FRACTAL ANALYSIS OF CANCELLOUS BONE IN DISEASE

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"Over the mountains
Of the Moon,
Down the Valley of the Shadow,
Ride, boldly ride,"
The shade replied -
"If you seek for Eldorado!"

from Eldorado
Edgar Allan Poe

Errata Sheet

Page	Para	Line	
Viii	3	4	"effect" should be "affect".
X	2	2	"remodeling" should be "remodelling".
10	5	5	"Figure 1.2d" should be "Figure 1.2c".
11	legend		"F_D =Maximum Feret's diameter, δ = Fractal dimension" inserted.
12	1	5-6	Should be "(Figure 1.3a), where the perimeter is the …".
17	2	14	"modeling" should be "modelling".
24	1	3	"where" should be "were".
36	1	1	"figure x" should be "Figure 2.2d".
51	2	4	"difficult" should be deleted.
66	1	7	"remodeling" should be "remodelling".
66	2	2	second instance of "was constructed" should be deleted.
67	1	2	"bone multicellular unit" should be "basic multicellular unit".
68	legend		"remodeling" should be "remodelling".
69	1	2	"remodeling" should be "remodelling".
69	1	5	"remodeling" should be "remodelling".
114	1	5	"Aaron *et al* (1985)" should be "Aaron *et al* (1987)".
114	1	8	"Thomson" should be "Thomsen".
114	1	8	"Chavassieux and Meunier 2001" should be deleted.
116	2	9	"modeling" should be "modelling".
116	2	10	"remodeling" should be "remodelling".
125	legend 1		"between" should inserted after "differences".
125	legend 2		"between" should inserted after "differences".
131	1	1	"Hildebrand and Ruegsegger 1997" should be deleted.
135	legend		"Parfitt *et al* 1987" inserted at end.
135	2	7	"P1" should be "P2".
136	1	2	"Hahn *et al* 1992" inserted at end.
154	1	11	"Figure 4.4x and 4.4y" should be deleted.
154	2	7	"Figures 4.4x and 4.4y" should be deleted.
154	2	8	"independent" should be "different".
155	1	2	"Figures 4.4x and 4.4y" should be deleted.
169	1	1	"with the normal" should be "and normals".
173	1	3	"stained" should be deleted.
197	2	4	"is" should be deleted.
241	2	6	"remodeling" should be "remodelling".
244	3	9	"The" should be "the".
245	2	6	"modeling" should be "modelling".
245	3	5	"remodeling" should be "remodelling".

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ABSTRACT

The principal aim of this thesis was to develop and implement a standardised protocol for the fractal analysis of cancellous bone architecture. Cancellous bone structure from different skeletal sites in groups of osteoporotic, osteoarthritic and normal individuals was analysed. The results of fractal analysis were explained in the context of conventional bone histomorphometry and *a priori* knowledge to advance the understanding of cancellous bone architecture.

There has been much effort devoted to the pursuit of descriptors of cancellous bone complexity. The aim of these endeavours has been to develop morphological descriptors of bone quality that explain the functional properties of the cancellous bone structure for age-related changes, the effect of disease processes or the effect of therapeutic agents on the diseased skeleton. The fractal analysis of the complexity of cancellous bone architecture promises to be an exciting addition to existing analytical techniques.

The establishment of a standardised methodology for the fractal analysis of cancellous bone encompassed many components. Knowledge of the stereological and histomorphometric principles that are employed in currently available techniques enabled a comprehensive examination of the factors that effect the measurement of the fractal dimensions. The methodology presented in this thesis has been optimised specifically for measuring sectional fractal dimensions in histological sections of cancellous bone.

The sectional fractal dimensions show that, over three ranges of scale, cancellous bone is effectively fractal at multiple sites in the normal skeleton. The three sectional fractal dimensions describe different morphological

compartments of the cancellous bone structure. Fractal 1 describes the surface texture of the trabeculae, fractal 2 describes the shape or form of individual trabeculae and fractal 3 describes the spatial arrangement or overall architecture of the cancellous bone.

This thesis reports that in the normal skeleton there are differences between skeletal sites for the fractal dimensions, which are dependent on the functional properties of the skeletal sites. Fractal 2 and fractal 3 for subchondral cancellous bone is greater than vertebral body and iliac crest cancellous bone, which indicates greater morphological complexity. Also, fractal 2 and fractal 3 in subchondral cancellous bone show an age-related decrease, which suggests that the cancellous bone structure becomes less complex with age. This inter-ostotic variability in response to ageing is indicative of the heterogeneity in functional properties of cancellous bone in the skeleton.

In this thesis, fractal analysis has been shown to detect morphological differences in the cancellous bone between normals, osteoporotics and osteoarthritics in the compressive and tensile trabeculae of the femoral head and the iliac crest. These data have provided new insights into the mechanisms of change to cancellous bone structure in ageing and in disease.

Age-related changes in the structural parameters of cancellous bone are seen at all the skeletal sites in the normals but are only present in the compressive trabeculae of the femoral head in the osteoporotics and not at all in the osteoarthritics. These observations indicate that these disease processes are associated with an uncoupling of the control mechanisms that affect cancellous bone structural complexity. In the normals, the fractal dimensions only show age-related change in the tensile trabeculae of the femoral head, suggesting that fractal analysis is not suitable for detecting the age-related changes that are quantified by the structural parameters of cancellous bone in these study groups

but the fractal dimensions detect underlying cancellous bone complexity independent of age.

For the osteoporotics, fractal 1 is the same at all skeletal sites. This suggests that the relative levels of remodeling activity are the same for both normals and osteoporotics. Fractal 2 for both the compressive and tensile trabeculae in the femur is significantly lower for the osteoporotics than the normals but in the iliac crest, fractal 2 is the same. This implies that in the femoral head the osteoporotics have trabeculae that are significantly less complex in shape than the normals. This phenomenon is not seen in the iliac crest, which is usually the site of diagnostic biopsy. Therefore, biopsies for diagnosis of osteoporosis may not show changes in cancellous bone structural complexity that are evident in disease affected sites. The structural parameters of cancellous bone show that osteoporotics lose whole trabeculae due to perforation of trabeculae, through decreased Tb.N and increased Tb.Sp. This leads to less interconnection between trabeculae, loss of branching and more rounded trabeculae, hence the trabeculae are less complex in shape. For fractal 3, in compressive and tensile regions of the femur the osteoporotics are significantly lower than the normals and in the iliac crest the osteoporotics are the same as the normals. This indicates that in the femoral head the spatial arrangement of the trabeculae within the cancellous structure of the osteoporotics is less complex. The structural parameters of cancellous bone show that there is loss of whole trabeculae, which is associated with increased spatial separation between the trabeculae as bone is lost.

For the osteoarthritics, fractal 1 is the same as the normals at all skeletal sites. Fractal 2 for the compressive trabeculae in the femoral head is significantly higher for the osteoarthritics than the normals but in the tensile trabeculae of the femoral head and the iliac crest fractal 2 for the osteoarthritics is the same as the normals. This implies that in the compressive trabeculae of the femoral head the osteoarthritics have trabeculae that are significantly more complex in

shape than the normals. The structural parameters of cancellous bone show that the compressive trabeculae of the femoral head are thicker, more numerous and less widely separated with greater BV/TV than the normals. This leads to greater interconnectivity between trabeculae and more complex branching, hence the trabeculae are more complex in shape. For fractal 3, in the compressive and tensile regions of the femoral head the osteoarthritics and the normals are the same but in the iliac crest the osteoarthritics are lower than the normals. This indicates that the spatial arrangement of the trabeculae within the cancellous structure of the osteoarthritics does not change in response to the disease process in subchondral cancellous bone adjacent to the articular lesion but in the iliac crest the spatial arrangement of the trabeculae in osteoarthritics is less complex in shape. The structural parameters of cancellous bone show that BV/TV is increased in the compressive and tensile trabeculae of the femoral head but not in the iliac crest of the osteoarthritics. This indicates that the spatial complexity of the trabecular arrangement within the cancellous structure of osteoarthritics changes independently of changes in cancellous bone structure detected by the structural parameters of cancellous bone.

The sectional fractal dimensions have detected differences in morphological complexity between the normals and disease groups and between the skeletal sites. These novel data have been obtained using an innovative technique that is not dependent on assumptions based on conceptual models of cancellous bone structure. *A priori* knowledge of bone biology is utilised to enable the fractal analysis to measure specific morphological entities within the cancellous bone structure. The fractal dimensions have identified changes in the morphological complexity of specific components of the cancellous structure, which are not identified by existing model-based morphometric techniques. This has enabled new understanding of how change to cancellous bone structure occurs as a result of a disease process. Fractal analysis is a novel tool that will prove useful for the study of changes in cancellous bone structure due to disease and to

study the use of therapies to alter or maintain the quality of cancellous bone architecture.

DECLARATION

This work contains no material that has been accepted for the award of any degree or diploma in any university or other terirary instititution and to the best of my knowledge contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis when deposited in the University library, being available for loan and photocopying.

Ian H Parkinson

27/6/2002

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PUBLICATIONS ARISING

Parkinson IH, Fazzalari NL.

Methodological principles for fractal analysis of trabecular bone.

Journal of Microscopy 198:134-142 (2000).

Parkinson IH, Fazzalari NL.

Fractal analysis of trabecular bone: A standardised methodology.

Image Analysis and Stereology 19:45-49 (2000).

Parkinson IH, Fazzalari NL.

Goodness of fit on a modified Richardson plot by residual analysis.

Fractals 8:261-265 (2000).

Parkinson IH, Fazzalari NL.

Structural Complexity of Cancellous Bone: A Fractal Analysis.

Bone 28:S200 (2001).

AWARDS

Best Paper: International Quantimet and Stereoscan User Conference, Cambridge, UK, October 1995.

Postgraduate Travelling Fellowship 2001, Faculty of Health Sciences, University of Adelaide.