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Title	Quantitative knee cartilage measurement at MR imaging of patients with anterior cruciate ligament tear
Author(s)	Kato, Kazuki; Kamishima, Tamotsu; Kondo, Eiji et al.
Citation	Radiological physics and technology, 10(4), 431-438 https://doi.org/10.1007/s12194-017-0415-4
Issue Date	2017-12
Doc URL	https://hdl.handle.net/2115/72265
Rights	This is a post-peer-review, pre-copyedit version of an article published in Radiological physics and technology. The final authenticated version is available online at: http://dx.doi.org/10.1007/s12194-017-0415-4
Type	journal article
File Information	Radiol Phys Technol 10(4)_431-438.pdf

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Title Page

Quantitative Knee Cartilage Measurement at MR Imaging of Patients with Anterior Cruciate Ligament Tear

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Abstract

In previous studies, numerous approaches were proposed that assess knee cartilage volume quantitatively by using 3D magnetic resonance (MR) imaging. However, clinical use of these approaches is limited because it is prone to metal artifact in postoperative cases. Our purpose in this study was to validate a method for knee cartilage volume quantification by using conventional MR imaging in patients who underwent anterior cruciate ligament (ACL) reconstruction surgery. The study included 16 patients who underwent MR imaging before and 1 year after ACL reconstruction surgery. Knee cartilage volumes were measured by our computer-based method with use of T1-weighted sagittal images. We classified the cartilage into 8 regions and made comparisons between preoperative and postoperative cartilage volumes in each region. There was a significant difference between preoperative and postoperative cartilage volumes with regard to medial posterior weight-bearing, medial posterior, lateral posterior weight-bearing, and lateral posterior portions ($p=0.006$, $p=0.023$, $p=0.017$ and $p=0.002$, respectively). These results were consistent with the previous studies showing that knee cartilage loss occurs frequently in these portions due to an anterior subluxation

of the tibia accompanied by ACL tear. With our method, knee cartilage volumes could be quantitatively measured with conventional MR imaging in patients who underwent ACL reconstruction surgery.

Key Words

knee cartilage: anterior cruciate ligament: magnetic resonance imaging

Introduction

Hyaline cartilage covering the surface of the diarthrodial joint is important for normal joint function and can transmit and distribute pressure without sustaining substantial wear [1,2]. In addition, because articular cartilage provides a nearly frictionless gliding surface, these forces can be transmitted during dynamic joint activity [3–8]. In order to satisfy these complex functional requirements, articular cartilage shows unique morphologic features and biomechanical properties that are unmatched by artificial material [1,2,9,10]. Observing cartilage destruction and loss is important for evaluating osteoarthritis (OA) [11,12].

Magnetic resonance (MR) imaging has been in use for cartilage evaluation for many years because it provides high soft-tissue contrast and spatial resolution. MR imaging enables direct qualitative and quantitative visualization and evaluation of the cartilage [13]. In recent years, some investigators have developed computer-based methods to create 3D cartilage reconstruction from magnetic resonance images [12,14–17]. These methods can be used for assessment of cartilage degeneration and cartilage loss quantitatively by evaluation of cartilage volume, while the methods have high susceptibility to metal artifacts due to their sequence design depending on the gradient echo technique, which is not recommended for quantitative analysis of cartilage in

post-operative status.

Anterior cruciate ligament (ACL) tear leads to anterior subluxation of the tibia with engagement of the anterior femoral condyle against the posterior tibial plateau [18–23]. As a result, cartilage loss occurs in the anterior femoral condyle and posterior tibial plateau [19,21]. In addition, 74% of patients who underwent ACL reconstruction surgery displayed some signs of radiographic OA within 7 years post-surgery. Thus, OA is common in ACL-reconstructed knees [24]. Therefore, our purpose in this study was to verify a quantification method for knee cartilage volumes by using conventional MR imaging in patients who had undergone ACL reconstruction surgery.

Materials and methods

Patients

The study included 16 patients who underwent MR imaging before and 1 year after ACL reconstruction surgery (Tables 1,2). This study was conducted in accordance with the Declaration of Helsinki and its updates and was approved by the local ethics committee. Informed consent was obtained from all of the patients.

MR imaging

All patients in this study group underwent MR imaging, with T1-weighted images obtained before (baseline) and 1 year after (follow-up) ACL reconstruction surgery. MR images were performed with the Achieva 1.5T A-series (Philips) and the Achieva 3.0T TX (Philips). Imaging parameters are summarized in Table 3. In follow-up studies, special care was taken so that the slice position was identical to that of the baseline study.

Image analysis

In this study, we used an original software in which cartilage is manually segmented from MR images taken at baseline and at follow-up, and the interval difference in cartilage volume between baseline and follow-up is displayed with Microsoft Excel and a color map.

The original software was developed with Microsoft Visual C# 2013. The MR images taken at baseline and at follow-up were imported into the software. Then, 3 steps for cartilage segmentation and volumetry were followed.

Step-1: semi-automated bone segmentation for bone area elimination at bone/cartilage interface

The interface between the subchondral bone and its cartilage is a sharp curvilinear line in most cases. Therefore, to eliminate bone pixels from volumetry of the cartilage, all the slices in each MR study were binarized automatically by Otsu's method [25], and fused images of the binary images and the original images were created (Fig.1). Here, the threshold was selected to separate bony structures from the soft tissues including cartilage, a pixel value larger than the threshold was displayed in green, and a pixel value less than the threshold was displayed with that of the original images. The green pixels containing bone area were then automatically extracted from the display. When the bone was not completely displayed in green, we manually eliminated the signal from the bone by mouse dragging operation. Extracting the bone using automatic binarization facilitated easier segmentation of the cartilage boundary for the subsequent processing, thus reducing the time for segmentation without affecting the accuracy of cartilage quantification.

Step-2: manual segmentation of the knee cartilage at its interface to joint space

We manually segmented the articular side of the knee cartilage which we deemed cartilage by mouse dragging operation. The segmented part was displayed in red (Fig.2). During cartilage segmentation, the pixels formally displayed in green were never

repainted as red, so that the bony areas were not added to the knee cartilage volumes. In baseline and follow-up images, we carefully performed this operation only on a slice judged to be the same section by observing between baseline and follow-up slices where articular cartilage is visible. The number of slices used for image analysis therefore resulted in the same for baseline as for follow-up. The total of the measured areas was calculated as volume.

Step-3: automated sub-region (8-regions) segmentation and volume calculation

We divided the segmented cartilage into quarters from the pixel where the cartilage exists at the most anterior position to the pixel at the most posterior position in the slices with the cartilage, and divided these into medial and lateral portions. We defined the 8 regions as lateral anterior, lateral anterior weight-bearing, lateral posterior weight-bearing, lateral posterior, medial anterior, medial anterior weight-bearing, medial posterior weight-bearing, and medial posterior portions (Fig.3.). The way we segmented the cartilage came from the findings of previous studies; ACL tear leads to anterior subluxation of the tibia with impaction of the anterior femoral condyle against the posterior tibial plateau along with cartilage loss in the anterior femoral condyle and posterior tibial plateau [19,21]. The amount of cartilage volume change was obtained by

158 subtraction of the volume of the baseline from that of the follow-up, and color mapping
159 was performed based on the value of these changes (Fig.4.).
160 One radiological technologist with three months of experience and enough
161 prior knowledge about the position of the cartilage performed computer-based analysis
162 twice with a half of year interval. In order to examine the validity of the original
163 software, pre- and post-operative knee cartilage was quantified using our software
164 (which includes semi-automatic and manual segmentation) and an image analysis
165 software called ImageJ (National Institutes of Health, Bethesda, MD) in one case
166 (20-year-old, male). In ImageJ, we manually segmented cartilage utilizing the “Polygon
167 selection” tool.
168
169 Statistical analysis
170 SPSS version 22.0 (IBM Corp, New York, NY) for Windows was used for statistical
171 analysis. When we compared the paired samples, normality was tested by the
172 Shapiro-Wilk test and did not find normality; we therefore performed the Wilcoxon
173 signed-rank test, which is a nonparametric test.
174 Intra-observer agreement was estimated using intra-class correlation
175 coefficients (ICC) employing a one-way random effects model for intra-observer

agreement. ICC values were interpreted as poor agreement for values between 0 and 0.20, fair agreement for values between 0.21 and 0.40, moderate agreement for values between 0.41 and 0.60, substantial agreement for values between 0.61 and 0.80, and almost perfect for values between 0.81 and 1.00 [25]. We compared the time taken per slice between the original software and ImageJ in a Wilcoxon signed-rank test.

Results

There was a significant difference between baseline and follow-up cartilage volumes in the medial posterior weight-bearing, medial posterior, lateral posterior weight-bearing, and lateral posterior portions (p=0.006, p=0.023, p=0.017, and p=0.002, respectively). However, there was no significant difference between baseline and follow-up cartilage volumes in the medial anterior, medial anterior weight-bearing, lateral anterior, and lateral anterior weight-bearing portions (p=0.352, p=0.098, p=0.642, and p=0.602, respectively), as shown in Table 4. A representative case is shown in Fig.5.

Intra-observer agreement of knee cartilage volume in 8 regions was almost perfect (ICC = 0.955; 95% confidence interval [95% CI], 0.943-0.965). Intra-observer agreement for delta values (difference between the baseline and follow-up) was substantial (ICC = 0.803; 95% CI, 0.732-0.857). The knee cartilage volume in the original software/ImageJ was 2108/2038 mm3 (0.094% difference) and 2108/2110 mm3 (3.4% difference) at the baseline and follow-up, respectively. The mean time (± standardized deviation) taken with the original software and ImageJ was 50.9 (± 10.1) and 131 (± 0.000788) seconds, respectively (p = 0.00004).

Discussion

In this study, we evaluated cartilage volumes in 16 patients before and 1 year after ACL reconstruction surgery. There was a significant difference between baseline and follow-up cartilage volumes in each of 4 regions (medial posterior weight-bearing, medial posterior, lateral weight-bearing posterior, and lateral posterior portions). In previous studies, quantitative knee cartilage evaluation was conducted using 3D-MR images [12,14–17], but to the best of our knowledge, there were no studies in which there was a quantitative evaluation of postoperative cartilage volume as in this study. T1-weighted images are used routinely for the analysis of anatomic structures. Moreover, they have an advantage over gradient echo sequences and fat suppression images, being free form postoperative metal artifacts. Therefore, this method could be applied immediately to clinical practice.

Previous investigations reported that ACL tear leads to anterior subluxation of the tibia with impaction of the anterior femoral condyle against the posterior tibial plateau along with cartilage loss in the anterior femoral condyle and posterior tibial plateau [19,21]. Also, previous studies showed that ACL-reconstructed knees had greater contact along the medial ridge of the medial plateau and the posterior aspect of the lateral plateau, compared to healthy contralateral knees and to the knees of healthy persons during exercise [15]. Furthermore, in another study, 74% of the patients who

had undergone ACL reconstruction surgery showed several signs of radiographic OA within 7 years after surgery, indicating that early-onset OA is common in ACL-reconstructed knees [24]. For these reasons, cartilage loss may occur in the anterior femoral condyle and posterior tibial condyle at the time of ACL tear. In this study, the results that there was a significant difference between baseline and follow-up cartilage volumes in the medial posterior weight-bearing, medial posterior, lateral weight-bearing posterior, and lateral posterior portions were consistent with this hypothesis. That may suggest that our newly proposed method could successfully quantify knee cartilage volume.

In this study, we showed that there is significant reduction in the reasonable anatomical location of the knee cartilage in patients who underwent ACL reconstruction surgery. Moreover, the knee cartilage volumes can be evaluated by using the conventional MR images with our software. We consider this is due to careful scan planning in terms of stable slice selection and imaging parameter, including slice thickness and slice gap. Together with compatible results from the data using the free software of ImageJ, we considered our cartilage volumetry was to be valid.

In our study results, the knee cartilage volumes did not show any significant difference in the anterior and anterior weight-bearing portions of both medial and lateral

sides. This may be attributed to the fact that we could not divide segmented cartilage into the femoral side and the tibial side. In our study population, as ACL tears were caused by trauma, cartilage wear was considered to be localized. For more sensitive detection of the localized cartilage loss, measurement of cartilage volume should be performed on the femoral side and the tibial side separately. However, in this study, it was difficult to separate the cartilage into the femoral side and the tibial side on the T1-weighted sagittal images.

We believe that as the original software used in this study is accurate, reproducible, and less time-consuming, it can be applied to the comparison among the procedures of ACL reconstruction. In a previous study, the comparison among the procedures of ACL reconstruction was performed, but the investigations evaluated ACL by arthroscopy, whereas a cartilage evaluation was not done [26]. We considered that adding cartilage evaluation to one of the prognostic evaluations might reveal signs of OA, which is considered to occur frequently in ACL-reconstructed knees.

Our study had several limitations. First, the devices used for MR images differ between inter- and intra- patients due to the retrospective design of this study. However, the MR parameters used in this study did not differ greatly between the devices, and the results of this research implied that cartilage volume may be quantified by use of

routine images, independent of the device. The second limitation was the small number of patients included in this study. Further study on more patients is needed for confirmation of the results. Thirdly, although the cartilage region is clearly depicted using 3D imaging methods such as the 3D-FISP sequence, we have no 3D imaging methods available for comparison. However, we believe that it is meaningful to quantitatively evaluate cartilage using 2D-T1w MR images although accuracy for cartilage volumetry may be inferior to 3D sequences due to the slice gap. Finally, because our original software was not free from manual segmentation for the most part, cartilage evaluation could be subjective and time-consuming. Moreover, when conducting similar research in other institutes, there is a possibility that some variation may occur depending on the analyst's skill. Therefore, in order fundamentally to solve these problems, we need to build a new algorithm for automating our original software.

Conclusion

Knee cartilage volumes could be measured quantitatively with conventional MR imaging in patients who underwent ACL reconstruction surgery.

Compliance with ethical standards

Conflict of interest

All authors have no conflicts of interest to disclose.

Ethical approval

All procedures in studies involving human participants were performed in accordance with the ethical standards of the Faculty of Health Sciences, Hokkaido University, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was waivered by the ethical committee of Faculty of Health Sciences, Hokkaido University as this was a retrospective study.

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361

Table 1. Characteristics of patients

	Value
Total no. of subjects included	16
Age. mean (range) in years	30.1 (13-58)
Sex. female/male	7/9
Knee. right/left	5/11

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Table 2. Athletic activity or situation associated with the injury, and period from injury to surgery

Case number	Situation	Days	Sex	Age [years]
1	tumble	756	M	36
2	rugby	92	M	19
3	ski	85	M	55
4	soccer	3626	M	32
5	basketball	136	F	13
6	badminton	0	M	19
7	tumble	139	F	45
8	gym vault	111	M	18
9	gym vault	15706	F	58
10	volleyball	57	F	15
11	volleyball	1461	F	51
12	volleyball	100	M	49
13	volleyball	85	F	16
14	triathlon	110	M	20
15	rugby	93	M	19
16	soccer	24	F	17

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Table 3. Acquisition parameters of MR imaging

Magnetic Field Strength [T]	1.5	3
Sequence	SE T1WI	
Section	sagittal	
Slice Thickness [mm]	3	
FA [degree]	90	
NEX	2	
Slice Gap [mm]	0.3	
TR [msec]	500 or 579	700 or 800
TE [msec]	15	10 or 12
ETL	3 or 4	3
BW [Hz]	230 - 259	242 - 255
Pixel Size [mm]	0.222 × 0.222 - 0.390 × 0.390	0.273 × 0.273 - 0.3125 × 0.3125
No. of Slices	23 or 24	23 or 25

370

Table 4. Comparison between baseline and follow-up cartilage volume in each region

Regions		n	Baseline		Follow-up		P value (<0.05)
			Mean [mm^3]	SD [mm^3]	Mean [mm^3]	SD [mm^3]	
Medial	Anterior	16	31.8	29.0	31.2	43.1	0.352
	Anterior weight-bearing	16	203	54.6	171	65.4	0.098
	Posterior weight-bearing	16	309	69.2	252	82.4	0.006
	Posterior	16	321	105	310	86.2	0.023
Lateral	Anterior	16	115	96.4	89.8	50.3	0.642
	Anterior weight-bearing	16	164	74.5	153	84.6	0.605
	Posterior weight-bearing	16	376	96.8	320	113	0.017
	Posterior	16	351	107	278	71.7	0.002

371 SD = standard deviation

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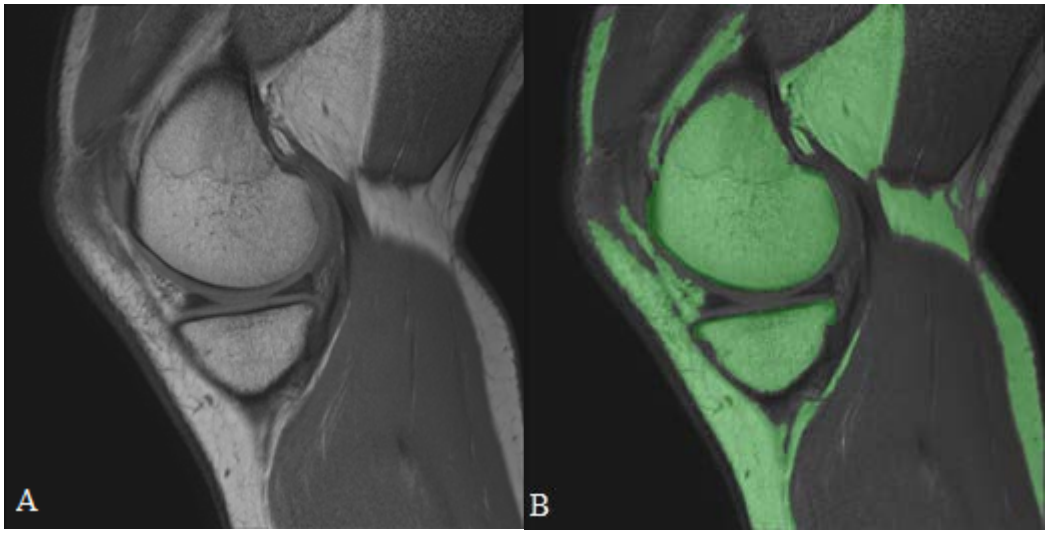


Fig.1. Original image (A) and fused image (B)

Fig.2. Segmentation of cartilage at fused image

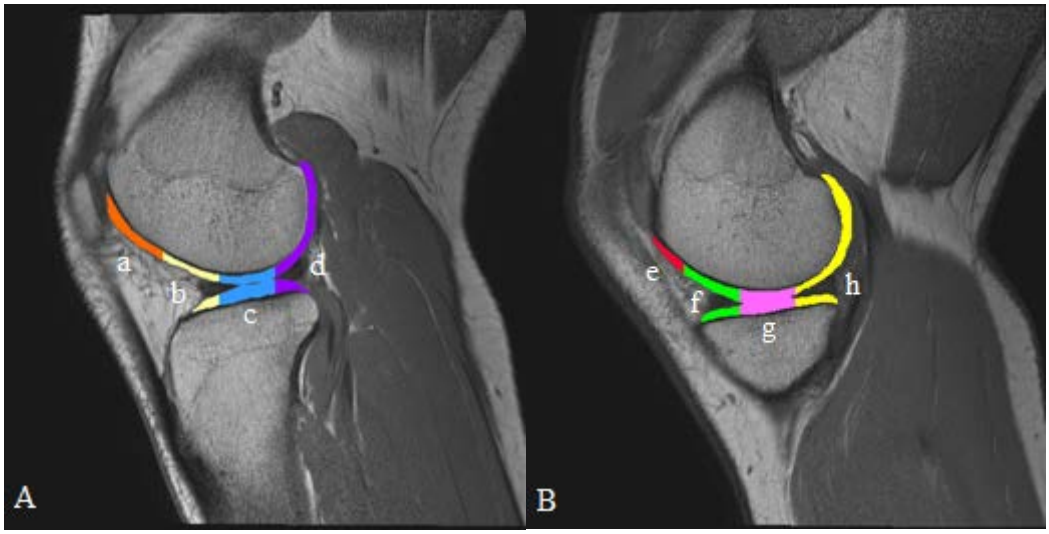


Fig.3. Cartilage classification into 8 regions.

(A) Sagittal MR image of the lateral side of the knee (B) Sagittal MR image of the medial side of the knee. (a) Lateral anterior portion (b) Lateral anterior weight-bearing portion (c) Lateral posterior weight-bearing portion (d) Lateral posterior portion (e) Medial anterior portion (f) Medial anterior weight-bearing portion (g) Medial posterior weight-bearing portion (h) Medial posterior portion

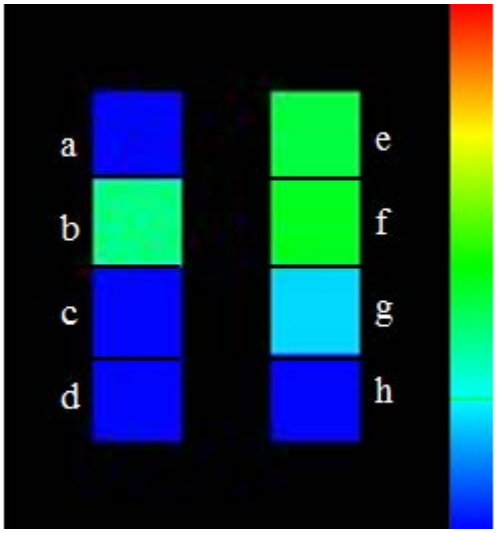
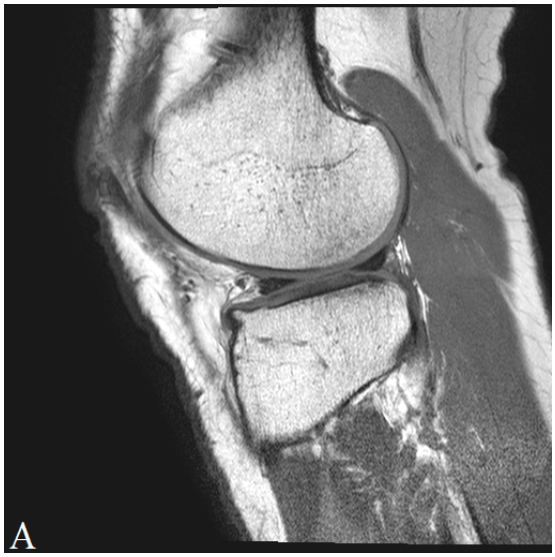


Fig.4. Cartilage volume map in a 36-year-old man’s right knee

The closer to red, the larger the difference between the follow-up and baseline is to the positive value. The closer to blue, the larger the difference between the follow-up and baseline is to the negative value. Green indicates almost unchanged.

(a) Lateral anterior portion (b) Lateral anterior weight-bearing portion (c) Lateral posterior weight-bearing portion (d) Lateral posterior portion (e) Medial anterior portion (f) Medial anterior weight-bearing portion (g) Medial posterior weight-bearing portion (h) Medial posterior portion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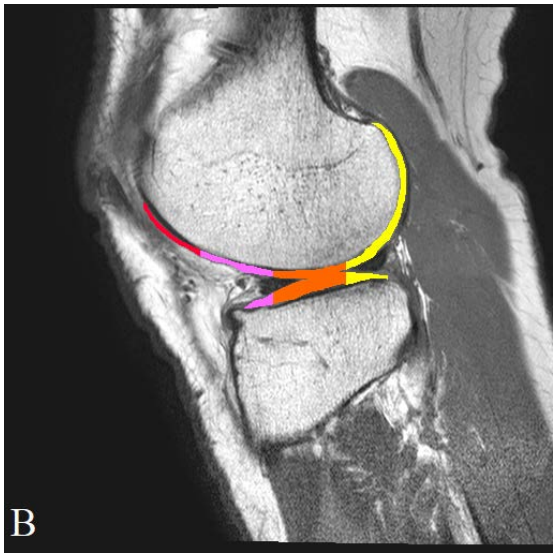
B

C

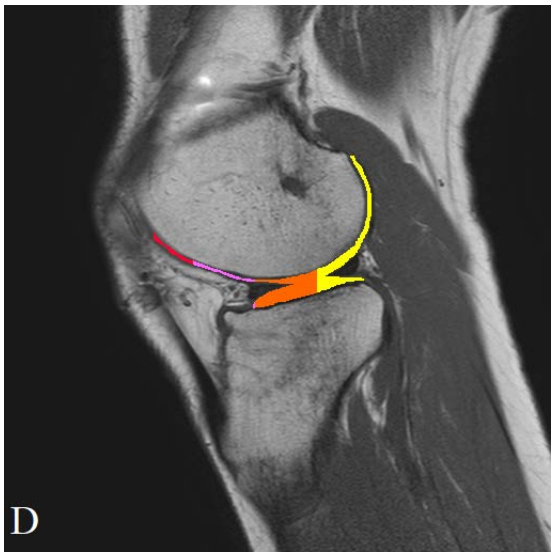

Fig.5. Example of a case with significant cartilage volume loss at multiple cartilage regions.

Sagittal T1-w MR images of knee in 36-year-old man before and 1 year after ACL reconstruction surgery. (A) baseline image. (B) is colored cartilage of (A). (c) is followup image. (D) is colored cartilage of (C). The cartilage volume at baseline (followup) was 70.9 (37.6), 131.3 (43.8), 484.9 (314.0) and 458.0 (313.0) mm3 in anterior, anterior weight-bearing, posterior weight-bearing and posterior at baseline, respectively. These interval changes are difficult to recognize using conventional visual assessment.