HIP FRACTURE RISK PREDICTIONS BY X-RAY COMPUTED TOMOGRAPHY

by

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Abstract

Fractures of the proximal femur represent a national health problem of crisis proportions. More than 250,000 hip fractures occur annually, resulting in costs in excess of 7 billion dollars per year. While there is growing evidence that certain therapeutic measures such as estrogen replacement can help retard bone loss and thus reduce hip fracture incidence, some treatment modalities are themselves associated with significant risks. It becomes increasingly important, therefore, to identify only those patients at greatest risk of fracture so that appropriate therapy can be instituted. New diagnostic imaging modalities such as quantitative computed tomography (QCT) could be employed for this purpose if appropriate tissue characterization procedures and fracture risk predictors are developed. Hence, the objective of this research was to investigate the mechanisms of proximal femur fracture through the use of QCT coupled with the finite element method of structural analysis, from which verified biomechanical predictors of hip fracture risk could be developed. To address this goal, it was initially imperative to study the material properties of both the trabecular and cortical bone within the proximal femur and to develop QCT based characterization techniques. Thus, four pairs of fresh human proximal femora were imaged with a conventional CT scanner from which fifty cylindrical trabecular bone specimens were fabricated and tested in compression. It was demonstrated that bone density ($R^2 = 0.73$), elastic modulus ($R^2 = 0.89$) and compressive strength ($R^2 = 0.89$) could be determined accurately and noninvasively by using single-energy QCT. In addition, the material properties of the metaphyseal shell were investigated through the use of three-point bending tests with 150 prismatic plate specimens. Both the elastic modulus and tensile strength were shown to be reduced from that measured within the femoral diaphysis by 33 and 21 percent respectively. Though the majority of this reduction could be attributed to density, architectural differences were also implied by the observed decrease in the ratio of longitudinal to transverse moduli (2.1 diaphyseal, 1.8 metaphyseal) and strength (2.7 diaphyseal, 2.0 metaphyseal). Structural analysis was subsequently performed on two intact femora using the displacement based finite element method. Three-dimensional, linear and nonlinear finite element models were noninvasively generated for the intact bones by using geometry and material property data obtained from QCT images and the appropriate QCT-material property regressions derived previously. Each bone was then instrumented with strain gages and tested to failure in one of either two loading configurations: a simplified one-legged stance or fall. For both loading conditions, the
maximum calculated von Mises effective strain from the linear analysis was predictive of in-vitro bone failure to within 8 percent. The results of the nonlinear analyses also exhibited excellent agreement with the in-vitro fracture location and failure load, but in addition provided insight into the fracture process by demonstrating internal trabecular failure and subsequent load transferal to the metaphyseal shell just prior to structural collapse. During one-legged stance, the critical failure strains were developed within the primary tensile trabeculae at the subcapital region of the femoral neck. In contrast, for the simulated fall, critical failure strains were observed within the intertrochanteric region, suggesting that QCT measurements at this sight would be a sensitive predictor of intact bone strength during falls. To verify this hypothesis, 12 intact human femora were scanned by QCT and subsequently tested to failure under the simulated fall conditions. A highly significant positive linear correlation was observed between the load at bone failure and the product of the average trabecular bone QCT value and total bone cross-sectional area as measured from a QCT image made through the intertrochanteric region ($R^2=0.93$). Similarly good correlation was observed when using average intertrochanteric trabecular QCT data alone ($R^2=0.89$). In conclusion, these results demonstrate that intact bone failure can be accurately modeled using the finite element method and that for the particular fall loading configuration studied, intact bone strength can be predicted noninvasively with high accuracy using QCT.

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# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstract</td>
<td>2</td>
</tr>
<tr>
<td>Acknowledgements</td>
<td>4</td>
</tr>
<tr>
<td>Contents</td>
<td>6</td>
</tr>
<tr>
<td>1.0 Introduction</td>
<td>8</td>
</tr>
<tr>
<td>1.1 Hip Fracture Risk Factors</td>
<td>9</td>
</tr>
<tr>
<td>1.1.1 Osteomalacia</td>
<td>9</td>
</tr>
<tr>
<td>1.1.2 Osteoporosis</td>
<td>11</td>
</tr>
<tr>
<td>1.1.3 Gender</td>
<td>13</td>
</tr>
<tr>
<td>1.1.4 Calcium and Vitamin D</td>
<td>15</td>
</tr>
<tr>
<td>1.1.5 Age</td>
<td>19</td>
</tr>
<tr>
<td>1.1.6 Race and Geography</td>
<td>21</td>
</tr>
<tr>
<td>1.1.7 Trauma</td>
<td>23</td>
</tr>
<tr>
<td>1.2 Fracture Classification</td>
<td>26</td>
</tr>
<tr>
<td>1.2.1 Femoral Neck Fractures</td>
<td>26</td>
</tr>
<tr>
<td>1.2.2 Intertrochanteric Fractures</td>
<td>29</td>
</tr>
<tr>
<td>1.3 Mechanism of Injury</td>
<td>33</td>
</tr>
<tr>
<td>1.3.1 Epidemiologic Studies</td>
<td>33</td>
</tr>
<tr>
<td>1.3.2 Experimental Studies</td>
<td>36</td>
</tr>
<tr>
<td>1.4 Fracture Prediction Methods</td>
<td>42</td>
</tr>
<tr>
<td>1.4.1 Photon Absorptiometry</td>
<td>42</td>
</tr>
<tr>
<td>1.4.2 Compton Scattering</td>
<td>47</td>
</tr>
<tr>
<td>1.4.3 Singh Index</td>
<td>48</td>
</tr>
<tr>
<td>1.4.4 Photodensitometry</td>
<td>50</td>
</tr>
<tr>
<td>1.4.5 Radiogrammetry</td>
<td>51</td>
</tr>
<tr>
<td>1.4.6 Computed Tomography</td>
<td>54</td>
</tr>
<tr>
<td>1.5 Osteoporosis Therapy</td>
<td>62</td>
</tr>
<tr>
<td>1.5.1 Vitamin D</td>
<td>62</td>
</tr>
<tr>
<td>1.5.2 Calcium</td>
<td>63</td>
</tr>
<tr>
<td>1.5.3 Fluoride</td>
<td>65</td>
</tr>
<tr>
<td>1.5.4 Estrogen</td>
<td>67</td>
</tr>
<tr>
<td>1.5.5 Calcitonin</td>
<td>69</td>
</tr>
<tr>
<td>1.5.6 Exercise</td>
<td>70</td>
</tr>
<tr>
<td>1.6 Mechanical Properties of Bone</td>
<td>72</td>
</tr>
<tr>
<td>1.6.1 Cortical Bone</td>
<td>72</td>
</tr>
<tr>
<td>1.6.2 Trabecular Bone</td>
<td>83</td>
</tr>
<tr>
<td>1.7 Loads on the Proximal Femur</td>
<td>93</td>
</tr>
<tr>
<td>1.7.1 Two-legged Stance</td>
<td>94</td>
</tr>
<tr>
<td>1.7.2 One-legged Stance</td>
<td>94</td>
</tr>
<tr>
<td>1.7.3 Dynamic Analysis</td>
<td>96</td>
</tr>
<tr>
<td>1.7.4 Falls</td>
<td>99</td>
</tr>
</tbody>
</table>
1.0 Introduction

Hip fractures represent a major proportion of the afflictions leading to morbidity and mortality among the elderly. The United States, with one of the highest fracture rates worldwide, has in excess of 225,000 cases per year. These high rates signify a major burden on today's health care resources. With an average hospital stay of twenty days, the annual direct cost is approximately one billion dollars. When including outpatient care, medication, visiting nurses and lost earnings, this total cost exceeds 7 billion dollars per year (Holbrook, 1984; Owen et al., 1980).

In addition to being a common event, the average patient age and numerous potential complications leads to significant mortality. It has been estimated that one third of all deaths which are attributable to accidents involve hip fractures (US Department of Health, 1978). When put in terms of the number of fracture patients, these figures suggest that 19% of patients with hip fracture die within the year as a result of the fracture itself (Adelson and Dseasohn, 1964; Miller, 1978).

To begin to understand the etiology of hip fracture, it is necessary to become familiar with many issues. This section presents a general review of data presented in the literature regarding the current concepts of risk assessment, mechanisms of injury and modes of therapy. In addition, a discussion on the current understanding of the material properties bone and femoral loading is included.
1.1 Hip Fracture Risk Factors

In an attempt to improve treatment and prevention of proximal femur fracture, many investigators have sought to find common risk factors among fracture groups. Investigations currently concentrate on those conditions known to influence the quantity and quality of bone such as osteoporosis and osteomalacia, as well as those associated with an increased propensity for trauma. Some of the major variables currently thought to influence the magnitude of osteopenia and hence fracture risk are, gender, serum calcium and vitamin D, age, or race. While no one factor is suspected of acting alone, the interaction of several agents most likely contributes to the patients demise. The evidence accumulated to date as to the influence of the above mentioned factors on proximal femur fracture is presented below.

1.1.1 Osteomalacia

Osteomalacia results in impaired mineralization of the organic bone matrix as a result of defects in metabolism or alterations in mineral availability. Pathologically, there is a marked increase in unmineralized bone or osteoid, and usually a demonstrable decrease in the rate of mineralization as shown by tetracycline labeling. The etiology is most commonly a disturbance in vitamin D metabolism caused by adult nutritional deficiency, malabsorption syndromes, liver and renal disease, inadequate sunlight, alcoholism, or steroid therapy. Drugs such as dilantin and excessive ingestion of phosphate-binding antacids such as aluminum
hydroxide may produce osteomalacia while genetic and environmental factors may also play an important role (Robbins et al., 1984).

The bulk of reported evidence serves to refute the claim that osteomalacia is a common factor in femoral fracture populations (Frish et al., 1982; Boyce et al., 1982; Lips et al., 1982; Fantini et al., 1982). Wicks (1982) in a study of an Australian population of 125 fracture patients, failed to find a single case of osteomalacia when examining the femoral heads. This finding is in agreement with a study of 35 femoral heads from fracture cases examined in the United Kingdom by Hodgkinson (1971) as well as with a study of iliac crest biopsies in 36 patients by Evans et al. (1981). Wooton (1971, 1982) in a study of 110 hip fracture patients reported evidence of osteomalacia in only seven of eighty biopsies performed. However, contrasting evidence has been published. Studies carried out in the United Kingdom (Gallagher et al., 1972; Jenkins et al., 1973; Aaron et al., 1974) report biopsies have revealed osteomalacia in over 30 percent of patients with fractured femoral necks. Hoikkala et al. (1982), using histomorphometric techniques found that 24% of 58 hip fracture patients had biochemical findings consistent with osteomalacia.

In summary, the reported frequency of osteomalacia in femoral neck fracture populations varies from 0 to 37 percent. This variability is partly due to varying criteria used to diagnose the disease (biochemical tests may be normal in osteomalacia but histological examination indicating excessive osteoid confirms the diagnosis, Hoikk et al., 1982)). While the presence of osteomalacia does greatly increases the likelihood of fracture, it is not a common affliction and consequently does not account for a significant number of fractures of the proximal femur.
1.1.2 Osteoporosis

Osteoporosis is the most common bone disorder in the United States and is so widespread that its onset is thought to be inevitable with old age. This disease is characterized by a decrease in bone mass producing porosity and fragility. Most often the condition is seen in patients who have no clear biochemical defect in the major constituents of bone; collagen and mineral. In these cases it is believed that the disorder is the result of aberrant cellular activity; either an increase in osteoclastic activity, a decrease in osteoblastic activity or an asynchrony between the two. The observation that women with hip fractures have reduced bone mineral in the proximal femur but no discernible bone loss in the lumbar spine or radius, has lead to the speculation that two different types of osteoporotic syndromes exit (Riggs, 1982). However, regardless of type, studies have demonstrated increased levels in urinary calcium in the early stages of osteoporosis, suggesting that increased bone resorption is primarily responsible (Nordin et al., 1985).

The role of osteoporosis in hip fracture still remains controversial. Some authors have found significant differences in bone density between fracture groups and controls, while others report observing none. Stevens et al. (1962), reported radiologic evidence of osteoporosis in 82% of 80 patients with intertrochanteric fractures and 71% of 75 patients with femoral neck fractures. They also found histologic evidence of osteoporosis in 47% of 70 intertrochanteric fractures and 33% of 60 femoral neck fractures. Pogund (1977) diagnosed osteoporosis on the basis of lateral x-rays of the spine and reported it present in 32% of 389 hip fracture
subjects as compared to 8% of 3,535 controls. Aitken (1984), studied a series of 200 women who experienced femoral neck fracture and quantified generalized osteoporosis by using metacarpal morphometry. He observed that of 195 women who fractured as a result of minor trauma, 82% had osteoporosis, although their values were within the range of controls. Therefore, he concluded that the absence of generalized osteoporosis is no protection against a hip fracture.

Cummings (1985) reviewed 15 studies conducted between 1960 and 1982 which investigated the role of osteoporosis in hip fracture. He reported that the case-controlled studies suggest patients with hip fracture are more osteoporotic, although the magnitude of difference with controls is controversial. Cummings continued by conjecturing that the discrepancies among the results may be partly due to ascertainment bias in collecting the data. In studies where this type of bias is minimized, by using such means as automated measuring methods, patients with hip fracture have only marginally less bone mass than controls.

Melton and Riggs (1985) attempted to clarify the discrepancies in reported results on the connection between osteoporosis and hip fracture. They suggest that osteoporosis should not be defined in terms of relative differences in bone mass between fracture groups and age-adjusted controls. Rather, it should be defined in terms of absolute levels of bone mass. They demonstrated that age-related fractures were relatively uncommon among people with bone mass densities (BMD) above 1.0 gm/cm², with an increase in fracture incidence with declining BMD.

The inconclusiveness of any studies to date on the role of osteoporosis
in hip fracture support the hypothesis that other factors are equally important. This observation suggests that reduced bone mass may be a necessary but not sufficient condition for the majority of fractures. Additional factors such as postural instability and femoral geometry are likely equally as important in defining fracture risk, and thus all must be considered when determining a comprehensive fracture prediction technique.

1.1.3 Gender

Women are reported to have a considerably higher likelihood for hip fracture than do men (Boyce and Vessey, 1985; Wooton, 1982). Up to 33 percent of women can expect to experience a hip fracture during their lifetime, while the percentage for men is only 17. Fracture rates for both sexes are generally increase approximately equally with age until the fourth decade wherein women experience a dramatic increase in occurrence following menopause. The peak rate of fracture of 3,317 per 100,000 is seen for women (at age 85) whereas for men the peak value is half that, 1,833 (also at age 85) (Melton and Riggs, 1983).

Mazess (1983), suggested that the observed difference in fracture rates between women and men could be the result of post menopausal changes in cortical bone resorption rates. In addition, the age of onset of cancellous bone loss appears to be equally as important. He reports that both women and men have similar rates of trabecular bone loss with age, beginning in early adulthood (6-8 percent per decade). This rate has not conclusively been shown to increase in post menopausal women. Cortical bone loss also
has similar density reduction rates between men and women (3 percent per decade), however women do show a marked increased rate of compact bone loss after menopause. Mazes suggested that the decreased trabecular bone density observed in fracture groups as compared to controls, is due to a lower initial density and not an increased resorption rate. This early onset of trabecular bone loss could lead to an increased deficit of trabecular bone relative to compact bone in the 50-60 age group.

It appears then, that both the loss of ovarian function as well as age, are important factors in the development of involutional osteoporosis in women. The increase in fracture rates occurring near the time of menopause highlight this change in hormonal status (Meema, 1975). Estrogen therefore, has been suspected as a key factor in controlling bone function. To date, however, no direct receptors for the various forms of known estrogens have been identified on bone-cell surfaces (Lane, 1983). It is believed that estrogen and PTH function in an antagonistic fashion and that in the absence of estrogen, bone is more sensitive to the action of PTH (Nordin et al., 1985). Decreased hormone levels can be seen not only in primary estrogen deficiency states but also in anti-estrogen metabolic conditions such as hyperprolactinemia (Klibanski, 1980; Lane, 1983) and therefore, studies of these additional populations may also serve to help elucidate the influences of estrogens on bone formation.

More recently however, the results of a large-scale epidemiologic study have contradicted the hypothesis that menopause is a key event in the development of osteoporosis (Brody et al, 1984). The authors report that hip fracture rates for white women start a steep climb between ages 40 and 44-15 to 20 years earlier than generally believed. The incidence curve
appears to continue to rise smoothly, with no apparent inflection around the time of menopause or thereafter. Their findings concur with the conclusions of Mazes and suggest that the higher number of hip fractures found among white women result from their incidence rate beginning to rise about five years earlier than those for black women, white men, and black men. According to their calculations, postponing the early rise in hip fracture incidence in white women by about five years would reduce overall hip fractures in this high-risk group by about 50 percent.

These studies highlight that the influence of gender is still not definitively known. As Brody and colleagues (1984) suggest, the increased susceptibility of white women cannot be attributed solely to either race or sex, since there is no consistent evidence of a gender effect among blacks or of a race effect among men.

1.1.4 Calcium and Vitamin D

Two dietary factors are presented throughout the literature as potentially playing a significant role in the occurrence of hip fracture: calcium and vitamin D. Since both are important for bone mineralization, the use of the serum levels of these compounds for predicting fracture risk is partially based on the theory that osteomalacia (reduced mineralization) increases a patient's fracture potential.

Calcium

Calcium, the principal mineral of the human skeleton and the most
abundant cation of the body, is essential to the integrity and function of cell membranes, neuromuscular excitability, transmission of nerve impulses, multiple enzymatic reactions, and regulation of parathyroid hormone secretion. Therefore it is no wonder that the human serum calcium concentration is kept remarkably constant between 9 and 10 mg/100ml. The total amount of calcium in the human body ranges from 1000 to 1200 grams with approximately 99% of the body calcium residing in the skeleton and the other 1% present in the extracellular and intracellular spaces. With the neurological and enzymatic functions of calcium as a top priority, the plasma levels of calcium are maintained largely by calling on the minerals reservoir within bone (Slatopolsky, 1984).

The primary factor in the regulation of extracellular calcium is parathyroid hormone (PTH). A reduction in plasma calcium stimulates PTH, which in turn increases serum calcium by, 1) increasing the activity and number of osteoclasts, inducing bone resorption, and consequently mobilizing calcium from bone, 2) augmenting calcium reabsorption by the kidney, and 3) increasing calcium absorption by the small intestine, indirectly, due to greater production of 1,25(OH)₂ vitamin D₃. With such a large percentage of body calcium residing in the bone mass, factors affecting calcium metabolism may lead to skeletal derangements (Bloom and Fawcett, 1975).

Serum calcium concentrations and hence osteoclastic activity (via PTH) can be influenced by changes in intake, absorption, and excretion of calcium. Some investigators have reported that calcium intake was low in osteoporotic subjects (Harrison, 1981; Lutwak, 1963). It has been recommended that before menopause, 1000 mg/day of calcium is adequate, but after
menopause, women need 1500 mg/day - equivalent to 1.25 quarts of milk daily (Pogrudn et al 1986). However, others have suggested that increasing the dietary calcium did not prevent bone loss (Garn, 1967). In addition, several authors report no difference in calcium absorption between hip fracture groups and controls (Wooton, 1979; Nordin et al., 1985). Taken together, these studies suggest that an increase in calcium excretion may be responsible for increased bone resorption. This hypothesis is supported by the observed differences of this parameter between men and women: urinary calcium excretion decreases with age in men as the result of an adrenal calcium-saving mechanism, however this is not true in women (Mazzoulli et al., 1982). An explanation for this observation was presented by Peacock et al. (1985), who suggested that in postmenopausal women, decreases in estrogen levels modify the PTH setpoint. This changed setpoint leads to elevated serum PTH levels and hence an elevated calcium mobilization from bone, which in turn results in increased serum calcium levels. The increased serum calcium then results in the observed elevated calcium excretion.

Therefore, while serum calcium may be a useful measure of the process of bone resorption and hence fracture risk measurements of calcium intake and absorption appear to be of little diagnostic value.

**Vitamin D**

The serum level of vitamin D has also been investigated to determine its influence on proximal femur fracture. The main source of vitamin D in man is endogenous vitamin D₃ produced by the ultraviolet irradiation of 7-dehydrocholesterol in the skin. Vitamin D then undergoes hydroxylation in
the liver to produce 1,25-dihydroxyvitamin D, the physiologically important, active form of the vitamin. The main source of exogenous vitamin D in the United States is milk. The daily requirement of vitamin D in infants is about 400 units; in older adults the requirement is as low as 70 units per day.

Physiological amounts of vitamin D in the diet are necessary to maintain the normal mineralization process in bone and to promote the intestinal absorption of calcium and phosphorus. Dietary deficiency of vitamin D increases the amount of osteoid tissue in the skeleton and decreases normal mineralization. Low calcium, low phosphate and a number of hormones (estrogens, prolactin, growth hormones) all act in vivo to stimulate the production of the active form of vitamin D. It has its major effect in three target organs, 1) the intestine, increasing calcium and phosphate absorption, 2) the skeleton, stimulating osteoclastic activity leading to bone resorption and calcium mobilization, and 3) the kidney, stimulating resorption of calcium and phosphate. Deficiency of vitamin D can therefore lead to rickets in children and to osteomalacia on adults. While nutritional osteomalacia is extremely rare in the United States, most cases are usually caused by an increased requirement for the vitamin (Gallagher and Riggs, 1978).

As in the debate over the correlation between serum calcium and fracture rates, there is also argument as to the importance of serum levels of vitamin D (Nordin et al., 1985). Although it has been reported that serum levels of vitamin D do decrease with age, which is thought to be the result of a failure of the aging kidney (Galinsky et al., 1982), there has been limited success in using this parameter for separating fracture patients
from controls. Wooton et al. (1979) used a protein binding assay to measure the 24(OH)D₃ concentration and found no significant difference between fracture groups and controls. Conversely, in a study of 125 fracture patients and 75 controls, Lips et al. (1982), reported that serum 25(OH)D, as measured by a binding assay, was significantly lower in fracture patients than controls. Therefore, while serum levels of vitamin D may be the important component in the disease state for some, it is not a universal finding in all hip fracture populations and is therefore not always a useful yardstick by which to measure fracture risk.

1.1.5 Age

After closure of the physes, bones continue to change their anatomical dimensions by gradually increasing the periosteal and endosteal diameters (Ruff and Hayes, 1982). At menopause in women, and more gradually in elderly men, the endosteal diameter increases at a greater rate than does the periosteal diameter, leading to a net loss of cortical bone. Likewise, it has been observed that bone density decreases with age (Sandler et al., 1982). This pattern of changing bone geometry and decreased density can give rise to a significantly increased risk of femoral neck fracture. Therefore, not unexpectedly, several studies have observed that the incidence of hip fractures increases exponentially with age in both sexes (Frandsen, 1983; Wooten, 1982; Melton and Riggs, 1985). Concurrent with this age related change authors note overall increases in fracture rate statistics. Wallace (1983), reported increases in incidence of between six and ten percent per year. Johnell (1984) observed that over the past thirty
years the number of hip fractures in his study population has increased by a factor of six. Elabdien (1984), reported an increase from 43 per 10,000 in 1965 to 65 per 10,000 in 1980 in the city of Uppsala, Sweden. These dramatic, progressive increases are beyond what could be explained by changing population demographics alone (Boyce, 1985; Zetterberg, 1984). The combination of demographic and pure fracture rate changes can have significant consequences for future generations. It has been projected that these trends could potentially result in a three-fold increase in the number of hip fractures over the next 20 years (Frandsen, 1983).

Boyce (1985) suggested that this increase in the age-specific incidence must be due to changes in the etiology of the fracture; that is, the emergence of new risk factors or an increase in severity or prevalence of previously existing factors. Baker et al. (1980) compared the UK rates for 1956 and 1975 and found that for women, the increase was confined to those aged under 75 and was most pronounced in the 55-64 age group. Wallace (1983) studied the rates over the period 1971-77 and found the greatest increase in women aged over 75, with virtually no increase in the under-65 group. These findings may indicate a cohort effect, with the raised incidence applying to patients born after 1890 (Boyce, 1985). The elevated rates would then be expected to "work their way through" the population by the end of the present decade.

Along with the observed increase of hip fracture rates, there has been reported changes in fracture type with age. Hedlund et al. (1985) studied the incidence of cervical and trochanteric fractures in a population in Stockholm, Sweden from 1972 through 1981. They reported that the incidence of both fracture types did not change in the age group 50-74 years. In
males 75 years and older, the incidence of both fracture types caused by moderate trauma increased annually by 5-6 percent. However, in females 75 years and older, the incidence of trochanteric fractures caused by moderate trauma increased annually by 6 percent, whereas the incidence of cervical fractures increased only marginally. Zetterberg et al. (1984) observed similar trends in a population from Goteborg Sweden. Dretakis and Christodoulou (1983) actually reported a decrease in cervical fractures with age; from 72% to 30% of proximal femur fractures during the 6th to 9th decade in females, while in males the proportions remained the same.

These observations have been explained by noting that cortical and trabecular bone contribute to bone strength in different relative amounts in the neck and greater trochanter. Hedlund and others (Melton and Riggs, 1985; Zetterberg, 1984) suggest that the risk of hip fracture is more dependent on the quality of the more metabolically active trabecular bone than that of cortical bone. This hypothesis is supported in part by the observations of Aitken (1984). He reported that women who were not osteoporotic had sustained cervical fractures almost twice as commonly as trochanteric fractures, whereas women who were severely osteoporotic had sustained trochanteric fractures twice as often as cervical fractures.

1.1.6 Race and Geography

Enormous variations of fracture rates have been observed within different countries and ethnic groups. In general, regardless of geographic location, non-white populations tend to have one half the fracture rate as
do whites. Engh et al. (1968), studying the patient population in a Virginia mental institution, reported an annual rate per 100,000 of 24.4 for white women above age 45 versus 6.3 in a similar group of black women, and 12.2 in white men versus 2.7 in black men. European and American-born Jewish women in Jerusalem have higher rates of hip fracture than do women in that city of Asian or African descent or those who are native-born Israelis (Melton and Riggs; 1983).

The pattern of occurrence of hip fractures within various ethnic groups varies as much as the overall rates between ethnic groups. Among the Bantu, the incidence of hip fracture increases only minimally with age, and rates for men are slightly higher than those for women. Among Chinese and Malay residents of Singapore, rates for males are also higher than those for women, but the incidence among both sexes does rise modestly with increasing age. The pattern for Indian residents of Singapore resembles that of Western men and women (Melton and Riggs, 1983).

No generally agreed upon reason has been described for the observed racial fracture rate differences. American blacks have been reported to have greater bone density levels than whites of the same age and sex. Conversely, the Bantu, with the lowest observed fracture rates, have similar bone densities as Johannesburg whites, who demonstrate similarly high fracture rates as American whites (Solomon, 1968).

Many other variables have been proposed to explain these observed differences such as diet, exposure to sunlight, propensity for trauma associated with social class and degree of industrialization, and level of physical activity. With the expected complexity of interactions between
geography, genetics, diet, and climate, it will be difficult to ever understand the true contributions of these variables.

1.1.7 Trauma

Femoral neck fracture is the end result of about 1 in 15 falls in the elderly (Wootton et al., 1982), and therefore the cause and type of fall is a significant variable in the formula for predicting risk. It has even been suggested that postural instability is the major determinant for femoral neck fracture (Aitken, 1984; Melton and Riggs, 1985; Wicks et al., 1982). As a person ages his strength and coordination decrease, reflex time increases, sensory perceptions decrease, gait becomes uncertain and subsequently the aged constitute roughly 72% of those who die annually from falls (Rodstein, 1964; Nickens, 1983). In addition to age the presence of debilitating conditions such as parkinsonism, hemiplegia, stroke, cardiac rhythm defects or alcoholism can also markedly increase an individuals probability for trauma. The most common type of fall in the elderly is from a standing height or less and it has been estimated that one third or more of all elderly individuals experience such a fall yearly (Melton and Riggs, 1985). However, since the degree of trauma needed to induce fracture decreases with age (Bauer, 1958), it has been suggested that fracture may not require any overt trauma at all and may even occur under the loads imparted during quiet walking (Reeves, 1977).

Several studies have investigated the nature of falls in the elderly focusing on the characteristics of these falls that change with age.
Sheldon (1960) investigated 500 fall patients, 59 of whom sustained femoral neck fracture. He classified the cause of falling as either extrinsic (environmental) or intrinsic (physiological), which differentiates 2 types of postural instability. Of the cases reported by Sheldon, 34% were identified as accidental or extrinsic and 25% as due to "drop attacks" or intrinsic (a drop attack was defined an event in which the patient suddenly finds herself on the floor with no recollection of what precipitated the event). It is thought that most of these drop attacks are caused by transient cerebral anoxemia initiated by extension of the head and rotation of the neck which compresses vertebral arteries already narrowed by atherosclerosis (Rodstein, 1964). A study of 384 patients and 226 controls was performed by Brocklehurst et al. (1978). They reported a higher incidence of chronic brain syndrome and poor physical condition in fracture groups than controls. Tripping was the cause of falls in younger groups (35% for those under age 65) while drop attacks were more common in older individuals (25% for those over age 75).

An individuals level of physical activity has also been reported to affect the type of fracture present. Trochanteric fractures usually occur in patients with markedly impaired physical activity and muscular weakness, while more active individuals with good muscular condition tend to fracture the femoral neck (Dretakis and Christodoulou, 1983). This observation may be a clue to defining the femoral loading which results in each of these types of fracture. More likely this is just another observation of the reported trend that older individuals (who are also more incapacitated) suffer intertrochanteric fractures in higher percentages because of an increased loss of cancellous bone over cortical bone.

In summary, it seems that about one third of falls are caused by
environmental factors and are manifested by tripping or slipping. Another fifth are caused by drop attacks or syncope, a fifth to a third due to loss of balance and the remainder due to miscellaneous factors such as collisions or seizures (Melton and Riggs, 1983).
1.2 Fracture Classification

1.2.1 Femoral Neck Fractures

Several methods for the classification of femoral neck fracture exist. The primary goal of these classification systems is to give information pertaining to, 1) the possibility of obtaining a stable and anatomical reduction, and 2) the risk of secondary fracture following internal fixation (Ganz, 1979; Jensen, 1980). The most common classification techniques are based on three fracture characteristics, 1) anatomical location of the fracture, 2) the direction of the fracture angle, and 3) displacement of the fracture fragments.

Anatomic Location

Fractures of the proximal femur are commonly divided into intra-articular (intracapsular; within the joint capsule) and extra-articular (extracapsular) groups (Delee, 1984). intra-articular fractures are in turn divided into subcapital and transcervical types. Some authors also include a basicervical classification, referring to fractures occurring at the base of the neck (Heppenstall, 1980), while others include these base of the neck fractures within the extracapsular group (Delee, 1984). The extra-articular classification includes most commonly intertrochanteric fractures, which will be discussed below.

The term subcapital refers to those fractures which occur at the junction of the femoral head and neck. The term transcervical refers to those fractures which pass across the neck midway between the femoral head
the greater trochanter. Distinguishing between these two types of fracture can be difficult using radiographs alone (Garden, 1974). Kleenerman and Marcuson (1970) conducted a study of twenty femoral heads removed at operation for primary prosthetic replacement. They noted that the heads showed a very constant pattern of fracture; the fracture line passing from the epiphysial scar on the superior aspect of the neck, along the ascending trabeculae to the calcar. No transverse cervical fractures were seen in this series and the authors suggested that they are likely very rare, with many true subcapital fractures being misdiagnosed as transcervical due to x-ray parallax.

Fracture Angle

The direction of the fracture line within the femoral neck has also been used to classify femoral neck fractures. Pauwels (1935) defined three groups, 1) type I, a fracture 30 degrees from the horizontal, 2) type II, a fracture 50 degrees from the horizontal, and 3) type III, a fracture 70 degrees from the horizontal (Fig. 1.2.1). The observed fracture angle on plane film radiographs however, has been shown to be highly influenced by the direction of the x-ray projection and on the orientation of the proximal femur during examination (Garden, 1974). The true direction of the fracture line has been reported to be fairly constant between 45 and 60 degrees (Linton, 1944) and thus this classification method is of little clinical value (DeLee, 1984).

Fracture Displacement

The amount of fracture displacement is an important parameter for
Figure 1.2.1: Pauwel's classifications of femoral neck fractures. From Heppenstall, (1980).

- 28 -
evaluating stability and thus the ultimate healing rate (Heppenstall, 1980). Garden (1961), noted that the various types of subcapital fractures were actually different degrees of displacement of a single fracture type, and hence proposed a classification based on the amount of displacement of the fracture. Type I is an incomplete fracture, and is present with minimal or no displacement. Type II is a complete fracture but is present with minimal or no displacement. Type III has displacement but the posterior retinaculum is intact and frequently shortening and external rotation of the distal fragment is present. Type IV has displacement with disruption of the retinaculum and loss of all continuity between the proximal and distal fragments. This loss of continuity allows the femoral head to remain in normal relationship with the acetabulum.

1.2.2 Intertrochanteric Fractures

Boyd and Anderson (1961) differentiated four types of trochanteric fractures. Type I is a linear fracture through the intertrochanteric region. Type II is defined as comminuted (broken into fragments) fracture within the intertrochanteric region. Type III is a trochanteric fracture with an associated subtrochanteric fragment. Type IV is an oblique fracture of the proximal portion of the shaft of the femur, involving the subtrochanteric region (Fig. 1.2.2).

Jensen (1980) conducted a study of 234 patients presenting with trochanteric fractures who were subsequently treated with sliding screw-plate internal fixation systems. Five classification systems were evaluated
Figure 1.2.2: Boyd classification of trochanteric fractures. From Boyd and Anderson, (1961).
as to their ability to give reliable information about the possibility of achieving anatomical reduction and the risk of secondary fracture dislocation. The Evans classification system was determined to contain the most information (Fig. 1.2.3). The second best system was determined to be one considering only the primary dislocation of the fracture.
Figure 1.2.3: Evan's classification of trochanteric fractures. From Jensen (1980).
1.3 Mechanism of Injury

1.3.1 Epidemiologic Studies

Knowledge of the specific nature of injury is important when attempting to determine fracture risk. Consequently, there is much debate concerning the events ultimately leading to hip fracture; whether the fall causes the fracture or a spontaneous fracture leads to the fall (Sloan and Holloway, 1981). It has been suggested that one of three mechanisms of injury are the cause of the majority of hip fractures (DeLee, 1984). The first is that of a direct blow over the greater trochanter as the result of a fall (Linton, 1944). The second mechanism is that of external rotation of the lower extremity. This motion results in the posterior neck impinging on the acetabulum, causing the neck to buckle (Scheck, 1959). The third mechanism is that of fatigue, which as a result of repeated cyclical loading, produces micro-cracks along the superior neck, at the head-neck junction (Freeman et al., 1974). In younger patients however, fracture is most commonly caused by major trauma, usually resulting in a hip joint force directed along the shaft of the femur (Protzman and Burkhalter, 1976).

The most common fracture mechanism appears to be a medially directed load applied to the greater trochanter. In a investigation of 365 intracapsular fracture patients, Linton (1944) reported that the majority (70 percent) stated the fracture was caused by a "blow on the hip" (Table 1.3.1). However, no consistent fracture pattern was observed. This loading allegedly caused an almost equal number of the different forms of fracture observed. Backman (1957), also reported that the majority of fractures
resulted from this loading mechanism. Of 102 patients with cervical femoral neck fracture, 84 recounted a fall on the hip as the cause. Eighteen of these patients did not know if they had fallen but were found to have evidence of trauma over the trochanteric region.

Table 1.3.1 - Different types of fractures as compared with their mode of origin (from Linton, 1944)

<table>
<thead>
<tr>
<th>Fracture types</th>
<th>Abduction</th>
<th>Intermedial</th>
<th>Adduction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Blow on the hip</td>
<td>4</td>
<td>27</td>
<td>9</td>
</tr>
<tr>
<td>Fall Backwards</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fall in non-reported way</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Slipped without falling</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fall forwards</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Fall from a height</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knocked down by vehicle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leg locked under body</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kicked against an object</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown reason</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The second suggested mechanism of fracture is based on observations of common fracture displacements. Scheck (1959), in a review of lateral x-rays of 100 intracapsular fractures, noted that 89 showed a typical angulation between the head and neck fragments with the head rotated posteriorly. He concluded that since the incidence is so high, the displacement must be caused either by the fracture mechanism or by forces acting on the fragments subsequent to fracture. Scheck discusses two mechanisms which could explain this. The first mechanism occurs when the posterior rim of the acetabulum impinges in the posterior aspect of the neck, causing the neck to buckle and fragment. This mechanism is supported by the observed comminution of the cortex of the posterior surface on the
neck, as found in 62 percent of the fractures in his study. A second possible mechanism for this fracture pattern is a result of the geometry of the femoral neck. Scheck observed that the head and neck have a curved longitudinal axis, the convexity of which is directed anteriorly. Thus a medial force applied at the greater trochanter will cause the anterior aspect of the neck to fail under tension while the posterior aspect fails in compression, with the separation of a butterfly fragment.

The third suggested fracture mechanism is fatigue; a result of the rate of cyclic damage out pacing that of repair. Sloan and Holloway (1981) conducted a prospective study of 54 cervical fracture patients. Sixty-nine percent of the patients could give some cause for their fall, although the information did not show any clear trend. Thirty-one percent felt that they had fallen because their hip had given way. A majority of these patients (60 percent) gave a clear history of previous pain in the affected hip. Almost everyone in the study group fell onto the side of the fracture. A much higher incidence of intracapsular fractures was found in the group who felt their hip had given way (77 percent) compared with the remainder (40 percent). The authors concluded that fatigue is a significant cause of hip fracture in the elderly.

Freeman et. al. (1974) conducted microscopic examination of sixteen femoral head and neck necropsy specimens in an attempt to quantify the role of fatigue in senile femoral neck fractures. They reported that trabecular fractures were more common in the area of the junction of the head and neck (56 percent). The relationship between the number of fatigue fractures and bone density in each specimen suggested there exists a threshold bone density of 0.5 gram/cm³, below which fatigue fractures appear in excessive
numbers. They concluded that senile subcapital fractures in osteoporotic patients are primarily due to fatigue and not the impact of a fall. Urozvit, et al. (1977) reported results which support this finding; that trabecular stress fractures are a normal occurrence, and the majority of such fractures seem to occur at the head-neck junction.

Watson (1975) conducted a similar microscopic study of the trabeculae in femoral heads taken at autopsy. Two separate populations were examined, 1) a high risk group of British patients, and 2) a low risk group from India and China. Eleven specimens from senile femoral neck fractures were found to have many more microfractures than the specimens from Asians. The numbers of fractures were similar to those found by Freeman et al. (1974). In addition it was observed that many more fractures (an average of 44.5) existed in thin trabeculae whereas the thick trabeculae, that exist in a band extending from the calcar to the fovia, contained much fewer fractures (an average of 5.5). Since the subcapital region contains a large proportion of thin trabeculae, these results tend to support the findings of Freeman et al. (1974), that subcapital fractures are commonly initiated by fatigue microfracture.

1.3.2 Experimental Studies

The goal of experimental studies of femoral neck fracture is to elucidate the in vivo conditions under which these events occur. A primary requisite, however, is that the fractures produced be representative of those seen in the clinical setting. The validity of conclusions drawn from
these experimental studies, thus, need to be viewed in light of the clinical significance of the resulting fracture patterns.

In an attempt to determine the cause of fracture in the trochanteric region of the femur Spears and Owen (1949), studied 150 femora under in vitro loading conditions. A dynamic force (via a pendulum) was applied in the medial direction at the lateral trochanteric region. During this loading the distal end of the femur was held fixed and the head was supported in a lead form representing the acetabulum. Surface stresses were investigated using a stresscoat technique. While all fractures were produced in the intertrochanteric region, the results seem to show that the failure occurs in compression in the lateral trabeculae first and then proceeds medially.

In a study of 115 embalmed femoral specimens, Smith (1953), attempted to elucidate the role of muscular or intrinsic forces in femoral neck fracture. He described a typical clinical fracture as transverse or transverse oblique with the distal fragment displaced upward. Forty-three femora were subject to vertical loading through a partially intact pelvis or medial loading applied to the greater trochanter. While no cervical fractures were observed, there were 24 trochanteric, 2 head and 16 pelvic fractures produced at an average load of 1994 lbs. A second series of tests were conducted with impact loading with similar results; one pelvic, 28 trochanteric and 3 femoral head fractures produced. A third series of tests were conducted in which the femoral neck was loaded in three-point bending, with the plane of the applied loads being coincident with the neck axis in the anterior-posterior directions. This loading mode produced fractures comparable to those seen clinically at an average load of 900 lbs. Smith
stated that this loading mode is similar to that present with the foot fixed on the ground and the external rotators active. He also stated that this condition is likely present during most neck fractures, the fall being secondary. Backman (1957) however, demonstrated that this loading mode does not accurately simulate the influence of the external rotary muscles, and in fact a correct analysis of Smith's load example would produce anteflexion of the head, which is clinically uncommon. Therefore, while useful information can be obtained from the first two series of tests, the third series is of little clinical value.

Backman (1957) has compiled the most extensive results to date pertaining to the possible mechanisms of proximal femur fracture. He stated that a fall on the hip is the simplest and most natural explanation, besides being the most common cause recorded in case histories. Experimental investigations were conducted with 99 fresh human femora. In all experiments the trauma was represented by a medially directed load applied at the greater trochanter. An estimate of the impact force for a 50 kg person was derived to be 7840 N, although some of the values used in the calculations appeared somewhat arbitrary. Backman suggests that given the magnitude of this force, muscular forces likely play only a minor role in femoral neck fracture. However, since fracture occurs at much lower loads (3800 N), muscular forces (1300 N) can have a significant contribution at that instance. Several different orientations of the femur, with respect to the applied load, were investigated. A large range of fracture patterns were observed with no clear correlation to the type of applied load, although transcervical fractures were the most common. In general, it was noted that the force required for subcapital fractures was small compared to other types. Also, subcapital fractures arose gradually, not suddenly in
a brittle fashion like the other types of fracture which occurred. Since no clear fracture pattern/load case trend was apparent, he concluded that the localization and character of the fracture is largely determined by a combination of the quality of the bone and the type of trauma. However, two loading conditions were observed to more commonly produce fracture patterns similar to those seen in vivo. The first condition arises when the patient lands on the lateral aspect of the buttock rather than directly on the greater trochanter. In this case the gluteal muscles give some support to the posterior aspect of the neck while the resultant joint contact force acts in the posterior direction. The second loading condition was one with combined bending, shearing, compression and torsional forces. The torsional forces applied were consistent with those measured to occur due to friction within the joint.

Hirsh and Frankel (1960) also investigated the influence of muscular forces on the observed fracture patterns in the femoral neck. A complete pelvi-femoral preparation was taken from a fresh cadaver and the muscles removed. Strain gauges were glued to the neck of the femur on the upper and lower cortices. For the condition of one-legged stance it was reported that the influence of the abductors acted to decrease the tensile stresses on the superior aspect of the neck. However, the actions of other muscle groups surrounding the hip (iliopsoas, adductors, gluteus maximus and short rotators) had no influence on these upper cortical stresses. Fractures produced with vertical loading only, traversed from the subcapital area of the upper cortex almost straight down to the lesser trochanter. These fractures had little in common with those seen clinically. In a separate series of experiments, the influence of muscles acting about the hip were simulated by applying a compressive force along the axis of the neck. The
type of fracture could be varied according to the direction of the axially applied load. Subcapital fractures with a typical clinical appearance were obtained when joint force was directed upward and laterally in the direction of the superior aspect of the greater trochanter. If the joint force was directed downward, toward the lesser trochanter, transcervical fractures were observed. The authors concluded that muscle forces are therefore important in determining fracture type and location. However, the direction of the joint forces reported here are very similar to those produced by lateral trauma on the greater trochanter as demonstrated by Backman (1957), and do not necessarily need to result from muscular contraction at all.

Griffiths et. al. (1971) conducted in vitro experimental studies to determine the influence of fatigue in femoral neck fracture. Thirty-seven specimens of the proximal third of an adult human femur were taken at necropsy. A single load was applied to the femoral head at an angle of 22.5 degrees to the diaphyseal axis. The loads were imparted cyclically at a frequency of 15 cycles/min for a period of up to 10,000 cycles. Fifteen specimens sustained fracture, the pattern described as resembling impacted subcapital fractures. However, in figures of typical specimens, the fracture patterns appear to be transcervical or basicervical. The results indicated that up to middle age, loads of about ten times body weight are required to produce fatigue failure in 10,000 cycles. The propensity of fatigue fracture was seen to decrease with age up to about the age of seventy, at which time a load of five times body weight was sufficient to produce fracture in some specimens. As noted by the authors, ten thousand cycles is equivalent to a walk at reasonable pace of about three hours duration. Since peak hip loads during gait can reach 6 times body weight
(Rohrle et. al., 1984), a young individual with a backpack, or an older individual, can easily meet the above criteria for fatigue fracture. As the time for generation of trabecular bone packets and hence repair is fairly long (69 days; Lips et. al. 1978), in vitro fatigue tests of this duration could accurately reflect the in vivo situation.

In summary, it appears that the occurrence and type of fracture is highly dependent on the condition of the proximal femur (bone quality and geometry) as well as the mode of loading that is applied. Since a particular femur can only be tested to failure once, the failure mode most likely to produce fracture or the true influence of loading configuration on the ultimate fracture type, cannot be elucidated from experimental studies alone. As demonstrated by Backman (1957), there are many combinations of load magnitude and direction that can occur during a fall. To attempt to simulate all of these would be impractical and unnecessary. It is likely that given an individuals local bone quality and geometry, the onset of fracture under the simplified loading conditions, such as vertical (simulating conditions under which fatigue fractures occur) or medial loading (simulating conditions under which trauma fractures occur), is a good indicator of the patients relative fracture risk under the common, actual, in vivo loading conditions.
1.4 Fracture Prediction Methods / Quantification of Bone Mass

Several parameters have been used as a measure of hip fracture risk (Dalen et al., 1976; Frendensborg and Nilsson, 1976; Leichter et al., 1981; Mizrahi, 1984). The most frequently cited indices involve photodensitometric or radiographic measures of the density of bone in the proximal femur (Colbert and Bachtell, 1981; Meema, 1981). As well as analyzing bone quality in the proximal femur, several techniques focus on bone in other, easier to access regions, such as the distal radius. Unfortunately, these methods may measure different properties of bone, at different sites in the body, where different types of bone exist (Leichter et al., 1981; Dalen and Jacobson, 1974). In addition, particular disease states may be manifested differently in different regions of the body (Riggs et al., 1982). Therefore, discrepancies between the various methods used for quantifying osteoporosis or fracture risk are expected. Many review articles covering quantitative bone assessment have been written (Sandler and Herbert, 1981; Mazess, 1983). This section contains a condensed review of the tools currently available for the determination of bone density and fracture risk. These technologies include; photon absorptiometry, Compton scattering, the Singh index, photodensitometry, and quantitative computed tomography (QCT).

1.4.1 Photon Absorptiometry

The technique of single photon absorption (SPA) makes use of a low
Energy photon beam for the determination of bone mineral content (Cameron and Sorenson, 1963; Sorenson and Cameron, 1967). The method consists of a collimated photon source and a collimated crystal detector system. The sample, which includes bone and surrounding tissue, is placed between the source and detector. From measurements of the intensity of the transmitted beam, made at intervals across the bone, the total mineral content of the bone can be determined. Highly accurate and reproducible results have been reported for determining radial bone density (Schlender and von Segger, 1976; Grubb et al., 1984;) and predicting in vitro radial fracture loads (Horsman et al., 1983). However, this technique is only applicable to the appendicular skeleton and is applied chiefly at the forearm or distal radius.

There are three major limitations in the usefulness of this technique for quantifying fracture risk at anatomical sites other than those directly measured. Firstly, is the inability of this technique to separate the density of the individual components of bone; cortical and cancellous. This issue is important since appendicular and axial skeletal sites contain different ratios of cancellous to cortical bone (Table 1.4.1), and cancellous bone has been shown to have a higher turnover rate than cortical bone (Bauer et al., 1929). Secondly, appendicular cortical mineral status may be different from axial trabecular status (Richardson et al., 1985). Therefore, SPA may not be a sensitive predictor of bone mineral state, or fracture risk, in regions other than the measuring site. Thirdly, changes in appendicular bone mass may be different from the changes in the axial skeleton. This is due to the apparent existence of two types of osteoporotic bone loss (Riggs et al., 1982), which affect the axial and appendicular skeleton differently. Patients with spinal fragility fractures
are thought to suffer primarily from postmenopausal osteoporosis, which is characterized by disproportionate trabecular bone loss in the axial skeleton. Conversely, patients with hip and radial fractures are thought to suffer from senile osteoporosis, which is characterized by a proportionate loss of both cortical and trabecular bone. Thus, although bone measurements on the radius can indicate overall skeletal status in normal subjects, and to a lesser degree in osteoporotic patients (Mazess et al., 1984; Smith et al., 1975; Robin et al., 1982; Gupta et al., 1984), these measurements may be inaccurate as a measure of the spinal state (Wahner et al., 1977, Reinbold et al., 1986). Recently, however, it has been suggested that analysis of a more distal site in the radius, where trabecular bone occupies greater than 50% of the mass, may yield a more accurate assessment of spine fracture potential (Awbrey et al., 1984, Manicourt et al., 1981).

Table 1.4.1 - Trabecular and cortical bone at common sampling sites (from Wahner et al., 1983)

<table>
<thead>
<tr>
<th>Bone</th>
<th>Site</th>
<th>Cortical Bone %</th>
<th>Trabecular Bone %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radius</td>
<td>midshaft</td>
<td>&gt;90</td>
<td>&lt;10</td>
</tr>
<tr>
<td></td>
<td>distal</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>Femur</td>
<td>neck</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>trochanter</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Spine</td>
<td>lumbar</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>

The increased number of Colles' fractures observed in hip fracture patients (Owen et al., 1982), suggests a correlation may exist between hip and radial bone quality. In support of this hypothesis, some authors report lower radial BMC values in the forearms of women with femoral neck
fracture than in controls, though only a few of the observations are definitely outside the normal limits (Fredensborg and Nilsson, 1977; Jensen et al., 1983). Several other investigators have also reported small, but significant differences in radial BMC between hip fracture patients and controls (Wooton et al., 1979; Khairi et al. 1976; Alhava and Karjalainen, 1973; Harma et al., 1985). However, using dual photon absorptiometry, it has also been reported that proximal femur bone densities correlate poorly ($R=0.4$) with radial values (Mazess, 1985).

Direct measurement of bone mineral content of the neck of excised femora via SPA has been shown to correlate well with in vitro neck fracture loads. Leichter et al. (1982) determined the magnitude of single joint force at failure for 18 proximal femora. The correlation between the force at failure and BMC as measured in the femoral neck was determined to be significant ($R=0.68$, $p<0.001$). Dalen et al. (1976), using similar techniques, also found significant correlations between force at fracture and femoral neck BMC ($R=0.89$). However, the simplified loading conditions used in these studies makes it difficult to extrapolate the results to in vivo situations.

SPA therefore, seems to yield useful results for determining overall skeletal bone status or radial fracture potential but, as yet, cannot satisfactorily predict in vivo fracture in other areas such as the hip and spine.

The method of dual photon absorption (DPA) makes use of two separate photon energies, and thus can distinguish between the attenuation coefficients of two different media, such as bone and soft tissue (Roos and
Skoldborn, 1974). This allows the measurement of bone mineral content in the axial skeleton, where large amounts of soft tissue are present (Dunn et al., 1980). The absorptiometer consists of a rectilinear scan mechanism and a photon source and detector, which enable reconstruction of two dimensional plots of transmitted intensity, or bone density. With the use of certain averaging procedures, DPA can accurately measure bone mass and density, and is only slightly affected by either surrounding tissue, or fat changes in the bone marrow (a 10% change in bone marrow fat content produced less than 0.6% change in the measured BMC, Wahner et al., 1985).

The bone mineral content of excised lumbar vertebrae, as measured by DPA, has been shown to correlate well (R=0.86) with the ultimate strength under axial loading (Hansson et al., 1980). Bone mineral content of the spine and/or the proximal femur has also been used to differentiate between spinal fracture groups and controls. It has been reported that in patients with known osteoporosis, the use of DPA can separate spinal fracture patients from controls with 80% probability (Raymakers et al., 1986). In the proximal femur and femoral shaft, there has been reported high correlations between BMC, as determined by DPA, and the amount of hydroxyapatite in the in vitro specimen (Bohr and Schaadt, 1985). Likewise, there has been some reported success in using bone mineral content of proximal femora (Riggs et al., 1982), and femoral shaft (Bohr and Schaadt, 1983), for separating hip fracture patients from controls.

While there is need for further studies, this technique appears to be a potentially valuable tool for the diagnosis and monitoring of both patients with osteoporosis and overt fracture.
1.4.2 Compton scattering

The Compton scattering technique determines density by measuring the scattered radiation from the tissue under investigation (Webber, 1981). The intensity of this scattered radiation is dependent both on the electron density of the sample and the angle at which the scatter is measured. With the use of a high energy source, a collimated detector, and correction techniques, bone density measurements can be made within a small volume (2 to 10 cm$^3$, Mazess, 1983) of trabecular bone, while minimizing the influence of surrounding cortical bone.

In a study of 314 adults aged 55 to 75 years, bone density measured in the distal radius (by Compton scattering) was found to be a better predictor of osteoporosis than BMC measured by SPA in the same site (Robin et al., 1982). The ability of Compton scattering technique to selectively measure only trabecular bone was cited as the reason for the better selectivity. Bone density was found to be decreased by 25% in the older, osteoporotic population. The reproducibility of the Compton scattering technique was reported to be 2%, while 40% of the SPA measurements were so widely variable that they could not be used at all.

Leichter et al. (1982) measured the in vitro breaking force for 32 human femora. Of three parameters used for the proximal femur (Singh index, BMC via SPA, and bone density via Compton scattering), the trabecular bone density measured by Compton scattering exhibited the best correlation to the breaking stress ($R=0.87$, $p<0.001$; and $r=0.84$, $p<0.001$, Mizrahi et al., 1982). A fair correlation between true density and estimated bone density
was observed ($R=0.62$, $p<0.001$).

These studies demonstrate that Compton scattering can be a good predictor of femoral neck fracture under simplified conditions in vitro. However, there have been no studies performed that evaluate the usefulness of this tool for predicting fracture loads in vivo or for separating fracture patients from controls.

1.4.3 Singh Index

In 1970, Singh et al. reported that the progressive changes occurring in osteoporosis could be measured by observing the trabecular patterns within the proximal femur. Six different patterns were recognized (Fig. 1.4.1), and later, (1972) they reported a clear separation could be made between persons with and without spinal crush fractures by using this index. Since then many authors have tried to reproduce these positive results. In general, while the use of the Singh index has been shown to be better at separating fracture patients from controls than other radiographic techniques (Horsman et al., 1982; Lips et al., 1984), the index is believed to have little clinical value. Kranedonk et al. (1972) found no correlation between the Singh index and radial bone mineral content as measured by SPA and thus concluded that the index was a poor predictor of generalized osteoporosis. Khairi et al. (1976), in a study of 106 women, reports no correlation between the Singh index and subsequent fracture. Pogrud et al. (1981), conducted a study of 550 hip fracture patients to assess the effectiveness of using the Singh index to identify patients at risk. The
Figure 1.4.1: Singh's index of osteoporosis. From Wahner et al., (1977)
interpretation of the Singh index was found to be difficult and not easily reproducible, and no definite correlation between the Singh index and hip fracture was found. Wicks et al. (1982) conducted a study of the femoral heads from 125 patients with fracture of the femoral neck. They report that the Singh index was unreliable as a radiological indicator of the bone content of the femoral heads.

Experimental studies of in vitro loads on excised femora have also demonstrated the limited usefulness of the Singh index. Leichter et al. (1982) reported a correlation was between bone density and shear stress at failure, but there was a poor correlation observed between the breaking stress and the Singh index. Therefore, the general consensus is that the Singh index is difficult to apply in a reproducible manner and shows little correlation with generalized osteoporosis and subsequent risk of fracture.

1.4.4 Photodensitometry

The technique of photodensitometry typically consists of a computer controlled densitometer which scans an x-ray image with a light beam. The data are analyzed by computer for the determination of bone mineral density. Photodensitometry makes use of the theory that the optical density of a radiographic image of bone is roughly proportional to the mineral mass. However, this relationship is only approximate, even with the use of compensatory reference wedges (Mazess, 1983). The two major sources of error are, 1) polychromaticity of the source radiation used which results in beam hardening, and 2) radiation scattering as the result of the
uncollimated source. Usually, radiographs of the hands or wrists are used to minimize patient exposure to radiation and to reduce beam hardening effects due to overlaying tissue.

A complete discussion of the application of this technique to the phalanges is described by Colbert and Bachtell (1981). They reported high correlations between the results of phalangeal photodensitometry and total body neutron activation ($R = 0.88$, $p<0.001$), as well as with SPA of the distal radius ($R=0.78$, $p<0.002$).

While the application of this technique to axial skeletal structures involves the increased influence of beam hardening and radiation scattering, some optimistic results have been reported. Vose and Mack (1963) conducted in vitro failure tests on 10 excised femora. They report a strong correlation between the roentgenographic bone density of the region known as Ward's triangle (Fig. 1.4.2) and the ultimate fracture load. This technique was later applied to fracture risk in vivo (Vose and Lockwood, 1963), and was shown to give adequate separation between fracture patients and controls. The density in the Ward's triangle area of 0.20 cm/cm. aluminum equivalency was determined as the cut off point between those at risk for fracture and controls.

1.4.5 Radiogrammetry

Radiogrammetry involves the morphometric measurement of cortical bone from radiographs as an estimate of bone mass. While in many regions of
Figure 1.4.2: Relationship between the ultimate yield load and roentgenographic density of Ward's triangle. From Vose and Mack (1963)
interest the total bone mass has contributions from both cortical and cancellous bone, morphometric measurement is capable of quantifying the cortical component only. The best locations then, for applying this technique are the tubular bones of the appendicular skeleton (Meema and Meema, 1981). In addition to neglecting the trabecular component, this technique cannot quantify intra-cortical porosity. Therefore, it has been shown that cortical thickness measurements are not a sensitive method for the determining the degree of osteopenia (Meema and Meema, 1969).

The correlation between morphometry of the metacarpals and hip fracture risk was investigated by Lips et al. (1984). Values of cortical thickness were found to be similar between fracture patients and controls. Also, poor correlations between the cortical index and histomorphometric analysis of iliac crest biopsies were reported. Horsman et al. (1983), investigated the relationship between measurements of radial cortical width and in vitro radial fracture loads. The correlation was significant (R=0.75; p<0.01), however, cortical width was found to be much less useful than bone mineral content for the quantification of osteoporosis.

The cortical width in the femoral neck has also been investigated as a possible indicator of hip fracture risk. Although differences have been observed between hip fracture groups and controls (Nilsson and Hagberg, 1976), the use of femoral or metacarpal cortical widths were found to be less useful in distinguishing fracture patients than the Singh index (Horsman et al., 1982). In light of the above mentioned results, the use of cortical thickness appears to be of little clinical value for distinguishing patients at risk for fracture.
1.4.6 Computed Tomography

The use of quantitative computed tomography (QCT) for the accurate assessment of bone status has been suggested by many authors (Revak, 1980; Elsasser and Reeve, 1980; Genant et al., 1985). The first clinically useful CT scanner was developed by Hounsfield (1973). Currently, third generation scanners employ a broad fan-beam x-ray source that is rotated in a continuous 360 degree motion (Fig. 1.4.3). The fan-beam is focused on a large array of detectors, with one complete sweep being performed in approximately five to ten seconds. A total of several hundred thousand measurements are made during one rotation. The data are transmitted to a computer for the necessary processing to generate a single cross sectional image. The thickness of the cross-sectional slice is usually between 0.5 to 1.3 centimeters and is divided into numerous volume elements (voxels). An x-ray attenuation value is determined for each volume, based on the density and atomic number of the tissue within it. The attenuation values are expressed as CT numbers (Hounsfield units), typically on a scale of -1000 for air, zero for water and +1000 for dense bone. Typical CT parameters are: 1.5 millimeters for spatial resolution; 0.5 percent for density resolution; and 1.5 rads for radiation exposure (Genant et al., 1980). The precision (reproducibility) of QCT in the spine has been reported to be 1%-3% for single-energy (80 kVp) and 3%-5% for dual-energy (80 kVp/140kVp) (Genant et al., 1982).

There are three basic advantages to using QCT to measure bone properties and estimate fracture risk. First, a two dimensional display of the data permits both identification of anatomy and separate measurement of both
Figure 1.4.3: Schematic representation of a third-generation computed tomography scanner. From Genant et al., (1980).
cortical and cancellous bone. Second, the ability to determine linear absorption coefficients in easily defined volumes enables the measurement of density. Third, use of a dual energy mode enables the accurate determination of mineral content in the presence of variable amounts of fat and soft-tissue.

Several sources of device-dependent error exist which must be understood when assessing the validity of CT results (Macoviski, 1983; Muller, 1985; Elsasser, 1980). These errors consist of the beam hardening effect, the partial volume effect, scan noise, and scan to scan noise (McCullough, 1977; Lampmann et al., 1984). Other measurement errors can be induced by changes in tissue composition from patient to patient, tissue changes within a particular patient over time, as well as with difficulties in obtaining repeatable patient positioning (Dunscombe, 1984).

Beam Hardening Effect

The x-ray source for CT scanners is polychromatic. Consequently, when this beam passes through tissue, the lower energy photons are absorbed more than the higher energy ones. This creates a shift in the photon energy distribution curve toward the higher energies. The remaining x-rays are termed 'hard', having a high effective photon energy. This higher energy results in a higher penetrability, and as a result, the effective linear attenuation coefficient ($\mu_T$) will decrease with increasing material thickness. This beam hardening effect results in decreased CT density values for structures deep within the body (Lampmann et al., 1984).

A theoretical investigation of the influence of beam hardening was
conducted by Wiessberger et al. (1978). Changes in water path length of 5 cm. resulted in a apparent 6.6% loss in bone mineral. Consequently, measurements of samples residing within areas of thick, overlaying tissue could be subject to significant errors. However, dual energy scanning as well as correction techniques are available to reduce the magnitude of this type of error.

Partial Volume Effect

The thickness of the CT slice is variable, from approximately 1.5 to 12 mm. Within a homogenous structure, thick slices result in better accuracy as the result of reduced noise. However, spatial resolution is decreased due to partial volume effects. The partial volume effect occurs when a voxel is filled with two different tissue types, both of which have very different attenuation coefficients. Artifacts are thus introduced into the image. Knowledge of the three dimensional shape and homogeneity of the structure to be scanned, should therefore be used to select the optimal CT slice thickness.

Scan Noise

When scanning a uniform object, the CT numbers are distributed randomly about an average value. The spread of the values about the mean is referred to as scan or photon noise. The low-contrast detectability of a scanner is dependent not only on the scan noise but also on the number of pixels observed. The reported CT value for a region of interest is the mean of the group pixel means. The standard deviation of the regional CT number is the standard deviation of the pixel means, which is defined to be the standard
deviation of any pixel value divided by the square root of the number of pixels. Therefore the more pixels within a region of interest, the lower the effective noise.

**Scan to Scan Noise**

In addition to the photon noise within one scan, there may be significant CT number variation between scans. Two causes of this are, 1) scanner calibration drift, resulting in a change in the linear attenuation coefficient per CT number, and 2) a drift in the CT number of water with time. The use of calibration phantoms can reduce the effect of scanner variability and assure scan to scan and machine to machine accuracy.

**Changes in Proportion of Marrow Fat**

Most of the x-ray attenuation responsible for the QCT number is due to marrow (Mazess and Vetter, 1985; Table 1.4.2). Therefore subtle changes in bone density can be masked by the large changes in marrow fat content with age (Dunhill et al., 1967). An increase in the ratio of fatty marrow to hemopoietic marrow combined with an increase of total marrow (a decrease in bone density), can lead to significant errors in bone density measurements made with single energy QCT in the elderly, osteoporotic population. This can result in a 50% reduction in mineral being reflected by only a 10% change in total measured density. Thus a change of 100 mg/cm³ in fat produces a change of about 14 mg/cm³ in apparent density, which can result in an error of 25–40 mg/cm³ or 30% in older subjects (Mazess, 1983). However, by applying age and gender matched corrections, this underestimation can be partially corrected for, resulting in the fat-
induced inaccuracy of 4-5 mg/cm³ or about 1/6 that of the normal biologic variation (Richardson et al., 1985). The potential difficulty in using such global corrections is that fat content has been reported to vary significantly within local regions of bone (Laval-Jeantet et al., 1986). However, these fat content numbers represent the total amount of fat within the samples tested and not the percentage of marrow that is fat. Therefore, this large variation of fat content presented by Laval-Jeantet et al. (1986) more likely represent a large variation in specimen density.

Table 1.4.2 - Volumetric composition of trabecular bone (from Mazess and Vetter, 1985)

<table>
<thead>
<tr>
<th></th>
<th>Concentration mg/cm³</th>
<th>Percent of total volume</th>
<th>Percent of total volume</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>young</td>
<td>old</td>
<td>young</td>
</tr>
<tr>
<td>Mineral</td>
<td>200</td>
<td>100</td>
<td>6.7</td>
</tr>
<tr>
<td>Matrix</td>
<td>120</td>
<td>65</td>
<td>9.4</td>
</tr>
<tr>
<td>Marrow</td>
<td>728</td>
<td>587</td>
<td>72.8</td>
</tr>
<tr>
<td>Fat</td>
<td>100</td>
<td>300</td>
<td>11.1</td>
</tr>
<tr>
<td>Total</td>
<td>1158</td>
<td>1052</td>
<td></td>
</tr>
</tbody>
</table>

Changes in Bone Composition

In osteoporosis, the elemental composition of bone tissue does not change significantly (Jowsey, 1964), thus the change in linear attenuation coef. (u_L) is easily interpreted as being due directly to bone loss. In osteomalacia, however, the mineral phase is depleted, so there is not only a change on the gross density but also in the tissue composition. Therefore, the interpretation of changes in u_L are not obvious when osteomalacia is present. To address this problem Wiessberger et al. (1978) conducted a theoretical study of the changes present in osteomalacia.
Changes in $u_t$ were found to be divided into a fraction due to mineral loss and a fraction due to changes in elemental composition. The sensitivity of QCT to these different types of bone material change is dependent on the particular photon energy used. Measurements of $u_t$ made at 140 keV are relatively independent of elemental changes and are proportional to bone density, while measurements made with 27 keV, 60 keV, and 120 keV reflect the elemental composition of bone to a greater extent. Increases in unmineralized bone would then be indistinguishable from increases in bone mineral or total bone if 140 keV, and to a lesser extent 120 keV, were used. Spectral changes due to mineral loss from surrounding bone was estimated to be 0.13% additional apparent mineral loss per 1% mineral actually lost. It was also estimated that the change in the effective linear attenuation coefficient per unit fraction of mineral lost is about 8.6 times greater in cortical than in cancellous bone. (Weissberger et al., 1978). Therefore, although cancellous bone is metabolically more active and loses more mineral, similar changes in CT number over time are observed in cortical bone.

By scanning a substance of known composition (calibration phantom) simultaneously with a patient, accurate characterization of tissue properties may be made. The use of a phantom allows for the comparison of results between different machines (Levi, 1982), as well as complete or partial elimination of scan to scan noise and beam hardening effects (Dunscombe, 1984).

Computed Tomography has been shown to provide a very accurate measurement of bone density. McBroom et al. (1985) reports a highly significant positive correlation ($R^2 = 0.89$, $p < 0.001$) between apparent
density and corrected CT numbers of cancellous bone samples taken from the lumbar spine. Vertebral failure loads were also significantly correlated to CT numbers ($R^2 = 0.81$, $p < 0.001$). In a study of 31 patients, Reich et al. (1976) report a good correlation between CT numbers and SPA values of the distal radius ($R = 0.72$). However, a better correlation was found between CT numbers and calcium content taken from 10 cadaver tibias ($R = 0.97$). Bradley et al. (1978) also reports a linear correlation ($R = 0.89$) between CT number and calcium content of cancellous bone from the lumbar spine.

The use of spinal CT to isolate populations at risk for fracture also shows great promise. Firooznia et al., (1986), report that in a sample population of 186 females aged 47 to 84 years, 87% of vertebral fracture patients, 38% of hip fracture patients and 82% of patients with both, had spinal BMC (as measured by QCT) values below the fifth percentile for healthy, premenopausal women. The use of low-dose CT of the radius has also been suggested as a sensitive and safe way to monitor osteoporosis (Ruegsegger et al., 1981). A precision of 0.3% in measuring trabecular bone allows detection of a 1% change in trabecular bone density. Weekly intervals of evaluation were suggested for patients at risk for immobilization osteoporosis, while 3-month intervals were determined as being adequate for postmenopausal osteoporosis patients.

Similar results can be expected for evaluating bone status within the proximal femur since images made with CT have been shown to accurately reproduce the concentration and orientation of the major trabeculae within this region (Kerr et al., 1986).
1.5 Osteoporosis Therapy

Several therapeutic regimens for the treatment of osteoporosis are widely used. These include, 1) vitamin D and calcium alone or in combination, 2) fluoride, alone or with vitamin D and calcium, 3) estrogen, and more recently 4) calcitonin.

1.5.1 Vitamin D

It has been observed that early after menopause women have a reduced serum level of $1,25(\text{OH})_2\text{D}_3$ and concomitant decreased intestinal absorption of calcium (Caniggia et. al. 1963). Thus, supplementation with vitamin D has been suggested to be an effective treatment for the prevention or cessation of osteoporosis (Section 1.1.4). However, the value of this treatment has not been conclusively demonstrated. In a study of 38 postmenopausal women, Gennari et. al.(1982) reported that while the patient group treated with $1,25(\text{OH})_2\text{D}_3$ (1 ug/day) demonstrated increased intestinal calcium absorption, they also showed a rise in plasma and urinary calcium and urinary excretion of hydroxyproline (the most reliable indicator of bone collagen resorption). Since, as the authors mention, $1,25(\text{OH})_2\text{D}_3$ is a powerful bone resorbing agent, the increased plasma and urinary calcium levels could be due to both increased absorption of calcium and increased release of calcium from bone. The authors concluded that $1,25(\text{OH})_2\text{D}_3$ treatment corrects only calcium hypoabsorption and not increased bone loss, and thus this therapy might best be combined with estrogen replacement to
achieve an effective regimen.

Christiansen (1982) investigated the influence vitamin D therapy with a study population of 315 patients. Patients treated with 1,25(OH)₂D₃ alone (0.25ug/day) had similar decreased in BMD as observed in controls (2% over the first year). However, when this preparation was combined with estrogen, a small enhancement of the positive effect of estrogen was observed, but the amount was not statistically significant. The authors concluded that both the decreased intestinal absorption of calcium seen early after menopause and the reduced serum level of 1,25(OH)₂D₃ in postmenopausal women with osteoporosis represent an adaptation to an increased mobilization of skeletal calcium in the hormone-deficient women. Treatment with this vitamin D metabolite is therefore without value.

1.5.2 Calcium

It appears that a negative calcium balance exits in osteoporotic women, possibly due to a combination of factors: decreased intake, decreased absorption, increased excretion or increased mobilization (Harrison, 1981; Lutwak, 1963; Nordin, 1985; Wooton, 1979). It is believed that these decreased levels of serum calcium can lead to increased bone resorption via an increased level of PTH (Section 1.1.4). However, the results of investigations on the effect of increased dietary calcium are not conclusive. Many authors have suggested that increased amounts of dietary calcium are required to maintain homeostasis (Gallagher and Riggs, 1978; Seeman and Riggs, 1991). These studies indicate that before menopause,
1,000 mg/day of calcium is adequate to maintain body calcium, while afterward, women need about 1,500 mg/day. The average American diet, exclusive of dairy products, provides approximately 500 mg of calcium per day (Mallette, 1982). Thus it has been suggested that after menopause women need an additional 1000 mg or approximately 5 glasses of milk daily. In support of this, Riggs et al. (1982), reported that patients receiving calcium only (1500 mg/day) had a vertebral fracture rate of approximately one half of that observed in the control group over a 12 year period.

In a recent investigation into the influence of calcium supplementation however, has demonstrated less favorable results. Riis et al (1987), conducted a two year study on postmenopausal bone loss. Three treatment groups were studied, 1) percutaneous estrogen, 2) oral calcium (2000 mg/day), and 3) placebo. Bone mineral content in the forearm and spine remained constant for the estrogen group but decreased significantly in the groups receiving calcium and placebo. The calcium treated group had a tendency for slowed loss of compact bone as compared with the placebo group but the rate of trabecular bone loss was the same. The results suggest that while calcium supplementation may have a minor effect in maintaining the quality of compact bone, it has little effect on the more metabolically active trabecular bone. As mentioned by the authors, trabecular bone has a higher rate of turnover during the years just after menopause, and hence these results might change as the duration of study increases.
1.5.3 Fluoride

Sodium fluoride therapy in osteoporosis has been shown to result in a significant increase in total osteoid volume and osteoid seam width (Kleerekoper et al. 1982). However, while moderate doses of fluoride favor bone formation and mineralization, high doses can lead to low breaking strength and low elasticity due to irregular mineralization and texture of the bone (Gedalia and Simkin, 1982). These high levels of fluoride (greater than 9,000 ppm) have been shown to result in decreased mineralization and increased endosteal bone resorption due to increased osteoclastic activity (Gedalia and Simkin, 1982). Therefore moderate doses are required (80-100 mg/day) for the beneficial effects of this drug. However, the observation of increased osteoid formation has lead some authors to conclude fluoride can induce osteomalacia and have therefore recommended the combined use of calcium and or vitamin D with fluoride (Jowsey et al. 1968).

The efficacy of a combined regimen of fluoride with calcium and vitamin D was investigated by Riggs et al. (1982). They reported that patients that relieved fluoride alone (50 mg/day) had a slightly (419/304) reduced (though not statistically significant) rate of vertebral fracture than those who did not receive fluoride in their treatment. When data for the first year was excluded there was a larger, statistically significant difference (61 percent). The authors noted that time is necessary for the fluoride therapy to increase vertebral bone mass. The best results however, were observed (834/53) with a combination of estrogen, fluoride and calcium with the rationale being that fluoride, a potent stimulator of bone formation, works synergistically with estrogen, a potent inhibitor of bone
resorption. Parenthetically, they also noted that a significant minority of the population studied had no response to the fluoride treatment and hypothesized that this subpopulation had an intrinsic abnormality in osteoblast function.

Menczel et al. (1982) also investigated the efficacy of fluoride/calcium treatment with a study population of 115 subjects. The majority (81%) of the group with fluoride treatment (20mg/day fluoride, 1.060 mg/day calcium) showed no decrease in bone density during the two year treatment period, while in 19% there was a slight increase in bone density. Conversely, in the control population over the same time period, there was an observed decrease in bone density of 25.3% for nonosteoporotic and 29.7% for osteoporotic patients.

While fluoride combined with calcium appears to be beneficial, the efficacy of fluoride combined with vitamin D alone has been questioned. Christiansen (1982), in a study of 315 patients rated the influence of several fluoride treatment regimens by measuring bone mineral content using single photon absorptiometry. Patients treated with fluoride and vitamin D (20mg/day NaF, 2,000 IU vitamin D3) had an observed decrease in BMC of 3.7 percent over the two year study period, compared to the control population which had an observed decrease of only 3.3%.

Kleerekoper et al. (1982) reported findings similar to Christiansen; that the inclusion of vitamin D with the treatment regimen of fluoride (NaF, 50mg/day) not only prevents the increase in bone formation induced by fluoride alone but actually reduces bone turnover to below pretreatment values. They concluded that the observed osteoid increase with fluoride
treatment is not the result of the presence of osteomalacia but rather the increase in bone matrix synthesis. Therefore the administration of vitamin D is not warranted and can actually be counter productive.

It is important to note that adverse patient reactions to fluoride treatment have also been reported, with the major complaints being rheumatic and gastrointestinal symptoms (Riggs et al; 1982).

1.5.4 Estrogen

It is now generally agreed upon that estrogen therapy reduces the accelerated rate of bone resorption observed in osteoporosis (Gordan, 1985). While no receptors for estrogen on bone have been observed (Lane, 1983), the actions of estrogen seem to be mediated by the thyroid hormone calcitonin (Chesnut et. al, 1982). However, along with its positive effects, estrogen therapy has been suspected to increase the risk of some forms of cancer (breast, endometrial) as well as to increase the propensity for hypertension and heart disease (a conclusion drawn from experience with estrogen use for oral contraception).

Using quantitative computed tomography, Ettinger et. al. (1982) quantified the influence of estrogen in several dose levels on the progression of osteoporosis. Patients taking a placebo or 0.15 mg of conjugated estrogens per day displayed a mean annual loss of 9.6% in trabecular bone mineral in the lumbar vertebra. Patients taking 0.3 to 0.45 mg per day showed a mean annual vertebral mineral loss of 8.6%, while those
taking 0.6 mg daily had unchanged values of vertebral bone mineral. The authors concluded that 0.6mg of conjugated estrogen per day is the appropriate level for effective treatment of osteoporosis induced bone loss.

Paganini-Hill et. al. (1981) conducted a study of treatment efficacy for the prevention of hip fracture with a study population of 20,000. The use of oral estrogens was found to be inversely proportional to hip fracture risk, with the degree of protection increasing with the duration of use. The greatest benefit was observed in oophorectomized women who had a calculated risk ratio of 0.14 (as compared to 0.86 for women with intact ovaries, and 0.62 for patients taking calcium alone).

Similar positive results of estrogen therapy were reported by Meema et. al. (1975) from a study of 82 postmenopausal women. Bone mineral loss of 9.1 mg/cm2 was reported for castrates and 6.9 mg/cm2 for those with natural menopause. With estrogen treatment (0.625 or 1.25 mg/day) there was an actual increase in annual bone mineral of on average 3.25 mg/cm2.

While these potential benefits of estrogen therapy are usually weighed against the potential hazards, harmful effects of this treatment regimen may be less common that first feared. While Hoover et al. (1976), reported no significant increased risk of breast cancer in estrogen-treated women, Gordon (1985), actually observed a reduced risk of breast cancer in those patients under estrogen therapy. Endometrial carcinoma has also been reported to be a major risk of estrogen therapy (Smith et al. 1975). Gordon (1985) reports, however, that the incidence of endometrial carcinoma in women can be greatly reduced by using a cycled regimen of a progestational
compound with the estrogen. In addition, while large dose oral contraceptives have been shown to be related to an increased risk of myocardial infarction, thrombophlebitis, and embolism, no such increase has been found with postmenopausal estrogens (Gordon, 1985).

1.5.5 Calcitonin

Calcitonin, a physiological inhibitor of bone resorption, has been the suspected link between estrogen and bone loss (Chesnut et. al. 1982). This connection is suspected for two reasons; 1) the striking gender difference in circulating levels, and 2) the gradual decrease observed with age (Hillyard et al. 1978). The major physiological function of calcitonin appears to be the protection of the skeleton against excessive resorption by opposing the resorptive actions of 1,25(OH)₂D and parathyroid hormone (PTH).

Stevenson et al. (1981) investigated the influence of estrogen therapy on plasma levels of calcitonin, PTH, and 1,25(OH)₂D in two groups of 7 postmenopausal women. The results demonstrated a definite rise in plasma calcitonin with estrogen therapy with a subsequent return to normal with withdrawal of treatment. A decrease in plasma calcium and a rise in PTH were also observed. These results suggest that the positive effects of estrogens on the maintenance of bone mass are, at least, partially mediated by calcitonin.

The usefulness of calcitonin has been investigated by several authors.
Agrawal et al (1982) conducted a study of 9 biopsy proven osteoporotic patients. The group treated with calcitonin increased their total body calcium by 3% at the end of two years. Chesnut et. al (1982) conducted a similar study of 45 postmenopausal osteoporotic women. At the end of 18 months the treated group demonstrated a significant increase in total body calcium as determined by total body neutron activation analysis. However, there was a reported cessation of response to calcitonin 26 months after initiation of treatment. This loss of response was thought to be the result of development of calcitonin antibodies, or loss of receptor sites for calcitonin.

While the use of calcitonin has potential for the side effect free treatment of osteoporosis, future work is needed to accurately assess the long term efficacy of the drug.

1.5.6 Exercise

The positive influence of exercise on bone mass has been demonstrated by many authors. Aloia et al (1978) investigated the effect of exercise in 18 postmenopausal women. One half of the subjects exercised for 1 hour three times a week for 1 year. The results indicated that total body calcium (as measured by total-body neutron activation) increased in the exercise group and decreased in the sedentary group (p<0.001). Bone mineral content in the distal radius (as measured by SPA) did not change significantly in either group. It has thus been suggested that exercise, together with calcium suppletionment, form a useful regimen for the prevention for involutional
bone loss (Korcok, 1982). It should be mentioned, however, that due to the potential risk of fracture induced by fatigue (Griffiths et al., 1971), the optimal level of exercise that is appropriate has not been defined: while a little can help, a lot can hurt.
1.6 Mechanical Properties of Bone

Long bones are composed of two different classes of bone, both of which exhibit different structural and mechanical properties. The first type forms the dense outer surfaces of long bones and is called cortical or compact. The second type lies within and is continuous with the cortical shell in the metaphyseal and epiphyseal regions. This type of bone is termed cancellous or trabecular. Trabecular bone consists of a three dimensional network of bony spicules which delineate numerous intercommunicating spaces filled by bone marrow. The classification of bone as cortical or cancellous is based on porosity, which is the proportion of the volume occupied by nonmineralized tissue. Cortical bone has a porosity of between 5 and 30 percent while cancellous bone porosity may range from 30 to more than 90 percent. The chemical composition and true density of cortical bone is very similar to that of cancellous bone (Gong et al, 1964), and as a result the distinction between very dense cancellous bone and very porous cortical bone is somewhat arbitrary. In fact, as will be discussed, formulae relating bone density to various mechanical properties have been presented and shown to be valid over a large range of observed density, including both cortical and cancellous bone (Carter and Hayes, 1976).

1.6.1 Cortical Bone

The mechanical properties of cortical bone are dependent on its structure and composition. Both of these properties vary considerably
throughout the skeleton and are influenced by many factors, not all of which are understood. Many authors have investigated the mechanical properties of the various regimes of cortical bone and have attempted to correlate their results with the microscopic and chemical characteristics. Two comprehensive papers on the mechanical properties of cortical bone have been presented by Reilly et al. (1974), and Carter and Spengler (1978). To help put the concepts into proper context, and to appreciate the complexity of the problem, a review of the development and morphology of cortical bone is required.

Bone consists of a solid mineral phase, an organic matrix of osteoid, and bone cells - osteocytes, osteoblasts, and osteoclasts. Osteocytes are merely osteoblasts that become incorporated within the matrix. Both the osteocytes and osteoblasts are uninucleate cells derived from primitive mesenchymal precursors. Osteoblasts are found along bone forming surfaces and may be in close approximation endosteally and subperiosteally but are more widely spaced throughout trabecular or cancellous bone. They contain an abundance of ribosomes involved in the synthesis of mainly collagen polypeptides and are rich in alkaline phosphatase. Osteoclasts are multinucleated cells which are involved in the resorption of bone. They are located along the endosteal surfaces and occasionally throughout cancellous bone. These cells contain acid phosphatase, collagenase, dehydrogenases, proteases, and carbonic anhydrase, which undoubtedly play roles in the resorption of bone (Robbins et al 1984).

The organic matrix of bone, synthesized by osteoblasts, is called osteoid before it is mineralized. It is 90 to 95 percent type I collagen embedded within a ground substance of glycosaminoglycans and linked to some
noncollagenous proteins, principally osteocalcin and osteonectin, both of which are involved in the deposition of calcium. Collagen fibers form the structural strength of the osteoid and are stabilized by intermolecular links to surrounding fibers.

Bone always develops by replacing pre-existing connective tissue. Two different modes of osteogenesis are recognized. When bone formation occurs directly in primitive connective tissue, it is called intramembranous ossification. When it takes place in pre-existing cartilage it is called endochondral ossification. (Bloom and Fawcett, 1975) In both types of bone formation the deposition of bone is essentially carried out in the same manner. The collagen is first laid down in sheets, producing lamellae along the endosteal and periosteal surfaces, as well as around trabeculae. Originally the collagen fibers have no preferred orientation and when this osteoid is mineralized it is called woven bone. Woven-fibered bone generally contains large, irregularly shaped vascular spaces with osteoblasts on the surrounding bone surface. These osteoblasts deposit successive layers of new bone, progressively diminishing the size of each vascular space. The resulting anastomosing, convoluted areas of bone, occupying what were previously vascular spaces, are called primary haversian systems, or primary osteons (McLean and Urist, 1968). Throughout adult life, the process of remodeling continually changes the architecture of the parent bone. This process of internal reorganization takes place by a coupled action of both osteoclasts and osteoblasts. The osteoclasts erode long cylindrical cavities in the primary bone, called secondary Haversian canals, which become occupied with blood vessels and become centers of subsequent lamellar bone deposition by osteoblasts. Within these concentric layers of lamellar bone, referred to as the secondary osteon, the collagen
fibers are then laid down in a more ordered fashion with the preferred orientation primarily along the long axis of the bone.

Mineralization of this mature osteoid produces what is called lamellar bone. Unlike primary osteons, these secondary osteons are always bounded by cement lines which are formed where osteoclastic activity ceases and osteoblastic bone formation resumes (Carter and Spengler, 1978). Irregular areas of bone between secondary osteons are called interstitial bone and represent the remnants of previous primary or secondary bone and therefore may be composed of woven bone or lamellar bone fragments. Neighboring haversian canals are connected by a fine network of channels called Volkmans canals, allowing the coordination of cells and the transfer of minerals into and out of bone (Bloom and Fawcett, 1975).

The diameter of long bones is increased by the deposition of subperiosteal, circumferential, lamellar bone. The processes of remodeling and subperiosteal deposition replace the original woven bone so that in the normal adult all cortical bone is lamellar. Lamellar bone consists of many sheets (thickness of 7um) separated by thin interlamellar cement bands (thickness of 0.1 um) (Ascenzi and Bocciarelli, 1967). Lamellar bone is found in primary osteons, and is formed when the rate of bone deposition is slow or moderate (Carter and Spengler 1978).

The mineral phase of bone is largely crystals of hydroxyapatite (CaPOOH). While the mineralization process is poorly understood it starts out with an amorphous collection of the mineral which is converted to the crystalline form with maturation. The crystals form between the cross linked collagen fibers adding strength and stability.
Mechanical properties

Bone is a complicated, two phase composite. The mineral phase, which has a high elastic modulus and low tensile strength, is imbedded within a collagen matrix which although strong under tension, has a low elastic modulus (Currey, 1969). The collagen fibers can have a random or highly ordered orientation and the amount of matrix present can vary dramatically within an individual and over time. Large variations in the mechanical properties have been observed. The differences are believed to be dependent on variations in tissue microstructure, mineralization, orientation, strain rate, and age.

Tissue microstructure

Walmsley (1959), studied the influence of the distribution of porosity through the cortex on bone elastic modulus. He demonstrated an increasing porosity at the endosteal surface which decreased toward the periosteal surface. This variation in porosity can have a great influence on the local mechanical properties. Carter and Hayes (1976), reported that the compressive strength of bone is proportional to the square of the apparent density, while the elastic modulus is proportional to the apparent density cubed (Carter and Hayes, 1977).

Along with this variation in porosity, a difference of bone microstructure between the endosteal and periosteal surfaces has also been observed (Walmsley, 1959; Meema and Meema, 1981). Bone near the endosteal surface has undergone more remodeling and thus contains more osteons and osteon fragments (Carter and Spengler 1978). Currey (1975), demonstrated
that increasing the amount of reconstruction or secondary haversian systems decreases tensile strength and modulus of elasticity. The numerous cement lines present with the many osteons introduces inherent weakness in this particular region. Conversely, on the periossteal surface where new bone is laid down, less remodeling has taken place and the primary architecture is circumferential lamellar bone. This lamellar bone contains no osteons with cement lines and is thus stronger.

The influence of osteons and cement lines was quantified by Evans and Bang (1966). They suggested that osteons and their fragments tend to decrease the tensile strength and modulus, while interstitial lamellae tend to increase these parameters. Also, the increased number of cement lines present in secondary haversian bone may include the benefit of increasing fatigue fracture resistance by serving as crack arrestors (Evans and Riolo 1970). Compressive strength, on the other hand, seems to be increased by large numbers of osteons. Evans and Vincentelli (1974), reported significant correlations between compressive strength and the percentage of osteons in the test sample break area. In summary, it appears that increased numbers of osteons tend to decrease the tensile strength of bone while increasing both the compressive strength and fatigue resistance.

In a study of bovine cortical bone, Lipson and Katz (1984), demonstrate that independent of mineral content, the tissue organization can also influence material properties. In regions where plexiform (nonorientated) bone was present, elastic modulus values were a measured 20 percent higher as compared to regions of pure haversian bone. The knowledge of the type of bone in a particular area is therefore as important as the local density in determining the mechanical properties.
Mineralization

Currey (1975), observed that increased ash content increases yield strength, tensile strength and modulus of elasticity. However, the low and high ash content samples were harvested from two different types of bone. Samples with a high ash content were obtained from haversian bone while samples with a low ash content were taken from primary bone. The differing tissue microstructures thus may have influenced the results. Burstein et al (1975), performed a similar study but instead used progressive decalcification of a single type of bone. They also reported a decrease in the tensile yield stress and ultimate stress but observed no change in the yield strain or ultimate strain unless decalcification was complete. The slope of the plastic region of the stress-strain curve remains constant throughout the decalcification process. The authors suggested that the mineral contributes the major portion of the tensile yield strength, while the slope or stiffness in the plastic region is a function only of the properties of collagen, which itself plays a minor role in the tensile yield strength of bone. In a more recent study, Currey (1984), reported that not only does a high value of mineral density produce a high value of Young's modulus, but also a low value of work to fracture.

Smith and Smith (1976), derived an exponential relationship between ultimate stress (compression and tension) and mineral density.

\[ \sigma_t = 0.524 \ e^{1.74M} \]
\[ \sigma_c = 0.547 \ e^{2.02M} \]

They also reported a temporal trend in femoral material properties.
Generally, the lowest values were found in specimens from the lateral/posterior quadrant, and the highest were found in samples from the medial/anterior quadrant. This supports the findings of Lipson and Katz (1984) for bovine femora.

Mineral density and ultimately strength, appear to be influenced by the local structure of collagen. An increased collagen cross-link density is thought to be associated with increased hydroxyapatite content, and therefore a decrease in cartilage cross-link density creates a decrease in bone strength (Lees and Davidson, 1977).

Orientation

Cortical bone has been shown to be transversely isotropic (Lang, 1970; Reilly and Burstein, 1975; Yoon and Katz, 1976). One principal material property axis is aligned with the primary haversian systems (longitudinal axis of long bones), while in the plane perpendicular to this axis, the material properties are isotropic. Therefore, five elastic constants completely describe the mechanical behavior. Reilly and Burstein (1975), conducted a series of experiments aimed to determine these elastic constants for human and bovine cortical bone (Table 1.6.1). Values obtained in tension were similar to those obtained in compression. The validity of the transversely isotropic model was tested by comparing actual modulii from 'off axis' test specimens to predicted values derived by the model. The tested specimens were usually stiffer than the theory predicted, which may be the result of the specimens being over constrained by the testing apparatus. The ratio between the ultimate tensile stress measured in the longitudinal direction and that measured in the transverse direction was
determined to be 2.6. The ratio for the values measured in compression was determined to be 1.6.

Table 1.6.1 - Elastic and ultimate constants for cortical bone (from Reilly and Burstein, 1975)

<table>
<thead>
<tr>
<th></th>
<th>Longitudinal</th>
<th>Transverse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elastic modulus</td>
<td>17000 MPa</td>
<td>11500 MPa</td>
</tr>
<tr>
<td>Shear modulus</td>
<td></td>
<td>3280</td>
</tr>
<tr>
<td>Poisson ratio</td>
<td>0.46</td>
<td>0.58</td>
</tr>
<tr>
<td>Tensile strength</td>
<td>133</td>
<td>51</td>
</tr>
<tr>
<td>Compressive strength</td>
<td>193</td>
<td>133</td>
</tr>
<tr>
<td>Torsional strength</td>
<td>68</td>
<td></td>
</tr>
</tbody>
</table>

Lipson and Katz (1984), measured the elastic modulus of bovine femoral bone using ultrasonic techniques. Measurements were made in the longitudinal, radial and transverse directions. Samples taken from haversian bone demonstrate transverse isotropy (Table 1.6.2). Samples of plexiform bone however appear anisotropic, the moduli in radial and tangential directions diaphyseal axis varied by 19%.

Table 1.6.2 - Average elastic moduli for bovine femoral bone (from Lipson and Katz, 1984)

<table>
<thead>
<tr>
<th></th>
<th>Radial</th>
<th>Direction</th>
<th>Longitudinal</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM quadrant</td>
<td>17260 MPa</td>
<td>21370 MPa</td>
<td>29760 MPa</td>
</tr>
<tr>
<td>PL quadrant</td>
<td>15390</td>
<td>16430</td>
<td>24660</td>
</tr>
</tbody>
</table>
Strain rate

Cortical bone has been shown to be a viscoelastic material and therefore the measured material properties are strain sensitive. Currey (1975), conducted tensile tests of cortical bone from bovine femora at strain rates from 0.00013 to 0.16 sec\(^{-1}\). He reported that a 1000 fold increase in the strain rate increases the measured tensile strength by over 50% and the elastic modulus by 10%. In a study of both human and bovine compact and cortical bone, Carter and Hayes (1977) determined both ultimate strength and elastic modulus to be proportional to the strain rate raised to the 0.06 power. These results underscore the importance of using physiologic strain rates when measuring bone properties.

Age

Throughout life, the morphology and composition of cortical bone are continually changing as a result of remodeling and certain disease states, such as osteoporosis. Kerley (1965), conducted microscopic investigations of 126 ground sections from human femora, tibia, and fibulae. Age correlations showed that increasing age was associated with: 1) a loss in the percentage of area occupied by subperiosteal circumferential lamellar bone; and 2) increased numbers of osteons and osteon fragments. These observations are consistent with changes due to years of remodeling.

Evans (1975), also observed these microscopic differences between bone samples from older and younger men. The number of osteons/mm\(^2\) and of osteon fragments/mm\(^2\) was greater in specimens from older men (smaller and more osteons). The bone from older men also tended to be more porous. Along with
these microscopic differences, Evans measured greater average breaking load, strength, strain, modulus and density in the samples of younger men. The absolute values of the results are questionable since the samples were taken from embalmed femora and tibia. The observed increase in porosity is the result of an increased depth of endosteal osteoclastic penetration (Parafitt, 1984). This process is a component of normal, age-related bone loss and results in the conversion of the inner third of the cortex into a structure that resembles trabecular bone.

Burstein et al (1976) investigated the mechanical properties of machined cortical bone specimens from human femora and tibia for a population ranging in age from twenty-one to eighty-six years (strain rate of 0.02 to 0.05 /sec). No significant differences were found between the mechanical properties of male and female specimens. Tibial specimens had greater ultimate strength, stiffness, and ultimate strain than femoral specimens. Consistent decreases with age for all mechanical properties except plastic modulus were found in the femoral but not the tibial specimens. The elastic modulus varied between 17.0 GPa (for the age range 20-29 yrs) to 15.6 GPa (for the age range 80-89 yrs), a decrease of 8 percent.

Dickenson et al (1981) focused specifically on differences of mechanical properties of cortical bone between normal and osteoporotic populations. Specimens were obtained from 11 women who experienced femoral neck fracture and had confirmed osteoporosis, and 11 age matched controls who died without hip fractures. They reported the osteoporotic bone sections had a significantly higher area occupied by cavities: 27 percent as opposed to 16 percent in normal bone. In addition there was a small but significant increase in the mineral content of the osteoporotic bone. Of the five
mechanical properties measured, three (stiffness, strength, and plastic energy absorbed before fracture) were significantly reduced, while yield stress and elastic energy absorption were almost unchanged. The elastic modulus for the normal subjects (average age 79 yrs) averaged 15.6 GPa which is the same result obtained by Burstein et al (1976). For the osteoporotic group (average age 81 yrs) the elastic modulus was decreased to 11.6 GPa. This is a decrease of 32 percent from the young healthy group. (strain rates were not reported)

The results of mechanical tests of old and osteoporotic bone correlate with the observed microstructural changes. Older bone contains more osteons, cement lines, and pores and is thus weaker.

1.6.2 Trabecular Bone

Trabecular bone is a porous material composed of an interconnecting network of rods and plates which develop during the process of endochondral ossification. During development, primitive pluripotential cells are carried into the interior of the cartilage model, which exists at the ends of forming, long bones. Some of these cells differentiate into hemopoietic material of the bone marrow. Others differentiate into osteoblasts which congregate and begin to deposit bone, forming the first trabeculae.

The mechanical properties of this material are dependent on many factors, which has consequently made efforts to quantify its behavior difficult. The most investigated characteristics of trabecular bone are
density and architecture. While cancellous bone has also been shown to be a viscoelastic material, it can be considered virtually elastic under in vivo loading conditions (Pugh et al., 1973).

Density

The density of cancellous bone can be defined in several ways. Apparent density is expressed as the total sample weight divided by the bulk sample volume. True density is defined as the sample weight divided by the volume of bone in the sample, which is usually measured by submersion techniques. Apparent density shows an approximately linear relationship between porosity and ash weight (McElhaney et al., 1970; Mueller et al., 1966). Therefore these two properties are an equally good measure of the amount of normally mineralized tissue.

The influence of density on the mechanical properties of trabecular bone has been investigated by several authors (Galante et al., 1970; Favenesi et al., 1984; Rohlmann et al., 1980, Nokso-Koivisto, 1984). Carter and Hayes (1976), tested specimens of human and bovine trabecular bone and observed large variations of apparent density (0.07 to 0.97 gm/cm³) but the true densities were approximately equal to that of compact bone (1.6 to 2.0 gm/cm³). (Gong et al. (1964), report a similar magnitude difference in ash weight between cancellous and cortical bone, 1.175 to 1.049 gm/cm³). The results of their study indicated that the compressive strength of bone is proportional to the square of the apparent density and to the strain rate raised to the 0.06 power. Gibson (1985), generated an analytical model of cancellous bone which represents the porous structure as a connected network of rods and plates. His model also supports a square law
relationship between density and Youngs modulus. In a later study, Carter and Hayes (1977), demonstrate that the compressive modulus of bone is proportional to the cube of the bone density.

Huskies et al (1984), performed a similar study with cancellous bone specimens from several different species, and indicated that a linear relationship between density and modulus, or strength, is equally accurate over the small ranges of density seen in a single species. A finite element model of the trabecular architecture also demonstrated that Poisson’s ratio is only weakly affected by apparent density, but depends strongly on the trabecular orientation.

Ducheyne et al (1977) also demonstrated strong correlations between bone density, strength and modulus but stated that density alone cannot completely explain the variation of material properties observed. They suggest that the trabecular architecture may possibly play an important role. Lindahl (1976), in a study of dried cancellous bone Lindahl reported that the observed reduction in strength parameters was considerably greater than the drop in apparent density, and thus also postulates that changes in microstructure and mineral content are also important. Harrigan et al (1981), attempted to quantify the role of architecture by developing a single equation for elastic modulus as a function of apparent density and trabecular orientation. They postulated that the elastic modulus is proportional to the apparent density raised to the 2.19 power and to a stereological parameter raised to the 2.7 power. However, these specimens were not tested in the principal material directions and hence a generalized relationship was not determined.
Throughout these studies several authors observed a linear relationship between strength and modulus, inferring an approximately constant strain at failure, despite the wide range of observed strengths. (Klever et al., 1984; Goldstein et al., 1983).

Cancellous specimens tested in tension have shown a similar relationship between strength and apparent density as seen in specimens tested in compression (Carter et al., 1979). The modulus of elasticity was found to be identical for the specimens tested in either tension or compression while the most prominent difference observed between the two testing modes was energy absorbed at failure. However, for trabecular specimens from the proximal humerus, Kaplan et al. (1985) reported the average strength in tension was 7.5 MPa or 60 percent of that measured in compression. Differences in testing protocol as well as the source of specimens may account for these discrepancies.

A relationship between shear strength and apparent density was determined for bovine trabecular samples by Stone et al. (1983). A power low relationship was postulated to exist, with the shear strength proportional to apparent density to the power 1.65. When a Hoffman failure surface was fitted to the shear and compressive test data, the failure ellipse indicated that the tensile strength was approximately one third of the mean compressive strength.

Architecture

The mechanical properties of cancellous bone cannot be defined by density alone since the properties vary with direction (Galante et al.,
The preferred orientation of cancellous bone is evident microscopically and in some cases macroscopically. Williams and Lewis (1982) describe three main types of trabecular architecture; plate-rod, plate-plate, and rod-rod. In the proximal tibia, the cancellous bone was determined to be approximately transversely isotropic, with the ratio of vertical to lateral stiffness ranging up to a factor of 10. The cancellous bone within the samples tended to form cylindrical arrangements vertically, which resulted in different failure modes in the vertical and horizontal directions.

Gibson (1985), described four types of trabecular architecture. He made use of an analytical model for cancellous bone to investigate the properties of these four types of bone that appear to predominate. At low densities, cancellous bone is made up of a network of rod-like elements which form open cells. At higher relative densities, it is made up of a network of plate-like elements forming closed cells. When loading is largely axial, the structure can develop cylindrical symmetry. The four resulting types of cancellous bone are then; open and closed celled asymmetric, and open and closed celled columnar. Analytical studies by Gibson demonstrated different failure modes for the various forms of bone, with the open cells failing by buckling and the closed cells failing by yielding.

Whitehouse and Dyson (1974), noted similar structural patterns in the proximal femur and describe the morphological relations to the four main groups of trabeculae as presented by Ward (1838). Townsend et al (1975), investigated the modulus of elasticity within the human patella and compared the results with a sheet and strut model. After determining the
orientation of the sheets using stereologic methods, the results from mechanical testing indicated a stiffness perpendicular to the sheets of approximately one half of that parallel to the sheets.

Harrigan et al (1980), collected cancellous bone samples from the distal end of human femora. Orientation of the sheets was determined by stereometric techniques and the blocks aligned so that one plane was parallel to the sheets. The strength of trabecular orientation was assessed on each face and the apparent density determined. Analysis showed that elastic modulus was empirically related to density raised to the 2.19 power and trabecular orientation raised to the 2.74 power.

As will be discussed below, Martens et al. (1983), Brown and Ferguson (1980) and Rohlmann et al. (1980) each investigated the mechanical properties of trabecular bone samples taken from the proximal femur and report strong anisotropic behavior.

Changes with age and disease

The strength of trabecular bone has been shown to decrease with age and disease (Weaver et al., 1966). Along with the often reported decrease in density, there appears to be changes in microstructure and mineral content as well. Trabecular thinning begins to become apparent in older individuals and seems to accompany the reduction in density. Ash content also decreases with age, beginning near age 60 (Weaver et al., 1966). The mineral content, however, appears to remain constant between age matched controls and osteoporotic populations (Jowsey, 1964). The combined influence of decreased density, modified architecture, and reduced mineral content can
have a profound influence on the resulting strength.

The age-related decrease in bone density has been reported by many authors. Riggs et al. (1982) measured bone mineral density (BMD) of the proximal femur, lumbar spine, or both by dual photon absorptiometry in 205 normal volunteers (123 women and 82 men; age range 20 to 92 yrs) and in 31 patients with hip fractures (26 women and 5 men; mean age, 78 yrs). For normal women, the regression of BMD on age was negative and linear at each site; overall decrease during life (age 20 to 90 yrs) was 58% in the femoral neck, 53% in the intertrochanteric region of the femur, and 42% in the lumbar spine. For the cervical region, bone diminution occurred at the rate of 0.0129 gm/cm² per year. For the intertrochanteric region, bone diminution occurred at a rate of 0.0108 g/cm² per year. These values however, include the influence of the surrounding cortical bone.

Histological studies of trabecular bone samples from patients with disuse osteoporosis were performed by Minaire et al. (1974). They reported a decrease of trabecular bone volume of 33% over 25 weeks which subsequently stabilized. Also present were an increase in osteoclastic resorption surfaces and depression of osteoblastic bone formation. The transient, rapid bone loss led to a new steady state of rarefied bone with a low rate of subsequent turn-over.

Mazess (1981), reports a loss of trabecular bone of between 6 and 8 percent per decade beginning at age 30. This rate was observed to be constant for both men and women with no change seen in post-menopausal women. A rate of bone loss of 8% per decade from age 30 corresponds to a total trabecular bone loss of 39 percent from age 30 to 90 (0.93 cubed).
Using the relationship between modulus and density as reported by Carter and Hayes (1977), one can estimate the change in elastic modulus caused by this 39 percent change on bone mass.

\[ E_1 = C(\rho)^3 = K (E_2) = K (C(0.62\rho)^3) \]

Solving for the ratio of the two elastic moduli results in \( K = 4.2 \), the trabecular modulus of the older individual being 0.24 or approximately one fourth that of the healthy, young individual.

It has been suggested that the observed architecture changes are the result of a particular type of age-related bone loss. Two types of bone loss (rapid and slow) have been proposed based on the quantum theory of bone formation (Parfitt, 1984). The quantum theory states that bone turnover occurs in anatomically discrete foci, within which remodeling activity lasts for approximately 4-6 months. A small piece of existing bone is removed by osteoclastic resorption, and within the cavity so formed, new bone is laid down until the defect is more or less completely repaired (Parfitt, 1979). Rapid bone loss is the result of excessive depth of osteoclastic resorption cavities. This leads to the removal of structural elements and a change in the local trabecular architecture, while the trabecular thickness remains unchanged. Rapid bone loss is thought to be the primary process present in age-related bone loss (Parfitt et al., 1983). This process can severely affect structural integrity since strength depends on continuity as well as density (Parfitt, 1984; Pugh, 1973). Slow bone loss results from incomplete refilling by osteoblasts of resorption cavities, leading to decreased trabecular width. This later process is thought to be the abnormality present in severe osteoporosis.
Lips et al. (1978) attempted to quantify slow cancellous bone loss by measuring trabecular mean wall thickness. Samples taken from the iliac crest have demonstrated that the mean trabecular wall thickness decreases with advancing age (average thickness is 50 um). The decrease is postulated to be the result of a decrease in osteoblast longevity rather than a decrease in osteoblast activity. The mean formation time of iliac trabecular bone packets was determined to be 69 days.

Trabecular bone properties in the proximal femur

Martens et al. (1983), studied the mechanical behavior of trabecular bone at the upper femoral region. Measurements were made along and at right angles to the femoral neck axis. The authors reported large variation in compressive strength and modulus of elasticity within and between femoral bone samples. Anisotropy and differences in anisotropy for the different regions were also observed. A significant correlation between mechanical properties (strength and modulus) and bone mineral content of the specimen was found. Along the neck axis the mean elastic modulus for the femoral head region was determined to be 900 (MN/mm²), for the femoral neck region 616 MN/mm², and for the intertrochanteric region 263 MN/mm² (strain rate; 7/sec).

Brown and Ferguson (1980) tested trabecular bone samples removed from the proximal femur. Samples were oriented such that faces corresponded with the superior-inferior, medial-lateral, and anterior-posterior directions. Low strain rate (0.004/sec) compression tests were performed, evaluating the apparent elastic modulus and yield strength, in the three perpendicular testing directions.
Rohmann et al (1980) measured the time independent properties of cancellous bone in the femoral head and condyles of 20 cadaveric human femora. In the femoral neck, samples were cut at right angles to the direction of loading in the one-legged stance position, while in the condyles the cuts were oriented at right angles to the diaphyseal axis. Using a strain rate of 0.0028/sec, they observed that the material properties varied greatly. Comparing the compressive strength of 299 samples from 8 individuals, the maximum value of 22.9 M/mm², is more than 40 times the minimal value of 0.56 N/mm² while the apparent density of the same specimens differ by a factor of 7 only.
1.7 Loads on Proximal Femur

To investigate the state of stress in the proximal femur and determine propensity for failure, several different classes of load cases should be considered. The four most general cases of interest are loads resulting from, 1) static two leg stance, 2) static one leg stance, 3) dynamic walking, and 4) falling. Many investigators have attempted to quantify the magnitude and direction of the important loads that influence the mechanics of the hip joint under various types of activity. The hip joint, surrounded by several groups of large muscles and strong ligaments, is a complicated structure which varies from individual to individual. Consequently, the uncertainty of these muscle and joint forces has slowed the understanding of this structure on the biomechanical level. Investigators have resorted to using simple load cases and/or making assumptions about forces in muscles based on their size, electrical activity, or the use of optimization techniques. To date, most is known about the forces surrounding the hip-joint only under the most simple conditions; one and two legged stance. Some authors have investigated the loads on the femoral head under more complicated loading conditions but information about forces in the musculature is lacking. Following is a summary of work reported in the literature regarding loading on the proximal femur under various conditions.
1.7.1 Two-legged Stance

Rydell (1966) reported that during two legged stance insignificant muscular forces act in the horizontal plane and therefore the horizontal component of the force acting at the hip joint is negligible. Quoting results of Pauwels (1935) he stated that the vertical component of the force on the femoral head is equal to 1/3 of the total body weight. The direction of the resultant force is along the mechanical axis of the femur as defined by Backman (1957) which passes through the center of the femoral head to a point located midway between the two femoral condyles. Due to the simplicity of this load case few authors can disagree with Rydell's conclusions, although the low magnitude of the resultant loads on the proximal femur have made this load case relatively uninteresting from the standpoint of investigating failure of the proximal femur or femoral prostheses.

1.7.2 One-legged Stance

The primary difference from two-legged stance is that significant muscular forces are now required to maintain static equilibrium. The principal muscle group needed to maintain stability are the abductors acting at the greater trochanter; the gluteus maximus and gluteus minimus. A single force is usually used to represent the combined action of these two muscles. A total of three forces are then seen to act on the torso, 1) gravity, 2) the resultant of the abductors, and 3) the joint reaction force
at the acetabulum. Several authors have investigated the directions and magnitudes of these forces. The first significant contribution to the resolution of forces in the hip joint was by Pauwels (1935). He determined that a joint force of 2.92 times body weight is directed downward at 15 degrees to the vertical on the femoral head, while the resultant muscle force at the greater trochanter of 2.13 times body weight is directed upward at 21 degrees to the vertical.

Inman (1947) used electromyography to study the action of the abductor muscles and to locate the line of action of the resultant force. For the level pelvis, the resultant abduction muscle force at the greater trochanter was determined vectorially to be 1.4 to 1.9 times body weight at 21 degrees to the vertical, and the joint force was determined to be 2.4 to 2.6 times body weight at 10 to 15 degrees to the vertical. Results for the pelvis sagging were higher, while those for the pelvis tilted upward were lower.

Rydell (1966) used an instrumented hip prosthesis to record forces on the femoral head during various activities. Although he mentions that the results are obtained under conditions that are not exactly physiological since the joint capsule and ligament structure were different that of a normal hip, his results are significant. During one-legged stance, he measured a joint force of 2.5 times body weight directed 12 degrees from the vertical. However, no attempt was made to quantify the magnitude or direction of the resultant abductor force.

Many attempts have been made using static analysis combined with knowledge of muscle anatomy to determine the joint and abductor forces.
Williams and Lissner (1962) gave an example of the one-legged stance where the angle between the line of action of the resultant abductor force and the horizontal is 71 degrees with a magnitude of 1.8 times body weight. The line of action of the joint force based on static equilibrium was found to be 78 degrees from the horizontal with a magnitude of 2.6 times body weight. Mcleish and Charnley (1970) used radiographic measurements to determine the relevant muscles acting at the greater trochanter and made assumptions about forces based on each muscles cross-section. Total muscle force was determined to be between 1.2 and 1.5 times body weight while the joint force was determined to be between 2.2 and 2.4 times body weight.

The above analyses assume a three force system and hence the resultant abductor force and the joint force are coplaner. Rybicki though, demonstrates that the resultant force on the head of the femur can make an angle of 8 to 10 degrees with the frontal plane during one legged stance. As a result, previous experimental and analytical studies of the femur have applied this planar force system in a horizontal plane coincident with the femoral neck axis (Rohlmann, 1982; Vichnin, 1986). However, the subtleties of how the direction and magnitude of this force system might vary for different femoral antetorsion and cervico-diaphyseal angles has not been addressed in the literature.

1.7.3 Dynamic Analysis

Dynamic joint forces can be determined by a number of techniques. Previous investigations have made use of cinematographic measurements,
instrumented prostheses, and/or optimization methods. Sherig and Arvikar (1975) developed a mathematical model of the lower extremities and torso having 42 equilibrium equations with 31 muscle forces and assuming quasi-static loading conditions. Since there were 62 more unknown variables than equations, an objective function was chosen that minimized the sum of all the muscle force plus four times the sum of the moments at all the joints. A maximum hip joint force of 5.4 times body weight was calculated to occur just after the heel strike phase of gait. The angle of the peak force component is 8 degrees medial and 8 degrees posterior to the horizontal. The major muscles active during the heel strike phase were determined to be the abductor group consisting of the gluteus minimus, gluteus medius and tensor facial latae. The force generated by this group of muscles during the heel strike phase was determined to be 155 kg. Since no mention was made of the gait velocity, subject body weight and direction of muscular loads, it is difficult to extrapolate this data to other cases.

Paul (1976) used 16mm cine cameras and a six-channel force plate dynamometer to gather gait data. Using anatomical dimensions obtained from test subjects, the equations of equilibrium were solved to determine forces around the hip joint. The lines of action of simplified ligamentous and muscular groups were inferred from the measured dimensions corresponding to the relative angular position of the limb segments as viewed in the frontal and sagittal planes. The averaged maximum of hip joint forces for normal walking speeds were determined to be 4.9 times body weight with the load directions being at 21 degrees medial to the femoral mechanical axis as viewed in frontal plane and 12 degrees anterior to the mechanical axis as viewed in the sagittal plane. Muscle force magnitudes and directions were not mentioned.
Crowninshield et al. (1978) also used biplanar photography along with a force plate to gather information on gait. The collected data was used along with a mechanical model of a lower extremity consisting of 68 constraint equations for the hip, knee and ankle joint including the action of 30 muscles. An optimization technique that applies an objective function based on muscle size and allowable forces was used to solve for the desired joint and muscle loads. For walking speeds that varied from 0.95 to 1.05 m/sec, the averaged maximum hip joint force was 4.6 times body weight directed along a line 27 degrees medial to a vertical line as viewed anterior to posterior in the frontal plane and 24 degrees posterior to a vertical line as viewed from medial to lateral in the sagittal plane. Predicted muscle force and EMG activity were given for the gait cycles of the subjects modeled.

Rohrle et al. (1984) using an optimization procedure that minimizes muscle forces, obtained a maximum hip joint force during the heel strike phase of gait of 4.3 times body weight at a walking speed of 1.2 m/sec. The resultant force is directed along a line 0.6 degrees medial to the vertical as viewed anterior to posterior and 12 degrees posterior to a vertical line as viewed medial to lateral. The maximum joint force throughout the gait cycle however, was found to be 6.4 times body weight and occurred during the toe-off phase. Calculated muscle forces were given for the heel strike and toe off phases of gait but no information on leg orientation at these times was discussed.

Patriarco et al. (1981) used an optical kinematic data acquisition system and an analytical optimization procedure to specifically determine muscle forces during a walking cycle. At a walking speed of 1.04 m/sec, the
resultant hip joint torque and force was determined and found to be similar to results of Crowninshield et al (1978). No hip joint contact force was mentioned but detailed leg orientation and muscle forces were presented. The locations of muscle origins and insertions were also available (Patriarco, 1982). The authors concluded that the precision achieved in calculating joint torques dominates the muscle force distribution and is more influential in predicting muscle force activity than the mathematical techniques and assumptions used to compensate for muscle redundancy.

Methods using instrumented endoprostheses can give a more accurate measurement of joint contact forces, although information on muscle forces are not determined. Rydell (1966) performed such an experiment implanting a prosthesis having strain gages applied to the neck. At similar walking speeds as considered by Crowninshield, Rydell reports a maximum force of 3.3 times body weight which deviates no more than 30 degrees from the femoral diaphyseal axis. English and Kilvington (1979) also implanted an instrumented prosthesis in a patient. They reported peak loads of 2.7 times body weight at intermediate walking speeds but their results are of little use because they only measured loads acting along the axis of the prosthetic neck.

1.7.4 Falls

To date no data is available on the forces generated around the hip joint during accidental falls. By investigating the type of falls that are common, one can approximate the loading present on the proximal femur
during these events. An increase in the propensity for falling is usually accompanied by poor physical activity and muscular atrophy. Specifically there has been reported a decrease in the size of fast twitch muscle fibers in the elderly (Aniansson et al. 1984). Therefore, as a first approximation, muscular loads may play only a minor role in generating load on the proximal femur during falls. More important are height of the fall, body orientation, and the constraints ligaments place on the range of motion of the femur.

The major circumstances surrounding falls in the elderly have been reported to be: 1) drop attacks or confusion 25%-45% (Sheldon, 1960); 2) tripping while ascending or descending stairs 25% (Lucht, 1971); and 3) other extrinsic causes such as a loose rug or slippery surface 39% (Lucht, 1971).
2.0 Femoral Trabecular Bone Properties by QCT

Trabecular bone plays a major role in maintaining the structural integrity of the proximal femur. Within the subcapital region, where the majority of cervical fractures are observed to occur (Kleenerman and Marcuson, 1970), trabecular bone accounts for an estimated 70 percent of bone strength (Lotz et al., 1987). Therefore, the success of any noninvasive technique for the estimation of proximal femur fracture risk relies on the accurate estimate of this tissue's mechanical properties.

The structural properties of trabecular bone are dependent on many factors, the most investigated of these being density. Carter and Hayes (1976), tested specimens of human and bovine trabecular bone spanning a large range of apparent density (0.07 to 0.97 gm/cm³). Their results indicated that the compressive strength is proportional to the square of the apparent density,

\[ S = 55\rho^2, \]

for a strain rate of 0.03 sec⁻¹ where \( S \) is in MPa and \( \rho \) is in gm/cm³. In addition, the compressive modulus was observed to be proportional to the apparent density cubed,

\[ E = 3070(\rho)^3, \]

also for a strain rate of 0.03 sec⁻¹, where \( E \) is in MPa. Huskies et al. (1984), performed similar studies with cancellous bone specimens from several different species, and indicated that a linear relationship between
density and modulus, or strength, is equally accurate over the small ranges of density seen in a single species. More recently, Rice et al. (1988), presented a thorough statistical review of previously published data for trabecular bone. They suggest that both Young’s moduli and strength are proportional to the square of apparent density and hence are proportional to each other.

Ducheyne et al. (1977) also demonstrated a strong relationship between bone density, strength and modulus but reported that density alone could not completely explain the variation of material properties observed. They suggested that trabecular architecture also plays an important role. Harrigan et al. (1981) attempted to quantify this role of architecture by developing a single equation for elastic modulus as a function of apparent density and trabecular orientation. They postulated that the elastic modulus is proportional to the apparent density raised to the 2.2 power and to a stereological parameter raised to the 2.7 power. However, two major experimental studies of trabecular bone properties in the proximal femur (Brown and Ferguson, 1980; Martens et al., 1983) have shown that density differences result in ten to one hundred fold differences in properties, whereas anisotropy accounts for two to four fold differences. Hence, it is reasonable to assume that a first order estimation of the material properties of trabecular bone can be made with knowledge of density alone.

Many non-invasive techniques are currently used for the estimation of bone density. Photodensitometry involves a radiographic measure of bone density, but when applied to the axial skeleton the accuracy suffers from large influences of beam hardening and radiation scattering (Colbert and Bachtell, 1981). Single photon absorptiometry (SPA) has been reported to
yield highly accurate and reproducible results for the determination of appendicular bone density (Grubb et al., 1984). This technique however, is not applicable to regions of the axial skeleton due to its inability to separate out the influence of overlaying tissue. Dual photon absorptiometry (DPA) has been shown useful at determining bone density of the axial skeleton where large amounts of soft tissue are present (Dunn et al., 1980), but interpretation of the results must be made with care due to their strong sensitivity to changes in bone cross-sectional geometry. In addition, the trabecular bone density as measured by these techniques is influenced by the surrounding cortical bone, the magnitude of which depends on the particular anatomical site under investigation.

Quantitative computed tomography (QCT) provides a number of advantages over other techniques (Revak, 1980; Genant et al., 1985). These include the ability to determine linear absorption coefficients in easily defined volumes, which enables a detailed mapping of bone density, including the separation of cancellous and cortical bone. However, there are some inherent limitations in the accuracy of this technique. Using single energy scans, the presence of variable amounts of fat within the marrow can introduce errors in the estimate of bone density on the order of 30% (Nazess and Veter, 1985). Also, when scanning structures deep within the body, the beam hardening effect can result in a decrease in the effective linear attenuation coefficient and a underestimation of tissue density (Lampmann et al., 1984). Despite these sources of error, the ability to predict the material properties of trabecular bone from QCT data of the spine and tibia has been documented (McBroom et al., 1985; Hvid et al., 1987). The purpose of this study was to extend these studies to the proximal femur by investigating the value of quantitative computed
tomography for the assessment of apparent density, strength and elastic modulus of trabecular bone in this region.

2.1 Materials and Methods

Forty-nine cylindrical specimens of human trabecular bone were machined from the left femur of four fresh/frozen human pairs ranging in age from 28 to 90 years. The human femora were harvested from individuals whom had no documented disorders which would affect bone strength (other than possibly osteoporosis). After removal of the soft tissue, the proximal one third of each bone was placed in a specially designed acrylic tank (Fig. 2.1). The distal end of each specimen was then rigidly clamped such that the plane formed by the neck and diaphyseal axis was parallel to the bottom surface of the box. Along the bottom of the box a rectangular nylon bar served as a reference axis. A calibration phantom, consisting of five chambers, each with different concentrations of K$_2$HPO$_4$ (0,5,10,20 and 30 gm/100cc) was also included in each scan. A laser target incorporated within the scanner, was used to align the specimen within the gantry. Five millimeter thick scans were made at five millimeter intervals along the neck axis from the base of the femoral neck toward the femoral head (Fig. 2.2).

Scans were performed using a GE 8800 scanner set at 120 KVP, 240 MAS, and a 25mm field. The resulting pixel resolution was approximately 0.7 mm. The images were reconstructed using a Gould FD5000 imaging processing system and in-house software. After reconstruction, scale factors were determined for each image and reference axes were placed at a predefined
Figure 2.1: Proximal femur within acrylic tank.
**Figure 2.2:** Location of QCT scans within the femoral neck.
corner of the cross-section of the nylon reference bar (Fig. 2.3). The location of each specimen was determined within the appropriate cross-section and the mean specimen QCT number calculated.

While still within the acrylic tank, the bones were imbedded in a rigid polyurethane foam (402A, 402B; Atlas Industries) to maintain the relative position of the bone to the reference axis. The bone/foam composite was then removed from the box and frozen at -20 degrees centigrade. While still frozen, the composite was sectioned (band saw with new 18 tooth/inch blade running at 3000 ft/min) such that the resulting bone slabs coincided with the scanned regions. Cylindrical specimens with a diameter of 9 mm were then cut from each slab using a hole saw (17 teeth/inch) at 640 rpm, the cylindrical axis of each specimen being perpendicular to the cut faces of each slab. The opposing flat faces of each specimen were then ground parallel using a metallurgical grinder with 300 grit paper while being kept moist with normal saline. After grinding, the specimens were stored at -20 degrees centigrade until testing. Prior to testing, they were thawed and kept fully moist.

The specimens were tested in compression using an electro-hydraulic materials testing system (Model 1331, Instron Corp., Canton Ma) at a strain rate of 0.03 sec\(^{-1}\) until the specimens were compressed to 85 percent of their original length (15 percent strain). The load was measured by the calibrated load cell of the test system, and specimen deformation was measured by an axial extensometer mounted directly on the load platens near the specimen. The data was collected using an IBM personal computer and analyzed using in house software. A fast fourier transform was performed to determine the frequency content of the signal to determine the
Figure 2.3: QCT image of cross-section through the femoral neck.
appropriate cutoff frequency for a low-pass filter to eliminate superimposed noise. Based on the determined cutoff frequency, the appropriate constants for a five-point low-pass filter were determined and the data filtered.

The slope of the load-deflection curve was determined by calculating the regression line in a moving cell fashion for a series of \( n \) consecutive points starting at the beginning of the data and stepping up to the peak load (where \( n \) = the number of data points to the peak load divided by four). For example, where there were 250 data points to the peak load, \( n = 63 \) and regression lines were determined from points 0 to 62, 1 to 63, 2 to 64 ... 187 to 250. The regression line with the best \( r^2 \) was used to represent the slope of the load-deflection curve in its most linear region. This method gave repeatable results which corresponded well with values obtained by hand from recordings of the load-deflection data. This slope was then multiplied by the initial specimen length and divided by the initial specimen cross-sectional area to obtain the elastic modulus. The ultimate strength was determined by dividing the highest load carried by the specimen before collapse by the initial specimen cross-sectional area.

After testing, the specimen tissue and apparent densities were measured using the technique presented by Carter and Hayes (1977). The marrow was first removed from the specimens by ultrasonic cleaning with ethanol. Next, the specimens were immersed in distilled water and vacuum degassed, and then weighed while suspended from an analytical balance (Mettler #H51AR, Hightstown NJ) to determine the submerged weight. They were then centrifuged at 8,000g on blotting paper for fifteen minutes to remove residual water from the pores and weighed in air to determine the hydrated
tissue weight. The volume of bone tissue in cubic centimeters was calculated as the difference between the hydrated tissue weight and submerged weight expressed in grams. Tissue density of the specimen was found by dividing hydrated tissue weight by bone tissue volume. Apparent density of the specimen was calculated by dividing hydrated tissue weight by bulk volume of the specimen as determined by micrometer measurements prior to testing.

2.2 Results

The relationship between specimen apparent density and corrected QCT number is shown in Figure 2.5. The expression which best describes the data was

$$\rho = 0.012(QCT) + 0.17$$  \hspace{1cm} (2.1)

(R² = 0.73, see = 0.081gm/cc, p<0.001) where ρ is the apparent density (gm/cc) and QCT is the corrected QCT number (%K₂HPO₄). In order to determine if distinct density/QCT relationships existed for each individual, separate linear regressions were calculated for the groups of specimens from each donor. The resulting standard errors of both the regression slope and intercept demonstrated that no significant difference (t<2.0; p>0.05) existed between each individual regression and that for the pooled population. This indicates that no systematic error existed between the density/QCT relationships for each donor and that expression 2.1 accurately describes the pooled set of data.
Figure 2.4: Typical stress-strain curve.
Figure 2.5: Apparent density versus corrected QCT.
Compressive Strength

Previous studies have demonstrated that the strength could be expressed as a power function of density (Carter and Hayes, 1977). Anticipating similar results, the data was plotted on log-log scales (Fig. 2.6). The data were well described by a line with slope 1.8,

\[ S = 25\rho^{1.8} \]  \hspace{1cm} (2.2)

\( R^2 = 0.93, \ p < 0.001, \ \text{see} = 2.28 \ \text{MPa} \), where \( S \) is the compressive strength (MPa) and \( \rho \) is the apparent density (gm/cc).

Figure 2.7 displays the relationship between the compressive strength and the corrected QCT number. The data are well described by a line with slope 1.4,

\[ S = 0.07(QCT)^{1.4} \]  \hspace{1cm} (2.3)

\( R^2 = 0.89, \ p < 0.001, \ \text{see} = 2.78 \ \text{MPa} \).
Figure 2.6: Compressive strength versus apparent density.
Figure 2.7: Compressive strength versus corrected QCT.
Compressive Modulus

The relationship between the compressive modulus of each specimen and the specimen apparent density is displayed in Figure 2.8. Plotting the data on log-log scales demonstrates the data is described well by a line with slope 1.4,

$$E = 1310(p)^{1.40}$$  \hspace{1cm} (2.4)

($R^2 = 0.91, p<0.001, \text{see}=158 \text{ MPa}$), where $E$ is the elastic modulus (MPa).

Figure 2.9 displays the relationship between the elastic modulus and the corrected QCT number. A good correlation is also observed, with the relationship well described by the expression,

$$E = 11(\text{QCT})^{1.2}$$  \hspace{1cm} (2.5)

($R^2 = 0.89, p<0.001, \text{see}=168 \text{ MPa}$).

An approximately linear relationship exists between the strength and elastic modulus

$$S = 0.012(E)^{1.04}$$  \hspace{1cm} (2.6)

($R^2=0.94, \text{see} = 2.03 \text{ MPa}; \text{Fig. 2.10}$) which suggested a constant strain at failure. A plot of failure strain (strain at maximum stress) versus specimen apparent density demonstrates that indeed failure strain is
Figure 2.8: Compressive modulus versus apparent density.
Figure 2.9: Compressive modulus versus corrected QCT.
Figure 2.10: Compressive strength versus elastic modulus.
independent of density ($R^2 = 0.12$, $F = 6.7$; Fig. 2.11), with the resultant mean being 2.7 percent.

2.3 Discussion

Our results demonstrate that a strong relationship exists between trabecular bone apparent density and corrected QCT number. The variability in the data resulted in errors on the order of 20 percent, being defined as the standard error of the density-QCT regression divided by the population mean density. This accuracy lies between the values of 8 and 30 percent reported elsewhere for single energy QCT (Genant et al., 1985; Hazess and Vetter, 1985).

Strength correlated significantly with apparent density, being proportional to density raised to the 1.8 power. Expression 2.2 is in fair agreement with that presented by Carter and Hayes (1977). Results of a two-tailed t-test revealed no statistically significant difference between the exponents 1.8 and 2.0 ($t < 2.0$; $p > 0.05$), but the constant multiplier presented by Carter and Hayes is significantly higher than that determined here. Architectural differences between specimens used in the two studies likely accounts for this disparity. In general, the specimens tested in this study were fabricated with the testing axis parallel to the femoral cervical axis and hence at some angle to what may be considered the 'principal' architectural direction; that of the primary compressive trabeculae (Fig. 2.2). Yet, the testing axis of other specimens closely aligns with the 'principal' direction of a secondary system of trabeculae.
Figure 2.11: Ultimate strain versus apparent density.
known as the principal tensile trabeculae. This diversity of architecture within the specimen population is suggested by the somewhat large (thirty-four percent) standard error in the regression between strength and density.

Corrected QCT was also a good predictor of strength, the standard error of the regression being 22 percent greater than that for the relationship between strength and apparent density. This magnitude of this additional error is consistent with that due to variable amounts of marrow fat (Laval-Jeantat et al., 1986). The increased variability is most noticeable at low specimen densities (Fig. 2.7), where a larger portion of specimen volume is composed of marrow.

The elastic modulus also correlated well with specimen apparent density. The power relationship presented here however, differs significantly \((t>2.0, p=0.05)\) from the cubic expression presented by Carter and Hayes (1977) and the squared relationship suggested by Rice et al. (1988). These differences also may be due to architectural differences, as mentioned above.

As with compressive strength, specimen elastic modulus correlated well with corrected QCT number. However, in contrast to the strength data, only a small additional error (6%) was apparent in the modulus/QCT relationship over and above that observed for the modulus/density relationship. This reduction in 'fat-induced' error is likely the result of a weaker dependence of modulus on density; that is, if modulus is less dependent on density than strength, errors in density measured via QCT (due to fat variability) will not affect modulus estimates as strongly as it will those
for strength. Nonetheless, increased variability is still apparent in the modulus vs QCT data at low specimen densities (Fig. 2.9), again suggesting the influence of marrow fat variability.

The linear relationship between strength and modulus presented here was statistically identical to that presented by Klever et al. (1984) and further supports the hypothesis of a constant strain at failure for trabecular bone (0.027 percent).

In summary, the data presented here demonstrate that apparent density, compressive strength and elastic modulus can be predicted with good accuracy using single-energy QCT. Although this is true, it is important to realize that these specimens were all tested in the same direction relative to the anatomical cervical axis, which serves to partially normalize to a particular architecture. As a result, the QCT data like density, is likely only serving as a relative measure of material properties, the true orthotropic values being dependent on the local architecture. Still, subtle differences in architecture and marrow fat content likely do exist between specimens in this study, and yet the majority of the variance (90 percent) in the strength and elastic modulus data could be explained by corrected QCT alone.

Fat content remains an important variable to consider when using single-energy QCT to follow the progression of osteoporosis within a particular patient, where significant changes in fat content can mask small changes in bone density (Mazess and Vetter, 1985). Nevertheless, fat content may not be as critical when using QCT data for analytical studies, such as finite element analysis, where the required discretization of data results in loss
of subtle details of the three-dimensional material variation. Provided the
good correlation observed between single-energy QCT and material property
data, additional uncertainty introduced through not incorporating fat
content, would likely not likely the results of such analytical
investigations.
3.0 Material Properties of Metaphyseal Bone in the Proximal Femur

The elastic and ultimate properties of femoral cortical bone have been measured by many investigators. These efforts have primarily focused on diaphyseal bone, where the thick cortex allows harvesting of specimens of sufficient size for standard tension and compression tests. However, the mechanical properties of the thin cortical shell at the ends of long bones is less well understood. Previous finite element and analytic studies have assumed that this thin cortex has similar mechanical properties to bone in the diaphyseal region. Recent investigations of subchondral bone in the femoral head (Brown and Vrahas, 1984) and the metaphyseal bone in the proximal tibia (Murray et al., 1984) however, have suggested that this cortical shell may have markedly reduced mechanical properties in comparison to diaphyseal bone. If this is true, the contribution of cortical bone to the strength of these regions has been overestimated in many previous analytic studies. In addition, since osteoporosis is thought to affect trabecular and cortical bone at different rates and at different times (Riggs et al., 1982), this issue is important to consider when investigating the influence of this disease on the load carrying capacity of the proximal femur. Overestimating the contribution of the cortical shell would lead to an underestimate of the osteoporosis-linked decrease in proximal femur strength, which is thought to be primarily due to a reduced of the metabolically active trabecular bone.

The thin geometry of the cortical shell in the proximal femur precludes the fabrication of standard specimens for tensile and compression tests. Other investigators have overcome this difficulty by using nonstandard
specimen geometries. For example, to determine the material properties of subchondral bone in the femoral head, Brown and Vrăhas (1984), fabricated spherical caps which were tested under polar point loads and the material properties were inferred from corresponding analytical shell solutions. Similarly, Murray et al. (1984), fabricated thin disks from the proximal tibia that were tested as centrally loaded circular plates. The irregular geometry of the cortical shell in the proximal femur also necessitates the use of very thin specimens. Therefore, flat, rectangular prismatic plates, fabricated from cortical bone in the proximal femur, were tested in three-point bending and the elastic modulus and ultimate strength inferred from comparisons between experimental results and the corresponding analytical thin plate solutions. The objectives of this study were: 1) to validate the formulations for deriving the elastic modulus and ultimate strength from three-point bending load-deflection data using specimens of wood and acrylic; and 2) to determine if there exists a significant difference between the modulus and strength of the thin cortical shell within the proximal femur and that of diaphyseal bone.

3.1 Materials and Methods

A total of 158 cortical shell specimens were machined from the left femur of five fresh/frozen femora, harvested from human cadavers ranging in age from 28 to 90 years. The specimens were taken in both the longitudinal and circumferential directions from the distal femoral neck, intertrochanteric and diaphyseal regions. Within the femoral neck, the longitudinal direction aligned with the femoral neck axis. The bone
specimens were prepared by first thawing frozen bones and sectioning them at several locations (Fig. 3.1). Next, portions of the cortex along with the underlying trabecular bone were removed from each section using a hand saw. The thickness of the cortical shell was then measured using metric calipers and the trabecular bone carefully ground away using a metallurgical grinder, first on 300 and then 600 grit abrasive paper. After achieving a planar endosteal surface free of defects, the specimen was inverted and a minimum of material ground from the periosteal surface until a thin region of constant thickness was obtained. The local architecture was observed by transmission light microscopy at low magnification (10x). Where a definite Haversian architecture was observed, an effort was made to align the axes of the specimen with the material axes. The resulting plate thickness ranged from 0.18 to 0.4 mm. The specimen widths were held near 5.0 mm while the lengths were maintained at 7.0 mm. All bone samples were kept moist with normal saline during all phases of fabrication and testing.

The specimens were tested using an electro-hydraulic materials testing system (Model 1331, Instron Corp., Canton Ma.) with specially designed hardware to apply the three-point bending loads (Fig. 3.2). This bending load was applied at such a rate so as to produce a strain rate of 0.05 sec$^{-1}$ at the location of maximum stress at the bottom surface of the plate. The resulting data was collected using an IBM personal computer and analyzed using in house software. A fast fourier transform was performed to determine the frequency content of the signal and the appropriate cutoff frequency for a low-pass filter to eliminate superimposed noise. Based on the determined cutoff frequency, the appropriate constants for a five-point low-pass filter were determined and the data filtered.
Figure 3.1: Section Locations within the proximal femur.
Figure 3.2: Three-point bending test hardware.
After testing, the specimens were dried and weighed on an analytical balance to an accuracy of 1 mg (Mettler #H51AR, Hightstown NJ). Densities were calculated by dividing specimen volume (as determined from moist specimen dimensions) by the specimen dry weight.

Provided that a typical specimen had a small thickness as compared with its width and length, the analytic relationship used to estimate the elastic modulus from the load-deflection data was based on the theory of thin plates (Timoshenko and Woinowsky-Krieger, 1959).

\[ E = \frac{PL^3(1-\nu^2)}{48 \delta I} \]  (3.1)

where \( E \) is the Young's modulus (MPa), \( \nu \) is the Poisson ratio, \( P \) is the applied load (Nt), \( L \) is the specimen length (mm), \( \delta \) is the specimen deflection at mid span (mm), and \( I \) is the cross sectional moment of inertia (mm\(^4\)).

Expression 1 is dependent on both the elastic modulus \( E \) and the Poisson ratio \( \nu \). The value of \( \nu \) was not measured but rather was assigned a value of 0.3 (Brown and Vrahos, 1984). A sensitivity analysis of the influence of variations of \( \nu \) (from between 0.2 to 0.4) on the calculated modulus \( E \) was performed and demonstrated that errors resulting from variation of \( \nu \) were small as compared to those from other sources.

Additional refinement to expression 1 was made to account for the concentrated nature of the applied loads (Timoshenko and Goodier, 1970):

\[ E = \frac{PL^3(1-\nu^2)}{48 \delta I} + \frac{PL}{4c} \left( \frac{6}{5} - \frac{3\nu}{4} \right) - 0.21P \]  (3.2)
Assuming \( v = 0.3 \) gives
\[
E = \left( \frac{P}{h} \right) \left( \frac{L^3}{52.7 \cdot 1} \right) \left( 1 + 2.85 \left( \frac{h}{L} \right)^2 - 0.84 \left( \frac{h}{L} \right)^3 \right).
\] (3.3)

The slope of the load-deflection curve used in expression 3 (\( \Delta P/\Delta \delta \)) was determined by calculating a best fit regression line to the data. This regression line was calculated in a moving cell fashion for a series of \( n \) consecutive points starting at the beginning of the data and stepping up to the peak load, where \( n \) = the number of data points to the peak load divided by four. For example, where there were 250 data points to the peak load, \( n = 63 \) and regression lines were determined for points 0 to 62, 1 to 63, 2 to 64 ... 107 to 250. The regression line with the best \( R^2 \) was used to represent the slope of the load-deflection curve in its most linear region. This method gave repeatable results which corresponded well with values obtained by hand from recordings of the load-deflection data.

The travel of the indenter was assumed to equal the beam deflection (Fig. 3.3). Therefore, any local deformations present at the points of load application would lead to an overestimation of the true beam deflection. The magnitude of this local plastic flow varies for different specimen materials and indenter geometries. Thus the magnitude of the local deformation was determined experimentally using the three-point test indenter and the particular specimen material of interest. We assumed that this deformation is a function of the applied load, the specimen width, and the specimen thickness

\[
\delta = f(P,b,h)
\] (3.4)

where \( P \) is the applied load, \( b \) is the specimen width, and \( h \) is the
thickness (Fig. 3.3). To determine the nature of expression (3.4), experiments were performed with oak and acrylic. These studies consisted of the application of a concentrated load to a slab of material while recording the resulting force/displacement relationships (Fig. 3.4).

The results demonstrated an initial nonlinear region at the initiation of contact, followed by a highly linear zone (Fig. 3.5). This linear region was used to determine a relationship between the contact load and the local deformation. Slab tests were performed for a series of specimen widths and thicknesses in order to determine their influence on the magnitude of the local deformation. A linear relationship of the following form was assumed

$$\left( \frac{\Delta P}{\Delta \delta} \right)_d = \frac{1}{\Phi} = K_1 (b) + K_2 (h) + K_3$$  \hspace{1cm} (3.5)

where $1/\Phi$ is the slope of the local deformation/deflection curve, $w$ is the specimen width and $t$ is the specimen thickness. By measuring $1/\Phi$ from the results of the slab tests of several samples of varying widths and thicknesses, the constants $K_1$, $K_2$ and $K_3$ were determined for each material. Thus, given the specimen width, the value of $\Phi$ was determined for each sample, and the deflection due only to the local deformation ($2\Delta P \Phi$) was subtracted from the total beam deflection $\delta$. This gives a modified form of the equation (3.3)

$$E = K \left( \frac{\Delta P}{\Delta \delta - 2\Delta P \Phi} \right) ,$$ \hspace{1cm} (3.6)

where $K$ is the constant multiplier of equation (3.3). The factor of 2 in the denominator is required since the local deformations are occurring both at the top and at the bottom of the beam (Fig. 3.6).
Figure 3.3: Beam dimension definitions.
Figure 3.4: Slab test configuration.
Figure 3.5: Slab load-deflection curve.
\[ \triangle P = \text{Applied Load} \]
\[ \triangle D = \text{Measured Displacement} \]
\[ \text{True Deflection} = \triangle D - 2 \triangle P \phi \]

**Figure 3.6:** Modified beam model.
The expression used to estimate the material ultimate strength assumed brittle behavior, with no yielding occurring in the material prior to failure. In this situation the stress varies linearly from the neutral axis, and beam theory, with a correction for the concentrated nature of the applied loads, applies:

$$\sigma_{\text{max}} = \frac{PLc}{4I} - 0.133 \left( \frac{P}{bc} \right), \quad (3.7)$$

where $c$ is one half the beam thickness, $b$ is the specimen width and $P$ is equal to the highest load ($P_{\text{ult}}$) carried by the specimen before fracture (Timoshenko and Goodier, 1970). This calculated breaking strength of the beam can be related to the material ultimate tensile strength by the experimentally determined parameter; the 'rupture factor' (Roark, 1975). This rupture factor is defined as the calculated maximum stress in the outer fibers of the beam at failure divided by the ultimate tensile stress of the material. This parameter signifies that a finite portion of the specimen cross-section needs to fail before structural failure results. For brittle materials this factor is reported to be between 1.60 and 1.75. Therefore, the material ultimate tensile strength can be related to the calculated maximum stress by

$$S_u = \left( \frac{\sigma_{\text{max}}}{R} \right) \quad (3.8)$$

where $S_u$ is the material ultimate tensile strength and $R$ is the rupture factor.

Given the numerous measurements performed for each calculation of modulus and strength, some estimate of the maximal absolute error inherent
in the results is appropriate. This error was determined given the magnitude of error present in the measurement of the specimen dimensions and the assumption of a Poisson ratio of 0.3. The bounds for the calculated parameter $\Delta F$ (modulus or strength) was determined given the bounds for the error of each of the variables $\Delta a_i$ (specimen length $l$, width $b$, thickness $h$, and Poisson ratio $\nu$). Using elementary calculus of errors

$$\Delta F = \sum_{i=1}^{k} \Delta a_i \left| \frac{f(x_1(a_1, \ldots, a_k))}{x_1} \right|, \quad (3.9)$$

where $f(x_1)$ represents the partial derivative of the function with respect to each of the variables. For the calculation of the elastic modulus, using equations (3.1) and (3.9) the resulting expression for the error bounds is

$$\Delta E = \frac{P}{4\delta} \left( \Delta l \left( \frac{3l^2(1-\nu^2)}{bh^3} \right) + \Delta b \left( \frac{l}{b^2h^2} \right) + \Delta h \left( \frac{3l^2(1-\nu^2)}{bh^4} \right) + \Delta \nu \left( \frac{3}{bh^3} - \frac{2\nu}{bh^3} \right) \right). \quad (3.10)$$

For the calculation of the bending strength, using equations (3.7) and (3.9), the resulting expression for the bounds of error is:

$$\Delta S = \frac{3P}{2} \left( \Delta l \left( \frac{1}{bh^2} \right) + \Delta b \left( \frac{1}{b^2h^2} \right) + \Delta h \left( \frac{2l}{bh^3} \right) \right). \quad (3.11)$$

The error bars displayed in all following figures represent the range of total error in the dependent variable as determined from the above formulations.

To verify the accuracy of the above formulations for determining the elastic modulus and ultimate strength, specimens fabricated from materials with known properties (wood and acrylic) were tested. Rectangular beams of varying thickness (0.4, 0.6, 0.8, 1.0mm) and of width and length similar to
what was expected for the bone samples, were fabricated from bulk material. In addition, a series of acrylic tensile specimens were fabricated to determine the true elastic modulus and strength. These cylindrical specimens were 4.5mm in diameter and 26mm long. They were tested to failure using the electro-hydraulic system, with the load measured using the calibrated load cell of the test system and the specimen deformation measured using a contact extensometer (Model #2620-532, Intron Corp, Canton Ma) attached directly to the specimen over a known gage length (12.5 mm).

3.2 Results

To estimate the influence of local deformations on the determination of the elastic modulus, a series of 12 slab load-deflection tests were performed for both wood, and acrylic. Multiple regression was performed with the data and the values of $K_1$, $K_2$ and $K_3$ for use in equation (3.5). These data are listed in Table 3.1 along with the results of an F-test (F), the significance level (p), and regression coefficient ($R^2$) for each regression.

<table>
<thead>
<tr>
<th>Material</th>
<th>$K_1$</th>
<th>$K_2$</th>
<th>$K_3$</th>
<th>F</th>
<th>p</th>
<th>$R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Oak</td>
<td>140</td>
<td>730</td>
<td>810</td>
<td>6</td>
<td>0.006</td>
<td>0.31</td>
</tr>
<tr>
<td>Acrylic</td>
<td>680</td>
<td>-1250</td>
<td>2000</td>
<td>46</td>
<td>0.0001</td>
<td>0.81</td>
</tr>
</tbody>
</table>
Wood

A typical load-deflection curve for oak tested in bending is shown in Figure 3.7a while the influence of the local deformations in the calculation of $E$ is demonstrated in Figure 3.7b. Without the correction for local deformations, the estimated value of $E$ was highly dependent on the material thickness, being approximately 20,000 MPa for a thickness of 0.04 mm and 10,400 MPa for a thickness of 1.0 mm ($F=78$, $p=0.0001$, $R^2=0.84$). When the correction for the local deformation was included (Fig. 3.7c), this dependency of the elastic modulus on thickness was reduced. However, a slight over-correction was introduced, resulting in an increase in the estimated modulus with thickness ($F=7.0$, $p=0.02$, $R^2=0.33$). The mean value of $E$ for the corrected data was determined to be 19950 MPa (see=3755).

The maximum fiber stress of the oak specimens was calculated using equation (3.7). The resulting values demonstrated no significant correlation with thickness ($F=0.90$, $p=0.36$, $R^2=0.3$), with the mean bending strength calculated to be 277 MPa (see=22). Using an assumed rupture factor for wood of 1.84 (Roark,1943), the calculated ultimate compressive strength was estimated to be 150 MPa.

The mean value of both the elastic modulus and compressive strength presented above are greater than that presented in the literature; 12,300 MPa and XXX MPa respectively. This is likely due to two factors, the first being that the mechanical properties of wood can vary greatly depending on such factors as moisture content. Secondly, the wood beam samples were fabricated from material between the porous growth rings. The exclusion of this porous material will serve to increase the measured properties as
Figure 3.7a: Wood beam load-deflection curve.
Figure 3.7b: Uncorrected wood modulus versus specimen thickness.
Figure 3.7c: Corrected wood modulus versus specimen thickness.
compared to literature values for the aggregate material.

Acrylic

Uniaxial tensile tests of six acrylic specimens fabricated from the same bulk material as the beam specimens were performed to determine the true elastic modulus and ultimate tensile strength. These tests resulted in an average modulus of 2980 MPa (see = 330) and average tensile strength of 72 MPa (see=4) both of which are within the published values of 2414 to 3102 MPa and 55 to 75 MPa respectively (Modern Plastics Encyclopedia, 1983).

Three-point bending test were performed with 16 acrylic specimens ranging in thickness from 0.4 to 1.2 mm. A typical load-deflection curve is presented in Figure 3.8a. The trend of decreasing modulus with thickness that was apparent for the wood specimens was not observed for acrylic (F=0.4, p=0.5, \( R^2 = 0.02 \)), the resulting mean modulus being 2890 MPa (see=270). Incorporating the local deformation correction again resulted in a slight over-correction, manifested as an apparent increase in modulus with specimen thickness \( (F=5,p=0.05,R^2 = 0.26; \text{ Fig. 3.8b}) \). The mean outerfiber strength, calculated using equation (3.7), was determined to be 126 MPa (see=12). Given the true tensile strength of 72 MPa, the bending strength and ultimate tensile stress were related by a rupture factor of 1.75.

The elastic modulus data as determined from the bending tests did not differ significantly from the values obtained from the tensile tests (t-test; \( t=0.62,p=0.5 \)). Therefore equation (3.3), which was used to determine the elastic modulus, appears to give accurate results. Also, since the
Figure 3.8a: Acrylic beam load-deflection curve.
Figure 3.8b: Uncorrected acrylic modulus versus specimen thickness.
Figure 3.8c: Corrected acrylic modulus versus specimen thickness.
value of the rupture factor (1.75) is within the expected range, the three-point bending test also appears to be an accurate method for the determination of the ultimate tensile strength. Since the geometry of the bone specimens were similar to those of acrylic, this empirical rupture factor of 1.75 was also applied to the cortical shell data.

Bone – Elastic Modulus

Slab tests were performed with 5 cortical bone specimens to determine the magnitude of $1/\phi$. The value this parameter was estimated to be approximately 4500. However, given the average bone specimen size, the magnitude of the error introduced by the local deformation was found to be small. All finished specimens were less than 0.5 mm in thickness, resulting in an error in the calculated modulus of less than 1 percent. Therefore, this correction for local deformations was not performed for the bone specimens.

Thirty-six specimens obtained from the femoral diaphysis were analyzed separately. Typical load-deflection curves for the longitudinal and transverse bone specimens are shown in Figures 3.9a and 3.9b and the results are presented in Table 3.4. The elastic modulus data (Fig. 3.10a) for the longitudinal direction demonstrated a significant correlation with specimen density ($R^2=0.60, p<0.001, \text{see}=1680 \text{ MPa}$), the mean value being 12700 MPa. In the transverse direction however, there was only a slight, non-significant variation of modulus with density (Fig. 3.10b, $R^2=0.22, p=0.05, \text{see}=1380 \text{ MPa}$), with the mean determined to be 5990 MPa. In addition, the resulting ratio of longitudinal to transverse moduli of was 2.1.
Figure 3.9a: Diaphyseal bone load-deflection curve for specimens fabricated in the longitudinal direction.
Figure 3.9b: Diaphyseal bone load-deflection curve for specimens fabricated in the transverse direction.
Figure 3.10a: Diaphyseal bone longitudinal modulus versus specimen apparent density.
Figure 3.10b: Diaphyseal bone transverse modulus versus specimen apparent density.
TABLE 3.4 - Diaphyseal specimen data

<table>
<thead>
<tr>
<th>Bone</th>
<th>Age</th>
<th>n</th>
<th>Orientation</th>
<th>E (MPa)</th>
<th>$\sigma_{\text{max}}$ (MPa)</th>
<th>$\delta$ (gm/cm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H399</td>
<td>81</td>
<td>7</td>
<td>Longitudinal</td>
<td>11030 (1180)</td>
<td>216 (12)</td>
<td>1.65 (0.05)</td>
</tr>
<tr>
<td>F</td>
<td>5</td>
<td></td>
<td>Transverse</td>
<td>5500 (645)</td>
<td>66 (10)</td>
<td>1.66 (0.03)</td>
</tr>
<tr>
<td>H449</td>
<td>27</td>
<td>5</td>
<td>Longitudinal</td>
<td>14660 (700)</td>
<td>250 (27)</td>
<td>1.82 (0.02)</td>
</tr>
<tr>
<td>M</td>
<td>4</td>
<td></td>
<td>Transverse</td>
<td>7210 (1080)</td>
<td>102 (24)</td>
<td>1.82 (0.03)</td>
</tr>
<tr>
<td>H458</td>
<td>70</td>
<td>3</td>
<td>Longitudinal</td>
<td>10380 (150)</td>
<td>191 (25)</td>
<td>1.66 (0.09)</td>
</tr>
<tr>
<td>F</td>
<td>2</td>
<td></td>
<td>Transverse</td>
<td>5350 (333)</td>
<td>74 (12)</td>
<td>1.72 (0.03)</td>
</tr>
<tr>
<td>H369</td>
<td>82</td>
<td>2</td>
<td>Longitudinal</td>
<td>12250 (1070)</td>
<td>217 (17)</td>
<td>1.70 (0.11)</td>
</tr>
<tr>
<td>M</td>
<td>3</td>
<td></td>
<td>Transverse</td>
<td>4960 (510)</td>
<td>72 (8)</td>
<td>1.69 (0.03)</td>
</tr>
<tr>
<td>H427</td>
<td>66</td>
<td>2</td>
<td>Longitudinal</td>
<td>15530 (50)</td>
<td>256 (5)</td>
<td>1.81 (0.04)</td>
</tr>
<tr>
<td>F</td>
<td>2</td>
<td></td>
<td>Transverse</td>
<td>5210 (2700)</td>
<td>98 (7)</td>
<td>1.82 (0.06)</td>
</tr>
</tbody>
</table>

| Mean Value | | Longitudinal | 12740 (2610) | 225 (28) | 1.72 (0.10) |
|            | 17 | Transverse   | 5990 (1520)  | 83 (21)  | 1.73 (0.07) |

One hundred and twenty-two specimens were also fabricated from the cortical shell within the distal femoral neck and intertrochanteric regions. Since the cortical shell within these areas demonstrated large variations in thickness around the periphery of the bone (with the inferomedial cortex being much thicker than the superolateral cortex), the data was tabulated in two groups to determine if any regional differences in modulus exist. Tables 3.5 and 3.6 present the elastic and ultimate property summary data for the superolateral and inferomedial regions. Included also in these tables are the values for the specimen densities.
### TABLE 3.5 - Proximal, superolateral specimen data

<table>
<thead>
<tr>
<th>Bone</th>
<th>Age Gender</th>
<th>n</th>
<th>Orientation</th>
<th>E  MPa</th>
<th>$\sigma_{\text{max}}$ MPa</th>
<th>$\delta$ gm/cm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>H399</td>
<td>81 F</td>
<td>11</td>
<td>Longitudinal</td>
<td>8770 (1610)</td>
<td>161 (34)</td>
<td>1.49 (0.13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13</td>
<td>Transverse</td>
<td>6040 (1170)</td>
<td>87 (16)</td>
<td>1.62 (0.09)</td>
</tr>
<tr>
<td>H449</td>
<td>27 M</td>
<td>9</td>
<td>Longitudinal</td>
<td>10410 (2060)</td>
<td>208 (39)</td>
<td>1.63 (0.07)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10</td>
<td>Transverse</td>
<td>4800 (1880)</td>
<td>76 (24)</td>
<td>1.65 (0.15)</td>
</tr>
<tr>
<td>H458</td>
<td>70 F</td>
<td>3</td>
<td>Longitudinal</td>
<td>9010 (2920)</td>
<td>184 (70)</td>
<td>1.63 (0.09)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4</td>
<td>Transverse</td>
<td>4440 (830)</td>
<td>100 (23)</td>
<td>1.65 (0.09)</td>
</tr>
<tr>
<td>H369</td>
<td>82 M</td>
<td>5</td>
<td>Longitudinal</td>
<td>8380 (1970)</td>
<td>157 (42)</td>
<td>1.63 (0.08)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9</td>
<td>Transverse</td>
<td>5200 (1690)</td>
<td>85 (16)</td>
<td>1.69 (0.09)</td>
</tr>
<tr>
<td>H427</td>
<td>66 F</td>
<td>2</td>
<td>Longitudinal</td>
<td>10300 (2120)</td>
<td>169 (58)</td>
<td>1.76 (0.06)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>Transverse</td>
<td>8130</td>
<td>114</td>
<td>1.58</td>
</tr>
<tr>
<td></td>
<td>Mean Value</td>
<td>31</td>
<td>Longitudinal</td>
<td>9280 (1995)</td>
<td>177 (44)</td>
<td>1.58 (0.12)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>37</td>
<td>Transverse</td>
<td>5380 (1610)</td>
<td>86 (21)</td>
<td>1.65 (0.11)</td>
</tr>
</tbody>
</table>

### TABLE 3.6 - Proximal, inferomedial specimen data

<table>
<thead>
<tr>
<th>Bone</th>
<th>Age Gender</th>
<th>n</th>
<th>Orientation</th>
<th>E  MPa</th>
<th>$\sigma_{\text{max}}$ MPa</th>
<th>$\delta$ gm/cm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>H399</td>
<td>81 F</td>
<td>14</td>
<td>Longitudinal</td>
<td>8820 (2790)</td>
<td>154 (40)</td>
<td>1.52 (0.14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4</td>
<td>Transverse</td>
<td>4630 (1410)</td>
<td>70 (23)</td>
<td>1.41 (0.05)</td>
</tr>
<tr>
<td>H449</td>
<td>27 M</td>
<td>7</td>
<td>Longitudinal</td>
<td>11390 (2240)</td>
<td>207 (32)</td>
<td>1.68 (0.10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6</td>
<td>Transverse</td>
<td>5480 (1730)</td>
<td>100 (35)</td>
<td>1.65 (0.15)</td>
</tr>
<tr>
<td>H458</td>
<td>70 F</td>
<td>3</td>
<td>Longitudinal</td>
<td>8440 (3060)</td>
<td>133 (46)</td>
<td>1.59 (0.08)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6</td>
<td>Transverse</td>
<td>5120 (440)</td>
<td>94 (4)</td>
<td>1.70 (0.05)</td>
</tr>
<tr>
<td>H369</td>
<td>82 M</td>
<td>3</td>
<td>Longitudinal</td>
<td>10050 (790)</td>
<td>207 (33)</td>
<td>1.68 (0.09)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td>Transverse</td>
<td>5020 (440)</td>
<td>79 (7)</td>
<td>1.71 (0.07)</td>
</tr>
<tr>
<td>H427</td>
<td>66 F</td>
<td>2</td>
<td>Longitudinal</td>
<td>13650 (390)</td>
<td>238 (14)</td>
<td>1.71 (0.05)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4</td>
<td>Transverse</td>
<td>7900 (3390)</td>
<td>88 (21)</td>
<td>1.63 (0.06)</td>
</tr>
<tr>
<td></td>
<td>Mean Value</td>
<td>29</td>
<td>Longitudinal</td>
<td>9860 (2790)</td>
<td>177 (47)</td>
<td>1.59 (0.14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25</td>
<td>Transverse</td>
<td>5550 (1900)</td>
<td>88 (22)</td>
<td>1.63 (0.14)</td>
</tr>
</tbody>
</table>
The resultant mean values of the elastic modulus in both the longitudinal and transverse directions did not differ significantly (t=0.93, p=0.36) for the superolateral and inferomedial groups and hence these two populations were combined. In the longitudinal direction, the mean value of the elastic modulus of the proximal specimens was 9560 MPa or 33 percent less than that measured within the diaphyseal region (12740 MPa). This difference was significant at p=0.05. However, there was also a significant difference in the density of the groups, with the mean proximal bone density (1.52 gm/cc) determined to be 9 percent less than that measured for the diaphyseal specimens (1.72 gm/cc).

In the transverse direction, however, there was no significant difference (t=1.16, p=0.24) in the mean value of the elastic modulus for the proximal region (5470 MPa) and that measured within the diaphysis (5988 MPa). Despite this lack of a significant difference in transverse moduli, the density of the proximal-transverse population (1.64 gm/cc) was significantly less (t=3.8, p<0.001) than that of the diaphyseal-transverse population (1.73 gm/cc). In addition, the resulting longitudinal to transverse moduli ratio was 1.76 or 17 percent less than that in the diaphysis.

Bone - Strength

The mean value of the maximum fiber stress for the diaphyseal bone tested in the longitudinal direction was determined to be 225 MPa (see=20). Using the estimated rupture factor of 1.75, the resultant ultimate tensile strength was 128 MPa. In the transverse direction, the maximum fiber stress of the diaphyseal bone was 83 MPa (see=21), corresponding to an ultimate tensile strength of 47 MPa. Both the longitudinal and transverse strengths
varied significantly with density, as shown in Figures 3.11a and 3.11b ($R^2=0.51, p<0.0001, \text{see}=14.0$ MPa; and $R^2=0.70, p<0.0001, \text{see}=6.1$ MPa respectively).

As with the elastic modulus, the population means for maximum stress in both the longitudinal and transverse directions did not differ significantly ($t=0.011, p=1.0$) for the two proximal groups and hence these two populations were pooled. The longitudinal ultimate tensile strength in the proximal region was 101 MPa (177/1.75) or 21 percent less than that measured within the diaphysis. This proximal population also demonstrated a significant ($t=6.02, p<0.0001$), 8 percent reduction in density from the diaphyseal specimens. In contrast, there was no significant difference ($t=0.69, p=0.50$) between the measured transverse strength within the proximal region (50 MPa or 87/1.75) and that measured within the diaphysis (47 MPa or 83/1.75). However, even with this apparent equality in transverse strength, the transverse proximal population also demonstrated a significant decrease in density (5 percent) from that of the diaphysis.

3.3 Discussion

The elastic properties of diaphyseal bone are well understood, supporting a transversely isotropic model. The elastic constants for femoral diaphyseal bone in tension have been presented by Reilly and Burstein (1975) as:
Figure 3.11a: Diaphyseal bone longitudinal maximum fiber stress versus specimen apparent density.
Figure 3.11b: Diaphyseal bone transverse maximum fiber stress versus specimen apparent density.
\[ E_{\text{longitudinal}} = 17000 \, \text{MPa} \]
\[ E_{\text{transverse}} = 11500 \, \text{MPa} \]

The results from the three-point bending tests presented here differ from these values. For diaphyseal bone, the mean longitudinal modulus was 12740 MPa or 25 percent lower than that reported above. However, the average diaphyseal specimen density of 1.72 gm/cc is well below that which would be expected for young healthy bone (1.95 gm/cc). Using the linear regression derived from our data, specimens with a density of 1.95 gm/cc have an estimated modulus of 16500 MPa, which is close to the published value. In addition, the calculated transverse modulus of 5990 MPa was also significantly less (48 percent) than that reported above. However, the transverse data demonstrated no significant variation with density and hence this variable does not explain the large discrepancy. This observed difference is possibly due to an increased sensitivity of the bending test, combined with the small specimen thicknesses, to local defects. The diaphyseal specimens tested here exhibited an haversian architecture, the canals of which could potentially occupy a large portion of the cross-section of specimens fabricated in the transverse direction. This would have the effect of decreasing the effective moment of inertia and leading to an underestimate of the material elastic modulus based on surface dimensions alone. Based on an average canal diameter of 90 microns and average specimen dimensions, the effective moment of inertia would be overestimated by 50 percent, leading to the observed 50 percent difference in the bending modulus.

The specimens fabricated from the proximal femur demonstrated significantly decreased mechanical properties from those of the diaphysis.
Within the proximal femur, the mean value of the longitudinal elastic modulus was 9650 MPa or 33 percent less than that measured for the diaphysis (12740 MPa). This difference is partially explained by observing the specimen modulus/density trends. For the total population (proximal and diaphyseal specimens), a linear regression fitted to the modulus vs. density data results in an $R^2$ of only 0.42 (Fig. 3.12). Thus, only 42 percent of the variance in the modulus of the total, longitudinal data can be explained by density alone. However, the transverse elastic moduli did not differ significantly differently between the diaphyseal (5990 MPa) and proximal (5470 MPa) populations despite a significant density difference. Therefore, it is likely that the measured difference between the proximal and diaphyseal moduli is not due to density differences alone, but that architectural differences also exist. This is further supported by the measured difference in the ratio of longitudinal to transverse moduli for the diaphyseal (2.12) and proximal (1.76) groups. Figures 13 show transmission light micrographs (20x) of specimens taken from the diaphyseal and proximal regions. Architectural differences are apparent, although such features were not observed in all proximal specimens.

For the cortical shell within the proximal femur, our overall mean values for the elastic properties were:

\[
\begin{align*}
E_{\text{longitudinal}} & = 9650 \text{ MPa} \\
E_{\text{transverse}} & = 5470 \text{ MPa} \\
\rho & = 1.62 \text{ gm/cm}^3
\end{align*}
\]

These calculated values of the elastic modulus $E_l$ and $E_t$ are associated with coefficients of variation of 2400 MPa and 1760 respectively, which are
Figure 3.12: Longitudinal modulus versus apparent density for the total population of bone specimens (diaphyseal and proximal).
Figure 3.13: Transmission light micrographs (20x) of diaphyseal beam specimen (above) and proximal beam specimen (below).
near those reported by other investigators for pure tension or compression (Burstein et al., 1976; Currey and Butler, 1975; Dickenson et al., 1981).

The ultimate tensile strength of femoral diaphyseal bone has also been subject to much investigation. Reilly and Burstein (1975) found the values of the ultimate tensile strengths to be:

\[
\begin{align*}
\text{Longitudinal } \sigma_{ult} &= 133 \text{ MPa} \\
\text{Transverse } \sigma_{ult} &= 51 \text{ MPa}
\end{align*}
\]

For the data presented here, the use of a rupture factor of 1.75 resulted in the diaphyseal ultimate tensile strength for the longitudinal (128 MPa) and transverse (47 MPa) specimens which did not differ significantly from those values presented by Reilly and Burstein (p<2.0). This was observed despite the density differences as suggested by the modulus data between our population and that of Reilly and Burstein. Since the flexural rigidity, from which the modulus was estimated, is sensitive to defects throughout the entire structure this observation is reasonable. However, the strength is dependent only on the material where the failure occurs, presumably at the center of the beam where the bending moment is the greatest (for three-point bending). The use of four-point bending would produce a region of constant bending stress in which failure would occur at the weakest location. Therefore, if four-point bending were used, it could be expected that the strength data would demonstrate similar sensitivities to heterogeneous porosity as the modulus data and as a result similar differences from the reported values.

The proximal specimens demonstrated a 21 percent decrease in
longitudinal strength as compared to diaphyseal bone. As with the elastic modulus, this difference could not be explained by density alone. However, in the transverse direction, no significant difference in strength was observed between the diaphyseal (47 MPa) and proximal (50 MPa) groups. Consequently, the ratio of longitudinal to transverse strength (2.7 diaphyseal, 2.0 proximal) differed significantly for the two regions. Together, this data supports the hypothesis that there exists a slight decrease in anisotropy for the proximal specimens.

The overall values for the ultimate strengths of the cortical shell within the proximal femur are:

\[
\text{Longitudinal } \sigma_{\text{ult}} = 101 \text{ MPa} \\
\text{Transverse } \sigma_{\text{ult}} = 50 \text{ MPa}
\]

These calculated values of the ultimate tensile strength are associated with a standard deviation of approximately 25 percent.

The characteristics of the load-deflection data demonstrate additional differences between the longitudinal and transverse populations. The specimens fabricated in the transverse direction failed in a more brittle fashion, with the strain at failure in the longitudinal direction being approximately four-five times that in the transverse direction (Fig. 3.8). This also agrees with the observations of others (Reilly and Burstein, 1975).

In summary, the use of three-point bending experiments potentially result in greater uncertainty in the estimation of specimen material
properties than standard tensile or compression tests. The three primary sources of this additional uncertainty are; 1) the inability of the analytic formulations to completely account for the complex stress state which includes regions of compression, tension and plastic deformation; 2) inclusion of errors inherent in the added dimensional measurements which must be made for each experiment; and 3) the small specimen geometries, resulting in an increased sensitivity to material defects. The validation studies performed with acrylic demonstrate that the determination of elastic modulus and ultimate tensile strength can be made with good accuracy for defect free material. In addition, the experiments performed with the oak specimens demonstrate the need to consider the magnitude of the local deformation at the site of load application. However, for small specimen thicknesses (< 0.5 mm) this local deformation resulted in less than 1 percent error and hence was

Other investigators studying the mechanical properties of the metaphyseal shell or subchondral bone have reported values for elastic modulus and strength which are markedly reduced from those of diaphyseal bone. Murray et al. (1984) estimated the elastic modulus and strength of the metaphyseal shell from the proximal tibia by testing thin disks. The moduli varied from 1400 to 7100 MPa, and the maximum stress at failure from 90 to 310 MPa. Brown and Vrahas (1984), measured the elastic modulus of the subchondral bone of the femoral head and reported a mean value of 1370 MPa. The results of our study however, suggest that the thin cortical shell within the distal femoral neck and intertrochanteric region has only slightly reduced mechanical properties from those in the diaphysis, and that the majority of this difference is due to a reduced density. Architectural differences are also implied with the ratio of longitudinal
to transverse moduli and strength within the proximal femur (1.5 and 2.0) being almost one and one half times less than that measured within the diaphysis (2.1 and 2.7).
4.0 Stress Distributions in the Proximal Femur During Gait and Falls

Few data exist regarding the magnitude of loads and the resulting stress distributions associated with proximal femoral fracture, either during normal activities or from a fall. While finite element analysis has been used extensively as a technique to determine stresses throughout the femur, the focus of previous studies has been primarily on the diaphyseal region, with little information reported for the femoral neck. Although experimental studies of femoral neck fracture have been performed (Smith, 1953; Backman, 1957; Hirsh and Frankel, 1960; Leichter et al., 1982, Esses et al., in prep.), the emphasis has been on elucidating the load conditions responsible for clinically observed fracture patterns and not on determining the resulting stress distributions. In addition, analytical models based on beam theory for the determination of neck stresses have been presented (Williams and Svensson, 1971; Mizrahi et al., 1984), but the results of these studies are limited by the geometric and material property simplifications inherent in such techniques.

The propensity of hip fracture varies significantly between individuals and is dependent on a number of host factors including bone density and geometry. Currently, the presence of osteopenia (reduced bone tissue) is the major determinant used for the identification of patients at high risk. It has been reported that trabecular bone is lost at a rate of 8 percent per decade from age 30 (Mazess, 1982). This represents a nearly 30% loss of trabecular bone by age 70. Cortical bone is also affected, displaying a reported 32% decrease in elastic modulus for samples obtained from osteoporotic patients (Dickenson et al., 1981).
Interindividual variations in the global geometry of the proximal femur could also increase fracture risk by altering the effect of both joint and muscle forces. For the modern human population, the cervico-diaphyseal angle, which represents the angle between the neck and diaphyseal axes, has a reported mean of approximately 128 degrees with a standard deviation of 6 (Fig. 4.1). The antetorsion angle, which represents the rotation of the neck axis out of the frontal plane, has a mean of approximately 14 degrees with a standard deviation of 8 (Ruff, 1981). This normal variation in bone geometry could potentially act to increase risk for fracture above that which would be predicted from bone density measurements alone.

There is also controversy concerning the relative importance of bone type, cortical and trabecular, in resisting fracture of the proximal femur. The current belief is that the load is distributed in proportion to the volume fraction of tissue (intertrochanteric region, 50% cortical and 50% trabecular: cervical region, 75% cortical and 25% trabecular) (Melton, 1983). The knowledge of which tissue is most important for structural integrity, combined with data on where osteoporotic fractures most often occur, would aid in understanding the nature and progression of osteoporosis. Also, since the capability of separately resolving cortical and trabecular bone can vary depending on the particular non-invasive imaging techniques employed, the understanding of how loads are distributed would be important in developing procedures for the in vivo evaluation of osteoporotic fracture risk.

The objective of the present analysis was to investigate how changes in global material and geometric properties affect stresses within the proximal femur and hence fracture risk. The variables studied include
Figure 4.1: Reference axes and geometric definitions for the proximal femur. From Ruff (1983).
cortical and trabecular bone material properties, cervico-diaphyseal angle, antetorsion angle and diaphyseal bowing. In addition, the load distribution between cortical and trabecular bone was investigated to determine which bone type was most important for the structural integrity of the proximal femur. Linear, three-dimensional finite element models were analyzed to predict the stress distribution within the femoral neck during three phases of gait (heel-strike, one-legged stance and toe-off) as well as during one particular type of fall.

4.1 Materials and Methods

A database of 80 human femurs (Ruff, 1981), representative of the modern population, was available for investigating the normal variation of geometry as well as generating finite element models. After preparation, all femurs had been embedded in a rigid foam and sectioned at 15 locations (Fig. 4.2). All sections were subsequently digitized and analyzed yielding numerous properties of the composite sections (Ruff, 1988). Several of these geometric parameters (cervico-diaphyseal angle, antetorsion angle, diaphyseal bowing, area and principal moments of inertia) were used to isolate a particular femur which represented the 'normal' from the parent population. Additional sections were then cut through the femoral neck and greater trochanter of the modeled femur to increase the geometric information in these areas.

Seven models were generated of the proximal one third of the femur (Table 4.1). All mesh geometries were permutations of the 'normal' (model
Figure 4.2: Cross-section locations within the femur. From Ruff (1983).
1) and were composed of 20 node isoparametric brick elements as well as an assortment of transition elements, wedge elements and partially constrained brick elements. A total of 532 elements and 2300 nodes were used (Fig. 4.3). Partially constrained 16-node brick elements represented a the portion of the cortical shell of the intertrochanteric and cervical regions with element aspect ratios of greater than 10 (Cheal, 1985). This element type eliminates the numerical ill-conditioning that results from using elements with poor aspect ratios while maintaining displacement interpolation compatibility with neighboring 20-node brick elements.

Models two through five were designed to study the effects of the normal variation of both cervico-diaphyseal and antetorsion angles. These were modifications of the original 'normal' model, representing plus and minus one and one half standard deviation in both cervico-diaphyseal angle (models 2 and 3) and antetorsion angle (models 4 and 5). In order to determine how to modify the 'normal' mesh geometry to represent models 2 thru 5, an analysis was performed using the existing femoral geometric database. The orientation of each bone section (Fig. 4.2) was quantified by noting the direction of the maximum area moment of inertia relative to the global xy plane. Data from the total population were grouped in such a way as to observe if specimens with plus and minus one and one half standard deviations of either the cervico-diaphyseal or antetorsion angle differed significantly from those with the mean value. There was observed no statistically significant difference (p=0.05) in the direction of the principal moments of inertia between femurs with various cervico-diaphyseal angles. Therefore, to represent cervico-diaphyseal angles of 136 (model 2) and 118 (model 3) degrees, the mesh normal geometry (model 1) was modified gradually, throughout the intertrochanteric region by rotating sections 9
Figure 4.3: Finite element mesh.
through 11 about their line of intersection (Fig. 4.4).

In contrast, a one-way analysis of variance demonstrated that significant geometric difference (F>8.0; p<0.002) between femurs with various antetorsion angles existed, and were present throughout the proximal one third of the femur. The orientation of the major moment of inertia of the cross-sections revealed that a twisting of the proximal femur occurs in those bones with antetorsion angles differing from the population mean. Therefore, element geometries distal to the greater trochanter were appropriately modified to represent antetorsion angles of 27 (Model 4) and 3 degrees (Model 5) (Fig. 4.5). Sections 1 through 4 were rotated about the z axis by plus (model 4) and minus (model 5) 18 degrees. Likewise, sections 5 and 6 were rotated by 15 degrees, and sections 7 to 19 were rotated in a rigid body fashion by 12 degrees.

To investigate the influence of diaphyseal geometry on femoral neck and intertrochanteric stresses, a sixth model was generated which was all degrees of freedom were deleted for nodes below the lesser trochanter. Since no significant correlation existed between the values of cervico-diaphyseal angle, antetorsion angle and diaphyseal bowing in this population, each parameter was varied independently.
Figure 4.4: Modifications for representing differences in cervico-diaphyseal angle.
Figure 4.5: Modifications for representing differences in antetorsion angle.
Table 4.1 - FEA Model Summary

<table>
<thead>
<tr>
<th>Model</th>
<th>Cervico-diaphyseal Angle</th>
<th>Antetorsion Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - Normal</td>
<td>127</td>
<td>15</td>
</tr>
<tr>
<td>2 - Plus 9°CD</td>
<td>136</td>
<td>15</td>
</tr>
<tr>
<td>3 - Minus 9°CD</td>
<td>118</td>
<td>15</td>
</tr>
<tr>
<td>4 - Plus 12°AT</td>
<td>127</td>
<td>27</td>
</tr>
<tr>
<td>5 - Minus 12°AT</td>
<td>127</td>
<td>3</td>
</tr>
<tr>
<td>6 - Constrained</td>
<td>127</td>
<td>15</td>
</tr>
<tr>
<td>7 - Osteoporotic</td>
<td>127</td>
<td>15</td>
</tr>
</tbody>
</table>

All analyses assumed linear, isotropic material behavior. The values of elastic modulus and Poisson ratio for the cortical and cancellous bone are presented in Table 4.2. The elastic modulus of the metaphyseal shell within the intertrochanteric and neck regions was reduced from that of diaphyseal bone in similar proportion to the reductions observed within the proximal tibia (Murray et al., 1984). For models 1 thru 6, the elastic moduli of the trabecular bone were heterogeneous and based on the results of Brown and Ferguson (1980) as well as Martens et al. (1983) (Table 4.3).

Model 7 was geometrically identical to model 1 but incorporated reduced material properties representative of the osteoporotic state. The elastic modulus of cortical bone from osteoporotic individuals has been reported to be reduced by approximately 32 percent from normal (Dickenson et al., 1981), therefore the modulus for all elements representing both the diaphyseal cortex and the metaphyseal shell were reduced uniformly by this amount. The mechanical properties of osteoporotic cancellous bone have not been specifically reported. However, assuming that the elastic modulus is proportional to the apparent density cubed (Carter and Hayes, 1977), a reported 8 percent per decade loss of trabecular bone mass (Mazess, 1982) represents a 66 percent decrease in elastic modulus by age 70. Therefore
for model 7, the modulus of the trabecular bone was uniformly reduced by 66 percent from the values used in Model 1 (Table 4.3).

**TABLE 4.2 - Material properties of the cortex and metaphyseal shell.**

<table>
<thead>
<tr>
<th>Shell Thickness</th>
<th>Elastic Modulus</th>
<th>Poisson Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 - 0.9 mm</td>
<td>3.0 GPa</td>
<td>0.45</td>
</tr>
<tr>
<td>1.0 - 1.9</td>
<td>7.0</td>
<td>0.45</td>
</tr>
<tr>
<td>2.0 - 2.9</td>
<td>12.5</td>
<td>0.45</td>
</tr>
<tr>
<td>3.0 -</td>
<td>17.0</td>
<td>0.45</td>
</tr>
</tbody>
</table>

**TABLE 4.3 - Material properties of trabecular bone**

<table>
<thead>
<tr>
<th>Location</th>
<th>Normal</th>
<th>Osteoporotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral Head</td>
<td>900 MPa</td>
<td>300 MPa</td>
</tr>
<tr>
<td></td>
<td>620</td>
<td>200</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>620</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td>450</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td>260</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>30</td>
</tr>
<tr>
<td>Intertrochanteric</td>
<td>620</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td>450</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>30</td>
</tr>
</tbody>
</table>

Four load cases were analyzed for all models (Tables 4.4 and 4.5). Load case 1 was representative of one-legged stance as presented by Williams and Lissner (1962). Load cases 2 and 3 represented the heel-strike and toe-off phases of gait (Fig. 4.6). The direction and magnitudes of the joint contact force and muscular loads for these two cases were adapted from the gait optimization studies of Patriarco et al. (1981) and Crowninshield (1978). The period of peak joint contact force for heel-strike and toe-off were determined to be at 15 and 45 percent of the gait cycle respectively.
Figure 4.6a: Posterior view of the muscle and joint contact loads acting on the proximal femur during heel-strike.
Figure 4.6b: Posterior view of the muscle and joint contact loads acting on the proximal femur during toe-off.
The results of EMG studies (Patriarco, 1982) were then used to determine which muscles were active at these specific periods. At heel-strike the muscles represented were the gluteus minimus, medius and maximus, while those at toe-off were the gluteus minimus and medius as well as the psoas. Next, the pelvic origins for each muscle were located based on scaled data presented by Patriarco (1982), while the corresponding insertions were located on the finite element mesh based on bony landmarks. Provided the orientation of the femur relative to the pelvis during each phase of gait (Patriarco, 1982), the appropriate Euler transformations were then performed to determine the unit vectors representing the direction of each of the applied muscle force in the coordinate system of the finite element model. Since the magnitude of the resultant hip contact force was not provided by Patriarco, the results of Crowninshield (1978) were used. This was justified by observing that the values presented for both the resultant moment and force about the hip joint were very similar for both studies. These values of the joint contact force were presented in a pelvic coordinate system and thus the appropriate Euler transformations were performed, as above, to determine the direction and magnitude in the coordinate system of the finite element model. In addition, since the coordinate system used by Patriarco to define the orientation of the femur relative to the pelvis incorporated the location of the femoral head, the direction of muscular and joint loads were recalculated for each of models 1 thru 5 where the proximal geometry had been modified.

Load case 4 represented a fall with a medially directed load applied to the greater trochanter. The direction of this contact force was adapted from the experimental work of Backman (1957). This particular fall load case was shown by Backman to produce clinically significant (subcapital)
fractures under \textit{in vitro} test conditions. The magnitude of the fall force used in this analysis was based on simple measurements performed during simulated falls. Using pressure sensitive film (Prescale MA+C R270 10M, Fugi Photo Film Co., Tokyo 106) attached to the skin above the lateral greater trochanter, the peak fall force was recorded during four falls by a healthy volunteer on a hard-wood floor. The falls were conducted such that the lateral aspect of the hip came in direct contact with the floor. The results demonstrated that the average peak force measured over the greater trochanter was approximately 11 times body weight.

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|l|}
\hline
\textbf{Force Location} & \textbf{Heel-strike} & \textbf{Toe-off} & \textbf{One-legged stance} & \textbf{Fall} \\
\hline
Glut max (-.46, .17, .87) & (-.48, -.33, .81) & (-.40, .14, .91) & \\
Glut med (-.28, .62, .73) & (-.23, .10, .97) & \\
Glut min (-.30, .65, .70) & (-.26, .17, .95) & \\
Psoas & (-.36, .85, .38) & \\
Joint (-.42, -.12, -.91) & (-.44, -.05, -.91) & (.29, -.10, -.95) & (.50, -.80, .34) & \\
Troch & & & (-.50, .80, -.34) & \\
\hline
\end{tabular}
\caption{Summary of loads, unit vectors}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|l|}
\hline
\textbf{Force Location} & \textbf{Heel-strike} & \textbf{Toe-off} & \textbf{One-legged stance} & \textbf{Fall} \\
\hline
Glut. max & 0.64 & 0.32 & 2.60 & \\
Glut. med & 0.72 & 0.86 & \\
Glut. min & 0.54 & 0.61 & \\
Psoas & 0.65 & \\
Joint & 4.20 & 3.90 & 1.80 & 11.0 & \\
Trochanter & & & & 11.0 & \\
\hline
\end{tabular}
\caption{Summary of loads, magnitude (x body weight)}
\end{table}

The analyses were performed using ADINA (ADINA Engineering, inc., Watertown, Massachusetts 02172), a general displacement-based finite element code. In-house software was used to calculate the three-dimensional nodal strains, von Mises yield stresses, principal stresses and direction
cosines. Pre- and postprocessing were performed by FEMGEN and FEMVIEW (Jordan, Apostal, Ritter Associates, Inc., Davisville, Rhode Island 02854). To determine the distribution of load between the cortical shell and trabecular core, the model results were isolated along four planes through the proximal femur (Fig. 4.7). Section planes 1 to 3 were oriented perpendicular to the cervical axis at the subcapital, mid-cervical and basi-cervical regions respectively, while section 4 transected the intertrochanteric region. The average normal stress to each plane was calculated for the appropriate element faces, then multiplied by the area of the element face, and summed for each material.

4.2 Results

Principal stress data are presented graphically as vector plots, with the length of each vector reflecting the magnitude and the direction reflecting the component direction. Compressive stress components are indicated with crossbars on the vectors. Contour plots are also used to present some of the results.

Load conditions

The displacement (magnified x20) of the finite element mesh during each of the four load cases is shown in Fig. 4.8. During one-legged stance, the femoral head is displaced distally with no deflection in the anterior-posterior direction. Heel-strike and toe-off resulted in similar displacements of the proximal femur with the combined actions of the joint
Figure 4.7: Finite element mesh displaying section locations at the: 1) subcapital; 2) mid-neck; 3) basicervical; and 4) intertrochanteric regions.
Figure 4.8: Displacement of the FEA mesh during each load case; medial-lateral view with anterior to the left.
and muscular loads serving to twist the proximal diaphysis, displacing the femoral head in the inferior-anterior direction. However, in response to impact loads on the greater trochanter as from a fall, the situation was reversed, with the head being displaced in the superior-posterior direction.

Vector plots of the resultant surface principal compressive stresses are displayed in Figure 4.9. During gait, a concentration of high compressive stress was present at the base of the femoral neck and medial intertrochanteric region. In contrast, during impact from a fall, large compressive stresses were present in the region of the superior-posterior neck and posterior trochanteric region, the peak magnitude being 4.3 times that present during gait.

The stress patterns observed within the trabecular bone were consistent with those calculated for the cortical surface. Figure 4.10 presents effective von Mises failure stress contour plots at the mid-neck (location 2). Again, the results indicate that the peak stresses occur in the inferior neck during gait, while at impact from a fall, these peak stresses occur in the superior-posterior region. In conjunction with this difference in stress location, the peak effective failure stress within the trabecular bone during the simulated fall is 4.7 times that present during gait.

During gait, the regions of highest stress within the cervical trabecular bone corresponded with the location of the system of trabeculae known as the primary compressive group (Fig. 4.11). Contour plots of the von Mises stress calculated within the trabecular bone for sections through the femoral head, subcapital, and mid-neck regions during one-legged stance
Figure 4.9: Vector plot of the surface principal compressive stress component P3; medial-lateral view with anterior to the left.
Figure 4.10: Contour plots of von Mises stress within the trabecular bone at the mid-neck location; lateral-medial view with anterior to the right.
Figure 4.11: Location of the major trabecular systems within the proximal femur: a) secondary compression group; b) primary compression group; and c) principal tension group. From 'Studies on the Anatomy and Function of Bones and Joints' ed. F. Evans.
are presented in Figure 4.12. Within the base of the femoral head, the peak failure stress was located slightly above the section centroid. This location of peak stress was observed to be more inferior at the subcapital region and is located in the most inferior trabecular bone at the mid-neck region. The model results demonstrated similar trends during heel-strike as shown in Figure 4.13. However, during a fall, the effective stresses in the trabecular bone were greatest in the superior neck, within the trabeculae which are commonly referred to as the primary tensile group (Fig. 4.11).

In addition, the contour plot of the strain calculated normal to each of the section planes (Fig. 4.14) suggests that the stress state during gait deviates significantly from simple bending since no neutral axis is observed. The strain pattern demonstrates a circular symmetry with the peak values being within the trabecular bone.

Variation of proximal geometry and material properties

Changes in global geometry were observed to modify the cervical stresses significantly for all load cases studied. The maximum von Mises stresses present at each region and during each load case are shown in Tables 4.6 to 4.9. During gait, the largest stresses within each section were observed for the model representing plus 9 degrees in the cervico-diaphyseal angle (Model 3). These stress values were from 17 to 30 percent greater than those observed in the normal bone. However, at impact from a fall, the peak von Mises stress occurred the model representing a decrease in antetorsion angle of 12 degrees (Model 5), being from 20 to 50 percent above that observed in the normal bone.
Figure 4.12: Contour plot of von Mises stress within the trabecular bone during one-legged stance at three sites: 1) femoral head; 2) subcapital; and 3) mid-neck. Medial-lateral view with anterior to the right.
Figure 4.13: Contour plot of von Mises stress within the trabecular bone during heel-strike at three sites: 1) femoral head; 2) subcapital; and 3) mid-neck. Medial-lateral view with anterior to the right.
Figure 4.14: Contour plot of strain normal to sections thru the femoral head and subcapital regions during one-legged stance; lateral-medial view, anterior to the right.
Modifying the cortical and trabecular bone material properties also resulted in significant changes in cervical stresses. The maximum von Mises stresses calculated for the osteoporotic model (Model 7) were found to be greater than those for normal bone. This increase was largest at the subcapital region; from 33 to 45 percent.

The geometry of the femoral diaphysis did not appear to influence the stresses within the proximal femur. The results from the model constrained at the lesser trochanter (Model 6) did not differ significantly from those of the normal bone (Tables 4.5 to 4.8).

Load distribution

The percentage of total load supported by the cortical and trabecular bone was approximately constant for all load cases. The cortical bone supports 30% of the load at the subcapital region (section 1, Figure 4.7), 50% of the load at the mid-neck (section 2), 96% of the load at the base of the neck (section 3) and 80% of the load at the intertrochanteric region (section 4). At impact of a fall, the percentage of load carried by the trabecular bone is similar to that calculated for gait for sections within the neck (1 to 3) and is increased slightly, to approximately 30%, within the intertrochanteric region (section 4).
### TABLE 4.5 - Maximum von Mises stress at subcapital region

<table>
<thead>
<tr>
<th>Model</th>
<th>Stance</th>
<th>Heel Strike</th>
<th>Toe-off</th>
<th>Fall</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - Normal</td>
<td>7.2 MPa</td>
<td>11.0 MPa</td>
<td>10.0 MPa</td>
<td>41.0 MPa</td>
</tr>
<tr>
<td>2 - Plus 9°CD</td>
<td>11.0</td>
<td>8.4</td>
<td>9.0</td>
<td>43.0</td>
</tr>
<tr>
<td>3 - Minus 9°CD</td>
<td>8.4</td>
<td>14.0</td>
<td>13.0</td>
<td>38.0</td>
</tr>
<tr>
<td>4 - Plus 12°AT</td>
<td>5.9</td>
<td>6.8</td>
<td>6.1</td>
<td>29.0</td>
</tr>
<tr>
<td>5 - Minus 12°AT</td>
<td>8.3</td>
<td>11.0</td>
<td>9.8</td>
<td>61.0</td>
</tr>
<tr>
<td>6 - Constrained</td>
<td>7.2</td>
<td>11.0</td>
<td>10.0</td>
<td>41.0</td>
</tr>
<tr>
<td>7 - Osteoporotic</td>
<td>9.6</td>
<td>16.0</td>
<td>14.0</td>
<td>56.0</td>
</tr>
</tbody>
</table>

### TABLE 4.6 - Maximum von Mises stress at the mid-neck region

<table>
<thead>
<tr>
<th>Model</th>
<th>Stance</th>
<th>Heel Strike</th>
<th>Toe-off</th>
<th>Fall</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - Normal</td>
<td>19.0 MPa</td>
<td>42.0 MPa</td>
<td>39.0 MPa</td>
<td>135.0 MPa</td>
</tr>
<tr>
<td>2 - Plus 9°CD</td>
<td>16.0</td>
<td>31.0</td>
<td>30.0</td>
<td>154.0</td>
</tr>
<tr>
<td>3 - Minus 9°CD</td>
<td>26.0</td>
<td>53.0</td>
<td>48.0</td>
<td>122.0</td>
</tr>
<tr>
<td>4 - Plus 12°AT</td>
<td>19.0</td>
<td>41.0</td>
<td>40.0</td>
<td>140.0</td>
</tr>
<tr>
<td>5 - Minus 12°AT</td>
<td>20.0</td>
<td>43.0</td>
<td>37.0</td>
<td>173.0</td>
</tr>
<tr>
<td>6 - Constrained</td>
<td>19.0</td>
<td>42.0</td>
<td>39.0</td>
<td>135.0</td>
</tr>
<tr>
<td>7 - Osteoporotic</td>
<td>24.0</td>
<td>53.0</td>
<td>47.0</td>
<td>168.0</td>
</tr>
</tbody>
</table>

### TABLE 4.7 - Maximum von Mises stress at the base of the neck region

<table>
<thead>
<tr>
<th>Model</th>
<th>Stance</th>
<th>Heel Strike</th>
<th>Toe-off</th>
<th>Fall</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - Normal</td>
<td>78.0 MPa</td>
<td>130.0 MPa</td>
<td>130.0 MPa</td>
<td>561.0 MPa</td>
</tr>
<tr>
<td>2 - Plus 9°CD</td>
<td>85.0</td>
<td>110.0</td>
<td>110.0</td>
<td>608.0</td>
</tr>
<tr>
<td>3 - Minus 9°CD</td>
<td>100.0</td>
<td>150.0</td>
<td>150.0</td>
<td>515.0</td>
</tr>
<tr>
<td>4 - Plus 12°AT</td>
<td>72.0</td>
<td>110.0</td>
<td>120.0</td>
<td>655.0</td>
</tr>
<tr>
<td>5 - Minus 12°AT</td>
<td>76.0</td>
<td>85.0</td>
<td>88.0</td>
<td>796.0</td>
</tr>
<tr>
<td>6 - Constrained</td>
<td>78.0</td>
<td>130.0</td>
<td>130.0</td>
<td>562.0</td>
</tr>
<tr>
<td>7 - Osteoporotic</td>
<td>84.0</td>
<td>140.0</td>
<td>140.0</td>
<td>608.0</td>
</tr>
</tbody>
</table>

### TABLE 4.8 - Maximum von Mises stress at the intertrochanteric region

<table>
<thead>
<tr>
<th>Model</th>
<th>Stance</th>
<th>Heel Strike</th>
<th>Toe-off</th>
<th>Fall</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - Normal</td>
<td>37.0 MPa</td>
<td>55.0 MPa</td>
<td>55.0 MPa</td>
<td>182.0 MPa</td>
</tr>
<tr>
<td>2 - Plus 9°CD</td>
<td>43.0</td>
<td>57.0</td>
<td>58.0</td>
<td>248.0</td>
</tr>
<tr>
<td>3 - Minus 9°CD</td>
<td>52.0</td>
<td>75.0</td>
<td>68.0</td>
<td>173.0</td>
</tr>
<tr>
<td>4 - Plus 12°AT</td>
<td>40.0</td>
<td>61.0</td>
<td>62.0</td>
<td>192.0</td>
</tr>
<tr>
<td>5 - Minus 12°AT</td>
<td>40.0</td>
<td>52.0</td>
<td>48.0</td>
<td>276.0</td>
</tr>
<tr>
<td>6 - Constrained</td>
<td>38.0</td>
<td>55.0</td>
<td>54.0</td>
<td>187.0</td>
</tr>
<tr>
<td>7 - Osteoporotic</td>
<td>38.0</td>
<td>58.0</td>
<td>57.0</td>
<td>197.0</td>
</tr>
</tbody>
</table>

- 195 -
TABLE 4.9 - Deviation of von Mises from normal at subcapital region (%)

<table>
<thead>
<tr>
<th>Model</th>
<th>Stance</th>
<th>Heel Strike</th>
<th>Toe-off</th>
<th>Fall</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - Normal</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2 - Plus 9°C-D</td>
<td>-25</td>
<td>-25</td>
<td>-10</td>
<td>+3</td>
</tr>
<tr>
<td>3 - Minus 9°C-D</td>
<td>+17</td>
<td>+27</td>
<td>+30</td>
<td>-7</td>
</tr>
<tr>
<td>4 - Plus 12°AT</td>
<td>-18</td>
<td>-38</td>
<td>-39</td>
<td>-31</td>
</tr>
<tr>
<td>5 - Minus 12°AT</td>
<td>+15</td>
<td>0</td>
<td>-2</td>
<td>+48</td>
</tr>
<tr>
<td>6 - Constrained</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7 - Osteoporotic</td>
<td>+33</td>
<td>+45</td>
<td>+40</td>
<td>-36</td>
</tr>
</tbody>
</table>

4.3 Discussion

Within the femoral neck, the heel-strike and toe-off phases of gait resulted in a two-fold increase in failure stress levels over those present during one-legged stance. However, the resultant stress patterns during all phases of gait were similar, with the peak trabecular stresses residing within the primary compressive system of trabeculae and the peak cortical stresses residing within the calcar. On impact from a fall however, the stress distributions were very different from those observed during gait, with the primary tensile group of trabeculae appearing to be the principal source of strength in the subcapital region. This finding is of great potential significance for osteoporotic patients. Based on Wolff's law, the forces that control bone remodeling will help maintain bone tissue in regions that are highly stressed during the common activity of gait (the primary compressive trabeculae). Conversely, it may be expected that regions of low stress during these common activities will lose bone at a higher rate (primary tensile trabeculae). Hence, it could be expected that there is a disproportionate increase in traumatic (fall) fracture risk over
spontaneous (gait) fracture risk. The suggested failure mechanism of crushing of the primary tensile group and tensile failure of the calcar femorale in response to a fall is supported by the clinical observation that a majority of subcapital fractures are marked by comminution of the posterior/superior cortex with concomitant posterior dislocation of the femoral head (Scheck, 1980). It should also be noted that the magnitude of the load at fall used here (11.0 x body weight) is an estimate based on the simple experiments discussed here and magnitudes during actual trauma may vary significantly. Therefore, the results presented here demonstrate differences in failure mechanism between gait and falls only for the particular case modeled, and cannot necessarily be generalized for all falls.

The results of this parametric study demonstrate that global bone geometry is an important variable to include when assessing femoral fracture risk. Femora with a cervico-diaphyseal angle less than the normal of 127 degrees experience increases of up to 30 percent in the stress levels during normal gait, while those with an antetorsion angle below the normal of 15 degrees experience increases of near 50 percent in the stress levels during falls. The decreased cervico-diaphyseal angle results in larger bending stresses due to an increased angle between the gait joint force and the cervical axis. Likewise, by increasing the antetorsion angle, the angle between the fall joint force and the cervical axis is increased, also leading to an increase in cervical bending and a concomitant increase in cortical stress. These results may prove important for accurately implementing fracture risk assessment techniques. Such techniques currently quantify fracture risk based on local measurements of bone geometry and material properties. Our results demonstrate that in order to reflect
accurately the true structural risk for fracture, this locally determined parameter needs to be modified to reflect the particular global bone geometry.

Diaphyseal geometry appeared to have little or no effect on femoral neck stresses. However, the models presented here assume static conditions. Since diaphyseal bowing likely modifies total femoral stiffness, a correlation of cervical stresses with diaphyseal bowing may have been observed if dynamic models of the entire femur were used.

These parametric results should be viewed in light of an important assumption that was made throughout the study. This assumption was that there is no direct dependency of joint load/direction on the proximal bone geometry. The optimization studies, from which the load and muscular forces were adapted, were based on data from too few patients to elucidate global femoral geometry effects. However, the modeled joint loads did vary indirectly with changes in antetorsion and cervico-diaphyseal angle. This was a result of the Patriarco coordinate system (in which the load vectors were defined) being defined partially by the location of the center of the femoral head.

Our results on the contribution of cortical and trabecular bone within the proximal femur differ from the prevailing notion in the literature. We show that there is a shift in the distribution of load from mainly trabecular bone near the femoral head (70%), to primarily cortical bone at the base of the femoral neck (96%). While this may be true, only one type of fall was investigated in this study. These load distributions may vary with different fall loading conditions and thus should be further
investigated. Nonetheless, this result has potentially significant implications for the use and interpretation of data obtained using noninvasive imaging techniques. For the accurate \textit{in vivo} assessment of hip fracture risk, our results suggest that it may prove necessary to quantify the relative structural contributions of each tissue. This capability however, is currently not available with some diagnostic technologies. The method of dual photon absorptiometry (DPA), for example, results in the integration of density data from both the trabecular and overlaying cortical bone within the region of interest. When using this technique therefore, it is not possible to quantify these tissues separately. Quantitative computed tomography (QCT) however, does allow the unique quantification of both geometry and density from trabecular and cortical bone and consequently may prove to be a more accurate method for the assessment of femoral fracture risk.

The results of the osteoporotic analysis (Model 7) demonstrated that this condition leads to dramatically increased stress levels, most notably in the subcapital region during heel-strike (45 percent) where the cervical strength is primarily determined by trabecular bone. These results, together with the observation that spontaneous fractures of the proximal femur usually occur in the subcapital region (Kleenerman and Marcuson, 1970), supports the hypothesis that such fractures result from reduced strength of trabecular bone (Melton, 1982), and are thus consistent with the progression of senile osteoporosis.
5.0 Fracture Prediction for the Proximal Femur Using
QCT Generated Finite Element Analysis

Fracture of the hip is a significant problem in the world adult population, with in excess of 250,000 cases reported per year in the United States alone (U.S. Public Health Service, 1985). While evidence suggests that certain therapeutic regimens can retard bone loss and thus stabilize fracture risk (Paganini-Hill et al., 1981), these treatments themselves can pose significant health risks. Therefore, it is important to identify and institute therapy for only those who are at greatest risk for fracture. Accordingly, many noninvasive techniques have been proposed for the assessment of in vivo hip fracture risk. These methods are typically based on measurements of bone density at various sites within the proximal femur, such as the Ward's triangle region. While generally good results have been reported for in vitro studies (Mizrahi et al., 1984; Leichter et al., 1982; Dalen et al., 1976; Phillips et al., 1975; Vose and Mack, 1963), only limited success has been described when using such measures to prospectively separate fracture patients from controls (Sartoris et al., 1985; Eriksson and Widhe, 1988; Mazess et al., in press; Bohr and Schaadt, 1983). There are several reasons for this difficulty in translating in vitro results into clinical success. One important reason is that many variables act in concert to determine in vivo fracture risk, such as bone strength, loading type (direction and magnitude), and probability of trauma (Aitken, 1984; Melton, 1983; Wicks et al., 1982); whereas when performing in vitro studies, the influence of only a few of these parameters is investigated. In addition, in vitro femoral specimens are usually fractured under loading configurations that represent one-legged stance. During actual falls however, the loading conditions are likely much
different from those present during gait and hence would produce very
different stress distributions. Furthermore, the structural significance of
proposed 'regions of interest' at which noninvasive measurements are made
has not been demonstrated in any rigorous manner, even for these simplified
loading conditions. To develop an accurate fracture risk assessment
 technique, it is important to investigate the isolated structural behavior
of the proximal femur, from which the location of structurally significant
regions that should be focused upon may be identified.

The finite element method of analysis has two main advantages over other
techniques for the structural analysis of the proximal femur. The first is
that this method allows for the representation of the complex geometric and
material property distribution, which normally present difficulties when
attempting to perform such analyses with closed form or experimental
techniques. The second advantage is that while an intact bone can be tested
to failure only once, a finite element model which has been shown to
accurately represent bone stresses, can be 'tested' innumerable times
allowing the investigation of many different loading conditions. For this
study, finite element models of intact proximal femora were created using
geometry and density data derived noninvasively from quantitative computed
tomography (QCT) images. QCT was chosen because it has been shown to be an
accurate technique for the assessment of intact bone status (Genant et al.,
1985; Elsasser and Reeve, 1980; Revak, 1980). In addition, with this
imaging modality, both the geometry and density can be determined, and
consequently it becomes possible to generate finite element models of
intact bones with accurate representation of the complex variation of these
parameters. The objectives of this aspect of the research were to: 1) use
QCT generated finite element models of intact femora to investigate the
isolated structural behavior of the proximal femur subject to loading conditions approximating one-legged stance and one particular type of fall; and 2) test the correspondence between these finite element analyses and in vitro fracture studies of the corresponding intact femora to determine how well this technique can model the complex process of bone failure.

5.1 Materials and Methods

Two fresh femora, harvested from human cadavers (female, age 66 and 70 years) and stored at -20°C, were used (Table 5.1). While in a water bath, both bones were imaged using a GE 8800 scanner operating at 120 KVP and 240 MAS as described in Section 2.0.

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Gender</th>
<th>Age</th>
<th>Cause of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>F</td>
<td>70</td>
<td>Pulmonary Edema</td>
</tr>
<tr>
<td>B</td>
<td>F</td>
<td>66</td>
<td>Respiratory Failure</td>
</tr>
</tbody>
</table>

5.1.1 Finite Element Mesh

The QCT images were reconstructed using a Gould FD5000 imaging processing system and in-house software. After reconstruction, scale factors were determined for each image and reference axes placed at a predefined corner of the cross-section of the nylon reference bar (Fig.
5.1). The images were then photographed and the mesh for the entire bone planned. The mesh connectivity, consisting over of 3100 nodes representing 214 cortical and 453 trabecular 20 node brick elements, was then created using the preprocessor FEMGEN (Jordan, Apostal, Ritter Associates Inc., Davisville, Rhode Island). The mesh was next traced onto sketches of each cross-section, photographed, projected on to a digitizer (Cybergraph system; Talos Systems, Scottsdale, Arizona), and the x-y-z coordinate for each nodal point determined (Fig. 5.2).

Material Properties

Once the mesh geometry was established, faces of trabecular elements coincident with each QCT slice were superimposed on the appropriate image and the average QCT number for each element face was calculated (Fig. 5.3). In addition for each slice, QCT data was sampled from each chamber of the included phantom. The QCT value versus the percent concentration of K$_2$HPO$_4$ for each chamber were found to fall on a straight line ($R^2$=0.998). The slope and intercept of this line were then used to correct the average data for scanner drift (Genant and Cann, 1983). Next, a QCT value for each trabecular element was determined by averaging the data for the two element faces which lay on consecutive images. Using the pre-determined correlations between corrected QCT number and bone modulus and strength (Section 2.0), these element QCT data were then converted into estimates of the material properties. Due to the large number of trabecular elements, it was impractical to represent the complete range of material properties suggested by the QCT data. Therefore, 10 different groups were used, each representing a range of bone density of 0.06 gm/cc (Table 5.2). Each trabecular element was then assigned the material properties of the set

- 203 -
Figure 5.1: QCT image through the femoral neck.
Figure 5.2: Finite element mesh of model A (above) and model B (below).
Figure 5.3: OCT image with trabecular mesh superimposed.
which was closest to its estimated value.

Table 5.2 - Trabecular bone material properties (All models)

<table>
<thead>
<tr>
<th>Material Set</th>
<th>% K_2HPO_4</th>
<th>Density (gm/cc)</th>
<th>Modulus (MPa)</th>
<th>Strength (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.4</td>
<td>0.22</td>
<td>65</td>
<td>0.60</td>
</tr>
<tr>
<td>2</td>
<td>9.1</td>
<td>0.28</td>
<td>160</td>
<td>1.50</td>
</tr>
<tr>
<td>3</td>
<td>13.8</td>
<td>0.33</td>
<td>260</td>
<td>2.80</td>
</tr>
<tr>
<td>4</td>
<td>18.4</td>
<td>0.39</td>
<td>360</td>
<td>4.10</td>
</tr>
<tr>
<td>5</td>
<td>23.1</td>
<td>0.44</td>
<td>480</td>
<td>5.70</td>
</tr>
<tr>
<td>6</td>
<td>27.8</td>
<td>0.50</td>
<td>600</td>
<td>7.40</td>
</tr>
<tr>
<td>7</td>
<td>32.5</td>
<td>0.56</td>
<td>720</td>
<td>9.20</td>
</tr>
<tr>
<td>8</td>
<td>37.1</td>
<td>0.62</td>
<td>840</td>
<td>11.00</td>
</tr>
<tr>
<td>9</td>
<td>41.8</td>
<td>0.67</td>
<td>970</td>
<td>13.00</td>
</tr>
<tr>
<td>10</td>
<td>46.5</td>
<td>0.73</td>
<td>1100</td>
<td>15.00</td>
</tr>
</tbody>
</table>

The material properties used to represent both the diaphyseal cortical bone and the metaphyseal shell were based on previous measurements of bone strength and modulus (Section 3.0). The elements representing the metaphyseal shell were at a minimum 1 mm thick for both models. To reflect a decreased thickness where appropriate (as measured on the contralateral bone of each pair), the elastic modulus was reduced by one third to one half. Consequently, three material sets were used to represent cortical bone within each model: one for diaphyseal bone; a second for the metaphyseal shell; and a third with a reduced elastic modulus for elements less than 1 mm thick (Tables 5.3 and 5.4).

Two types of analyses were performed for each bone. The first assumed linear behavior, with the trabecular bone being represented as isotropic and the cortical bone and metaphyseal shell represented as transversely isotropic. The trabecular bone elastic moduli were highly heterogeneous,
being determined by QCT data, and were given a uniform Poisson ratio of 0.3. The longitudinal and circumferential cortical elastic moduli were determined from previous studies (Section 3.0). The shear moduli, having not been measured, were based on the results of Reilly and Burstein (1975) and scaled by the particular value of the longitudinal modulus used in each material set (Table 5.3). For example, Reilly and Burstein presented a value of the shear modulus component $G_{12}$ as 3.60 GPa when the longitudinal modulus $E_3$ was 17.0 GPa. In this analysis, where the diaphyseal cortical modulus $E_3$ was determined to be 15.5 GPa the value of the shear modulus component $G_{12}$ was estimated to be 3.60(15.5/17.0) or 3.28 GPa.

<table>
<thead>
<tr>
<th>Model</th>
<th>Location</th>
<th>$E_1$</th>
<th>$E_2$</th>
<th>$E_3$</th>
<th>$G_{12}$</th>
<th>$G_{23}$</th>
<th>$G_{31}$</th>
<th>$\nu_{12}$</th>
<th>$\nu_{13}$</th>
<th>$\nu_{23}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Diaph</td>
<td>11.0</td>
<td>11.0</td>
<td>16.3</td>
<td>3.46</td>
<td>3.15</td>
<td>3.15</td>
<td>0.58</td>
<td>0.31</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>Meta</td>
<td>7.4</td>
<td>7.4</td>
<td>11.0</td>
<td>2.31</td>
<td>2.11</td>
<td>2.11</td>
<td>0.58</td>
<td>0.31</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>Reduced</td>
<td>2.8</td>
<td>2.8</td>
<td>3.5</td>
<td>0.90</td>
<td>0.82</td>
<td>0.82</td>
<td>0.58</td>
<td>0.31</td>
<td>0.31</td>
</tr>
<tr>
<td>B</td>
<td>Diaph</td>
<td>10.5</td>
<td>10.5</td>
<td>15.5</td>
<td>3.28</td>
<td>2.98</td>
<td>2.98</td>
<td>0.58</td>
<td>0.31</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>Meta</td>
<td>7.0</td>
<td>7.0</td>
<td>10.4</td>
<td>2.00</td>
<td>2.20</td>
<td>2.00</td>
<td>0.58</td>
<td>0.31</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>Reduced</td>
<td>3.5</td>
<td>3.5</td>
<td>5.2</td>
<td>1.00</td>
<td>1.10</td>
<td>1.00</td>
<td>0.58</td>
<td>0.31</td>
<td>0.31</td>
</tr>
</tbody>
</table>

The second set of analyses assumed nonlinear, isotropic behavior for both the cortical and trabecular bone. The complex nonlinear behavior of trabecular bone was represented by a material formulation originally designed for concrete (Bathe and Ramaswamy, 1979). The concrete model employs three basic features to describe material behavior: 1) a nonlinear stress-strain relation including strain-softening to allow for weakening of the material under increasing compressive stresses; 2) a failure envelope that defines cracking in tension and crushing in compression; and 3) a
strategy to model the post-cracking and crushing behavior of the material (Fig. 5.4; Appendix).

The nonlinear behavior of the cortical bone was represented by an isotropic bilinear material law, with a linear stress-strain relationship to yield and a second, reduced linear stress-strain relationship thereafter (Fig. 5.5). Again, the elastic modulus and yield strength of cortical bone were derived from previous studies (Section 3.0). The tangent moduli ($E'$) were based on the results of Burstein et al. (1976) and scaled by the longitudinal elastic modulus of each material set (Table 5.4).

Table 5.4 - Cortical Material Properties - Nonlinear Models

<table>
<thead>
<tr>
<th>Model</th>
<th>Location</th>
<th>$E$ (GPa)</th>
<th>$E'$ (GPa)</th>
<th>$\nu$</th>
<th>$\sigma_{y}$ (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Diaph</td>
<td>16.3</td>
<td>1.01</td>
<td>0.48</td>
<td>111</td>
</tr>
<tr>
<td></td>
<td>Meta</td>
<td>10.4</td>
<td>0.64</td>
<td>0.48</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>Reduced</td>
<td>3.5</td>
<td>0.22</td>
<td>0.48</td>
<td>88</td>
</tr>
<tr>
<td>B</td>
<td>Diaph</td>
<td>15.5</td>
<td>0.78</td>
<td>0.48</td>
<td>123</td>
</tr>
<tr>
<td></td>
<td>Meta</td>
<td>10.4</td>
<td>0.52</td>
<td>0.48</td>
<td>117</td>
</tr>
<tr>
<td></td>
<td>Reduced</td>
<td>5.2</td>
<td>0.26</td>
<td>0.48</td>
<td>117</td>
</tr>
</tbody>
</table>

Due to processing limitations, the nonlinear analyses could not be performed with the entire 3100 node mesh. Therefore, the elements distal to the lesser trochanter were removed and this truncated model, consisting of 2550 nodes, used instead (Fig. 5.6). Displacement boundary constraints, derived from the linear analyses, were applied to the distal most free surface in order to maintain solution accuracy within the intertrochanteric region. In addition, the nonlinear material behavior was applied only to a
Figure 5.4: Uniaxial stress-strain material law used for the nonlinear representation of trabecular bone. From Bathe and Ramaswamy, 1979.
Figure 5.5: Elastic-plastic material model used to represent the nonlinear behavior of cortical bone.
Figure 5.6: Truncated finite element models used in the nonlinear analyses.
subset of the elements; those in regions where the linear analyses had demonstrated peak stresses were present (Fig. 5.7).

Applied Loads

Two load cases were analyzed, one for each model. The first, used only with model A, consisted of a distributed compressive load (445 Nt.) applied to the superior aspect of the femoral head and directed parallel the diaphyseal axis (Fig. 5.8a). This load geometry has been shown to approximate one-legged stance (Rohlmann et al., 1983) and was represented primarily because it was easily reproduced in vitro, allowing strain-gage verification of the finite element results. The second load case, used only for model B, represented one particular type of fall in which the posterolateral aspect of the greater trochanter comes in contact with the ground (Backman, 1957). This situation would arise when a patient slips and falls, landing on the lateral buttock with the posterolateral aspect of the greater trochanter coming in contact with the ground. For this case, a posterolaterally directed load (222 Nt.) was applied to the femoral head with an equal and opposite reaction load applied to the lateral greater trochanter (Fig. 5.8b). The direction of the loads were such that both the diaphyseal and neck axes form an angle of 30 degrees with the plane perpendicular to the applied loads (horizontal). These directions represent the patient hitting with the thigh at an angle of 30 degrees to the ground, with their torso rotated slightly to the side of contact. For both load cases, the joint load was distributed over 9 adjacent nodes such that the resultant passed through the anatomic center of the femoral head. To balance the applied loads in both models, all degrees-of-freedom were deleted for the nodes on the most distal face of the diaphysis.
Figure 5.7: Distribution of linear and nonlinear material properties within the truncated finite element models.
Figure 5.8a: Loading configuration used for model A; a joint contact load directed parallel to the diaphyseal axis.
Figure 5.8b: Loading configuration used for model B; a posterolaterally directed load applied to the femoral head with an equal and opposite reaction load applied to the lateral greater trochanter.
The behavior of the nonlinear material law used for trabecular bone was such that small load increments were required for an accurate solution. Preliminary studies, based on cylinders of trabecular bone, demonstrated that good results were obtained with load increments equal to one fourth the load required for the structure to become nonlinear (Appendix). Consequently, based on the results of the in vitro intact bone studies, a model load increment of 448 Nt. was chosen for model A while a load increment of 224 Nt. was chosen for model B.

Failure Criteria

To predict local bone failure for the linear analyses, a von Mises yield criterion was applied to the stress results for elements representing cortical bone, and both a von Mises and Hoffman yield criterion were applied to the stress results for elements representing trabecular bone. The Hoffman failure theory (Hoffman, 1976) assumes linear terms to account for different tensile and compressive strengths, and has been demonstrated to fit experimental trabecular bone data well for the $\tau_{xy} - \sigma_{xx}$ plane (Stone et al., 1983). In principal stress space, the theory is given by

$$c_1(\sigma_2 - \sigma_3)^2 + c_2(\sigma_3 - \sigma_1)^2 + c_3(\sigma_1 - \sigma_2)^2$$

$$+ c_4\sigma_1 + c_5\sigma_2 + c_6\sigma_3 = 1 \quad (5.1)$$

where

$$c_1 = c_2 = c_3 = \frac{1}{2}\frac{S_t}{S_c}$$

$$c_4 = c_5 = c_6 = \frac{1}{S_t} - \frac{1}{S_c} ,$$
and where \( S_t \) is the ultimate strength in tension and \( S_c \) is the ultimate strength in compression. If \( S_t \) and \( S_c \) are equal, Equation 5.1 reduces to the von Mises yield function. The compressive strength of trabecular bone was estimated directly using the QCT-strength regressions presented in Section 2.0, while the tensile strength was assumed to be approximately one-third the compressive strength (Stone et al., 1983).

For the nonlinear models, the failure behavior of trabecular bone was represented within the finite element analysis. That is, at any particular load step when an element was predicted to fail (based on the input parameters defining a failure surface and local principal stress state), the element stiffness was reduced in an appropriate, predefined way. This behavior resulted in increased loading of the surrounding elements as would be expected in a true local failure. The compression failure envelope for trabecular bone, used in conjunction with the concrete material law, was defined in principal stress space so as to represent the Hoffman failure surface (Expression 5.1). For cortical bone, while yielding was modeled within the finite element analysis, no ultimate failure behavior was represented and thus the calculated von Mises stress was used as described above to estimate when local cortical bone failure had occurred.

Throughout this discussion, the model results for elements representing the cortical shell, primary compressive trabeculae and primary tensile trabeculae are presented separately. The primary compressive trabecular system extends from the superior aspect of the femoral head down to the medial calcar, while the primary tensile trabecular system traverses along the superior aspect of the femoral neck (Fig. 5.9). By noting the average QCT data for element faces coincident with the mesh section locations
Figure 5.9: Schematic representation of the proximal femur displaying the location of the major trabecular systems; secondary compressive group (A), primary compressive group (B), and primary tensile group (C).
throughout the femoral neck (Fig. 5.10), the elements representing either the primary compressive or primary tensile trabeculae were isolated (Fig. 5.11). At these section locations, the maximum von Mises and/or Hoffman failure stress was calculated for coincident element faces. The maximum effective stress for each element face was then divided by the element tensile strength to determine a critical stress ratio or factor of safety for that element. A peak stress ratio at each section was then determined for each of three element groupings.

Several authors have demonstrated a constant strain at failure for bone, and thus suggest that a measure of material strain may be a good indicator of bone strength (Vahey et al., 1987). With this in mind, an effective von Mises strain was also calculated for each element. Based on the results of trabecular compression tests (Section 2.0) and literature data for cortical bone (Burstein et al., 1976), a uniform ultimate failure strain of 3 percent was assumed for all materials in order to calculate the critical failure strain ratio.

The analyses were performed using ADINA (ADINA Engineering, Inc., Watertown Mass 02172), a general displacement-based finite element code (Bathe, 1982). ADINA provided the interpolation of elemental integration point stresses to the nodal points. In-house software calculated the three-dimensional nodal strains, modified von Mises yield stresses, and principal stresses and their direction cosines.

5.1.2 in vitro mechanical testing

To conduct mechanical testing, each bone was sectioned at the mid-
Figure 5.10: Location of sections at which model results were investigated.
Figure 5.11a: Medial-lateral view (anterior to the left) of trabecular elements representing the primary compressive and primary tensile trabeculae at each cervical section for model A.
Figure 5.11b: Medial-lateral view (anterior to the left) of trabecular elements representing the primary compressive and primary tensile trabeculae at each cervical section for model B.
diaphysis, and the distal end was embedded within an aluminum fixture. Next, each bone was instrumented with 9 strain gage rosettes. The location of the gages was such that three rosettes were coplainer at three specified locations; subcapital, basicervical and subtrochanteric (Fig. 5.12). The gages used were stacked, 45-degree rosettes with an active gage length of 3.18 mm (#FABR-12-35SX, BLH Electronics, Waltham MA). The bone surface was prepared and gages bonded as presented by Carter et al. (1980). At each strain gage location the periosteum was removed, the bone surface prepared with 180 grit sandpaper and then degreased with ethanol. A thin film of cyanoacrylate (Permabond 101) was applied to the bone surface and the gage pressed firmly to the prepared bone surface for approximately 3 minutes. To act as a strain relief, a small strip of 6 solder pads was attached at the base of each rosette and each gage lead soldered to one pad. The gages were then coated with a liquid acrylic (M-Coat D, Micromeasurements Inc., Raleigh, NC) and allowed to dry for 15 minutes. Twisted pairs of 18 gage wire, approximately 36 inches long, were connected to each gage via the solder pads. Each gage was connected as an active branch of a Wheatstone bridge employing one dummy gage (120 ohm) for temperature compensation. Each bridge was part of an Optilog data collection system (Optim Electronics, Gaithersburg, MD) which sequentially sampled each strain gage. The data were collected from the Optilog using an IBM personal computer and commercially available software (Labtech Notebook).

Both femurs were then tested to failure in one of two different loading modes, corresponding to those of finite element analyses, using a hydraulic materials testing system (model 1331, Instron Corp., Canton Ma). With the distal end rigidly fixed, bone A was tested to failure with a single load applied to the femoral head and directed parallel to the diaphyseal axis.
Figure 5.12: Strain gage locations for both instrumented femurs. Locations correspond to medial (A), anterior (B) and lateral (C) at section 4; inferior (A), superior/anterior (B) and superior/posterior (C) at sections 12 and 15.
The second bone (B) so as to simulate a fall by positioning it in such a way that both the diaphyseal and neck axes formed an angle of 30 degrees with the horizontal. The distal end of the bone was rigidly fixed with the lateral aspect of the greater trochanter in contact with the platform of the hydraulic actuator. A single vertical load was applied to the femoral head, directed in the anatomic posterolateral direction.

5.2 Results

The load-deflection behavior of the intact bones during the in vitro failure tests is shown in Figure 5.13. These plots demonstrate that bone A began to yield at near 1960 Nt and failed at 3825 Nt, while bone B began to yield at near 770 Nt and subsequently failed at 1430 Nt.

Linear Finite Element Analysis

The values of measured and calculated maximum principal strains for each gage location are presented in Tables 5.5 and 5.6. The location numbers correspond to model sections (Fig. 5.10), while the letter designation refers to the circumferential location of the gage within each section (Fig. 5.11). Strain gage 4B of bone A failed during the in vitro experiment and hence no data were collected at this location. For bone A, the difference between the model and experimental results varied from between 1 and 200 percent, with the best agreement observed in the diaphyseal region (location A and C). However, for bone B, poorer agreement was observed, with the difference between the model and experimental results ranging from
Figure 5.13a: Load-deflection curve from the in vitro failure test of bone A.
Figure 5.13b: Load-deflection curve from the \textit{in vitro} failure test of bone B.
8 to 550 percent. The majority of this variance occurred at six specific gages; 2 for bone A and 4 for bone B.

<table>
<thead>
<tr>
<th>Location</th>
<th>FEA Principal Strain Results (x10(^{-3}))</th>
<th>Experiment Principal Strain Results (x10(^{-3}))</th>
<th>Percent Difference</th>
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</thead>
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<td>P3</td>
<td>P1</td>
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<tr>
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<tr>
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<td>0.</td>
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<tr>
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<tr>
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<th>Experiment Principal Strain Results (x10(^{-3}))</th>
<th>Percent Difference</th>
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<tr>
<td>15C</td>
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<td>-0.661</td>
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Principal surface stress vectors are presented for models A and B in Figs. 5.14a and 5.14b respectively. For model A, the peak tensile stresses (P1) were observed in the superior cortex of the femoral neck, while the
Figure 5.14a: Principal surface stress vectors P1 and P3 for model A (simulated one-legged stance), presented for the posterior (top) and anterior surfaces.
Figure 5.14b: Principal surface stress vectors P1 and P3 for model B (simulated fall), presented for the posterior (top) and anterior surfaces.
maximum compressive stresses (P3) were within the medial calcar region. As expected, the stress state was very much different for model B, where the maximum tensile and compressive stresses both occurred in the proximal intertrochanteric region on the anterior and posterior sides respectively. When the results of both models were scaled such that the applied loads were of equivalent magnitude, the peak cervical stresses at impact of a fall in bone B were 2.6 (P1) and 1.3 (P3) times greater than those calculated for one-legged stance in bone A. The direction of these principal stress vectors for bone B demonstrate that while the femoral neck was primarily in bending the diaphysis was in torsion.

Contour plots of the effective von Mises stress within the metaphyseal shell are presented in Figs. 5.15a and 5.15b for several cross-sections through the finite element mesh. For model A (one-legged stance), the peak failure stresses occur within the superior and inferior bone throughout the femoral neck. In contrast, Figure 5.15b demonstrates how for model B (fall), the peak stresses occur on the anterior and posterior surfaces. The von Mises stress within the internal trabecular bone for each model are presented in Figures 5.15a and 5.15b. These figures demonstrate that within the cervical region for both models, trabecular stresses were concentrated within elements representing the primary compressive system of trabeculae.

Plots of the peak value of the ratio between the calculated von Mises stress and the estimated failure stress versus model location are presented in Figures 5.17 and 5.18, with separate curves for cortical bone, the primary compressive trabeculae and primary tensile trabeculae. This ratio reaches unity when the von Mises failure stress becomes equal to the bone
Figure 5.15a: Contour plot of the von Mises effective stress at sections 14 and 12 of bone A. These demonstrate that during simulated one-legged stance, peak cervical stresses occur in the superior and inferior cortical surfaces.
Figure 5.15b: Contour plots of the von Mises effective stress at sections 14 and 12 of bone B. These demonstrate that during a simulated fall, peak cervical stresses occur in the anterior and posterior cortical surfaces.
Figure 5.16a: Contour plot of the von Mises effective stress within the trabecular bone at section 14 of bone A (one-legged stance) demonstrating stress concentration within the primary compressive trabeculae.
**Figure 5.16b:** Contour plot of the von Mises effective stress within the trabecular bone at section 14 of bone B (fall) demonstrating stress concentration within the primary compressive trabeculae.
Figure 5.17a: For the cortical bone in bone A (OLS), the plot of the maximum ratio between the calculated element von Mises stress and estimated ultimate stress at each section location, demonstrating a peak at the inferior surface at section 12.
Figure 5.17b: For the primary compressive trabeculae in bone A (OLS), the plot of the maximum ratio between the calculated element failure stresses and estimated ultimate stress at each section location demonstrating a peak at section 14.
Figure 5.17c: For the primary tensile trabeculae in bone A (OLS), the plot of the maximum ratio between the calculated element failure stresses and estimated ultimate stress at each section location, demonstrating a peak at section 14.
Figure 5.18a: For the cortical bone in bone B (fall), the plot of the maximum ratio between the calculated element von Mises stress and estimated failure stress at each section location, demonstrating a peak at the posterior surface of section 10.
Failure Stress/Ultimate Stress
Primary Compressive Trabeculae

Figure 5.18b: For the primary compressive trabeculae in bone B (fall), the plot of the maximum ratio between the calculated element von Mises stress and estimated failure stress at each section location, demonstrating a peak at section 14.
Figure 5.18c: For the primary tensile trabeculae in bone B (fall), the plot of the maximum ratio between the calculated element failure stresses and estimated ultimate stress at each section location, demonstrating peak stresses at section 14.
Figure 5.18d: For the intertrochanteric trabeculae in bone B (fall), the plot of the maximum ratio between the calculated element failure stresses and estimated ultimate stress at each section location, demonstrating peak stresses at section 10.
strength and hence local failure is expected. For model A, the peak cortical stress ratio occurred at the inferior surface at base of the neck (Section 11), while for model B, this peak cortical stress ratio occurred at the posterior intertrochanteric region (Section 10). In both models, the stress ratio decreases gradually in both the proximal and distal directions. By extrapolating linearly, cortical failure for bone A was expected at 448/0.14 or 3200 N, which is 16 percent below the observed in vitro failure load (Table 5.7). Likewise for model B, cortical bone failure was expected at 224/0.14 or 1600 N, which is 12 percent higher than that observed in vitro.

Table 5.7 - Results: Linear FEA and in-vitro bone studies

<table>
<thead>
<tr>
<th>Model</th>
<th>Analysis</th>
<th>Failure Criteria</th>
<th>Experiment (N)</th>
<th>FEA (N)</th>
<th>Percent Difference</th>
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<tr>
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<td>vM Stress 1957</td>
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<td>-21</td>
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<td></td>
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<td>Linear</td>
<td>vM Stress 3825</td>
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<td>-18</td>
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<td>vM Strain</td>
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<td>-5</td>
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For model A, the peak trabecular stress ratio occurred in the primary compressive trabeculae at section 14. This value, 0.5, suggests that trabecular failure begins much earlier than cortical bone failure, becoming unity at 870 N. In contrast, while a peak cervical trabecular stress ratio
occurs at the same location for model B, the maximum value is reached within the intertrochanteric region (0.62).

Plots of the peak strain ratios are presented in Figures 5.19 and 5.20 for models A and B respectively. For model A, the cortical bone trends were somewhat different than those observed for the stress data (Fig. 5.17). The peak strain value occurred on the superior aspect of the femoral neck at section 13. This strain ratio (0.13) reaches 1 at 3530 Nt which is within 8 percent of the in vitro fracture load. In contrast, the trends of the strain ratios for the trabecular bone were similar to those presented in Figure 5.16, with the peak value also occurring at section 14 (0.18). This value reaches unity at 2400 Nt, which is 22 percent higher than the load at which the experimental data suggests the intact bone began to behave nonlinearly (1960 Nt).

For model B, the trends in the peak strain ratios were similar to the stress ratio data for both cortical and trabecular bone. The peak cortical strain ratio was 0.17 and occurred within the posterior cortex at section 10. This ratio can be extrapolated to an expected failure load of 1360 Nt, or 5 percent lower than that in vitro. The peak trabecular strain ratio was 0.30 and occurred within the intertrochanteric region at section 9. This ratio becomes unity at 740 Nt, which is 4 percent lower that the load at which the experimental data demonstrated that the intact bone began to behave nonlinearly (778 Nt).

Nonlinear Finite Element Analyses - Model A

Plots of the cortical bone critical stress ratio for the nonlinear model
Figure 5.19: For bone A (OLS), the plot of the maximum ratio between the calculated element von Mises strain and estimated ultimate strain at each section location, demonstrating a peak at section 14 within the compressive trabeculae.
Figure 5.20: For bone B (fall), the plot of the maximum ratio between the calculated element von Mises strain and estimated ultimate strain at each section location, demonstrating a peak at section 9 within the intertrochanteric trabeculae.
of specimen A are presented in Figure 5.21a. The results for 3 of the 8 load cases are displayed; 445, 3110 and 3560 Newtons. At the first load step (445 N) the model behaved linearly and the data suggest that the peak stress ratio existed within the medial cortex at section 11. This result agrees with the linear, transversely isotropic analysis of bone A presented above. At load step 7 (3110 Nt) the stress ratio becomes approximately constant for sections 8 thru 14. Proximally, this stress ratio decreased markedly at sections 15 and 16. However, at load case 8, a dramatic reversal was observed in this stress profile, with the peak stress ratio reaching the critical value of 1 at section 15, within the superior aspect of the neck. For the next load step (4030 Nt) the stiffness matrix was no longer positive definite and the analysis could not continue. Therefore structural collapse was predicted between 3560 and 4030 Nt.

<table>
<thead>
<tr>
<th>Model</th>
<th>Analysis</th>
<th>Failure Criteria</th>
<th>Experiment (N)</th>
<th>FEA (N)</th>
<th>Percent Difference</th>
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The peak stress ratios for the primary compressive and tensile trabeculae are presented in Figs. 5.21b and 5.21c. During load step 1 these stress ratios were approximately constant near 0.30. However, at load step 7 the stress ratio for the primary compressive trabeculae developed a peak at section 14. Subsequently at load step 8, there was a marked decrease in this stress ratio at section 14, signifying the initiation of trabecular
Figure 5.21a: For cortical bone of the nonlinear model of bone A (OLS), the plot of the maximum ratio between the calculated element von Mises stress and estimated ultimate stress at each section location for three load steps, demonstrating a sudden increase within the superior cortical surface of section 15 at 3590 Nt.
von Mises/ultimate stress
Primary Compressive Trabeculae

Figure 5.21b: For compressive trabeculae of the nonlinear model of bone A (OLS), the plot of the maximum ratio between the calculated element von Mises stress and estimated ultimate stress at each section location for three load steps, demonstrating a sudden decrease within section 14 at 3590 Nt.
Figure 5.21c: For tensile trabeculae of the nonlinear model of bone A (OLS), the plot of the maximum ratio between the calculated element von Mises stress and estimated ultimate stress at each section location for three load steps.
failure. This trabecular failure is demonstrated more dramatically through contour plots of the effective von Mises stress presented in Figures 5.22a thru c. These figures show that local failure begins at load step 7 for the elements representing the primary compressive trabeculae at section 14. Complete failure with stress release subsequently occurs within this region at load step 8.

The load at which the model results demonstrate the initiation of significant structural yielding can be illustrated with the values of the largest and smallest eigenvalues of the ensemble stiffness matrix (Table 5.8). A significant change is observed in the smallest eigenvalue at load step 5. This implies the onset of significant nonlinearity between 1780 and 2220 Newtons.

<table>
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**Table 5.9 - Eigenvalues $\lambda_1$ and $\lambda_n$ and condition number, Bone A**

Nonlinear analysis - Model B

Plots of the cortical bone critical stress ratio for the nonlinear model of specimen B are presented in Figure 5.23a. The results for 3 of the 8
Figure 5.22a: Contour plot of the von Mises effective stress for trabeculae of the nonlinear model of bone A (OLS) within section 14 at 450 Nt, demonstrating peak stresses within the primary compressive trabeculae.
Figure 5.22b: Contour plot of the von Mises effective stress for trabeculae of the nonlinear model of bone A (OLS) within section 14 at 3140 Nt, demonstrating the initiation of trabecular failure.
Figure 5.22c: Contour plot of the von Mises effective stress for trabeculae of the nonlinear model of bone A (OLS) within section 14 at 3590 Nt, demonstrating significant failure within the compressive trabeculae.
Figure 5.23a: For cortical bone of the nonlinear model of bone B (fall), the plot of the maximum ratio between the calculated element von Mises stress and estimated ultimate stress at each section location for three load steps, demonstrating yielding within both the anterior and posterior surfaces of section 9 at 1570 Nt.
load cases are displayed; 222, 890 and 1560 Newtons. At the first load step (222 N), the model behaved linearly with the data demonstrating that the peak stress ratio exists within the posterior cortex at section 9. At load step 4 (890 Nt), the relative magnitude of this stress peak at section 9 increases, being 0.86. At load step 7 (1560 Nt), the posterior cortical stresses become approximately equal at 0.87 which signifies cortical yielding. On the anterior surface of the bone, the stress ratio demonstrates two peaks of equal magnitude, one at section 9 and the other at section 13. For the next load step (1780 Nt) the stiffness matrix was no longer positive definite and the analysis could not continue. Therefore structural collapse was predicted between 3560 and 4030 Nt.

The peak stress ratios for the primary compressive, primary tensile, and intertrochanteric trabeculae are presented in Figs. 5.23b thru 5.23d. During load step 1 these stress ratios were approximately constant being 0.2, 0.2 and 0.3 respectively. At load step 4, peaks in the stress ratio data are observed for the compressive (section 14) and intertrochanteric trabeculae (section 10). These trends remain approximately constant for load case 7, which infers that no trabecular failure had occurred. Contour plots of the von Mises stress are presented in Fig. 5.24 for section 9. These figures demonstrate that trabecular failure begins in this region at 1570 Nt.

A significant change is observed in the smallest eigenvalue at load step 4. This implies the onset of significant nonlinearity between 670 and 890 Newtons.
Figure 5.23b: For compressive trabeculae of the nonlinear model of bone B (fall), the plot of the maximum ratio between the calculated element von Mises stress and estimated ultimate stress at each section location for three load steps.
von Mises/ultimate stress
Primary Tensile Trabeculae

Figure 5.23c: For tensile trabeculae of the nonlinear model of bone B (fall), the plot of the maximum ratio between the calculated element von Mises stress and estimated ultimate stress at each section location for three load steps, demonstrating increases within sections 11 and 12 at 1570 Nt.

- 259 -
von Mises/ultimate Stress
Intertrochanteric Trabecular Bone

Figure 5.23d: For intertrochanteric trabeculae of the nonlinear model of bone B (fall), the plot of the maximum ratio between the calculated element von Mises stress and estimated ultimate stress at each section location for three load steps.
Figure 5.24: Contour plot of the von Mises effective stress within the trabecular bone at section 9 of bone B (fall) at 1570 Nt, demonstrating the initiation of trabecular failure.
Table 5.10 - Eigenvalues $\lambda_1$ and $\lambda_n$ and condition number, Bone B

<table>
<thead>
<tr>
<th>Load Step</th>
<th>Load Magnitude (Nt)</th>
<th>$\lambda_1 \times 10^2$</th>
<th>$\lambda_n \times 10^7$</th>
<th>Condition Number $\log_{10}(\lambda_n/\lambda_1)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>222</td>
<td>1.581</td>
<td>0.969</td>
<td>4.8</td>
</tr>
<tr>
<td>2</td>
<td>445</td>
<td>1.566</td>
<td>0.969</td>
<td>4.8</td>
</tr>
<tr>
<td>3</td>
<td>670</td>
<td>1.551</td>
<td>0.969</td>
<td>4.8</td>
</tr>
<tr>
<td>4</td>
<td>890</td>
<td>0.901</td>
<td>0.969</td>
<td>5.0</td>
</tr>
<tr>
<td>5</td>
<td>1110</td>
<td>0.597</td>
<td>0.968</td>
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<tr>
<td>6</td>
<td>1330</td>
<td>0.334</td>
<td>0.967</td>
<td>5.5</td>
</tr>
<tr>
<td>7</td>
<td>1560</td>
<td>0.037</td>
<td>0.966</td>
<td>6.4</td>
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</tbody>
</table>

5.3 Discussion

The application of the finite element method for both two and three dimensional analysis of the proximal femur is becoming routine. However, the majority of published studies investigate issues regarding the use of femoral prostheses, and hence focus on regions distal to the greater trochanter (Rohlmann et al., 1982; Huiskes et al., 1981; Vichnin and Batterman, 1986). A few detailed analyses of the femoral neck have been presented, but again, no emphasis was placed on cervical or intertrochanteric fracture (Brown and DiGioia, 1984; Orr et al., 1988). However, finite element analysis has been used with good success to predict the strength of diaphyseal bone (Hipp et al., 1988), but similar results have not been presented for structures which are primarily trabecular. This thesis demonstrates that the finite element method of analysis, with geometries and material properties generated from the noninvasive imaging technique QCT, can provide an excellent method for estimating the intact strength of the proximal femur. In addition, through
the use of nonlinear analysis, substantial insight can be obtained regarding the events occurring just prior to fracture.

The results of our linear analyses correlated well with the observed in vitro bone behavior, with the calculated von Mises strain providing the best indicator of both bone yield and failure. When employing this failure criteria, the finite element analysis predicted bone failure to within 8 percent of the experimental fracture loads for both load cases. The onset of structural yielding was observed to result from the initiation of trabecular failure and was also predicted with good accuracy by using the strain failure criteria. In general, the use of this strain criteria resulted in more accurate predictions than when employing the calculated von Mises stress. This was likely the result of the strain distributions being more well behaved than the corresponding stress distributions. For instance, when the material properties are highly heterogeneous as was the case here, and in conjunction elements with different material properties are adjacent, nonphysiologic stress concentrations may be introduced as the result of element geometry alone. However, due to the requirements of interelement compatibility, the strain distributions will not likely demonstrate such dramatic interelement gradients (Fig. 5.25). These large interelement stress differences may also be eliminated by using more, but smaller elements. Convergence studies in this regard are warranted, but given the success of the present analysis, may not be critical.

The nonlinear analyses also performed well when used to predict both yield and fracture loads, but in addition, illuminated the events which occur just prior to structural collapse. For model A, which represented a modified one-legged stance loading configuration, trabecular failure
Figure 5.25: Contour plots of von Mises stress (above) and strain (below) within section 9 for the linear analysis of bone B (fall).
within the primary compressive trabeculae appeared to be an initiating event for bone fracture, resulting in sudden load transferal to the adjacent metaphyseal shell. The location of the critical stress that was subsequently reached within the shell (superior neck, section 15) corresponded very well with the location at which fracture initiated during the in vitro failure test of bone A (Fig. 5.26). The finite element analysis could not continue to the next load step due to the severe mesh distortion, indicating structural collapse at between 3560 and 4030 Newtons. The actual specimen failed at 3825 Nt, which is within 7 percent of the FEA results. In addition, by observing the solution eigenvalues, the initiation of bone yielding was predicted within 13 percent of that observed in vitro.

For model B, which represented one type of fall, the events leading to failure were somewhat different. Fracture was predicted within the intertrochanteric region (Section 9), where both the anterior and posterior cortices were observed to yield. This location is also very close to where the in vitro fracture was observed (Fig. 5.27). However, no sudden dramatic trabecular failure, such as that seen for bone A, was predicted by the analysis at the time of fracture. Instead, the failure mechanism appeared to be primarily cortical yielding with subsequent trabecular bone failure. This difference in failure mode between model A and B supports the results of Section 4.0, which demonstrate that within the subcapital region, trabecular bone supports the majority of the applied load, and hence trabecular failure should initiate bone fracture. Conversely, within the intertrochanteric region, cortical bone provides the primary source of strength, and therefore the stresses in this tissue should proceed to fracture in a predictable fashion with no sudden
Figure 5.26: X-ray of bone A after the *in vitro* failure experiment demonstrating transcervical fracture.
Figure 5.27: X-ray of bone B after the in vitro failure experiment demonstrating intertrochanteric fracture.
increase due to internal trabecular failure.

In contrast to the yield and failure studies, our strain gage data correlated poorly with the linear, anisotropic finite element results. Comparisons between strain gage and finite element data has been presented by several authors, the results of which can be used to determine the degree of agreement expected. Huiskes et al., (1981) conducted an in-depth strain gage study of the femoral diaphysis and reported agreement between beam theory and strain gage data of better than 50 percent when the principal elastic modulus was assumed to be 20 GPa. Similarly, Rohlmann et al., (1981) compared the results of detailed finite element studies of the femur with strain gage data collected from the contralateral bone. The finite element model was typically stiffer than the experimental bone, with reported principal strain data of up to 40 percent less that measured from the corresponding strain gages. In general, both studies demonstrate best correspondence in the mid-diaphysis, away from the metaphyseal regions both distally and proximally. In contrast, significant discrepancies exist between the our FEA results and the strain gage data. Where these differences are appreciable, the finite element model predicts larger strains than were measured experimentally. This observation suggests that the likely reason for these large errors is poor gage bonding to the bone surface. When excluding the 6 gages with dramatic differences from the FEA results (2 from bone A and 4 from bone B), the differences between the model and experiment are similar in magnitude to those reported by others. Therefore, while our strain gage data is not sufficient to validate the model results independently, some of the data do correspond to within the expected degree of accuracy published by other workers.
The structural importance of the Ward's triangle region has been stressed by several authors (Vose and Mack, 1963), primarily in regard to the use of noninvasive techniques for fracture risk assessment (Mazess et al., 1988). While the interest in Ward's triangle originated from observations that it is the area in which bone loss appears first (Kerr et al., 1986), this observation alone does not prove structural significance. In fact, the finding that bone in this region is lost first may well indicate its lack of structural importance. Accordingly, the results of our structural analysis demonstrate that this region (Sections 11 and 12 for both models) is relatively unimportant in regard to both cortical and trabecular bone stresses and strains. As demonstrated in Figs. 5.19 and 5.20, critical strain regions exist more distal, within the intertrochanteric region for one-legged stance (bone B), and more proximal, within the subcapital region during impact of a fall (bone A). Consequently, it is likely that Ward's triangle will not be the most sensitive location to make noninvasive bone measurements for the assessment of fracture risk. Rather, the intertrochanteric region would appear to be the most sensitive site to assess fall fracture risk, as would the subcapital region for one-legged stance. The dramatic loss in density observed in the Ward's triangle region is likely just the consequence of this region having a initially reduced bone density relative to surrounding tissue. A similar process has been noted in the spine, where the nature of the initial trabecular architecture results in the false appearance of preferential bone loss with the progression of osteoporosis (Snyder et al., 1988). This being the case, measurements at this site may initially be sensitive to bone status, but once the majority of trabecular bone is lost (resulting in the classic appearance of the Ward's triangle), continued measurements at this location will be rather
insensitive to further changes.

While the loading conditions modeled in this study were not meant to accurately represent those present in vivo, the primary significance of this research is that finite element analysis can be used to accurately predict bone failure provided the loads are accurately known. Therefore, it remains to determine accurately the nature of the loads present during actual trauma before in vivo fracture risk can be assessed using finite element analysis. Although this is true, QCT generated finite element analysis may not be the most efficient technique for clinical fracture risk assessment. At present only the determination of trabecular bone material properties is performed in any automated fashion, and generating a well behaved mesh geometry from the QCT images is still a process which requires much user intervention. Rather, finite element analysis will likely be of most value for gaining understanding of the processes that occur during bone failure and how simpler, more cost efficient measures could be better applied to assess bone strength in vivo. Accordingly, the goal of the next chapter of this thesis was to make use of the results of this section and to determine the QCT based parameters that best relate to the fracture load of intact femoral specimens tested to failure in vitro under the 'fall' loading conditions presented in this section.

There are several potential limitations in this study. First, is the use of isotropic material properties for trabecular bone in both the linear and nonlinear analyses. While the trabecular bone within the femoral neck and intertrochanteric regions has been shown to demonstrate significant anisotropic behavior (Martens et al., 1983; Brown and Ferguson, 1980; Snyder et al., 1988), Brown et al., (1984) demonstrated
that the incorporation of anisotropic properties into two-dimensional models of the proximal femur results in no significant changes in the stress distributions. However, these two-dimensional analyses presented by Brown et al. were performed only for simulated one-legged stance in which the applied loads closely align with the principal material directions. During a fall this is not the case and hence such insensitivity to anisotropy may not be apparent. Therefore the importance of the isotropy assumption should be investigated.

A second limitation was the simplicity of the fall case considered. Several clinical studies have been performed to attempt to elucidate the most common type of trauma resulting in hip fracture. In an investigation of 365 intracapsular fracture patients, Linton (1944) reported that the majority (70 percent) stated that the fracture was caused by a 'blow on the hip'. Similar results were reported by Backman (1957) who reports that 84 of 102 fracture patients recounted a fall on the hip as the cause of fracture. In addition, several experimental studies have been performed with the goal of identifying the intrinsic (muscular) and extrinsic (applied) forces required to produce clinically significant fracture types (Spears and Owen, 1949; Smith, 1953; Backman, 1957). Yet, no quantitative data exist regarding the magnitude and direction of forces, both intrinsic and extrinsic, present during falls. The complexity of the problem is compounded by the number of variables which exist, such as patient height and weight, presence of overlaying soft tissue, direction of fall, and location of impact. The simplified fall case considered here demonstrates that significantly different failure modes can exist for different loading conditions. However, more data regarding the magnitude and direction of the loads present during trauma are needed before the nature of in vivo
In summary, the finite element method of analysis was shown to accurately predict both structural yielding and catastrophic failure for two disparate loading conditions. For a simplified one-legged stance configuration, the primary compressive trabeculae of the subcapital region was the site at which failure initiated. In contrast, during a simplified fall (meant to represent the situation when a patient lands on the lateral buttock/greater trochanter), failure of the cortical bone at intertrochanteric region was predicted. These results further suggest that the intertrochanteric region may be the most sensitive site at which to make noninvasive measurements for the assessment of in vivo fall fracture risk.
6.0 Fall Fracture Risk of the Proximal Femur

by Quantitative Computed Tomography

In response to the dramatic increase in hip fracture rates, much effort has been made toward the development of techniques by which the risk of fracture could be quantified. A number of in vitro studies have been performed in attempts to elucidate femoral structural behavior and develop non-invasive techniques for the estimation of femoral fracture risk in vivo. Vose and Mack (1963), tested 10 proximal femora with a single joint load directed parallel to the diaphyseal axis. Roentgenographic bone density was measured across the mid neck noting values at the lateral cortex, Ward's triangle, and medial cortex. Density measured within the Ward's triangle area was reported to provide the best correlation with fracture load although no statistical analyses were presented. Phillips et al. (1975), utilized data from quantitative radiography of the proximal femur to estimate the moment of inertia within the mid-neck region. The load required to cause failure of the cortical bone on the superior aspect of the neck was then estimated by employing beam theory. This value was reported to correlate well with the actual failure loads of specimens tested under 'standing' conditions, although again no statistical analysis was presented.

Dalen et al. (1976), measured bone mineral content (BMC) through the center of the femoral neck using single photon absorptiometry (SPA) and related this value to the ultimate force at fracture of test specimens loaded parallel to the diaphyseal axis. The BMC was found to correlate moderately with the ultimate force ($R^2=0.61$). Leichter et al. (1982),
tested intact femora to failure with a single joint load directed at 9° lateral to the diaphyseal axis. Bone density was measured across the mid-neck using Compton scattering. In addition to the fracture load, the surface area of the fracture was measured, with the ultimate load divided by the fracture surface area being presented as a fracture shear stress. Bone density was reported to correlate moderately with fracture load ($R^2=0.66$) and to fracture 'shear' stress ($R^2=0.76$). Mizrahi et al. (1984) used composite beam theory to calculate the ultimate tensile stress on the superior aspect of the femoral neck for intact femora tested with a single joint load applied at 9° to the diaphyseal axis. Bone density was measured by Compton scattering at a site 1 cm inferomedial to the superior surface of the neck. The ultimate stress was reported to correlate well with bone density ($R^2=0.71$). Sartoris et al. (1985), used a dual-energy projection radiographic technique to measure bone mineral content in 19 pairs of cadaver femora. The bones were broken with a single joint load applied at the femoral head and directed toward the center of the knee. Positive linear correlation was reported between dual-energy measurements and dry density ($R^2=0.71$), ash fraction ($R^2=0.71$), cross-sectional cortical bone area ($R^2=0.53$) and, to a lesser degree, force required for fracture ($R^2=0.29$).

Esses et al. (in prep.) demonstrated that single-energy quantitative computed tomography (QCT) could be used to estimate noninvasively the apparent density ($R^2=0.60$) and compressive strength ($R^2=0.83$) of trabecular bone within the subcapital region of fresh, human femora. Eight intact femora were tested to failure with a single joint load applied parallel to the diaphyseal axis. A significant linear correlation was observed between the force required to create a cervical fracture and the average QCT value
within the subcapital region ($R^2 = 0.64$).

In all of these studies, femoral specimens were tested to failure under loading configurations representing one-legged stance. However, it has been reported that greater than 90% of all hip fractures are associated with trauma due to falls (Alffram, 1964; Melton and Riggs, 1983), during which the applied loads are likely much different that those present during gait. Consequently, the application of the results of these in vitro fracture studies to an in vivo, traumatic situation is questionable. The purpose of this aspect of the research was to extend the studies of Esses et al. (in prep.) to the loading associated with falls, and thereby investigate the value of QCT for the prediction of the loads required to induce femoral fracture under controlled in vitro conditions designed to represent one particular type of fall.

6.1 Materials and Methods

Twelve pairs of proximal femora, harvested from fresh human cadavers (age 53–81 years) and stored at -20°C, were used (Table 6.2). All bones were imaged using a GE 9800 scanner operating at 120 KVP and 240 MAS as described in Section 2.0 (Fig. 6.1).

Finite element analysis of the proximal femur (Section 5.0) has demonstrated that critical stress regions exist near the base of the femoral neck and within the intertrochanteric region during simulated falls. In addition, a secondary peak in bone stress occurs at the
Figure 6.1: QCT image made through the femoral neck.
subcapital region, within the primary compressive trabeculae. Therefore, QCT data were collected at these three specific locations for each specimen (Fig. 6.2). Image 1 was made perpendicular to the cervical axis and coincided with the subcapital region; the junction of the femoral head and neck. Image 2 was made perpendicular to the cervical axis at the base of the femoral neck. Image 3 passed through the intertrochanteric region and was defined by the bisection of slice 2 and a line at the superior aspect of the lesser trochanter made perpendicular to the diaphyseal axis (Fig. 6.3). At each location, the average subcortical QCT value was calculated and corrected for scanner drift by subtracting the average QCT value for the H$_2$O chamber of the phantom. In addition at the intertrochanteric location, average QCT data were collected for a small region within the thick medial cortex.

Dimensional measurements were also made for each bone from plane film x-rays taken prior to testing. Radiographs were taken (40 sec @ 80 KV) with the anterior surface of each bone in direct contact with the x-ray film in order to minimize image magnification. These measurements included the femoral head diameter and neck length, and were made in the following manner. At the mid-neck, where the width was the smallest, a line was drawn perpendicular to the cervical axis (a in Fig. 6.4). A parallel line (b) was drawn within the femoral head at the point of its maximum width, the length of this used as the femoral head diameter. A third line (c) was drawn to represent the cervical axis by connecting the midpoints of line a and b. At the level just below the lesser trochanter, another line (d) was drawn perpendicular to the diaphyseal axis and the midpoint between medial and lateral periosteal surfaces was located. A parallel line (e) was drawn in similar fashion 7.5 cm distal to line (d). Finally, line (f) was drawn
Figure 6.2: Scout view demonstrating the location of the three scan locations.
Figure 6.3: OCT images made at the subcapital (top), basicervical (middle) and intertrochanteric (bottom) regions.
Figure 6.4: Measurements made from x-ray images of each bone to determine head diameter and neck length.
connecting the midpoints of (d) and (e). The length of line (c), from its intertrochanteric intersection of line (f) minus the head radius, was used to represent the neck length.

Several geometric parameters were also measured within each image using a version of the software package SLICE (Nagurka, 1980), adapted for use with a Gould PD5000 image processing system. These geometric measurements were made by first greylevel thresholding the QCT image so that only pixels representing bone were counted. Typically, for the calculation of total bone indices, a greylevel threshold of 1150 HU was chosen as the minimum needed to eliminate the inclusion of artifacts from surrounding soft tissue and water (Fig. 6.5a). When calculating separate cortical and trabecular parameters, 2000 HU was used to distinguish these two tissues (Fig. 6.5b). Second, each pixel within a defined subregion, was checked to determine if its value exceeded the threshold, and if so, it was included in the calculation of section aerial properties. These properties, determined for both the total area of bone and separately for the cortical and trabecular regions, included area, and the principal area moments of inertia translated to the calculated section centroid.

Cross-sectional parameters based on the theory of composite beams were also calculated. For a beam of two materials it can be shown that the stress in each is related to the elastic modulus and moment of inertia by

\[
\sigma_{x1} = \frac{MyE_1}{E_1 I_1 + E_2 I_2}, \quad \sigma_{x2} = \frac{MyE_2}{E_1 I_1 + E_2 I_2},
\]

(6.1)

where \(\sigma_x\) is the normal axial stress, \(M\) is the applied moment at the section, \(E\) is the modulus of elasticity, \(I\) is the moment of inertia about
Figure 6.5: OCT of the intertrochanteric region greylevel thresholded at a) 1150 HU (above) and b) 2000 HU.
the neutral axis, and \( y \) is the distance from the neutral axis to the point of interest (Timoshenko and Gere, 1972). By rearranging terms, the applied force can be expressed as a function of the sectional properties by

\[
F = \frac{\sigma_{x1} (E_1 I_1 + E_2 I_2)}{y l E_1} = \frac{\sigma_{x2} (E_1 I_1 + E_2 I_2)}{y l E_2},
\]

(6.2)

where \( F \) is the applied force, and \( l \) is the perpendicular distance from the line of action of the applied force to the section of interest. Setting the normal axial stress equal to the material ultimate stress, the force \( F \) becomes the applied force at material failure. Since the finite element analyses performed in Section 5.0 demonstrated that peak local strain was a good measure of bone failure, and that the strain at failure is approximately constant (0.03) for both cortical and trabecular bone (Section 2.0, Burstein and Reilly, 1976), ultimate strain was used in Eq. 6.2 instead of ultimate stress. With this substitution, Eq. 6.2 becomes equivalent for both materials, being

\[
F_f = \frac{\varepsilon_u (E_1 I_1 + E_2 I_2)}{y l},
\]

(6.3)

where \( \varepsilon_u \) is the ultimate strain and \( F_f \) is the load at failure. Therefore the neck parameter

\[
\frac{E_c I_c + E_t I_t}{y l}
\]

was calculated at each of the three sections of interest, where \( y \) was one half the maximum anterior-posterior dimension at each section and \( l \) was the distance from the center of the femoral head to the section of interest,
and the subscripts c and t represent cortical and trabecular bone respectively. The elastic modulus of trabecular bone, $E_t$, was estimated from the average subendosteal QCT data at each section by employing the QCT-modulus relationship derived in Section 2.0. Since a relationship between cortical QCT and mechanical properties was not measured, the value of $E_c$ was assumed to be the mean value for the metaphyseal specimens from proximal femora (9650 MPa) as presented in Section 3.0.

The strength of each intact femur was measured experimentally in such a way as to represent one particular type of fall. This loading configuration was one of many investigated experimentally by Backman (1957), and was chosen because it was reported to result in clinically significant fracture types. This case represents the situation in which the patient falls to the side, with the greater trochanter coming in contact with the ground. This situation was simply modeled as an anteromedially directed force applied to the lateral greater trochanter with a parallel and opposite reaction load applied to the femoral head (Fig. 6.6). The direction of the loads were such that both the diaphyseal and neck axes formed an angle of 30 degrees with the plane perpendicular to the applied loads. Each bone was sectioned at the mid-diaphysis level and the distal end rigidly fixed with the lateral aspect of the greater trochanter in contact with the horizontal platform of the hydraulic actuator. A single vertical load was then applied to the femoral head at a displacement rate of 0.70 mm/sec until failure was reached. The magnitude of the applied load was measured by the calibrated load cell of the test system while the specimen deformation was measured using the calibrated LVDT of the hydraulic actuator. The data were collected using a personal computer (IBM) and commercially available software (Labtech Notebook, Wilmington, MA 01887). In addition to the
Figure 6.6: Schematic representation of the loads applied to the femoral specimens.
ultimate load, the energy to failure was also estimated by calculating the area under the load-deflection curve up to the point of specimen collapse. All specimens failed by transcervical, intertrochanteric or basicervical fracture (Table 6.2).

Correlation coefficients, standard deviations and linear regressions were calculated using the software package RS1 (BBN Software Products, Cambridge, MA 02238), with the size of the resulting coefficients of determination interpreted using the classification scheme presented by Hinkle et al., (1979), shown in Table 6.1.

<table>
<thead>
<tr>
<th>Rule of Thumb for Interpreting the Size of a Coefficient of Determination (From Hinkle et al., 1979)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.90 to 1.00 (-0.90 to -1.00)</td>
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<tr>
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<tr>
<td>0.00 to 0.30 (0.00 to -0.30)</td>
</tr>
</tbody>
</table>

6.2 Results

A typical load-deflection curve is presented in Figure 6.7. In the initial portion of the curve, nonlinearities are observed which represent local crushing primarily at the location of the applied load at lateral greater trochanter. As the load increases, a second region of nonlinearity is reached which represents the initiation of structural yielding.
Figure 6.7: Typical specimen load-deflection curve.
Table 6.2 - Bone Data

<table>
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<tr>
<th>Specimen</th>
<th>Gender</th>
<th>Age</th>
<th>Listed Cause of Death</th>
<th>Failure Load (Nt)</th>
<th>Type of Fracture</th>
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<td>1326</td>
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<tr>
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<td>66</td>
<td>Respiratory Failure</td>
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<td>F</td>
<td>63</td>
<td>Cardio-Pulm Arrest</td>
<td>2446</td>
<td>intertroch</td>
</tr>
<tr>
<td>H613L</td>
<td>F</td>
<td>62</td>
<td>Pulmonary Arrest</td>
<td>1935</td>
<td>transcervical</td>
</tr>
</tbody>
</table>

High positive correlation was observed between the specimen fracture load and the subcapital average subcortical QCT (Fig. 6.8a; Table 6.3), while moderate positive correlation was observed for the other subcapital indices; the average subcortical QCT times trabecular bone area (Fig. 6.8b) and the average subcortical QCT times the minimum principal trabecular bone moment of inertia (Fig. 6.8c). The low correlation between the fracture load and the subcapital measure, the composite beam parameter was not significant (Fig. 6.8d).

At the basiscervical location, moderate positive correlation was observed between the fracture load and all biomechanical indices. In particular, the average trabecular QCT times trabecular bone area (Fig. 6.9a), average trabecular QCT times section moment of inertia (Fig. 6.9d) and the composite beam parameter provided the best results (Fig. 6.9f).

In general, the most significant relationship between fracture load and the bone measures was obtained within the intertrochanteric region. A high positive correlation was observed for the intertrochanteric trabecular
Figure 6.8a: Fracture load versus the subcapital average trabecular QCT value.
Figure 6.8b: Fracture load versus the subcapital average trabecular QCT value times the trabecular bone area.
Figure 6.8c: Fracture load versus the subcapital average trabecular QCT value times section minimum moment of inertia.
Figure 6.8d: Fracture load versus the subcapital composite beam parameter.
Figure 6.9a: Fracture load versus the basicervical trabecular bone QCT value.
Figure 6.9b: Fracture load versus the basicervical trabecular bone QCT value times the trabecular bone area.
Figure 6.9c: Fracture load versus the basicervical trabecular bone QCT value times the total bone area.
Figure 6.9d: Fracture load versus the basicervical trabecular bone QCT value times the section minimum moment of inertia.
Figure 6.9e: Fracture load versus the basicervical cortical bone minimum moment of inertia.
Figure 6.9f: Fracture load versus the basicervical composite beam parameter.
average QCT (Fig. 6.10a) and the average QCT times trabecular bone area (Fig. 6.10b). The average QCT times total bone area provided a very high positive correlation with fracture load (Fig. 6.10c), resulting in the the best predictor of bone strength of all those measured. A moderate to low correlation was observed between the fracture load and the other intertrochanteric indices; cortical bone minimum moment of inertia (Fig. 6.10d), and the composite beam parameter (Fig. 6.10e).

The trabecular bone QCT data at the subcapital and intertrochanteric regions were moderately correlated (Fig. 6.11a) with each other and to a lesser degree with the basicervical (Ward's triangle) trabecular bone QCT (Fig. 6.11b). However, the cortical calcar QCT demonstrated no significant correlation with either subcapital or intertrochanteric trabecular data (Fig. 6.11c). In addition, no significant correlation was observed between the load at fracture and specimen age (Fig. 6.11d).

Finally, the energy to failure was observed to vary significantly between bones, ranging from 16 to 51 Nm with a mean of 26.5 (std = 11 Nm).
Figure 6.10a: Fracture load versus intertrochanteric trabecular bone QCT value.
Figure 6.10b: Fracture load versus intertrochanteric trabecular bone QCT value times trabecular bone area.
Figure 6.10c: Fracture load versus intertrochanteric trabecular bone QCT value times total bone area.
Figure 6.10d: Fracture load versus intertrochanteric trabecular bone QCT value times section minimum moment of inertia.
Figure 6.10e: Fracture load versus intertrochanteric cortical bone minimum moment of inertia.
Figure 6.10f: Fracture load versus intertrochanteric composite beam parameter.
Figure 6.11a: Subcapital trabecular bone QCT value versus intertrochanteric trabecular bone QCT value.
Figure 6.11b: Basicervical trabecular bone QCT value versus intertrochanteric trabecular bone QCT value.
Figure 6.11c: Calcar cortical bone QCT value versus intertrochanteric trabecular bone QCT value.
Figure 6.11d: Fracture load versus specimen age. Filled symbols represent males.
Table 6.3 - Observed correlations between fracture force and bone indices.

<table>
<thead>
<tr>
<th>Location</th>
<th>Parameter</th>
<th>Correlation Coefficient R²</th>
<th>Standard Error of Regression see (Nt)</th>
<th>Significance Level p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcap.</td>
<td>Av. Trab. QCT</td>
<td>0.72</td>
<td>586</td>
<td>0.0004</td>
</tr>
<tr>
<td></td>
<td>Av.QCT x Trab. Area</td>
<td>0.68</td>
<td>629</td>
<td>0.0009</td>
</tr>
<tr>
<td></td>
<td>Av.QCT x Total I</td>
<td>0.58</td>
<td>727</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>Composite Param.</td>
<td>0.32</td>
<td>917</td>
<td>0.053</td>
</tr>
<tr>
<td>Basi.</td>
<td>Av. Trab. QCT</td>
<td>0.48</td>
<td>804</td>
<td>0.012</td>
</tr>
<tr>
<td></td>
<td>Av.QCT x Trab. Area</td>
<td>0.50</td>
<td>787</td>
<td>0.010</td>
</tr>
<tr>
<td></td>
<td>Av.QCT x Bone Area</td>
<td>0.54</td>
<td>760</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>Av.QCT x Total I</td>
<td>0.55</td>
<td>749</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>Cortical I</td>
<td>0.48</td>
<td>806</td>
<td>0.013</td>
</tr>
<tr>
<td></td>
<td>Composite Param.</td>
<td>0.66</td>
<td>655</td>
<td>0.0014</td>
</tr>
<tr>
<td>Troch.</td>
<td>Av. Trab. QCT</td>
<td>0.87</td>
<td>397</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td></td>
<td>Av.QCT x Trab. Area</td>
<td>0.89</td>
<td>366</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td></td>
<td>Av.QCT x Bone Area</td>
<td>0.93</td>
<td>296</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td></td>
<td>Av.QCT x Total I</td>
<td>0.65</td>
<td>658</td>
<td>0.0015</td>
</tr>
<tr>
<td></td>
<td>Cortical I</td>
<td>0.48</td>
<td>803</td>
<td>0.012</td>
</tr>
<tr>
<td></td>
<td>Composite Param.</td>
<td>0.46</td>
<td>817</td>
<td>0.015</td>
</tr>
</tbody>
</table>

6.3 Discussion

The use of quantitative computed tomography as an indirect measure of bone density provided an excellent predictor of in vitro femur strength during a simulated fall. Data from the intertrochanteric region furnished the best correlation with fracture, supporting the results of previous finite element analyses (Section 5.0). These finite element models demonstrated that during a fall, the peak stresses are developed within the intertrochanteric region.

While several investigators have also reported bone density to be an important variable for in vitro fracture risk (Vose and Mack, 1963;
Dalen et al., 1976; Leichter et al., 1982), their studies were performed with loads representing one-legged stance and with measurements made in the mid-neck region only. The results of these studies indicated that Ward's triangle was the critical region for the integrity of the femoral neck and thus should be the site at which measurements are made for noninvasive fracture risk assessment (Mazess and Wahner, 1988). However, our study using loads representing a fall demonstrates that while data from within the Ward's triangle region correlate moderately with bone strength, measures at this site are relatively insensitive predictors of fracture during loading conditions representative of in vivo trauma.

At the basicervical and intertrochanteric sites, the inclusion of geometric data along with QCT estimated density resulted in improved predictability of the fracture load. While the importance of geometric factors has been emphasized previously (Phillips et al., 1975; Mizrahi et al., 1982; Fredensborg and Nilsson, 1977; Horsman et al., 1982; Esses et al., in prep.), the issue of what and where to measure to obtain the most sensitive indicator of bone strength has not been adequately resolved. Our results demonstrate that the combination of trabecular bone average QCT data with total bone area at the intertrochanteric site provides an excellent predictor of intact bone strength ($R^2 = 0.93$, $\text{SEE} = 296 \text{ Nt}$). While the composite beam parameter included more structural geometric information at each site, this data may be too specific to the particular measurement location to provide a general predictor of intact bone strength. That is, since all the specimens did not fracture at the same location, a detailed parameter which assumes a particular mode of failure (bending) at one particular location may not be expected accurately predict the fracture load in all cases. Even when considering
only those specimens which fractured near the location of the measured composite parameter, this criteria did not appear to perform particularly well. When using the minimum of the three composite parameters calculated for each bone (subcapital, basicervical, or intertrochanteric), improved predictability of the fracture force was observed ($R^2=0.76$, see=549 Nt), but this parameter still did not perform as well as even trochanteric trabecular QCT data alone. Perhaps, if this parameter were measured in a continuous fashion throughout the proximal femur, local minimum values would be observed which were missed when only measuring at three sites, and consequently better predictability would result.

Of all the parameters measured, the best indicator of bone strength was obtained by the simple combination of a measure of bone size (total bone cross-sectional area at the intertrochanteric site) and bone material properties (average trabecular bone QCT at the intertrochanteric site). The simplicity of this result implies that data obtained through the use of other noninvasive imaging modalities may perform equally well. For instance, when using photon absorptiometry, measurements of both cross-sectional area as well as an average attenuation coefficient can be made (Martin and Burr, 1984). Therefore, a parameter similar to the one proposed here could potentially be measured in situ using dual photon absorptiometry, although no separation of the contributions of cortical and trabecular bone could be made. Indeed, DPA has been used in prospective clinical studies to measure bone status (bone mineral density) at the intertrochanteric site and to relate this parameter to fracture incidence. Melton et al. (1985) measured bone mineral density (BMD) with DPA at a cervical and
intertrochanteric site within the proximal femur for 300 women. Hip fracture incidence rate was investigated as a function of the measured BMD at both sites. Best fit regressions demonstrated a quadratic relationship between cervical BMD and fracture incidence ($R^2=0.97$) and a cubic relationship between intertrochanteric BMD and incidence ($R^2=0.99$). These relationships reflect a greater change in fracture incidence for a given change in intertrochanteric BMD than for an equivalent change in cervical BMD. In a similar study, Mazess et al., (in press) measured BMD within three sites within the proximal femur (cervical, Ward's triangle and intertrochanteric) for 423 females. The BMD at the femoral sites were approximately 25 to 30 percent below age-matched controls, with the largest difference being at the intertrochanteric site (28 percent). Eriksson et al., (1988) measured BMD at 4 sites within the proximal femur (mid-neck, Ward's triangle, intertrochanteric and total trochanteric areas) for controls and patients with either cervical or intertrochanteric fractures. For intertrochanteric fractures, the BMD as measured within the total trochanteric region demonstrated the largest difference from the control group (27 percent). In all these studies, BMD was determined from the measured bone mineral content within a region of interest divided by the projected scan area of that region. This data therefore includes integration of both cortical and trabecular bone density and no measure of the bone cross-sectional area. However, their findings support our results that the intertrochanteric site is the more sensitive location for the estimation of hip fracture risk.

The moderate correlation between average subcortical QCT data from the intertrochanteric and subcapital sites demonstrates that trabecular
bone status at these two locations may be related. Yet this relationship is not strong enough to allow subcapital QCT to be an equally good predictor of fall fracture load as is the intertrochanteric data. In contrast, our data demonstrate that no significant correlation exists between intertrochanteric trabecular and cortical bone QCT. While the sensitivity of QCT to cortical bone properties has not been demonstrated, these data suggest that bone loss within these tissues may be uncoupled. In addition our data also demonstrates that no significant relationship existed between the specimen age and failure load, which points out the limitations with using comparisons of measured parameters against those from age and gender matched controls as an indication of fracture risk. Rather, as presented by Melton et al., (1985), the use of an absolute value as an assessment threshold, will likely result in the best identification of those at greatest risk.

The estimated energy to failure varied significantly between bones. However, this value is dependent on many factors in addition to the structural behavior within the proximal femur, such as the diaphyseal length and torsional rigidity, and the amount of local crushing at the lateral trochanter. In addition, the lack of surrounding soft tissue and the quasi-static nature of load application precludes direct comparisons between this measured value and estimates of the energy imparted to the hip at impact of a fall. However, our data suggests that much less energy is required to break the proximal femur than that which is potentially available during a fall. For example, for a 50 kg. person falling from a height of 1 meter, the potential energy available is approximately 500 Nm. This value is an order of magnitude greater than the data presented here. Therefore, since a hip is not broken every time
someone falls, significant energy is likely absorbed by other means such as soft tissue, muscle contraction, and outstretched hands. This observation further emphasizes the need to investigate and understand the process of falling.

There are three important limitations of this study. The first is the use of single-energy QCT, which has been demonstrated to be influenced by variations in marrow fat content (Mazess, 1983; Laval-Jeantet, 1986). Nonetheless, the excellent results obtained when using intertrochanteric data demonstrate that when estimating structural properties, the errors introduced from marrow fat variation may not be critical. However, given the relatively small size of this sample (n=12) and the uncertainty of the actual marrow fat content within each bone, this issue cannot be adequately addressed with our data. The second limitation was that only a simplified fall was investigated. Many clinical and experimental studies have been performed to in an attempt to identify the common types of falls and the resulting intrinsic (muscular) and extrinsic (applied) forces on proximal femur (Backman, 1957; Smith, 1953; Spears and Owen, 1949; Linton, 1944). Yet no quantitative data exists regarding the magnitude and direction of forces present during actual falls. The complexity of this problem is compounded by the number of variables which exist, such as patient height and weight, presence of overlaying soft tissue, direction of fall and location of impact. Ideally, the most severe, clinically relevant loading condition should be used in this type of study. However, at this time sufficient quantitative information is not available. The third limitation is that no true subcapital fractures were produced in the tested specimens, and therefore the usefulness of these techniques for
predicting fracture risk cannot be assessed for this particular fracture type.

In summary, our results demonstrate that bone strength can be determined in vitro under controlled loading conditions representing one type of fall by using a parameter combining average QCT data and cross-sectional area. However, the application of this technique for the determination of femoral strength in vivo will require the investigation and solution of other potential problems such as appropriate patient positioning and beam hardening due to surrounding soft tissue. Moreover, the determination of femur strength in situ will solve only a portion of the problem of establishing individual risk of hip fracture. In order to place isolated femur strength in proper context, the magnitude and direction of impact loads resulting from falls need to be quantified. Additional studies are required which will investigate the relationship between the direction and magnitude of resultant fall forces and such parameters as patient height, weight, the amount of overlaying soft tissue, direction of the fall, location of the impact, and patient muscle tone. Nonetheless, worst case scenarios need to be developed such that bone strength can be converted to an estimate of the factor of safety. Second, and equally important, is the determination of individual probability of trauma (Melton and Riggs, 1985). Patients with certain pre-existing disorders are known to be at increased risk of falling and hence are more likely to subject fragile bones to critical levels of stress (Brookehurst et al., 1978; Lipsitz, 1986). These factors therefore, all need to be considered when developing a comprehensive hip fracture risk prediction technique.
7.0 Recommendations

The results presented in this thesis have begun to address the basic questions regarding the mechanism of fracture of the proximal femur. While encouraging results have been presented regarding the estimation of intact bone strength using QCT, there is likely much more to be gained by the continuation of this research. Specifically, the tools explored here for the structural analysis of the proximal femur have not been exhaustively utilized. The finite element method of analysis is most useful as an iterative tool by which structural insight may be gained through the variation of material properties and loading configurations. In this regard, there are several studies which should be performed to further elucidate the mechanics of the proximal femur. First, while two dimensional analyses of the proximal femur have suggested that the incorporation of anisotropic trabecular material properties may not be important in structural analysis during one-legged stance (Brown and DiGioia, 1984), this may not be true during the impact of a fall. During gait, the direction of the joint contact loads align closely with the major material axis of the trabeculae of the primary compressive system and thus the material property assumptions in directions perpendicular to this direction will not likely influence the results significantly. However, at impact from a fall, a posterolaterally directed load applied to the femoral head acts perpendicular to the major material axis of the primary compressive trabeculae and consequently the off-axis material property assumptions become more important. Current studies (Snyder, 1988), have made it possible to define the three dimensional orthotropic material properties of the trabecular bone within the proximal femur and hence the incorporation
of this data into the linear finite analysis should be performed. It may well be that the assumption of isotropy results in significant overestimation of the true bone strength at the impact of a fall, especially within the subcapital region where the trabeculae are highly orientated.

A second area of continued research should be the investigation of additional fall load cases. While it may prove difficult to accurately determine the loads actually present in vivo during falls, the finite element method would be useful to identify a 'worst case' set of loads which could be used to estimate minimum bone strength. Thus, a broad range of anatomically possible fall directions should be considered and the one which presents the most severe state of stress could be used in further analyses. It would be of interest to determine if during the most severe type of fall, the intertrochanteric region is still the most sensitive site to noninvasively estimate fracture risk. This strategy would result in a conservative estimate of bone strength and consequently may be the most appropriate for future clinical trials.

Refinement of the finite element mesh should be also considered. The mesh used in the present analysis incorporates a relatively large element size. Provided the significant heterogeneity of the material property distribution of the trabecular bone, improved solution accuracy may be obtained with a smaller element size. However, for the nonlinear analyses, the current model size is at the limit of system capability and hence if the element size is appreciable reduced, the amount of the proximal femur represented will need to be decreased. Such a reduction in bone representation may pose a significant problem, in that fractures may occur.
anywhere from the subcapital to intertrochanteric regions and thus the entire neck and trochanter must be represented in order not to miss a potential fracture. Still, given the good results obtained using the current mesh geometry, further element size reduction may not be warranted.

The results of the finite element analyses presented in Sections 4.0 and 5.0 may also have significant ramifications for the design of femoral prostheses. These results have begun to elucidate the structural behavior of the proximal femur and hence how prostheses may be designed to most optimally integrate with natural function. It appears that the 'mechanical axis' of the femoral neck does not correspond with the neck axis, as commonly referred to in the literature. Rather, most notably in those with marked osteoporosis, the proximal femur behaves as a composite column, with the proximal portion composed of the primary compressive system of trabeculae and the distal portion composed of the cortical bone of the medial calcar (Fig. 7.1). The model of a column in compression as opposed to a tube in bending could provide insight into the design of prostheses which result in a more physiologic distribution of stress and hence longer implant life. Specifically, an implant which completely straddles the medial calcar, such that the direct compressive load is applied to the cortex in this region may prove advantageous (Fig. 7.2).

Since intertrochanteric fracture is not the only type observed clinically, a femoral specimen which has failed by subcapital fracture in vitro should be modeled as those in Section 5.0 to add further insight into the process of proximal femur fracture. In addition, several studies have reported trends in fracture type with age, suggesting a dependence on bone density. Therefore it may be useful to perform a parametric study with
Figure 7.1 Figure of the proximal femur displaying an estimate of the true 'mechanical axis' of the femoral neck.
Figure 7.2  Schematic representation of a potential modification to prosthesis designs based on the composite column theory.
models similar to those used in Section 5.0 to investigate how the progression of osteoporosis affects the location and type of fracture. It may result that, independent of the load configuration, the progression of osteoporosis causes a shift in the 'stress critical site', consequently resulting in fracture at a different location.

Three types of femoral failure were noted in the specimens tested in vitro; transcervical, basicervical and intertrochanteric. None fractured by classic, clinically important subcapital fracture. Therefore, in conjunction with the additional modeling studies of fall subcapital fractures, bones which have failed in this way should be added to the in vitro study presented in Section 6.0 to determine if the intertrochanteric still the best location for noninvasive fracture risk assessment.

Single-energy QCT proved to be an excellent technique for the assessment of in vitro fracture risk for the specific population of specimens tested. However, these specimens represent only a narrow range of donor age. Marrow fat content can vary significantly with age (Dunhill, 1967), and this variation has been reported to lead to significant errors in the estimation of bone density with single energy techniques (Mazess, 1983). Consequently, additional work should be performed to assess the influence of marrow fat content on the predictors of fracture risk presented here. This should include the addition of specimens obtained from a broader range of donors to the in vitro fall fracture study. If needed, the use of dual-energy techniques, such as dual-energy QCT and dual photon absorptiometry, should be explored to determine if they provide greater accuracy in the assessment of intact bone strength by eliminating the effects of soft tissue and bone marrow.
8.0 Appendix – Concrete Material Law Used for Trabecular Bone

Trabecular bone exhibits a complex structural response with various important nonlinearities; including a nonlinear stress-strain behavior, tensile cracking and compressive crushing. Presently, most investigators using finite element models approximate this behavior by incorporating material models such as; isotropic linear elastic, orthotropic linear elastic, and bilinear isotropic. These material approximations fail to model the important asymmetry of the trabecular bone stress-strain behavior in compression and tension; namely being essentially linear to ultimate failure in tension and highly nonlinear to the crushing in compression with post-crushing strain softening. However, a material model that incorporates these critical features has been developed for modeling concrete structures (Bathe and Ramaswamy, 1979). (Portions of this text are taken from that article and the reader is referred to it for more detail.)

This concrete model employs three basic features to describe material behavior; 1) a nonlinear stress-strain relation including strain-softening to allow for the weakening of the material under increasing compressive stresses, 2) a failure envelope that defines cracking in tension and crushing in compression, and 3) a strategy to model the post-cracking and crushing behavior of the material. Under uniaxial conditions there is assumed to be three phases to the material law: 1) zero stress to tensile failure, in which there is a linear stress-strain relation; 2) zero stress to the minimum (crushing) stress in compression; and 3) from the minimum stress to the ultimate stress in compression (Fig. 8.1). For cases 2 and 3 a parabolic stress-strain relationship is used.
Figure 8.1 Material model uniaxial stress - strain law. From Bathe and Ramaswamy, 1979.
The material is considered isotropic when subjected to tension or low compression, low compression defined as \( \sigma_{p3} > \kappa \sigma_c \) (typically \( \kappa = 0.4 \)). If the material is under high compression, \( \sigma_{p3} < \kappa \sigma_c \) an orthotropic stress-strain matrix with directions of orthotropy defined by the principal stress directions is employed.

The tensile failure envelope is shown in Figure 8.2. It is noted that considering one principal stress direction, the tensile strength of the material does not change with the introduction of tensile stresses in the other principal stress directions. However, the presence of compressive stresses in one or more of the other principal directions does change this tensile strength. Tensile failure occurs if the tensile stress in a principal stress direction exceeds the material tensile failure stress. In this case it is assumed that a plane of failure develops perpendicular to the principal stress direction. The effect of this type of material failure is that the normal and shear stiffness across the plane of failure are reduced, and the corresponding normal stress is released. The normal and shear stresses are reduced by constant factors; \( \eta_n \) is used as the normal stiffness reduction factor (typically 0.001), while \( \eta_s \) is the shear stiffness reduction factor (typically 0.5).

To model compressive failure, a failure surface in principal stress space is defined by 24 discrete stress values for various ratios of \( \sigma_1 \) to \( \sigma_c \), as well as for various relationships between \( \sigma_2 \) and \( \sigma_3 \) (Fig. 8.3). Six values of \( \sigma_1/\sigma_c \) determine at which stress magnitudes of \( \sigma_1 \) the discrete two-dimensional failure envelopes are input. These two-dimensional failure envelopes are defined by the failure stress values of \( \sigma_3/\sigma_c \) that correspond to the stress magnitudes \( \sigma_2 = \sigma_1, \sigma_2 = 0.5 \sigma_3 \) and \( \sigma_2 = \sigma_3 \). To identify if
Figure 8.2 Triaxial tensile failure envelope. From Bathe and Ramaswamy, 1979.
Figure 8.3 Triaxial compressive failure envelope. From Bathe and Ramaswamy, 1979.
compression failure has occurred, the largest principal stress $\sigma_{p1}$ is employed to establish by interpolation a biaxial failure envelope on $\sigma_{p2}$ and $\sigma_{p3}$. The material has crushed if the stress state corresponding to $\sigma_{p2}$ and $\sigma_{p3}$ lies on or outside this biaxial failure envelope. If the material has crushed in compression, it is assumed that the material strain-softens into all directions until the minimum principal strain reaches the ultimate strain. When the minimum principal strain becomes equal to the ultimate strain, all stresses are completely released, and from then on the material has no more stiffness.

To determine if this material law could be used for trabecular bone, a finite element model was generated to simulate a simple cylindrical specimen tested in compression (Fig. 8.4). The modeled bone specimen was taken from the femoral neck, being fabricated with a diameter of 9.87 mm and a length of 7.87 mm. The average corrected QCT value for the specimen taken in situ was 175 HU. The stress-strain curve for the specimen tested to failure in uniaxial compression is shown in Figure 8.5. By employing regressions obtained for QCT versus strength and elastic modulus (Section 2.0), the elastic modulus was estimated to be 170 MPa, and the ultimate strength in compression to be -5.5 MPa. In addition, based on the results of Kaplan et al (1985), the ultimate strength in tension was approximated to be 60% of that in compression, or 3.36 MPa. The concrete model requires 31 input variables, those used in this analysis are presented below.
\[ E_0 = 170 \text{ MPa} \quad - \text{constant Young's modulus in tension} \]
\[ \nu = 0.40 \quad - \text{Poisson Ratio} \]
\[ \alpha = 0.0 \quad - \text{Coef. of thermal expansion} \]
\[ \sigma_t = 3.36 \text{ MPa} \quad - \text{ultimate tensile strength} \]
\[ \sigma_c = -5.5 \text{ MPa} \quad - \text{minimum compressive (crushing) stress} \]
\[ \varepsilon_c = -0.054 \quad - \text{strain at minimum compressive stress} \]
\[ \sigma_u = -4.37 \text{ MPa} \quad - \text{ultimate compressive stress} \]
\[ \varepsilon_u = -0.095 \quad - \text{strain at ultimate compressive stress} \]

The compressive failure envelope for trabecular bone has not yet been completely defined, and thus the 24 parameters required to define the surface in principal stress space were calculated based on the Hoffman failure theory (Hoffman, 1976). This failure theory assumes linear terms to account for different tensile and compressive strengths and was demonstrated to fit test data reasonably well for the \( \tau_{xy} - \varepsilon_{xx} \) plane (Stone et al., 1983). For principal stress space, the theory is given by

\[
C_1(\sigma_2 - \sigma_3)^2 + C_2(\sigma_3 - \sigma_1)^2 + C_3(\sigma_1 - \sigma_2)^2 \\
+ C_4\sigma_1 + C_5\sigma_2 + C_6\sigma_3 = 1
\]

where
\[
C_1 = C_2 = C_3 = \frac{1}{2\, S_t S_c} \\
C_4 = C_5 = C_6 = \frac{1}{S_t} - \frac{1}{S_c}
\]

and where \( S_t \) is the ultimate strength in tension and \( S_c \) is the ultimate strength in compression.
Figure 8.4 Axisymmetric 113 node model of a cylindrical specimen.
Figure 8.5 Stress-strain curve from uniaxial stress compression test.
\[
\begin{align*}
\text{SP1(1)} &= \frac{\sigma_{p1}}{\sigma_c} = 0.0 \\
\text{SP1(2)} &= \frac{\sigma_{p1}}{\sigma_c} = 0.25 \\
\text{SP1(3)} &= \frac{\sigma_{p1}}{\sigma_c} = 0.50 \\
\text{SP1(4)} &= \frac{\sigma_{p1}}{\sigma_c} = 0.75 \\
\text{SP1(5)} &= \frac{\sigma_{p1}}{\sigma_c} = 1.0 \\
\text{SP1(6)} &= \frac{\sigma_{p1}}{\sigma_c} = 1.2 \\
\text{SP3(1,1)} &= \frac{\sigma_{p3}^{1,1}}{\sigma_c} = 1.00 \\
\text{SP3(2,1)} &= \frac{\sigma_{p3}^{2,1}}{\sigma_c} = 1.41 \\
\text{SP3(3,1)} &= \frac{\sigma_{p3}^{3,1}}{\sigma_c} = 1.80 \\
\text{SP3(4,1)} &= \frac{\sigma_{p3}^{4,1}}{\sigma_c} = 2.18 \\
\text{SP3(5,1)} &= \frac{\sigma_{p3}^{5,1}}{\sigma_c} = 2.54 \\
\text{SP3(6,1)} &= \frac{\sigma_{p3}^{6,1}}{\sigma_c} = 2.86 \\
\text{SP3(1,2)} &= \frac{\sigma_{p3}^{1,2}}{\sigma_c} = 1.38 \\
\text{SP3(2,2)} &= \frac{\sigma_{p3}^{2,2}}{\sigma_c} = 1.83 \\
\text{SP3(3,2)} &= \frac{\sigma_{p3}^{3,2}}{\sigma_c} = 2.32 \\
\text{SP3(4,2)} &= \frac{\sigma_{p3}^{4,2}}{\sigma_c} = 2.83 \\
\text{SP3(5,2)} &= \frac{\sigma_{p3}^{5,2}}{\sigma_c} = 3.35 \\
\text{SP3(6,2)} &= \frac{\sigma_{p3}^{6,2}}{\sigma_c} = 3.76 \\
\text{SP3(1,3)} &= \frac{\sigma_{p3}^{1,3}}{\sigma_c} = 1.26 \\
\text{SP3(2,3)} &= \frac{\sigma_{p3}^{2,3}}{\sigma_c} = 1.68 \\
\text{SP3(3,3)} &= \frac{\sigma_{p3}^{3,3}}{\sigma_c} = 2.14 \\
\text{SP3(4,3)} &= \frac{\sigma_{p3}^{4,3}}{\sigma_c} = 2.61 \\
\text{SP3(5,3)} &= \frac{\sigma_{p3}^{5,3}}{\sigma_c} = 3.10 \\
\text{SP3(6,3)} &= \frac{\sigma_{p3}^{6,3}}{\sigma_c} = 3.50
\end{align*}
\]
The remaining parameters were set to

\[
\begin{align*}
\text{BETA} &= 0.75 \quad \text{principal stress ratio, } \beta \\
\text{GAMMA} &= 1 \quad \text{uniaxial critical strains scaling factor} \\
\text{KAPA} &= 0.5 \quad \text{control parameter for changing material law, } \kappa \\
\text{CLFN} &= -1 \quad \text{constant used for loading function} \\
\text{STIFAC} &= 0.0001 \quad \text{normal stiffness reduction factor, } \eta_n \\
\text{SHEFAC} &= 0.5 \quad \text{shear stiffness reduction factor, } \eta_s \\
\text{TREF} &= 0 \quad \text{reference temp - not used}
\end{align*}
\]

For strain controlled loading, the model results are presented with the experimental data in Figure 8.6. The FEA model results are shifted slightly to the right in this figure since the model does not represent the contact nonlinearities which were present in initial portion of the experimental data. To obtain a well behaved solution it was important to use small strain increments, here strain steps of 0.065 or \( \epsilon_u / 11 \) were used. For strain controlled loading, the strain-softening portion of the curve could only be reached if no equilibrium iterations were used. For uniaxial compression with strain controlled loading, the concrete material law appears to behave well and accurately represents the stress-strain behavior of trabecular bone.

Since applied loads will be used in the finite element models of the intact bones, it was important to also investigate the stress controlled behavior of this material law. Models were run with and without stiffness reformations and/or equilibrium iterations. Using no stiffness reformations or equilibrium iterations, the applied and predicted material stress versus strain behavior is presented in Figure 8.7. This figure demonstrates that when using no stiffness reformations or equilibrium iterations the predicted stress is always smaller than the applied stress. The model results presented in Figure 8.8 demonstrate that the model response is
Figure 8.6 Uniaxial stress-strain response of the model run with strain controlled loading.
Figure 8.7 Uniaxial stress-strain response of the model run with stress controlled loading and no stiffness reformations or equilibrium iterations.
Figure E.8 Uniaxial stress-strain response of the model performed with stress controlled loading with and without stiffness reformations and equilibrium iterations.
similar as long as either stiffness reformations, equilibrium iterations or both are used. Therefore, due to the large amount of CPU time required to perform the equilibrium iterations, it was decided to perform the analyses with stiffness reformations alone.

Input parameters for intact bone models

The input data for the concrete material law used in the finite element models of two intact bones are presented below. The size of the load increment used in each model was based on results of the cylinder FEA studies and the in-vitro intact bone failure tests, being one fourth that required for the structure to become nonlinear (448 Nt. for bone A; 224 Nt. for bone B). Table 8.1 presents partial input data for each of the 10 material sets used in both models. These data were based partially on the trabecular bone study presented in Section 2.0.
Table 8.1 - Trabecular bone nonlinear material law input data

<table>
<thead>
<tr>
<th>Material Set</th>
<th>$E_0$ (MPa)</th>
<th>$\nu$</th>
<th>$\sigma_0$ (MPa)</th>
<th>$\sigma_C$ (MPa)</th>
<th>$\epsilon_C$ (x10^-2)</th>
<th>$\sigma_U$ (MPa)</th>
<th>$\epsilon_U$ (x10^-2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65</td>
<td>0.30</td>
<td>0.30</td>
<td>-0.60</td>
<td>-2.7</td>
<td>-0.4</td>
<td>-4.7</td>
</tr>
<tr>
<td>2</td>
<td>160</td>
<td>0.30</td>
<td>0.90</td>
<td>-1.50</td>
<td>-2.7</td>
<td>-1.2</td>
<td>-4.7</td>
</tr>
<tr>
<td>3</td>
<td>260</td>
<td>0.30</td>
<td>1.70</td>
<td>-2.80</td>
<td>-2.7</td>
<td>-2.2</td>
<td>-4.7</td>
</tr>
<tr>
<td>4</td>
<td>360</td>
<td>0.30</td>
<td>2.40</td>
<td>-4.10</td>
<td>-2.7</td>
<td>-3.3</td>
<td>-4.7</td>
</tr>
<tr>
<td>5</td>
<td>480</td>
<td>0.30</td>
<td>3.40</td>
<td>-5.70</td>
<td>-2.7</td>
<td>-4.6</td>
<td>-4.7</td>
</tr>
<tr>
<td>6</td>
<td>600</td>
<td>0.30</td>
<td>4.40</td>
<td>-7.40</td>
<td>-2.7</td>
<td>-5.8</td>
<td>-4.7</td>
</tr>
<tr>
<td>7</td>
<td>720</td>
<td>0.30</td>
<td>5.50</td>
<td>-9.20</td>
<td>-2.7</td>
<td>-7.2</td>
<td>-4.7</td>
</tr>
<tr>
<td>8</td>
<td>840</td>
<td>0.30</td>
<td>6.60</td>
<td>-11.00</td>
<td>-2.7</td>
<td>-8.7</td>
<td>-4.7</td>
</tr>
<tr>
<td>9</td>
<td>970</td>
<td>0.30</td>
<td>7.30</td>
<td>-13.00</td>
<td>-2.7</td>
<td>-10.4</td>
<td>-4.7</td>
</tr>
<tr>
<td>10</td>
<td>1100</td>
<td>0.30</td>
<td>9.10</td>
<td>-15.00</td>
<td>-2.7</td>
<td>-12.0</td>
<td>-4.7</td>
</tr>
</tbody>
</table>

The input parameters used for definition of the compressive failure surface were determined by solution of the Hoffman failure surface and are presented below.

\[
\text{SP1}(1) = \frac{\sigma_{1}}{\sigma_c} = 0.0 \\
\text{SP1}(2) = \frac{\sigma_{2}}{\sigma_c} = 1.00 \\
\text{SP1}(3) = \frac{\sigma_{3}}{\sigma_c} = 2.00 \\
\text{SP1}(4) = \frac{\sigma_{4}}{\sigma_c} = 3.00 \\
\text{SP1}(5) = \frac{\sigma_{5}}{\sigma_c} = 4.00 \\
\text{SP1}(6) = \frac{\sigma_{6}}{\sigma_c} = 5.00 \\
\text{SP3}(1,1) = \frac{\sigma_{3,1}}{\sigma_c} = 1.00 \\
\text{SP3}(2,1) = \frac{\sigma_{2,1}}{\sigma_c} = 2.56 \\
\text{SP3}(3,1) = \frac{\sigma_{3,1}}{\sigma_c} = 3.94 \\
\text{SP3}(4,1) = \frac{\sigma_{4,1}}{\sigma_c} = 5.26 \\
\text{SP3}(5,1) = \frac{\sigma_{5,1}}{\sigma_c} = 6.53 \\
\text{SP3}(6,1) = \frac{\sigma_{6,1}}{\sigma_c} = 7.78 \\
\text{SP3}(1,2) = \frac{\sigma_{1,2}}{\sigma_c} = 1.39
\]
\[
\begin{align*}
\text{SP3}(2,2) &= \frac{\sigma_{p3}^2}{\sigma_c} = 3.37 \\
\text{SP3}(3,2) &= \frac{\sigma_{p3}^3}{\sigma_c} = 5.48 \\
\text{SP3}(4,2) &= \frac{\sigma_{p3}^4}{\sigma_c} = 7.61 \\
\text{SP3}(5,2) &= \frac{\sigma_{p3}^5}{\sigma_c} = 9.75 \\
\text{SP3}(6,2) &= \frac{\sigma_{p3}^6}{\sigma_c} = 11.90 \\
\text{SP3}(1,3) &= \frac{\sigma_{p3}^{1,3}}{\sigma_c} = 1.27 \\
\text{SP3}(2,3) &= \frac{\sigma_{p3}^{2,3}}{\sigma_c} = 3.11 \\
\text{SP3}(3,3) &= \frac{\sigma_{p3}^{3,3}}{\sigma_c} = 5.07 \\
\text{SP3}(4,3) &= \frac{\sigma_{p3}^{4,3}}{\sigma_c} = 7.05 \\
\text{SP3}(5,3) &= \frac{\sigma_{p3}^{5,3}}{\sigma_c} = 9.04 \\
\text{SP3}(6,3) &= \frac{\sigma_{p3}^{6,3}}{\sigma_c} = 11.03
\end{align*}
\]

The remaining parameters were set to

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>BETA</td>
<td>0.75</td>
<td>principal stress ratio, $\beta$</td>
</tr>
<tr>
<td>GAMMA</td>
<td>1</td>
<td>uniaxial critical strains scaling factor</td>
</tr>
<tr>
<td>KAPA</td>
<td>0.5</td>
<td>control parameter for changing material law, $\kappa$</td>
</tr>
<tr>
<td>CLFN</td>
<td>-1</td>
<td>constant used for loading function</td>
</tr>
<tr>
<td>STIFAC</td>
<td>0.0001</td>
<td>normal stiffness reduction factor, $\eta_n$</td>
</tr>
<tr>
<td>SHEFAC</td>
<td>0.5</td>
<td>shear stiffness reduction factor, $\eta_S$</td>
</tr>
<tr>
<td>TREF</td>
<td>0</td>
<td>reference temp - not used</td>
</tr>
</tbody>
</table>
9.0 REFERENCES


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- 348 -


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- 359 -


