新北市政府106年度自行研究報告

研究主題:
中文：
使用電腦輔助系統進行超音波影像之膝關節軟骨量化及分析
英文：
Knee Articular Cartilage Evaluation in Musculoskeletal Ultrasound Using Computer-aided Quantitative System

研究機關：新北市立聯合醫院
研究人員：李忠謙
研究期程：106.1.1-106.12.31

新北市政府衛生局編印
印製年月:106年12月

新北市政府106年度自行研究計畫表

填 表 人：李忠謙

填表日期：105.10.29

聯絡電話：0978695369

計　畫　名　稱	使用電腦輔助系統進行超音波影像之膝關節軟骨量化及分析		
研究機關及人員	計畫主持人：新北市立聯合醫院骨科 李忠謙主任	期　　程	自106年1月1日至106年12月31日
目　　的	本研究計畫目的為發展電腦輔助量化及分析系統自動偵測及量化分析膝關節之軟骨組織。此電腦輔助量化分析系統的完成，可讓醫師在進行膝關節超音波檢查後，快速獲得膝關節軟骨組織之量化資料。		
方　　法	本計畫提出的主要研究主題為發展電腦輔助量化分析系統於膝關節超音波之上，第一步驟先將超音波影像進行優化處理，藉由分析解剖學上的資訊，進行自動化軟骨組織偵測，並標出軟骨組織之淺部及深部邊緣，完成軟骨組織之淺部及深部邊緣後，即可對膝關節之軟骨組織進行定量及分析。		
經　　費	315,000元		
備　　註			

備註：

一、研究機關及人員：包括研究機關、實際研究人員及參與工作人員。

二、方法：如研究方法之訂定、問題之發掘、研究設計、資料之蒐集與分析、解決方案之研擬、研究報告之提出。

三、已提報之自行研究計畫因故撤銷辦理者，應敘明原因行文通知。

四、自行研究報告內容應力求與所屬局處業務相關。

新北市政府 106 年度自行研究成果摘要表

計　　畫　　名　　稱	使用電腦輔助系統進行超音波影像之膝關節軟骨量化及分析
期　　　　　　　　程	自 106 年 1 月 1 日至 106 年 12 月 31 日
經　　　　　　　　費	315,000 元
緣　起　與　目　的	本研究計畫目的為發展電腦輔助量化及分析系統自動偵測及量化分析膝關節之軟骨組織。此電腦輔助量化分析系統的完成，可讓醫師在進行膝關節超音波檢查後，快速獲得膝關節軟骨組織之量化資料。
方　法　與　過　程	本計畫提出的主要研究主題為發展電腦輔助量化分析系統於膝關節超音波之上，第一步驟先將超音波影像進行優化處理，藉由分析解剖學上的資訊，進行自動化軟骨組織偵測，並標出軟骨組織之淺部及深部邊緣，完成軟骨組織之淺部及深部邊緣後，即可對膝關節之軟骨組織進行定量及分析。
研究發現及建議	The collected cases included 104 knee ultrasound images from 7 males and 9 females. The accuracy of cartilage thickness between the proposed computer-aided quantitative system when compared with manual measure by the orthopedic surgeon was 88.53% at IN, 85.69% at LC, and 83.98% at MC respectively. The overall accuracy of the proposed CAD system in cartilage measurement was 86.07%. In conclusion, the proposed automatic computer-aided system can provide the quick, inexpensive, and accurate additional information of knee cartilage identification and thickness measurement for the physicians to evaluate the severity of osteoarthritis.
備　　　　　　　　註	

新北市政府 106 年度自行研究計畫執行情形季報表

填表日期：

計畫名稱	研究機關及人員	期程		執行情形概述	備註
		起	訖		
使用電腦輔助系統進行超音波影像之膝關節軟骨量化及分析	新北市立聯合醫院骨科 李忠謙主任	106.01.01	106.12.31	IRB 通過，病歷資料收集中。	
使用電腦輔助系統進行超音波影像之膝關節軟骨量化及分析	新北市立聯合醫院骨科 李忠謙主任	106.01.01	106.12.31	收集個案影像資料，並進行去連結處理，同時進行量化分析系統之程式改良。	
使用電腦輔助系統進行超音波影像之膝關節軟骨量化及分析	新北市立聯合醫院骨科 李忠謙主任	106.01.01	106.12.31	資料檢索中，期中報告已完成。	
使用電腦輔助系統進行超音波影像之膝關節軟骨量化及分析	新北市立聯合醫院骨科 李忠謙主任	106.01.01	106.12.31	期末報告完成。	

Abstract

Osteoarthritis is one of the most common joint disease at knee. Osteoarthritis is characterized by focal cartilage degeneration and progression loss of cartilage. The roentgenogram is the primary radiological examination for diagnosis of knee osteoarthritis, but revealed only indirect signs of articular cartilage abnormalities and is not sensitive to minor changes in cartilage conditions and thickness. In this study, an automatic computer-aided quantitative (CAQ) system for measurement of knee cartilage thickness using ultrasound images was developed in evaluating the severity of cartilage wear which represents the severity of knee osteoarthritis. After ultrasound images are acquired, the cartilage area were segmented from these images by Markov random field (MRF) models. For segmented cartilage area, the delineation of cartilage boundary was marked automatically by spline interpolation algorithm and superficial and deep boundaries were smoothed for preparation of marks for measurement positions. The thickness of femoral trochlea cartilage was measured by the proposed automatic computer-aided system. The three positions of measurement were done automatically at the lateral condyle (LC), the intercondylar area (IN), and the medial condyle (MC) respectively. The collected cases included 104 knee ultrasound images from 7 males and 9 females. The accuracy of cartilage thickness between the proposed computer-aided quantitative system when compared with manual measure by the orthopedic surgeon was 88.53% at IN, 85.69% at LC, and 83.98% at MC respectively. The overall accuracy of the proposed CAD system in cartilage measurement was 86.07%. In conclusion, the proposed automatic computer-aided system can provide the quick, inexpensive, and accurate additional information of knee cartilage identification and thickness measurement for the physicians to evaluate knee joint cartilage condition and the severity of osteoarthritis.

Keywords: osteoarthritis, knee cartilage, cartilage thickness, ultrasound, computer-aided

Introduction

Osteoarthritis is the most common joint disease affecting the elderly patients, and the knee is involved most commonly among peripheral joints[1]. The prevalence of knee osteoarthritis increases with age[2]. The knee osteoarthritis is known as a condition of joint cartilage and meniscus wearing which is an irreversible process[3] and associated with synovial inflammation, weakened muscle, joint alignment, structural change at subchondral bone. Patients with knee osteoarthritis have symptoms of knee pain, swelling, limitation of joint movement, stiffness and further deformity. The diagnosis of knee osteoarthritis begins with physical examination and can be confirmed by radiological studies [4].

The plain X-rays are the most common radiological examination for diagnosis of knee osteoarthritis and are considered as the gold standard for evaluation of severity of osteoarthritis. The Kellgren and Lawrence system [5] is the method of classifying the severity of knee osteoarthritis from 0 to 4 according to joint space narrowing, osteophyte and bony deformity. However, the diagnosis of knee osteoarthritis by radiographs has the limitation to directly visualize articular cartilage and other soft tissue which is involved in the pathophysiology of osteoarthritis [6,7]. To evaluate cartilage wearing and lesions and intra-articular inflammation, magnetic resonance imaging (MRI) and ultrasound (US) would be prescribed by physicians [8].

Cartilage abnormalities are primary features of osteoarthritis, and repetitive and chronic intra-articular inflammation in the knee joint was considered contribute to the progression of knee osteoarthritis [9-11]. Bony change and deformity can be recognized in radiographic images which have little information of cartilage condition due to inability of direct visualization of articular cartilage. The soft tissue structures such as joint cartilage, meniscus and synovium are visualized on US and MRI. US and MRI have comparable diagnostic performance for the assessment of femoral cartilage, effusion and synovial thickening[12]. Compared with MRI, the advantages of US are that it is quick, inexpensive, easy to assess, dynamic and with few contraindications. Therefore, the ultrasonography has been proved previously to be a valid and reliable method for femoral cartilage evaluation [13-17]. Knee US imaging could also detect articular abnormalities, such as effusions, synovitis, and intra-articular bodies [18,19]. However, knee US imaging still exist several limitations which are an operator-dependent technique with existence of intra-rater and inter-rater reliability [20], learning curve variability dependent on the operator experience, and limited application of deeper articular structure and subchondral bone due to the properties of sound.

The purpose of this study is to develop automatic computer-aided quantitative (CAQ) system using knee musculoskeletal US image to evaluate the thickness of femoral trochlea cartilage automatically and validate clinical application of US for evaluation of knee OA. This is the first study of computer-aided quantification system for evaluation of knee cartilage to the best of our knowledge. The assessment system could provide confident and quick results of knee cartilage thickness measurements, and it would be helpful to assist the physicians in assessing the degree of cartilage wear and the severity of knee osteoarthritis.

Materials and Methods

Patients and data acquisition

After excluding images with poor quality, the database used in this study consisted of 104 knee ultrasound images in 16 adult patients collected from January 2013 to July 2016. The 16 cases were those of 7 men and 9 women aged 26-65 years (mean age, 42.6 years).

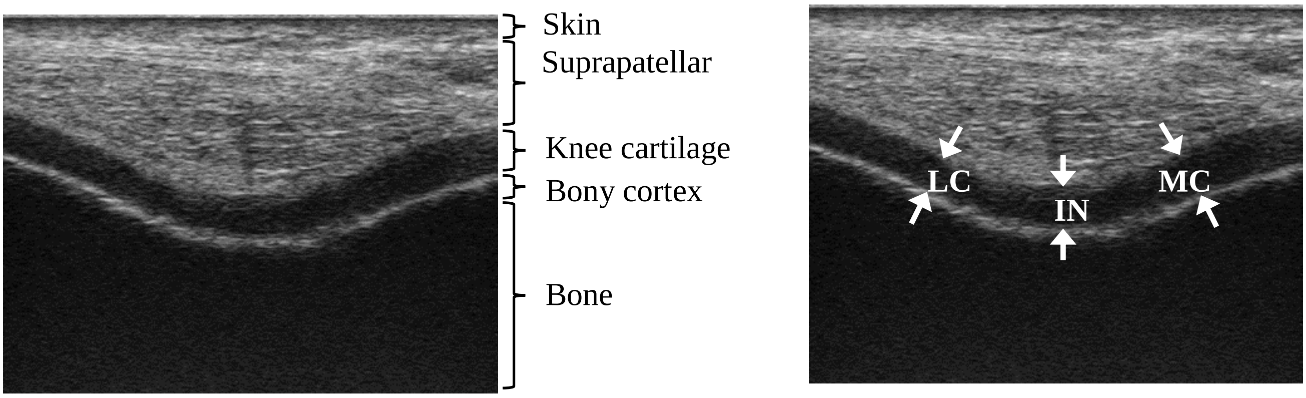
The knee ultrasound images in the collected database were generated using an ALOKA alpha-7 ultrasound scanner (Hitachi-Aloka Medical, Tokyo, Japan) with linear array probe (scan width: 36mm) ranging from 5 to 13 MHz. The settings of the ultrasound scanner such as gain compensation were consistent for all patients. During examination, the postures of the examined patients were standard sitting position with knee hyperflexion (Fig. 1) and examination schedule were followed.

Figure.1 Transducer placement for femoral cartilage measurement with knee

hyperflexion.

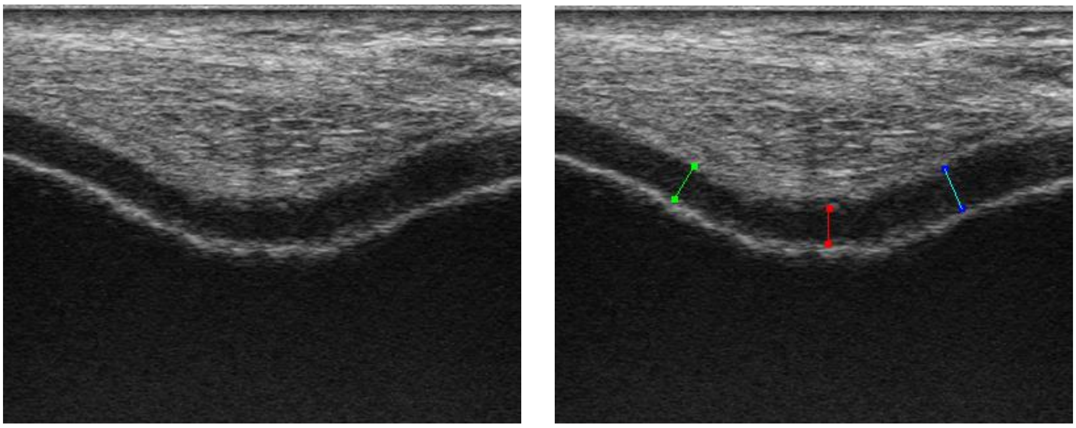
Cartilage Thickness Measurement

The cartilage thickness was measured in intercondylar notch (IN), lateral condyle (LC), and medial condyle (MC) with the transducer placed transversely to the knee above the patella region. Figure 2 reveals the anatomy on knee ultrasound. The position of LC and MC measurement was midpoint of intercondylar notch and lateral and medial edges of the ultrasound images or cartilage margins. To evaluate accuracy of the cartilage thickness measurement by the proposed CAQ system, a program tool was designed for the orthopedic surgeon to perform the measurement manually. By using the program tool, the orthopedist manually located and measured the cartilage thickness at three positions of IN, LC, and MC. For every image, the measurement of femoral articular cartilage thickness was performed by an orthopaedic surgeon who expertizes musculoskeletal ultrasound (Fig. 3) and the data was used to be compared with the proposed CAQ system. Manual measurement by the physicians was performed by using a program tool developed in this study to facilitate the procedures and data output.



(a) (b)

Figure 2. (a) Representation of knee anatomy on knee ultrasound. (b) Measurement of femoral articular cartilage thickness at intercondylar notch (IN), lateral condyle (LC), and medial condyle (MC).



(a) (b)

Figure 3. Ultrasound images of the femoral cartilage (a) with intercondylar notch (IN, red line), lateral condyle (LC, green line), and medial condyle cartilage (MC, blue line) thickness measurement (b) by an orthopaedic surgeon.

Methods

After acquisition, the knee ultrasound images were drawn out from the scanner and stored as 8-bit images with pixel value ranging from 0 to 255. The CAQ system was started with quality enhancement, and followed with cartilage area segmentation, cartilage area detection, boundary delineation and automatic thickness measurement. Figure 3 represent the flowchart of CAQ system for automatic measurement of femoral articular cartilage.

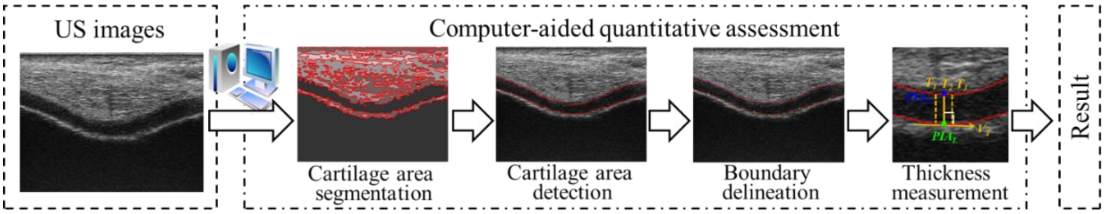


Fig. 3. Flowchart of the developed computer-aided quantitative assessment system for thickness measurement of the cartilage area in US.

Quality Enhancement

In US images, speckle noise usually reduces the image quality and biases the segmentation result. To overcome this problem, quality enhancement was used as a pre-processing to reduce speckle noise and enhance image contrast, which was performed by a sigmoid filter. The sigmoid operator is a non-linear transform of mapping a selected range of the gray values in a given image into a specific gray value range with a very smooth and continuous transition. For each pixel in a US image I, we assume G(x, y) is the gray-value of a pixel, and the new gray-value, G', enhanced by the sigmoid operator is expressed as:

$$G' = (Max - Min)\frac{1}{\left(1+e^{-\left(\frac{G-\beta}{\alpha}\right)}\right)} + Min, \quad (1)$$

where Max(=255) and Min(=0) are the maximum and minimum gray values in the output image, α and β denote the width and median of the selected gray value range in the input image.

Cartilage Area Segmentation

Cartilage area segmentation was used to separate a given US image into regions, where each region was a collection of pixels associated with homogeneous intensity and texture. In this study, the MRF analysis was used to classify pixels in a given US image into several pixel classes by referring textural constraints of the neighboring pixels. To perform MRF analysis, in the US image *I*, let $\Lambda = \{\omega_1, \omega_2, ..., \omega_i\}$ denoted a set of N_L labels, where $1 < i < N_L$, and *f* was the observed textural feature in *I*. For initialization, each pixel in *I* was labeled as $\omega_i \in \Lambda$ according to the feature vector *v* extracted from *I*, and probability distribution of the segmentation ω_i with the given *v* can be expressed as $P(\omega_i | v)$. Then, the Bayes rule is exploited to obtain $P(\omega_i | v)$ by

$$P(\omega_i|v) = {P(v|\omega_i)P(\omega_i)}/{P(v)}, \quad (2)$$

where $P(v)$ was constant. For the MRF model, an optimal segmentation labeling $\hat{\omega}$ was obtained by maximizing the probability distribution $P(\omega_i|v)$ via the maximum a posteriori (MAP), and was expressed as

$$\hat{\omega} = \underset{\omega_i \in \Lambda}{argmax}\, P(\omega_i|v). \quad (3)$$

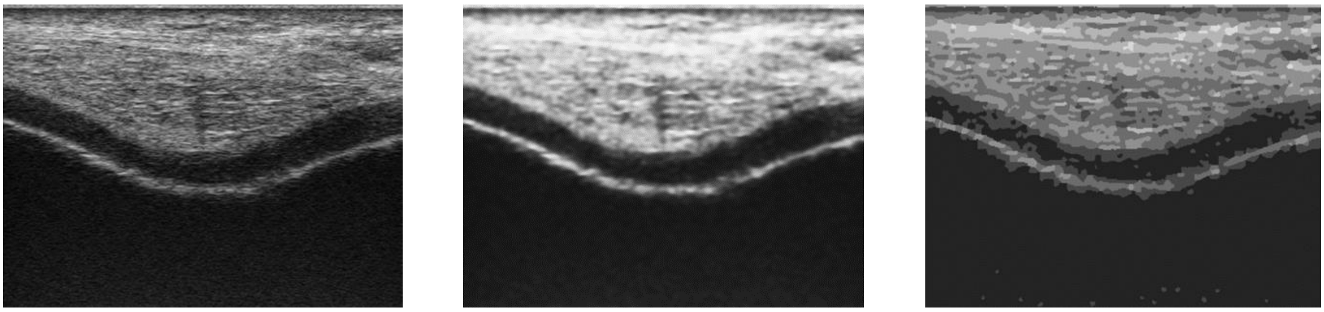
According to Eq. (2), the constant $1/P(v)$ is dropped while only the maximum $\hat{\omega}$ was interested, and the optimal labeling $\hat{\omega}$ for each pixel can be obtained by suing the MAP, which was replaced by

$$\hat{\omega} = \underset{\omega_i \in \Lambda}{argmax}\, P(v|\omega_i)\, P(v). \quad (4)$$

Thus, by using MRF analysis, all the pixels in I were segmented into non-overlapping regions, and each region was labeled as class-i according to the corresponding optimal labeling $\hat{\omega} = \omega_i$. The pixels in a region labeled as class-i was assigned with a replacement gray-value g(i), which was calculated by

$$g(i) = \left\lfloor (i-1) \times \frac{Max}{N_L - 1} \right\rfloor, \quad (5)$$

where *Max* was the maximum gray-value range in *I*. To illustrate the cartilage area segmentation, an original cartilage US image was shown in Fig. (a), and the corresponding image processed by the sigmoid operation was shown in Fig. (b). Then, after applying the MRF analysis with N_L = 8, the MEF segmentation of Fig. 4(b) was shown in Fig. (c), where the pixel gray-values were assigned by Eq. (5).



(a) (b) (c)

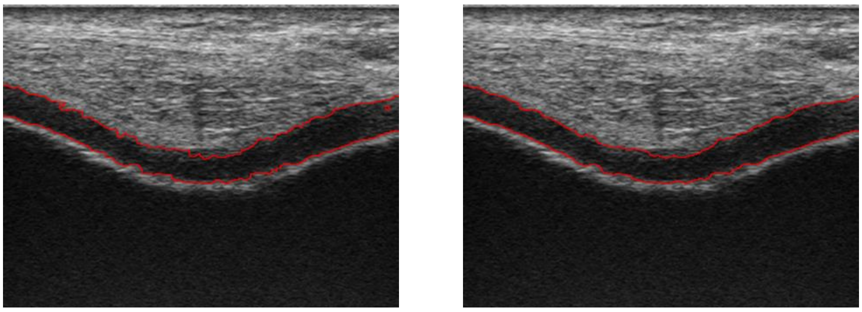
Fig. 4. (a) An original cartilage ultrasound image, (b) the image after noise removal and contrast enhancement, and (c) the MRF segmentation with N_L = 8.

Cartilage Area Detection

To extract the desired cartilage area, cartilage area detection was performed based on a merging scheme to collect and detect dark areas from the segmented regions. The merging scheme was composed of three steps and two thresholding values of coarse fusion and fine tuning, which were described as follows:

1. For initialization, each segmented region associated with $g(i) = 0$ were selected as seed regions, and TH_{ME1} and TH_{ME2} were threshold values for the coarse merging and fine tuning , where $1 \leq TH_{ME1} < TH_{ME2} \leq N_L$.
2. The coarse fusion was executed from $i = 1$ to TH_{ME1} to iteratively merge the adjacent segmented regions associated with $g(i)$. The merged regions with the first two large areas were selected as the candidates of bone and cartilage regions.
3. In the fine tuning procedure, the merging process was started from two candidate regions, and regions associated with gray-values less than $g(i)$ were merged into the adjacent candidate region, from $i = 0$ to TH_{ME2}. The regions were labeled as parts of the bony cortex, while they were selected by both of the candidate regions for merging at i-iteration.

In this study, TH_{ME1} was pre-defined as the maximal i associated with $g(i) < Avg_I$, where Avg_I was the gray-value mean of all pixels in I. In addition, TH_{ME2} was chosen as $TH_{ME1}+2$ empirically. After the fine tuning procedure, the candidate region with the largest area was labeled as the cartilage area. Then, morphological operators, such as dilation and erosion, were exploited to fill miss-segmented regions and to smooth the boundaries of the detected cartilage area. In Fig. 5(a), the cartilage area was detected by applying the presented merging scheme on the MRF segmentation. There was a miss-segmented region at the right side within the cartilage area, which was filled after applying morphological operation, as shown in Fig. (b).

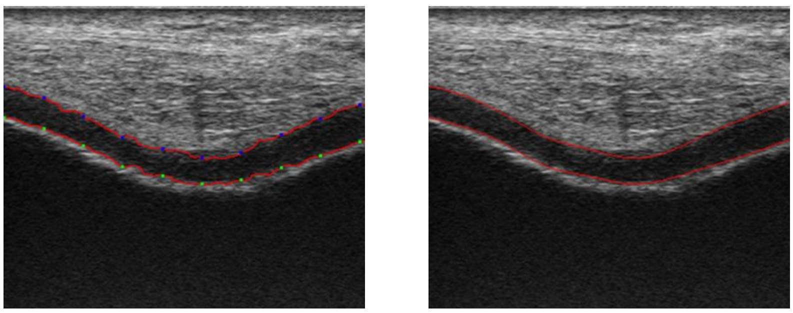


(a) (b)

Fig. 5. (a) The cartilage area detected by the presented merging scheme, and (b) the cartilage area processed by morphological operation.

Boundary Delineation

The boundary delineation was presented to refine and smooth the two detected cartilage boundaries, to approximate the real cartilage boundaries, and was composed of sample point selection and spline interpolation. In sample point selection, a constant interval between two adjacent sample points on x-axis was exploited to select two sets of sample points from the detected boundaries, which were denoted as SP1 and SP2, respectively. If there were more than one point at the same x-coordinate selected from SP1/SP2, the y-coordinate of the corresponding sample point was average of the y-coordinates of those selected points. Spline interpolation〔35〕 was a term of interpolation where the input points were estimated using a mathematical function of piecewise polynomials to minimize the interpolation error. By using spline interpolation, two smoothing curves denoted as B_{Upper} and B_{Lower}, are generated to pass exactly through the sample points of SP1 and SP2, respectively. In Fig. (a), the blue-color and green-color points were the selected as SP1 and SP2, and fitted by using spline interpolation to generate the smoothing boundaries of the detected cartilage area, as shown in Fig. (b).



(a) (b)

Fig. 6. (a) The sample point selection applied on B_{Upper} (blue) and B_{Lower} (green), and (b) the curve fitting of the selected sample points via the spline interpolation.

Thickness Measurement

The thickness of the cartilage area, denoted as T_C, was measured on the three target positions at IN, LC and MC. For this purpose, the intersection points of IN, LC and MC should be located at the refined B_{Upper} and B_{Lower} , as superficial and deep boundaries, respectively. To locating the position of IN, the lowest point of B_{Lower} was selected as an intersection point of IN, and denoted as PIA_L. Then, the other intersection point of IN, denoted as PIA_U, can be acquired while the vector V_N of PIA_L

and PIA_U satisfies the following equation,

$$VT \bullet VN = 0, \tag{6}$$

where V_T was the tangent vector at PIA_L. The position of LC was sought in the left side of B_{Upper} and B_{Lower} from IN. The middle point between PIA_L and the highest point of B_{Lower} in the left side was selected as an intersection point of LC, and denoted as PLC_L. The other intersection point of LC was located by using the same method for locating PIA_U. Also, the two intersection points of MC, denoted as PMC_U and PMC_L, were located by using the same method for locating those of LC.

Thickness measurement at IN, LC, and MC was performed by measuring the segments of PIA_U and PIA_L, PLC_U and PLC_L, and PMC_U and PMC_L. In addition, to increase accuracy and robustness, for each target position, thickness measurement was performed by averaging thicknesses of three segments, T_1, T_2, and T_3. The T_2 was the original thickness at the target position, and T_1 and T_3 were with 2-pixels interval from the left and right of the target position. Fig. illustrated the procedure of thickness measurement at IN for the boundary delineation in Fig. (b).

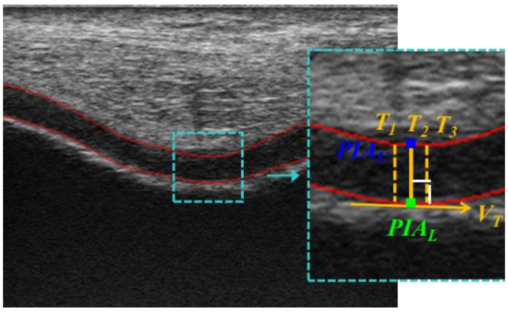


Fig. 7. Illustration of thickness measurement for the position of IN. The V_T was the

tangent vector for B_{Lower} on PIA_L, the thickness of IN was measured by averaging thicknesses of three segments, T_1, T_2, and T_3.

Results

The thickness measurement of the three target positions at IN, MC, and LC, which were automatically obtained by the proposed CAQ system, was compared with measures by the orthopedic surgeon to determine the accuracy of proposed CAQ system. The accuracy was represented by MIND (minimum of difference), MAXD (maximum of difference), MD (mean of difference), and SDD (standard deviation of difference) of the thickness measurement for all images. For 104 US images, Table 1 shows the comparison of the difference between the automatic measures by the proposed CAQ system and manual measures by the orthopedic surgeon. The mean of difference were 0.32±0.25 mm at LC, 0.28±0.22 mm at IN and 0.35±0.28 mm at MC. The accuracy of the assessment system was were 85.69%, 88.53%, and 83.98% at LC, IN, and MC with the overall accuracy of 86.07%. with the overall accuracy was 85.95%. The deviation of the measurement positioning by proposed CAQ system were 0.81±0.72 mm at LC, 0.75±0.55 mm at IN, and 0.89±0.76 mm at MC while compared with manual positioning by the orthopedic surgeon (Table 2).

Difference	Thickness measurement		
	LC	IN	MC

MAXE (mm)	0.68	0.61	0.89
MINE (mm)	0.01	0.01	0.02
ME (mm)	0.32	0.28	0.35
SD (mm)	0.25	0.22	0.28

Table 1 Comparison of the maximum (MAXD), minimum(MIND), mean(MD), and standard deviation(SDD) of measurement errors between the thickness measurement by the proposed system and the orthopedist.

Deviation	Measurement positioning		
	LC	IN	MC
MAXE (mm)	2.12	1.92	2.33
MINE (mm)	0.1	0.1	0.2
ME (mm)	0.81	0.75	0.89
SD (mm)	0.72	0.55	0.76

Table 2 The maximum, minimum, mean, and standard deviation of position deviation between the system result and measures of the orthopedic surgeon at the positions of LC, IN and MC for all cases.

Discussion

The cartilage thickness measurement is an important parameter of structural joint damage in osteoarthritis and other inflammatory arthritis. To monitor joint disease progression and evaluate therapeutic response, the assessment of cartilage condition is important[21].

In this study, we proposed an automatic computer-aided quantitative (CAQ) assessment system for femoral articular cartilage thickness measurement on musculoskeletal ultrasound which includes automatic knee articular cartilage segmentation and thickness measurement. In the proposed system, the cartilage area segmentation was performed on the 2-D B-mode ultrasound images and the spline interpolation was applied to refine the superficial and deep boundaries of the cartilage area to approach the real boundaries. The three positions of IN, LC, and MC were located automatically by CAQ system for thickness measurement, and the thickness of femoral articular cartilage was automatically measured by the proposed system. The measurement results of CAQ was compared with the measurements by the orthopedic surgeon. The accuracy of the proposed CAQ system for the positions at LC, IN, and MC was 85.69%, 88.53%, and 83.98%, respectively, with the overall accuracy of 86.07%. Based on the experiment results, the knee cartilage thickness measurement by the proposed system is comparable to the measurements by the orthopedic surgeon. The experiment results demonstrates that the proposed system provides confident, fast and inexpensive method for the measurement of knee articular cartilage thickness.

The measurement of femoral articular cartilage thickness have been shown acceptable inter-examiner and intra-examiner reliability in previous human studies[22-24]. Nevertheless, this study was conducted to demonstrate the accuracy of the proposed CAQ system in measuring knee articular cartilage thickness when compared the measures by one orthopedic surgeon who was familiar with musculoskeletal ultrasound. Further studies of multi-examiner assessment and comparison with proposed CAQ system are needed to prove the benefit of low variability and reproducibility of the CAQ system in measuring the joint cartilage thickness.

Ultrasound is considered to be an operator-dependent examination. The variability in assessing cartilage thickness on ultrasound images is related to inappropriate positioning and inclination of the transducer, and interface and artefacts appeared especially when performed by less-experienced sonographers. The proposed CAQ system could provide a useful tool for training of less-experienced sonographers.

More experiments will be accomplished in the future to explore the clinical application of the proposed CAQ system. To improve the accuracy of the knee cartilage thickness assessment, the advanced segmentation method and merging method should be developed to improve the cartilage boundary detection, especially on ultrasound images with cartilage lesions which revealed poor cartilage margins. More cases including variable cartilage morphologies should be collected to demonstrate the robustness and reliability of the proposed system to facilitate clinical application. Furthermore, the proposed CAQ system is a quantitative system including articular cartilage segmentation and automatic cartilage delineation, the quantitative texture features could be extracted from area of cartilage delineation by the proposed system and then analyzed for detection and diagnosis of articular cartilage lesions in the future.

In conclusion, the proposed CAQ system provides a useful, confident, fast and inexpensive quantitative assessment for the physicians to evaluate the degree of cartilage wearing of knee joint on ultrasound images.

Acknowledgements

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