Repeatability of quantification of extrusion of the medial meniscus in knee osteoarthritis using three-dimensional models

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SUMMARY

Objective: Meniscal damage is one of risk factors for the development of knee osteoarthritis (KOA). Medial meniscal extrusion (MME) is associated with the progression of cartilage loss in the medial compartment. The objective of this study was to determine the intra-rater repeatability of our method of three-dimensionally analyzing MME in patients with KOA.

Design: Eight knees with medial KOA were examined in participants aged between fifty and eighty years old. We created three-dimensional models of the tibia and medial meniscus using a 0.4 Tesla MRI scanner and embedded a local coordinate system into the tibia. Repeatability of measurements of the MME volume and width were tested using intraclass correlation coefficient (ICC).

Results: The ICC for measuring the MME volume was 0.998 [95% confidence interval, 0.992, 1.000]. Measurement error for the MME volume was 0.5–7.0%. The ICC for measuring the MME width was 0.983 [0.924, 0.996]. Measurement error for the MME width was 0.0–11.4%. There was no correlation between the MME volume and width (r = 0.565, p = 0.145).

Conclusions: This study concluded that three-dimensional volume and width measurements of the MME by a single rater using MRI images had high repeatability even in the limited image quality. The result of non-significant correlation between the MME width and volume suggests that MME width measured using a low-magnet MRI scanner not considered reliable. Further studies are needed to determine the association between the MME volume and disease progression of KOA.

1. Introduction

There is a pressing need to develop methods of treating and preventing knee osteoarthritis (KOA). The number of patients with symptomatic KOA has been estimated to be 7.8 million in Japan [1] and 15.1 million in the United States [2]. In recent years, magnetic resonance imaging (MRI) allows to capture detailed pathologic changes due to KOA, even in asymptomatic individuals [3]. Medial KOA involves a greater amount of meniscal extrusion than that occurring in individuals without KOA [4]. Presence of MME was associated with prevalent frequent knee symptoms such as knee pain and stiffness at 12-month visit at the odds ratio of 1.64 [95% confidence interval: CI 1.02, 2.62] [5]. Moreover, KOA grade 2 or worse on Kellgren-Lawrence classification, meniscal tear, and presence of meniscal meniscal extrusion (MME) at the baseline were associated with the onset of cartilage defect after 30 months of follow up [6]. Therefore, MME may contribute to symptoms and progression of KOA.

Accurate and precise measurement of MME would allow longitudinal comparisons of KOA. Several methods of measuring MME quantitatively or semi-quantitatively have been proposed [5,7–10]. Whole-Organ Magnetic Resonance Imaging Score (WORMS) as a semi-quantitative method using the Likert scale had difficulties in measuring and comparing MME in detail [7,8,11]. The MRI Osteoarthritis Knee Score (MOAKS) evaluated meniscal extrusion by grading 0–4; grade 0: <2 mm;
Comparisons of longitudinal measurements for MME will require a reliable method of defining the contours of the tibial plateau and medial meniscus, so that the distance of MME can be determined with sufficient reproducibility. Previously proposed 2D methods involved the medial edge of the medial tibial plateau [13–16] or medial edge of the medial articular cartilage [9,17,18]. However, using the medial edge of the tibial plateau as a reference point [13–16] is problematic since it may develop osteophyte formations that may change its contour over time. Similarly, the medial edge of the articular cartilage [9,17,18] may also demonstrate degeneration and cannot provide a consistent reference point for a longitudinal study. Therefore, the optimal measurement method must avoid using anatomical landmarks affected by osteophytes or degeneration as reference points for determining MME. Accordingly, such a reference point would provide more consistent results in measuring MME. Moreover, MME width may be suppressed by the medial collateral ligament and may not be the best index of pathology. Therefore, the volume of the medial meniscus outside the contour of the tibia may be of interest to determine whether the distance is an appropriate index for MME.

We developed a three-dimensional (3D) method for measuring MME that avoids the potential errors caused by changes in osteophytes around the medial tibial plateau [19]. However, this new method requires validation. The objective of this study was to determine intra-rater repeatability of the 3D measurement method for MME, as a part of developing a new method of measuring MME three-dimensionally. We hypothesized that measuring the MME volume and width using a consistent reference for determining MME. Accordingly, such a reference point would provide more consistent results in measuring MME. Moreover, MME width may be suppressed by the medial collateral ligament and may not be the best index of pathology. Therefore, the volume of the medial meniscus outside the contour of the tibia may be of interest to determine whether the distance is an appropriate index for MME.

We developed a three-dimensional (3D) method for measuring MME that avoids the potential errors caused by changes in osteophytes around the medial tibial plateau [19]. However, this new method requires validation. The objective of this study was to determine intra-rater repeatability of the 3D measurement method for MME, as a part of developing a new method of measuring MME three-dimensionally. We hypothesized that measuring the MME volume and width using 3D models would not involve clinically significant intra-rater error. Validation of the 3D method of measuring the MME would allow longitudinal observations and comparisons between different laboratories in future studies. In order to verify the hypothesis, we examined KOA patients with the MME to assess intra-rater repeatability.

2. Methods

2.1. Trial design

This study examined intra-rater repeatability. This study was based on image data obtained as baseline data in a randomized controlled trial (RCT) investigating the effect of exercise therapy in patients with KOA. The study protocol was approved by the institutional review board of the local hospital (approval number: 2010-14) and registered at UMIN Clinical Trials Registry (UMIN000028944). We recruited participants at a seminar on KOA held by the local hospital. Written informed consent was obtained from all the participants included in the study.

2.2. Participants

Inclusion criteria for this study were: 1) Japanese aged between fifty and eighty years old; 2) primary KOA; 3) Kellgren-Lawrence classification grade 1, 2 or 3; and 4) consent to participate after receiving a thorough explanation of the protocol and expected risks. Exclusion criteria were: 1) any history of rehabilitation for KOA; 2) secondary KOA; 3) history of knee injury or surgery; 4) presence of other physical disability, mental disorder, or inability to communicate clearly; or 5) inability to undergo MRI. A priori sample size calculation was performed using R version 2.8.1. Eight participants were needed to determine the reliability under the condition of alpha level of 0.05, a power of 0.8, and a k of two.
[0.16, 0.40] mm/0.92 [0.59, 1.26] in the Z-axis as single rater conducted the embedding process twice at an interval of three days [21]. The same tibial model was used for the first and second measurements.

2.5. Outcomes

The MME volume was defined as the volume of the medial meniscus outside the contour of the tibial cross section. First, the tibial cross section was created by cutting the model below the tibial plateau where the contour of the cross section was not affected by osteophytes (Figs. 2a, b). The contour of the plane 4.0 mm below the tibial plateau plane was observed and bony protrusion was recognized as osteophyte at the observed plane. The cross section was thickened inferiorly for 20 mm thickness to create a tibial cross section volume (Fig. 2c). Then, the medial meniscus was translated inferiorly so that the superior surface of the medial meniscus was covered by the tibial cross section model, and the MME width was the distance on the Z-axis measured from the most medial point of the tibial cross section model and the most medial point of the medial meniscus (Fig. 3).

2.6. Statistical analysis

An experienced rater performed manual segmentation of the medial meniscus, then performed the segmentation again one week later. The error in the MME volume and width were calculated. In addition, the Pearson’s correlation coefficient between the MME volume and width was calculated at a significance level of α = 0.05. Statistical analysis for repeatability was performed using intraclass correlation coefficient (ICC). ICC and 95% CI were calculated with the use of SPSS Statistics version 21 (IBM Corporation, Armonk, NY) based on a single-measures (k = 2), absolute-agreement, one-way random effects model.

3. Results

Six females and two males of the medial KOA patients were included as the participants. Means [95% CI] of age, height, weight, and BMI were 56.4 [52.7, 60.2] years, 152.1 [146.9, 157.2] cm, 62.6 [51.4, 73.7] kg, and 27.0 [22.8, 31.3] kg/m², respectively. Four participants were classified with Kellgren-Lawrence classification grade 1, and four participants were classified with grade 2. No participants had narrowing of the lateral femoro-tibial compartment. Two participants had doubtful osteophyte of the lateral compartment. All the participants had osteophyte in the medial tibial plateau, and none of 8 had osteophytes at 4.0 mm below the tibial plateau plane.

The MME volume at first and second measurements were 493.5 [224.8, 742.2] mm³ and 505.4 [250.1, 760.8] mm³, respectively. The MME width at first and second measurements were 2.8 [1.8, 3.7] mm and 2.7 [1.9, 3.5] mm, respectively. The ICC for measuring the MME volume was 0.998 [0.992, 1.000] (range: 186.3–1060.5 mm³) (Fig. 5). The measurement error of MME volume was 2.7% [0.5–7.0%] (range: 0.5–7.0%). The ICC for measuring the MME width was 0.983 [0.924, 0.996] (range: 1.5–4.5 mm) (Fig. 6). The measurement error of MME width was 0.7% [0.0–11.4%] (range: 0.0–11.4%). There was no correlation between the MME volume and width (r = 0.565, p = 0.145) (Fig. 7).

4. Discussion

The objective of this study was to determine intra-rater repeatability of our 3D method of measuring the MME. The ICC for the MME volume was 0.998, and the ICC for width was 0.983. This new method of measuring the MME volume and MME width was highly repeatable. In addition, there was no correlation between the MME volume and MME width.

The range of the MME width was 1.5–4.5 mm in this study. Bruns et al. [22] showed that MME width in women with no osteophytes...
radiographically (mean age 55.0 years old) was 1.64 ± 0.92 mm on a single slice of coronal MRI. Wenger et al. [13] reported that MME width in patients with knee pain (mean age 62.7 ± 9.4 years) was 2.65 ± 1.71 mm. Bloecker et al. [17] reported that MME width in patients with medial joint narrowing (mean age 61.3 ± 9.2 years) was 3.35 ± 1.96 mm on a single slice of coronal MRI. Our findings were comparable to the values reported by previous studies. Our method would be useful for longitudinal study to determine changes in MME because the effects of the osteophytes were excluded.

The MME volume was not correlated with the MME width. The MME width was measured at the center line between the anterior and posterior tangent of the tibial plateau in the current study, which would be disregard the MME other than the particular location including supero-inferior thickness and antero-posterior extrusion. On the other hand, the MME volume was extruded part of the medial meniscus from the tibial plateau measuring not only the medio-lateral translation of the medial meniscus, but also the other directions. The medial meniscus will change its volume and shape due to loading condition such as loading dose, various activities, or presence of injuries. Moreover, the amount of the MME might depend on knee alignment or kinematics. These differences would have caused non-significant correlation (p = 0.145) between the MME width and volume, which may involve a beta-error due to the small sample size. It has been shown that in normal knees, the medial meniscus moves medially by 3.3 ± 2.27 mm from full extension to 90° flexion [15]. If the tibia translates laterally during knee extension, the medial femoral condyle may push the medial meniscus medially causing medial extrusion during knee extension. Saari et al. [23] reported that the tibia translates laterally by 0.5 mm during knee extension, but it is unclear whether this excursion has a significant influence on MME. Further study is needed to determine the association of MME with kinematics of the knee joint. Our previous study analyzed the association between the MME width and volume, which add our knowledge of MME measurement for future studies. Although there was high intra-rater repeatability using the MRI device with a 0.4 Tesla magnet which is commonly used in orthopaedic clinics, the result of non-significant correlation between the MME width and volume suggests that MME width measured by 2D MRI images in the clinics are not considered reliable as compared with MME volume. Therefore, the association between the MME width and disease progression of KOA shown in the previous studies should be revisited, which should be confirmed by MME volume in future studies.

The strength and novelty of our new method of measuring MME volume and width are the use of 3D models of the tibia and medial meniscus, with highly repeatable techniques for segmentation and embedding the bony coordinate system to determine the tibial cross...
Fig. 6. This scatter graph shows the correlation between repeated measurements of the MME width.

Fig. 7. This scatter graph shows no correlation between the measured MME volume and MME width.
section as a reference for the edge of the medial tibial plateau. Geurmazi et al. [24] showed that osteophyte was observed by using MRI in 74% of the patients with Kellgren-Lawrence grade 0. Wulka et al. [25] showed that the tibial plateau size in females over 40 years old is increased due to larger osteophytes around the tibial plateau. The previous studies showed that MME width measured two-dimensionally using MRI changed over a few years [17,22]. However, there is a possibility that longitudinal enlargement of osteophytes occurs around the medial tibial plateau and that the MME width is affected. It is also a limitation in this study that the medial meniscus width was measured on only one coronal MRI slice and may not include the changes demonstrated on other slices. Dube et al. [26] measured the volume and area of MME between the baseline and 12-month post-up using the most outer contour of the medial tibial plateau looking down from the above as the reference point, which clearly includes the contour of osteophytes. The MME volume by Dube et al. [26] and from the current study were 507.26 mm³ and 493.5 mm³, respectively. The current study included patients in their 50’s and a direct comparison of these data is not valid due to the different populations. Therefore, there is a need for further improvement by excluding the effects of osteophyte changes and establishing 3D analysis of MME. In addition to the conceptual advantage, our method was proven to be highly repeatable. The reproducibility of embedding the local coordinate system in this study was high and the mean error of Z translation was 0.21 [0.03, 0.40] mm [21]. The repeatability of manual segmentation of the medial meniscus was also high. Accordingly, our new method should allow precise measurement of longitudinal morphological changes of the tibial plateau and the MME volume and width over the years.

This method had several limitations. Firstly, the MRI sequence in this study was not an optimal sequence for the meniscus. The contours of the medial meniscus and other tissues were blurred to some extent. Nevertheless, the intra-rater repeatability was sufficient. Segmentation of the meniscal meniscus itself could be conducted in T1 images because the contour of the medial meniscus could be clearly discriminated from the surrounding tissues. On the other hand, the cortex was visualized clearly and the tibial reference of the MME could be valid and repeatable. Secondly, longitudinal trial error of the position of the knee or mobility of the meniscal meniscus would affect the repeatability of the medial meniscus position between two MRI scanning sessions. Further studies would be needed to determine the longitudinal trial error. Thirdly, inter-rater agreement was not tested in this study. One rater segmentation has an advantage in reducing inter-rater errors in a small study with 8 samples. However, it has a limited generalizability. Agreement between multiple observers would increase the reliability of the measurement method. Finally, this study did not include testing of embedding the coordinate system. Ikuta et al. [21] determined the repeatability of segmentation of the tibias and embedding the coordinate system. This study determined repeatability of the medial meniscus segmentation and measurement of the MME since this study used the same tibial models at first and second measurements. Combining these findings would improve the true error caused by the measurement system.

5. Conclusions

This study concludes that the 3D volume and width measurement of MME by a single rater using MRI images have high repeatability even in the limited image quality. Although there was high intra-rater repeatability using the MRI device with a 0.4 T magnet which is commonly used in orthopaedic clinics, the result of non-significant correlation between the MME width and volume suggests that MME width measured in the clinics are not considered reliable. This method of excluding the effect of the morphological change of the tibial osteophyte may provide precise information and allow longitudinal measurements of MME in order to assess the predictor of the development of KOA. Further studies are needed to determine the association between the MME volume and disease progression of KOA.

Author contributions
- Study conception and design: Sadakyo, Sadamatsu, Gamada.
- Recruitment of patients: Sadakyo, Sadamatsu.
- Analysis and interpretation of the data: Watanabe, Hoshi, Gamada.
- Drafting of the article: Watanabe, Hoshi.
- Critical revision of the article for important intellectual content: Hoshi, Sadamatsu, Gamada.
- Final approval of the article: Watanabe, Hoshi, Sadakyo, Sadamatsu, Gamada.

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Ethical approval

This study was based on image data obtained as baseline data in an RCT investigating the effect of exercise therapy in patients with KOA. The RCT protocol was approved by the Medical Research Ethics Committee in Sadamatsu Hospital (approval number: 2010-14) and registered at UMIN Clinical Trials Registry (UMIN000028944). All procedures performed in studies involving human participants were in accordance the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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