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Original contribution

# A fast method for the quantification of fat fraction and relaxation times: Comparison of five sites of bone marrow

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ABSTRACT

*Purpose:* Bone marrow is found either as red bone marrow, which mainly contains haematopoietic cells, or yellow bone marrow, which mainly contains adipocytes. In adults, red bone marrow is principally located in the axial skeleton. A recent study has introduced a method to simultaneously estimate the fat fraction (FF), the T1 and T2* relaxation times of water (T1w, T2*w) and fat (T1f and T2*f) in the vertebral bone marrow. The aim of the current study was to measure FF, T1w, T1f, T2*w and T2*f in five sites of bone marrow, and to assess the presence of regional variations.

*Methods:* MRI experiments were performed at 1.5 T on five healthy volunteers (31.6 ± 15.6 years) using a prototype chemical-shift-encoded 3D multi-gradient-echo sequence (VIBE) acquired with two flip angles. Acquisitions were performed in the shoulders, lumbar spine and pelvis, with acquisition times of <25 seconds per sequence. Signal intensities of magnitude images of the individual echoes were used to fit the signal and compute FF, T1w, T1f, T2*w and T2*f in the humerus, sternum, vertebra, ilium and femur.

*Results:* Regional variations of fat fraction and relaxation times were observed in these sites, with higher fat fraction and longer T1w in the epiphyses of long bones. A high correlation between FF and T1w was measured in these bones (R = 0.84 in the humerus and R = 0.84 in the femur). In most sites, there was a significant difference between water and fat relaxation times, attesting the relevance of measuring these parameters separately.

*Conclusion:* The method proposed in the current study allowed for measurements of FF, T1w, T1f, T2*w and T2*f in five sites of bone marrow. Regional variations of these parameters were observed and a strong negative correlation between the T1 of water and the fat fraction in bones with high fat fractions was found.



## 1. Introduction

Bone marrow is a tissue located in the central cavities of the long bones and in the cavities of the trabecular bones. This tissue is principally composed of haematopoietic cells and adipocytes, and it is responsible for the production of erythrocytes, platelets and leucocytes [1,2]. Bone marrow is found either as red bone marrow, which mainly contains haematopoietic cells or yellow bone marrow, which mainly contains adipocytes. Red bone marrow is predominant during childhood; it is then gradually replaced by yellow bone marrow. In adults, red bone marrow principally remains in the axial skeleton, namely the skull, ribs, sternum, scapulae and vertebrae, as well as in parts of the peripheral skeleton: in the ilium and the epiphyses of the humerus and the femur [1].

Quantitative chemical-shift-encoded MRI has been widely used to study bone marrow composition. A recent study [3] has shown the presence of regional variations in the composition of bone marrow with higher fat fraction and lower diffusion coefficient in the peripheral skeleton compared to the axial skeleton. Quantitative MRI can also be used as a non-invasive tool to diagnose bone marrow pathologies. The fat fraction and the T1 and T2* relaxation times have been shown to be relevant biomarkers of the pathophysiological status of this tissue. For

*Abbreviations:* VIBE, volumetric interpolated breath-hold examination; CAIPIRINHA, controlled aliasing in parallel imaging results in higher acceleration; CV, coefficient of variation.

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instance, the vertebral fat fraction decreased in patients suffering from bone marrow malignancies [4] and it increased after treatment in patients who received chemotherapy [5]; the vertebral fat fraction was found to be higher in osteoporotic patients than in healthy volunteers [6,7]. The quantification of T1 and T2* is also of interest in several pathologies of the bone marrow. For instance, in a number of studies it was found that osteoporotic patients had a longer vertebral common-T2* [8–11] and a shorter vertebral common-T1 [11] than healthy volunteers; and that the T1 of water was higher in vertebrae with malignancies than in healthy vertebrae [12,13].

Recently, a method based on fast chemical-shift imaging was proposed to measure the fat fraction and the separate T1 and T2* of water and fat (FF, T1w, T1f, T2*w and T2*f) in the bone marrow with two acquisitions [14]. In this method, the MR signal is modelled as the weighted sum of water and fat signals and the signal intensity sampled in the tissue is fitted to the signal equation to quantify FF, T1w, T1f, T2*w and T2*f.

As previous studies have shown regional variations of bone marrow fat fractions, and given the importance of T1 and T2* as biomarkers, the aim of the current study was to measure FF, T1w, T1f, T2*w and T2*f in multiple sites of bone marrow in healthy volunteers and to assess the presence of regional variations for these parameters.

## 2. Materials and methods

### 2.1. Magnetic resonance imaging (MRI)

All experiments were conducted according to the procedures approved by the local Institutional Review Board. A group of 5 healthy volunteers (age range 20–58 years, mean age 31.6 ± 15.6 years, 3 women and 2 men) were enrolled in the current study.

Experiments were performed on a 1.5 T MR system (MAGNETOM Aera, Siemens Healthcare, Erlangen, Germany) in the shoulders (coronal acquisition), the lumbar spine (sagittal acquisition) and the pelvis (coronal acquisition) using the regular spine and body receiver coils. The imaging protocol consisted of a prototype chemical-shift-encoded 3D multi-gradient-echo sequence (volumetric interpolated breath-hold examination, VIBE [15]) acquired with two flip angles in consecutive runs.

The scanning parameters used in the VIBE sequence were optimised in a previous study [14] and were as follows: repetition time TR = 8.21 ms, four echoes acquired in a single TR (TE1/TE2/TE3/TE4 = 1.18/2.34/4.4/6.8 ms), bandwidth 1220 Hz/pixel, parallel imaging using CAIPIRINHA (controlled aliasing in volumetric parallel imaging results in higher acceleration) with an acceleration factor R = 2 in the phase encoding direction and R = 2 in the slice encoding direction resulting in a total acceleration factor of R = 4, 60 slices of 4 mm thickness; the sequence was performed with flip angles of 5° and 15°. Sagittal acquisitions in the lumbar spine were performed with: matrix 192 × 256, field of view 315 × 420 $mm^2$ and partial Fourier 6/8, resulting in an acquisition time of 16 s per sequence. Coronal acquisitions in the shoulder and the pelvis were performed with: matrix 256 × 256, field of view 420 × 420 $mm^2$ and no partial Fourier, resulting in an acquisition time of 23 s per sequence. Lumbar spine and shoulder acquisitions were performed with breath-holds.

### 2.2. Data analysis

Regions of interest (ROIs) were drawn with ImageJ (NIH, Bethesda, MD, http://imagej.nih.gov/ij/) by a radiologist (J.L., 15 years of experience). Twelve ROIs were drawn for each volunteer: one in each the upper epiphyses of the right and left humerus, one in the sternum, one in each of the five lumbar vertebrae L1 to L5 (in the anterior part of the vertebral body to avoid vascular artefacts), one in each lateral side of the ilium and one in each the upper epiphyses of the right and left femur. The ROIs were placed on the images acquired at TE2 with the flip angle of 5°, and were copied to the other images. Each ROI had an area of 52 voxels and was positioned in the bone marrow with care to avoid voxels with cortical bone and partial volume effects. For each of the twelve ROIs, ROI-averaged signal intensities and standard deviations were measured in the magnitude images of the four individual echoes acquired with the two flip angles.

Signal analysis was performed according to the method described in [14]. In this method, the signal intensity of a spoiled gradient echo sequence is modelled as the weighted sum of water and fat signals with separate T1 and T2* relaxation times for water and fat. In contrast to the method described in [14], the fat signal model used here consisted of the four main peaks of the vertebral bone marrow MR spectrum (0.9, 1.3, 2–2.2 and 5.3 ppm with relative peak areas of 9%, 63%, 15% and 7%, respectively) recently characterised by Karampinos et al. [16]. The signal intensity is therefore a function of the sequence parameters (TR, TE and flip angle) and the tissue parameters (S0, FF, T1w, T1f, T2*w and T2*f). In each of the twelve ROIs, the averaged signal measured on the magnitude images acquired at the four echo times and with the two flip angles was fitted to the signal equation, and FF, T1w, T1f, T2*w and T2*f were determined. The ambiguity between water and fat signals arising from the use of magnitude data was resolved by assuming that T1w was higher than T1f [17,18].The fitting was performed with in-house-built scripts written in Mathematica (Wolfram Research, Champaign, IL, USA).

The parameters computed in the right and left humerus were averaged, and so were the parameters computed in the five lumbar vertebrae (L1 to L5), in the right and left ilium and in the right and left femur.

### 2.3. Statistical analysis

The coefficient of variation (CV) was computed for each parameter (FF, T1w, T1f, T2*w and T2*f) in the five sites of bone marrow studied. The differences between the cohort-mean water and fat relaxation times were assessed with *t*-tests for T1 relaxation times (T1w versus T1f) and for T2* relaxation times (T2*w versus T2*f) on each site. The presence of a correlation between the fat fraction and the T1 of water was assessed by computing the Pearson correlation coefficient for each site. The threshold $p < 0.01$ was chosen for statistical significance. Statistical analyses were performed with MATLAB (MathWorks, Natick, MA, USA).

## 3. Results

A set of MR images acquired on a volunteer at the first echo time (TE = 1.18 ms) is displayed in Fig. 1; it represents the five sites of bone marrow studied. Data fitting and parameter quantification were successful for all sites despite a wide range of tissue parameters encountered; the example of a signal fit performed in one vertebra and in the humerus is shown in Fig. 2. The averaged values for fat fraction, T1 and T2* relaxation times of water and fat computed in the bone marrow of the humerus, sternum, vertebra, ilium and femur are given in Table 1. Several results from this table can be outlined. First, the fat fractions were higher in the epiphyses of long bones (humerus and femur) than in the sternum, vertebra and ilium; for instance the mean fat fraction was 74 ± 11% in the humerus versus 42 ± 15% in the vertebra. In addition, the inter-individual variability of the fat fraction depended on the site of bone marrow considered: the coefficient of variation ranged between 8% in the ilium and 32% in the sternum. Second, the estimates of T1w varied from 621 ± 110 ms in the vertebra to 815 ± 333 ms in the humerus with a large inter-individual variability (CVs between 18% in the vertebra and 54% in the femur); the estimates of T1f varied from 224 ± 92 ms in the sternum to 330 ± 20 ms in the vertebra with a smaller inter-individual variability (lower CVs). Third, the estimates of T2*w varied from 4.7 ± 3.5 ms in the humerus to 12.7 ± 5.4 ms in the vertebra. The estimates of T2f varied from 15.9 ± 3.9 ms in the vertebra to 30.0 ± 2.4 ms in the humerus. The coefficients of determination of