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Magnetic resonance microscopy of trabecular bone

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Background. *Bone diseases such as osteoporosis lead to changes in the trabecular bone mass and architecture. Improved methods for the quantitative assessment of trabecular bone are needed to better understand the role of trabecular architecture in bone strength. MR microscopy (MRM), with its ability to achieve resolutions below 50 μm, has proved to be particularly useful for the ex vivo evaluation of the complex architecture of trabecular bone. In this study, we describe the use of projection reconstruction (PR) with MRM for the quantitative evaluation of the three-dimensional structure of trabecular bone explants and for the prediction of their biomechanical properties.*
Material and methods. *High-resolution 3D PR and trabecular bone explants were analysed to determine standard morphologic parameters such as trabecular bone volume fraction (BV/TV or Vv), trabecular thickness (Tb.Th) and trabecular separation (Tb.Sp). Segmentation of the high-resolution images into bone and bone marrow was obtained by using a Bayesian approach. The derived parameters were finally included in non-linear mathematical models for the prediction of Young's modulus (YM).*
Results. *The parameters derived from the PR spin-echo were found to be stronger predictor of YM (R^2 = 0.86) than those derived from the conventional spin-echo images (R^2 = 0.75) used for comparison.*
Conclusions. *This ex vivo approach should be readily adaptable to the studies in human subjects.*

Key words: bones - ultrastructure; magnetic resonance imaging, magnetic resonance microscopy; projection reconstruction, Young's modulus

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Introduction

Bone diseases lead to changes in the trabecular bone structure that are not only characterised by reduction of bone mass but also by modifications of the bone architecture often accompanied by atraumatic fractures.[1] Osteoporosis is nowadays a problem of primary importance, which mainly affects women and elderly people. In Europe, the number of bone fractures related to osteoporosis amounts to more than one million per year and this number is expected to rise dramatically over the coming years because the percentage of elderly people that is already high is still increasing. As a consequence, there is a great need to develop accurate methods for the evaluation of the status of bone tissue in order to achieve an early diagnosis of the disease and to determine the level of fracture risk as well as to provide therapeutic intervention in high risk patients and to monitor the effects of therapy. Several investigations have indicated that, besides bone mineral density (BMD), also trabecular architecture can be an important factor in assessing bone strength.[2,3]

The accurate in vivo observation of the microstructure of the bone is today not feasible, but the use of magnetic resonance imaging (MRI) techniques in the area of osteoporosis appears very promising.[4-6] Among these techniques, the most powerful methodology for the *ex vivo* study of trabecular bone is certainly magnetic resonance microscopy (MRM), which also able to provide detailed information on the trabecular bone structure. Recently, we have proposed the use of short-TE projection reconstruction (PR) MR microscopy for the study of healthy and osteoporotic bone explants.[7] The aim of this study was to verify the potential of the PR method in the characterisation of trabecular bone architecture and in the prediction of its mechanical properties.

Material and methods

Sixteen specimens consisting of cylindrical bone plugs (∅=4mm) were obtained from load-bearing and no-load-bearing regions of porcine humeral heads. The explants were examined at 7.05 T using a Bruker AM300 instrument equipped with a vertical wide-bore magnet and a microimaging accessory. All the explants were studied in the air using a 5mm diameter radio frequency (RF) coil. Short-TE proton MR microimages were acquired using a 3D spin-echo (TE = 3.0 ms, TR = 1.0 s) sequence according to the projection reconstruction (PR) method with constant gradient step and partial echo-acquisition already described.[8] This method provided images with a final voxel resolution of 41×41×82 μm^3. Spin-echo microimages (TE = 6.2 ms, TR = 1.0 s) were obtained on the same explants by the standard Fourier transform imaging method. The Young's modulus was measured on other sixteen bone specimens excised from adjacent areas to those used for the explants subjected to MR microscopy.

After interpolation to obtain an isotropic voxel resolution, the main standard structural parameters such as trabecular bone volume fraction (BV/TV or Vv), trabecular thickness (Tb.Th), and trabecular separation (Tb.Sp) were derived from contiguous cross sections of binary images using the *t3m* software.[9] Segmentation of the high resolution images into bone and bone marrow was obtained by adopting a Bayesian approach based on the Markov random field model where the likelihood function was locally adaptive.[10] The derived structural parameters were finally included in non linear mathematical models for the prediction of Young's modulus (YM) of the trabecular bone explants.

Results

Figure 1 shows a 2D section of a 3D PR microimage of an intact specimen of porcine trabecular bone. The morphologic parameters obtained from the PR images were compared with those extracted from the standard FT images. In Table 1, the morphologic parameters extracted from the PR and standard FT images of the load-bearing bone specimens are reported, whereas Table 2 presents the corresponding data derived for the bone specimens excised from no-load-bearing regions. The best prediction of the mechanical properties of the examined trabecular bone explants were obtained by using the following non linear model derived from the equation proposed by Hwang et al.:[11]

$$YM=Vv*(a+b/Tb.Sp+c/Tb.Sp^2+d/Tb.Sp^3)+Tb.Th*(e+f/Tb.Sp+g/Tb.Sp^2+h/Tb.Sp^3)+k \quad [1]$$

which included simultaneously Vv, Tb.Th and 1/Tb.Sp. Figures 2 and 3 show the relationships between the Young modulus measured experimentally and that predicted using the structural parameters derived from the PR and standard FT images, respectively. The parameters extracted from the PR images were found to be stronger predictors of YM (R^2 = 0.86) than those derived from the standard FT images (R^2 = 0.75).

Discussion

In this study, short-TE PR method was adopted to minimise the susceptibility effect at the bone-marrow interface, which may lead to overestimation of the trabecular thickness as

Table 1. Standard morphologic parameters estimated from projection reconstruction (PR) and conventional FT spin-echo images of porcine trabecular bone explants from load-bearing regions.

	PR method			FT method		
Sample	**Vv**	**Tb.Th**	**Tb.Sp**	**Vv**	**Tb.Th**	**Tb.Sp**
	%	**mm**	**mm**	**%**	**mm**	**mm**
1	0.680	0.289	0.136	0.720	0.399	0.155
2	0.796	0.329	0.084	0.789	0.428	0.115
3	0.697	0.266	0.116	0.754	0.444	0.135
4	0.714	0.281	0.113	0.559	0.287	0.227
5	0.662	0.215	0.109	0.738	0.356	0.126
6	0.613	0.217	0.137	0.542	0.225	0.190
7	0.609	0.219	0.141	0.664	0.301	0.152
8	0.558	0.193	0.153	0.539	0.202	0.173
9	0.695	0.264	0.116	0.637	0.241	0.137
Mean	0.669	0.253	0.123	0.660	0.320	0.157
S.D.	0.070	0.044	0.021	0.097	0.090	0.035

Table 2. Standard morphologic parameters estimated from projection reconstruction (PR) and conventional FT spin-echo images of porcine trabecular bone explants from no-load-bearing regions.

	PR method			FT method		
Sample	**Vv**	**Tb.Th**	**Tb.Sp**	**Vv**	**Tb.Th**	**Tb.Sp**
	%	**mm**	**mm**	**%**	**mm**	**mm**
1	0.481	0.144	0.155	0.275	0.103	0.270
2	0.532	0.197	0.174	0.268	0.119	0.326
3	0.379	0.119	0.195	0.425	0.150	0.203
4	0.359	0.128	0.229	0.433	0.126	0.166
5	0.470	0.162	0.183	0.349	0.110	0.205
6	0.394	0.146	0.225	0.459	0.144	0.169
7	0.440	0.152	0.193	0.556	0.213	0.170
Mean	0.436	0.150	0.193	0.395	0.138	0.216
S.D.	0.062	0.025	0.027	0.104	0.037	0.061

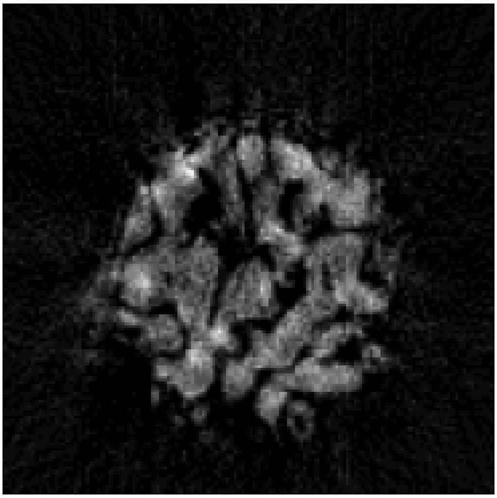

Figure 1. 2D section of a 3D projection reconstruction spin-echo image of a porcine trabecular bone specimen.

reported by Majumdar and co-workers.[12] The results reported in Table 1 and Table 2 do not seem to show significant differences in Tb.Th for the PR and FT method. This is probably due to the fact that the morphologic parameters were computed on isotropic image voxels with a 41 μm^3 resolution. However, the PR-derived structural data appear to be more accurate as their SD resulted lower than those calculated for the FT-derived values. Even though a spin-echo scheme was adopted in this study, we foresee that the PR method can also be of great advantage in the case of gradient-echo sequences. This implies that the PR method can be readily implemented on modern clinical MRI scanners. Moreover, our best model for the prediction of Young's

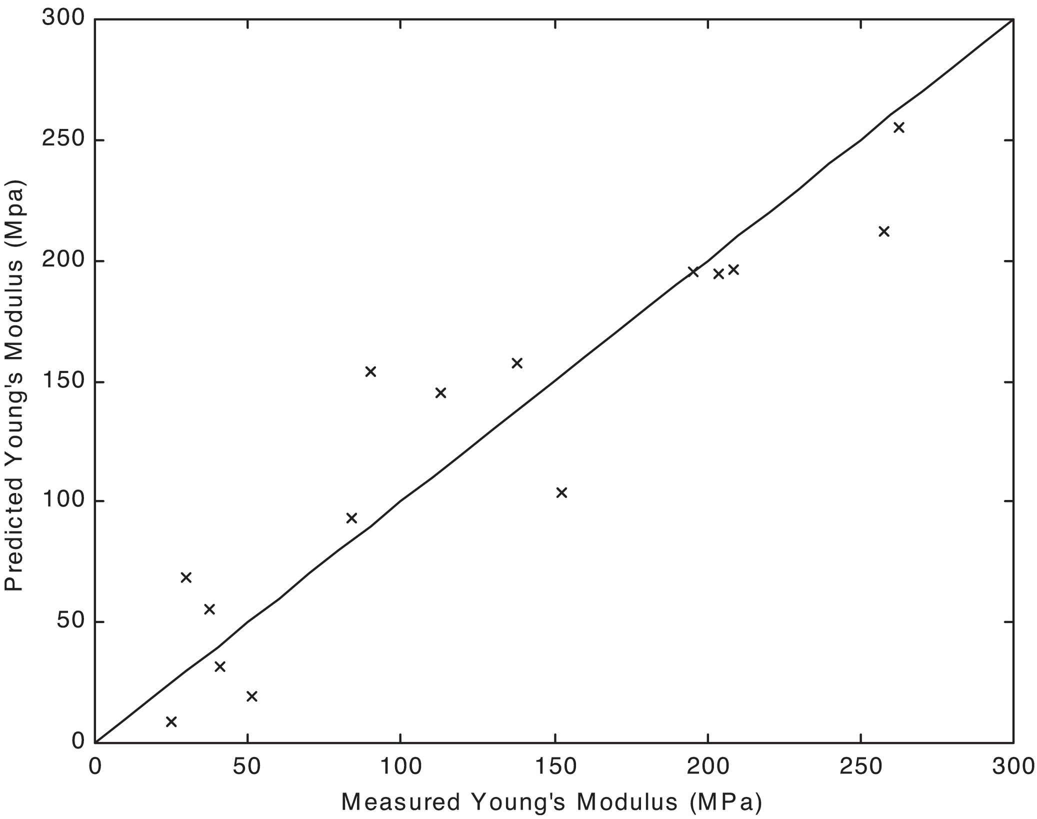

Figure 2. Experimental Young's modulus versus predicted Young's modulus. Predicted YM values were calculated including the morphologic parameters Vv, Tb.Th and 1/Tb.Sp derived from PR images in the equation 1 (R^2 = 0.86).

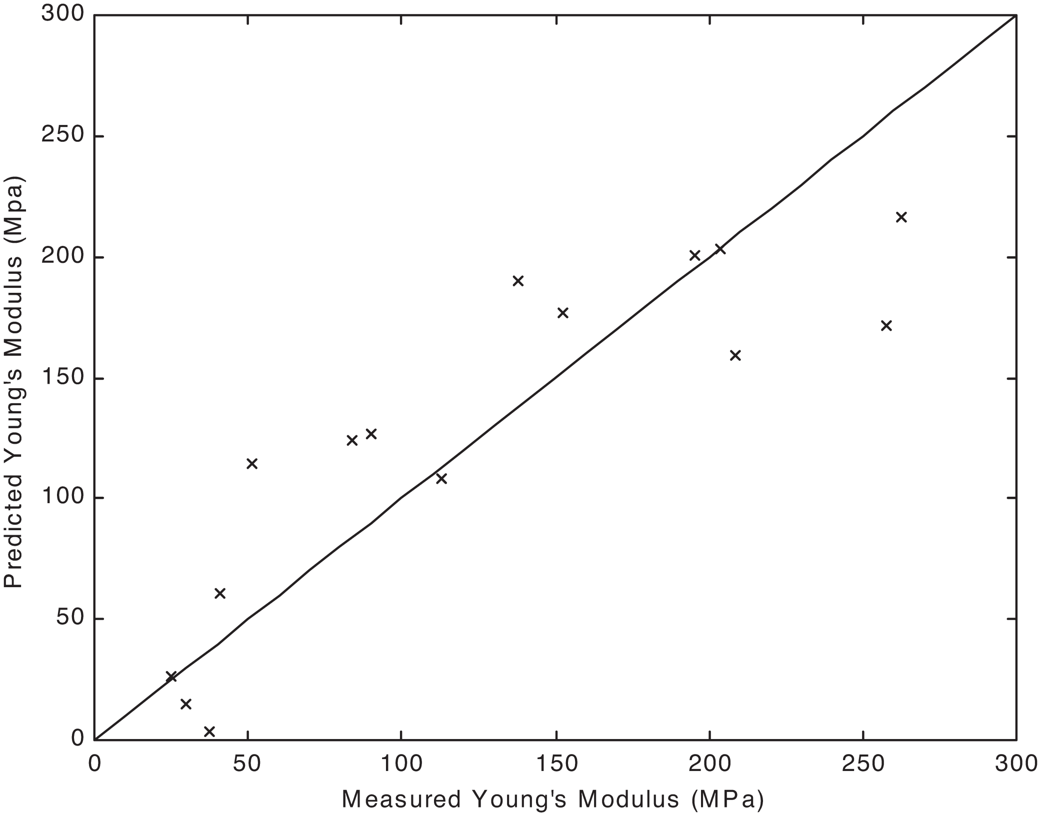

Figure 3. Experimental Youngīs modulus versus predicted Young's modulus. Predicted YM values were calculated including the morphologic parameters Vv, Tb.Th and 1/Tb.Sp derived from conventional FT images in the equation 1 (R^2 = 0.75).

modulus can contribute to a more accurate in vivo evaluation of the mechanical properties of the trabecular bone.

Since the risk of bone fractures seems to be strongly related to bone architecture, the described PR-based approach may provide a relevant contribution to the clinical MRI investigation of trabecular bone in ageing and osteoporosis.

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