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Computational Aspects of Treatment Planning for Neutron Capture Therapy

by

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Abstract

Boron Neutron Capture Therapy (BNCT) is a biochemically targeted form of binary radiation therapy that has the potential to deliver radiation to cancers with cellular dose selectivity. Accurate and efficient treatment planning calculations are essential to maximizing the efficacy of BNCT and ensuring patient safety. This thesis investigates computational aspects of BNCT treatment planning with the aim of improving both the accuracy and efficiency of the planning process as well as developing a better understanding of differences in computational dosimetry that exist between the different BNCT clinical sites around the world.

A suite of computational dosimetry reference problems were developed as a basis for comprehensively testing, comparing, and analyzing current and future BNCT treatment planning systems (TPSs) under conditions relevant to both patient planning and planning system calibration. Using these reference problems, four of the TPSs that have been used in clinical BNCT (MacNCTPlan, NCTPlan, BNCT_Rtpe, and SERA) were compared to reference calculations performed with the well-benchmarked Monte Carlo radiation transport code MCNP5. The comparison of multidimensional dose data in the form of dose profiles, isodose contours, dose difference distributions and dose-volume histograms yielded many clinically significant differences. Additional calculations were performed to further investigate and explain significant deviations from the reference calculations.

A combined 81 brain tumor patients have been treated in dose escalation trials of Neutron Capture Therapy (NCT) in the USA at Harvard-Massachusetts Institute of Technology (MIT) and Brookhaven National Laboratory (BNL). Pooling the clinical data from these and other trials will allow the evaluation of the safety and efficacy of NCT with more statistical rigor. However, differences in physical and computational dosimetry between the institutions that make a direct comparison of the clinical dosimetry difficult must first be addressed before clinical data can be compared. This study involves normalizing the BNL clinical dosimetry to that of Harvard-MIT for combined NCT dose response analysis using analysis of MIT measurements and calculations with the BNL treatment planning system (TPS), BNCT_Rtpe, for two different phantoms. The BNL
TPS was calibrated to dose measurements made by MIT at the Brookhaven Medical Research Reactor (BMRR) in the BNL calibration phantom, a Lucite cube, and then validated by MIT dose measurements at the BMRR in an ellipsoidal water phantom. Using the newly determined TPS calibration, treatment plans for all BNL patients were recomputed, yielding reductions in reported mean brain doses of 10% on average in the initial 15 patients treated with the 8 cm collimator and 27% in the latter 38 patients treated with a 12 cm collimator. These reductions in reported doses have clinically significant implications for those relying on reported BNL doses as a basis for initial dose selection in clinical studies and reaffirm the importance of collaborative dosimetric comparisons within the NCT community. The dosimetric adjustments allowed the BNL clinical data to be legitimately combined with the Harvard-MIT clinical data for a combined dose response analysis of the incidence of radiation-induced somnolence syndrome. Probit analysis of the composite data set for the incidence of somnolence yielded ED_{50} values of 5.76 Gy_w and 14.4 Gy_w for mean and maximum brain dose.

The applicability and optimization of variance reduction techniques for BNCT Monte Carlo treatment planning calculations were investigated using MCNP5. The pre-existing variance reduction scheme in the Monte Carlo model of the fission converter beam (FCB) at MIT was optimized, resulting in improved energy-dependent neutron and photon weight windows. Using these weight windows, a more precise surface source representation of the FCB was produced downstream at the patient position with improved statistical properties that increased the mean efficiency of in-phantom dose calculations by a factor of 9. The variance reduction techniques available in MCNP were also explored as a means of increasing the efficiency of dose calculations in the patient model. By disabling implicit neutron capture and using fast neutron source biasing and photon production biasing techniques, the mean efficiency of dose calculations was improved by a factor of 2.2.

Constructing an accurate description of a neutron beam is critical to achieving accurate calculations of dose in NCT treatment planning. This study compares two methods of neutron beam source definition commonly used in BNCT treatment planning calculations, the phase space file (MCNP surface source file) and source variable probability distributions (MCNP SDef). To facilitate the comparison, a novel software tool was developed to analyze MCNP surface source files and construct MCNP SDef representations. This tool was applied to the MIT FCB, which has a well-validated Monte Carlo model. Each source type (surface source file and SDef) was used to simulate transport of the beam through voxel models of the modified Snyder head phantom, where doses were calculated. Compared to the surface source file, the initial dose calculations with the SDef produced significant errors of ~15%. Using a patched version of MCNP that allowed the observed radial dependence of the relative azimuthal angle to be modeled in the SDef, errors in all dose components in the head phantom at D_{max} were reduced to acceptably small levels with none being statistically significant except for the induced photon error of 0.5%. Errors in the calculated doses introduced by sampling the azimuthal component of particle direction uniformly in the SDef vary spatially, are phantom-dependent, and thus cannot be accurately corrected by a simple scaling of doses.
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I would like to dedicate this thesis to all those that have been stricken with cancer and faced it with great courage and fortitude.
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INTRODUCTION

Figure 1.1 The $^{10}$B nucleus captures a thermal neutron ($\sigma_A=3837$ b) to produce two densely ionizing particles, $^4$He and $^7$Li, that deposit their energy along very short tracks that are comparable in length to the diameter of most cells. This reaction forms the basis of BNCT. (Reprinted from Kiger$^5$).

Figure 1.2 Relevant neutron interactions in tissue that are responsible for the majority of the patient dose during BNCT. While all contribute to a non-specific and unavoidable background dose, the preferential accumulation of $^{10}$B in tumor cells provides the targeting necessary to achieve therapeutic advantage. 57

Figure 1.3 Boron and neutron kerma factors$^4$ for ICRU adult brain tissue.$^6$ The boron kerma factors reflect the $1/v$ shape of the $^{10}$B neutron absorption cross section and are scaled for a $^{10}$B concentration of 15 $\mu$g/g. The total neutron kerma data are the weighted sum of kerma from those isotopes found in brain tissue. At thermal neutron energies, the main contribution is from nitrogen (via the $^{14}$N(n,p)$^{14}$C reaction) while hydrogen (via the $^1$H(n,n')$^1$H reaction) is the main contributor at fast neutron energies. 59

Figure 1.4 Energy level diagram representing the deexcitation of $^{11}$B* after the capture of a thermal neutron to $^7$Li or to an intermediate excited state ($^7$Li*), which releases a 478 keV $\gamma$-ray as it deexcites. Although not depicted here, an $\alpha$ particle ($^4$He) also results from the deexcitation of $^{11}$B*. 61

Figure 1.5 Screen capture of the BNCT treatment planning system, NCTPlan, displaying total weighted brain isodose contours (in Gy$_w$) for a patient treated at Harvard-MIT. 63

Figure 1.6 Screen capture of the BNCT treatment planning system, NCTPlan, displaying the total weighted brain dose-volume histogram for a patient treated at Harvard-MIT. 69

Figure 1.7 2D and 3D representations of the voxel (a,b), univel (c,d), and NURBS (e,f) (Non-Uniform Rational B-Splines) modeling techniques employed by MacNCTPlan and NCTPlan, SERA, and BNCT_Rtpe, respectively, to model the patient anatomy for BNCT treatment planning calculations. (Reprinted with permission from Kiger and Kumada$^{40}$). 71
INTERCOMPARISON OF NEUTRON CAPTURE THERAPY TREATMENT PLANNING SYSTEMS

Figure 2.1 Sagittal (a), coronal (b), and transverse (c) views through the analytical model of the modified Snyder ellipsoidal head phantom used for the reference dosimetry calculations. A brain tumor was modeled by a 4 cm diameter sphere. The anatomical regions were modeled using ICRU 46 adult whole brain, adult whole cranium, and adult skin biological materials.

Figure 2.2 Transverse and oblique views through the analytical model of the leg phantom used for the reference dosimetry calculations. The phantom was derived from measurements of CT image data of a human leg from the Visual Human Project. Two superficial tumors, modeled by a sphere and an arc shape, were added to simulate BNCT treatment of peripheral melanoma. The different anatomical regions were modeled using ICRU 46 adult muscle, adult cortical bone, adult connective tissue, and adult skin biological materials.

Figure 2.3 Energy spectra for the thermal and generic epithermal neutron beams simulated as part of the reference dosimetry calculations. The generic epithermal neutron beam was taken from the pre-existing suite of reference dosimetry calculations\textsuperscript{14} while the thermal neutron beam was modeled after the M11 thermal neutron beam at MIT.\textsuperscript{50} Both beams were normalized to a neutron flux of $1 \times 10^{10} \text{n/cm}^2\text{s}$.

Figure 2.4 Simulated treatment field orientations for the head and leg phantoms. Both 1- and 3-field irradiations were simulated for the head phantom. The disc source for the single field irradiation of the leg phantom was rotated 35° from the lateral x axis.

Figure 2.5 Transverse, coronal, and sagittal views of the various mesh tallies used within MCNP5 to produce the reference depth-dose (1×10×10 mm), isodose (1×1×2 mm), and dose-volume (2×2×2 mm) data for the ellipsoidal head phantom. The mesh used to calculate dose-volume data for the brain tumor is not shown but consisted of 1×1×1 mm tally volumes.

Figure 2.6 Thermal neutron flux and percent difference $(100\times[\text{TPS}−\text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. SERA and BNCT_Rtpe data are calculated at (default) intervals of 5 mm. MCNP5 served as the reference for percent difference calculations.

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Figure 2.8 Thermal neutron flux and percent difference \((100\times[\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the large rectangular water phantom for different representations of the SERA voxel data. The uninterpolated SERA voxel data were read and interpolated using MATLAB for comparison to the interpolated output of seraPlan to illustrate interpolation errors in the line and point edit data. The data produced using 3D cubic interpolation served as the reference for percent difference calculations since it produced the closest agreement to the reference calculations.

Figure 2.9 Thermal neutron flux and percent difference \((100\times[\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the large rectangular water phantom for MATLAB interpolations of voxel data from each TPS. The uninterpolated voxel data from each TPS were read and interpolated using MATLAB to illustrate the agreement with MCNP5 when interpolation errors are eliminated. MCNP5 served as the reference for percent difference calculations.

Figure 2.10 Total neutron cross sections for H\(_2\)O used by MCNP and SERA in transport calculations. Cross section data for both include the S(\(\alpha,\beta\)) thermal neutron scattering treatment for hydrogen in light water. The energy range \((0.414 \text{ eV} \leq E_n \leq 4.46 \text{ eV})\) is highlighted and expanded to better illustrate the difference in cross sections. This energy range represents ~9% of the neutrons at the thermal neutron flux peak (2.0 cm depth) in the large rectangular water phantom.

Figure 2.11 Boron dose rate for a \(^{10}\)B concentration of 15 \(\mu\)g/g and percent difference \((100\times[\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

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Figure 2.13 Ratio of nitrogen dose rate to thermal neutron flux as a function of depth in the large rectangular water phantom. For SERA, edit
mesh atomic densities corresponding to brain ($\rho = 1.04 \text{ g/cm}^3$) and lung ($\rho = 0.25 \text{ g/cm}^3$) were specified in two separate simulations. When an edit mesh composition of lung was used in SERA, the density of water in the phantom was reduced to 0.25 g/cm$^3$ to approximate neutron transport through adult human lung. The ratios illustrate that SERA nitrogen (hydrogen and boron) kerma factors are scaled at runtime by the mass density of the edit mesh material.

Figure 2.14  Boron dose rate for a $^{10}$B concentration of 15 μg/g and percent difference ($100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}}$) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. Multigroup boron neutron kerma factors from BNCT Rtmp and SERA were used in MCNP5 calculations of boron dose rates, which served as the reference for BNCT Rtmp and SERA percent difference calculations, respectively.

Figure 2.15  Thermal neutron (and nitrogen) dose rate and percent difference ($100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}}$) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.16  Comparison of BNCT Rtmp and SERA multigroup (94 energy groups) nitrogen and hydrogen neutron kerma data to the corresponding pointwise continuous ICRU kerma data. The percent difference between the INL and ICRU kerma data was calculated with the ICRU kerma data as the reference. The INL hydrogen kerma data does not include the contribution from the recoil deuteron which leads to large differences in the thermal neutron energy range. The vertical dashed line represents the energy cutoff at 0.5 eV that is used to separate the thermal and fast neutron dose components in the reference MCNP5 calculations. No such energy binning is used in BNCT Rtmp or SERA.

Figure 2.17  Comparison of BNCT Rtmp and SERA multigroup (94 energy groups) nitrogen and hydrogen neutron kerma data to pointwise continuous reference total brain neutron kerma data. The percent difference between the summed INL nitrogen and hydrogen kerma data and the total brain kerma data was calculated with the total brain kerma data as the reference. The vertical dashed line represents the energy cutoff at 0.5 eV that is used to separate the thermal and fast neutron dose components in the reference MCNP5 calculations. No such energy binning is used in BNCT Rtmp or SERA.

Figure 2.18  Nitrogen dose rate and percent difference ($100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}}$) as a function of depth along the central beam axis in the large rectangular water phantom for each
planning system. Multigroup INL nitrogen neutron kerma factors were used in MCNP5 calculations of nitrogen dose rates, which served as the reference for percent difference calculations. Nitrogen dose rates calculated with ICRU 63 nitrogen kerma factors are included as a point of comparison.

Figure 2.19 Fast neutron (and hydrogen) dose rate and percent difference \(100 \times \frac{[TPS - \text{Ref}]}{\text{Ref}_{\max}}\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.20 Hydrogen dose rate and percent difference \(100 \times \frac{[TPS - \text{Ref}]}{\text{Ref}_{\max}}\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. Multigroup INL hydrogen neutron kerma factors were used in MCNP5 calculations of hydrogen dose rates, which served as the reference for percent difference calculations. The fast neutron source biasing run mode was not used for BNCT_Rtpe or SERA (i.e., run modes “NGD” were used). Hydrogen dose rates calculated with ICRU 63 hydrogen kerma factors are included as a point of comparison.

Figure 2.21 Fast neutron flux and percent difference \(100 \times \frac{[TPS - \text{Ref}]}{\text{Ref}_{\max}}\) as a function of depth along the central beam axis in the large rectangular water phantom for different representations of the SERA voxel data. The uninterpolated SERA voxel data were read and interpolated using MATLAB for comparison to the interpolated output of seraPlan to illustrate interpolation errors in the line and point edit data. The data produced using 3D cubic interpolation served as the reference for percent difference calculations since it produced the closest agreement to MCNP5.

Figure 2.22 Total neutron dose rate (thermal+fast and hydrogen+nitrogen) and percent difference \(100 \times \frac{[TPS - \text{Ref}]}{\text{Ref}_{\max}}\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.23 Induced photon dose rate and percent difference \(100 \times \frac{[TPS - \text{Ref}]}{\text{Ref}_{\max}}\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.24 Photon kerma factors used in the reference, BNCT_Rtpe, and SERA calculations of induced and incident photon dose and the percent difference of the BNCT_Rtpe and SERA kerma data from the reference kerma data. The reference data are pointwise continuous while the BNCT_Rtpe and SERA kerma data have 70 and 86 energy groups, respectively.
Figure 2.25 Induced photon dose rate and percent difference \(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_{\text{max}}}\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. Multigroup photon kerma factors from BNCT_Rtpe and SERA were used in MCNP5 calculations of induced photon dose rates, which served as the reference for BNCT_Rtpe and SERA percent difference calculations, respectively.

Figure 2.26 Incident photon dose rate and percent difference \(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_{\text{max}}}\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.27 Incident photon dose rate and percent difference \(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_{\text{max}}}\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. Multigroup photon kerma factors from BNCT_Rtpe and SERA were used in MCNP5 calculations of incident photon dose rates, which served as the reference for BNCT_Rtpe and SERA percent difference calculations, respectively. The \(-2\%\) difference reflects a subtle normalization error in BNCT_Rtpe and SERA incident photon dose rates.

Figure 2.28 Total biologically weighted brain dose rate and percent difference \(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_{\text{max}}}\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.29 Axial sections through the BNCT_Rtpe NURBS model, SERA univel model, MacNCTPlan and NCTPlan mixed-material voxel models of the ellipsoidal head phantom used to simulate BNCT treatment of a brain tumor.

Figure 2.30 Thermal neutron flux and percent difference \(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_{\text{max}}}\) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. SERA and BNCT_Rtpe data are calculated at (default) intervals of 5 mm. MCNP5 served as the reference for percent difference calculations.

Figure 2.31 Different NCTPlan voxel models of the head phantom that resulted from shifting the phantom image data in 1 mm steps along its minor axis (the central axis of the beam). The phantom’s biological materials are color coded by density, and white tick marks have been added to indicate the front and back edges of the un-shifted phantom.

Figure 2.32 Uninterpolated NCTPlan thermal neutron flux voxel data and percent difference \(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_{\text{max}}}\) as a function of depth along the central beam axis in the ellipsoidal head phantom for
different NCTPlan models of the head phantom that resulted from shifting the phantom image data varying distances along the central beam axis in relation to the voxel mesh. MCNP5 served as the reference for percent difference calculations.

Figure 2.33 Boron dose rate for a $^{10}$B concentration of 15 μg/g and percent difference (100×[TPS−Ref]/Ref$_{max}$) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.34 Fast neutron (and hydrogen) dose rate and percent difference (100×[TPS−Ref]/Ref$_{max}$) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. The fast neutron source biasing run mode was not used for BNCT_Rtpe or SERA (i.e., run modes “NGD” were used) because doing so results in a significant −47% difference at the phantom entrance. MCNP5 served as the reference for percent difference calculations.

Figure 2.35 Uninterpolated NCTPlan fast neutron dose rate voxel data and percent difference (100×[TPS−Ref]/Ref$_{max}$) as a function of depth along the central beam axis in the ellipsoidal head phantom for different NCTPlan models of the head phantom that resulted from shifting the phantom image data varying distances along the central beam axis in relation to the voxel mesh. MCNP5 served as the reference for percent difference calculations.

Figure 2.36 Induced photon dose rate and percent difference (100×[TPS−Ref]/Ref$_{max}$) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.37 Uninterpolated NCTPlan induced photon dose rate voxel data and percent difference (100×[TPS−Ref]/Ref$_{max}$) as a function of depth along the central beam axis in the ellipsoidal head phantom for different NCTPlan models of the head phantom that resulted from shifting the phantom image data varying distances along the central beam axis in relation to the voxel mesh. MCNP5 served as the reference for percent difference calculations.

Figure 2.38 Total biologically weighted brain dose rate and percent difference (100×[TPS−Ref]/Ref$_{max}$) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.39 Axial sections through the BNCT_Rtpe NURBS model, SERA univel model, MacNCTPlan and NCTPlan mixed-material voxel models of the leg phantom used to simulate BNCT treatment of peripheral melanoma.
Figure 2.40  Thermal neutron flux and percent difference \((100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the leg phantom for each planning system. SERA and BNCT_Rtpe data are calculated at (default) intervals of 5 mm. MCNP5 served as the reference for percent difference calculations.

Figure 2.41  Boron dose rate for a \(^{10}\text{B}\) concentration of 22.5 µg/g and percent difference \((100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.42  Fast neutron (and hydrogen) dose rate and percent difference \((100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.43  Induced photon dose rate and percent difference \((100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.44  Incident photon dose rate and percent difference \((100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.45  Total biologically weighted skin dose rate and percent difference \((100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure 2.46  Boron isodose contours for a \(^{10}\text{B}\) concentration of 15 µg/g in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.

Figure 2.47  Difference in boron dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference boron dose for a 1-field irradiation of the head phantom.

Figure 2.48  Incident photon isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.

Figure 2.49  Transverse and coronal views through the ellipsoidal head phantom overlaid with the coarse scoring mesh from each TPS to illustrate the relative orientation of each mesh with the phantom and the beam path (shaded region). The mesh element centers in
BNCT_Rtpe and SERA are offset by 5 mm in each dimension from the mesh element centers of MacNCTPlan and NCTPlan. The beam is aligned with mesh element edges in BNCT_Rtpe and SERA whereas it is aligned with mesh element centers in MacNCTPlan and NCTPlan. Each tally volume is 1 cm³, and only a portion of each mesh is shown.

Figure 2.50 Incident photon dose rate and percent difference (100×[TPS−Ref]/Ref$_{max}$) for each planning system as a function of the lateral distance (in the transverse plane) from the central beam axis in the ellipsoidal head phantom. MCNP5 served as the reference for percent difference calculations.

Figure 2.51 Total biologically weighted brain isodose contours in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.

Figure 2.52 Difference in total biologically weighted brain dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the head phantom.

Figure 2.53 Total biologically weighted brain isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.

Figure 2.54 Total biologically weighted tumor isodose contours in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.

Figure 2.55 Difference in thermal neutron flux in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron flux for a 1-field irradiation of the leg phantom.

Figure 2.56 Difference in boron dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference boron dose for a 1-field irradiation of the leg phantom.

Figure 2.57 Total biologically weighted tumor isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.
Figure 2.58 Total biologically weighted tumor isodose contours in an oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.

Figure 2.59 Total biologically weighted dose-volume histograms for brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. The default output from seraPlot is shown along with a corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose).

Figure 2.60 Total biologically weighted dose-volume histograms for brain tumor for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Figure 2.61 Total biologically weighted dose-volume histograms for brain for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Figure 2.62 Total biologically weighted dose-volume histograms for the brain tumor for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Figure 2.63 Total biologically weighted dose-volume histograms for skin for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Figure 2.64 Total biologically weighted dose-volume histograms for tumor 1 (spherical tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Figure 2.65 Total biologically weighted dose-volume histograms for tumor 2 (arc-shaped tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.
CHAPTER THREE

COMPARISON OF DOSES DELIVERED IN CLINICAL TRIALS OF NEUTRON CAPTURE THERAPY IN THE USA

Figure 3.1 Comparison of (annotated) BNCT_Rtpe raster images of the 12 cm BMRR collimator used to calibrate the treatment planning system and to calculate patient doses for planning. The collimator modeled in the TPS calibration (left) using the Lucite cube phantom was not as thick and provided less beam collimation and thus yielded lower calculated in-phantom doses. The effect of calibrating the TPS in this configuration is to overestimate doses in the patient (right), where a thicker collimator was used.

Figure 3.2 BNCT_Rtpe calculations scaled to MIT measurements in the BNL calibration phantom, a Lucite cube. Dose component scaling factors were derived from the least squares fitting of BNCT_Rtpe calculations to MIT measurements. The plotted calculation lines are the product of the scale factors (shown in the legend) and doses calculated by BNCT_Rtpe.

Figure 3.3 Scaled BNCT_Rtpe calculations and MIT dose measurements in the MIT ellipsoidal head phantom. Scaling factors are those derived from the data of Figure 3.2. The plotted calculation lines are the product of the scale factors (shown in the legend) and doses calculated by BNCT_Rtpe.

Figure 3.4 Original vs. revised (a) mean and (b) maximum biologically weighted brain doses for the BNL patients. The solid line represents equality of revised and original dosimetry.

Figure 3.5 Contributions to the adjusted mean and maximum physical brain doses (unweighted) for the BNL patients.

Figure 3.6 Original and revised treatment plans for a BNL patient treated with 3 fields using the 12 cm collimator after the fuel shuffle. The isodose contours are displayed as a percentage of the biologically weighted brain dose in the voxel containing the maximum thermal neutron flux under the original dosimetry (15.6 Gyw). The contours were plotted with the BNL treatment planning system, BNCT_Rtpe.

Figure 3.7 Original and revised total biologically weighted dose-volume histograms for the brain, tumor, and target volumes of a BNL patient treated with 3 fields using the 12 cm collimator after the fuel shuffle.

Figure 3.8 Maximum brain dose versus mean brain dose for the combined BNL and Harvard-MIT patient data. Filled symbols represent patients that developed radiation-induced somnolence syndrome. The retreatment of 1 previously treated BNL patient as well as the 2 Harvard-MIT patients for which somnolence could not be
evaluated due to confounding factors were censored from the analysis.

Figure 3.9 Dose response curves for radiation-induced somnolence for the combined BNL and Harvard-MIT patient data based on the mean or maximum weighted brain dose. The 95% confidence intervals are indicated by the pairs of dashed lines.

Figure 3.10 Dose response curves for radiation-induced somnolence for the revised and original biologically weighted mean brain doses for the BNL patients only. The revised BNL doses resulted in an ED_{50} that was 26% lower than for the original dosimetry (6.42 Gy_{w} vs. 4.75 Gy_{w}).

CHAPTER FOUR

APPLICATION OF VARIANCE REDUCTION IN MONTE CARLO TREATMENT PLANNING CALCULATIONS

Figure 4.1 Neutron current energy spectrum inside the beam aperture (r ≤ 5.9 cm) of the MIT FCB. The uncertainties have been intentionally increased by an order of magnitude to better illustrate the effectiveness of the energy-dependent weight windows at reducing uncertainties across a broad range of neutron energies.

Figure 4.2 Two dimensional distributions of dose rate, relative error, and FOM (Figure-Of-Merit) calculated for the incident photon dose component of the MIT FCB in a voxel model of the modified Snyder head phantom. Streak artifacts of high in-phantom incident photon dose, high uncertainty, and low FOM resulting from the “unlucky” rouletting of neutrons and excessive splitting of the subsequent induced photons during upstream Monte Carlo calculations of the FCB beam line are evident. The color bars are log scale.

Figure 4.3 Monte Carlo model of the MITR-II reactor core and FCB beam line illustrating the series of MCNP calculations and surface source (SS) files used to create a surface source representation of the beam downstream at the patient position (beam aperture) for use in BNCT treatment planning calculations.

Figure 4.4 Flowchart outlining the systematic approach taken to minimize production of problematic high weight tracks and subsequent splitting into excessive numbers of duplicate tracks during the Monte Carlo simulations of the FCB beam line that resulted from neutrons rouletting to high weights and producing photons which were split multiple times. The process was repeated until the production of high weight tracks, as manifest by excessive numbers (> 100) of duplicate tracks recorded on the surface source at the patient position, had been sufficiently reduced.
Figure 4.5 Original (from 2002) and new neutron and photon weight windows for those cells along the central axis of the FCB beam line. The thin vertical lines that segment the weight windows represent the boundaries of different regions of the beam line. Neutron and photon weight windows were increased moving radially outward from the beam central axis.

Figure 4.6 Histogram of the number of duplicate photon tracks within the FCB surface source file at the patient position and the subsequent effect they had on in-phantom incident photon dose rates, relative errors, and FOM before and after adjustments to upstream weight windows. By adjusting the weight windows, the mean number of identical photon tracks per independent history was reduced from 102 to 2.96, and streak-artifacts of high dose and high uncertainty were eliminated while the FOM was increased significantly. The value plotted at $10^0$ tracks represents the number of unique tracks (no duplicates) within the surface source file. The color bars are log scale.

Figure 4.7 Boron and fast neutron dose rate, relative error, and FOM (Figure-Of-Merit) distributions in the transverse plane of the modified Snyder head phantom on the FCB central axis before and after adjustments to the weight windows used for transport through the beam line. The mean, minimum, and maximum FOM values increased for both dose components as a result of the adjustments. The color bars are log scale.

Figure 4.8 Induced photon and total weighted brain dose rate, relative error, and FOM (Figure-Of-Merit) distributions in the transverse plane of the modified Snyder head phantom on the FCB central axis before and after adjustments to the weight windows used for transport through the beam line. The mean, minimum, and maximum FOM values increased for both dose components as a result of the adjustments. The color bars are log scale.

Figure 4.9 Detailed description of the series of simulations and surface source files used to produce a more accurate surface source representation of the FCB at the patient position. In total, 1.07 CPU years of simulation time and 88 GB of computer storage were used.

Figure 4.10 Comparison of calculated and measured doses in the MIT ellipsoidal head phantom. MCNP calculations with the FCB surface source were scaled to match physical dosimetry measurements using least squares fitting; dose scale factors for each component are listed in the legend.

Figure 4.11 FOM (Figure-Of-Merit) distributions for in-phantom dose tallies in the transverse beam line plane which result from employing different variance reduction techniques during coupled neutron/photon transport simulations of the generic epithermal neutron beam in a voxel model of the modified Snyder head.
phantom. Larger FOM values indicate more efficient dose calculations. The color bars are log scale.

Figure 4.12 FOM (Figure-Of-Merit) distributions for in-phantom dose tallies in the transverse beam line plane which result from employing different variance reduction techniques during coupled neutron/photon transport simulations of the generic epithermal neutron beam in a voxel model of the modified Snyder head phantom. Larger FOM values indicate more efficient dose calculations. The color bars are log scale.

Figure 4.13 Percent difference in the mean FOM (Figure-Of-Merit) for in-phantom dose tallies when compared to simulations using the default photon production biasing parameter of $-1$. As the biasing parameter is increased to 0, more induced photons are produced with appropriately adjusted (lower) weights so as to maintain a fair Monte Carlo game and provide unbiased results. Increasing photon production dramatically improves the efficiency of calculating the induced photon dose, but this comes with the expense of reduced efficiency for other dose components such as the boron dose.

Figure 4.14 Cylindrical weight windows mesh superimposed on a 1 cm$^3$ voxel model of the modified Snyder head phantom and irradiated with a 10 cm diameter monodirectional epithermal neutron disc source. The neutron and photon weight windows in those regions of the mesh labeled with an ‘X’ were intentionally made very large ($1 \times 10^{25}$) to terminate tracking calculations for all particles escaping from the phantom.

CHAPTER FIVE

NEUTRON BEAM SOURCE DEFINITION TECHNIQUES FOR NEUTRON CAPTURE THERAPY TREATMENT PLANNING

Figure 5.1 Parameters used to define the particle position and direction (indicated by the bold arrow) in the SDef source representations. $r$ and $\phi$ are sampled to determine position $(x,y)$. The polar angle $\theta$ and the relative azimuthal angle $\phi'$, defined relative to the track’s radial vector, determine particle direction.

Figure 5.2 Track information from the surface source file is scored into an array of fine radial, energy, polar angle $(\theta)$, and relative azimuthal angle $(\phi')$ bins such as illustrated here. This finely binned information is grouped into coarse regions for the $r$, $E$, and $\theta$ source variables, as indicated by the thick dashed lines. In each coarse region (e.g., the shaded region), a unique marginal probability distribution is computed for each of the 4 source variables. The product of each region’s marginal probability
distributions in $r$, $E$, $\theta$ and $\phi'$ is used to model the joint probability distribution $P_{i,j,k}(r, E, \theta, \phi')$ in that region.

**Figure 5.3** Comparison of the joint probability distribution of polar angle $\theta$ and energy ($P(\theta,E)$) with the product of the marginal distributions ($P(\theta)$-$P(E)$) for the radial region corresponding to the beam aperture ($r \leq 5.9$ cm) of the MIT FCB. Large percent differences indicate a high degree of inseparability between the two source variables. The alternating shaded/white areas demarcate different coarse regions of the r-E-$\theta$ phase space.

**Figure 5.4** Comparison of the joint probability distribution of radius and energy ($P(r,E)$) with the product of the marginal distributions ($P(r)$-$P(E)$). The alternating shaded/white areas demarcate different coarse regions of the r-E-$\theta$ phase space.

**Figure 5.5** Comparison of the joint probability distribution of radius and polar angle $\theta$ ($P(r,\theta)$) with the product of the marginal distributions ($P(r)$-$P(\theta)$) for the thermal, epithermal, and fast neutron energy groups. The alternating shaded/white areas demarcate different coarse regions of the r-E-$\theta$ phase space.

**Figure 5.6** Radial distribution of neutron current for different energy and angular regions of the phase space at the plane of the beam aperture of the MIT FCB. Line thickness encodes the thermal, epithermal and fast neutron energy groups while solid and dashed lines represent polar angle regions of $0^\circ \leq \theta \leq 20^\circ$ and $20^\circ < \theta \leq 90^\circ$, respectively. For the radial region outside the beam collimator ($r > 11.8$ cm, right of the vertical line) where the neutron current is orders of magnitude smaller than in the aperture, only one $\theta$ bin was used to help reduce fluctuations in the distribution resulting from few particles.

**Figure 5.7** Energy spectrum of the neutron current in different radial and angular regions on the beam aperture plane of the MIT FCB. Line thickness encodes the different radial regions on each plot with the top plot representing $0^\circ \leq \theta \leq 20^\circ$ and the bottom $20^\circ < \theta \leq 90^\circ$. In the outermost radial region ($11.8$ cm $< r \leq 30$ cm) $\theta$ was scored into only one bin ($0^\circ \leq \theta \leq 90^\circ$) to reduce statistical fluctuations. Energy bins of equal lethargy (10 per decade) were used to score the particle weight.

**Figure 5.8** Polar angle ($\theta$) probability distributions calculated in each of 4 radial regions and 3 energy regions. Line thickness encodes the thermal, epithermal and fast neutron energy groups. The particle weight was scored into $2^\circ$ bins from $0^\circ$ to $90^\circ$.

**Figure 5.9** Radial distribution of incident photon current for different energy and angular regions of the phase space at the plane of the beam aperture of the MIT FCB. Line thickness encodes the 3 energy groups while solid and dashed lines represent polar angle regions of $0^\circ \leq \theta \leq 20^\circ$ and $20^\circ < \theta \leq 90^\circ$, respectively. For the radial
region outside the beam collimator \((r > 11.8 \text{ cm})\) where the photon current is orders of magnitude smaller than in the aperture, only one \(\theta\) bin was used to help reduce fluctuations in the distribution resulting from few particles.

**Figure 5.10** Energy spectrum of the incident photon current in different radial and angular regions on the beam aperture plane of the MIT FCB. Line thickness encodes the different radial regions on each plot with the top plot representing \(0^\circ \leq \theta \leq 20^\circ\) and the bottom \(20^\circ < \theta \leq 90^\circ\). In the outermost radial region \((11.8 \text{ cm} < r \leq 30 \text{ cm})\) \(\theta\) was scored into only one bin \((0^\circ \leq \theta \leq 90^\circ)\) to reduce statistical fluctuations. 100 keV energy bins were used to score the particle weight.

**Figure 5.11** Polar angle \((\theta)\) probability distributions for the incident photons calculated in each of 3 radial regions and 3 energy regions. Line thickness encodes the energy groups. The particle weight was scored into 2\(^\circ\) bins from \(0^\circ\) to \(90^\circ\).

**Figure 5.12** Probability distributions of the relative azimuthal angle \(\phi'\) inside the beam aperture of the MIT FCB determined from the surface source file and the fitted model. The nonuniform distribution shows a preference for outward angles \((|\phi'| < \pi/2)\). \(r_0\) is the radius of the beam aperture, 5.9 cm, and \(b\) is a fitted constant. Radial bins range from 0 to 5.9 cm in \(-1\) cm steps. \(P(\phi')\) is shown averaged over the radial bins and is limited to \(0 \leq \phi' \leq \pi\) for this comparison. In the modifications to MCNP5, the fitted model is symmetric about \(
\phi'=0\) and is sampled from \(-\pi\) to \(+\pi\).

**Figure 5.13** Comparison of dose rates calculated in the modified Snyder head phantom using different beam source models for the MIT FCB and a source to surface distance of 3.0 cm. Solid lines represent the reference doses calculated with the surface source while dashed and dash-dot lines represent data for the SDef models with and without \(\phi'\) dependence, respectively. Isodose labels represent a percentage of the maximum dose rate in the phantom computed with the surface source for each dose component. Error bars (1 \(\sigma\)) in the depth-dose plots are omitted for clarity in cases where they are negligibly small.

**Figure 5.14** Total biologically weighted brain dose-volume histograms produced by simulating the irradiation of the Snyder head phantom (SSD=3.0 cm) with the different source representations of the MIT FCB. The time required to deliver a maximum brain dose of 12.5 Gy\(_w\) with the surface source model (13.47 minutes) was used to convert to units of absolute dose. Dose component scaling factors, derived from calculations with the SDef model and standard version of MCNP in large rectangular water phantom (column 4 of Table 5.1), were applied to the SDef doses.
in the head phantom to simulate the planning system calibration routinely performed at some institutions. The resulting disagreement between the uniform $\phi'$ SDef and the surface source curves (8.7%, 7.3%, and 11.6% in mean, minimum, and maximum brain dose, respectively) illustrates that the errors introduced during patient planning by sampling $\phi'$ uniformly are not corrected by calibrating the planning system in a reference phantom.

CHAPTER SIX

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE WORK

APPENDIX A

REFERENCE DATA FOR NEUTRON CAPTURE THERAPY TREATMENT PLANNING SYSTEMS

Figure A.1 Thermal neutron flux and percent difference $(100\times[TPS−Ref]/Ref_{max})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. SERA and BNCT_Rtpe data are calculated at (default) intervals of 5 mm. MCNP5 served as the reference for percent difference calculations.

Figure A.2 Boron dose rate for a $^{10}$B concentration of 15 $\mu$g/g and percent difference $(100\times[TPS−Ref]/Ref_{max})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.3 Thermal neutron (and nitrogen) dose rate and percent difference $(100\times[TPS−Ref]/Ref_{max})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.4 Fast neutron (and hydrogen) dose rate and percent difference $(100\times[TPS−Ref]/Ref_{max})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.5 Induced photon dose rate and percent difference $(100\times[TPS−Ref]/Ref_{max})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.6 Incident photon dose rate and percent difference $(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_\text{max}})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.7 Total biologically weighted brain dose rate and percent difference $(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_\text{max}})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.8 Total biologically weighted tumor dose rate and percent difference $(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_\text{max}})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.9 Thermal neutron flux and percent difference $(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_\text{max}})$ as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. SERA and BNCT Rtpe data are calculated at (default) intervals of 5 mm. MCNP5 served as the reference for percent difference calculations.

Figure A.10 Boron dose rate for a $^{10}$B concentration of 15 $\mu$g/g and percent difference $(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_\text{max}})$ as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.11 Thermal neutron (and nitrogen) dose rate and percent difference $(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_\text{max}})$ as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.12 Fast neutron (and hydrogen) dose rate and percent difference $(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_\text{max}})$ as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.13 Induced photon dose rate and percent difference $(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_\text{max}})$ as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.14 Incident photon dose rate and percent difference $(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_\text{max}})$ as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
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Figure A.16  Total biologically weighted tumor dose rate and percent difference $(100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.17  Thermal neutron flux and percent difference $(100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the leg phantom for each planning system. SERA and BNCT_Rtpe data are calculated at (default) intervals of 5 mm. MCNP5 served as the reference for percent difference calculations.

Figure A.18  Boron dose rate for a $^{10}\text{B}$ concentration of 22.5 $\mu$g/g and percent difference $(100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.19  Thermal neutron (and nitrogen) dose rate and percent difference $(100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.20  Fast neutron (and hydrogen) dose rate and percent difference $(100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.21  Induced photon dose rate and percent difference $(100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.22  Incident photon dose rate and percent difference $(100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.23  Total biologically weighted skin dose rate and percent difference $(100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.

Figure A.24  Total biologically weighted tumor dose rate and percent difference $(100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
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Figure A.26  Boron isodose contours for a $^{10}$B concentration of 15 μg/g in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.27  Thermal neutron (and nitrogen) isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.28  Thermal neutron (and nitrogen) isodose contours in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.29  Fast neutron (and hydrogen) isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

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Figure A.31  Induced photon isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.32  Induced photon isodose contours in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for
each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

**Figure A.33** Incident photon isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

**Figure A.34** Incident photon isodose contours in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

**Figure A.35** Total biologically weighted brain isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

**Figure A.36** Total biologically weighted brain isodose contours in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

**Figure A.37** Total biologically weighted tumor isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

**Figure A.38** Total biologically weighted tumor isodose contours in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

**Figure A.39** Boron isodose contours for a $^{10}$B concentration of 15 μg/g in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

**Figure A.40** Boron isodose contours for a $^{10}$B concentration of 15 μg/g in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.41 Thermal neutron (and nitrogen) isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.42 Thermal neutron (and nitrogen) isodose contours in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.43 Fast neutron (and hydrogen) isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.44 Fast neutron (and hydrogen) isodose contours in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.45 Induced photon isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.46 Induced photon isodose contours in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.47 Incident photon isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.49 Total biologically weighted brain isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.50 Total biologically weighted brain isodose contours in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.51 Total biologically weighted tumor isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.52 Total biologically weighted tumor isodose contours in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.53 Boron isodose contours for a $^{10}$B concentration of 22.5 μg/g in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.54 Boron isodose contours for a $^{10}$B concentration of 22.5 μg/g in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.55 Thermal neutron (and nitrogen) isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment
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Figure A.56 Thermal neutron isodose contours in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.57 Fast neutron (and hydrogen) isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.58 Fast neutron isodose contours in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.59 Induced photon isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.60 Induced photon isodose contours in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.61 Incident photon isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.62 Incident photon isodose contours in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.63 Total biologically weighted skin isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.64  Total biologically weighted skin isodose contours in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.65  Total biologically weighted tumor isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

Figure A.66  Total biologically weighted tumor isodose contours in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.

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Figure A.81 Difference in total biologically weighted tumor dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the head phantom.

Figure A.82 Difference in total biologically weighted tumor dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the head phantom.

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Figure A.99 Difference in thermal neutron flux in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron flux for a 1-field irradiation of the leg phantom.

Figure A.100 Difference in thermal neutron flux in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron flux for a 1-field irradiation of the leg phantom.

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Figure A.102 Difference in boron dose in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference boron dose for a 1-field irradiation of the leg phantom.

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Figure A.104 Difference in thermal neutron dose in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron dose for a 1-field irradiation of the leg phantom.

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Figure A.106 Difference in fast neutron dose in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference fast neutron dose for a 1-field irradiation of the leg phantom.

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Figure A.111 Difference in total biologically weighted skin dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the leg phantom.

Figure A.112 Difference in total biologically weighted skin dose in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the leg phantom.

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Figure A.114 Difference in total biologically weighted tumor dose in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the leg phantom.

Figure A.115 Boron dose-volume histograms for brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. The default output from seraPlot is shown along with a corrected interpretation of the SERA dose-volume data (with a -5% shift in dose).

Figure A.116 Thermal neutron (and nitrogen) dose-volume histograms for the brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a -5% shift in dose) is shown instead of the default seraPlot output.

Figure A.117 Fast neutron (and hydrogen) dose-volume histograms for the brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a -5% shift in dose) is shown instead of the default seraPlot output.

Figure A.118 Induced photon dose-volume histograms for the brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a -5% shift in dose) is shown instead of the default seraPlot output.
Figure A.119 Incident photon dose-volume histograms for the brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Figure A.120 Total biologically weighted dose-volume histograms for brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. The default output from seraPlot is shown along with a corrected interpretation of the SERA dose-volume data (with a −5% shift in dose).

Figure A.121 Boron dose-volume histograms for the brain for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

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Table B.1  Hardware for the master and 11 slave nodes of the cluster. All components were purchased new except the video cards for the slave nodes which were purchased used on eBay. The components were purchased individually at a total cost of 10,074.52 and manually assembled over 3.5 months during the summer of 2005. 725
Preface

Throughout this thesis, blank pages have been inserted where necessary to ensure that all color pages are single-sided to increase readability when printed. All such pages are labeled as being intentionally left blank and are assigned a page number despite being blank.
CHAPTER ONE

Introduction

1.1 Introduction to Boron Neutron Capture Therapy

The ineffectiveness of conventional therapies against certain types of cancer has continually led to the search for more effective forms of treatment. However, the primary goal of even the experimental forms of cancer therapy remains the ability to deliver highly localized damage to cancer cells while sparing the surrounding healthy normal tissue. In conventional radiotherapy, this is most often achieved through the geometric targeting of the tumor with highly collimated and shaped beams of radiation, but selectively targeting cancer at the cellular level remains an elusive goal. If dose targeting could be improved, higher doses could be delivered to the tumor cells which could potentially lead to better local tumor control, even for those cancers that have proven to be radioresistant. An experimental therapy that can provide such selective cellular targeting is Boron Neutron Capture Therapy (BNCT).

1.1.1 Concepts of BNCT

Boron Neutron Capture Therapy is a biochemically targeted form of binary radiation therapy that has the potential to treat cancers that have proven to be resistant to more conventional therapies due to its selective dose targeting.\textsuperscript{1,2} In BNCT, dose
targeting is achieved by selectively loading the stable isotope $^{10}$B into the malignant tissue via a tumor-selective boronated pharmaceutical infused directly into the patient’s bloodstream. The biochemical selectivity of the boronated compound allows large concentrations of $^{10}$B to accumulate in the tumor cells relative to normal tissue (3 to 4 times more), essentially differentiating normal and cancer cells. The $^{10}$B compound alone is (usually) not toxic to cells; actually it is eliminated naturally from the body within a reasonable time frame after infusion. However, when the malignant tissue that has been preloaded with $^{10}$B is irradiated with a collimated beam of low energy neutrons, the large (relative to other nuclei present in the tissue) microscopic absorption cross section of the $^{10}$B nuclei for thermal neutrons results in $^{10}$B(n,α)$^7$Li neutron capture reactions that produce two densely ionizing particles, $^4$He and $^7$Li, that deposit their energy along very short tracks (~4 $\mu$m for $^7$Li and ~7 $\mu$m for $^4$He) comparable in length to the diameter of most cells. This neutron capture reaction is illustrated in Figure 1.1 and forms the basis of the selective targeting in BNCT. The result is that the dose from $^{10}$B capture reactions is selectively delivered only to those cells where $^{10}$B nuclei and thermal neutrons are present. While neutrons do interact with the other isotopes present in tissue to create a non-specific and unavoidable background dose in BNCT, the preferential accumulation of $^{10}$B in tumor cells and its large neutron absorption cross section provides the dose targeting necessary to ultimately result in a therapeutic gain.

1.1.2 Dose Components in BNCT

A complex radiation field is produced in the irradiated volume during BNCT due to the presence of 5 different dose components that have different LET (linear energy transfer) and different spatial distributions. These 5 dose components include the boron
dose produced by the $^{10}$B(n,$\alpha$)$^7$Li reaction, thermal neutron dose mainly from the $^{14}$N(n,p)$^{14}$C reaction, fast neutron dose mainly from the $^1$H(n,n')$^1$H proton recoil reaction, induced photon dose from photons created inside the patient mainly via the $^1$H(n,$\gamma$)$^2$H reaction, and incident photon dose from those photons that are produced upstream and outside of the patient. The relevant neutron interactions that occur in tissue during BNCT are illustrated in Figure 1.2.
Figure 1.2 Relevant neutron interactions in tissue that are responsible for the majority of the patient dose during BNCT. While all contribute to a non-specific and unavoidable background dose, the preferential accumulation of $^{10}$B in tumor cells provides the targeting necessary to achieve therapeutic advantage.
1.1.2.1 Boron Dose

The selective cellular dose targeting that forms the basis of BNCT is provided by the capture of thermal neutrons (\(E_n < 0.5\text{ eV}\)) by \(^{10}\text{B}\) nuclei. BNCT takes advantage of the high natural probability that a \(^{10}\text{B}\) nucleus will capture a thermal neutron that is due to the large absorption cross section of \(^{10}\text{B}\) which has a \(1/v\) shape (where \(v\) is the speed of the incident neutron). This \(1/v\) shape is reflected in the boron kerma (kinetic energy released per unit mass) shown in Figure 1.3. The \(^{10}\text{B}\) absorption cross section for a 0.025 eV neutron (\(v=2200\text{ m/s}\)) is 3837 barns while the corresponding cross section for \(^{14}\text{N}\) is over 3 orders of magnitude less, 1.7 b. Upon capturing a thermal neutron, the \(^{10}\text{B}\) immediately forms unstable \(^{11}\text{B}^*\), which decays within \(\sim 10^{-15}\) seconds into \(^4\text{He}\) and \(^7\text{Li}\) nuclei. However, 94% of the \(^{11}\text{B}^*\) nuclei will initially decay into an unstable excited state of \(^7\text{Li}^*\) which releases a 480 keV photon as it deexcites to \(^7\text{Li}\). This process is represented in an energy level diagram in Figure 1.4. Both of the high LET heavy charged particles that result from the capture reaction will deposit their energy along relatively short tracks which acts to confine the energy (and dose) to those cells containing the \(^{10}\text{B}\) nuclei. Conversely, the large mean free path of the 480 keV photon results in energy being transported away from the reaction site; therefore, this \(\gamma\)-ray contributes to the non-specific background dose in BNCT.

1.1.2.2 Thermal Neutron Dose

As illustrated in Figure 1.2, thermal neutrons can also be absorbed by the 2.2% of normal brain that is \(^{14}\text{N}\) to produce a proton and \(^{14}\text{C}\) via the \(^{14}\text{N}(n,p)^{14}\text{C}\) capture reaction, releasing 0.626 MeV. This neutron capture reaction is the predominate mechanism by which thermal neutrons contribute locally absorbed dose in normal tissue. In Figure 1.3, \(^{14}\text{N}\) kerma contributes 96.3% of the total neutron kerma at thermal neutron energies. \(^1\text{H}\)
nuclei (10.7% of normal brain) can also absorb thermal neutrons to produce high LET recoil deuterons and low LET 2.22 MeV photons. While the recoil deuterons are only responsible for 2.5% of the total neutron kerma at thermal neutron energies, the induced photons, whose dose is separately tracked and accounted for (section 1.1.2.3), contribute significantly to the non-specific background dose in BNCT and therefore reduce the therapeutic gain.

Figure 1.3  Boron and neutron kerma factors\(^4\) for ICRU adult brain tissue.\(^6\) The boron kerma factors reflect the \(1/v\) shape of the \(^{10}\text{B}\) neutron absorption cross section and are scaled for a \(^{10}\text{B}\) concentration of 15 μg/g. The total neutron kerma data are the weighted sum of kerma from those isotopes found in brain tissue. At thermal neutron energies, the main contribution is from nitrogen (via the \(^{14}\text{N}(n,p)^{14}\text{C}\) reaction) while hydrogen (via the \(^{1}\text{H}(n,n')^{1}\text{H}\) reaction) is the main contributor at fast neutron energies.
Figure 1.4  Energy level diagram representing the deexcitation of $^{11}$B* after the capture of a thermal neutron to $^7$Li or to an intermediate excited state ($^7$Li*), which releases a 478 keV γ-ray as it deexcites. Although not depicted here, an α particle ($^4$He) also results from the deexcitation of $^{11}$B*.

1.1.2.3 Photon Dose

For computation, the photon dose is often separated into induced and incident components. As illustrated in Figure 1.2, induced photons are produced in the patient, mainly by the thermal neutron absorption reactions of $^1$H. Incident photons are produced outside of the patient (via neutron interactions in the beam line or from those photons originating in the reactor core) and contribute dose in the patient during BNCT. However, the relative contribution from the low LET incident photons is usually small for well-designed neutron beams.

1.1.2.4 Fast Neutron Dose

The external beam of low energy (epithermal) neutrons used to irradiate the targeted anatomical region to provide thermal neutrons for capture by $^{10}$B is usually contaminated with fast neutrons ($E_n > 10$ keV). These fast neutrons, unlike the lower
energy neutrons, are not initially absorbed on interaction in tissue but rather predominantly scatter and thermalize in collisions with $^1$H to contribute dose mainly via the high LET recoil protons that are produced. However, the application of resonance scattering materials like Al, F, S, Ar to differentially filter out fast neutrons limits the fast neutron contamination of clinical beams to result in a dose component that is usually a small percentage of the total. Also, fast neutrons do indeed interact with the other nuclei present in tissue in large concentrations (e.g., $^{12}$C and $^{16}$O), but the dose that results from those interactions is a small percentage of the dose contributed by fast neutrons at neutron energies below ~1 MeV. At neutron energies above ~1 MeV, the neutron kerma contributed by these isotopes increases significantly as shown in Figure 1.3.

1.1.2.5 Weighted Dose

Estimating the biological effectiveness of the total dose delivered during BNCT is difficult due the complex mixture of high and low LET radiation and the differing biological effectiveness of each. Therefore, to account for these differences in radiation quality, each dose component is multiplied by a relative biological effectiveness (RBE) value that is determined experimentally, generally using an animal model, for the irradiated tissue and specified relative to low LET photon radiation. Factors relating to the biodistribution of the boronated compound used in the therapy are folded into the RBE to produce a compound biological effectiveness (CBE) factor for the boron dose component that is specific to each boron compound and tissue. The (total) weighted dose is the sum of all dose components weighted by the appropriate RBE or CBE and is expressed as Gy$_w$ (weighted Gray) to indicate that it is a weighted dose. The weighted
dose is presumed to be approximately equivalent in effect to the same dose of photon radiation.

1.1.3 Physical and Computational Dosimetry of BNCT

The ability to measure the dose in a clinical beam is an essential aspect of BNCT. Usually, this involves performing measurements of the thermal neutron flux, fast neutron dose, and photon dose both in-air and in a reference phantom and then using the appropriate $^{10}$B and $^{14}$N kerma factors to convert the measurements of thermal neutron flux into boron and thermal neutron dose. At the Massachusetts Institute of Technology (MIT), measurements of the 2200 m/s (0.025 eV) thermal neutron flux are made with Au foil activation analysis using the cadmium difference method, and measurements of fast neutron and photon dose rates are performed using the dual ion chamber technique. However, the techniques used to make the flux and dose measurements are not standardized for NCT and therefore the physical dosimetry can vary among clinical sites, which obstructs comparison of clinical data from different sites.

The measurements of flux and dose in the neutron beam are used to calibrate the treatment planning system (TPS) to ensure that the doses calculated during the planning process are an accurate representation of those delivered during treatment. The custom computer programs used for treatment planning vary among BNCT clinical sites, and that is important because significant differences exist between these programs that are difficult to quantify. This lack of standardization in NCT computational dosimetry presents another obstacle to pooling clinical data. Nevertheless, significant steps have been taken by the International Dosimetry Exchange to address both the differences in physical and computational dosimetry.
1.1.4 Clinical Trials of BNCT

Although still an experimental therapy, neutron capture therapy is by no means a new concept. It was first suggested by Locher in 1936, only 4 years after Chadwick discovered the neutron. However, it would not be until the 1950s and 1960s that the very first clinical trials of BNCT would be initiated at Brookhaven National Laboratory (BNL) and MIT. The results from these initial clinical trials of BNCT for human brain tumors were however discouraging. Retrospective analyses of these trials have indicated that both failed to sufficiently deliver the two essential components required for BNCT; the low energy neutrons beams used did not provide the penetration necessary to sufficiently deliver thermal neutrons to the deep malignant tissue and the boron-delivery agent was not sufficiently selective for the tumor which resulted in large $^{10}$B concentrations in the brain and skin. Therefore, the selective cellular dose targeting that is essential to BNCT was not achieved, a considerable background dose was delivered to the normal tissue, and no noticeable tumor control resulted.

While these discouraging results led to the closing of the initial BNCT clinical trials in the United States in 1961, clinical studies of BNCT using thermal neutron beams were resumed in Japan by 1968. Basic research in neutron capture therapy continued in the United States with the focus on correcting the shortcomings of those initial clinical trials. More specifically, this involved the development of higher energy epithermal neutron beams with deeper penetration and boron delivery agents with improved biological selectivity. These efforts resulted in the design and construction of dedicated epithermal ($0.5 \text{ eV} \leq E_n \leq 10 \text{ keV}$) neutron beams that allowed thermal neutrons to be delivered to deep-seated tumors. Also, new boronated pharmaceuticals, such as the amino acid derivative p-boronophenylalanine (BPA) and a sulfhydryl borane (BSH), with
much improved biochemical selectivity for the malignancies that are most often the target of BNCT were developed. Other technologies important for BNCT were also developed like techniques for the macroscopic and microscopic quantification of the boron biodistribution (e.g., PGNAA\textsuperscript{24,25} and HRQAR\textsuperscript{26,27}) along with new techniques for more accurate dose measurement and calculation, including three-dimensional treatment planning software, that helped maximize the efficacy of the treatment while ensuring the safety of the patient. Due to these significant advances, interest in BNCT was renewed, which eventually led to clinical trials at various sites in the USA,\textsuperscript{28-31} Japan,\textsuperscript{32,33} Europe\textsuperscript{34-38} and Argentina\textsuperscript{39} and extension from primary brain tumors to other diverse sites such as subcutaneous melanoma, intracranial melanoma metastacies, head and neck malignancies, liver tumors, and other thoracic targets.

1.1.5 Treatment Planning for BNCT
As in any form of radiotherapy, accurate treatment planning is essential to BNCT. Before a patient is treated with BNCT, detailed treatment planning calculations are performed for each patient to customize the therapy to that patient’s anatomy and maximize dose to the tumor while respecting dose limits on normal tissues. Evaluating dose distributions using isodose contours and dose-volume histograms for different beam orientations or different combinations of beams allows development of an optimal treatment plan that maximizes dose to the target volume while ensuring that the doses that will be delivered during treatment are safe for the patient. An example of the different dose data used in BNCT treatment planning are shown in Figure 1.5 and Figure 1.6, where isodose contours and a dose-volume histogram are shown for a patient treated at Harvard-MIT. Calculating the dose delivered during BNCT is complex due to the
required radiation transport and the presence of multiple dose components, which depend strongly on the tissue composition. Therefore, a treatment planning system for BNCT must provide the tools necessary to construct individualized patient models, perform particle transport calculations through that model, compute estimates of the various dose components, and analyze the dose distribution by calculating isodose contours and dose-volume histograms for the relevant anatomical structures. A recent review by Kiger and Kumada discusses the requirements for BNCT treatment planning in detail.40

Custom computer programs have been developed that address the computational requirements of BNCT treatment planning. Currently, 5 different treatment planning systems (TPSs) have been used in the clinical trials of BNCT in the Americas, Europe and Asia: BNCT_Rtpe (BNCT Radiation Therapy Planning Environment),41-43 SERA (Simulated Environment for Radiotherapy Applications),44,45 MacNCTPlan,46,47 NCTPlan,48,49 and JCDS (JAERI Computational Dosimetry System).50,51 All of these TPSs are similar in that they utilize Monte Carlo algorithms for radiation transport exclusively because of their ability to provide a detailed treatment of physics and geometry. Nevertheless, despite these similarities and the common goals, significant differences exist between these planning systems (e.g., in modeling techniques, kerma factors, dose reporting, radiation source definition) that make it difficult to directly compare patient doses from different BNCT clinical sites that were calculated with different TPSs. As an example of these differences, the techniques employed by the planning systems to model the patient anatomy for the particle transport are illustrated in Figure 1.7.
Figure 1.5  Screen capture of the BNCT treatment planning system, NCTPlan, displaying total weighted brain isodose contours (in Gy$_w$) for a patient treated at Harvard-MIT.
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Figure 1.6  Screen capture of the BNCT treatment planning system, NCTPlan, displaying the total weighted brain dose-volume histogram for a patient treated at Harvard-MIT.
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Figure 1.7 2D and 3D representations of the voxel (a,b), univel (c,d), and NURBS (e,f) (Non-Uniform Rational B-Splines) modeling techniques employed by MacNCTPlan and NCTPlan, SERA, and BNCT_Rtpe, respectively, to model the patient anatomy for BNCT treatment planning calculations. (Reprinted with permission from Kiger and Kumada⁴⁰).
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Although the Monte Carlo method is regarded as the most accurate method for radiation transport and dose calculations, the algorithms are not inherently accurate. In addition to accurate physics models, cross sections, and geometric models, the accuracy of Monte Carlo treatment planning calculations depends on using an accurate representation of the radiation source. However, accurately defining the radiation source is one of the most difficult aspects of the entire treatment planning process. Two of the techniques that exist for defining the radiation source are binary phase space (or MCNP$^{52}$ surface source) files and MCNP SDef source probability models. There are advantages and disadvantages to each technique.

Regardless of which technique is used to define the radiation source, it is common, especially in reactor-based BNCT, to define the source at a position close to the patient (e.g., as close as 1 cm) to allow the computational resources to be focused on dose calculations in the patient and not wasted on repeating computationally expensive transport computations upstream of the patient. This precalculation is feasible because the number of configurations possible with an epithermal neutron beam is very small. However, accurately defining the radiation source at a position downstream involves performing detailed Monte Carlo (or alternatively discrete-ordinates) calculations of the beam line. During these Monte Carlo calculations, the nature of the deep-penetration shielding problem often requires that nonanalog Monte Carlo (or variance reduction) techniques be employed to ensure that an adequately precise representation of the radiation source is produced at the downstream location.
1.2 Research Goals and Thesis Organization

This thesis investigates many of the computational aspects of BNCT treatment planning with the aim of improving both the accuracy and efficiency of the planning process as well as the understanding of differences in computational dosimetry that exist between different clinical sites. Therefore, it begins with an in-depth intercomparison of 4 of the different TPSs that have been used for treatment planning in BNCT clinical trials. Understanding the differences between the planning systems helps to further address some of the technical obstacles that prevent patient dose data from different clinical sites from being pooled. If differences in physical and computational dosimetry are properly addressed, pooling patient dose data from different clinical sites is indeed possible as is illustrated in Chapter 3 using patient data from BNL and Harvard-MIT and the work of the International Dosimetry Exchange.12,13

The Monte Carlo variance reduction techniques utilized during the detailed calculations of the neutron beam line are essential to ensuring that an accurate representation of the source is available in the subsequent treatment planning calculations. The techniques available for those calculations are reviewed in Chapter 4 and are also investigated as a means to increase the computational efficiency of dose calculations in the patient. The research described in Chapter 4 is used to produce a more precise surface source representation of the MIT Fission Converter Beam (FCB)21,53 with improved statistical properties that is used in Chapter 5 to directly compare two of the techniques available to model the radiation source for BNCT treatment planning calculations. A brief summary of the work presented in this thesis and the conclusions
reached in each chapter will be included in Chapter 6 along with recommendations for future work. A more detailed introduction to the major thesis chapters follows.

1.2.1 Intercomparison of Neutron Capture Therapy Treatment Planning Systems

In Chapter 2, a pre-existing suite of reference computational dosimetry problems is extended from depth-dose profiles in a single phantom to include multiple phantoms (a large rectangular water phantom, the modified Snyder head phantom, and a cylindrical leg phantom derived from CT data from the Visual Human Project), thermal and epithermal neutron beam spectra, and multi-dimensional dose data (isodose contours and dose-volume histograms) relevant to BNCT treatment planning. The extended set of references problems is then used as the basis for a detailed comparison of the 4 TPSs available at Harvard-MIT, BNCT_Rtpe, SERA, MacNCTPlan, and NCTPlan, to reference dosimetry calculations performed using the well-benchmarked Monte Carlo radiation transport code, MCNP5. The complete set of reference data and comparisons with data output by each treatment planning system are included in Appendix A.

1.2.2 Comparison of Doses Delivered in Clinical Trials of Neutron Capture Therapy in the USA

Before patient dose data from different BNCT clinical sites can be pooled together for combined dose response analysis, differences in physical and computational dosimetry between the clinical sites must first be resolved. Chapter 3 describes the normalization of BNL clinical dosimetry to that of Harvard-MIT. Using MIT measurements made at BNL (as part of the International Dosimetry Exchange and calculations with the BNL treatment planning system (BNCT_Rtpe), a relationship between the patient doses reported by BNL and doses measured by MIT in a reference phantom is determined. This derived relationship (in the form of dose component scale
factors) is then validated using calculations and MIT measurements in a different phantom. The BNL patient doses are recomputed using these scale factors, and the revised BNL clinical data are pooled with that of Harvard-MIT for a combined dose response analysis.

1.2.3 Application of Variance Reduction in Monte Carlo Treatment Planning Calculations for Neutron Capture Therapy

Chapter 4 investigates the application and optimization of variance reduction in the two phases of Monte Carlo treatment planning calculations, radiation transport calculations to define the beam source and dose calculations in the patient. First, calculations with MCNP are used to investigate and improve the pre-existing variance reduction scheme in the Monte Carlo model of the MIT Fission Converter Beam. Using an 11 node Beowulf cluster (described in Appendix B), a more precise surface source representation of the FCB with improved statistical properties is produced downstream at the patient position and validated using physical dosimetry measurements in the MIT ellipsoidal head phantom. The variance reduction techniques available in MCNP are also explored as a means of increasing the computational efficiency of dose calculations in the patient.

1.2.4 Neutron Beam Source Definition Techniques for Neutron Capture Therapy Treatment Planning

Constructing an accurate description of a neutron beam is critical to achieving accurate calculations of dose for NCT treatment planning. Chapter 5 uses the more precise surface source representation of the FCB created in Chapter 4 to compare two of the methods of neutron beam source definition available: MCNP surface source files and MCNP SDef source probability distributions. Each source definition type is used to
simulate transport of the beam through voxel models of the modified Snyder head phantom and a large rectangular water phantom where doses were calculated and compared for each source type. The development of a software tool that converts MCNP surface source models into MCNP SDefs is described as is the patch of the MCNP5 source code that allows the neutron and photon source angular distributions to be completely specified with an SDef.
1.3 References


49. S.J. González, G.A. Santa Cruz, W.S. Kiger III, M.R. Palmer, P.M. Busse, and R.G. Zamenhof, “NCTPlan, the New PC version of MacNCTPlan: Improvements and Verification of a BNCT Treatment Planning System,” in Research and


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2.0 Abstract

Currently, 5 different treatment planning systems (TPSs) are or have been used in clinical trials of Neutron Capture Therapy (NCT) at various sites worldwide: MacNCTPlan, NCTPlan, BNCT_Rtpe, SERA, and JCDS. This chapter describes work performed to comprehensively test and compare 4 of these NCT treatment planning systems in order to facilitate the pooling of patient data from the different clinical sites for analysis of the combined clinical results as well as to provide an important quality assurance tool for existing and future TPSs. Three different phantoms were used to evaluate the planning systems under conditions relevant to both patient planning and TPS calibration: the modified Snyder head phantom, a large rectangular water phantom, and a human leg phantom simulating a peripheral melanoma treatment. The comparison of dose profiles, isodose contours, dose difference distributions and dose-volume histograms to reference calculations performed with the well-benchmarked Monte Carlo radiation transport code MCNP5 yielded many clinically significant and interesting differences.
Each of the planning systems deviated from the reference calculations, with the newer systems (i.e., SERA and NCTPlan) most often yielding better agreement than their predecessors (i.e., BNCT_Rtpe and MacNCTPlan). Additional calculations were performed to further investigate and explain the sources of significant deviations from the reference calculations when they were observed in the planning systems. The combination of simple phantoms and sources with more complicated and realistic planning conditions has produced a well-rounded and useful suite of test problems for NCT treatment planning system analysis. Furthermore, such dosimetric comparisons play an essential role in helping to overcome obstacles, such as a lack of standardization in computational dosimetry, that prevent legitimate comparisons of patient data within the global NCT community.

2.1 Introduction

As in conventional radiotherapy, a detailed treatment plan is required in BNCT to ensure both the safety of the patient and to maximize the efficacy of the treatment. However, treatment planning for BNCT is more difficult due to the presence of multiple dose components as well as the requirement for a detailed physics model to treat this scatter-dominated radiation transport problem. Therefore, any treatment planning system (TPS) used for BNCT must adequately address these issues as well as provide the dose visualization and analysis tools necessary for effective radiotherapy treatment planning. Currently, 5 different treatment planning systems have been used in the clinical trials of BNCT in the Americas, Europe and Asia: BNCT_Rtpe (BNCT Radiation Therapy
While all BNCT planning systems depend on Monte Carlo particle transport algorithms, each provides a unique planning environment and has been responsible for introducing different innovations to the BNCT treatment planning process. However, the differences (e.g., in modeling techniques, kerma factors and dose reporting) that make each planning system unique also make it difficult to directly compare calculated patient doses from different BNCT clinical sites. While differences in physical and computational dosimetry have begun to be addressed through the International Dosimetry Exchange, this first order approach to clinical dosimetry normalization would indeed benefit from a more detailed comparison of the planning systems under conditions relevant to BNCT treatment planning.

2.1.1 BNCT Treatment Planning Systems

Each of the treatment planning systems used in BNCT is able to produce a treatment plan by providing the tools necessary to construct individualized patient models, perform particle transport calculations, and compute estimates of the various dose components present during BNCT and analyze the dose distribution. These dose components include the boron dose produced by the $^{10}\text{B}(n,\alpha)^7\text{Li}$ reaction, thermal neutron dose mainly from the $^{14}\text{N}(n,p)^{14}\text{C}$ reaction, fast neutron dose mainly from the $^1\text{H}(n,n')^1\text{H}$ proton recoil reaction, induced photon dose from photons created inside the phantom mainly via the $^1\text{H}(n,\gamma)^2\text{H}$ reaction, and the incident photon dose from those photons which are produced upstream in the beam line, outside the patient. In providing the
basic functionality required for effective BNCT treatment planning, the planning systems provide different techniques for model construction, material (tissue) compositions, kerma factors, neutron and photon cross sections, and Monte Carlo based radiation transport algorithms. It is significant differences in these essential aspects that make comparing calculated patient doses from different clinical sites difficult and that further emphasize the need for such a rigorous evaluation of the treatment planning systems. The features of each TPS which are relevant to the intercomparison will be discussed below and, as such, the following discussion is not meant to be a comprehensive description of each TPS.

2.1.1.1 BNCT_Rtpe

Developed at Idaho National Laboratory (INL) specifically for BNCT, BNCT_Rtpe was first used in 1994 during the BNCT trials at Brookhaven National Laboratory (BNL). Running on a Hewlett Packard® (HP) Unix workstation, BNCT_Rtpe utilizes a special-purpose Monte Carlo transport code, rtt_MC, to perform the necessary neutron and photon transport calculations. Before using rtt_MC, the patient’s anatomical structures are outlined on each CT or MR image slice by placing a set of control points. These user-defined control points are used to construct a 3D NURBS (Non-Uniform Rational B-Splines) model which defines the geometry for Monte Carlo transport calculations. In constructing the model, each user-defined anatomical region is assigned a specific user-defined material composition so that the appropriate cross section data are used for the transport calculations. The neutron and photon sources are defined in BNCT_Rtpe as probability distributions on a planar surface among geometric primitives defining those structures external to the patient anatomy.
such as a collimator and its aperture. Transport calculations are performed during user-defined run modes with the default being NFGD (Neutron, Fast neutron bias, induced and incident Gamma, and dose editing modes). During the rtt_MC transport calculations, a 30×30×30 mesh of 1 cm³ tally volumes is superimposed over the NURBS geometry defining the patient for scoring volume-averaged estimates of neutron fluence which are integrated against energy-dependent kerma factors to provide estimates of dose in each 1 cm³ volume of the scoring mesh. The multi-group cross section and kerma data are stored in a binary file in a format inherited from the RAFFLE code¹⁷ that was developed at INL during the 1970’s and 1980’s. 94 energy groups are used to define the neutron cross section and kerma data (22 thermal energy groups for 0 ≤ E_n ≤ 0.414 eV, 40 epithermal energy groups for 0.414 eV < E_n ≤ 9.12 keV, and 32 fast energy groups for 9.12 keV < E_n ≤ 16.9 MeV), and 70 groups are used for photon cross section and kerma data. Neutron cross section data were derived mainly from the ENDF/B-V nuclear data library,¹⁸ but neutron cross section data from ENDF/B-IV were used in the thermal neutron energy range for select elements (e.g., ¹⁰B and ¹⁴N). Photon cross section data were derived from the DLC-99/HUGO library,¹⁹ which is based on ENDF/B-V. The kerma data are read at runtime, and the neutron kerma is scaled by the user-defined edit mesh atomic densities (in atoms/barn cm and considered constant for the mesh) to provide volume-averaged estimates of boron, nitrogen, hydrogen, and photon dose rates for each mesh element. The same set of photon kerma factors are used in calculating dose regardless of the composition of the anatomical region in which dose is being computed as is done in most NCT planning systems. The dose tallies have no energy boundaries, meaning that a neutron of any energy can contribute to the neutron dose component tallies. However, in
the BNCT_Rtpe fast neutron source biasing mode (i.e., run mode “F”), wherein the fast neutron portion of the source spectrum is sampled for better convergence of the hydrogen dose rate, only those neutrons above a given energy (the default biasing energy cutoff is 9.12 keV) contribute to the hydrogen dose rate. A custom 3D cubic interpolation subroutine is used to calculate dose or flux at any point within the coarse $30\times30\times30$ tally mesh. This interpolated dose and flux information can be displayed as dose vs. depth profiles, isodose contours for transverse or coronal planes, and dose-volume histograms for any user-defined region of the patient anatomy. In addition to treatment planning for the BNL clinical trials, BNCT_Rtpe has been in BNCT clinical trials at Espoo (Finland) and Petten (The Netherlands).

2.1.1.2 SERA

Developed jointly by INL and Montana State University and released in 1998 as a successor to BNCT_Rtpe, SERA inherited some source code from BNCT_Rtpe and thus shares many of the same features. Therefore, only the differences between BNCT_Rtpe and SERA that relevant to this intercomparison will be mentioned here. SERA divides the treatment planning process into several logical steps and provides a distinct program or module (i.e., seraImage, seraModel, sera3d, seraCalc, seraPlan, seraDose, seraPlot) for each step. In SERA, univels (uniform volume elements) replace NURBS as the technique for modeling complex patient anatomy and allow faster transport calculations by employing integer arithmetic to perform the required ray tracing. Univels are defined as right parallelepipeds with a cross-sectional area equal to that of a pixel and a thickness equal to the slice thickness of the CT or MR image. Defining univels in this manner preserves the geometric fidelity of the original medical image data while allowing rapid
interrogation of the transport geometry. Using graphical interface tools provided by seraModel, each pixel on every CT or MR image slice is assigned to a user-defined anatomical region (e.g., brain, tumor, bone) by “painting” it a specific color. This user input is constructed into a 3D univel model of the patient anatomy that is used by the custom transport module, seraMC, to perform the necessary Monte Carlo transport calculations. Multiple fields are weighted and combined with seraPlan so that the appropriate multi-dimensional dose data can be produced and visualized with seraPlot and seraDose. For SERA, boron and photon kerma data as well as photon cross section data were updated from BNCT_Rtpe whereas neutron cross section data remained the same. However, the cross section library for SERA was expanded to include data for other elements (e.g., bismuth, iron, chromium, and molybdenum). A finer energy grid was used to represent the updated boron and photon kerma data in SERA resulting in an increase in the number of energy groups from 94 to 717 for boron kerma and from 70 to 86 for photon kerma. Photon cross section data were updated to ENDF/B-VI\textsuperscript{18} from the DLC-99/HUGO library\textsuperscript{23}. SERA has been used for treatment planning for BNCT clinical trials at Espoo (Finland),\textsuperscript{20} Studsvik (Sweden),\textsuperscript{24} and Kyoto (Japan).\textsuperscript{25}

2.1.1.3 MacNCTPlan

MacNCTPlan was developed in the Pascal programming language for the Power Macintosh\textsuperscript{™} platform at Harvard-MIT and imbedded within the public domain image processing program NIH Image (developed at the U.S. National Institutes of Health and available on the Internet at http://rsb.info.nih.gov/nih-image/). MacNCTPlan thresholds the CT image data into primary materials (i.e., air, normal tissue, and bone) with a user-defined region of interest (ROI) used to delineate tumor. A $21 \times 21 \times 25$ mesh of 1 cm$^3$
voxels is superimposed over the thresholded image data and MacNCTPlan calculates in 20% increments the volume fraction of the primary materials and tumor within each element of the voxel mesh. Using the calculated volume fractions, the material definitions for air, normal tissue, bone, and tumor are mixed accordingly to result in a material specification for each voxel. The voxel mesh and the corresponding mixed materials are constructed into a lattice model so that a customized version of the Monte Carlo transport code MCNP4B,26 modified with the speed tally patch27-30 to decrease computation time in specially constructed lattice geometries, can be used to perform the necessary transports calculations. Due to its extended development history, MCNP brings well-benchmarked and detailed treatments of neutron and photon transport physics as well as a broad range of functionality (e.g., in terms of source definition techniques, cross section data, variance reduction techniques, and tally specification) to the treatment planning process. Along with the neutron or photon source definition, the appropriate energy-dependent boron, neutron and photon kerma factors are added to the MCNP input deck so that volume-averaged estimates of fluence in each 1 cm$^3$ element of the voxel mesh can be converted to estimates of boron, thermal and fast neutron, and photon dose. Unlike in BNCT_Rtpe and SERA, a defined neutron energy cutoff of 0.5 eV is used to separate the neutron dose into thermal and fast components to facilitate comparison of calculated doses with dose measurements. After performing the neutron and photon transport calculations with MCNP, the calculation results are loaded into MacNCTPlan where the coarse 21×21×25 dose matrix is interpolated to the resolution of the original medical image data (i.e., ~ 1 mm). The interpolated data are then visualized in the form of dose vs. depth profiles, isodose contours for any arbitrary plane, and dose-volume
histograms for each user-defined ROI. MacNCTPlan has been used in the BNCT clinical trials at Harvard-MIT (USA)\textsuperscript{31,32} and Rez (Czech Republic).\textsuperscript{33}

2.1.1.4 \textit{NCTPlan}

\textit{NCTPlan} was developed in a collaboration between Harvard-MIT and the Comisión Nacional de Energía Atómica (CNEA) of Argentina. Despite its many similarities to MacNCTPlan, it represents more than a direct port of MacNCTPlan to Microsoft Visual Basic\textsuperscript{TM} and the x86 platform. Like MacNCTPlan, \textit{NCTPlan} constructs a mixed-material voxel model from the thresholded CT image data and uses MCNP4B with the speed tally patch to perform the neutron and photon transport calculations in the lattice model of the patient. Also, like MacNCTPlan, the calculation results are loaded into \textit{NCTPlan} for dose interpolation, analysis and visualization. However, the algorithms responsible for voxel model construction, dose interpolation and calculation of dose-volume histograms were greatly improved in \textit{NCTPlan} which results in differences worthy of further investigation. Clinical trials at Harvard-MIT,\textsuperscript{31,32} Petten (The Netherlands),\textsuperscript{34} and CNEA (Argentina)\textsuperscript{35} have used \textit{NCTPlan} for clinical treatment planning.

2.1.2 Previous Work

Considerable comparative work between the various treatment planning systems has been performed previously. A comparison of voxel-by-voxel dose differences between MacNCTPlan and \textit{NCTPlan} for two randomly selected patients from the Harvard-MIT BNCT clinical trials produced agreement within $\pm 4\%$.\textsuperscript{36} Another comparison of these two planning systems to MCNP reference calculations in the Snyder head phantom reported that the improved algorithms in \textit{NCTPlan} produced more accurate
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Comparing NCTPlan calculations in the modified Snyder head phantom with reference calculations using monoenergetic, monodirectional beams demonstrated generally good agreement except at shallow depths where NCTPlan underestimated the dose resulting from the interactions of thermal neutrons. By simulating a variety of beams and transport geometries (water-filled cylinder, water-filled ellipsoid, and a Harvard-MIT patient), a comparative study between MacNCTPlan and BNCT_Rtpe found differences in the ellipsoidal phantom as large as 14.5% in maximum photon doses and 17.5% in maximum fast neutron doses, isodose contours in the patient that agreed to within a few millimeters, and dose-volume histograms which were similar in shape. Comparisons of MacNCTPlan, SERA, and MCNP thermal neutron fluence profiles in a rectangular water phantom and an ellipsoidal head phantom from various monoenergetic neutron beams produced differences as large as 21% for MacNCTPlan and 20% for SERA. These differences were attributed to the material mixing and voxelization techniques of MacNCTPlan and the inability of the multigroup data format of SERA to accurately model resonances in cross section data. Similar findings were produced in a separate study that also modeled monoenergetic neutron beams with SERA, but better agreement between SERA and MCNP was achieved when the energy spectra of the simulated neutron beams spanned at least 1 of the 94 neutron energy groups in SERA. Previous comparisons of the TPSs have not been limited solely to simple phantoms and beams but have included actual BNCT clinical beams and patients. A study comparing the dose-volume histograms calculated by BNCT_Rtpe and SERA for 10 BNCT patients treated at the Finnish Research Reactor (FiR 1) discovered differences as large as ~10%, which were attributed to the more
accurate volumetric calculations in SERA. A study using the hyperthermal neutron beam at the RA-6 reactor in Argentina reported that fast neutron dose rates calculated by SERA in both a large rectangular water phantom and a cylindrical water phantom underestimated the corresponding physical dosimetry measurements and NCTPlan calculations by an average of 22%. Similarly, a comparison of SERA and JCDS (using a detailed JCDS model with 2×2×2 mm voxels and a 5×5×5 mm scoring mesh) for a 2-field brain cancer patient resulted in differences of 22% in the maximum fast neutron dose rate to brain. However, differences in the maximum biologically weighted doses for the brain, planning target volume (PTV), and tumor were much smaller at 3%, 3%, and 4%, respectively.

When considered as a whole, the previous work indeed represents a valuable resource of intercomparative data, but the rather limited scope of each study (i.e., limited in terms of the number of TPS and the type of dose data compared, usually only depth-dose profiles) combined with the wide variety of different irradiation conditions represented makes it difficult to extrapolate the findings of any one particular comparison to another. Moreover, the previous studies generally make only limited efforts to understand and explain the differences between planning systems. Therefore, preliminary work towards standardizing such comparisons of BNCT treatment planning systems was done previously through the development of a set of reference dosimetry calculations represented as dose vs. depth profiles in the modified Snyder head phantom, and that work serves as the basis for the intercomparison described here.
2.1.3 Objectives

In this chapter, that preliminary work was extended to form a more comprehensive set of reference problems which subjects the treatment planning systems to a variety of conditions relevant to BNCT treatment planning. The original set of reference problems was extended to include both simple and complex phantoms. The simulated irradiations of a large rectangular water phantom and the modified Snyder head phantom with an epithermal neutron beam as well as the irradiation of a leg phantom with a thermal neutron beam allowed the planning systems to be evaluated under different geometric conditions that are relevant either to clinical irradiations or calibration conditions at some institutions. Using analytical representations of these 3 phantoms with the well-benchmarked Monte Carlo radiation transport code MCNP5\textsuperscript{43} and the most up-to-date neutron and photon cross sections, material compositions, and kerma factors available, clinically relevant multidimensional dose data in the form of dose vs. depth profiles, isodose contours, and dose-volume histograms were calculated and compared to the corresponding output from BNCT_Rtpe, SERA, MacNCTPlan, and NCTPlan. Using analytical representations of each phantom in the reference calculations avoided introducing the geometric approximations that are characteristic of each treatment planning system. Extending the reference dose data to include isodose contours and dose-volume histograms was also significant since it is those representations of dose that are actually used in clinical treatment planning. While the intercomparison includes only those treatment planning systems available to the authors at the time the work was performed, a primary goal during the development and application of these reference dosimetry calculations was to facilitate the inclusion of other BNCT treatment planning systems as they become available or are developed in the future.
2.2 Methods and Materials

The reference data consist of MCNP5 calculations of dose and flux at finely spaced points in various analytical phantoms which are post-processed with custom MATLAB (The MathWorks, Natick, MA) functions in order to produce multi-dimensional dose and flux data relevant to BNCT treatment planning. This reference data are subsequently compared to output from each BNCT treatment planning system to produce a comprehensive dosimetric intercomparison.

2.2.1 Phantoms

The criteria for selecting or designing phantoms to include as part of the reference calculations were relatively simple. Each of the phantoms had to be simple enough that an analytical representation with no geometric approximations could be created but still represent irradiation conditions relevant to the BNCT treatment planning calculations. The large rectangular water phantom, similar to that used in the International Dosimetry Exchange, is a cube 40 cm on a side modeled entirely of light water (H₂O). Since both the geometry and material are easily modeled by the treatment planning systems, the large water phantom provided a good basis with which to begin the intercomparison since any potential differences due to modeling technique or material specification are avoided. Also, the large water phantom is representative of the phantoms used at some BNCT clinical facilities to calibrate their treatment planning systems.

To simulate conditions relevant to treatment planning for BNCT of intracranial disease, the modified Snyder head phantom was modeled using three ellipsoids to define the boundaries of brain, skull, and skin and irradiated with a generic epithermal neutron beam. To make the phantom more relevant to BNCT of intracranial tumors, a tumor
was modeled as a 4 cm diameter sphere (volume of 33.5 cm$^3$), added to the center of the brain ellipsoid, and shifted 2 cm along the lateral x-axis to make it tangential to the center coordinate of the brain. Sagittal, coronal, and transverse views of the analytical representation of the head phantom are shown in Figure 2.1. Each region in the head phantom was modeled using the corresponding ICRU 46 biological material: adult whole brain ($\rho=1.04$ g/cm$^3$), adult whole cranium ($\rho=1.61$ g/cm$^3$), and adult skin ($\rho=1.09$ g/cm$^3$). $^{10}$B concentrations of 15, 52.5, and 22.5 $\mu$g/g$^{45}$ were explicitly modeled in brain ($1.0 \times$ blood [$^{10}$B]), tumor ($3.5 \times$ blood [$^{10}$B]$^{46}$ and skin ($1.5 \times$ blood [$^{10}$B]$^{47}$), respectively, to correctly account for neutron flux depression due to the capture of thermal neutrons by $^{10}$B nuclei. It should be noted that the voxel modeling technique used by MacNCTPlan and NCTPlan did not permit the layer of skin to be modeled separately due to the limitation of 4 primary materials, so skin was represented as soft tissue (i.e., adult whole brain + 15 $\mu$g/g $^{10}$B) in calculating the mixed materials. With its curved surfaces and heterogeneous composition, the head phantom tested the ability of each planning system to model the complex anatomical structures and biological materials that are required for accurate BNCT treatment planning.

Since BNCT has not been limited solely to intracranial tumors$^{35,48}$ a leg phantom was created to simulate BNCT of peripheral melanoma of the human leg. The dimensions of the leg phantom anatomy were derived from CT data from the Visual Human Project.$^{49}$ Cylinders 25 cm in length and 9.75 cm, 9.35 cm, 7.0 cm, 2.25 cm, and 1.15 cm in diameter were used to model skin, the connective tissue between the skin and muscle, muscle, tibia, and fibula, respectively. Two superficial tumors were also modeled as part of the leg phantom: a spherical tumor with a diameter of 1.5 cm and volume of 1.77 cm$^3$.  

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and an arc-shaped tumor with a volume of 19.2 cm³. Transverse and oblique slices through the leg phantom are shown in Figure 2.2. Each region in the leg phantom was modeled with the corresponding ICRU 46 biological material: adult muscle (ρ=1.05 g/cm³), adult cortical bone (ρ=1.92 g/cm³), adult connective tissue (ρ=1.03 g/cm³), and adult skin (ρ=1.09 g/cm³). ¹⁰B concentrations of 15, 52.5, 15, and 22.5 μg/g were explicitly modeled in muscle (1.0 × blood [¹⁰B]), tumor (3.5 × blood [¹⁰B]), connective tissue (1.0 × blood [¹⁰B]), and skin (1.5 × blood [¹⁰B]), respectively. The regions of connective tissue and skin were both modeled as muscle in MacNCTPlan and NCTPlan since their mixed material voxel models were limited to the 4 primary materials of air, muscle, bone, and tumor. The greater curvature of the leg phantom surface, the use of a thermal neutron beam, and the superficial location of the tumors subjected each planning system to irradiation conditions significantly different from the head phantom and large rectangular water phantom.
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Figure 2.1 Sagittal (a), coronal (b), and transverse (c) views through the analytical model of the modified Snyder ellipsoidal head phantom used for the reference dosimetry calculations. A brain tumor was modeled by a 4 cm diameter sphere. The anatomical regions were modeled using ICRU 46 adult whole brain, adult whole cranium, and adult skin biological materials.
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Figure 2.2  Transverse and oblique views through the analytical model of the leg phantom used for the reference dosimetry calculations. The phantom was derived from measurements of CT image data of a human leg from the Visual Human Project. Two superficial tumors, modeled by a sphere and an arc shape, were added to simulate BNCT treatment of peripheral melanoma. The different anatomical regions were modeled using ICRU 46 adult muscle, adult cortical bone, adult connective tissue, and adult skin biological materials.
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2.2.2 Neutron and Photon Sources

As for the phantoms, neutron and photons beams that were easy to model in each of the treatment planning systems and also relevant to BNCT were selected for the reference calculations. The generic epithermal neutron beam from the pre-existing suite of reference calculations\textsuperscript{14} was also used in this work as the neutron source for both the large rectangular water phantom and head phantom. The monodirectional 10 cm diameter disc source was modeled as 10\% thermal neutrons (0.001 eV to 0.5 eV), 89\% epithermal neutrons (0.5 eV to 10 keV), and 1\% fast neutrons (10 keV to 2 MeV). The disc source was sampled uniformly in area (i.e., radius sampled from $p(r) \sim r$) and was normalized to a neutron flux of $1 \times 10^{10}$ n/cm$^2$s.

To simulate treatment planning for BNCT of peripheral melanoma with the leg phantom, a monodirectional 10 cm diameter thermal neutron disc source was modeled using the energy spectrum of the M11 thermal neutron beam\textsuperscript{50} at MIT as a basis. For MCNP5, a combination of different built-in functions were used to model the source probability distributions in the thermal, epithermal and fast regions of the thermal beam’s energy spectrum. The Maxwell fission spectrum, with parameters tuned to represent the Maxwellian thermal neutron distribution, was employed to model the thermal neutron peak below 1 eV. The Power law represented the nearly $1/E$ distribution in the epithermal neutron portion of the spectrum and the Watt fission spectrum modeled the fast neutrons above $\sim 100$ keV. The Maxwell fission energy spectrum ($p(E) = CE^{1/2}\exp(-E/a)$ with $a=3.25 \times 10^{-8}$ MeV), 165 points approximating the Power law ($p(E) = c|E|^a$ with $a=-1.1575$) for 0.32 eV $\leq E_n \leq$ 10 MeV, and the Watt fission energy spectrum ($p(E) = C\exp(-E/a)\sinh(bE)^{1/2}$ with $a=0.988$ MeV and $b=2.249$ MeV$^{-1}$) were modeled and sampled with frequencies of 99.87\%, 0.11\%, and 0.02\%, respectively. In MCNP, the
Power law was not available to model energy probability distributions without modifying the source code, so a piecewise linear function defined with a fine energy grid was instead used to approximate the Power law from 0.32 eV to 10 MeV. For BNCT_Rtpe and SERA, the neutron energy spectrum of the thermal beam was modeled using the maximum allowed 100 energy bins. For all calculations, the disc source was sampled uniformly in area and normalized to a neutron flux of $1 \times 10^{10}$ n/cm$^2$s. The generic epithermal and thermal neutron beam energy spectra are both shown in Figure 2.3.

The same incident photon source was modeled for all 3 phantoms: a monoenergetic and monodirectional disc source of 2 MeV photons 10 cm in diameter and normalized to a flux of $2 \times 10^8$ $\gamma$/cm$^2$s. This normalization was calculated so that the maximum incident photon dose rate would be approximately 10% of the maximum induced photon dose rate on the central beam axis in the head phantom.
Figure 2.3  Energy spectra for the thermal and generic epithermal neutron beams simulated as part of the reference dosimetry calculations. The generic epithermal neutron beam was taken from the pre-existing suite of reference dosimetry calculations\textsuperscript{14} while the thermal neutron beam was modeled after the M11 thermal neutron beam at MIT.\textsuperscript{50} Both beams were normalized to a neutron flux of $1 \times 10^{10}$ n/cm$^2$s.
2.2.3 Monte Carlo Simulations

2.2.3.1 Geometric Models

An exact analytical model with no geometric approximations of each phantom was constructed from geometric primitives using combinatorial geometry in MCNP5 v. 1.40 and these analytical models were used for the reference dose calculations. MATLAB was used to produce the corresponding DICOM format images (with 0.977 mm/pixel in-plane resolution and 2 mm slice thickness) of each phantom which were then processed and imported into each planning system and used to construct a 3D model of each phantom native to each TPS (i.e., voxel, NURBS, or univel model) just as if planning for an actual patient. It should be noted that the image data for the large water phantom was constructed so that the phantom surface was aligned with the voxel mesh of MacNCTPlan and NCTPlan to ensure that no material mixing of water and air occurred in any of the voxels at the air-phantom interface. Thus, all voxels in the mesh were modeled as either 100% water or 100% air. Also, for MacNCTPlan and NCTPlan, additional slabs of water were added around the $21\times21\times25 \, \text{cm}^3$ voxel mesh for the large rectangular water phantom so that the resulting model was equivalent in size to the analytical representation used in the reference calculations (i.e., $40\times40\times40 \, \text{cm}^3$).

2.2.3.2 Cross Sections

The most up-to-date cross section data available at the time this work was performed were used for the reference calculations. Each treatment planning system used its default cross section data. The MCNP5 transport calculations utilized as the reference as well as the MCNP4B calculations performed for MacNCTPlan and NCTPlan all used neutron and photon cross section data from the MCNP ENDF60 library, which were derived from the ENDF/B-VI nuclear data library. Both BNCT_Rtpe and SERA
employed multigroup neutron cross section data (94 energy groups) derived mainly from the ENDF/B-V nuclear data library, but cross section data from ENDF/B-IV was used in the thermal neutron energy range (i.e., $E_n < 0.414$ eV) for some elements (e.g., $^{10}$B and $^{14}$N). Thermal neutron cross section data for hydrogen in light water was based on experimental work by Nelkin\textsuperscript{52} and Haywood\textsuperscript{53} performed in the 1960’s. The neutron cross section data modeled by BNCT\textsubscript{Rtpe} and SERA for the various materials of the three phantoms were compared and found to be identical, but their photon cross section data differ. BNCT\textsubscript{Rtpe}’s photon cross section data were derived from the DLC-99/HUGO library,\textsuperscript{19} which is based on ENDF/B-V, while SERA utilized updated photon cross section data from ENDF/B-VI. The $S(\alpha,\beta)$ thermal neutron scattering treatment for hydrogen in light water was utilized for all the Monte Carlo transport calculations. In BNCT\textsubscript{Rtpe} and SERA, the $S(\alpha,\beta)$ thermal neutron scattering treatment for CH\textsubscript{2} was additionally used in modeling the various biological materials.

2.2.3.3 Kerma Factors and Dose

Neutron and photon kerma factors\textsuperscript{14} for ICRU 46 adult whole brain were used in the large rectangular water phantom and head phantom for the reference calculations as well as for MacNCTPlan and NCTPlan. For all 3 phantoms, the same $^{10}$B kerma factors\textsuperscript{14} were used for the reference, MacNCTPlan, and NCTPlan calculations. In BNCT\textsubscript{Rtpe} and SERA, the edit mesh atomic densities for boron, nitrogen, and hydrogen (in atoms/barn cm), which scale the corresponding elemental neutron kerma factors, were specified for ICRU 46 adult whole brain. In addition, carbon and oxygen densities were input for SERA to include their contributions in the calculation of total dose. In calculating photon dose with BNCT\textsubscript{Rtpe} and SERA, the same sets of brain photon
kerma factors are used regardless of the anatomical region where the photon dose is actually being computed. The photon kerma factors are updated in SERA and are therefore different from those used by BNCT_Rtpe. Since BNCT_Rtpe and SERA only report total photon dose, minor adjustments were made to rtt_MC and seraMC to separate the photon dose into induced and incident components. In the irradiation of the leg phantom, skin was the dose-limiting tissue, so neutron kerma factors for ICRU 46 adult skin were used for reference, MacNCTPlan, and NCTPlan calculations along with photon kerma factors for ICRU 44 adult skeletal muscle, which were calculated from NIST data. Muscle photon kerma factors differ from skin photon kerma factors by less than 1% for photon energies above 150 keV and by ~0.4% at 2.2 MeV (i.e., the energy of the photon produced by the $^1\text{H}(n,\gamma)^2\text{H}$ reaction). In the corresponding BNCT_Rtpe and SERA simulations with the leg phantom, edit mesh atomic densities corresponding to ICRU 46 adult skin were used. In all three phantoms, the energy-dependent kerma factors were used to calculate the 5 main dose components present during BNCT. The boron dose, thermal and fast neutron dose, induced and incident photon dose were also weighted by RBE or CBE factors of 1.3, 3.2, 3.2, 1.0, and 1.0, respectively, and summed to produce the total biologically weighted brain dose in the head phantom. Similarly, RBE factors of 2.5, 3.2, 3.2, 1.0, and 1.0 were used to calculate the total biologically weighted skin dose in the leg phantom. The total biologically weighted tumor dose was also calculated for the head phantom and leg phantom tumors using the same RBE factors as for brain, except for the boron dose, which was scaled by 3.8 instead of 1.3.
2.2.3.4 Field Arrangements

Simulated irradiation of the large water phantom utilized a single field perpendicular to the phantom surface aligned to the center of the phantom. For the head phantom, dose data for single-field and combined 3-field irradiations were calculated. The simulated single-field treatment plan used a lateral field (ipsilateral). Contralateral and vertex fields were added to produce the 3-field plan. The central axes of the ipsilateral and contralateral fields were aligned with the geometric center of the tumor while the central axis of the vertex field was aligned with the z-axis which is tangent to the tumor. The ipsilateral, contralateral, and vertex fields were fluence-weighted by factors of 0.5, 0.25, and 0.25, respectively. For the leg phantom, the disc source was rotated 35° from the x-axis for a single lateral anterior oblique field orientation. Figure 2.4 illustrates the field orientations for the head and leg phantoms.

2.2.3.5 Dose Data

Each treatment planning system was used to produce dose vs. depth profiles along the central beam axis (at ~1 mm increments for MacNCTPlan and NCTPlan, at 5 mm increments for BNCT_Rtpe and SERA), isodose contours in orthogonal planes on the beam central axis, and dose-volume histograms for brain and tumor in the head phantom and for skin and both tumors in the leg phantom. Additionally, for a more detailed understanding of the agreement between the isodose contours lines, the unmasked, interpolated 2D dose data, from which each planning system plots isodose contours, was extracted and used to calculate 2D dose difference distributions. To calculate the corresponding reference data to which each TPS was compared, MCNP5 mesh tallies of various sizes were used in simulations with analytical models of the phantoms. For dose vs. depth profiles, a uniform mesh of 1×10×10 mm tally volumes centered on the central
beam axis was used. The dose grid for isodose contours was calculated using a 2 mm thick tally mesh with 1 mm in-plane resolution. For dose-volume data in the head phantom, the brain was enclosed in a mesh of $2 \times 2 \times 2$ mm tally volumes while a finer mesh of $1 \times 1 \times 1$ mm volumes was superimposed over the tumor. For the leg phantom, a cylindrical mesh tally was used for both the skin and the arc-shaped tumor (#2) while a cartesian mesh of $1 \times 1 \times 1$ mm tally volumes was used for the spherical tumor (#1). Figure 2.5 shows a sample of the mesh tallies used within MCNP to calculate the multidimensional reference dose data in the head phantom.

The results of the MCNP5 mesh tallies were read into MATLAB and processed to produce data that could be directly compared to the output of each treatment planning system. Thus, for the sake of this intercomparison, the reference data or calculations refer to MCNP5 calculations of dose or particle flux in the analytical phantoms using various mesh tallies followed by post-processing with custom MATLAB functions. For instance, custom MATLAB functions were developed to calculate via numerical integration the partial volume fractions for each element of the rectangular or cylindrical scoring mesh intersecting the border of a structure, and these partial volumes were used to account for partial volume effects when calculating the reference dose-volume histograms. The reference isodose contours were directly compared to those plotted separately with MCNP5 (using MCPLOT\textsuperscript{43}) to verify the accuracy of the MATLAB post-processing and contour plotting functions. To facilitate the direct comparison of isodose contours between each TPS and the reference, the contours were plotted for absolute dose rather than as a percentage of a reference dose. In order to calculate dose, treatment times for each planning system were computed using realistic BNCT dose prescriptions for each
phantom: a maximum brain dose of 12.5 Gy$_w$ for the head phantom and a minimum tumor dose of 24 Gy$_w$ for the leg phantom. Similarly, plotting the dose-volume data output from each TPS as percent volume vs. percent of the reference dose would have made a direct comparison difficult since the reference doses were different for each TPS. Therefore, using the treatment times calculated using the reference data, the dose-volume data from each TPS and the reference were plotted as percent volume vs. absolute dose.

1.5×10$^9$ source particles were simulated for each field and phantom during the reference MCNP5 coupled neutron/photon (i.e., mode np) and incident photon (i.e., mode p) calculations, and each simulation was performed in parallel on an 11 node Beowulf cluster. 5×10$^7$ source particles were simulated during sequential runs for MacNCTPlan, NCTPlan, BNCT_Rtpe, and SERA to sufficiently reduce the uncertainties associated with Monte Carlo simulation to insignificant levels. While BNCT_Rtpe and SERA do not report uncertainties for tallied quantities, simulating 5×10$^7$ particles has been shown to produce adequately converged calculations for all dose components.$^{57}$ The Monte Carlo transport module of BNCT_Rtpe, rtt_MC, was ported to x86 Linux so that better statistics could be rapidly achieved by running more particle histories with newer computer hardware. Source biasing of fast neutrons and photon production biasing was used in MCNP5 (for reference calculations) and MCNP4B (for MacNCTPlan and NCTPlan calculations) to reduce the variance of the fast neutron and induced photon dose component tallies. The lattice speed tally patch$^{30}$ was utilized for MCNP4B transport calculations for the MacNCTPlan and NCTPlan voxel models of all 3 phantoms. Unless otherwise noted, BNCT_Rtpe and SERA were run in their default modes of “NFGD” which includes the default fast neutron source biasing mode.
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Figure 2.4  Simulated treatment field orientations for the head and leg phantoms. Both 1- and 3-field irradiations were simulated for the head phantom. The disc source for the single field irradiation of the leg phantom was rotated 35° from the lateral x axis.
Figure 2.5 Transverse, coronal, and sagittal views of the various mesh tallies used within MCNP5 to produce the reference depth-dose (1×10×10 mm), isodose (1×1×2 mm), and dose-volume (2×2×2 mm) data for the ellipsoidal head phantom. The mesh used to calculate dose-volume data for the brain tumor is not shown but consisted of 1×1×1 mm tally volumes.
2.3 Results

The complete set of reference data (including all dose components) and the comparison to corresponding data from each treatment planning system is included in Appendix A. Since the complete set includes 156 plots and 44 tables, only a representative subset will be presented here for discussion.

2.3.1 Dose vs. Depth Profiles

To facilitate the direct comparison of dose and flux profile data from each planning system to that of the reference, differences between each TPS and the reference were calculated as a function of depth in the phantoms and plotted as percentages of the maximum reference dose or flux (i.e., as $100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_{\text{max}}}$). Percent differences were calculated in this manner to prevent differences in small doses (at depth in the phantom) from obscuring the comparison in the more important high dose region. Percent difference vs. depth profiles are included directly below the corresponding dose and flux profiles for all 3 phantoms.

2.3.1.1 Large Rectangular Water Phantom

This section reports the comparison of 1D dose and flux profiles in the large rectangular water phantom from each TPS with the reference.

2.3.1.1.1 Thermal Neutron Flux

Since in excess of 90% of the total biologically weighted dose in BNCT is derived from the interactions of thermal neutrons with boron, nitrogen and hydrogen, accurate calculations of the thermal neutron flux are absolutely essential to accurate BNCT treatment planning. Therefore, comparisons of thermal neutron flux profiles are an appropriate starting point for any intercomparative discussion. Figure 2.6 shows the
thermal neutron flux calculated by MCNP5, BNCT_Rtpe, SERA, MacNCTPlan, and NCTPlan as well as the percent difference of each TPS from the reference MCNP5 calculations as a function of depth in the large rectangular water phantom. Each TPS deviates from the reference calculations with the largest differences occurring at the phantom entrance. The deviations in flux in the rectangular water phantom indicate the presence of differences that are independent of both kerma factors and geometric modeling technique. For each TPS, the thermal neutron flux data result from interpolating the volume-averaged flux from a coarse scoring mesh of 10×10×10 mm elements. In each TPS, the geometric center points of these cubic tally volumes correspond to ½ integral depths in the rectangular water phantom (e.g., 0.5 cm, 1.5 cm, 2.5 cm, etc). At these ½ integral depths, MacNCTPlan and NCTPlan produce relatively good agreement by underestimating the reference thermal neutron flux by less than 3%, which is understandable considering the smaller tally volumes (0.1 cm³ vs. 1 cm³) used in the reference calculations. If the reference thermal neutron flux is averaged over an equivalent volume (i.e., 10 reference mesh elements) and compared to uninterpolated MacNCTPlan and NCTPlan voxel flux data, the differences are not statistically significant. It is also worth noting that averaging the reference thermal neutron flux profile data over 1 cm³ (i.e., the tally volume utilized by all the TPSs) alone produces a 1% decrease in the maximum reference thermal neutron flux and a 37% increase in flux at the phantom surface. However, the exact effect of volume averaging depends on the position on the scoring mesh with respect to the phantom, and that position is different for reference, MacNCTPlan/NCTPlan, and BNCT_Rtpe/SERA calculations. Nevertheless, the linear interpolation between the voxels is unable to accurately model
the curvature of the reference flux profile, especially at the phantom entrance, where differences as large as 17% and 13% are observed for MacNCTPlan and NCTPlan, respectively. Accordingly, the largest differences for MacNCTPlan and NCTPlan occur close to the voxel edges at approximately integral depths in the phantom. On the downstream side of the thermal neutron flux peak, at depths greater than ~2.5 cm, the curvature of the reference flux profile is relatively low, so the linear interpolation performed by MacNCTPlan and NCTPlan produce improved agreement that is within ~4.5% and ~2% of the reference, respectively. However, the improved agreement at these depths uncovers a different “sawtooth” pattern in the percent difference profiles of MacNCTPlan and NCTPlan that indicates the presence of subtle interpolation errors in both TPSs. Although the pattern for MacNCTPlan is different from that of NCTPlan, both are ~1.5% from crest to trough. At the depth corresponding to the reference biologically weighted dose maximum ($d_{\text{max}}$), 1.9 cm, MacNCTPlan and NCTPlan differ from the reference thermal neutron flux by 4.2% and 3.8%, respectively.

In Figure 2.6, BNCT_Rtpe and SERA produce thermal neutron flux profiles very similar to each other, as expected, given the similarities in their transport codes and their identical neutron cross section data. Both BNCT_Rtpe and SERA overestimate the maximum thermal neutron flux at 2.0 cm depth by ~6% and flux along the downstream side of the peak from 1% to 5%. The interpolation error observed in both MacNCTPlan and NCTPlan in Figure 2.6 motivated calculation of more finely spaced flux data (at 0.1 mm rather than the 5 mm default intervals) from BNCT_Rtpe and SERA to compare with the reference. The resulting finely spaced SERA thermal neutron flux data are shown in Figure 2.7 along with the percent difference of that data from the reference MCNP5
calculations. The BNCT_Rtpe data are very similar to the SERA data and are omitted for clarity. The SERA data exhibits discontinuities in the thermal neutron flux (and percent difference) profile at integral depths in the phantom, which correspond to voxel edges. For instance, the difference reaches 6.5% at 2.0 mm depth and then suddenly drops to 3.4% at 2.01 mm depth. This discontinuity in the finely spaced line edit data indicates a problem with the SERA (and BNCT_Rtpe) interpolation algorithm. Moreover, when the SERA line edit data are compared to the uninterpolated voxel flux data in Figure 2.7, it is evident that the (interpolated) line edit data at the voxel centers do not coincide with the voxel values. This problem is generally masked by the use of coarser sampling intervals (the default is 5 mm) so that the discontinuity is not apparent. If the uninterpolated SERA coarse voxel data are read and interpolated using MATLAB’s cubic algorithm (BNCT_Rtpe and SERA employ a custom 3D cubic-like interpolation algorithm), the discontinuities at the voxel edges are eliminated as expected in Figure 2.7. Similarly, if the uninterpolated NCTPlan voxel data are read and linearly interpolated using MATLAB (MacNCTPlan and NCTPlan employ a custom 3D linear interpolation), the interpolation error in NCTPlan observed in Figure 2.6 and Figure 2.7 is corrected.

To further investigate the interpolation error in SERA (and BNCT_Rtpe), the SERA voxel data was interpolated at 0.1 mm intervals using several different methods in MATLAB and compared to uninterpolated voxel data as well as seraPlan line and point edits (at positions corresponding to voxel center points). The resulting comparison is shown in Figure 2.8 where the percent difference is calculated with respect to 3D cubic interpolation since it provides the best agreement with the reference MCNP5 calculations. The line edit flux data from seraPlan exhibit discontinuities at voxel edges
as large as 4%. The magnitude of these jumps depends on the curvature of the voxel data, with the largest occurring in regions of high curvature (e.g., the thermal neutron flux peak). Moreover, the point edit flux data, which are sampled at the voxel center points where the effect of interpolation should be to return the voxel-averaged value, match the seraPlan line edit data and exhibit disagreements of up to ~2% with the uninterpolated SERA voxel data. While 1D and 3D linear interpolation produce identical flux data, neither interpolation method is able to accurately model the curvature of the thermal neutron flux peak. Even 1D cubic interpolation results in differences as large as 2.5% in regions of high curvature. Nevertheless, when the interpolation error is eliminated by using MATLAB to interpolate the coarse voxel data, agreement with the reference calculations is improved, as shown in Figure 2.9. Due to the similarities between the BNCT_Rtpe and SERA data as well as between the MacNCTPlan and NCTPlan data, only data for SERA and NCTPlan are represented in Figure 2.9 for clarity. The characteristic patterns of percent difference for NCTPlan are no longer present, resulting in ~2% better agreement at a depth of 4.5 cm. Also, 3D cubic interpolation of the NCTPlan voxel data is better able to model the curvature of the reference flux profile, resulting in as much as a 3% improvement in agreement at integral depths over linear interpolation. The agreement for SERA at the thermal neutron flux maximum improves by ~3% using MATLAB’s 3D cubic interpolation, and discontinuities are eliminated. However, even when interpolation errors are corrected in Figure 2.9, SERA (and BNCT_Rtpe) still overestimate the reference thermal neutron flux at the peak and along the downstream side.
Disagreement in flux in the absence of geometric approximations indicates differences in transport calculations and therefore warrants closer examination of the SERA and MCNP5 neutron cross sections for H2O, shown in Figure 2.10. The MCNP5 S(α,β) thermal neutron scattering cross sections for hydrogen in light water are defined up to higher neutron energies than the corresponding data in SERA, resulting in an energy region (0.414 eV ≤ E_n ≤ 4.46 eV which is highlighted and expanded in Figure 2.10) where SERA and MCNP5 cross sections differ by up to 15%. Therefore, during SERA transport calculations in the large rectangular water phantom, neutrons in this energy range (16% of neutrons at the phantom entrance and 9% of neutrons at 2.0 cm depth) are subjected to cross sections that are as much as 15% lower than the corresponding MCNP5 cross sections, which in SERA (and BNCT_Rtpe) may contribute to a higher maximum thermal neutron flux and a more penetrating beam. Conversely, the large difference in cross sections at neutron energies below ~1 meV does not significantly affect the thermal neutron flux agreement since a very small percentage of neutrons are in that very low energy range (0.2% of neutrons at 2.0 cm depth). It should also be noted that the comparison of total neutron cross sections in Figure 2.10 is a rather simplistic representation of more complex data. Therefore, it is important not to oversimplify the explanation of the observed disagreement in thermal neutron flux since other factors, like differences in transport physics between rtt_MC, seraMC, and MCNP5, are also very likely responsible but difficult to evaluate.
Figure 2.6 Thermal neutron flux and percent difference (100\times[TPS−Ref]/Ref_{max}) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. SERA and BNCT_Rtpe data are calculated at (default) intervals of 5 mm. MCNP5 served as the reference for percent difference calculations.
Figure 2.7 Thermal neutron flux and percent difference ($100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_{\text{max}}}$) as a function of depth along the central beam axis in the large rectangular water phantom for different representations of the SERA and NCTPlan voxel data. The uninterpolated voxel data from SERA and NCTPlan were read and interpolated using MATLAB for comparison to the interpolated output of each TPS, as well as MCNP5, to illustrate the interpolation errors in both TPSs. SERA data (solid line) are evaluated at intervals of 5 mm. MCNP5 served as the reference for percent difference calculations.
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Figure 2.8  Thermal neutron flux and percent difference \((100 \times \text{[TPS–Ref]/Ref}_{\text{max}})\) as a function of depth along the central beam axis in the large rectangular water phantom for different representations of the SERA voxel data. The uninterpolated SERA voxel data were read and interpolated using MATLAB for comparison to the interpolated output of seraPlan to illustrate interpolation errors in the line and point edit data. The data produced using 3D cubic interpolation served as the reference for percent difference calculations since it produced the closest agreement to the reference calculations.
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Figure 2.9 Thermal neutron flux and percent difference (100×[TPS−Ref]/Ref\textsubscript{max}) as a function of depth along the central beam axis in the large rectangular water phantom for MATLAB interpolations of voxel data from each TPS. The uninterpolated voxel data from each TPS were read and interpolated using MATLAB to illustrate the agreement with MCNP5 when interpolation errors are eliminated. MCNP5 served as the reference for percent difference calculations.
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Figure 2.10 Total neutron cross sections for H$_2$O used by MCNP and SERA in transport calculations. Cross section data for both include the $S(\alpha,\beta)$ thermal neutron scattering treatment for hydrogen in light water. The energy range ($0.414 \, \text{eV} \leq E_n \leq 4.46 \, \text{eV}$) is highlighted and expanded to better illustrate the difference in cross sections. This energy range represents $\sim9\%$ of the neutrons at the thermal neutron flux peak (2.0 cm depth) in the large rectangular water phantom.
2.3.1.1.2 Boron Dose

Figure 2.11 shows the comparison of boron dose rate profiles for the 4 TPSs with the reference in the large rectangular water phantom for a $^{10}$B concentration of 15 $\mu$g/g. Given the dependence of the boron dose on the thermal neutron flux, it is not surprising that the comparison of boron dose rates exhibits many of the same features observed with the thermal neutron flux. The $\pm 9\%$ to 15\% differences for MacNCTPlan and NCTPlan at depths less than $\sim 2.5$ cm are again due to the inability of linear interpolation to model the curvature of the reference dose profile using dose data from a coarse scoring mesh. At depths greater than 2.5 cm, interpolation error results in characteristic “sawtooth” patterns in the percent difference profiles of MacNCTPlan and NCTPlan, underestimating the reference boron dose rates by less than 5\% and 2.5\%, respectively. This agreement is nearly identical to that observed in the comparison of thermal neutron flux, which is expected since identical boron kerma factor data are used. However, BNCT_Rtpe boron dose rates in Figure 2.11 are $\sim 1.5\%$ larger than the corresponding SERA values at most depths despite their nearly identical thermal neutron flux profiles. This observation is consistent with the differences in boron kerma data shown in Figure 2.12. Over the neutron energy range $4$ meV $\leq E_n \leq 0.25$ MeV, the mean differences between the multigroup BNCT_Rtpe (94 energy groups) and SERA (717 energy groups) boron kerma factors and the pointwise continuous reference boron kerma factors are $\pm 1.1\%$ and $\pm 2.5\%$, respectively, which explains the $\sim 1.5\%$ difference between the BNCT_Rtpe and SERA boron dose rates observed in Figure 2.11. However, the disagreement for BNCT_Rtpe and SERA at $d_{\text{max}}$, 10.5\% and 9.1\%, respectively, is larger than that predicted from the combination of differences in the calculated thermal neutron flux, and kerma factors, and the interpolation error. The worse agreement results from
both BNCT_Rtpe and SERA improperly scaling the boron, nitrogen, and hydrogen neutron kerma factors by the mass density of the edit mesh biological material at runtime. This was determined through numerical experiments with the two TPSs and through review of their source code. In calculating the edit mesh composition for BNCT_Rtpe and SERA, the density of ICRU adult brain ($\rho = 1.04 \text{ g/cm}^3$) is used to convert $1 \mu g / \text{g} \, ^{10}\text{B}, 2.2\%$ nitrogen, and $10.7\%$ hydrogen into the corresponding atomic densities in atoms/barn·cm as required by both TPSs. Since these edit mesh atomic densities are used by BNCT_Rtpe and SERA to directly scale the elemental boron, nitrogen, and hydrogen kerma data (in units of cGy·barn·g) without any consideration of the edit mesh material density* (which should divide energy per unit volume to yield dose), the resulting dose rates are improperly multiplied by the density of ICRU adult brain, $1.04 \text{ g/cm}^3$. Therefore, in addition to the $\sim 3\%$ overestimation of the reference maximum thermal neutron flux by BNCT_Rtpe and SERA and the $\sim 3\%$ interpolation error, a $4\%$ error is introduced by improperly scaling the boron kerma data, producing maximum boron dose rates $9$-$10\%$ larger than the reference.

To better illustrate the runtime scaling of INL kerma data, the nitrogen dose rates calculated by MCNP5 and SERA in the large rectangular water phantom were divided by the corresponding thermal neutron flux to compare the relative scale of the kerma factors actually used for dose calculations since the ration of nitrogen dose to thermal neutron flux should be relatively constant. An additional SERA simulation was performed in the large rectangular water phantom where the density of water was reduced by a factor of $4$ to approximate BNCT dose calculations for human lung, which have been investigated

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* This seems to be a result of improperly assuming that the mass density will always be $1.0 \text{ g/cm}^3$. 
using SERA.\textsuperscript{58} Accordingly, the SERA edit mesh compositions for \textsuperscript{10}B, nitrogen, and hydrogen in that simulation were specified for adult human lung with a density of 0.25 g/cm\textsuperscript{3}. The resulting ratios of nitrogen dose rate to thermal neutron flux for these three simulations are shown in Figure 2.13. When an edit mesh composition for brain is specified in SERA, the dose to flux ratio for SERA is larger than the corresponding MCNP5 ratio by a factor equal to the mass density of brain in g/cm\textsuperscript{3}, 1.04. Likewise, when an edit mesh composition for lung is specified in SERA, the SERA ratio is reduced by a factor of 4 confirming that the SERA nitrogen kerma factors had in fact been multiplied by the mass density of lung.

To better understand the influence that different boron kerma factors have on calculations of boron dose rates, especially in terms of continuous energy vs. multigroup, the multigroup BNCT\_Rtpe and SERA boron kerma factors from Figure 2.12 were multiplied by 1.04 and used in MCNP5 calculations of boron dose rate profiles in the large rectangular water phantom. When the resulting boron dose rate profiles are compared to BNCT\_Rtpe and SERA as shown in Figure 2.14, the differences (e.g., \textasciitilde7\% difference in maximum boron dose rates) are reduced to levels consistent with the agreement in thermal neutron flux. If the MCNP5 boron dose rate profiles calculated using BNCT\_Rtpe and SERA multigroup boron kerma factors are compared to the MCNP5 profiles calculated with reference pointwise continuous boron kerma factors, the differences that result (3.3\% for BNCT\_Rtpe kerma data and 1.3\% for SERA kerma data at 2.0 cm depth) are almost entirely due to differences in magnitude between the boron kerma data (\textasciitilde1.1\% for BNCT\_Rtpe and \textasciitilde2.5\% for SERA as shown in Figure 2.12) and the 4\% error resulting from improperly scaling the INL boron kerma data by mass.
density. Therefore, when simulating realistic (i.e., polyenergetic) beams with a broad neutron spectrum, any differences that are introduced by approximating continuous energy kerma data with multigroup kerma data are small compared to these other errors.
Figure 2.11  Boron dose rate for a $^{10}$B concentration of 15 $\mu$g/g and percent difference $(100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure 2.12 Boron neutron kerma factors used in the reference, BNCT_Rtpe, and SERA calculations of boron dose and the percent difference of the BNCT_Rtpe and SERA kerma data from the reference kerma data. The reference data are pointwise continuous while the BNCT_Rtpe and SERA kerma data have 94 and 717 energy groups, respectively.
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Figure 2.13  Ratio of nitrogen dose rate to thermal neutron flux as a function of depth in the large rectangular water phantom. For SERA, edit mesh atomic densities corresponding to brain ($\rho = 1.04$ g/cm$^3$) and lung ($\rho = 0.25$ g/cm$^3$) were specified in two separate simulations. When an edit mesh composition of lung was used in SERA, the density of water in the phantom was reduced to 0.25 g/cm$^3$ to approximate neutron transport through adult human lung. The ratios illustrate that SERA nitrogen (hydrogen and boron) kerma factors are scaled at runtime by the mass density of the edit mesh material.
Figure 2.14  Boron dose rate for a $^{10}$B concentration of 15 μg/g and percent difference $(100 \times \frac{[TPS - \text{Ref}]}{\text{Ref}_{\text{max}}})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. Multigroup boron neutron kerma factors from BNCT_Rtpe and SERA were used in MCNP5 calculations of boron dose rates, which served as the reference for BNCT_Rtpe and SERA percent difference calculations, respectively.
2.3.1.1.3 Thermal Neutron Dose

The reference MCNP5, MacNCTPlan, and NCTPlan thermal neutron dose rate profiles as well as BNCT_Rtpe and SERA nitrogen dose rate profiles in the large rectangular water phantom are compared in Figure 2.15. Not surprisingly, MacNCTPlan and NCTPlan exhibit similar agreement to that observed in the thermal neutron flux comparison in Figure 2.6. Linear interpolation between the elements of the coarse scoring mesh, centered at ½ integral depths in the phantom, is unable to accurately model the curvature of the reference dose profile which results in significant differences (−9% to 16%) at shallow depths. When the curvature of the reference profile decreases, agreement improves to within 5% for MacNCTPlan and NCTPlan, and characteristic patterns produced by interpolation error are observed. Nevertheless, NCTPlan generally produces better agreement than MacNCTPlan by 2-3%.

BNCT_Rtpe and SERA do not calculate the dose from thermal neutrons in the same manner as the reference calculations. Whereas the reference calculations, as well as MacNCTPlan and NCTPlan, use total brain neutron kerma factors (i.e., weighted sum of kerma from $^1$H, $^{14}$N, $^{12}$C, $^{16}$O, $^{31}$P, sulfur, and chlorine) and a definite energy cutoff ($E_n \leq 0.5$ eV) to define the dose from thermal neutrons, BNCT_Rtpe and SERA use multigroup nitrogen kerma factors (represented with 94 energy groups) to calculate the dose from the $^{14}$N(n,p)$^{14}$C reaction for all neutron energies. In Figure 2.15, BNCT_Rtpe and SERA produce nearly identical nitrogen dose rate profiles due to the similarity of their transport codes and identical nitrogen kerma factors. BNCT_Rtpe and SERA nitrogen dose rates overestimate the reference peak thermal neutron dose rate by ~10%, which is due to differences in thermal neutron flux calculations (refer to Figure 2.9), interpolation error
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(refer to Figure 2.7), and the improper scaling of nitrogen kerma factors by the mass density of the edit mesh (refer to Figure 2.13). A comparison of the INL multigroup nitrogen kerma factors to nitrogen kerma factors from ICRU Report 63\textsuperscript{59} indicates an average difference of only $\sim$1% as shown in Figure 2.16. When compared to total brain neutron kerma factors, as shown in Figure 2.17, the INL nitrogen kerma factors are on average 4% lower in the thermal neutron energy range since the total brain neutron kerma includes contributions from other elements other than nitrogen. In fact, $\sim$2.5% and $\sim$1% of the reference thermal neutron dose rate at 2.0 cm depth is from hydrogen and chlorine, respectively. However, the lack of an upper energy boundary to the BNCT\_Rtpe and SERA nitrogen dose tally allows an epithermal and fast neutron contribution to the nitrogen dose (e.g., 2.3% of the nitrogen dose at 2.0 cm depth is from neutrons above 0.5 eV) that helps compensate for the 4% difference in nitrogen and total brain neutron kerma factors. While this epithermal and fast neutron contribution to the nitrogen dose is properly accounted for in the thermal and fast neutron dose accounting scheme, it does not contribute to the reference thermal neutron dose in Figure 2.15, but it does contribute to the nitrogen dose in BNCT\_Rtpe and SERA. To further address the significance of using different kerma data, the multigroup INL nitrogen kerma factors (which were multiplied by 1.04 to simulate BNCT\_Rtpe and SERA’s runtime multiplication of kerma factors by the mass density of the edit mesh) as well as ICRU nitrogen kerma factors from Figure 2.16 were used in MCNP5 to calculate nitrogen dose rates in the large rectangular water phantom as shown in Figure 2.18. Using INL nitrogen kerma factors in MCNP5 produces a maximum nitrogen dose rate $\sim$6.8% lower than BNCT\_Rtpe and SERA (which is consistent with the $\sim$3% difference in thermal neutron flux and the $\sim$3%
interpolation error) and 4% higher than calculated with ICRU nitrogen kerma factors (which is consistent with the runtime multiplication of the INL kerma factors by the mass density of the edit mesh).
Figure 2.15 Thermal neutron (and nitrogen) dose rate and percent difference \((100\times[TPS-Ref]/Ref_{max})\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure 2.16  Comparison of BNCT_Rtpe and SERA multigroup (94 energy groups) nitrogen and hydrogen neutron kerma data to the corresponding pointwise continuous ICRU kerma data. The percent difference between the INL and ICRU kerma data was calculated with the ICRU kerma data as the reference. The INL hydrogen kerma data does not include the contribution from the recoil deuteron which leads to large differences in the thermal neutron energy range. The vertical dashed line represents the energy cutoff at 0.5 eV that is used to separate the thermal and fast neutron dose components in the reference MCNP5 calculations. No such energy binning is used in BNCT_Rtpe or SERA.
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Figure 2.17 Comparison of BNCT_Rtpe and SERA multigroup (94 energy groups) nitrogen and hydrogen neutron kerma data to pointwise continuous reference total brain neutron kerma data. The percent difference between the summed INL nitrogen and hydrogen kerma data and the total brain kerma data was calculated with the total brain kerma data as the reference. The vertical dashed line represents the energy cutoff at 0.5 eV that is used to separate the thermal and fast neutron dose components in the reference MCNP5 calculations. No such energy binning is used in BNCT_Rtpe or SERA.
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Figure 2.18 Nitrogen dose rate and percent difference (100×[TPS−Ref]/Ref\text{max}) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. Multigroup INL nitrogen neutron kerma factors were used in MCNP5 calculations of nitrogen dose rates, which served as the reference for percent difference calculations. Nitrogen dose rates calculated with ICRU 63 nitrogen kerma factors are included as a point of comparison.
2.3.1.1.4 Fast Neutron Dose

The reference MCNP5, MacNCTPlan, and NCTPlan fast neutron dose rates as well as BNCT_Rtpe and SERA hydrogen dose rates are shown as a function of depth in the large rectangular water phantom and compared in Figure 2.19. The nearly $\sim 7\%$ disagreement for MacNCTPlan and NCTPlan at the surface of the phantom is due to the inability of data linearly interpolated from the coarse voxel mesh to model the sudden change in the fast neutron dose rate. MacNCTPlan and NCTPlan deviate from the reference calculations by less than 3% and 1%, respectively, at $\frac{1}{2}$ integral depths (voxel center points). However, at depths in between, characteristic patterns of larger percent difference (up to 2.2%) are observed, especially for NCTPlan, and due to error in the interpolation algorithms of these TPSs.

BNCT_Rtpe and SERA do not calculate the dose from fast neutrons in the same manner as the reference MCNP5 calculations. BNCT_Rtpe and SERA use multigroup hydrogen kerma factors (represented with 94 energy groups) to calculate the dose from the $^1\text{H}(n,n')^1\text{H}$ proton recoil reaction for all neutron energies rather than to tally dose from neutrons above 0.5 eV using total brain neutron kerma factors. In Figure 2.19, BNCT_Rtpe and SERA hydrogen dose rates underestimate the reference fast neutron dose rate by 46% at the phantom entrance. Several factors contribute to this significant disagreement. In Figure 2.16, the comparison of INL and ICRU 63 hydrogen kerma factors show significant differences at neutron energies below $\sim 50$ eV because the INL hydrogen kerma factors do not include kerma from the recoil deuteron that results from neutron capture by hydrogen $[^1\text{H}(n,\gamma)^2\text{H}]$. In fact, INL hydrogen kerma factors drop to 0 at neutron energies below 0.414 eV. A separate MCNP5 simulation with both ICRU and
INL hydrogen kerma factors indicated that kerma from the recoil deuteron is responsible for 5.4% of the hydrogen dose at a depth of 1.0 cm. Therefore, the underestimation of the reference fast neutron dose rates by BNCT_Rtpe and SERA is at least partially due to incomplete INL hydrogen kerma factors. Another MCNP5 simulation also showed that ~13% of the reference fast neutron dose at 1.0 cm depth is from elements other than hydrogen (8% from $^{14}$N, 4% from $^{16}$O, and 1% from chlorine), so the hydrogen dose will naturally underestimate the fast neutron dose, especially when the significant thermal neutron contribution to the hydrogen dose (via the recoil deuteron) is not included. If kerma from the recoil deuteron is included in MCNP5 hydrogen dose calculations (with ICRU hydrogen kerma factors), the contribution of thermal neutrons below 0.5 eV to the hydrogen dose helps partially compensate for the ~13% of the fast neutron dose that is from elements other than hydrogen to result in a hydrogen dose at 1.0 cm depth that underestimates the fast neutron dose by only ~5%. Nevertheless, the largest contribution to the significant underestimation of the reference fast neutron dose rates in Figure 2.19 results from an energy cutoff for the BNCT_Rtpe and SERA fast neutron source biasing run mode (run mode F) that is set too high. After completing the normal neutron transport calculations (run mode N), the hydrogen dose rates are cleared and reset to zero in preparation for the biased fast neutron calculations since the codes do not permit hydrogen dose data from the two run modes to be combined. When the default biased fast neutron run mode is used, neutrons greater than 9.12 keV are sampled from the source (with appropriately adjusted weights) and tracked in order to tally hydrogen dose and fast neutron flux until their energy falls below 9.12 keV, at which point tracking stops. Therefore, only those neutrons with energy greater than 9.12 keV contribute to the
BNCT_Rtpe and SERA hydrogen dose rates, but a separate MCNP5 simulation using the multigroup INL hydrogen kerma factors indicated that ~33% of the hydrogen dose at 1.0 cm depth is from neutrons below 9.12 keV. Thus, the default biasing energy cutoff is set too high and therefore contributes significantly to the drastic underestimation of reference fast neutron dose rates by hydrogen dose rates. If BNCT_Rtpe and SERA simulations with the biased fast neutron mode disabled are compared to MCNP5 calculations using INL multigroup and ICRU 63 pointwise continuous hydrogen kerma factors, the agreement improves significantly as shown in Figure 2.20. It is interesting to note that in Figure 2.20 the contribution of the recoil deuteron to the ICRU hydrogen kerma factors helps to produce higher hydrogen dose rates at depths beyond 6 mm despite the INL hydrogen kerma data having been increased by 4% to model the runtime scaling by the edit mesh mass density in BNCT_Rtpe and SERA. Also, the presence of noticeable statistical fluctuations in the hydrogen dose rate (and percent difference) profiles of BNCT_Rtpe and SERA in Figure 2.20 despite having simulated $3.3\times10^8$ and $9.9\times10^7$ particles, respectively, helps illustrate the importance of the biased fast neutron run mode. However, the default setting is not appropriate for an epithermal neutron beam and results in a significant underestimation of the hydrogen dose rate, so it must be adjusted to a value that is appropriate for the neutron source.

In attempting to compensate for poor convergence of the fast neutron flux and “Ultra” dose (typically from carbon and oxygen) in SERA, a subtle error was introduced in the interpolation code of seraPlan that affects only interpolated fast neutron flux and “Ultra” dose data. To illustrate this error, fast neutron flux data from seraPlan line (at 0.1

* SERA will crash when transitioning from one run mode to another (e.g., N to G) if the number of particles simulated exceeds 8 digits or 99,999,999.
mm intervals) and point edits are shown in Figure 2.21 and compared to data interpolated from the same coarse voxel data using MATLAB. The interpolation error in seraPlan results in a stepped fast neutron flux profile that produces differences as large as 15% when compared to 3D cubic interpolation from MATLAB; similar results are observed for interpolated “Ultra” doses. It is important to understand that this interpolation error is different from that shown in Figure 2.7 (which affects all interpolated data in both BNCT_Rtpe and SERA) and is only present in interpolated fast neutron flux and “Ultra” dose data produced by seraPlan.

2.3.1.1.5 Total Neutron Dose

Approximately 98% of the reference total neutron dose (i.e., thermal + fast neutron dose) at 2.0 cm depth in the large rectangular water phantom is from neutron interactions with nitrogen (77%) and hydrogen (21%), and the rest is mainly from interactions with oxygen (0.89%), chlorine (0.84%), and carbon (0.27%). Thus, a comparison of the summed nitrogen and hydrogen dose from BNCT_Rtpe and SERA to the reference total neutron dose should almost eliminate any disagreement that results from differences in dose definitions; one should expect the summed hydrogen and nitrogen doses to underestimate the reference total neutron dose by only 2% at 2.0 cm depth. The comparison of summed INL nitrogen and hydrogen kerma factors to reference total brain neutron kerma factors in Figure 2.17 predicts a larger underestimation since the INL hydrogen kerma factors lack the contribution from the recoil deuteron which results in an average difference in kerma of $-4.3\%$ for $4.1\,\text{meV} \leq E_n \leq 2\,\text{MeV}$. However, the INL nitrogen and hydrogen kerma factors in Figure 2.17 are multiplied at runtime by the mass density of the edit mesh material in $\text{g/cm}^3$, 1.04. Therefore, if differences in
kerma data were the only source of disagreement, the summed nitrogen and hydrogen dose from BNCT_Rtpe and SERA would underestimate the reference total neutron dose by −0.3%. When other sources of disagreement between BNCT_Rtpe, SERA, and the reference are considered, such as differences in thermal neutron flux (~3%) and interpolation error (~3%), the predicted percent difference at 2.0 cm depth increases to 5.7%. This predicted disagreement is actually quite close to the observed disagreement in Figure 2.22 where the summed nitrogen and hydrogen dose from BNCT_Rtpe and SERA overestimate the reference total neutron dose at 2.0 cm depth by 5.2% and 5.5%, respectively. If SERA “Ultra” dose (from carbon and oxygen) is summed with the nitrogen and hydrogen dose, the disagreement between SERA and the reference increases from 5.5% to 6.5%, which is consistent with the observation that neutron interactions with those elements included in the “Ultra” dose are responsible for ~1% of the total neutron dose. Thus, although comparing BNCT_Rtpe and SERA nitrogen + hydrogen dose to the reference thermal + fast neutron dose avoids differences in dose definition, other sources of disagreement persist. Meanwhile, MacNCTPlan and NCTPlan produce agreement in total neutron dose rate, −4.3% and −2.9% at 2.0 cm depth, respectively, that is simply a combination of the agreement in thermal and fast neutrons dose rate because both TPSs defines thermal and fast neutron dose in a manner identical to the reference calculations. For instance, the difference for NCTPlan is a combination of the 1.8% overestimation of the fast neutron dose rate in Figure 2.19 and the −4.8% underestimation of the thermal neutron dose rate in Figure 2.15.
Figure 2.19 Fast neutron (and hydrogen) dose rate and percent difference $(100 \times [\text{TPS}_{\text{Ref}} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Hydrogen dose rate and percent difference (100×[TPS−Ref]/Ref_{max}) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. Multigroup INL hydrogen neutron kerma factors were used in MCNP5 calculations of hydrogen dose rates, which served as the reference for percent difference calculations. The fast neutron source biasing run mode was not used for BNCT_Rtpe or SERA (i.e., run modes “NGD” were used). Hydrogen dose rates calculated with ICRU 63 hydrogen kerma factors are included as a point of comparison.
Figure 2.21  Fast neutron flux and percent difference \(100 \times \frac{[\text{TPS} - \text{Ref}]}{\text{Ref}_{\text{max}}}\) as a function of depth along the central beam axis in the large rectangular water phantom for different representations of the SERA voxel data. The uninterpolated SERA voxel data were read and interpolated using MATLAB for comparison to the interpolated output of seraPlan to illustrate interpolation errors in the line and point edit data. The data produced using 3D cubic interpolation served as the reference for percent difference calculations since it produced the closest agreement to MCNP5.
Figure 2.22 Total neutron dose rate (thermal + fast and hydrogen + nitrogen) and percent difference \((100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
2.3.1.1.6 Induced Photon Dose

Figure 2.23 compares induced photon dose rate profiles from each TPS to the reference in the large rectangular water phantom. Since induced photons are produced by the interactions of thermal neutrons, it is not surprising that the differences for MacNCTPlan and NCTPlan induced photon dose rates are similar to those observed for the thermal neutron flux in Figure 2.6. However, the comparison of thermal neutron flux produced worse agreement at shallow depths. For instance, at a depth of 8 mm, the difference in induced photon dose rate for MacNCTPlan is $-2.3\%$ while there is a $-6.6\%$ difference in thermal neutron flux at the same depth. Similarly, for NCTPlan, the difference in induced photon dose rate is $-4.1\%$, and the difference in thermal neutron flux at that depth is $-9.1\%$. This improved agreement at shallow depths can be attributed to the different shapes and positions of the induced photon dose rate and thermal neutron flux peaks. The linear interpolation employed by MacNCTPlan and NCTPlan is better able to estimate dose rates along the upstream edge of the induced photon dose rate peak since it broader and occurs 4 mm deeper in the phantom than the thermal neutron flux peak. On the downstream edge of the peak at depths greater than 2.4 cm, NCTPlan produces better agreement than MacNCTPlan by $-2\%$, and both TPSs exhibit their characteristic interpolation error.

In Figure 2.23, the differences between BNCT_Rtpe and SERA induced photon dose rate profiles (e.g., 8% at 2.5 cm depth) are not consistent with the similarities expected and largely observed for other dose components with these two TPSs. The differences in induced photon dose rates arise from rather significant differences in photon kerma factors; comparing BNCT_Rtpe and SERA photon kerma factors with
those used in the reference calculations, as shown in Figure 2.24, demonstrates large differences that reach a maximum of 136% difference at $E_\gamma=60$ keV. BNCT_Rtpe also differs from SERA in the number of photon kerma and cross section energy groups (70 for BNCT_Rtpe vs. 86 for SERA) and in the assignment of a point kerma value of $9.58 \times 10^{-12}$ Gy cm$^2$ to 2.2 MeV photons (from the $^1$H(n,$\gamma$)$_2^2$H reaction) only which is 4.2% larger than the corresponding SERA multigroup kerma and 8.1% larger than the reference value calculated from NIST data. However, since a separate MCNP5 simulation indicated that 97% of the maximum induced photon dose rate is from photons above 1 MeV, the differences for BNCT_Rtpe induced photon dose rates (~11% at 2.5 cm depth) are not as large as might be expected given the differences in photon kerma factors shown in Figure 2.24. Therefore, while very significant differences in photon kerma are indeed present for BNCT_Rtpe, photons in the energy range where the largest differences occur do not significantly contribute to the induced photon dose rate. For SERA, better agreement with the reference photon kerma factors (3.7% at 2.2 MeV) translates into better agreement in induced photon dose rates (3.6% at 2.5 cm depth). To further illustrate that the disagreement in induced photon dose rates is mainly attributable to differences in photon kerma factors, BNCT_Rtpe and SERA multigroup photon kerma factors were used in MCNP5 simulations to calculate induced photon dose rate profiles in the large rectangular water phantom, and the resulting dose data are compared to BNCT_Rtpe and SERA in Figure 2.25. When differences in photon kerma are eliminated, the agreement of BNCT_Rtpe and SERA with reference MCNP5 calculations is within 1.5%. Nevertheless, it is important to point out that BNCT_Rtpe and SERA treat induced photons as isotropic volume sources calculated from photon production
tallies in each $1\text{ cm}^3$ volume of the tally mesh calculated during the normal neutron run mode (run mode N). As a result, the position of induced photons within each tally voxel is not preserved as in MCNP5 transport calculations (where neutron-induced photons are stored in a bank for later transport), and induced photons will only be sampled in those regions of the geometry covered by the $30\times30\times30\text{ cm}^3$ tally mesh. The limitation of the tally mesh size and photon production did not appear to introduce any significant differences into the induced photon dose calculations in the large rectangular water phantom since the tally mesh sufficiently covered the region of interest along the central beam axis. Nevertheless, it is important to be aware of this issue since it may cause variable photon production in the collimator in more realistic clinical situations; i.e., coverage of the collimator by the tally mesh can affect photon production there.

2.3.1.1.7 Incident Photon Dose

Figure 2.26 compares incident photon dose rate profiles from each TPS to the reference in the large rectangular water phantom. MacNCTPlan and NCTPlan produce excellent agreement to within 1.5% and 1.0% of the reference, respectively. For the reference dose profile, the curvature that is characteristic of the other reference dose component profiles is not present, so linear interpolation between the coarse voxels is better able to model the reference dose rate profile. The voxel doses for MacNCTPlan and NCTPlan are not statistically different from the reference incident photon doses, but interpolation error causes the interpolated dose data to deviate from the voxel data, especially at depth, and produce the observed disagreement. If MATLAB is used to linearly interpolate the voxel doses, agreement improves to within 0.4% at all depths. BNCT_Rtpe and SERA produce different induced photon dose rates profiles mainly due
to the differences in photon kerma data, shown in Figure 2.24. For 2.0 MeV photons, the BNCT_Rtpe photon kerma factor is 5% larger than the reference value while the SERA photon kerma factor is 1.2% smaller which helps to explain the relative magnitude of their dose rate profiles with respect to the reference. If differences due to photon kerma factors are removed by using multigroup photon kerma factors from BNCT_Rtpe and SERA in MCNP5 calculations of incident photon dose rates in the large rectangular water phantom, the percent differences for both TPSs shift to roughly −2% for all depths, as shown in Figure 2.27, perhaps indicating the presence of a systematic difference. Upon further investigation, a subtle error in the BNCT_Rtpe and SERA photon dose calculations was found that resulted in the incident photon dose rates being too low. However, the error in the incident photon dose rates can be predicted by

$$\frac{D_{\text{corr}}}{D_{\text{orig}}} = \frac{\text{gam}_\text{ratio} + \text{gp}_\text{tot}}{\text{gam}_\text{ratio} + \text{gp}_\text{tot} - (\text{gam}_\text{ratio} \times \text{gp}_\text{tot})}$$

(2.1)

where \(\text{gam}_\text{ratio}\) (\(\gamma/\text{cm}^2\text{s}\)) is the BNCT_Rtpe or SERA incident photon yield \((\gamma/\text{cm}^2\text{s})\) divided by the total source particle yield \((n+\gamma/\text{cm}^2\text{s})\) and \(\text{gp}_\text{tot}\) (\(\gamma/\text{cm}^2\text{s}\)) is the number of induced photons per source neutron. Both \(\text{gam}_\text{ratio}\) and \(\text{gp}_\text{tot}\) are reported in BNCT_Rtpe and SERA output files. Since Eq. 2.1 will always evaluate to a value that is greater than 1, the original uncorrected incident photon dose rates \(D_{\text{orig}}\) will always be smaller than the corresponding corrected values \(D_{\text{corr}}\). When applied to the BNCT_Rtpe and SERA calculations in the large rectangular water phantom with the generic epithermal neutron and monoenergetic 2 MeV incident photon beams \((\text{gam}_\text{ratio}=0.0196, \text{gp}_\text{tot}=0.4188)\), Eq. 2.1 evaluates to 1.019. This indicates that the BNCT_Rtpe and SERA incident photon dose rates in Figure 2.26 and Figure 2.27...
should be scaled up by 1.019 ($D_{\text{corr}} = 1.019 \times D_{\text{orig}}$) to correct for the error. This corrective scaling compensates for the roughly constant $-2\%$ difference in Figure 2.27 to produce very good agreement with the incident photon dose rates calculated with MCNP5 using BNCT_Rtpe and SERA photon kerma factors. A closer examination revealed that the error also affects the induced photon dose as predicted by

$$\frac{D_{\text{corr}}}{D_{\text{orig}}} = 1 - \frac{\text{gam}_\text{ratio}^2}{\text{gam}_\text{ratio} + \text{gp}_\text{tot} - (\text{gam}_\text{ratio} \times \text{gp}_\text{tot})}$$  \hspace{1cm} (2.2)

This equation will always evaluate to less than unity indicating that the original uncorrected induced photon dose rates ($D_{\text{orig}}$) will always be larger than the corrected values ($D_{\text{corr}}$). However, for the generic epithermal neutron and monoenergetic 2 MeV incident photon beams, Eq. 2.2 indicates that $D_{\text{corr}} = 0.9991 \times D_{\text{orig}}$, so the error in induced photon dose is not actually significant. Although the errors described by Eqs. 2.1 and 2.2 will affect the total photon dose, they counteract each other to result in a very small net difference. For instance, when the incident photon dose is $\sim 10\%$ of the induced photon dose, the error in the total photon dose is less than 0.1\%, and is therefore neither noticeable nor significant. Even if the incident photon yield is increased by a factor of 5 to produce an incident photon dose that is $\sim 50\%$ of the induced photon dose, the error in the total is still only approximately $-1.3\%$. 
Figure 2.23 Induced photon dose rate and percent difference (100×[TPS–Ref]/Ref_{max}) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
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Photon kerma factors used in the reference, BNCT_Rtpe, and SERA calculations of induced and incident photon dose and the percent difference of the BNCT_Rtpe and SERA kerma data from the reference kerma data. The reference data are pointwise continuous while the BNCT_Rtpe and SERA kerma data have 70 and 86 energy groups, respectively.
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Figure 2.25 Induced photon dose rate and percent difference \((100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_\text{max}})\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. Multigroup photon kerma factors from BNCT_Rtpe and SERA were used in MCNP5 calculations of induced photon dose rates, which served as the reference for BNCT_Rtpe and SERA percent difference calculations, respectively.
Figure 2.26  Incident photon dose rate and percent difference \((100\times[TPS-\text{Ref}]/\text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure 2.27  Incident photon dose rate and percent difference \((100\times[TPS-\text{Ref}]/\text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. Multigroup photon kerma factors from BNCT\_Rtpe and SERA were used in MCNP5 calculations of incident photon dose rates, which served as the reference for BNCT\_Rtpe and SERA percent difference calculations, respectively. The \(\pm 2\%\) difference reflects a subtle normalization error in BNCT\_Rtpe and SERA incident photon dose rates.
2.3.1.1.8 Total Biologically Weighted Dose

Total biologically weighted brain dose rate profiles from each TPS are compared to the reference in the large rectangular water phantom in Figure 2.28. MacNCTPlan and NCTPlan underestimate the reference maximum at 1.8 cm depth by $-3.3\%$ and $-3.7\%$, respectively, which is mainly due to the inability of the linearly interpolated dose data to match the curvature of the reference dose data at the dose peak. Better agreement occurs at integral depths in the phantom which correspond to the geometric centers of voxels from the coarse scoring mesh, but interpolation error and larger tally volumes produce differences even at those depths as large as $-1.8\%$. The largest differences occur at the phantom entrance where MacNCTPlan and NCTPlan overestimate the reference by 11$\%$ and 8$\%$, respectively. BNCT_Rtpe and SERA overestimate the reference maximum weighted dose rate by 8.4$\%$ and 5.9$\%$, respectively. This disagreement is a rather complex combination of disagreement resulting mainly from differences in calculated thermal neutron flux, interpolation error, the improper multiplication of the neutron and boron kerma factors by the mass density of the edit mesh, and differences in photon kerma factors. The better agreement observed for SERA relative to BNCT_Rtpe is mainly a result of more accurate photon kerma factors and the resulting better agreement in induced photon dose rate, which contributes 23$\%$ of the maximum weighted dose rate.

During an intercomparison such as this, it is important to not only report the magnitude of the disagreement but also to understand the causes. Determining the source(s) of disagreement observed in the large rectangular water phantom between MacNCTPlan/NCTPlan and the reference is relatively simple because differences in
kerma factors, cross section data, and Monte Carlo transport calculations* are avoided as are geometric approximations which limits the possibilities and simplifies the explanation. Conversely, several factors contribute to the disagreement between BNCT_Rtpe/SERA and the reference calculations, making it more difficult to unfold and explain. The disagreement in each dose component is attributable to some combination of the following: differences in calculated neutron or photon flux, interpolation error, differences in kerma factors, improper runtime multiplication of neutron and boron kerma factors by the mass density of the edit mesh material, differences in dose definition, a biasing and cutoff energy for the fast neutron source biasing run mode that is too high, and the photon normalization error. The contributions of these factors to the total disagreement observed for BNCT_Rtpe and SERA in the large rectangular water phantom are shown in Table 2.1 and Table 2.2, respectively.

Some additional explanation is required as to how the different factors were assessed. A depth of 2.0 cm was chosen as the evaluation point partially because it is approximately the location of the total weighted dose maximum and partially to exclude the disagreement at the phantom entrance due to differences in tally volumes between the TPSs and the reference (1 cm$^3$ vs. 0.1 cm$^3$). Differences in thermal neutron (defined by the INL planning systems as $E_n \leq 0.414$ eV), fast neutron ($E_n > 9.12$ eV), induced photon, and incident photon flux were calculated by comparing flux data interpolated by MATLAB (to eliminate the interpolation error) from coarse BNCT_Rtpe and SERA voxel data to corresponding MCNP5 data. To compute photon flux, patched versions of both rtt_MC and seraMC with kerma factors set to unity had to be used since neither

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* Differences between MCNP4B, used with MacNCTPlan and NCTPlan, and MCNP5 v. 1.40 are very small.
calculates photon flux by default. The interpolation error is not constant for all dose components. Instead, it depends upon the gradient of the particular dose component at the evaluation point and is therefore larger for peaked profiles (e.g., boron dose) than for dose profiles exhibiting little curvature (e.g., incident photon dose). Since the influence of different kerma factors depends on the spectrum (and hence depth), the values listed in Table 2.1 and Table 2.2 are differences in dose at 2.0 cm depth that result from comparing MCNP5 calculations with multigroup INL kerma data to similar calculations with reference (boron and photon) or ICRU (hydrogen and nitrogen) pointwise continuous kerma data. For instance, the MCNP5 dose rate at 2.0 cm depth from INL hydrogen kerma factors was 9.2% smaller than calculated with ICRU hydrogen kerma factors, which is mainly because the INL hydrogen kerma factors do not include the contribution from the recoil deuteron, so −9.2% is listed as the difference in kerma factors for the fast neutron dose component. Kerma scaling refers to the improper runtime multiplication of BNCT_Rtpe and SERA boron and neutron kerma data by the mass density of the edit mesh material, so using edit mesh densities for ICRU adult brain results in a 4% increase in neutron and boron dose rates. To quantify the disagreement due solely to differences in dose definitions, MCNP5 calculations of nitrogen and hydrogen dose using ICRU nitrogen and hydrogen kerma factors with no energy boundaries were compared to MCNP5 calculations of thermal and fast neutron dose with total brain neutron kerma factors and an energy boundary at 0.5 eV (distinguishing thermal and fast neutron dose). The 4.7% underestimation of the fast neutron dose by the hydrogen dose is larger than the 1.3% underestimation of the thermal neutron dose by nitrogen dose because nitrogen represents a larger percentage of the thermal neutron dose
(96.5%) that hydrogen dose does of the fast neutron dose (87%). MCNP5 was also employed to estimate the percentage of the hydrogen dose from neutrons below the default energy cutoff (9.12 keV) for the BNCT_Rtpe and SERA fast neutron source biasing run mode. The resulting 21.7% indicates that using the default fast neutron source biasing run mode is the single largest contributor to the underestimation of the reference fast neutron dose rate by BNCT_Rtpe and SERA. The disagreement due to the photon normalization error was calculated using Eqs. 2.1 and 2.2 and is specific to the neutron and photon source as well as the simulated geometry. The differences predicted by combining the independent sources of disagreement (sum of differences) for each dose component agree well with the observed values (actual differences), differing by at most 0.8% for BNCT_Rtpe and 1.5% for SERA. While many of the specific values listed in Table 2.1 and Table 2.2 are likely unique to the simulated source and geometry, the more general process of identifying the various sources of the observed disagreement should apply to any dosimetric intercomparison involving BNCT_Rtpe or SERA.
Figure 2.28  Total biologically weighted brain dose rate and percent difference \((100 \times [TPS - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Table 2.1  Percent differences between BNCT_Rtpe and reference MCNP5 dose rates at 2.0 cm depth along the central beam axis in the large rectangular water phantom. The differences for each dose component are resolved into contributing components, and the product of these components is shown for comparison to the actual differences. BNCT_Rtpe does not calculate thermal and fast neutron dose components in the same manner as the reference MCNP5 calculations but instead calculates the dose from neutron interactions with nitrogen and hydrogen thus leading to differences in “Dose Definition”. “Flux” represents differences in thermal neutron flux (for boron and thermal neutron dose), fast neutron flux (for fast neutron dose), and photon flux (for induced and incident photon dose). BNCT_Rtpe overestimates the reference total biologically weighted brain and tumor doses by 8.4% and 10.1%, respectively.

<table>
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<tr>
<th>Source of Disagreement</th>
<th>Dose Components</th>
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<tr>
<td></td>
<td>Boron</td>
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<tr>
<td>Flux</td>
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<td>Interpolation Error</td>
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<tr>
<td>Kerma Factors</td>
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<td>Kerma Scaling</td>
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<tr>
<td>Dose Definition</td>
<td>----</td>
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<tr>
<td>Fast Neutron Src. Biasing</td>
<td>----</td>
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<tr>
<td>Normalization Error</td>
<td>----</td>
</tr>
<tr>
<td>Sum of Differences</td>
<td>9.7%</td>
</tr>
<tr>
<td>Actual Differences</td>
<td>10.5%</td>
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Table 2.2 Percent differences between SERA and reference MCNP5 dose rates at 2.0 cm depth along the central beam axis in the large rectangular water phantom. The differences for each dose component are resolved into contributing components, and the product of these components is shown for comparison to the actual differences. SERA does not calculate thermal and fast neutron dose components in the same manner as the reference MCNP5 calculations but instead calculates the dose from neutron interactions with nitrogen and hydrogen thus leading to differences in “Dose Definition”. “Flux” represents differences in thermal neutron flux (for boron and thermal neutron dose), fast neutron flux (for fast neutron dose), and photon flux (for induced and incident photon dose). SERA overestimates the reference total biologically weighted brain and tumor doses by 5.9% and 8.5%, respectively.

<table>
<thead>
<tr>
<th>Source of Disagreement</th>
<th>Dose Components</th>
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<tbody>
<tr>
<td></td>
<td>Boron</td>
</tr>
<tr>
<td>Flux</td>
<td>3.1%</td>
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<tr>
<td>Actual Differences</td>
<td>9.1%</td>
</tr>
</tbody>
</table>
2.3.1.2 Ellipsoidal Head Phantom

The features observed during the comparison of depth-dose data in the large rectangular water phantom do not arise from approximations in the geometric representations of the phantom, so they are present in the comparison in the head phantom as well. Therefore, an in-depth discussion of the same features will not be repeated. Instead, the main focus in the head phantom is to develop a better understanding of how geometric approximations affect the accuracy of dose calculations and to compare the multi-dimensional dose data (i.e., isodose contours and dose-volume histograms) that is used in clinical treatment planning. The simplest way to identify the effect of the geometric approximations introduced by each TPS is to compare agreement in the presence of those approximations, as in the head phantom, to agreement in the absence of them, as in the large rectangular water phantom. Axial sections through the BNCT_Rtpe NURBS model, SERA univel model, and MacNCTPlan/NCTPlan mixed-material voxel models of the ellipsoidal head phantom are shown in Figure 2.29. Each TPS represents the ellipsoidal head phantom in a manner that is clearly distinct from the others. Even the mixed-material voxel models produced by MacNCTPlan and NCTPlan are different from each other in that different mixed materials are modeled in 192 voxels or 5.8% of the total number of non-air voxels. NCTPlan’s improved voxelization algorithm result in a more accurate and symmetrical voxel model of the head phantom than the asymmetrical model produced by MacNCTPlan.38
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Figure 2.29  Axial sections through the BNCT_Rtpe NURBS model, SERA univel model, MacNCTPlan and NCTPlan mixed-material voxel models of the ellipsoidal head phantom used to simulate BNCT treatment of a brain tumor.
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2.3.1.2.1 Thermal Neutron Flux

Figure 2.30 shows the thermal neutron flux calculated by MCNP5, BNCT_Rtpe, SERA, MacNCTPlan, and NCTPlan as well as the difference of each TPS from the reference MCNP5 calculations as a function of depth along the central beam axis in the ellipsoidal head phantom. The largest differences for MacNCTPlan (25%) and NCTPlan (10%) occur at the phantom entrance where data linearly interpolated from the coarse scoring mesh are unable to match the sharp increase in the reference thermal neutron flux profile. The agreement improves at depths beyond the phantom entrance, but MacNCTPlan and NCTPlan still underestimate the maximum reference thermal neutron flux (at a depth of 2.1 cm) by $-5.1\%$ and $-5.4\%$, respectively. Part of the disagreement at all depths in the head phantom is due to interpolation error in both TPSs. If the coarse voxel data from MacNCTPlan and NCTPlan are linearly interpolated with MATLAB to eliminate interpolation error, agreement improves for both MacNCTPlan (e.g., 10% to 2%) and NCTPlan (e.g., $-2.2\%$ to $0.1\%$) at 1.0 cm depth. Also, as observed in the large rectangular water phantom, averaging over a larger tally volume contributes to the underestimation of the maximum reference thermal neutron flux by MacNCTPlan and NCTPlan. If the reference thermal neutron flux is averaged over a tally volume equivalent to that used by MacNCTPlan and NCTPlan ($1\ cm^3$), a 1% decrease in the reported maximum reference thermal neutron flux results and the agreement with MacNCTPlan and NCTPlan improves slightly. Nevertheless, for both TPSs, the best agreement with the reference occurs at depths corresponding to voxel center points. However, the differences at those depths are ~2-3 times larger than observed in the rectangular water phantom due to the presence of geometric approximations. For
instance, on the deep side of the thermal neutron flux peak at a depth of 3.0 cm, MacNCTPlan and NCTPlan underestimate the reference thermal neutron flux in the head phantom by −8.9% and −6.7%, respectively, whereas in the large rectangular water phantom the corresponding percent differences are −4.5% and −2%.

A specific geometric approximation present in the voxel models of MacNCTPlan and NCTPlan is due to the limitation of 4 primary materials. This limitation causes MacNCTPlan and NCTPlan to model the head phantom’s skin as brain, which has both a lower density (1.09 g/cm³ vs. 1.04 g/cm³) and $^{10}$B concentration (22.5 μg/g vs. 15.0 μg/g) than skin. A separate simulation with MCNP5 indicated that modeling the skin as brain produces a 1.3% increase in the thermal neutron flux at 3 mm depth and a 0.6% increase in the maximum thermal neutron flux. Looking along the central beam axis in the head phantom provides an example of other geometric approximations introduced in the voxelization process which are also partially responsible for the disagreement in Figure 2.30. The central axis of the beam line intersects the analytical model of the head phantom at x=7.25 cm and travels through ~5 mm of skin (ρ=1.09 g/cm³) and ~6 mm of bone (ρ=1.61 g/cm³) before entering the brain. However, in the MacNCTPlan and NCTPlan voxel models of the head phantom, the beam line enters a mixture of tissue (brain) and bone (60% tissue, 40% bone, ρ=1.268 g/cm³) upon crossing the voxel edge at x=7.5 cm (0.25 cm earlier) and travels 2 cm through that mixture before entering brain. Therefore, in the voxel models, neutrons reaching the phantom surface have already been transported through a non-air mixture which increases neutron scattering and thermalization beyond that of the analytical model. So, agreement with the analytical model will depend to some extent upon the radiological depth of the analytic phantom
surface, defined as $\rho x$, where $x$ is the distance neutrons must travel through a non-air mixture before reaching the phantom surface and $\rho$ is the density of that mixture. Better agreement is expected as the radiological depth of the analytic phantom surface approaches zero in the voxel model. If the average radiological depth of the phantom surface is calculated in a $6\times6$ cm$^2$ region about the central beam axis for the MacNCTPlan and NCTPlan voxels models of the head phantom, the MacNCTPlan model is $\sim20\%$ larger, which is due to differences in voxelization algorithms between the two TPSs and is at least partially responsible for the worse agreement between MacNCTPlan and the reference calculations. Also, the observed shift in MacNCTPlan’s and NCTPlan’s thermal neutron flux peaks (most noticeable on the deep side) is estimated, at a thermal neutron flux of $2.0\times10^{10}$ n/cm$^2$s, to be 5.2 mm and 3.8 mm, respectively. These shifts are similar to the corresponding average radiological depths calculated (in a $6\times6$ cm$^2$ area about the central beam axis) for the voxel models of MacNCTPlan (4.5 mm) and NCTPlan (3.9 mm).

To further investigate these observations, different NCTPlan mixed-material voxel models of the head phantom were created with NCTPlan by shifting the phantom image data in 1 mm steps along its minor axis, which is parallel to the ipsilateral beam line. Axial sections through the resulting voxel models are shown in Figure 2.31, and the corresponding uninterpolated thermal neutron flux voxel data for a representative subset of those models are shown in Figure 2.32 where each is compared to the reference calculations. The uninterpolated voxel data are shown to prevent the interpolation error in NCTPlan from obscuring the comparison. The voxel model that minimizes the radiological depth of the analytic phantom surface (20% smaller than the next closest
model) also produces the best agreement with the reference calculations in Figure 2.32 (e.g., 0.69% at 1.5 cm depth). In other words, shifting the head phantom image data by 8 mm better aligns the phantom surface with the upstream edges of the first non-air voxels encountered by beam neutrons to result in improved agreement with the analytical model. The range of agreement displayed in Figure 2.32 illustrates the influence that geometric approximations can have on the accuracy of treatment planning calculations and therefore underscores the importance of using a model with smaller voxels to help minimize that influence. However, assigning the volume-averaged flux or dose to the voxel’s center-of-mass rather than to its geometric center for interpolation has been proposed as a means to produce better agreement in data interpolated at or near the phantom surface.60 The interpolated MacNCTPlan and NCTPlan thermal neutron flux data shown in Figure 2.30 suggests that such a change would produce better agreement because the linear interpolation between the 1 cm⁳ tally volumes is unable to match the sharp increase in the reference thermal neutron flux at the phantom surface.

In Figure 2.30, geometric approximations appear to have much less of an adverse effect on the agreement between BNCT_Rtpe/SERA and the reference due to the modeling techniques those TPSs employ. The agreement at the thermal neutron flux maximum in the head phantom is actually 1.5-2 times better than in the large rectangular water phantom (3-4% vs. 6%) for both BNCT_Rtpe and SERA, indicating that NURBS and univels are as equally capable of modeling the curved surfaces of the head phantom as they are the flat surfaces of the large rectangular water phantom. In addition, it is possible that the worse agreement in the large rectangular water phantom is due to the increased number of interactions (compared to transport calculations in the head
phantom) that could magnify the significance of any differences that exist in transport physics between rtt_MC, seraMC, and MCNP5. Also, $S(\alpha,\beta)$ thermal neutron scattering data for hydrogen in both light water and polyethylene were defined for each biological material (except ICRU cranium where doing so would have meant artificially increasing the concentration of hydrogen) in the BNCT_Rtpe and SERA models of the head phantom whereas only the $S(\alpha,\beta)$ treatment for hydrogen in light water was allowed in the MCNP5 reference calculations. Further investigation revealed that while using both $S(\alpha,\beta)$ treatments does produce differences in the thermal neutron spectrum when compared to using only one, the differences (e.g., 0.5% in the maximum thermal neutron flux) are insignificant so long as the free gas treatment is avoided (which supports data originally reported by Goorley et al.\textsuperscript{14}).
Figure 2.30  Thermal neutron flux and percent difference ($100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}}$) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. SERA and BNCT_Rtpe data are calculated at (default) intervals of 5 mm. MCNP5 served as the reference for percent difference calculations.
Figure 2.31 Different NCTPlan voxel models of the head phantom that resulted from shifting the phantom image data in 1 mm steps along its minor axis (the central axis of the beam). The phantom’s biological materials are color coded by density, and white tick marks have been added to indicate the front and back edges of the un-shifted phantom.
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Figure 2.32  Uninterpolated NCTPlan thermal neutron flux voxel data and percent difference \((100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the ellipsoidal head phantom for different NCTPlan models of the head phantom that resulted from shifting the phantom image data varying distances along the central beam axis in relation to the voxel mesh. MCNP5 served as the reference for percent difference calculations.
2.3.1.2.2 Boron Dose

The comparison of boron dose rates in the head phantom is shown in Figure 2.33, and the dose rates are scaled for a $^{10}$B concentration of 15 μg/g. When compared to the agreement in the large rectangular water phantom (Figure 2.11), NCTPlan produces better agreement in the head phantom on the shallow side of the peak (−1.0% vs. −7.8% at 1.0 cm depth) and worse agreement on the deep side of the peak (−7.2% vs. −2.5% at 3.0 cm depth) While MacNCTPlan and NCTPlan both underestimate the reference maximum boron dose rate by −5.4% (at a depth of 2.2 cm), a more accurate voxel model as well as an improved interpolation algorithm helps NCTPlan produce better agreement than MacNCTPlan by 4.3% at 1.0 cm depth and by 2.0% at 3.0 cm depth. BNCT_Rtpe and SERA produce worse agreement (7.5% at a depth of 2.0 cm) with reference boron dose rates than with reference thermal neutron flux due the improper runtime multiplication of boron kerma factors by the mass density of ICRU brain, 1.04 g/cm$^3$. While geometric approximations do not significantly affect the agreement of either TPS, SERA produces 1-2% better agreement than BNCT_Rtpe at deeper depths in the head phantom.

2.3.1.2.3 Fast Neutron Dose

In Figure 2.34, MacNCTPlan and NCTPlan underestimate the reference fast neutron dose rate at the head phantom entrance by 28% and 40%, respectively, which is largely due to interpolation error in both TPSs. The agreement at the entrance improves significantly, to −7.5%, if MATLAB is used to linearly interpolate the coarse voxel data from each TPS. While NCTPlan produces better agreement than MacNCTPlan by 1-5% at depths beyond the entrance, agreement with the reference is still 2-3 times worse than observed in the rectangular water phantom, in the absence of any geometric
approximations. When uninterpolated fast neutron dose rate voxel data from different NCTPlan voxel models are compared in Figure 2.35, the significant interpolation error at the phantom entrance is removed, indicating better agreement in the NCTPlan uninterpolated voxel data than represented by the interpolated profile data in Figure 2.34. Also, shifting the phantom by 2 mm produces the worst agreement with the reference partially because the resulting voxel model maximizes the radiological depth of the analytic phantom surface which contributes to a more significant underestimation of the reference fast neutron dose rates (−7.9% at 1.0 cm depth) than observed for any of the other models (1-1.5% at 1.0 cm depth).

Since the default energy cutoff for the fast neutron source biasing run mode of BNCT_Rtpe and SERA is inadequate for the generic epithermal neutron beam and results in significant underestimations (−46%) of the reference fast neutron dose rates, hydrogen dose rates produced with that run mode disabled are shown in Figure 2.34 to allow closer examination of the agreement in the absences of such large differences. BNCT_Rtpe and SERA underestimate the reference dose rates by 8-10% at the phantom entrance which is approximately consistent with the agreement in the large rectangular water phantom and the data in Table 2.1 and Table 2.2, which indicate that incomplete INL hydrogen kerma factors (i.e., missing kerma from the recoil deuteron) contribute significantly (9.2%) to the underestimation of the reference fast neutron dose rates. However, no additional significant differences in dose rates are introduced for BNCT_Rtpe or SERA as a result of geometric approximations in the head phantom.
Figure 2.33  Boron dose rate for a $^{10}$B concentration of 15 $\mu$g/g and percent difference $(100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure 2.34  Fast neutron (and hydrogen) dose rate and percent difference \((100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. The fast neutron source biasing run mode was not used for BNCT_Rtpe or SERA (i.e., run modes “NGD” were used) because doing so results in a significant \(-47\%\) difference at the phantom entrance. MCNP5 served as the reference for percent difference calculations.
Figure 2.35  Uninterpolated NCTPlan fast neutron dose rate voxel data and percent difference \((100 \times \text{TPS} - \text{Ref}) / \text{Ref}_{\text{max}}\) as a function of depth along the central beam axis in the ellipsoidal head phantom for different NCTPlan models of the head phantom that resulted from shifting the phantom image data varying distances along the central beam axis in relation to the voxel mesh. MCNP5 served as the reference for percent difference calculations.
2.3.1.2.4 Induced Photon Dose

The comparison of induced photon dose rates to the reference calculations in the head phantom is shown in Figure 2.36. The odd shapes observed in the percent difference profiles of MacNCTPlan and NCTPlan at shallow depths up to 1.25 cm are due to interpolation error, and these shapes are replaced with much smoother profiles if MATLAB is used to perform the 3D linear interpolation. The interpolation error is also worse for MacNCTPlan than for NCTPlan, and interpolated doses from MacNCTPlan are 3-5% different than the MATLAB values which helps give the impression in Figure 2.36 that doses calculated by MacNCTPlan and NCTPlan are more different from each other than they actually are. For instance, at 1 cm depth, the induced photon dose rate calculated by MacNCTPlan is 8% larger than the corresponding NCTPlan value. However, when the interpolation error in both TPSs is eliminated, the MacNCTPlan dose rate is only 2% larger than the NCTPlan value. Nevertheless, both TPSs produce 2-3 times worse agreement in the head phantom than in the large rectangular water phantom (−5.5% vs. −2% at 3.0 cm depth) due to the geometric approximations inherent in 1 cm³ voxel models. When the head phantom image data are aligned differently with the voxel mesh and uninterpolated voxel data are plotted, better agreement in the induced photon dose rates are observed at the entrance in Figure 2.37; shifting the phantom image data by 8 mm results in a 1% difference at the entrance. All of the NCTPlan voxel models shown in Figure 2.37 produce agreement at least as good as the interpolated NCTPlan data in Figure 2.36.

In Figure 2.36, the 9.2% and 3.1% overestimation of the reference maximum induced photon dose rate by BNCT_Rtpe and SERA, respectively, is mainly due to those
differences in photon kerma factors shown in Figure 2.24 and summarized in Table 2.1 and Table 2.2. In those tables, differences in photon kerma factors alone are shown to be responsible for BNCT_Rtpe and SERA overestimating the reference induced photon dose rates by 9.6% and 2.8%, respectively, which is consistent with the disagreement observed in Figure 2.36. Also, the agreement between both TPSs and the reference in the head phantom is not significantly affected by geometric approximations since both employ modeling techniques (i.e., NURBS and univels) that do an adequate job of maintaining the geometric fidelity of the phantom.

2.3.1.2.5 Total Biologically Weighted Dose

The total biologically weighted brain depth-dose rate profiles for each TPS and the reference are shown in Figure 2.38 along with the corresponding percent differences from the reference as a function of depth in the head phantom. At the total weighted dose maximum, MacNCTPlan and NCTPlan underestimate the reference value by −5.0% and −4.8%, respectively, while BNCT_Rtpe and SERA overestimate the reference value by 5.0% and 3.5%, respectively. For MacNCTPlan and NCTPlan, the best agreement in total biologically weighted brain dose rate occurs at depths corresponding to voxel center points. At a depth of 2.3 cm (which corresponds to a voxel center), MacNCTPlan and NCTPlan underestimate the reference doses by −5.7% and −4.5%, respectively, where the worse agreement for MacNCTPlan is due to a significant interpolation error in that TPS. However, in the absence of geometric approximations in the large rectangular water phantom, the agreement in total weighted dose at ½ integral depths corresponding to voxel center points is better (e.g., −2.9% and −1.9% at a depth of 2.5 cm for MacNCTPlan and NCTPlan, respectively). If the head phantom image data are shifted by
8 mm to where the phantom surface is better aligned with the upstream edges of the first non-air voxels encountered by the source neutrons, the resulting NCTPlan voxel model produces improved agreement of \(-2\%\) at those depths corresponding to voxel center points. For BNCT_Rtpe and SERA, the agreement in the head phantom is actually better than observed in the large rectangular water phantom by 2-3\%, indicating that no significant geometric approximations are introduced by modeling the head phantom with NURBS or univels.
Figure 2.36  Induced photon dose rate and percent difference \((100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_{\text{max}}})\) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure 2.37 Uninterpolated NCTPlan induced photon dose rate voxel data and percent difference \((100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the ellipsoidal head phantom for different NCTPlan models of the head phantom that resulted from shifting the phantom image data varying distances along the central beam axis in relation to the voxel mesh. MCNP5 served as the reference for percent difference calculations.
Figure 2.38  Total biologically weighted brain dose rate and percent difference (100×[TPS−Ref]/Ref_{max}) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
2.3.1.3 Leg Phantom

Simulating the treatment of superficial tumors in the leg phantom with a thermal neutron beam intentionally shifts the emphasis of comparison closer to the phantom surface where the dose from the thermal neutron beam is high and significant disagreement is observed in both the large rectangular water phantom and head phantom. Axial sections through the BNCT_Rtpe NURBS model, SERA univel model, and MacNCTPlan/NCTPlan mixed-material voxel models of the leg phantom are shown in Figure 2.39. The mixed-material voxel models produced by MacNCTPlan and NCTPlan are different from each other due to the improved voxelization algorithm of NCTPlan. While only 1.1% of the non-air voxels are different between the two models, all differences occur in voxels at or close to the phantom surface in close proximity to the tumors. It is also rather clear in Figure 2.39 that 1 cm$^3$ are too large relative to the dimensions of the different regions of the leg phantom and the curvature of the phantom surface to accurately model the phantom.

2.3.1.3.1 Thermal Neutron Flux

Figure 2.40 shows the thermal neutron flux calculated by MCNP5, BNCT_Rtpe, SERA, MacNCTPlan, and NCTPlan as well as the percent difference of each TPS from the reference MCNP5 calculations as a function of depth along the central beam axis in the leg phantom. Simulating a thermal neutron beam produced a thermal neutron flux peak at a depth of 1.5 cm in the leg phantom that was 2.3 cm narrower (evaluated at ¾ the maximum flux) and 1.8 cm shallower than observed in the head phantom. Interpolating data from a coarse scoring mesh of 1 cm$^3$ tally volumes did not accurately model the relatively narrow peak or the very steep dose gradient at the phantom entrance which results in BNCT_Rtpe, SERA, MacNCTPlan and NCTPlan underestimating the
maximum thermal neutron flux by $-10\%$, $-8.9\%$, $-19\%$, and $-15\%$, respectively. It should be noted that the coarseness of the SERA line edit data (calculated at 5 mm intervals with seraPlan) masks the actual level of agreement ($-8.9\%$) at the thermal neutron flux maximum instead giving the appearance that it is only $-5\%$. Identical spacing was requested for BNCT_Rtpe line edit data, but rtt_MC automatically adjusted the spacing in order to provide interpolated data at all region boundaries. Given the dimensions of the leg phantom, a scoring mesh of 1 cm$^3$ tally volumes does not provide the resolution necessary to adequately match the high gradient of the reference thermal neutron flux peak. If the reference thermal neutron flux data are averaged over 1 cm$^3$ (i.e., 10 reference tally volumes), the peak is shifted by 2 mm to a deeper depth, its width is increased by 1.0 cm, and the maximum value is decreased by 6.8\% as a result of volume averaging. On the deep side of the peak at depths beyond $\sim1.0$ cm, where the curvature of the reference flux profile is relatively low, the agreement for all TPSs improves to within 5\% of the reference. In addition to producing the largest underestimation of the reference thermal neutron flux maximum, MacNCTPlan is also the only TPS that consistently overestimates the reference thermal neutron flux at depths greater than $\sim1.5$ cm, and both results are due to inaccuracies in the MacNCTPlan voxel model that adversely affect the agreement in the thermal neutron flux. Also, if MATLAB is used to interpolate the MacNCTPlan and NCTPlan coarse voxel data, the fluctuations observed in Figure 2.40 at depths beyond 1.0 cm are replaced by smoother flux data.
Figure 2.39 Axial sections through the BNCT_Rtpe NURBS model, SERA univel model, MacNCTPlan and NCTPlan mixed-material voxel models of the leg phantom used to simulate BNCT treatment of peripheral melanoma.
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Figure 2.40 Thermal neutron flux and percent difference (100×[TPS−Ref]/Ref\textsubscript{max}) as a function of depth along the central beam axis in the leg phantom for each planning system. SERA and BNCT\textsubscript{Rtpe} data are calculated at (default) intervals of 5 mm. MCNP5 served as the reference for percent difference calculations.
2.3.1.3.2 Boron Dose

When comparing boron dose rates in the leg phantom that have been scaled to a $^{10}$B concentration of 22.5 μg/g (for skin), the agreement shown in Figure 2.41 for MacNCTPlan (19% at 4 mm depth) and NCTPlan (15% at 4 mm depth) is nearly identical to the agreement observed in thermal neutron flux because the boron dose rates were calculated using identical $^{10}$B kerma factors and the $1/\nu$ shape of that kerma factor emphasizes the thermal portion of the neutron energy spectrum. However, differences in $^{10}$B kerma factors do exist between BNCT_Rtpe, SERA, and the reference, and they significantly affect the agreement shown in Figure 2.41. The differences in $^{10}$B kerma factors are a combination of the average differences shown in Figure 2.12 (−2.5% for BNCT_Rtpe and −1.0% for SERA) and those due to the improper runtime scaling of BNCT_Rtpe and SERA $^{10}$B kerma factors by the mass density of ICRU skin, 1.09 g/cm$^3$. Therefore, BNCT_Rtpe and SERA boron dose rates in the leg phantom result in a −4.2% and −3.5% underestimation of the maximum reference boron dose rate and a 5.4% and 3.2% overestimation of the reference on the deep side of the peak at 1 cm depth, respectively.

2.3.1.3.3 Fast Neutron Dose

Each TPS underestimates the maximum reference fast neutron dose rate in Figure 2.42; MacNCTPlan and NCTPlan do so by −5.5% while BNCT_Rtpe and SERA underestimate it by −3%. MacNCTPlan and NCTPlan also underestimated the maximum reference fast neutron dose rate in the head phantom in Figure 2.34, and in Figure 2.35, it was shown to be due to the geometric approximations that are characteristic of the orientation of the phantom within the voxel mesh. The fluctuations in the MacNCTPlan
and NCTPlan fast neutron dose data are produced by the interpolation algorithms within each TPS and are eliminated if MATLAB is used to perform the linear interpolation. BNCT_Rtpe and SERA underestimate the reference fast neutron dose rates at shallow depths by ~3% despite using hydrogen kerma factors that have been improperly multiplied by 1.09, the density of ICRU skin in g/cm$^3$. The BNCT_Rtpe and SERA hydrogen dose rates do not include contributions from neutrons below 9.12 keV because the default fast neutron source biasing run mode was utilized for calculations in the leg phantom (refer to section 2.3.1.1.4). A separate MCNP5 calculation of the hydrogen dose rate in the leg phantom using ICRU hydrogen kerma factors indicated that 60% of the hydrogen dose rate is from interactions of thermal neutrons (via the recoil deuteron) due to the nearly 4 orders of magnitude difference between thermal and fast neutron flux. Therefore, even if the default fast neutron source biasing run mode were to be disabled, allowing all neutron energies to contribute to the hydrogen dose, BNCT_Rtpe and SERA would still dramatically underestimate the reference hydrogen dose as a result of their incomplete hydrogen kerma factors in the thermal neutron energy region. Thus, BNCT_Rtpe and SERA underestimate the maximum reference hydrogen dose rate by 55%, but the contribution of the hydrogen dose to the total neutron dose is so small (e.g., 2% of maximum reference total neutron dose) that this large underestimation is not significant. However, both codes produce much better agreement with the reference fast neutron dose rate because the 0.5 eV energy cutoff employed in the reference calculations excludes the contribution from thermal neutrons and the improper runtime multiplication of the INL hydrogen kerma factors by 1.09 compensates for the contribution of kerma from elements besides hydrogen to the reference fast neutron dose,
which is absent in BNCT_Rtpe and SERA. Therefore, the differences observed in Figure 2.42 between BNCT_Rtpe/SERA hydrogen dose rates and reference fast neutron dose rates are largely due to differences in fast neutron flux.

2.3.1.3.4 Induced Photon Dose

In Figure 2.43, MacNCTPlan and NCTPlan significantly underestimate the maximum reference induced photon dose rate in the leg phantom by −15.5% and −12.6%, respectively. Both MacNCTPlan and NCTPlan underestimated the maximum thermal neutron flux in Figure 2.40 and that certainly contributed to the underestimation of the dose from photons produced by the reactions of thermal neutrons. However, part of the significant underestimation of the reference induced photon dose rates is due to the limitation of 4 primary materials in the voxel models of MacNCTPlan and NCTPlan. If the reference simulation is repeated with the analytical model of the leg phantom changed to include only air, bone, normal tissue (muscle) and tumor, the maximum induced photon dose rate is decreased by 4%. Also, averaging the reference dose data over 1 cm³ further reduces the maximum induced photon dose rate by 2%. On the deep side of the peak, NCTPlan underestimates the reference induced photon dose rates by 5-10% while MacNCTPlan manages to produce better agreement than NCTPlan at deeper depths. MacNCTPlan’s overestimation of the thermal neutron flux at those depths results in more induced photons, increased induced photon dose rates, and better agreement with the reference calculations.

In Figure 2.43, BNCT_Rtpe overestimates the maximum reference induced photon dose rate by 3% while SERA underestimates it by −3.5%. Like MacNCTPlan and NCTPlan, both BNCT_Rtpe and SERA significantly underestimate the maximum
reference thermal neutron flux in Figure 2.40, but the differences in photon kerma factors that are shown in Figure 2.24 help compensate for a lower thermal neutron flux to produce the agreement observed. Similarly, on the deep side of the induced photon dose rate peak, SERA produces better agreement than BNCT_Rtpe (e.g., −1.4% vs. 5.2% at a depth of 2.0 cm) due to SERA’s improved photon kerma factors. It should also be noted that discontinuities as large as 5% are observed in the BNCT_Rtpe and SERA flux and dose rate data in the leg phantom if finely spaced (i.e., < 1 mm) line edit data are plotted. The interpolation error identified in both TPSs (and shown for SERA in Figure 2.7) produces these discontinuities at several depths in the phantom.

2.3.1.3.5 Incident Photon Dose

In Figure 2.44, MacNCTPlan and NCTPlan produce agreement within 1% of the reference incident photon dose rates in the leg phantom. The fluctuations in the MacNCTPlan and NCTPlan incident dose rates, most noticeable in the percent difference profiles and larger for MacNCTPlan, are produced by the interpolation algorithms of each TPS. BNCT_Rtpe and SERA result in approximately constant 4.3% and −2.8% differences, respectively. The observed disagreement for BNCT_Rtpe and SERA is a result of differences in photon kerma factors as well as the photon normalization error that is defined by Eq. 2.1. For the irradiation of the leg phantom with the thermal neutron beam, Eq. 2.1 evaluates to 1.0146 and indicates that the normalization error is responsible for BNCT_Rtpe and SERA underestimating the reference incident photon dose rates by −1.5%. Table 2.1 and Table 2.2 estimate, albeit for the comparison in the large rectangular water phantom, that differences in photon kerma factors alone are responsible for BNCT_Rtpe overestimating the reference incident photon dose rates by
6.2% and SERA underestimating them by $-1.1\%$. These differences combine with the normalization error to produce the disagreement observed in Figure 2.44 for BNCT_Rtpe and SERA.

### 2.3.1.3.6 Total Biologically Weighted Dose

The total biologically weighted skin dose rates from each TPS and the reference are shown in Figure 2.45 along with the corresponding percent difference of each TPS from the reference as a function of depth in the leg phantom. At a depth of 4 mm, MacNCTPlan and NCTPlan underestimate the maximum reference total weighted skin dose rate by $-18\%$ and $-14\%$, respectively, while BNCT_Rtpe and SERA underestimate it by $-3.5\%$. In the leg phantom, the BNCT_Rtpe and SERA neutron and boron dose rates are improperly scaled up by 1.09 which actually helps compensate for the disagreement at shallow depths, where all TPSs significantly underestimate the thermal neutron flux and hence the total weighted dose rate, but also contributes to higher dose rates on the deep side of the dose peak that overestimate the reference by 3-6%. Due to differences in their respective voxel models of the leg phantom, MacNCTPlan and NCTPlan result in total weighted skin dose rates that significantly differ from each other with MacNCTPlan producing 5-10% lower weighted dose rates than NCTPlan at the dose peak and then 5-10% larger values on the backside of the dose peak. Likewise, the more accurate NCTPlan voxel model produces 4% better agreement with the maximum reference total weighted skin dose than does the MacNCTPlan model.
Figure 2.41  Boron dose rate for a $^{10}$B concentration of 22.5 μg/g and percent difference (100×[TPS−Ref]/Ref$_{max}$) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure 2.42 Fast neutron (and hydrogen) dose rate and percent difference \((100 \times \frac{[\text{TPS} - \text{Ref}]}{\text{Ref}_{\text{max}}})\) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure 2.43  Induced photon dose rate and percent difference \((100\times[\text{TPS-Ref}/\text{Ref}_{\text{max}}])\) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure 2.44  Incident photon dose rate and percent difference (100×[TPS−Ref]/Ref_{max}) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
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Figure 2.45 Total biologically weighted skin dose rate and percent difference \((100\times[TPS-Ref]/Ref_{max})\) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
2.3.2 Isodose Contours and Dose Difference Distributions

To facilitate the direct comparison of 2D dose data from each TPS to the reference, screen captures of isodose contours from each TPS were overlaid with reference contours after the treatment time (or, equivalently, monitor units) from each TPS had been used to convert the dose rate data for both the TPSs and the reference to units of absolute dose. The treatment times shown in Table 2.3 for each planning system and the reference were calculated based on realistic BNCT dose prescriptions for each phantom type: a maximum brain dose of 12.5 Gy\textsubscript{w} for the head phantom and a minimum tumor dose of 24 Gy\textsubscript{w} for the leg phantom. For the head phantom, the treatment times are all within 5-6% of the reference, but larger disagreement, such as 10% for BNCT\_Rtpe and 17% for MacNCTPlan, are observed for the leg phantom. It is worth noting that limitations in the TPSs often prevented a uniform set of isodose line levels (dose values) from being plotted for all the TPSs for a given dose component. However, even in those instances, the differences in the plotted contour levels from one TPS to another are small and do not in any way affect the comparison between each TPS and the reference.

<table>
<thead>
<tr>
<th>Table 2.3</th>
<th>Treatment time in minutes required to deliver a maximum brain dose of 12.5 Gy\textsubscript{w} for the head phantom or a minimum tumor dose of 24 Gy\textsubscript{w} for the leg phantom.</th>
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<tbody>
<tr>
<td></td>
<td><strong>Treatment Time (minutes)</strong></td>
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<tr>
<td></td>
<td><strong>Head Phantom</strong></td>
</tr>
<tr>
<td></td>
<td>1 field</td>
</tr>
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<td>Reference</td>
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</tr>
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</tr>
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<td>SERA</td>
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<td>MacNCTPlan</td>
<td>3.34</td>
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<tr>
<td>NCTPlan</td>
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contours; the reference contour levels in every plot are matched to those used by the TPS. A more detailed analysis of the 2D dose data from each TPS is also included in the form of dose difference distributions. Dose differences, defined as TPS – Reference, were calculated using the interpolated and unmasked 2D dose matrix from each TPS and plotted as percentages of the maximum reference dose for both orthogonal planes containing the central beam axis. This finer grained comparison is meant to compliment the more conventional but coarser comparison of isodose contours. It is important to note that when discussing the agreement observed in 2D dose difference distributions, all agreement is specified relative to the reference dose maximum. For example, a 5% difference in boron dose for a TPS at a given location indicates that the dose difference (TPS – Reference) is 5% of the reference boron dose maximum rather than the reference boron dose at that location.

2.3.2.1 Ellipsoidal Head Phantom

This section reports the comparison of 2D dose distributions (i.e., isodose contours and dose difference distributions) in the head phantom. For all of the dose components, refer to sections A.3.1 and A.4.1 of Appendix A.

2.3.2.1.1 Boron Dose

Boron isodose contours from each TPS are shown in Figure 2.46 for a 1-field irradiation of the head phantom, and the reference contours have been overlaid as dashed lines. BNCT_Rtpe does not allow isodose contours to be color coded, so contour labels have been added manually. The comparison of isodose contours demonstrate agreement in 2D that is consistent with that observed in the comparison of 1D depth-dose rate profiles. In Figure 2.33, BNCT_Rtpe and SERA dose rates along the central beam axis
overestimate the maximum reference boron dose rate by ~6%. Likewise, in Figure 2.46, both BNCT_Rtpe and SERA overestimate the reference in the high dose region to the extent that the highest dose reference contour is not plotted which implies a DTA (distance-to-agreement) for contours in that region of at least 4-8 mm. However, the agreement for BNCT_Rtpe and SERA improves with depth and lateral distance from the central beam axis to result in less than 1 mm of separation for the lower dose contours. In Figure 2.33, MacNCTPlan and NCTPlan boron depth-dose rates overestimate the reference boron dose rates at shallow depths and subsequently underestimate them at depths beyond 0.5-1.5 cm. While the contours for MacNCTPlan and NCTPlan in Figure 2.46 are too coarse to adequately illustrate the agreement close to the surface, the underestimation of the reference boron dose rates by both TPSs is clearly evident and results in contours separated by 5-9 mm in the high dose region. While the agreement improves for lower dose contours, MacNCTPlan and NCTPlan contours are still shifted from the reference by ~4 mm and ~2 mm, respectively. Also, MacNCTPlan’s lowest dose contour appears to trace around the edges of voxels from the coarse scoring mesh, resulting in a stepped contour that indicates problems in the contouring algorithm of MacNCTPlan.

To illustrate the agreement in between the particular isodose lines shown in Figure 2.46, the corresponding boron dose difference distribution for each TPS is shown in Figure 2.47 with outlines of the skin, skull, brain, and tumor superimposed in black. The largest disagreement for BNCT_Rtpe and SERA occurs at the boron dose maximum where larger tally volumes, interpolation error, and improperly scaled boron kerma factors combine to overestimate the reference dose by ~6%. Also, the interpolation error
in both BNCT_Rtpe and SERA (refer to Figure 2.7) result in two thin vertical, parallel strips in the high dose region at approximately x=4.15 cm and x=5.45 cm where the dose differences are elevated by ~1% above those on either side. If MATLAB’s cubic algorithm is used to interpolate the coarse voxel data from BNCT_Rtpe and SERA, not only are those strips eliminated but the dose differences in the high dose regions are reduced from 5-6% to 2-3%. For MacNCTPlan and NCTPlan, the 6-7% underestimation of the reference dose rates in the high dose region is partially due to interpolation error and partially due to the inability of dose data linearly interpolated from the coarse 1 cm³ scoring mesh to match the curvature of the reference dose data. The very well defined “checker board” pattern in the dose difference distributions is actually a 2D representation of the “sawtooth” pattern observed when comparing depth-dose profiles in Figure 2.33. Interestingly, both MacNCTPlan and NCTPlan produce this characteristic pattern. If MATLAB is used to linearly interpolate the coarse voxel data from MacNCTPlan and NCTPlan, these checkerboard patterns are eliminated, but the agreement does not change significantly for either TPS. It should also be noted that the boron dose difference distributions for all TPSs are symmetrical about the central beam axis because the phantom itself is symmetrical about the beam axis in the transverse plane.
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Figure 2.46  Boron isodose contours for a $^{10}$B concentration of 15 μg/g in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.
Figure 2.47  Difference in boron dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference boron dose for a 1-field irradiation of the head phantom.
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2.3.2.1.2 Incident Photon Dose

Incident photon isodose contours from each TPS are compared to reference contours in a transverse plane of the head phantom in Figure 2.48. Due to the monodirectionality of the incident photon beam and the relatively low number of interactions incident photons experience in the phantom before escape, the dose gradient inside the beam is relatively flat, so that even a small difference in incident photon dose will translate into a relatively large DTA for contours. BNCT_Rtpe overestimates the reference incident photon dose by ~4% due mainly to the differences in photon kerma factors shown in Figure 2.24, but that 4% difference results in a separation of ~1.5 cm for contours at shallow depths. Similarly, SERA underestimates the reference photon dose by ~3% due mainly to the incident photon normalization error, but that difference results in contours at shallow depths that are shifted by ~1.1 cm from the reference. The reference lateral incident photon dose gradient is flat out to the edge of the beam at \( y = \pm 5 \) cm where the dose decreases by 95% just beyond the edge of the beam. However, BNCT_Rtpe and SERA calculate sharp increases in the incident photon dose, as large as 10%, near the edge of the beam that subsequently result in isodose contours that extend to deeper depths in the phantom within ~1 cm of the lateral beam edges and thus produce “horns” in the isodose contours. These misshapen contours are due to a combination of the interpolation algorithms employed by BNCT_Rtpe and SERA and the steep lateral dose gradient at the edges of the monodirectional photon beam. Similar shapes are produced when MATLAB is used to interpolate the coarse voxel dose data from BNCT_Rtpe and SERA with its cubic interpolation algorithm and plot the contours. While these differences near the lateral edges of the beam do not produce any significant
disagreement in total weighted dose due to the relatively small contribution of the incident photon dose, it does emphasize the importance of evaluating the different representations and individual components of dose data since differences are not always confined to the central beam axis and can potentially be masked by summation.

MacNCTPlan and NCTPlan produce very good agreement with the reference incident photon isodose contours, especially at shallow depths where the DTA is less than 1 mm. However, the agreement gets slightly worse with depth, and the DTA along the central beam axis for the lowest dose contour is 6 mm and 3 mm for MacNCTPlan and NCTPlan, respectively. Laterally, the contours of MacNCTPlan and NCTPlan do not fully extend out to the edges of the beam but instead span to within 5-10 mm of reference contours at the phantom surface. To understand this behavior, transverse and coronal views through the head phantom are shown in Figure 2.49 with a portion of the coarse scoring mesh from each TPS overlaid and with the beam path through each mesh shaded. The edges of the beam are aligned with mesh element edges in BNCT_Rtpe and SERA whereas they are aligned with mesh elements centers in MacNCTPlan and NCTPlan. Therefore, in this case, it happens that BNCT_Rtpe and SERA are better able to model the sharp reference dose gradient at the lateral edges of the beam because the beam edges align with the edges of the scoring mesh elements. To better illustrate this effect, the lateral incident photon dose rate profile from each TPS is shown in Figure 2.50 as a function of the distance from the central beam axis. The position of the monodirectional photon beam within the coarse scoring mesh and the extremely steep dose gradient prevent MacNCTPlan and NCTPlan from accurately estimating the reference incident photon dose from 4-6 cm which results in a shallower dose gradient, 35 to −50%
differences, and isodose contours that do not fully extend out to the edges of the beam. The shifted scoring mesh alone allows BNCT_Rtpe and SERA to better estimate the steep reference dose gradient and produce contours that are closer to the reference laterally by ~5 mm. The horns in the dose distribution are however visible here near the lateral edges of the beam. These observations further emphasize the problems with employing such a coarse scoring mesh, especially when steep dose gradients are present; although this is an extreme case, alignment of the beam edges with the dose mesh edges should not be needed for accurate calculations.
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Incident Photon Dose

Figure 2.48  Incident photon isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.
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Figure 2.49 Transverse and coronal views through the ellipsoidal head phantom overlaid with the coarse scoring mesh from each TPS to illustrate the relative orientation of each mesh with the phantom and the beam path (shaded region). The mesh element centers in BNCT_Rtpe and SERA are offset by 5 mm in each dimension from the mesh element centers of MacNCTPlan and NCTPlan. The beam is aligned with mesh element edges in BNCT_Rtpe and SERA whereas it is aligned with mesh element centers in MacNCTPlan and NCTPlan. Each tally volume is 1 cm$^3$, and only a portion of each mesh is shown.
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Figure 2.50 Incident photon dose rate and percent difference ($100 \times \frac{[TPS−Ref]}{Ref_{max}}$) for each planning system as a function of the lateral distance (in the transverse plane) from the central beam axis in the ellipsoidal head phantom. MCNP5 served as the reference for percent difference calculations.
2.3.2.1.3 Total Biologically Weighted Dose

Figure 2.51 shows the total weighted brain isodose contours for each TPS and the reference in the coronal plane containing the central beam axis. BNCT_Rtpe underestimates the reference total weighted brain dose in the high dose region by ~5% which results in a DTA in that region of at least 7-10 mm. The agreement improves for the lower dose contours where the BNCT_Rtpe contours are within 1-2 mm of the reference. SERA produces better agreement with the reference contours than BNCT_Rtpe due to slight differences in their respective boron kerma factors which, when scaled at runtime by the mass density of the edit mesh, places the SERA boron kerma factors in better agreement with the reference kerma factors. The largest differences occur in the high dose region where SERA overestimates the reference by ~4% and produces contours 3-5 mm from the reference, but the DTA for the lower dose contours is 1 mm or less. MacNCTPlan and NCTPlan produce noticeably worse agreement at all depths partially as a result of geometric approximations introduced by using a coarse 1 cm³ voxel model. For the 2 highest dose contours, the agreement is also not uniform in that both TPSs, especially MacNCTPlan, produce better agreement on the shallow side of the contour than on the deep side. Nevertheless, for the highest dose contour of 11.9 Gyw, the DTA for MacNCTPlan is 7-9 mm and 6-9 mm for NCTPlan, but the agreement improves to result in a DTA of ~4 and ~2.5 mm, respectively, for the lower dose contours. Stepped MacNCTPlan contours are also observed indicating the presence of problems within the contouring algorithm.

The corresponding total biologically weighted brain dose difference distribution for each TPS is shown in Figure 2.52 and overlaid with outlines of the skin, skull, brain,
and tumor. BNCT_Rtpe and SERA underestimate the reference dose in the skin by 1-4% and overestimate the reference dose in the brain by 2-5% and 1-4%, respectively, partially because of the difference in tally volumes between the $1 \times 1 \times 2$ mm reference mesh and the $10 \times 10 \times 10$ mm scoring mesh of BNCT_Rtpe and SERA. SERA produces slightly better agreement with the reference in the high dose region in the brain because the improperly scaled SERA boron kerma factors are closer to the reference by 1-2% than the scaled BNCT_Rtpe kerma factors. MacNCTPlan and NCTPlan both underestimate the reference maximum total weighted brain dose by ~5% due to differences in tally volumes and geometric approximations.

Figure 2.53 shows the total biologically weighted brain isodose contours for each TPS and the reference that result from a 3-field irradiation of the head phantom. BNCT_Rtpe overestimates the reference in the high dose region by ~5% which results in a DTA of at least 7-11 mm for the highest dose contour, but the agreement improves to ~3.5% at deeper depths along the ipsilateral beam axis and to 1-2% laterally. However, the parallel opposed beams produce a relatively flat dose gradient on the contralateral side of the phantom where there is only a 10% deviation in doses between the depths of 1.5 and 8 cm. Therefore, the ~3.5% differences in that region actually results in a DTA of ~1.3 cm for the 6.49 Gy$_w$ contour. SERA produces better agreement and overestimates the reference doses by ~2% in the high dose region which results in a DTA for the highest dose contour of ~3 mm. On the contralateral side of the phantom, the dose differences are 1-2% and also result in a DTA of ~3 mm. The agreement is also very good laterally with a DTA of less than 1 mm for the lower dose contours. MacNCTPlan and NCTPlan both underestimate the reference dose by ~6% in the high dose region.
which results in a DTA of 5-9 mm and 5-7 mm, respectively. At shallow depths on the contralateral side of the phantom, MacNCTPlan produces worse agreement than NCTPlan (e.g., −6.4% vs. −2.7% at a depth of 1.5 cm) due to inaccuracies in the MacNCTPlan voxel model along the contralateral surface of the phantom like those shown in Figure 2.29. For the 3 lowest dose contours, the DTA for both MacNCTPlan and NCTPlan is in the 2-4 mm range.

Figure 2.54 compares the total biologically weighted tumor isodose contours for each TPS and the reference that result from a 3-field irradiation of the head phantom. BNCT_Rtpe and SERA overestimate the reference in the high dose region by ~5% and ~4%, respectively which correspond to a DTA in that region of 5-10 mm. The DTA decreases for the lower dose contours, but a noticeable gap of 1.2-2.3 cm is created because the ~42 Gy_w contours of BNCT_Rtpe and SERA extend further towards the contralateral side of the phantom than do the reference contours. However, these large gaps represent an overestimation of the reference dose in that region by BNCT_Rtpe and SERA of only 5% and 2.5%, respectively. MacNCTPlan and NCTPlan underestimate the reference in the high dose region by as much as 10% which results in a DTA of ~1.2 cm for the highest dose contour. MacNCTPlan produces similar agreement to NCTPlan on the ipsilateral side but worse agreement near the entrance for both the contralateral (e.g., 2.5× worse at 1.5 cm depth) and vertex (e.g., 1.25× worse at 1.5 cm depth) beams due to inaccuracies in the MacNCTPlan voxel model. A large separation is observed in a section of the 41.0 Gy_w contour where the reference contour extends 2.1 cm and 3.7 cm beyond the MacNCTPlan and NCTPlan contours, respectively, towards the contralateral side of the phantom. However, these large differences in contours represent a mere 2-4%
underestimation of the reference in that region of the phantom where the dose gradient is low.

**Total Biologically Weighted Brain Dose**

![Isodose contours](image)

**Figure 2.51** Total biologically weighted brain isodose contours in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.
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Figure 2.52 Difference in total biologically weighted brain dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the head phantom.
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Figure 2.53  Total biologically weighted brain isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.
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Figure 2.54  Total biologically weighted tumor isodose contours in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.
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2.3.2.2 Leg Phantom

This section reports the comparison of 2D dose and thermal neutron flux distributions (i.e., isodose contours and dose or flux difference distributions) in the leg phantom. For all of the dose components, refer to sections A.3.2 and A.4.2 of Appendix A.

2.3.2.2.1 Thermal Neutron Flux

Figure 2.55 shows the 2D thermal neutron flux difference distribution for each TPS in the traverse plane of the leg phantom on the beam central axis with superimposed outlines of skin, tumors, bone and muscle. BNCT_Rtpe and SERA both underestimate the reference thermal neutron flux maximum at 4 mm depth in the phantom by 9-10% because 1 cm³ tally volumes are too large to accurately represent the narrow thermal neutron flux peak. In fact, a region of underestimation ~6.5 cm wide borders the entire beam-facing surface of the phantom and encompasses the shallow side of both tumors. However, regions where BNCT_Rtpe and SERA overestimate the reference flux by 4-6% and 2-4%, respectively, are also observed (e.g., at x=−4.2 cm). If MATLAB is used to interpolate (via cubic interpolation) the coarse voxel data from BNCT_Rtpe and SERA, the differences in those same regions decrease by 1-2%, thus identifying interpolation error as a significant contributor to the disagreement in those regions. Other than in these regions, the thermal neutron flux differences in the leg phantom are all within 2% for BNCT_Rtpe and SERA. MacNCTPlan and NCTPlan also underestimate the reference thermal neutron flux at shallow depths by as much as 19% and 15%, respectively. However, on the deep side of the tumors, MacNCTPlan overestimates the reference flux by as much as 14% whereas NCTPlan produces agreement in that same region within 2%. While the underestimation of the reference at shallow depths is due in large part to
the coarseness of the scoring mesh and voxel model relative to the dimensions of the leg phantom, MacNCTPlan’s significant disagreement at deeper depths are mainly attributable to interpolation error and inaccuracies in its voxel model like those shown in Figure 2.39. If MATLAB is used to linearly interpolate MacNCTPlan’s coarse voxel data, the “checker board” pattern is eliminated and agreement on the deep side of the tumors improves by 4-5%. Similarly, two distinct regions of ~4% overestimation are present in the flux difference distribution for NCTPlan, but the agreement improves to within ~2% at each spot if MATLAB is used to linearly interpolate NCTPlan’s coarse voxel data.

2.3.2.2.2 Boron Dose

Figure 2.56 shows the 2D boron dose difference distribution for each TPS in a traverse plane of the leg phantom on the beam central axis with superimposed outlines of skin, tumors, bone and muscle. The boron dose difference distributions for MacNCTPlan and NCTPlan are nearly identical to their respective thermal neutron flux difference distributions shown in Figure 2.55 because in the boron kerma factors used are also identical. However, that is not the case for BNCT_Rtpe and SERA because their boron kerma factors differ, and, more importantly, because they have been improperly scaled at runtime by 1.09, the density of ICRU skin in g/cm³. As a result, boron dose differences as large as 8-12% are observed on the deep side of the tumors. The scaling also actually improves agreement to 5-6% at shallow depths by compensating for BNCT_Rtpe and SERA’s underestimation of the reference thermal neutron flux.

2.3.2.2.3 Total Biologically Weighted Dose

Figure 2.57 compares the total biologically weighted tumor isodose contours for
each TPS with the reference in the transverse plane of the leg phantom containing the central beam axis. Both BNCT_Rtpe and SERA significantly underestimate the reference thermal neutron flux in the high dose region as shown in Figure 2.55, but scaling the neutron and boron kerma factors up at runtime by the mass density of ICRU skin (1.09) actually compensates for the underestimation to produce contours that are 5 mm from the reference contour along the beam line and 2-3 mm laterally. However, that scaling also results in BNCT_Rtpe and SERA overestimating the reference doses beyond the tumors to produce DTA of 2-4 mm for the lower dose contours. MacNCTPlan deviates substantially from the reference contour in the high dose region and thus results in a contour that is 1/3 the width of the reference contour and shifted by ~1.2 cm laterally. These differences are due to interpolation error as well as inaccuracies in the MacNCTPlan voxel model. Agreement improves in the lower dose contours where the DTA is generally within 5 mm and MacNCTPlan’s contours span the same lateral distance as the reference contours. NCTPlan produces better agreement than MacNCTPlan in the high dose region as evidenced by its isodose contour being centered about the central beam axis and spanning 2/3 the lateral width of the reference contour. Agreement improves significantly in the lower dose contours where the DTA are generally less than 1 mm which is actually better agreement than observed for the head phantom (Figure 2.51).

Figure 2.58 compares the total biologically weighted tumor isodose contours of MacNCTPlan and NCTPlan with the reference in the oblique plane of the leg phantom containing the central beam axis. Since it was not possible to plot contours for this oblique plane in BNCT_Rtpe or SERA, they have been omitted from the comparison in
this plane.∗ MacNCTPlan produces significant differences in the high dose region where its contour does not extend to the same width as the reference either axially or along the beam line. On the deep side of the tumor, MacNCTPlan overestimates the reference doses by as much as 11% due to interpolation error and inaccuracies in its voxel model which results in a DTA as large as 3 mm. Also, the lower dose MacNCTPlan contours are stepped and appear to trace along the edges of the 1 cm³ tally volumes rather than being smooth like those of NCTPlan. NCTPlan produces better agreement than MacNCTPlan like in the transverse plane, but the highest dose NCTPlan contour does not span the same axial distance as the reference contour instead extending within ~1.4 cm of the reference contour’s superior and inferior edges. However, agreement for the lower dose (≤ 16.5 Gyₜ) contours is excellent with DTA within 1 mm, which is surprising when the coarseness of the tally mesh and the voxel model relative to the leg phantom dimensions is considered.

∗ Isodose contours for the oblique plane were successfully calculated with seraPlan, but seraPlot would not display them correctly.
Figure 2.55  Difference in thermal neutron flux in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron flux for a 1-field irradiation of the leg phantom.
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Figure 2.56  Difference in boron dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference boron dose for a 1-field irradiation of the leg phantom.
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Figure 2.57  Total biologically weighted tumor isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.
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Figure 2.58  Total biologically weighted tumor isodose contours in an oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table 2.3 was used to convert the reference dose rates to absolute dose.
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2.3.3 Dose-Volume Histograms

Each TPS produced a unique reference dose when calculating the treatment plans. Therefore, the reference treatment times from Table 2.3 were used to convert the dose-volume data from each TPS into units of absolute dose to allow for a direct comparison with the corresponding reference dose-volume data. The volumes calculated by each TPS for the various anatomical regions in the head and leg phantoms are shown in Table 2.4 and the corresponding analytical volumes are included for comparison. Clearly, SERA and NCTPlan produce more accurate volume estimates than their respective predecessors. For instance, BNCT_Rtpe and MacNCTPlan calculate volumes for brain that are 95% and 75% of the analytical volume, respectively, whereas SERA and NCTPlan produce volume estimates that are within 0.03% of the analytical volume. These more accurate volume estimates are a direct result of the improved accuracy of SERA’s univel models over that of BNCT_Rtpe NURBS models and the algorithmic improvements in NCTPlan compared to MacNCTPlan. It should be noted, however, that

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<th>Structure Volume (cm³)</th>
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<th>Leg Phantom</th>
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NCTPlan produced a different volume for brain (1403.27 cm$^3$) when calculating the fast neutron DVH resulting from a 1-field irradiation of the head phantom. This reproducible and erroneous volume calculation was not reproduced for the 3-field irradiation, any other regions, or dose components nor was anything similar observed in MacNCTPlan. Also, in Table 2.4, there is no MacNCTPlan or NCTPlan entry for leg phantom skin. MacNCTPlan and NCTPlan ROI files for skin were successfully created and displayed by both TPSs, but their resulting volume estimates were 12× the analytical volume. The clearly erroneous DVHs indicated that neither TPS was able to accurately calculate dose-volume data for regions like skin that have interior holes. In this case, the skin ROI was represented by a single concave C-shaped contour with the two ends of the C nearly touching.

When comparing dose-volume data, the level of agreement can be reported as the difference in dose for a given volume fraction (the horizontal distance between DVHs) or the difference in volume fraction for a given dose (the vertical distance between DVHs). The former was utilized for a majority of this analysis. However, since is also common in radiotherapy to report the volume fraction of a given anatomical region that received a dose greater than some pre-determined value, brain $V_8$ values (i.e., the fraction of brain volume that received $\geq 8$ Gy$_{eq}$) from each TPS are also reported and compared with the reference. To extract such data from the binned BNCT_Rtpe dose-volume histograms, the lower left or low dose corner of the each bin for a given DVH was connected, and the dose data were linearly interpolated from the resulting curve.
2.3.3.1 Ellipsoidal Head Phantom

Figure 2.59 shows the total biologically weighted dose-volume histograms for brain resulting from a 1-field irradiation of the head phantom for 3.16 minutes (i.e., the reference treatment time from Table 2.3). Conventional and binned representations of the reference data are included to facilitate its comparison to both the binned dose-volume data from BNCT_Rtpe and the more conventional integral dose-volume histograms from the other TPSs. By default, seraPlan calculates dose-volume data in 10\% increments of its reference dose, and then seraPlot assigns the corresponding percent volume to the center of each dose bin in order to plot a conventional DVH. As shown in Figure 2.59, this interpretation of the SERA dose-volume data results in a systematic 5\% (i.e., $\frac{1}{2}$ default bin width) shift to higher doses and worse agreement with the reference. If the same seraPlan dose-volume data are instead re-plotted at the low dose edge of each bin rather than at the center, better agreement with the reference DVH is observed in Figure 2.59. Therefore, only the corrected interpretation of the SERA dose-volume data with a $-5\%$ shift in dose will be included in subsequent figures, where it will be labeled as such.

The corresponding mean, minimum, and maximum total weighted brain doses are shown in Table 2.5. Data for MacNCTPlan is not listed because the code does not report this information. The agreement with the reference in both Figure 2.59 and Table 2.5 is consistent with the trends identified when evaluating the other forms of dose data. BNCT_Rtpe and SERA generally overestimate the reference whereas MacNCTPlan and NCTPlan generally underestimate, and SERA and NCTPlan generally produce better agreement than their respective predecessors. In Table 2.5, maximum brain doses for BNCT_Rtpe, SERA, and NCTPlan differ from the reference by 5.7\%, 4.0\%, and $-5.3\%$, respectively, which is consistent with the agreement observed in the total weighted dose
profiles (refer to Figure 2.38). In Figure 2.59, BNCT_Rtpe, SERA, MacNCTPlan, and NCTPlan produce $V_8$ brain volume fractions of 10.0%, 11.1%, 6.0%, and 7.0%, respectively. When compared to the reference $V_8$ of 8.6%, BNCT_Rtpe, SERA, MacNCTPlan, and NCTPlan result in differences of 16.7%, 29.2%, −29.9%, and −18.2%, respectively. When the same SERA dose-volume data are interpreted differently than seraPlot and re-plotted correctly, the resulting DVH produces a $V_8$ volume fraction of 9.3% which overestimates the reference value by only 8.9% and represents much improved agreement from the seraPlan interpretation. Both BNCT_Rtpe and MacNCTPlan produce improved agreement at higher doses and lower volumes whereas SERA and NCTPlan produce relatively consistent agreement across a range of doses. SERA produces better agreement than BNCT_Rtpe because of improvements in modeling technique (i.e., univels vs. NURBS) that result in a more accurate model of the phantom for both transport and DVH calculations. While MacNCTPlan and NCTPlan employ the same modeling technique, their DVH algorithms are different. MacNCTPlan’s rather simplistic DVH algorithm results in large disagreement whereas the clearly significant algorithmic improvements made in NCTPlan are largely responsible for the better agreement.

Figure 2.60 shows the total biologically weighted dose-volume histograms for tumor resulting from a 1-field irradiation of the head phantom for 3.16 minutes. The corresponding dose statistics are shown in Table 2.5 where BNCT_Rtpe, SERA, and NCTPlan minimum tumor doses differ from the reference by 14%, 3.5%, and −6.5%, respectively. Overall, the agreement shown in Figure 2.60 is similar to that observed for brain. BNCT_Rtpe and SERA on average overestimate the reference dose delivered to a
given volume of tumor by ~6.5% and ~4.5%, respectively, while NCTPlan consistently underestimates the reference doses by ~4%. At low doses, MacNCTPlan underestimates the reference by 10-15%, but the agreement improves significantly to within 2-4% at higher doses and small volumes.

The total biologically weighted dose-volume histograms for brain resulting from a 3-field irradiation of the head phantom for a total of 5.66 minutes are shown in Figure 2.61. The corresponding dose statistics are reported in Table 2.6 where maximum brain doses for BNCT_Rtpe, SERA, and NCTPlan differ from the reference by 5.8%, 3.2%, and ~5.9%, respectively. These maximum brain doses indicate agreement similar to that observed for the 1-field DVH. The V₈ brain volume fractions produced by BNCT_Rtpe, SERA, MacNCTPlan and NCTPlan are read from Figure 2.61 to be 21.4%, 17.9%, 11.0%, and 12.0%, respectively. When compared to the reference value of 15.2%, the differences for BNCT_Rtpe, SERA, MacNCTPlan and NCTPlan are calculated to be 40.5%, 17.6%, −27.6%, and −21.4%, respectively. The agreement for BNCT_Rtpe and SERA is significantly worse than observed for the for 1-field irradiation. Closer examination of the reference DVH in Figure 2.61 reveals a bend in the reference histogram at ~8 Gyₑ that the coarse BNCT_Rtpe and SERA dose-volume data (the default 10% dose bins were used) are not able to accurately match, which results a large overestimation of the V₈ volume fraction. Otherwise, SERA and NCTPlan again produce rather consistent agreement (approximately 2.2% and −5.5%, respectively) in dose in Figure 2.61. BNCT_Rtpe overestimates the reference doses at low doses by 10-14%, but the agreement improves to ~6.5% at higher doses, which is similar to the behavior observed for a 1-field irradiation. At low doses and large volumes, MacNCTPlan
significant underestimates the references doses by more than 25%, but the agreement improves significantly, to within 5-8%, at doses above 6 Gy\textsubscript{w}. While MacNCTPlan is observed to underestimate the total weighted reference isodose contours in Figure 2.53, the disagreement is significantly less than 25%. Therefore, the large disagreement observed in the dose-volume data is an artifact of MacNCTPlan’s simplistic DVH algorithm.

Figure 2.62 shows the total biologically weighted dose-volume histograms for tumor resulting from a 3-field irradiation of the head phantom for a total of 5.66 minutes. The corresponding dose statistics are listed in Table 2.6 where BNCT\textsubscript{Rtpe}, SERA, and NCTPlan minimum tumor doses differ from the reference by 11%, 4.4%, and −4.2%, respectively. Overall, the agreement observed for each TPS in Figure 2.62 is similar to that produced when comparing tumor dose-volume data from a 1-field irradiation. BNCT\textsubscript{Rtpe} and SERA consistently overestimate the reference doses delivered to a given tumor volume fraction by 6.5-7.5% and 3.3-5%, respectively. At low tumor doses, MacNCTPlan and NCTPlan underestimate the reference by 6-7.5% and 4.5%, respectively, which represents an improvement for MacNCTPlan from the 1-field DVH. At higher doses, the agreement for MacNCTPlan improves to within −4% whereas NCTPlan’s agreement does not change significantly.
Table 2.5  Total biologically weighted dose statistics in Gy<sub>w</sub> for brain and tumor resulting from a single-field irradiation of the head phantom with the generic epithermal neutron beam for 3.16 minutes.

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Table 2.6  Total biologically weighted dose statistics in Gy<sub>w</sub> for brain and tumor resulting from a 3-field irradiation of the head phantom with the generic epithermal neutron beam for 5.66 minutes.

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Figure 2.59  Total biologically weighted dose-volume histograms for brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. The default output from seraPlot is shown along with a corrected interpretation of the SERA dose-volume data (with a −5% shift in dose).
Figure 2.60  Total biologically weighted dose-volume histograms for the brain tumor for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.
Figure 2.61  Total biologically weighted dose-volume histograms for brain for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.
Figure 2.62 Total biologically weighted dose-volume histograms for the brain tumor for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.
2.3.3.2 Leg Phantom

This section reports the comparison of dose-volume data from each TPS with the reference for the skin and both tumors in the leg phantom. For all of the dose components, refer to section A.5.2 of Appendix A.

2.3.3.2.1 Skin

The total biologically weighted dose-volume histograms for skin resulting from a 3-field irradiation of the leg phantom for 1.38 minutes are shown in Figure 2.63. It should be noted that the DVHs are only for skin in the treated volume which is bounded axially within 6 cm of the beam central axis. Also, MacNCTPlan and NCTPlan are omitted from the comparison because neither was able to accurately calculate dose-volume data for concave regions like skin. In the Harvard-MIT clinical trials of BNCT for intracranial disease using the fission converter beam, the biologically weighted dose at 5 mm depth along the central beam axis was recorded as the maximum skin dose, so that method was repeated for the leg phantom. The MacNCTPlan and NCTPlan total biologically weighted dose rates at 5 mm depth were read from Figure 2.45 and multiplied by the reference treatment time of 1.38 minutes. The resulting values as well as the other dose statistics for skin are shown in Table 2.7 where the BNCT_Rtpe, SERA, MacNCTPlan, and NCTPlan maximum skin doses differ from the reference by 5.7%, 6.6%, −5.4%, and −10%, respectively. In Figure 2.63, the conventional representation of the reference dose-volume data is not entirely smooth but rather exhibits some waviness (e.g., at ~12 Gy) because the cylindrical scoring mesh used in the reference calculations did not consist of uniform tally volumes. The scoring mesh was intentionally made finer in the high dose region to better handle the high dose gradient and coarser in the low dose regions to improve dose statistics on the contralateral side of the phantom. Both BNCT_Rtpe and
SERA produce significant disagreement at low doses with both underestimating the reference by as much as $-48\%$ and $-18\%$, respectively, but agreement improves significantly to within $10\%$ for doses above $11 \text{ Gy}_w$. It is also worth noting that the maximum incident photon dose to skin reported by SERA was nearly $7\times$ larger than the reference value ($0.75 \text{ Gy vs. } 0.11 \text{ Gy}$; refer to Table A.31) which suggests a potential problem with SERA’s custom 3D dose interpolation algorithm and steep dose gradients much like that which produced the “horns” in the incident photon isodose contours in Figure 2.48. Nevertheless, while the agreement for skin DVHs is not excellent, it is good given that BNCT_Rtpe and SERA use dose interpolated from a mesh of $1 \text{ cm}^3$ tally volumes to estimate the dose in the $2 \text{ mm}$ thick layer of skin.

2.3.3.2.2 Tumor 1 (spherical tumor)

Figure 2.64 shows the total biologically weighted dose-volume histograms for tumor 1 (i.e., the spherical tumor) resulting from a 1-field irradiation of the leg phantom for 1.38 minutes. The corresponding dose statistics are shown in Table 2.7 where minimum tumor doses for BNCT_Rtpe, SERA, and NCTPlan differ from the reference by $9.9\%$, $7.9\%$, and $1.0\%$, respectively. In Figure 2.64, BNCT_Rtpe overestimates the reference DVH doses by as much as $12\%$ at lower doses, but the agreement steadily improves to $2.3\%$ at high doses and small volumes. SERA produces slightly better agreement by overestimating the reference by $6\text{-}10\%$ at smaller doses to actually underestimating the reference by $1.5\%$ at the highest doses. These observations are consistent with the agreement observed in the 2D boron difference distributions in Figure 2.56 where both BNCT_Rtpe and SERA underestimate the reference boron in the high dose region of the tumor and overestimate the reference doses in the low dose region of
the tumor. Since the minimum tumor dose occurs on the deep side of the tumor, BNCT_Rtpe and SERA overestimate the reference minimum tumor dose in Table 2.7. Similarly, in Figure 2.56, MacNCTPlan underestimates the reference boron dose on the shallow or high dose side of the tumor and overestimates the reference dose on the deep side or low dose side. Therefore, MacNCTPlan overestimates the reference doses by as much as 7% at lower doses and underestimates the reference at the higher doses by as much as 9%, which when combined results in a much steeper DVH than the reference. NCTPlan does not overestimate the reference on the deep or low dose side of the tumor in Figure 2.56, so it produces a very good estimate of the reference minimum tumor dose in Table 2.7. However, NCTPlan does underestimate the reference doses on the high dose side of the tumor, which produces the disagreement in the dose-volume data, as much as −12% in Figure 2.64, observed at high doses.

2.3.3.2.3 Tumor 2 (arc-shaped tumor)

The total biologically weighted dose-volume histograms for tumor 2 (i.e., arc-shaped tumor) resulting from a 1-field irradiation of the leg phantom for 1.38 minutes are shown in Figure 2.65. The corresponding dose statistics are reported in Table 2.7 where BNCT_Rtpe, SERA, and NCTPlan minimum tumor doses differ from the reference by 8.0%, 4.5%, and −8.4%, respectively. Due partially to the improper scaling of the boron doses, both BNCT_Rtpe and SERA overestimate the references doses on the deep side of the tumor in Figure 2.56. Therefore, both BNCT_Rtpe and SERA overestimate the minimum reference tumor dose as well as the DVH doses for large volumes by 10-12% and 6-8%, respectively. Agreement improves for both TPSs at higher DVH doses and smaller tumor volumes to within 2-5%. The agreement is clearly worse for MacNCTPlan
and NCTPlan. In Figure 2.56, the arc-shaped tumor is almost completely enclosed within a region of significant underestimation where disagreement reaches $-25\%$ and $-17\%$ for MacNCTPlan and NCTPlan, respectively. Therefore, the disagreement in the corresponding dose-volume data for that tumor is not particularly surprising. MacNCTPlan underestimates the references doses for large tumor volumes in excess of 40%, but agreement improves at higher doses to within 10-15%. NCTPlan consistently underestimates by the reference DVH doses by 10-13%.

The level of agreement observed for the subcutaneous tumors is significantly worse for all TPSs than observed for the brain tumor in Figure 2.59 because the brain tumor was positioned deep enough in the head phantom to avoid the region of significant disagreement near the phantom surface where, in the thermal neutron beam, the dose gradients are even steeper. On the other hand, the superficial location of all of the structures of interest in the leg phantom exposed those regions to the significant disagreement at shallow depths that resulted from a combination of excessively large tally volumes, interpolation error, and geometric approximations (from coarse MacNCTPlan and NCTPlan voxel models).
Table 2.7 Total biologically weighted dose statistics in Gy$_w$ for skin, tumor 1 (spherical), and tumor 2 (arc-shaped) resulting from a 1-field irradiation of the leg phantom with a thermal neutron beam for 1.38 minutes. Maximum skin doses for MacNCTPlan and NCTPlan were recorded at a depth of 5 mm on the central beam axis.

<table>
<thead>
<tr>
<th></th>
<th>Dose (Gy$_w$)</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>minimum</td>
<td>maximum</td>
</tr>
<tr>
<td>Skin</td>
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<td></td>
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</tr>
<tr>
<td>Reference</td>
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</tr>
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<td>----</td>
<td>12.69</td>
</tr>
<tr>
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<td>----</td>
<td>----</td>
<td>12.07</td>
</tr>
<tr>
<td>Tumor 1</td>
<td></td>
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<td></td>
</tr>
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<tr>
<td>Tumor 2</td>
<td></td>
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</tr>
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<tr>
<td>NCTPlan</td>
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<td>23.10</td>
<td>37.86</td>
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</table>
Figure 2.63  Total biologically weighted dose-volume histograms for skin for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.
Figure 2.64  Total biologically weighted dose-volume histograms for tumor 1 (spherical tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.
Figure 2.65  Total biologically weighted dose-volume histograms for tumor 2 (arc-shaped tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.
2.4 Discussion

This analysis has uncovered a number of differences between planning systems and specific issues with individual planning systems, some new and some previously reported. Many of the differences are clinically significant and some are quite surprising. A number of factors may have contributed to these findings. The TPSs used in BNCT are not commercial software packages but are research software with very small user bases and are usually developed by small teams of physicists, engineers, and sometimes students with very limited budgets. All current BNCT TPSs use Monte Carlo algorithms, which are widely regarded as the most accurate method available for dose calculation. Monte Carlo dose calculations, however, are not inherently accurate, meaning that the particular software implementation must be properly tested to prevent or correct subtle problems that frequently arise during the software development process. Statistical error in Monte Carlo calculations may have masked some issues; the computational power available to rapidly provide results with very low uncertainties in this study has not always been available.

The many deviations from the reference data encountered in this study underscore the importance of understanding differences between planning systems before clinical dosimetry from different institutions can be legitimately compared. These results also emphasize the value and utility of such a reference data set during the TPS development process. Many of the issues with the TPSs uncovered in this study could have been easily detected and eliminated early in the development process if this suite of test problems and reference data had been available. We hope that the availability of the reference data
from this suite of test problems will help to improve the accuracy and uniformity of BNCT planning systems.

All of the TPSs produce data deviating from the reference. While fully understanding the causes behind such deviations is indeed important, the clinical significance of the observed differences between the TPSs and the reference calculations also needs to be properly addressed. The significance of the differences depends at least partially on the measured quantity used to calibrate the planning system because some differences will “cancel out” when the TPS is calibrated to measurements while others will persist. Since the observed disagreement is actually the sum of differences from several different sources, especially for BNCT_Rtpe and SERA, calibrating the planning system cannot possibly eliminate them all. For instance, calibrating BNCT_Rtpe or SERA to physical dosimetry measurements of thermal neutron flux (as appears to be done quite frequently;\textsuperscript{13,61} refer to Chapter 3) will not correct for the improper multiplication of neutron and boron dose rates by the mass density of the edit mesh material. Therefore, even if the planning system is tuned to produce good agreement with measurements of thermal neutron flux, differences in calculated dose will persist. If, however, BNCT_Rtpe and SERA are calibrated to the neutron or boron dose, those differences will be eliminated, at least for planning calculations with the same edit mesh material density. This observation underscores the importance of calibrating treatment planning systems using dose, which is a more clinically relevant quantity, rather than relying on thermal neutron flux for calibration. Nevertheless, tuning the planning system to the improperly multiplied neutron or boron doses will likewise produce worse agreement in thermal neutron flux and the induced photon dose. Some sources of
disagreement will persist regardless of how the planning systems are calibrated. Differences due to interpolation error or erroneous kerma factors (e.g., BNCT_Rtpe photon kerma factors) or geometric approximations cannot be eliminated by tuning the planning system because the disagreement they produce is not constant but rather dependent on the specific details of the treatment planning calculations. Other sources of disagreement, such as that produced by the fast neutron source biasing mode in BNCT_Rtpe and SERA or the systematic shift of DVH data by seraPlot, can indeed be avoided simply by being aware that they do exist and then taking the steps necessary to prevent them. will not correct for the improper multiplication of neutron and boron dose rates by the mass density of the edit mesh material. Therefore, even if the planning system is tuned to produce good agreement with measurements of thermal neutron flux, differences in calculated dose will persist. If, however, BNCT_Rtpe and SERA are calibrated to the neutron or boron dose, those differences will be eliminated, at least for planning calculations with the same edit mesh material density. This observation underscores the importance of calibrating treatment planning systems using dose, which is a more clinically relevant quantity, rather than relying on thermal neutron flux for calibration. Nevertheless, tuning the planning system to the improperly multiplied neutron or boron doses will likewise produce worse agreement in thermal neutron flux and the induced photon dose. Some sources of disagreement will persist regardless of how the planning systems are calibrated. Differences due to interpolation error or erroneous kerma factors (e.g., BNCT_Rtpe photon kerma factors) or geometric approximations cannot be eliminated by tuning the planning system because the disagreement they produce is not constant but rather dependent on the specific details of
the treatment planning calculations. Other sources of disagreement, such as that produced by the fast neutron source biasing mode in BNCT_Rtpe and SERA or the systematic shift of DVH data by seraPlot, can indeed be avoided simply by being aware that they do exist and then taking the steps necessary to prevent them.

More realistic beams, such as the MIT fission converter beam (FCB)\textsuperscript{62,63}, and transport geometries, such as the RANDO\textsuperscript{®} anthropomorphic phantom (The Phantom Laboratory, Salem, NY), were considered for inclusion in the reference problems but were ultimately excluded in favor of more simplistic phantoms and neutron beam spectra. Many differences between planning systems and problems with individual planning systems were discovered using the simple phantoms and beams in this study. Using more realistic phantoms and beams would, in our view, make evaluation and interpretation of the results more difficult. Comparisons using more realistic beams and phantoms are useful and important, but only after more fundamental evaluations are performed, as in this study. One of the conclusions reached in Chapter 5 was that the only way to accurately model the complex 5-dimensional probability distribution describing the spatial, energy, and angular characteristics of a radiation beam like the FCB was to use a patched version of the Monte Carlo transport code or a phase space file. However, neither of those methods was feasible for BNCT_Rtpe or SERA, so it would have been nearly impossible to accurately model a clinical beam like the FCB in those TPSs. Also, comparing calculations to only physical dosimetry measurements severely limits the types of dose data that can be compared. So, using a well-benchmarked Monte Carlo code like MCNP5 as the reference allowed more flexibility in the types of reference dose data that could be calculated and thus enabled a more in-depth and clinically relevant
comparison. Other phantoms were considered as was using actual image data of human anatomy, but it would have been very difficult to investigate the effects of geometric approximations since such anatomy could not be modeled for the reference transport calculations without introducing such approximations.

It was initially intended that electron transport would be included in the reference dose calculations, but doing so proved to be difficult. Mesh tallies and the ability to tally independently from the transport geometry were absolutely essential to the reference calculations, but MCNP5 v. 1.40 unfortunately lacked the ability to tally dose from electrons with a mesh tally. Therefore, MCNPX v2.6.a	extsuperscript{64} was investigated as a possible solution as it did include such functionality. However, it was discovered during initial simulations that MCNPX mesh tallies produced wrong answers if the boundary of a mesh element coincided with that of an internal geometry boundary. Therefore, the only other option was to write a custom tally routine for MCNP5, and that is beyond the scope of this work.

During the comparison of multi-dimensional dose data, it was made clear that 1 cm	extsuperscript{3} volumes are insufficient for both a scoring mesh and a voxel model. There was indeed a time when using a relatively coarse mesh was required because the computational resources available could not achieve the desired level of uncertainty in smaller tally volumes within a reasonable period of time. However, with the computational resources currently available for treatment planning calculations, that limitation no longer exists, so smaller tally volumes and a finer voxel model	extsuperscript{11,65} have been and should continue to be implemented to achieve more accurate models of the patient anatomy and improved dose calculations.
2.5 Conclusions

The pre-existing suite of reference dosimetry calculations\textsuperscript{14} has been extended to include multiple phantoms, neutron beam spectra, and multi-dimensional dose data relevant to BNCT treatment planning. The resulting suite of reference data were used as a basis of comparison for four BNCT treatment planning systems: BNCT\textsubscript{Rtpe}, SERA, MacNCTPlan, and NCTPlan. All 4 planning systems deviated significantly from the reference calculations with SERA and NCTPlan generally producing better agreement than their respective predecessors, BNCT\textsubscript{Rtpe} and MacNCTPlan. Additional effort was focused on understanding and explaining the causes of the disagreement observed. Other BNCT treatment planning systems could easily be analyzed once they become available. This intercomparison of planning systems begins to address the obstacles in computational dosimetry that prevent the legitimate pooling of BNCT clinical outcomes while also providing a quality assurance tool for existing and future treatment planning systems.
2.6 References


9. S.J. González, G.A. Santa Cruz, W.S. Kiger III, M.R. Palmer, P.M. Busse, and R.G. Zamenhof, “NCTPlan, the New PC version of MacNCTPlan: Improvements and Verification of a BNCT Treatment Planning System,” in *Research and


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3.0 Abstract

A combined 81 brain tumor patients have been treated in dose escalation trials of Neutron Capture Therapy (NCT) in the USA at Harvard-Massachusetts Institute of Technology (MIT) and Brookhaven National Laboratory (BNL). Pooling the clinical outcomes from these trials will allow the evaluation of the safety and efficacy of NCT with more statistical rigor. However, differences in physical and computational dosimetry between the institutions that make a direct comparison of the clinical dosimetry difficult must first be addressed before clinical data can be compared. This chapter describes work performed to normalize the BNL clinical dosimetry to that of Harvard-MIT for combined NCT dose response analysis. This normalization involved analysis of MIT measurements and calculations using the BNL treatment planning system (TPS), BNCT_Rtpe, for two different phantoms. The BNL TPS was calibrated to dose measurements made by MIT at the Brookhaven Medical Research Reactor (BMRR) in the BNL calibration phantom, a Lucite cube, and then validated by MIT dose measurements at the BMMR in an
ellipsoidal water phantom. Using the newly determined TPS calibration, treatment plans for all BNL patients were recomputed, yielding reductions in reported mean brain doses of 10% on average in the initial 15 patients treated with the 8 cm collimator and 27% in the latter 38 patients treated with a 12 cm collimator. These reductions in reported doses have clinically significant implications for those relying on reported BNL doses as a basis for initial dose selection in clinical studies and reaffirm the importance of collaborative dosimetric comparisons within the NCT community.

3.1 Introduction

Given the considerable expense and time required to conduct trials of BNCT along with the understanding that the number of patients having been treated with Boron Neutron Capture Therapy (BNCT) at the various sites in the Americas, Europe, and Asia is steadily growing, it would indeed be advantageous to be able to pool the clinical outcomes from different sites together so the safety and efficacy of BNCT could be analyzed in much greater detail. However, significant differences in the physical and computational dosimetry such as differences in dose measurement techniques, treatment planning codes, and methods of dose prescription impede direct comparisons of clinical results. Nevertheless, significant steps have been taken to properly address these differences in dosimetry,\textsuperscript{1-3} and these efforts form the foundation for the work described in this chapter.

In order to better understand the differences in dose measurement techniques, Massachusetts Institute of Technology (MIT) made measurements of thermal neutron flux, fast neutron dose rate, and photon dose rate at the Brookhaven Medical Research
Reactor (BMRR) in both the Brookhaven National Laboratory (BNL) and MIT calibration phantoms: a 14×14×14 cm Lucite cube and an ellipsoidal head phantom, respectively. These MIT measurements in the BNL beam and calibration phantom are essential to any retrospective analysis attempting to compare patient doses from the two clinical sites. This dosimetric comparison between BNL and MIT was later expanded to include clinical sites in Europe as part of the International Dosimetry Exchange. A similar collaboration was necessary to properly analyze differences in computational dosimetry. Using the physical dosimetry measurements made by MIT at the different clinical sites and treatment plans produced by each group, scale factors were calculated to normalize the clinical dosimetry at each site to that of Harvard-MIT.

Similarly, this chapter describes the normalization of the BNL clinical dosimetry to that of Harvard-MIT. Using the MIT measurements made at BNL in the Lucite cube calibration phantom as well as the corresponding calculations performed using the BNL treatment planning system, dose component scale factors were derived to determine the relationship between the patient doses reported by BNL and doses measured by MIT. These scale factors were then applied to calculations of dose in the ellipsoidal head phantom and compared to MIT measurements in order to confirm that the scale factors are valid for phantoms (and patients) other than the BNL cube phantom in which they were derived. After using these scale factors to recompute BNL patient doses, the revised BNL clinical data were pooled with those of Harvard-MIT for a combined dose response analysis.
3.1.1 Clinical Trials of BNCT in the USA

3.1.1.1 Brookhaven National Laboratory

Between 1994 and 1999, 54 brain tumor patients were treated in dose escalation trials at BNL.6-8 During the clinical trials, patients diagnosed with glioblastoma multiforme (GBM) were treated in a series of dose escalation protocols via boronophenylalanine-fructose (BPA-F) mediated NCT with epithermal neutrons delivered at the BMRR in 1 or 2 fractions with between 1 and 3 fields. The BPA-F was infused over 2 hours at doses ranging from 250 to 355 mg/kg. Treatment planning at BNL was performed using the Monte Carlo-based BNCT_Rtpe (BNCT Radiation Therapy Planning Environment)9-11 planning system developed at Idaho National Laboratory (INL). For calibration of the treatment planning system, measurements of thermal neutron flux via Au foil activation analysis, and photon dose rate with thermoluminescent dosimeters (TLDs) were made in the BNL Lucite cube phantom and measurements of the fast neutron dose rate via the dual chamber technique were made in-air.3,12 In addition to calibration measurements, monthly measurements of thermal neutron flux and photon dose rate were made in the same cube phantom as part of the quality assurance (QA) protocol at BNL. During the clinical trials at BNL, two significant changes were made to the epithermal neutron beam at the Brookhaven Medical Research Reactor: the 8 cm collimator was replaced with a 12 cm collimator in 199612 and the fuel elements were rearranged in 1998 to increase neutron beam intensity. The first 15 patients were treated with the 8 cm collimator and the latter 39 were treated with the 12 cm collimator: 23 before the fuel shuffle and 16 afterwards. The workstation used at BNL for treatment planning as well as records of the BNL QA measurements were moved to MIT and used for this analysis.
3.1.1.2 Harvard-MIT

Between 1994 and 2003, 27 patients were treated for intracranial disease in dose escalation trials of NCT at Harvard-MIT.\textsuperscript{13-15} Patients with either GBM or intracranial melanoma metastases were treated with BPA-F mediated NCT with the epithermal neutrons delivered by either the MIT M67 thermal beam\textsuperscript{16} or the MIT fission converter beam (FCB)\textsuperscript{17} in 1 or 2 fractions with between 1 and 3 fields. The BPA-F was infused over 1-1.5 hours at doses ranging from 250 to 350 mg/kg or 14.0 g/m\textsuperscript{2}.\textsuperscript{18,19} Planning for the Harvard-MIT patients was performed using MacNCTPlan\textsuperscript{20} and its successor NCTPlan\textsuperscript{4,21} that were developed in-house or in collaboration with the Comisión Nacional de Energía Atómica (CNEA) of Argentina, respectively. The planning system was calibrated for each beam in an ellipsoidal head phantom\textsuperscript{22} using measurements of thermal neutron flux made with Au foil activation analysis using the cadmium difference method\textsuperscript{23} as well as measurements of fast neutron and photon dose rates made using the dual chamber technique.\textsuperscript{24,25} Planning system calculations for the FCB were also validated using measurements on multiple axes in a large rectangular water phantom.\textsuperscript{26} For the Harvard-MIT clinical trials, 21 patients were treated with the MIT M67 beam and 6 with the MIT FCB.

3.2 Methods and Materials

3.2.1 Normalization of Clinical Dosimetry

Normalization of the BNL and Harvard-MIT clinical dosimetry involved the determination of dose scale factors to account for the differences in physical and computational dosimetry and convert doses reported by BNL to doses reported by MIT.
These scale factors were derived through analysis of the MIT measurements made at the BMRR\textsuperscript{3} and comparison with calculations performed by the treatment planning system used at BNL, BNCT\textsubscript{Rtpe}.

MIT measurements of the 2200 m/s (0.025 eV) neutron flux in the BNL cube phantom and ellipsoidal head phantom were converted to boron and thermal neutron dose using the kerma factors\textsuperscript{27} of $8.67 \times 10^{-14}$ Gy cm\(^2\) and $1.79 \times 10^{-13}$ Gy cm\(^2\), respectively. The \(^{10}\text{B}\) kerma factor corresponds to a \(^{10}\text{B}\) concentration of 1 \(\mu\text{g/g}\). The thermal neutron kerma factor was calculated for ICRU 46\textsuperscript{28} adult whole brain composition which has a density of 1.04 g/cm\(^3\) and has a \(^{14}\text{N}\) concentration of 2.2% by mass. In addition to these measurements of boron and thermal neutron dose, MIT measurements of in-air and in-phantom photon and fast neutron dose in the cube phantom were used to determine the scaling of the fast neutron, incident and induced photon dose components.

The MIT measurement conditions were modeled in BNCT\textsubscript{Rtpe} using BNL’s most up-to-date source definition for the BMRR epithermal beam and a NURBS (Non-Uniform Rational B-Splines) model of the BNL cube phantom. The NURBS modeling technique is needed to accurately model the irregular shapes of the human anatomy like the skin, skull, tumor, etc. In BNL’s original calibration calculations, the cube phantom was modeled in BNCT\textsubscript{Rtpe} using simple geometric primitives and combinatorial geometry (CG), but a NURBS model of the cube was chosen for this analysis since it is the modeling technique used in patient planning. Moreover, when reviewing the original BNCT\textsubscript{Rtpe} calibration simulations, a subtle geometric error in the modeling of the BMRR 12 cm diameter collimator assembly with the CG cube phantom was discovered. The full 13.32 cm thickness of the lithiated-polyethylene collimator was truncated at a
thickness of 8 cm, with the other 5.32 cm modeled as vacuum. Figure 3.1 illustrates the difference between the collimator assembly modeled in the original calibration simulations with a CG cube and that used in patient treatment planning with a NURBS model of a patient. To determine the effect of this modeling error on the TPS calibration, in-phantom doses calculated using the correct model of the NURBS cube were least squares fit to doses calculated using the cropped collimator and the CG cube. This error was not present in the earlier calibration calculations using the 8 cm diameter collimator assembly nor was it present in the patient planning calculations. The atomic densities for $^{10}\text{B}$ ($6.01\times10^{-8}$ atoms/barn cm or 1 $\mu$g/g), hydrogen ($6.32\times10^{-2}$ atoms/barn cm or 10.7% by mass) and nitrogen ($7.91\times10^{-4}$ atoms/barn cm or 1.84% by mass) that are used solely to scale the elemental kerma factors for dose calculations were the same as used in BNL’s patient planning calculations. 50 million neutron and photon histories were tracked for the calibration calculations and $^{10}\text{B}$, thermal and fast neutron, and incident and induced photon doses were calculated at depths in the phantom corresponding to the MIT measured values. Incident photon and fast neutron doses were also calculated in-air. Least squares fitting the resulting BNCT_Rtpe calculations in the cube phantom to the MIT measurements produced individual scaling factors for each of the computed dose components. These dose component scaling factors were then validated by applying them to similar BNCT_Rtpe calculations of dose along the central axis in the MIT calibration phantom, the ellipsoidal head phantom (modeled in BNCT_Rtpe using NURBS), and comparing the scaled calculations to corresponding MIT measurements made at the BMRR.
Figure 3.1 Comparison of (annotated) BNCT_Rtpe raster images of the 12 cm BMRR collimator used to calibrate the treatment planning system and to calculate patient doses for planning. The collimator modeled in the TPS calibration (left) using the Lucite cube phantom was not as thick and provided less beam collimation and thus yielded lower calculated in-phantom doses. The effect of calibrating the TPS in this configuration is to overestimate doses in the patient (right), where a thicker collimator was used.

Due to changes made at the BMRR during the clinical trials, these dose scale factors were not applicable to all of the BNL patients but rather only to those 16 patients treated under irradiation conditions similar to when the MIT measurements were made, i.e., with the 12 cm collimator after the fuel element shuffle. The effects of the fuel element shuffle on patient dose had to be properly assessed as part of the retrospective analysis. Since the available BNL measurement data made after the shuffle were limited to the monthly QA measurements, averages of the thermal neutron flux and photon dose rate from these monthly measurements at two depths (3.5 and 7.0 cm) and 3 axes positions (central beam axis and 2 lateral axes) were calculated and least squares fit to BNL measurements\textsuperscript{12} made prior to the fuel element shuffle. The resulting adjustments were applied to the neutron and photon dose scaling components to account for changes.
caused by the fuel shuffle, producing a new set of dose scaling factors for the patients treated with the 12 cm diameter collimator and before the fuel rod shuffle in 1998. This adjusted set of dose scaling factors was also applied to the 8 cm collimator patients, since no changes upstream of the collimator were made. However, before the scale factors could be applied to the 8 cm collimator patients, the contribution from the collimator modeling error had to be removed since it was not present for those patients.

3.2.2 Updates to the BNL Treatment Planning System

The treatment plans for all BNL patients were recomputed with the newly determined and validated TPS calibration that provided corrected doses calibrated to Harvard-MIT clinical dosimetry. However, adjustments to the BNL patient treatment planning data were not limited only to the dose scale factors. The specialized Monte Carlo transport module of BNCT_Rtpe, rtt_MC, was ported to run on x86 Linux so that better statistics could be rapidly achieved by running more particle histories on newer computer hardware. With the capability to run faster, the number of neutron and photon histories simulated, originally 0.5 to 1.0 million, was increased to 15 million histories per field, significantly reducing the statistical uncertainty of the calculated doses. To avoid the repetition of particle histories that could occur if the period of the random number generator is exceeded, the random number generator used by rtt_MC\textsuperscript{29} in the Monte Carlo transport calculations, which has a period of \(\sim 500\) million,\textsuperscript{30} was replaced with the Modified Lagged Fibonacci generator that is part of the Scalable Parallel Random Number Generators (SPRNG)\textsuperscript{31} library v. 2.0 and has a period of \(\sim 10^{394}\) random numbers. The photon kerma factors used by BNCT_Rtpe to calculate photon doses were replaced with those updated values used in its successor, SERA (Simulated Environment for
BNCT_Rtpe assigns a point kerma value of $9.58 \times 10^{-12} \text{ Gy cm}^2$ to those 2.2 MeV photons resulting from the $^1\text{H}(n,\gamma)^1\text{H}$ reaction, and this value was updated to the corresponding value calculated from NIST data$^{33}$ of $8.92 \times 10^{-6} \text{ Gy cm}^2$. The tissue compositions used in the BNCT_Rtpe NURBS model of each patient were updated with a combination of adult whole brain, adult whole cranium, and adult skin materials, as defined by ICRU 46 with $^{10}\text{B}$ concentrations in the brain ($1.0 \times$ blood $[^{10}\text{B}]$), tumor ($3.5 \times$ blood $[^{10}\text{B}]$), and skin ($1.5 \times$ blood $[^{10}\text{B}]$)$^{18,34}$ explicitly modeled in the transport calculations to correctly account for neutron flux depression due to the capture of thermal neutrons by $^{10}\text{B}$ nuclei.$^{35,36}$ Dose-volume histograms for brain, tumor, and target were calculated for each patient, and the weighting factors used in the calculation of total biologically weighted dose were 3.2 for both fast and thermal neutrons, 1.3 for $^{10}\text{B}$, and 1.0 for photons.$^{37}$ These weighting factors are identical to those used for the Harvard-MIT patients with the exception of the photon dose component. For the 21 patients treated with the MIT M67 beam, a dose rate reduction factor of 0.5$^{13}$ was applied to the photon dose component to account for the low dose rate in the M67 beam. The most accurate source model of the BMRR epithermal neutron beam was used for all patients along with the appropriate model of either the 8 or 12 cm collimator assembly.

**3.2.3 Dose Response Analysis**

Once the dose scale factors were applied to the recomputed BNL patient doses, the Harvard-MIT and BNL clinical data were pooled together for a combined dose response analysis of radiation-induced somnolence syndrome. Somnolence syndrome is characterized by an otherwise unexplained fatigue and drowsiness that develops within a few weeks after cranial radiation.$^{38}$ Somnolence is not a dose-limiting toxicity and is
considered to be an acceptable side-effect of radiotherapy. However, somnolence precedes more significant and serious neurological changes that occur at higher doses, such as brain necrosis, which are desirable to avoid. Although somnolence is not a particularly well-defined endpoint, analysis of the somnolence dose response may allow important information on the tolerance of normal brain to NCT to be extracted. The presence or absence of somnolence syndrome for each patient in the combined data set was scored (as a binary endpoint), and probit analysis was performed to determine the dose that results in somnolence in 50% of the patients (effective dose 50% or ED$_{50}$).

### 3.3 Results

MIT dose measurements made in the Lucite cube are shown with the scaled BNCT$_{Rtpe}$ calculations (and scale factors) in Figure 3.2, and the scale factors are also reported in the top section of Table 3.1 in column 2. The scaled calculations of dose rates agree well with measurements and lie within 1 standard deviation of the measured values at nearly all measurement points. For the fast neutron dose component, the calculated values fall within one standard deviation of the measurements at all depths in the BNL cube phantom beyond 1 cm. Due to the large uncertainty (30-100%) associated with the in-phantom fast neutron measurements, the fast neutron scaling factor was determined from the in-air measurement of fast neutron dose where the measurement error was significantly smaller, at 16%. Therefore, the scaled in-air calculation of fast neutron dose lies directly beneath the measured value. Similarly, the scaled in-air incident photon calculation is beneath the measured value. The scaling factors derived in the cube phantom were then applied to BNCT$_{Rtpe}$ calculations in the ellipsoidal head phantom,
and the resulting scaled calculations are compared to MIT measurements in Figure 3.3. Agreement between MIT measurements and the scaled BNCT_Rtpe calculations in the ellipsoidal head phantom is very good.

![Graph showing dose rate vs. depth in BNL Cube Phantom (cm)](image)

**Figure 3.2** BNCT_Rtpe calculations scaled to MIT measurements in the BNL calibration phantom, a Lucite cube. Dose component scaling factors were derived from the least squares fitting of BNCT_Rtpe calculations to MIT measurements. The plotted calculation lines are the product of the scale factors (shown in the legend) and doses calculated by BNCT_Rtpe.
Table 3.1  Dose component scaling factors used to normalize BNL dosimetry to that of Harvard-MIT. The scale factor for each dose component is resolved into 3 contributing components which were derived independently from the total scale factor. Patients were divided into 3 groups based on the changes in beam collimation and rearrangement of the BMRR fuel. A set of dose scaling factors was derived for each group.

<table>
<thead>
<tr>
<th>Dose Component</th>
<th>Scale Factor</th>
<th>Product of Components</th>
<th>Components of scale factor</th>
<th>Difference between BNCT_Rtpe and BNL measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Measurement Techniques</td>
<td>Collimator Error</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 cm collimator after BMRR fuel shuffle (16 patients)</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>boron</td>
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<tr>
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<tr>
<td>fast neutron</td>
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<td>0.59</td>
<td>0.69</td>
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<tr>
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<td>0.93</td>
</tr>
<tr>
<td>induced photon</td>
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<td>0.73</td>
<td>0.85</td>
<td>0.91</td>
</tr>
<tr>
<td>12 cm collimator before BMRR fuel shuffle (23 patients)</td>
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<tr>
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<td>0.77</td>
<td>0.93</td>
<td>0.91</td>
</tr>
<tr>
<td>thermal neutron</td>
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<td>0.94</td>
<td>0.93</td>
<td>0.91</td>
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</tr>
<tr>
<td>incident photon</td>
<td>1.34</td>
<td>1.55</td>
<td>0.85</td>
<td>0.93</td>
</tr>
<tr>
<td>induced photon</td>
<td>0.68</td>
<td>0.69</td>
<td>0.85</td>
<td>0.91</td>
</tr>
<tr>
<td>8 cm collimator (15 patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>boron</td>
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<td>0.83</td>
<td>0.93</td>
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</tr>
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</tr>
<tr>
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</tr>
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<td>1.37</td>
<td>0.85</td>
<td>---</td>
</tr>
<tr>
<td>induced photon</td>
<td>0.74</td>
<td>0.77</td>
<td>0.85</td>
<td>---</td>
</tr>
</tbody>
</table>
Without adjustment, these scale factors are only valid for the last 16 patients treated at BNL due to changes in beam collimation and the fuel element rearrangement at the BMRR during the clinical trials. Thus, to properly address these changes, the BNL patients were grouped according to irradiation conditions, and a unique set of dose component scaling factors was derived and applied to each group. The effect of the fuel element rearrangement in 1998 was found by scaling post-shuffle BNL dose measurements to corresponding pre-shuffle measurements via least squares analysis. The neutron dose component scale factors (derived from MIT measurements after the shuffle)
were scaled by 0.94 while the photon dose scale factors were scaled by 0.97 to account for the effects of the shuffle. The resulting set of scale factors are applicable to those BNL patients treated with the 12 cm collimator before the fuel shuffle and are shown in the middle section of Table 3.1 in column 2. Except for the adjustment due to the modeling error of the 12 cm collimator, this set of scale factors should also be applicable to the patients treated with the 8 cm collimator since no changes were made in the beam line upstream of the collimator, which is modeled in the patient transport calculation as illustrated in Figure 3.1. Therefore, to account for the lack of the collimator modeling error, the scale factors for the 8 cm collimator patients were derived from the scale factors for the 12 cm collimator patients before the fuel shuffle by dividing out the contribution of the collimator error (column 5) to the scale factors. The scale factors for the 8 cm collimator patients are listed in the bottom section of Table 3.1 in column 2.

To further analyze the dose scaling factors, calculations independent from those used to derive the scale factors were performed to resolve each scale factor into 3 component parts: the scaling due to differences in physical dosimetry measurement techniques between BNL and MIT, the scaling due to the collimator modeling error, and the scaling resulting from differences between BNCT_Rtpe calculations and BNL measurements. The scaling due to differences in physical dosimetry was calculated by least squares fitting BNL measurements to MIT measurements made in the BNL Lucite cube under similar irradiation conditions. This component of the scaling was assumed to be constant for all the patients regardless of beam collimation and fuel element arrangement. Similarly, the scaling due to the collimator modeling error was assumed to be unchanged by the fuel shuffle. For the last component of scaling, BNCT_Rtpe
calculations in the BNL cube phantom were least squares fit to the corresponding BNL measurements. The 3 resulting components are listed in the last 3 columns of Table 3.1 under “Components of scale factor” and labeled as “Measurement Techniques”, “Collimator Error”, and “Difference between BNCT_Rtpe and BNL measurements”. The product of these 3 components is also shown in column 3 of Table 3.1 to provide a point of comparison to the independently derived total scale factors shown in column 2. The very good agreement between the total scaling and the product of the 3 components is an important validation of the dose scale factors.

The treatment plan for each BNL patient was recomputed, and the appropriate set of dose scaling factors from Table 3.1 was applied to normalize the patient doses to Harvard-MIT clinical dosimetry. The adjusted mean and maximum brain doses are plotted against the original brain doses in Figure 3.4. The mean brain doses of the initial 15 patients treated with the 8 cm collimator were reduced by 10% while an average reduction of 28% was calculated for the 23 patients treated with the 12 cm collimator before the fuel shuffle and 25% for the 16 patients treated after the fuel shuffle. Corresponding reductions in maximum brain dose of 8%, 26% and 21% were calculated for the same groups of patients. Figure 3.5 shows the component doses for the adjusted average and maximum brain physical doses.

Figure 3.6 compares original and adjusted total biologically weighted brain isodose contours for an example BNL patient treated with 3 fields using the 12 cm diameter collimator after the fuel shuffle. Isodose levels represent a percentage of the total biologically weighted brain dose delivered to the point of maximum thermal neutron flux using the original BNL dosimetry. The 70% contour from the revised dosimetry is
approximately equivalent to the 90% to 95% contours from the original dosimetry which is consistent with the average reduction in mean and maximum brain doses of 25% and 21%, respectively. Figure 3.7 shows original and revised total biologically weighted dose-volume histograms for brain, tumor, and target volumes for the same BNL patient. The reductions in dose are, as expected, quite large.

Once properly normalized with the appropriate set of dose scale factors, the BNL patient dosimetry was compared to the Harvard-MIT patient dosimetry as is done in Figure 3.8, which shows the maximum brain dose vs. the mean brain dose for each patient of the combined data set. Filled symbols in Figure 3.8 indicate those patients who developed radiation-induced somnolence syndrome. Probit analysis was used to construct a dose response curve for the incidence of somnolence syndrome for the combined BNL and Harvard-MIT patient data. The resulting probit curves are shown in Figure 3.9 with ED50 values of 5.76 Gy_w and 14.4 Gy_w for mean and maximum brain dose, respectively. As Figure 3.9 shows graphically, the corresponding 95% confidence intervals for the ED50 values are [5.22 Gy_w, 6.56 Gy_w] and [12.6 Gy_w, 20.3 Gy_w]. The dose response curves for the original and revised BNL mean brain doses are shown in Figure 3.10. Adjusting the BNL dosimetry reduced the ED50 for mean brain dose for the BNL patients by 26%, from 6.42 Gy_w to 4.75 Gy_w.
Figure 3.4 Original vs. revised (a) mean and (b) maximum biologically weighted brain doses for the BNL patients. The solid line represents equality of revised and original dosimetry.
Figure 3.5 Contributions to the adjusted mean and maximum physical brain doses (unweighted) for the BNL patients.
Figure 3.6 Original and revised treatment plans for a BNL patient treated with 3 fields using the 12 cm collimator after the fuel shuffle. The isodose contours are displayed as a percentage of the biologically weighted brain dose in the voxel containing the maximum thermal neutron flux under the original dosimetry (15.6 Gy\textsubscript{w}). The contours were plotted with the BNL treatment planning system, BNCT\_Rtpe.
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Figure 3.7 Original and revised total biologically weighted dose-volume histograms for the brain, tumor, and target volumes of a BNL patient treated with 3 fields using the 12 cm collimator after the fuel shuffle.
Figure 3.8 Maximum brain dose versus mean brain dose for the combined BNL and Harvard-MIT patient data. Filled symbols represent patients that developed radiation-induced somnolence syndrome. The retreatment of 1 previously treated BNL patient as well as the 2 Harvard-MIT patients for which somnolence could not be evaluated due to confounding factors were censored from the analysis.
Figure 3.9  Dose response curves for radiation-induced somnolence for the combined BNL and Harvard-MIT patient data based on the mean or maximum weighted brain dose. The 95% confidence intervals are indicated by the pairs of dashed lines.
3.4 Discussion

The excellent agreement between the adjusted calculations in the ellipsoidal phantom and MIT measurements demonstrates that the dose scale factors (derived in the cube phantom) are not specific to a particular phantom and validates the application of the factors to the BNL patients. The significant deviation of these dose component scale factors from unity was determined to be a result of 3 contributors: differences in measurement techniques between BNL and MIT, a subtle geometric error in some of
BNL’s TPS calibration calculations, and differences between BNCT_Rtpe calculations and BNL measurements.

Differences in physical dosimetry between BNL and MIT, (e.g., BNL’s measurement of the group thermal neutron flux vs. MIT’s measurement of the 2200 m/s neutron flux, the use of TLDs vs. ionization chambers to measure photon dose) were shown to be significant and such differences must be properly addressed when comparing dosimetry from different clinical sites. BNL measurements of photon dose yielded values larger than corresponding MIT measurements by 15% while differences in fast neutron measurements were nearly 30% larger.

Also contributing to the dose component scaling factors was a geometric error in the BNCT_Rtpe model of the 12 cm collimator assembly and the cube phantom used in BNL’s original calibration calculations. The thickness the BMRR collimator assembly was not modeled correctly, which resulted in less collimation of the neutron beam and lower calculated doses in the calibration phantom. Because the beam intensity was increased in the TPS to compensate for the lower doses calculated in the phantom and because the error present in the calibration simulation was absent in patient calculations, the patient doses were overestimated; this factor increases calculated doses by 7-10%. Although the convenience of using combinatorial geometry to represent a phantom in calibration calculations is tempting, it is important to calibrate the treatment planning system under the same computational conditions that are used for patient planning in order to avoid such subtle errors. Calculations of the thermal neutron flux using the cropped 12 cm collimator assembly and the CG cube phantom produced excellent agreement with BNL calculations of thermal flux, as expected since that model was used
in calibrating the planning system. However, when BNL measurements of thermal neutron flux were converted to dose and compared to BNCT_Rtpe calculations, the calculated boron and thermal neutron dose rates were systematically 4% larger than the BNL measurements. This finding, a deviation between calibration to thermal neutron flux and calibration to derived dose rates, confirms that it is more appropriate to calibrate treatment planning systems using dose, which is a more clinically relevant quantity, rather than to rely on thermal neutron flux for calibration.

The scaling factors for the $^{10}$B, thermal neutron, and induced photon dose components should be nearly identical since all depend on the thermal neutron flux. However, the scale factors in column 2 of Table 3.1 seem to differ. The reason that the thermal neutron scale factor is higher than the $^{10}$B scale factor is that the thermal neutron scale factors account for the difference in thermal neutron kerma factors, which primarily is due to the ~20% difference in the $^{14}$N concentration used in clinical treatment planning between Brooks brain composition (1.84%) used for the original BNL treatment planning and ICRU brain composition (2.2%) used for MIT treatment planning. If this difference is removed, then the thermal neutron scale factor is reduced to 0.84, which is close to the $^{10}$B scale factor of 0.82. Similarly, the induced photon scale factor was found to be different from the $^{10}$B scale factor. Differences in photon dose measurement techniques (column 4 of Table 3.1) are larger than the corresponding values for the $^{10}$B and thermal neutron components which results in the total photon scaling being further from unity.

Previous such analyses of the combined Harvard-MIT and BNL clinical data have been reported. However, these analyses did not fully account for all the differences in

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* In Chapter 2, this 4% difference was found to be due to the improper scaling of BNCT_Rtpe neutron and boron dose calculations by the mass density of the edit mesh, which was 1.04 g/cm$^3$ for ICRU adult brain.
the physical and computational dosimetry between the two sites that are included as part of this work. In a previous analysis, all of the dose component scaling factors (0.92, 0.92, 0.73, and 0.74 for boron, thermal neutron, fast neutron, and total photon dose scaling, respectively) were significantly closer to unity than those derived in this work. The 12 cm collimator modeling error had not been discovered at the time of that analysis, so the BNCT_Rtpe simulations that were performed to derive the scaling factors did not contain the modeling error. If the scale factors from that work are multiplied by the collimator error (column 5 of Table 3.1), better agreement in the neutron dose scale factors is produced. However, the total photon dose scale factors from the two analyses will still be different due the different photon kerma factors used in the BNCT_Rtpe simulations. Also, in that analysis a single set of scale factors was applied to all patients, and the patients’ plans were not recomputed with the updates to the BNCT_Rtpe planning system that were an important part of this analysis. Performing the planning calculations again on the original BNL workstation for that analysis would have taken ~280 days whereas porting rtt_MC, the Monte Carlo transport module in BNCT_Rtpe, to x86 Linux allowed the planning calculations for all 54 patients to be completed in ~2 days on an 11 node Beowulf cluster (described in Appendix B). Being able to rapidly compute plans with more histories was a significant advantage in that it allowed for better statistics and much improved convergence of the Monte Carlo dose calculations. The improved dose convergence that directly resulted from simulating 15 to 30 times more neutron and photon histories (5×10^5 or 1×10^6 vs. 1.5×10^7) per field than the original BNL calculations alone (no other corrections) was significant enough to produce

* To be more precise, the collimator modeling error was inadvertently and unknowingly corrected.
biologically weighted reference brain doses as much as 5.1% lower.

In Figure 3.9, the steeper response curve and the smaller confidence interval for the mean dose indicate a stronger correlation between mean brain dose and somnolence than for the maximum brain dose. Analyzing the pooled patient data produced confidence intervals for the ED$_{50}$ values for mean and maximum brain dose that were 3.4 and 1.6 times narrower, respectively, than resulted from analyzing the Harvard-MIT or BNL patient data separately, further illustrating the value of patient pooling when attempting such statistical analysis in NCT.

The work described in this chapter defined a quantitative relationship between treatment plans calculated for BNL patients and doses measured by MIT and used this relationship to make adjustments to clinical doses reported by BNL that are necessary for a combined dose response analysis. The BNL patient dosimetry was normalized to the Harvard-MIT clinical dosimetry (rather than vice versa) because MIT has made dose measurements in 8 of the 11 neutron beams recently used for clinical BNCT with a standard dosimetric approach as part of the International Dosimetry Exchange. Normalizing the BNL clinical dosimetry to that of Harvard-MIT using the derived relationship facilitates the comparison of BNL clinical data not only to Harvard-MIT but also to the other clinical sites. The resulting large reductions in reported doses from the BNL clinical trials of NCT have clinically significant implications for those in the NCT community relying on doses reported by BNL as a basis for initial dose selection in clinical studies. These results also demonstrate the validity of the approach to dosimetric normalization proposed by the International Dosimetry Exchange$^{26}$ and the Treatment Planning Exchange as well as provide an example of what can be achieved within the
framework of such collaborative dosimetric comparisons. These collaborative efforts are designed to address differences in physical and computational dosimetry which impede the analysis and comparison of NCT clinical data from different sites worldwide and provide a dosimetric basis for the collective analysis of clinical data. Furthermore, these findings should provide strong motivation for actively participating in such efforts.

### 3.5 Conclusions

A relationship between BNL clinical dosimetry and Harvard-MIT clinical dosimetry was determined and validated. This relationship was used to adjust the recomputed BNL dosimetry so that it could be legitimately pooled together with Harvard-MIT patient data for a dose response analysis for radiation-induced somnolence syndrome. The BNL patient doses were significantly lowered due to differences in dose measurement techniques between BNL and MIT, a subtle geometric modeling error present in BNL’s calibration calculations, and small differences between BNL's measurements and calibration calculations. The significantly narrower confidence intervals about the resulting ED$_{50}$ values illustrated the importance of pooling dosimetry from different clinical sites as well as participating in those efforts which attempt to facilitate the direct comparison of clinical dosimetry.
3.6 References


Computational Aspects of Treatment Planning for Neutron Capture Therapy


4.0 Abstract

Treatment planning for Neutron Capture Therapy (NCT) most often begins with detailed radiation transport calculations of the beam line to produce a radiation source definition close to the patient position to avoid repeating the computationally expensive calculations of the beam line for each patient. When using Monte Carlo simulations, the difficulty associated with this deep-penetration shielding problem often requires that nonanalog Monte Carlo algorithms, or variance reduction techniques, be used to ensure that enough unique track information reaches the downstream patient position to produce a source representation with good accuracy and precision for the subsequent dose calculations in the patient. This chapter investigates the applicability and optimization of variance reduction for both parts of NCT Monte Carlo treatment planning calculations: calculations of the neutron beam line and the subsequent dose calculations in the patient. During the first phase of this analysis, MCNP was used to improve the pre-existing variance reduction in the Monte Carlo model of the Massachusetts Institute of
Technology (MIT) fission converter beam (FCB) resulting in optimized energy dependent neutron and photon weight windows. A simulation of the FCB beam line with these weight windows using an 11 node Beowulf cluster produced a more precise surface source representation of the FCB downstream at the patient position with improved statistical properties that directly resulted in a $9\times$ increase in the mean efficiency of in-phantom dose calculations. The new surface source model of the FCB was also validated using physical dosimetry measurements in the MIT ellipsoidal head phantom. During the second phase of this analysis, the variance reduction techniques available in MCNP were also explored as a means of increasing the computational efficiency of dose calculations in the patient using a voxel model of the modified Snyder head phantom and a generic epithermal neutron beam. By disabling implicit neutron capture and using fast neutron source biasing and photon production biasing techniques, the mean efficiency of the total weighted brain dose calculations can be improved by a factor of 2.2.

4.1 Introduction

Treatment planning calculations for BNCT are in some ways more complicated than those for conventional radiotherapy since a detailed physics model is required to properly treat the scatter-dominated radiation transport processes and multiple dose components that result. Thus, all current BNCT treatment planning systems use Monte Carlo radiation transport algorithms since they are widely considered to be the most accurate method of calculation available. However, Monte Carlo simulations are computationally intensive, and the precision of the calculated doses depends on the number of particle histories simulated. Because dose targeting in NCT is achieved
through biochemical selectivity of the neutron capture agent rather than through geometric targeting of highly collimated and shaped beams of radiation, epithermal neutron beams generally have few degrees of freedom and a very limited number of configurations. Beam modifying devices are usually limited to a small number of circular collimators or a device that permits insertion of a neutron absorber\textsuperscript{1} or moderator\textsuperscript{2} into the beam to effect a spectrum shift. The very small number of configurations possible with an epithermal neutron beam enables precalculation of radiation sources a short distance from the patient, e.g., as close as 1 cm. In contrast, medical linear accelerators, with their motorized jaws and multileaf collimators, have an extremely large number of possible configurations, effectively preventing precalculation. This approach allows the majority of the computational effort in the BNCT treatment planning process to be focused on dose calculations in the patient rather than on repeating, for each patient, Monte Carlo calculations of the entire fixed beam line which are external to and largely independent of the patient geometry and position. Nevertheless, calculations of the beam line are obviously an essential part of the treatment planning process since the accuracy and precision of dose in the patient are critically dependent on detailed upstream calculations.

Detailed radiation transport computations (using the Monte Carlo or discrete ordinates methods) of the neutron beam line are performed to define the radiation source at a position close to the patient. In Monte Carlo calculations, exact track characteristics such as position, direction, energy, and (statistical) weight of all particle histories crossing a plane, which is usually at the beam aperture near the patient position, are recorded to a binary phase space file (or “surface source” file in MCNP\textsuperscript{3} parlance) or are
scored to construct a probability distribution for a given source characteristic, similar to the result from a discrete ordinates calculation. The binary track information from the phase space file can either converted into a set of probability distributions describing the beam characteristics\(^4\) (as described in Chapter 5) or sampled directly in subsequent transport simulations into the patient geometry. In sampling the surface source directly, the dose precision in the patient is limited by the amount of unique track information sampled; this limitation is referred to as the latent variance\(^5\) of the phase space file. While the surface source can indeed be sampled multiple times to improve the statistics for those dose components that are derived from the thermal neutron flux, the effectiveness of oversampling is very limited for fast neutrons and incident photons due to their longer mean free paths and comparatively infrequent interactions in the patient. Therefore, ensuring that adequate unique track information is recorded to the surface source file during upstream calculations of the beam line is essential to achieving acceptably low levels of uncertainty for in-patient dose calculations.

When the phase space file at the beam aperture of the fission converter beam\(^6,7\) at MIT was calculated, the low natural probability that particles originating in the MITR-II reactor core would reach the beam aperture required that nonanalog Monte Carlo algorithms be used to ensure that sufficient track information was recorded downstream at the beam aperture within a reasonable simulation time using the moderate computational resources available. Therefore, mathematical tricks known as variance reduction techniques were employed during the Monte Carlo simulations to help accomplish that goal and thus reduce the uncertainty or variance for subsequent dose calculations in the patient.
4.1.1 Variance Reduction Techniques

An analog Monte Carlo model (which is directly analogous to what naturally occurs) is sufficient so long as a significant portion of the naturally sampled particles contribute to the estimated quantity. However, in deep-penetration shielding problems, this is rarely the case, and as a result unacceptably high natural variance is produced for the estimated quantities. So, in those cases, the model is intentionally biased to artificially increase the probability that a sampled particle will contribute to a given estimated quantity and thus help reduce the uncertainty associated with that quantity. While the model will indeed no longer be analogous to the natural transport (i.e., it is nonanalog), the estimated quantity itself will be the same as the analog model if the effect of biasing is properly accounted for and removed. To accomplish this, each particle track is assigned a weight (statistical weight that is unrelated to particle mass) which is updated as that track is transported through the simulated geometry and subjected to various interactions and variance reduction events. If a given track should contribute to a tally, its contribution to the scored quantity will be will be appropriately adjusted using its weight to maintain a fair Monte Carlo game and prevent biasing the scored quantity.

The well-benchmarked Monte Carlo radiation transport code, MCNP, provides several robust variance reduction techniques that act to reduce the uncertainties inherent to Monte Carlo calculations while also ensuring that the estimated quantities are not biased as a result of the variance reduction techniques. Most of the techniques involve playing Russian Roulette with a particle whereby the weight of a given particle, $W_0$, is increased to $W_f$ (where $W_f > W_0$) with probability $W_0/W_f$ or set to 0 and terminated (or killed) with probability $1 - W_0/W_f$. Thus, on average, particle weight is preserved from the corresponding analog Monte Carlo model, but computational time is not wasted.
tracking particles with low weight. However, effective variance reduction can indeed be tricky because it cannot usually be applied universally but rather must be tuned to a specific transport problem in order to provide optimal results, which can sometimes be a time-consuming trial and error process. To better understand the tuning process, a brief introduction to those variance reduction techniques that were explored as part of this analysis is included here. Further discussion may be found in the MCNP manual or the Los Alamos National Laboratory (LANL) report by Booth and Hendricks.

4.1.1.1 Implicit Capture

If a relatively large amount of computational effort has been devoted to transporting a particle into a given tally region, it would be highly inefficient if that particle were to be absorbed just prior to contributing to the tally. Therefore, implicit capture (as opposed to analog capture) is employed to ensure that the particle will always survive absorption but with a weight appropriately adjusted to reflect the nonanalog event: $W(1-\sigma_a/\sigma_t)$ where $\sigma_a$ and $\sigma_t$ are the microscopic absorption and total cross sections, respectively, and $W$ is the incident particle weight. Tracking continues for the particle until it escapes the geometry or reaches the weight cutoff. Implicit capture increases the probability that a particle will still contribute to the scored quantity but also increases the computation time per history. Nevertheless, along with Russian Roulette (via the weight cutoff game), implicit capture is the only other variance reduction technique enabled by default for neutrons in MCNP.

4.1.1.2 Geometry Splitting

It is inefficient to track particles into unimportant parts of the problem geometry where the probability of the particle contributing to either the quantity being scored or
the surface source being recorded is very low. Therefore, geometry splitting allows computational effort to be directed away from such regions of the problem geometry and focused on those that have a higher probability of contributing to the tally or surface source. To achieve this, the transport geometry is sufficiently segmented into cells, and each cell is assigned an importance that is proportional to the estimated contribution that the particles in that cell will make to the scored quantity. During the transport calculations, if a particle of weight $W_0$ leaves a cell with importance $I_0$ to enter a cell with lower importance $I_1$, Russian Roulette is played with the probability of survival being $I_1/I_0$ and the weight of the surviving particle equal to $W_0 I_0/I_1$. Conversely, if the particle enters a cell with higher importance ($I_1 > I_0$) and $I_1/I_0$ is an integer $n$, then the particle is split upon entering the new cell into $n$ identical particles each with a weight of $W_0/n$. If $I_1/I_0$ is not an integer value, $n$ is calculated by rounding the ratio down to the nearest integer, and then splitting into $n+1$ particles with $I_1/I_0 − n$ probability or into $n$ particles with $1 − (I_1/I_0 − n)$ probability with each particle assigned a new weight of $W_0 I_0/I_1$ regardless. It is important to note that each particle track resulting from the split will be subjected to a different random number sequence in the subsequent tracking calculations and will likely experience a different sequence of events. Splitting does not occur in void cells since doing so would only result in extra tracking calculations that are not needed due to the uninhibited path each particle will travel to the next surface. Overly excessive rouletting and/or splitting are generally avoided in order to help prevent both the permanent loss of unique track information and the creation of large amounts of duplicate track information, which is inefficient.
4.1.1.3 Photon Production Biasing

During coupled neutron/photon transport calculations, photons are created from neutron collisions. The weight of the resulting induced photon $W_p$ is calculated as $W_n(\sigma_\gamma/\sigma_T)$ where $W_n$ is the neutron weight and $\sigma_\gamma$ and $\sigma_T$ are the photon production and total neutron cross sections, respectively. This photon weight is compared to a threshold weight, $W_iI_s/I_i$, which is specified as the product of the ratio of the collision cell neutron importance to the source cell neutron importance, $I_s/I_i$, and the value of the PWT card in MCNP for the given cell, $W_i$. If $W_i < 0$, the starting weight of the current neutron history, $W_s$, is folded into the factor to produce a threshold weight of $|W_i|W_sI_s/I_i$. When the PWT card is not used, $W_i$ is assigned the default value of $-1$. If the induced photon weight is above the threshold, then one or more photons will be banked or saved for subsequent tracking calculations each with a weight of $W_p/N_p$ where $N_p$ is the number of photons created as calculated by $(W_pI_s)/(5I_sW_i)$. However, if the induced photon weight is below the threshold, Russian Roulette is played for the photon with a survival probability of $W_pI_i/(W_iI_s)$. Therefore, adjusting the threshold weight via the entry on the PWT card in MCNP allows the number and weight of neutron-induced photons to be controlled. As the threshold is lowered, more neutron-induced photons will be produced, up to a maximum of 10 per collision, but with appropriately adjusted weights so as to not bias the calculations. A unique random number sequence will be used for each neutron-induced photon created thereby increasing the probability that one or more will contribute to the quantity being scored or the surface source being recorded. If photon weight windows are used, the entries on the PWT card are ignored, and $W_i$ is set to the minimum photon weight window for the each cell.
4.1.1.4 Weight Cutoff

Once the weight of a particle has dropped to a sufficiently low value, it is inefficient to continue tracking the insignificant particle. The weight cutoff helps to reduce such inefficiency by rouletting particles when their weight falls below a user-defined threshold. Since the weight cutoff was originally designed for use with geometry splitting, the weight cutoff game depends on the ratio of source cell importance to current cell importance, \( R \), as well as two user-defined parameters, \( WC1 \) and \( WC2 \). Russian Roulette is played if the particle’s weight, \( W_0 \), falls below \( WC2 \times R \) with a probability of survival equal to \( W_0 / (WC1 \times R) \). If the particle survives, it is assigned a weight of \( WC1 \times R \), and the transport continues. If negative values of \( WC1 \) or \( WC2 \) are specified, then \( |WC1| \times W_s \) and \( |WC2| \times W_s \) are substituted for \( WC1 \) and \( WC2 \), respectively, where \( W_s \) is the minimum weight assigned to a source neutron by MCNP. The default values of \( WC1 \) and \( WC2 \) for neutrons and photons are \(-0.50 \) and \(-0.25 \), respectively. For coupled neutron/photon transport calculations, the photon weight cutoffs are set equal to the corresponding neutron values unless explicitly changed by the user using the CUT card.

4.1.1.5 Weight Windows

Through the use of particle splitting and Russian Roulette, weight windows help focus computational effort on particles that have a higher probability of contributing to the scored quantity. To accomplish this, a range of acceptable weights define a “weight window” for each cell. If a particle enters the cell or undergoes a collision within the cell, the particle’s weight is evaluated to determine whether it falls within, above, or below the window so that the appropriate action can be taken. If the weight is within the window, then no action is taken for the particle in that cell. If the particle weight is below the
window, then the Russian Roulette game is played, and if the particle is not terminated, it is assigned a weight that is within the weight window for that cell. When the particle weight is above the upper bound of the window, then it is split so that the resulting particles all have a weight within the window. For complex transport geometries such as the MIT FCB, it is very difficult to manually produce effective neutron and photon weight windows. Therefore, MCNP includes the ability to easily generate weight windows via the MCNP weight windows generator. The weight windows generator calculates the importance of each cell using Eq. 4.1 with the user specifying a tally bin for which the weight windows will be optimized.

\[
\text{Importance} = \frac{\text{total score for user defined tally resulting from particles and their progeny entering the cell}}{\text{total weight entering cell}} (4.1)
\]

MCNP assigns weight windows that are inversely proportional to the importance calculated for a cell. As particles are transported from the source towards a particular region of interest, the importance of the cells along its path increases while the weight windows for those same cells decrease. By using the weight windows generated in a previous run in a subsequent calculation of the weight windows, a more optimal set of weight windows can be iteratively calculated. Weight windows can be space-energy or space-time dependent, so if using cell-by-cell weight windows it is important to have sufficiently segmented the problem geometry to properly model the spatial dependence of weight windows. If the weight window is zero for a given cell, then weight windows are disabled, and particles in the cell are subjected to the weight cutoff game. Also, the relative magnitude of the neutron and photon weight windows in a given cell allow control over the number and weight of neutron-induced photons produced in that cell.
during coupled neutron/photon transport calculations. The value of $W_i$ used to calculate the weight threshold for induced photons (section 4.1.1.3) is set to the minimum photon weight window for each cell. However, before banking the induced photons, each is (appropriately) rouletted if it is below the photon weight window. As with geometry splitting, large fluctuations in the weight windows for adjacent cells should be avoided in order to prevent significant rouletting and/or splitting of particles. The ratio of weight windows between adjacent cells is recommended to be $\leq 4$.

4.1.1.6 Energy Cutoff

If the energy of a tracked particle falls below a user defined value (neutron default is 0.0 MeV, photon default is 100 keV), then the transport calculations for that particle are terminated without playing Russian Roulette. Therefore, if the energy cutoff is not carefully selected for a given problem, then particles that could potentially contribute to one or more tallies could be prematurely terminated resulting in biased or wrong answers. However, using an appropriate energy cutoff can increase computational efficiency by not wasting computational effort on tracking insignificant histories.

4.1.1.7 Source Biasing

It is often advantageous to distort the natural source probability distribution so that certain portions of the distribution that would otherwise be sampled infrequently will be preferentially sampled in order to help lower the uncertainties for one or more scored quantities. For example, in BNCT it is important to minimize the fast neutron contamination in the epithermal neutron beam since fast neutrons lead to a non-specific background dose that lowers the therapeutic ratio. Therefore, in an analog Monte Carlo model of a BNCT neutron beam line, the fast portion of the neutron energy spectrum is
sampled relatively infrequently which can lead to large uncertainties when calculating the fast neutron dose in the patient. One method of reducing these uncertainties is to sample the fast portion of the source neutron energy spectrum more frequently but with a reduced particle weight so as to not bias the resulting calculations.

4.1.2 Original Variance Reduction for the MIT FCB

In 2002, detailed calculations of the constructed FCB beam line were performed in order to produce a surface source representation at the patient position for treatment planning calculations for the BNCT clinical trials at Harvard-MIT. Past experiences using Monte Carlo transport calculations to design the FCB had indicated that neutron and photon weight windows would result in the most computationally efficient calculations of the beam line. Therefore, the MCNP weight windows generator was used to produce space- and energy-dependent neutron and photon weight windows for each cell of the well-segmented FCB model geometry. For neutrons, weight windows were generated for 7 energy groups with the following upper energy boundaries: 0.01 eV, 0.1 eV, 1 eV, 10 keV, 100 keV, 1 MeV, and 20 MeV. Likewise, photon weight windows were generated for 2 energy groups with upper energy boundaries of 0.55 MeV and 100 MeV. Using 7 separate simulations, the neutron weight windows in each of the 7 energy groups were optimized using scores from the corresponding energy bin of a neutron current tally inside the aperture ($r \leq 5.9$ cm) at the beam aperture plane. The weight windows for the appropriate energy group from these 7 individual simulations were manually combined to yield a complete set of energy dependent neutron weight windows. Optimizing the neutron weight windows for each energy group independently ensured effective variance reduction across a broad range of neutron energies as shown in Figure
4.1 where the uncertainties (which have been intentionally increased by an order of magnitude to better illustrate the effect) are reasonably uniform at energies outside of the epithermal neutron energy range. Photon weight windows were generated during similar simulations but were instead optimized for a tally of the A-150 tissue equivalent plastic photon dose at the beam aperture plane. Using these neutron and photon weight windows, transport calculations of the FCB beam line were performed on a dual 1.7 GHz Intel® Xeon™ processor workstation in several steps, beginning with criticality calculations of the MITR-II reactor core and ending with the production of a combined neutron and photon surface source downstream at the beam aperture plane. In preparation for dose calculations in the patient, the neutron and photons tracks were separated so that induced and incident photons could be calculated separately. This series of simulations resulted in a 337 MB (megabyte) surface source file containing only neutron tracks (3,674,093 neutron tracks from 59,517 independent histories) and a 351 MB surface source file of photons tracks only (3,862,520 photon tracks from 23,891 independent histories). Before patient planning commenced, both surface source files were validated using physical dosimetry measurements\textsuperscript{13,14} in the MIT ellipsoidal head phantom\textsuperscript{15,16} and in a large rectangular water phantom\textsuperscript{17}. 
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Figure 4.1 Neutron current energy spectrum inside the beam aperture ($r \leq 5.9$ cm) of the MIT FCB. The uncertainties have been intentionally increased by an order of magnitude to better illustrate the effectiveness of the energy-dependent weight windows at reducing uncertainties across a broad range of neutron energies.

4.1.3 Treatment Planning with the MIT FCB

After selecting several possible treatment field orientations using NCTPlan,$^{15,18}$ the FCB neutron and photon surface source files were each sampled once during separate MCNP simulations and tracked into a voxel model of the patient anatomy to calculate the dose components present in BNCT. From validation calculations with the FCB neutron and photon surface source files, dose component scaling factors were derived by least squares fitting calculated doses to physical dosimetry measurements made in-phantom
and in-air. The scale factors for the boron, thermal and fast neutron, and induced photon dose components were unity while a scale factor of 2.48 was applied to the incident photon dose because MCNP is unable to model delayed gammas. These scale factors calibrated NCTPlan calculations to physical dose measurements and helped ensure that the patient doses calculated during in the treatment planning process were an accurate representation of what would be actually delivered during treatment. For the 7 patients treated with the FCB, the average CPU times for the coupled neutron/photon (mode np) and photon (mode p) treatment planning simulations were 45.9 and 14.2 minutes per field, respectively.

Distinctive streak artifacts of high dose and large uncertainty in the incident photon dose distribution would later be identified when examining the 2-dimensional dose distributions in the patient; these artifacts were determined to be due to high weight or excessive duplicate photon tracks. An example of these streak artifacts is shown in Figure 4.2. This problem indicated that the variance reduction used in the upstream calculations of the beam line may be suboptimal. The rather large ratio of tracks to independent histories, 61.7 for the neutron surface source and 160 for the photon surface source, also suggest that there may be too much particle splitting and not enough unique track information. The artifacts also make it difficult to accurately calibrate the planning system for the incident photon dose component. Despite the dramatic appearance of the streak artifacts in Figure 4.2, it is important to understand that the clinical significance of these problems is small because the incident photon dose is a small component of the total weighted brain dose, contributing 3.4% at $D_{\text{max}}$. Also, it is important to recognize that the variance reduction scheme that was ultimately responsible for creating the
problems was produced by the MCNP weight windows generator and was the best variance reduction scheme available at the time and it appeared to perform very well for most dose components.
Figure 4.2  Two dimensional distributions of dose rate, relative error, and FOM (Figure-Of-Merit) calculated for the incident photon dose component of the MIT FCB in a voxel model of the modified Snyder head phantom. Streak artifacts of high in-phantom incident photon dose, high uncertainty, and low FOM resulting from the “unlucky” rouletting of neutrons and excessive splitting of the subsequent induced photons during upstream Monte Carlo calculations of the FCB beam line are evident. The color bars are log scale.
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4.1.4 Objectives

With increasingly powerful computational resources routinely available, it is understandable to simply employ a brute force approach to Monte Carlo treatment planning calculations whereby a sufficiently large number of particles are simulated in order to achieve the desired level of dose precision. However, more computationally efficient approaches are usually available that would better facilitate the planning process and thus help result in a more optimal and accurate treatment plan. Therefore, this chapter describes analysis to help reduce the uncertainties that are inherent in Monte Carlo treatment planning calculations for BNCT. The analysis was divided into two logical phases. In phase I, the original variance reduction of the FCB Monte Carlo model was reevaluated and further optimized in an attempt to improve the surface source representation of the MIT FCB beam line at the patient position and subsequently produce increased dose accuracy and precision in the patient. Having a more accurate surface source definition of the MIT FCB would not only benefit future retrospective analyses of the FCB patient data but would also facilitate the comparison of the different source definitions techniques available for NCT treatment planning (Chapter 5). While variance reduction is most often essential, especially in reactor-based BNCT, to the Monte Carlo calculations of the beam line, it is not often employed for the subsequent dose calculations in the patient. Therefore, in phase II, the focus was shifted to dose calculations in the patient where considerable effort was devoted to investigating the effectiveness of the various variance reduction techniques at improving the computational efficiency. In those calculations, even modest gains in efficiency would be advantageous since calculations of patient dose are often repeated several times for different beam orientations during the BNCT treatment planning process.
4.2 Materials and Methods

Both phase I and II of this work required the often difficult task of comparing different types of variance reduction. So, throughout the course of this analysis, a given variance reduction technique was ultimately evaluated based on its ability to reduce the uncertainties of in-patient dose calculations. The test case used to evaluate different variance reduction schemes in this study was a single-field irradiation of the Snyder head phantom.19 NCTPlan was used to create a 1 cm³ voxel model of the modified Snyder head phantom, and a 4 cm diameter sphere was added to the phantom to model the intracranial disease that is often the target of BNCT. The different regions of the Snyder head phantom were modeled using adult whole brain and adult whole cranium, as defined by ICRU Report 46.20 A concentration of 15 μg/g of $^{10}$B was explicitly modeled in the brain and $3.5\times$ that concentration was modeled in the tumor. Neutron, photon, and $^{10}$B kerma factors21 for ICRU 46 adult whole brain material were used to compute the 5 dose components present in BNCT: the $^{10}$B(n,$\alpha$)$^{7}$Li reaction, thermal neutron dose mainly from the $^{14}$N(n,p)$^{14}$C reaction, fast neutron dose mainly from the $^{1}$H(n,n$'$)$^{1}$H proton recoil reaction, induced photon dose from photons created inside the patient mainly via the $^{1}$H(n,$\gamma$)$^{2}$H reaction, and incident photon dose from those photons which were produced upstream and outside of the patient.21 The total biologically weighted brain dose was calculated as the sum of the boron, thermal neutron, fast neutron, induced photon and incident photon dose components weighted by RBE or CBE factors22 of 1.3, 3.2, 3.2, 1.0, and 1.0, respectively.
To evaluate the computational efficiency and overall effectiveness of a particular variance reduction technique, it is useful to define the Figure-of-Merit (FOM) as follows:\(^3\)

\[
\text{FOM} \equiv \frac{1}{(\text{relative error})^2 \times \text{CPU time}}
\]  

(4.2)

The relative error of a tally is its standard deviation divided by its estimated mean and varies inversely with the square root of the number of particle histories simulated. In other words, the relative error of a given tally can be reduced by a factor of \(N\) by simulating \(N^2\) times as many particle histories. CPU time is the total time (summed for all CPUs for parallel calculations) required to complete the simulation and is directly proportional to the number of simulated histories. Given these proportionalities, the FOM should roughly be constant and independent of runtime or the number of histories simulated. A variance reduction technique with a larger FOM for a given tally is more efficient at reducing uncertainties than other techniques with smaller FOM values. To facilitate the comparison of the different forms of variance reduction, custom MATLAB (The MathWorks, Natick, MA) functions were used to read and graphically display the 2-dimensional dose, relative error, and FOM distributions for the dose components calculated in the 1 cm\(^3\) voxels of the head phantom.

For phase I calculations, the Monte Carlo model of the MIT FCB incorporating the \(^6\)Li filter assembly\(^1\) (with the \(^6\)Li filter out) was used with the original energy-dependent neutron and photon weight windows as a starting point in a search for more optimal variance reduction to increase the amount of unique track information reaching the beam aperture while also decreasing the excessive numbers of duplicate tracks. Once
sufficiently effective variance reduction was obtained, the calculations of the FCB beam line were repeated with a significantly increased number of simulated histories to produce a new surface source file at the beam aperture plane. Previously reported physical dosimetry measurements\(^1\) of boron, thermal and fast neutron, and photon dose for the FCB along the central axis of the MIT ellipsoidal head phantom were used for model validation. The physical dosimetry of the MIT FCB has been described elsewhere.\(^{17,23}\) When needed, custom MATLAB functions were employed to read, write, and manipulate binary MCNP surface source files.

In phase II, irradiation of the voxel model of the head phantom with a generic epithermal neutron beam\(^{21}\) was simulated using different forms of variance reduction available in MCNP (section 4.1.1). The mean efficiency of the in-phantom dose calculations resulting from each variance reduction type was compared to a baseline MCNP simulation with only the default variance reduction (i.e., implicit capture and weight cutoff) enabled to appropriately gauge the effectiveness of that particular technique at reducing the variance. For each variance reduction technique, the relevant parameters were adjusted in a trial-and-error process to optimize the variance reduction for the transport problem without biasing the dose calculations. The monodirectional 10 cm diameter disc source was modeled as 10% thermal neutrons ($1 \times 10^{-9}$ eV to 0.5 eV), 89% epithermal neutrons (0.5 eV to 10 keV), and 1% fast neutrons (10 keV to 2 MeV). The disc source was sampled uniformly in area and was normalized to a neutron flux of $1 \times 10^{10}$ n/cm$^2$/s. This beam was chosen so that the corresponding MCNP source definition, represented as a series of probability distributions, would be an appropriate analogue to those actual clinical BNCT beams that are represented in a similar manner. To provide an
appropriate incident photon dose component in the calculation of the total weighted dose rate, a 2 MeV monoenergetic and monodirectional photon disc source was simulated and normalized to $2 \times 10^8 \, \gamma/cm^2s$. MCNP5 version 1.40 was used to perform all Monte Carlo calculations in both phases of the work, and all simulations were performed in parallel on a Beowulf cluster (described in Appendix B) composed of 11 nodes with AMD® Athlon 64™ 3200+ (2.0 GHz) 64 bit processors and 2 GB RAM.

4.3 Results

4.3.1 Phase I: Detailed Calculations of the Neutron Beam Line

The detailed Monte Carlo calculations of the MIT FCB beam line were divided into a series of 3 simulations with each resulting in a surface source file at a different location along the beam line. This method of segmenting of the transport geometry allowed downstream calculations to be repeated as needed without having to first repeat the time-consuming upstream portion of the calculations and does not introduce any significant approximations. A cross-sectional view of the Monte Carlo model of the FCB beam line outlining the simulations performed and surface source files written is shown in Figure 4.3. In the first simulation, a criticality calculation of the MITR-II reactor core was performed and used to produce a fission volume source file in the core, and only default variance reduction (no weight windows) was used during the criticality calculation. The neutron track information from that fission volume source was sampled during the second simulation and transported to the edge of the graphite reflector, immediately before the fission converter, where a second surface source file was recorded. For the third simulation, the neutron tracks from the surface source file at the
edge of the graphite reflector were sampled, transported through the fission converter and collimator to the beam aperture plane via coupled neutron/photon calculations, and written to a surface source file at the patient position along with photons tracks resulting from neutron interactions. It should be noted that photons originating in the core were not simulated since they have been shown to represent only a very small fraction of the incident photon dose at the beam aperture. Since a great majority of the photons that contribute to incident photon dose at the patient position originate downstream of the fission converter, coupled neutron/photon calculations were used to produce the mixed particle surface source representation at the patient position. This single surface source file of neutron and photons tracks was split into separate neutron and photon surface source files by transporting particles an infinitesimal distance to a new surface where new surface source files were written in separate runs. This allows the induced (induced in the phantom) and incident (incident on the phantom) photon dose components to be calculated separately in subsequent simulations through the patient geometry and for those results to be independently scaled for planning system calibration.

Using the model, simulations, and surface source files depicted in Figure 4.3, energy dependent neutron and photon weight windows were calculated for the entire FCB beam line from reactor core to patient position using the MCNP weight windows generator with the original weight windows serving as initial estimates. Weight windows were calculated for the 7 original neutron energy groups (with upper boundaries of 0.01 eV, 0.1 eV, 1 eV, 10 keV, 100 keV, 1 MeV, and 20 MeV) but only 1 photon energy group and were optimized for boron and incident photon dose rate calculations in the

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* The neutron surface source file was created using the cards “mode n” and “ssw pty n” and the photon surface source with “mode p” and “ssw pty p”.
spherical tumor of an analytical model of the modified Snyder head phantom simulated at the patient position. To better model the energy dependence of the neutron weight windows and ensure adequate variance reduction across a range of neutron energies, 7 simulations were performed (1 simulation for each neutron energy group) in which weight windows for each of the seven neutron energy groups were individually optimized using the corresponding energy bin of the tumor boron dose tally. The resulting optimized weight windows for each neutron energy group were copied from the appropriate simulation and manually combined to form a new set of neutron weight windows. The entire process was repeated with this new set of weight windows in order to further optimize the weight windows. After this second iteration was complete, the resulting final set of weight windows was used in calculations of the FCB beam line to produce the surface source at the patient position (i.e., “SS 3” in Figure 4.3). It should also be noted that the number of particles simulated during computations of weight windows was increased by a factor of 36, which was determined so that the storage requirements for the 3 surface source files produced would not exceed the limits of the hard disk storage available. While significantly increasing the number of particle histories used to generate weight windows did not necessarily improve the estimates of windows for cells along the central beam axis, those cells that were rarely visited before experienced an increase in the number of tracks which improved the estimate of the importance function in those regions.
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Figure 4.3  Monte Carlo model of the MITR-II reactor core and FCB beam line illustrating the series of MCNP calculations and surface source (SS) files used to create a surface source representation of the beam downstream at the patient position (beam aperture) for use in BNCT treatment planning calculations.
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Subsequent in-phantom dose calculations with the newly created surface source file exhibited streak artifacts of elevated incident photon dose and uncertainty, as shown in Figure 4.2, similar to those produced by the original FCB surface source file created in 2002. Excessively high weight tracks split into many duplicates were suspected to be responsible. To investigate this, custom MATLAB functions were used to read the binary track information recorded to SS 3 and calculate the number of identical neutron and photon tracks per independent particle history. Excessive numbers of identical neutron and photon tracks were identified and determined to be the cause of the observed streak artifacts. So, a systematic approach was employed to identify and address the source(s) of this duplicate track information, and that process is represented as a flowchart in Figure 4.4. The first step was to identify those independent particle histories with large numbers of duplicate tracks from SS 3. Each of these problematic histories were then read from SS 2 upstream and written individually to short surface source files along with all their associated tracks. The DBCN (debug information) and RAND (random number generator) cards were employed in the subsequent MCNP simulations with these short, single-history surface source files to exactly reproduce each track’s path from the edge of the graphite reflector to the beam aperture and provide detailed information about all interactions and variance reduction events along the way. This detailed track information revealed that in certain regions of the FCB beam line geometry (off the central beam axis) select fission neutrons were being scattered and surviving consecutive 1-for-5 Russian Roulette events in adjacent cells and being increased in weight by a factor of 5 each time. In one instance, a neutron survived a series of consecutive Russian Roulette events to have its weight increased by nearly 3 orders of magnitude. These high weight
neutrons would then produce the maximum of 10 induced photons upon interacting in the cadmium layer that lines the upstream edge of the lead photon shield. The resulting photons directed downstream towards the beam aperture would then be subjected to consecutive 5-for-1 particle splitting events through the lead shield and then multiple 2-for-1 splitting events in the collimator, all of which helped produce a cascade of identical tracks directed towards the beam aperture plane. As these problematic regions were identified, the weight windows in these regions were adjusted to reduce the ratio of the weight windows in adjacent cells and therefore limit the effect of unlucky variance reduction events and excessive particle splitting. This process was repeated until the problematic weight windows upstream of the lead shield had been sufficiently corrected.
Sample SS 2, transport all particle histories to patient position using modified weight windows, and record SS 3.

Use custom MATLAB functions to read and analyze SS 3. Identify those independent histories with excessive numbers of duplicate tracks.

For each identified problematic particle history, read all associated tracks from the upstream SS 2 and write them to a new, short surface source file using custom MATLAB functions.

Sample the new, short surface source file containing the problematic histories, and debug each track with the MCNP DBCN card as it is transported through the geometry to identify those regions of the FCB beam line geometry where rouletting to a very high weight or excessive splitting occurs.

Manually adjust weight windows in problematic regions.

Repeat until problematic high weight tracks have been eliminated.

Figure 4.4 Flowchart outlining the systematic approach taken to minimize production of problematic high weight tracks and subsequent splitting into excessive numbers of duplicate tracks during the Monte Carlo simulations of the FCB beam line that resulted from neutrons rouletting to high weights and producing photons which were split multiple times. The process was repeated until the production of high weight tracks, as manifest by excessive numbers (> 100) of duplicate tracks recorded on the surface source at the patient position, had been sufficiently reduced.
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While that process successfully minimized the production of high weight particles, the problem of excessive particle splitting events due to decreasing weight windows in the collimator remained. A separate calculation of the beam line indicated that 90.7% of the photon track weight reaching the beam aperture was from upstream of the beam collimator which meant that decreasing the weight windows through the collimator to result in additional particle splitting, as recommended by the MCNP weight windows generator, was very likely unnecessary and ultimately counterproductive for efficiency. So, the neutron and photon weight windows in the collimator were set to be constant in the longitudinal direction for each energy group, using values for the first cell after the lead photon shield for cells on the central axis. The original (from 2002) and corrected neutron and photon weight windows for those cells along the central axis of the beam line are shown in Figure 4.5. Notice that the original weight windows produced by the MCNP generator decreased by over 2 orders of magnitude in the collimator. Moving radially outward from the beam’s central axis, the new neutron and photon weight windows were manually increased to help focus computational effort on transporting particles towards the beam aperture.

Using the corrected neutron and photon weight windows, the calculations of the FCB beam line were repeated starting with SS 2 at the edge of the graphite reflector and ending with a new surface source at the patient position. Directly as a result of the changes in the neutron and photon weight windows, the runtime required to perform the transport calculations through the FCB beam line was reduced by a factor of 3.2 and the size of the resulting surface source was reduced by a factor of 200, from 34 GB to 170 MB. The new surface source file contained many fewer duplicate neutron and photon
tracks, as illustrated in Figure 4.6, which shows a histogram of the number of duplicate photon tracks per history. The mean number of duplicate photon tracks per independent history was reduced from 102 to 2.97. Since the problematic high weight particles were absent, severe streak artifacts in the subsequent in-phantom incident photon dose rate calculations were also resolved. Although the incident photon relative error in Figure 4.6 is indeed higher (5% vs. 7.5% at incident photon dose maximum) after the adjustments due to less track information, limiting the excessive number of identical photon tracks and subsequently avoiding the significant wasted computational expense of transporting them into the phantom increased the mean efficiency (FOM) of the in-phantom incident photon dose calculations by a factor of 185. Similarly, the mean number of duplicate neutron tracks per independent history was reduced from 31.0 to 2.37, and select particle histories that had in excess of 200,000 identical neutron tracks were eliminated. Therefore, the mean efficiency of in-phantom boron and fast neutron dose calculations was increased by factors of 5 and 23.8, respectively, as shown in Figure 4.7. The mean efficiency of in-phantom induced photon and total weighted brain dose calculations were likewise increased by factors if 2.7 and 9.1, respectively, as shown in Figure 4.8. The mean, minimum, and maximum FOM values for all in-phantom dose tallies before and after the changes to the weight windows are listed in Table 4.1. Small regions of large uncertainty and low efficiency (relative to the values in adjacent voxels) in the boron and induced photon (and hence total weighted brain) dose were eliminated by adjusting the weight windows. It should also be noted that the adjustments to the weight windows produced a small but statistically significant 1% decrease in the boron dose in a region on the ipsilateral side of the phantom that included the maximum boron dose. However, this
difference is small compared to the error in the physical dosimetry measurements used to calibrate the planning system and is therefore not clinically significant.

The adjustments to the neutron and photon weight windows described above improved variance reduction and computational efficiency significantly. These improvements did not, however, increase the number of unique photon tracks and independent histories reaching the beam aperture. To improve this aspect of the calculation, other forms of variance reduction were investigated for use in the calculations of the FCB beam line. It was thought that developing a scheme whereby photon production biasing could be separated and controlled independently from the photon population control (splitting and Russian Roulette during transport) would produce stronger variance reduction and more unique photons at the beam aperture plane. So, the corrected neutron weight windows were still used, but the corrected photon weight windows were inverted, appropriately scaled, and input as cell importances to guide the resulting biased spatial importance sampling. Similarly, the corrected photon weight windows were used to derive cell-by-cell entries for the PWT (photon production biasing card) card to control photon production biasing. After expending significant effort to find more optimal photon importance functions and photon biasing parameters, the mean FOM for in-phantom tallies of boron, fast neutron, and incident photon dose rates were still factors of 7.8, 7.7, and 4.8 times lower than the corresponding values produced with weight windows. Therefore, it was concluded that the corrected energy-dependent weight windows were indeed the best available solution for this transport problem.
Figure 4.5  Original (from 2002) and new neutron and photon weight windows for those cells along the central axis of the FCB beam line. The thin vertical lines that segment the weight windows represent the boundaries of different regions of the beam line. Neutron and photon weight windows were increased moving radially outward from the beam central axis.
Figure 4.6 Histogram of the number of duplicate photon tracks within the FCB surface source file at the patient position and the subsequent effect they had on in-phantom incident photon dose rates, relative errors, and FOM before and after adjustments to upstream weight windows. By adjusting the weight windows, the mean number of identical photon tracks per independent history was reduced from 102 to 2.96, and streak-artifacts of high dose and high uncertainty were eliminated while the FOM was increased significantly. The value plotted at $10^0$ tracks represents the number of unique tracks (no duplicates) within the surface source file. The color bars are log scale.
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Figure 4.7  Boron and fast neutron dose rate, relative error, and FOM (Figure-Of-Merit) distributions in the transverse plane of the modified Snyder head phantom on the FCB central axis before and after adjustments to the weight windows used for transport through the beam line. The mean, minimum, and maximum FOM values increased for both dose components as a result of the adjustments. The color bars are log scale.
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Induced photon dose rate, relative error, and FOM (Figure-Of-Merit) distributions in the transverse plane of the modified Snyder head phantom on the FCB central axis before and after adjustments to the weight windows used for transport through the beam line. The mean, minimum, and maximum FOM values increased for both dose components as a result of the adjustments. The color bars are log scale.
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Table 4.1 FOM (Figure-Of-Merit) statistics for dose tallies in the voxel model of the modified Snyder head phantom before and after adjustments to the weight windows in the Monte Carlo calculations of the FCB beam line. The adjustments reduced the number of high weights tracks and excessive particle splitting, thereby increasing computational efficiency by limiting the duplicate track information recorded to the surface source file used in the phantom dose calculations.

<table>
<thead>
<tr>
<th>Dose Component</th>
<th>Before Adjustments</th>
<th>After Adjustments</th>
<th>After/Before Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Min.</td>
<td>Max.</td>
</tr>
<tr>
<td>Boron</td>
<td>47.4</td>
<td>0.024</td>
<td>190</td>
</tr>
<tr>
<td>Thermal Neutron</td>
<td>48.0</td>
<td>0.024</td>
<td>190</td>
</tr>
<tr>
<td>Fast Neutron</td>
<td>1.3</td>
<td>0.003</td>
<td>5.0</td>
</tr>
<tr>
<td>Induced Photon</td>
<td>22.3</td>
<td>0.030</td>
<td>79.4</td>
</tr>
<tr>
<td>Incident Photon</td>
<td>1.7</td>
<td>0.072</td>
<td>4.6</td>
</tr>
<tr>
<td>Total Weighted Brain</td>
<td>30.5</td>
<td>0.041</td>
<td>223</td>
</tr>
</tbody>
</table>

With confidence that the neutron and photon weight windows were sufficiently optimal forms of variance reduction for the FCB beam line calculations, the amount of unique neutron and photon track information reaching the patient position was increased by brute force. Each neutron track from SS 2 was sampled 50×, at weights appropriately reduced to 1/50th their stored values, in a simulation that required in excess of 1 CPU year of computer time. Relevant details for the simulations performed and surface source files produced for the final calculations of the FCB beam line are shown in Figure 4.9. The resulting neutron and photon surfaces sources files at the patient position (i.e., SS 3a and SS 3b in Figure 4.3 and Figure 4.9) were used in simulations with the MIT ellipsoidal head phantom to produce in-phantom dose rates for comparison to corresponding physical dosimetry measurements. Dose component scaling factors were derived by least squares fitting calculated doses to measurements. The resulting scaling factors for the boron, thermal neutron, fast neutron, and induced photon dose components
were determined to be 0.95, which is within 1 $\sigma$ of previous scale factors.$^{10,15}$ The incident photon dose component scaling factor was determined to be 1.95; this large deviation from unity results from the inability of MCNP to model delayed gammas. In Figure 4.10, comparison of the scaled calculations with measured dose rates demonstrates excellent agreement.
Criticality calculations of the MITR-II reactor core
Run Mode: n
Cycles: 1100 kcode cycles of 360,000 particles
per cycle with 100 settle cycles
Run time: 98.5 CPU hours

Transport to the edge of the graphite reflector
Run Mode: n
SS resampling factor: 1x
Run time: 12 CPU days

Transport to the patient position
Run Mode: np
SS resampling factor: 50x
Run time: 1.03 CPU years

Figure 4.9 Detailed description of the series of simulations and surface source files used to produce a more accurate surface source representation of the FCB at the patient position. In total, 1.07 CPU years of simulation time and 88 GB of computer storage were used.
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Figure 4.10  Comparison of calculated and measured doses in the MIT ellipsoidal head phantom. MCNP calculations with the FCB surface source were scaled to match physical dosimetry measurements using least squares fitting; dose scale factors for each component are listed in the legend.
4.3.2 Phase II: Dose Calculations in the Patient

In phase II, the focus of the analysis was shifted from calculations of the beam line to dose calculations in a voxel model of the modified Snyder head phantom to determine whether any of the variance reduction techniques available in MCNP could increase computational efficiency and facilitate the treatment planning process. A simple MCNP SDef model of a generic epithermal neutron beam was used instead of the surface source model of the FCB since surface source representations usually contain some “built-in” variance reduction as a result of the techniques applied in upstream calculations. Nevertheless, most of the variance reduction techniques investigated could readily be adapted to either form of source definition with little effort. The techniques investigated were neutron and photon energy cutoff, neutron and photon weight cutoff, fast neutron source biasing, photon production biasing, and neutron and photon weight windows. For each of these techniques, a trial and error process was used to tune the technique to the given transport problem in order to produce more optimal variance reduction. Therefore, the results shown and discussed for each technique are actually the culmination of many separate simulations. The different techniques, as well as combinations of techniques, were compared based on their ability to increase the FOM for in-phantom dose calculations without biasing the calculated dose rates. A coupled neutron/photon simulation with each variance reduction technique was compared to a corresponding baseline simulation with only the default variance reduction enabled (implicit capture and weight cutoff). The resulting 2-dimensional FOM distributions for in-phantom boron, fast neutron, induced photon, and total weighted brain dose calculations are shown in Figure 4.11 and Figure 4.12 for the baseline simulation (labeled implicit capture) and simulations with each variance reduction technique. The
The corresponding ratios ($FOM_{VR}/FOM_{Base}$) of mean in-phantom FOM values are listed in Table 4.2 for each biasing technique and dose component. In Table 4.2, results are also included for both analog and implicit capture when relevant.

### 4.3.2.1 Implicit Capture

With implicit capture enabled for neutrons (as in the baseline simulation), the runtime was 30% longer than for analog capture. Therefore, any gains in reducing the variance for the in-phantom dose calculations were more than offset by the increased computation time per neutron history that is a characteristic disadvantage of implicit capture. The mean FOM for the boron and thermal neutron dose components were essentially unchanged from the simulation with analog capture, but the corresponding mean fast neutron, induced photon and total weighted brain FOM values increased by 42%, 38%, and 16%, respectively, by disabling implicit capture for neutrons.

### 4.3.2.2 Energy Cutoff

When the neutron energy cutoff was raised to $5\times10^{-4}$ eV, the maximum boron dose was decreased by 2% due to prematurely terminated neutron tracks. Similarly, if the photon energy cutoff was increased to 500 keV, the maximum induced photon dose was decreased by 2.3%. Therefore, neutron and photon energy cutoffs of $1\times10^{-4}$ eV and 100 keV were selected, respectively, to prevent biasing the dose calculations. However, such relatively small increases in the energy cutoffs (default values are 0.0 eV for neutrons and 1 keV for photons) understandably failed to significantly decrease the computation time and therefore resulted in no improvement in the efficiency of the dose calculations.
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Figure 4.11 FOM (Figure-Of-Merit) distributions for in-phantom dose tallies in the transverse beam line plane which result from employing different variance reduction techniques during coupled neutron/photon transport simulations of the generic epithermal neutron beam in a voxel model of the modified Snyder head phantom. Larger FOM values indicate more efficient dose calculations. The color bars are log scale.
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Figure 4.12  FOM (Figure-Of-Merit) distributions for in-phantom dose tallies in the transverse beam line plane which result from employing different variance reduction techniques during coupled neutron/photon transport simulations of the generic epithermal neutron beam in a voxel model of the modified Snyder head phantom. Larger FOM values indicate more efficient dose calculations. The color bars are log scale.
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Table 4.2  
Ratio of the mean in-phantom FOM (Figure-Of-Merit), relative to a baseline simulation with the default MCNP variance reduction, implicit capture, for dose calculations in the voxel model of the modified Snyder head phantom that result from employing different variance reduction techniques during coupled neutron/photon simulations with the generic epithermal neutron beam. The variance reduction parameters used for each technique are the result of a trial and error process performed to tune the specific technique to the given transport problem in order to maximize effectiveness. Results are included for both analog (A) and implicit (I) neutron capture.

<table>
<thead>
<tr>
<th>Variance Reduction Technique(s)</th>
<th>Neutron Capture</th>
<th>Thermal Neutron</th>
<th>Fast Neutron</th>
<th>Induced Photon</th>
<th>Total Weighted Brain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implicit Capture (default)</td>
<td>I</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Analog Capture</td>
<td>A</td>
<td>1.01</td>
<td>1.42</td>
<td>1.38</td>
<td>1.16</td>
</tr>
<tr>
<td>Photon Prod. Biasing</td>
<td>A</td>
<td>0.88</td>
<td>1.24</td>
<td>3.09</td>
<td>1.55</td>
</tr>
<tr>
<td>Photon Prod. Biasing</td>
<td>I</td>
<td>0.90</td>
<td>0.91</td>
<td>2.53</td>
<td>1.44</td>
</tr>
<tr>
<td>Weight Cutoff</td>
<td>I</td>
<td>0.95</td>
<td>1.38</td>
<td>1.33</td>
<td>1.13</td>
</tr>
<tr>
<td>Fast Neutron Src. Biasing</td>
<td>A</td>
<td>0.82</td>
<td>23.0</td>
<td>1.11</td>
<td>1.44</td>
</tr>
<tr>
<td>Fast Neutron Src. Biasing</td>
<td>I</td>
<td>0.74</td>
<td>14.5</td>
<td>0.72</td>
<td>1.18</td>
</tr>
<tr>
<td>Weight Windows Mesh</td>
<td>I</td>
<td>0.78</td>
<td>1.10</td>
<td>2.68</td>
<td>1.42</td>
</tr>
<tr>
<td>Energy Cutoff</td>
<td>I</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Fast Neutron Src. + Photon Prod. Biasing</td>
<td>A</td>
<td>0.72</td>
<td>0.71</td>
<td>20.2</td>
<td>2.47</td>
</tr>
<tr>
<td>Fast Neutron Src. + Photon Prod. Biasing + Wgt. Cut</td>
<td>I</td>
<td>0.75</td>
<td>0.75</td>
<td>14.7</td>
<td>2.03</td>
</tr>
</tbody>
</table>
4.3.2.3 Weight Cutoff

After performing several simulations with different weight cutoff parameter pairs (\(WC1\) and \(WC2\), described in section 4.1.1.4), the parameters were set at \(-1.5\) and \(-0.75\), respectively, and resulted in the FOM data listed in Table 4.2 and displayed in Figure 4.12 for the weight cutoff. The mean efficiency for total weighted brain dose calculations was increased by 13% over the baseline simulation, where the default \(WC1\) and \(WC2\) values of \(-0.5\) and \(-0.25\) were used, due to the significant increase in the efficiency of the fast neutron and induced photon dose calculations. Increasing the absolute values of the weight cutoff parameters from their default settings helps reduce (via Russian Roulette) the number of low weight neutron tracks produced by implicit capture and decreases the runtime by 28%. Nevertheless, larger increases (16% for total weighted brain dose calculations) in the dose calculation efficiency are observed by simply disabling implicit neutron capture.

4.3.2.4 Photon Production Biasing

As the photon production biasing parameter (specified via the PWT card) was incrementally increased from the default value of \(-1\) to 0 to increase the production of induced photons, the mean FOM for the in-phantom induced photon dose calculations increased by a factor as large as 5.5, as shown in Figure 4.13. However, that increase in FOM comes at the expense of reduced efficiency for other dose components, like the boron dose. Therefore, it is important to fully understand how a particular variance reduction technique affects the efficiency of all dose calculations. Figure 4.13 also indicates that there is no significant benefit, in terms of the efficiency of the total weighted brain dose calculations, in increasing the photon production biasing parameter above \(-0.25\). So, that value was chosen as the photon production biasing parameter to
produce the induced photon dose FOM distribution shown in Figure 4.11 where biasing photon production more than triples (3.09×) the mean efficiency of induced photon dose calculations when used with analog capture.

![Graph showing photon production biasing parameter vs. difference in mean FOM from default setting](image)

**Figure 4.13** Percent difference in the mean FOM (Figure-Of-Merit) for in-phantom dose tallies when compared to simulations using the default photon production biasing parameter of \(-1\). As the biasing parameter is increased to 0, more induced photons are produced with appropriately adjusted (lower) weights so as to maintain a fair Monte Carlo game and provide unbiased results. Increasing photon production dramatically improves the efficiency of calculating the induced photon dose, but this comes with the expense of reduced efficiency for other dose components such as the boron dose.
4.3.2.5 Fast Neutron Source Biasing

The natural sampling frequency of the generic epithermal neutron beam was defined to be 10%, 89%, and 1% for the thermal, epithermal, and fast regions of the neutron energy spectrum, respectively. To decrease the uncertainties associated with the fast neutron dose rates, the source sampling frequency was biased so that fast neutrons would be sampled more frequently but at a decreased weight. Similar to photon production biasing, the FOM for the fast neutron dose calculations could be increased rather dramatically by significantly biasing the source sampling frequencies. However, that increase would come at the expense of decreased efficiency for the other dose components. So, a trial-and-error approach was taken to find the fast neutron source biasing parameters that provided a sufficient balance. When the thermal, epithermal, and fast regions of the source spectrum were sampled with biased frequencies of 1%, 70%, and 20% respectively, the fast neutron portion of the energy spectrum was oversampled by a factor of 20, and the starting weight of each fast neutron was appropriately decreased from the default value of 1 to 0.05 to properly account for the biasing. As a result of the biasing alone, the mean FOM for the in-phantom fast neutron dose calculations was increased by a factor of 14.5, and the significant increase in efficiency is clearly evident in Figure 4.11. However, that increase comes at the expense of decreased efficiency of boron, thermal neutron and induced photon dose calculations. Nevertheless, the decrease in the efficiency of the other dose calculations is not so dramatic as to decrease the efficiency of the total weighted brain dose calculations.

4.3.2.6 Weight Windows

Investigation of weight windows for treatment planning calculations was motivated by a report that a weight windows variance reduction tool was being
developed at the University of Michigan for one of the Idaho National Laboratory treatment planning systems. The voxel model of the modified Snyder head phantom was represented in MCNP as a lattice in order to take advantage of the lattice speed tally patch. Therefore, the most plausible approach to investigating weight windows was to use the weight windows mesh since it is independent of the problem geometry and could be easily rotated and translated into the desired orientation with the beam during treatment planning calculations. Alternatively, if the voxel model were to be constructed in the cell model, cell-by-cell importances or weight windows could be specified, but it would be much more difficult to adjust the variance reduction as the field orientation is changed. Different orientations of the weight windows mesh were calculated, but the most efficient calculations with the monodirectional disc source resulted when the edge of the cylindrical weight windows mesh was aligned with the front edge of the phantom. This increased the efficiency of the transport calculations by preventing those particles that scatter out of the phantom from being needlessly split or rouletted since they are no longer important to the dose calculation. However, this gain in efficiency was only marginal. Each element of the weight windows mesh was 2 cm thick along the beam line with a diameter of 10.5 cm just large enough fully enclose the outer boundary of the voxel model of the head phantom. An outer layer of mesh elements completely external to the phantom were used to terminate tracking calculations for those neutron and photons tracks escaping from the phantom. The orientation of the cylindrical weight windows mesh with respect to the phantom and the disc source is shown in Figure 4.14.

The MCNP weight windows generator was used to produce weight windows for each element of the mesh for 3 neutron energy groups (with upper boundaries of 0.5 eV,
10 keV, 20 MeV) and 1 induced photon energy group. For each neutron and photon energy group, 3 separate simulations were performed to produce weight windows optimized for the corresponding in-phantom dose tally at 3 different depths (2, 6, and 12 cm) along the beam line. The resulting 3 sets of weight windows (1 for each depth) were examined for each neutron and photon energy group and combined into one set to better address the differences in the weight windows for dose calculations at different depths in the phantom. The resulting weight windows for each neutron and photon energy group were then written into an appropriately formatted wwinp file for use with MCNP.

For a fixed number of particles, subsequent simulations with these weight windows produced runtimes that were over 4× longer than simulations without them. Thus, the computational efficiency was actually significantly decreased for all dose calculations (e.g., −43% for boron dose calculations) except for a small 5% increase in the efficiency of induced photon dose calculations. This decrease in efficiency resulted from excessive and unnecessary splitting in the phantom. To eliminate the excessive particle splitting occurring in the phantom, the weight windows for all neutron energy groups were set to a constant value of unity in all 8 mesh elements. Likewise, a constant photon weight window of 0.25 was specified for all 8 mesh elements since the previous analysis of photon production biasing had shown that to be a rather optimal value. These adjustments to the neutron and photon weight windows decreased the runtime by 80% and increased FOM values for all dose component tallies by 2-5× when compared to simulations with the steeper weight windows produced by the MCNP generator. These constant weight windows failed to produce an increase in efficiency, when compared to the baseline simulation, for any of the individual dose component calculations except for
the induced photon dose where a significant 80% increase was observed. However, that increase in efficiency was significant enough to produce a 19% increase in the mean efficiency of the total weighted brain dose calculations. To further optimize the variance reduction of the weight windows mesh, the appropriate parameter was adjusted so that particle weight was evaluated at boundary crossings only (as opposed to the default where this is performed at collisions and boundary crossings) to determine if splitting or rouletting was required to keep the particle within the boundaries of the weight window. This change further increased the mean efficiency of the boron, fast neutron, induced photon, and total weighted brain dose calculations by an additional 4%, 3.5%, 3.9% and 2.7%, respectively. Therefore, these flat weight windows were used to produce the FOM distribution shown in Figure 4.12 and the values listed in Table 4.2 for the weight windows mesh. Nevertheless, the lack of any spatial variation in the neutron and photon weight windows essentially result in variance reduction that could otherwise be achieved by combining the weight cutoff game and photon production biasing. Weight windows do not provide any additional gain in computational efficiency and are therefore a suboptimal variance reduction solution for in-phantom dose calculations.
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Figure 4.14  Cylindrical weight windows mesh superimposed on a 1 cm$^3$ voxel model of the modified Snyder head phantom and irradiated with a 10 cm diameter monodirectional epithermal neutron disc source. The neutron and photon weight windows in those regions of the mesh labeled with an ‘X’ were intentionally made very large (1×10$^{25}$) to terminate tracking calculations for all particles escaping from the phantom.
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4.3.2.7 Combined Photon Production and Fast Neutron Source Biasing

The analysis thus far has considered simulations with only a single variance reduction technique. However, it is possible to employ more than one variance reduction technique in the same simulation. Therefore, different combinations were explored based on their observed effectiveness when used individually. Out of the several possible combinations investigated, combining fast neutron source biasing and photon production biasing produced the largest increases in the mean computational efficiency when all the dose component calculations were considered. As shown in Table 4.2, the dramatic increase in the efficiency of the fast neutron dose \((20.2\times)\) and induced photon dose \((2.47\times)\) calculations (due in part to disabling implicit neutron capture) overcome the comparatively small decrease in the efficiency of the boron and thermal neutron dose \((0.72\times)\) calculations to result in total weighted brain dose calculations that are \(2.2\times\) more efficient on average than default MCNP calculations (with neutron implicit capture enabled) that are most commonly performed in BNCT treatment planning. As is evident in Table 4.2, a similar level of efficiency in the total weighted brain dose calculations can be achieved using fast neutron source biasing and photon production biasing with implicit capture enabled if the weight cutoff is increased above the default values to limit the computational effort devoted to low weight tracks. However, combining implicit capture with fast neutron source and photon production biasing results in a rather significant decrease in efficiency (compared to the corresponding simulation where it is disabled) for the fast neutron and induced photon dose calculations.
4.4 Discussion

Repeating the original radiation transport calculations of the FCB beam line with more histories would not correct the issues resulting from the suboptimal weight windows produced by the MCNP weight windows generator. The resulting high weight tracks produced distinctive regions of large uncertainty in the incident photon dose in the patient while the excessive duplicate track information resulted in highly inefficient dose calculations and significantly inflated computer storage requirements. Therefore, considerable computational effort was spent to identify and correct the cause of these problems as well as to investigate the effectiveness of other forms of variance reduction. The complexity of the Monte Carlo model of the FCB beam line meant undertaking a time consuming trial and error process to evaluate potential variance reduction techniques and optimize the effectiveness of the technique determined to be the best available (i.e., weight windows). The effectiveness of different forms of variance reduction or the differences produced by altering parameters for a given technique were all evaluated using relevant in-phantom dose calculations similar to those used in clinical BNCT treatment planning. Optimizing weight windows for in-phantom tumor dose tallies rather than in-air flux tallies at the beam aperture did not result in many dramatic changes in the weight windows plotted in Figure 4.5. The most noticeable change occurred in the neutron weight windows for the 0.1 eV to 1 eV energy group where the original weight windows (from 2002) are more sloped through the aluminum and lead shield and result in a weight window at the collimator entrance that is an order of magnitude lower than the corresponding new weight window. However, any differences are relatively small compared to those in the collimator that result from manually adjusting the neutron and
photon weight windows in that region to a constant value to reduce particle splitting. However, the optimal weight windows for the collimator are likely somewhere in between the constant values used and the sloped set produced by MCNP. The relatively unobstructed path through the collimator along the central beam axis from the lead shield to the beam aperture plane suggest that drastically decreasing the weight windows along that path to result in particle splitting is not warranted and is counterproductive. Conversely, flat weight windows limit the number of unique photon tracks reaching the beam aperture plane. Of course, this issue points to the even larger problem of the MCNP weight windows generator failing to produce an adequate importance function. The phase space was sufficiently subdivided in space and energy, but the weight windows produced by MCNP were clearly less than optimal. Adding an angular dependence to the weight windows would likely help, but the magnitude of that effect is hard to estimate.

As a result of the work to optimize the neutron and photon weight windows and the computational resources of the Beowulf cluster, the number of independent neutron and photon independent particle histories at the beam aperture was increased by factors of 352 and 598, respectively. While the increased information is indeed advantageous for the precision of all subsequent dose calculations, it is particularly important for the calculations of fast neutron and incident photon dose rates in the patient. The effectiveness of sampling the surface source file multiple times to increase dose precision is more limited for these dose components than the other dose components due to the comparatively low number of interactions each experiences in the phantom before thermalization or escape. The increase in unique track information in the surface source file also allows conversion into an SDef representation using the methods presented in
Chapter 5 with greater accuracy and precision. In addition to the significant increase in unique track information when compared to the original surface source files from 2002, the ratios of the number of tracks to independent histories were decreased from 61.7 and 160, for the neutron and photon surface source files at the patient position, respectively, to 2.0 for both. Therefore, computation time was not spent during the dose calculations in the phantom handling duplicate track information which increased in the mean, minimum, and maximum FOM for all dose components. For instance, the mean, minimum, and maximum FOM values for the total weighted brain dose calculations were increased by factors of 9.1, 358, and 6.0, respectively.

The subsequent validation calculations reaffirmed the earlier findings of good agreement with physical dosimetry measurements. All of the calculated dose component scale factors, except for the incident photon scale factor, were within $1\sigma$ of those used in treatment planning for the Harvard-MIT clinical trial of BNCT. The large incident photon dose component scale factor was due to the inability of MCNP to properly model delayed gammas. Although the incident photon dose is a small contributor to the total biologically weighted dose, the 21% decrease in the scale factor underscores the importance of devoting computational effort to produce an accurate representation of the beam at the patient position. While the exact details of the variance reduction might indeed be specific to the FCB beam line, the broader applicability of these findings are in the overall process that was used to arrive at those details and the motivation to perform such work.

The work performed on the variance reduction of the FCB beam line provided considerable experience in executing MCNP in parallel with surface source files as large
as 42 GB. Therefore, a few important observations drawn from that experience will be shared. The version of MCNP used for these calculations was compiled with a pre-release version of a patch from the X-5 Monte Carlo team, which is responsible for MCNP development, that allowed the slave processes during parallel simulations to access surface source files locally rather than to have 11 complete copies sent over the network from the master process at beginning of the simulation. This was essential to the completion of this work given the large size of the surface source files involved. Consider the parallel simulation executed on 11 nodes that reads the fission volume source for transport to the edge of the graphite reflector. The patched MCNP executable allowed each of the 11 slave processes to read from the same copy of the fission volume source since each slave process had a “local” copy of the file available via an NFS mounted directory. If not for this patch, 11 copies of the 33 GB file would have been sent to the slave processes over the network only to then be transferred back to the master node as each slave process wrote the file to an NFS mounted directory. The startup time required to transfer such massive amounts of data over the network, as well as the storage requirements (12 copies×33 GB), would have made these simulations impossible with our hardware. Since simulations with SS 2 at the edge of the graphite reflector were repeated so frequently during the course of this work, a copy of SS 2 was transferred to each slave node’s local disk drive so that each slave process would be able to read from its own local copy, thus greatly reducing network traffic and the startup times for the parallel simulations dependent upon that surface source file. This functionality is now included in version 1.50 of MCNP5. There was also a significant variation observed in the time required for the slave processes to complete the transport calculations for their
assigned portion of tracks from the surface source file. It was not unusual for multiple nodes to lie dormant for significant amounts of time (i.e., 30 – 60 minutes) waiting for all the nodes to reach the rendezvous point. Since the dormancy seemed (counter intuitively) to increase as rendezvous points were made less frequent, shorter rendezvous intervals were chosen to prevent nodes from getting out of sync and wasting significant computational resources.

During the 50× sampling of SS2 that required over 1 CPU year to perform, unavoidable excessive warning messages regarding track weights starting outside of a given weight window were written to the simulation output file until there was no more free disk space available, thus causing the simulation to crash. This was a result of the error counter, a signed 4-byte integer overflowing from the maximum integer to the minimum and causing the error message to be written for every track. Therefore, a custom MCNP executable was created with the problematic error message disabled for that simulation, and the MCNP development team was notified of the problem.

Exploring the variance reduction for dose calculations in the head phantom was obviously quite different than for the beam line of the FCB. Thus, it is not surprising that the variance reduction technique that was found to be the best solution for the beam line calculations, energy-dependent weight windows, was found to be suboptimal for the dose calculations in the phantom. Despite considerable effort to tune the weight windows mesh to produce more efficient dose calculations, the increases in computational efficiency were indeed marginal compared to other methods. The relatively small transport geometry represented by the voxel model of the phantom did not warrant the constant splitting and rouletting that is characteristic of weight windows. Surprisingly,
implicit neutron capture, which is enabled by default, proved to be inefficient as well. The dimensions of the head phantom or a patient’s anatomy and the distances neutrons and photon must be tracked to contribute to a scored quantity are small compared to deep penetration problems like the FCB beam line. Therefore, modified sampling methods such as fast neutron source biasing and photon production biasing, and perhaps forced collisions (for fast neutron and incident photon dose calculations), are more effective than population control methods such as weight windows.

When using the different variance reduction techniques, it was important to ensure that the resulting doses were not biased in the process. Increasing the neutron and photon energy cutoffs beyond certain energies resulted in the termination of particle tracks that would have contributed dose in the phantom, thus resulting in lowered and incorrect dose rates. However, most forms of variance reduction employ Russian Roulette instead of simply terminating tracks in order to help avoid biasing answers. It is also important to understand that an increase in the FOM for a given dose component tally usually comes at the expense of another, as Figure 4.13 indicates for the boron and induced photon dose rate tallies. Fast neutron source biasing and photon production biasing each predictably increased the mean FOM for the fast neutron and induced photon dose rate tallies, respectively, but, the effectiveness of a given form of variance reduction should be properly investigated for all dose component tallies to ensure that other dose calculations are not actually being made more inefficient. Combining fast neutron source biasing with photon production biasing resulted in calculations of the total weighted brain dose rate that were over twice as efficient as the default MCNP calculations (with neutron implicit capture) at reducing the uncertainty. Thus, the same
level of precision for the total weighted dose could be achieved in less than half the runtime. Although an MCNP SDef representation of an actual clinical neutron beam should be substantially more complex than the generic epithermal neutron beam, these results indicate that it is indeed possible to achieve more efficient calculations of the total weighted dose rate. The need for improvements in computational efficiency will become more important as voxel sizes smaller than 1 cm$^3$ become more frequently employed for more accurate modeling of the patient anatomy.

4.5 Conclusions

Manually optimizing the energy dependent neutron and photon weight windows used in the Monte Carlo computations of the FCB beam line help to produce a surface source file at the patient position with significantly less duplicate track information thereby allowing for increased computationally efficiency while also correcting existing problems due to high weight tracks. The more accurate surface source representation was successfully validated using physical dosimetry measurements. Also, several variance reduction techniques were investigated in an attempt to increase the computational efficiency of in-phantom dose calculations for BNCT treatment planning. The different variance reduction techniques were each tuned in a trial-and-error process to the transport problem and then compared in their effectiveness at reducing the uncertainty associated with in-phantom dose calculations while also maintaining sufficient dose accuracy. By combining both fast neutron source biasing and photon production biasing and disabling implicit neutron capture, the mean computational efficiency of the total weighted brain dose calculations was increased by a factor of 2.2.
4.6 References


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Neutron Beam Source Definition Techniques for Neutron Capture Therapy Treatment Planning

5.0 Abstract

Constructing an accurate description of a neutron beam is critical to achieving accurate calculations of dose in neutron capture therapy (NCT) treatment planning. This chapter compares two different methods of neutron beam source definition. The first method involves performing a detailed simulation of the neutron beam line and recording the characteristics of all particle histories to a phase space file referred to as a “surface source.” The second method involves representing the beam characteristics as a set of probability distributions using the MCNP general source definition card or SDef. To facilitate the comparison, a software tool was developed for analyzing surface source files and constructing probability distributions to represent the source in treatment planning simulations. Simulations in this study were performed using the MCNP Monte Carlo radiation transport code with the MIT fission converter beam (FCB), which has a well-validated MCNP model, serving as the test neutron beam. Each source type (surface source file and SDef) was used to simulate transport of the beam through voxel models of
the modified Snyder head phantom and a large rectangular water phantom where doses were calculated. When compared to dose calculations with the surface source file, the initial calculations with the SDef produced significant errors of 15.2% and 10.7% at $D_{\text{max}}$ in the head phantom and rectangular water phantom, respectively. Using a patched version of MCNP that allowed the observed radial dependence of the relative azimuthal angle to be modeled in the SDef, errors in all dose components in the head phantom at $D_{\text{max}}$ were reduced to acceptably small levels with none being significant ($P \geq 0.13$) except for the 0.5% error in the induced photon dose. Similar error reductions were obtained for the large water phantom. Errors in the calculated doses introduced by sampling the azimuthal component of particle direction uniformly in the SDef vary spatially and are phantom-dependent and thus cannot be accurately corrected by a simple scaling of doses.

### 5.1 Introduction

Boron Neutron Capture Therapy (BNCT) has been used to treat a variety of cancers at various sites worldwide: in the USA,\textsuperscript{1-4} in Japan,\textsuperscript{5,6} in Europe\textsuperscript{7-11} and in Argentina.\textsuperscript{12} For clinical trials of BNCT, accurate treatment planning calculations are required to ensure the safety of the patient and the maximum efficacy of the therapy. However, the presence of multiple dose components, some of which depend strongly on tissue composition, as well as the scatter-dominated radiation transport require dose calculations that are more complicated than those for conventional radiotherapy. Thus, BNCT treatment planning systems utilize Monte Carlo simulations exclusively because solution of the Boltzmann transport equation is required in this scatter-dominated
problem. Due to its ability to provide a detailed treatment of physics and geometry, Monte Carlo algorithms are widely held to be the most accurate method of radiation transport and dosimetry calculation available. In spite of this ability, Monte Carlo based treatment planning is critically dependent on using an accurate model of the radiation source for the Monte Carlo radiation transport computations. Failure to use an accurate source model adversely affects the accuracy of computations and the resulting treatment plan. However, accurately defining the radiation source is one of the most difficult aspects of the entire treatment planning process because it requires producing an adequately accurate representation of the 5-dimensional probability distribution describing the spatial, energy, and angular characteristics of a radiation beam. Several methods for defining the radiation source have been used clinically in BNCT treatment planning.

5.1.1 Methods of Source Definition

In Monte Carlo simulations for NCT treatment planning, it is inefficient to simulate transport of particles from the reactor core or accelerator target all the way through the beam line for each patient. Therefore, other techniques are used that are more efficient that define a source term for planning simulations a short distance from the patient. Two methods of defining a neutron beam source for NCT treatment planning involve the use of binary phase space files (surface sources) or explicitly defining spatial, energy and angular probability distributions in the code used for the radiation transport calculations. Each of these methods has significant advantages and disadvantages.
5.1.1.1 *Surface Source Files*

In the first method of source definition, detailed Monte Carlo radiation transport computations of the neutron beam line are performed, and the characteristics of all particle histories crossing a plane are recorded to a phase space file often referred to as a “surface source.” This binary phase space file contains exact track characteristics, such as position, direction, energy, and (statistical) weight of all particle histories at a given position in the treatment geometry, which is usually at the beam aperture near the patient position. The particle tracks from the phase space file are sampled in subsequent simulations of particle transport through the patient geometry thus allowing the computational resources to be focused on dose calculations in the patient and not wasted on repeating expensive transport computations upstream of the patient. The primary benefit of using a surface source file is that it introduces no significant approximations into the source description, which should lead to improved dose accuracy. The drawbacks of this method include the extremely large (GB) size of the unportable binary files, lower computational efficiency, increased start-up times for parallel computations, and limitations on the number of particles that can be simulated and the dose precision achievable, which results from the finite amount of track information recorded in the surface source file. This limitation on the dose precision achievable with a surface source file is also known as its latent variance.\textsuperscript{13}

5.1.1.2 *Probability Distributions*

Detailed probability distributions describing the spatial, energy and angular distribution must be created from previous computations of the neutron beam line. This usually involves computing the distributions of particle current\textsuperscript{14} using a Monte Carlo or discrete ordinates transport code, but an auxiliary code may also be used to compute
probability distributions from a phase space file. The flexibility and detail allowed in defining these probability distributions for the subsequent transport calculations depends on the transport code used. In the case of the well-benchmarked code MCNP,\textsuperscript{15} the general source definition card (SDef) is used to define the probability distributions usually a few centimeters from the patient on an in-air plane corresponding to the beam aperture. Modeling the collimator assembly and other structures upstream of the aperture are not necessary for the subsequent dose calculations in the patient since the neutron and photon current scattering off the patient and back upstream into the collimator assembly and then back into the patient is negligibly small at \(< 1\%\). Also, modeling the source in this manner does not suffer from any of shortcomings of the surface source files, yet regardless of which transport code is used, grouping the track information into discrete bins may involve significant approximations and loss of information that reduces the accuracy of computed doses. The magnitude of these approximations may be particularly sensitive to the binning structure used, especially in those sections of the spectrum where the distribution changes rapidly. The fact that the probability distributions for the source variables (energy spectrum, spatial distribution, angular distribution) may be inseparable is also problematic for this method.

5.1.2 Objectives

This chapter compares two different methods of defining a neutron beam source for NCT treatment planning calculations, the surface source (phase space file) and SDef (probability distributions). A surface source model of a neutron beam is converted into a MCNP SDef model using a suite of tools designed and developed specifically for this purpose. In-phantom dose data produced by the surface source model are compared to
dose data produced by the SDef model to evaluate the accuracy of the doses computed by the SDef and hence the magnitude of the approximations introduced by the conversion process. If the inherent approximations could be limited to the extent that they produce no significant differences in dose when compared to calculations with surface sources, then the use of SDefs in NCT treatment planning calculations would indeed be advantageous since the shortcomings of using surface sources could be avoided without compromising accuracy. The various steps in the conversion process as well as the tools developed to perform the conversion will also be discussed.

5.2 Methods and Materials

The well-validated Monte Carlo transport code MCNP\textsuperscript{15} was used for all radiation transport calculations. MCNP is also used to perform the transport calculations for NCT treatment planning systems such as MacNCTPlan,\textsuperscript{16} NCTPlan,\textsuperscript{17} MiMMC,\textsuperscript{18,19} and JCDS.\textsuperscript{20}

5.2.1 Neutron Beam and Phantoms

The neutron beam used as a test case in this study is the MIT fission converter beam (FCB),\textsuperscript{21,22} which has been used in clinical trials of BNCT\textsuperscript{4} and has a Monte Carlo model and surface source representation that have been well-validated against physical measurements made in both an ellipsoidal head phantom\textsuperscript{23} and a large rectangular water phantom.\textsuperscript{23,24} In preparation for the work described in this chapter, considerable effort was expended to improve the pre-existing variance reduction in the FCB model, resulting in energy-dependent neutron and photon weight windows optimized to increase the amount of unique track information reaching the beam aperture while also limiting
excessive numbers of duplicate tracks. The improvements made to the variance reduction of the FCB model, as well as the work used to produce them, are discussed in Chapter 4. After producing a new surface source at the FCB beam aperture with a significantly increased amount of neutron and photon track information, the FCB model was validated again with the new surface source, reaffirming earlier findings of good agreement between calculations and in-phantom physical dosimetry measurements. The derived dose component scaling factors that are indicative of the agreement of calculations and measurements were within 1 standard deviation of unity for all dose components except the incident photon dose, which resulted in a scale factor of 1.95 due to the inability of MCNP to model delayed gammas.

5.2.2 Probability Distribution Construction

The surface source file written at the beam exit of the MIT FCB was converted into a set of probability distributions formatted for the MCNP SDef card using a suite of custom MATLAB (The MathWorks, Natick, MA) functions. Using MATLAB to manipulate and analyze the binary track data rather than relying upon MCNP tallies helped to expedite the iterative conversion process greatly. However, an important early test of the custom software was to compare its output of binned particle weight directly to MCNP tallies to ensure that the binary surface source file was being read and processed correctly. Track weight is directly proportional to the probability that a given track will occur and is properly adjusted by variance reduction techniques to ensure a fair Monte Carlo game and unbiased answers. The neutron and photon track information was read directly from the binary surface source file, and track weight was scored into a 4D array of radial (r), energy (E), polar angle (θ), and relative azimuthal angle (φ') bins for each
particle type, neutron and gamma. As shown in Figure 5.1, the relative azimuthal angle $\phi'$ is defined for the purposes of this work as the angle between the particle’s radial position vector (at an angle $\phi$) and the projection of the particle’s direction onto the source plane. The circular symmetry of the FCB collimator and the emerging neutron beam permits this compact and convenient representation of the source geometry using polar coordinates.

Figure 5.1  Parameters used to define the particle position and direction (indicated by the bold arrow) in the SDef source representations. $r$ and $\phi$ are sampled to determine position $(x,y)$. The polar angle $\theta$ and the relative azimuthal angle $\phi'$, defined relative to the track’s radial vector, determine particle direction.
Limiting the loss of information in binning the particle weight meant carefully selecting appropriately sized fine bins for each source variable. The scheme for neutrons was a mixture of 2, 5 and 10 mm bins for radius, 10 logarithmically spaced bins per decade for energy, and 2 degree bins for $\theta$ and $\phi'$. Similar binning was used for photons except that 100 keV energy bins were used for all energies except below 1 MeV where finer bins of 25 keV were needed to more accurately model peaks in the energy distribution. To construct the probability distributions needed for the SDef, the r-E-$\theta$ phase space was broken into several coarse rectangular regions (no segmentation was used in the $\phi'$ direction). In each coarse region, marginal probability distributions* for each source variable (r, E, $\theta$, $\phi'$) were computed from the binned track data. Figure 5.2 illustrates the fine binning of the track information and the coarse rectangular regions of the phase space, each of which has a unique marginal probability distribution for each source variable. These marginal distributions are sampled in the SDef model and actually define the source. The products of these marginal distributions were graphically and quantitatively compared to the corresponding joint probability distributions for source variable pairs in order to guide selection of the boundaries of the coarse phase space regions to minimize the differences between the two and thus produce an accurate probability model of the source. This iterative process involved selecting a set of boundaries for each source variable to define the coarse phase space, plotting and reviewing the agreement between the marginal and joint probability distributions in each rectangular region of that phase space, and then adjusting the boundaries as needed to

* For a joint distribution $f(x, y)$ of the random variables X and Y, the marginal distributions of X alone and Y alone are given by $g(x) = \int_{-\infty}^{\infty} f(x, y) \, dy$ and $h(y) = \int_{-\infty}^{\infty} f(x, y) \, dx$, respectively.
improve agreement. This process was repeated until sufficient agreement was observed or until limitations* of MCNP were reached. In order to achieve the required level of source dependency with the MCNP SDef, congruent source planes† were used, one for each coarse region of the phase space and each with its own marginal probability distributions for \( r, E, \theta \) and \( \phi' \).

\[
P_{i,j,k}(r,E,\theta,\phi') \equiv P_{i,j,k}(r) \cdot P_{i,j,k}(E) \cdot P_{i,j,k}(\theta) \cdot P_{i,j,k}(\phi')
\]

Figure 5.2 Track information from the surface source file is scored into an array of fine radial, energy, polar angle (\( \theta \)), and relative azimuthal angle (\( \phi' \)) bins such as illustrated here. This finely binned information is grouped into coarse regions for the \( r, E, \) and \( \theta \) source variables, as indicated by the thick dashed lines. In each coarse region (e.g., the shaded region), a unique marginal probability distribution is computed for each of the 4 source variables. The product of each region’s marginal probability distributions in \( r, E, \theta \) and \( \phi' \) is used to model the joint probability distribution \( P_{i,j,k}(r,E,\theta,\phi') \) in that region.

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* MCNP allows a maximum of 999 source variable distributions.
† Degenerate planar surfaces with different MCNP problem numbers but the identical geometric parameters.
5.2.2.1 Direction Sampling in MCNP5

In the standard method of direction sampling in MCNP, the polar angle $\theta$ is first sampled from a user-defined distribution in the SDef. Then, the relative azimuthal angle $\phi'$ is sampled uniformly from $-\pi$ to $+\pi$. However, in this study we determined that for the MIT FCB, $\phi'$ is not uniformly distributed and thus is not accurately modeled by the uniform sampling in MCNP. Instead, values of $|\phi'| < \pi/2$ are preferred (i.e., particles directed radially outward, away from the beam center), and, inside the beam aperture, this preference has a radial dependence that increases with distance from the beam center. Therefore, MCNP5 v1.40 was modified to allow the radial dependence of $\phi'$ to be accurately modeled using either a radially dependent offset cosine function or other standard user-defined distributions (e.g., a combination of line segments) as needed. The accuracy of the model was assessed by plotting the percent difference between the modeled and actual $\phi'$ distributions as a function of $\phi'$ for each region of the phase space.

In the radial region corresponding to the beam aperture, the probability distribution of $\phi'$ was modeled by Eq. 5.1,

$$P(\phi') = \frac{1}{2\pi} + b \frac{r}{r_0} \cos(\phi')$$

where $r_0$ is the radius of the beam aperture, 5.9 cm, and $b$ is a fitted constant which was determined via least squares fitting. This function is an empirical fit to the simulated joint $r$-$\phi'$ distribution that was found to match the sampled data well. One of the important properties of this probability distribution function is that, at the center of the beam ($r=0$), the $\phi'$ distribution is uniform. From symmetry arguments, one should expect uniformity of the $\phi'$ distribution at the center of the beam since there is no preferred direction. Since
the integral of Eq. 5.1 is not invertible, the distribution was sampled using the rejection method.\textsuperscript{25} For those radial regions outside of the beam aperture where the particle flux is significantly lower and the radial dependence of $\phi'$ is small, the $\phi'$ distribution is not well-described by the offset cosine function. The radially independent $\phi'$ probability distribution in these radial regions was modeled in the source definition by a series of line segments determined using least squares fitting. The modified MCNP executable was subjected to rigorous testing to ensure the patch worked exactly as intended within its limited scope.

\textbf{5.2.3 Monte Carlo Computations}

Using the MiMMC (Multi-Modal Monte Carlo) treatment planning system,\textsuperscript{18} 4 mm mixed-material voxel models of the modified Snyder head phantom\textsuperscript{26} and the large rectangular water phantom were constructed for radiation transport simulation with MCNP. The water phantom is a cube 40 cm on a side modeled entirely of light water while the Snyder head phantom is modeled using adult whole brain and adult whole cranium, as defined by ICRU Report 46.\textsuperscript{27} These two distinctly different phantoms allow the source definition techniques and the dose distributions they produce to be evaluated and compared under different geometric conditions, one relevant to clinical irradiations, and the other relevant to calibration conditions at some institutions. For consistency with both Harvard-MIT patient planning and calibration conditions, a 3 cm air gap was modeled between the beam aperture and the head phantom while the large water phantom was modeled adjacent to the beam aperture with no air gap. To further investigate the agreement of the different source definition techniques as a function of the source to
surface distance (SSD), additional simulations in the head and large water phantoms were performed with air gaps of 0 and 3 cm, respectively.

The transport simulations were performed in each phantom using MCNP5 v. 1.40 with the 3 different source models for the MIT FCB: a surface source representation and SDef models with and without $\phi'$ dependence. Simulations using an SDef with a $\phi'$ dependence employed a modified version of MCNP as described above. Two simulations per source model were used for dose calculations in each phantom. A coupled neutron/photon simulation (via “mode np”) was performed to sample neutrons from the source plane and transport them, along with any photons they produce, through the phantom while a photon-only simulation (via “mode p”) was performed to sample and transport only photons from the source. Neutron, photon, and $^{10}$B kerma factors$^{28}$ for ICRU 46 adult whole brain material were used to convert calculations of voxel-averaged neutron and photon fluence into the various dose components present in BNCT. The 5 calculated dose components include the boron dose via the $^{10}$B(n,$^\alpha$)$^7$Li reaction, thermal neutron dose mainly from the $^{14}$N(n,p)$^{14}$C reaction, fast neutron dose mainly from the $^1$H(n,n')$^1$H proton recoil reaction, induced photon dose from photons created inside the phantom mainly via the $^1$H(n,$^\gamma$)$^2$H reaction, incident photon dose from those photons that were produced upstream and outside of the phantom. The total biologically weighted brain dose was calculated as the sum of the boron, thermal neutron, fast neutron, induced photon and incident photon dose components weighted by RBE (Relative Biological Effectiveness) and CBE (Compound Biological Effectiveness) factors$^{29}$ of 1.3, 3.2, 3.2, 1.0, and 1.0, respectively.
Doses calculated in the head phantom were compared using isodose contours and dose vs. depth profiles along the central beam axis. In the SDef source models, source biasing of the fast neutrons was used, and photon production biasing was employed in all source models to improve statistics at depth in the phantoms. Although not as flexible or transparent as using variance reduction with the SDef, the surface source file has “built-in” variance reduction as a result of the energy-dependent weight windows used throughout the FCB beam model. To improve statistics when using the surface source file, which has limited particle information, the surface source file was sampled 15 times. Due to scattering in the phantom, sampling each neutron and photon track multiple times will result in different particle histories in the phantom and increase the chance that a track will be scored in the phantom. This significantly improves statistics for dose components that depend on the thermal flux, i.e., the boron, thermal neutron, and induced photon dose components. However, the effectiveness of multiple sampling is limited for fast neutrons and incident photons due to the relatively low number of interactions each experiences in the phantom before thermalization or escape. Simulations were performed in parallel on a Beowulf cluster (described in Appendix B) of 11 nodes with AMD® Athlon 64™ 3200+ (2.0 GHz) 64 bit processors and 2 GB RAM.

5.3 Results

For both neutrons and photons, a simple SDef with minimal phase space segmentation as well as a more segmented and complex SDef were created using the software suite. The simple SDef was created to help clearly illustrate the process while
the more complicated SDef was used to obtain a higher level of accuracy for comparisons with in-phantom dose calculations using the surface source model of the FCB.

Using the simple phase space segmentation scheme, Figure 5.3, Figure 5.4, and Figure 5.5 show a representative portion of the graphical comparisons used to determine the coarse region boundaries of the phase space and evaluate the accuracy of the calculated distributions for \((\theta, E)\), \((r, E)\), and \((r, \theta)\), respectively. Each of these figures shows the joint probability distribution(s) for a given source variable pair, the product(s) of the marginal distributions and the percent difference between the two. The joint distributions were produced by binning the particle weight from the surface source file, and the marginal distributions are actually defined in the SDef to model the joint distributions. Areas where the differences are very large (e.g., >30%) represent a significant degree of coupling between the probability distributions for that pair of source variables. The product of the marginal distributions produces adequately good agreement (~1% to 5%) with the joint distributions in those regions of the phase space responsible for producing a majority of the in-phantom dose, namely the epithermal energy region in the beam aperture. Any noticeable features, such as discontinuities or areas of large disagreement, in the plots of the marginal and joint distributions were seen as possible locations for coarse region boundaries. Once a boundary was assigned, the plots were reproduced to assess the change in agreement between the joint distribution and the product of the marginal distributions. In Figure 5.3, a noticeable feature is present around \(\theta = 20^\circ\) in the percent difference plot, and assigning a coarse region boundary at \(\theta = 20^\circ\) produced much better agreement between the joint and marginal distributions. In Figure 5.4, noticeable lines in the percent difference plots are seen at approximately \(r = 5.9\) cm
and $r = 11.8$ cm, so radial region boundaries were set at those particular radii and improve agreement. It should be noted that the region boundaries selected are in fact connected to the physical geometry of the FCB. For instance, $\sim 20^\circ$ is the angle between the sloped inner wall of the collimator cone and the beam aperture surface while the radial region boundaries represent the interfaces of different physical regions. For the simple neutron SDef, four concentric radial regions were selected: $0$ cm $\leq r \leq 5.9$ cm (beam aperture), $5.9$ cm $< r \leq 7$ cm (aperture/collimator interface to 1 cm inside the collimator wall), $7$ cm $< r \leq 11.8$ cm (the collimator wall), and $11.8$ cm $< r \leq 30$ cm (outside the collimator wall). Three energy regions corresponding to thermal ($1 \times 10^{-3}$ eV $\leq E \leq 0.5$ eV), epithermal ($5$ eV $< E \leq 10$ keV) and fast ($10$ keV $< E \leq 20$ MeV) neutrons were used. For all but the outermost radial region, two $\theta$ regions were used ($0^\circ \leq \theta \leq 20^\circ$, $20^\circ < \theta \leq 90^\circ$). However, due to the lower number of particle tracks in the outermost radial region, $\theta$ was not split in that radial region to reduce statistical fluctuations in the distribution. The resulting radial distributions of neutron current, neutron current energy spectra, and polar angle probability distributions for each region of the phase space are shown in Figure 5.6, Figure 5.7, and Figure 5.8, respectively. Inside the beam aperture, the neutron current distribution is nearly constant. Therefore, the radial probability distribution defined in the SDef for the radial region corresponding to the beam aperture increases linearly because the radial distribution of neutron current and the radial probability distribution are related by a factor of the radius.
Figure 5.3  Comparison of the joint probability distribution of polar angle $\theta$ and energy ($P(\theta,E)$) with the product of the marginal distributions ($P(\theta)\cdot P(E)$) for the radial region corresponding to the beam aperture ($r \leq 5.9$ cm) of the MIT FCB. Large percent differences indicate a high degree of inseparability between the two source variables. The alternating shaded/white areas demarcate different coarse regions of the r-E-\theta phase space.
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Figure 5.4  Comparison of the joint probability distribution of radius and energy ($P(r, E)$) with the product of the marginal distributions ($P(r) \cdot P(E)$). The alternating shaded/white areas demarcate different coarse regions of the r-E-θ phase space.
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Figure 5.5 Comparison of the joint probability distribution of radius and polar angle $\theta$ ($P(r, \theta)$) with the product of the marginal distributions ($P(r) \cdot P(\theta)$) for the thermal, epithermal, and fast neutron energy groups. The alternating shaded/white areas demarcate different coarse regions of the r-E-$\theta$ phase space.
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Figure 5.6 Radial distribution of neutron current for different energy and angular regions of the phase space at the plane of the beam aperture of the MIT FCB. Line thickness encodes the thermal, epithermal and fast neutron energy groups while solid and dashed lines represent polar angle regions of $0^\circ \leq \theta \leq 20^\circ$ and $20^\circ < \theta \leq 90^\circ$, respectively. For the radial region outside the beam collimator ($r > 11.8$ cm, right of the vertical line) where the neutron current is orders of magnitude smaller than in the aperture, only one $\theta$ bin was used to help reduce fluctuations in the distribution resulting from few particles.
Figure 5.7 Energy spectrum of the neutron current in different radial and angular regions on the beam aperture plane of the MIT FCB. Line thickness encodes the different radial regions on each plot with the top plot representing $0^\circ \leq \theta \leq 20^\circ$ and the bottom $20^\circ < \theta \leq 90^\circ$. In the outermost radial region ($11.8 \text{ cm} < r \leq 30 \text{ cm}$) $\theta$ was scored into only one bin ($0^\circ \leq \theta \leq 90^\circ$) to reduce statistical fluctuations. Energy bins of equal lethargy (10 per decade) were used to score the particle weight.
Figure 5.8  Polar angle ($\theta$) probability distributions calculated in each of 4 radial regions and 3 energy regions. Line thickness encodes the thermal, epithermal and fast neutron energy groups. The particle weight was scored into 2° bins from 0° to 90°.
In order to produce the more complicated neutron SDef, plots such as those shown in Figure 5.3, Figure 5.4, and Figure 5.5 were carefully examined, and the phase space was further segmented. Radial boundaries were placed at 4 cm, 5.9 cm, 7.5 cm, 11.8 cm, 17 cm, 22 cm, and 30 cm, energy boundaries were placed at 0.2 eV, 5 eV, 2 keV, 50 keV, 1 MeV, and 20 MeV, and θ boundaries were placed at 12°, 18°, 26°, 35°, and 60°. It should be noted that increasing the segmentation by adding region boundaries has no significant effect on the total simulation time since more than 99.3% of the computational effort is spent tracking the particles and not in sampling the SDef. However, there is a limit on the amount of segmentation that can be used in constructing an SDef since MCNP5 will not allow more than 999 distributions in a SDef.

For the simple photon SDef model, the radial boundaries were the same as for the simple neutron SDef except that the 7 cm boundary was removed resulting in 3 radial regions. Three energy regions (0 ≤ E ≤ 600 keV, 600 keV < E ≤ 2 MeV, and 2 MeV < E ≤ 10 MeV) and two segments in θ (0° ≤ θ ≤ 20° and 20° < θ ≤ 90°) were specified. The resulting radial distributions of incident photon current, incident photon current energy spectra, and polar angle probability distributions for each region of the phase space are shown in Figure 5.9, Figure 5.10, and Figure 5.11. To construct the more complicated photon SDef, radial boundaries were placed at 2 cm, 4 cm, 5.9 cm, 7 cm, 9 cm, 11.8 cm, 15 cm, 20 cm, and 30 cm, energy boundaries at 400 keV, 600 keV, 2 MeV, and 10 MeV, and θ boundaries at 20°, 26°, 36°, 46°, 56°, and 66°.
Figure 5.9  Radial distribution of incident photon current for different energy and angular regions of the phase space at the plane of the beam aperture of the MIT FCB. Line thickness encodes the 3 energy groups while solid and dashed lines represent polar angle regions of $0^\circ \leq \theta \leq 20^\circ$ and $20^\circ < \theta \leq 90^\circ$, respectively. For the radial region outside the beam collimator ($r > 11.8$ cm, right of the vertical line) where the photon current is orders of magnitude smaller than in the aperture, only one $\theta$ bin was used to help reduce fluctuations in the distribution resulting from few particles.
Figure 5.10  Energy spectrum of the incident photon current in different radial and angular regions on the beam aperture plane of the MIT FCB. Line thickness encodes the different radial regions on each plot with the top plot representing $0^\circ \leq \theta \leq 20^\circ$ and the bottom $20^\circ < \theta \leq 90^\circ$. In the outermost radial region ($11.8 \text{ cm} < r \leq 30 \text{ cm}$) $\theta$ was scored into only one bin ($0^\circ \leq \theta \leq 90^\circ$) to reduce statistical fluctuations. 100 keV energy bins were used to score the particle weight.
Figure 5.11  Polar angle ($\theta$) probability distributions for the incident photons calculated in each of 3 radial regions and 3 energy regions. Line thickness encodes the energy groups. The particle weight was scored into $2^\circ$ bins from $0^\circ$ to $90^\circ$.
Before performing any in-phantom dose calculations with the neutron or photon SDef models, the software suite used to create them was verified in a closed loop test. To perform the test, the newly created MCNP SDef source model of the MIT FCB was sampled in MCNP to write a binary surface source representation of the SDef. The software suite was then used to generate a SDef model from this binary surface source for the sole purpose of comparison with the original SDef. This testing and the resulting excellent agreement between the two SDef models helped to ensure the accuracy of the conversion process.

Figure 5.12 compares the radial dependence of $\phi'$ observed in the surface source with the fitted model described by Eq. 5.1 for epithermal neutrons in the radial region corresponding to the FCB beam aperture for $0^\circ \leq \theta \leq 90^\circ$, demonstrating very good agreement. However, as the phase space is segmented in $\theta$, the excellent agreement between the fitted model and the sampled $\phi'$ distribution deteriorates somewhat. Least squares analysis produced $b$ values of 0.043, 0.042, and 0.045 for the thermal, epithermal and fast energy regions of the phase space inside the beam aperture for $0^\circ \leq \theta \leq 20^\circ$, respectively. For $20^\circ < \theta \leq 90^\circ$, the resulting $b$ values were 0.109, 0.077, and 0.092 for the same energy regions. Outside the aperture, strong radial dependence of $\phi'$ was not observed, so other radially independent probability distributions of piecewise linear form were used. For photons, the shape of the $\phi'$ distribution was more complex than for the neutrons. Thus, the $\phi'$ distribution in each region of the phase space was analyzed in order to determine whether the offset cosine function or other radially independent distributions provided the best fit.
Figure 5.12 Probability distributions of the relative azimuthal angle $\phi'$ inside the beam aperture of the MIT FCB determined from the surface source file and the fitted model. The nonuniform distribution shows a preference for outward angles ($|\phi'| < \pi/2$). $r_0$ is the radius of the beam aperture, 5.9 cm, and $b$ is a fitted constant. Radial bins range from 0 to 5.9 cm in ~1 cm steps. $P(\phi')$ is shown averaged over the radial bins and is limited to $0 \leq \phi' \leq \pi$ for this comparison. In the modifications to MCNP5, the fitted model is symmetric about $\phi'=0$ and is sampled from $-\pi$ to $+\pi$.

Figure 5.13 compares isodose contours and depth vs. dose profiles along the central beam axis for the two complex SDef source models ($\phi'$ uniform and nonuniform) to reference data computed with the surface source in the head phantom at a source to surface distance of 3.0 cm. Table 5.1 summarizes the results for the head phantom and the large water phantom, reporting the error in maximum dose rate for the two SDef source models as compared to the reference surface source model. Significantly elevated dose rates as much as 15.2% higher than the reference surface source results were
computed with the SDef model. In the standard version of MCNP, only a uniform $\phi'$ distribution can be simulated with a SDef source model. Shifts in the isodose contours to deeper depths (and higher dose rates) for all dose components are clearly evident with the uniform $\phi'$ distribution. When the nonuniform $\phi'$ distribution was modeled accurately using the patched version of MCNP, the agreement between the SDef and the surface source improved dramatically, resulting in excellent agreement in the isodose contours. However, despite the dramatic improvement in the agreement in the incident photon contours between the surface source and the SDef with the nonuniform $\phi'$ distribution, differences are still evident at deeper depths in the phantom. However, this may be a result of noise (latent variance) in the surface source file. Nevertheless, this small disagreement (3.0% difference at 4.5 cm) in a dose component which in total represents only \(~6\%\) of the maximum total biologically weighted dose is acceptable and, given the difficulty experienced in modeling the complicated joint probability distributions for the incident photon, is not completely unexpected. Also, the data in Table 5.1 show that the error produced by not accurately modeling the $\phi'$ distribution is dependent upon the phantom as well as the distance from the source plane to the surface of the phantom. When the observed nonuniform $\phi'$ distribution of the FCB was modeled in the neutron and photon SDefs, good agreement with the surface source model was achieved regardless of the phantom or the distance from its surface to the source plane. However, evaluating the agreement in the large water phantom simply by looking in a single voxel at $D_{\text{max}}$ might not be a sufficient means of comparison. Thus, the mean disagreement was calculated for those voxels in the large water phantom which received at least 50% of the maximum dose for a given dose component. The resulting mean errors were less than
0.5% for all dose components except the fast neutrons and incident photons which produced mean errors of $3.3 \pm 3.7\%$ and $2.7 \pm 2.0\%$, respectively, when compared to the surface source model. A similar analysis was also performed in the head phantom for the simple and complex neutron and photon SDefs in order to evaluate the effect a more complex SDef has on the agreement with the surface source model. The resulting mean error values, as well as the error at $D_{\text{max}}$ for each dose component, are shown in Table 5.2. As expected, increasing the segmentation of the phase space and hence the complexity of the SDef resulted in better agreement with the surface source model. However, the improvement for the fast neutrons and incident photons was negligible indicating that further improvements in these two components may require another approach. Nevertheless, the disagreement between the dosimetry for the surface source model and the SDef model with the nonuniform $\phi'$ distribution is small compared to the uncertainties usually associated with physical dosimetry measurements in NCT.\textsuperscript{30,31}

To further illustrate the clinical significance of these findings, dose component scaling factors, derived from calculations with the uniform $\phi'$ SDef model in large rectangular water phantom (column 4 of Table 5.1), were applied to the uniform $\phi'$ SDef doses in the head phantom to simulate the planning system calibration routinely performed at some institutions. The total biologically weighted brain dose-volume histograms produced by simulating the irradiation of the Snyder head phantom (SSD=3.0 cm) with the different source representations of the MIT FCB are compared in Figure 5.14. The time required to deliver a maximum brain dose of 12.5 Gy$_w$ with the surface source model (13.47 minutes) was used to convert to units of absolute dose to facilitate a more direct comparison of the dose-volume data. The resulting disagreement between the
scaled SDef and the surface source curves (8.7%, 7.3%, and 11.6% in mean, minimum, and maximum total weighted brain dose, respectively) clearly indicates that the errors introduced during patient planning by sampling $\phi'$ uniformly are not corrected by calibrating the planning system in a reference phantom. Meanwhile, the agreement with the surface source dose-volume data improves significantly if the nonuniform $\phi'$ distribution is modeled accurately using the patched version of MCNP (0.5%, 2.4%, 0.3% in mean, minimum, and maximum total weighted brain dose, respectively). While the exact process and/or phantoms used to calibrate the planning system may depend on the institution, the approach used here represents a relatively effective analogue of the calibration methodology commonly used at various clinical BNCT sites.

Table 5.3 reports the statistical uncertainty for each dose component at $D_{\text{max}}$ in the ellipsoidal head phantom. The fast neutron and incident photon dose errors from the surface source run are the largest at 1.2% and 2.1% respectively, due to the limited amount of track information and the limited effect that multiple track sampling has on these two dose components. Table 5.4 contains simulation statistics for both the coupled neutron/photon and incident photon simulation into the ellipsoidal head phantom using the surface source and the SDef.
Figure 5.13  Comparison of dose rates calculated in the modified Snyder head phantom using different beam source models for the MIT FCB and a source to surface distance of 3.0 cm. Solid lines represent the reference doses calculated with the surface source while dashed and dash-dot lines represent data for the SDef models with and without $\phi'$ dependence, respectively. Isodose labels represent a percentage of the maximum dose rate in the phantom computed with the surface source for each dose component. Error bars (1 $\sigma$) in the depth-dose plots are omitted for clarity in cases where they are negligibly small.
Table 5.1  Error in maximum dose rate for SDef source models compared to the surface source reference values for the Snyder ellipsoidal head phantom and large rectangular water phantom for source to surface distances of 0 and 3.0 cm. Uncertainties are 1 $\sigma$.

| Dose Component     | Source to Surface Distance = 0 cm | | |  
|--------------------|----------------------------------| |  
|                    | Head Phantom | Large Water Phantom |  
|                    | $\phi'$ Uniform | $\phi'$ Nonuniform | $\phi'$ Uniform | $\phi'$ Nonuniform |  
| Boron              | 7.4 ± 0.2% | 0.3 ± 0.2% | 3.7 ± 0.2% | 0.4 ± 0.2% |  
| Thermal neutron    | 7.4 ± 0.2% | 0.3 ± 0.2% | 3.7 ± 0.2% | 0.4 ± 0.2% |  
| Fast neutron       | 4.2 ± 1.1% | 2.7 ± 1.1% | 2.3 ± 1.1% | 1.8 ± 1.1% |  
| Induced photon     | 8.1 ± 0.2% | 0.1 ± 0.2% | 2.5 ± 0.1% | 0.3 ± 0.1% |  
| Incident photon    | 3.0 ± 2.0% | 0.3 ± 2.0% | 0.0 ± 2.1% | −1.0 ± 2.1% |  
| Total weighted brain dose | 7.6 ± 0.2% | 0.2 ± 0.2% | 3.9 ± 0.1% | 0.5 ± 0.1% |  

<p>| Source to Surface Distance = 3.0 cm | | |</p>
<table>
<thead>
<tr>
<th>Dose Component</th>
<th>Head Phantom</th>
<th>Large Water Phantom</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\phi'$ Uniform</td>
<td>$\phi'$ Nonuniform</td>
</tr>
<tr>
<td>Boron</td>
<td>14.9 ± 0.2%</td>
<td>0.3 ± 0.2%</td>
</tr>
<tr>
<td>Thermal neutron</td>
<td>14.9 ± 0.2%</td>
<td>0.3 ± 0.2%</td>
</tr>
<tr>
<td>Fast neutron</td>
<td>10.2 ± 1.2%</td>
<td>0.8 ± 1.2%</td>
</tr>
<tr>
<td>Induced photon</td>
<td>13.5 ± 0.2%</td>
<td>0.5 ± 0.2%</td>
</tr>
<tr>
<td>Incident photon</td>
<td>10.0 ± 2.1%</td>
<td>−2.8 ± 2.1%</td>
</tr>
<tr>
<td>Total weighted brain dose</td>
<td>15.2 ± 0.2%</td>
<td>0.4 ± 0.2%</td>
</tr>
</tbody>
</table>

Table 5.2  Mean absolute value of dose error for all voxels receiving $\geq 50\%$ of the maximum dose and the error in maximum dose rate for the simple and complex SDef source models with nonuniform $\phi'$ compared to the surface source reference values for the Snyder ellipsoidal head phantom and a source to surface distances of 3.0 cm. Uncertainties are 1 $\sigma$.

<table>
<thead>
<tr>
<th>Dose Component</th>
<th>Simple SDef</th>
<th>Complex SDef</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Error</td>
<td>Error at $D_{\text{max}}$</td>
<td>Mean Error</td>
</tr>
<tr>
<td>Boron</td>
<td>1.6 ± 0.4%</td>
<td>2.2 ± 0.2%</td>
</tr>
<tr>
<td>Thermal neutron</td>
<td>1.6 ± 0.4%</td>
<td>2.0 ± 0.2%</td>
</tr>
<tr>
<td>Fast neutron</td>
<td>2.3 ± 1.7%</td>
<td>−1.1 ± 1.2%</td>
</tr>
<tr>
<td>Induced photon</td>
<td>1.4 ± 0.3%</td>
<td>2.0 ± 0.2%</td>
</tr>
<tr>
<td>Incident photon</td>
<td>3.2 ± 2.3%</td>
<td>2.2 ± 2.1%</td>
</tr>
<tr>
<td>Total weighted brain dose</td>
<td>1.6 ± 0.5%</td>
<td>2.2 ± 0.2%</td>
</tr>
</tbody>
</table>

444
Figure 5.14  Total biologically weighted brain dose-volume histograms produced by simulating the irradiation of the Snyder head phantom (SSD=3.0 cm) with the different source representations of the MIT FCB. The time required to deliver a maximum brain dose of 12.5 Gy\textsubscript{w} with the surface source model (13.47 minutes) was used to convert to units of absolute dose. Dose component scaling factors, derived from calculations with the SDef model and standard version of MCNP in large rectangular water phantom (column 4 of Table 5.1), were applied to the SDef doses in the head phantom to simulate the planning system calibration routinely performed at some institutions. The resulting disagreement between the uniform $\phi'$ SDef and the surface source curves (8.7%, 7.3%, and 11.6% in mean, minimum, and maximum brain dose, respectively) illustrates that the errors introduced during patient planning by sampling $\phi'$ uniformly are not corrected by calibrating the planning system in a reference phantom.
Table 5.3  Statistical uncertainty (1σ) in percent of the maximum dose rates for calculations in the head phantom for a source to surface distance of 3.0 cm. Each neutron and photon track from the surface source was sampled 15 times to improve in-phantom dose statistics while the SDef data corresponds to 400 million neutrons and photons.

<table>
<thead>
<tr>
<th>Dose Component</th>
<th>Statistical Uncertainty at D_{max} (%)</th>
<th>Surface Source</th>
<th>SDef</th>
</tr>
</thead>
<tbody>
<tr>
<td>boron</td>
<td>0.12</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>thermal neutron</td>
<td>0.12</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>fast neutron</td>
<td>1.16</td>
<td>0.44</td>
<td></td>
</tr>
<tr>
<td>induced photon</td>
<td>0.10</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>incident photon</td>
<td>2.07</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>total weighted brain dose</td>
<td>0.15</td>
<td>0.09</td>
<td></td>
</tr>
</tbody>
</table>

Table 5.4  Simulation statistics for the transport calculations in the ellipsoidal head phantom using the surface source and the complex neutron and photon SDefs. The np mode represents a coupled neutron/photon simulation while mode p simulates only incident photons. The total number of tracks sampled for the surface source is the product of the resampling factor and the number of distinct tracks in the surface source file, whereas for the SDef it is the number of histories from the MCNP input deck.

<table>
<thead>
<tr>
<th>Source Type</th>
<th>Mode</th>
<th>Number of Independent Histories</th>
<th>Number of Distinct Tracks</th>
<th>Total Number of Tracks Sampled</th>
<th>Resampling Factor</th>
<th>CPU Time (CPU h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface</td>
<td>np</td>
<td>$2.10 \times 10^7$</td>
<td>$4.29 \times 10^7$</td>
<td>$6.44 \times 10^8$</td>
<td>15</td>
<td>205.2</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>$1.43 \times 10^7$</td>
<td>$2.86 \times 10^7$</td>
<td>$4.29 \times 10^8$</td>
<td>15</td>
<td>11.4</td>
</tr>
<tr>
<td>SDef</td>
<td>np</td>
<td>$4.00 \times 10^8$</td>
<td>$4.00 \times 10^8$</td>
<td>$4.00 \times 10^8$</td>
<td>---</td>
<td>122.1</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>$4.00 \times 10^8$</td>
<td>$4.00 \times 10^8$</td>
<td>$4.00 \times 10^8$</td>
<td>---</td>
<td>12.9</td>
</tr>
</tbody>
</table>
5.4 Discussion

The custom suite of MATLAB scripts used in the SDef construction not only greatly expedited the iterative conversion process but also facilitated the analysis of the SDef at several intermediate steps to help guide the process towards producing optimal coarse region boundaries. Our tool produces source definition files for our two treatment planning codes, NCTPlan\textsuperscript{17,23} and MiMMC\textsuperscript{18,19} which use MCNP for dose calculations. Other NCT treatment planning systems that use MCNP (e.g., JCDS\textsuperscript{20}) could easily use this tool to produce source definitions with little or no modification. Producing source definition files for other codes, e.g. SERA, would require only minor modifications to our software. Since this tool could easily be applied to other neutron beams, it is available on request.

The preference for outwardly directed particle tracks in the actual source distribution produces lower dose rates relative to an SDef with a uniform distribution of φ' because outwardly directed particles have a greater tendency to miss the phantom and not deposit any energy. Modeling the radial dependence of the relative azimuthal angle in MCNP produced significantly better agreement between in-phantom dose rates calculated using the surface source and SDef, reducing the error in total biologically weighted dose from greater than 15% to less than 1%. Using this modification and the sophisticated MATLAB tool to analyze the surface source file and construct the SDef, the approximations in source modeling were minimized to result in excellent agreement with the dose rates in two different phantoms calculated using the surface source file.

Using versions of MCNP not modified with the patch described here, the SDef source model (uniform φ') and surface source models have both been used at Harvard-
MIT and elsewhere in clinical treatment planning for NCT. To some extent, the dose error resulting from using a uniform $\phi'$ distribution with the standard SDef model can be accounted for in planning system calibration by dose rate scaling. However, dose rate scaling corrects this problem only approximately since the effect of this error is not spatially uniform; i.e., with the planning system tuned to give good agreement on the central axis, agreement will be poorer laterally. This adjustment is also phantom-dependent as seen from Table 5.1, indicating that using a set of simple dose-scaling factors to correct for the nonuniform $\phi'$ distribution is not viable. In Figure 5.14, a difference of 11.6% in the maximum total weighted brain dose was observed between the SDef (with uniform $\phi'$ distribution) and the surface source even though dose component scale factors, derived in the large rectangular water phantom, had been applied to the SDef doses. Therefore, calibrating the planning system using measurements in a reference phantom will not fully correct the error in the subsequent dose calculations in a patient. Within this framework, the correct solution is to accurately model the $\phi'$ distribution using a patched version of MCNP or a surface source file.

The two NCT treatment planning systems developed at Idaho National Lab (INL), BNCT_Rtpe (BNCT Radiation Therapy Planning Environment) and its successor SERA (Simulated Environment for Radiotherapy Applications), use special-purpose Monte Carlo transport codes that require the neutron and photon sources to be defined as probability distributions. For these codes to determine each source particle’s starting direction, the polar angle $\theta$ is sampled from up to 10 user-defined equiprobable angular bins, and then the relative azimuthal angle $\phi'$ is sampled uniformly from $-\pi$ to $+\pi$. Thus, if the actual $\phi'$ distribution is not uniformly distributed as for the MIT FCB, errors for in-
phantom dose rates similar to those reported in this chapter using the standard unpatched version of MCNP might be expected with BNCT_Rtpe and SERA. However, a different modeling approach is generally used in these codes that may, at least to some extent, avoid the problem observed here with the angular distribution. For example, in the clinical trials of BNCT at Brookhaven National Laboratory, the Brookhaven Medical Research Reactor (BMRR) was modeled in BNCT_Rtpe in the 15 cm thick beam collimator 13.3 cm upstream of the beam aperture and not directly at the beam aperture plane as for the MIT FCB.\textsuperscript{37,38} Requiring BNCT_Rtpe to transport the sampled source particles through the collimator for each planning calculation may help to define the neutron and photon angular and spatial distribution at the beam exit, thus likely reducing errors due to a nonuniform $\phi'$ distribution like those observed in the simulations reported here. In this chapter we have not studied the question of whether specifying a simple (flat radial distribution and uniform $\phi'$ distribution) source inside the collimator upstream of the exit will provide adequate accuracy for the spatial and angular distributions at the beam exit and, more importantly, good dosimetric accuracy in-phantom. Clearly, this is a topic that warrants further study.

The coupled neutron/photon simulation using the surface source took 68\% longer to run, only to produce larger uncertainties for the fast neutrons and uncertainties of comparable magnitude for the other neutron dose components. However, it should be noted that the number of histories simulated for each source type was much larger than would be needed clinically. Simulating more particle tracks was necessary for this analysis to reduce the statistical uncertainty for the fast neutron and incident photon dose components. This also made it easier to assess small differences in in-phantom doses.
between the different source models. Nevertheless, given that the standard deviations varies inversely with the square root of the number of sampled tracks, the surface source would need to be run factors of 1.2, 7.0, 1.1 and 69 times longer to achieve levels of uncertainty in the boron, fast neutron, induced photon and incident photon dose rates, respectively, comparable to those in the SDef run. For the boron and induced photon dose rates, this could be achieved by further increasing the resampling factor for the surface source to beyond 15. However, to further decrease uncertainty in the fast neutron and incident photon dose components, the upstream simulation of the neutron beam line would need to be run longer to produce more track information in the surface source file, which would then lead to issues regarding the size (~400 GB) of the resulting surface source file and the length of the simulation needed to produce it (~67 CPU years on our cluster).

As demonstrated here, surface source files and SDefs offer both advantages and disadvantages as methods of defining a neutron beam for NCT treatment planning. While surface source files introduce no significant approximations into the source definition and can potentially provide “built-in” variance reduction for subsequent simulations, limitations on dose precision, lower computational efficiency, especially for parallel computations, and the large size of the unportable binary files are significant drawbacks. While SDefs do not suffer from any of these same disadvantages and also provide greater source transparency as well as more flexibility in variance reduction, constructing a SDef source model can potentially involve significant approximations that would significantly reduce the accuracy of the calculated doses. However, using the tools outlined in this chapter, the approximations in the SDef construction process were limited so as to
provide excellent agreement with the surface source and thus physical dosimetry measurements of the FCB.

In this chapter, the Monte Carlo model of the FCB epithermal neutron beam, as realized through a detailed surface source file, was employed as the reference standard for comparison with the SDef models. The accuracy of a computational model depends on the physics model as well as the cross sections and the fidelity of the model geometry and composition to the real world. The Monte Carlo model of the MIT research reactor and FCB is very detailed and has been well-validated with dose measurements in-air and in phantoms. Therefore, the FCB surface source model was used as the reference because the level of resolution and detail in the neutron spatial, energy, and angular probability distributions that can obtained through a Monte Carlo simulation far exceeds what is attainable with measurements. Moreover, it is generally only the marginal distribution for a given source variable that is obtained with measurements whereas the joint probability distribution is only determined by calculation. Furthermore, these findings indicate that a high level of detail regarding the beam’s spectral characteristics is required to construct an adequately accurate model of the neutron beam from probability distributions and obtain accurate dose calculations throughout the phantom.

The modification of the MCNP5 source code to enable simulation of angular distributions with nonuniform relative azimuthal angles has broader applications than those outlined in this work. Essentially, any attempt to model a radiation source with a significantly nonuniform relative azimuthal angle distribution will produce errors unless that non-uniformity is modeled in the transport calculations. The adjustments to the MCNP5 source introduced in here could easily be extended and/or tuned to the needs of a
particular transport problem. We expect it may be directly applicable to situations like computed tomography (CT) dosimetry and applications with circular collimators (e.g., stereotactic radiosurgery or Cyberknife).

5.5 Conclusions

A software tool has been developed to convert MCNP surface source models into MCNP SDefs. The surface source model of the MIT FCB was successfully converted into a MCNP SDef, which produced very good agreement with in-phantom dose rates calculated using the well-benchmarked surface source model. However, achieving such agreement required modifications to the MCNP source code to allow the nonuniform \( \phi' \) distribution for the FCB to be accurately modeled. Using a surface source file or a modified version of MCNP is the only way to accurately model the nonuniform \( \phi' \) distribution since the errors introduced by sampling \( \phi' \) uniformly are phantom-dependent and thus cannot be corrected using a set of dose-scaling factors. The conversion process, as well as the software suite used, could be easily employed for other neutron beams.
5.6 References


Computational Aspects of Treatment Planning for Neutron Capture Therapy


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6.1 Summary and Conclusions

Accurate and efficient treatment planning calculations are essential to maximizing the efficacy of Boron Neutron Capture Therapy (BNCT) and ensuring the safety of the patient. Therefore, this thesis has explored many of the computational aspects of BNCT treatment planning with the aim of improving both the accuracy and efficiency of the planning process. This thesis also sought to develop a better understanding of differences in computational dosimetry that exist between BNCT clinical sites to help address the obstacles that prevent pooling of clinical data for combined analysis.

6.1.1 Intercomparison of Neutron Capture Therapy Treatment Planning Systems

A suite of computational dosimetry reference problems were developed to test, compare, and analyze current and future BNCT treatment planning systems under conditions relevant to both patient planning and planning system calibration. These reference problems were based on an pre-existing set of problems which was greatly expanded to include multiple phantoms (a large rectangular water phantom, the modified
Snyder head phantom,\textsuperscript{2} and a cylindrical leg phantom), thermal and epithermal neutron beam spectra, and the multi-dimensional dose data (isodose contours and dose-volume histograms) that are commonly used in treatment planning. While the head and leg phantoms are meant to represent the different human anatomy that has been irradiated during BNCT, the large rectangular water phantom was included because it is used in planning system calibration at some institutions and its simple geometry can be represented by all of the planning systems without any geometric approximations. Using these newly designed reference problems, 4 of the treatment planning systems (TPSs) that have been used clinically (BNCT\textsubscript{Rtpe},\textsuperscript{3,5} SERA,\textsuperscript{6,7} MacNCTPlan,\textsuperscript{8,9} and NCTPlan,\textsuperscript{10,11}) were compared to reference dosimetry calculations performed using the well-benchmarked Monte Carlo radiation transport code, MCNP5.\textsuperscript{12} These reference calculations made use of analytical representations of the 3 phantoms as well as and the most up-to-date neutron and photon cross sections, material compositions, and kerma factors available to ensure that the reference data were not adversely influenced by geometric approximations or inaccurate transport calculations. The resulting comparison of the reference dose data to that directly output by each TPS resulted in many clinically significant and interesting differences, and additional effort was focused on understanding and explaining the causes of the observed disagreement.

Each of the planning systems deviated significantly from the reference calculations, with SERA and NCTPlan generally producing better agreement than their respective predecessors, BNCT\textsubscript{Rtpe} and MacNCTPlan. For BNCT\textsubscript{Rtpe} and SERA, the deviations from the reference calculations observed in the depth-dose profiles were resolved into the following factors: differences in calculated neutron or photon flux
(which result from differences in physics models, transport algorithms, and cross section data), interpolation errors, differences in kerma factors, the improper runtime multiplication of neutron and boron kerma factors by the edit mesh density, differences in dose definition, a biasing and cutoff energy for the fast neutron source biasing run mode that is too high, and a photon normalization error. Conversely, the observed disagreement for MacNCTPlan and NCTPlan was usually easier to resolve into contributing factors and was most often attributed to a characteristic interpolation error discovered in both TPSs and the geometric approximations associated with relatively large 1 cm$^3$ voxel models. During the intercomparison, it became increasingly clear, especially in the leg phantom where a thermal neutron beam is used, that the 1 cm$^3$ volumes are insufficient for use in either a scoring mesh or a voxel model. Smaller volumes should be used to improve dose calculation and geometric modeling accuracy. Furthermore, the differences observed between the TPSs are an example of the obstacles that prevent patient data from different clinical sites from being combined; doses reported by clinical sites that have used different TPSs cannot be legitimately combined until those obstacles are properly addressed by developing a better understanding of the magnitudes and causes of the differences between the planning systems. This study has done much towards resolving these issues.

6.1.2 Comparison of Doses Delivered in Clinical Trials of Neutron Capture Therapy in the USA

Once differences in physical and computational dosimetry are adequately addressed, clinical data from different sites can indeed be pooled together as was successfully done for clinical data from BNL (Brookhaven National Laboratory) and Harvard-MIT (Massachusetts Institute of Technology). To accomplish that, a relationship
between BNL and Harvard-MIT clinical dosimetry was determined and validated using MIT physical dosimetry measurements made at BNL in two different phantoms as part of the International Dosimetry Exchange.\textsuperscript{13,14} This relationship was used to recompute the BNL patients’ dosimetry, normalizing it to the Harvard-MIT clinical dosimetry. This relationship (in the form of dose component scaling factors) was further resolved into several contributing factors. Differences in physical dosimetry techniques between BNL and Harvard-MIT, the presence of a subtle geometric modeling error in BNL’s calibration calculations, and small differences between BNL’s measurements and calibration calculations combined to lower the reported BNL patient doses significantly. The reductions in mean brain doses averaged 10\% in the initial 15 patients treated with the 8 cm collimator, 28\% for the 23 patients treated with the 12 cm collimator before the fuel shuffle, and 25\% for the final 16 patients treated after the fuel shuffle. This adjustment enabled the BNL clinical data to be legitimately pooled together with Harvard-MIT patient data for a dose response analysis for radiation-induced somnolence syndrome. Probit analysis of the composite data set yielded $ED_{50}$ values for the incidence of somnolence of 5.76 Gy\textsubscript{w} and 14.4 Gy\textsubscript{w} for mean and maximum brain dose, respectively. As a direct result of the increased sample size of the larger patient pool, the confidence intervals of the $ED_{50}$ values were narrowed significantly. Also, the adjustments to the BNL patient doses reduced the $ED_{50}$ for the mean brain dose of the BNL patients alone by 26\%. The reductions in the reported doses from the BNL clinical trials are clinically significant and have important implications for those within the NCT community relying on the BNL clinical data to choose initial doses in clinical trials of BNCT. Furthermore, these findings should provide strong motivation for all institutions
undertaking human BNCT clinical trials to participate in dosimetric intercomparisons like the International Dosimetry Exchange.\textsuperscript{13,14}

6.1.3 Application of Variance Reduction in Monte Carlo Treatment Planning Calculations for Neutron Capture Therapy

The energy dependent neutron and photon weight windows used in the detailed Monte Carlo computations of the MIT fission converter beam (FCB)\textsuperscript{15} were optimized to produce a surface source file at the patient position with significantly less duplicate track information that resulted in a 9-fold increase in the mean computationally efficiency of the subsequent in-phantom total weighted dose calculations and a very large, 200-fold decrease in the size of the binary file (34 GB vs. 0.17 GB) for the same number of starting histories. Problems in the incident photon dose distribution (streak artifacts of high dose and large uncertainty) associated with high weight tracks were also corrected. The Beowulf cluster (described in Appendix B and constructed to facilitate the work in this thesis) was used for simulations with the optimized weight windows to increase the unique track information reaching the patient position and result in a more accurate surface source representation. The new MCNP surface source representation of the FCB was successfully validated using physical dosimetry measurements.\textsuperscript{16,17}

Several of the variance reduction techniques available in MCNP were also investigated in an attempt to increase the computational efficiency of in-phantom dose calculations for BNCT treatment planning using calculations in an NCTPlan voxel model of the Snyder head phantom. The efficiency and accuracy of dose calculations in the head phantom with different variance reduction techniques were compared to a baseline simulation with the default MCNP variance reduction (implicit capture and weight cutoff). By combining both fast neutron source biasing and photon production biasing
and disabling implicit neutron capture, the mean computational efficiency of the total weighted brain dose calculations in the phantom voxel model was increased by a factor of 2.2, meaning that by using these techniques the same level of precision for the total weighted dose could be achieved in less than half the runtime.

### 6.1.4 Neutron Beam Source Definition Techniques for Neutron Capture Therapy Treatment Planning

Two methods of neutron beam source definition commonly used in BNCT treatment planning calculations (MCNP surface source and MCNP SDef) were compared. A surface source is a binary file that contains exact track characteristics, such as position, direction, energy, and (statistical) weight of all particle histories at a given position in the treatment geometry, and the tracks from this file are sampled in subsequent simulations of particle transport through the patient geometry. The radiation source can also be defined by detailed probability distributions (via the SDef card) that describe the spatial, energy and angular characteristics of the beam. These two techniques were compared by simulating transport through a 4 mm³ voxel model of the modified Snyder head phantom. To facilitate the comparison, a software tool (called ss2sdef) was developed to analyze MCNP surface source files and construct MCNP SDef source probability models. A novel feature of this software tool is the analysis of the separability of different source variable probability distributions. Since it is the marginal distributions of the source variables that are sampled to determine source particle characteristics, the software tool allows evaluation of how well the product of the marginal probability distributions for two source variables (e.g., energy and polar angle) approximate the actual joint distribution of the source variables through comparison and error plots. This feature, especially the error plots, greatly facilitates selection of boundaries for
segmenting the phase space to improve the fidelity of the source representation. This software suite was used to analyze the surface source model of the MIT FCB and construct a SDef representation. The analysis of the FCB surface source showed that the source variables are, to a large degree, inseparable and that a high degree of segmentation of the source phase space (e.g., 252 regions) is needed to obtain an accurate representation of the source for treatment planning. When compared to dose calculations in the head phantom with the surface source file, the SDef produced significant errors (e.g., 15.2% at $D_{\text{max}}$). Using a patched version of MCNP5 that allowed the observed radial dependence of the relative azimuthal angle to be modeled by the SDef, errors in all dose components in the head phantom at $D_{\text{max}}$ were reduced to acceptably small levels with none being statistically significant ($P \geq 0.13$) except for the 0.5% error in the induced photon dose. Therefore, it was concluded that a modified version of MCNP or a surface source file is required to accurately model the neutron and photon angular distributions since the errors introduced by using a uniform distribution for the relative azimuthal angle vary spatially, are phantom-dependent, and thus cannot be corrected using a set of dose-scaling factors.

6.2 Future Work

The evaluation of the 4 planning systems with the reference data produced results that were sometimes alarming. These results provide a compelling argument that improved quality assurance is needed for NCT treatment planning systems. The suite of test problems developed here could play an important role assessing the other existing and future planning systems. A primary goal during the development and application of
the suite of reference dosimetry calculations was to facilitate the inclusion of other BNCT treatment planning systems as they become available or are developed in the future. Other planning systems, such as JCDS, THORplan, and MiMMC could easily be included in the intercomparison. Also, now that a basic understanding of how the planning systems compare has been developed, the reference problems could be extended to include more realistic beams and phantoms based on human image data. Also, calculations of dose using electron transport should be included (if a reliable computational tool can be found for the coupled neutron-photon-electron dose calculations) as part of the reference calculations to properly evaluate the accuracy of estimating dose with kerma, especially near the patient surface.

MIT has made dose measurements in 8 of the 11 neutron beams recently used for clinical BNCT with a standard dosimetric approach as part of the International Dosimetry Exchange. This wealth of measurement data provides the basis necessary to address differences in physical and computational dosimetry and pool patient data from other clinical sites with that from BNL and Harvard-MIT. Analysis of the head phantom measurement and calculation data for the Treatment Planning Exchange should continue. It was analysis of this data for BNL that lead to the detailed dosimetric analysis of Chapter 3.

The variance reduction techniques investigated using the generic epithermal neutron beam and head phantom should be assessed in a clinical beam, like the surface source and SDef representations of the FCB, to ensure that the significant increases in the computational efficiency of dose calculations transcend any specific beam or irradiation conditions. It should also be possible to partially or fully apply the variance reduction
techniques that increased computational efficiency (fast neutron source biasing, photon production biasing, disabling implicit capture) to other treatment planning systems, like SERA.

In Chapter 5, two methods of neutron beam source definition were investigated, surface source files and SDef probability distributions. As used in NCTPlan, both methods locate planar sources in air a short distance from the patient. With the SDef representation, a large and rather complicated set of probability distributions is needed to accurately model the source. The two INL (Idaho National Laboratory) treatment planning systems, BNCT_Rtpe and SERA, take a different approach. In addition to the patient, they include part of the collimator in the computational model and sample a relatively simple set of source probability distributions inside the collimator to define the source. Transporting particles from a source plane through the collimator for each planning calculation may help to define the neutron and photon angular and spatial distributions at the beam exit and therefore reduce errors due to inaccurately modeling the source. The accuracy of this technique should be evaluated, especially for the short (e.g., 5 cm) thicknesses of collimator sometimes used in models. The tools developed in Chapter 5 would greatly facilitate this analysis and could be easily be adapted, as needed, to work with other TPSs.

Also, further work should be performed to get the patch to MCNP5 that was developed to allow the neutron and photon angular distributions to be accurately modeled incorporated into standard MCNP. The patch is essential to being able to accurately model the FCB with SDef probability distributions, and therefore it is likely to be beneficial to other groups within the NCT community. However, it could also be
extended to apply to other transport problems, such as computed tomography (CT) dosimetry and applications with circular collimators (e.g., stereotactic radiosurgery or Cyberknife).

This thesis has provided various observations of BNCT treatment planning that could be used to improve the MiMMC treatment planning system that is currently being developed to overcome many of the limitations of NCTPlan. MiMMC provides a unique platform to test and incorporate new features into the treatment planning process, and its open source licensing also provides a level of transparency that facilitates more rapid development and code review than otherwise possible. Given the small group usually responsible for the development and testing of BNCT treatment planning systems, openness is important as it prevents spending valuable manpower implementing and testing features that already exist. Therefore, it is believed that MiMMC may represent a positive step forward towards more standardized BNCT computational dosimetry.

Drawing from the overall experience of this thesis work and extrapolating to the future, it is believed that BNCT treatment planning would benefit greatly from some basic level of standardization since many of the significant differences that currently exist between the planning systems could have been prevented if such standardization had existed during their respective development and testing. An appropriate starting point for standardization would be acceptance of a common set of kerma factors and dose definitions.
6.3 References


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A.1 Introduction

The complete set of reference data described in Chapter 2 is included here. For the large rectangular water phantom, ellipsoidal head phantom, and leg phantom, relevant dose data are displayed from each planning system (BNCT_Rtpe, SERA, MacNCTPlan and NCTPlan) and compared to the corresponding reference data (MCNP5 and post-processing by MATLAB). For the head phantom, both single and multi-field data are included. The data are grouped by type: dose vs. depth profiles along the central beam axis, isodose contours and dose difference distributions for orthogonal beam planes, and dose-volume histograms for the relevant anatomical structures in the phantom. Within each type, the data are further organized by dose component: thermal neutron flux, boron dose, thermal neutron (and nitrogen) dose, fast neutron (and hydrogen) dose, induced photon dose, incident photon dose, and total biologically weighted dose.

The calculated data in the large water and ellipsoidal head phantoms were produced by simulating a monodirectional generic epithermal neutron beam, 10 cm in
diameter, normalized to a neutron flux of $1 \times 10^{10}$ n/cm$^2$s. For the leg phantom, the simulated neutron source was a monodirectional thermal neutron beam 10 cm in diameter normalized to a neutron flux of $1 \times 10^{10}$ n/cm$^2$s. The simulated photon source for all 3 phantoms was a 2.0 MeV monoenergetic and monodirectional 10 cm diameter disc source normalized to a flux of $2 \times 10^8 \gamma$/cm$^2$s.

To facilitate the direct comparison of isodose contours between each treatment planning system and the reference, the contours were plotted in units of absolute dose rather than as a percentage of a reference dose. In order to calculate dose, treatment times for each planning system were calculated based on realistic BNCT dose prescriptions for each phantom type: a maximum brain dose of 12.5 Gy$_w$ for the head phantom and a minimum tumor dose of 24 Gy$_w$ for the leg phantom. The resulting treatment times for each planning system and the reference are shown in Table A.1. Similarly, plotting the dose-volume data from each TPS as percent volume vs. percent of the reference dose would have made a direct comparison difficult since the reference doses were different for each TPS. So, using the reference treatment times from Table A.1, the dose-volume data from each TPS and the reference were plotted as percent volume vs. absolute dose.

<table>
<thead>
<tr>
<th>Table A.1</th>
<th>Treatment time in minutes required to deliver a maximum brain dose of 12.5 Gy$_w$ for the head phantom or a minimum tumor dose of 24 Gy$_w$ for the leg phantom.</th>
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</thead>
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<tr>
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<td>Head Phantom</td>
</tr>
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<td></td>
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<tr>
<td>Reference</td>
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</tr>
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<tr>
<td>SERA</td>
<td>3.04</td>
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<tr>
<td>MacNCTPlan</td>
<td>3.34</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>3.33</td>
</tr>
</tbody>
</table>
A.2 Dose vs. Depth Profiles

A.2.1 Large Rectangular Water Phantom

Figure A.1  Thermal neutron flux and percent difference \((100 \times \text{[TPS–Ref]/Ref}_{\text{max}})\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. SERA and BNCT_Rtpe data are calculated at (default) intervals of 5 mm. MCNP5 served as the reference for percent difference calculations.
Figure A.2  Boron dose rate for a $^{10}$B concentration of 15 μg/g and percent difference $(100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.3  Thermal neutron (and nitrogen) dose rate and percent difference $(100 \times \text{[TPS−Ref]/Ref}_{\text{max}})$ as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.4 Fast neutron (and hydrogen) dose rate and percent difference \((100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.5  Induced photon dose rate and percent difference (100×[TPS−Ref]/Ref_{max}) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.6  Incident photon dose rate and percent difference (\(100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_{\text{max}}}\)) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.7 Total biologically weighted brain dose rate and percent difference 
($100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}}$) as a function of depth along the central beam 
axis in the large rectangular water phantom for each planning system. 
MCNP5 served as the reference for percent difference calculations.
Total biologically weighted tumor dose rate and percent difference (100\times[TPS–Ref]/Ref_{max}) as a function of depth along the central beam axis in the large rectangular water phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
A.2.2 Head Phantom

![Thermal Neutron Flux (Head Phantom)](image)

**Figure A.9** Thermal neutron flux and percent difference ($100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}}$) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. SERA and BNCT Rtpe data are calculated at (default) intervals of 5 mm. MCNP5 served as the reference for percent difference calculations.
Figure A.10  Boron dose rate for a $^{10}$B concentration of 15 μg/g and percent difference \((100\times[TPS-Ref]/\text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.11 Thermal neutron (and nitrogen) dose rate and percent difference \((100 \times \text{TPS-Ref}/\text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.12 Fast neutron (and hydrogen) dose rate and percent difference \((100\times[TPS-\text{Ref}]/\text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
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Figure A.13  Induced photon dose rate and percent difference ($100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}}$) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.14 Incident photon dose rate and percent difference \((100\times[TPS-\text{Ref}]/\text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.15  Total biologically weighted brain dose rate and percent difference \((100 \times [\text{TPS} - \text{Ref}]/\text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.16 Total biologically weighted tumor dose rate and percent difference \((100 \times [TPS_{\text{Ref}} - \text{Ref}]/\text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the ellipsoidal head phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
A.2.3 Leg Phantom

Figure A.17 Thermal neutron flux and percent difference \((100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the leg phantom for each planning system. SERA and BNCT_Rtpe data are calculated at (default) intervals of 5 mm. MCNP5 served as the reference for percent difference calculations.
Figure A.18  Boron dose rate for a $^{10}$B concentration of 22.5 $\mu$g/g and percent difference $(100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})$ as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.19  Thermal neutron (and nitrogen) dose rate and percent difference \((100\times[TPS-\text{Ref}]/\text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.20 Fast neutron (and hydrogen) dose rate and percent difference \((100\times[\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.21  Induced photon dose rate and percent difference ($100 \times \text{[TPS−Ref]/Ref}_\text{max}$) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.22  Incident photon dose rate and percent difference \((100\times[TPS-\text{Ref}]/\text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.23 Total biologically weighted skin dose rate and percent difference \((100 \times \frac{\text{TPS} - \text{Ref}}{\text{Ref}_{\text{max}}})\) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
Figure A.24  Total biologically weighted tumor dose rate and percent difference \((100 \times [\text{TPS} - \text{Ref}] / \text{Ref}_{\text{max}})\) as a function of depth along the central beam axis in the leg phantom for each planning system. MCNP5 served as the reference for percent difference calculations.
A.3 Isodose Contours

A.3.1 Head Phantom

Boron Dose

Figure A.25  Boron isodose contours for a $^{10}$B concentration of 15 $\mu$g/g in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.26  Boron isodose contours for a $^{10}$B concentration of 15 μg/g in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Thermal Neutron Dose

Figure A.27  Thermal neutron (and nitrogen) isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.28 Thermal neutron (and nitrogen) isodose contours in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
Fast Neutron Dose

Figure A.29  Fast neutron (and hydrogen) isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Fast Neutron Dose

Figure A.30  Fast neutron (and hydrogen) isodose contours in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Induced Photon Dose

Figure A.31 Induced photon isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Induced Photon Dose

Figure A.32 Induced photon isodose contours in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Appendix A: Reference Data for Neutron Capture Therapy Treatment Planning Systems  

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Incident Photon Dose

![Incident Photon Isodose Contours](image)

Figure A.33  Incident photon isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Appendix A: Reference Data for Neutron Capture Therapy Treatment Planning Systems  J.R. Albritton

Incident Photon Dose

Figure A.34 Incident photon isodose contours in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Total Biologically Weighted Brain Dose

Figure A.35  Total biologically weighted brain isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Total Biologically Weighted Brain Dose

Figure A.36 Total biologically weighted brain isodose contours in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
Total Biologically Weighted Tumor Dose

Figure A.37 Total biologically weighted tumor isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
Total Biologically Weighted Tumor Dose

Figure A.38  Total biologically weighted tumor isodose contours in the coronal plane containing the central beam axis for a 1-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
Figure A.39  Boron isodose contours for a \(^{10}\text{B}\) concentration of 15 μg/g in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.40 Boron isodose contours for a $^{10}$B concentration of 15 μg/g in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.41  Thermal neutron (and nitrogen) isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.42  Thermal neutron (and nitrogen) isodose contours in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Fast Neutron Dose

Figure A.43  Fast neutron (and hydrogen) isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.44  Fast neutron (and hydrogen) isodose contours in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.45 Induced photon isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Appendix A: Reference Data for Neutron Capture Therapy Treatment Planning Systems  J.R. Albritton

Induced Photon Dose

Figure A.46  Induced photon isodose contours in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.47 Incident photon isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.48 Incident photon isodose contours in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Total Biologically Weighted Brain Dose

Figure A.49  Total biologically weighted brain isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Total Biologically Weighted Brain Dose

Figure A.50  Total biologically weighted brain isodose contours in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Total Biologically Weighted Tumor Dose

Figure A.51 Total biologically weighted tumor isodose contours in the transverse plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.52  Total biologically weighted tumor isodose contours in the coronal plane containing the central beam axis for a 3-field irradiation of the head phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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A.3.2 Leg Phantom

Boron Dose

Figure A.53 Boron isodose contours for a $^{10}$B concentration of 22.5 μg/g in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Boron Dose

Figure A.54  Boron isodose contours for a $^{10}$B concentration of 22.5 $\mu$g/g in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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 Thermal Neutron Dose

Figure A.55  Thermal neutron (and nitrogen) isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Thermal Neutron Dose

![Contour Maps](image)

Figure A.56  Thermal neutron isodose contours in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Fast Neutron Dose

Figure A.57  Fast neutron (and hydrogen) isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Fast Neutron Dose

Figure A.58  Fast neutron isodose contours in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Induced Photon Dose

**Figure A.59** Induced photon isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Induced Photon Dose

Figure A.60  Induced photon isodose contours in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Incident Photon Dose

BNCT_Rtpe

SERA

MacNCTPlan

NCTPlan

Figure A.61 Incident photon isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.62 Incident photon isodose contours in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Figure A.63  Total biologically weighted skin isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Appendix A: Reference Data for Neutron Capture Therapy Treatment Planning Systems  J.R. Albritton

Figure A.64  Total biologically weighted skin isodose contours in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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### Total Biologically Weighted Tumor Dose

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Figure A.65  Total biologically weighted tumor isodose contours in the transverse plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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Total Biologically Weighted Tumor Dose

Figure A.66 Total biologically weighted tumor isodose contours in the oblique plane containing the central beam axis for a 1-field irradiation of the leg phantom. Each planning system’s contours (solid) are overlaid with the reference contours (dashed) after the treatment time for each planning system from Table A.1 was used to convert the reference dose rates to absolute dose.
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A.4 Dose Difference Distributions

A.4.1 Head Phantom

Figure A.67 Difference in thermal neutron flux in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron flux for a 1-field irradiation of the head phantom.
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Figure A.68  Difference in thermal neutron flux in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron flux for a 1-field irradiation of the head phantom.
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Figure A.69  Difference in boron dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference boron dose for a 1-field irradiation of the head phantom.
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Appendix A: Reference Data for Neutron Capture Therapy Treatment Planning Systems  

Figure A.70  Difference in boron dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference boron dose for a 1-field irradiation of the head phantom.
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Figure A.71  Difference in thermal neutron (and nitrogen) dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron dose for a 1-field irradiation of the head phantom.
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Figure A.72  Difference in thermal neutron (and nitrogen) dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron dose for a 1-field irradiation of the head phantom.
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Figure A.73  Difference in fast neutron (and hydrogen) dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference fast neutron dose for a 1-field irradiation of the head phantom.
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Figure A.74 Difference in fast neutron (and hydrogen) dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference fast neutron dose for a 1-field irradiation of the head phantom.
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Figure A.75  Difference in induced photon dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference induced photon dose for a 1-field irradiation of the head phantom.
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Figure A.76  Difference in induced photon dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference induced photon dose for a 1-field irradiation of the head phantom.
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Figure A.77  Difference in incident photon dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference incident photon dose for a 1-field irradiation of the head phantom.
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Figure A.78  Difference in incident photon dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference incident photon dose for a 1-field irradiation of the head phantom.
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Figure A.79  Difference in total biologically weighted brain dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the head phantom.
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Figure A.80  Difference in total biologically weighted brain dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the head phantom.
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Figure A.81 Difference in total biologically weighted tumor dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the head phantom.
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Figure A.82  Difference in total biologically weighted tumor dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the head phantom.
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Figure A.83  Difference in thermal neutron flux in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron flux for a 3-field irradiation of the head phantom.
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Figure A.84  Difference in thermal neutron flux in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron flux for a 3-field irradiation of the head phantom.
Figure A.85  Difference in boron dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference boron dose for a 3-field irradiation of the head phantom.
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Figure A.86 Difference in boron dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference boron dose for a 3-field irradiation of the head phantom.
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Figure A.87 Difference in thermal neutron (and nitrogen) dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron dose for a 3-field irradiation of the head phantom.
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Figure A.88 Difference in thermal neutron (and nitrogen) dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron dose for a 3-field irradiation of the head phantom.
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Figure A.89  Difference in fast neutron (and hydrogen) dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference fast neutron dose for a 3-field irradiation of the head phantom.
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Figure A.90 Difference in fast neutron (and hydrogen) dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference fast neutron dose for a 3-field irradiation of the head phantom.
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Figure A.91  Difference in induced photon dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference induced photon dose for a 3-field irradiation of the head phantom.
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Figure A.92  Difference in induced photon dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference induced photon dose for a 3-field irradiation of the head phantom.
Figure A.93  Difference in incident photon dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference incident photon dose for a 3-field irradiation of the head phantom.
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Appendix A: Reference Data for Neutron Capture Therapy Treatment Planning Systems

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Figure A.94  Difference in incident photon dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference incident photon dose for a 3-field irradiation of the head phantom.
Appendix A: Reference Data for Neutron Capture Therapy Treatment Planning Systems  

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Figure A.95  
Difference in total biologically weighted brain dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 3-field irradiation of the head phantom.
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Figure A.96 Difference in total biologically weighted brain dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 3-field irradiation of the head phantom.
Total Biologically Weighted Tumor Dose Difference (TPS – Ref)

Figure A.97 Difference in total biologically weighted tumor dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 3-field irradiation of the head phantom.
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Figure A.98 Difference in total biologically weighted tumor dose in the coronal plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 3-field irradiation of the head phantom.
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A.4.2 Leg Phantom

Figure A.99  Difference in thermal neutron flux in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron flux for a 1-field irradiation of the leg phantom.
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Figure A.100  Difference in thermal neutron flux in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron flux for a 1-field irradiation of the leg phantom.
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Figure A.101 Difference in boron dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference boron dose for a 1-field irradiation of the leg phantom.
Figure A.102 Difference in boron dose in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference boron dose for a 1-field irradiation of the leg phantom.
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Figure A.103  Difference in thermal neutron (and nitrogen) dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron dose for a 1-field irradiation of the leg phantom.
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Figure A.104 Difference in thermal neutron dose in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference thermal neutron dose for a 1-field irradiation of the leg phantom.
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Figure A.105 Difference in fast neutron (and hydrogen) dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference fast neutron dose for a 1-field irradiation of the leg phantom.
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Figure A.106 Difference in fast neutron dose in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference fast neutron dose for a 1-field irradiation of the leg phantom.
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Figure A.107  Difference in induced photon dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference induced photon dose for a 1-field irradiation of the leg phantom.
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Figure A.108 Difference in induced photon dose in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference induced photon dose for a 1-field irradiation of the leg phantom.
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Figure A.109  Difference in incident photon dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference incident photon dose for a 1-field irradiation of the leg phantom.
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Figure A.110 Difference in incident photon dose in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference incident photon dose for a 1-field irradiation of the leg phantom.
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Figure A.111 Difference in total biologically weighted skin dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the leg phantom.
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Figure A.112 Difference in total biologically weighted skin dose in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the leg phantom.
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Figure A.113 Difference in total biologically weighted tumor dose in the transverse plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the leg phantom.
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Figure A.114 Difference in total biologically weighted tumor dose in the oblique plane containing the central beam axis expressed as a percentage of the maximum reference total weighted dose for a 1-field irradiation of the leg phantom.
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A.5 Dose-Volume Histograms

Table A.2  Volumes in cm$^3$ of the various anatomical regions in the head and leg phantoms as calculated by each treatment planning system. The analytical volumes are also included as a point of comparison. MacNCTPlan and NCTPlan skin volumes are not included because neither planning system was able to accurately calculate dose-volume data for concave regions like skin.

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<th>Leg Phantom</th>
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A.5.1 Head Phantom

A.5.1.1 Brain

Figure A.115  Boron dose-volume histograms for brain for brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. The default output from seraPlot is shown along with a corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose).

Table A.3  Boron dose statistics for brain resulting from a 1-field irradiation with the generic epithermal neutron beam for 3.16 minutes.

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<th>Boron Dose (Gy)</th>
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Figure A.116 Thermal neutron (and nitrogen) dose-volume histograms for the brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.4 Thermal neutron (and nitrogen) dose statistics for brain resulting from a 1-field irradiation with the generic epithermal neutron beam for 3.16 minutes.

<table>
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<th>Thermal Neutron Dose (Gy)</th>
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Figure A.117 Fast neutron (and hydrogen) dose-volume histograms for the brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.5 Fast neutron (and hydrogen) dose statistics for brain resulting from a 1-field irradiation with the generic epithermal neutron beam for 3.16 minutes.

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<td>NCTPlan</td>
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Figure A.118 Induced photon dose-volume histograms for the brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Table A.6 Induced photon dose statistics for brain resulting from a 1-field irradiation with the generic epithermal neutron beam for 3.16 minutes.

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Figure A.119 Incident photon dose-volume histograms for the brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Table A.7 Incident photon dose statistics for brain resulting from a 1-field irradiation with the generic epithermal neutron beam for 3.16 minutes.

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<th>maximum</th>
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<td>SERA</td>
<td>0.15</td>
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<td>0.36</td>
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<td>NCTPlan</td>
<td>0.14</td>
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Figure A.120 Total biologically weighted dose-volume histograms for brain for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. The default output from seraPlot is shown along with a corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose).

Table A.8 Total biologically weighted dose statistics for brain resulting from a 1-field irradiation with the generic epithermal neutron beam for 3.16 minutes.

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<th>Total Biologically Weighted Dose ($Gy_w$)</th>
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</thead>
<tbody>
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<tr>
<td>Reference</td>
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<tr>
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<td>3.08</td>
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<tr>
<td>NCTPlan</td>
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</table>
Figure A.121  Boron dose-volume histograms for the brain for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.9  Boron dose statistics for brain resulting from a 3-field irradiation with the generic epithermal neutron beam for 5.66 minutes.

<table>
<thead>
<tr>
<th>Boron Dose (Gy)</th>
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<th>minimum</th>
<th>maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>1.68</td>
<td>0.14</td>
<td>4.58</td>
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<tr>
<td>BNCT_Rtpe</td>
<td>1.82</td>
<td>0.17</td>
<td>4.92</td>
</tr>
<tr>
<td>SERA</td>
<td>1.78</td>
<td>0.17</td>
<td>4.92</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>1.55</td>
<td>0.13</td>
<td>4.32</td>
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</tbody>
</table>
Figure A.122  Thermal neutron (and nitrogen) dose-volume histograms for the brain for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Table A.10  Thermal neutron (and nitrogen) dose statistics for brain resulting from a 3-field irradiation with the generic epithermal neutron beam for 5.66 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Thermal Neutron Dose (Gy)</th>
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</thead>
<tbody>
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<tr>
<td>Reference</td>
<td>0.23</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>0.25</td>
</tr>
<tr>
<td>SERA</td>
<td>0.24</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>0.21</td>
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</tbody>
</table>
Figure A.123  Fast neutron (and hydrogen) dose-volume histograms for the brain for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.11  Fast neutron (and hydrogen) dose statistics for brain resulting from a 3-field irradiation with the generic epithermal neutron beam for 5.66 minutes.

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<tr>
<th></th>
<th>Fast Neutron Dose (Gy)</th>
<th>mean</th>
<th>minimum</th>
<th>maximum</th>
</tr>
</thead>
<tbody>
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<td>Reference</td>
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<td>0.072</td>
<td>0.0022</td>
<td>0.38</td>
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<td>0.062</td>
<td>0.0021</td>
<td>0.26</td>
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<tr>
<td>SERA</td>
<td></td>
<td>0.062</td>
<td>0.0000</td>
<td>0.27</td>
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<tr>
<td>NCTPlan</td>
<td></td>
<td>0.069</td>
<td>0.0041</td>
<td>0.33</td>
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</table>
Figure A.124 Induced photon dose-volume histograms for the brain for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Table A.12 Induced photon dose statistics for brain resulting from a 3-field irradiation with the generic epithermal neutron beam for 5.66 minutes.

<table>
<thead>
<tr>
<th>Reference</th>
<th>BNCT_Rtpe</th>
<th>SERA</th>
<th>NCTPlan</th>
</tr>
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<tbody>
<tr>
<td>mean</td>
<td>1.88</td>
<td>2.09</td>
<td>1.91</td>
</tr>
<tr>
<td>minimum</td>
<td>0.60</td>
<td>0.70</td>
<td>0.63</td>
</tr>
<tr>
<td>maximum</td>
<td>3.56</td>
<td>3.89</td>
<td>3.64</td>
</tr>
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</table>
Figure A.125 Incident photon dose-volume histograms for the brain for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.13 Incident photon dose statistics for brain resulting from a 3-field irradiation with the generic epithermal neutron beam for 5.66 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Incident Photon Dose (Gy)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>minimum</td>
<td>maximum</td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>0.27</td>
<td>0.0047</td>
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<tr>
<td>BNCT_Rtpe</td>
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<td>0.0000</td>
<td>0.62</td>
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<tr>
<td>SERA</td>
<td>0.26</td>
<td>0.0000</td>
<td>0.63</td>
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<tr>
<td>NCTPlan</td>
<td>0.26</td>
<td>0.0051</td>
<td>0.51</td>
<td></td>
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</table>
Figure A.126 Total biologically weighted dose-volume histograms for the brain for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.14 Total biologically weighted dose statistics for brain resulting from a 3-field irradiation with the generic epithermal neutron beam for 5.66 minutes.

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<th>mean</th>
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<th>maximum</th>
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</thead>
<tbody>
<tr>
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<td>BNCT_Rtpe</td>
<td>5.72</td>
<td>1.01</td>
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<td>SERA</td>
<td>5.43</td>
<td>0.92</td>
<td>12.90</td>
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<tr>
<td>NCTPlan</td>
<td>4.94</td>
<td>0.82</td>
<td>11.76</td>
</tr>
</tbody>
</table>
A.5.1.2 Brain Tumor

Figure A.127 Boron dose-volume histograms for the brain tumor for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Table A.15 Boron dose statistics for the brain tumor resulting from a 1-field irradiation with the generic epithermal neutron beam for 3.16 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Boron Dose (Gy)</th>
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<tr>
<td>Reference</td>
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<tr>
<td>BNCT_Rtpe</td>
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</tr>
<tr>
<td>SERA</td>
<td>8.78</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>7.94</td>
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</table>
Figure A.128 Thermal neutron (and nitrogen) dose-volume histograms for the brain tumor for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a –5% shift in dose) is shown instead of the default seraPlot output.

Table A.16 Thermal neutron (and nitrogen) dose statistics for the brain tumor resulting from a 1-field irradiation with the generic epithermal neutron beam for 3.16 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Thermal Neutron Dose (Gy)</th>
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<td>Reference</td>
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<tr>
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<tr>
<td>SERA</td>
<td>0.34</td>
</tr>
<tr>
<td>NCTPlan</td>
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</table>
Figure A.129  Fast neutron (and hydrogen) dose-volume histograms for the brain tumor for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a \(-5\%\) shift in dose) is shown instead of the default seraPlot output.

Table A.17  Fast neutron (and hydrogen) dose statistics for the brain tumor resulting from a 1-field irradiation with the generic epithermal neutron beam for 3.16 minutes.

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<tr>
<th></th>
<th>Fast Neutron Dose (Gy)</th>
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<tr>
<td>SERA</td>
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<td>NCTPlan</td>
<td>0.073</td>
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</table>
Figure A.130  Induced photon dose-volume histograms for the brain tumor for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.18  Induced photon dose statistics for the brain tumor resulting from a 1-field irradiation with the generic epithermal neutron beam for 3.16 minutes.

<table>
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<tr>
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<th>Induced Photon Dose (Gy)</th>
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<tbody>
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<tr>
<td>Reference</td>
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<tr>
<td>BNCT_Rtpe</td>
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<td>SERA</td>
<td>2.39</td>
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<tr>
<td>NCTPlan</td>
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</table>
Figure A.131 Incident photon dose-volume histograms for the brain tumor for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Table A.19 Incident photon dose statistics for the brain tumor resulting from a 1-field irradiation with the generic epithermal neutron beam for 3.16 minutes.

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<th>Incident Photon Dose (Gy)</th>
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<td></td>
<td>mean</td>
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<tr>
<td>Reference</td>
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</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>0.29</td>
</tr>
<tr>
<td>SERA</td>
<td>0.27</td>
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<tr>
<td>NCTPlan</td>
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</table>
Figure A.132  Total biologically weighted dose-volume histograms for the brain tumor for a 1-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.20  Total biologically weighted dose statistics for the brain tumor resulting from a 1-field irradiation with the generic epithermal neutron beam for 3.16 minutes.

<table>
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<th></th>
<th>Total Biologically Weighted Dose (Gyₜₜ)</th>
<th>mean</th>
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<th>maximum</th>
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<tr>
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<td>19.37</td>
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<td>37.41</td>
<td>17.65</td>
<td>64.60</td>
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<td>NCTPlan</td>
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<td>33.88</td>
<td>15.94</td>
<td>58.44</td>
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</table>
Figure A.133 Boron dose-volume histograms for the brain tumor for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Table A.21 Boron dose statistics for the brain tumor resulting from a 3-field irradiation with the generic epithermal neutron beam for 5.66 minutes.

<table>
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<tr>
<th></th>
<th>Boron Dose (Gy)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>minimum</td>
<td>maximum</td>
</tr>
<tr>
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<td>6.13</td>
<td>14.88</td>
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<tr>
<td>BNCT_Rtpe</td>
<td>10.34</td>
<td>6.82</td>
<td>15.31</td>
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<tr>
<td>SERA</td>
<td>10.10</td>
<td>6.53</td>
<td>15.44</td>
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<tr>
<td>NCTPlan</td>
<td>9.17</td>
<td>5.90</td>
<td>13.92</td>
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</table>
Figure A.134 Thermal neutron (and nitrogen) dose-volume histograms for the brain tumor for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.22 Thermal neutron (and nitrogen) dose statistics for the brain tumor resulting from a 3-field irradiation with the generic epithermal neutron beam for 5.66 minutes.

<table>
<thead>
<tr>
<th>Reference</th>
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<th>SERA</th>
<th>NCTPlan</th>
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</thead>
<tbody>
<tr>
<td>mean</td>
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<td>maximum</td>
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<td>0.38</td>
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<td>0.40</td>
<td>0.26</td>
<td>0.59</td>
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<td>0.39</td>
<td>0.25</td>
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<td>0.36</td>
<td>0.23</td>
<td>0.54</td>
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</table>
Figure A.135  Fast neutron (and hydrogen) dose-volume histograms for the brain tumor for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.23  Fast neutron (and hydrogen) dose statistics for the brain tumor resulting from a 3-field irradiation with the generic epithermal neutron beam for 5.66 minutes.

<table>
<thead>
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<th>Fast Neutron Dose (Gy)</th>
<th>mean</th>
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<th>maximum</th>
</tr>
</thead>
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<tr>
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<td>0.060</td>
<td>0.15</td>
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<td>BNCT_Rtpe</td>
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<tr>
<td>SERA</td>
<td>0.085</td>
<td>0.062</td>
<td>0.12</td>
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<td>NCTPlan</td>
<td>0.090</td>
<td>0.061</td>
<td>0.15</td>
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</table>
Figure A.136  Induced photon dose-volume histograms for the brain tumor for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Table A.24  Induced photon dose statistics for the brain tumor resulting from a 3-field irradiation with the generic epithermal neutron beam for 5.66 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Induced Photon Dose (Gy)</th>
<th></th>
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<td>maximum</td>
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</tr>
<tr>
<td>Reference</td>
<td>3.06</td>
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<td>3.58</td>
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<td>BNCT_Rtpe</td>
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<td>2.82</td>
<td>3.88</td>
<td></td>
</tr>
<tr>
<td>SERA</td>
<td>3.12</td>
<td>2.55</td>
<td>3.61</td>
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</tr>
<tr>
<td>NCTPlan</td>
<td>2.89</td>
<td>2.39</td>
<td>3.37</td>
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</table>
Figure A.137 Incident photon dose-volume histograms for the brain tumor for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.25 Incident photon dose statistics for the brain tumor resulting from a 3-field irradiation with the generic epithermal neutron beam for 5.66 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Incident Photon Dose (Gy)</th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>minimum</td>
<td>maximum</td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>0.47</td>
<td>0.45</td>
<td>0.49</td>
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<tr>
<td>BNCT_Rtpe</td>
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<td>0.47</td>
<td>0.51</td>
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</tr>
<tr>
<td>SERA</td>
<td>0.45</td>
<td>0.44</td>
<td>0.48</td>
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<td>NCTPlan</td>
<td>0.47</td>
<td>0.45</td>
<td>0.49</td>
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</table>
Figure A.138  Total biologically weighted dose-volume histograms for the brain tumor for a 3-field irradiation of the head phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.26  Total biologically weighted dose statistics for the brain tumor resulting from a 3-field irradiation with the generic epithermal neutron beam for 5.66 minutes.

<table>
<thead>
<tr>
<th>Total Biologically Weighted Dose (Gy_w)</th>
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<th>minimum</th>
<th>maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>41.69</td>
<td>27.22</td>
<td>62.91</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
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<td>30.24</td>
<td>64.83</td>
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<td>SERA</td>
<td>43.39</td>
<td>28.41</td>
<td>64.61</td>
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<tr>
<td>NCTPlan</td>
<td>39.65</td>
<td>26.09</td>
<td>59.17</td>
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</table>
A.5.2 Leg Phantom

A.5.2.1 Leg Phantom Skin

Figure A.139 Boron dose-volume histograms for skin for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.27 Boron dose statistics for leg phantom skin resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
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<th>Boron Dose (Gy)</th>
<th>mean</th>
<th>minimum</th>
<th>maximum</th>
</tr>
</thead>
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<td>4.03</td>
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<td>0.000</td>
<td>4.30</td>
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<tr>
<td>SERA</td>
<td>0.80</td>
<td>0.000</td>
<td>4.30</td>
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Figure A.140 Thermal neutron (and nitrogen) dose-volume histograms for skin for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $\pm 5\%$ shift in dose) is shown instead of the default seraPlot output.

Table A.28 Thermal neutron (and nitrogen) dose statistics for leg phantom skin resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
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<tr>
<th></th>
<th>Thermal Neutron Dose (Gy)</th>
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</thead>
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<tr>
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</tr>
<tr>
<td>Reference</td>
<td>0.14</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
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<tr>
<td>SERA</td>
<td>0.14</td>
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</table>
Figure A.141  Fast neutron (and hydrogen) dose-volume histograms for skin for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.29  Fast neutron (and hydrogen) dose statistics for leg phantom skin resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Fast Neutron Dose (Gy)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>minimum</td>
<td>maximum</td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>0.0025</td>
<td>0.000</td>
<td>0.0074</td>
<td></td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>0.0023</td>
<td>0.000</td>
<td>0.0086</td>
<td></td>
</tr>
<tr>
<td>SERA</td>
<td>0.0028</td>
<td>0.000</td>
<td>0.0110</td>
<td></td>
</tr>
</tbody>
</table>
Figure A.142  Induced photon dose-volume histograms for skin for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Table A.30  Induced photon dose statistics for leg phantom skin resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th>Induced Photon Dose (Gy)</th>
<th>mean</th>
<th>minimum</th>
<th>maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>0.30</td>
<td>0.065</td>
<td>0.98</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>0.28</td>
<td>0.070</td>
<td>1.06</td>
</tr>
<tr>
<td>SERA</td>
<td>0.28</td>
<td>0.062</td>
<td>1.02</td>
</tr>
</tbody>
</table>
Figure A.143 Incident photon dose-volume histograms for skin for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Table A.31 Incident photon dose statistics for leg phantom skin resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th>Incident Photon Dose (Gy)</th>
<th>mean</th>
<th>minimum</th>
<th>maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>0.050</td>
<td>0.000</td>
<td>0.11</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>0.050</td>
<td>0.000</td>
<td>0.17</td>
</tr>
<tr>
<td>SERA</td>
<td>0.048</td>
<td>0.000</td>
<td>0.75</td>
</tr>
</tbody>
</table>
Figure A.144 Total biologically weighted dose-volume histograms for skin for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.32 Total biologically weighted dose statistics for leg phantom skin resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes. The maximum skin dose for MacNCTPlan and NCTPlan was recorded at 5 mm depth along the central beam axis.

<table>
<thead>
<tr>
<th></th>
<th>Total Biologically Weighted Dose (Gy$_w$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
</tr>
<tr>
<td>Reference</td>
<td>2.88</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>2.46</td>
</tr>
<tr>
<td>SERA</td>
<td>2.78</td>
</tr>
<tr>
<td>MacNCTPlan</td>
<td>----</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>----</td>
</tr>
</tbody>
</table>
### A.5.2.2 Leg Phantom Tumor 1 (spherical tumor)

**Figure A.145** Boron dose-volume histograms for tumor 1 (spherical tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

**Table A.33** Boron dose statistics for tumor 1 (spherical tumor) resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th>Boron Dose (Gy)</th>
<th>mean</th>
<th>minimum</th>
<th>maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>7.82</td>
<td>5.66</td>
<td>9.67</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>8.39</td>
<td>6.25</td>
<td>9.75</td>
</tr>
<tr>
<td>SERA</td>
<td>8.16</td>
<td>6.14</td>
<td>9.53</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>7.36</td>
<td>5.72</td>
<td>8.53</td>
</tr>
</tbody>
</table>
Figure A.146 Thermal neutron (and nitrogen) dose-volume histograms for tumor 1 (spherical tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.34 Thermal neutron (and nitrogen) dose statistics for tumor 1 (spherical tumor) resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Thermal Neutron Dose (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
</tr>
<tr>
<td>Reference</td>
<td>0.58</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>0.62</td>
</tr>
<tr>
<td>SERA</td>
<td>0.61</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>0.55</td>
</tr>
</tbody>
</table>
Figure A.147 Fast neutron (and hydrogen) dose-volume histograms for tumor 1 (spherical tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Table A.35 Fast neutron (and hydrogen) dose statistics for tumor 1 (spherical tumor) resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Fast Neutron Dose (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
</tr>
<tr>
<td>Reference</td>
<td>0.0067</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>0.0066</td>
</tr>
<tr>
<td>SERA</td>
<td>0.0069</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>0.0069</td>
</tr>
</tbody>
</table>
Figure A.148  Induced photon dose-volume histograms for tumor 1 (spherical tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.36  Induced photon dose statistics for tumor 1 (spherical tumor) resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Induced Photon Dose (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
</tr>
<tr>
<td>Reference</td>
<td>1.08</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>1.09</td>
</tr>
<tr>
<td>SERA</td>
<td>1.03</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>0.93</td>
</tr>
</tbody>
</table>
Figure A.149 Incident photon dose-volume histograms for tumor 1 (spherical tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.37 Incident photon dose statistics for tumor 1 (spherical tumor) resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th>Incident Photon Dose (Gy)</th>
<th>mean</th>
<th>minimum</th>
<th>maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>0.109</td>
<td>0.106</td>
<td>0.111</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>0.113</td>
<td>0.112</td>
<td>0.115</td>
</tr>
<tr>
<td>SERA</td>
<td>0.106</td>
<td>0.105</td>
<td>0.109</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>0.108</td>
<td>0.099</td>
<td>0.109</td>
</tr>
</tbody>
</table>
Figure A.150  Total biologically weighted dose-volume histograms for tumor 1 (spherical tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.38  Total biologically weighted dose statistics for tumor 1 (spherical tumor) resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Total Biologically Weighted Dose (Gy₃₀)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
</tr>
<tr>
<td>Reference</td>
<td>32.80</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>35.09</td>
</tr>
<tr>
<td>SERA</td>
<td>34.22</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>30.76</td>
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</tbody>
</table>
A.5.2.3 Leg Phantom Tumor 2 (arc-shaped tumor)

Figure A.151 Boron dose-volume histograms for tumor 2 (arc-shaped tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a $-5\%$ shift in dose) is shown instead of the default seraPlot output.

Table A.39 Boron dose statistics for tumor 2 (arc-shaped tumor) resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th>Boron Dose (Gy)</th>
<th>mean</th>
<th>minimum</th>
<th>maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>8.97</td>
<td>6.00</td>
<td>10.23</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>9.45</td>
<td>6.49</td>
<td>10.74</td>
</tr>
<tr>
<td>SERA</td>
<td>9.32</td>
<td>6.28</td>
<td>10.55</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>7.98</td>
<td>5.54</td>
<td>9.08</td>
</tr>
</tbody>
</table>
Figure A.152 Thermal neutron (and nitrogen) dose-volume histograms for tumor 2 (arc-shaped tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.40 Thermal neutron (and nitrogen) dose statistics for tumor 2 (arc-shaped tumor) resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Thermal Neutron Dose (Gy)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>minimum</td>
<td>maximum</td>
</tr>
<tr>
<td>Reference</td>
<td>0.67</td>
<td>0.45</td>
<td>0.76</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>0.69</td>
<td>0.48</td>
<td>0.79</td>
</tr>
<tr>
<td>SERA</td>
<td>0.69</td>
<td>0.47</td>
<td>0.78</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>0.59</td>
<td>0.41</td>
<td>0.67</td>
</tr>
</tbody>
</table>
Figure A.153 Fast neutron (and hydrogen) dose-volume histograms for tumor 2 (arc-shaped tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.41 Fast neutron (and hydrogen) dose statistics for tumor 2 (arc-shaped tumor) resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Fast Neutron Dose (Gy)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>minimum</td>
<td>maximum</td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>0.0069</td>
<td>0.0064</td>
<td>0.0072</td>
<td></td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>0.0068</td>
<td>0.0063</td>
<td>0.0070</td>
<td></td>
</tr>
<tr>
<td>SERA</td>
<td>0.0069</td>
<td>0.0069</td>
<td>0.0083</td>
<td></td>
</tr>
<tr>
<td>NCTPlan</td>
<td>0.0068</td>
<td>0.0061</td>
<td>0.0075</td>
<td></td>
</tr>
</tbody>
</table>
Figure A.154  Induced photon dose-volume histograms for tumor 2 (arc-shaped tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a ~5% shift in dose) is shown instead of the default seraPlot output.

Table A.42  Induced photon dose statistics for tumor 2 (arc-shaped tumor) resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Induced Photon Dose (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
</tr>
<tr>
<td>Reference</td>
<td>1.09</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>1.11</td>
</tr>
<tr>
<td>SERA</td>
<td>1.04</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>0.90</td>
</tr>
</tbody>
</table>
Figure A.155 Incident photon dose-volume histograms for tumor 2 (arc-shaped tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.43 Incident photon dose statistics for tumor 2 (arc-shaped tumor) resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Incident Photon Dose (Gy)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>minimum</td>
<td>maximum</td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>0.109</td>
<td>0.108</td>
<td>0.111</td>
<td></td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>0.114</td>
<td>0.112</td>
<td>0.116</td>
<td></td>
</tr>
<tr>
<td>SERA</td>
<td>0.107</td>
<td>0.105</td>
<td>0.134</td>
<td></td>
</tr>
<tr>
<td>NCTPlan</td>
<td>0.109</td>
<td>0.108</td>
<td>0.110</td>
<td></td>
</tr>
</tbody>
</table>
Figure A.156  Total biologically weighted dose-volume histograms for tumor 2 (arc-shaped tumor) for a 1-field irradiation of the leg phantom. Conventional and binned representations of the reference data are included. A corrected interpretation of the SERA dose-volume data (with a −5% shift in dose) is shown instead of the default seraPlot output.

Table A.44  Total biologically weighted dose statistics for tumor 2 (arc-shaped tumor) resulting from a 1-field irradiation with a thermal neutron beam for 1.38 minutes.

<table>
<thead>
<tr>
<th></th>
<th>Total Biologically Weighted Dose (Gy_w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
</tr>
<tr>
<td>Reference</td>
<td>37.44</td>
</tr>
<tr>
<td>BNCT_Rtpe</td>
<td>39.39</td>
</tr>
<tr>
<td>SERA</td>
<td>38.77</td>
</tr>
<tr>
<td>NCTPlan</td>
<td>33.24</td>
</tr>
</tbody>
</table>
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APPENDIX B

Construction of a Beowulf Cluster for Monte Carlo Computations

B.1 Introduction

To facilitate the computationally intensive research described in this thesis, a Beowulf cluster was constructed during the summer of 2005. Monte Carlo algorithms are very well-known for their parallelizability, so constructing a high-performance homogeneous cluster from common personal computer hardware was a relatively inexpensive and efficient way to decrease the computation time. Even for large numbers of sequential computations such as those performed in Chapter 3, the cluster proved to be an invaluable resource that allowed a more thorough investigation than would have otherwise been possible within the given time frame. However, the success of a cluster, especially one assembled from standard component parts, was certainly not guaranteed, so considerable effort was devoted to properly designing, constructing and testing the cluster in order to prevent problems that could potentially limit its effectiveness. Since the cluster was an essential tool for this thesis work, a brief overview of its hardware, software, and performance characteristics will be presented here.
B.2 Hardware

During the initial planning stages, estimates for pre-packaged computing clusters were obtained from few different companies, but none were able to provide the desired level of customization within the defined price range. Therefore, the decision was made to build the cluster from “scratch” using standard off-the-shelf component parts. However, before any purchases were made, a variety of research and tests were first performed to maximize the computational power to cost ratio (i.e., simulated particle histories per minute per dollar). Once an appropriate design was determined, enough components were purchased to fully assemble 1 node, and that node was subjected to a variety of tests designed to fully stress the system’s hardware. After observing satisfactory stability and performance, enough components were ordered to construct 1 master node and 10 additional slave nodes. The relevant hardware used in the master and slave nodes is listed in Table B.1.

The master or head node consists of dual 250 GB hard drives operating in a mirrored RAID (Redundant Array of Independent Disks) array for real time data backup to protect against sudden disk failure. In addition, nightly differential backups are performed and written to removable DVD media via the dual DVD±RW drives. The master node’s video card supplies dual monitor support. The dual integrated gigabit network interfaces on the master node allow a connection to both the outside world, so that users can gain access remotely, and to each slave node via the gigabit network switch. The slave nodes are actually similar to the master node but with a few notable differences. Each slave node has 2 GB RAM and an 80 GB hard drive for local storage. While each slave node is headless (no monitor), cheap second-hand video cards
Table B.1  Hardware for the master and 11 slave nodes of the cluster. All components were purchased new except the video cards for the slave nodes which were purchased used on eBay. The components were purchased individually at a total cost of 10,074.52 and manually assembled over 3.5 months during the summer of 2005.

<table>
<thead>
<tr>
<th>Component</th>
<th>Master Node</th>
<th>Slave Node (11×)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPU</td>
<td>single core 2.0 GHz AMD 64-bit Athlon 3200+</td>
<td></td>
</tr>
<tr>
<td>Motherboard</td>
<td>MSI K8N Neo4 Platinum</td>
<td>MSI K8N Neo4-F</td>
</tr>
<tr>
<td>Memory</td>
<td>512MB DDR PC3200 (2×)</td>
<td>1GB DDR PC3200 (2×)</td>
</tr>
<tr>
<td>Hard Disk</td>
<td>Seagate 250GB SATA (2×)</td>
<td>Seagate 80GB SATA</td>
</tr>
<tr>
<td>Video</td>
<td>Nvidia GeForce 6200 (PCIe)</td>
<td>Matrox Millennium (PCI)</td>
</tr>
<tr>
<td>Network</td>
<td>Dual Integrated Gigabit NIC</td>
<td>Integrated Gigabit NIC</td>
</tr>
<tr>
<td>Optical Drive</td>
<td>Dual Layer 16× DVD±RW (2×)</td>
<td>none</td>
</tr>
<tr>
<td>Case</td>
<td>Antec Plus1000 w/ 480W PS</td>
<td>Antec SLK1650 w/ 350W PS</td>
</tr>
<tr>
<td>Network Switch</td>
<td>NETGEAR 24-port 10/100/1000 Mbps</td>
<td></td>
</tr>
</tbody>
</table>

purchased on eBay were installed so that a monitor could be connected for diagnostic purposes in the event that remote login from the master node was not possible. It is also worth mentioning that in ~4 years of use the only hardware failures were in motherboard and case cooling fans, which were still under warranty at the time and replaced free of charge. However, even those hardware failures did not affect the normal operation of the cluster as temperatures remained relatively stable until the fans could be replaced. A rear view of all 11 fully assembled slave nodes is shown in Figure B.1.

## B.3 Software

The master and all 11 slave nodes run the 64-bit Debian GNU/Linux operating system. It was chosen primarily because it is free, open and has a reputation within the Linux community of valuing stability over new cutting-edge features. Also, the robust
software package management system allows easy access to system updates as well as a huge repository of over 20,000 software titles. Custom Linux kernels (v. 2.6.18) were compiled for the master and slave nodes to better tune the operating system to the specific hardware. A 32-bit compatibility layer was also installed so that 32-bit binaries could be executed seamlessly. Each user’s home directory on the master node is served to all slave nodes via a network file system (NFS) mount, and “passwordless” logins, which are essential to parallel simulations, are permitted between the master and slave nodes via the Secure Shell (ssh) protocol. Custom shell scripts were developed to perform nightly differential backups to DVD as well as monitor the health of the system hardware. The Ganglia Monitoring System (http://ganglia.info/) allows certain characteristics of the cluster (e.g., CPU load, CPU temperature, network traffic, free disk space) to be monitored graphically, even remotely, from a web browser. Robust job scheduling is provided by the Sun Grid Engine (http://gridengine.sunsource.net/), and SystemImager (http://wiki.systemimager.org/) is used to keep the system software on the 11 slave nodes in sync with each other and up-to-date (files and directories related to the operating system are not served via NFS but rather are stored locally on each slave node). The Cluster Command and Control (C3) tool suite (http://www.csm.ornl.gov/torc/C3/) was installed to provide very useful cluster-wide administration and management tools. Rather remarkably, the only software that was not free and open source was the Intel® Fortran 90 compiler required to compile custom versions of the Monte Carlo transport codes, MCNP5 and MCNPX. Planning, assembly, and post-configuration of the cluster took 3.5 months total during the summer of 2005.
B.4 Performance

Since completion of the cluster, uptime (i.e., time since last reboot) has consistently been measured in months with the current uptime approaching 1 year. Planned power outages are the most frequent cause for rebooting the cluster. Over 8,700 jobs have been submitted to the cluster in ~4 years of use with the research presented in Chapter 4 alone requiring over 1000 separate simulations totaling 3.2 CPU years of simulation time. Shortly after the cluster was made fully operational, benchmarks were performed to test both its efficiency and peak performance. As shown in Figure B.2, the simulation speed (i.e., simulated particle histories/minute) increases linearly with the number of nodes, and that relationship holds out to 11 nodes. The speedup factor (defined relative to the runtime on 1 node) at 11 nodes is actually 10.9, but that still represents greater than 99% efficiency. To test the peak performance of the cluster, version 1.0a of the High-Performance Linpack Benchmark (http://www.netlib.org/benchmark/hpl/), which is the same benchmark used to consistently rank the fastest supercomputer sites in the world (http://www.top500.org/), was employed. That benchmark indicated that the cluster is capable of performing 33.5 billion floating point operations per second or 33.5 gigaFLOPS.

* As of 06/2009, a cluster at Los Alamos National Laboratory (LANL), named Roadrunner, is the world’s fastest supercomputer and is capable of sustaining more than 1.1 petaFLOPS or $1.1 \times 10^{15}$ (1.1 quadrillion) floating point operations per second (http://www.top500.org).
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Figure B.1  All 11 fully assembled and operational slave nodes. Each slave node is connected via the gigabit network switch, positioned above the second tier of nodes, to the master node (whose dual monitor console is visible in the background). The master node also allows remote access.
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Figure B.2  Simulation speed and speedup factor (defined relative to the runtime on 1 node) as a function of the number of uniprocessor cluster nodes used in the test parallel Monte Carlo simulation with MCNP5 version 1.40. The measured efficiency is very close to ideal and is greater than 99% at 11 nodes. At peak performance, the cluster is capable of performing 33.5 billion floating point operations per second or 33.5 gigaFLOPS.