

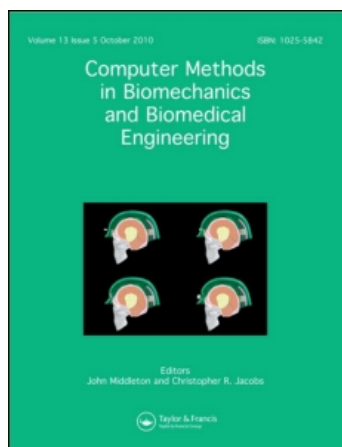
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Quantification of Bone Microarchitecture with the Structure Model Index

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The deterioration of cancellous bone structure due to aging and disease is characterized by a conversion from plate elements to rod elements. Consequently the terms "rod-like" and "plate-like" are frequently used for a subjective classification of cancellous bone. In this work a new morphometric parameter called Structure Model Index (SMI) is introduced, which makes it possible to quantify the characteristic form of a three-dimensionally described structure in terms of the amount of plates and rod composing the structure. The SMI is calculated by means of three-dimensional image analysis based on a differential analysis of the triangulated bone surface. For an ideal plate and rod structure the SMI value is 0 and 3, respectively, independent of the physical dimensions. For a structure with both plates and rods of equal thickness the value lies between 0 and 3, depending on the volume ratio of rods and plates.

The SMI parameter is evaluated by examining bone biopsies from different skeletal sites. The bone samples were measured three-dimensionally with a micro-CT system. Samples with the same volume density but varying trabecular architecture can uniquely be characterized with the SMI. Furthermore the SMI values were found to correspond well with the perceived structure type.

Keywords: Morphometry, structural parameters, structure classification, micro-CT, trabecular bone structure

1. INTRODUCTION

Since bone strength depends on the amount of bone tissue and on the microarchitecture of bone (Dalen *et al.*, 1976, Ciarelli *et al.*, 1991), it is important to be able to quantify both these properties. A wide range of techniques has been developed for the non-invasive assessment of bone mass and mass

density, such as peripheral and axial quantitative computed tomography, single — and dual-energy x-ray absorptiometry. The non-invasive assessment of architectural features is not yet available in the clinic. Invasive techniques provide bone samples which are then sectioned. Three-dimensional information is achieved by deriving morphometric parameters from two-dimensional sections using

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stereological techniques. Established parameters next to bone volume density (BV/TV) are e.g. trabecular thickness (Tb.Th), trabecular separation (Tb.Sp) and trabecular number (Tb.N), calculated indirectly assuming a plate model (Whitehouse, 1974, Parfitt *et al.*, 1987). The orientation of trabecular structure is another important factor responsible for the anisotropic material properties of bone (Cowin, 1985). The orientation and degree of anisotropy (DA) can be estimated from e.g. mean intercept length measurements (Harrigan and Mann, 1984). Of increasing interest are topological quantities such as connectivity (for a review see Compston, 1994) and fractal dimension (Weinstein *et al.*, 1992). Connectivity derived from two-dimensional sections can only give restricted information of the three-dimensional topology, but has nevertheless been shown to correlate with mechanical strength of trabecular bone (Mellish *et al.*, 1991). The use of fractal analysis for the characterization of topological properties of cancellous bone is a relatively new approach, its usefulness is still a matter of debate (Cross *et al.*, 1993, Chung *et al.*, 1994). Other methods are strut, node and termini analysis (Garrahan *et al.* 1986) or the calculation of Euler numbers using stereological techniques (Gundersen *et al.*, 1993).

The availability of three-dimensional measuring techniques opens new possibilities to analyze the architecture of cancellous bone. Three-dimensional image processing methods allow to derive unbiased morphometric parameters in a direct way. Examples of such techniques are direct volume and surface determination (Guilak, 1994), model independent assessment of thickness (Hildebrand and Rüegsegger, 1997) and three-dimensional connectivity estimation (Odgard and Gundersen, 1993).

In this paper three-dimensional methods for the quantification of the architectural type of cancellous bone are developed, allowing to directly quantify the frequently used subjective classification of cancellous bone as "plate-like" and "rod-like". The work is based on mathematical models which relate the volume and surface to a form dependent quantity and a linear measure corresponding to the thickness of

the structure. By evaluating a variety of form dependent measures with the help of three-dimensional micro-CT images of trabecular bone samples, we found an optimal parameter and called it *Structure Model Index* (SMI). The SMI value of an ideal plate structure is 0, and for an ideal cylindrical rod structure it is 3, independent of the physical dimensions of the structure. Applied to a mixed structure of plates and rods, the SMI assumes values between 0 and 3.

2. METHODS

2.1. Mathematical Model

Usually simple geometrical models are used to describe and quantify the complex structure of trabecular bone. The model are selected such that relevant features of the structure are described adequately. In classical bone histomorphometry quantities such as volume, surface, thickness and separation are of prime interest. They are therefore used as parameters in the geometrical models. The structure type is, however, assumed to be constant. An example is the well established plate model introduced by Parfitt *et al.* 1983: the model consists of periodically arranged parallel plates and the parameters are plate thickness and separation. Other models used are rods and spherical objects or mixtures of plates and rods (Martin, 1984, Fazzalari *et al.* 1989).

Our model shall allow to quantify the type of structure. In the search of such a model, we start with a family of models where the structure volume V depends on a linear measure r and the structure surface S is the derivative of the volume with respect to r .

$$V = f(r), \quad S = \frac{\partial V}{\partial r} = f'(r) \quad (1)$$

r is taken as the half thickness (or the radius) of the structural elements and is assumed constant over the entire structure. A simple representative of this family is

$$V = kr^e, \quad e \geq 1 \quad (2)$$

where e describes the type of structure and k and r are scale dependent, geometric parameters. With $e = 1$ we have a plate structure, k is the surface area of the plates. With $e = 2$ a rod structure is

described, k is proportional to the length of the rods. A model with spherical elements would be described with $e = 3$, probably useful for marrow cavities (spherical void).

2.2. Model Type Parameters

Let us now assume that volume, surface and thickness are directly determined from measured structures. The exponent e in (2) is then simply

$$e = \frac{V'(r) \cdot r}{V(r)} = \frac{S \cdot r}{V} \quad (3)$$

We generalize this finding to define a *structure volume exponent*

$$\text{SVE} = \frac{S \cdot r}{V} \quad (4)$$

For a structure consisting of both plates and rods with volume V_p and V_r , respectively we consider the model

$$V = V_p + V_r = k_1 r + k_2 r^2 \quad (5)$$

The pertaining SVE expression for this model is

$$\text{SVE} = \frac{(k_1 + 2k_2 r) \cdot r}{k_1 r + k_2 r^2} = \frac{1 + 2\epsilon}{1 + \epsilon} \quad (6)$$

with rod-plate volume ratio ϵ defined as

$$\epsilon = \frac{V_r}{V_p} = \frac{k_2}{k_1} r \quad (7)$$

For ideal geometrical objects the SVE assumes the values 1, 2 and 3 for plates, rods and spheres, respectively. An object consisting of plates and rods will have an SVE value between 1 and 2, according to (6). If applied to non-ideal objects the SVE parameter tends to be insensitive. One reason for this behavior is that thickness of the structure should precisely be in accordance to the surface density (S/V) of the structure, a condition which is not always met by real, measured structures. To avoid this problem the relative surface deviation ($S'(r)/S(r)$) is introduced and, since the $e - 1$ is the exponent of the surface area in equation (2)

$$e - 1 = \frac{S'(r) \cdot r}{S(r)} = \frac{ke(e-1)r^{e-2}}{ker^{e-1}} \cdot r \quad (8)$$

again we generalize this finding and define a *structure surface exponent* SSE

$$\text{SSE} = \frac{S' \cdot r}{S} \quad (9)$$

which, for a model containing both plates and rods leads to

$$\text{SSE} = \frac{2\epsilon}{1 + 2\epsilon} \quad (10)$$

Applied to cancellous bone structure the SSE parameter gives plausible results. Obviously the assumption of a constant thickness is too strict for the SVE parameter. A certain variability, as observed in reality (Hildebrand and Rüegsegger, 1997), has to be accepted. With the SSE parameter the variation of thickness seems less critical.

Since precise thickness measurements are not always possible — as in *in vivo* situations — it would be nice to have a thickness independent parameter to describe the model type of a structure. Equations (3) and (8) suggest to divide the exponent of the surface area with the exponent of the volume of the model in (2)

$$\frac{e-1}{e} = \frac{S'(r) \cdot V(r)}{S(r)^2} \quad (11)$$

again we generalize this finding and define a *structure model index* SMI

$$\text{SMI} = 6 \cdot \frac{S' \cdot V}{S^2} \quad (12)$$

The factor 6 is introduced to obtain simple integer values for ideal plates, cylinders and spheres, the SMI values for these models are namely 0, 3 and 4, respectively. For a model containing both plates and rods we get

$$\text{SMI} = 12 \cdot \frac{\epsilon + \epsilon^2}{1 + 4(\epsilon + \epsilon^2)} \quad (13)$$

So it is possible to get the rod-to-plate ratio purely from measures derived from the volume and the surface.

2.3. Implementation Techniques

The proposed methods require model independent assessment of the employed quantities. Typically the

analysed structures are described using binary voxel images, from which morphometrical quantities can be directly assessed.

The structure surface area S is determined by triangulating the surface of a voxel image and calculating the total area of the triangles. For the surface triangulation the Marching Cubes method (Lorensen and Cline, 1987) is applied. Structure volume V is calculated in a similar way by defining polyhedrons inside the structure according to the triangulated surface (Guilak, 1994).

For the direct estimation of thickness, a method based on three-dimensional distance transformation of the voxel image is used (Hildebrand and Rügsegger, 1997). With this technique a volume weighted mean thickness is calculated independently of the structure type.

For the calculation of the SSE and SMI the surface area derivative S' is required. To accomplish this we developed a new technique. A variation of the structure thickness is thereby simulated by translating the triangulated surface in its normal direction. An estimation of the surface area derivative is then estimated with a differential calculation. This procedure can be divided in to the following processing steps:

1. Triangulation of the surface and calculation of the total surface area $S(r)$
2. Calculation of the mean surface normal direction at all triangle vertices. This is done by averaging all normal vectors of the triangles connected to the same vertex.
3. Displacement of the vertices in the positive (outward) direction of the appertaining normal by a small distance of Δr .
4. Recalculation of the surface area $S(r + \Delta r)$ posterior to vertices displacement
5. Calculation of the approximal derivative of the surface area $S'(r)$ as the differential coefficient $\{S(r + \Delta r) - S(r)\}/\Delta r$

The magnitude of the displacement Δr can be selected quite uncritically between 1/10 and 1/1000 of a voxel side length, leading to almost the same value. The lower limit is dependent on the dynamic of the variables (i.e. number of bits in the floating point format) used to represent the surface values. The derived value may be corrupted if a structure with a rough surface is analyzed. For this reason the surface was smoothed prior to calculation of volume, surface and surface derivative, by averaging the positions of the vertices locally. An example

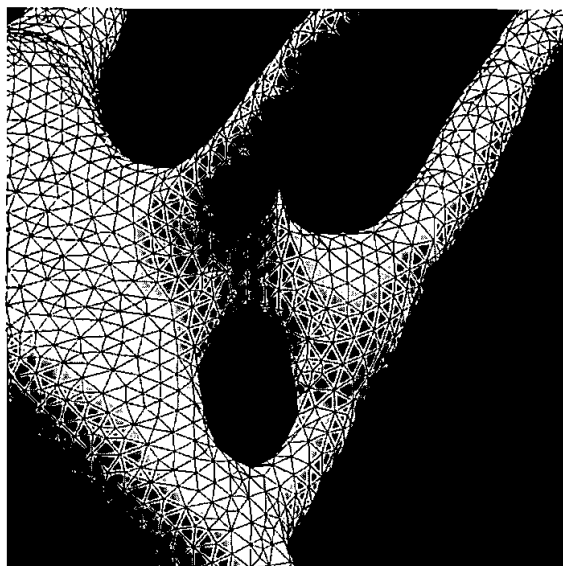


FIGURE 1 Surface triangulation of a voxel image used for volume, surface and surface derivative estimation. The surface is smoothed by averaging the positions of the vertices locally. The picture shows a close up from a trabecular structure measured with a micro-CT.

of such a smoothed triangulated surface is given in Figure 1.

To verify the correctness of the surface derivative approximation, the surface area is calculated indirectly as the differential coefficient of the volume ($\{V(r + \Delta r) - V(r)\}/\Delta r$). The so calculated area deviated from the directly calculated surface area less than 0.2 percent for the images used in this study.

3. MATERIALS

3.1. Measuring System

We used a newly developed high-resolution micro computed tomograph (μ CT) to measure biological tissue samples non-destructively (Rüeggsegger *et al.*, 1995). The system is based on a compact fan-beam type CT scanner. An X-ray tube with a microfocus is used as a source, a CCD-array as a detector. Typically, tissue samples with a diameter of 8 mm and a length of up to 36 mm are measured. Spatial resolution is 28 μ m and the used voxel size is $14 \times 14 \times 14 \mu\text{m}^3$.

3.2. Cancellous Bone Samples

To evaluate the proposed model parameters we examined a set of 8 human bone biopsies with various structural characters in terms of morphometrical parameters and perceived structure type. All selected samples origin from different donors and were taken from three different sites; lumbar spine, iliac crest and femoral head. The volume of interest (VOI) was a cubic region with a side length of 4 mm equivalent to 286^3 voxels. The used biopsies are a subset of the bone samples of the European Union project *BIOMED I "Assessment of Quality of Bone in Osteoporosis"* (Dequeker, 1994).

3.3. Three-dimensional Structure Analysis

The acquired gray-level voxel images are segmented and displayed with three-dimensional image

processing techniques (Müller *et al.*, 1994). The three-dimensional structural analysis, including the image segmentation, are carried out fully automatically without any operator interaction. All image processing modules are built in to the software package *IPL (Image Processing Language)* developed at our lab. All primary parameters are written to a data bank. The derived parameters are then automatically calculated from the primary parameters using a database query program. For image reconstruction and processing an AlphaStation 500/333 (Digital Equipment Corporation, Maynard, MA, USA) was used. Reconstruction of the μ CT images are carried out online during the measurement.

In addition to the proposed SVE, SSE and SMI parameters, the following three-dimensional parameters are calculated: Bone volume density (BV/TV), Bone surface density (BS/BV), model independent trabecular thickness (Tb.Th), trabecular thickness standard deviation (Tb.Th.SD) and mean intercept number (N_{MIL}). Bone volume, surface area and thickness are calculated using the techniques described in Section 2.3. The mean intercept number is the mean number of intersection points between uniformly distributed test lines and the surface of the trabecular structure divided with the total length of the test lines. The parameter is calculated using three-dimensional mean intercept length estimation (see e.g. Whitehouse, 1974). The value N_{MIL} corresponds to the trabecular number (Tb.N) if a plate model is assumed. For arbitrary structures it is related to the mean separation of the surfaces of the structure.

4. RESULTS

The morphometric parameters of the evaluated samples are given in Table I, the respective shaded surface representation in Figures 3, 4 and 5. The relation between the structure type parameters and the bone volume density is given in Figure 2.

The two samples from the lumbar spine (A and B) have a characteristic rod-like structure and a low volume density (0.065 and 0.064). According to the SMI values (2.66 and 1.94), sample A has a more

TABLE 1 Three-dimensional morphometric parameters derived from micro-CT measurements of human cancellous bone biopsies from the lumbar spine (LS), the iliac crest (IC) and the femoral head (FH)

Sample	Site	Pat. no	Sex	Age [Y]	SVE [I]	SSE [I]	SMI [I]	BV/TV [I]	BS/BV [mm ⁻¹]	Tb.Th [mm]	Tb.Th.SD [mm]	N _{MIL} [mm ⁻¹]
A	LS	51	F	76	1.53	0.676	2.66	0.065	22.6	0.135	0.048	1.13
B	LS	45	F	60	1.38	0.447	1.94	0.064	23.8	0.116	0.041	1.18
C	IC	69	F	80	1.38	0.476	2.06	0.124	17.6	0.157	0.066	1.45
D	IC	67	M	82	1.40	0.384	1.65	0.124	16.5	0.169	0.085	1.39
E	IC	48	F	75	1.20	0.211	1.05	0.129	19.0	0.126	0.045	1.62
F	FH	25	M	72	1.24	0.206	1.00	0.223	17.2	0.144	0.040	2.30
G	FH	55	M	60	1.16	0.031	0.16	0.222	13.6	0.171	0.056	2.03
H	FH	60	M	83	1.20	0.029	0.14	0.320	10.8	0.223	0.071	2.17

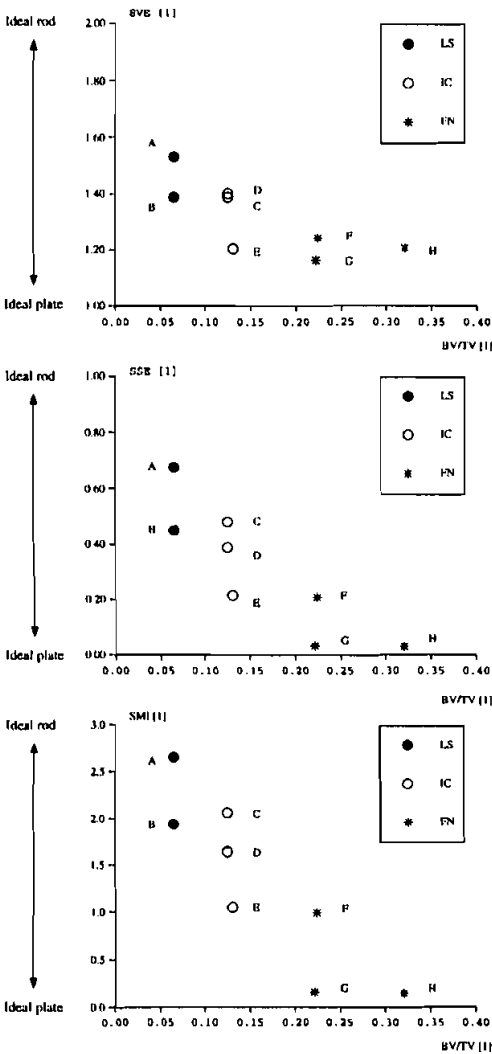


FIGURE 2 SVE, SSE and SMI in relation to bone volume density (BV/TV) for the evaluated bone biopsies (sample identification according to Table 1).

pronounced rod structure compared to sample B. This can be verified in the visualizations (Figure 3): Sample B has several plates with interconnecting rods, whereas sample A has almost a pure rod structure, with only a few plate segments.

In the iliac crest samples (C, D and E) the volume density is almost twice as high as that of the lumbar spine samples (0.124, 0.124 and 0.129). The structure architecture consists of both plates and rods. The corresponding SMI values indicate different degrees of plates and rods (2.06, 1.65 and 1.05). This can again be verified by observing the three-dimensional architecture of the samples (Figure 4): Sample C is quite rod-like, sample E is quite plate-like and sample D is in-between.

The samples from the femoral head (F, G and H) are more dense and plate-like than the ones selected from the two other sites. Consequently the volume densities are higher (0.223, 0.222 and 0.320) and the derived SMI values are lower (1.00, 0.16 and 0.14). In the appertaining visualizations of the samples (Figure 5) this can also be confirmed. In the structure of sample F just a few rods can be observed, whereas the structure of sample G resembles almost a perfect plate structure. The denser structure of sample H is also very plate-like and has a SMI value similar to that of sample G, but is significantly thicker.

Similar SMI values and different volume densities can also be found between the samples B and C and between the samples E and F. In both cases the difference in volume is due to a combination of thicker structure and smaller separation of the samples C and F compared with samples B and E.



FIGURE 3 Micro-CT images of biopsies taken from the lumbar spine (Sample A and B). SI, LM and AP indicate the directions superior-inferior, lateral-medial and anterior-posterior, respectively.

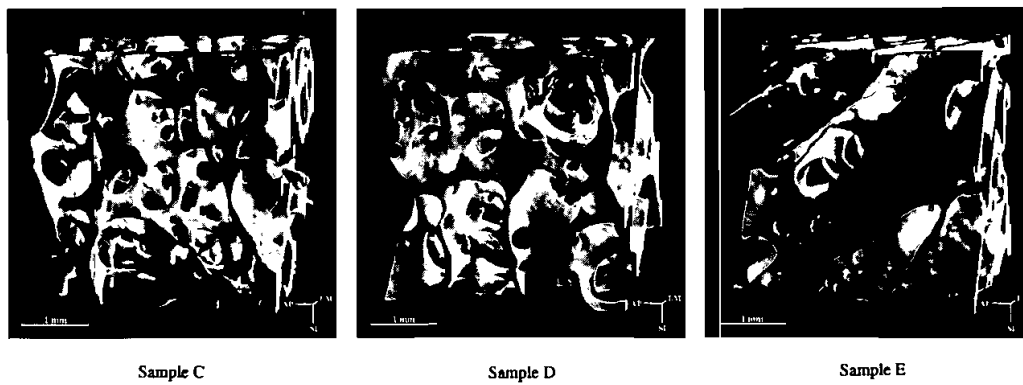


FIGURE 4 Micro-CT images of biopsies from the iliac crest (Sample C, D and E).

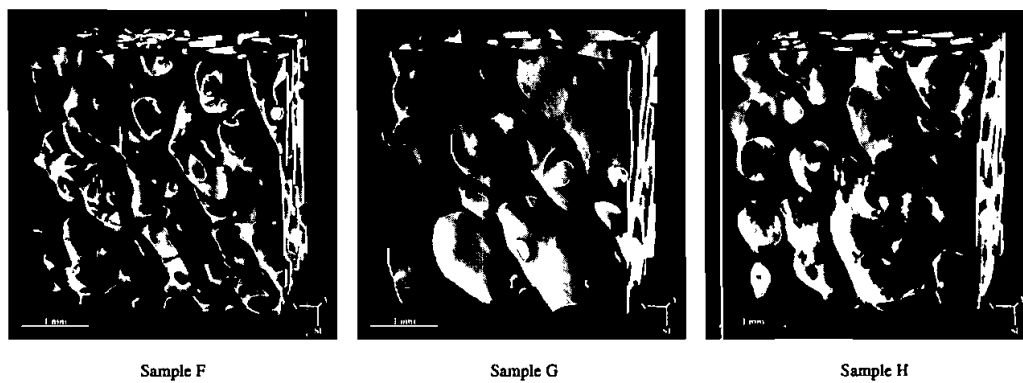


FIGURE 5 Micro-CT image of biopsies from the femoral head (Sample F, G and H). SI indicates the superior-inferior direction. X and Y are unspecified directions.

The resulting SSE values are almost equivalent to the ones achieved using SMI (Figure 2). Compared to the SMI results, the SSE values show a smaller dynamic range in relation to the ideal values; 0 for plates and 1 for cylindrical rods. The dynamic range for the SVE values are even smaller and some data are no longer reliable (e.g. sample D, C).

5. DISCUSSION

We introduced methods for a scale invariant assessment of the structure model type. With the model type parameters it is possible to classify a structure as plate-like, rod-like or spherical and also to derive the rod-plate ratio in mixed structures. Instead of assuming a fixed model constitution for the theoretical considerations, more flexible models were used as a basis, where the model type was included as a parameter.

Three different parameters (SVE, SSE and SMI) are evaluated in this work ideally giving equivalent information on the structure type. Applied to real objects, however, they behave quite differently, depending on the sensitivity to deviation from the ideal models. Thickness is e.g. assumed constant, but as can be seen by the derived thickness standard deviation of the examined structures (Table I), the variation of thickness is not negligible. Another shortcoming of the models is that intersections between structure elements, e.g. between rods and plates, not are accounted for. For the simple SVE parameter such deviations from the model lead to dubious values when applied to non-ideal structures like trabecular bone. For the SSE parameter the variations in thickness are less critical and the parameter gives plausible values for examined cancellous bone samples. The intersections of structure parts have a less critical influence on the parameters. This was verified with synthetic test objects. The explanation for this is that the region of intersections does not contribute to a substantial part of any of the used quantities used in the calculation of the parameters.

The SMI parameter is introduced to get a thickness independent measure for the model type. This is especially of importance for *in vivo* measurements with their notoriously bad spatial resolution. For our samples, measured with a high-resolution micro-CT system, we expect similar results as with the SSE parameter which is nicely shown in Figure 2.

An established two-dimensional parameter to quantify the form of trabecular bone structure is the Trabecular Bone Pattern Factor (TBPf) introduced by Hahn *et al.*, 1992. The TBPf is used to estimate the connectedness by means of the ratio of concave to convex surfaces and is calculated as the change of perimeter length divided by the change of area by a dilatation of the structure by one pixel. The TBPf is in fact a quantity similar to a two-dimensional approximation of the relative surface deviation (RSD) introduced to derive the SSE parameter. Consequently, the TBPf is something close to the relative perimeter deviation in two dimensions. Since TBPf was shown to be sensitive to age-related bone loss (Grote, *et al.* 1995), an interesting possibility is to use the RSD as a three-dimensional correspondence to TBPf. The RSD parameter is in contrast to the proposed structure type parameters not scale invariant and depends on the structure thickness by a constant model type (see Equation 9).

Mechanical properties of cancellous bone have been shown to depend not only on apparent density but also on the structural model (Gibson, 1985): rod-like elements forming open cells were shown to have a different relation between mechanical properties and apparent density than plate-like elements forming closed cells. An interesting issue of future work would therefore be to examine the relation of the SMI and the mechanical properties of trabecular bone samples.

The purpose of the proposed SMI parameter is to present an independent structural parameter next to other directly estimated quantities such as volume, surface area and thickness. Since the SMI parameter gives no direct information on connectivity, it should be complemented with a parameter which directly quantifies the connectedness of a three-dimensional structure. This can be achieved

by calculating the Euler characteristic of three-dimensional data (Odgaard and Gundersen, 1993). The proposed set of independently assessed parameters could be valuable to define the pathological state of cancellous bone more precisely and to investigate the consequences of bone remodeling due to aging, disease or altered loading conditions.

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