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Quantitative Magnetic Resonance Imaging Detects Changes in Meniscal Volume *in Vivo* After Partial Meniscectomy

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Abstract

Background—Quantifying changes in meniscal volume *in vivo* before and after partial meniscectomy (PM) could help elucidate the mechanisms involved in osteoarthritis development after meniscal injury and its surgical treatment.

Purpose/Hypothesis—To determine whether quantitative MRI (qMRI) could detect the immediate reduction in meniscal volume created by PM, while ruling out changes in unresected structures. We hypothesized that qMRI would be reliable for determining meniscal volume within the repeated images of unresected menisci. Additionally, we expected no significant difference in volume between the uninjured menisci of the injured knees and the same menisci of the uninjured knees.

Study Design—Controlled laboratory study.

Methods—Ten subjects with meniscal tears were evaluated with 3T MRI before and after arthroscopic PM. Manual segmentation was used to create models of the menisci and to determine the pre- and post-operative meniscal volumes for each subject. The responsiveness and reliability of qMRI for determining meniscal volume *in vivo* were evaluated using these measurements. We expected a decrease in volume of the resected menisci, but not in the uninjured menisci, after surgery.

Results—The mean pre-operative volume of the injured menisci was significantly greater than the mean post-operative volume ($2896 \pm 277 \text{ mm}^3$ vs. $2480 \pm 277 \text{ mm}^3$; $p=0.000$). There was no significant difference between the mean pre- and post-operative volumes of the uninjured menisci ($2687 \pm 256 \text{ mm}^3$ vs. $2694 \pm 256 \text{ mm}^3$; $p=1.000$).

Conclusions—Manual segmentation demonstrated a significant reduction in the volume of the surgically resected menisci after PM, but no significant change in the volume of unresected meniscal tissue, indicating that the manual segmentation method is responsive.

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Conflict of Interest

None of the authors have any relationships with commercial parties that pertain to the material presented in or related to this manuscript.

Clinical Relevance—This approach offers a novel, reliable method to study the relationship between the volume of meniscal tissue removed during PM and subsequent patient outcomes during long-term clinical studies.

Keywords

Meniscectomy; Imaging; Knee; Quantitative MRI; Osteoarthritis

Introduction

The menisci of the knee are fibrocartilagenous load-bearing structures responsible for increasing cartilage contact area and decreasing contact stress within the tibiofemoral (TF) joint^{1, 26, 32, 35, 42, 45}. These structures are thought to play a role in shock absorption, joint congruity, and articular cartilage nutrition, and are essential for long-term joint function^{6, 24, 44}. Meniscal injury is known to alter knee joint contact mechanics³¹, and may disrupt the load-bearing capabilities of the meniscus, thereby adversely affecting articular cartilage metabolism. Meniscal injuries, therefore, may place the knee joint at risk for early osteoarthritis (OA).

Total meniscectomy, a procedure in which the entire damaged meniscus is excised, was once a standard treatment for meniscal tears, but has since been identified as a risk factor for OA^{18, 33, 41}. Partial meniscectomy (PM), in which the torn portion of the meniscus is removed, while the unaffected, stable portion is left intact, is routinely performed to eliminate the painful symptoms and dysfunction that can accompany meniscal tears. While regarded as an improvement, it is unknown whether PM decreases OA risk compared with total meniscectomy^{3, 4, 12-14, 21, 22, 27-29, 37-41}.

The relationship between meniscal injury, PM, and OA is poorly understood. The effects of meniscal tears and varying degrees of PM on TF joint contact mechanics have been studied in finite element models and cadaver specimens^{31, 46}, but the results may differ *in vivo*, and the amount of meniscal tissue removed and subsequent OA risk remain unknown. Of particular clinical interest is whether there is a critical amount of meniscal tissue that can be removed during PM without compromising the load-bearing, shock-dissipating, and nutritional support capabilities of the meniscus. While the amount of meniscus removed during surgery may not be the only factor associated with the outcome of PM, it almost certainly plays a significant role. Tracking these patients may help determine the existence of such a threshold. These data could help surgeons predict OA risk after PM, and may help determine when the procedure is the best treatment option for meniscal tears, and when alternative treatments should be considered. Such studies necessitate a quantitative method that can reliably assess changes in meniscal volume and dimensions *in vivo* with sufficient accuracy to track changes in patients over time.

Quantitative magnetic resonance imaging (qMRI) has been used to assess morphological changes in knee articular cartilage^{5, 8, 10, 11, 15, 16, 25, 30}, and to estimate meniscus allograft size⁴³. Our group recently validated a qMRI approach for evaluating meniscal volume *ex vivo* using phantom and cadaver models⁹. However, in order for this method to be applied in long-term clinical studies, it must first be validated *in vivo*.

The purpose of this study was to assess the responsiveness of qMRI for determining meniscal volume *in vivo* before and after PM in subjects with unilateral meniscal tears. The main focus was to determine whether qMRI could detect the immediate reduction in meniscal volume created by partial resection, while simultaneously ruling out changes in unresected structures. Ten subjects participated; their injured and uninjured knees were

imaged before and after PM. The specific aims were: (1) to determine whether qMRI could detect a decrease in the volume of surgically resected menisci *in vivo* following partial resection; (2) to determine the reliability of the method for quantifying meniscal volume *in vivo* by repeated imaging of the uninjured menisci; and (3) to determine whether the volume of the contralateral uninjured meniscus could be used to estimate the pre-injury volume of the injured meniscus. We hypothesized that there would be a decrease in the volume of the resected menisci, but not in the uninjured menisci, after surgery (Hypothesis 1). We also expected the qMRI method to be reliable for determining meniscal volume within the repeated images of the unresected menisci (Hypothesis 2). Additionally, we expected no significant difference in pre-operative volume between the menisci of the injured knees and the same menisci of the contralateral knees (Hypothesis 3).

Materials and Methods

Subjects

Study approval was granted by the Institutional Review Boards of Brown University and Rhode Island Hospital prior to subject recruitment. Male and female subjects between the ages of 18 and 50 years who were candidates for arthroscopic PM were eligible for inclusion in the study. Subjects whose injury had occurred more than 12 months before surgery, those with a prior knee injury for which they sought medical attention, or with diseases predisposing them to cartilage damage were excluded from the study. The subjects represented a consecutive sample of those eligible and willing to participate, whose MRIs could be scheduled prior to surgery. No participating subjects were excluded after surgery for any reason.

Ten subjects (9 males, 1 female) with a mean age of 36.2 years (range 22-48 years) were included. The causes of injury varied among subjects. Five subjects underwent unilateral partial medial meniscectomy, 4 subjects underwent unilateral partial lateral meniscectomy, and 1 subject underwent both medial and lateral PM within the same knee.

MR Imaging

MR imaging was performed on both knees of each subject, an average of 11.5 days (range 2 – 44 days) before and 27.2 days (range 14 – 46 days) after surgery; the time between pre- and post-operative MRI assessments averaged 39.7 days (range 18 – 71 days). Each knee was imaged on a 3T MR imaging system (Siemens Trio, Erlangen, Germany), using a commercially available circular polarized knee coil. The medial and lateral menisci of each knee were imaged using the T2*-weighted, 3D-CISS sequence (Fig. 1) [Constructive Interference in the Steady State; TR/TE/FA: 12.5/6.3/35°; FOV: 160mm; matrix: 512×512; in-plane resolution/slice thickness/interslice gap: 0.3125/1.0/0mm; bandwidth: 130 Hz/pixel; averages: 1; acquisition time: 13 minutes, 36 seconds] at both time points⁹.

Manual Segmentation

The menisci of each scan were independently segmented in both the sagittal and coronal planes by a single experienced examiner using commercial software (Mimics 9.11, Materialise, Ann Arbor, MI). Each subject's scans were segmented consecutively, but the examiner was blinded to operative status and patient information. Because the segmentation process is binary, the external contour of each meniscus was segmented without noting any degenerative signal within the meniscal tissue. Once segmented, the menisci were reconstructed, and a 3D voxel model of each structure was created. Each voxel model was wrapped with a triangular mesh to create a virtual solid model⁸⁻¹⁰. Each virtual model captured both the volume and morphology of each meniscus (Fig. 2).

Meniscal Volume

Once a virtual solid model of each meniscus was created from manual segmentation, the volume of each model was determined by surface integration⁹. The volumes of the right medial, right lateral, left medial, and left lateral menisci of each subject were recorded both before and after PM. The pre- and post-operative volumes of the surgically resected menisci were compared to demonstrate that the method could detect the change in volume of the meniscus following PM (Aim 1; Fig. 3a). The pre- and post-operative images of the menisci that were not treated surgically were used to establish the repeatability of the technique (Aim 2; Fig. 3a). Additionally, the pre-operative volumes of the injured and uninjured menisci were compared in order to demonstrate that the volume of the contralateral uninjured meniscus could be used to estimate the pre-injury volume of the injured meniscus (Aim 3; Fig. 3b).

Statistical Analyses

Meniscal volumes were compared using mixed linear modeling. Within-subject, knee, and meniscus correlations were accounted for by including random effects for the intercept and a term for the interaction of these factors. Additionally, repeated measurements of the same meniscus were modeled with correlated error. A variance components variance-covariance structure was used for both random and repeated effects. Orthogonal contrast statements were used to test the hypotheses associated with each specific aim. P-values for multiple comparisons were adjusted using the Holm test (sequential Bonferroni). The test-retest reliabilities of uninjured meniscal volumes were estimated based on the intraclass correlation coefficient (ICC) for a fixed set of ratings. Statistical analyses were carried out in SAS (Version 9.1.3, Service Pack 4; SAS Institute, Cary, NC). Meniscal volumes were normally distributed.

A post-hoc power analysis was conducted to estimate the smallest changes detectable (2-tailed $\alpha = 0.05$) with 10 subjects at powers of 80, 90, and 95% in the uninjured compartments (Table 1). This analysis was informed by the standard deviations and the correlations between the pre- and post-operative measurements of the menisci. The detectable changes can be interpreted as the size of changes at or above that which could be effectively ruled out with probabilities 80, 90, and 95%.

Results

The pre-operative volumes of the injured medial and lateral menisci were significantly greater than the post-operative volumes (adjusted $p=0.000$ for both; Fig. 4). The post-operative volumes of the injured medial and lateral menisci were a mean of 16.8% and 12.1% less, respectively, than the pre-operative volumes of those menisci (Hypothesis 1).

There was no statistically significant difference between the pre- and post-operative volumes of the uninjured menisci in the operated knees (adjusted $p=1.000$; Fig. 4). Similarly, there was no significant difference between the pre- and post-operative volumes of the menisci of the contralateral uninjured knees (adjusted $p=1.000$; Fig. 4). The post-operative volumes of the uninjured menisci differed by a mean of 0.83% from the pre-operative volumes of the uninjured menisci (Hypothesis 2). The ICCs for the uninjured medial and lateral menisci were 0.91 and 0.93, respectively (Hypothesis 2).

There was also no statistically significant difference between the pre-operative volumes of the uninjured medial menisci of the injured knees and the medial menisci of the uninjured knees (mean difference of 13.8%; adjusted $p=1.000$). The same result was seen for the pre-operative volumes of the uninjured lateral menisci (mean difference of 7.4%; adjusted $p=1.000$). Additionally, there was no statistically significant difference between the pre-

operative volumes of the injured medial menisci and the medial menisci of the uninjured knees (mean difference 0.6%; adjusted $p=0.963$). The same result was seen for the pre-operative volumes of the injured lateral menisci and the lateral menisci of the uninjured knees (mean difference 18.4%; adjusted $p=1.000$). Complete results are seen in Table 2 (Hypothesis 3).

Discussion

Although meniscal injury and PM have been correlated with early OA ^{2, 3, 7, 14, 17-20, 22, 23, 27, 34, 36, 37, 41}, to date, a cause-effect relationship between these has not been established.

An accurate, reliable method that can quantify changes in meniscal volume and dimensions *in vivo* would allow PM patients to be tracked over time, thereby helping to elucidate the mechanisms involved in early OA development. Such a method could also be used to size meniscal allografts. The method proposed in this study would provide a valuable tool for both applications.

By showing statistically significant reductions in the volume of the resected menisci after surgery, the present study demonstrates that qMRI is sensitive enough to detect the surgical removal of meniscal tissue. The measured volume reduction was not a product of bias, since no reduction was detected in the volumes of the uninjured menisci, despite 95% power to detect changes in volume of 97mm³. These results suggest that the described MR-based imaging and segmentation method is a responsive and reliable tool for determining a change in meniscal volume *in vivo* after PM. This quantitative method may be useful in future long-term studies designed to evaluate the outcome of meniscal injury and PM.

It is possible that a loss of meniscal volume at the time of injury may affect the pre-operative meniscal volumes indicated by our segmentation method. Preliminary data have shown that it is possible to use the volume of the contralateral, uninjured meniscus to estimate the pre-injury volume of an injured meniscus if necessary ⁹. In the present study (Aim 3), the mean pre-operative volumes of the uninjured medial and lateral menisci within the injured knees differed from the mean volumes of the same menisci within the uninjured knees by 13.8% and 7.4%, respectively. Additionally, the mean pre-operative volumes of the injured medial and lateral menisci differed from the mean volumes of the same menisci within the uninjured knees by 0.6% and 18.4%, respectively. It is likely that the lateral menisci that underwent partial resection were more damaged during injury, contributing to the higher percent difference between these menisci and their uninjured counterparts. These differences were not statistically significant, and further suggest that contralateral menisci may be useful to estimate the pre-injury volumes of injured menisci, particularly when an injured meniscus is badly damaged.

Because the relationships between meniscal injury, PM, and OA are not well understood, it is possible that the volume of meniscal tissue removed during surgery may not be as meaningful as the location from which it is removed, and the status of the outer rim of the meniscus. The 3D voxel models created from our manual segmentation procedure capture both volume and morphology, so it will be possible to use these models to assess not only the volume of meniscal tissue removed during surgery, but also the location from which it is removed and the status of the meniscal rim.

Stone et al. used a similar MR-based approach to size meniscal allografts ⁴³. The technique involved the segmentation of 1.5T MR images in the sagittal plane. MR-based meniscal volumes were compared to water displacement volumes to determine accuracy. Stone et al. reported the water displacement volumes to be approximately 2500mm³, which align well with the meniscal volumes estimated in the present study. While precise, their MR-based

measurements consistently underestimated actual meniscal volumes by 20 and 44% for the medial and lateral menisci, respectively. In contrast, our group recently completed an *ex vivo* evaluation of the meniscal segmentation approach described in the present study⁹. By segmenting 3T MR images in both the sagittal and coronal planes, we were able to create 3D virtual models of cadaver menisci. We then compared the volumes of these models to water displacement-based volumes of the same menisci, excised from the cadaver knee. We noted coefficients of variation of less than 4% for both medial and lateral menisci, and MR-based volumes that were within 5% of water displacement volumes, indicating the technique was both reliable and accurate *ex vivo*. The responsiveness of this method for measuring meniscal volume has been further confirmed *in vivo* by the present study, wherein pre- and post-operative volumes of the uninjured menisci across subjects showed a difference of only 0.83% (range 0.16-1.57%), while the volumes of the injured menisci showed a difference of 14.4% (range 12.1-16.8%) before and after PM. An *in vivo* assessment is necessary to account for the errors introduced by motion and blood flow artifacts, which were found to be negligible.

There are several limitations associated with the present study. First, the number of subjects studied was relatively small (n=10). However, we were able to detect statistically significant decreases in meniscal volume after surgery in the treated menisci with this sample size, while simultaneously ruling out changes in the control menisci. Our post-hoc power analysis suggests that with 10 subjects, the study was adequately powered to detect changes in meniscal volume (Table 1). Additionally, the purpose of this study was to validate the described MR-based segmentation method *in vivo* so that the method can be used in the design of future long-term clinical studies.

Second, the design of this study did not allow for any direct accuracy assessment of meniscal volume. The nature of the arthroscopic PM procedure did not allow us to measure the amount of meniscal tissue removed from each subject's knee during surgery. Attempts were made to filter each piece of tissue removed during preliminary studies, but because each arthroscopy involved some shaving and debridement of the injured meniscus, measurement was not feasible. However, our group has conducted studies using phantom and cadaver models to assess the accuracy and reliability of our meniscal segmentation technique *ex vivo*⁹. In future studies, it may prove useful to study accuracy by taking intra-operative measurements of the resected menisci, and comparing those to dimensions of the 3D voxel models created by our segmentation method.

Despite these limitations, the results of the present study, particularly when combined with the *ex vivo* work evaluating the accuracy of the method⁹, indicate that MR-based segmentation is a responsive and reliable method for evaluating meniscal volume *in vivo* before and after PM. This method can be applied in future long-term studies of the outcomes of PM, which may begin to elucidate the mechanisms that drive the relationship between meniscal injury, PM, and early OA.

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Figure 1.
Sagittal view of a knee imaged with the Constructive Interference in the Steady State (CISS) sequence, from which the menisci were segmented.

Figure 2. MR-based 3D models of a subject's medial meniscus with a radial tear in the posterior region (a) before and (b) after partial meniscectomy. The virtual 3D models created in this study captured both volume and morphology of the menisci.

Figure 3.

Flow charts depicting the use of data gathered from each subject. Each subject had one injured and one uninjured knee, both of which underwent MRI before and after the injured knee underwent arthroscopic partial meniscectomy. (a.) Aims 1 and 2 compared the volumes of the injured and uninjured menisci, respectively, before and after partial meniscectomy. (b.) Aim 3 compared the pre-operative volumes of the injured and uninjured menisci.

Figure 4.

Least squares mean volumes (mm³) of the menisci of the injured (left 4 sets of columns) and uninjured (right 2 sets of columns) legs, before and after arthroscopic partial meniscectomy. Labels “Inj,” “Uninj,” “Lat,” and “Med” denote Injured, Uninjured, Lateral, and Medial, respectively. * denotes adjusted p=0.000. Error bars indicate $\pm$ standard errors.

Table 1

Detectable changes in meniscal volume at power as a function of location.

<u>Leg</u>	<u>Meniscus</u>	<u>Compartment Status</u>	<u>Detectable Change (mm³)</u>		
			<u>80%</u>	<u>90%</u>	<u>95%</u>
Injured	Lateral	Uninjured	71	82	92
Injured	Medial	Uninjured	6	6	7
Uninjured	Lateral	Uninjured	110	127	143
Uninjured	Medial	Uninjured	113	130	146

Table 2

Pre-operative least squares mean meniscal volumes (mm^3) and their least squares standard errors (SE) as a function of leg (injured vs. uninjured), meniscus (medial vs. lateral), and compartment status (injured vs. uninjured). Direct comparisons were made between the injured and uninjured leg for each group of menisci by calculating the percent difference.

Leg	Meniscus	Compartment Status	Mean (SE) Pre-op Volume (mm^3)	Percent Difference
Injured	Medial	Uninjured	3268 (324)	13.8%
Uninjured	Medial	Uninjured	2817 (205)	
Injured	Lateral	Uninjured	2249 (290)	7.4%
Uninjured	Lateral	Uninjured	2415 (205)	
Injured	Medial	Injured	2833 (265)	0.6%
Uninjured	Medial	Uninjured	2817 (205)	
Injured	Lateral	Injured	2958 (290)	18.4%
Uninjured	Lateral	Uninjured	2415 (205)	