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On the Significance of Motion Degradation in High-Resolution 3D μ MRI of Trabecular Bone

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Abstract

Rationale and Objectives—Subtle subject movement during high-resolution 3D μ MR imaging of trabecular bone (TB) causes blurring, thereby rendering the data unreliable for quantitative analysis. In this work, the effects of translational and rotational motion displacements have been evaluated qualitatively and quantitatively.

Materials and Methods—In Experiment I, motion was induced by applying various simulated and previously observed *in vivo* trajectories as phase shifts to k-space or rotation angles to k-space segments of a virtually motion-free data set. In Experiment II, images that were visually free of motion artifacts from two groups of 10 healthy individuals, differing in age, were selected for probing the effects of motion on TB parameters. In both experiments, images were rated for motion severity and the scores were compared to a focus criterion, the normalized gradient squared (NGS).

Results—Strong correlations were observed between the motion quality scores and the corresponding NGS values ($R^2 = 0.52$ – 0.64 ; $p < 0.01$). The results from Experiment I demonstrated consistently lower image quality and alterations in structural parameters of 9–45% with increased amplitude of displacements. In Experiment II, the significant differences in structural parameter group means of the motion-free images were lost upon motion degradation. Autofocusing, a post-processing correction method, partially recovered the sharpness of the original motion-free images in 13/20 subjects.

Conclusion—Quantitative TB structural measures are highly sensitive to subtle motion-induced degradation which adversely affects precision and statistical power. The results underscore the influence of subject movement in high-resolution 3D μ MRI and its correction for TB structure analysis.

Keywords

3D μ MRI; Trabecular bone; Translational and Rotational motion; Virtual bone biopsy

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INTRODUCTION

Osteoporosis, a disorder of bone remodeling imbalance, is usually assessed on the basis of bone mineral density (BMD), a surrogate marker of bone strength, typically obtained by dual energy x-ray absorptiometry (1, 2). Despite its ubiquity in the assessment of bone integrity, BMD does not yield insights into bone quality, a somewhat elusive physical property based on the integrity of trabecular and cortical bone microstructure (1). Three-dimensional μ MRI acquisition and processing techniques enable direct visualization and quantification of trabecular bone (TB) architecture in response to aging or drug treatment of osteoporosis (3, 4). One such suite of 3D image acquisition and processing methods, the virtual bone biopsy (VBB) (5), has demonstrated reproducible and accurate quantification of TB architectural measures at peripheral locations. A number of investigators have performed structural analysis in patients at the distal radius (6, 7), tibia (8) and calcaneus (9) *in vivo*. The structural changes at these peripheral sites are strongly associated with similar changes occurring elsewhere in the skeleton (10, 11), can be predictive of fracture status (12, 13) and serve as useful markers for monitoring disease status.

The ability to accurately retrieve the 3D architectural features of TB depends on several parameters that include signal-to-noise ratio (SNR), voxel size, accurate co-registration of baseline and follow-up images in longitudinal studies and motion during data acquisition (3). Motion degradation in MRI can be attributed to macroscopic motion that encompasses both 1) physiological motion, from respiration, cardiac pulsations or peristalsis and 2) involuntary subject movement during the scan. While the former probably have minor effects, the latter are the key source of loss of image sharpness in μ MRI of the distal extremities (14). The problem is exacerbated by the high resolution necessary for accurate retrieval of the 3D architecture of trabecular networks, which demand relatively long scan times (~10–15 minutes), even though parallel imaging has the potential to substantially shorten acquisition times (15). Given image pixel sizes on the order of 100 μ m, even sub-millimeter displacements arising from involuntary motion can be detrimental for TB micro-images and they are difficult to prevent despite employing tight immobilization (16).

Rigid body motion-derived errors in the VBB-based structural and topological parameters can also mask treatment effects in longitudinal studies of bone disease (14). Song *et al.* showed that the apparent bone volume fraction (BVf; bone volume/total volume) decreases by 8–12% due to translational shifts in 3D Fast Large Angle Spin Echo (FLASE) acquisitions (17). Further, Gomberg *et al.* reported relative errors of up to 80% in TB structural and topological parameters in simulations of translational and rotational motion (16). More recently, Lin *et al.* showed that a 2° rotation reduces the normalized gradient squared (NGS), a metric for image sharpness, by up to 4% with a concomitant relative error in some of the topological parameters of up to 20% (14). Translational motion is expressed in k-space as a linear phase shift along the direction of motion, whereas a rotation in image space generates a commensurate rotation in k-space, leading to more complex artifacts from k-space inconsistencies (18). The sensitivity of high-resolution 3D acquisition schemes to small displacements, whether translational or rotational, puts into question the utility of serial clinical data unless appropriate corrections to the data can be made. Alternatively, motion-degraded images may have to be discarded on the basis of an image quality rating scheme (11, 19) or some objective quantitative metric of image sharpness (14).

Several correction methods exist to address rigid body motion in 3D μ MRI techniques for TB microstructural characterization. The utility of these methods relies on the detection of the pose changes which need to be decoupled from the correction routine. The most straightforward approach to correct for translational motion is via navigator echoes from

which the x- and y- displacements can be extracted (17, 20). Possible drawbacks of this approach are the requirements for the acquisition of additional data that may prolong scan time and in general, some a priori knowledge of the type of motion to be encountered is needed for optimal design of the navigator. Retrospective motion correction methods use a variety of k-space based algorithms to correct for displacements during the scan. One such method is referred to as autofocusing (14, 21, 22) which allows for correction of both, translational and rotational displacements by yielding optimal values for an image focus criterion for motion-remedied blocks of k-space lines. A broader understanding of the level and implications of motion degradation in 3D μ MRI of TB incorporating translational and rotational motion induction trajectories may enable a more robust correction of the resultant motion artifacts.

The purpose of this study was to quantitatively evaluate the effects of translational and rotational motion on TB microstructural parameters by applying various retrospectively derived *in vivo* and simulated motion trajectories to essentially motion- and artifact-free high-quality 3D TB micro-images of the distal tibia. In Experiment I, the robustness of an image rating scheme was assessed with respect to translational and rotational motion corruption by applying various motion trajectories to one TB image. Motion scores were then compared to an image sharpness criterion and the effects of motion on TB structural and topological parameters were analyzed. In Experiment II, the effects of 20 unique retrospectively derived translational motion trajectories on structural parameters in TB images from two groups of healthy subjects differing in mean age were evaluated. Here, the goal was to test whether varying levels of motion degradation would mask the underlying differences in quantitative structural parameters between two groups.

MATERIALS AND METHODS

Motion Simulation Theory

Inverse Fourier transformation was first performed along k_z to separate the k-space data for each slice. Motion was then simulated on a slice-by-slice basis. Rigid body translational motion, for which all locations of the object undergo identical displacements, was simulated by multiplying the k-space data by the appropriate phase factors prior to Fourier reconstruction (18) (Figure 1).

This operation results in a phase error such that the corrupted signal, $\tilde{s}(k_x, k_y)$, is related to the true signal $s(k_x, k_y)$ by,

$$\tilde{s}(k_x, k_y) = e^{-i\varphi(k_x, k_y)} s(k_x, k_y) \quad (1)$$

where

$$\varphi(k_x, k_y) = 2\pi(k_x\Delta_x + k_y\Delta_y) \quad (2)$$

Here, Δ_x and Δ_y are the applied translational shifts in the x and y directions, respectively, for each k-space line.

For the purpose of rotational motion induction, k_y -space (460 total lines) was divided into 3 segments, each covering ~150 contiguous phase-encode lines. Rotations of varying angles θ were then applied to any of the three segments of k-space, at the start, middle or at the end of the acquisition. The rotations were decomposed into three simple shears given that a

rotation matrix is equal to the product of three shearing matrices (23, 24). Since the component shears can be applied solely in the x-direction or solely in the y-direction, a rotation can be split into three one-dimensional operations. The final image was derived by summing the rotated and un-rotated sub-images obtained from each segment using a product of shear transformations. A detailed treatment of rotational motion induction can be found elsewhere (23).

Image Acquisition, Reconstruction and Pre-processing

Image data from an ongoing clinical translational study involving healthy control subjects were acquired on a Siemens 1.5T Sonata system (Erlangen, Germany) equipped with gradients of maximum amplitude and slew rate of 40 mT/m and 200 T/m/s, respectively. Twenty-one subjects (12 females, 9 males, age range= 19–53 years) provided informed consent in accordance with study guidelines of the Institutional Review Board. The left distal tibia of each subject underwent a single examination.

Both feet of each subject were secured on a polyvinyl chloride platform at a 135° degree angle relative to the shin, using a vacuum bag and Velcro® straps to ensure immobilization during the scan interval. A custom-designed receive-only, dual-element phased-array coil was used for imaging the left ankle. Axial and sagittal localizer gradient-echo and spin-echo images (total duration, 1min 43s) were acquired to prescribe the high-resolution imaging slab for the 3D high-resolution scan performed with a modified fast large-angle spin-echo (FLASE) sequence (duration, 15min 23s) (25, 26) and the following scan parameters: TR/TE = 80/11.8 ms (60% fractional acquisition), flip angle= 140°, bandwidth= 17 KHz, FOV= 70×64×13 mm³, R>L phase encoding and image matrix size= 512×460×32 providing a voxel size of 137×137×410 μm³. Navigator data (256 points, dwell time= 40 μs) along two projection directions (x and y) were acquired in a slab outside the imaging region in intervals of 160 ms to track translational shifts during the scan (26).

K-space data was reconstructed in a step-wise manner by 1) homodyne reconstruction of the partial readout, 2) apodization using a Fermi filter to reduce Gibbs ringing and 3) 3D Fourier transformation to image space, followed by square root sum of squares (SRSS) combination of the independent element images. The SRSS combined images were subjected to an automated masking technique to define the TB region by disconnecting the soft-tissue components external to the periosteum (27). SNR was computed as the ratio of the mean marrow signal intensity (within the masked TB region) to that of the mean of a noise-only region free of signal and artifacts using square regions-of-interest (40×40 pixels).

Post-Processing and Analysis

All images were subjected to VBB processing (27) by first performing BVF mapping to generate 3D grayscale maps where pure bone was assigned an intensity of 100 and pure marrow was attributed a value of zero (28). The mean BVF (bone volume/total volume) was derived from the 3D BVF images as $\sum BVF_i$, where BVF_i is the fractional occupancy of bone in the i th voxel, summed over all voxels in a given region-of-interest. Topological features were classified according to digital topological analysis (DTA) after skeletonization of the BVF images (27) in order to convert the trabecular plates to surfaces and trabecular rods to curves. DTA parameters evaluated include the volume densities of curves (C) and surface (S)-type voxels, as well as two composite parameters, surface-to-curve (S/C) ratio, i.e. ratio of plate-like to rod-like trabeculae and erosion index (EI), i.e. ratio of the sum of parameters expected to increase with osteoclastic resorption to the sum of those expected to decrease (29).

Experiment I

A high-quality 3D FLASE image (SNR= 12.7) with a voxel size of $137 \times 137 \times 410 \mu\text{m}^3$, served as a reference. This image was subjected to 14 x- and y- translational motion trajectories: 5 *in vivo* trajectories derived from retrospective analysis of patient images (Table 1) and 9 simulated trajectories that modeled abrupt patient movements (Table 2). Each point within an input motion trajectory (460 total y- phase encodings in the FLASE acquisition) represented the average shift for a given 2-second period during a scan. The x- and y- shifts were applied as phase factors to the k-space data of the “still” image resulting in motion-corrupted images upon Fourier transformation. The image was further subjected to 18 simulated rotational motion trajectories that were modeled as step functions to simulate abrupt displacements with subsequent return to the original position (Table 3). Rotations were induced for a given segment (~150 lines/segment at the start or center of k-space) of k_y phase encoding lines and rotation was around the z-axis (in-plane rotation). Rotations to the final 1/3rd segment of k-space were not applied as preliminary tests showed that the results were identical to rotations induced for the first 150 k_y lines.

Each motion-corrupted image was then independently rated by four experienced raters on a scale of 1–4 for the level of motion corruption (1: minimal, 2: slight blurring, 3: significant blurring and 4: severe blurring). The tibial TB region was then masked and the NGS was computed for each mask according to (30, 31):

$$NGS = \sum_{i,j} \frac{(|G_{i,j}|^2)}{\left(\sum_{i,j} |G_{i,j}| \right)^2} \quad (3)$$

where $|G_{i,j}|$ is the pixel intensity gradient at voxel coordinate (i, j) and is computed from the square root of the sum of squares of x and y gradients over all images. The gradients were computed by using a simple nearest neighbor filter of $[-1, 1]$. All masked images subsequently underwent VBB processing to quantify the effect of motion on structure and topology.

Experiment II

A retrospective analysis utilizing VBB processing was undertaken on a set of 3D FLASE data of 20 healthy individuals. All images were rated as being essentially free of motion. The data were divided into two groups of 10 based on the subject's age: 1) Young (19–26 years, median=24.5 years) and 2) Middle-aged (40–53 years, median=44 years). A one-way analysis of variance indicated that the group means of the TB parameters evaluated between the two groups were significantly different ($p= 0.009$ to 0.02). Each of the 20 data sets was then subjected to one of 20 randomly-assigned, different x- and y- translational motion trajectories derived from retrospective analysis of the navigator-based data correction from ongoing patient scans in the authors' lab. The trajectories ranged from -0.25 to $+10.5$ pixels along x and -0.3 to $+12.5$ pixels along the y-axis. The average aggregate displacements ranged from 3.6 to 4 pixels ($\sim 520 \mu\text{m}$) along both, x and y in both groups. Similar to the translational motion degradation scheme implemented in Experiment I, the x- and y- shifts were applied as phase factors to the k-space data of the original scans resulting in motion-corrupted images upon inverse Fourier transformation (Figure 1). Following motion-degradation, each data set was subjected to autofocusing motion correction (14, 31) in order to determine if the loss in image sharpness could be recovered.

In our implementation of autofocusing, motion was estimated by optimizing the NGS value of reconstructed images by applying a range of trial motions as phase shifts to segments of k-space lines or views. The algorithm initiated at a k-space region (“the motion-free” base) near $k_y=0$ and adjacent segments were motion-corrected independently (31). The motion-free base was then expanded by including the two corrected segments in a center-out manner following which the next two segments were processed, and so forth. This iterative process was continued until the entire k-space was assumed to be motion-remedied. We used 8-view segments and the rotational and translational search range between two neighboring segments was selected as ($\theta = \pm 1.0^\circ$; $x, y = \pm 8$ pixels) in steps of 0.25° and $1/4$ pixels as reported previously (14). The computation time was ~4 hours per data set on a Linux workstation with a 2.6 GHz AMD Opteron quad-core processor and 32 GB of RAM.

All original, motion-degraded and autofocusing-corrected images were graded for motion severity on a new finer scale of 1–10 (1: worst, 10: motion-free) in a blinded fashion by 3 raters. This new scale enabled a wider selection of motion scores for the higher number of cases (20 motion-free, 20 motion-degraded and 20 autofocusing-corrected) that had to be evaluated. Next, the tibial TB regions were masked on the motion-induced and autofocusing-corrected images, NGS computations were performed and each masked image underwent VBB processing.

Statistics

Statistical analyses were performed with JMP 7.0 (SAS Institute, Cary, NC) and SigmaStat 4.0 (Aspire International Software, Ashburn, VA). Fleiss’ κ coefficient test was used to measure the inter-rater agreement from the image ‘motion-quality’ evaluations (32). This test calculated the degree of agreement in classifications over that which would be expected purely due to chance. The test output, κ coefficient, is the ratio between the observed and expected frequencies and ranges from -1 (no agreement) to 1 (perfect agreement). A one-way ANOVA was performed to compare the group means of TB parameters for the 1) original and motion-corrupted data to evaluate whether subject motion affects group differentiation and 2) motion-corrupted and autofocusing-corrected data to determine if group differentiation could be re-established following correction. Linear regression analyses were performed with Pearson’s correlation coefficient and significance level of the F-test to assess correlations between mean motion scores versus NGS values for 33 images (1 original, 14 translational motion-degraded and 18 rotational motion-degraded) in Experiment I. In Experiment II, regression analysis was performed to determine the following correlations: 1) percent differences in mean motion scores versus NGS values between the original and motion-corrupted images and 2) percent differences in mean motion versus NGS between the motion-corrupted and autofocusing-corrected images of 20 healthy young and middle-aged subjects.

RESULTS

Experiment I

The NGS values of the translational and rotational motion-degraded images were reduced by 0.8–2.4%. The perceived reduction in the quality of the motion-degraded images upon visual inspection by the raters mirrored the change in NGS values for both categories of motion-induced degradation (Figure 2). Motion induction led to blurring of TB microstructural features. Higher motion scores (greater degradation) correlated negatively with the corresponding NGS values for translational ($R^2=0.52$, $p<0.01$) and rotational ($R^2=0.64$, $p<0.01$) motion (Figure 2). Displacements applied during the central k_y intervals (i.e., low spatial frequencies) resulted in lower image NGS values and higher mean motion scores compared to motion induced at peripheral k_y intervals (high spatial frequencies). The inter-

inter-rater reliability metric, $\kappa = 0.42$, from the evaluation of all 33 images indicated a moderate level of agreement between the 4 raters. Figure 3 shows 3D FLASE distal tibia images from a 43-year-old healthy female. The uncorrupted image received a mean motion score of 1.0 signifying virtually no motion. The native translational x (blue) and y (red) motion trajectories are displayed below the NGS value of the image and correspond to the trajectories from Tables 1 and 2. Increased translational motion along x and y yielded consistently higher motion scores and lower NGS values (down to 1.4% reductions) which depended not only on the amplitude of motion applied to the image, but also the k-space interval during which the shifts occurred (Figure 3B, C). Motion induction using *in vivo* translational motion trajectories generated images that were degraded to a lesser extent (lower motion scores and higher NGS values; Table 1 and Figure 3B) compared to images degraded with synthetic step-function-based trajectories (Table 2, Figure 3C). Figure 4 demonstrates the effects of rotational motion in images of the same subject. Here, greater angular rotational displacements resulted in a steeper decline in NGS (down to 2.4%), particularly when rotations were applied during the acquisition of low spatial frequencies (Figure 4B, C).

Figure 5 displays the change in structural and topological parameters for varying levels of translations (3, 6 and 9 pixels) and rotations (0.05° – 5°) simulated on the ‘still’ dataset for both, peripheral and central k_y intervals. The direction and magnitude of changes resulting from both types of motion varied for different parameters. Apparent BVF, S/C and S decreased whereas EI and C increased with successive levels of motion. The magnitude of the percent differences in these parameters was greater for translations and rotations occurring at the central $150\text{ }k_y$ lines. Overall, considering both peripheral and central k_y intervals, the mean percent reduction in S/C was greater than BVF for translational (25% decrease vs. 8% decrease, $p < 0.001$, paired t-test) and rotational (19% decrease vs. 2% decrease, $p < 0.001$, paired t-test) motion, as brought about by an increase in the apparent mean number of curve voxels (11–14%) and fewer surface voxels (10–20%).

Experiment II

The NGS values of the translational motion-degraded images were consistently reduced (1.3–7.7%, $p < 0.001$) relative to the original un-corrupted images in all 20 cases, which was paralleled by large decreases in motion scores (4–68% decreases, $p < 0.001$). A strong correlation ($R^2 = 0.62$, $p < 0.001$) was observed between the percent differences of both image quality measures (Figure 6). On average, motion degradation resulted in significant reductions in apparent BVF (8–9%) and S/C (24–29%) and increases in EI (32–40%) within both groups ($p < 0.001$). Figure 7 displays representative images and the applied motion trajectories for comparison between two individuals from each group, where motion-induction led to a reduction in both, the mean motion score and NGS values for both datasets. A comparison of the percent differences in TB structural parameters of both subjects before and after motion-induction (Figure 7C) by different trajectories revealed that strong age-related effects in the parameters that was apparent in the motion-free images (decreases in BVF and S/C (5–16%) and an increase in EI (18%)) were substantially attenuated and the original direction of change was reversed following motion degradation. Similar differences in the means were also observed in other comparisons between the two groups. Overall, the measured difference in mean BVF values between the young ($11.1 \pm 0.6\%$) and the middle-aged ($10.3 \pm 0.7\%$) group in the original data (7.6% difference, $p = 0.009$) was lower (6.3%) following motion degradation and significance was lost ($p = 0.06$) (Figure 8A, B). Similar reductions in group differences were also detected for the topological parameters, S/C and EI (Figure 8C–F).

Upon autofocusing-based motion correction, image quality improved in 13 of 20 subjects as evidenced from the change in motion quality scores (mean increase = 28%) and NGS values

(up to 5%). The percent differences of both image quality measures were strongly correlated ($R^2 = 0.68$, $p < 0.001$). On average, motion correction led to an increase in the measured BVF and S/C (4–18%) and a reduction in EI (12–15%) in both groups. The difference in mean values between the two groups were 6.5% for BVF ($p = 0.05$), 13.4% for S/C ($p = 0.09$) and 17% for EI ($p = 0.04$), suggesting that although autofocusing helped recover some of the sharpness of the original motion-free images in the majority of instances, it was not entirely successful at restoring the significance in the parameter group means observed earlier in the original motion-free data (data not shown).

DISCUSSION

Rigid body translational and rotational motion can impair the quality of 3D high-resolution TB micro-images. Since the voxel dimensions in 3D FLASE along the x- and y-axes are one third of the voxel size along the slice direction, z (137 μm^2 vs. 410 μm), in-plane motion is more detrimental and also more likely to occur than through-plane motion (along the tibial axis). Furthermore, TB is anisotropic with its preferential orientation along the slice direction. Motion degradation can blur fine structural features of the TB network (16) and critically affects reproducibility of TB structural and mechanical parameters (33, 34). Despite using tight limb immobilization, the degradation of TB images from involuntary subject-induced motion occurs more frequently due to the relatively long acquisition times and poses challenges of optimal correction strategy in longitudinal studies (35, 36). Here, pre-existing patient conditions, especially in elderly subjects (e.g. twitching or restless leg syndrome cause discomfort) lead to poor compliance for remaining still during scanning, often resulting in repeat scans. Therefore, understanding the impact of subject motion on the images and the means to overcome these detrimental effects is important.

This study was designed to examine the impact of varying levels of translational and rotational motion degradation on high-resolution 3D micro-images of TB structure. We were interested in evaluating the extent to which the presence of each type of motion can mask group differences in the microstructural parameters and the implications of motion in serial studies of osteoporosis monitoring disease or treatment-based effects. The current work is an extension of an earlier study to explore the effects of motion on TB parameters (16). The findings from our motion-based simulations are: 1) subjective image motion quality scores correlated with an objective metric of image sharpness, the NGS (Figures 2, 6), 2) the correlations between motion quality scores and NGS were associated with the level of translational or rotational displacements applied at specific k-space intervals (Figures 3–4), 3) motion affected TB structural parameters lowering the apparent BVF and S/C and increasing EI (Figure 5), 4) translational displacements during acquisition on the order of 2–3 pixels (300–400 μm), or 0.7° rotations were sufficient to blur images and preclude further analysis, 5) the age-related difference in TB parameters between two distinct groups of healthy individuals was masked after motion degradation (Figures 7–8) and 6) autofocusing correction was able to partially restore the sharpness of the original images which had been motion-degraded by application of smoothly varying trajectories. Although several translational motion trajectories that varied in amplitude were employed in this study (0.5–12.5 pixels), rotations beyond 5° were not applied in order to avoid artifacts from overlapping edges in k-space (23). Furthermore, based on data from ongoing clinical studies in our lab, we do not encounter rotations greater than 1.5° on average, as detected by autofocusing.

Motion degradation was observed to adversely impact the topology of the TB network to a greater extent than BVF as concluded from the observed changes in S/C and EI (Figures 5, 7–8). Due to the small size of human bone trabeculae (100–150 μm), the detection of microstructural TB alterations (e.g. the conversion of plates to rods due to remodeling-

induced bone loss, or vice versa, bone accretion from therapeutic intervention), depends upon SNR and voxel size (3, 34, 37). Here, our results bring motion to the forefront as another covariate which can significantly hinder the detection of subtle TB microstructural changes. Song and Wehrli first implemented navigator-echo based motion detection in 3D FLASE TB images of the distal radius (voxel size: $137 \times 137 \times 500 \mu\text{m}^3$) and reported decreases in BVF of 12% following translational shifts of up to 6 pixels along x and y (17). A 6-pixel in plane shift corresponds to $820 \mu\text{m}$. Gomberg *et al.* simulated translational (up to 5 pixels in steps of 0.5 pixel) and rotational (20 rotations up to 1.2°) displacements in 3D FLASE data sets of the distal tibia using similar voxel sizes as in our study and evaluated the change in TB parameters. They observed reductions in BVF and S/C of 17–27% and 29–80%, respectively, for 2–3 pixel translations and minimum rotations of 0.5° (16). Increases in EI of the same order of magnitude as S/C were also observed.

Our results (shown in Figure 5) are in agreement with those from the above previous reports. However, in this current study, we also examined the effects of various retrospectively derived *in vivo* and simulated translational and rotational motion trajectories (52 in total from Experiments I and II) on the TB microstructural parameters. Furthermore, we showed that significant differences in parameter group means between subject groups can be masked due to motion. Retrospectively derived trajectories (Table 1) varied smoothly in time and induced blurring throughout the tibia (Figures 3B, 7B). However, the simulated trajectories (Tables 2–3) mimicked step-function like jerks or involuntary muscular contractions and resulted in more severe blurring in peripheral tibial aspects (Figures 3C, 4B–C). Such detrimental effects in image quality also appeared to manifest in the relative change in TB parameters following varying levels of motion degradation (Figure 5). Similar fluctuations in apparent TB parameters have previously been reported for single-step rotations from -2° to 2° (14). Our results from Experiment II also lend weight to the impact of motion in longitudinal patient studies probing treatment efficacy. In a serial study of hypogonadal men given testosterone replacement therapy, Benito *et al.* demonstrated improvements of up to 11% in VBB-derived TB parameters of the distal tibia such as BVF and S/C, after 24 months of treatment (38). Similarly, others have reported an increase in BVF and S/C of 7% and 8.6%, respectively, following 24 months of estradiol therapy in a group of postmenopausal women serially scanned with 3D FLASE (36). Given the findings of our study, such significant effects denoting improvements in TB microarchitecture could be obscured by even subtle motion degradation.

The availability of motion correction methods in the realm of 3D high-resolution TB μMRI is limited. Navigator-based motion detection and correction has proven reliable for correction of in-plane translations (17). The 3D FLASE pulse sequence utilizes a long TR (80ms) where, following readout of the imaging data, a separate excitation pulse can be incorporated to acquire navigator data. This pulse excites a slice adjacent to the imaging slab and navigator readouts along the x- and y-axis are acquired in an alternating manner. Thereafter, the acquired data are motion-corrected, line-by-line from the translational shifts detected from correlations of each navigator projection with an arbitrary reference location (26). This type of navigator-based motion correction can only adequately resolve translational shifts in the course of high-resolution 3D imaging. Although other navigator-based or self-navigating rigid body motion compensation techniques exist that can resolve both, translational and rotational motion (39–43), they have not yet been adopted for 3D μMRI of TB. A retrospective motion-correction technique able to address both in-plane rigid body translations and rotations in 3D μMRI is autofocusing (21), more recently perfected for high-resolution TB imaging by Lin *et al.* (14, 31). In Experiment II of our study, we used autofocusing to ameliorate the image quality following translational motion degradation in both, the young and middle-aged groups. This correction approach was not successful at improving the image quality in 7/20 subjects possibly due to an abrupt pixel shift along x or

y that occurs during an eight-view segment being corrected in the algorithm (e.g. y-axis motion trajectory in Figure 7A). Autofocusing assumes a piecewise constancy in translations and rotations thus making smoothly varying trajectories more amenable to correction rather than abrupt shifts, which cannot be accurately recovered and compensated (31).

Our findings would also translate to imaging studies of other organs, as rigid body motion during scanning is a commonplace occurrence in head and body imaging. More suitably, these results are applicable to high-resolution imaging where involuntary subject motion can be expected, even for short data acquisition times. High-resolution peripheral quantitative computed tomography (HR-pQCT) is another modality often utilized for 3D imaging of TB microstructure. Despite the short acquisition times (~3minutes), subject motion is also detrimental in HR-pQCT, resulting in streaks, smearing and discontinuities of cortical and TB structures (44). From our results, it appears that large, sudden displacements, such as jerks, occurring during acquisition of low spatial frequencies (central k_y lines) contribute to the most severe artifacts and TB microstructural parameter alterations (Figures 3C, 4C and 5). Furthermore, translations and rotations do not occur in isolation in the clinical realm and the impact of a model incorporating both types of motion on quantitative parameters will have to be explored in the future. Further work is also needed to identify locations in k-space where the joint occurrence of translational and rotational displacements is particularly critical.

CONCLUSIONS

Quantitative TB structural measures are highly sensitive to subtle motion-induced degradation which adversely affects precision and statistical power. The level of translational or rotational motion displacements does not have to be severe with aggregate displacements during the scan on the order of 2–3 pixel (300–400 μm) translations or 0.7° rotations sufficient to blur images and cause significant errors in the derived structural parameters.

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Figure 1. Schematic representation of the motion-corruption chain. In the displayed example, translational displacements of up to 5 pixels (X) and 10 pixels (Y) were applied resulting in image quality degradation. Magnified insets depict sharp (original) and blurred (motion-induced) regions of the trabecular bone network.

Figure 2. Comparison of mean motion scores vs. NGS for simulations of translational and rotational motion. The solid regression line is fitted to the uncorrupted image (gray circle) and 14 images with varying levels of induced translations (*in vivo* trajectories - green circles (Table 1), synthetic trajectories- black circles (Table 2)). The dashed regression line is fitted to 18 images with various degrees of induced rotations (red and blue triangles, Table 3) and the original image. Red and blue represent rotations applied during peripheral and central k_y intervals, respectively.

Figure 3.

Original (A) and translational motion corrupted (B, C) images. B) An *in vivo* translational motion trajectory (trajectory #5 from Table 1) applied to the original data yielded a mean motion score of 1.5 and reduction in NGS of 0.9% relative to A. C) A simulated trajectory mimicking an involuntary muscular movement (trajectory #9 from Table 2) yielded a poorer motion score and NGS value (relative to A).

Figure 4.

Original (**A**) and rotational motion degraded (**B**, **C**) images. **B**) A 2° rotation (trajectory #16 from Table 3) applied to the original data yielded a mean motion score of 2.75 and reduction in NGS of 1.9% relative to **A**. **C**) A 5° rotation (trajectory #18 from Table 3) yielded a poorer motion score and NGS value (relative to **A**).

Figure 5. Percent difference in TB structural parameters for translational (**A**, **B**) and rotational (**C**, **D**) motion-corrupted images by simulated trajectories. Single-step x-displacements of 3, 6 and 9 pixels were applied to the peripheral (**A**) and central (**B**) k_y intervals (150 phase encodes). Similarly, 9 single-step rotations from 0.05° – 5° (Table 3) were applied to each, peripheral (**C**) and central (**D**) k_y intervals. Structural parameters include bone volume fraction (BVF), surface-to-curve (S/C) ratio, surface voxels (S), curve voxels (C) and erosion index (EI).

Figure 6. Comparison of percent differences in mean motion and NGS values between the original and motion-corrupted images of 10 young and 10 middle-aged healthy subjects.

Figure 7. Comparison of images (**A**-26 year-old; **B**-51 year-old) and percent differences in the TB measures (**C**) between the two subjects before and after motion degradation with two different and randomly assigned translational motion trajectories. Existing differences in BVF (5%), S/C (16%) and EI (18%) between the two individuals were substantially reduced and the direction of change was reversed following motion induction.

Figure 8. Original (motion-free) and motion-induced scatter-plots of bone volume fraction (**A, B**), surface-to-curve ratio (**C, D**) and Erosion index (**E, F**) demonstrating the masking of healthy age-related differences after motion induction in two groups (Young and middle-aged) of 20 subjects. Diamonds denote the 95% confidence intervals about the means.

Table 1

Range of retrospective *in vivo* translational motion trajectories providing displacements along X and Y for each of the five trajectories.

Trajectory No.	X motion	Y motion
	pixels (range)	pixels (range)
1.	4.0 (−1.0 to 3.0)	4.0 (−1.8 to 2.2)
2.	6.0 (−4.5 to 1.5)	4.4 (−2.2 to 2.2)
3.	8.0 (−2.5 to 5.5)	5.3 (−2.2 to 3.1)
4.	7.0 (−3.5 to 3.5)	4.5 (−3.1 to 1.4)
5.	2.8 (−1.3 to 1.5)	2.3 (−1.3 to 1.0)

Table 2

Synthetic translational motion trajectories. The step-function displacements (in pixels) along X and Y are given for different k_y intervals.

Trajectory No.	X motion		Y motion	
	pixels	k_y interval	pixels	k_y interval
1.	3.0	1–150	0.0	0
2.	6.0	1–150	0.0	0
3.	9.0	1–150	0.0	0
4.	0.0	0	3.0	200–350
5.	0.0	0	6.0	200–350
6.	0.0	0	9.0	200–350
7.	1.0	1–150	3.0	1–150
8.	3.0	200–350	3.0	200–350
9.	6.0	1–200	9.0	200–350

Table 3

Simulated rotational motional trajectories. In-plane rotations (in degrees) are given for various k_y intervals.

Trajectory No.	Rotation	k_y interval
1.	0.05°	0–150
2.	0.10°	0–150
3.	0.20°	0–150
4.	0.05°	151–300
5.	0.10°	151–300
6.	0.20°	151–300
7.	0.35°	0–150
8.	0.70°	0–150
9.	1.25°	0–150
10.	2.0°	0–150
11.	3.0°	0–150
12.	5.0°	0–150
13.	0.35°	151–300
14.	0.70°	151–300
15.	1.25°	151–300
16.	2.0°	151–300
17.	3.0°	151–300
18.	5.0°	151–300