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Age-Related Changes in the Morphology and Deformational Behavior of Knee Joint Cartilage

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Objective. **Alterations of cartilage morphology and mechanical properties occur in osteoarthritis, but it is unclear whether similar changes also take place physiologically during aging, in the absence of disease. In this in vivo study, we tested the hypothesis that thinning of knee joint cartilage occurs with aging and that elderly subjects display a different amount of cartilage deformation than do young subjects.**

Methods. **We evaluated 30 asymptomatic subjects ages 50–78 years. Morphologic parameters for the knee cartilage (mean and maximum thickness, surface area) were computed from magnetic resonance imaging data. Results were compared with those in 95 young asymptomatic subjects ages 20–30 years. Deformation of the patellar cartilage was determined after the subjects performed 30 knee bends.**

Results. **There was a significant reduction of patellar cartilage thickness in elderly women (−12%; $P < 0.05$), but not in elderly men (−6%). Femoral cartilage was significantly thinner in both sexes (−21% in women, −13% in men; $P < 0.01$), whereas tibial cartilage thickness displayed only nonsignificant trends (−10% in women, −7% in men). Patellar cartilage deformation was −2.6% in elderly women and −2.2% in elderly men. These values were significantly lower ($P < 0.05$) than those in young subjects.**

Conclusion. **We confirmed the hypothesis that knee cartilage becomes thinner during aging, in the absence of cartilage disease, but that the amount of reduction differs between sexes and between compartments of the knee joint. We show that under in vivo loading conditions, elderly subjects display a lower level of cartilage deformation than do healthy young subjects.**

Morphologic and biochemical changes are known to occur in articular cartilage with age-related pathologic processes, such as osteoarthritis (OA) (1). It is unclear, however, whether changes in cartilage morphology (e.g., thinning) also occur during normal (physiologic) aging, in the absence of cartilage disease. The characterization of age-related changes in cartilage thickness can make it possible to distinguish between the normal aging process and pathologic alterations. Quantitative data on cartilage thinning may permit the establishment of T score (difference between patients and healthy young subjects, expressed in standard deviations) and Z score (difference between patients and healthy subjects of the same age) systems for OA. These scoring systems are currently used for the evaluation of bone loss in osteoporosis and require reference data throughout various age groups. However, quantitative values for articular cartilage have not yet been established.

Previous studies of cadavers have reported significant cartilage thinning with age in the patella of women but not men when arthritis cases were included (2). But, no changes in cartilage thickness in the human shoulder were found (3). Based on magnetic resonance imaging (MRI) studies, Karvonen et al (4) reported significant cartilage thinning with age in the weight-bearing aspect of the femoral condyles of subjects without OA, but no changes in the posterior aspect of the femoral condyles, in the tibia, or in the patella. It is, however, questionable whether such local measurements are accurate, reproducible, and representative of the entire cartilage plate.

Quantitative, 3-dimensional MRI now offers

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the possibility to determine the cartilage thickness in vivo throughout the total cartilage plates (5). These measurements have been validated against several accepted (invasive) techniques (6,7) and have been shown to permit highly reproducible measurements in living subjects (4,6).

Previous in vitro studies have reported changes in human cartilage biochemistry with age, such as a decrease in proteoglycan (PG) synthesis and content (8) as well as in the interstitial water content (1). These changes may explain alterations in the mechanical properties of articular cartilage. Some in vitro experiments have suggested that the compressive (9,10) and tensile (11) stiffness of articular cartilage decreases with age. These results have fostered the hypothesis that elderly individuals display a larger amount of cartilage deformation under a given load in vivo (exercise), and that this increase in deformation may initiate or accelerate the OA process. However, other in vitro experiments have indicated that an increase in pentosidine levels with age may render the cartilage stiffer (12), potentially leading to less deformation of the cartilage in vivo, and rendering the cartilage more brittle, causing a faster progression of cartilage degeneration (13).

Changes in deformational behavior with age have potential implications for the mechanical strains to which tissue-engineered cartilage transplants are subjected within their target environment, and in particular for the design and preoperative testing of these constructs.

Since MRI has recently also made it possible to investigate the deformational behavior of patellar cartilage in vivo (14), the aim of the current study was to use this method to determine morphologic and deformational properties of knee joint cartilage in elderly subjects. Specifically, we tested the hypothesis that thinning of knee joint cartilage occurs physiologically with aging, in the absence of cartilage disease, and that elderly subjects display a different amount of cartilage deformation in vivo than do young subjects.

SUBJECTS AND METHODS

In this cross-sectional study, the right knee joints of 15 women (mean ± SD age 61 ± 9.8 years, range 50–78 years) and 15 men (age 60 ± 5.0 years, range 53–74 years) who volunteered to participate in the study were investigated. Those with a history of knee pain, trauma, or surgery were not included in the study.

The subjects were examined with a 1.5T scanner (Magnetom Vision; Siemens, Erlangen, Germany). A previously validated fat-suppressed gradient-echo sequence (6,7) was used to acquire sagittal data sets of the knee (resolution $0.31 \times 0.31 \times 1.5$ mm^3). Three of the women and 4 of the men were excluded from further investigation because of visible cartilage lesions at the medial patellar facet or at the femoral condyles.

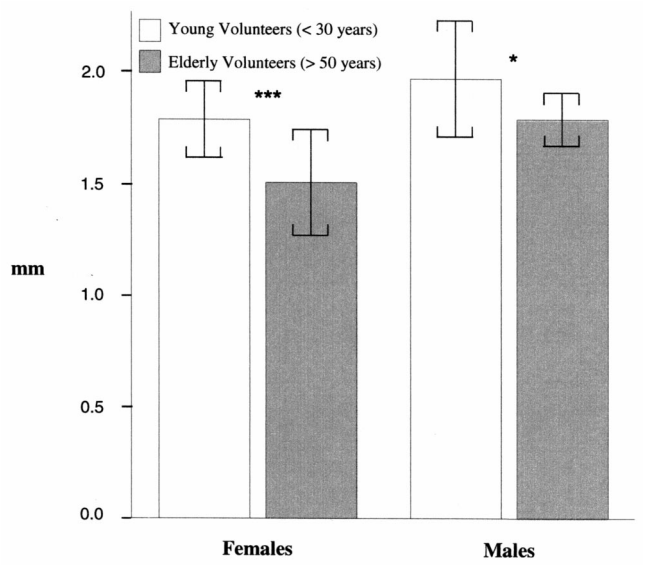

Figure 1. Knee joint cartilage thickness (averaged from the patellar, femoral, and tibial cartilage) in young (20–30 years) and elderly (50–78 years) volunteers. Values are the mean ± SD. $* = P < 0.05$; $*** = P < 0.001$.

Two transverse data sets of the patellar cartilage were obtained at the same resolution. After initial data acquisition, the volunteers were asked to perform 30 deep knee bends (flexion angle ~120°). The subjects were then repositioned in the magnet within 45 seconds, and a transverse data set of the patellar cartilage was acquired from 90 seconds to 320 seconds after the end of the exercise.

Segmentation was performed on a graphics computer (Octane Duo; Silicon Graphics, Mountain View, CA) on a section-by-section basis, using a B-spline snake algorithm (6). All cartilage plates were reconstructed 3-dimensionally, and the size of the joint surface area and the bone–cartilage interface area (more specifically, the boundary between the calcified and the noncalcified cartilage) were computed after triangulation. The femoral cartilage plate was divided interactively into the facies patellaris femoris (the trochlea) and the medial and lateral femoral condyles. The mean and maximum cartilage thicknesses were computed independently of the original section orientation with a 3-dimensional Euclidean distance transformation algorithm (4). The thickness values were compared with data in 46 young healthy women (mean ± SD age 25.2 ± 3.2 years) and 49 men (age 25.8 ± 3.2 years) (age range for all subjects 20–30 years).

To determine the deformational behavior of the patellar cartilage, the thickness values obtained from the data set acquired after knee bends were subtracted from those before exercise. These values were related to data from 12 healthy young women and men (14). Statistical significance of the

Table 1. Morphology of the knee joint cartilage in young and elderly subjects, grouped according to sex*

Group, cartilage plate	Young subjects	Elderly subjects	Difference, %	*P*
Women	n = 46	n = 12		
Mean thickness (mm)				
Patella	2.49 ± 0.39	2.19 ± 0.19	−12	<0.05
Femur (total)	1.67 ± 0.21	1.32 ± 0.28	−21	<0.001
Facies patellaris	1.87 ± 0.23	1.62 ± 0.44	−13	<0.01
Medial condyle	1.51 ± 0.31	1.20 ± 0.22	−21	<0.01
Lateral condyle	1.62 ± 0.23	1.30 ± 0.27	−20	<0.01
Tibia				
Medial plateau	1.43 ± 0.27	1.30 ± 0.27	−10	NS
Lateral plateau	1.87 ± 0.28	1.70 ± 0.24	−10	NS
Maximum thickness (mm)				
Patella	5.39 ± 1.12	4.37 ± 0.51	−19	<0.01
Femur (total)	4.06 ± 0.69	3.47 ± 0.68	−15	<0.01
Facies patellaris	3.93 ± 0.47	3.68 ± 1.01	−6	NS
Medial condyle	3.41 ± 0.80	2.50 ± 0.46	−27	<0.001
Lateral condyle	3.23 ± 0.46	2.62 ± 0.49	−19	<0.01
Tibia				
Medial plateau	3.59 ± 1.20	3.12 ± 0.76	−13	NS
Lateral plateau	4.57 ± 0.71	3.56 ± 0.81	−22	<0.01
Men	n = 49	n = 11		
Mean thickness (mm)				
Patella	2.67 ± 0.44	2.52 ± 0.37	−6	NS
Femur (total)	1.87 ± 0.27	1.63 ± 0.08	−13	<0.01
Facies patellaris	2.17 ± 0.31	1.79 ± 0.15	−18	<0.001
Medial condyle	1.66 ± 0.32	1.45 ± 0.18	−13	<0.05
Lateral condyle	1.78 ± 0.35	1.62 ± 0.17	−9	NS
Tibia				
Medial plateau	1.59 ± 0.32	1.58 ± 0.27	−1	NS
Lateral plateau	2.05 ± 0.42	1.91 ± 0.29	−7	NS
Maximum thickness (mm)				
Patella	5.79 ± 0.87	5.32 ± 0.99	−8	NS
Femur (total)	4.75 ± 0.59	3.98 ± 0.43	−16	<0.001
Facies patellaris	4.68 ± 0.62	3.85 ± 0.51	−18	<0.001
Medial condyle	3.55 ± 0.59	3.14 ± 0.38	−12	<0.05
Lateral condyle	3.76 ± 0.57	3.37 ± 0.47	−11	<0.05
Tibia				
Medial plateau	3.99 ± 1.28	3.40 ± 0.78	−15	NS
Lateral plateau	4.85 ± 0.87	3.74 ± 0.59	−23	<0.001

* Values are the mean ± SD of the mean and maximum thickness, the joint surface area, and the bone–cartilage interface (see Subjects and Methods for details). *P* values were determined by Mann-Whitney U test. NS = not significant.

differences were calculated with a nonparametric test (Mann-Whitney U test).

RESULTS

The mean knee joint cartilage thickness in elderly women (average of all cartilage plates) was significantly lower (−15%; $P < 0.001$) than that observed in the young women (Figure 1). The mean thickness in elderly men was also significantly lower than that in young men (9%; $P < 0.05$) (Figure 1). The differences between the elderly and the younger subjects were not the same for the different compartments of the knee joint cartilage.

The mean cartilage thickness of the patella was 12% lower ($P < 0.05$) and the maximum thickness was 19% lower ($P < 0.01$) in elderly women compared with young women (Table 1). For elderly men, a smaller difference was found relative to younger individuals (−6% for the mean and −8% for the maximum thickness). These differences did not attain statistical significance. In the femur, the mean and maximum cartilage thicknesses in elderly individuals were significantly lower, but the difference also varied between compartments (from −6% to −27%) (Table 1). The tibial cartilage plates displayed only trends toward cartilage thinning (−1% to −10% for the mean thickness), with only the maximum thickness values of the lateral tibial

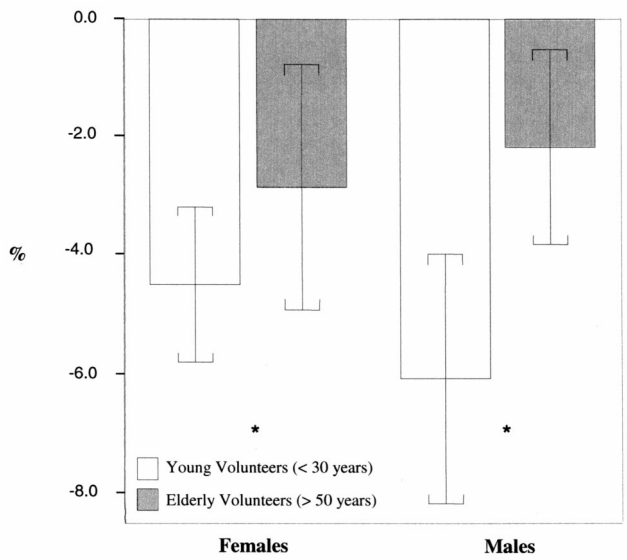

Figure 2. Percentage differences in the mean patellar cartilage thickness (after 30 deep knee bends) in young (20–30 years) and elderly (50–78 years) volunteers. Values are the mean ± SD. $* = P < 0.05$.

cartilage reaching statistical significance (−22% [$P < 0.01$] in women, and −23% [$P < 0.001$] in men).

The size of the bone–cartilage interface and the joint surface area showed no significant difference between the young and the elderly women and men, except for the size of the femoral cartilage plate of the elderly men (data not shown).

Patellar cartilage deformation was 2.6 ± 1.7% (mean ± SD) in elderly women, and 2.2 ± 1.7% in elderly men (Figure 2). The deformation was significantly lower ($P < 0.05$) than that observed in young individuals, where the deformation was 4.5 ± 1.3% in women, and 6.2 ± 2.1% in men.

DISCUSSION

In this study, we tested the hypothesis that thinning of knee joint cartilage occurs physiologically with aging, in the absence of cartilage disease, and that elderly subjects display a different amount of cartilage deformation in vivo compared with young subjects. We found a significant reduction of cartilage thickness in the femur of elderly women and men and in the patella of elderly women. In contrast, the patellar cartilage of elderly men and the tibial cartilage plates of elderly men and women displayed only trends toward cartilage thinning, the differences in which did not attain statistical significance.

Karvonen et al (4) found a similar pattern of cartilage thinning in the weight-bearing region of the femoral cartilage plates and the tibia. However, in contrast to our results and the results reported by Meachim et al (2), they did not report a reduction of patellar cartilage thickness in elderly women. This discrepancy may be due to Meachim's inclusion of subjects with OA or their inclusion of the medial and the lateral patellar facet (2); Karvonen et al (4) analyzed only the central aspects of the patella. Our analysis offers the advantage that the entire joint surface is included in the analysis, and the current data indicate that the amount of age-related patellar cartilage thinning may indeed be sex-specific, being higher in women than in men.

In the tibia, changes in the mean cartilage thickness between young and elderly asymptomatic subjects did not attain statistical significance in either sex. These findings differ from those reported in individuals with OA, in which highly significant thinning has been observed (4). A substantial loss of cartilage volume has also been reported in MRI-based studies performed prior to total knee arthroplasty (6).

Our current findings suggest that it is possible to apply T score and Z score systems for effectively distinguishing between normal (physiologic) aging and pathologic tissue loss in femorotibial OA. Our data on knee joint cartilage morphology in healthy elderly individuals presented in this study could therefore serve as a first reference for calculating specific Z scores in individual patients. Given the standard deviation of ~15% for the mean thickness of the knee joint cartilage plates, a total of 9 healthy subjects will be required in each age group (e.g., decade) to achieve a standard error of the mean of 5%. With this number of subjects, the error for estimating the actual mean value in the population is <10% at a 95% confidence level. To reduce this error to <5% (with an SEM of 2.5%), a total of 36 individuals is required for each group.

In view of some experimental investigations (9–11), the smaller amount of patellar cartilage deformation after dynamic loading in elderly individuals was unexpected. Those studies have reported a reduced compressive and tensile stiffness of articular cartilage with age (and more so with OA). There are 2 potential explanations for this discrepancy: More recent studies have indicated that cartilage may become not more compliant, but stiffer, with aging. For example, Bank et al (12) found an increase in nonenzymatic glycation product levels (specifically, pentosidine) in mature articular cartilage with age, and an association of higher pentosidine levels with a stiffer collagen network in

instantaneous unconfined compression. It has also been reported that pentosidine crosslinks may render the cartilage more brittle, causing a faster progression of cartilage degeneration (13). In view of the decreasing water content with age (2) and the strong negative linear correlation between water content and equilibrium modulus (9), it may also be that the decrease in interstitial water is responsible for an increase in cartilage stiffness. Another potential explanation for the decrease of in vivo deformation with aging is that elderly individuals apply different motor strategies during physical exercise (15), potentially leading to lower joint loads during exercise.

The observation of a smaller amount of cartilage deformation in elderly subjects has important implications for cartilage biology and the clinical management of OA. In conjunction with a general decline in chondrocyte function with age, a decrease in mechanical stimulation of the cells under in vivo loading conditions in elderly subjects may explain the age-related decrease in proteoglycan synthesis (8). This reduction in matrix synthesis may also provide a potential explanation for the thinning of knee joint cartilage observed in our study. Our observations indicate that the onset of OA in elderly individuals is not explained by the suspected increase in cartilage deformation due to altered mechanical properties, and that cartilage transplants will be subjected to smaller rather than higher strains within their target environment in elderly subjects. Finally, the observation that cartilage becomes more compliant in OA (1,9) indicates that it may be more effective to measure the functional properties (deformational behavior) of articular cartilage to differentiate between normal (physiologic) aging and pathologic processes rather than to determine morphologic parameters alone.

The current study focused on the analysis of the deformational behavior of patellar cartilage because (unlike for the tibia) short acquisition times and a very high precision (~1–1.4%) can be achieved with a transverse section orientation. Further efforts are required to establish comparable protocols for reliably measuring femorotibial cartilage compression in young and elderly individuals in vivo, and to determine whether these cartilage plates behave differently or similarly compared with the patella.

In conclusion, our study confirms the hypothesis that thinning of knee joint cartilage occurs physiologically with aging, in the absence of cartilage disease. However, the reduction is higher in some (femoral) cartilage plates than in others (tibia) and differs between the sexes (patella). Our findings show that elderly subjects do not display a higher amount of cartilage deformation in vivo than do young subjects, but that the deformation is considerably less than in the young. These data provide a basis for the quantitative assessment of morphologic and functional cartilage properties in OA versus those observed during normal (physiologic) aging, using an entirely noninvasive imaging modality.

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REFERENCES

1. Grushko G, Schneidermann R, Maroudas A. Some biochemical and biophysical parameters for the study of the pathogenesis of osteoarthritis: a comparison between the processes of ageing and degeneration in human hip cartilage. Connect Tissue Res 1989; 19:149–76.
2. Meachim G, Bentley G, Baker R. Effect of age on thickness of adult patellar articular cartilage. Ann Rheum Dis 1977;36:563–8.
3. Meachim G. Effect of age on thickness of adult articular cartilage at the shoulder joint. Ann Rheum Dis 1971;30:43–6.
4. Karvonen RL, Negendank WG, Teitge RA, Reed AH, Miller PR, Fernandez-Madrid F. Factors affecting articular cartilage thickness in osteoarthritis and aging. J Rheumatol 1994;21:1310–8.
5. Stammberger T, Eckstein F, Englmeier K-H, Reiser M. Determination of 3D cartilage thickness data from MR imaging: computational method and reproducibility in the living. Magn Reson Med 1999;41:529–36.
6. Burgkart R, Glaser C, Hyhlik-Dürr A, Englmeier K-H, Reiser M, Eckstein F. Magnetic resonance imaging–based assessment of cartilage loss in severe osteoarthritis: accuracy, precision, and diagnostic value. Arthritis Rheum 2001;44:2072–7.
7. Graichen H, Springer V, Flamann T, Stammberger T, Glaser C, Englmeier K-H, et al. High-resolution, selective water-excitation MR imaging for quantitative assessment of thin cartilage layers: validation with CT-arthrography and A-mode ultrasound. Osteoarthritis Cartilage 2000;8:106–14.
8. DeGroot J, Verzijl N, Bank RA, Lafeber FPJG, Bijlsma JWJ, TeKoppele JM. Age-related decrease in proteoglycan synthesis of human articular chondrocytes: the role of nonenzymatic glycation. Arthritis Rheum 1999;42:1003–9.
9. Armstrong CG, Mow VC. Variations in the intrinsic mechanical properties of human cartilage with age, degeneration and water content. J Bone Joint Surg Am 1982;64:88–94.
10. Armstrong CG, Bahrani AS, Gardner DL. In vitro measurement of articular cartilage deformations in the intact human hip joint under load. J Bone Joint Surg Am 1979;61:744–54.
11. Kempson GE. Age-related changes in the tensile properties of human articular cartilage: a comparative study between the femoral head of the hip joint and the talus of the ankle joint. Biochim Biophys Acta 1991;1075:223–30.
12. Bank RA, Bayliss MT, Lafeber FPJG, Maroudas A, TeKoppele JM. Ageing and zonal variation in post-translational modification

of collagen in normal human articular cartilage: the age-related increase in non-enzymatic glycation affects biomechanical properties of cartilage. Biochem J 1998;15:345–51.
13. DeGroot J, Verzijl N, Wenting-van Wijk M, Jacobs K, Van Roermund P, Bank RA, et al. Nonenzymatic glycation increases the severity of osteoarthritis in the canine ACLT model: a biochemical basis for age as a risk factor of OA [abstract]. Transactions of the 47th Annual Meeting of the Orthopaedic Research Society, February 25–28, 2001, San Francisco, CA. p. 227.
14. Eckstein F, Lemberger B, Stammberger T, Englmeier KH, Reiser M. Patellar cartilage deformation in vivo after static versus dynamic loading. J Biomech 2000;33:819–25.
15. Papa E, Cappozzo A. Sit-to-stand motor strategies in able-bodied young and elderly subjects. J Biomech 2000;33:1113–22.