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Quantitative assessment of trabecular bone micro-architecture of the wrist via 7 Tesla MRI: preliminary results

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Abstract

Object—The goal of this study was to determine the feasibility of performing quantitative 7T magnetic resonance imaging (MRI) assessment of trabecular bone micro-architecture of the wrist, a common fracture site.

Materials and methods—The wrists of 4 healthy subjects (1 woman, 3 men, 28±8.9 years) were scanned on a 7T whole body MR scanner using a 3D fast low-angle shot (FLASH) sequence (TR/TE = 20/4.5ms, 0.169 × 0.169 × 0.5mm). Trabecular bone was segmented and divided into 4 or 8 angular subregions. Total bone volume (TBV), bone volume fraction (BVF), surface-curve

ratio (SC), and erosion index (EI) were computed. Subjects were scanned twice to assess measurement reproducibility.

Results—Group mean subregional values for TBV, BVF, SC, and EI (8 subregion analysis) were as follows: 8489 ± 3686 , 0.27 ± 0.045 , 9.61 ± 6.52 ; and 1.43 ± 1.25 . Within each individual, there was subregional variation in TBV, SC, and EI ($>5\%$), but not BVF ($<5\%$). Intersubject variation ($\sim 12\%$) existed for all parameters. Within-subject coefficients of variation were $\sim 10\%$.

Conclusion—This is the first study to perform quantitative 7T MRI assessment of trabecular bone micro-architecture of the wrist. This method could be utilized to study perturbations in bone structure in subjects with osteoporosis or other bone disorders.

Keywords

MRI; 7 Tesla; Ultra high field; Wrist; Trabecular bone; Micro-architecture; Osteoporosis

Introduction

Osteoporosis affects 10 million Americans resulting in 2 million fractures per year and \$17 billion in direct annual costs for fracture care [1]. The United States National Institutes of Health has defined it as a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture [2]. Although areal bone mineral density (BMD), as measured by dual-energy x-ray absorptiometry (DEXA) is the current standard-of-care test utilized to diagnose osteoporosis, it has limitations. For example, DEXA cannot account for other properties of bone that contribute to its ability to resist deformation, such as its geometry and micro-architecture. Indeed, only 50% of the variation in whole bone strength is attributable to variation in BMD [3, 4]. Furthermore, because DEXA is a 2-dimensional technique in which photons are projected onto a planar surface, BMD measurements can be rendered inaccurate secondary to vascular calcifications or osteophytes that overlie bone.

Over the last decade, high resolution (<0.2 mm in-plane) imaging techniques have proven to be powerful methods to identify the perturbations in trabecular bone micro-architecture in subjects with osteoporosis [5–8]. High resolution peripheral quantitative computed tomography (HRpQCT) can allow imaging of the distal radius and distal tibia with up to 81 micron isotropic voxel size [7, 8]. Magnetic resonance imaging (MRI), though unable to match the resolution of HRpQCT, can still image trabecular bone with up to 0.137micron in-plane spatial resolution [6] and has been used to detect trabecular bone micro-architectural changes in osteoporosis [5, 6], renal disease [9], estrogen supplementation [10], and in response to physical activity [11]. The arrival of high field (HF, ~ 3 T) and ultra high field (UHF, ~ 7 T) MR scanners with the inherent increased signal-to-noise ratio (SNR) available holds promise for imaging with increased spatial resolution and decreased scan times [12–16]. High spatial resolution allows for more accurate depiction of individual plates and rods that compose the trabecular bone micro-architectural network, and decreased scan times can decrease the chance for motion artifact in imaging examinations that aim to resolve submillimeter structures.

The wrist is a common site of fracture in osteoporotic patients [1]. High resolution MRI studies performed on conventional field strength scanners reveal decreased trabecular thickness, number, and connectivity and increased trabecular separation in osteoporotic patients compared with matched controls [5, 6]. To our best knowledge, only three studies have performed MRI of the wrist at UHF [17–19] and in these studies, quantitative assessment of trabecular bone microarchitecture was not performed. Therefore, the goal of this feasibility study was to perform MRI of the wrist at 7T and quantitative analysis of

trabecular bone micro-architecture. As a secondary goals, we also carried out subregional analysis of trabecular bone micro-architecture (by dividing the distal radius into angular segments) and we evaluated measurement reproducibility by scanning subjects twice. We hypothesized that subregional analysis might identify local variation in trabecular bone parameters. We also hypothesized that it would be possible to obtain good measurement reproducibility for trabecular bone parameters.

Materials and methods

Volunteers

This study had institutional review board approval, and written informed consent was obtained. Four healthy volunteers (1 woman, 21 years; 3 men, 33 ± 9.3 years) without history of trauma, surgery, arthropathy, or metabolic/endocrinologic disorder were recruited.

MRI Scanning

Subjects were scanned on a 7T whole body MR scanner (Siemens, Erlangen, Germany) in the prone position with the dominant wrist extended in front of them (“superman” position). We used an in-house constructed radiofrequency coil consisting of two curved “clamshell” sections. The initial use of this coil along with B1+ field maps and coil sensitivity/SNR maps was previously described [19]. Each clamshell section consists of an inner layer containing four overlapped 48-mm circular receive coils and an outer layer (15 mm above the inner layer) containing two 70-mm square overlapped transmit loop coils. Transmit power is split into four equal parts by a cascade of Wilkinson dividers and applied to the transmit loops with a birdcage-like phase relationship. The wrist was placed in between the two clamshell sections. Small foam pads used for routine clinical MRI scans were placed at volar and dorsal aspects of the wrist to minimize patient motion. Finally, the coil was secured to the table by Velcro straps.

Axial images of trabecular bone were obtained with a 3-dimensional fast low-angle shot (FLASH) sequence (TR/TE = 20/4.5ms, flip angle= 10° , bandwidth= 130Hz/ pixel, 30 axial images, FOV = 86×86 mm, matrix = 512×512 (resolution = 0.169×0.169 mm), 0.5 mm slice thickness, TA = 4min 6 s). Subjects were scanned two times (30min apart with re-positioning between scans) to determine measurement reproducibility (see Statistical Analysis below).

Image registration

Before image analysis, image registration was applied to the MR data sets in order to ensure that measurements were made in the same location for each subject. The algorithm utilized was based on the mutual information-based rigid-body registration technique [20]. In brief, the mutual information registration criterion states that the mutual information of the image intensity values of corresponding voxel pairs is maximal if the images are geometrically aligned [20]. After using this registration algorithm to ensure that measurement locations were as similar as possible, image analysis was then performed on the original datasets.

Segmentation and subregional division via principal components analysis

All images were made anonymous before image analysis. Trabecular bone of the distal radius was manually segmented on MR images using a two-dimensional graphical interface by drawing a boundary approximately 1 mm from the endosteal surface of cortical bone. Each manually segmented region of interest (ROI) was further subdivided into either four or eight angular subregions using a computerized algorithm as described in the following.

Let SI_i denote the set of pixels manually marked on the i th image slice as belonging to a specific ROI, and let cg_i denote the center of gravity of those pixels. In order to compensate for angular variations of positioning the patient's wrist with respect to the MR scanner coordinate system and patient-specific variations in the shape of ROI, a reference line is computed from a specific ROI using its 3D shape. First, the best fit line for the cg_i from different slices is computed and considered as the central axial line for the ROI; let L denote the central axial line. In order to standardize in-plane angular regions, the pixels within the manually drawn ROI are projected on a plane P orthogonal. The major axis of the projected points is computed by principle component analysis (PCA) and is used as the reference line for angular subdivision. Finally, the cylindrical space around the central axial line is divided into eight angular subregions with respect to the reference line. This process is schematically illustrated in Fig. 1a while division on one image slice into four and eight subregions is shown in Fig. 1b and c.

Generation of apparent bone volume fraction (BVF) maps

Bone volume fraction (BVF) images were then computed using a local marrow intensity computation approach without requiring a global thresholding. In a BVF image, pixel intensity corresponds to the fractional occupancy of bone. Total bone volume (TBV) was calculated based on the total number of pixels occupied by bone weighted by pixel intensity. Next, subvoxel processing was applied, in which voxels were subdivided and signal intensities were re-distributed among the subvoxels. This produces images with apparent higher spatial resolution.

Digital topological analysis (DTA) image and quantitative assessment of topology

Digital topological analysis [21, 22] is a fully three-dimensional method that accurately determines the topological class (e.g., surfaces, curves, junctions, and edges) of each individual location in a digitized structure that has been applied for quantifying quality of trabecular bone architectural make-up [22]. Before applying DTA, a binarized trabecular bone image is skeletonized to a network of one- and two-dimensional structures representing rods and plates, respectively. DTA involves three steps; the first one is inspecting each bone voxel's 26 neighborhood (i.e., the voxels within the $3 \times 3 \times 3$ kernel) and computation of the numbers of objects, tunnels, and cavities under a hypothetical conversion of the central voxel to marrow. A partial classification of each bone voxel is determined from these three numbers using a look-up-table for an idealized network of surfaces and curves. A unique topological classification is then achieved using the results of partial classification and another look-up-table solving for local topological ambiguities in digital manifolds and their junctions [21, 22]. These topological classes are used to compute several topological parameters for trabecular bone networks. We focused on two specific parameters, namely, the SC ratio and the erosion index (EI). The SC ratio represents the trabecular plate to rod ratio, which has clinical importance, being known to decrease in subjects with osteoporosis [5, 6]. The EI is a surrogate of network connectivity and represents the ratio of parameters expected to increase during osteo-clastic resorption (curve, curve-edge, surface-edge, profile-edge, curve-curve junctions) relative to those expected to decrease (surface and surface-surface). A higher EI indicates a decrease in network connectivity. In subjects with osteoporosis, connectivity between rods has been shown to decrease [5, 6].

Statistical analysis

Statistical analysis was performed using SPSS (Chicago, Illinois). For each individual, mean values (of the two scans) for TBV, BVF, SC, and EI were computed for the distal radius analyzed: (1) as a whole ROI, (2) as 4 subregions, and (3) as 8 subregions. Mean subregional values and standard deviations for TBV, BVF, SC, and EI were calculated. Within a given individual, the percent variation across subregions (Var) was calculated as

the subregional standard deviation divided by the subregional mean multiplied by 100. For the group, mean values and standard deviations for TBV, BVF, SC, and EI were also computed for the wrist analyzed: (1) as a whole ROI, (2) as 4 subregions, and (3) as 8 subregions. The percent biological variation across subjects (BVar) was calculated as the group standard deviation divided by the group mean multiplied by 100. As subjects were scanned twice, measurement reproducibility for the whole radius was assessed by computing the within-subject root mean square coefficient of variation and the intraclass correlation coefficient.

Results

Representative axial 7T MR images of trabecular bone of the wrist from each subject are shown in Fig. 2a to d. A co-registered image from scans 1 and 2 for a subject is shown in Fig. 3. For each subject, TBV, BVF, surface-curve (SC) ratio, and EI are shown in Table 1 for the distal radius analyzed: (1) as a whole ROI, (2) as 4 subregions, and (3) as 8 subregions. The results show that within each individual, there is subregional variation in TBV, surface-curve ratio, and EI, but not in BVF (<5%) (Table 1). For the group as a whole, biological variation between subjects was detected for all parameters whether the wrist was analyzed as one whole ROI or analyzed on a subregional level (Table 2). There was good measurement reproducibility for TBV, BVF, surface-curve ratio, and EI as assessed by a within-subject root mean square coefficient of variation 10% and an intraclass correlation coefficient 0.91 (Table 3).

Discussion

This study demonstrates for the first time the feasibility of performing quantitative assessment of trabecular bone micro-architecture of the wrist via 7T MRI. This study also provides evidence that subregional variation in trabecular bone micro-architecture of the wrist may exist, even in healthy subjects. Altogether, this method may represent a new means by which to study pathologic alterations in bone structure of the wrist, which is a common site of fracture.

The main advantage of scanning at UHF is the increased intrinsic signal available. In general, in an MR experiment, the signal from the sample is proportional to the square of the static magnetic field (B_0^2). By treating the coil and sample as resistors in series, SNR can be given by the equation:

$$\frac{\text{Signal}}{\text{Noise}} = \frac{B_0^2}{\text{Noise}_{\text{coil}} + \text{Noise}_{\text{sample}}} = \frac{B_0^2}{\sqrt{aB_0^{1/2} + bB_0^2}}$$

where the terms $aB_0^{1/2}$ and bB_0^2 represent the contributions from coil noise and sample noise, respectively [23, 24]. With increasing field strength, sample noise predominates over coil noise, and as a result, SNR scales approximately linearly with B_0 . (For a more thorough treatment of SNR at UHF, see reference [24].) The increased SNR of UHF can be translated into increased spatial resolution and scanning speed, and improved ability to detect low gamma nuclei (^{23}Na , ^{31}P , ^{13}C). Numerous technical obstacles exist to scanning at UHF, including changes in T1 and T2 relaxation rates (increase in T1 and decrease in T2), maintenance of B_1 field homogeneity, increased chemical shift and susceptibility artifact, and greater acoustic noise and energy deposition. However, the increase in number of

publications describing UHF musculoskeletal MRI over the last few years provides evidence that these technical obstacles are surmountable [11, 14, 17–19, 25–28].

The wrist imaging performed in this study could be similarly performed on any 7T scanner. For patient positioning, we used the “superman position” (patient prone with wrist extended above the head). This is used routinely for clinical wrist MRI examinations. We also followed clinical wrist MRI protocols in that we placed foam pads at the volar and dorsal aspects of the wrist to reduce patient motion. The chance for motion artifact was also likely reduced because the image acquisition time was only 4 min 6s, whereas typical trabecular bone imaging exams on conventional field strength scanners last approximately 15–25 min. 7T coils are not widely available, and the clamshell 8 channel receive coil we used was custom-made in-house [19]. However, as 7T scanners become more widely available, vendors are more likely to manufacture coils for imaging body parts, such as the wrist.

BMD, as measured by DEXA, is the current imaging standard utilized by clinicians to diagnose osteoporosis, assess fracture risk, and determine whether antiresorptive therapy should be initiated. However, BMD has numerous limitations. There is a tenfold increase in fracture risk with aging that is independent of BMD [29], and the majority of patients who suffer fractures do not meet BMD criteria for osteoporosis [30]. Trabecular bone is a major contributor to bone strength, and bone biopsy studies have shown that trabecular bone micro-architecture is deranged in subjects with osteoporosis [5, 6]. Over the last decade, great effort has been devoted to the development of non-invasive imaging techniques to quantitatively assess trabecular bone micro-architecture in vivo [5, 6].

The plates and rods that compose the trabecular bone micro-architectural network are less than 200 microns in dimension. Thus, to adequately resolve these structures, high-resolution images are required ($0.169 \times 0.169 \times 0.5$ mm in this study), which in turn demands imaging under high SNR conditions. Trabecular bone imaging is therefore greatly facilitated by the move to higher field strength. A few studies have evaluated trabecular bone micro-architecture of the knee and ankle at 7T [11, 25, 26], and in one of these studies, 7T MRI was able to detect subtle changes in trabecular bone micro-architecture between a group of Olympic athletes and healthy controls [11].

Even though MRI of trabecular bone micro-architecture of the distal radius has been performed successfully at conventional field strength for several years [5, 6], a similar situation was present for the knee and ankle a few years ago. Trabecular bone imaging in these locations was also already being successfully performed at 1.5 and 3T [31–33]. The benefit of 7T for imaging of trabecular bone remains to be determined, but this may ultimately reside in the ability to image non-peripheral locations, such as the hip and spine, where osteoporotic fractures frequently occur and have great morbidity [1]. In these locations, overcoming increased specific absorption rate (SAR) will remain a challenge since SAR is proportional to B_0^2 and since these locations are near abdominal and pelvic organs that have high energy absorption because of their dielectric properties [24]. Nevertheless, the construction of a 7T wrist coil and the performance of 7T wrist trabecular bone imaging represent perhaps initial steps toward making hip and spine imaging at 7T possible.

Subregional analysis of trabecular bone has been applied to study local bone micro-architectural alterations in the knee of subjects with osteoarthritis [31, 33, 34]. These studies, which were carried out at 1.5 and 3 T, demonstrated differences in trabecular bone micro-architecture in the medial knee compartment compared with the lateral compartment. Furthermore, the trabecular bone changes correlated with changes in cartilage parameters. The results of our study provide evidence that subregional variation in trabecular bone

micro-architecture of the wrist may exist, even in healthy subjects. This subregional variation is unlikely to be due to poor measurement precision, as the within-subject coefficients of variation were low and intraclass correlation coefficients were high. The presence of local variation in trabecular bone micro-architecture may have implications for the prediction of fracture risk and fracture location in subjects with osteoporosis. For example, if bone quality is locally decreased within a certain portion of the distal radius, this may represent the location where a person is more likely to sustain a fragility fracture.

We note that in this study there is high inter-subject variation for the trabecular bone parameters (BVar, Table 2). The likely explanation for this is that there is normal variation in bone quality even among healthy subjects. Just as healthy subjects can have differences in macroscopic bone structure such as femur length, diameter, or cross-sectional area, they are likely to have differences in bone micro-architecture. In addition, although the subjects did not have a known medical disorder and did not use medication, differences in nutrition or physical activity levels could result in differences in bone quality. As one specific example, subject number 4 had a high whole radius SC (17.52) compared with subjects number 2 (9.23) and 3 (9.76), even though all of these subjects had similar BVF (0.28–0.3). Since SC decreases in subjects with osteoporosis [6], it would appear that subject number 4 might have improved bone quality compared with subjects number 2 and 3. This is purely a conjecture. The results raise the possibility that topological parameters of trabecular bone micro-architecture provide additional, complementary information about bone quality not provided by BVF [6, 35].

This study has several limitations. Firstly, the number of subjects scanned was low. As a result, the values of the trabecular bone measures obtained likely do not necessarily reflect those of the general population. Secondly, we did not perform a comparison with trabecular bone measures obtained at conventional field strength (1.5 or 3T), nor did we perform a comparison with a reference standard such as microcomputed tomography. This will be an important step to validate 7T measurements and determine if comparisons can be made between field strengths. Thirdly, we used a gradient-echo to image trabecular bone. Gradient-echo-based sequences have been extensively utilized at 1.5 and 3T, and more recently at 7T to image trabecular bone [5, 26, 31, 33, 36]. However, they have the disadvantage of greater sensitivity to off-resonance effects from magnetic field inhomogeneity and chemical shift dispersion. This can result in artifactual broadening of the trabecular bone signal void. Spin-echo-based sequences, such as 3D fast large-angle spin-echo (3D FLASE), are less sensitive to off-resonance effects and at conventional field strength can provide a resolution of $0.137 \times 0.137 \times 0.4$ mm in vivo [6, 15]. Recently, a spin-echo sequence has been successfully adapted for use at 7T (3D fast spin-echo with out-of-slab cancellation through phase alternation, 3D FSE-OSC) [16, 27]. This may allow even more accurate imaging of trabecular bone at 7T to be possible. As a final limitation, we did not scan any subjects with osteoporosis as we felt this was beyond the scope of this feasibility study. Therefore, we cannot comment on whether high resolution MRI of the wrist at 7T can discriminate between subjects with and without bone disorders. However, this has been demonstrated for high resolution MRI of the wrist at 1.5T [35, 37]. Also, as mentioned above, high resolution MRI of the distal femur/proximal tibia at 7T is capable of detecting statistically significant improvements in trabecular bone micro-architecture in a group of elite athletes compared with matched controls [11].

Conclusion

In conclusion, we demonstrate the feasibility of performing quantitative analysis of trabecular bone micro-architecture of the wrist via 7T MRI with good measurement precision (within-subject coefficient of variation 10% and intra-class correlation coefficient

0.91). This analysis can be performed in a subregional fashion, and the results suggest that local variations in trabecular bone micro-architecture may exist even in healthy subjects. In the future, this method could be used to provide further insight into the trabecular bone micro-architectural abnormalities that exist in subjects with osteoporosis. It could also be used to study the pathogenesis of other musculoskeletal disorders that affect the bones of the wrist, such as rheumatoid arthritis.

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Fig. 1.

a Illustration demonstrating the angular subregional (R) division of the distal radius around a major axis reference line computed by principal components analysis (PCA). ROI = Region of interest. **b** Computed angular subdivisions (4) on one image slice of a manually drawn ROI on an MR data set. **c** Computed angular subdivisions (8) on one image slice of a manually drawn ROI on an MR data set

Fig. 2.

a Subject 1 (S1): representative axial 7T MR image of the wrist (TR/TE = 20/5.1 m s, 0.169×0.169 mm, 0.5 mm slice thickness, 30 axial images acquired in 4min 6s). **b** Subject 2 (S2): same scanning parameters as for Subject 1. **c** Subject 3 (S3): same scanning parameters as for Subject 1. **d** Subject 4 (S4): same scanning parameters as for Subject 1

Fig. 3. Axial 7T MR images of the wrist of one subject from scan number 1 (*left panel*) and scan number 2 (*middle panel*), followed by a co-registered image (*right panel*)

Table 1
Mean values (of two measurements) for total bone volume (TBV), bone volume fraction (BVF), surface-curve ratio (SC), and erosion index (EI) for the distal radius analyzed: (1) as a whole ROI, (2) as 4 subregions, and (3) as 8 subregions

	TBV	Var (%)	BVF	Var (%)	SC	Var (%)	EI	Var (%)
<i>Radius as a whole</i>								
Subject 1	46,478 ± 856	1.8	0.20 ± .002	1	1.69 ± 0.18	10.6	2.94 ± 0.15	5.1
Subject 2	63,245 ± 214	0.3	0.28 ± 0.006	2.1	9.76 ± 0.1	1	0.84 ± 0.02	2.3
Subject 3	136,752 ± 1,970	1.4	0.29 ± 0.016	5.5	9.23 ± .3	3.3	0.93 ± 0.09	9.6
Subject 4	98,069 ± 3,569	3.6	0.30 ± 0.008	2.6	17.52 ± 1.92	10.9	0.64 ± 0.034	5.3
<i>Mean subregional values (radius divided into 4 subregions)</i>								
Subject 1	10,042 ± 1,753	17	0.20 ± 0.008	4.1	1.69 ± 0.39	23	3.18 ± 0.92	29
Subject 2	13,323 ± 3,652	27	0.28 ± 0.011	3.9	9.83 ± 2.23	23	0.86 ± 0.097	11.3
Subject 3	25,816 ± 12,498	48	0.28 ± 0.0017	0.6	9.15 ± 0.9	9.8	0.92 ± 0.04	4.3
Subject 4	20,212 ± 3,918	19	0.30 ± 0.008	2.6	17.8 ± 2.03	11	0.63 ± 0.038	5.9
<i>Mean subregional values (radius divided into 8 subregions)</i>								
Subject 1	5,021 ± 1,991	39	0.19 ± 0.007	3.7	1.66 ± 0.39	24	3.31 ± 0.93	28
Subject 2	5,921 ± 2,325	39	0.28 ± 0.013	4.6	9.96 ± 2.26	23	0.86 ± 0.096	11
Subject 3	12,908 ± 6,950	54	0.28 ± 0.003	1	9.21 ± 1.1	12	0.93 ± 0.048	5.2
Subject 4	10,106 ± 4,099	41	0.30 ± 0.01	3.2	17.62 ± 2.3	13	0.64 ± 0.041	6.4

For the 4-subregion and 8-subregion analysis, mean subregional values and the percent variation across subregions (Var) are reported. For the distal radius analyzed as a whole, Var represents the coefficient of variation for the two measurements for each subject

Table 2

Group mean values (including both measurements for each subject) and biological variation across the group (BVar) for total bone volume (TBV), bone volume fraction (BVf), surface-curve ratio (SC), and erosion index (EI) for the distal radius analyzed: (1) as a ROI, (2) as 4 subregions (SR), and (3) as 8 subregions

Group mean values	TBV	BVar (%)	BVF	BVar (%)	SC	BVar (%)	EI	BVar (%)
<i>Radius as a whole</i>	86,136 ± 40,004	46	0.27 ± 0.049	18	9.53 ± 6.46	67	1.33 ± 1.07	80
<i>Radius as 4 subregions</i>	17,348 ± 7,058	40	0.26 ± 0.045	17	9.62 ± 6.58	68	1.40 ± 1.19	85
SR1	14,978 ± 5,334	35	0.28 ± 0.041	15	9.96 ± 6.28	63	1.14 ± 0.71	63
SR2	23,967 ± 15,032	63	0.28 ± 0.045	16	11.34 ± 7.5	66	1.26 ± 1.05	83
SR3	14,027 ± 5,118	36	0.27 ± 0.04	15	9.84 ± 7.06	71	1.3 ± 1.06	81
SR4	18,017 ± 7,031	39	0.27 ± 0.03	12	8.7 ± 5.59	64	1.1 ± 0.52	48
<i>Radius as 8 subregions</i>	8,489 ± 3,686	43	0.27 ± 0.045	17	9.61 ± 6.52	67	1.43 ± 1.25	87
SR1	9,680 ± 3,659	38	0.27 ± 0.043	16	9.53 ± 6.02	63	1.21 ± 0.77	64
SR2	4,978 ± 1,701	34	0.27 ± 0.053	20	10.34 ± 6.35	61	1.35 ± 1.18	87
SR3	9,359 ± 6,495	69	0.27 ± 0.056	21	11.15 ± 7.99	71	1.55 ± 1.62	104
SR4	14,100 ± 8,073	57	0.26 ± 0.05	19	10.69 ± 7.45	69	1.39 ± 1.24	89
SR5	8,481 ± 4,137	49	0.27 ± 0.05	19	9.88 ± 8.16	82	1.86 ± 2.13	115
SR6	5,209 ± 1,982	38	0.26 ± 0.043	17	8.87 ± 5.81	66	1.48 ± 1.34	90
SR7	6,229 ± 2,234	36	0.26 ± 0.04	15	8.01 ± 5.49	68	1.46 ± 1.16	79
SR8	11,353 ± 5,541	49	0.26 ± 0.03	12	8.43 ± 5.48	65	1.16 ± 0.59	51

Table 3
Measurement reproducibility for the whole radius, radius as 4 subregions, and radius as 8 subregions, as assessed by the within-subject root mean square coefficient of variation (RMS-CV) and the intraclass correlation coefficient

	TBV	BVF	SC	EI
<i>Radius as a whole</i>				
Within-subject RMS-CV	0.021	0.022	0.08	0.079
Intraclass correlation coefficient	0.99	0.95	0.94	0.98
<i>Radius as 4 subregions</i>				
Within-subject RMS-CV				
SR1	0.031	0.018	0.038	0.051
SR2	0.037	0.019	0.06	0.06
SR3	0.035	0.024	0.082	0.023
SR4	0.033	0.022	0.032	0.032
Intraclass correlation coefficient				
SR1	0.99	0.96	0.97	0.98
SR2	0.99	0.97	0.95	0.99
SR3	0.99	0.96	0.99	0.98
SR4	0.99	0.95	0.99	0.94
<i>Radius as 8 subregions</i>				
Within-subject RMS-CV				
SR1	0.032	0.024	0.086	0.07
SR2	0.019	0.021	0.021	0.051
SR3	0.045	0.025	0.064	0.05
SR4	0.025	0.035	0.041	0.057
SR5	0.026	0.029	0.042	0.016
SR6	0.029	0.026	0.074	0.039
SR7	0.029	0.029	0.06	0.08
SR8	0.022	0.026	0.098	0.07
Intraclass correlation coefficient				
SR1	0.99	0.95	0.92	0.97
SR2	0.98	0.96	0.97	0.98
SR3	0.99	0.97	0.97	0.99
SR4	0.99	0.96	0.96	0.99
SR5	0.99	0.95	0.99	0.99
SR6	0.99	0.95	0.98	0.98
SR7	0.99	0.95	0.99	0.97
SR8	0.99	0.91	0.98	0.98