Heat Transfer Between Blood Vessels and Perfused Tissue During Hyperthermia Therapy

by

Jeffrey Jay Breedlove
B.S. Mechanical Engineering, MIT 1994

Submitted to the Department of Mechanical Engineering in Partial Fulfillment of the Requirements for the Degree of Master of Science

at the Massachusetts Institute of Technology

February 1997

© 1997 Jeffrey Jay Breedlove
All rights reserved

The author hereby grants to MIT permission to reproduce and to distribute publicly paper and electronic copies of this thesis document in whole or in part.

Signature of Author .......................................................... Jeffrey Breedlove
Department of Mechanical Engineering
September 15, 1996

Certified by .......................................................... Dr. W. H. Newman
Research Scientist
Thesis Supervisor

Certified by .......................................................... Dr. H. F. Bowman
Director, MIT Hyperthermia Program
Thesis Supervisor

Accepted By .......................................................... Professor Ain A. Sonin
Chairman, Committee on Graduate Students

APR 16 1997
Heat Transfer Between Blood Vessels and Perfused Tissue During Hyperthermia Therapy

by

Jeffrey Jay Breedlove

Submitted to the Department of Mechanical Engineering on September 15, 1996 in partial fulfillment of the requirements for the Degree of Master of Science in Mechanical Engineering

Abstract

Hyperthermia is a cancer treatment method that destroys tumors by elevating the temperature of the cancerous tissue above 43 °C for a specified amount of time. Unfortunately, healthy tissue is also susceptible to necrosis when its temperature is elevated. The goal of most hyperthermia treatments is to destroy an entire tumor while minimizing damage to the surrounding healthy tissue.

The efficacy of hyperthermia therapy is enhanced by using appropriate thermal models to plan, monitor, and evaluate treatments. In many patients, the treated tissue volume contains thermally-significant blood vessels that are capable of cooling surrounding cancerous cells to subtherapeutic temperatures. Thermal models should, therefore, have the ability to account for the local effects of individual blood vessels. Simple analytical models assume flow inside blood vessels is always thermally fully-developed. These models are inappropriate because the thermal entrance length of all, except for the smallest, blood vessels is large when compared to the dimensions of a large tumor. Numerical solutions to the coupled equations of heat transfer and fluid flow are accurate, but computationally intense. This thesis presents a simple, empirically-derived model that accurately quantifies the effects that individual blood vessels have on hyperthermia temperature fields. The model is validated with extensive numerical results that encompass a realistic range of tissue and vessel parameters. The model was designed to be incorporated into the Basis Element Method developed at MIT, however, it is general enough to be used in conjunction with any temperature calculation tool.

Thesis Supervisor: Dr. W. H. Newman
Title: Research Scientist

Thesis Supervisor: Dr. H. F. Bowman
Title: Director, MIT Hyperthermia Program
# Table of Contents

1 Introduction..................................................................................................................13  
1.1 Hyperthermia ...........................................................................................................13  
1.2 Thermal Modelling ................................................................................................14  
1.3 Blood Vessels........................................................................................................16  

2 Tissue Heating Techniques .......................................................................................17  
2.1 Heated Antennae .....................................................................................................17  
2.2 Electrical Current ...................................................................................................17  
2.3 Microwaves and Ultrasound Waves .......................................................................18  

3 Bioheat Transfer .........................................................................................................25  

4 The Basis Element Method .........................................................................................33  

5 Heat Transfer to Blood Vessels ..................................................................................37  
5.1 Governing Heat Transfer Equations .......................................................................38  
5.2 Mixing-Cup Temperature .......................................................................................40  
5.3 The Graetz Problem ...............................................................................................40  
5.4 Numerical Calculations with NEKTON ....................................................................42  
5.5 Heat Transfer Coefficient and Thermal Entrance Region .....................................46  
5.6 Thermal Entrance Region of Blood Vessels ........................................................48  
5.7 Region of Tissue Thermally Affected by a Blood Vessel .......................................49  
5.8 Far-Field Temperature Elevation in Heated Tissue ...............................................53  

6 Thermal Model ............................................................................................................55  
6.1 Relationship Between Mixing-Cup and Tissue Temperature ..............................55  
6.2 Empirical Characterization of Mixing-Cup Temperature in a Vessel .................57  
6.3 Temperature in the Vicinity of Thermally-Significant Blood Vessels ..................81  

7 Determination of Blood Vessel Parameters ..............................................................83  
7.1 X-Ray Angiography ...............................................................................................83  
7.2 Computerized Tomography (CT) ...........................................................................85  
7.3 Ultrasound .............................................................................................................85  
7.4 Magnetic Resonance Imaging ...............................................................................89  
7.5 Creation of a 3-D Vascular Tree from 2-D Image Planes .......................................91  
7.6 Recommendation ..................................................................................................93  

8 Recommendations for Further Work .........................................................................95  

Appendix A: Reduction of Equations (6.27) - (6.33) .....................................................97  

References ......................................................................................................................103
List of Figures

Figure 1.1: Temperature-duration thresholds for histologic damage to mammalian tissues in vivo. Figure taken from Lele (1987). ................................................................. 13

Figure 2.1: Speed of sound in selected biological materials. Figure taken from Wells (1977). ................................................................................................................... 19

Figure 2.2: Speed of sound in selected biological materials. Figure taken from Wells (1977). ................................................................................................................... 20

Figure 2.3: Attenuation coefficient of ultrasound waves in selected biological materials. Figure taken from Wells (1977). ................................................................. 21

Figure 2.4: Attenuation of plane electromagnetic waves and plane ultrasound waves in muscle. Figure taken from Lele (1987). .................................................................. 22

Figure 4.1: 2-D representation of the BEM. ................................................................. 35

Figure 5.1: Heated, perfused tissue surrounds a straight, cylindrical blood vessel that carries hydrodynamically fully-developed flow. Volumetric power deposition inside the tissue steps from zero to $Q_o$ at $z = 0$. .................................................................................................................. 38

Figure 5.2: Mixing-cup temperature of steady, laminar, hydrodynamically fully-developed flow in a circular tube. Temperature of the tube wall is 0 °C for negative z, and 6 °C for positive z. Fluid is blood. Diameter of tube is 1 mm. Average flow velocity is 1 cm/s. RMS difference for 68 points is 0.0142 °C. .......................................................................................................... 44

Figure 5.3: Mixing-cup temperature of steady, laminar, hydrodynamically fully-developed flow in a circular tube. Temperature of the tube wall is 0 °C for negative z, and 6 °C for positive z. Fluid is blood. Diameter of tube is 3 mm. Average flow velocity is 2 cm/s. RMS difference for 68 points is 0.0080 °C. .......................................................................................................... 45

Figure 5.4: Mixing-cup temperature of steady, laminar, hydrodynamically fully-developed flow in a circular tube. Temperature of the tube wall is 0 °C for negative z, and 6 °C for positive z. Fluid is blood. Diameter of tube is 5 mm. Average flow velocity is 26 cm/s. RMS difference for 68 points is 0.0133 °C. ............................................................................................................. 46

Figure 5.5: Nusselt number for steady, laminar, hydrodynamically fully-developed flow in a circular tube ........................................................................................................... 47

Figure 5.6: Temperature field generated by NEKTON. Volumetric power deposition in the tissue is zero for negative z, and 0.4 W/cm³ for positive z. Perfusion in the tissue is 100 ml/100ml-min ($L_p = 0.3$ cm). Diameter of the vessel is 3 mm. Average flow velocity is 2 cm/s. Solid lines on the axis planes delineate projections of the vessel wall. Dashed lines on the axis planes are located 3 perfusion lengths from the projection of the vessel wall. ...... 51
**Figure 5.7:** Temperature field generated by NEKTON. Volumetric power deposition in the tissue is zero for negative \( z \), and 0.02 W/cm\(^3\) for positive \( z \). Perfusion in the tissue is 5 ml/100ml-min \( (L_p = 1.34 \text{ cm}) \). Diameter of the vessel is 3 mm. Average flow velocity is 2 cm/s. Solid lines on the axis planes delineate projections of the vessel wall. Dashed lines on the axis planes are located 3 perfusion lengths from the projection of the vessel wall.

**Figure 6.1:** Mixing-cup temperature elevation for seven combinations of vessel and tissue parameters.

**Figure 6.2:** Normalized mixing-cup temperature elevation.

**Figure 6.3:** Normalized mixing-cup temperature elevation versus Graetz number.

**Figure 6.4:** Normalized mixing-cup temperature elevation versus Breedlove number.

**Figure 6.5:** Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 100 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative \( z \), and \( 5.333 x 10^{-1} \text{ W/cm}^3 \) for positive \( z \) \( (T_{\text{far-field}} = 8 \degree \text{C}) \). Diameter of the vessel is 1 mm. Average flow velocity is 1 cm/s (Torell and Nilsson, 1978). RMS difference for 97 points is 0.0780 \degree \text{C}.

**Figure 6.6:** Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 5 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative \( z \), and \( 2.6667 x 10^{-2} \text{ W/cm}^3 \) for positive \( z \) \( (T_{\text{far-field}} = 8 \degree \text{C}) \). Diameter of the vessel is 1 mm. Average flow velocity is 1 cm/s (Torell and Nilsson, 1978). RMS difference for 97 points is 0.0622 \degree \text{C}.

**Figure 6.7:** Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 100 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative \( z \), and \( 6.6667 x 10^{-2} \text{ W/cm}^3 \) for positive \( z \) \( (T_{\text{far-field}} = 1 \degree \text{C}) \). Diameter of the vessel is 1 mm. Average flow velocity is 1 cm/s (Torell and Nilsson, 1978). RMS difference for 97 points is 0.0098 \degree \text{C}.

**Figure 6.8:** Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 5 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative \( z \), and \( 3.3333 x 10^{-3} \text{ W/cm}^3 \) for positive \( z \) \( (T_{\text{far-field}} = 1 \degree \text{C}) \). Diameter of the vessel is 1 mm. Average flow velocity is 1 cm/s (Torell and Nilsson, 1978). RMS difference for 97 points is 0.0078 \degree \text{C}.

**Figure 6.9:** Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 100 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative \( z \), and \( 4.0 x 10^{-1} \text{ W/cm}^3 \) for positive \( z \) \( (T_{\text{far-field}} = 6 \degree \text{C}) \). Diameter of the vessel is 3 mm. Average flow velocity is 2 cm/s (Torell and Nilsson, 1978). RMS difference for 93 points is 0.0356 \degree \text{C}.

**Figure 6.10:** Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 5 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative \( z \), and \( 2.0 x 10^{-2} \text{ W/cm}^3 \) for positive \( z \) \( (T_{\text{far-field}} = 6 \degree \text{C}) \). Diameter of the vessel is 3 mm. Average flow velocity is 2 cm/s (Torell and Nilsson, 1978). RMS difference for 89 points is 0.0350 \degree \text{C}.
Figure 6.11: Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 25 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative $z$, and $1.0 \times 10^{-1}$ W/cm$^3$ for positive $z$ ($T_{\text{far-field}} = 6$ °C). Diameter of the vessel is 5 mm. Average flow velocity is 26 cm/s (Ferguson and Roach, 1972). RMS difference for 93 points is 0.0117 °C.  

Figure 6.12: Volumetric power deposition described by Equations (6.24) - (6.25).

Figure 6.13: Comparison between Equations (6.27) - (6.33) and data generated with NEKTON. Perfusion in the tissue is 100 ml/100ml-min. $Q_A''''_{\text{max}} = 5.3333 \times 10^{-1}$ W/cm$^3$. ($T_{\text{far-field}})_{\text{max}} = 8$ °C. Diameter of the vessel is 1 mm. Average flow velocity is 1 cm/s (Torell and Nilsson, 1978). RMS difference for 109 points is 0.0524 °C.

Figure 6.14: Comparison between Equations (6.27) - (6.33) and data generated with NEKTON. Perfusion in the tissue is 5 ml/100ml-min. $Q_A''''_{\text{max}} = 2.6667 \times 10^{-2}$ W/cm$^3$. ($T_{\text{far-field}})_{\text{max}} = 8$ °C. Diameter of the vessel is 1 mm. Average flow velocity is 1 cm/s (Torell and Nilsson, 1978). RMS difference for 109 points is 0.0380 °C.

Figure 6.15: Comparison between Equations (6.27) - (6.33) and data generated with NEKTON. Perfusion in the tissue is 100 ml/100ml-min. $Q_A''''_{\text{max}} = 5.3333 \times 10^{-1}$ W/cm$^3$. ($T_{\text{far-field}})_{\text{max}} = 8$ °C. Diameter of the vessel is 3 mm. Average flow velocity is 2 cm/s (Torell and Nilsson, 1978). RMS difference for 101 points is 0.0410 °C.

Figure 6.16: Comparison between Equations (6.27) - (6.33) and data generated with NEKTON. Perfusion in the tissue is 5 ml/100ml-min. $Q_A''''_{\text{max}} = 2.6667 \times 10^{-2}$ W/cm$^3$. ($T_{\text{far-field}})_{\text{max}} = 8$ °C. Diameter of the vessel is 3 mm. Average flow velocity is 2 cm/s (Torell and Nilsson, 1978). RMS difference for 109 points is 0.0343 °C.

Figure 6.17: Comparison between Equations (6.27) - (6.33) and data generated with NEKTON. Perfusion in the tissue is 25 ml/100ml-min. $Q_A''''_{\text{max}} = 1.0 \times 10^{-1}$ W/cm$^3$. ($T_{\text{far-field}})_{\text{max}} = 6$ °C. Diameter of the vessel is 5 mm. Average flow velocity is 26 cm/s (Ferguson and Roach, 1972). RMS difference for 97 points is 0.0073 °C.

Figure 6.18: Superposition of vessel properties used to represent a bifurcation.

Figure 7.1: The presence of bones and highly perfused tissue can limit information obtained from x-ray angiography: (a) fictitious tissue volume, (b) resulting x-ray angiogram.

Figure 7.2: Frequency spectrum for (a) transmitted signal, (b) reflected signal for blood flowing away from the receiver, and (c) reflected signal for blood flowing toward the receiver.

Figure 7.3: (a) Frequency spectrum of transmitted signal, (b) frequency spectrum of received signal in tissue with low perfusion (c) frequency spectrum of received signal in tissue with high perfusion.

Figure 7.4: Parabolic velocity profile for fully-developed, laminar flow in a blood vessel. Shape of this profile is approximate since it assumes that blood is a Newtonian fluid.
Figure 7.5: The shape of a vessel image on an image plane is related to the angle at which the vessel crosses the image plane. .................................................................92

Figure 7.6: Image plane spacing is too large to keep track of some vessels. .................93
List of Tables

Table 5.1: Constants for Equation (5.16) ................................................................. 42

Table 5.2: Thermal Entrance Lengths of Vessels in the Human Circulatory System .. 49

Table 5.3: Typical Perfusion Lengths Encountered During Hyperthermia .............. 50
Chapter 1

Introduction

1.1 Hyperthermia
Hyperthermia is an experimental cancer treatment modality that destroys tumors by elevating the temperature of the cancerous tissue above 43 °C for a specified amount of time (normal body temperature is 37 °C). The exact time required for cell death to occur has been experimentally determined to be a function of temperature. Figure 1.1 is a summary of experimental data.

Figure 1.1: Temperature-duration thresholds for histologic damage to mammalian tissues in vivo. Figure taken from Lele (1987).
Unfortunately, healthy tissue is also susceptible to necrosis when its temperature is elevated. The goal of most hyperthermia treatments is to destroy an entire tumor while minimizing damage to the surrounding healthy tissue.

Hyperthermia therapy is most commonly administered as an adjunct to other cancer treatment techniques. Hyperthermia is most effective at killing cells in the G phase of the cell cycle, while radiation therapy is most effective at killing cells in the S phase of the cell cycle. As a result, applying both hyperthermia and radiation therapy within an hour of each other helps ensure that all malignant cells are destroyed. Furthermore, hyperthermia sensitizes surviving cells to damage by radiation and increases the cytotoxic activity of several classes of chemotherapeutic drugs such as alkylating agents, antimetabolites, and antibiotics (Lele, 1987).

1.2 Thermal Modelling
Many different tissue heating methods can be used to generate hyperthermia temperature fields. The ability to calculate the temperature field that results from an applied power deposition field offers many benefits to hyperthermia treatment centers. When this ability is linked with power applicator information, it can be used by clinicians to predict how varying specific power applicator parameters affects subsequent temperature fields. Using a temperature calculation algorithm enhances pre-treatment planning by allowing clinicians to simulate treatments with patient information obtained from CT scans. Clinicians can use simulated treatments to determine the feasibility of hyperthermia treatment, select the most appropriate power applicator or combination of applicators, and choose the optimal physiological treatment delivery portal or combination of portals. If a temperature calculation algorithm performs with sufficient speed, it can be used to monitor the temperature field in tissue during treatment. This minimizes the number of invasive temperature probes required and helps clinicians detect under-heated and over-heated tissue in
all regions of the treatment volume. As a result, the power deposition field can be modified during treatment to ensure that all regions of the tissue are properly heated. After a hyperthermia treatment is completed, a temperature calculation algorithm can be used to reconstruct the therapy. Therapy reconstruction provides clinicians with a history of the temperature field that existed in the tissue during the treatment. This information helps them evaluate the treatment and gain knowledge that can be used to improve future treatments.

The widely accepted finite element and finite difference methods are capable of calculating accurate hyperthermia temperature fields (Charney and Levin, 1988; Charney and Levin, 1989; Mooibroek and Lagendijk, 1991; Chen and Roemer, 1992; Breedlove et al., 1995). These calculation schemes, however, are computationally intense and cannot currently be used in real-time to monitor treatment delivery. Most existing hyperthermia programs utilize one of these two numerical methods for pre-treatment planning and post-treatment reconstruction. Treatment delivery is monitored with sparse thermometry. The temperature of the tissue at non-measured locations is estimated by a clinician who relies on personal judgement and past experience. Utilizing a clinician’s judgement to determine temperature is inexact and often results in improper heating of the treatment volume. The need for a calculation algorithm that can be used in real-time by clinicians to help make treatment delivery decisions prompted the creation of the Basis Element Method (BEM) (Newman et al., 1990; Martin et al., 1992; Newman, 1993; Martin, 1995). The BEM utilizes a Green’s Theorem approach to calculate three-dimensional, steady-state, temperature fields. The governing equations of the BEM are derived from the Pennes bioheat equation (Pennes, 1948). Newman et al. (1995) report that the BEM is capable of generating accurate, real-time, temperature fields.
1.3 Blood Vessels

The BEM uses a continuum approach to model biological heat transfer during hyperthermia treatment. This continuum approach neglects the local effects that "thermally significant" blood vessels have on the temperature field in the tissue. Overgaard and Nielsen (1980) report that tumor regrowth following hyperthermia treatment occurs preferentially in tissue that surrounds blood vessels. Blood vessels that flow from unheated regions of the body into heated tissue volumes cool the tissue that surrounds them. In many cases, this reduces the temperature of the surrounding cancerous cells to sub-therapeutic levels. As a result, malignant cells survive and proliferate. Once the impact that individual blood vessels have on hyperthermia temperature fields is quantitatively understood, vessel cooling can be compensated for by depositing the appropriate amount of power in regions of tissue that surround thermally significant vessels.

The main objective of this thesis is to show how the BEM can be modified so that it accurately accounts for the local effects of thermally significant blood vessels. Chapter 2 discusses several heating techniques that are commonly used to administer hyperthermia. Chapter 3 summarizes bioheat transfer models created by several researchers. Chapter 4 explains the Basis Element Method. Chapter 5 investigates heat transfer to blood vessels. Chapter 6 presents and validates a blood vessel model that can be incorporated into the Basis Element Method. Chapter 7 discusses methods that can be used to obtain the blood vessel parameters required by the BEM vessel model. Chapter 8 recommends work that should be performed to further validate the BEM vessel model.
Chapter 2

Tissue Heating Techniques
Several tissue heating techniques can be used for hyperthermia treatment. The most common modes of tissue heating utilize heated antennae, electrical current induced in the tissue, microwaves, or ultrasound waves. All of these heating methods can be applied both invasively and non-invasively. Invasive heating methods possess a major problem. These methods physically disturb the malignant tissue. As a result, viable cancer cells may be released into the blood stream. These cells may migrate to other parts of the body and proliferate into metastatic tumors several years after treatment. Metastases can also occur when tumors are surgically removed. This concern has promoted the development of non-invasive cancer treatment methods. The following paragraphs describe the heating methods mentioned above and discuss their limitations.

2.1 Heated Antennae
Several antennae containing electrical heaters can be inserted into a volume of tissue and used to therapeutically heat it. The heat generated inside each antenna is transferred to the tissue that surrounds it. The degree of spatial control of the temperature field resulting from this type of heating depends on the spacing between adjacent antennae and on the ability to control the heat generated and conducted along the axis of each antenna. The number of antennae that can be inserted into the tissue is limited by patient discomfort.

2.2 Electrical Current
Tissue heating with electrical current is accomplished by inserting several antennae into the tissue and imposing an electrical potential between adjacent electrodes. This potential creates an electrical current that passes through the tissue and dissipates power according to
\[ Q = I^2 R \]  \hspace{1cm} (2.1)

where \( Q \) is the power dissipated in the tissue, \( I \) is the current that flows through the tissue, and \( R \) is the electrical resistance of the tissue. The spatial resolution of the power deposition field created with this type of heating depends on the distance between adjacent electrodes. The number of antennae that can be inserted into the tissue is, again, limited by patient discomfort.

2.3 Microwaves and Ultrasound Waves
Microwaves are electromagnetic waves, while ultrasound waves are pressure waves. Both types of waves obey the following equation:

\[ c_w = f\lambda \]  \hspace{1cm} (2.2)

where \( c_w \) is the speed of the wave, \( f \) is the frequency of the wave (in Hz), and \( \lambda \) is the wavelength. Electromagnetic waves propagate at the speed of light, \( c_l \). The speed of light depends primarily on the dielectric properties of the material through which the wave propagates. Pressure waves propagate at the speed of sound, \( c_s \). The speed of sound depends on the acoustic properties of the medium through which the wave propagates. The speed of sound in selected biological materials is presented in Figures 2.1 and 2.2.

The frequency of microwaves and ultrasound waves which can be used to effectively heat tumors is limited. The smallest volume over which these types of power can be focussed is approximately equal to the dimension of the wavelength cubed. Lele (1987) reports that microwaves travelling through muscle at 2450 MHz and 915 MHz possess wavelengths of 1.8 cm and 4.5 cm respectively, while ultrasound waves travelling through muscle at 3 MHz and 1 MHz possess wavelengths of 0.05 cm and 0.15 cm respectively. Therefore, 2450 MHz and 915 MHz microwave power can only be used to selectively heat relatively large volumes of tissue with characteristic lengths larger than or equal to
1.8 cm and 4.5 cm respectively, while 3 MHz and 1 MHz ultrasound can be used to selectively heat volumes of tissue with characteristic lengths larger than or equal to 0.05 cm and 0.15 cm respectively. The ability to accurately focus power on small subvolumes of a tumor is important since tumors are often irregularly shaped and located adjacent to critical organs and tissues.

![Diagram of speed of sound in biological materials]

**Figure 2.1:** Speed of sound in selected biological materials. Figure taken from Wells (1977).
**Figure 2.2:** Speed of sound in selected biological materials. Figure taken from Wells (1977).

The rate of volumetric heat generation by electromagnetic waves and pressure waves in a material is proportional to the intensity of the waves. The intensity of plane waves is attenuated exponentially according to Equation (2.3) (Wells, 1977).

\[ I(z) = I_0 \exp(-2\mu_a z) \]  \hspace{1cm} (2.3)

In this equation, \( z \) is distance in the direction of wave propagation, \( I(z) \) is the intensity of the waves (units = power per length squared), \( I_0 \) is the intensity of the waves at \( z \) equal to zero, and \( \mu_a \) is the attenuation coefficient of the waves in a specific medium (units =
nepers per length). The magnitude of the attenuation coefficient depends on the frequency of the waves and the material through which the waves propagate. In general, the attenuation coefficient of a specific material increases as the frequency of the waves increases. Some literature sources report attenuation coefficients in units of decibels (dB) per unit length. Decibels can be converted to nepers by noting that:

$$1 \text{ neper} = 20 \left( \log_{10}e \right) \text{ dB} = 8.686 \text{ dB}$$  \hspace{1cm} (2.4)

Figure 2.3 gives the attenuation coefficient of ultrasound waves in selected biological materials.

**Figure 2.3:** Attenuation coefficient of ultrasound waves in selected biological materials. Figure taken from Wells (1977).
Figure 2.4 shows how the intensity of plane electromagnetic waves and plane ultrasound waves is attenuated in muscle. This figure quantifies the trade-off between penetration depth and wavelength.

![Graph showing intensity attenuation of electromagnetic and ultrasound waves](image)

**Figure 2.4:** Attenuation of plane electromagnetic waves and plane ultrasound waves in muscle. Figure taken from Lele (1987).

When pressure waves encounter a density discontinuity, a portion of the waves' intensity is reflected, while the remainder is transmitted through the discontinuity. Large density discontinuities are found in the body at soft tissue/bone and soft tissue/gas interfaces. For a detailed description of how pressure waves behave at density discontinuities, see Wells (1977) and Breedlove (1994a).

Microwaves can be effectively used to non-invasively heat tumors near the surface of the body. Because the attenuation coefficient of microwaves in tissue is large, however, tumors that reside more than 1-2 cm from the surface of the body cannot be selectively heated with non-invasive microwave applicators. Tumors that exist deep below the sur-
face of the body can only be selectively heated with interstitial microwave antennae or 
microwave applicators designed to be inserted into the body through an orifice such as the 
esophagus, rectum, or urethra.

Ultrasound can be used to non-invasively heat both surface tumors and deep-seated 
tumors. Because ultrasound waves possess a large attenuation coefficient in bone, how-
ever, tumors that are surrounded by bone (cranial tumors, etc.) cannot be heated with 
ultrasound. Tumors that reside near bone can only be heated with ultrasound if the ultra-
sound waves can be projected on the tumor through a soft tissue portal. Because pressure 
waves are reflected when they encounter a large density discontinuity, tumors that lie near 
gas cavities (lungs, stomach, intestines, etc.) are difficult to treat with ultrasound.

Hyperthermia therapy for the MIT/Dana Farber Cancer Institute Hyperthermia Pro-
gram is administered with an array of 56 plane-wave ultrasound transducers (33 mm x 33 
mm each) which operate coherently at 1 MHz. These transducers are rigidly attached to 
the concave surface of a 23.8 cm radius hemisphere. This device is coupled to patients 
through a water filled bolus bag that contacts both the transducers and the patient. By 
specifying the intensity of the power emitted from each transducer, the power deposition 
field in the tissue can be controlled with a high degree of spatial resolution. This allows 
the shape of the resulting temperature field to be customized for a specific treatment so 
that the entire tumor receives a therapeutic dose of energy while damage to healthy tissue 
is minimized.
Chapter 3

Bioheat Transfer
Heat transfer in biological tissue is complex. In addition to conduction in the solid tissue, heat is convected by blood that flows through the tissue. Blood vessels vary in size, flow rate, orientation, and location. The largest blood vessel in the human body is the ascending aorta. In a typical human body, this vessel is 25 mm in diameter and carries blood flowing at an average velocity of 22 cm/s (Ferguson and Roach, 1972). The peak velocity in a typical ascending aorta is 63 cm/s (Whitmore, 1968). The smallest blood vessels in the human body are the capillaries. Capillaries are 5-10 μm in diameter and carry blood flowing at an average velocity of 0.05-0.1 cm/s (Whitmore, 1968). Crezee and Lagendijk (1992) reviewed the work of Ferguson and Roach (1972) to determine the likelihood of turbulent flow in blood vessels. In this study, the effects of pulsatile flow and bifurcations were considered. Crezee and Lagendijk concluded that turbulence will occur only in the largest arteries and veins in the human body.

The density of vessels in human tissue is on the order of 10,000 vessels per cubic centimeter (Baish, 1994). Current vessel imaging equipment is unable to locate the smallest vessels. Even if knowledge of the location, size, and flow rate of all of the vessels in a tissue volume is assumed, accounting for all of these vessels individually in a mathematical model is not feasible with current computer technology.

Many researchers have developed mathematical modelling tools that can be used to predict bioheat transfer. These tools include:

- Continuum bioheat transfer equations
- Idealized analytical models that estimate the effects of individual blood vessels
- Numerical temperature calculation algorithms
Continuum equations are capable of accurately predicting gross temperature fields, however, they do not account for the local effects of individual blood vessels. As a result, temperature gradients near vessels are not predicted by these equations. Idealized analytical models are often used in conjunction with continuum equations to estimate the individual effects of thermally significant blood vessels. Most of these analytical models assume that the flow is always thermally fully-developed. Data presented in Section 5.6 shows that this assumption is inappropriate. Specifically, Table 5.2 shows that the thermal entrance length of all, except for the smallest, blood vessels is large when compared to the dimensions of a large tumor. Heat transfer to thermally undeveloped flow is greater than it is to thermally fully-developed flow. As a result, models based on the assumption of thermally fully-developed flow underpredict the amount of heat that is transferred to blood vessels. Numerical temperature calculation algorithms combine vessel models with a continuum equation to create a mechanism capable of generating three-dimensional temperature fields. Typically, numerical algorithms are more versatile than analytical methods because they allow irregular geometries, material properties, and boundary conditions to be discretized onto a calculation grid. Although many numerical algorithms are sophisticated enough to generate very accurate data, most are too computationally intense to be used in real-time.

The most widely used continuum bioheat transfer equation was proposed by Pennes (1948). The Pennes equation represents the heat transfer effects of blood flow with a temperature dependent heat sink. The basic assumption in the Pennes model is that blood enters the tissue at a fixed arterial temperature and leaves the tissue at the local tissue temperature. Physically, this requires that all heat transfer between the tissue and the blood occurs in the capillaries.
Wulff (1974) criticized the Pennes model, and introduced his own continuum bioheat transfer equation. Wulff's "directed perfusion" model accounts for the effects of blood flow with a convective energy transport term. This term contains the vector dot product of the local temperature gradient and the local volume averaged blood velocity.

Chen and Holmes (1980) created a continuum model for bioheat transfer. Like the Pennes model, the partial differential equation that they derived includes a temperature-dependant heat sink term. This term, however, is slightly different than the one proposed by Pennes. In addition to a heat sink term, the model proposed by Chen and Holmes utilizes an enhanced conduction term and a convective energy transport term to account for heat transfer to blood.

Weinbaum and Jiji (1985) also derived a continuum bioheat transfer equation. This equation accounts for the effects of blood flow with an enhanced thermal conductivity tensor. The local value of this tensor is determined from vascular geometry and flow velocity. In deriving this equation, Weinbaum and Jiji made the simplifying assumption that the tissue temperature is equal to the mean of the arterial and venous temperatures. The "effective thermal conductivity" model developed by Weinbaum and Jiji can often be simplified by assuming isotropy and reducing the thermal conductivity tensor to a scalar.

Baish (1994) proposed a continuum bioheat transfer model that calculates temperature based on a statistical approach. Baish's algorithm generates a fictitious vascular tree that is physiologically similar to an actual vascular tree, numerically calculates the steady-state temperature field in the tissue based on the fictitious vasculature, and performs statistical analysis on the temperature field. The output of this algorithm is the most probable temperature at a point in the tissue and the uncertainty in temperature resulting from the possible proximity of blood vessels.
Baish et al. (1986a) compared the performances of the Pennes, directed perfusion, and effective conductivity continuum bioheat transfer models with three idealized vascular models. The three vascular models consisted of: an array of unidirectional vessels, an array of countercurrent vessels, and a set of large arteries that supply small vessels which drain into large veins. This comparison was performed by using analytical and finite difference methods to calculate temperature profiles in one-dimensional heated tissue. Blood flowing in vessels was assumed to be steady, laminar, hydrodynamically fully-developed, and thermally fully-developed.

Charney et al. (1990) compared one-dimensional temperature fields generated with the Pennes and effective conductivity equations with data obtained from a rigorous three-equation model. Charney et al. showed that the Pennes model is more accurate than the effective conductivity model under certain conditions, while the effective conductivity model is more accurate than the Pennes model under other conditions. Charney et al. concluded that a hybrid model of the two should be formed.

Crezee and Lagendijk (1990) performed experiments with an isolated, perfused, bovine kidney to evaluate the performances of the Pennes equation and the effective conductivity equation. Specifically, these experiments were conducted to determine the relative effectivenesses of the two models in regions of tissue surrounding an artificial blood vessel. When predicting temperature fields with the continuum models, they assumed that the flow rate in the artificial vessel was large enough so that the temperature gradient along the axis of the vessel could be neglected. They also assumed that temperature in the tissue was fixed to a constant value at a somewhat arbitrary distance from the vessel wall, that there was no volumetric heat generation, and that flow in the artificial vessel was steady, laminar, hydrodynamically fully-developed, and thermally fully-developed.
Victor and Shah (1976) investigated heat transfer to blood in the entrance region of a circular tube. In their analysis, blood flow was assumed to be steady, laminar, hydrodynamically undeveloped, and thermally undeveloped as it entered the tube. The two specific situations that were studied in this paper are: constant wall temperature and constant wall heat flux. The non-Newtonian behavior of blood was represented with the Casson equation

\[ \tau_s = \left( \sqrt{\tau_y} + \sqrt{\mu \frac{\partial V_z}{\partial y}} \right)^2 \]  

(3.1)

where \( \tau_s \) is shear stress, \( \tau_y \) is yield stress, \( \mu \) is constant viscosity, \( V_z \) is axial velocity, and the \( y \)-axis is perpendicular to the tube axis. Governing equations were solved numerically. Results were validated by comparing them with experimental data, previously published data for Newtonian fluids (\( \tau_y = 0 \)), and analytical expressions that characterize steady, laminar, fully-developed flow. In this publication, Nusselt number (dimensionless heat transfer coefficient) is plotted as a function of Graetz number (dimensionless distance along the axis of the tube) for both the constant wall temperature and the constant wall heat flux cases.

Chato (1980) presented a three-dimensional, idealized, analytical model for heat transfer in tissue surrounding a vessel. Chato’s model neglects perfusion, volumetric power deposition, and axial heat flow in the tissue. Temperature in the tissue is fixed to a constant value at a somewhat arbitrary distance from the vessel wall. Flow in the vessel is assumed to be steady and laminar. Chato’s model accounts for the entrance region of the vessel and treats blood as a non-Newtonian fluid. Chato accomplished this by using a Nusselt number equation that he derived by fitting an expression to data presented in Victor and Shah (1976). Specifically, Chato used data from Victor and Shah that represents blood entering a tube with a constant wall temperature.
Lagendijk (1982) also derived a three-dimensional, idealized, analytical model for heat transfer in tissue surrounding a blood vessel. This model was revised by Crezee and Lagendijk (1992). The revised model neglects axial heat flow in the tissue, accounts for volumetric power deposition, and utilizes the effective thermal conductivity approach to represent the effects of perfusion. Flow in the vessel is assumed to be steady, laminar, hydrodynamically fully-developed, and thermally fully-developed. The temperature in the tissue is fixed to a constant value at a somewhat arbitrary distance from the vessel wall. Crezee and Lagendijk described how their model can be altered so that it includes the effects of the thermal entrance region. Crezee and Lagendijk did not, however, perform the difficult steps necessary to incorporate the thermal entrance region into their analytical model.

Veins and arteries in the human body often flow parallel and countercurrently to each other. Chato (1980) derived a simple model for heat transfer between countercurrent vessels. Chato's model neglects heat transfer between the countercurrent pair and the surrounding tissue. Baish et al. (1986b) extended the work of Weinbaum and Jiji (1985) to create a model for heat exchange between countercurrent vessels. The model presented by Baish et al. includes heat transfer from the vessel pair to the surrounding tissue. The models created by Chato and Baish et al. both assume that the heat transfer coefficients between the vessels and the tissue are independent of thermal development of the flows. Crezee and Lagendijk (1992) used the conduction coupling parameters proposed by Baish et al. to append their idealized model so that it is capable of describing the effects of countercurrent vessel pairs.

Lagendijk et al. (1984) presented a three-dimensional, time-dependant, finite difference computer algorithm. This algorithm was improved by Mooibroek and Lagendijk (1991). The calculation scheme utilizes the explicit forward difference heat balance tech-
nique to calculate temperature in tissue that contains discreet blood vessels. The effects of perfusion can be represented with either the Pennes equation or the effective thermal conductivity equation. Steady, laminar, hydrodynamically fully-developed, and thermally fully-developed blood flow is assumed inside all vessels.

Charney and Levin (1988) used a finite element routine to calculate transient and steady-state temperatures in heated tissue surrounding countercurrent artery/vein pairs. In these numerical simulations, vessel temperatures were prescribed, the Pennes equation was used to account for perfusion, and blood flowing in the vessels was assumed to be steady, laminar, hydrodynamically fully-developed, and thermally fully-developed. Charney and Levin used data from their simulations to validate the use of the conduction coupling parameters presented by Baish et al. (1986b).

Charney and Levin (1989) performed one-dimensional, transient and steady-state, finite difference simulations on a heated tissue volume that contains a fictitious, branching, countercurrent, vessel network. Charney and Levin utilized the conduction coupling parameters presented by Baish et al. (1986b). The effects of perfusion were accounted for with a modified Pennes heat sink term in which the arterial temperature is a function of location and time. Results were compared with data obtained using the Pennes equation.

Baish (1990) suggested that countercurrent artery/vein pairs can be treated as highly conductive fibers in a less conductive medium. Baish developed analytical expressions for the conductivity and radii of the conductive fibers. Baish recommended that his conductive fiber approach be combined with well-established, composite material, heat transfer analysis methods to predict temperature in tissue.

Chen and Roemer (1992) simulated hyperthermia treatments with a steady-state, finite difference algorithm. Their finite difference model is based on the Pennes equation, and includes the individual effects of several discreet blood vessels. In their simulations, ves-
sels pass through the heated tissue volume, supply blood to the capillaries, and drain blood from the tissue. Flow rate in the vessels, and the arterial temperature in the Pennes heat sink term are functions of location in the tissue. Flow in the vessels is assumed to be steady, laminar, hydrodynamically fully-developed, and thermally fully-developed.

The hyperthermia team at the Massachusetts Institute of Technology developed a rapid, three-dimensional, steady-state, temperature calculation algorithm called the Basis Element Method (Newman et al., 1990; Martin et al., 1992; Newman, 1993; Martin, 1995). This numerical method is based on the Pennes equation and utilizes the Green’s Theorem approach. Martin (1995) experimentally validated the accuracy of the Basis Element Method. Newman et al. (1995) and Martin (1995) have shown that this approach is capable of generating temperature fields in real-time.

H.F. Bowman at MIT has significantly advanced thermal modelling of blood flow for hyperthermia. Bowman (1980) first used the term “thermally-significant vessels” to describe blood vessels that produce temperature perturbations in the surrounding tissue that cannot be mathematically explained with the Pennes bioheat equation. Bowman (1981) discussed the heat transfer mechanisms that govern biological heat transfer during hyperthermia. Bowman (1982) performed a parametric analysis that demonstrated the relative effects that perfusion and thermal conductivity have on temperature distributions for various configurations of ultrasound induced hyperthermia. Bowman (1984) reviewed methods to estimate tissue perfusion. Bowman et al. (1975) compiled the available measured data on human thermal properties. Bowman et al. (1991) experimentally illustrated the influence that anesthesia has on local temporal perfusion levels, and displayed the need for dense thermometry to adequately characterize tumor thermal dose. Bowman et al. (1995) introduced routine measurement of tumor perfusion during clinical hyperthermia.
Chapter 4

The Basis Element Method

The need for a temperature calculation algorithm capable of generating accurate, real-time, three-dimensional, temperature fields that occur in biological tissue during hyperthermia treatment, prompted the creation of the BEM (Newman et al., 1990; Martin et al., 1992; Newman, 1993; Martin, 1995). Newman et al. (1995) reports that the BEM is capable of calculating temperature fields in 60 seconds with an RMS error of less than 0.3 °C. Calculating an equivalent temperature field with a commercially available spectral element package (NEKTON) requires 2,000 seconds (Newman et al., 1995).

The BEM utilizes an approximation of the Green’s Theorem approach to calculate steady-state temperature at discrete locations in the treated tissue. According to the Green’s Theorem approach: if a power deposition field is represented with an infinite number of infinitesimal (point) power sources, the temperature elevation at a specific location can be calculated by integrating the temperature elevation contributions from all of the point sources. The temperature elevation contribution from a single point source is calculated as if the point source is the sole source of power inside the tissue. The BEM approximates the Green’s Theorem approach by summing the temperature elevation contributions from a finite number of spatially discrete power sources. Each of these sources consists of a spherically symmetric volumetric power generation. Since the power deposition field is discretized with spheres possessing finite radii, it is only represented approximately. As the radii of the spherical sources approaches zero, the BEM temperature approximation approaches the exact Green’s Theorem solution.
The steady-state, temperature elevation contribution from a source is calculated by analytically solving the steady-state form of the Pennes bioheat equation (Pennes, 1948). The complete Pennes bioheat equation is

\[
\frac{1}{\alpha} \frac{\partial T}{\partial t} = \nabla^2 T - \left( \frac{1}{L_p^2} \right) T + \frac{Q''}{k_t}
\]

(4.1)

where,

\[
L_p = \sqrt{\frac{k_t}{\omega \rho_{bl} c_{bl}}}
\]

(4.2)

\(\alpha\) = tissue thermal diffusivity \hspace{1cm} \(\omega\) = perfusion rate
\(T\) = temperature elevation \hspace{1cm} \(\rho_{bl}\) = blood density
\(t\) = time \hspace{1cm} \(c_{bl}\) = blood specific heat
\(Q''\) = volumetric power deposition \hspace{1cm} \(k_t\) = tissue thermal conductivity

The Pennes equation is a continuum model that describes the balance between thermal energy storage, conduction, heat transferred by perfusion, and applied power. In this model, the heat transfer effects of perfusion are represented with a temperature dependent heat sink. Charney et al. (1990) show that the Pennes approximation yields acceptable results for global temperature field calculations associated with hyperthermia. Because the Pennes equation is a continuum model, however, it does not predict local temperature gradients induced by individual blood vessels.

The temperature elevation contribution from a source is attenuated exponentially with a space constant equal to the perfusion length, \(L_p\) (see Equation (4.2)). As a result, sources that are greater than a few perfusion lengths away from the point where temperature is...
being calculated can be neglected to save computational time. Figure 4.1 displays a 2-D representation of the BEM.

![Figure 4.1: 2-D representation of the BEM.](image)

In this figure, sources with centers inside the large dark circle are shaded. Only the temperature elevation contributions from these sources are summed to calculate temperature at the center of the large circle. Temperature elevation contributions from sources with centers outside the large circle are not included in the summation. The parameter \( n \), in Figure 4.1, is chosen to specify a trade-off between accuracy and computational time. The number of calculations required to determine temperature at a point is proportional to the cube of \( nL_p \).

The radii of the spherical sources is another calculation parameter that is chosen to specify a trade-off between accuracy of temperature calculations and computational time required. As the radii of the sources is decreased, the power deposition field is more precisely discretized. As a result, more accurate temperature calculations are obtained. This effect is most dramatic in regions where the gradient of the power deposition field is large. The number of calculations required to determine temperature at a point is inversely proportional to the cube of the sphere radii in that region. For a complete explanation of all of
the parameters that affect the accuracy and computational effort of BEM temperature calculations, consult Breedlove (1994b).

The BEM accounts for tissue property discontinuities and boundary conditions by utilizing a calculation strategy similar to the Method of Images used in electrostatic field calculations. Boundaries are accommodated by situating combinations of sources and sinks on opposite sides of the boundary location. These sources and sinks are positioned and powered such that the appropriate boundary condition is satisfied. For detailed information on this subject, see Martin (1995).
Chapter 5

Heat Transfer to Blood Vessels
It is very difficult to analytically solve the coupled partial differential equations that govern heat transfer between a blood vessel and heated, perfused tissue. This is true even if steady-state, axial symmetry, and uniform tissue properties are assumed. Section 5.1 presents the equations that govern the axially-symmetric, steady problem. The difficulty involved in obtaining a complete analytical solution is then discussed.

The solution to a simplified problem is presented in Section 5.3. This simplified problem neglects heat transfer in the tissue and considers only the single partial differential equation that governs heat transfer inside the vessel. Although this simplified solution does not capture all of the physics of the actual problem, it provides insight about the functional dependencies that can be expected. This analytical solution is used in Section 5.4 to validate the accuracy of the commercially-available, numerical, temperature calculation software that is used extensively throughout this document.

The remaining sections in this chapter quantify important blood vessel heat transfer parameters. Section 5.5 defines the heat transfer coefficient and thermal entrance length of a blood vessel. Section 5.6 presents thermal entrance lengths for specific blood vessels in the human circulatory system. The data presented in this section displays the importance that the thermal entrance region has on heat transfer to blood vessels. Section 5.7 quantifies the volume of tissue that is thermally affected by a blood vessel. Section 5.8 derives the temperature at a distance that is far from thermally-significant vessels.
5.1 Governing Heat Transfer Equations

The basic problem of heat transfer between heated, perfused tissue and a straight, cylindrical blood vessel carrying steady, hydrodynamically fully-developed flow is illustrated in Figure 5.1.

\[ Q^\prime\prime = 0 \]

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure51.png}
\caption{Heated, perfused tissue surrounds a straight, cylindrical blood vessel that carries hydrodynamically fully-developed flow. Volumetric power deposition inside the tissue steps from zero to \( Q_o \) at \( z = 0 \).}
\end{figure}

This problem is simplified by assuming that all processes are steady, the tissue properties are uniform, the vessel radius is constant, the mass flow rate in the vessel is constant, and the power deposition inside the vessel is zero. The equations that govern this problem are:

\[ \frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial T_i}{\partial r} \right) + \frac{\partial^2 T_i}{\partial z^2} - \left( \frac{1}{L_p} \right) T_i = -\frac{Q^\prime\prime}{k_i} \quad \text{for} \quad r > R_o \]

\[ \frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial T_b}{\partial r} \right) + \frac{\partial^2 T_b}{\partial z^2} - \frac{\mu}{\alpha} \frac{\partial T_b}{\partial z} = 0 \quad \text{for} \quad r < R_o \]

with the following boundary conditions:
\[ T_t(r, z = -\infty) = 0 \quad (5.3) \]

\[ T_b(r, z = -\infty) = 0 \quad (5.4) \]

\[ T_t(r, z = \infty) = \frac{Q_w L_p^2}{k_t} \quad (5.5) \]

\[ T_b(r, z = \infty) = \frac{Q_u L_p^2}{k_t} \quad (5.6) \]

\[ \frac{\partial T_t}{\partial r} (r = \infty, z) = 0 \quad (5.7) \]

\[ \frac{\partial T_b}{\partial r} (r = 0, z) = 0 \quad (5.8) \]

\[ T_t(r = R_o, z) = T_b(r = R_o, z) \quad (5.9) \]

\[ k_t \frac{\partial T_t}{\partial r} (r = R_o, z) = k_b \frac{\partial T_b}{\partial r} (r = R_o, z) \quad (5.10) \]

In these equations, \( T_t \) is the temperature of the tissue, \( T_b \) is the temperature of the blood inside the vessel, \( u \) is the velocity of the blood, \( R_o \) is the radius of the vessel, \( k_t \) is the thermal conductivity of the tissue, \( k_b \) is the thermal conductivity of the blood, \( \alpha \) is the thermal diffusivity of the blood, \( Q'' \) is the volumetric power deposition in the tissue, and \( L_p \) is the perfusion length defined in Equation (4.2). Since the flow is assumed to be hydrodynamically fully-developed, the velocity of the blood is given by Equation (5.11).

\[ u = u_{\max} \left( 1 - \frac{r^2}{R_o^2} \right) \quad (5.11) \]

In this equation, \( u_{\max} \) is the velocity of the blood at \( r = 0 \). If axial heat conduction in the flow is neglected, Equation (5.2) reduces to:

\[ \frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial T_b}{\partial r} \right) - \frac{u}{\alpha} \frac{\partial T_b}{\partial z} = 0 \quad \text{for} \quad r < R_o \quad (5.12) \]

Equations (5.1) and (5.12) are both of the Sturm-Liouville type. If these two equations were not coupled to each other through Equations (5.9) and (5.10), individual solutions to
both could be obtained by employing the method of separation of variables (Arpaci, 1991). Obtaining a solution for the coupled equations, however, requires that the eigenfunctions of both equations in the axial direction have the same form. This constraint cannot be satisfied because Equations (5.1) and (5.12) have different forms.

5.2 Mixing-Cup Temperature

Analysis of heat transfer to internal flows is often performed using the mixing-cup temperature of the flow. The mixing-cup temperature of a flow, $T_m$, is defined in Lienhard (1987) to be

$$
T_m \equiv \frac{\int \rho c_p u T dA}{\int \rho c_p u dA} = \frac{\text{energy flow rate}}{(\text{mass flow rate})c} \tag{5.13}
$$

where $T$ is temperature, $\rho$ is density, $c_p$ is specific heat, and $u$ is the velocity of the flow perpendicular to the differential area, $dA$. Mixing-cup temperature is the cross-sectional, mass flow rate weighted, average temperature of the flow. Physically, the mixing-cup temperature is the temperature that would be obtained if fluid at a particular cross-section was allowed to flow into a container and then thoroughly mixed.

5.3 The Graetz Problem

This section presents the analytical solution to the Graetz problem. The solution to the Graetz problem quantifies heat transfer to steady, hydrodynamically fully-developed flow inside a cylindrical tube. The Graetz problem does not consider heat transfer in the medium that surrounds the flow. Although the solution to the Graetz problem does not capture all of the physics involved when there is heat transfer between perfused tissue and a blood vessel, it provides insight about the functional dependencies that can be expected.
Heat transfer to fluid flowing in circular tubes has been investigated by Graetz (1885), Sellars et al. (1956), Siegel et al. (1958), and Kays and Crawford (1980). Graetz (1885) calculated the temperature profile of fluid flowing in a circular tube under steady, laminar conditions where there is a step change in the temperature of the tube wall at \( z = 0 \) (the \( z \)-axis points in the direction of the tube axis). Graetz assumed that the flow was isothermal and hydrodynamically fully-developed at \( z = 0 \). Kays and Crawford (1980) state that the Graetz solution is an accurate approximation when the velocity profile is not fully-developed, if the Prandtl number of the fluid is greater than 5. In performing his calculations, Graetz neglected axial conduction of heat in the flow. Kays and Crawford state that this assumption is valid as long as the product of the Reynolds number and the Prandtl number is greater than 100. The Reynolds number and the Prandtl number are dimensionless parameters defined in Equations (5.14) and (5.15) respectively.

\[
\text{Reynolds number} \equiv Re \equiv \frac{p \bar{u} D}{\mu} \quad (5.14)
\]

\[
\text{Prandtl number} \equiv Pr \equiv \frac{v}{\alpha} \quad (5.15)
\]

In these equations, \( \rho \) is density, \( \bar{u} \) is average velocity, \( D \) is diameter, \( \mu \) is viscosity, \( v \) is kinematic viscosity, and \( \alpha \) is thermal diffusivity.

The partial differential equation that governs the Graetz problem is of the Sturm-Liouville type. Therefore, it can be solved by employing the method of separation of variables (Arpaci, 1991). The solution to the Graetz problem, in terms of the mixing-cup temperature, is given by Kays and Crawford (1980) to be:

\[
\frac{T_0 - T_m}{T_0 - T_e} = 8 \sum_{n = 0}^{\infty} \frac{G_n}{\lambda_n^2} \exp\left(-\lambda_n^2 \frac{z}{Re Pr}\right) \quad (5.16)
\]

where, fluid flows in the positive \( z \)-direction, \( T_m \) is the mixing-cup temperature, \( T_0 \) is the temperature of the wall for \( z > 0 \), \( T_e \) is the temperature of the fluid for \( z < 0 \), \( \lambda_n^2 \) and \( G_n \) are
constants, and \( R \) is the radius of the tube. The values of \( \lambda_n^2 \) and \( G_n \) are listed in Table 5.1.

<table>
<thead>
<tr>
<th>( n )</th>
<th>( \lambda_n^2 )</th>
<th>( G_n )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7.312</td>
<td>0.749</td>
</tr>
<tr>
<td>1</td>
<td>44.62</td>
<td>0.544</td>
</tr>
<tr>
<td>2</td>
<td>113.8</td>
<td>0.453</td>
</tr>
<tr>
<td>( &gt;2 )</td>
<td>( (4n+8/3)^2 )</td>
<td>( 1.1276\lambda_n^{-1/3} )</td>
</tr>
</tbody>
</table>

Sellars et al. (1956) and Siegel et al. (1958) extended the work of Graetz. Sellars et al. made approximations necessary to calculate the complete set of eigenvalues and constants for the Graetz solution. Sellars et al. used the Graetz solution and the method of superposition to form a Stieltjes integral that can be used to calculate temperature profiles in the fluid when the wall temperature varies arbitrarily along the \( z \)-axis. Sellars et al. also performed calculations to determine temperature profiles in the fluid when the heat flux at the tube wall is prescribed instead of the temperature. Siegel et al. took a different approach than Sellars et al. to determine temperature profiles in the fluid when the heat flux at the tube wall is prescribed. The work of Siegel et al. resulted in a solution with a more complete set of eigenvalues and constants than was previously determined by Sellars et al.

5.4 Numerical Calculations with NEKTON

NEKTON Version 2.85\(^1\) is a commercially available software package used extensively in this thesis to generate temperature fields. NEKTON uses the spectral element method to solve coupled fluid mechanics and heat transfer problems. NEKTON allows the use of a temperature dependant heat sink to represent the effects of perfusion (as in the Pennes bio-heat equation).

---

1. Copyright 1991 by Nektonics, Inc. and the Massachusetts Institute of Technology.
Figures (5.2) - (5.4) compare results obtained with NEKTON to the analytical solution of the Graetz problem (Equation (5.16)). This comparison was performed to demonstrate that the author is capable of using NEKTON to accurately calculate the temperature fields presented in this document. In all three figures, the temperature of the tube wall is 0 °C for negative $z$, and 6 °C for positive $z$. The fluid is blood. The tube diameter and flow velocity used to generate Figure 5.2 represent a 1 mm diameter vein (Torell and Nilsson, 1978). This vessel estimates the least thermally-significant vessel that will be considered when calculating temperature fields for hyperthermia. Smaller vessels are difficult to detect, and equilibrate very rapidly with the temperature of surrounding tissue. The tube diameter and flow velocity used to create Figure 5.3 represent a 3 mm diameter vein (Torell and Nilsson, 1978). Parameters used to produce Figure 5.4 represent the femoral artery (Ferguson and Roach, 1972). The femoral artery was chosen to estimate the most thermally-significant vessels likely to reside near tissue treated with hyperthermia.
Figure 5.2: Mixing-cup temperature of steady, laminar, hydrodynamically fully-developed flow in a circular tube. Temperature of the tube wall is 0 °C for negative $z$, and 6 °C for positive $z$. Fluid is blood. Diameter of tube is 1 mm. Average flow velocity is 1 cm/s. RMS difference for 68 points is 0.0142 °C.
Figure 5.3: Mixing-cup temperature of steady, laminar, hydrodynamically fully-developed flow in a circular tube. Temperature of the tube wall is 0 °C for negative $z$, and 6 °C for positive $z$. Fluid is blood. Diameter of tube is 3 mm. Average flow velocity is 2 cm/s. RMS difference for 68 points is 0.0080 °C.
Figure 5.4: Mixing-cup temperature of steady, laminar, hydrodynamically fully-developed flow in a circular tube. Temperature of the tube wall is 0 °C for negative $z$, and 6 °C for positive $z$. Fluid is blood. Diameter of tube is 5 mm. Average flow velocity is 26 cm/s. RMS difference for 68 points is 0.0133 °C.

5.5 Heat Transfer Coefficient and Thermal Entrance Region

Equation (5.17) defines the heat transfer coefficient, $h$, for flow in a circular tube.

$$Q' = hD\pi (T_w - T_m)$$  \hspace{1cm} (5.17)

In this equation, $Q'$ is the amount of heat per unit length transferred to the fluid, $T_w$ is the temperature of the tube wall, and $T_m$ is the mixing-cup temperature of the flow. The heat transfer coefficient can be evaluated analytically for the situations investigated by Graetz, Sellars et al., and Siegel et al. Figure 5.5 displays two relationships between Nusselt num-
Nusselt number and Graetz number, $G_z$ (Kays and Crawford, 1980). Nusselt number and Graetz number are defined as

$$Nu = \frac{hD}{k_f}$$

(5.18)

$$Gz = \frac{z/R}{RePr}$$

(5.19)

where, $k_f$ is the thermal conductivity of the fluid.

**Figure 5.5:** Nusselt number for steady, laminar, hydrodynamically fully-developed flow in a circular tube.

In this figure, the solid line depicts the Nusselt number when there is a step change in the temperature of the tube wall at $z = 0$, while the dashed line corresponds to the Nusselt number when there is a uniform heat flux at the tube wall for $z > 0$. 

47
In both cases displayed in Figure 5.5, the Nusselt number approaches a constant value as the Graetz number increases. This constant is 3.658 for the constant wall temperature case and 4.364 for the constant wall heat flux case. The region where the Nusselt number is larger than its downstream constant value is called the thermal entrance region of the flow. Physically, the thermal entrance region is the portion of the flow where thermal boundary layers originating from opposite sides of the tube do not contact each other. The part of a flow that is not in the thermal entrance region is considered thermally fully-developed. According to Kays and Crawford (1980), the distance in the flow direction, $z_{et}$, required for a hydrodynamically fully-developed flow to become thermally fully-developed in a tube with a circular cross-section is

$$z_{et} = 0.05RePrD = \frac{0.05D^2 \bar{u}}{\alpha}$$  \hspace{1cm} (5.20)

5.6 Thermal Entrance Region of Blood Vessels
Many researchers have simplified the analysis of heat transfer between tissue and blood vessels by neglecting the thermal entrance region of the vessel. Although this assumption greatly simplifies the calculation, it is only valid for very small vessels. Table 5.2 displays the length of the thermal entrance region for several vessels found in the human body. Thermal entrance length was calculated with Equation (5.20). Properties of blood were taken to be: density = 1000 kg/m$^3$, viscosity = 0.0035 kg/m-sec, thermal conductivity = 0.6 W/m-K, specific heat = 4000 J/kg-K (Crezee and Lagendijk, 1992). The last column in Table 5.2 corresponds to the location where diameter and velocity data for each vessel was obtained. Reference "F" is Ferguson and Roach (1972), reference "V" is van de Vosse (1987), and reference "W" is Whitmore (1968).
Table 5.2: Thermal Entrance Lengths of Vessels in the Human Circulatory System.

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Diameter [mm]</th>
<th>Average Velocity [cm/s]</th>
<th>Reynolds Number</th>
<th>Thermal Entrance Length [cm]</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending aorta</td>
<td>25</td>
<td>22</td>
<td>1571</td>
<td>4582</td>
<td>F</td>
</tr>
<tr>
<td>Internal carotid artery</td>
<td>4</td>
<td>50</td>
<td>571</td>
<td>266</td>
<td>F,V</td>
</tr>
<tr>
<td></td>
<td>6.2</td>
<td>14.5</td>
<td>257</td>
<td>186</td>
<td></td>
</tr>
<tr>
<td>Femoral artery</td>
<td>5</td>
<td>26</td>
<td>371</td>
<td>216</td>
<td>F</td>
</tr>
<tr>
<td>Renal artery</td>
<td>4</td>
<td>50</td>
<td>571</td>
<td>266</td>
<td>F</td>
</tr>
<tr>
<td>Capillaries</td>
<td>0.005-0.01</td>
<td>0.05-0.1</td>
<td>0.0007-0.003</td>
<td>4x10^{-7}-4x10^{-6}</td>
<td>W</td>
</tr>
<tr>
<td>Large veins</td>
<td>5-10</td>
<td>15-20</td>
<td>214-571</td>
<td>125-666</td>
<td>W</td>
</tr>
<tr>
<td>Venae cavae</td>
<td>20</td>
<td>11-16</td>
<td>629-914</td>
<td>1468-2133</td>
<td>W</td>
</tr>
</tbody>
</table>

5.7 Region of Tissue Thermally Affected by a Blood Vessel

The Pennes bioheat equation predicts that thermal perturbations are damped exponentially with a space constant equal to the perfusion length, $L_p$. The perfusion length was defined in Chapter 4 to be:

$$L_p = \sqrt{\frac{k_t}{\omega \rho_{bl} c_{bl}}} \quad (5.21)$$

Equation (5.21) shows that this parameter is inversely proportional to the perfusion level, $\omega$. Perfusion in heated tissue may rise above 100 ml/100ml-min (ml of blood per 100 ml of tissue per min), while perfusion in damaged tissue may approach zero ml/100ml-min. Table 5.3 displays values of perfusion length for a range of perfusion levels encountered during typical hyperthermia treatments. The calculations performed to generate Table 5.3 use the properties of blood presented in Section 5.6.
Table 5.3: Typical Perfusion Lengths Encountered During Hyperthermia.

<table>
<thead>
<tr>
<th>Perfusion Level, $\omega$ [ml/100ml-min]</th>
<th>Perfusion Length, $L_p$ [mm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>13.4</td>
</tr>
<tr>
<td>20</td>
<td>6.71</td>
</tr>
<tr>
<td>40</td>
<td>4.74</td>
</tr>
<tr>
<td>60</td>
<td>3.87</td>
</tr>
<tr>
<td>80</td>
<td>3.35</td>
</tr>
<tr>
<td>100</td>
<td>3.00</td>
</tr>
</tbody>
</table>

The presence of perfusion causes the significant thermal effects of a blood vessel to be limited to the region of tissue that is located less than 3 perfusion lengths away from the vessel wall. Figure 5.6 and Figure 5.7 show temperature fields generated by NEKTON in which a 3 mm diameter vein flows through perfused tissue. There is a step change in volumetric power deposition in the tissue at $z = 0$. Power deposition in the vessel is zero. Flow is steady, laminar, and hydrodynamically fully-developed. The effects of perfusion were treated as a temperature dependant heat sink (Pennes bioheat equation). Thermal conductivity of the tissue is 0.6 W/m-K (Crezee and Lagendijk, 1992). Properties of blood are those given in Section 5.6. Average flow velocity in the vessel is 2 cm/s (Torell and Nilsson, 1978). Perfusion in the tissue is 100 ml/100ml-min in Figure 5.6 and 5 ml/100ml-min in Figure 5.7. The solid lines on the axis planes delineate projections of the vessel wall. The dashed lines on the axis planes are located 3 perfusion lengths from the projection of the vessel wall.
**Figure 5.6:** Temperature field generated by NEKTON. Volumetric power deposition in the tissue is zero for negative $z$, and 0.4 W/cm$^3$ for positive $z$. Perfusion in the tissue is 100 ml/100ml-min ($L_p = 0.3$ cm). Diameter of the vessel is 3 mm. Average flow velocity is 2 cm/s. Solid lines on the axis planes delineate projections of the vessel wall. Dashed lines on the axis planes are located 3 perfusion lengths from the projection of the vessel wall.
Figure 5.7: Temperature field generated by NEKTON. Volumetric power deposition in the tissue is zero for negative z, and 0.02 W/cm$^3$ for positive z. Perfusion in the tissue is 5 ml/100ml-min ($L_p = 1.34$ cm). Diameter of the vessel is 3 mm. Average flow velocity is 2 cm/s. Solid lines on the axis planes delineate projections of the vessel wall. Dashed lines on the axis planes are located 3 perfusion lengths from the projection of the vessel wall.
5.8 Far-Field Temperature Elevation in Heated Tissue

The Pennes bioheat equation predicts that the temperature elevation of uniformly heated tissue \((Q'' = Q_0'')\) will reach a constant steady-state value if the tissue is a sufficient number of perfusion lengths away from all thermal perturbations. The value of this far-field temperature elevation can be determined by setting all of the derivatives in the Pennes bioheat equation to zero

\[
\frac{1}{\rho c} \frac{\partial T}{\partial t} = \nabla \cdot \left( \frac{1}{\rho c} \right) T + \frac{Q_0''}{k_f} \tag{5.22}
\]

This leaves:

\[
T_{\text{far-field}} = \frac{Q_0'' L_p^2}{k_f} \tag{5.23}
\]
Chapter 6

Thermal Model
This chapter presents a model that accurately quantifies the effects that individual blood vessels have on hyperthermia temperature fields. Section 6.1 derives an expression that characterizes the relationship between the mixing-cup temperature of blood in a vessel and the temperature of the unheated, perfused tissue that surrounds the vessel. The derivation assumes that the vessel carries blood with a mixing-cup temperature that varies arbitrarily along the axis of the vessel. Section 6.2 derives and validates an empirical relationship that characterizes the mixing-cup temperature inside a vessel that flows through arbitrarily heated, perfused tissue. Section 6.3 describes how the information presented in Sections 6.1 and 6.2 can be used to calculate temperature in the vicinity of thermally-significant blood vessels.

6.1 Relationship Between Mixing-Cup and Tissue Temperature
This section presents an expression that characterizes the relationship between the mixing-cup temperature of blood in a vessel and the temperature of the unheated, perfused tissue that surrounds the vessel. The derivation assumes that the vessel carries blood with a mixing-cup temperature elevation, $T_{mc}$, that varies arbitrarily along the axis of the vessel. There is no volumetric power deposition in the tissue, the vessel is straight and cylindrical, and axial heat conduction in the tissue is neglected. A criterion is established that can be used to determine the validity of neglecting axial conduction.

The partial differential equation that governs axially symmetric heat transfer in perfused tissue is
\[
\frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial T_t}{\partial r} \right) + \frac{\partial^2 T_t}{\partial z^2} - \left( \frac{1}{L_p^2} \right) T_t = 0 \quad \text{for} \quad r > R
\] (6.1)

where \( T_t \) is the temperature elevation of the tissue, \( L_p \) is the perfusion length defined in Equation (4.2), \( R \) is the radius of the vessel, \( r \) is distance from the center of the vessel, and \( z \) is distance along the axis of the vessel in the direction of blood flow. Equation (6.1) can be simplified if axial heat conduction in the tissue is neglected. Axial conduction can be neglected when

\[
\frac{\partial T_t}{\partial z} \ll \frac{\partial T_t}{\partial r} \quad (6.2)
\]

Equations (6.3) and (6.4) approximate the order of magnitude of the terms in Equation (6.2).

\[
\frac{\partial T_t}{\partial z} \sim \frac{dT_{mc}}{dz} \quad (6.3)
\]

\[
\frac{\partial T_t}{\partial r} \sim \frac{-T_{mc}}{L_p} \quad (6.4)
\]

Therefore, Equation (6.2) can be estimated by

\[
\frac{dT_{mc}}{dz} \ll \frac{-T_{mc}}{L_p} \quad (6.5)
\]

If this criterion is satisfied, Equation (6.1) reduces to

\[
\frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial T_t}{\partial r} \right) - \left( \frac{1}{L_p^2} \right) T_t = 0 \quad \text{for} \quad r > R
\] (6.6)

The boundary conditions for Equation (6.6) are

\[
\frac{\partial T_t}{\partial r} = 0 \quad \text{at} \quad r = \infty \quad (6.7)
\]

\[
k \frac{\partial T_t}{\partial r} = Q' \quad \text{at} \quad r = R \quad (6.8)
\]
where \( k_t \) is the thermal conductivity of the tissue, and \( Q'' \) is the circumferentially-averaged rate of heat flux into the vessel. \( Q'' \) is related to the mixing-cup temperature in the vessel through a simple energy balance.

\[
Q'' = \left( \frac{\dot{m} c_{bl}}{2 k \pi} \right) \frac{dT_{mc}}{dz}
\]

(6.9)

In this equation, \( \dot{m} \) is the mass flow rate of blood in the vessel, and \( c_{bl} \) is the specific heat of blood. The solution to Equation (6.6) with boundary conditions (6.7) and (6.8) is

\[
T_t = \left[ \frac{-Q'' L_p}{k_0 K_1 \left( \frac{R}{L_p} \right)} \right] K_0 \left( \frac{r}{L_p} \right)
\]

(6.10)

where \( K_\nu \) is a modified Bessel function of the second kind of order \( \nu \) (Arpaci, 1991). Substitution of Equation (6.9) into Equation (6.10) yields

\[
T_t = \left[ \frac{-\dot{m} c_{bl} L_p}{2 R \pi k_0 K_1 \left( \frac{R}{L_p} \right)} \right] K_0 \left( \frac{r}{L_p} \right) \left( \frac{dT_{mc}}{dz} \right)
\]

(6.11)

### 6.2 Empirical Characterization of Mixing-Cup Temperature in a Vessel

This section presents the derivation of an empirical relationship that characterizes the mixing-cup temperature of blood in a vessel that flows through a region of arbitrarily heated tissue. Subsection 6.2.1 discusses the source of the data from which the relationship was deduced. Subsection 6.2.2 establishes the empirical “building-block” equations that were used to derive the complete relationship. The building-block equations characterize the mixing-cup temperature of blood in a vessel that flows from a region of tissue with no volumetric power deposition into a region of tissue with a uniform volumetric power deposition. Subsection 6.2.3 demonstrates the accuracy of the building-block equations for the range of parameters that are expected in hyperthermia. Subsection 6.2.4 utilizes the building-block equations to derive the complete relationship that characterizes mixing-cup tem-
temperature when volumetric power deposition in the tissue varies arbitrarily. Subsection 6.2.5 uses this relationship to calculate the mixing-cup temperature of a vessel that flows through a region of tissue with a specific, spatially-varying, volumetric power deposition. Subsection 6.2.6 validates the accuracy of the complete empirical relationship by comparing the mixing-cup temperature calculated in Subsection 6.2.5 to data generated with NEKTON.

6.2.1 Empirical Data
The empirical analysis and numerical validations presented in this chapter were performed with data generated by NEKTON. In all NEKTON simulations, flow inside the vessel is steady, laminar, and hydrodynamically fully-developed; blood inside the vessel enters the tissue at body temperature far from where heating occurs; the heat transfer effects of perfusion are treated as a temperature dependent heat sink; volumetric power deposition inside the vessel is zero; and volumetric power deposition in the tissue is a function only of distance along the axis of the vessel. Contrary to the steady flow assumption, flow inside blood vessels is pulsatile. This is especially true for arteries. Chato (1980) states that pulsatility increases heat transfer between a vessel and the tissue that surrounds it. The assumption of laminar flow is satisfactory except when the largest vessels in the human body are considered (Crezee and Lagendijk, 1992; Ferguson and Roach, 1972). Using Equation (5.15) and property values presented in Section 5.6, the Prandtl number of blood is equal to 23.3. Because this value is much greater than one, hydrodynamic boundary layers grow much faster than thermal boundary layers. Therefore, blood flow can be considered hydrodynamically fully-developed. Neglecting power deposition inside large vessels is reasonable since they occupy only a small percentage of the tissue volume and the attenuation coefficient of ultrasound power in blood is low (Wells, 1977; Baish et al., 1986a; Roemer, 1991; Dorr and Hynynen, 1992). Since power deposition in the tissue is
constrained to be a function only of position along the axis of the vessel, it is set to the area-averaged volumetric power deposition defined by

\[
Q_{A^\infty} = \frac{\int_0^{2\pi} \int_0^R \frac{Q'' r dr d\theta}{r} \cdot 2\pi (R + 3L_\rho)}{\int_0^{2\pi} \int_0^R r dr d\theta}
\]  \hspace{1cm} (6.12)

6.2.2 Empirical Building-Block Equations
Examination of NEKTON data led to the development of an empirical relationship that characterizes the mixing-cup temperature of a blood vessel flowing through perfused tissue that contains a step change in volumetric power deposition. This subsection presents: the seven sets of NEKTON data from which the empirical relationship was derived, a three-step normalization of the NEKTON data, and the three piecewise-continuous equations that constitute the empirical relationship.

Figure 6.1 displays the mixing-cup temperature elevation calculated by NEKTON for seven combinations of tissue and vessel parameters. These seven sets of data encompass the range of conditions that are most appropriate for hyperthermia. The tissue and blood properties used to create this figure are presented in Chapter 5. In all seven cases, the vessel length was set to 20 cm. It is unlikely that a longer blood vessel will exist inside a hyperthermia treatment volume.
Figure 6.1: Mixing-cup temperature elevation for seven combinations of vessel and tissue parameters.

The dashed line, solid line, x’s, and o’s in Figure 6.1 all represent a 1 mm diameter vein with an average flow velocity of 1 cm/s (Torell and Nilsson, 1978). As discussed in Section 5.4, this vessel estimates the least thermally significant vessel that will be considered when calculating temperature fields for hyperthermia. For the dashed line: perfusion in the tissue is 100 ml/100ml-min; and volumetric power deposition in the tissue is zero for negative $z$, and $5.3333 \times 10^{-1}$ W/cm$^3$ for positive $z$ ($T_{\text{far-field}} = 8 \, ^\circ\text{C}$). For the solid line: perfusion in the tissue is 5 ml/100ml-min; and volumetric power deposition in the tissue is zero for negative $z$, and $2.6667 \times 10^{-2}$ W/cm$^3$ for positive $z$ ($T_{\text{far-field}} = 8 \, ^\circ\text{C}$). For the x’s:
perfusion in the tissue is 100 ml/100ml-min; and volumetric power deposition in the tissue is zero for negative z, and $6.6667 \times 10^{-2}$ W/cm$^3$ for positive z ($T_{\text{far-field}} = 1 \, ^{\circ}\text{C}$). For the o's: perfusion in the tissue is 5 ml/100ml-min; and volumetric power deposition in the tissue is zero for negative z, and $3.3333 \times 10^{-3}$ W/cm$^3$ for positive z ($T_{\text{far-field}} = 1 \, ^{\circ}\text{C}$).

The dash-dot line and +’s represent a 3 mm diameter vein with an average flow velocity of 2 cm/s (Torell and Nilsson, 1978). For the dash-dot line: perfusion in the tissue is 100 ml/100ml-min; and volumetric power deposition in the tissue is zero for negative z, and $4.0 \times 10^{-1}$ W/cm$^3$ for positive z ($T_{\text{far-field}} = 6 \, ^{\circ}\text{C}$). For the +’s: perfusion in the tissue is 5 ml/100ml-min; and volumetric power deposition in the tissue is zero for negative z, and $2.0 \times 10^{-2}$ W/cm$^3$ for positive z ($T_{\text{far-field}} = 6 \, ^{\circ}\text{C}$).

The *’s represent a typical femoral artery with a 5 mm diameter and an average flow velocity of 26 cm/s (Ferguson and Roach, 1972). As discussed in Section 5.4, the femoral artery estimates the most thermally significant vessel likely to reside near tissue treated with hyperthermia. Perfusion in the tissue is 25 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative z, and $1.0 \times 10^{-1}$ W/cm$^3$ for positive z ($T_{\text{far-field}} = 6 \, ^{\circ}\text{C}$).
Mixing-cup temperature elevation can be normalized by dividing it by the far-field temperature elevation calculated with Equation (5.23). The results of this normalization are illustrated in Figure 6.2.

![Graph showing normalized mixing-cup temperature elevation vs distance along the vessel axis](image)

**Figure 6.2**: Normalized mixing-cup temperature elevation.

As a result of the normalization, sets of data are now coincident in cases where volumetric power deposition is the only differing input (the dashed line coincides with the x’s, and the solid line coincides with the o’s).

The solution to the Graetz problem presented in Section 5.3 suggests that the data in Figure 6.2 may be further reduced by plotting the normalized mixing-cup temperature elevation as a function of the Graetz number of the vessel defined by Equation (5.19). Figure
6.3 illustrates that the functional dependency of normalized mixing-cup temperature elevation cannot be completely characterized by the Graetz number.

![Graph showing normalized mixing-cup temperature elevation versus Graetz number.](image)

**Figure 6.3:** Normalized mixing-cup temperature elevation versus Graetz number.

Through careful examination and extraordinary insight, it was discovered that the normalized mixing-cup temperature elevation depends almost entirely on a dimensionless parameter that has been eponymously named the “Breedlove number”. The Breedlove number, $Br_z$, is defined as:

$$Br_z = \left( \frac{z}{RePr} \right) \left( \frac{R}{L_p} \right)^{3/8} \quad (6.13)$$

The Breedlove number is the product of the Graetz number and a length ratio raised to the three-eighths power. Figure 6.4 displays the seven sets of data plotted as normalized mix-
ing-cup temperature elevation versus Breedlove number. The figure shows that the functional dependency on the Breedlove number breaks down in the vicinity of the power deposition discontinuity \((z = 0)\). In this region of tissue, the abrupt change in power deposition causes perfusion effects to dominate.

\[
Br_z = \left( \frac{z/R}{RePr} \right) \left( \frac{R}{L_p} \right)^{3/8}
\]

**Figure 6.4:** Normalized mixing-cup temperature elevation versus Breedlove number.
The normalized data plotted in Figure 6.4 was used to develop the following three piecewise-continuous empirical equations:

\[
\frac{T_{mc}k_t}{Q_A^{''}L_p^2} = C_1 \exp\left(\frac{z}{L_p}\right) \quad \text{for} \quad Br_z \leq 0
\]  \hspace{1cm} (6.14)

\[
\frac{T_{mc}k_t}{Q_A^{''}L_p^2} = \frac{C_2 - C_1}{C_2} \left[1 - \exp\left(-3.26 Br_z\right)\right] + C_1 \quad \text{for} \quad 0 \leq Br_z \leq 0.15
\]  \hspace{1cm} (6.15)

\[
\frac{T_{mc}k_t}{Q_A^{''}L_p^2} = 1 - \exp\left(-3.26 Br_z\right) \quad \text{for} \quad Br_z \geq 0.15
\]  \hspace{1cm} (6.16)

where,

\[
C_1 = \frac{1}{2} \left[1 - \exp\left(-2.4 Br_{t_p}^{0.94}\right)\right]
\]  \hspace{1cm} (6.17)

\[
C_2 = 1 - \exp\left[-3.26 \left(0.15\right)\right]
\]  \hspace{1cm} (6.18)

\[
Br_{t_p} = \left(\frac{L_p/R}{RePr}\right)\left(\frac{R}{L_p}\right)^{3/8}
\]  \hspace{1cm} (6.19)

These building-block equations can be used to determine the mixing-cup temperature elevation of a vessel that carries blood through perfused tissue where volumetric power deposition steps from zero to \(Q_A^{''}\) at \(z = 0\). The accuracy of the building-block equations is established in the next subsection. The building-block equations are then utilized in Subsection 6.2.4 to derive a more generally applicable relationship that can be used to calculate mixing-cup temperature when volumetric power deposition in the tissue varies arbitrarily.
6.2.3 Accuracy of the Building-Block Equations
The figures in this subsection compare Equations (6.14) - (6.16) with the NEKTON data presented in Figure 6.1. As previously stated, tissue and vessel parameters span the range of values that is expected for hyperthermia.

Figure 6.5: Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 100 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative \(z\), and \(5.3333 \times 10^{-1}\) W/cm\(^3\) for positive \(z\) \((T_{\text{far-field}} = 8\,^\circ\text{C})\). Diameter of the vessel is 1 mm. Average flow velocity is 1 cm/s (Torell and Nilsson, 1978). RMS difference for 97 points is 0.0780 °C.
Figure 6.6: Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 5 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative $z$, and $2.6667 \times 10^{-2}$ W/cm$^3$ for positive $z$ ($T_{\text{far-field}} = 8$ °C). Diameter of the vessel is 1 mm. Average flow velocity is 1 cm/s (Torell and Nilsson, 1978). RMS difference for 97 points is 0.0622 °C.
Figure 6.7: Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 100 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative $z$, and $6.6667 \times 10^{-2}$ W/cm$^3$ for positive $z$ ($T_{\text{far-field}} = 1 \, ^\circ \text{C}$). Diameter of the vessel is 1 mm. Average flow velocity is 1 cm/s (Torell and Nilsson, 1978). RMS difference for 97 points is 0.0098 $^\circ \text{C}$. 
Figure 6.8: Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 5 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative \( z \), and \( 3.3333 \times 10^{-3} \) W/cm\(^3\) for positive \( z \) (\( T_{\text{far-field}} = 1^\circ \text{C} \)). Diameter of the vessel is 1 mm. Average flow velocity is 1 cm/s (Torell and Nilsson, 1978). RMS difference for 97 points is 0.0078 \(^\circ\)C.
Figure 6.9: Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 100 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative $z$, and $4.0 \times 10^{-1}$ W/cm$^3$ for positive $z$ ($T_{\text{far-field}} = 6$ °C). Diameter of the vessel is 3 mm. Average flow velocity is 2 cm/s (Torell and Nilsson, 1978). RMS difference for 93 points is 0.0356 °C.
Figure 6.10: Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 5 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative $z$, and $2.0 \times 10^{-2}$ W/cm$^3$ for positive $z$ ($T_{\text{far-field}} = 6^\circ$C). Diameter of the vessel is 3 mm. Average flow velocity is 2 cm/s (Torell and Nilsson, 1978). RMS difference for 89 points is 0.0350 $^\circ$C.
Figure 6.11: Comparison between Equations (6.14) - (6.16) and data generated with NEKTON. Perfusion in the tissue is 25 ml/100ml-min. Volumetric power deposition in the tissue is zero for negative $z$, and $1.0 \times 10^{-1}$ W/cm$^3$ for positive $z$ ($T_{\text{far-field}} = 6$ °C). Diameter of the vessel is 5 mm. Average flow velocity is 26 cm/s (Ferguson and Roach, 1972). RMS difference for 93 points is 0.0117 °C.

6.2.4 Arbitrary Volumetric Power Deposition

A superposition of Equations (6.14) - (6.16) can be used to determine the mixing-cup temperature elevation inside a vessel when the volumetric power deposition in the tissue varies arbitrarily along the axis of the vessel. Let Equation (6.20) represent Equations (6.14) - (6.16).

$$\frac{T_{mc} k_t}{Q_{\text{in}}^2 L_p} = F(z)$$

(6.20)

Equation (6.20) gives the mixing-cup temperature elevation in the vessel when the volu-
metric power deposition in the tissue steps from zero to \( Q_A''' \) at \( z = 0 \). If there are \( n \) steps in volumetric power deposition, the mixing-cup temperature elevation in the vessel is given by

\[
T_{mc} = \left( \frac{L_p}{k_j} \right)^2 \sum_{i=1}^{n} Q_{Ai}''' F(z - \xi_i)
\]  

(6.21)

where \( Q_{Ai}''' \) is the increase in volumetric power deposition at \( z = \xi_i \). If volumetric power deposition in the tissue changes infinitesimally with \( z \), the mixing-cup temperature elevation in the vessel is given by

\[
T_{mc} = \left( \frac{L_p}{k_j} \right)^2 \int_{\xi = -\infty}^{\xi = \infty} F(z - \xi) \frac{dQ_A'''}{d\xi} d\xi
\]  

(6.22)

where \( \xi \) is a dummy variable for \( z \). If both types of changes in volumetric power deposition are present, the mixing-cup temperature elevation in the vessel is given by:

\[
T_{mc} = \left( \frac{L_p}{k_j} \right)^2 \sum_{i=1}^{n} Q_{Ai}''' F(z - \xi_i) + \left( \frac{L_p}{k_j} \right)^2 \int_{\xi = -\infty}^{\xi = \infty} F(z - \xi) \frac{dQ_A'''}{d\xi} d\xi
\]  

(6.23)

For a complete derivation of a similar equation based on the solution to the Graetz problem, consult Kays and Crawford (1980).

### 6.2.5 Specific Example

The accuracy of Equation (6.23) was demonstrated by comparing its predictions with data generated by NEKTON. The problem that was solved consists of a vessel that flows through tissue with a volumetric power deposition described by Equations (6.24) - (6.25).

\[
Q_A''' = 0 \quad \text{for}\quad z \leq 0 \quad \text{and}\quad z \geq 20 \text{ cm}
\]  

(6.24)

\[
Q_A''' = \frac{Q_A'''_{\text{max}}}{2} \left\{ 1 + \cos \left[ (z - 10) \frac{\pi}{10} \right] \right\} \quad \text{for}\quad 0 \text{ cm} \leq z \leq 20 \text{ cm}
\]  

(6.25)

This volumetric power deposition is sketched in Figure 6.12.
Figure 6.12: Volumetric power deposition described by Equations (6.24) - (6.25).

Substituting Equations (6.24) and (6.25) into Equation (6.23) yields:

\[
T_{mc} = \left( -\frac{Q_{A,\text{max}}}{20k_i} \right) \left( \frac{L_p^2\pi}{20k_i} \right) \int_{\xi = 0}^{\xi = 20} F(z - \xi) \sin \left( \frac{(\xi - 10)\pi}{10} \right) d\xi
\]  \hspace{1cm} (6.26)

Inserting the definition of \( F(z) \) into Equation (6.26) gives:

\[
T_{mc} = \left( -\frac{Q_{A,\text{max}}}{20k_i} \right) \left( \frac{L_p^2\pi}{20k_i} \right) \int_{\xi = 0}^{\xi = 20} C_1 \exp \left( \frac{z - \xi}{L_p} \right) \sin \left( \frac{(\xi - 10)\pi}{10} \right) d\xi
\]

for \( z \leq 0 \text{ cm} \)  \hspace{1cm} (6.27)
\[ T_{mc} = \left( \frac{-Q_{A \max}^m L_p^2 \pi}{20k_t} \right) \left\{ \int_{\xi = 0}^{\xi = z - \frac{0.15}{Br'}} \left[ 1 - \exp\left(-3.26Br_z - \xi\right) \right] \sin\left( (\xi - 10) \frac{\pi}{10} \right) \, d\xi + \right. \\
\left. \int_{\xi = z - \frac{0.15}{Br'}}^{\xi = z} \left[ \frac{C_2 - C_1}{C_2} \left[ 1 - \exp\left(-3.26Br_z - \xi\right) \right] + C_1 \right] \sin\left( (\xi - 10) \frac{\pi}{10} \right) \, d\xi + \right. \\
\left. \int_{\xi = z}^{\xi = 20} C_1 \exp\left(\frac{z - \xi}{L_p}\right) \sin\left( (\xi - 10) \frac{\pi}{10} \right) \, d\xi \right\} \\
\text{for } 0 \text{ cm} \leq z \leq 20 \text{ cm} \text{ and } \left( z - \frac{0.15}{Br'} \right) \geq 0 \text{ cm} \quad (6.28) \]

where, \( Br' \) is defined as:

\[ Br' = \left( \frac{1}{R} \left( \frac{R}{Re Pr(L_p)} \right) \right)^{3/8} \quad (6.29) \]

and has units of cm\(^{-1}\).

\[ T_{mc} = \left( \frac{-Q_{A \max}^m L_p^2 \pi}{20k_t} \right) \left\{ \int_{\xi = 0}^{\xi = z} \left[ \frac{C_2 - C_1}{C_2} \left[ 1 - \exp\left(-3.26Br_z - \xi\right) \right] + C_1 \right] \sin\left( (\xi - 10) \frac{\pi}{10} \right) \, d\xi + \right. \\
\left. \int_{\xi = z}^{\xi = 20} C_1 \exp\left(\frac{z - \xi}{L_p}\right) \sin\left( (\xi - 10) \frac{\pi}{10} \right) \, d\xi \right\} \\
\text{for } 0 \text{ cm} \leq z \leq 20 \text{ cm} \text{ and } \left( z - \frac{0.15}{Br'} \right) \leq 0 \text{ cm} \quad (6.30) \]
\[ T_{mc} = \left( -\frac{Q_{A}^{m} L_{p}^{2} \pi}{20 k_{t}} \right) \left\{ \begin{array}{l} \xi = z - \frac{0.15}{B r'} \\
\int_{\xi = 0}^{\xi = 20} \left[ 1 - \exp (-3.26 Br_{z-\xi}) \right] \sin \left[ (\xi - 10) \frac{\pi}{10} \right] d\xi + \\
\int_{\xi = 0}^{\xi = 20} \left[ \frac{C_{2} - C_{1}}{C_{2}} \left[ 1 - \exp (-3.26 Br_{z-\xi}) \right] + C_{1} \right] \sin \left[ (\xi - 10) \frac{\pi}{10} \right] d\xi, \end{array} \right. \]

for \( z \geq 20 \text{ cm} \) and \( 0 \text{ cm} \leq \left( z - \frac{0.15}{B r'} \right) \leq 20 \text{ cm} \) \hspace{1cm} (6.31)

\[ T_{mc} = \left( -\frac{Q_{A}^{m} L_{p}^{2} \pi}{20 k_{t}} \right) \left\{ \begin{array}{l} \xi = z - \frac{0.15}{B r'} \\
\int_{\xi = 0}^{\xi = 20} \left[ 1 - \exp (-3.26 Br_{z-\xi}) \right] \sin \left[ (\xi - 10) \frac{\pi}{10} \right] d\xi, \end{array} \right. \]

for \( z \geq 20 \text{ cm} \) and \( \left( z - \frac{0.15}{B r'} \right) \leq 0 \text{ cm} \) \hspace{1cm} (6.32)

\[ T_{mc} = \left( -\frac{Q_{A}^{m} L_{p}^{2} \pi}{20 k_{t}} \right) \left\{ \begin{array}{l} \xi = z - \frac{0.15}{B r'} \\
\int_{\xi = 0}^{\xi = 20} \left[ 1 - \exp (-3.26 Br_{z-\xi}) \right] \sin \left[ (\xi - 10) \frac{\pi}{10} \right] d\xi, \end{array} \right. \]

for \( z \geq 20 \text{ cm} \) and \( \left( z - \frac{0.15}{B r'} \right) \geq 20 \text{ cm} \) \hspace{1cm} (6.33)

Equations (6.27) - (6.33) are reduced in Appendix A.
6.2.6 Accuracy of Complete Empirical Relationship

Figures (6.9) - (6.13) compare Equations (6.27) - (6.33) with data generated by NEKTON.

![Graph showing Mixing-Cup Temperature Elevation vs Distance Along Axis of Vessel]

**Figure 6.13:** Comparison between Equations (6.27) - (6.33) and data generated with NEKTON. Perfusion in the tissue is 100 ml/100ml-min. $Q_A''''_{max} = 5.3333 \times 10^{-1}$ W/cm$^3$. $(T_{far-field})_{max} = 8$ °C. Diameter of the vessel is 1 mm. Average flow velocity is 1 cm/s (Torell and Nilsson, 1978). RMS difference for 109 points is 0.0524 °C.
Figure 6.14: Comparison between Equations (6.27) - (6.33) and data generated with NEKTON. Perfusion in the tissue is 5 ml/100ml-min. $Q_A''_{\text{max}} = 2.6667 \times 10^{-2}$ W/cm$^3$. $(T_{\text{far-field}})_{\text{max}} = 8^\circ$C. Diameter of the vessel is 1 mm. Average flow velocity is 1 cm/s (Torell and Nilsson, 1978). RMS difference for 109 points is 0.0380°C.
Figure 6.15: Comparison between Equations (6.27) - (6.33) and data generated with NEKTION. Perfusion in the tissue is 100 ml/100ml-min. $Q_A''''_{\text{max}} = 5.3333 \times 10^{-1}$ W/cm$^3$. $(T_{\text{far-field}})_{\text{max}} = 8$ °C. Diameter of the vessel is 3 mm. Average flow velocity is 2 cm/s (Torell and Nilsson, 1978). RMS difference for 101 points is 0.0410 °C.
Figure 6.16: Comparison between Equations (6.27) - (6.33) and data generated with NEKTON. Perfusion in the tissue is 5 ml/100ml-min. $Q_A^{'''}_{\text{max}} = 2.6667 \times 10^{-2}$ W/cm$^3$. $(T_{\text{far-field}})_{\text{max}} = 8$ °C. Diameter of the vessel is 3 mm. Average flow velocity is 2 cm/s (Torell and Nilsson, 1978). RMS difference for 109 points is 0.0343 °C.
Figure 6.17: Comparison between Equations (6.27) - (6.33) and data generated with NEKTON. Perfusion in the tissue is 25 ml/100ml-min. $Q_A^{\text{max}} = 1.0 \times 10^{-1}$ W/cm$^3$. $(T_{\text{far-field}})_{\text{max}} = 6$ °C. Diameter of the vessel is 5 mm. Average flow velocity is 26 cm/s (Ferguson and Roach, 1972). RMS difference for 97 points is 0.0073 °C.

6.3 Temperature in the Vicinity of Thermally-Significant Blood Vessels

This section describes how to use the information presented in Sections 6.1 and 6.2 to calculate temperature in the vicinity of thermally-significant blood vessels. First, the mixing-cup temperature of each thermally-significant vessel should be calculated with Equation (6.23). The change in tissue temperature caused by each vessel should then be determined with Equation (6.11). This temperature change field should be added to the temperature elevation field that is calculated assuming there are no thermally-significant vessels. As discussed in Section 5.7, the thermal effects of a particular vessel are only significant in
the region of tissue that is less than three perfusion lengths from the wall of the vessel. Therefore, the method described in this paragraph should only be invoked to calculate temperature at locations that are sufficiently close to a thermally-significant vessel.

The location, radius, and average flow velocity of all thermally-significant vessels must be determined before the blood vessel model described in this chapter can be used (see Chapter 7). The term “average flow velocity” refers to a cross-sectionally and temporally averaged velocity. The radius and average flow velocity of a vessel change along its axis. If the changes are gradual, axially averaged values may be inserted into the vessel model. If the changes are abrupt (i.e., at a bifurcation), the superposition illustrated in Figure 6.18 is suggested.

![Diagram of vessel properties](image)

**Figure 6.18:** Superposition of vessel properties used to represent a bifurcation.

In this superposition, \( R_4 \) and \( v_4 \) are chosen such that

\[
\frac{1}{R_3} \left( \frac{R_3}{3/8} \right) = \frac{1}{R_1} \left( \frac{R_1}{3/8} \right) + \frac{1}{R_2} \left( \frac{R_2}{3/8} \right) + \frac{1}{R_4} \left( \frac{R_4}{3/8} \right)
\]

(6.34)

This approach has not been tested.
Chapter 7

Determination of Blood Vessel Parameters
In order to use the BEM blood vessel model developed in Chapter 6, the location, diameter, and mass flow rate of all vessels being accounted for must be known. Several medical imaging techniques exist that are capable of determining the location and cross-sectional geometry of blood vessels in biological tissue. A few of these methods are: x-ray angiography, computerized tomography (CT), ultrasound, and magnetic resonance imaging (MRI). Ultrasound and MRI possess the additional ability to determine flow velocity. If cross-sectional geometry and flow velocity are known, mass flow rate can be calculated with Equation (7.1).

\[ \dot{m} = \int_A \rho_{bl} \left( \hat{v} \cdot \hat{n} \right) dA \]  

(7.1)

In this equation, \( \rho_{bl} \) is the density of blood, \( \hat{v} \) is the vector velocity of blood flow, and \( \hat{n} \) is a unit vector normal to the differential area, \( dA \). This chapter describes the various medical imaging techniques and discusses their limitations.

7.1 X-Ray Angiography
X-ray angiography utilizes a radio-opaque dye and x-rays to produce a 2-D image of blood vessels on an x-ray film. The first step in x-ray angiography is to inject the radio-opaque dye into the large vessels that carry blood to the tissue volume of interest. After a time period that is sufficient for the dye to flow into all of the vessels in the volume, an x-ray of the volume is taken. Because x-rays are unable to pass through the dye, vessels carrying the dye appear as clear images on the developed x-ray films.

The greatest problem with x-ray angiography is that it only produces a two-dimensional representation of the vasculature. Although some three-dimensional information
can be obtained by x-raying the tissue volume from different angles, human interpretation and analysis is required to convert the films into a three-dimensional image. Interpreting the developed films is often difficult since vessels that cross each other at different depths in the tissue appear to intersect each other in the same plane. The fact that bones and highly perfused tissue are opaque to x-rays adds to this problem. Bones are always opaque to x-rays because they are dense. Highly perfused tissue, like that found in the kidney, is opaque to x-rays when the blood that it is perfused with contains the radio-opaque dye. Figure 7.1 displays an example of how the presence of highly perfused tissue and bones can limit information obtained from x-ray angiography.

Figure 7.1: The presence of bones and highly perfused tissue can limit information obtained from x-ray angiography: (a) fictitious tissue volume, (b) resulting x-ray angiogram.

Valk, et al. (1985) reproduced an actual x-ray angiogram that exhibits this problem. This angiogram shows a bladder that is full of radio-opaque dye that has been filtered from the blood by the kidneys. Because the bladder contains radio-opaque dye, the blood vessels behind it and in front of it do not show up on the angiogram.
Using x-ray angiography to image vessels possesses several other drawbacks. One problem is that the radio-opaque dye only stays inside the tissue volume for a limited amount of time. Consequently, if the x-rays are taken too long after the dye has been injected, the presence of vessels will not be accurately detected. X-raying a tissue volume at different time intervals and monitoring the time required to clear the dye from different regions provides qualitative information about perfusion and blood vessel flow rates. X-ray angiography does not, however, provide any quantitative information about perfusion or vessel flow rates. Another drawback associated with x-ray angiography is that the time required to develop and analyze the x-ray films prohibits imaging vessels in real-time. A further problem with x-ray angiography is that it exposes the patient to radiation. This is a concern since most hyperthermia patients also receive radiation treatment.

7.2 Computerized Tomography (CT)
Computerized tomography is used to create two-dimensional images that represent parallel planes of tissue. The two-dimensional images are created by x-raying the tissue from all directions in a single plane. These two-dimensional images can be combined to create three-dimensional output. As with x-ray angiography, CT can be used to locate blood vessels if the vessels are injected with a radio-opaque dye prior to CT scanning. The big advantage that CT has over x-ray angiography is that CT output is not distorted by overlapping tissues. Although CT is capable of adequately locating vessels in a tissue volume, it does not provide any quantitative information concerning blood flow velocities.

7.3 Ultrasound
Ultrasound can be used to non-invasively determine the density field inside tissue. This is important for locating organ boundaries and interfaces between different tissue types. Ultrasound systems measure tissue density by insonating the tissue and measuring the
intensity of the reflected ultrasound. The intensity of the reflected signal is used to determine the density of the reflecting tissue, while the time delay between sending and receiving the signal is used to calculate the distance of the reflecting tissue from the receiver. Although a contrast agent can be injected into the tissue to improve ultrasound measuring capabilities, its presence is not required as it is in x-ray angiography. Unlike x-ray angiography, ultrasound output is not distorted by overlapping tissues.

In addition to possessing the ability to identify different tissue types, ultrasound systems can be used to locate blood vessels and quantitatively measure blood flow velocity. Ultrasound can be used to measure flow velocity because it is a pressure wave. The frequency of a pressure wave exhibits a doppler shift when it is reflected by a moving surface. In the case of blood flow, the moving surfaces that reflect the ultrasound waves are tightly packed clusters of erythrocytes (red blood cells) (Wells, 1994)\(^1\). The velocity of blood, \(v_b\), is related to the doppler shift in frequency by

\[
v_b = \frac{c}{2f_1} (f_{rec} - f_1)
\]

(7.2)

Where \(f_1\) is the primary frequency of the transmitted waves, \(f_{rec}\) is the primary frequency of the reflected waves, and \(c\) is the speed of sound inside the tissue (Wells, 1994). The primary frequency of the reflected waves must be determined by performing spectral analysis. Sketches of frequency spectrums for typical transmitted and received signals are displayed in Figure 7.2.

\---

1. Individual erythrocytes do not reflect an appreciable amount of ultrasound because their characteristic length dimensions are two orders of magnitude smaller than the wavelength of typical ultrasound waves. An erythrocyte is a biconcave disk with a diameter of approximately 8 µm and a thickness of around 2 µm. A typical ultrasound wave possesses a frequency of 3 MHz and has a wavelength of 0.5 mm in blood (Wells, 1994).
Figure 7.2: Frequency spectrum for (a) transmitted signal, (b) reflected signal for blood flowing away from the receiver, and (c) reflected signal for blood flowing toward the receiver.

This figure shows that if the red blood cells are moving away from the receiver, the frequency of the reflected waves is decreased. On the other hand, if the red blood cells are moving toward the receiver, the frequency is increased.

Ultrasound systems possess one minor problem when used to measure flow velocities. The doppler shift in frequency only provides information about the component of the flow velocity in the direction of the receiver. As a result, the net direction of the flow must be discerned before the mass flow rate in the vessel can be calculated. Wells (1994) describes systems in which the net direction of the flow is determined by either transmitting or receiving the ultrasound signal from two different directions.

Several ultrasound systems exist that are capable of producing two-dimensional, color images of tissue density and flow speed in real-time (Weils, 1994). These images represent planes of tissue that are perpendicular to the ultrasound transmitter. One typical ultrasound visualization system produces images consisting of 800 velocity vectors at a rate of 25 images per second (Wells, 1994). Although the output of typical ultrasound systems repre-
resents a single plane of tissue, Wells (1994) describes a system that creates color, three-dimensional output by combining two-dimensional images that represent parallel planes of tissue. This system produces images that represent 33 planes of tissue that are spaced in 5 mm intervals. Wells is unclear whether this, or any ultrasound system currently being used, is capable of generating three-dimensional output in real-time. The literature search performed while creating this document did not reveal the existence of any ultrasound systems capable of real-time, three-dimensional, flow velocity measurement. Examples of two-dimensional and three-dimensional color output from several ultrasound systems can be found in Wells (1994) and van der Woude, et al. (1994).

In addition to quantitatively measuring flow velocities, ultrasound systems can be used to qualitatively measure perfusion. Unlike vessel blood flow, perfusion in a small (but macroscopic) volume of tissue occurs nearly equally in all directions. Although there are exceptions, this generalization adequately characterizes perfusion in most regions of the human body. Sketches of typical transmitted and received ultrasound signals in perfused tissue are displayed in Figure 7.3.

![Figure 7.3](image)

**Figure 7.3:** (a) Frequency spectrum of transmitted signal, (b) frequency spectrum of received signal in tissue with low perfusion (c) frequency spectrum of received signal in tissue with high perfusion.
This figure shows that the frequency spectrum of the received signal is shorter and wider than the frequency spectrum of the transmitted signal, but possesses the same primary frequency. The two frequency spectrums possess the same primary frequency because the average velocity of the blood flowing in the tissue is zero. The average velocity is zero because the blood is flowing equally in all directions. The width of the frequency spectrum of the received signal is proportional to the perfusion level. By comparing the widths of the frequency spectrums of signals received from different regions of the tissue, perfusion level can be qualitatively discerned. This qualitative information can help clinicians decide where to place perfusion measurement probes during hyperthermia treatment, and provide information concerning the volume of tissue in which a perfusion measurement probe characterizes perfusion level.

7.4 Magnetic Resonance Imaging

MRI, like ultrasound, is capable of locating blood vessels and measuring their flow velocities. MRI uses a magnetic field to produce two-dimensional images of the tissue at different depths in the scanned volume. In these images, tissues possessing different properties appear as different shades of gray. If desired, these shades of gray can be automatically color coded. As with ultrasound, several two-dimensional MRI images can be combined to create three-dimensional output. Unlike x-ray angiography, MRI output is not distorted by overlapping tissues.

MRI can be used to measure flow velocities because spatial velocity and acceleration gradients inside the scanned tissue affect the received MRI signal. Blood flow in vessels always exhibits a cross-sectional velocity gradient. An idealized example of a velocity profile inside a blood vessel is sketched in Figure 7.4.
Figure 7.4: Parabolic velocity profile for fully-developed, laminar flow in a blood vessel. The shape of this profile is approximate since it assumes that blood is a Newtonian fluid.

Fortunately, the velocity gradient inside a blood vessel is steepest at the vessel wall. This fact helps MRI accurately determine the locations of vessel boundaries. Once the velocity gradient at several locations in a cross-section of a blood vessel has been measured with MRI, flow velocity can be calculated through numeric integration.

One problem with using MRI to determine the locations and flow velocities of blood vessels occurs because flow in some vessels is pulsatile. This is especially true for arteries. In a typical human ascending aorta, for example, velocity drops from peak of 63 cm/second (Whitmore, 1968) in midsystole to nearly zero cm/second in late diastole. Because MRI requires a velocity gradient to detect vessels, an MRI snapshot taken during late diastole may not detect the presence of important vessels. Von Schultess and Higgins (1985) display several examples of this problem. This problem can be avoided by not relying on one MRI snapshot to characterize a plane of tissue. Instead, two or three MRI snapshots should be taken within a single cardiac cycle.
MRI output can be displayed in several ways. Flow velocity can be displayed on a three-dimensional image of the tissue by using a color code. Alternately, MRI data can be displayed as a two-dimensional picture of the tissue with distance perpendicular to the image plane, cross-sectional area of blood vessels, or flow velocity color coded. Valk et al. (1985) and Hale et al. (1985) show some examples of ways in which MRI data can be displayed.

Although MRI is the most accurate method discussed in this chapter for locating vessels and measuring their flow velocities, it is not practical for real-time use during hyperthermia treatment. One typical MRI system is capable of producing 40 black and white, two-dimensional images in 17 minutes (Hale et al., 1985). In this system, each image plane pixel represents 1.7 x 1.7 mm to 2.0 x 2.0 mm of tissue, and the distance between adjacent image planes is 2 mm. Analysis of the images and color coding requires additional time. Even if MRI systems were capable of creating color images in real-time, they could not be used during hyperthermia treatment. This results from the fact that strong magnetic fields inside the MRI scanning cylinder prohibit the presence of metal objects. Since all hyperthermia power applicators in current use contain metal, hyperthermia and MRI cannot be conducted simultaneously.

7.5 Creation of a 3-D Vascular Tree from 2-D Image Planes
Vessel data must be three-dimensional to be useful. CT, ultrasound, and MRI generate finitely-spaced, two-dimensional image planes. Three-dimensional data created from finitely-spaced image planes is sometimes inaccurate. A three-dimensional vascular tree is constructed from image planes by connecting the vessel images on adjacent planes. In accomplishing this task, the shape of each vessel image is used to help find the corresponding image on the adjacent plane. This is done by trying to estimate the angle at which each vessel crosses each image plane. Figure 7.5 is a sketch that illustrates how the
shape of a vessel image on a plane is related to the angle at which the vessel crosses the plane.

**Figure 7.5:** The shape of a vessel image on an image plane is related to the angle at which the vessel crosses the image plane.

The minimum vessel size that can be detected with CT, ultrasound, and MRI depends on the area of tissue that each image plane pixel represents and the distance between adjacent image planes. Vessels with cross-sectional areas smaller than the area of tissue that an image plane pixel represents will not be detected. In addition, vessels that are oriented parallel to the image planes and possess diameters smaller than the plane spacing may not be detected. An example of this is sketched in Figure 7.6.
Figure 7.6: Image plane spacing is too large to keep track of some vessels.

7.6 Recommendation
Although MRI is the most accurate method considered in this document for locating blood vessels and measuring their flow velocities, it is expensive and cannot be used during treatment. Therefore, MRI should be conducted only before each patient’s first hyperthermia treatment to get an initial assessment of his/her vasculature and anatomy. If MRI is used this way, it will be a valuable and economical tool for treatment planning.

The diameter and blood flow rate of vessels vary during a hyperthermia treatment. Initially, vessels dilate as the body tries to cool the heated tissue by increasing blood flow to the region. If the treatment lasts long enough, tissue damage and blood coagulation will cause blood flow to decrease and vessels to collapse. Vessel size and flow velocity should be monitored in real-time during treatment to help clinicians make proper treatment delivery decisions. Real-time monitoring should be conducted with an ultrasound system. This ultrasound system should also be used to monitor relative perfusion during the treatment.
Chapter 8

Recommendations for Further Work

Several actions should be conducted to continue the work presented in this document. The effects of pulsatile flow, non-Newtonian behavior of blood, and power deposition inside the vessel should be quantified. This can be accomplished by performing numerical simulations with NEKTON. In situations where these effects are significant, the vessel model presented in Chapter 6 should be appended with appropriate correction factors. Next, the Basis Element Method computer code should be modified so that it includes the vessel model. After the computer code is modified, a series of validations are required. Initial validations should be conducted with NEKTON. Temperature fields generated with the modified Basis Element Method and NEKTON should be compared for increasingly complex vascular geometries. These vascular geometries should include: straight vessels with axially invariant flow rates, curved vessels with axially invariant flow rates, vessels with axially varying radii and flow rates, vessels that are thermally close to other vessels, and branching vessels. After completing the numerical validations, the accuracy of the modified Basis Element Method should be experimentally tested. This can be accomplished with a modified version of the porcine experiments described in Martin (1995). As a final task, the trade-off between improved temperature field accuracy and increased computational effort should be quantified.

---

1. In the human circulatory system, the radius and flow rate of an artery gradually decrease in the direction of flow as blood is distributed to small vessels that branch off of the primary vessel. Conversely, the radius and flow rate of a vein gradually increase in the direction of flow as blood is collected from small vessels that join the primary vessel.
Appendix A

Reduction of Equations (6.27) - (6.33)
The integrals in Equations (6.27) - (6.32) can be grouped into two categories. These categories are represented by Equations (A.1) and (A.2).

\[
\int_{\xi_1}^{\xi_2} A \sin \left( (\xi - 10) \frac{\pi}{10} \right) d\xi
\]  
(A.1)

\[
\int_{\xi_1}^{\xi_2} A \exp \left[ B (z - \xi) \right] \sin \left[ (\xi - 10) \frac{\pi}{10} \right] d\xi
\]  
(A.2)

In these equations, \( A \) and \( B \) are arbitrary constants. The solution to Equation (A.1) is:

\[
\int_{\xi_1}^{\xi_2} A \sin \left( (\xi - 10) \frac{\pi}{10} \right) d\xi = \frac{-10A}{\pi} \left\{ \cos \left( (\xi_2 - 10) \frac{\pi}{10} \right) - \cos \left( (\xi_1 - 10) \frac{\pi}{10} \right) \right\}
\]  
(A.3)

The solution to Equation (A.2) can be obtained with the help of the following identity (Gradshteyn and Ryzhik, 1965):

\[
\int e^{ax} \sin (bx) \, dx = \frac{e^{ax} (asinx - bcosx)}{a^2 + b^2}
\]  
(A.4)

Applying Equation (A.4) to Equation (A.2) yields the following:

\[
\int_{\xi_1}^{\xi_2} A \exp \left[ B (z - \xi) \right] \sin \left[ (\xi - 10) \frac{\pi}{10} \right] d\xi =
\]

\[
\frac{A \exp \left[ -B (\xi_2 - z) \right]}{B^2 + \left( \frac{\pi}{10} \right)^2} \left\{ -B \sin \left[ (\xi_2 - 10) \frac{\pi}{10} \right] - \frac{\pi}{10} \cos \left[ (\xi_2 - 10) \frac{\pi}{10} \right] \right\} -
\]

\[
\frac{A \exp \left[ -B (\xi_1 - z) \right]}{B^2 + \left( \frac{\pi}{10} \right)^2} \left\{ -B \sin \left[ (\xi_1 - 10) \frac{\pi}{10} \right] - \frac{\pi}{10} \cos \left[ (\xi_1 - 10) \frac{\pi}{10} \right] \right\}
\]  
(A.5)
Using Equations (A.3) and (A.5), Equations (6.27) - (6.32) are reduced to:

\[
T_{mc} = \left( \frac{-Q_{A_{\text{max}}} L_p^2 n}{20 k_f} \right) \left( \frac{\pi}{10} \right)^3 \left[ \exp \left( \frac{z - 20}{L_p} \right) \right] \left[ \frac{1}{L_p^2} + \left( \frac{\pi}{10} \right)^2 \right] - \left[ \exp \left( \frac{z}{L_p} \right) \right] \left[ \frac{1}{L_p^2} + \left( \frac{\pi}{10} \right)^2 \right]
\]

for \( z \leq 0 \) cm \hspace{1cm} (A.6)
\[ T_{nc} = \left( \frac{Q_{A_{max}}^m L_p^2 \pi}{20k_t} \right) \left( \frac{10}{\pi} \right) \left\{ \cos \left[ \left( z - \frac{0.15}{Br} - 10 \right) \frac{\pi}{10} \right] + 1 \right\} + \]

\[ \left( \frac{Q_{A_{max}}^m L_p^2 \pi}{20k_t} \right) \left( \frac{C_2 - C_1}{C_2} + C_1 \right) \left( \frac{10}{\pi} \right) \left\{ \cos \left[ \left( z - 10 \right) \frac{\pi}{10} \right] - \cos \left[ \left( z - \frac{0.15}{Br} - 10 \right) \frac{\pi}{10} \right] \right\} + \]

\[ \left( \frac{Q_{A_{max}}^m L_p^2 \pi}{20k_t} \right) \exp \left[ -3.26 \left( \frac{0.15}{10} \right) \right] \left( \frac{\pi}{10} \right) \left\{ \frac{3.26Br}{(3.26Br)^2 + \left( \frac{\pi}{10} \right)^2} \right\} \left\{ 3.26Br \sin \left[ \left( z - \frac{0.15}{Br} - 10 \right) \frac{\pi}{10} \right] - \pi \right\} + \]

\[ \pi \cos \left[ \left( z - \frac{0.15}{Br} - 10 \right) \frac{\pi}{10} \right] \left\{ \frac{Q_{A_{max}}^m L_p^2 \pi}{20k_t} \right\} \left( \frac{\pi}{10} \right) \left\{ \frac{3.26Br}{(3.26Br)^2 + \left( \frac{\pi}{10} \right)^2} \right\} \left\{ \frac{\pi}{10} \right\} + \]

\[ \left( \frac{Q_{A_{max}}^m L_p^2 \pi}{20k_t} \right) \left( \frac{C_2 - C_1}{C_2} \right) \left[ \frac{1}{(3.26Br)^2 + \left( \frac{\pi}{10} \right)^2} \right] \left\{ 3.26Br \sin \left[ \left( z - 10 \right) \frac{\pi}{10} \right] - \pi \cos \left[ \left( z - 10 \right) \frac{\pi}{10} \right] \right\} - \]

\[ \left( \frac{Q_{A_{max}}^m L_p^2 \pi}{20k_t} \right) \left( \frac{C_2 - C_1}{C_2} \right) \left[ \frac{\exp \left[ -3.26 \left( \frac{0.15}{10} \right) \right]}{(3.26Br)^2 + \left( \frac{\pi}{10} \right)^2} \right] \left\{ 3.26Br \sin \left[ \left( z - \frac{0.15}{Br} - 10 \right) \frac{\pi}{10} \right] - \pi \cos \left[ \left( z - 10 \right) \frac{\pi}{10} \right] \right\} - \]

\[ \frac{\pi}{10} \cos \left[ \left( z - \frac{0.15}{Br} - 10 \right) \frac{\pi}{10} \right] + \left( \frac{-Q_{A_{max}}^m L_p^2 \pi}{20k_t} \right) \left( \frac{\pi}{10} \right) C_1 \left[ \frac{\exp \left( \frac{z - 20}{L_p} \right)}{\left( \frac{1}{L_p} \right)^2 + \left( \frac{\pi}{10} \right)^2} \right] - \]

\[ \left( \frac{-Q_{A_{max}}^m L_p^2 \pi}{20k_t} \right) C_1 \left[ \frac{1}{\left( \frac{1}{L_p} \right)^2 + \left( \frac{\pi}{10} \right)^2} \right] \left\{ \frac{-1}{L_p} \sin \left[ \left( z - 10 \right) \frac{\pi}{10} \right] - \pi \cos \left[ \left( z - 10 \right) \frac{\pi}{10} \right] \right\} \]

for \( 0 \text{ cm} \leq z \leq 20 \text{ cm} \) and \( \left( z - \frac{0.15}{Br} \right) \geq 0 \text{ cm} \)

(A.7)
\[ T_{mc} = \left( \frac{Q_A^{\prime \prime \prime}}{20k_t} \right) \left( \frac{L_p^2 \pi}{C_2 - C_1} \right) \left( \frac{C_2 - C_1}{C_2} + C_1 \right) \left( \frac{10}{\pi} \right) \{ \cos \left[ (z - 10) \frac{\pi}{10} \right] + 1 \} + \]

\[ \left( \frac{Q_A^{\prime \prime \prime}}{20k_t} \right) \left( \frac{L_p^2 \pi}{C_2} \right) \left( \frac{1}{(3.26Br)^2 + \left( \frac{\pi}{10} \right)^2} \right) \{ 3.26Br \sin \left[ (z - 10) \frac{\pi}{10} \right] - \frac{\pi}{10} \cos \left[ (z - 10) \frac{\pi}{10} \right] \} - \]

\[ \left( \frac{Q_A^{\prime \prime \prime}}{20k_t} \right) \left( \frac{L_p^2 \pi}{C_2} \right) \left[ \exp \left( -3.26Br_z \right) \right] \left( \frac{\pi}{10} \right) + \left( \frac{-Q_A^{\prime \prime \prime}}{20k_t} \right) \left( \frac{L_p^2 \pi}{10} \right) \left( \frac{\pi}{10} \right) \left( \frac{1}{L_p^2 + \left( \frac{\pi}{10} \right)^2} \right) \}

\[ \left( \frac{-Q_A^{\prime \prime \prime}}{20k_t} \right) \left( \frac{L_p^2 \pi}{C_1} \right) \left[ \frac{1}{L_p^2 + \left( \frac{\pi}{10} \right)^2} \right] \left\{ -\frac{1}{L_p} \sin \left[ (z - 10) \frac{\pi}{10} \right] - \frac{\pi}{10} \cos \left[ (z - 10) \frac{\pi}{10} \right] \right\} \]

for \( 0 \text{ cm} \leq z \leq 20 \text{ cm} \) \quad \text{and} \quad \left( z - \frac{0.15}{Br} \right) \leq 0 \text{ cm}

\text{(A.8)}
\[ T_{mc} = \left( \frac{Q_{\text{max}}}{20k_t} \right) \left( L_r^2 \pi \right) \left( \frac{10}{\pi} \right) \left\{ \cos \left[ \left( z - \frac{0.15}{Br'} - 10 \right) \frac{\pi}{10} \right] + 1 \right\} + \]

\[ \left( \frac{Q_{\text{max}}}{20k_t} \right) \left( L_r^2 \pi \right) \left( C_2 - C_1 \right) \left( \frac{10}{\pi} \right) \left[ \cos \left[ \left( z - \frac{0.15}{Br'} - 10 \right) \frac{\pi}{10} \right] + \exp \left[ -3.26 \left( 0.15 \right) \frac{\pi}{10} \right] \left[ 3.26Br' \sin \left[ \left( z - \frac{0.15}{Br'} - 10 \right) \frac{\pi}{10} \right] \right] \right. \]

\[ \left. \frac{\pi}{10} \cos \left[ \left( z - \frac{0.15}{Br'} - 10 \right) \frac{\pi}{10} \right] \right\} - \left( \frac{Q_{\text{max}}}{20k_t} \right) \left( L_r^2 \pi \right) \left( C_2 - C_1 \right) \left( \frac{10}{\pi} \right) \left[ \frac{\exp \left[ -3.26Br' \right]}{(3.26Br')^2 + \left( \frac{\pi}{10} \right)^2} \left( \frac{\pi}{10} \right) - \exp \left[ -3.26Br'z_{-20} \right] \right. \]

\[ \left. \frac{\pi}{10} \cos \left[ \left( z - \frac{0.15}{Br'} - 10 \right) \frac{\pi}{10} \right] \right\} - \left( \frac{Q_{\text{max}}}{20k_t} \right) \left( L_r^2 \pi \right) \left( C_2 - C_1 \right) \left( \frac{10}{\pi} \right) \left[ \exp \left[ -3.26 \left( 0.15 \right) \frac{\pi}{10} \right] \left[ 3.26Br' \sin \left[ \left( z - \frac{0.15}{Br'} - 10 \right) \frac{\pi}{10} \right] \right] \right. \]

\[ \left. \frac{\pi}{10} \cos \left[ \left( z - \frac{0.15}{Br'} - 10 \right) \frac{\pi}{10} \right] \right\} \]

for \( z \geq 20 \text{ cm} \) and \( 0 \text{ cm} \leq \left( z - \frac{0.15}{Br'} \right) \leq 20 \text{ cm} \)  

(A.9)

\[ T_{mc} = \left( \frac{Q_{\text{max}}}{20k_t} \right) \left( L_r^2 \pi \right) \left( C_2 - C_1 \right) \left( \frac{10}{\pi} \right) \left[ \frac{\exp \left[ -3.26Br'z_{-20} \right] - \exp \left[ -3.26Br' \right]}{(3.26Br')^2 + \left( \frac{\pi}{10} \right)^2} \right] \left( \frac{\pi}{10} \right) \]

for \( z \geq 20 \text{ cm} \) and \( \left( z - \frac{0.15}{Br'} \right) \leq 0 \text{ cm} \)  

(A.10)
\[
T_{mc} = \left( \frac{Q_{A_{\text{max}}}}{20k_t} \right)^2 \left[ \frac{\exp(-3.26Br_z - 20) - \exp(-3.26Br_z)}{(3.26Br')^2 + \left( \frac{\pi}{10} \right)^2} \right] \left( \frac{\pi}{10} \right)
\]

for \( z \geq 20 \text{ cm} \) and \( \left( z - \frac{0.15}{Br'} \right) \geq 20 \text{ cm} \)

(A.11)
References


THESIS PROCESSING SLIP

FIXED FIELD

ill ________________ name ____________

index ________________ biblio ________________

▶ COPIES

Archives  Aero  Dewey  Eng  Hum

Lindgren  Music  Rotch  Science

TITLE VARIES  □  ____________________________

NAME VARIES:  □  ____________________________

IMPRINT:  (COPYRIGHT) ____________________________

▶ COLLATION:  107p

▶ ADD. DEGREE:  ____________  ▶ DEPT.:  ____________________________

SUPERVISORS:  ____________________________

__________________________  ____________________________

__________________________  ____________________________

__________________________  ____________________________

__________________________  ____________________________

__________________________

NOTES:

cat'r:  ____________________________  date:  ____________________________

▶ DEPT:  M.E.  ▶ YEAR:  1997  ▶ DEGREE:  M.S.

▶ NAME:  BREEDLOVE, Jeffrey Jay