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A Registration-based Autofocusing Technique for Automatic Correction of Motion Artifacts in Time-Series Studies of High-Resolution Bone MRI

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Abstract

Purpose—To develop a registration-based autofocusing (RAF) motion correction technique for high-resolution trabecular bone (TB) imaging and to evaluate its performance on in-vivo MR data.

Materials and Methods—The technique combines serial registration with a previously developed motion correction technique – autofocusing – for automatic correction of subject movement degradation of MR images acquired in longitudinal studies. The method was tested on in-vivo images of the distal radius to measure improvements in serial reproducibility of parameters in 12 women (ages 50–75 years), and to compare with the navigator echo-based correction and autofocusing. Further, the technique’s ability to optimize the sensitivity to detect simulated bone loss was ascertained.

Results—The new technique yielded superior reproducibility of image-derived structural and mechanical parameters. Average coefficient of variation across all parameters improved by 12.5%, 27.0%, 33.5% and 37.0%, respectively, following correction by navigator echoes, autofocusing, and the RAF technique (without and with correction for rotational motion); average intra-class correlation coefficient increased by 1.2%, 2.2%, 2.8% and 3.2%, respectively. Further, simulated bone loss (5%) was well recovered independent of the choice of reference image (4.71% or 4.86% with respect to using either the original or the image subjected to bone loss) in the time series.

Conclusion—The data suggest that our technique simultaneously corrects for intra-scan motion corruption while improving inter-scan registration. Further, the technique is not biased by small changes in bone architecture between time-points.

Keywords

motion correction; MRI; trabecular bone; reproducibility

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Introduction

Since the inception of magnetic resonance imaging (MRI), acquisition of high-quality in-vivo images has been hampered by subject motion-related artifacts, such as ghosting and blurring. Motion-induced artifacts reduce the reliability of image-based quantitative analysis as well as the data's diagnostic usefulness (1–3). In particular, if the nature or extent of motion differs between scans in longitudinal studies, motion-induced artifacts can potentially mask subtle changes, critical in evaluating interventional effects. Although advanced acquisition techniques that are less sensitive to motion exist, they often compromise image resolution, contrast and signal-to-noise ratio (SNR) (4). Therefore, in spite of improved hardware, image acquisition and reconstruction techniques, subject motion remains a major challenge in quantitative high-resolution MRI.

Problems from subject motion are exacerbated in trabecular bone (TB) imaging due to the relatively long scan times and the high spatial resolution required to accurately retrieve the bone's 3D micro-structure. Artifacts from involuntary subject movement have been shown to reduce the reliability of image-based quantitative assessment of the TB network, for example, TB structural and topological parameters. Song et al (5) showed that translational displacements during the scan can lower apparent bone volume fraction (BV/TV: bone volume divided by total volume) by 8–12%. Gomberg et al (2) found that even a rotation of as little as 0.5° can result in substantial errors in the image-derived structural parameters. Lin et al (3) further reported that a rotation of 2° can cause relative errors of up to 20% in derived topological parameters. In a more recent study, Bhagat et al (6) found that motion-induced displacements occurring close to the center of k-space caused greater errors than those occurring during scanning of k-space periphery. Furthermore, Lin et al (3) demonstrated that changes in structural parameters caused by rotation are consistent with those expected from bone loss thereby indicating that subtle movement could falsely suggest a trabecular bone structural degradation.

Rigid-body translation and rotation resulting from involuntary subject movement during the scan are the most dominant source of artifacts in high-resolution MR (μ MR) imaging of TB. Several techniques have been proposed for retrospectively removing motion-induced image artifacts, including navigator echo-based correction (5,7) and auto-correction or autofocusing (AF) (1,3,4,8,9). Navigator-based techniques collect additional data using additional echoes (sometimes in conjunction with additional excitation pulses) to track motion in specific directions. Although effective to reduce translational motion artifacts when imaging TB, this technique may require extra scan time. In addition, the compensation for rotational displacements requires more complicated navigators such as orbital (10) or spherical navigators (11), which have so far not been used in TB imaging. In contrast, autofocusing is capable of correcting both in-plane translations and rotations, even in cases of non-rigid motion of the surrounding anatomy by confining the analysis to the trabecular bone region only. The technique aims to optimize an image focus criterion (e.g. the normalized gradient squared value) by applying a series of trial corrections to probe for motion-induced displacements without the need for additional data. However, coverage of an adequate search range can be computationally intensive. In addition, most metrics used in practice require calculation of image gradients, a process that is susceptible to noise.

In this work, a new motion correction technique is described that combines serial registration with autofocusing. The rationale underlying this approach is as follows: In serial studies it is likely that some scans are less motion degraded than others. If one of the image datasets is essentially motion-free, this dataset may be used to provide a priori information that can be exploited for correction of motion in the other images. To evaluate the technique's performance, three motion correction techniques were applied to in-vivo micro-MR images of the distal radius, an anatomic site where rotational subject motion occurs more frequently. First, image quality achieved with the proposed technique was compared to that obtained using the navigator echoes or autofocusing. The second objective was to explore the effectiveness of the new technique for improving the serial reproducibility of image-derived TB structural and mechanical parameters. Finally, it was investigated whether the sensitivity for the detection of bone loss will be affected after applying this registration-based autofocusing technique.

Methods

Registration-based autofocusing

The registration-based autofocusing (RAF) approach involves three steps. First, we assume that one image in the time series of acquired images is of higher quality than the remaining ones (i.e., sharper due to less motion corruption). We use the normalized gradient squared (NGS) (12) value (in addition to visual inspection) to select this relatively motion-free image, which is then used as a "reference" to correct the other motion-degraded images in the time series (henceforth referred to as "corrupted images"). Then in step one a pattern-based registration (13) is performed to resample the reference image to each of the corrupted images. Next (i.e., in step two), motion-induced displacements in each of the corrupted images are corrected based on the reference in the following manner. As in traditional autofocusing (9), k-space data of the corrupted image is divided into small segments (along in-plane phase-encoding direction (k_y) to ensure that data in each segment is acquired contiguously), which are corrected one at a time (starting from the center of k-space and moving outward) by applying a series of trial rotations and translations (the remaining segments being fixed). The objective here is to maximize the normalized cross-correlation of the corrupted and reference images within a region of interest (typically TB region), as opposed to optimizing an image sharpness metric, e.g., the NGS value, for individual scans separately in the traditional autofocusing technique (9). This segment-based optimization is performed in an iterative way, i.e., when all segments with a given size have been optimized, a new iteration starts with a reduced segment size. Finally, in step three, if there are more than two time points in the series, this step involves resampling the corrupted images after correction back to their reference for subsequent quantitative analysis (see Figure 1 for an illustration of the procedure). By optimizing the mutual correlation between serial images after rough registration, the technique simultaneously corrects for intra-scan motion corruption and improves inter-scan registration.

During the second step described above, the correction for each segment is performed as follows: Each time, the k-space segment to be corrected is first transformed to image space to yield its image contribution. This image contribution is subtracted from the full image (a

combination of those already corrected and those not yet corrected), and then corrected by directly applying trial displacements. Subsequently, the corrected image contribution is added back yielding an updated full image. Incremental translation (fractional pixel shifts) can be achieved by means of either zero-filling before fast Fourier transform (FFT) (9) (which can be done once for the whole image so that all subsequent corrections can be performed in image space) or linearly-increasing phase terms in k-space (where all trial fractional translations are calculated once in k-space and saved to a buffer). For trial rotations, three successive shear transformations are applied to approximate in-plane rotation as described in (14). The range for trial rotations and translations was $-1^\circ \leq \theta \leq 1^\circ$ and $-8 \leq x, y \leq 8$ pixels, respectively, with increments of 0.2° and $(0.25, 0.25)$ pixels (all rotations and translations considered were in-plane; see (3) and subsequent discussion for justification). To investigate the contribution from prior registration, a smaller search range ($-1^\circ \leq \theta \leq 1^\circ$; $-3 \leq x, y \leq 3$ pixels) but same increment size was also utilized as well as a translation-only correction performed with a range of $(-3 \leq x, y \leq 3)$ pixels and an increment of 0.5 pixel. The segment size used in the RAF technique was fixed to 10 k_y lines in all experiments and one iteration was performed to minimize computation time.

Image acquisition

In-vivo μ MR images of the right distal radius from eighteen female subjects (age ranges 50–75 years) were selected from a previous study (15). All subjects signed an informed consent in accordance with study guidelines of the institutional review board. Each subject had been scanned three times (baseline, follow-up 1 and 2) over the course of eight weeks, with a mean interval between scans of 20 days. Images were acquired with a modified 3D fast large-angle spin-echo (FLASE) pulse sequence (16) with the following parameters: imaging volume = $70 \times 42 \times 13$ mm³, voxel size = $137 \times 137 \times 410$ μ m³, TR (repetition time) / TE (echo time) = 80/10 ms, flip angle = 140° , NEX (number of excitations) = 1, and scan time = 10.4 minutes. With slice-encoding (k_z) being on the innermost loop during acquisition, the 10 k_y lines in each segment are temporally closest to each other. Data was acquired in the standard linear way along the k_y direction. A navigator echo scheme alternating between the x-axis and y-axis in subsequent TRs was incorporated following each readout as described in (5). All scans were performed on a Siemens 1.5T MAGNETOM Sonata MR scanner (Siemens Medical Solution, Erlangen, Germany), using a transmit-receive elliptical birdcage wrist radiofrequency coil (InsightMRI, Worcester, MA). Details regarding the setup of the RF coils along with the positioning device are provided in (15).

Experiments

Two experiments were conducted to evaluate the performance of the algorithm. In the first experiment, in-vivo images of the distal radius at all three time points were utilized to evaluate the technique's effectiveness on improving serial reproducibility in terms of structural and mechanical parameters in longitudinal studies. Results from the various motion correction techniques were compared between each other as well as with those obtained without motion correction. The second experiment was designed to investigate whether applying the technique would affect the sensitivity on detecting bone loss, which is critical in longitudinal studies, e.g. to evaluate treatment effectiveness. Specifically, bone loss was simulated in the distal radius images at a given time point, and BV/TV computed

after applying the RAF technique to determine whether the applied bone loss was altered by the technique.

In the first experiment, five sets of images were generated for each scan dataset for comparison: no correction, navigator-based correction, autofocusing correction, translation only as well as rotation/translation combined RAF technique. Specifically, the navigator data collected during the FLASE acquisition was utilized to correct for translational motion as described in (5); an autofocusing algorithm was applied in a manner identical to previous work (1,3,4,8,9) except that the NGS value (the image sharpness metric they used) was calculated only inside the ROI (TB region) to correct for combined rotational and translational motion (search range: -1° θ 1° and -8 x, y 8 pixels; increments: 0.25° and $(0.25, 0.25)$ pixels; segment size: $8 k_y$ lines); the RAF algorithm comprised of translation-only and combined rotation and translation (parameters used will be given in the Results).

Image processing

Original reconstructed images, or images corrected using the navigator data or the autofocusing algorithm were first co-registered to ensure consistent region of interest (ROI) across all time points (this step was skipped for the RAF motion-corrected images). Six subjects were excluded due to failed registration (due to motion degradation or ineffective motion correction by navigator echoes or autofocusing) resulting in a total of twelve groups of datasets. Minor image intensity variations were then corrected for all datasets using a local thresholding algorithm (17). Subsequently, the TB region was semi-manually segmented from each resultant image and processed to generate a 3D grayscale bone volume fraction (BVF) map (3D array). Individual voxel intensity in the BVF maps represents the fractional occupancy of bone in that voxel, ranging from 0% for pure marrow to 100% for pure bone. These 3D arrays were then used in the following analyses.

Calculation of structural and mechanical parameters

Trabecular bone structural and topological parameters (BV/TV, surface-to-curve ratio (S/C) and erosion index (EI)) were calculated by digital topological analysis (DTA) (18) based virtual bone biopsy (VBB) processing (19). Average 3D trabecular thickness (Tb.Th) was calculated using the fuzzy-distance transform method (18), and average trabecular spacing (Tb.Sp) and trabecular number (Tb.N) were derived from the calculated Tb.Th according to (20).

Axial stiffness was estimated by applying simulated compressive loading within the linear elastic regime via a voxel-based micro-finite element (μ FE) analysis as described in (21). Voxels in the BVF map were first converted to hexahedral finite elements. Tissue-level modulus (YM of each element) was linearly scaled by the bone volume fraction (BVF) value at that voxel using $YM = BVF \times 15 \text{ GPa}$; and Poisson's ratio set to 0.3. A small strain (0.05%) was applied to nodes at the proximal surface of the TB region while nodes at the distal surface were fixed in the axial direction. Nodes at both the proximal and distal surfaces were free to move in the transverse plane. Subsequently, a linear FE system was established by setting the total force at equilibrium to zero, and solved for the equilibrium

displacements using a parallel preconditioned conjugate gradient method (21). Axial stiffness was finally obtained as the resultant primary stress divided by the applied strain.

Trabecular bone yield and post-yield behavior was simulated by solving a series of nonlinear systems with incrementally applied strains using a nonlinear FE program (22) where trabecular tissue was modeled as an elasto-plastic material. Material nonlinearity was considered by adjusting tissue-level modulus according to a tissue-level effective strain-based criterion at each iteration. A nonlinear system was thereby established and iteratively solved for the resultant apparent stress for each applied strain. Boundary conditions were set to represent axial compression with no friction along the transverse directions (as described in the above linear case). The stress-strain curve was thereafter obtained as the best fitted cubic polynomial to these points of applied strains and corresponding stresses. Lastly, the apparent yield stress and strain were obtained based on the 0.2% offset rule (23). The maximum stress value of the stress-strain curve was set as the ultimate stress and its corresponding strain value was used as the ultimate strain. In addition, modulus of resilience was calculated as the integral of the fitted polynomial to the stress-strain curve from zero to the yield strain point. Similarly, toughness was calculated as the area up to the ultimate strain point.

Evaluation of reproducibility

The coefficient of variation (CV) and the intra-class correlation coefficient (ICC) were calculated to evaluate the serial reproducibility and reliability of the TB structural and mechanical parameters.

Evaluation of sensitivity to detect bone loss

To simulate bone loss, we applied homogeneous erosion similar to that described in (24). Specifically, bone volume fractions of TB surface voxels were gradually reduced in random fashion until the desired reduction in bone volume (5%) was reached. The following two procedures were then designed and implemented on images of the distal radius at a single time point (chosen from images pertaining to three time points for a set of relatively motion-free images). In total, 12 images were thereby selected and utilized in this experiment. Figure 2 illustrates the two procedures.

Procedure I

Step 1: Simulate bone loss (corresponding to a 5% reduction in bone volume fraction – BV/TV) to the original acquired image (Image0) to obtain Image1, which will be referred to as ‘L’;

Step 2: Add translational displacements to ‘L’ to obtain Image2, referred to as ‘LM’. The translational motion trajectories used here were detected by navigator echoes in previous in-vivo studies (see Figure 3 showing four examples).

Step 3: Run the RAF algorithm on ‘LM’ using the originally acquired image (Image0) as the reference to obtain Image3, which will be referred to as ‘LMC1’;

Step 4: Run the RAF algorithm on 'LM' using the image with simulated bone loss (Image1) as the reference to obtain Image4, which will be referred to as 'LMC2';

Step 5: Compare bone loss between 'LMC1' and 'LMC2' in terms of BV/TV.

Procedure II

Step 1: Add translational motion (as used in Procedure I) to the original image (Image0) to obtain Image5, which will be referred to as 'M';

Step 2: Run the RAF motion correction algorithm on 'M' with the original image (Image0) as the reference to obtain Image6, which will be referred to as 'MC1';

Step 3: Compare bone loss in terms of BV/TV between 'M' and 'LM' (the latter was obtained from Procedure I) as well as between 'MC1' and 'LMC1' (the latter was obtained from Procedure I).

Statistical analysis

The changes in parameters between with and without applying various motion correction techniques as well as between various motion correction techniques were assessed using analysis of variance (ANOVA). The comparisons of bone loss between different datasets were assessed using two-sided paired Student's t-test when data were normally distributed, and nonparametric Wilcoxon signed rank test when data were not normally distributed. All statistical analyses were performed using JMP Discovery Software (JMP 9.0; SAS Institute Inc., Cary, NC, USA), with $p < 0.05$ indicating statistical significance.

Results

Sample data

Figure 4 shows a motion-corrupted image of a subject and the corrected images obtained from the navigator-based technique, autofocusing, and the RAF technique (without and with correction for rotational displacements). The search range in the RAF technique for the translation-only correction was $(-3 \text{ } x, y \text{ } 3 \text{ pixels})$ with an increment of 0.5 pixel (Figure 4d); for the combined trial rotations and translations the range was $(-1^\circ \text{ } \theta \text{ } 1^\circ; -3 \text{ } x, y \text{ } 3 \text{ pixels})$ with increments of 0.2° and $(0.25, 0.25)$ pixels (Figure 4e), and $(-1^\circ \text{ } \theta \text{ } 1^\circ; -8 \text{ } x, y \text{ } 8 \text{ pixels})$ with the same increments (Figure 4f). Motion artifacts are appreciably reduced in all corrected images compared to the originally acquired corrupted image. The percent changes of the normalized gradient squared (NGS) values, used here as the image sharpness metric, relative to no correction are 0.07%, 1.09%, 3.73%, 3.90% and 3.92%, respectively. Also notable are the improved sharpness in trabecular structural features inside the marked regions. The three images (Figure 4d–f) corrected by the RAF technique (without and with applying trial rotations) are visually indistinguishable; all of them are visually comparable to the autofocusing corrected image and superior to the navigator-echo corrected image. We therefore only report results obtained from applying the smaller search range in the following experiments (with rotation correction: $-1^\circ \text{ } \theta \text{ } 1^\circ; -3 \text{ } x, y \text{ } 3 \text{ pixels}$; without rotation correction: $-3 \text{ } x, y \text{ } 3 \text{ pixels}$, corresponding respectively to the parameters chosen for Figures 4d and 4e).

Evaluation of reproducibility

CVs and ICCs averaged across all structural and mechanical parameters were compared between various motion correction techniques for all twelve subjects (Figure 5). We note that all correction methods yielded decreased average CV and increased average ICC compared to the uncorrected data. For both structural and mechanical parameters, the RAF technique that included rotation correction yielded the lowest average CV and highest average ICC, followed by the RAF technique without rotation correction, followed by autofocusing and navigator correction. The average CV over all parameters (structural and mechanical) decreased from 5.6% to 4.9%, 4.1%, 3.7% and 3.5%, respectively for the navigator-based technique, autofocusing, the RAF technique (without and with rotation correction). Similarly, average ICC increased from 0.948 to 0.959, 0.969, 0.974 and 0.978, respectively.

Table 1 lists the average CV and ICC of each parameter: BV/TV, selected structural (S/C, EI, Tb.Th, Tb.N, Tb.Sp) and mechanical parameters (axial stiffness, yield strain, yield stress, ultimate strain, ultimate stress, modulus of resilience and toughness), obtained with and without various motion correction techniques. The differences between corrected and uncorrected parameters as well as between corrected parameters from various techniques were normally distributed ($p < 0.05$). RAF and autofocusing yielded improved reproducibility relative to that found for uncorrected values ($p < 0.05$ for Tb.N, Tb.Sp, stiffness, yield stress, ultimate strain, ultimate stress, modulus of resilience and toughness). Additionally, RAF also outperformed uncorrected BV/TV and yield strain ($p < 0.05$), and was found to superior to navigator-echo correction for yield strain and modulus of resilience ($p < 0.05$). Navigator correction yielded better reproducibility except for S/C, EI, axial stiffness, yield strain/stress and ultimate stress. For most of the parameters (except Tb.N and Tb.Sp), RAF with rotation correction performed slightly better than when only translational motion was corrected for. However, the slight improvement achieved with rotation correction entailed a considerable penalty in computation time (127 versus 6 minutes per 3D dataset). Overall, the RAF data was suggestive of yielding improved reproducibility relative to autofocusing (Figure 5) but the comparisons did not reach statistical significance. We note that results from autofocusing were not significantly more reproducible than those from navigator correction. However, the improvements from RAF relative to navigator correction were statistically significant for some parameters.

Among the structural parameters, Tb.N and Tb.Sp benefited most in terms of mean CV and ICC whereas S/C was affected little by motion correction. Reproducibility improved fairly uniformly for all mechanical parameters.

Detection sensitivity of bone loss from motion corrupted images

Figure 6 provides means and standard errors of the detected bone loss (relative to the applied reduction in BV/TV) for the twelve groups of datasets. When the distal radius dataset was subjected to simulated motion corruption by applying trajectories actually observed during in-vivo imaging, the resulting images ('M' in Figure 6) showed an average of 4.03% reduction in BV/TV compared to the BV/TV computed from uncorrupted images. When the same motion trajectory was applied to images previously subjected to 5% simulated bone

loss, the detected average reduction in BV/TV was 8.10% ('LM' in Figure 6). After subjecting these motion degraded images comprising simulated bone loss to the RAF algorithm (without rotation correction), the average detected reduction in BV/TV was 4.71% when using the original image as the reference ('LMC1' in Figure 6), and 4.86% when using the image subjected to bone loss ('LMC2' in Figure 6). These two values of detected bone loss were not significantly different from each other and both were not significantly different from the 5% value expected to be detected, suggesting that using either the original image or the image with simulated bone loss as reference during the motion correction procedure both recover the actual bone loss. Similarly, RAF (with rotation correction) yielded similar average reduction in BV/TV (4.22% when using the original image as the reference and 4.26% when using the image subjected to bone loss). In addition, the change in BV/TV after applying motion correction to images with only simulated motion ('MC1') was -0.13% (not significantly different from 0%) compared to BV/TV of the original image, showing the effectiveness of the RAF technique as well. Further, the differences in reduction of BV/TV were 4.07% between motion corrupted images with and without bone loss (comparing 'LM' and 'M' in Figure 6), and 4.84% between motion corrected images with and without bone loss (comparing 'LMC1' and 'MC1'). The latter was not significantly different from the 5% ground truth, demonstrating that the RAF technique does not mask the effect of bone loss when using the original image as the reference.

Discussion

We have developed a registration-based autofocusing motion correction technique in which correlation between serial images is maximized as an image quality metric, thereby simultaneously correcting for intra-scan motion corruption and improving inter-scan registration. The new technique has been tested on in-vivo distal radius datasets and its performance compared to previously verified techniques. For most of the data, autofocusing and, more so the RAF technique, outperformed translational navigator correction. The primary reason is likely that navigators correct for translational displacements only. In addition, the correlation used in the RAF technique, or the NGS value calculated in autofocusing, to evaluate image sharpness was calculated only inside the region of interest (the TB region here), which guarantees that all motion under consideration is rigid, whereas the navigator correction does not have such a feature and neither does it address non-rigid deformations. However, the calculation of NGS values involves derivatives, which is prone to noise, especially within the high-frequency regions. Furthermore, the RAF technique makes use of prior information in a time series with the aid of the least motion corrupted image set as reference; such prior information assists the search process. Another advantage of the new technique is its efficiency in terms of computation time. Our results suggest that in-plane trial rotations may not need to be considered, thus only two degrees of displacements (in-plane trial translations) need to be tested and their search ranges reduced after a prior registration, thereby significantly improving the computational efficiency.

Lowered CV and increased ICC for both structural and mechanical parameters demonstrate improved reproducibility compared to the alternative methods considered. Reproducibility significantly determines statistical power in longitudinal studies such as the ability to detect changes due to aging or disease, or to assess the response to treatment. Besides correction

for involuntary subject movement during the scan, effective registration has been shown to be a critical determinant of reproducibility (2). Although registration was performed in all datasets, it was enhanced by the RAF technique at no extra cost, which may explain the improved reproducibility. Therefore, the registration-based autofocusing technique simultaneously achieves enhanced registration and motion correction.

The data used for performance evaluation of the various correction algorithms is germane because it is fair to assume that given the short intervals between repeat exams (mean interval 20 days), remodeling induced changes in actual bone structure are negligible. The various longitudinal studies from the authors' and other laboratories suggest that structural parameters vary measurably only over the time course of 1–2 years (25–28), and only when treatment is involved.

The sensitivity of the method to detect the effect of bone loss was also evaluated. It is critical to ensure that the motion correction procedure does not mask subtle changes caused by actual temporal changes from treatment. The current study found that the detected fractional bone loss induced by simulation on actual images was not adversely affected by the application of the proposed method. Further, the detected fractional bone loss was not significantly affected by the choice of the reference images (i.e., those with or without simulated bone loss), suggesting that the choice of reference does not bias the detectability of bone loss.

One might argue that motion correction may not be clinically significant when the actual changes in bone structure and biomechanics caused by treatment or disease far exceed those detected before and after applying motion correction. However, this is typically not the case. For example, in the present study, the mean relative difference in BV/TV between pre- and post RAF correction measurements was about 3%, whereas the average changes in BV/TV observed in previous longitudinal studies were often as small as 1% (29,30). Furthermore, the results from our bone loss experiment show that subject motion during scanning detected in-vivo caused apparent changes in BV/TV comparable to actual ones. Therefore, changes in estimates of bone structure and biomechanics resulting from involuntary subject motion during scanning can easily surpass actual changes from treatment or disease progression.

The present study has some limitations. First, the proposed motion correction technique only applies to longitudinal studies, since data from more than one time-point are needed among which at least one acquired image set needs to be relatively motion-free. Nevertheless, even if all acquired images are motion-corrupted to various degrees, the one rated of best quality may first be autofocusing corrected, subsequently serving as reference. Second, only in-plane rigid-body motion was considered and corrected. Although the present program can be extended to compensate for 3D motion as well at the cost of increased computation time, it has been shown that motion along the through-plane direction is likely to be less serious than that occurring in-plane (3). In addition, in-plane resolution is often higher than through-plane. Our regional calculation of the cost function (the normalized cross-correlation) further constrains motion to be essentially rigid within the ROI, which is a reasonable assumption for hard tissues.

In conclusion, a new registration-based autofocusing motion correction technique has been presented and its feasibility and practicality was evaluated relative to various established correction techniques. The results suggest improved reproducibility of the derived TB structural and mechanical parameters, primarily due to the enhanced registration. The sensitivity of the technique to detect changes from bone loss suggests that the technique does not mask subtle treatment effects on TB microstructure and biomechanics.

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Figure 1.

a) Processing steps in the RAF motion correction technique: each corrupted image is corrected based on its co-registered reference image from the same time series; b) Illustration of step two in (a): k-space is divided into segments, each of which is corrected sequentially by applying trial displacements to maximize the correlation with the reference within ROI (the TB region).

Figure 2.

Diagrams for evaluation of the RAF technique's sensitivity to detect bone loss: (a) Procedure I – apply the technique to images subjected to simulated bone loss and motion, and compare the resultant BV/TVs between using different references (the original image and the original image plus bone loss); (b) Procedure II – apply the technique to images subjected to only simulated motion using the original image as reference, and then compare the resultant BV/TVs with those obtained from Procedure I.

Figure 3.

Four examples of the twelve in-vivo translational motion trajectories (red: x displacement; blue: y displacement) used in the bone loss experiment. The twelve trajectories were detected by Navigator echoes in the distal tibiae and randomly chosen from a previous study, and then randomly assigned to the twelve datasets.

Figure 4.

(a) Motion-corrupted image, (b) navigator-based technique corrected image, (c) AF corrected image, (d) RAF corrected image (without correction for rotational motion, search range of translation $[-3\ 3]$ with an increment of 0.5 pixel), (e) RAF corrected image (with correction for rotation, search range of translation $[-3\ 3]$ with an increment of 0.25 pixel), (f) RAF corrected image (with correction for rotation, search range of translation $[-8\ 8]$ with an increment of 0.25 pixel) of the distal radius from a subject. Motion artifacts in all corrected images are reduced. The percent changes of NGS relative to no correction are 0.07%, 1.09%, 3.73%, 3.90% and 3.92%, respectively. Note improved sharpness of trabecular structures inside the marked regions.

Figure 5.

Average CVs and ICCs for structural and mechanical parameters estimated from the twelve groups of datasets of in-vivo TB images of the distal radius acquired at three time-points for various motion correction techniques as indicated in the figure. (* denotes $p < 0.05$).

Figure 6.

Mean and standard error of the detected absolute change in BV/TV of L (the original image with applied bone loss of 5%), LM (original image with simulated bone loss and simulated motion), LMC1 (the image after applying RAF to 'LM' with the original image as the reference), LMC2 (the image after applying the RAF technique to 'LM' with 'L' as the reference) and M (the original image with simulated motion only) obtained from the twelve subjects. The average changes in BV/TV of 'LMC1' and 'LMC2' were not significantly different from each other and neither was significantly different from the applied 5% bone loss.

Table 1

Average CV and ICC for structural and mechanical parameters obtained with and without application of the motion correction techniques examined.

	Group A: Without motion correction	Group B: Navigator-based motion-corrected data	Group C: Autofocusing corrected data	Group D: Registration-based motion-corrected data (translation only)	Group E: Registration-based motion-corrected data (translation and rotation)
BV/TV	4.18	3.41	3.11	2.98	2.84*
S/C	7.21	7.32	6.27	5.48	5.41
EI	7.02	7.26	6.33	5.17	5.15
Tb.Th	1.97	1.95	1.35	1.50	1.61
Tb.N	4.03	3.00	2.86*	2.74*	2.17*
Tb.Sp	4.39	3.22	3.10*	2.96*	2.37*
E_z	6.48	5.11	4.66*	3.90*	3.74*
ϵ_y	1.36	1.48	1.05	0.77*	0.73*
σ_y	7.65	6.62	5.23*	4.48*	4.23*
ϵ_u	3.83	3.82	3.22	3.26	2.93
σ_u	7.43	6.23	5.15*	4.53*	4.47*
U_r	8.58	7.77	5.56*	4.99*	4.70*
K_c	8.70	6.54	5.92*	5.64*	5.53*
BV/TV	0.934	0.963	0.959	0.965	0.969
S/C	0.977	0.979	0.973	0.986	0.989
EI	0.958	0.946	0.970	0.988	0.981
Tb.Th	0.915	0.934	0.952	0.945	0.941
Tb.N	0.912	0.950	0.951	0.952	0.970
Tb.Sp	0.915	0.949	0.950	0.959	0.972
E_z	0.978	0.973	0.972	0.983	0.986
ϵ_y	0.935	0.946	0.957	0.976	0.976
σ_y	0.973	0.971	0.973	0.985	0.989
ϵ_u	0.916	0.945	0.976	0.990	0.994

	Group A: Without motion correction	Group B: Navigator-based motion-corrected data	Group C: Autofocusing corrected data	Group D: Registration-based motion-corrected data (translation only)	Group E: Registration-based motion-corrected data (translation and rotation)
	σ_u	0.973	0.971	0.972	0.984
	U_T	0.970	0.970	0.970	0.989
	K_C	0.964	0.970	0.965	0.977

Note: BV/TV = bone volume fraction; S/C = surface-to-curve ratio; EI = erosion index; Tb.Th = trabecular thickness; Tb.N = trabecular number; Tb.Sp = trabecular spacing; E_Z = axial stiffness; ϵ_y = yield strain; σ_y = yield stress; ϵ_u = ultimate strain; σ_u = ultimate stress; U_T = modulus of resilience and K_C = toughness.

* denotes that the marked group and group A are significantly different ($p < 0.05$); denotes that the marked group and group B are significantly different ($p < 0.05$).