Chord distributions across 3D digital images of a human thoracic vertebra

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Radiation dose estimates to the trabecular region of the skeleton are of primary importance due to recent advancements in nuclear medicine. Establishing methods for accurately calculating dose in these regions is difficult due to the complex microstructure of this anatomic site and the typical ranges of beta-particles in both bone and marrow tissues. At the present time, models of skeletal dosimetry used in clinical medicine rely upon measured distributions of straight-line path lengths (chord lengths) through bone and marrow regions. This work develops a new three-dimensional, digital method for acquiring these distributions within voxelized images. In addition, the study details the characteristics of measuring chord distributions within digital images and provides a methodology for avoiding undesirable pixel or voxel effects. The improved methodology has been applied to a digital image (acquired via NMR microscopy) of the trabecular region of a human thoracic vertebra. The resulting chord-length distributions across both bone trabeculae and bone marrow cavities were found to be in general agreement with those measured in other studies utilizing different methods. In addition, this study identified that bone and marrow space chord-length distributions are not statistically independent, a condition implicitly assumed within all current skeletal dosimetry models of electron transport. The study concludes that the use of NMR microscopy combined with the digital measurement techniques should be used to further expand the existing Reference Man database of trabecular chord distributions to permit the development of skeletal dosimetry models which are more age and gender specific. © 2001 American Association of Physicists in Medicine. [DOI: 10.1118/1.1380211]

I. INTRODUCTION

The skeleton represents an organ system for which estimates of radiation absorbed dose are of key importance. Not only is the skeleton serviced by a complex vascular system, but it also serves as the “housing” for the hematopoietic marrow, the tissues responsible for the production of the various formed elements released to circulating blood. The interlaced geometry of the osseous and marrow tissue regions within trabecular bone necessitates that a discussion of the radiation dose to one region cannot take place without some consideration of its effect on the other tissues. For example, radiation treatment of an osteosarcoma is limited by the corresponding radiation damage to healthy marrow. Conversely, radiation ablation of marrow prior to marrow transplantation may be limited by radiation damage to healthy osteogenic tissue of the endosteum.

Recent advancements in nuclear medicine have enhanced the need for improved trabecular bone dosimetry. In radioimmunotherapy, radiation dose to the active bone marrow has been established as a limiting factor in this treatment modality. 1–5 It is well known that radiation can lead to cancers in both the skeletal and hematopoietic systems. Of these cancers, osteosarcomas and leukemia are of major concern. Consequently, it becomes important to accurately determine the absorbed dose to these tissues for differing therapy agents and treatment regimes. With improved dosimetric models for trabecular skeletal regions, unintended risks associated with these therapies may be reduced through refinements in treatment strategies.

A. Bone structure/physiology

There are two main types of bone in terms of histological structure. Cortical bone is the hard compact structure that comprises the outer cortex of all skeletal sites, and is primarily featured as the outer layer of the diaphyses of long bones. Cortical bone accounts for ~80% of the total skeletal mass. 6 The dominant structure within cortical bone is the Haversian canal. The Haversian canals, along with the smaller Volkmann’s canals, are pathways the circulatory system uses to supply nutrients to osteocytes located within the osseous tissue of cortical bone. Dosimetry models of cortical bone have been developed by Beddoe 7,8 and Akabani, 9 and, more recently, by Bouchet and Bolch. 10

The second type of bone, and the area of interest in this research, is trabecular bone. Trabecular bone, also referred to as spongy bone, consists of a complex network of bone spicules, which define the boundaries of the marrow cavities. Bone marrow within these cavities may be hematopoietically active (red marrow), inactive (yellow marrow), or a mixture of both. The active marrow is responsible for the production of
of the various blood cell lines, while inactive marrow is predominantly composed of adipocytes (fat cells). Trabecular bone is found in the inner regions of the vertebra, ribs, skull, pelvis, and the ends of the long bones.

At the surfaces of the osseous tissues, either within the Haversian canals of cortical bone or the marrow cavities of trabecular bone, there exists a thin layer of osteogenic cells called the endosteum. A similar layer exists on the exterior of the cortical bone called the periosteum.

The geometry and composition of the trabecular region of the skeleton creates several unique dosimetry problems. Since cavities of active marrow in the adult are located within the trabecular regions of the skeleton, the dimensions of the two interlacing regions must be accurately known in order to calculate absorbed dose to these sites. The anisotropic structure of this region further complicates dosimetry studies in that it is difficult to apply any uniform modeling technique to such a complex geometry. Furthermore, the small sizes of trabeculae and marrow cavities, relative to the typical beta particle ranges, imply that medium-to-higher energy electrons may traverse several cavities while continuously depositing their kinetic energy.

B. Studies at the University of Leeds

F. W. Spiers, in his work with skeletal dosimetry, was the first to recognize that trabecular bone dosimetry required detailed knowledge of the trabecular microstructure. His research group at the University of Leeds developed optical scanning methods for determining frequency distributions of straight-line path lengths through both bone and marrow regions. Spiers and his students subsequently utilized these chord-length distributions in their studies of beta particle dosimetry for trabecular bone sites. In contrast to the optical techniques of Spiers, the present study looks at the methods for obtaining these distributions within digital images.

C. Chord-length distributions

All current beta-particle dosimetry models for trabecular bone are in some way based upon the trabecular and marrow chord-length distributions measured by Spiers. The frequency of chord lengths through convex bodies has been studied within applications varying from acoustics to ecology. Chord lengths are defined by the intersection of a straight line or ray with two boundaries. There are a variety of methods for obtaining these distributions dependent upon the origin and direction of the rays relative to the object of interest. As pointed out by Eckerman, "Failure to note the distinct nature of these distributions can result in misunderstanding of some aspects of the radiation transport processes." Three fundamental methods of randomly obtaining these frequency distributions are relevant in trabecular dosimetry: mean-free-path randomness (μ-randomness), interior radiator randomness (I-randomness), and surface radiator randomness (S-randomness).

Mean-free-path randomness was used in the work of Beddoe at the University of Leeds, and is the method utilized at the University of Florida. Several people have studied the mathematics of chord distributions across simple geometric shapes.

II. BACKGROUND

A. Chord distributions across a square/rectangle

Of particular interest in this study is the nature of chord-length distributions across squares and rectangles, the typical shapes of pixels within a 2D digital image. Of course, various features seen in chord-length distributions generated across rectangular targets (e.g., pixels within 2D images) are easily extended to those seen in chord-length distributions generated across cubical targets (e.g., voxels within 3D images).

Figure 1(a) illustrates rays crossing a square at a given angle of intersection. For angle θ, there is a maximum chord length generated interior to the square when the ray extends across opposite sides of the square. This maximum chord length L is thus equal to

\[ L = W \sec \theta, \]

where W is the dimension of the square. Furthermore,
The relative number of chords of length $L$ is equal to $(W-x)/W$ since a chord is fired from equally spaced increments along the side of the square. The distance $x$ is given as:

$$x = W \tan \theta.$$  

By setting $f(L) = (W-x)/W$, where $f(L)$ is the relative frequency of chords of length $L$, one may write the frequency of chord lengths as:

$$f(L) = 1 - \tan \left( \arccos \left( \frac{W}{L} \right) \right).$$  

A plot of this expression is shown in Fig. 2 for an arbitrary pixel of width $W=100$. When viewed within a larger distribution of chord lengths from a 3D digital image, this pixel (or voxel) effect "A" will result in a series of tailed spikes as shown in Fig. 3 (discussed below).

Also obvious in Fig. 1(a) is the fact that a linear distribution of chord lengths of length less than $W \cdot \sec(\theta)$ will be measured. These chords will be measured with constant frequency regardless of the angle of incidence for all chords of length less than $W$. As a result of this pixel effect "B," a straight line of equal nonzero probability is expected within the chord-length distribution from zero to a chord length equal to the pixel width. For chord lengths ranging from $W$ to $W \cdot \sec(\theta_{\max})$, there will be a linear decrease in their frequency as the frequency of sampling angles is also constant during chord length acquisition. Note that at $\theta_{\max}=45^\circ$ for a square pixel, $\sec(\theta_{\max}) = 1.414$, and thus for a pixel resolution of 59 $\mu$m, this maximum reach of pixel effect "B" will extend out to 83 $\mu$m. Obviously, in the range from 59 to 83 $\mu$m, or $W$ to $W \cdot \sec(\theta_{\max})$, this effect is superimposed by pixel effect "A." In summary, there exists two pixel effects resulting from contributions of chords resulting from rays traversing from one side of the pixel to the opposite side (effect "A"), and from chords resulting from rays traversing from one side to an adjacent side of the same pixel (effect "B"). Analogous effects are found in rays traversing voxels within a 3D image.

The chord-length distribution across a square has also been derived by Kellerer,\textsuperscript{17} yielding

$$f(L) = \begin{cases} \frac{1}{2W} & \text{for } L \leq W \\ \frac{W^2}{L^2 \sqrt{L^2-W^2}} - \frac{1}{2W} & \text{for } W < L \leq \sqrt{2}W \end{cases}$$  

Note that this equation implicitly includes both pixel effects for chord lengths within the range $W$ to $W \cdot \sec(\theta)$.

For the case of rectangular pixels, pixel effect "B" is slightly more complicated. Figure 1(b) represents rays crossing a rectangular pixel. For this case it is necessary to determine the value of $\theta_m$ where the largest chord across a single rectangular pixel will transition from $|W_x \cdot \sec(\theta)|$ to $|W_y \cdot \csc(\theta)|$. Since

$$\theta_{m} = \arctan \left( \frac{W_y}{W_x} \right), \text{ then}$$

$$L_{\max} = \begin{cases} |W_x \cdot \sec(\theta)|, & \text{for } \theta = 0 \rightarrow \theta_m, \ 90^\circ + \theta_m \rightarrow 180^\circ + \theta_m, \ 270^\circ + \theta_m \rightarrow 360^\circ \\ |W_y \cdot \csc(\theta)|, & \text{for } \theta = \theta_m \rightarrow 90^\circ + \theta_m, \ 180^\circ + \theta_m \rightarrow 270^\circ + \theta_m \end{cases}.$$  

This relationship will be used to remove both pixel effects, and their 3D equivalent voxel effects, from measured chord-length distributions acquired from 2D and 3D NMR images of trabecular bone.

Pixel effect "A" results in a chord distribution containing spikes as shown in Fig. 3. This distribution was obtained from an NMR image of human trabecular bone (see Sec. II below). Since the pixels have a finite resolution, a chord length is not accurate to a level of 1 $\mu$m, so it is necessary to group the chord distribution data, or place them into bins of a defined width.
Grouping the data thus removes the presence of the pixel effect peaks. A binwidth equal to the smallest resolution is chosen in order to smooth the distribution, a feature necessary for its implementation in dosimetry models.

Coleman\textsuperscript{21} has derived the $\mu$-chord distributions through a cube of unit width. The result is as follows:

\[
 f(L) = \begin{cases} 
 \frac{8L^3 - 3L^4}{3\pi L^3} & \text{for } 0 < L \leq 1 \\
 \frac{6\pi + 6L^4 - 1 - 8(2L^2 + 1)\sqrt{L^2 - 1}}{3\pi L^3} & \text{for } 1 < L \leq \sqrt{2} \\
 \frac{6\pi - 3L^4 - 5 + 8(L^2 + 1)\sqrt{L^2 - 2} - 24\arctan(\sqrt{L^2 - 2})}{3\pi L^3} & \text{for } \sqrt{2} < L \leq \sqrt{3} 
\end{cases}
\]  

(8)

The shape of this distribution is plotted in Fig. 4 and compared to that of the square both of unit dimension.

Data acquisition by Spiers and his students at the University of Leeds was performed in two dimensions. Of course, the desired end result is a set of distributions that approximate the omnidirectional pathlengths of beta particles through the trabecular region. These are obtained by combining the chord distributions obtained within each of the three orthogonal planes. “In the case of bones which show no apparent symmetry, scans in three orthogonal planes can be combined directly to give an omnidirectional distribution.”\textsuperscript{13} If this statement by Beddoe et al. for directly combining 2D chords from orthogonal planes is valid, the two curves in Fig. 4 should match. Three orthogonal planes through a cube would result in chords from three sets of two-dimensional squares, which when combined give the distribution for a square, not for a cube. Nevertheless, the shapes are similar, and for dosimetry purposes, probably do not result in significant differences.

B. Chord distributions across spherical objects

The relationships for chord-length distributions within a circle and a sphere are easily derived. The chord distribution across a circle is given as:

\[
 f(L) = \frac{L}{4R\sqrt{R^2 - \left(\frac{L}{2}\right)^2}}. 
\]  

(9)

The corresponding frequency distribution of chords across a sphere is given as:

\[
 f(L) = \frac{L}{2R^2}. 
\]  

(10)

These distributions are compared in Fig. 5.

C. Imaging techniques for studying trabecular architecture

While the research of Spiers and his students was superb in its level of detail and completeness, future improvements in skeletal dosimetry, particularly for medical applications, require an expanded database of marrow and trabecular chord distributions. These databases should more fully encompass variations in trabecular microstructure with both subject, age, and gender. Newer techniques in medical imaging can now be applied to this particular task.

In 1996, studies were initiated at the University of Florida\textsuperscript{22–27} to look at techniques that could be used to improve on, or expand, the microstructure database gathered at the University of Leeds. This work resulted in the selection
of nuclear magnetic resonance (NMR) microscopy coupled with image processing techniques to obtain chord distributions in a human thoracic vertebra.19

III. MATERIALS AND METHODS

In order to study the consequences of measuring chord lengths in a digital image, studies were performed on two different simple voxelized shapes. First, chord lengths were measured across a mathematically created cube in order to verify the relationships discussed previously. Next, a three-dimensional digital image of a sphere was created. Obviously, a voxelized sphere no longer maintains the smooth edges of a mathematical sphere. The chord distributions for a sphere have been mathematically derived, and provide a method for quantifying pixel effects, and their corresponding voxel effects, in the measured chord distributions. Techniques for their removal were then developed.

A. Chord lengths across a voxelized sphere

A sphere was created with a relative radius of 500 units. The sphere was then voxelized with each cubical voxel of relative length 10. Chord distributions were then acquired across this body using a variety of different methods. Chord distributions can be acquired in either two dimensions or three dimensions. In fact, up to this point, chord distributions for skeletal dosimetry have only been acquired using two-dimensional techniques. Previous research at the University of Florida,19,23 as well as at the University of Leeds,7,13 has assembled final chord distributions from multiple two-dimensional slices taken in each of the three orthogonal image planes.

In this present work, however, three-dimensional images of trabecular bone have been acquired allowing for direct three-dimensional measurement techniques. By acquiring chord distributions with both two-dimensional and three-dimensional techniques and comparing their results, one can test the previous statement by Beddoe et al. regarding the adequacy of 2D techniques.

The method used to acquire chord distributions involves firing parallel isotropic rays across the 3D voxelized image. When the ray intersects two boundary points for the tissue media (bone or marrow in this case), the distance of the resulting chord is measured and assigned as the chord length. These methods are simple enough when dealing with an object defined by a continuous surface boundary. They become more difficult when dealing with voxelized objects, due to the pixel/voxel effects discussed and derived earlier.

In this study, two chord acquisition techniques have been developed to reduce the influence of pixel/voxel effects “A” and “B.” Chord distributions acquired under these two Minimum Acceptable Chord (MAC) criteria are then compared against chord distributions acquired in which every chord length is measured regardless of its size or origin. In chord acquisitions made under the first minimum acceptable chord criterion, MAC-1, each measured chord is forced to cross a minimum distance from one face of a single voxel to its parallel face on the opposite side. In other words, chords that result from a ray that crosses from one face of a voxel to its orthogonal adjacent side are ignored in the development of the chord distribution. Mathematically, the measured chord length is compared to a calculated minimum distance given in Eq. (7) based on the ray’s angle of incidence relative to the voxel orientation. Chords acquired under this MAC-1 criterion guarantee that the ray moves at a minimum of one resolution distance in either the x or y dimension for 2D images. For 3D images, the chord length must equal a minimum of one resolution distance in either the x or y or z dimension.

The second chord acceptance criteria, MAC-2, goes a step further in that it guarantees that the ray moves a resolution distance in two dimensions for 2D images, and in all three dimensions for 3D images, if the resulting chord is to be included in the chord distribution. Figure 6 gives a visual depiction of the MAC-1 and MAC-2 chord-length selection criteria. In this study, chords are acquired with and without the use of the MAC-1 and MAC-2 selection criteria. The resulting chord distributions are then compared for both 2D and 3D images.

B. Specimen preparation and NMR image acquisition

Images were previously obtained of trabecular regions within a human thoracic vertebra. The subject, from whom the specimen was obtained, was a 52-year-old male trauma victim with no known metabolic disorders that would present an abnormal skeletal structure. Details of the specimen preparation are described in Jokisch et al.19 Cylindrical cores were drilled from the vertebral bodies using a coring bit of 12-mm inner diameter. Subsequently, the bone marrow was removed by immersing the cored samples in 5% sodium hypochlorite aqueous solution for several hours and rinsing repeatedly with hot water. One of these samples was then suspended in 1 mM Gd-DTPA aqueous solution within a 13-mm inner diameter glass vial for subsequent NMR imaging at 600 MHz.
One cylindrical vertebral core was subsequently imaged using a Varian Unity Spectrometer having an active bore diameter of 15 mm and operating at a 600-MHz proton resonance frequency (1.4 T magnetic field strength). A 15-mm-diameter standard high-resolution radiofrequency (rf) coil was used to obtain sufficient sensitivity and rf field homogeneity. A conventional 3D spin-echo sequence was applied to obtain a fully three-dimensional image of the sample. A gradient amplitude of 11.4 G cm\(^{-1}\) was applied along the read axis (y), with maximum phase encoding gradients of 8.9 and 7.7 G cm\(^{-1}\) applied along the x and z directions, respectively. The repetition and echo times were 300 ms and 24 ms, respectively. The field-of-view for the x,y,z axes was 15\(\times\)15 \(\times\)10 mm\(^3\), and a voxel spatial resolution of 59\(\times\)59 \(\times\)78 \(\mu\)m\(^3\) was achieved. It is from this image set that both marrow and trabecular chord-length distributions were obtained.

C. Image processing

Three image-processing steps are required prior to making estimates of marrow cavity and trabecular chord distributions. These steps include image thresholding, image segmentation, and image filtering. In order to measure chord distributions, it is desirable to separate the marrow cavities from the bone trabeculae by assigning a gray-level threshold that effectively segments the image into only bone and marrow voxels. Image thresholding is performed automatically by a user-written C-code that incorporates the tissue classification model of Chung et al.\(^{25}\) This technique applies a Rayleigh–Gaussian distribution to the histogram and calculates the optimal threshold value using techniques described in Jokisch et al.\(^{19}\) The final image-processing step involves elimination of single voxels of anomalously high or low intensity arising from signal noise through the application of a median filter to the binary image following image segmentation. Other investigators performing analyses on NMR images of human trabecular bone have applied median filters.\(^{28–31}\) In this work, a minimal neighborhood area of 3 \(\times\)3\(\times\)3 voxels was chosen for image filtering.

D. Statistical independence of bone and marrow chord lengths

One of the assumptions of a chord length-based dosimetry model of trabecular bone is that bone and marrow chord lengths are statistically independent of one another. A chord-length-based dosimetry model samples randomly and alternately from the marrow and bone chord distributions. It is very possible, however, that there is an association between the occurrence of chords of given lengths in the two media. In other words, in the real trabecular bone structure, large marrow chords may follow smaller than average bone chords. This association seems likely upon visual examination of an image of the trabecular region of the skeleton, where different regions appear to have different 3D structural characteristics. Existing distribution-based models do not account for a dependence of a bone (or marrow) chord-length distribution upon the value of the previously selected marrow (or bone) chord length.

During the acquisition of the chord lengths, data can be acquired which may test the statistical independence of these two distributions. This acquisition is performed by recording distributions of marrow chord lengths separately and indexing them to the previous bone chord length.

IV. RESULTS AND DISCUSSION

A. Chord lengths across a voxelized cube

Chord lengths were acquired across a voxelized cube. The cube was placed orthogonal to the voxelization, to insure that there would not be any geometrical differences between a mathematically “perfect” cube and the voxelized cube. The results are shown in Fig. 7. The cube was set to have a unit length, width, and height. Figure 7 shows good agreement between the mathematically derived results and measured results. The peaks that are seen in the measured sample after unit width are due to angular sampling. Chords are fired in discrete angles, and as the discrete step is decreased, the distribution would smooth into the neighbor values. Firing chords over many angles quickly becomes computer-time limited, and may not be necessary for accurate dosimetry.

B. Chord lengths across a voxelized sphere

For this study, chords were fired across a voxelized sphere and compared to the theoretical result of Eq. (10). Unlike the cube, the voxelized sphere does have a slightly different geometry from the “perfect” sphere. Chord distributions were acquired both with and without the use of either the MAC-1 or MAC-2 criteria. Additionally, measurements were made using either 2D images (and subsequently combined across all three orthogonal planes), or they were made directly within the 3D image. Figure 8 displays the measured chord distributions across the voxelized sphere of radius equal to 500 units using both 2D and 3D techniques. There are differences at very low chord lengths in that some voxel effects are picked up only under three-dimensional chord length acquisitions. Nevertheless, one observes that the general shape
of the two-dimensional results more closely approximate the expected spherical distribution, and not the chord distribution of a circle (see Fig. 5).

Figure 9 displays the results for the chord distribution acquired without the use of either MAC criteria to those acquired with the use the MAC-1 or MAC-2 selection criteria. These results were all obtained using three-dimensional acquisition of the chord lengths. As expected, the greatest peak at small chord lengths was found without the use of either the MAC-1 or MAC-2 criteria. The second highest peak was found in which the MAC-1 criterion was applied. It is important to note that the three acquisition methods only vary at small chord lengths, and that the general shape of the distribution for the body being measured is preserved in all cases.

Figure 10 illustrates this point further by comparing the chord distributions acquired under either the MAC-1 or MAC-2 selection criteria against the expected mathematical result for a “perfect” sphere. The frequency of the small chords is critical when calculating the average chord length. All six acquisitions produce a different mean chord length as shown in Table I. The use of the MAC-2 selection criteria resulted in a mean chord length closest to those of the non-voxelized “perfect” sphere.

Figure 11 displays a 3D representation of the cored trabecular bone sample as acquired on the 600-MHz spectrometer. As noted earlier, the image was acquired in a voxel matrix format of 256×256×128 with a spatial resolution of 59 ×59×78 μm³ per image voxel. A representative slice extracted from this 3D image is shown in Fig. 12 for the transverse-viewing plane. Evident within the figure are susceptibility artifacts (bright pixels) occurring within voxels adjacent to the bone surfaces. These enhanced image signals are attributable to the large magnetic susceptibility differential between the water within the marrow spaces and the tissues within the bone trabeculae. For those surface voxels partially encompassing both marrow and bone (partial volume averaging), the enhanced signal from the water within those voxels will preferentially favor the creation of pure marrow voxels during image segmentation resulting in a slight thinning of the bone trabeculae. These artifacts can be reduced significantly by imaging over longer times at lower field strengths (e.g., 4.7 T).

A three-dimensional region of interest was selected from which a gray-level histogram was constructed for each im-

![Fig. 8. Comparison of chord lengths measured with 2D and 3D techniques across a voxelized sphere.](image1)

![Fig. 9. Chord distributions across a voxelized sphere using no minimum acceptable chord criterion, the MAC-1 criterion, or the MAC-2 criterion.](image2)

![Fig. 10. Comparison of chord distributions across a voxelized sphere using the two MAC criteria compared to the theoretical result for nonvoxelized sphere.](image3)

### Table I. Mean chord lengths within a voxelized sphere obtained with and without the use of minimum acceptable chord selection criteria. Results are given for both direct 3D chord acquisitions and those from the combination of 2D acquisitions in each of the three orthogonal image planes.

<table>
<thead>
<tr>
<th>Minimum acceptable chord criteria used</th>
<th>Chord acquisition methods used</th>
<th>Mean chord length (μm)</th>
<th>Ratio of mean chord to that for a perfect sphere</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Direct 3D</td>
<td>443.8</td>
<td>0.666</td>
</tr>
<tr>
<td>None</td>
<td>2D Orthogonal Planes</td>
<td>525.9</td>
<td>0.789</td>
</tr>
<tr>
<td>MAC-1</td>
<td>Direct 3D</td>
<td>573.7</td>
<td>0.861</td>
</tr>
<tr>
<td>MAC-1</td>
<td>2D Orthogonal Planes</td>
<td>614.1</td>
<td>0.921</td>
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<tr>
<td>MAC-2</td>
<td>Direct 3D</td>
<td>633.9</td>
<td>0.951</td>
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<tr>
<td>MAC-2</td>
<td>2D Orthogonal Planes</td>
<td>652.4</td>
<td>0.979</td>
</tr>
<tr>
<td>Perfect sphere</td>
<td></td>
<td>666.7</td>
<td>1.000</td>
</tr>
</tbody>
</table>

[Eq. (10)]
age. This same region of interest was used for the threshold calculation, chord distribution measurement, and voxel radiation transport performed in a subsequent study. Figure 13 shows the gray level histogram for the image obtained from NMR acquisition at 600 MHz (~14.1 T). As predicted under the tissue classification model of Chung et al., the distribution is bimodal and follows the Rayleigh–Gaussian distribution. As described earlier, nonlinear least-squares techniques are used to fit the histogram from which an optimal image threshold is selected by numerical solution.

Application of both a threshold for image segmentation and a median filter for removal of single high-or low-intensity voxels yields a binary image from which chord distributions may be obtained. Figure 14 displays a segmented and median filtered image of the single slice given in Fig. 12.

C. Trabecular and marrow cavity chord-length distributions

It is proposed that NMR microscopy be used to expand the original database of chord-length distributions reported by Spiers and his students for use in radiation dosimetry models of the skeleton. Correspondingly, it is of interest to compare chord distributions measured by the University of Leeds’ group to those measured in this work. Shown in Figs. 15 and 16 are the normalized chord length distributions for both trabeculae and marrow cavities, respectively, as measured by NMR microscopy and image analysis. Also shown, are the chord distributions for the cervical and lumbar vertebra as measured by the Leeds’ optical bone scanner and reported in Appendix C of Whitwell’s thesis.

For the trabecular chord distributions shown in Fig. 15, general agreement is seen between the three vertebrae. The peak at small chord lengths had not been observed in the thoracic vertebra reported in our earlier studies, yet...
analogous peaks in the distributions for the cervical and lumbar vertebrae had always been observed in the Leeds’ data. The appearance of the peak in the UF data is attributed to the application of the MAC-2 chord selection criterion during chord length acquisition designed to remove voxel effects “A” and “B.” The distributions for all three skeletal sites tail away with similar frequencies. There is one significant difference at ~450 μm for the thoracic vertebra measured here. It is postulated that this small peak in the distribution is a real feature of the imaged specimen. For the marrow chord distributions shown in Fig. 16, similar agreement is observed between the data for each of the spinal regions. Additionally, the distributions tail away with the same shape in chord frequency.

The publications from the University of Leeds’ group represent the only known published source of chord length distributions through trabeculae in the thoracic vertebra as measured with NMR microscopy and image processing (present study). Average chord lengths are frequently reported. Table II lists estimates of both the mean trabecular chord lengths and the mean marrow cavity chord lengths published in other studies. The mean chord lengths reported here for both the bone trabeculae (281 μm) and marrow cavities (1170 μm) have increased from what was reported previously (201 and 998 μm, respectively). These increases are primarily due to the use of the MAC-2 chord selection criterion, and the subsequent removal of very short chord lengths within the distribution.

Chung et al. estimate a mean trabecular thickness (±1 standard deviation) for 22 lumbar vertebral of 127±13 μm—a value much lower than our estimate of 281 μm for the thoracic vertebra. In a later study, however, the authors studied the variation of trabecular thickness with decreasing image slice thickness. The authors noted a convergence of the mean trabecular thickness to between 180 and 190 μm at slice thicknesses below 300 μm. Goulet et al. used QCT in their study of trabecular bone sites; no quantitative comparison with our data can be made considering the wide variety of skeletal sites included in their estimates. Our estimated mean trabecular thickness of 281 μm is consistent with light microscopy measurements reported by Mosekilde, Whitwell, and Beddoe. The latter study was conducted in part to show the biological variability of this microstructural parameter. The closest match is that with the measurement of Whitwell for the cervical vertebra.

Our estimated mean marrow cavity size of 1170 μm for a single thoracic vertebra is found to be intermediate to those reported by Whitwell for the neighboring cervical and lumbar vertebra (909 μm and 1233 μm, respectively) for a similarly aged male subject. In the study of Beddoe et al., the authors report a mean marrow cavity chord length of 1070 ± 128 μm for the lumbar vertebra.

**D. Statistical dependence of chord distributions**

One of the fundamental assumptions in the use of chord-length distributions as input to skeletal dosimetry models is that bone and marrow chord distributions are statistically independent of one another. To explore the validity of this assumption, separate marrow distributions were acquired and indexed to the previously seen bone chord length within the NMR image. To demonstrate the results graphically, Fig. 17 displays the mean marrow chord length as a function of the previously seen bone chord length. As predicted, there is a definite observable relationship between the length of a bone chord and the length of its successive marrow chord. If the distributions were truly statistically independent, one would simply observe a line of zero slope. Figure 17, however, shows that if a large bone chord length is encountered, the next marrow chord will be, on average, smaller than the overall mean marrow chord length.

Figure 18 displays these same results three-dimensionally. Marrow chord distributions are plotted with respect to the length of the previously encountered bone chord length. The entire 3D distribution is normalized to both the marrow chord and bone chord bin widths, and thus gives the overall
relative frequency for a successive combination of bone and marrow chords. These results suggest a possible improvement to existing chord-length-based dosimetry models in which one would no longer sample bone and marrow chord lengths from the same two distributions, but one would sample a unique marrow distribution indexed to the previously sampled bone chord. During particle transport, one would then sample a unique bone chord-length distribution indexed to the previously sampled marrow chord.

V. CONCLUSIONS

The problems associated with acquiring \( \mu \)-random chord distributions in voxelized objects have been discussed. It is concluded that voxel effects should be minimized, and two different methods have been presented based on establishing Minimum Acceptable Chord (MAC) selection criteria. It is recommended that the MAC-2 criterion be used to acquire chords across voxelized surfaces. It was noted that small differences do exist between two-dimensional and three-dimensional acquisitions, although they are probably too small to make significant differences in skeletal dosimetry. Nevertheless, the three-dimensional acquisition method is recommended, and will be utilized in future studies of chord-length distributions in human trabecular bone samples imaged via NMR microscopy.

![Fig. 17](image1.png)

**Fig. 17.** Mean marrow chord lengths with respect to the length of the previous bone chord.

<table>
<thead>
<tr>
<th>Study</th>
<th>Image technique</th>
<th>Skeletal site</th>
<th>Subject(s) age/gender</th>
<th>Mean trabecular chord length (( \mu )m)</th>
<th>Mean marrow chord length (( \mu )m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UF (present study)</td>
<td>NMR</td>
<td>Thoracic vertebra</td>
<td>52-y-old male</td>
<td>281</td>
<td>1170</td>
</tr>
<tr>
<td>Jokisch et al. (1998)</td>
<td>NMR</td>
<td>Thoracic vertebra</td>
<td>52-y-old male</td>
<td>201</td>
<td>998</td>
</tr>
<tr>
<td>Chung et al. (1993)</td>
<td>NMR</td>
<td>Lumbar vertebra</td>
<td>16 subjects</td>
<td>127±13</td>
<td>Not Reported</td>
</tr>
<tr>
<td>Chung et al. (1995)</td>
<td>NMR</td>
<td>Lumbar vertebra</td>
<td>24–86 y (mean 60 y)</td>
<td>180 to 190</td>
<td>Not Reported</td>
</tr>
<tr>
<td>Goulet et al. (1994)</td>
<td>QCT</td>
<td>Tibia, femur, iliac crest, radius, humerus, lumbar vertebra</td>
<td>Not reported</td>
<td>140±20</td>
<td>640±240</td>
</tr>
<tr>
<td>Whitwell (1973)</td>
<td>Sectioning/light microscopy</td>
<td>Lumbar vertebra</td>
<td>44-y-old male</td>
<td>280</td>
<td>909</td>
</tr>
<tr>
<td>Beddoo et al. (1976)</td>
<td>Sectioning/light microscopy</td>
<td>Lumbar vertebra</td>
<td>44-y-old male</td>
<td>246</td>
<td>1233</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>44-y-old male</td>
<td>235</td>
<td>1172</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>44-y-old male</td>
<td>207</td>
<td>953</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>52-y-old male</td>
<td>187</td>
<td>1310</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>48-y-old male</td>
<td>173</td>
<td>1040</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>44-y-old male</td>
<td>190</td>
<td>1144</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>39-y-old male</td>
<td>160</td>
<td>998</td>
</tr>
</tbody>
</table>

![Fig. 18](image2.png)

**Fig. 18.** Normalization of distributions displaying relative frequencies of bone and marrow chord length combinations. This plot could also be interpreted as displaying the bone chord distribution indexed to the length of the previously sampled marrow chord length, as well as the marrow chord distribution indexed to the length of the previously sampled bone chord length.
The microscopic structure of trabecular bone for a thoracic vertebral specimen was characterized by NMR microscopy combined with digital image processing. The resulting chord-length distributions across both bone trabeculae and bone marrow cavities were found to be in general agreement with those measured for the cervical and lumbar vertebrae in a similarly aged healthy adult male using physical sectioning and 2D automated light microscopy. As noted earlier, this latter data currently forms the foundation upon which all past and current standardized internal dosimetry models of the skeleton are based. The current study further demonstrates that NMR microscopy of trabecular bone may be used to augment and expand this database, thus providing an important tool for comparisons of various chord-based dosimetry models.

We have not been able to find significant discussion of the problems associated with measuring chord lengths in digital images in the literature. Published studies that make these measurements list only mean chord-length values. It is unclear as to how, or if, the pixel effects described in this paper were dealt with in these other studies. It seems possible that the pixel effects may have gone undetected if the codes were written solely for the purpose of obtaining mean chord lengths, and thus a distribution was never observed. Other studies derive mean lengths from other parameters, which cannot be used to obtain distributions of chord lengths.

Our work has additionally suggested that the assumption of statistical independence between bone and marrow chord lengths may be incorrect. This result could form a basis for differences in the dosimetry of the trabecular skeleton when comparing chord-based dosimetry models to more realistic voxel-based transport methods. A possible method of correcting standard chord-based transport methods, which would require selective sampling from a joint distribution based on the previously sampled chord length in the previous medium, has been suggested.

The chord-length distributions presented in this study are for a single cored sample of a thoracic vertebra, and are not presented as definitive results for all thoracic vertebrae. Note that a limited sample size (seven skeletal sites from one individual) did not deter the use of the Leeds’ data for use in skeletal dosimetry models adopted by both the Medical Internal Radiation Dosimetry (MIRD) Committee of the Society of Nuclear Medicine and the International Commission on Radiological Protection (ICRP). The potential use of NMR microscopy to assess larger data sets of chord distributions (with much greater ease than optical methods) should be pursued. Furthermore, an expanded database may allow the development of more age- and gender-specific models of skeletal dose. While such detailed models may not be necessary in radiation protection applications, it may be very important in applications to internal emitter therapies. These patients, particularly older females, for which marrow dose estimates are desired, may present trabecular bone morphologies very different from those defined by “Reference Man” attributable to bone loss diseases such as osteoporosis.

While skeletal dosimetry models based upon measured data of trabecular bone microstructure contribute greatly to our understanding of radiation effects to this organ system, they still require several assumptions regarding the transport of electrons and other charged particles through the “real” geometry of the region. Therefore, a more realistic transport model is sought against which models based on chord length distributions can be compared and validated.

ACKNOWLEDGMENTS

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