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Trabecular bone structure and strength - remodelling and repair

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Abstract

The strength of the spinal trabecular bone declines by a factor of 4-5 from the age of 20 to 80 years. At the same time, the volumetric (apparent) density declines by a factor of only 2. This discrepancy can be explained by the known power relationship between density and strength; this power relationship is based on the fact that trabecular bone is a porous material. To date, it has not been possible to determine or quantify the influence other factors may have in determining the strength of a loadbearing trabecular network. However, it is known that with age: 1) There is a loss of connectivity through osteoclastic perforations of horizontal struts. 2) There is an increase in anisotropy - again due to loss of horizontal struts, and perhaps also due to micro-modelling drift or to thickening of some vertical trabeculae. 3) The changes in the network can lead to the slenderness ratio between vertical and horizontal struts reaching a certain magnitude and thereby inducing buckling under compression. 4) Microdamage and microfractures will occur - mainly in these very loaded vertical struts. The microfractures will be repaired by microcallus formation, and these calluses will later be removed by the remodelling process. 5) Bone material quality will slightly change, leading to a decrease in collagen content and a relative increase in the degree of mineralisation. But, it is not known how these factors will influence the power relationship between density and strength. Nor is it known how different treatment regimens will affect the "natural" power relationship: will the same curve be followed, but in the opposite direction? Or will the curve be less or more steep? Will the gain in bone strength be larger if treatment is started early - on the steep part of the curve? Furthermore, as trabecular bone can never be isolated in vivo, other factors need to be investigated: The interplay between the cortical shell and the trabecular network; transmission of load; the interplay between soft tissues (cartilage, connective tissue, muscle) and bone; the shock absorbing capacity of the discs; and the hydraulic effect of the bone marrow. In order to answer these questions, more in vitro and in vivo studies on human bone in relation to aging, to immobilisation, to exercise and in relation to different treatment regimens are needed.

Keywords: Osteoporosis, Bone Density, Bone Structure, Human Vertebrae

Introduction

During normal aging there is a decrease in trabecular bone density of approx. 50%. However, at the same time the decrease in bone strength is much more pronounced and reaches values of 70-80%. This is caused by the non-linear relationship between trabecular density and strength.

Carter and Hayes showed as early as in 1977 that there is a power relationship between volumetric bone density and bone strength[4]. In their study they pooled trabecular and cortical bone and thereby achieved a large variation in density ("large density window"). The power of the relationship was found to be 2.

A more discriminating picture of the relationship between trabecular bone apparent density and strength has subsequently been established, with powers ranging from near 1 to about 3 - depending on the type of cancellous bone and the density "window" under investigation.

Mosekilde et al. (1987) and Ebbesen et al. (1997) found that both linear and power functions gave the same degree of correlation between trabecular bone density and strength[11,5].

This could, however, be explained by the use of a relatively small density window in these two studies as only cancellous bone from normal individuals was investigated. Had osteoporotic patients been included, then the power relationship might have shown its superiority.

The power relationship is based on the fact that cancel-

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lous bone is a porous material[4] - but the shape of the curve could be influenced by many different factors which are all tightly connected with bone remodelling and repair:

1. Loss of connectivity
2. Increase in anisotropy
3. Buckling of vertical struts (Euler buckling)
4. Microdamage, microfractures and repair
5. Change in material quality
6. Treatment regimes

Therefore, while the power relationship between density and strength is the main reason for the very pronounced decrease in bone strength with age, the other factors mentioned above might also play their own roles.

Materials and methods

1. Loss of connectivity due to osteoclastic perforations.

During normal aging, the remodelling process causes trabecular thinning and fortuitous osteoclastic perforations. This affects mainly the horizontal struts in a very oriented, loadbearing network as seen in the spine[12]. It has been difficult to quantify connectivity of trabecular bone, and one of the most optimal methods; measurements of connectivity density, have failed to show that connectivity has any influence per se on bone strength[15].

It should be noted, though, that this study focused on iliac crest bone biopsies (mainly plates, few perforations in relation to age, isotropic bone, non-loadbearing bone). A similar analysis has not yet been performed on spinal loadbearing cancellous bone.

However, there is no doubt that perforations as such lead to an accelerated bone loss (removal of unloaded struts) and thereby to accelerated decrease in bone strength over time[13,14].

2. Increase in anisotropy.

This is a direct effect of the above described loss of horizontal struts. However, other factors might also be important: There might be a compensatory increase in thickness of some of the loaded/strained vertical trabeculae (modelling drift). This is an issue which is still under debate and which cannot be resolved easily: it is not yet possible to follow changes in human trabecular structures in a longitudinal manner. Possibly some new techniques,

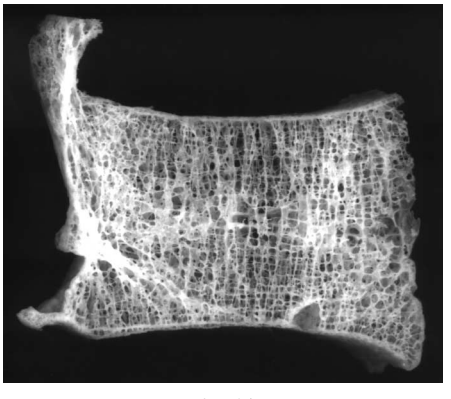

Fig. 1A

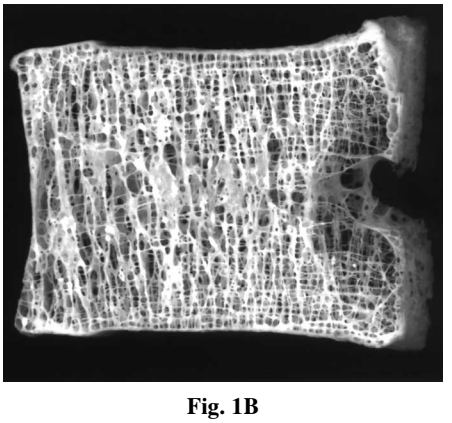

Fig. 1B

Figures 1A and 1B.
A. Vertebral body from an 85 year old man with osteophytes and a very clear diagonal stress-bridge in the trabecular network.
B. Vertebral body from an 80 year old man without osteophytes. The trabecular network is very regular.
(Photographs of midsagittal sections.)

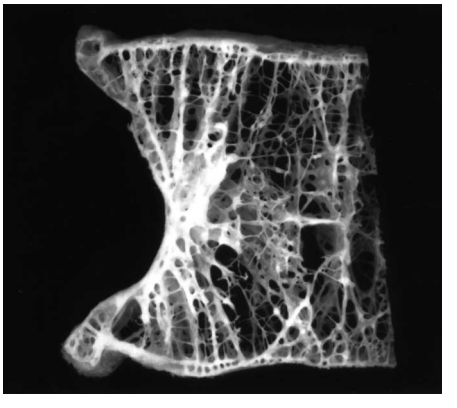

Fig. 2A

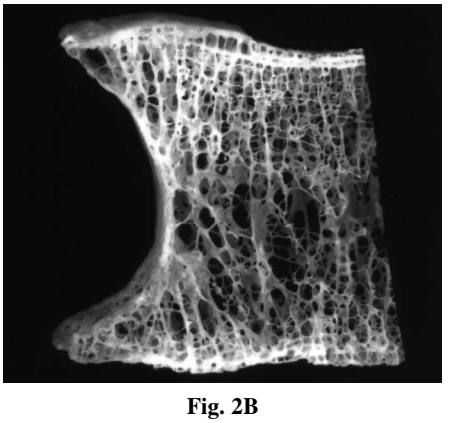

Fig. 2B

Figures 2A and 2B.
A. Vertebral body from a 91 year old man: clear trabecular thickening of struts between the endplates and the vertebral rim (a stress-bridge?).
B. Vertebral body from an 80 year old man without any "fortification" of the trabecular network.
(Photographs of 1/2 frontal sections.)

e.g. MR or μCT will one day be capable of making this possible.

However, the visual impression of sections from human vertebrae is clear: Trabecular structures under high stress or strain will be able to adapt to these through modelling drift and thickening. This is most clearly visualised with respect to loadbearing osteophytes - where load is transmitted from one vertebral body to the next through their osteophytes. Figure 1A shows such a vertebra where new stress-bridges are created at a diagonal to the central trabecular network. Such a stress-bridge is not seen in the vertebral body from a man of the same age but without osteophytes (Fig. 1B).

The described stress-bridges might also be formed in other parts of the trabecular network - in the form of thickenning of vertical struts in the existing regular trabecular network - transmitting load from one endplate to the other or transmitting load from the endplates to the cortical rim (Fig. 2A and B). These are typical examples of architectural adaptations of the human loadbearing trabecular bone to the high strain events[7,8,9].

3. Buckling of vertical struts (Euler buckling).

Bell et al. showed in 1967 that Euler buckling can be created due to loss of horizontal struts[2]. Because the strength of a trabecular structure is proportional to its radius squared, thinning of the vertical struts has a tremendous influence on strength. In a similar manner, the compressive strength of the network is proportional to the square of the distance between the supporting horizontal struts.

Furthermore, at a certain stage, when several horizontal struts have disappeared, the slenderness ratio of a long, unsupported vertical trabecula reaches a critical value, and the trabecula fails due to buckling under compression[16]. When this stage is reached - due to failure in adaptation? - the loss of strength is dramatic.

A clear example of this is seen in figure 3A (a vertebral fracture in a 79 year old woman); a few very long, unsupported vertical struts are seen. Figure 3B shows the vertebral body from a 67 year old women without osteoporosis. The difference between the disorientated structure in figure 3A and the well-connected structure in figure 3B is very clear.

4. Microdamage - microfracture and repair.

Microdamage of the bone tissue is a discrete lesion which

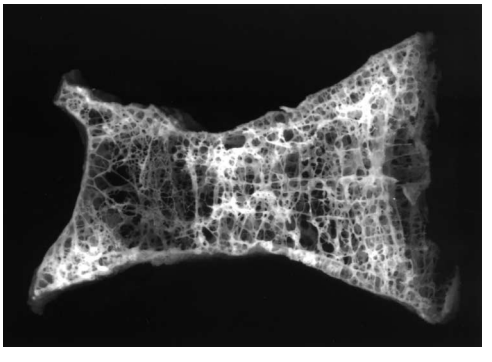

Fig. 3A

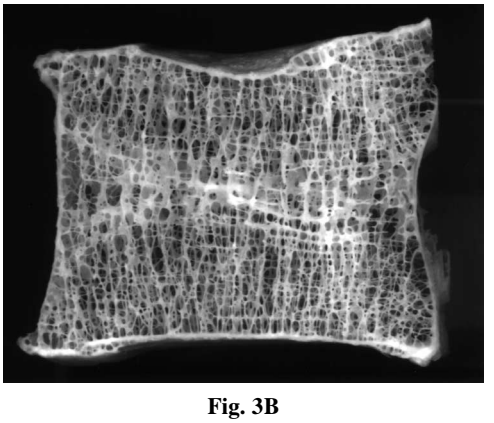

Fig. 3B

Figures 3A and 3B.
A. Vertebral body with an osteoporotic fracture (79 year old woman). There is a deterioration of the network, and some long vertical struts without any support are seen.
B. Vertebral body from a 67 year old woman without osteoporosis. The network is "perfectly" organised. (Photographs, midsagittal sections).

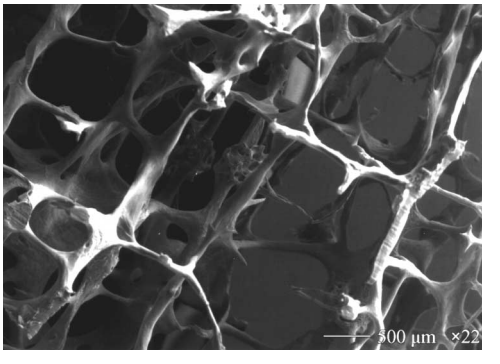

Fig. 4A

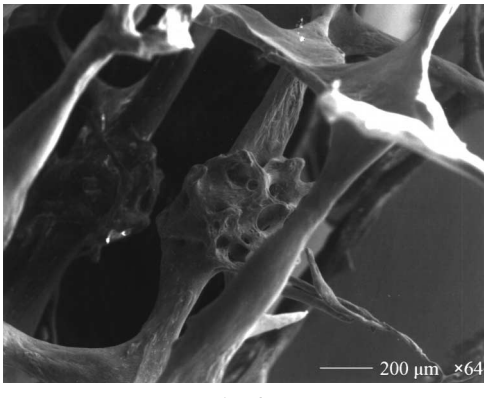

Fig. 4B

Figures 4A and 4B.
Scanning electron microscopy (SEM) showing multiple microcalluses on vertical struts (79 year old woman with vertebral fractures). The microcalluses are newly formed.
A. Shows the very loose network with two microcalluses in the background (magnification x22).
B. Clearly shows the two newly formed microcalluses (magnification x64).

will be repaired by the remodelling process[3,6]. Microfracture of a trabecular structure is a larger lesion and requires healing by the formation of woven bone - like a normal fracture. As in normal fracture healing, there is a massive demand for blood supply, and in newly formed microcalluses a tremendous amount of vessels are present (Fig. 4A and B). However, microcalluses do not accumulate in the network - they are removed by the remodelling process. Therefore, at a later stage the microcallus will have a very smooth surface with no entrances for vessels.

In the studies by Hansson and Roos[10] and by Vernon Roberts and Pirie[17] it has clearly been shown that the number of microcalluses per vertebral body is dependent not only on the age of the individual but also on the bone density. Vertebral bodies with low bone density had the highest number of microcalluses. In elderly individuals with very low bone density, more than 100 microcalluses have been counted per vertebral body[17].

Although microcalluses are mostly seen on vertical struts, they can also appear on horizontal supporting struts. The only requirement seems to be that there is still physical contact between the broken trabecular ends. Whether microcalluses should be regarded as a sign of poor architectural adaptation to prevailing strain, or whether they are a sign of a well-functioning repair mechanism is difficult to determine.

In the human spine, endplate depressions (Schmorl's depressions) are another site where microdamage and repair take place. Also, the number of Schmorl's depressions increases both with the age of the individual and with the decline in bone mass[10].

Immediately after a small fracture of an endplate, the disc tissue is forced into the vertebral body and can quickly occupy a large part of a vertebral body. To protect against this, a cup-shaped barrier of woven bone is rapidly formed around the fibrocartilage of the disc.

Concomitantly, microcalluses are often seen underneath the endplate depression. This is again a sign of a vigorous repair mechanism in a trabecular network which might not have been optimally adapted to strain/stress.

Fig. 5A

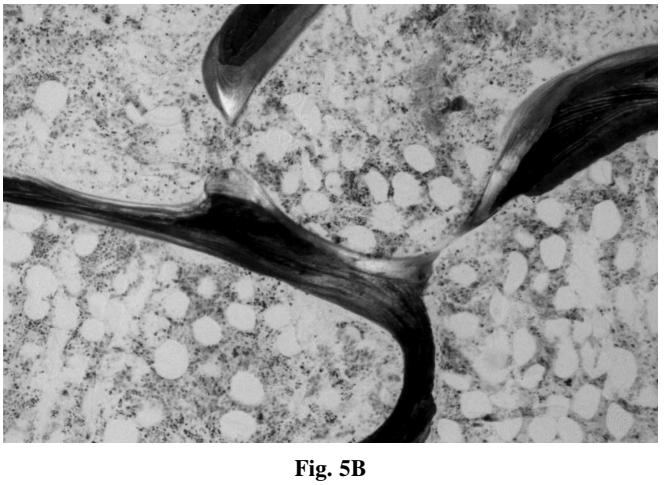

Fig. 5B

Figures 5A and 5B. Human trabecular bone. Undecalcified, 8μm thick sections stained with nuclear fast red.
A. The red colour is dependent on the age of bone tissue: the trabecular core is dark red, newer packets have lighter red to pink colours. (Normal light microscopy).
B. The same section investigated in polarised light with a λ-filter.

5. Changes in bone material quality.

In the described non-linear relationship between trabecular bone apparent density and strength, the bone material quality is considered constant. Whether this is the case during normal aging is a matter of debate. A recent study by Bailey et al.[1] has shown that during normal aging there is a relative decline in collagen content and an increase in mineralisation[1]. This indicates a decrease in real density with age. Whether this is due to: 1. osteocyte death; 2. increased mineralisation of the central trabecular bone core; or 3. a decline in turnover per se is not known (Fig. 5A and B).

The effect of this concerning microdamage and microfracture is not known. Just as it is still not known whether powerful antiresorptive agents (e.g. bisphos-

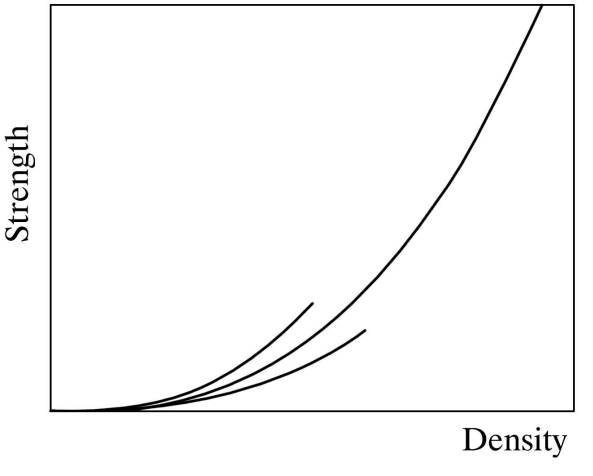

Figure 6. Schematic drawing of the power function between apparent density and strength. The thick curve shows the "natural" relationship. The two other curves indicate how treatment regimes might affect the relationship.

phonates) will change bone mineralisation after long-term treatment and thereby change bone material quality.

6. Treatment regimes versus trabecular architecture and strength.

At present we know that there is a power relationship between trabecular bone apparent density and strength. And we also know that there is a constant architectural adaptation to strain. But we do not know whether the described "natural" power relationship will be different during treatment regimes (pharmaceutical or mechanical): it could be steeper or, more probably, less steep (Fig. 6). At the same time, we do not know whether the efficacy of treatment is dependent on the time of initiation of treatment (Fig. 7). In theory, early prevention should be more effective that late treatment - taking the power relationship between density and strength into consideration: early prevention will act on the steep part of the power curve.

Therefore, a small increase in bone density would lead to a larger increase in bone strength. It should be stressed again that early prevention does not have to be pharmaceutical - it could also be weightbearing exercise or a combination of pharmaceutical intervention and weightbearing exercise.

Discussion

Having discussed the porous structure of trabecular bone and the adaptations of the trabecular network to mechanical demands, it should be stressed that trabecular bone does not function as an isolated unit - it will always be connected with the cortical shell. And, as trabecular bone architecture and mass change with age, so does the cortical bone. In the spine this is seen as a remodelling-induced thinning of the shell and a very slow periosteal apposition, leading to expanding of the vertebral body with age (modelling). The changes in the cortical shell are further influenced by the formation of osteophytes and the invasion of soft tissue into the vertebral body as such (Fig. 8A and B).

Therefore, concerning vertebral body strength, trabecular bone architecture does play a role, but so too do: trabecular bone density, bone size and cortical thickness. Additionally, concerning vertebral fracture liability, there are external factors which play a very important role: disc status, muscle protection and trauma. These external factors - like disc states - are often overlooked in clinical trials assessing vertebral deformities.

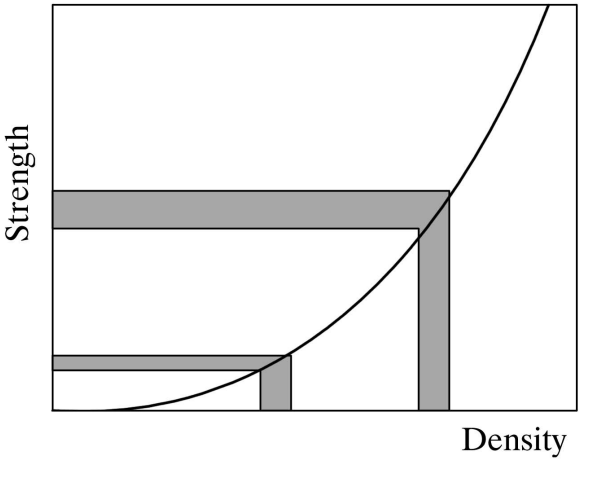

Figure 7. Schematic drawing of the power relationship between apparent density and strength. The effect of early and late treatment is indicated. Early treatment (at the steep part of the curve) induces a much larger strength response than late treatment.

Conclusion

During normal aging, the decrease in trabecular bone strength is much more pronounced than the decline in apparent density. This is mainly explained by the power relationship between trabecular bone density and strength,

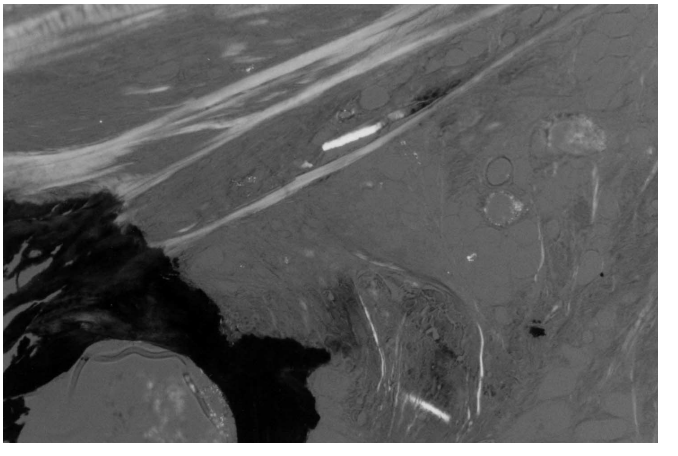

Fig. 8A

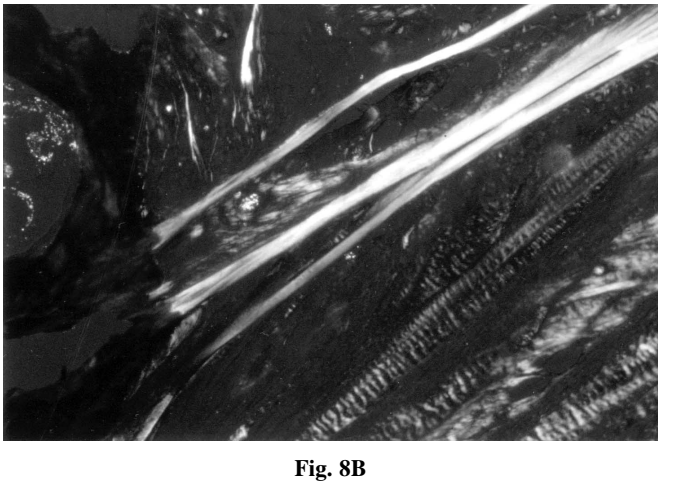

Fig. 8B

Figure 8A and 8B. Normal histological sections of the region close to the cortical shell of a vertebral body. Both normal histological sections are investigated in polarised light with a λ-filter.
A. Shows collagen fibres invading the marrow cavity and attaching themselves to trabecular struts.
B. Collagen fibres and muscle fibres invading the marrow cavity of a vertebral body. The collagen fibres are pulling on the trabecular structures.

as demonstrated in the static test situation. Dynamically, this relationship might be influenced by remodelling-induced deterioration of the network, modelling drift and microdamage and healing.

However, to date only very little is known concerning the role of these factors per se, furthermore, only very little is known concerning this relationship when treatment regimes are initiated with or without weightbearing exercise.

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