Image Registration in the T_2* Measurements of the Calcaneus Used to Predict Osteoporotic Fractures

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Abstract *The conventional criterion for fracture risk assessment is the bone mineral density (BMD) measured by X-ray absorptiometry. Even if there is a strong association between bone strength and BMD, nowadays it is well accepted that this is not a sufficiently reliable predictor of fracture risk in osteoporotic patients. Therefore, there is a growing need for a better predictor of bone strength. Several studies have confirmed that the T_2* relaxation time estimates based on magnetic resonance imaging (MRI) show a strong correlation with bone strength. In this paper, an image-processing tool for the reduction of motion artifacts in the T_2* measurements of the bone marrow of the calcaneus is described.*

Keywords: *osteoporosis, magnetic resonance imaging, image registration*

1. Introduction

The importance of noninvasive methods for fracture risk assessment is emphasized by the dramatic increase of osteoporosis incidence in elderly population. Osteoporosis is a metabolic bone disease leading to bone mass reduction and deterioration of the trabecular bone architecture with a consequent increase in bone fragility and susceptibility to fracture. There are two different types of bone present in the skeleton: cortical bone and trabecular bone. The dense cortical (compact) bone creates the rigid shell of bones while the trabecular (spongy) bone is found at the end of long bones, in vertebral bodies and flat bones. The trabecular bone constitutes a complicated three-dimensional structure of interconnected trabeculae (plate- and rod-like elements of the structure having a thickness approximately 0.1-0.2 mm), which is optimized for strength and lightness. The strength of this structure is determined not only by the amount of the bone mineral (which is assessed by the BMD parameter) but morphometric and topologic properties of the structure affect the bone mechanical properties to a significant degree as well. In fact, only about 60% of the bone strength variation can be explained by variations in bone mineral density. A clinical consequence of this is a large proportion of patients with normal BMD scores suffering osteoporotic fractures. Therefore, there is a need for a better bone strength predictor, which takes into account the bone structure arrangement as well. Several studies [2, 3] have demonstrated that the effective transverse relaxation time T_2* determined by magnetic resonance imaging (MRI) is significantly increased in the osteoporotic bone thus showing the potential of this technique in fracture risk assessment. A recent study at 3.0 Tesla [4] has confirmed that the calcaneus is a suitable surrogate site to assess vertebral osteoporosis and that T_2* is sensitive to alterations in bone quality not captured by density.

The magnetic resonance signal of the mineralized bone decays too fast to be measured using common MRI protocols. However, the trabecular bone cavities are occupied by bone marrow, having relatively long relaxation times T_1 and T_2. The bone marrow consists mainly of water and fatty acid triglycerides. A small difference (about 2.7 ppm) in magnetic susceptibility between the mineralized bone (containing higher atomic number elements, i.e. calcium and phosphorus) and the bone marrow causes a distortion of the polarizing magnetic field. This field inhomogeneity in turn leads to additional dephasing of the spin isochromats and thus modulates the effective transverse relaxation time T_2*. Using numerical simulations [5, 6] it can be shown that the induced field gradients depend on the morphometric properties of the trabecular bone structure (e.g. trabecular thickness and trabecular spacing). This field inhomogeneity is unfavorable at high resolution MRI of trabecular bone (where the resolution is comparable to the trabecular thickness) because is responsible for the apparent thickening of trabeculae in images acquired using gradient echo techniques. On the other hand, measurements of T_2* in low resolution images of the trabecular bone yield a potentially valuable indirect descriptor of bone properties.

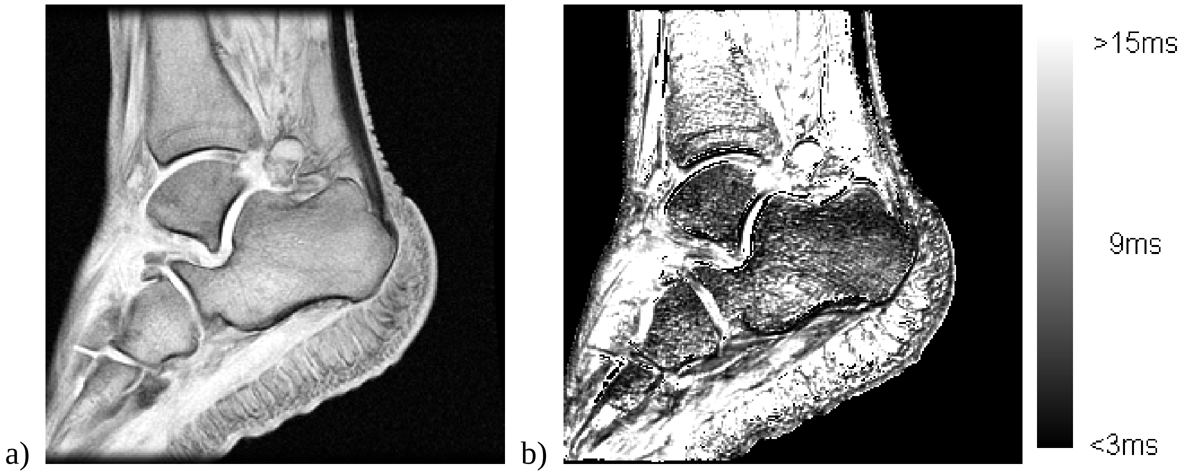

Fig. 1. a) Fast gradient echo image of the heel region acquired with echo time 3.1ms.
b) Corresponding map of T_2* values. The spatial density of trabecular bone structure in calcaneus is spatially variant, therefore changes in T_2* can be observed in different parts of the calcaneus.

2. Subject and Methods

Both calcanei of sixteen female subjects with age 62.3±11 (mean±std.) years and T-scores –3.3±1.8 (measured in the lumbar spine region using Quantitative Computed Tomography, QCT) were studied using a 3T GE Genesis-Signa whole body MRI scanner. Out of these subjects, six women suffered osteoporotic fractures of the spine documented by X-ray radiography. A two-dimensional fast gradient-echo sequence with variable echo time (TE), repetition time (TR) of 200 ms, flip angle of 30° and one acquisition was applied in the sagittal plane. A matrix of 256 × 256 was used with a field of view of 150 × 150 cm to yield a pixel size of 586 × 586 μm^2. The slice thickness was 5 mm. T_2* values of each calcaneus were calculated from a series of twenty-two images with echo times (TEs) ranging from 3.1 ms to 14 ms.

The free induction signal decay is approximately exponential and characterized by T_2* relaxation time constant. This value is estimated by nonlinear fitting of the exponential curve to image pixel intensities in consecutive images. A problem linked to the selected acquisition scheme is the region of interest motion between consecutive images. Due to the heterogeneity of the calcaneus, a shift by a few pixels may cause abrupt intensity changes in the fitted data and thus affect the precision of T_2* estimates. In order to suppress the influence of this motion, an image registration scheme was introduced to realign the acquired images.

Point-based and boundary-based (or surface in 3D imaging) image registration methods require manual or automatic feature extraction (e.g. anatomical landmarks selection or surface segmentation). These methods are sensitive to accurate selection of these features [7]. Therefore, the pixel-based (or voxel in 3D imaging) methods, which optimize a functional by measuring the similarity of all geometrically corresponding pixel pairs for some feature (e.g. intensity), seem to be the most suitable for this application. Several pixel-based methods have been proposed that optimize some global measure of the absolute difference between corresponding pixel intensities in a region of interest. In this case, it is assumed, however, that the intensities of the images are linearly correlated. The contrast ratio between various tissues in the sequence of the images acquired with different echo time values is changes due to different decay rates in these tissues. Therefore, the maximization of mutual information is the method of choice in this application.

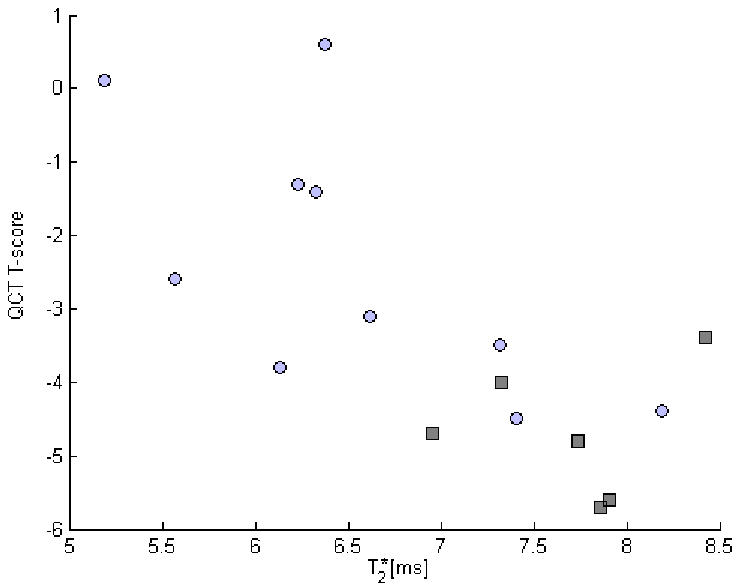

Fig. 2. QCT T-score (proportional to BMD) and corresponding T_2* values. The patients who suffered osteoporotic fractures are denoted by squares, those without fractures are denoted by circles.

The mutual information $I(A,B)$ of two arbitrary images A and B is defined by the formula [7]

$$I(A,B)=\sum_{a,b} p_{AB}(a,b)\log_2 \frac{p_{AB}(a,b)}{p_A(a)\cdot p_B(b)} \tag{1}$$

These images are related by a geometrical transformation T_α, i.e. pixel p in A having intensity a corresponds to $T_\alpha(p)$ in B with intensity b. $p_{AB}(a, b)$, $p_A(a)$, $p_B(b)$ are the joint and marginal distributions of the pair (a, b) and of a and b, respectively. It is postulated that images A and B are geometrically aligned by the transformation T_{α^*} for which $I(A,B)$ is maximal, i.e.

$$\alpha^* = \arg\max_\alpha I(A,B) \tag{2}$$

Distributions estimates are obtained by the joint image intensity histogram normalization. The partial volume (PV) distribution [7] was adopted in the histogram computation, where the contribution of the image intensity $b=B(p)$ to the joint histogram is distributed over the intensity values of all nearest neighbors of $T_\alpha(p)$ using the same weights as for trilinear interpolation. Another important implementation issue is to perform a small resampling of one of the images, such that the pixel grids of the reference and floating (transformed image) are no longer identical. If this step is omitted, the PV interpolation yields local maxima for such transformations $T_\alpha(p)$, where the pixel positions coincide exactly (e.g. shift by pixel size multiples). This may affect the optimization robustness.

A simple nonrigid (warping) image transformation was designed to take into account the region of interest motion in the acquired images. Two main axes, having intersection approximately in the subtalar region of the calcaneus, are defined. The first one is parallel to the fibula, and the second one heads from the subtalar region towards the foot point. These two axes are allowed to rotate around their intersection while the image is warped. Image warping introduces deformations into the bone regions of the images as well. Such deformations, however, proved to be non significant for limited foot motions. Typically, the first axe is fixed, and the direction angle of the second axe is one of the transformation parameters. Two other parameters define the translation of the axes intersection. Steepest descent method was adopted to perform the transformation parameters optimization.

3. Conclusion

In this paper, a simple image-processing tool designed for the realignment of calcaneus MR images was described. The method proved to be fully automated and robust. It is supposed that image registration may improve the precision of T_2* estimates.

In this preliminary study a significant correlation ($R = -0.72$, $p < 0.005$) was found between QCT T-score values and T_2* data. It may be noted, in the fig. 2, that patients, who suffered a fracture are well clustered in the right bottom part of the graph. A greater number of osteoporotic subjects is currently under investigation. This MRI study should allow us to estimate the fracture risk prediction capabilities of the method. It will be necessary, however, to define the region of the calcaneus, which is the most suitable for fracture risk prediction and to develop a method facilitating accurate selection of this region of interest.

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