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Bone mineral and other bone components in vertebrae evaluated by QCT and MRI

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Abstract. To evaluate the usefulness of assessing bone components using magnetic resonance imaging (MRI), the contributions of bone components, including mineral, fat and collagen, to bone mineral density (BMD) and T1 relaxation time (T1) were studied using phantoms. Excised human vertebrae were also evaluated by quantitative computed tomography (QCT) and MRI. T1 was shortened with increasing quantities of fat and collagen. In water, T1 was significantly affected by bone density, while in oil, T1 became slightly longer as bone density increased. The presence of fat and collagen caused under- and overestimations of BMD, respectively. There was good correlation between T1 and BMD in osteoporotic vertebrae and the vertebrae with long T1 showed an increased content of hematopoietic marrow and/or abnormally increased bone mineral. It was concluded that the experimental data showed that MRI can contribute to the assessment of bone quality.

Key words: Bone mineral density – Quantitative computed tomography – Magnetic resonance – Marrow fat – Collagen

Quantitative CT (QCT) is an established method for assessing the mineral content of bone in the vertebral spongiosa. The contribution of vertebral fat content to the accuracy of single-energy QCT has been discussed for years, and many investigators have tried to estimate the fat content in the vertebral spongiosa using QCT [2, 8, 9, 15, 16]. Magnetic resonance imaging (MRI) has been used to differentiate the water and fat signals [1, 4, 14].

We observed the influence of three bone components, mineral, fat, and collagen, on the bone mineral density (BMD) and T1 relaxation time experimentally, using phantoms. We also examined the correlation between T1 relaxation time and BMD in 94 excised human vertebral specimens and correlated the results with the histological findings, to ascertain the usefulness of CT and MRI. No previous report has assessed the influence of fat and collagen on BMD and T1 relaxation time using both QCT and quantitative MRI in the same series.

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Materials and methods

Phantoms

Phantoms containing composites of $CaCO_3$ to simulate mineral, cottonseed oil to simulate marrow fat, and agar to simulate collagen were prepared. One series contained various concentrations of $CaCO_3$ (50, 100, 150 mg/ml) and cottonseed oil (0, 10, 20, 30 mg/ml) with a constant 50 mg/ml agar concentration in water solutions. Another series contained various concentrations of agar (50, 100, 150, 200 mg/ml) and constant concentrations of $CaCO_3$ (100 mg/ml) and of cottonseed oil (10 mg/ml).

Vertebrae

We examined 94 lumbar vertebral (L1–4) specimens excised from 65 male and 29 female cadavers ranging in age from 11 to 85 years. No patients with primary hematopoietic disorders, such as leukemia, and aplastic anemia, were included. The excised vertebral bodies usually included the pedicles but not the posterior arches and transverse processes. All bones were fixed in 10% formalin solution for 2 or 3 days before the MRI and CT examinations. All the specimens were also examined histologically.

Magnetic resonance imaging

MRI was accomplished using a 1.5-T Signa system (GE Medical Systems). The vertebral specimens were scanned in a head coil using spin-echo techniques, and T1 data were obtained from two images with repetition times (TR) of 300 and 800 ms and an echo time (TE) of 20 ms (TR/TE = 300, 800/20). The T1 relaxation time was derived from a two-parameter-fit algorithm. The vertebrae were scanned using 3 mm thickness at midplane in sagittal and axial sections. A 256 × 192 data acquisition matrix was employed.

Quantitative CT

A Siemens Somatom DR-H was used for the CT examinations. This scanner is equipped with a rapid kVp switching system [13], which changes the peak voltage between 125 and 85 kVp from pulse to pulse, thereby ensuring the collection of all necessary data during one scan.

The following four images can be reconstructed from the raw data: the high-energy image (KV-HI; 125 kVp single-energy data), the low-energy image (KV-LO; 85 kVp single-energy data), the water-density image (MAT-LO) and the calcium density image (MAT-HI). A region of interest (ROI) was placed in the KV-HI and MAT-HI images to calculate the calcium content, expressed in milligrams calcium hydroxyapatite equivalent per cubic centimeter. The vertebrae were placed in a water bath and were scanned using an 8-mm-thick slice at midplane.

Results

Experimental data

Influence of fat and mineral on the T1 relaxation time and BMD. The measured *T1 relaxation time* plotted against the concentration of oil in different concentrations of $CaCO_3$ is shown in Fig. 1. In phantoms without oil, the T1 relaxation time lengthened as the $CaCO_3$ increased in concentration. In phantoms with oil, the T1 relaxation time was not significantly affected by the increase in $CaCO_3$ concentration [3]. This result (Fig. 1) is elaborated on in Fig. 2 for various mixtures of oil in varying concentrations between 100 and 300 mg/ml. The T1 relaxation time correlated closely with the concentrations of oil and became longer as the $CaCO_3$ concentrations increased.

Figure 3 shows the influence of fat on *bone mineral density* as assessed by QCT. There were close correlations between BMD and the concentrations of mineral. BMD estimated with single-energy QCT was more strongly influenced by fat than was BMD as estimated using dual-energy QCT.

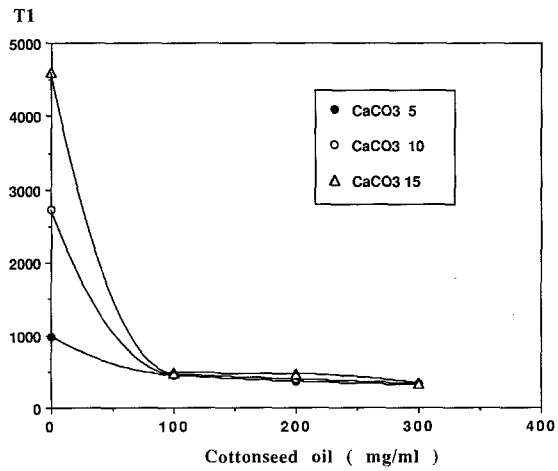


Fig. 1. T1 relaxation times with various concentrations of fat and mineral. In phantoms without oil, the T1 relaxation time becomes longer as the $CaCO_3$ concentration is increased. In phantoms with oil, the T1 relaxation time is not significantly affected by increased $CaCO_3$ concentrations

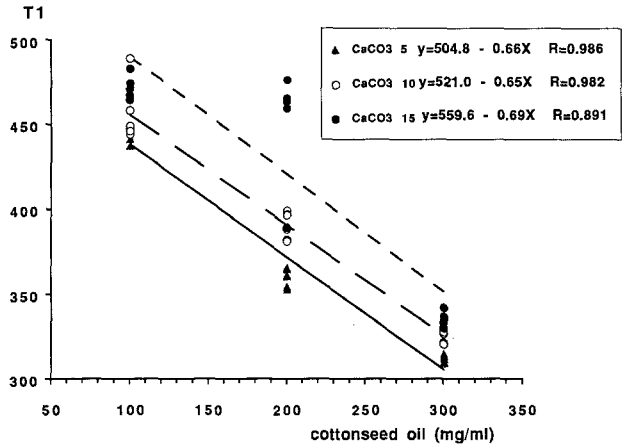


Fig. 2. T1 relaxation times with various concentrations of fat and mineral

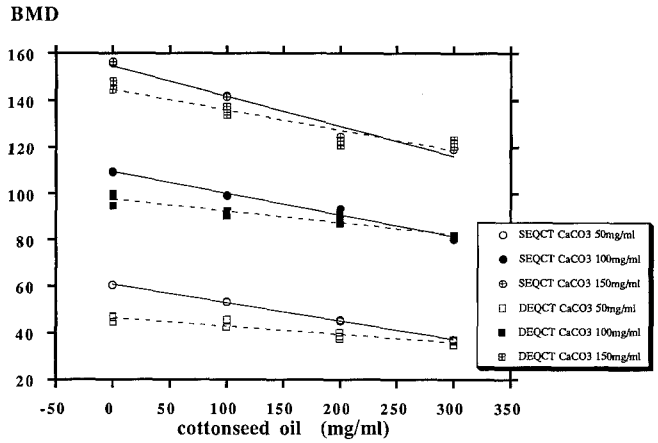


Fig. 3. Influence of fat on bone mineral density (BMD). BMD estimated with single-energy quantitative computed tomography (SEQCT) and with dual-energy quantitative computed tomography (DEQCT)

Influence of agar on T1 relaxation time and BMD. The influence of agar on *T1 relaxation times* was evaluated using phantoms containing various concentrations of agar but a constant concentration of 100 mg/ml $CaCO_3$ and 10 mg/ml cottonseed oil. T1 relaxation times decreased as agar concentrations increased (Fig. 4).

Figure 5 shows the influence of agar on *bone mineral density*. BMD estimated using single-energy QCT was strongly influenced by the concentration of agar, while BMD estimated using dual-energy QCT was not significantly influenced by agar concentration.

Evaluation of the cadaveric vertebrae

Relationship between the T1 relaxation time and BMD. Fifty-four vertebral specimens from patients without either metabolic disorders or bone marrow dysfunction showed T1 relaxation times between 220 and 400 ms. There was good correlation ($r=0.59$, $P<0.0001$) between T1 relaxation time and BMD as estimated by sin-

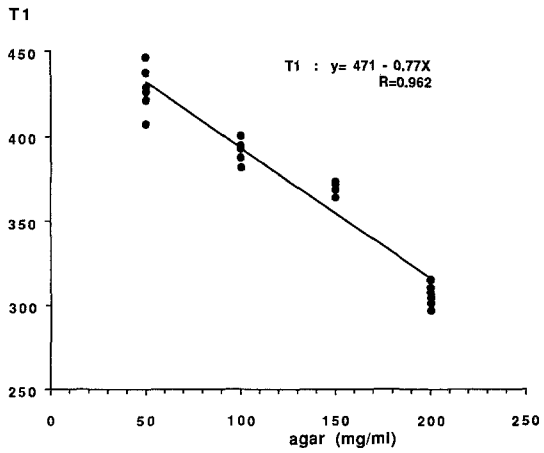


Fig. 4. T1 relaxation times in various concentrations of agar

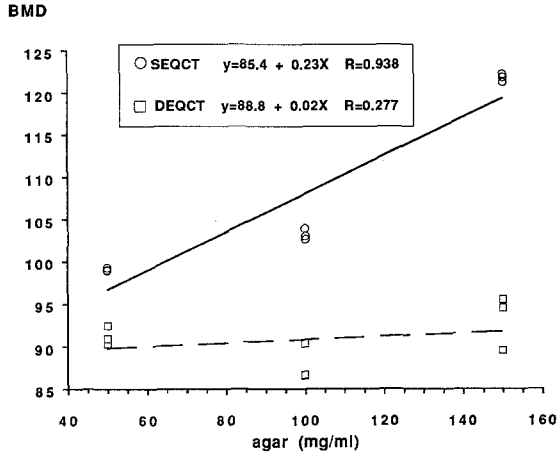
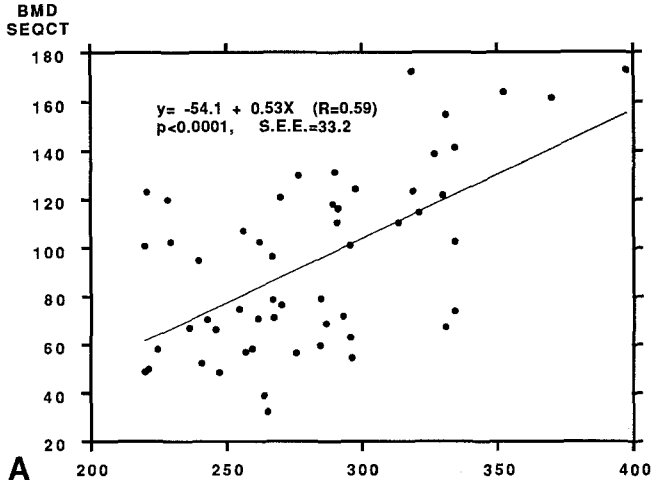


Fig. 5. BMD in various concentrations of agar



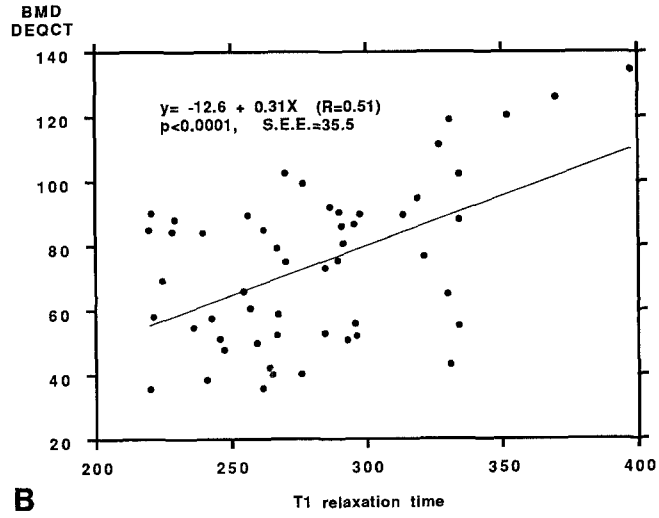


Fig. 6A, B. Good correlation exists between T1 relaxation times and BMD. **A** Correlation with BMD as estimated with SEQCT; **B** correlation with BMD as estimated by DEQCT

gle-energy QCT (Fig. 6A). There was also good correlation ($r=0.51$, $P<0.0001$) between T1 relaxation time and BMD as estimated by dual-energy QCT (Fig. 6B).

Vertebrae with long T1 relaxation times. Twenty-two vertebrae with increased cellularity histologically showed T1 relaxation times greater than 400 ms. These were from 13 patients who had had liver cirrhosis, seven who had been on hemodialysis, and two who had had diabetes mellitus. Four of the seven patients who had been on hemodialysis had manifest osteosclerosis.

Case 1 was the cadaver of a 57-year-old man with liver cirrhosis. CT revealed no abnormality and a T1-weighted image of the vertebra showed a low signal intensity (Fig. 7). Histologically, the cellularity of the vertebra was markedly increased.

Vertebrae from the four patients who had been on hemodialysis and who had marked osteosclerosis on CT also had relatively long T1 relaxation times, greater than 400 ms. In case 2, a 32-year-old woman, a reconstructed sagittal CT image showed osteosclerosis near the endplate, while a T1-weighted sagittal image showed low signal intensity in the same region (Fig. 8A). Histological study of this sclerotic region revealed numerous immature thin trabeculae and moderately increased cellularity, and some peritrabecular fibrosis (Fig. 8B). The focal, markedly low signal intensity was attributed to a combination of increased bone mineral and possible marrow fibrosis.

Vertebrae with short T1 relaxation times. Eighteen vertebrae exhibited T1 relaxation times less than 220 ms. All these specimens showed thin trabeculae and increased fat marrow histologically.

Discussion

It is well known that the presence of fat causes underestimation and the presence of collagen overestimation of

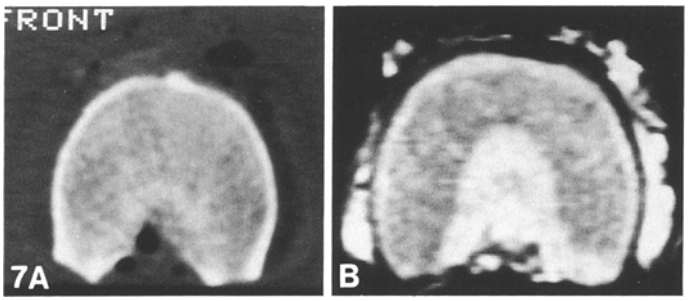
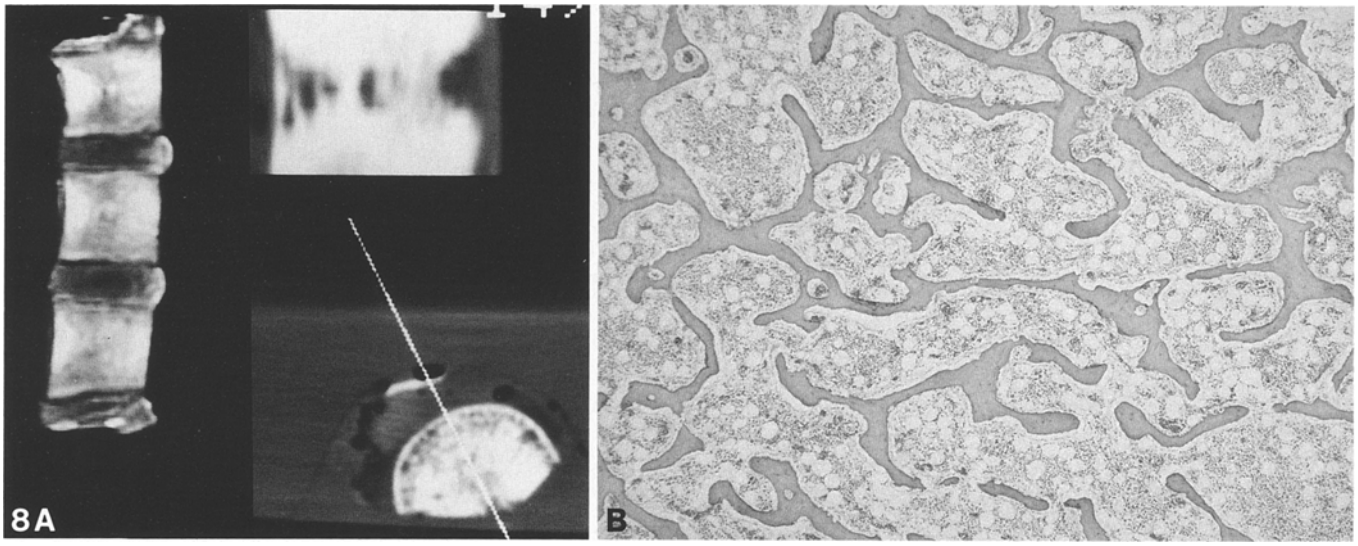


Fig. 7A, B. A 57-year-old man with hepatic cirrhosis (case 1). CT shows no abnormality (**A**) and the T1-weighted image (**B**) shows a low signal intensity throughout most of the vertebra, not including the subcortical region and the region around the nutrient foramen

Fig. 8A, B. A 32-year-old woman with chronic renal failure on maintenance hemodialysis (case 2). **A** A reconstructed sagittal CT image shows osteosclerotic changes near the endplate, while a T1-weighted sagittal image shows low signal intensity in the same region. **B** This osteosclerotic region shows numerous immature thin trabeculae



BMD. Some investigators have reported the influence of vertebral fat content on QCT [2, 8, 9, 15, 16]. The fact that the dual-energy QCT estimate is more accurate than the single-energy QCT estimate has been reported by many investigators [7, 10]. These results were confirmed in our experiments in which the influence of oil and agar on T1 relaxation times was observed in the same setting.

The results of our experiments using quantitative MRI showed that T1 relaxation time was significantly affected by bone density in water, while in oil, T1 relaxation times became only slightly longer as bone density increased. These data suggested a possibility that the bone appears low in signal intensity in some metabolic bone diseases with markedly increased bone mineral or with hypercellular marrow, and that the bone with increased fat or collagen appears relatively high in signal intensity. With regard to quantitative MRI of bone mineral, the effects of bone on proton NMR relaxation times of surrounding liquids have been reported by Davis et al [3]. They measured T1 relaxation times and T2* relaxation times by MR spectroscopy, and found that the mineral exerted no influence on T1 relaxation time in fat solution but that it had a significant influence on T2* relaxation time both in water and in oil. We studied the effect of mineral on T1 relaxation times using gelatinous phantoms, which are thought to bear a close resemblance to real bone. The results of our experiments were consistent with theirs in many respects. The discrepancy between our results and theirs can be attributed to differences in methods; they used MR spectroscopy and liquid phantoms, whereas we used MRI and gelatinous phantoms.

The T1 relaxation time of bone marrow is a combination of the short T1 relaxation time of marrow fat and the long T1 relaxation time of the water-laden normal or pathologic hematopoietic tissue. The replacement of hematopoietic tissue by fatty marrow may explain the shortening of T1 relaxation times; there have been several reports concerning the relationship between T1 relaxation time and cellularity of bone marrow [5, 12, 14, 18, 19]. In our study, the vertebrae with long T1 relaxation times revealed hypercellularity and/or markedly increased bone mineral, while the vertebrae with short T1 relaxation times revealed hypocellularity and were osteoporotic histologically.

The vertebral spongiosa consists of bone mineral and bone marrow (hematopoietic and fatty marrow). Our data show that bone loss is accompanied by an increase in fat content. The interaction between the bone metabolism and bone marrow has not been elucidated, but it is presumed that the functional cells in the bone marrow are involved in the process of bone remodeling. It is interesting that an increase in the quantities of fat is thought to precede osteopenia in certain cases of osteoporosis [15]. Further investigation is necessary, therefore, to clarify which change occurs earlier – the increase in fat content or the loss of mineral content – and also to clarify in which area osteoporosis occurs earliest.

Collagen and mineral are usually present in relatively

constant proportions in patients without specific metabolic bone disorders. In osteomalacia, renal osteodystrophy, and Gaucher disease [10, 17], the content of mineral and fat is an important factor influencing the BMD and T1 relaxation time. Measurements of T1 relaxation times may be useful for evaluating changes in bone quality, because patients on maintenance hemodialysis exhibit various types of bone change [11], such as increased collagen or increased fat or markedly increased mineralization.

In summary:

1. Experimentally, an increase in fat and collagen induces a shortening of the T1 relaxation time. T1 relaxation time in oil is not significantly affected by the quantity of mineral. The presence of fat causes underestimations of BMD, while the presence of collagen causes overestimations of BMD. Dual-energy QCT is more accurate than is either of the single-energy QCT estimates.
2. There is good correlation between the T1 relaxation time and BMD. Some vertebrae have long T1 relaxation times, probably due to increased hematopoietic marrow and markedly increased bone mineral. The bones with short T1 relaxation times probably contain increased amounts of fat; they revealed osteoporotic changes histologically.

This experimental and cadaver study shows that MRI can provide useful information about changes in bone composition.

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