Fully automatic three-dimensional MRI analysis for the cartilage and meniscus of the knee: Kanagawa Knee Study

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Abstract

Objective

We have developed a fully automatic three-dimensional MRI analysis software that measures the projected cartilage area ratio (PCAR) to allow for the quantification of the cartilage in the knee. Our objectives were to verify our software's accuracy for segmentation of cartilage and meniscus and to quantify cartilage and meniscus extrusion in our cross-sectional study. We also examined which cartilage quantification was most affected by age and analyzed the relationship between PCAR and meniscus extrusion.

Methods

MRI data from 108 subjects were selected for training, and Dice similarity coefficients were determined from 5 other subjects to verify the accuracy. Our cross-sectional study included other 561 subjects between 30–70 years of age. We quantified cartilage thickness, cartilage volume, and PCAR (0.0–1.5 mm) in medial femoral, lateral femoral, medial tibial, and medial lateral regions. Each region was divided into nine subregions, with particular focus on the medial central (mc) subregion. The medial meniscus coverage ratio (MMCR) was investigated as a quantification for meniscus extrusion.

Results

Dice similarity coefficients for cartilage and meniscus were both approximately 0.9. Among cartilage quantifications, the highest absolute value of the correlation coefficient with age was mcMT PCAR 1.0 mm in females and mcMT cartilage thickness in males. In females, mcMT PCAR 1.0 mm was correlated with MMCR, although MMCR was not correlated with age. In males, mcMT PCAR 0.0 mm was correlated with MMCR.

Conclusions

Our software showed high segmentation accuracy and provided numerous quantifications of cartilage related to age and meniscus extrusion.

Trial registration: UMIN, UMIN000032826. Registered 1 September 2018, https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr_view.cgi?recptno=R000037299

Introduction

Three-dimensional magnetic resonance imaging (3D MRI) analysis is useful for the quantification of cartilage and the meniscus in osteoarthritis of the knee [1–3]. However, this promising method is not popular at present because segmentation of cartilage and the meniscus often requires manual operation or correction, which requires time and effort. To solve these problems, automatic segmentation techniques using deep neural networks have been developed [4–7]. We have also recently developed a

system for automatic extraction of cartilage and meniscus using deep neural networks. The first purpose of our study was to verify the accuracy of our software for automatic cartilage and meniscus segmentation on knee MRI.

For quantification of knee cartilage using 3D MRI, cartilage thickness, volume, and thickness map are used in many cases [1, 8–13]. As another cartilage measurement, we recently proposed “projected cartilage area ratio” (PCAR), which was the ratio of the projected cartilage area with intended thickness to the region of interest (ROI). The cartilage thickness used in assessing PCAR can be adjusted according to disease conditions, so that even slight changes can be revealed in a relatively short period [14]. Furthermore, PCAR, unlike cartilage thickness and volume, may not be affected by body size and may have an advantage when analyzing the cartilage. However, in our past development, the 3D-reconstructed femoral cartilage was projected directly onto the 2D plane, so the apparent thickness in the 2D projection was greater than the actual thickness due to the slope of the cartilage. To overcome this problem, we have improved the 3D-reconstructed femoral cartilage to project radially onto the 2D plane. We also recently developed a PCAR evaluation for tibial cartilage. In addition, for more detailed analysis, we enabled PCAR evaluation in five regions (including the medial femoral condyle cartilage, lateral femoral condyle cartilage, trochlea femoral cartilage, medial tibial cartilage, and lateral tibial cartilage) and nine subregions.

The meniscus plays a critical role in shock absorption and is especially important in regulating load-bearing distribution. Meniscus extrusion is one of the strongest risk factors for the progression of osteoarthritis [15]. For the index of meniscus extrusion, the deviation width of the meniscus in the coronal view of 2D MRI or ultrasound images is often used [16]. However, in meniscus extrusion, the meniscus does not always simply displace externally, and an evaluation on only one plane cannot explain the pathological condition of the meniscus extrusion in detail. On the other hand, 3D MRI analysis can provide the meniscus extrusion area, volume, and meniscus coverage ratio (MCR), which covers the tibial cartilage area [3, 17, 18]. These indicators can be more useful for analyzing the relationship between meniscus extrusion and osteoarthritis.

Extensive epidemiological studies have shown that osteoarthritis of the knee increases with age and that it affects females more frequently than males [19–21]. However, it remains unknown whether PCAR and the quantification of meniscus extrusion are affected by age or gender. Furthermore, analyzing the relationship between PCAR and the quantification of meniscus extrusion will be useful for continued elucidation of the pathology of osteoarthritis. To address these factors, we collected 3D MRI knee data from 561 volunteers, including more than 50 females and 50 males in their 30 s, 40 s, 50 s, 60 s, and 70 s named Kanagawa Knee Study. The second purpose of our study was to quantify cartilage (including PCAR) and meniscus extrusion using 3D MRI analysis to examine whether these quantifications were affected by gender, body size, and age, as well as to analyze the relationship between PCAR and meniscus extrusion.

Materials And Methods

This study was approved by the Medical Research Ethics Committee of Tokyo Medical and Dental University and written informed consent was obtained from all participants. The protocols were enrolled in a database of the National University Hospital Council of Japan (UMIN000031924, UMIN000032826) and disclosed.

Magnetic resonance imaging (MRI)

Images were collected with a 3.0-T MRI (Achieva 3.0T TX; Philips) using 16-channel flex coils. The sagittal plane of the knee joint was imaged using both a fat-suppressed spoiled gradient echo (SPGR) sequence to extract cartilage and a proton density weighted imaging (PDWI 3D FSE/TSE) sequence to extract meniscus and bone. For both sequences, sagittal imaging was performed at an in-plane resolution of 0.31×0.31 mm, a partition thickness of 0.36 mm (320 slices), and a field of view of 150×150 mm.

Automatic segmentation algorithm of 3D MRI

We used 3D convolutional neural network model based on U-Net for our software [22]. The network used convolution with padding to improve the accuracy of edge extraction. As a loss function, we used Soft Dice loss [23] (Fig. 1).

For neural network construction, we randomly chose 10 healthy volunteers and 103 patients with knee pain who had visited our hospital between July 7, 2012, and July 24, 2018. These data were manually segmented by two authors (H.A. and A.H.) who had both trained as orthopedic surgeons for six years and had experience in the manual correction of over 200 knees. Segmentation data were converted by professional engineers (K.S. and J.M.) to train the neural network. To train the network to construct a region of interest (ROI) of the femoral subchondral bone and the medial/lateral tibial plateau, we manually segmented the ROI by using a reconstructed 3D knee model.

To validate our algorithm, 108 subjects among 113 were randomly selected for training. After training with 108 subjects, we computed the segmentation accuracy of another 5 subjects as one validation test. We performed the validation test three times, which selected another 108 subjects for training and 5 subjects for each test. After completing three validation tests, the software was trained by all data collected from 113 subjects and was then used for the cross-sectional research of this study.

Kanagawa Knee Study

We mainly recruited workers or retirees from the Kanagawa Prefectural Office and named this study “Kanagawa Knee Study.” We collected 561 datasets included more than 50 females and 50 males per age group (30s, 40s, 50s, 60s, and 70s). Those who had a history of lower limb surgery or who were diagnosed with rheumatoid arthritis or cancer were excluded. We announced recruitment of these subjects at the Kanagawa Prefectural Government between September 1, 2018 and August 30, 2019. Participants joined our study voluntarily. We collected their heights, weights, knee radiographs, and MRIs between November 3, 2018, and September 28, 2019, at the AIC Yaesu clinic of Tokyo.

Nomenclature and quantitative measurements for cartilage and the meniscus

To quantify cartilage, femoral (F) cartilage was radially projected and divided into three regions inside of the ROI of the femoral subchondral bone (blue outer line of Fig. 2A), femoral trochlea (TrF: anterior cartilage from proximal to inter condylar notch), medial femoral condyle (MF: medial cartilage from intercondylar notch to posterior), and lateral femoral condyle (LF: lateral cartilage from intercondylar notch to posterior) (Fig.2A). The tibial cartilage was vertically projected and divided into two areas inside the ROI of the medial/lateral tibial plateau (blue outer line of Fig. 2B), medial tibia (MT), and lateral tibia (LT) (Fig. 2B).

Each area was automatically divided into 3×3 subregions at equal intervals and named according to the previous report. From medial to lateral, the subregions in the TrF were named medial (m), central (c), and lateral (l). From proximal to distal, they were named proximal (p), intermediate (i), and distal (d) (Fig. 2A). From anterior to posterior, subregions in the other four parts (MF, LF, MT, and LT) were named anterior (a), medial (m), and posterior (p). From internal to external, they were named internal (i), central (c), and external (e) (Figs. 2A, 2B) [24].

Our software automatically computed cartilage average thickness (ThC), cartilage volume (VC), and projected cartilage area ratio (PCAR) in each region and subregion. Our software could also display the cartilage thickness mapping (Fig. 2C).

In this study, PCAR represented the ratio between the projected cartilage area and the total area of the ROI. PCAR = 1.0 meant that the entire ROI of the subchondral bone was covered by cartilage. PCAR = 0.0 meant that no cartilage covered the ROI of the subchondral bone. For example, a schematic diagram of the projected cartilage area (cartilage thickness ≥1.0 mm) is shown in Fig. 2D. As practical examples, the projected cartilage area (cartilage thickness ≥ 0.0 mm) is shown in Fig. 2E, and the projected cartilage area (cartilage thickness ≥ 1.0 mm) is shown in Fig. 2F. We evaluated PCAR for the threshold of cartilage thicknesses at ≥ 0.0 mm, ≥ 0.5 mm, ≥ 1.0 mm, and ≥ 1.5 mm. PCARs for the threshold of cartilage thicknesses at each of these measurements were named PCAR0.0, PCAR0.5, PCAR1.0, and PCAR1.5, respectively.

To evaluate the meniscus, medial and lateral meniscus volume, meniscus extrusion (ME) volume, ME area, and meniscus coverage ratio (MCR) were automatically computed. MCR was defined as the ratio between the overlapping area of the meniscus and the area of the ROI for the tibial plateau (Fig. 2G).

Statistical analysis

To evaluate the accuracy of automatic segmentation, we calculated the Dice similarity coefficient (DSC) between manual segmentation and automatic segmentation [25]. In each validation test, DSC was computed for five test subjects at the femoral bone, tibial bone, femoral cartilage, tibial cartilage, medial/lateral meniscus, femoral subchondral bone ROI, and medial/lateral tibia plateau ROI. After the three validation tests, we calculated the mean DSC of each test.

To compare gender differences in the quantification of cartilage and the meniscus, we used the Mann–Whitney U test. To evaluate the correlation between each quantitative value and age or other quantitative value, we used Spearman's rank correlation test. All statistical analyses were done using JMP® 14 (SAS Institute Inc., Cary, NC, USA). P values < 0.005 were considered statistically significant.

Results

Segmentation accuracy

The mean Dice similarity coefficient (DSC) of all tests combined was 0.985 for the femoral bone, 0.980 for the tibial bone, 0.911 for the femoral cartilage, 0.892 for the tibial cartilage, 0.916 for the medial meniscus, 0.891 for the lateral meniscus, 0.905 for the ROI of the femoral subchondral bone, and 0.888 for the ROI of the medial/lateral tibia plateau (Table 1).

Characteristics of study subjectsin the cross-sectional study

This study included 561 subjects: 277 females and 284 males (Table 2). The overall average age of the subjects was 53.7 ± 13.9 years for females and 55.2 ± 11.0 years for males. The body mass index was 22.5 ± 3.0 for females and 23.6 ± 3.2 for males. The rate of grade 3 or 4 on the Kellgren–Lawrence OA scale was 5.4% for females and 1.4% for males.

Gender differences in quantification of cartilage and the meniscus

The cartilage volume and thickness were significantly higher in males than in females in the MF, MT, LF, and LT (Table 3). PCAR was higher in males than females except for MT PCAR1.0 and LF PCAR0.0, 0.5, 1.0. The volume and area of the medial/lateral meniscus were higher in males than in females.

Correlation between cartilage quantifications and body size

Thickness and volume of femoral and tibial cartilage in each region were correlated with height in both genders (Table 4). On the other hand, the MF PCAR, LF PCAR, MT PCAR, and LT PCAR0.0-1.5 were not correlated with height. Even if they were correlated, their rs were less than 0.2 in both genders. There were no correlations between cartilage quantifications (CV, ThC, and PCAR) and weight and BMI (data not shown).

Correlation between cartilage quantification and age

Among the nine subregions in the MF, MT, LF, and LT, we focused on the medial central subregion because it was considered more representative than other subregions. In females, among cartilage quantifications (including PCAR0.0, 0.5, 1.0, 1.5, VC, and ThC for the MF, LF, MT, LT, mcMF, mcLF, mcMT, and mcLT), the highest absolute value of the correlation coefficient with age was mcMT PCAR1.0 (rs = -0.34) (Table 5). In males, the highest absolute value of the correlation coefficient with age was mcMT ThC (rs = -0.35). The second highest correlation coefficient with age was mcMT PCAR1.5 (rs = -0.33).

Correlation between the quantification of meniscus extrusion and age

In females, medial meniscus extrusion (MME) area and MME volume were correlated with age. The MMCR was not correlated with age (Table 6). In males, there were no correlations between the quantification of meniscus extrusion (MME area, MME volume, and MMCR) and age.

Correlation between projected cartilage area ratio (PCAR) and meniscus extrusion

In females, mcMT PCAR0.0, 0.5, and 1.0 were significantly correlated with MME area, MME volume, and MMCR (Table 6). In males, mcMT PCAR0.0, 0.5, and 1.0 were significantly correlated with MME area and MME volume. mcMT PCAR0.0 and 1.0 were also significantly correlated with MMCR. However, the absolute value of rs between them was less than 0.2.

Discussion

Our software provided high automatic segmentation accuracy for cartilage and the meniscus. The cartilage and meniscus volumes, and most PCARs, were higher in males than in females. Thickness and volume of femoral and tibial cartilage in each region were correlated with height, while MF PCAR0.0-1.5 and MT PCAR0.0-1.5 were not correlated in both genders. In our cartilage quantifications, the highest absolute values of the correlation coefficient with age were mcMT PCAR1.0 in females and mcMT ThC in males. In females, mcMT PCAR0.0-1.0 was correlated with MMCR, although MMCR was not correlated with age. In males, there were no correlations between the quantification of meniscus extrusion and age.

Among 561 volunteers in our cross-sectional study, 20 had visited hospitals for more than three months due to their knee symptoms for the right knee only, 15 had visited for more than three months for the left knee only, and 6 had visited for more than three months for both knees. This means that 25 volunteers (4.4%) had ever visited hospitals due to their knee symptoms. Those who had radiographic osteoarthritis at grade 3 or 4 on the Kellgren–Lawrence scale included 19 volunteers (3.4%). These data indicate that most of the subjects in this cross-sectional study were healthy.

Gender differences related to cartilage thickness is still a controversial concept. In our current study, the MT ThC was 1.75 ± 0.24 mm in females (n = 277) and 1.93 ± 0.25 mm in males (n = 284), meaning the MT ThC was significantly higher in males than in females ($p < 0.0001$). On the other hand, according to a 3D MRI study by Faber et al., the MT ThC was 1.20 ± 0.19 mm in females (n = 8) and 1.36 ± 0.15 mm in males (n = 9), meaning there was no significant difference between females and males [26]. The subjects in the study by Faber et al. were young, healthy volunteers (age 22 ± 2 years) and MRIs were performed with a 1.5 T fat-suppressed 3D gradient-echo sequence. The significant gender difference in cartilage thickness in these studies depended on the ages of the subjects and the imaging sequences, but the difference in sample number will greatly be affected. In our study, as is true of most quantifications of cartilage, quantifications of the meniscus (including meniscus coverage ratio) were significantly higher in males than in females. For analysis of cartilage and meniscus pathology, we should take gender differences into consideration.

In this study, thickness and volume of femoral and tibial cartilage in each region were correlated with height. This means that to accurately analyze these quantifications, it is necessary to correct these quantifications by considering the heights of each individual. On the other hand, MF PCAR0.0-1.5 and MT PCAR0.0-1.5 were not correlated with height. Therefore, PCARs are useful cartilage quantifications for examining the relationship to age since they do not need to be corrected for height.

In our cartilage quantifications, the highest absolute value of the correlation coefficient with age was mcMT PCAR1.0 (rs = -0.34) in females. In other words, in females, mcMT PCAR1.0 was more sensitive than thickness and volume at each region and subregion for age-related cartilage quantifications. In males, the highest absolute value of the correlation coefficient with age was mcMT ThC (rs = -0.35), and the second highest was mcMT PCAR1.5 (rs = -0.33). Though MT ThC was significantly correlated with height, MT PCAR1.5 without correction for height was correlated with age. Among mcMT PCAR0.0, 0.5, 1.0, 1.5, PCAR1.0 was highest in females, but PCAR1.5 was highest in males. This is due to the fact that cartilage is thicker in males than in females.

We also showed that MME area and volume were correlated with age in females. Achtnich et al. reported, using ultrasound examination, that the width of MME increased with age [27], and this was similar to our results, though the subjects in the Achtnich et al. study included 17 males in addition to 58 females. In our study, MMCR, which is considered an index that reflects meniscus function more directly than the MME area and MME volume, was not correlated with age in both genders. On the other hand, MMCR was associated with a decrease in mcMT PCAR, which was associated with age in both genders. These data mean that decreases in MMCR possibly promote decreases in MT cartilage over normal aging. At present, MRI is not recommended for early detection of osteoarthritis due to a lack of validated consensus [28]. Our findings suggest that mcMT PCAR is a useful quantification for detecting early knee osteoarthritis and that MMCR is an important risk factor.

In this study, we propose three limitations. First, the composition of the subjects in the cohort did not match that of the general population and this selection bias cannot be ignored. Second, the software was specific to the training cohort, and the performance was not the same to the different cohort. Third, though we obtained the cartilage quantification of nine subregions in the MF, MT, TrF, LF, and LT, we only focused on the medial central subregion because it was considered more representative than other subregions.

Conclusion

Our 3D U-Net algorithm showed high segmentation accuracy for knee cartilage and menisci. In our cross-sectional study, the absolute value of the correlation coefficient with age was high in females (mcMT PCAR1.0) and males (mcMT PCAR1.5). Though MMCR was not correlated with age, MMCR was correlated with mcMT PCAR1.0. Our software provided numerous quantifications of cartilage related to age and meniscus extrusion.

Abbreviations

3D MRI: Three-dimensional magnetic resonance imaging, PCAR: Projected cartilage area ratio, ThC: cartilage average thickness, VC: cartilage volume, ROI: region of interest, ME: meniscus extrusion, MME: medial meniscus extrusion, MCR: meniscus coverage ratio, MMCR: medial meniscus coverage ratio, SPGR: spoiled gradient echo, PDWI: proton density weighted imaging, TrF: femoral trochlea, MF: medial femoral condyle, LF: lateral femoral condyle, MT: medial tibia, LT: lateral tibia, DSC: Dice similarity coefficient, mc: medial central subregion

Declarations

Ethics approval and consent to participate

This study was approved by the Medical Research Ethics Committee of Tokyo Medical and Dental University and written informed consent was obtained from all participants. The protocol was enrolled in a database of the National University Hospital Council of Japan (UMIN000031924, UMIN000032826) and disclosed.

Consent for publication

This manuscript does not contain any individual data.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

Study conception and design: Aoki, Ozeki, Hyodo, Suzuki, Masumoto, and Sekiya. Acquisition of data: Aoki, Takanashi, Katano, Okanouchi, and Sekiya. Analysis and interpretation of data: Aoki, Ozeki, Miura, Matsuda, Fujiwara, and Sekiya.

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Tables

Table 1. Automatic segmentation accuracy.

	DSC (average ± SD)			
Subregions	1st test	2nd test	3rd test	Total
Femoral bone	0.985 ± 0.004	0.985 ± 0.007	0.983 ± 0.004	0.985 ± 0.005
Tibial bone	0.981 ± 0.008	0.978 ± 0.013	0.983 ± 0.002	0.980 ± 0.009
Femoral cartilage	0.905 ± 0.024	0.913 ± 0.034	0.916 ± 0.013	0.911 ± 0.024
Tibial cartilage	0.893 ± 0.072	0.868 ± 0.119	0.914 ± 0.009	0.892 ± 0.072
Medial meniscus	0.921 ± 0.012	0.906 ± 0.020	0.922 ± 0.014	0.916 ± 0.016
Lateral meniscus	0.893 ± 0.038	0.905 ± 0.033	0.875 ± 0.053	0.891 ± 0.041
ROI of femoral subchondral bone	0.905 ± 0.016	0.904 ± 0.019	0.906 ± 0.017	0.905 ± 0.016
ROI of medial/lateral tibia plateau	0.889 ± 0.036	0.884 ± 0.055	0.892 ± 0.022	0.888 ± 0.037

*DSC averages and SDs were calculated for the first to third tests with 5 subject data, for a total of 15 subject data.

Table 2. Characteristics of the study subjects.

Characteristic	Female	Male
Total	n=277	n=284
Age	53.7 ± 13.9	55.2 ± 11.0
30–39 years	n=56	n=52
40–49 years	n=61	n=62
50–59 years	n=53	n=50
60–69 years	n=55	n=57
70–79 years	n=52	n=63
Height: means ± SD (cm)	158.6 ± 7.1	168.4 ±5.5
Weight: means ± SD (kg)	56.7 ± 9.2	66.9 ± 11.2
Body mass index: means ±SD	22.5 ± 3.0	23.6 ± 3.2
Kellgren–Lawrence OA scale KL0/1/2/3/4	231/23/8/6/9	266/9/5/3/1

Table 3. Cartilage and meniscus quantification at medial compartment in both genders.

	Female	Male	p value
MF VC (mm^3)	2503 ± 416	3349 ± 531	< 0.0001
MF ThC (mm)	1.83 ± 0.25	2.02 ± 0.22	< 0.0001
MF PCAR0.0	0.99 ± 0.05	0.99 ± 0.01	0.01
MF PCAR0.5	0.99 ± 0.05	0.99 ± 0.01	0.01
MF PCAR1.0	0.98 ± 0.06	0.99 ± 0.01	0.002
MF PCAR1.5	0.85 ± 0.10	0.88 ± 0.07	0.001
LF VC (mm3)	2274 ± 370	3297 ± 492	< 0.0001
LF ThC (mm)	1.72 ± 0.23	1.94 ± 0.20	< 0.0001
LF PCAR0.0	0.99 ± 0.03	0.99 ± 0.04	0.90
LF PCAR0.5	0.99 ± 0.03	0.99 ± 0.00	0.99
LF PCAR1.0	0.99 ± 0.03	0.99 ± 0.01	0.32
LF PCAR1.5	0.84 ± 0.12	0.88 ± 0.08	< 0.0001
MT VC (mm^3)	1286 ± 227	1872 ± 334	< 0.0001
MT ThC (mm)	1.75 ± 0.24	1.93 ± 0.25	< 0.0001
MT PCAR0.0	0.99 ± 0.06	0.99 ± 0.01	< 0.0001
MT PCAR0.5	0.99 ± 0.05	0.99 ± 0.01	< 0.0001
MT PCAR1.0	0.95 ± 0.06	0.96 ± 0.03	0.53
MT PCAR1.5	0.71 ± 0.19	0.78 ± 0.13	< 0.0001
LT VC (mm3)	1537 ± 309	2203 ± 383	< 0.0001
LT ThC (mm)	2.20 ± 0.37	2.44 ± 0.32	< 0.0001
LT PCAR0.0	0.96 ± 0.05	0.97 ± 0.02	< 0.0001
LT PCAR0.5	0.96 ± 0.05	0.97 ± 0.03	< 0.0001
LT PCAR1.0	0.92 ± 0.06	0.94 ± 0.04	< 0.0001
LT PCAR1.5	0.79 ± 0.11	0.83 ± 0.08	< 0.0001
MM Volume (mm^3)	2179 ± 491	2974 ± 567	< 0.0001
MM Area (mm^2)	655 ± 88	834 ± 99	< 0.0001
MME Volume (mm^3)	300 ± 286	351 ± 217	0.0004

MME Area (mm^2)	75 ± 54	83 ± 39	0.001
MMCR	0.49 ± 0.09	0.52 ± 0.07	0.003
LM Volume (mm3)	2184 ± 480	2820 ± 475	< 0.0001
LM Area (mm2)	651 ± 82	818 ± 83	< 0.0001
LME Volume (mm3)	25 ± 60	14 ± 34	0.01
LME Area (mm2)	6.39 ± 13.3	3.49 ± 7.57	0.002
LMCR	0.66 ± 0.08	0.67 ± 0.06	0.28

Table 4. Correlation quantification of cartilage with height.

Quantification of each cartilage	rs	p value
Female		
F PCAR00	0.07	0.23
F PCAR05	0.07	0.21
F PCAR10	0.10	0.09
F PCAR15	0.12	0.06
F.ThC	0.18	0.003
F.VC	0.39	<.0001
LT PCAR00	0.08	0.21
LT PCAR05	0.07	0.25
LT PCAR10	0.08	0.18
LT PCAR15	0.13	0.04
LT.ThC	0.19	0.001
LT.VC	0.36	<.0001
MT PCAR00	-0.03	0.58
MT PCAR05	-0.04	0.54
MT PCAR10	0.01	0.82
MT PCAR15	0.11	0.06
MT.ThC	0.14	0.02
MT.VC	0.32	<.0001
Quantification of each cartilage	rs	p value
Male		
F PCAR00	0.04	0.48
F PCAR05	0.04	0.52
F PCAR10	0.09	0.13
F PCAR15	0.16	0.01
F.ThC	0.34	<.0001
F.VC	0.49	<.0001

LT PCAR00	0.15	0.01
LT PCAR05	0.15	0.01
LT PCAR10	0.14	0.02
LT PCAR15	0.15	0.01
LT.ThC	0.25	<.0001
LT.VC	0.43	<.0001
MT PCAR00	0.01	0.81
MT PCAR05	0.01	0.84
MT PCAR10	0.13	0.03
MT PCAR15	0.16	0.01
MT.ThC	0.20	<.0001
MT.VC	0.38	<.0001

Table 5. Correlation of PCAR, VC, and ThC with age.

Regions &	rs (p value)					
subregions	PCAR0.0	PCAR0.5	PCAR1.0	PCAR1.5	VC	ThC
Female						
MF	-0.14 (0.019)	-0.14 (0.025)	-0.06 (0.34)	-0.07 (0.27)	-0.01 (0.84)	0.02 (0.70)
LF	-0.23 (0.0001)	-0.21 (0.0005)	-0.11 (0.072)	0.07 (0.26)	-0.02 (0.69)	0.02 (0.76)
MT	-0.06 (0.30)	-0.07 (0.242)	-0.11 (0.080)	-0.16 (0.041)	-0.03 (0.59)	-0.12 (0.042)
LT	0.15 (0.013)	0.15 (0.016)	0.06 (0.30)	-0.06 (0.34)	-0.15 (0.0012)	-0.19 (0.012)
mcMF	-0.21 (0.0004)	-0.21 (0.0004)	-0.06 (0.30)	-0.06 (0.36)	0.03 (0.66)	0.05 (0.42)
mcLF	0.15 (0.014)	0.15 (0.014)	0.06 (0.35)	-0.03 (0.58)	-0.12 (0.054)	-0.04 (0.52)
mcMT	-0.21 (0.0004)	-0.21 (0.0004)	-0.34 (<0.0001)	-0.28 (<0.0001)	-0.16 (0.0063)	-0.25 (<0.0001)
mcLT	-0.12 (0.042)	-0.12 (0.042)	-0.13 (0.039)	-0.15 (0.016)	-0.12 (0.055)	-0.13 (0.038)
Male						
MF	-0.26 (<0.0001)	-0.25 (<0.0001)	-0.16 (0.0063)	-0.02 (0.71)	-0.09 (0.127)	-0.08 (0.206)
LF	-0.08 (0.19)	-0.08 (0.18)	-0.04 (0.50)	0.06 (0.31)	-0.10 (0.10)	-0.09 (0.13)
MT	-0.11 (0.066)	-0.11 (0.069)	-0.13 (0.028)	-0.17 (0.0034)	-0.15 (0.014)	-0.22 (0.0002)
LT	-0.02 (0.78)	-0.02 (0.76)	-0.02 (0.70)	-0.09 (0.12)	-0.14 (0.019)	-0.20 (0.0007)
mcMF	-0.10 (0.085)	-0.05 (0.38)	-0.05 (0.36)	-0.02 (0.73)	-0.10 (0.097)	-0.12 (0.045)
mcLF	-0.10 (0.094)	-0.10 (0.094)	-0.09 (0.15)	-0.09 (0.14)	-0.19 (0.0011)	-0.18 (0.0019)
mcMT	-0.13 (0.025)	-0.13 (0.025)	-0.18 (0.0018)	-0.33 (<0.0001)	-0.25 (<0.0001)	-0.35 (<0.0001)
mcLT	-	-	-	-0.06 (0.33)	-0.07 (0.22)	-0.10 (0.081)

-: The correlation coefficient could not be measured because they were all the same and had no variance.

Table 6. Correlation of age and mcMT with quantification of MM extrusion.

	rs (p value)				
	Age	mcMT PCAR0.0	mcMT PCAR0.5	mcMT PCAR1.0	mcMT PCAR1.5
Female					
MME Area	0.15 (0.012)	-0.32 (<0.0001)	-0.32 (<0.0001)	-0.19 (0.0017)	-0.05 (0.38)
MME Volume	0.15 (0.013)	-0.32 (<0.0001)	-0.32 (<0.0001)	-0.18 (0.0022)	-0.02 (0.67)
MMCR	0.001 (0.987)	0.30 (<0.0001)	0.30 (<0.0001)	0.25 (<0.0001)	0.28 (<0.0001)
Male					
MME Area	-0.09 (0.066)	-0.18 (0.0029)	-0.17 (0.0036)	-0.17 (0.0036)	-0.01 (0.82)
MME Volume	-0.11 (0.12)	-0.18 (0.0029)	-0.18 (0.0022)	-0.18 (0.0029)	-0.01 (0.90)
MMCR	0.03 (0.62)	0.17 (0.0033)	0.11 (0.057)	0.13 (0.033)	0.04 (0.54)

Figures

Fig. 1

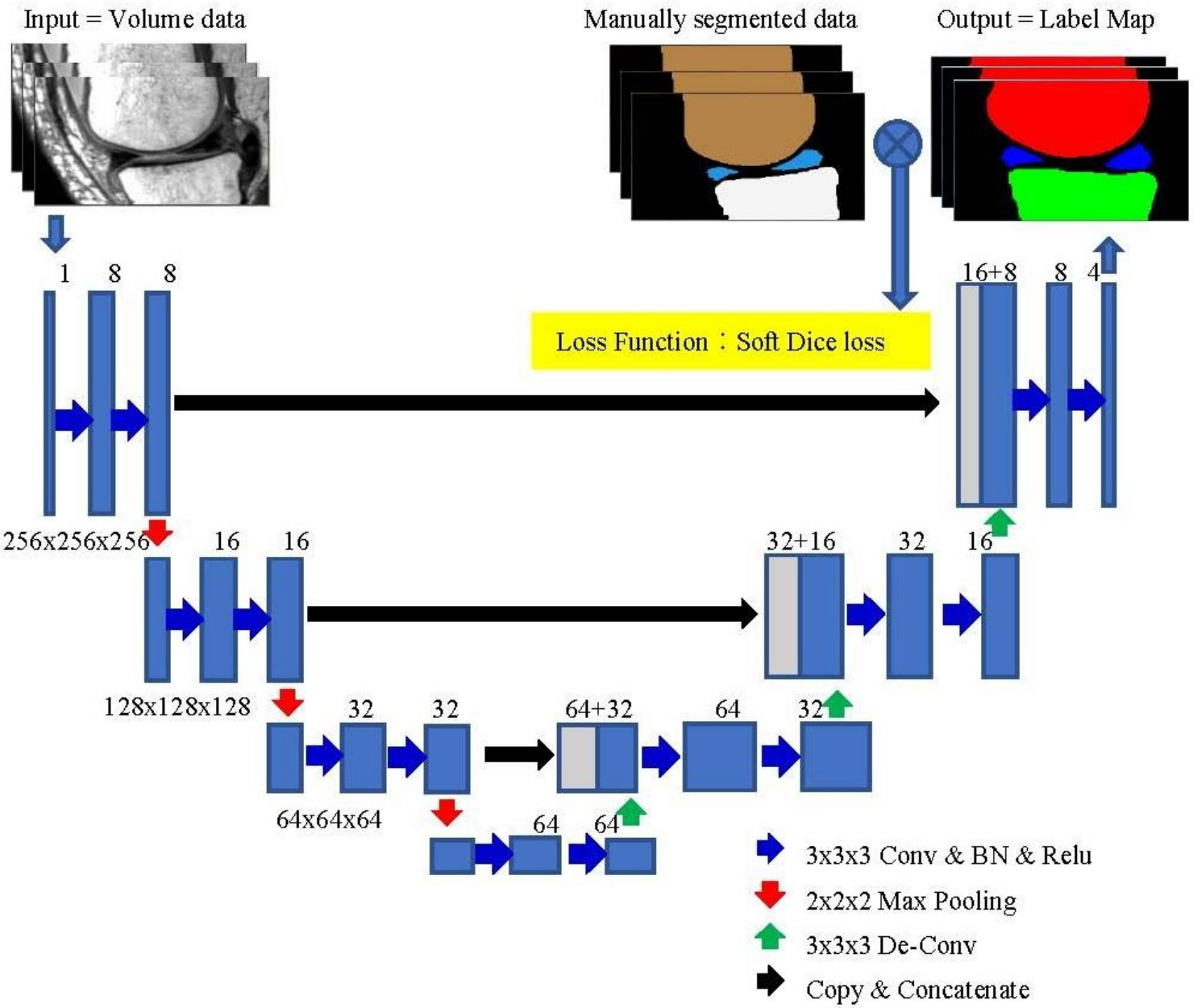

Figure 1

3D Convolutional Neural Network (3D-CNN) algorithm for segmentation of cartilage, meniscus, and bone. The 3D CNN was constructed based on U-Net. Encode layers were formed with 3x3x3 convolution layers, batch normalization, rectified linear unit, and 2x2x2 max pooling layers. As decode layers, 3x3x3 deconvolution layers were used.

Fig. 2

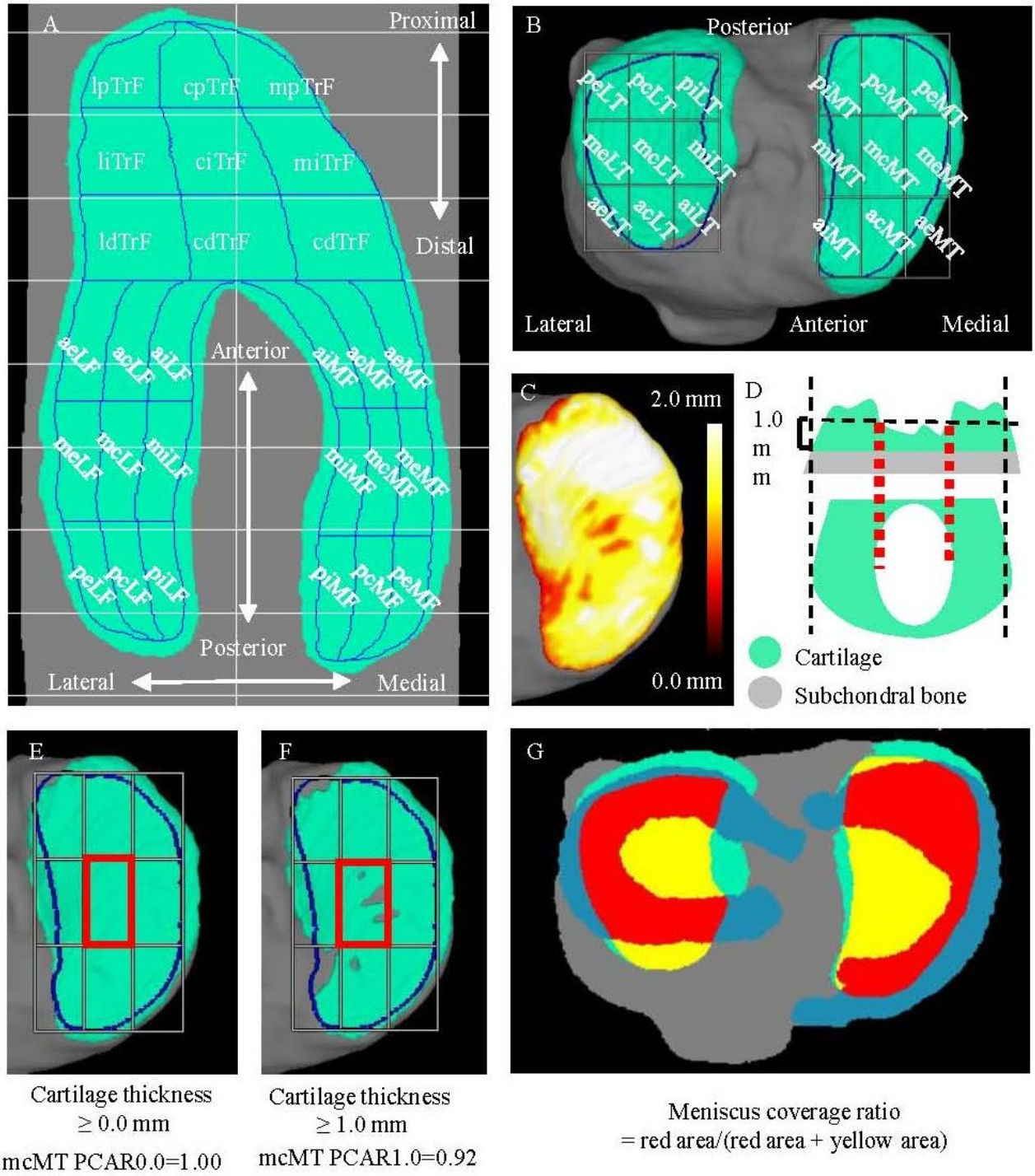

Figure 2

Projected cartilage area and meniscus coverage ratio. (A) Subregions of femoral cartilage. Green region is femoral cartilage, blue outer line means the ROI of the femoral subchondral bone and bule inner line means subregion automatically divided at equal intervals by CNN. (B) Subregions of tibial cartilage. Gray region is tibial bone, green region is femoral cartilage, blue outer line means the ROI of the femoral subchondral bone and bule inner line means subregion automatically divided at equal intervals by CNN.

(C) Cartilage thickness mapping in the medial tibia. (D) Schematic diagram of the projected cartilage area (cartilage thickness ≥ 1.0 mm). (E) Practical example of the projected cartilage area (cartilage thickness ≥ 0.0 mm) in the medial tibia. (F) Practical example of the projected cartilage area (cartilage thickness ≥ 1.0 mm) in the medial tibia. (G) Schematic diagram of the meniscus coverage ratio. Red part is overlapping area of meniscus and the medial/lateral tibial plateau region of interest (ROI). Red part + Yellow part is the medial/lateral plateau ROI. ROIs were reconstructed by CNNs. Green parts are cartilage located outside of ROI.