Slice Thickness in the Assessment of Medial and Lateral Tibial Cartilage Volume and Accuracy for the Measurement of Change in a Longitudinal Study

FLAVIA CICUTTINI, KEVIN F. MORRIS, MICHAEL GLISSON, ANITA E. WLUKA

ABSTRACT. ***Objective.*** The optimal magnetic resonance image (MRI) slice thickness required to assess cartilage volume accurately and efficiently in cross-sectional and longitudinal studies is unknown. We compared cartilage volume measured from MRI of the knees using different slice thicknesses (1.5 to 7.5 mm) and assessed longitudinal change.

Methods. A total of 123 subjects with osteoarthritis had baseline and followup MRI on their symptomatic knee at 2 years. Medial and lateral tibial cartilage volumes were calculated using increasing slice thickness by extracting each second, third, fourth, or fifth slice area to calculate total volume, which was compared to the "gold standard" volume calculated from the original 1.5 mm slices.

Results. There was little difference in the average medial and lateral tibial cartilage volume observed as the slice thickness increased from 1.5 to 7.5 mm; medial tibial cartilage volume ranged from 1750 µl to 1787 µl and lateral tibial cartilage volume ranged from 1949 µl to 2007 µl. There was also little absolute difference in the average change in medial and lateral tibial cartilage volume measured over 2 years. However, with increasing slice thickness, there was a decreased correlation between the tibial cartilage volume change calculated from the increased slice thickness, with the lowest correlation being 0.77 ($p < 0.001$) when the lateral cartilage volume calculated from the 7.5 mm slice was compared to the 1.5 mm slices.

Conclusion. Increasing slice thickness may provide sufficiently accurate measurement of tibial cartilage volume and change over time in some studies. This would result in reduction in MRI scanning and postimaging processing time, which has the potential of increasing the feasibility of this technique. (J Rheumatol 2004;31:2444–8)

Key Indexing Terms:
KNEE CARTILAGE MAGNETIC RESONANCE IMAGING SLICE THICKNESS

Osteoarthritis (OA) is a disease involving articular cartilage and the underlying bone. With increasing disease severity, articular cartilage is lost. However, the study of OA has been limited by the lack of a sensitive tool with which to measure the cartilage, as a marker of disease severity. The joint space has been used as a proxy for disease severity, with the underlying assumption that it consists primarily of articular cartilage[1]. However, the joint space contains many structures in addition to articular cartilage, including the menisci, synovium, and synovial fluid[2]. It is only an indirect measure of articular cartilage.

There has been increasing interest in direct measurement of articular cartilage from magnetic resonance images (MRI) as a possible outcome measure of OA[3,4]. This method has been validated against anatomic dissection, and it has been shown to be reproducible, with coefficients of variation of about 2%[4,5]. Subjects imaged by MRI are not exposed to any radiation, which is a significant ethical benefit of studies investigating factors contributing to the risk of OA in healthy subjects.

MRI is expensive, with the cost being proportional to imaging time. In addition, most techniques used to measure knee cartilage volume require significant and varying levels of postimaging processing[4,6]. Postimaging processing requires significant experience and training to achieve accurate and reproducible results, since most validated methods are not fully automated. This contributes to the cost of the method, and limits the more widespread application of this measure. One possible solution is to limit the structures measured within the knee, and thus limit the postprocessing time and possibly simplify the technique. We addressed this objective by comparing the relationship between the volume of tibial and femoral cartilage plates in the medial and lateral tibiofemoral joints in healthy subjects and those with OA[7]. We observed a significant relationship between tibial

From the Department of Epidemiology and Preventive Medicine, Monash University, Alfred Hospital, Prahran, Victoria; and the Centre for Clinical Neuroscience and Neurological Research, St. Vincent's Hospital, Melbourne, Australia.

Supported by the Center for Clinical Research Excellence (Therapeutics) and the National Health and Medical Research Council of Australia.

F. Cicuttini, FRACP, PhD, Associate Professor; M. Glisson, PhD Scholar; A.E. Wluka, FRACP, NHMRC Scholar, Department of Epidemiology and Preventive Medicine, Monash University; K.F. Morris, ME, FIEAust, Senior Researcher, Centre for Clinical Neuroscience and Neurological Research, St. Vincent's Hospital.

Address reprint requests to Dr. F. Cicuttini, Department of Epidemiology and Preventive Medicine, Alfred Hospital, Prahran, Victoria 3181, Australia. E-mail: flavia.cicuttini@med.monash.edu.au

Submitted November 18, 2003; revision accepted July 12, 2004.

and femoral cartilage volume in both healthy subjects and those with OA and in both compartments in a cross-sectional study[7] and with longitudinal change[8]. This suggests that it may be possible to simplify cartilage measurement by measuring one cartilage plate alone[8].

Most current work has focused on reducing slice thickness in order to improve accuracy of cartilage volume measurement. However, this results in increased MRI scanning time and an increase in the number of slices to be processed. There is currently no information available on the optimal slice thickness in terms of accuracy and efficiency in assessing cartilage volume cross-sectionally and over time. We compared cartilage volume measured from MRI of the knees using different slice thicknesses (1.5, 3, 4.5, 6.0, and 7.5 mm) and assessed longitudinal change.

MATERIALS AND METHODS

Subjects with OA who had been involved in longitudinal studies of knee cartilage within our unit over about 2 years and who had had a radiograph at baseline were included in this study. The study was approved by the ethics committee of the Alfred and Caulfield Hospitals in Melbourne, Australia. All subjects provided informed consent. Subjects with knee OA were recruited using a combined strategy including advertising through local newspapers and the Victoria branch of the Arthritis Foundation of Australia as well as collaboration with general practitioners, specialist rheumatologists, and orthopedic surgeons. Subjects were excluded if any form of arthritis other than OA was present, including evidence of chondrocalcinosis on plain radiographs or evidence of focal cartilage lesion on MRI to suggest a posttraumatic etiology.

At baseline, each asymptomatic subject had a weight-bearing anteroposterior tibiofemoral radiograph, taken in full extension, of the dominant knee. In the case of symptomatic subjects, both knees were imaged, but the knee with the least symptomatic radiographic OA was used as the study joint. These radiographs were independently scored in duplicate by a trained observer who used a published atlas to classify disease in the tibiofemoral joint[9]. The intraobserver reproducibility as measured by kappa statistic was 0.92 for tibial and 0.90 for femoral osteophytes, and 0.82 for medial and 0.80 for lateral joint space narrowing (kappa statistic).

Knee cartilage volume was determined by means of image analysis using the Osiris program[4,5]. The volumes of the medial tibial and lateral tibial knee cartilage plates were isolated from the total volume by manually drawing disarticulation contours around the cartilage boundaries on an image by image basis. All individual slice areas for each cartilage and each subject were subsequently recorded. The total area of each individual cartilage was then multiplied by the slice thickness to produce a volume estimate. These measurements were then repeated independently by a second researcher. This "all slice" estimate of cartilage volume (based on slice thickness of 1.5 mm) was used as the "gold standard" for later comparison.

Medial and lateral tibial cartilage volumes were calculated based on increasing slice thickness by extracting each second, third, fourth, or fifth slice area from the data file of each individual's medial and lateral tibial cartilage plate. These were then summed and this total was multiplied by the corresponding slice thickness (3.0, 4.5, 6.0, or 7.5 mm). In practical MR scanning the actual position of the first intersection of the cartilage will be unknown until after a scan is acquired. To simulate this real-practice situation, a second series of estimates was calculated by randomly selecting the slice that was the starting point.

Statistical analysis. Descriptive statistics for characteristics of the subjects were tabulated. Results were assessed for normality. To assess the relationship between medial and lateral tibial cartilage volumes calculated from the thinnest slices (1.5 mm) compared to those calculated from the increased slice thicknesses (3.0, 4.5, 6.0, and 7.5 mm), Spearman's correlation coefficients were calculated. Absolute over and under errors (i.e., irrespective of direction) for each cartilage volume measurement compared to that estimated from the 1.5 mm slice data are reported as the mean absolute values of the differences between the cartilage volumes based on the scans of 1.5 mm thickness and the measurements obtained from the increasing slice thickness. Absolute percentage error was obtained by dividing the absolute error by the cartilage volumes based on the data for the scan at 1.5 mm thickness. To assess the relationship between medial and lateral tibial cartilage volume, and changes in medial and lateral tibial cartilage volume, Spearman's correlation coefficients were calculated. A p value less than 0.05 (2-tailed) was considered statistically significant. All analyses were performed using SPSS (v. 10.0.5; SPSS, Chicago, IL, USA).

RESULTS

There was little difference in the average medial and lateral tibial cartilage volume obtained as the slice thickness increased from 1.5 to 7.5 mm. The medial tibial cartilage volume varied from 1750 µl to 1787 µl as the slice thickness increased from 1.5 mm to 7.5 mm (Table 1). The corresponding average lateral tibial cartilage volumes varied from 1949 µl to 2007 µl.

The absolute over and under-estimates of the medial and lateral tibial cartilage volumes increased as the slice thickness increased (Table 1). For the medial tibial cartilage volume this increase ranged from 4.8% using the 3.0 mm slice thickness to 7.4% when the volume was calculated from the 7.5 mm slices. For the lateral tibial cartilage volume this increase ranged from 4.2% using the 3.0 mm slice to 7.4% when the volume was calculated from the 7.5 mm slices. There was only a small reduction in the correlation between the medial tibial cartilage volumes calculated from the increased slice thickness, with the lowest correlation being 0.96 ($p < 0.001$) when the medial cartilage volume calculated from the 7.5 mm slice was compared to that calculated from the 1.5 mm slices (Table 1). Similarly, the correlation between the lateral tibial cartilage volume calculated from the 1.5 mm slices and that calculated from the 7.5 mm slices was $R = 0.95$ ($p < 0.001$). For slice thicknesses of 3.0 mm and 4.5 mm the average over and under-estimates of both medial and lateral cartilage volumes were 5.1% or less, with correlations of 0.98. When the medial and lateral tibial cartilage volumes were calculated by randomly selecting a different MRI slice as the starting point, there was very little difference in the mean cartilage volume calculated compared to the volume calculated when using slice number 1 as the first slice with the correlation being $R = 0.99$ ($p < 0.001$) for both the medial and lateral tibial cartilages.

We used the knee cartilage volume to assess change in cartilage volume over the study duration of 2 years to compare change measured by the different slice thicknesses (Table 2). There was little difference in the average medial and lateral tibial cartilage volume change observed as the slice thickness increased from 1.5 to 7.5 mm. However, there was a reduction in the correlation between the medial tibial cartilage volume change calculated from the increased

Table 1. Comparison of medial and lateral tibial cartilage volumes measured using MRI images acquired using different slice thickness, compared to the "gold standard" volume measured from 1.5 mm slice thickness.

	Section Thickness 1.5 mm	Section Thickness 3.0 mm	Section Thickness 4.5 mm	Section Thickness 6.0 mm	Section Thickness 7.5 mm
Medial tibial cartilage, µl					
Mean cartilage volume (SD)	1787 (507)	1750 (528)	1757 (500)	1763 (532)	1780 (548)
Absolute difference (SD)*		84 (78)	90 (70)	113 (96)	123 (93)
Absolute % difference (SD)		4.8 (4.6)	5.1 (4.0)	6.5 (5.1)	7.4 (6.1)
Correlation (R) of cartilage volume with that calculated using 1.5 mm slice thickness		0.98, $p < 0.000$	0.98, $p < 0.000$	0.96, $p < 0.000$	0.96, $p < 0.000$
Lateral tibial cartilage, µl					
Mean cartilage volume (SD)	1990 (606)	1949 (589)	1966 (598)	1997 (606)	2007 (597)
Absolute difference (SD)*		82 (81)	94 (83)	110 (76)	140 (117)
Absolute % difference (SD)*		4.2 (4.2)	4.8 (3.8)	6.0 (4.9)	7.4 (6.0)
Correlation (R) of cartilage volume with that calculated using 1.5 mm slice thickness		0.98, $p < 0.000$	0.98, $p < 0.000$	0.98, $p < 0.000$	0.95, $p < 0.000$

* Mean absolute differences and mean absolute percentage differences of cartilage volume measured using the different slice thicknesses compared to the volume measured from the 1.5 mm slice thickness.

Table 2. Comparison of change in medial and lateral tibial cartilage volumes over a 2 year period measured using MRI images acquired using different slice thicknesses, compared to the "gold standard" volume measured from 1.5 mm slices.

	Comparator	Change in Medial Tibial Cartilage Plate Using Different Section Thickness			
	Section Thickness 1.5 mm	3.0 mm	4.5 mm	6.0 mm	7.5 mm
Mean change in cartilage volume (SD), µl	576 (370)	616 (388)	625 (422)	582 (414)	590 (447)
Correlation (R) of change in cartilage volume with that calculated using 1.5 mm slice thickness		0.91, $p < 0.000$	0.91, $p < 0.000$	0.85, $p < 0.000$	0.81, $p < 0.000$
	Comparator	Change in Lateral Tibial Cartilage Plate Using Different Section Thickness			
	1.5 mm	3.0 mm	4.5 mm	6.0 mm	7.5 mm
Mean change in cartilage volume (SD), µl	258 (310)	210 (309)	207 (338)	265 (317)	280 (359)
Correlation (R) of change in cartilage volume with that calculated using 1.5 mm slice thickness		0.91, $p < 0.000$	0.90, $p < 0.000$	0.83, $p < 0.000$	0.77, $p < 0.000$

slice thickness, with the lowest correlation being 0.81 ($p < 0.001$) when the medial cartilage volume calculated from the 7.5 mm slice was compared to that calculated from the 1.5 mm slices (Table 2). Similarly, the correlation between the lateral tibial cartilage volume calculated from the 1.5 mm slices and that calculated from the 7.5 mm slices was 0.77 ($p < 0.001$). The standard deviation of the in change cartilage volume can be seen to increase for both the medial and lateral tibial cartilage volumes (Table 2).

DISCUSSION

Our data suggest that for slice thicknesses of 3.0 mm and 4.5 mm the average over and under-estimates of both medial and lateral cartilage volumes were 5.1% or less, with correlations of 0.98 between the cartilage volumes obtained using these slice thicknesses and those obtained from 1.5 mm slice thickness. There was very little change in the magnitude of the average loss of cartilage volume over 2 years as the slice thickness increased, although the standard deviation increased. There was, however, a gradual reduction in the correlation between the cartilage volume measured using 1.5 mm slice thickness and the increased slice thickness for individual subjects.

No previous study has examined the effect of increasing slice thickness on measurement of cartilage volume. We have previously shown that there is good correlation between cartilage volume measured using 1.5 mm slice thickness and anatomical dissection of cartilage[5], and that this method of measuring cartilage volume is sensitive for detecting change in tibial cartilage volume[4]. We showed that subjects with OA lose about 5% of their knee cartilage per annum[4]. In the current study we used this well described population to explore the effect of increasing the slice thickness on measurement of cartilage volume, while other meas-

urement variables were kept constant. We saw that increasing slice thickness resulted in surprisingly little change in the magnitude of the average cartilage volume loss over 2 years when cartilage volume was measured using 1.5 mm slice thickness and increasing slice thickness up to 4.5 mm. This can be explained by the spatial resolution decreasing with increasing slice thickness, and thus the variance in the data increasing because the remaining slices focus on different portions of the irregularly shaped cartilage. Depending on what particular surfaces remain, the overall volume may be increased or decreased. However, if this is random, then the mean will remain roughly the same, as we found.

The increase in the standard deviation of the average cartilage loss as the slice thickness increased would be expected to influence the sample size required in order to demonstrate a change in cartilage volume. For example, based on these data, if all other measurement variables were kept constant, it would be expected that for a given effect size, the sample size would increase by about 30% as the slice thickness increased from 1.5 mm to 7.5 mm at the medial tibial cartilage, and 35% at the lateral tibial cartilage. These observations only remain true for the average change in cartilage volume of a population, since we also observed a reduction in the correlation between the cartilage volume measured using 1.5 mm thick slices and the increasing slice thickness, suggesting that greater error is likely on an individual level.

This study has simply looked at the effect of increasing slice thickness while all other variables were kept constant. We used the measurements of a single, experienced observer. We did not rescan the study subjects, but simply estimated the cartilage volume by using every second, third, fourth, and fifth slice. This has merit in that it allowed us to examine the single effect of slice thickness in the situation where all other variables, such as repositioning the subject and measurement, were kept constant. The effects of these errors on measurement have been well documented[10,11]. One further potential problem of increased slice thickness is that there may be variability in the position at which the first MRI slice is positioned. When we examined this by randomly selecting the site at which cartilage volume estimate was started, we found strong correlation between cartilage volume estimations.

Intuitively, reducing the number of slices of tibial cartilage measured may seem unwise. However, it should be kept in mind that for a completely regular structure, such as a cylinder, the area of a single slice with length gives an exact volume. This principle can also be applied to more complex structures. Recent theory has been developed to estimate volume from a systematic sample of tissue slices of a given thickness and to predict the corresponding error[12,13]. A recent study was performed to determine the minimum number of MRI slices required to estimate the volumes of the cerebrum and of the compartments of gray matter and white matter[12]. Irrespective of slice thickness, a minimum of 3, 5, and 10 slices provided estimates of the true total volume of grey matter and white matter with coefficients of error of 10%, 5%, and 3%. For the cerebrum, a minimum of 2, 3, and 4 slices were required for coefficients of error of the same precision. The tibial cartilage is a relatively regular structure, so it is not surprising that a limited number of slices give an accurate estimate of the volume. By reducing the number of slices to 25% in 2 typical subjects tested, we estimated that the predicted increase would increase by less than 1% (data not shown). This is consistent with the relatively modest error that we observed in cartilage volume estimation when the slice thickness was increased.

Our combined data suggest that it may not be necessary to use very thin slice thickness in all studies examining joint cartilage. A major problem with routine use of MRI in the epidemiology of OA is the issue of feasibility. Currently, MRI is an expensive modality with limited access. However, postimaging processing requires significant experience and training to achieve accurate and reproducible results, since it is not an automated method[4,6]. This means that it is currently limited to few institutions. However, MRI is a very versatile tool and can be used to address a number of issues in knee OA, and we have already seen its potential in examining factors affecting knee cartilage[14,15].

For some purposes, increasing slice thickness may provide sufficiently accurate results. This would mean reduction in MRI scanning time. The cost of this technique is directly proportional to scanning time. In addition, there will also be a proportional reduction in postimaging processing time. This approach is analogous to the early work in the area of osteoporosis that was aimed at simplifying the measurement of bone mineral density (BMD), yet retaining clinically useful information. For example, increasing slice thickness by 3-fold will reduce imaging and postprocessing time by roughly one-third. This can be used to negotiate the cost of MRI. How the investigators then design their study will depend on the effect size they estimate will occur, the cost of the limited MRI, the estimated cost-savings of processing the images, and the feasibility and cost of recruiting study subjects. We believe that studies such as this one that aim to simplify assessment of articular cartilage will contribute useful data for the debate about the most efficient way of assessing the state of articular cartilage for different purposes. When more is known about structural change in OA, MRI may assist in routine clinical assessment in a way analogous to the use of BMD in management of osteoporosis.

ACKNOWLEDGMENT

We are grateful to Judy Hankin for her assistance in project management. We are also grateful to the subjects who gave their time to participate in the investigation.

REFERENCES

1. Altman R, Brandt K, Hochberg M, et al. Design and conduct of

clinical trials in patients with osteoarthritis: recommendations from a task force of the Osteoarthritis Research Society. Results from a workshop. Osteoarthritis Cartilage 1996;4:217-43.
2. Adam G, Bohndorf K, Prescher A, Drobnitzky M, Gunther RW. [NMR tomography of the cartilage structures of the knee joint with 3-D volume imaging combined with a rapid optical-imaging computer]. ROFO Fortschr Geb Rontgenstr Nuklearmed 1989;150:44-8.
3. Eckstein F, Schnier M, Haubner M, et al. Accuracy of cartilage volume and thickness measurements with magnetic resonance imaging. Clin Orthop 1998;352:137-48.
4. Wluka AE, Stuckey S, Snaddon J, Cicuttini FM. The determinants of change in tibial cartilage volume in osteoarthritic knees. Arthritis Rheum 2002;46:2065-72.
5. Cicuttini F, Forbes A, Morris K, Darling S, Bailey M, Stuckey S. Gender differences in knee cartilage volume as measured by magnetic resonance imaging. Osteoarthritis Cartilage 1999;7:265-71.
6. Eckstein F, Winzheimer M, Hohe J, Englmeier KH, Reiser M. Interindividual variability and correlation among morphological parameters of knee joint cartilage plates: analysis with three-dimensional MR imaging. Osteoarthritis Cartilage 2001;9:101-11.
7. Cicuttini FM, Wluka AE, Stuckey SL. Tibial and femoral cartilage changes in knee osteoarthritis. Ann Rheum Dis 2001;60:977-80.
8. Cicuttini F, Wluka A, Wang Y, Stuckey SL. Longitudinal study of changes in tibial and femoral cartilage in knee osteoarthritis. Arthritis Rheum 2004;50:94-7.
9. Altman RD, Hochberg M, Murphy WA, Wolfe F, Lequesne M. Atlas of individual radiographic features in osteoarthritis. Osteoarthritis Cartilage 1995;3 Suppl A:3-70.
10. Peterfy CG, van Dijke CF, Janzen DL, et al. Quantification of articular cartilage in the knee with pulsed saturation transfer subtraction and fat-suppressed MR imaging: optimization and validation. Radiology 1994;192:485-91.
11. Eckstein F, Westhoff J, Sittek H, et al. In vivo reproducibility of three-dimensional cartilage volume and thickness measurements with MR imaging. AJR Am J Roentgenol 1998;170:593-7.
12. McNulty V, Cruz-Orive LM, Roberts N, Holmes CJ, Gual-Arnau X. Estimation of brain compartment volume from MR Cavalieri slices. J Comput Assist Tomogr 2000;24:466-77.
13. Garcia-Finana M, Cruz-Orive LM, Mackay CE, Pakkenberg B, Roberts N. Comparison of MR imaging against physical sectioning to estimate the volume of human cerebral compartments. Neuroimage 2003;18:505-16.
14. Jones G, Glisson M, Hynes K, Cicuttini F. Sex and site differences in cartilage development: a possible explanation for variations in knee osteoarthritis in later life. Arthritis Rheum 2000;43:2543-9.
15. Wluka AE, Davis SR, Bailey M, Stuckey SL, Cicuttini FM. Users of oestrogen replacement therapy have more knee cartilage than non-users. Ann Rheum Dis 2001;60:332-6.