Correlation of Knee-Joint Cartilage Morphology With Muscle Cross-Sectional Areas vs. Anthropometric Variables

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ABSTRACT

We tested the hypothesis that muscle cross-sectional areas (MCSAs) are more highly (and independently) correlated with cartilage morphology than are body height and weight, and that the physiological reduction of cartilage thickness with aging is associated with a proportional, age-dependent decrease in MCSAs. In 59 asymptomatic individuals (23–75 years old), morphological parameters of the knee cartilages (volume, thickness, and bone–cartilage interface area), and MCSAs were determined from magnetic resonance imaging (MRI) data. Multiple regression models were used to calculate which proportion of the variability of the normal cartilage morphology can be predicted based on independent variables. MCSAs and body height and weight showed correlation coefficients of +0.66, +0.60, and +0.25, respectively, with knee-joint cartilage volume. The correlation coefficients with cartilage thickness were +0.44, +0.35, and +0.24, respectively. Age accounted for a significant ($P < 0.01$) reduction in cartilage thickness, but there was no proportional change of MCSAs. Approximately 76% of the variability of the knee cartilage volume could be predicted from independent variables in a multiple regression model with MCSAs contributing significant, independent information. In conclusion, we find that MCSAs are more highly correlated with cartilage morphology than are body height and weight. The significant decrease in cartilage volume and thickness with age is not associated with a proportional decrease in MCSAs. Anat Rec Part A 270A:175–184, 2003. © 2003 Wiley-Liss, Inc.

Key words: articular cartilage; muscle cross-sectional areas; anthropometric variables; magnetic resonance imaging; osteoarthritis

The development of magnetic resonance imaging (MRI) has made it possible to delineate articular cartilage in vivo (Recht et al., 1993; Peterfy et al., 1994; Eckstein et al., 1996). In conjunction with state-of-the-art three-dimensional (3D) postprocessing tools (qMRI) the technique has been shown to produce accurate and precise data on the cartilage morphology (volume, thickness, and surface area) of the knee in healthy individuals (Stammberger et al., 1999a; Hohe et al., 2002), and in patients with femorotibial osteoarthritis (OA) (Burgkart et al., 2001). Various studies have revealed that the knee-joint cartilage volume displays a high intersubject variability (Eckstein et al., 1998a, 2001a; Cicuttini et al., 1999; Jones et al., 2000), but little is known about the determinants of this

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variability. Several authors (Karvonen et al., 1994; Cova et al., 1996; Dalla Palma et al., 1997; Eckstein et al., 1998a, 2001a; Cicuttini et al., 1999; Jones et al., 2000) have investigated the correlation of knee-joint cartilage morphology with anthropometric variables such as body height, body weight, and age. Body height and weight have been shown to be only weakly correlated with cartilage volume (Dalla Palma et al., 1997; Eckstein et al., 1998a; Cicuttini et al., 1999; Jones et al., 2000), and in particular with cartilage thickness (Karvonen et al., 1994; Eckstein et al., 2001a). Considering that cartilage thickness may depend on the "loading history" of the joint (Kurrat and Oberländer, 1978; Müller-Gerbl et al., 1987; Carter et al. 1991; Eckstein et al., 1992; Adam et al., 1998), muscle cross-sectional areas (MCSAs) and muscle forces may provide better estimates of cartilage morphology than body height and weight or other anthropometric variables, because MCSAs have been shown to be strongly associated with muscle strength (Maughan et al., 1983; Brand et al., 1986), whereas joint loads are mainly determined by muscle force (An et al., 1997). MCSAs can be accurately and reproducibly determined with MRI (Narici et al., 1988; Walton et al., 1997; Mitsiopoulos et al., 1998; Zanetti et al., 1998). The identification of these factors can provide clues as to the structure–function relationship of articular cartilage.

The staging of OA of the knee is currently based on clinical examination (Kawasaki et al., 1998) and radiographic assessment of joint space width (Buckland-Wright et al., 1995a; Sun et al., 1997). However, radiography does not provide accurate results in the lateral compartment of the femorotibial joint (Buckland-Wright et al., 1995b), it cannot differentiate between femoral and tibial cartilage loss, and it requires highly standardized positioning procedures (ideally fluroscopy) to obtain reproducible data. The cartilage status measured with qMRI can provide estimates on the amount of cartilage volume loss for all surfaces and compartments of the knee. However, the high intersubject variability in the population (Eckstein et al., 2001a) makes it difficult to extrapolate the actual tissue loss in a given patient, and renders grading systems relatively insensitive (Burgkart et al., 2001). Therefore, the "physiological" (pre-OA) cartilage morphology has to be estimated based on independent variables that can be readily obtained from the patient. Ideally, these variables should be highly correlated with the normal cartilage morphology, but should themselves not be affected by the presence of OA.

The objective of this study, therefore, was to identify factors that are potentially associated with normal cartilage morphology, i.e., cartilage volume and thickness, and size of the surface area. We specifically tested the hypothesis that MCSAs are more highly (and independently) correlated with cartilage morphology than are body height and weight. We further tested the hypothesis that the physiological reduction of cartilage thickness with aging (Hudelmaier et al., 2001) is associated with a proportional age-dependent decrease in muscle force and cross-sectional area. Multiple regression models are employed to determine which proportion of the variability of the normal cartilage morphology can be predicted based on a set of measurable independent variables. This is of value for understanding the determinants of normal cartilage morphology, and for more reliably estimating the amount of tissue loss in OA.

MATERIALS AND METHODS

We investigated the right knee joints, MCSAs of the right leg, and anthropometric variables (body height and weight, and age) of 66 individuals (medical students or friends and relatives of the investigators). The volunteers had not previously performed any intensive form of sports, and displayed an average level of physical activity. Volunteers with a history of knee pain, trauma, or surgery were not included in the study. Because clinical symptoms are often weakly correlated with osteoarthritic lesions, and because cartilage lesions can be sufficiently detected with current protocols (Disler et al., 1995), the MR images were qualitatively read by an experienced radiologist. This led to the exclusion of three women and four men (>50 years old). We then analyzed the data from 29 women (38.9 ± 18.5 years old, range 23–75 years) and 30 men (38.2 ± 16.8 years old, range 23–74 years). Informed consent was obtained prior to the examination, and the study protocol was ratified by the local ethics committee.

Imaging was performed with a 1.5 T scanner (Magnetom VISION; Siemens, Erlangen, Germany) and a circularly polarized transmit-receive knee-coil (Siemens). A previously validated gradient-echo sequence (fast low-angle shot (FLASH-3D); repetition time (TR) = 17.2 msec, echo time (TE) = 6.6 msec, flip angle = 20°) with selective water excitation (Graichen et al., 2000; Glaser et al., 2001) was used to acquire sagittal data-sets of the right knee (in-plane resolution = 0.31 mm; section thickness = 1.5 mm, acquisition time = 9 min 15 sec) (Fig. 1a). In the next step, transverse images of the right leg were acquired at the thigh (midway between the knee-joint space and the greater trochanter) and the calf (at the point of maximum circumference, which was identified by visual inspection). A T1-weighted spin-echo sequence (TR = 532 msec, TE = 15 msec) was used for this purpose, at an in-plane resolution of 1.1 mm and a section thickness of 10 mm (Fig. 2a).

All data-sets were transferred to a graphics computer (Octane Duo, Silicon Graphics Inc., Mountain View, CA). Segmentation of the cartilage was performed on a section by section basis, using a semiautomatic B-spline Snake algorithm (Stammberger et al., 1999a), which uses a combination of image forces and model forces, to identify the cartilage contours. Each cartilage plate of the knee was segmented and reconstructed three-dimensionally (Fig. 1b), and the volume was calculated by numeric integration of the segmented voxels. The size of the articular surface and bone–cartilage interface area was computed after triangulation of the reconstructed cartilage plates (Hohe et al., 2002). The mean and maximal cartilage thickness values were calculated independently of the original section orientation, using a 3D Euclidian distance transformation algorithm (Stammberger et al., 1999b). The mean cartilage thickness for the entire knee was derived by averaging the mean cartilage thickness of all cartilage plates, and weighing them relative to the size of the respective bone–cartilage interface area (Eckstein et al., 2001a). These methods, which have precision errors of 2–4%, were described in detail in a recent review (Eckstein et al., 2001b). As a simple measure of bone size, the mediolateral diameter of the tibial head (THD) was determined by counting the number of slices in which the tibial cartilages were visualized. This value was multiplied with the section thickness.

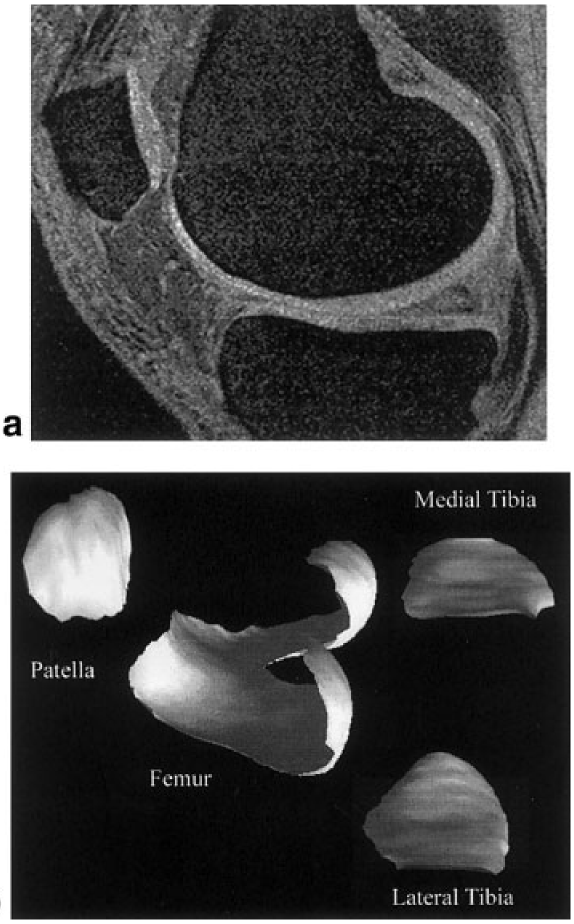

Fig. 1. **a:** Sagittal MR image of the knee, acquired with a T1-weighted gradient-echo sequence with selective water excitation (TR = 17.2 msec, TE = 6.6 msec, flip angle = 20°, in-plane resolution = 0.31 mm^2, slice thickness = 1.5 mm). Articular cartilage appears light gray; bones and bone marrow appear dark. **b:** Exploded figure of 3D computer reconstructions of the cartilage plates of the knee. Cartilage plates are not positioned in a physiologically correct manner.

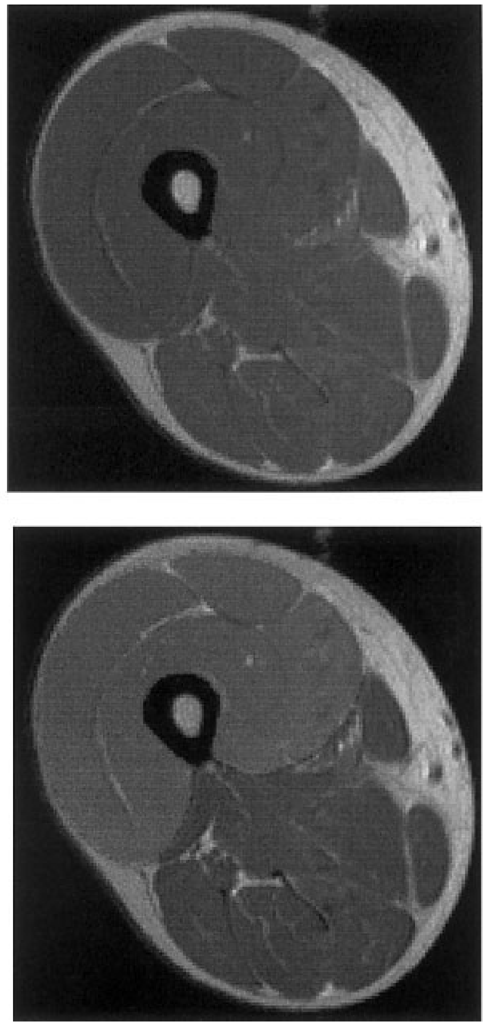

Fig. 2. **a:** Transverse MR image, acquired midway between the knee-joint space and the greater trochanter with a T1-weighted spin-echo sequence (TR = 532 msec, TE = 15 msec, in-plane resolution = 1.1 mm, slice thickness = 10 mm). **b:** The same image with a cross-sectional area of the quadriceps segmented (light gray).

The MCSAs were segmented in the acquisitions of the thigh and calf, excluding the bones, large septs, and vessels. Because of the importance of the extensor mechanism on knee-joint loading (An et al., 1997), the quadriceps femoris was additionally segmented as a separate entity (Fig. 2b). The precision was determined by additionally acquiring four datasets of the thigh and calf in four individuals after repositioning the leg. From those four acquisitions the coefficients of variation (CV%) were computed for each individual and each measurement site, and finally the root mean square (RMS) average (Glüer et al., 1995) was determined. The RMS averages were 2.4% for the total MCSA of the thigh, 1.7% for the MCSA of the quadriceps, and 2.0% for the total MCSA of the calf.

Statistical Analysis

Cartilage volumes of the total knee and of each cartilage plate were correlated with body weight and height, THD, and MCSAs of the thigh, quadriceps femoris, and calf, using the Pearson correlation coefficient for linear dependencies, after confirming a normal distribution of the variables. Because the cartilage volume depends on both the size of the bone–cartilage interface area (or joint surface area) and the cartilage thickness, correlation coefficients were also derived for these variables. Fischer z-transformation was used to determine whether certain correlation coefficients were significantly different from others. The parameters were also correlated with age, and the change per decade (relative to a 20-year-old subject) was calculated from the regression equations. Finally, we determined which proportion of the variability of cartilage morphology can be predicted from a multiple regression model including the above-described parameters. This was achieved by determining the adjusted multiple coefficient of determination (r^2) from stepwise linear regression analysis (forward mode).

RESULTS

The descriptive statistics for the anthropometric variables are listed in Table 1, and those for cartilage mor-

TABLE 1. Anthropometric parameters in the different groups

Parameter	All (n = 59)	Women (n = 29)	Men (n = 30)	Difference/ significance (%)
Age (years)	38.5 ± 17.5	38.9 ± 18.5	38.2 ± 16.8	− 2
Body weight (kg)	69.3 ± 12.8	60.1 ± 6.7	78.2 ± 10.9	+ 23***
Body height (cm)	173.0 ± 8.2	167.2 ± 5.9	178.6 ± 5.9	+ 6***
THD (cm)	7.0 ± 0.6	6.6 ± 0.5	7.5 ± 0.4	+ 12***
MCSA thigh (cm^2)	133.8 ± 27.8	112.3 ± 16.2	154.6 ± 19.7	+ 27***
MCSA quadriceps (cm^2)	61.3 ± 14.1	50.6 ± 9.0	71.6 ± 9.8	+ 29***
MCSA calf (cm^2)	69.5 ± 13.6	60.2 ± 9.3	78.6 ± 10.7	+ 23***

THD, tibia head diameter; MCSA, Muscle cross-sectional area.
***$P < 0.001$.

TABLE 2. Morphological parameters of knee cartilage in the different groups

Parameter	All (n = 59)	Women (n = 29)	Men (n = 30)	Difference/ significance (%)
Knee				
Volume (cm^3)	20.5 ± 4.8	16.9 ± 3.2	23.8 ± 3.5	+ 29***
BCI (mm^2)	89.9 ± 12.3	80.2 ± 8.6	99.2 ± 6.7	+ 19***
Mean thickness (mm)	1.8 ± 0.3	1.7 ± 0.2	1.9 ± 0.2	+ 11***
Max. thickness (mm)	5.6 ± 1.0	5.3 ± 0.9	5.9 ± 0.9	+ 11*
Patella				
Volume (cm^3)	3.7 ± 0.9	3.1 ± 0.6	4.2 ± 0.8	+ 26***
BCI (mm^2)	12.3 ± 1.7	11.2 ± 1.2	13.5 ± 1.2	+ 17***
Mean thickness (mm)	2.5 ± 0.5	2.4 ± 0.4	2.6 ± 0.6	+ 8
Max. thickness (mm)	5.3 ± 1.1	5.1 ± 1.0	5.6 ± 1.1	+ 9
Medial Tibia				
Volume (cm^3)	2.2 ± 0.6	1.8 ± 0.3	2.6 ± 0.5	+ 31***
BCI (mm^2)	10.9 ± 1.6	9.9 ± 1.3	12.0 ± 1.1	+ 17***
Mean thickness (mm)	1.6 ± 0.3	1.5 ± 0.3	1.7 ± 0.3	+ 12***
Max. thickness (mm)	4.0 ± 1.3	3.7 ± 1.1	4.3 ± 1.4	+ 14
Lateral Tibia				
Volume (cm^3)	2.7 ± 0.7	2.2 ± 0.4	3.2 ± 0.6	+ 21***
BCI (mm^2)	10.9 ± 1.9	9.4 ± 1.4	12.3 ± 1.2	+ 24***
Mean thickness (mm)	2.0 ± 0.4	1.9 ± 0.3	2.2 ± 0.4	+ 14**
Max. thickness (mm)	4.5 ± 1.0	4.4 ± 0.9	4.7 ± 1.0	+ 6
Femur				
Volume (cm^3)	11.9 ± 2.9	9.9 ± 2.1	13.9 ± 2.1	+ 29***
BCI (mm^2)	55.2 ± 7.7	49.8 ± 6.2	60.4 ± 4.8	+ 18***
Mean thickness (mm)	1.7 ± 0.3	1.5 ± 0.2	1.8 ± 0.2	+ 17***
Max. thickness (mm)	4.1 ± 0.8	3.7 ± 0.9	4.5 ± 0.6	+ 18***

THD, tibia head diameter; MCSA, muscle cross-sectional area; BCI, bone-cartilage interface.
*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

phology (cartilage volume, size of the bone–cartilage interface, and mean and maximal cartilage thickness) are shown in Table 2. Values are given for the entire sample and for women and men, separately. Basic anthropometric variables, MCSAs, and parameters of cartilage morphology (especially bone–cartilage interface areas) were significantly higher in men than in women (Tables 1 and 2).

In the total sample (Table 3), the volume of the knee cartilage was most highly correlated with the MCSA of the thigh ($r^2 = 0.66$) and the body height ($r^2 = 0.60$). The correlations with the MCSA of the quadriceps and calf were slightly lower, and those with the body weight and THD were significantly ($P < 0.01$) lower.

The size of the cartilage–bone interface area of the knee correlated most highly with the MCSA of the thigh and the body height ($r^2 = 0.66$ in both cases). Surprisingly, the THD was a weaker predictor of the size of the bone–cartilage interface (Table 3). The mean cartilage thickness correlated most highly with the MCSA of the thigh ($r^2 = 0.44$) and the body height ($r^2 = 0.35$), the association with the body weight ($r^2 = 0.14$) being significantly ($P < 0.05$) lower.

These observations also applied to the single cartilage plates of the knee (Table 3). Body height generally displayed a significantly higher correlation with cartilage volumes than did body weight, and the highest correlation with cartilage thickness was generally attained by the MCSA of the thigh. The MCSA of the quadriceps did not achieve a higher correlation coefficient with patellar cartilage than the entire MCSA of the thigh.

In the subsets of women and men, the cartilage volume was also most highly correlated with thigh MCSAs and body height (Tables 4 and 5). In women, body height and MCSAs were generally the better predictors of bone–cartilage interface area and cartilage thickness (Table 4), respectively, whereas the reverse was true in men.

As regards the correlation with age (Table 6), there was no significant decrease in thigh and calf MCSAs in either

TABLE 3. Correlation coefficients (r^2) of knee joint cartilage morphology correlated with anthropometric variables and muscle cross-sectional areas in women and men (n = 59)

Morphological parameter	Body weight	Body height	Tib. head diameter	Thigh MCSA	Quadriceps MCSA	Calf MCSA
Total knee joint cartilage						
Volume	0.29***	0.60***	0.23***	0.66***	0.53***	0.52***
BCI	0.48***	0.66***	0.55***	0.66***	0.54***	0.62***
Mean thickness	0.14**	0.35***	0.04	0.44***	0.39***	0.28***
Max. thickness	0.0	0.12**	0.0	0.14**	0.13**	0.09**
Patellar cartilage						
Volume	0.18***	0.41***	0.17**	0.55***	0.44***	0.41***
BCI	0.41***	0.50***	0.48***	0.52***	0.46***	0.50***
Mean thickness	0.01	0.10**	0.0	0.16**	0.13**	0.10**
Max. thickness	0.0	0.08*	0.0	0.14**	0.11**	0.09**
Medial tibial cartilage						
Volume	0.24***	0.56***	0.22***	0.46***	0.45***	0.31***
BCI	0.31***	0.53***	0.45***	0.38***	0.42***	0.35***
Mean thickness	0.07*	0.25***	0.02	0.27***	0.23***	0.14**
Max. thickness	0.0	0.12**	0.0	0.03	0.04	0.01
Lateral tibial cartilage						
Volume	0.28***	0.53***	0.21***	0.62***	0.48***	0.41***
BCI	0.42***	0.45***	0.49***	0.59***	0.44***	0.48***
Mean thickness	0.04	0.24***	0.0	0.24***	0.23***	0.12**
Max. thickness	0.0	0.17**	−0.01	0.07*	0.08*	0.03
Femoral cartilage						
Volume	0.35***	0.59***	0.21***	0.62***	0.56***	0.53***
BCI	0.41***	0.58***	0.46***	0.56***	0.50***	0.58***
Mean thickness	0.19***	0.38***	0.06*	0.45***	0.42***	0.31***
Max. thickness	0.14**	0.25***	0.04	0.22***	0.23***	0.26***

MCSA, muscle cross-sectional area; BCI, bone-cartilage interface.
$^*P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$.

women or men, but there was a decrease in quadriceps MCSA in the total sample and in women (–4% and –5% per decade, respectively). While there was no significant change in the size of the bone–cartilage interface area with age in either women or men, the mean cartilage thickness displayed a significant ($P < 0.01$) and relatively uniform (–4% per decade) decrease in most cartilage plates (Table 6). The decrease was generally stronger in women, and it was not always significant in men (Table 6).

The stepwise regression models showed that the MCSAs were relevant predictors of both the bone–cartilage interface area and the cartilage thickness, and provided information independently of body weight and height (Table 7). Generally, the MCSA of the total thigh was the best predictor, and no additional information was gained by including other MCSAs (quadriceps or calf) in the model. Body height was almost always included in the regression models (Table 7), and body weight and THD were included occasionally. When a standardized set of parameters was used by forcing the MCSA of the thigh, body height and weight, and age into the multiple regression models, we found that for the total sample, 76% of the variability of knee cartilage volume could be predicted. These models were able to predict a significantly ($P < 0.001$) higher percentage of the variability in the bone–cartilage interface area (84% for total knee) than in cartilage thickness (55% for total knee).

When the bone–cartilage interface area was included as a measure of bone size (derived from MRI) as an independent variable in stepwise regression models, this parameter generally replaced body height, leading to slightly improved prediction ($r^2 = 0.82$ for the total knee cartilage volume). Nevertheless, the MCSA of the thigh provided additional, independent information on the cartilage volume of all plates. The only exception was the patella, in which only age and bone size yielded significant information. The same was found in women, whereas in men the regression models generally included only age and bone size.

DISCUSSION

In this study we tested the hypotheses that MCSAs are more highly (and independently) correlated with cartilage morphology in comparison with body height and weight, and that the physiological decrease in cartilage thickness with aging is associated with an age-dependent decrease in MCSAs. We found that the MCSAs of the thigh display a higher correlation with cartilage volume than do basic anthropometric variables, and provide additional, independent information on cartilage morphology. MCSAs of the thigh are significantly better predictors of bone–cartilage interface area and cartilage thickness compared to body weight, but are only slightly superior compared to body height. Although the significant decrease in cartilage volume and thickness with age is not associated with a proportional decrease in MCSAs of the thigh, a significant decrease in patellar cartilage thickness and MCSA of the quadriceps was found in elderly women, but not in men.

This study has several limitations. A cross-sectional study can describe the correlation between dependent variables, but cannot prove a causal relationship between them. However, one aim of this study was to identify predictors of knee cartilage morphology, independently of whether these are a cause of, or are only associated with the dependent variable (cartilage morphology). A potential problem in painful OA may be that MCSAs are nega-

TABLE 4. Correlation coefficients (r^2) of knee joint cartilage morphology correlated with anthropometric variables and muscle cross-sectional areas in women (n = 29)

Morphological parameter	Body weight	Body height	Tib. head diameter	Thigh MCSA	Quadriceps MCSA	Calf MCSA
Total knee joint cartilage						
Volume	0.09	0.35***	−0.01	0.50***	0.46***	0.45***
BCI	0.29**	0.45***	0.19**	0.21**	0.13*	0.35***
Mean thickness	0.0	0.08	−0.15*	0.35***	0.42***	0.15*
Max. thickness	−0.02	0.04	−0.18*	0.17*	0.22**	0.07
Patellar cartilage						
Volume	0.03	0.24**	−0.03	0.31**	0.38***	0.22**
BCI	0.30**	0.50***	0.14*	0.07	0.08	0.28**
Mean thickness	−0.01	0.01	−0.15*	0.26**	0.31**	0.06
Max. thickness	−0.02	0.0	−0.21**	0.18*	0.20**	0.04
Medial tibial cartilage						
Volume	0.07	0.46***	0.0	0.35***	0.39***	0.26**
BCI	0.05	0.37***	0.14*	0.07	0.14*	0.10*
Mean thickness	0.0	0.14*	−0.12*	0.37***	0.34***	0.18**
Max. thickness	−0.02	0.13*	−0.07	0.06	0.06	0.08
Lateral tibial cartilage						
Volume	0.09*	0.38***	0.0	0.46***	0.44***	0.23**
BCI	0.17*	0.18**	0.12*	0.23**	0.15*	0.12*
Mean thickness	0.0	0.19**	−0.18*	0.28**	0.34***	0.13*
Max. thickness	−0.01	0.22*	−0.18*	0.07	0.18*	0.01
Femoral cartilage						
Volume	0.10*	0.28**	0.0	0.48***	0.41***	0.52***
BCI	0.27**	0.32**	0.15*	0.21**	0.10*	0.50***
Mean thickness	0.0	0.06	−0.09	0.29**	0.32**	0.14*
Max. thickness	0.0	0.03	0.0	0.07	0.08	0.16*

MCSA, muscle cross-sectional area; BCI, bone-cartilage interface.
*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

tively affected by the disease process, although current data (Slemenda et al., 1997; Brandt et al., 1999) indicate that these changes are much less than the intersubject variability reported in this study. Also, in unilateral OA it is possible to measure the contralateral limb. Another limitation is that we did not systematically assess the level of physical activity and/or the actual muscle strength of the subjects, as these are difficult to determine objectively. Furthermore, while the macromorphology of knee cartilage has been investigated, the microstructural properties have not. To date there is no established, noninvasive method for determining these properties in healthy volunteers. In the present study only the right knee joint was investigated, based on the observations that side differences in cartilage morphology are small (0–6% for the various parameters) and that side dominance of the limbs does not significantly influence side differences in knee cartilage macromorphology (Eckstein et al., 2002b).

Previous studies have shown that high-resolution gradient-echo sequences with fat-suppression or water excitation can provide valid information on cartilage volume and thickness (Eckstein et al., 1996, 1998b, 2000; Graichen et al., 2000; Burgkart et al., 2001; Glaser et al., 2001). For the protocol used in the current work, precision errors have been shown to range between 2% and 6% for cartilage volume, thickness, and size of the bone–cartilage interface area in the various compartments of the knee (Glaser et al., 2001; Eckstein et al., 2001b; Hohe et al., 2002). These precision errors are substantially lower than the variability observed between different subjects in this study, and the method is therefore suitable to test the given hypotheses. The advantage of the current methodology is that it can be applied in vivo, which allows the investigation of asymptomatic volunteers without cartilage lesions, and with known medical and social histories.

The validity and accuracy of MRI-based MCSA measurements have been tested by several groups (Narici et al., 1988; Walton et al., 1997; Mitsiopoulos et al., 1998; Zanetti et al., 1998). We determined the precision errors of the current protocol to be 2–3%. These values are substantially lower than the observed intersubject differences, indicating that the method is adequate for the given task.

Previous studies found a relatively weak association of cartilage morphology with body weight and height (Karvonen et al., 1994; Dalla Palma et al., 1997; Eckstein et al., 1998a, 2001a; Cicuttini et al., 1999; Jones et al., 2000). Jones et al. (2000) found a significant (albeit weak) correlation between muscle force and cartilage volume of the patella and the lateral tibia in children (9–18 years old), but no significant association in the medial tibia.

In the current study we show that in both young and elderly adults MCSAs can provide significant, independent information for predicting cartilage morphology. Our data show that with a mixed sample of men and women, and using anthropometric variables and MCSAs, it is possible to predict 76% of the variability in cartilage volume, 84% of that in bone–cartilage interface area, and 55% of that in mean cartilage thickness. Among the MCSAs, those of the thigh generally displayed the highest correlations. This was as expected, because the thigh musculature is more directly involved in knee-joint loading than the calf muscle. Although femoropatellar loading is mainly determined by the quadriceps (An et al., 1997), the correlation with femoropatellar cartilage morphology was not higher than that with the total thigh. This suggests that in order to determine MCSAs, it is sufficient to mea-

TABLE 5. Correlation coefficients (r^2) of knee joint cartilage morphology correlated with anthropometric variables and muscle cross-sectional areas in men (n = 30)

Morphological parameter	Body weight	Body height	Tib. head diameter	Thigh MCSA	Quadriceps MCSA	Calf MCSA
Total knee joint cartilage						
Volume	0.0	0.29**	0.0	0.23**	0.08	0.08
BCI	0.03	0.23**	0.22**	0.38***	0.12*	0.30**
Mean thickness	0.0	0.17*	−0.06	0.10*	0.02	0.02
Max. thickness	−0.09*	0.05	−0.04	0.01	0.0	0.0
Patellar cartilage						
Volume	−0.01	0.08	0.0	0.23**	0.04	0.10*
BCI	0.02	0.03	0.22**	0.27**	0.12*	0.15*
Mean thickness	0.0	0.09	0.0	0.07	0.01	0.05
Max. thickness	−0.02	0.08	0.0	0.08	0.0	0.07
Medial tibial cartilage						
Volume	0.0	0.17*	0.0	0.03	0.02	0.0
BCI	0.01	0.13*	0.18*	0.03	0.05	0.04
Mean thickness	−0.04	0.06	−0.04	0.0	0.0	0.0
Max. thickness	−0.06	0.06	−0.14*	0.0	0.0	−0.05
Lateral tibial cartilage						
Volume	0.0	0.14*	0.0	0.24**	0.03	0.06
BCI	0.03	0.04	0.24**	0.24**	0.0	0.17*
Mean thickness	−0.03	0.08	−0.14	0.06	0.03	0.0
Max. thickness	−0.01	0.17*	−0.12*	0.06	0.02	0.0
Femoral cartilage						
Volume	0.02	0.35***	0.0	0.18**	0.10*	0.09
BCI	0.02	0.23**	0.12*	0.25**	0.23**	0.14*
Mean thickness	0.0	0.18*	−0.10*	0.07	0.02	0.02
Max. thickness	0.0	0.21**	−0.15*	0.03	0.04	0.04

MCSA, muscle cross-sectional area; BCI, bone-cartilage interface.
*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

TABLE 6. Correlation coefficients, significance and percentual changes per decade of anthropometric parameters and knee joint cartilage morphology with age in women and men

Morph. parameter	All (n = 59)		Women (n = 29)		Men (n = 30)	
Body weight (kg)	0.01	1%	0.10	2%	0.01	1%
Body height (cm)	−0.07*	−1%	−0.05	0%	−0.21*	−1%
THD (cm)	0.14**	2%	0.35**	3%	0.20*	1%
MCSA thigh (cm^2)	−0.06	−3%	−0.16	−3%	−0.12	−3%
MCSA quadriceps (cm^2)	−0.08*	−4%	−0.26**	−5%	−0.11	−3%
MCSA calf (cm^2)	−0.02	−2%	0.0	0%	−0.11	−3%
Knee						
Volume (cm^3)	−0.11**	−4%	−0.18*	−4%	−0.25**	−4%
BCI (mm^2)	0.0	−1%	0.01	0%	−0.06	−1%
Mean thickness (mm)	−0.26***	−4%	−0.34**	−4%	−0.37***	−4%
Max. thickness (mm)	−0.20***	−4%	−0.30**	−5%	−0.14*	−4%
Patella						
Volume (cm^3)	−0.10*	−4%	−0.18*	−4%	−0.13	−4%
BCI (mm^2)	0.0	0%	0.03	1%	0.0	0%
Mean thickness (mm)	−0.12**	−4%	−0.30**	−5%	−0.04	−3%
Max. thickness (mm)	−0.14**	−4%	−0.30**	−6%	−0.04	−2%
Medial tibia						
Volume (cm^3)	−0.11*	−4%	−0.18*	−4%	−0.18*	−5%
BCI (mm^2)	0.0	1%	0.0	0%	−0.01	−1%
Mean thickness (mm)	−0.20***	−4%	−0.30**	−5%	−0.18*	−4%
Max. thickness (mm)	−0.18**	−7%	−0.15*	−6%	−0.22**	−8%
Lateral tibia						
Volume (cm^3)	−0.12**	−5%	−0.21*	−5%	−0.23**	−5%
BCI (mm^2)	−0.0	−1%	0.0	−1%	0.0	−1%
Mean thickness (mm)	−0.24***	−4%	−0.35**	−4%	−0.25**	−5%
Max. thickness (mm)	−0.41***	−7%	−0.38***	−7%	−0.46***	−8%
Femur						
Volume (cm^3)	−0.10*	−4%	−0.13	−4%	−0.22**	−4%
BCI (mm^2)	0.0	0%	0.0	0%	−0.02	−1%
Mean thickness (mm)	−0.22***	−4%	−0.24**	−4%	−0.48***	−5%
Max. thickness (mm)	−0.15**	−4%	−0.08	−4%	−0.42***	−5%

THD, tibia head diameter; MCSA, muscle cross-sectional area; BCI, bone-cartilage interface.
*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

TABLE 7. Adjusted r^2, parameters included in multiple regression analysis and adjusted r^2 of forced regression

Morph. parameter	Women and men (all variables)	Women and men (forced)	Women (forced)	Men (forced)
Knee				
Volume	0.76 (a,b,e)	0.75	0.59	0.44
BCI	0.84 (a,d,e,g)	0.79	0.53	0.45
Mean thickness	0.55 (c,e)	0.56	0.42	0.37
Max thickness	0.25 (c,e)	0.32	0.26	0.28
Patella				
Volume	0.54 (e)	0.61	0.36	0.32
BCI	0.66 (a,d,e)	0.67	0.57	0.25
Mean thickness	0.20 (b,e)	0.22	0.32	0.17
Max thickness	0.21 (b,e)	0.24	0.26	0.23
Medial tibia				
Volume	0.62 (a,b,e)	0.61	0.58	0.23
BCI	0.62 (a,d)	0.56	0.34	0.04
Mean thickness	0.36 (c,e)	0.38	0.41	0.14
Max thickness	0.28 (a,b,c)	0.26	0.19	0.25
Lateral tibia				
Volume	0.70 (a,b,e)	0.69	0.59	0.33
BCI	0.68 (d,e)	0.63	0.22	0.16
Mean thickness	0.36 (c,e)	0.41	0.43	0.19
Max thickness	0.46 (a,c)	0.47	0.44	0.41
Femur				
Volume	0.69 (a,e)	0.71	0.51	0.39
BCI	0.73 (a,d,g)	0.70	0.39	0.44
Mean thickness	0.53 (c,e)	0.54	0.28	0.41
Max thickness	0.34 (c,g)	0.30	−0.02	0.39

a, body height; b, body weight; c, age; d, tibia head diameter; e, musclearea thigh; f, musclearea quadriceps; g, musclearea calf.

sure MCSAs of the thigh, because MCSAs of the calf and quadriceps only provide redundant information.

It is notable that a significantly higher proportion of the variability in the bone–cartilage interface area can be predicted than in cartilage thickness. This demonstrates that the variability in cartilage thickness is the dominant source of variability in cartilage volume, which cannot be explained by anthropometric variables and MCSAs. Our data indicate that the processes involved in the formation of bone size may be more closely linked to these variables than the processes involved in determining cartilage thickness. However, it should be kept in mind that bone size and cartilage thickness are mainly determined during growth, and that the variables measured in adults may not necessarily reflect the variables present during the growth phase. In this context, however, it must be pointed out that the correlations were not significantly different in the young (20–30 years old) and elderly subjects (>50 years old).

It is not surprising that the bone–cartilage interface area is highly correlated with body height, since larger individuals have larger bones. However, 20–30% of the variability in the bone–cartilage interface area in the mixed sample (and an even higher proportion in subsets of women and men) is unexplained by body height. Surprisingly, a local parameter of bone size (the THD) does not provide better estimates of bone–cartilage interface area than body height—not even for the tibial cartilages. Potential reasons include a low correlation between the mediolateral and anterioposterior dimensions of the tibial plateau, and a high variability of the intercondylar area. In contrast, the MCSA of the thigh is a good and independent predictor of bone–cartilage interface area (although it is not better than body height).

With regard to cartilage thickness, MCSAs of the thigh tend to be better predictors than the anthropometric variables. The likely explanation is that the local mechanical loading history is a relevant factor in the formation of cartilage thickness (Müller-Gerbl et al., 1987; Carter et al., 1991). However, in a previous study (Eckstein et al., 2002a) in which triathletes were compared with physically inactive volunteers, no difference in cartilage thickness was observed (although differences were found in the bone–cartilage interface area). There may be independent factors that regulate both the cartilage thickness and the MCSAs, but these are currently not known.

The finding that body weight is a relatively poor predictor of both bone–cartilage interface area and cartilage thickness is consistent with previous observations (Cicuttini et al., 1999; Jones et al., 2000; Eckstein et al., 2001a). A possible explanation is that bone length and MCSAs may play a more important role in determining the mechanical loading history of the knee than does body weight, because the lever arms and maximal muscle forces are more important in determining the joint loads than is body weight alone (An et al., 1997).

Because body weight and height, and MCSAs generally attain higher values in men than in women, it is obvious that the correlation between these variables and the total sample are higher than in the subgroups of men and women. Nevertheless, significant correlations were, in general, also observed within each gender, showing that there truly exists a positive linear relationship between these variables and cartilage morphology, independently of gender differences. However, we cannot explain why the correlations were somewhat higher in women than in men. We also can not explain why MCSAs tend to be better predictors of cartilage thickness, and body height to be a better predictor of bone–cartilage interface area in women, whereas the opposite was observed in men.

Age shows significant negative correlation coefficients with the volume and thickness of the knee cartilage, but not with the size of the bone–cartilage interface, as shown in a prior study (Hudelmaier et al., 2001). A relatively consistent decrease (−4% per decade) in mean cartilage thickness was noted in all joint compartments. To our surprise, the MCSAs did not show a significant decrease with age, except for the quadriceps in women. However, the stronger decrease in quadriceps MCSA in women (compared with men) may correspond with the stronger decrease in patellar cartilage thickness. Nevertheless, we refute the hypothesis that the age-dependent decrease in cartilage thickness is generally caused by (or associated with) a decrease in MCSAs. Despite the nonsignificant changes in MCSAs, we cannot rule out the possibility that there is a significant decrease in muscle force in elderly subjects, as it is still a matter of controversy whether changes in muscle fiber type and alterations in recruitment (specific muscle force) occur with aging (Frontera et al., 2000; Cannon et al., 2001; Goodpaster et al., 2001; Urbancheck et al., 2001). Moreover, correlations between MCSAs and muscle strength have been shown to be only moderate (Dowling and Cardone, 1994; Bruce et al., 1997; Overend et al., 1992). An alternative explanation may be that cartilage thickness diminishes physiologically with aging (independent of a reduction in loading), due to impaired cellular function, reduced synthesis of matrix components, and lower extracellular water content.

In conclusion, we find that MCSAs are more highly (and independently) correlated with cartilage morphology in comparison with body height and weight, and bone size. The significant decrease in cartilage volume and thickness with age, however, is not associated with a proportional decrease in MCSAs of the thigh. Our data show that up to 76% of the variability of knee-joint cartilage volume can be predicted based on body height and weight, and MCSAs of the thigh in a sample of both genders, and about 59% and 44% can be predicted in women and men, respectively. The ability to identify factors that determine normal cartilage morphology helps us understand the structure–function relationships of normal cartilage, and it is of practical importance to be able to accurately estimate the amount of tissue loss in osteoarthritic patients.

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