Skeletal Radiol (2001) 30:144–150

ARTICLE

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Gender differences in knee joint cartilage thickness, volume and articular surface areas: assessment with quantitative three-dimensional MR imaging

Received: 19 June 2000
Revision requested: 4 August 2000
Revision received: 30 November 2000
Accepted: 6 December 2000

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Abstract *Objective*: To compare the cartilage thickness, volume, and articular surface areas of the knee joint between young healthy, non-athletic female and male individuals.
Subjects and design. MR imaging was performed in 18 healthy subjects without local or systemic joint disease (9 female, age 22.3±2.4 years, and 9 male, age 22.2±1.9 years.), using a fat-suppressed FLASH 3D pulse sequence (TR=41 ms, TE=11 ms, FA=30°) with sagittal orientation and a spatial resolution of $2\times0.31\times0.31$ mm^3. After three-dimensional reconstruction and triangulation of the knee joint cartilage plates, the cartilage thickness (mean and maximal), volume, and size of the articular surface area were quantified, independent of the original section orientation.
Results and conclusions: Women displayed smaller cartilage volumes than men, the percentage difference ranging from 19.9% in the patella, to 46.6% in the medial tibia. The gender differences of the cartilage thickness were smaller, ranging from 2.0% in the femoral trochlea to 13.3% in the medial tibia for the mean thickness, and from 4.3% in the medial femoral condyle to 18.3% in the medial tibia for the maximal cartilage thickness. The differences between the cartilage surface areas were similar to those of the volumes, with values ranging from 21.0% in the femur to 33.4% in the lateral tibia. Gender differences could be reduced for cartilage volume and surface area when normalized to body weight and body weight×body height. The study demonstrates significant gender differences in cartilage volume and surface area of men and women, which need to be taken into account when retrospectively estimating articular cartilage loss in patients with symptoms of degenerative joint disease. Differences in cartilage volume are primarily due to differences in joint surface areas (epiphyseal bone size), not to differences in cartilage thickness.

Keywords Cartilage · Knee joint · Gender · MR imaging · Cartilage thickness · Joint surface area

Introduction

Magnetic resonance (MR) imaging is an effective tool for visualizing articular cartilage with high contrast relative to the adjacent tissues under in vivo conditions [1, 2, 3]. Using high-resolution, fat-suppressed gradient-echo sequences and advanced three-dimensional (3D) digital postprocessing techniques, it has become possible to obtain accurate [2, 4, 5, 6, 7, 8, 9] and highly reproducible [4, 6, 10, 11, 12, 13, 14] data on the quantitative distribution of cartilage in the human knee joint, relatively independent of the specific section orientation and angulation.

The current approach in bone densitometry is to measure bone mass or density at a given anatomic site and to compare these parameters with those of a normal young (*T*-score) or age-matched (*Z*-score) reference population. This has initiated the present World Health Organization operational definition of osteoporosis, defining the disease as a loss of bone mass of more than 2.5 standard deviations below the normal value, and large data bases have been established documenting normal reference values for various geographical regions and ethnic groups [15, 16]. Since systematic differences have been described for most parameters between men and women [15, 16], the clinical measurements are usually related to a reference population of the same gender.

Equivalent approaches may be pursued for retrospectively estimating cartilage loss in patients with symptomatic joint disease such as rheumatoid and degenerative arthritis, but to date little quantitative data exists on the normal distribution of cartilage volume and thickness in young individuals. In a recent study Cicuttini et al. [17] examined the knees of 28 patients and reported that the cartilage volumes of the femur and patella, but not those of the tibia, were significantly larger in men than in women. However, these data comprised only volumetric information and were obtained in patients with knee pain, who did not represent a truly healthy population. To our knowledge, no previous study has examined gender differences in 3D cartilage thickness throughout entire cartilage plates and the size of the joint surface areas.

The objective of the present study was therefore to answer the following questions:

- What is the normal range of cartilage volumes, the mean and maximum thickness and surface area in all the knee joint cartilage plates of young healthy males and females?
- Are there systematic differences between men and women, and is the interindividual variability of the values in a mixed sample higher than that in groups of just one gender?
- Are the gender differences similar or different for the various morphologic parameters, such as cartilage volume, mean and maximal cartilage thickness, and surface areas?
- Can gender differences be reduced by normalizing the cartilage parameters to body height, body weight or bone size (tibial head diameter)?

Materials and methods

Imaging

We examined the right knee joints of nine young healthy women (age 22.3±2.4 years) and nine healthy young men (age 22.2±1.9 years). Individuals with previous knee trauma, knee pain, and other chronic diseases of the musculoskeletal system were excluded from the study. To eliminate the confounding influence of differences in physical activity between men and women, we only selected volunteers who had never practiced sports on a regular basis (also not during childhood and adolescence), and did not have a job that involved increased physical activity. All volunteers had a normal weight according to the definition of Thews and Vaupel [18]. The mean (±SD) weight of the women was 61.9 (±5.6) kg, and that of the men 74.9 (±9.3) kg; body height was 169 (±6) cm and 180 (±5) cm respectively. The volunteers were asked to physically rest for 1 h before the investigation, in order to avoid load-induced compression of the cartilage prior to imaging [19].

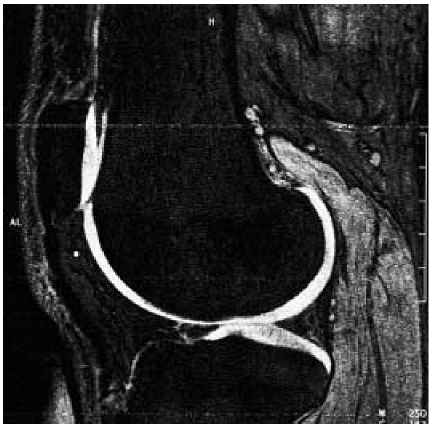

Fig. 1 Sagittal MR image (fat-suppressed 3D gradient-echo sequence) of the knee joint of a volunteer

MRI was performed with a 1.5 T magnet (Magnetom Vision, Siemens, Erlangen, Germany), a circular polarized extremity coil, and a fat-suppressed, 3D gradient-echo sequence (FLASH-3D: TR=45 ms, TE=11 ms, FA=30°, acquisition time=15 min). Sagittal images were obtained with a section thickness of 2 mm and an in-plane resolution 0.31×0.31 mm^2 (field of view=16 cm, matrix=512×512 pixels). The frequency encoding direction was chosen from superior to inferior, and the phase encoding direction from posterior to anterior (Fig. 1).

Digital image processing and statistical analysis

All data sets were digitally transferred to a multiprocessing computer (Octane Duo, Silicon Graphics, Mountain View, Calif.) with a high-performance graphic system. Segmentation of the patellar, femoral, medial, and lateral tibial cartilages was carried out interactively – section by section – by two observers (S.L. all femoral data sets, and R.M. all patellar and tibial data sets), using a B-spline Snake algorithm [12] developed in our groups. This algorithm uses a deformable model approach based on B-splines and has been shown to be more efficient and provide a higher precision than manual segmentation.

The cartilage volumes were determined after 3D reconstruction from the number of voxels attributed to the various cartilage plates. The mean and maximal cartilage thickness for the cartilage plates were computed after shape-based interpolation to isotropic voxel dimensions (0.31×0.31×0.31 mm^3), using a 3D Euclidean distance transformation [13]. This algorithm computes the minimal spatial distance from the articular surface to the cartilage–bone interface at about 1000 points per square centimeter of the articular surface, independent of the original section position and angulation.

Finally, the size of the articular surface and the cartilage–bone interface were calculated after interpolation and triangulation. For the thickness computations, the femur was separated into its trochlear component, and into the medial and lateral femoral condyle. This subdivision was not performed for cartilage volume

Table 1 Knee joint cartilage volume (ml): mean±standard deviation (range) of values in women and men, percentage difference (male vs female) normalized to female and significance level

	Women	Men	Difference (%)	Significance level (*P*)
Patella	2.97±0.72 (1.81–4.17)	3.56±0.48 (2.71–4.12)	+19.9	NS
Femur	11.8±1.4 (10.3–13.8)	15.0±2.6 (11.4–18.4)	+27.1	0.05
Medial tibia	1.31±0.29 (0.97–1.81)	1.92±0.49 (1.28–2.83)	+46.6	0.01
Lateral tibia	1.78±0.33 (1.28–2.24)	2.55±0.51 (1.56–3.05)	+43.3	0.01
Knee (total)	17.9±2.2 (14.5–21.9)	23.0±2.7 (18.8–27.0)	+28.5	0.01

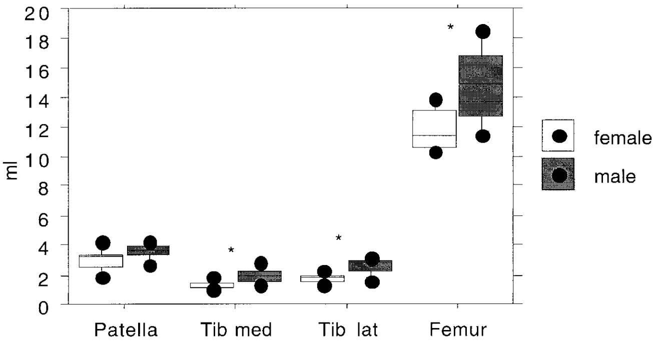

Fig. 2 Box plot showing the cartilage volumes in the knee joint plates of women and men. *Asterisks* indicate significant difference at the 5% level (Mann-Whitney *U*-test)

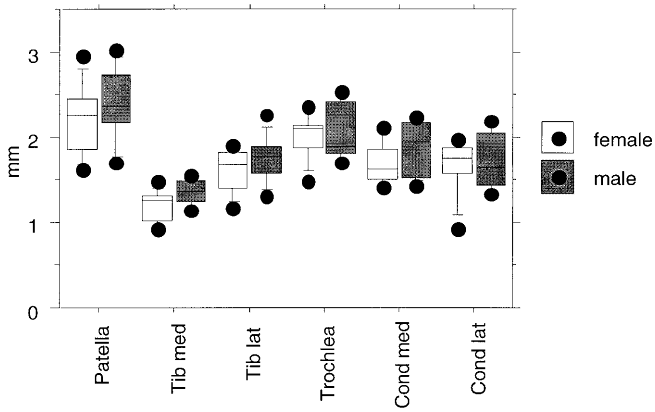

Fig. 3 Box plot showing the mean cartilage thickness in the knee joint plates of women and men

and surface area computations, since the subdivision does not follow a natural border. Whereas the precise point of subdivision directly determines the adjacent volumes and surfaces areas, the thickness values are only minimally affected by the choice of subdivision.

To evaluate whether the values were systematically different between men and women, a nonparametric test (Mann-Whitney *U*-test) was employed at a significance level of 5%. As differences between the genders may be due to differences in body height, body weight or bone size between men and women, a linear regression analysis was performed to examine the effect of these variables on the cartilage volume, mean thickness and surface areas. Results are presented as regression coefficients and *P* values of a paired *t*-test with the null hypothesis “body factor and cartilage parameter are not linearly dependent”. The cartilage parameters were then normalized to the different factors and a nonparametric test (Mann-Whitney *U*-test) was employed at a significance level of 5%.

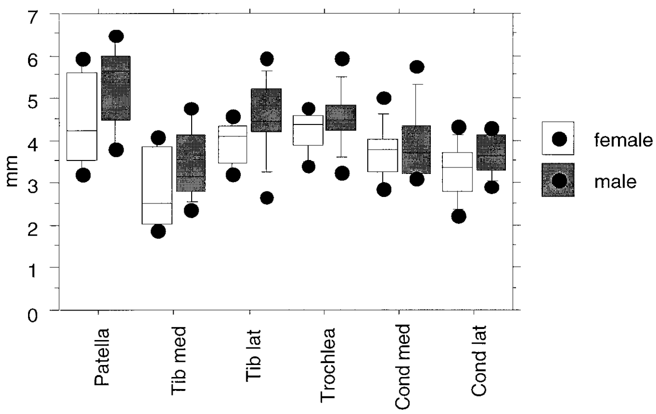

Fig. 4 Box plot showing the maximal cartilage thickness in the knee joint plates of women and men

Results

The cartilage volume was higher in men in all cartilage plates, the difference being statistically significant in the femur and tibia but not in the patella (Fig. 2). The gender-specific differences ranged from 19.9% in the patella to 46.6% in the medial tibia (Table 1). The range of normal values observed in men and women was high, the respective values being given in Table 1.

The gender-specific differences in the mean and maximal cartilage thickness were less pronounced than the differences in volume, and were not statistically significant in any of the joint surfaces (Figs. 3, 4). They ranged from 2.0% in femoral trochlea to 13.3% in the medial

Table 2 Mean knee joint cartilage thickness (mm): mean±standard deviation (range) of values in women and men, percentage difference (male vs female) normalized to female and significance level

	Women	Men	Difference (%)	Significance level (*P*)
Patella	2.20±0.43 (1.62–2.94)	2.39±0.42 (1.70–3.01)	+8.6	NS
Femur (total)	1.79±0.22	1.88±0.29	+5.0	NS
Trochlea	2.01±0.25 (1.48–2.35)	2.05±0.32 (1.74–2.54)	+2.0	NS
Medial condyle	1.69±0.24 (1.40–2.12)	1.86±0.31 (1.44–2.24)	+10.1	NS
Lateral condyle	1.65±0.33 (0.93–1.97)	1.73±0.32 (1.34–2.19)	+4.8	NS
Medial tibia	1.20±0.19 (0.92–1.48)	1.36±0.15 (1.14–1.54)	+13.3	NS
Lateral tibia	1.61±0.25 (1.16–1.90)	1.76±0.27 (1.31–2.27)	+9.3	NS
Knee (total)	1.86±0.24	2.01±0.31	+8.1	NS

Table 3 Maximal knee joint cartilage thickness (mm): mean±standard deviation (range) of values in women and men, percentage difference (male vs female) normalized to female and significance level

	Women	Men	Difference (%)	Significance level (*P*)
Patella	4.51±1.08 (3.20–5.95)	5.26±0.99 (3.79–6.44)	+16.6	NS
Femur	–	–	–	–
Trochlea	4.20±0.48 (3.38–4.78)	4.51±0.72 (3.26–5.95)	+7.4	NS
Medial condyle	3.73±0.67 (2.86–5.02)	3.89±0.85 (3.11–5.73)	+4.3	NS
Lateral condyle	3.29±0.64 (2.25–4.34)	3.69±0.47 (2.93–4.27)	+12.2	NS
Medial tibia	2.90±0.92 (1.90–4.06)	3.43±0.86 (2.40–4.78)	+18.3	NS
Lateral tibia	3.96±0.51 (3.22–4.59)	4.54±0.91 (2.69–5.94)	+14.6	NS

Table 4 Knee joint surface area size (mm^2): mean±standard deviation (range) of values in women and men, percentage difference (male vs female) and significance level

	Women	Men	Difference (%)	Significance level (*P*)
Patella	1047±123 (917–1265)	1289±158 (1014–1470)	+23.1	0.01
Femur	5478±655 (4612–6497)	6554±391 (5925–6888)	+21.0	0.01
Medial tibia	811±112 (679–1006)	1078±235 (807–1460)	+32.9	0.01
Lateral tibia	881±98 (678–991)	1175±147 (926–1388)	+33.4	0.01
Knee (total)	8218±795 (6918–9281)	10096±498 (9228–10670)	+22.9	0.01

tibia for the mean thickness (Table 2), and from 4.3% in the medial condyle to 18.3% in the medial tibia for the maximal thickness (Table 3).

Similar to cartilage volume, the size of the joint surfaces displayed larger gender-specific differences (Fig. 5) than the cartilage thickness values, the percentage differences ranging from 21.0% in the femur to 33.4% in the lateral tibia (Table 4).

For cartilage volume and surface areas, the interindividual variability was generally higher within the entire sample (9 men and 9 women) than that within the group of men and women, respectively. This, how-

Table 5 Interindividual variability (CV%, coefficient of variation=SD/mean×100) of morphologic cartilage parameters (*Th.* thickness) in the various surfaces in the entire sample (*n*=18), women and men, respectively

		Total sample	Women	Men
Patella	Volume	20%	24%	14%
	Mean Th.	18%	19%	18%
	Max. Th.	22%	24%	19%
	Surface area	16%	12%	12%
Femur	Volume	19%	11%	17%
	Surface area	13%	12%	6%
Trochlea	Mean Th.	14%	13%	16%
	Max. Th.	14%	11%	16%
Medial condyle	Mean Th.	16%	14%	17%
	Max. Th.	20%	18%	22%
Lateral condyle	Mean Th.	19%	20%	18%
	Max. Th.	17%	19%	13%
Medial tibia	Volume	31%	22%	26%
	Mean Th.	14%	16%	11%
	Max. Th.	29%	32%	25%
	Surface area	24%	14%	22%
Lateral tibia	Volume	27%	19%	20%
	Mean Th.	16%	15%	15%
	Max. Th.	18%	13%	20%
	Surface area	19%	11%	13%

Table 6 Correlation coefficients (*r*) and significance levels (*P*) for the linear correlation between the body factors body weight, body height, tibial head diameter and body weight×body height with the cartilage parameters volume, mean thickness and surface area

	Body weight	Body height	Tibial head diameter	Body weight * height
Cartilage volume				
Patella	0.56*	0.31	0.36	0.54*
Femur	0.66**	0.61**	0.30	0.71**
Medial tibia	0.61**	0.39	0.50*	0.61**
Lateral tibia	0.34	0.43	0.49*	0.38
Knee (total)	0.72***	0.62**	0.43	0.75***
Cartilage surface area				
Patella	0.60**	0.59*	0.38	0.64**
Femur	0.62**	0.82***	0.23	0.72***
Medial tibia	0.66**	0.49*	0.58*	0.67**
Lateral tibia	0.38	0.58*	0.51*	0.45
Knee (total)	0.70**	0.82***	0.41	0.78***
Mean cartilage thickness				
Patella	0.34	0.043	0.11	0.29
Femur	0.37	0.16	0.19	0.36
Medial tibia	0.23	0.005	0.30	0.20
Lateral tibia	0.17	0.073	0.30	0.16
Knee (total)	0.39	0.22	0.14	0.38

*$P<0.05$; **$P<0.01$; ***$P<0.001$

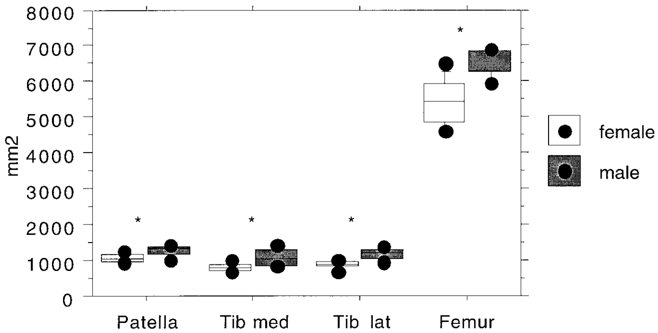

Fig. 5 Box plot showing the size of the articular surface areas in the knee joint plates of women and men. *Asterisks* indicate significant difference at the 5% level (Mann-Whitney *U*-test)

Table 7 Knee joint cartilage volume (ml) normalized to body weight (kg), body size (m), body weight×body size, and tibial head diameter (cm), respectively: percentage difference (male vs female) normalized to female and significance level

	Not normalized	Normalized to			
		Height	Weight	Weight× height	Tibial head diameter
Patella	19.9	12.3	0.1	–6.3	10.3
Femur	26.5*	18.7*	4.9	–1.7	15.1
Medial tibia	46.7**	37.5*	21.3	13.5	33.5*
Lateral tibia	42.8**	34.3*	20.9*	13.5	30.8*
Knee (total)	28.5**	20.6**	6.9	0.2	17.2*

*$P<0.05$; **$P<0.01$;***$P<0.001$

Table 8 Mean knee joint cartilage thickness (mm) normalized to body weight (kg), body size (m), body weight×body size, and tibial head diameter (cm), respectively: percentage difference (male vs female) normalized to female and significance level

	Not normalized	Normalized to			
		Height	Weight	Weight× height	Tibial head diameter
Patella	8.7	1.9	–9.8	–15.6	–1.3
Femur (total)	5.3	–1.3	–13.3*	–18.9*	–4.2
Medial tibia	13.4	6.0	–5.9	–12.1	3.2
Lateral tibia	9.3	2.5	–8.7	–14.5	0.0
Knee (total)	8.6	1.7	–10.3	–16.1*	–1.4

ever, did not apply to the mean and maximal thickness (Table 5).

Significant correlations of surface area and cartilage volume were found with body weight, body height and body weight×body height with the exception of the lateral tibia, and with the tibial head diameter (tibial cartilage). No significant correlation of these factors was observed with the mean cartilage thickness (Table 6). For

Table 9 Knee joint surface area size (mm^2) normalized to body weight, body size, body weight×body size, and tibial head diameter, respectively: percentage difference (male vs female) normalized to female and significance level

	Not normalized	Normalized to			
		Height	Weight	Weight× height	Tibial head diameter
Patella	23.1***	15.5*	2.9	–3.6	12.4
Femur	19.6***	12.4*	–0.1	–6.2	8.4
Medial tibia	32.9***	24.7*	10.0	3.1	20.9*
Lateral tibia	33.4***	25.4**	12.5	5.7	21.5**
Knee (total)	22.9***	15.4***	2.6	–3.7	11.5*

*P<0.05; **P<0.01;***P<0.001

both cartilage surface area and cartilage volume, the differences between men and women were reduced when normalized to body weight or body weight×body height. In this case, the gender differences did not remain statistically significant (Tables 7, 9). The gender differences in mean cartilage thickness changed direction when values were normalized to body weight or body weight× body height. In this case, women showed significantly higher values for the femur (Table 8). Gender differences were reduced slightly when values were normalized to body height or tibial head diameter (Table 8).

Discussion

In this study we examined gender-specific differences in the normal articular cartilage volume, thickness, and surface area in the human knee joint of healthy volunteers, using quantitative 3D MR imaging. We found a relatively high variability in these parameters, in both men and women, and significant differences between the genders for most parameters and surfaces. The current study shows that gender-specific differences in cartilage volume result primarily from a difference in joint size rather than cartilage thickness. This indicates that individuals with small joints yield higher ratios between cartilage thickness and size of the articular surface than those with large joints.

In previous studies, we have shown that the image protocol and image processing employed allow one to obtain accurate [2, 6, 7, 8] values on cartilage morphology including volume, thickness, and surface area. The advantage of this computational method is that the cartilage thickness is computed throughout the entire joint at approximately 1000 points per square centimeter of the articular surface. Thus the thickness value is not confined to a specific location that is difficult to define and reproduce in cross-sectional and longitudinal studies. In particular, the analysis is relatively independent of the specific position, orientation, and angulation of the section [8]. The differences between individuals are considerably higher than the precision errors of the technique upon repositioning of the joint [6, 10, 13, 14]. This underlines the fact that a reliable assessment can be made under in vivo conditions if adequate pulse sequences and digital postprocessing techniques are employed.

Several previous studies have indicated that men have a higher absolute knee joint cartilage thickness than women of the same age [20, 21, 22]. However, the current study suggests that gender-specific differences in cartilage volume and surface area sizes are considerably higher than the differences in thickness.

Cicuttini et al. [17] found statistically significant gender differences in cartilage volume in the femur (60%) and patella (47%), but not in the tibia (49%). The mean difference between the male and female cartilage volume of our subjects was similar in the tibia (43% medial plateau and 47% lateral plateau), whereas the volume differences in the patellar and femoral cartilage were only 20% and 27%, respectively.

These differences might be partly explained by the fact that Cicuttini et al. examined patients who suffered from knee pain (<3months), whereas the volunteers in our study were all healthy subjects. Furthermore the subjects in our group had never practiced sports on a regular basis. To what extent factors such as knee pain or physical (in)activity influence cartilage morphology will have to be examined in further studies with larger groups of volunteers.

Similarly to Cicuttini et al. [17] we found that differences in cartilage volume were not or only slightly dependent on body height or bone size. However, we found that cartilage volume shows a higher linear relationship with body weight and the product of body weight and body height.

In our study we have provided a first estimate of the normal range of cartilage volumes, thickness (mean and maximal), and surface areas in the knee joint cartilage of young healthy male and female individuals. We observed significant differences between men and women, suggesting that measurements in patients with cartilage loss [14] should be related to those in young individuals of the same gender, when absolute values of the cartilage parameters are used.

The interindividual variability in absolute cartilage values in a mixed sample is generally higher than that in groups of one gender only, indicating that the detection of tissue loss based on T-score systems (as currently employed in bone densitometry) is more effective when relating the value to that of young individuals of the same gender.

For cartilage volume and surface areas we have observed significant differences between men and women. Both variables seem to correlate with body weight and the product of body weight and body height. Normalization to these body factors greatly reduces the gender-specific differences. Therefore the interindividual variability in cartilage volume and surface areas within samples might be reduced by normalizing the cartilage values to these parameters, thus improving the accuracy of monitoring tissue loss based on a *T*-score system.

For rating cartilage thickness loss, however, absolute thickness values could be used without differentiation between the genders, as the gender-specific differences seem to be independent of the anthropometric variables examined.

Further efforts should be directed at creating larger, gender-specific data bases of normal cartilage morphology in young, healthy individuals. These will allow one to evaluate whether paired samples of men and women with similar body weight and height display similar or significantly different cartilage volumes, cartilage thickness, and articular surface areas. It will thus be possible to determine whether these differences are "truly" gender-specific or whether they can be explained by differences in anthropometric variables, such as body mass and body dimensions, between males and females.

Acknowledgements We would like to thank Tobias Stammberger for his help with the digital image analysis. The current study was performed within the framework of the doctoral thesis (in preparation) of Susanne Lukasz at the medical faculty of the Ludwig Maximilians University, Munich.

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