Predicting Bone Strength with SPENT (Sub Pixel Enhancement of Non-Uniform Tissue) and R2'

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Introduction To assess fracture risk in diseases such as osteoporosis, Bone Mineral Density (BMD) is typically measured using Dual-Energy X-ray Absoptiometry (DEXA). However, DEXA is limited by its accuracy, partly because it measures 'area' density rather than 'true' density. In addition, DEXA imparts a dose of radiation. MRI can provide a non-invasive investigation of bone density and structure[1]. However, image based MRI assessment of bone has been limited by the resolution and sensitivity available in a clinical setting. MR relaxometry has also been used to measure R_2', characterised by a loss of coherence through spatial variation in the main magnetic field B_0, which is related to the structure of bone[2,3]. In this work, a new method called SPENT[4] is investigated with R_2' as MR parameters that may be used to predict bone strength without requiring high resolution 3D imaging.

SPENT Theory SPENT is a method that sensitises images to the level of homogeneity of magnetisation within each pixel (see Fig.1c). This can be achieved by applying an additional gradient prior to the readout period to produce a 2π phase wrap across each pixel (effectively shifting the k-space window to obtain the next 'tile'). For a pixel with uniform magnetisation in the direction of the applied gradient, no coherent signal is formed and the pixel is dark. However, if the voxel has non-uniform magnetisation (e.g. if it lies on a boundary of two tissues such as bone and water) there will be a coherent signal produced[4]. A Normalised-SPENT (N-SPENT) image (Fig.1d) can be created by dividing the SPENT image (Fig.1c) by a standard image (Fig.1b). This removes the dependence of the SPENT signal intensity on the amount of magnetisation in each pixel. The average signal in the N-SPENT image over the volume of the bone cube is a measure of the magnetisation distribution that may be related to the structure of the bone.

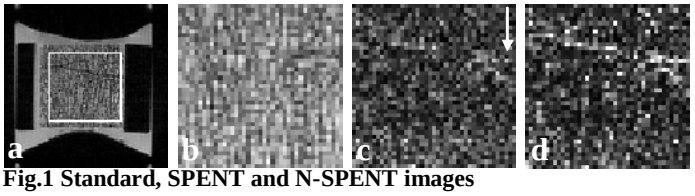

Fig.1 Standard, SPENT and N-SPENT images
a) A standard image of a bone cube in its holding device with a region (roi) entirely within the bone highlighted, **b)** the roi from **a**, **c)** a SPENT image of the same roi (investigating homogeneity in the direction indicated), **d)** a Normalised-SPENT (N-SPENT) image created by dividing **c** by **b**.

Methods Thirty $(1.5cm)^3$ bone samples were cut from excised human femoral heads. The location was selected using two perpendicular radiographs to lie in a region at the top of femur above Ward's triangle. Furthermore, the samples had their marrow removed and (for the MR measurements) replaced by water. The bone density was calculated from the dry weight of the bone cubes over their volume. In addition, some cubes had their BMD measured using DEXA. A close correlation (r^2=0.96, p<0.0001) was found between these two measurements of density. Young's Modulus (YM) was measured in the direction of trabecular structure (*x*) using mechanical tests carried out with an actuated test machine (Lloyds M30K, UK). All MRI measurements were performed on a 7T, 12cm bore, Bruker Avance spectrometer using a home built saddle coil. R_2' was measured from values of T_2 and T_2*. T_2 was obtained using a standard 2DFT spin echo sequence at 3 different echo times (TE=20,50 and 80ms, TR=3000ms). Similarly, T_2* was measured using a standard 2DFT gradient echo sequence (TE=5,15 and 25ms, TR=2000ms). The following parameters were used for both measurements: FoV=3cm, matrix size=96x96, 16 adjacent 1mm slices. To obtain the relaxation constants a 'least squares' linear fit was applied to the log of signal intensity (over a region lying entirely within the bone) v TE. Additionally, SPENT images (like those in Fig.1) were obtained using a standard spin echo, multislice 2DFT sequence, by applying an extra gradient prior to the acquisition in each of the *x*,*y* and *z* directions (corresponding to read/phase/slice). Standard images without the extra gradient were also obtained. The imaging parameters used were FoV=3cm, 96x96 matrix, 1mm slice thickness, TE=20ms, TR=1161.9. The average N-SPENT signal was calculated over a volume lying entirely within the bone cube for each individual direction (*x*,*y*,*z*).

Results The correlations between the different parameters were obtained using the JMP statistics package (SAS institute, Cary, NC, USA), see Table 1. YM and BMD correlate strongly (r^2=0.582, p <0.0001). R_2' correlates with both BMD (r^2=0.653, p<0.0001) and a little more weakly with YM (r^2=0.484, p<0.0001). SPENT correlates very highly with BMD in *all* the individual directions *x*,*y* and *z*. The *z* direction was best (r^2=0. 866, p<0.0001). SPENT is correlated with YM, though not as highly as with BMD, and *not in all* directions. The *x* direction (also the direction of trabecular structure) was not as significantly correlated to YM. The combined MR parameters gave a better correlation to YM (r^2=0.712), a measure of the biomechanical strength of bone, than was provided by BMD alone (r^2=0.582).

	YM r^2	BMD r^2
R2'	0.484*	0.653*
N-SPENT x	0.260**	0.702*
N-SPENT y	0.508*	0.689*
N-SPENT z	0.523*	0.866*
N-SPENT y+z	0.570*	
N-SPENT x,y,z & R2'	0.712*	
YM		0.582*
* p<0.0001, **p<0.01		

TABLE 1 Results Summary

Discussion The average N-SPENT signal in a single direction produced a similar measure to BMD. This was achieved using a 1mm slice thickness and an in-plane resolution of 0.31mm. This is a significantly larger resolution than is generally required for accurate bone volume assessment directly from images. To obtain an N-SPENT image took 3mins 43s, this time could be halved with little penalty in SNR simply by extending the readout length as opposed to performing separate acquisitions to obtain the standard and SPENT images. This suggests similar N-SPENT measurements may be possible at clinical field strength. The differences observed between the N-SPENT directions v YM could contain additional information.

Conclusions The average N-SPENT signal correlates very highly to BMD (r^2=0. 866 for the *z* direction). In combination with R_2', N-SPENT provided a better correlation to YM (r^2=0.712) than the BMD alone (r^2=0.582). Further work is required to translate the promising results displayed here into a useful in-vivo method for assessing bone fracture risk at clinical field strengths.

References **1.** Genant, H. K. et al. 1996, *J.Bone Miner.Res.*, vol. 11, no. 6, pp. 707-730. **2.** Ford, J. C., Wehrli, F. W., & Chung, H. W. 1993, *Magn Reson.Med.*, vol. 30, no. 3, pp. 373-379. **3.** Engelke, K., Majumdar, S., & Genant, H. K. 1994, *Magn Reson.Med.*, vol. 31, no. 4, pp. 380-387. **4.** Carmichael, D. W., Ordidge, R. J., and Yiannakas, M. 2002, *Proc.10th Annual Meeting of the ISMRM*, abs. 296.

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