

Feasibility of T and Z Scores From Magnetic Resonance Imaging Data for Quantification of Cartilage Loss in Osteoarthritis

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Objective. T scores (an indicator of the difference between patients and young healthy subjects) and Z scores (an indicator of the difference between patients and age-matched healthy subjects) are used in the diagnosis of osteoporosis and form the current basis for the definition of osteoporosis by the World Health Organization. We tested the feasibility of using T and Z scores derived from quantitative cartilage imaging with magnetic resonance imaging (MRI) for the diagnosis of osteoarthritis (OA).

Methods. High-resolution MR images of tibial cartilage were acquired from 126 young healthy adults (ages 20–35 years), 24 age-matched elderly healthy adults (ages 50–75 years), 7 OA patients prior to tibial osteotomy, and 7 OA patients prior to knee arthroplasty. Cartilage volume, thickness, surface area, and original joint surface area (before onset of disease) were determined in the medial and lateral tibia.

Results. The cartilage volume of the medial tibia of osteotomy patients with varus malalignment displayed moderate T scores (–1.0), and more negative T scores (–3.8) were observed in knee arthroplasty patients with varus malalignment. Normalization of the cartilage volume to the original joint surface area

substantially enhanced the scores in patients undergoing osteotomy (–2.3) and in patients undergoing knee arthroplasty (–5.5), and this was superior to the normalization ratios of cartilage volume to body height and cartilage volume to body weight, in terms of distinguishing the loss of articular cartilage.

Conclusion. Quantitative analysis of OA by MRI is feasible using T and Z scores. However, cartilage volume should be normalized to the individual joint surface area in order to maximize the discriminatory power of this technique for the diagnosis of OA.

In osteoporosis, deviations of bone density in patients versus normal subjects are generally expressed in terms of T scores and Z scores. These scores quantify the difference between the patients' values and the mean values in young healthy adults (T score) or in age-matched healthy adults (Z score) of the same sex, by dividing this difference by the standard deviation of the respective reference group. T scores currently form the basis for the operational diagnosis of osteoporosis by the World Health Organization (1), with thresholds defined as follows: a bone mineral density value (T score) of –1.0 to –2.5 SD below the mean value for young healthy adults is defined as osteopenia, and a score of less than –2.5 SD below the mean for young healthy adults is defined as osteoporosis. This system is now widely accepted in the management of osteoporotic bone loss (2).

In osteoarthritis (OA), diagnosis is currently based on systems of scoring the extent of pain and ability to function (e.g., the Western Ontario and McMaster Universities OA Index) or on radiographic findings (e.g., the Kellgren and Lawrence score). However, no validated, quantitative diagnostic approach currently exists that is based directly on the target tissue in OA, i.e., loss

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of articular cartilage. Magnetic resonance imaging (MRI) can delineate articular cartilage directly (3) and therefore represents a promising tool for quantifying cartilage loss in OA. In contrast to measurements of joint space width on radiographs, MR-based analysis of cartilage morphology is not confined in accuracy to the medial femorotibial compartment (4), is not affected by meniscal subluxation (5,6), and permits determination of the spatial distribution of cartilage loss within the joint surface (3,7). High-resolution T1-weighted, fat-suppressed or water-excitation gradient echo sequences have been shown to provide accurate data on cartilage volume and thickness in healthy joints (8) and were also recently validated in the joints of patients with severe OA prior to knee arthroplasty (7). A relatively large intersubject variability of normal cartilage volume has been reported in young healthy adults (9) and elderly healthy subjects (10). Because in a cross-sectional study, it is unknown whether the patient has displayed high or low cartilage volume before the onset of disease, this lack of information poses potential difficulties in retrospectively estimating the amount of cartilage tissue lost between the onset of disease and the time of investigation.

In this study, we tested the feasibility of utilizing T and Z scores for the diagnosis of OA in the context of quantitative cartilage imaging with MRI. Because a substantial percentage of the variability of cartilage volume is determined by the joint surface area, and because only a moderate correlation exists between cartilage volume and body height or body weight (9), we tested the following hypothesis: normalization of cartilage volume to the original joint surface area (before onset of disease) can reduce the intersubject variability among healthy adults and thus displays higher discriminatory ability (more negative T and Z scores) for distinguishing between patients and healthy adults than does cartilage volume alone or than does normalization of cartilage volume to body weight or to body height.

PATIENTS AND METHODS

We investigated the knee joints of 126 young healthy adults (50 women, 76 men, ages 20–35 years) and of 24 elderly (age-matched) healthy adults (13 women, 11 men, ages 50–75 years) (10). The subjects had no history of knee pain, knee trauma, knee surgery, ligament or meniscal injuries, or generalized disease of the musculoskeletal system. Subjects with cartilage lesions on the MR images had been excluded from the healthy reference groups (10). The age, body weight, and body height of the healthy adults are summarized in Table 1.

The patient cohort consisted of a group of 7 individuals with clinical indications for a high tibial osteotomy (6 with varus malalignment [range 6–15°] and 1 with valgus malalign-

ment [3°]), of whom 3 were women and 4 were men (ages 22–56 years). The knee angle was defined as the angle between the biomechanical axes of the femur and tibia. The other patient group comprised 7 individuals with a clinical indication for total knee arthroplasty (TKA) (5 with varus malalignment [range 9–18°], 1 with valgus malalignment [6°], and 1 with bicompartamental [medial and lateral] OA [2° varus]), of whom 5 were women and 2 were men (ages 60–85 years) (7).

Among the women in the osteotomy group, the mean $\pm$ SD body weight was 86.7 ± 15.3 kg, and the mean $\pm$ SD body height was 166.7 ± 5.8 cm. Among the men in the osteotomy group, the respective values for body weight and height were 89.3 ± 21.2 kg and 169.5 ± 6.1 cm. Among the women in the TKA group, the mean $\pm$ SD body weight was 77.0 ± 15.2 kg, and the mean $\pm$ SD body height was 164.0 ± 4.8 cm. Among the men in the TKA group, the respective values for body weight and height were 78.5 ± 4.9 kg and 169.0 ± 1.4 cm. Informed written consent was obtained from all subjects. The study protocol was ratified by the local ethics committee.

MRI was performed with a 1.5T magnet (Magnetom Vision; Siemens, Erlangen, Germany) and a circular polarized transmit–receive extremity coil. All subjects were investigated with the same type of MR sequence (spoiled, 3-dimensional [3D] gradient-echo sequence [fast low-angle shot] with selective water excitation; radiofrequency amplitude ratios 1:2:1; time to recovery 17.2 msec, time to echo 6.6 msec; flip angle 20°) (7,8,11). Sagittal data sets were acquired from 110 (42 women and 68 men) of the 126 young healthy volunteers (50 women and 76 men) and from all 24 elderly volunteers (section thickness 1.5 mm; in-plane resolution $0.31 \text{ mm} \times 0.31 \text{ mm}$; field of view 160 mm; matrix 512^2 pixels; acquisition time 9 minutes). Coronal data sets (7,11) were obtained from 16 young healthy adults (8 women and 8 men) (section thickness 1.2–1.5 mm; in-plane resolution $0.31 \text{ mm} \times 0.31 \text{ mm}$; acquisition time 6 minutes) and from all of the OA patients. We have previously shown that these protocols permit high precision of quantitative cartilage analysis in healthy subjects and in OA patients (7,8,11,12), and that the cartilage volume derived from preoperative in vivo imaging is consistent with the tissue volume of surgically removed cartilage (7).

All MRI data were transferred digitally to a workstation (Octane Duo; Silicon Graphics, Mountain View, CA). A semiautomated B-spline snake algorithm was used for the segmentation of the medial and lateral tibial cartilages (13). The cartilage volume of the tibial cartilage was computed by numeric integration of the voxels assigned to the medial and lateral cartilage plates during this process (3), and the mean and maximal thickness were determined 3-dimensionally, independent of the original section orientation, with a 3D Euclidean distance transformation (EDT) algorithm (12). The size of the bone cartilage interface area and of the joint surface area were determined with a triangulation algorithm (14). Note that in the patients, the EDT algorithm computes the thickness of the remaining cartilage plate, but does not account for the absence of thickness (zero thickness) of denuded cartilage areas. In order to account for the zero thickness of denuded areas, the cartilage volume is normalized to the “original” (before the onset of OA) size of the joint surface area.

Table 1. Quantitative cartilage parameters of the medial and lateral tibia in young healthy adults and age-matched healthy volunteers (total of 150)*

	Medial tibia							Lateral tibia									
	Age, years	BW, kg	BH, cm	Maximum thickness, mm	Mean thickness, mm	Volume, mm ³	Volume, BW ratio, mm ³ /kg	Volume, BH ratio, mm ³ /cm	Volume, SA ratio, mm ³ /mm ²	Maximum thickness, mm	Mean thickness, mm	Volume, mm ³	BW ratio, mm ³ /kg	BH ratio, mm ³ /cm	Volume, SA ratio, mm ³ /mm ²		
Women																	
Young adults (n = 50)																	
Mean	25.1	59.9	168.5	3.8	1.6	1,977	33.4	11.7	2.0	4.6	2.0	2,392	40.5	14.2	2.4		
SD	3.3	7.4	5.8	1.0	0.2	295	5.5	1.6	0.2	0.7	0.2	351	8.0	2.2	0.3		
CV, %	13	12	3	27	13	15	16	14	12	15	12	15	20	15	11		
Age-matched adults (n = 13)																	
Mean	62.2	65.3	163.8	3.3	1.4	1,640	25.2	10.0	1.7	3.8	1.8	2,017	30.7	12.3	2.1		
SD	9.8	7.9	8.2	0.7	0.3	298	3.8	1.5	0.3	0.9	0.2	456	4.6	2.8	0.3		
CV, %	16	12	5	20	19	18	15	15	15	23	14	23	15	23	13		
Men																	
Young adults (n = 76)																	
Mean	26.0	77.1	180.3	4.2	1.8	2,924	39.3	16.3	2.2	5.2	2.3	3,489	46.7	19.4	2.7		
SD	3.6	10.8	6.8	1.0	0.3	631	9.0	3.5	0.3	0.8	0.3	670	9.4	3.5	0.3		
CV, %	14	14	4	23	14	22	23	21	12	15	12	19	20	18	11		
Age-matched adults (n = 11)																	
Mean	59.1	80.6	175.1	3.4	1.6	2,338	29.8	13.3	2.0	3.7	1.9	2,806	35.5	16.0	2.3		
SD	5.4	13.4	4.2	0.8	0.3	363	6.9	2.1	0.3	0.6	0.3	402	7.0	2.2	0.3		
CV, %	9	17	2	23	17	16	23	16	15	16	16	14	20	14	14		

* BW = body weight; BH = body height; SA = articular surface area; CV = coefficient of variation in the sample.

Table 2. T and Z scores in patients undergoing tibial osteotomy (OT) (n = 7) and in patients undergoing total knee arthroplasty (TKA) (n = 7)*

	Medial tibia						Lateral tibia					
	Maximum thickness	Mean thickness	Volume	Volume: BW ratio	Volume: BH ratio	Volume: SA ratio	Maximum thickness	Mean thickness	Volume	Volume: BW ratio	Volume: BH ratio	Volume: SA ratio
Tibial OT												
Varus (n = 6)												
T score	-0.7	-0.7	-1.0	-2.1	-0.9	-2.3	-0.5	-0.2	-1.2	-2.1	-1.1	-0.7
Valgus (n = 1)												
T score	-1.3	-1.9	-1.0	-1.7	-1.1	-2.0	-2.4	-3.9	-3.4	-2.9	-3.2	-4.2
TKA												
Varus (n = 5)												
T score	-1.3	-2.2	-3.8	-4.0	-4.0	-5.5	-1.8	-2.5	-2.7	-2.8	-2.5	-4.5
Z score	-1.1	-1.0	-3.0	-3.7	-3.4	-4.0	-0.4	-1.5	-1.7	-2.6	-1.5	-3.2
Valgus (n = 1)												
T score	0.3	-0.8	-1.8	-1.3	-1.6	-3.2	-2.5	-3.0	-3.9	-2.8	-3.6	-4.8
Z score	1.2	0.2	-0.6	0.4	-0.5	-2.0	-1.0	-1.9	-2.2	-2.7	-2.1	-3.5
Bicompartmental												
OA varus (n = 1)†												
T score	-2.0	-3.2	-3.7	-3.5	-3.6	-6.3	-2.6	-2.8	-3.8	-3.7	-3.9	-6.1
Z score	-1.4	-2.1	-4.7	-3.2	-4.6	-5.0	-0.9	-1.4	-4.6	-3.5	-4.7	-4.5

* Among the tibial OT group, varus malalignment was a mean $\pm$ SD $9 \pm 3.3^\circ$ and valgus was 3° . Among the TKA group, varus malalignment was a mean $\pm$ SD $12.2 \pm 3.9^\circ$, valgus was 6° , and the bicompartmental OA was 2° varus. See Table 1 for other definitions.

† Presence of osteoarthritis (OA) in the medial and lateral femorotibial compartment.

The original medial and lateral tibial plateau surface area was segmented in a separate step by tracing the subchondral bone contours of the tibia. This segmentation process included denuded areas as well as the bone cartilage interface of the remaining cartilage, but did not include osteophyte surfaces. Repeated analysis from 4 separate scans (after repositioning of the joint) in 5 TKA patients revealed a root mean square (RMS) average SD of 30 mm^2 (RMS average coefficient of variation [CV] 2.6%) for the original joint surface area of the lateral tibia and an RMS average SD of 46 mm^2 (CV 5.1%) for that of the medial tibia, with the coefficients for the ratios of volume to original surface areas of the lateral and medial tibias being in the same range (RMS average CVs 3.5% and 5.9%, respectively). Finally, normalization of cartilage volume to joint surface area was compared with normalization of cartilage volume to body weight as well as cartilage volume to body height.

Potential systematic differences between sagittal and coronal image data in healthy young adults were assessed in women and men, using an unpaired *t*-test, with the level of significance being set at 1%. The patient data were compared with those from young healthy subjects and, if appropriate, also with those from age-matched (elderly) healthy subjects of the same sex. The absolute difference was divided by the SD of the mean value in the normal volunteers, to compute the T and Z score for each patient (2).

RESULTS

The normal values for quantitative cartilage parameters in the medial and lateral tibia of healthy young adult women and men (ages 20–35 years) and of healthy age-matched elderly subjects (ages 50–75 years) are

displayed in Table 1. With the exception of the maximal thickness of the medial tibia in the women, there was no significant difference between the sagittal and coronal data, and therefore these values were pooled. As shown previously (10,15), the women displayed smaller values for cartilage thickness and volume than did the men, and the elderly subjects displayed smaller values than did the young healthy adults. The variability in cartilage volume was effectively reduced when being normalized to the joint surface area, and this normalization was more effective than was normalization to body weight or body height (Table 1).

The average T score in osteotomy patients with varus malalignment was -1.0 for the cartilage volume of the medial tibia and -0.7 for the cartilage thickness. The score was substantially enhanced (rendered more negative) when cartilage volume was normalized to the original joint surface area (-2.3) (Table 2). After normalization, 3 patients displayed scores that were more negative than -2.5 (-2.8 to -5.1) and 3 patients exhibited more positive scores (-1.3 to -0.3), whereas before normalization, only 1 patient had displayed a value of less than -2.5 . Normalization to body weight and body height did not enhance T scores as effectively as did normalization to joint surface area (Table 2). Because 3 of the osteotomy patients were relatively young (ages 22, 35, and 40 years, respectively), no Z scores were computed for this group of patients. The

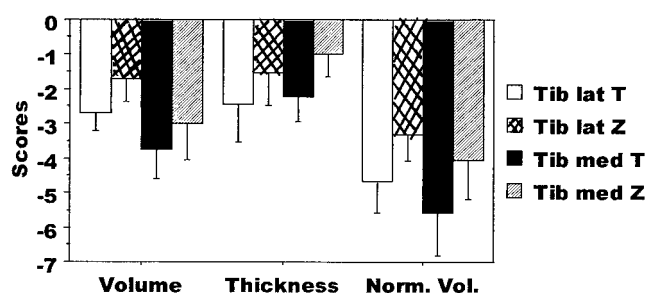


Figure 1. T and Z scores in the lateral tibia (Tib lat T and Tib lat Z, respectively) and medial tibia (Tib med T and Tib med Z, respectively) for cartilage volume, cartilage thickness (of the remaining cartilage plate), and cartilage volume normalized to the original joint surface area (Norm. Vol.) among the 5 patients with severe varus osteoarthritis prior to total knee arthroplasty. Bars show the mean and SD.

T score for the osteotomy patient with valgus malalignment was also substantially enhanced—in this case for the lateral tibial compartment—when cartilage volume was normalized to the original joint surface area (from -3.4 to -4.2 ; see Table 2).

Average T and Z scores for TKA patients with varus OA amounted to -3.8 and -3.0 , respectively, for the cartilage volume of the medial tibia, -2.2 and -1.0 , respectively, for the cartilage thickness, and -5.5 and -4.0 , respectively, for the normalized cartilage volume (Table 2 and Figure 1). After normalization to the joint surface area, all TKA patients displayed T scores (range -3.8 to -6.5) and Z scores (range -2.9 to -4.9) that were more negative than -2.5 . As expected, the T and Z scores in the lateral tibia were smaller than those in the medial tibia among the patients with varus OA (Table 2 and Figure 1), with the Z score being more negative than -2.5 in only 2 of the 5 patients.

The TKA patient with valgus OA displayed more negative scores at the lateral tibia than at the medial tibia, whereas the patient with bicompartamental OA showed highly negative scores at both the medial and the lateral side (Table 2). Again, normalization to body weight and body height was not as effective as normalization to the original joint surface area among these patients (Table 2).

DISCUSSION

In this pilot study we have shown that quantitative parameters of articular cartilage, as derived from high-resolution MR images, can be effectively used to apply a T and Z score system to quantitative assessment of OA. This study does not intend to systematically

investigate the amount of tissue loss at various stages of OA. For this latter purpose, the number of investigated patients would have to be higher, and patient groups would have been selected according to more stringent radiographic OA criteria. In contrast, our objective was to test the hypothesis that a T and Z score system can be successfully applied to patients with a clinical indication for joint surgery (tibial osteotomy or knee arthroplasty), and that normalization of cartilage volume to the original joint surface area (before onset of disease) increases the discriminatory power when making clear distinctions between patients and healthy adults, versus cartilage volume alone or versus normalization of cartilage volume to body weight and body height.

Application of T and Z scores critically depends on the availability of reliable data from healthy subjects. The first step was therefore to establish a large reference base for quantitative cartilage parameters in volunteers without joint disease. Because MRI is not based on ionizing radiation, image acquisition in healthy adults is not critical and, in contrast to radiography, large databases can be established for various age groups. In the present study, all image data (from volunteers and patients) were acquired on the same scanner and with the same type of MR sequence. Half of the data sets were segmented by one experienced user, and the data segmented by other users were checked for consistency with this subset. The magnitude of T and Z scores depends directly on the intersubject variability (standard deviation) in the reference group. One important step in the analysis was therefore to confirm that the variation for the entire sample was not higher than that of the subgroup investigated by one experienced user only. In this way we were able to exclude the possibility that interobserver differences in cartilage segmentation affected the scores computed in this study. Significant differences in bone mass and density have been reported between the sexes, continents, countries, ethnic groups, and even for various regions within the same country (2). All data reported herein (both from volunteers and from patients) were obtained from Bavarian residents of the same ethnicity, and therefore no bias should be involved in the comparison.

Since significant differences in quantitative cartilage parameters have been reported between men and women (15), T score systems must be derived from sex-specific reference data; otherwise, cartilage loss is underestimated in men and overestimated in women. We have shown previously that physiologic changes of cartilage morphology occur with aging, even in the absence of joint disease (10). Therefore, T scores should

be supplemented by Z scores, to express the difference between the patient and an age-matched (elderly) volunteer, if appropriate.

One problem with using cartilage volume as an outcome variable is its relatively large variability in the normal population. This variability has 2 different sources: one is the variability in cartilage thickness, which cannot be assessed retrospectively in patients, but the more important one is the variability in joint surface area (9). The original size of the joint surface (before the onset of the disease) is accessible by quantitative measurement in patients and can be reconstructed by determining the size of the remaining joint surface plus the size of the denuded joint area. It is important to note that when determining the size of the joint surface area, it is insufficient to measure the length in each sectional image and multiply it by the section thickness, because the joint surface is also curved in the z-direction of the data set. For this reason we have used a validated triangulation algorithm which is highly reproducible under in vivo imaging conditions (14).

We and other authors (9) have also proposed other parameters for normalizing cartilage volumes between individuals (e.g., normalizing to tibial head diameter, body weight, or body height). However, the correlation of these parameters with cartilage volume in healthy adults was shown to be less than that of the joint surface area (9), and these parameters proved less useful in enhancing T and Z scores in that study; moreover, the mean cartilage thickness was also less useful in this context, because cartilage does not generally display homogeneous thinning throughout the surface. A direct measure of cartilage thickness that does not account for the zero thickness of denuded areas is, therefore, less effective than is the ratio of cartilage volume to original joint surface area.

Both the absolute and the normalized cartilage volume displayed a surprising degree of variability among patients, particularly in those with clinical indications for tibial osteotomy. In the latter patients, scores in the medial tibial plateau of those with varus malalignment ranged from +1.5 to -3.5 for cartilage volume, and from -0.3 to -5.1 for normalized volumes (divided by surface area). Results in the lateral tibia were also variable, with values ranging from -0.3 to -2.0 (absolute scores), and from +0.9 to -2.2 (normalized scores). It is important to note that the indication for surgery was primarily based on clinical parameters (location of pain, degree of malalignment), and only to a minor extent on radiographic assessment of the joint. In order to correlate the clinical success of the osteotomy with MR-based

measures of cartilage morphology prior to operation, future studies will have to show whether T and Z scores of cartilage status (particularly the ratio between the medial and lateral side) are clinically helpful in deciding whether the patient will benefit from tibial osteotomy.

In the TKA group with varus malalignment, T scores for absolute cartilage volume varied from -2.6 to -4.7 in the medial tibia, and from -2.2 to -3.2 in the lateral tibia. Again, the scores were substantially enhanced (more negative) when cartilage volume was normalized to the original joint surface area (values of -3.8 to -6.5 in the medial tibia, and -3.7 to -5.7 in the lateral tibia). All patients were treated with a bilateral resurfacing prosthesis, but the ratio of medial to lateral scores may be used in the future to decide on whether a unilateral or bilateral prosthesis is more suitable for a given patient.

In conclusion, this report shows that quantitative assessment of OA by MRI is feasible using a T and Z score system. Because of the large intersubject variability in cartilage volume in healthy volunteers, normalization is required to achieve maximal discriminatory power. The most effective scores were obtained by normalization of cartilage volume to the original joint surface area. Future studies in larger patient cohorts and also in other knee compartments (e.g., patellar and femoral cartilage) will have to establish whether T and Z scores of normalized cartilage volume can be applied as effectively in the clinical management of knee OA as they have been in the determination of bone mineral density for the management of osteoporosis.

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