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Development of an Arthroscopic Ultrasound Probe for Assessment of Articular Cartilage Degeneration

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Abstract — **Quantitative assessment of articular cartilage is important for the early diagnosis of osteoarthritis, intra-operation joint tissue evaluation and judgment of repaired cartilage quality. This technique is also applicable to the cartilage if arthroscopic instrument embedding this technique can be developed. In this study, an arthroscopic water-jet ultrasound indentation probe was developed with the help of a small profile intra-articular ultrasound imaging (IAUS) catheter for the intra-articular measurement of cartilage condition. The probe can provide measurement of morphological, acoustical and mechanical properties of articular cartilage. Preliminary tests were conducted on 10 intact porcine knees with the guide of arthroscopy for the evaluation of cartilage degeneration, which was induced by trypsin digestion. Results showed the cartilage stiffness decreased significantly after the digestion ($p < 0.001$) with the measurement conducted by the developed probe. In summary, an arthroscopic ultrasound probe has been successfully developed and its utility in detecting the cartilage degeneration was demonstrated in this study. Future work includes the improvement of the probe design and studies on measurement of animal or human samples in vivo.**

I. INTRODUCTION

Osteoarthritis (OA) is a common joint disease especially seen in elderly people. One of the main tissues affected by this disease is the articular cartilage, which is a thin tissue covering the bony end in the joint and mainly provides mechanical support and lubrication during joint movement. In the USA, nearly 27 millions of patients were affected by this disease [1]. According to a survey conducted in Hong Kong, the direct cost for its treatment was up to HK$40,180 (~US$5,150) per person per year [2]. Cartilage shows some kind of degeneration when associated with OA. Currently, the degeneration of articular cartilage is diagnosed by a narrowed joint space as shown in X-ray radiographs or focal lesions as seen under the arthroscopic examination, which is either with limited resolution or can only evaluate the macroscopic surface disruption. Therefore, these two methods are not suitable for the detection of early degeneration of the articular cartilage. On the other hand, various treatment methods including cartilage transplant or tissue engineering for cartilage have been developed for repairing the degenerated cartilage [3]. How to quantitatively assess the quality of the repaired cartilage is a critical step for developing effective treatment schemes. Furthermore, in minimally-invasive operation, it is also useful to include the assessment of exposed articular cartilage to check its degeneration status. Therefore, it is necessary to develop new techniques and devices toward the directions of early detection of cartilage degeneration, assessment of repaired cartilage quality or intra-operation diagnosis of cartilage status.

Various medical imaging modalities have been explored for the quantitative assessment of cartilage degeneration. Using contrast agents, MRI has been demonstrated to be effective to detect the loss of proteoglycan (PG), and some techniques have been adopted or proposed for the diagnosis of OA [4], such as the dGEMRIC, which has been used in clinical practice [5]. However, because of high cost of MRI diagnosis, currently it is not yet so feasible to make it available for routine clinical use. CT, especially the contrast enhance computed tomography (CECT) is also useful for the study of cartilage degeneration [6]; it is still used in the laboratory research and one of its biggest limitations, i.e., radiation risk will be of concern when applied on patients. The near infrared spectroscopy (NIRS) has also been recently proposed for the assessment of cartilage lesion [7], but it lacks resolution in depth, and its clinical potential still need be investigated in future studies. In addition to NIRS, optical coherence tomography (OCT) is another optical technique which has been demonstrated to be useful for cartilage evaluation [8, 9]. Although with a high resolution, the penetration depth is limited for OCT, which may hinder its broad applications in cartilage research. Ultrasound method is a potential method for the quantitative assessment of cartilage status [10]. The value of ultrasound for sensitive detection of cartilage degeneration has been demonstrated [11] and nowadays it has been widely explored to incorporate this facility into the objective and quantitative assessment of articular cartilage degeneration in clinical applications, including the work described in the current study.

Previous studies have reported some work towards the direction of developing arthroscopic devices for cartilage assessment [7, 12-14]. For example, Dashefsky might have developed the earliest arthroscopic device to measure the softening of patellar cartilage in chondromalacia. Lyrra et al. [13] has developed an arthroscopic indentation device to measure the mechanical properties of articular cartilage in joints. A small indenter was installed at the device tip to mechanically indent the cartilage and measure the force response at a fixed indentation depth. Later, ultrasound was embedded in the arthroscopic device to measure more tissue properties [15]. However, an extra bolster was needed to switch between the measures of mechanical and acoustic properties, which was inconvenient in real clinical practice. Other developments of arthroscopic instruments are still in

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their infant stage and more efforts are needed to apply these techniques in clinical situations.

The water-jet ultrasound indentation is a method previously developed in our group for assessing the morphological, acoustical and mechanical properties of the soft tissue including articular cartilage [16, 17], which are potentially useful for the quantitative assessment of cartilage degeneration. In order to make this technique available for intra-articular arthroscopic operation, miniaturization of the probe is necessary. This study describes the development of such an ultrasound probe for the intra-articular assessment of cartilage status.

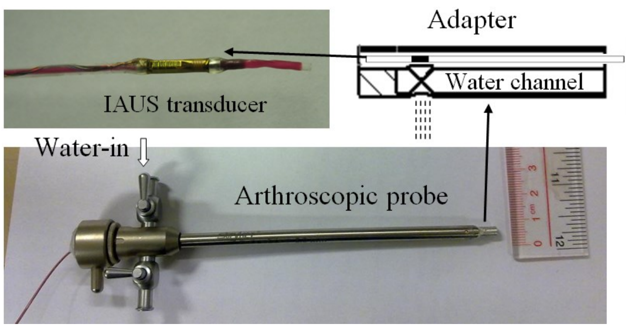

Figure 1. The developed arthroscopic probe which includes a water-jet ultrasound indentation system.

II. INSTRUMENT DEVELOPMENT AND EXPERIMENT

A. Instrument development

The developed probe is shown in Figure 1. It mainly consists of an adapter installed at the tip of an arthroscopic cannula with a diameter of 5.5 mm. In the adapter, an intra-articular ultrasound (IAUS) transducer was installed for collecting the ultrasound signal reflected from the articular cartilage. The IAUS transducer was adopted from an intravascular ultrasound system (In-Vision Gold, Volcano Inc., San Diego, CA, USA) with a specific catheter of 3.5 F (about 1.2 mm) in diameter and 20 MHz in central frequency (Ref 85900, Eagle Eye Gold, Volcano Inc., San Diego, CA, USA). This system was demonstrated to be very useful for the study of articular cartilage [18, 19]. Raw radiofrequency signals could be generated by the IAUS system. The essential part of the catheter, which had 64 ultrasound elements arranged cylindrically, was installed on top of the water-jet orifice for ultrasound signal collection.

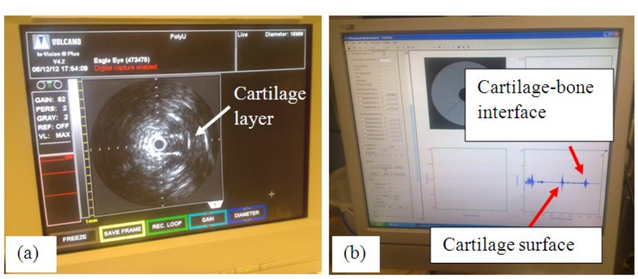

Figure 2. A typical view of the porcine articular cartilage on (a) IAUS and (b) custom designed software graphic user interface

The water was input from the side channel of the cannula and the water pressure was measured by a pressure sensor installed in series with the water pipe (not shown). Wire of the IAUS was output from the other side of the cannula, which was sealed with clay and glue for a successful production of the water-jet. Each image (360° view) (Figure 2a) consisted of 512 lines among which one line perpendicular to the cartilage surface was selected for studying the cartilage deformation. The ultrasound signal and water pressure signal were acquired at a frame rate of 30 Hz and then input to a PC for display and off-line signal processing. Custom-designed software interface programmed with C++ was used for the data display, storage and also off-line processing. The deformation of the cartilage was extracted by applying the cross-correlation algorithm to the cartilage surface reflected ultrasound signals during the water-jet indentation test. A-line ultrasound signal (Figure 2b) was used in the current study to extract the deformation of cartilage layer; however, when all the image signals could be input into PC in future studies, it was possible to analyze all other information of the cartilage including surface roughness and spatially averaged acoustical reflection [20].

B. Experimental test and analysis

Twelve intact porcine knees obtained from a local market were used for the experiment. These knees were obtained fresh within two hours post-mortem after the sacrifice of the pigs. Among them, 10 were used for the enzymatic treatment study and the remained two were used as a control group to study the effect of natural ageing without enzymatic treatment.

The developed probe was inserted into the knee joint and placed upon the cartilage under the guide of the arthroscopic observation (Figure 3). The test position was one point selected on cartilage of the femoral groove. In order to induce degenerative change to the articular cartilage, 0.25% trypsin-EDTA was used to digest the proteoglycans (PGs) [21], which has been widely adopted in previous studies as a model to simulate the early degeneration of articular cartilage [15, 17, 20, 22]. The digestion time was set to be four hours [20]. The trypsin solution was applied into the joint using the same arthroscopic channel with the developed probe. In this case, the water channel was used but trypsin solution, rather than tap water, was injected into the joint capsule. Enough solution was infilled in the capsule in order to immerse the cartilage region of interest so that enzyme could easily penetrate into the cartilage layer to digest the target components. The trypsin solution was also refilled into the capsule continuously by a small water pump during the treatment period in order to prevent the loss of enzyme solution by evaporation.

In order to measure the time (about 4 hours) effect on the cartilage stiffness, two extra tests were conducted in two extra intact knees to measure the change of cartilage stiffness along with time. No enzymatic treatment was applied to the two control knees and during the interval, the physiological saline solution was filled in the joint capsule to prevent the dehydration of the tissue.

Ultrasound signals from the cartilage layer were collected and the water-jet indentation test was conducted on the cartilage before and after the enzymatic treatment. Ultrasound signals with optimized incidence angle were used to measure the thickness of the cartilage. For the water-jet indentation test, a cyclic water pressure from zero to 330 kPa with a period time of 10 s was used to indent the cartilage and typically three cycles of loading and unloading were applied to the cartilage for each test. For each sample, three tests were conducted with a rest of at least 30 minutes between two consequent tests. The probe was fixed during the indentation test to prevent the movement of the probe in order to reduce its effect on the extraction of deformation.

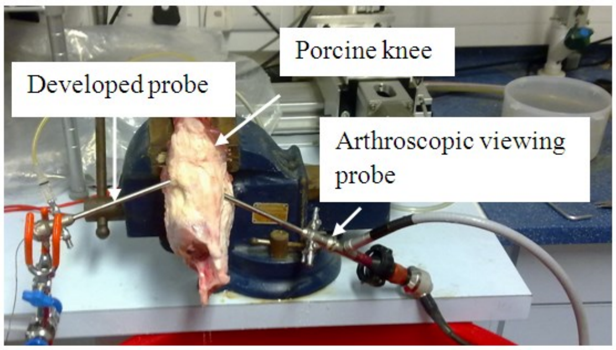

Figure 3. The setup for the porcine knee test

The articular cartilage was measured for the thickness and the stiffness under the water-jet indentation test. The thickness was calculated by the time of flight multiplied by the speed of sound in cartilage (1585m/s, [10]). For the indentation test, a stiffness coefficient with the following equation was used for the comparison:

$$S = (F/A)/(\Delta d/D_0)$$

where S is the stiffness coefficient with a unit of Pa, F is the indentation force calibrated from water pressure, A is the indentation area, Δd is the deformation of cartilage and D_0 is the initial thickness of the cartilage. For comparison, paired *t*-test was used to compare the change of thickness and stiffness before and after the degeneration.

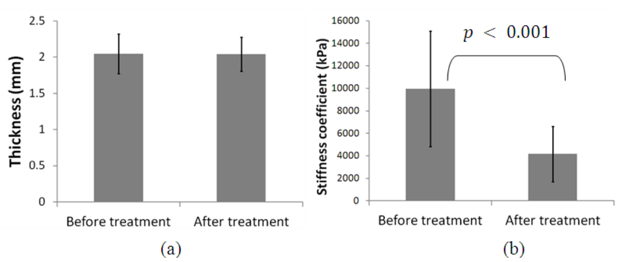

Figure 4. Test results of (a) thickness and (b) stiffness change before and after enzymatic digestion

III. RESULTS

The measurement was successfully conducted on all the porcine knees under arthroscopic guidance. There was no significant change of the cartilage thickness after the trypsin digestion (2.05 ± 0.27 mm vs. 2.04 ± 0.23 mm, $p > 0.05$). However, for the stiffness, there was a significant decrease after the trypsin digestion (9962 ± 5138 kPa vs. 4170 ± 2451 kPa, $p < 0.001$). A mean decrease of 53.6 ± 18.0% was revealed for the change of stiffness after the trypsin treatment. The original stiffness for the two control samples was 4445 kPa and 4154 kPa, respectively. The knees were kept hydrated and then the cartilage was re-tested after 4 hours of hydration. The corresponding stiffness became 4029 kPa and 3863 kPa. There was only a 9.4% and 7.0% decrease of stiffness for the two samples, which was much smaller than the mean decrease of 53.6% measured in the degeneration study.

IV. DISCUSSION

An arthroscopic ultrasound probe was successfully developed and fabricated in the current study. The developed probe fulfilled the requirement of measurement of versatile tissue properties of the articular cartilage in an arthroscopic operation. It has a proper size which can be inserted into the joint of big animals for direct measurement of the cartilage material properties. In order to make this tool ready for clinical applications, further improvement of the probe design and fabrication is needed and more pre-clinical trials should be planned in future studies.

Single element ultrasound transducer was adopted for the development of water-jet ultrasound indentation system in the prototype design [16, 23]. The system was also demonstrated to be useful for the characterization of articular cartilage degeneration [17]. Therefore, it is necessary to miniaturize this system into an arthroscopic one in order to make it available for clinical applications. In this study, single element ultrasound transducer was not considered because to specific reasons: the first was that no such small ultrasound transducer was readily available in the market for direct use; the second was that for an array ultrasound transducer with imaging capability, more characteristic parameters could be obtained from an ultrasound imaging of the cartilage, such as the surface roughness [20]. The 2-D signals were not used in the current study but they will be surely incorporated in future development of system and software.

The specific information that could be obtained from the probe was mainly limited by the ultrasound frequency and the orifice size. Based on the geometrical size of the adaptor and the position of the IAUS catheter, the angle that could be imaged for the external tissue was about 40°/360°=1/9 of the IAUS catheter in the current design. The total RF line number that can be viewed for external tissue was 512/9≈60, which was enough for calculating tissue material properties if all the ultrasound signal lines were collected for data analysis. On the other hand, the spatial resolution of the imaging was limited by the ultrasound frequency. According to the manufacturer's webpage information, the frequency can be as high as 45 MHz for the intravascular ultrasound catheter, and therefore, if higher spatial resolution is needed, a higher frequency IAUS catheter can be adopted for the intra-articular measurement. However, it should be noted that the penetration depth will be compromised when higher frequency is used. Based on practical requirements of spatial resolution and penetration depth, a proper frequency can be selected for cartilages with different thickness from different animal species.

For experimental study, the thickness of articular cartilage was supposed to be mainly contributed by the collagen network and therefore its thickness would not be significantly changed after the trypsin digestion. This has also been demonstrated in previous studies where no significant change of cartilage thickness was found after trypsin digestion [17, 20]. For the decrease of stiffness after digestion, one concern was that it might come from the natural degeneration of the material quality with time even without the effect of enzymatic digestion. The control group study might suggest that the main decrease of stiffness came from the enzymatic digestion, which was mainly caused by the depletion of proteoglycans after enzymatic treatment. The decrease of stiffness was mainly due to the reduction of fixed charge density and then the decrease of repulsive force in compression after the depletion of the PGs.

Only cartilages in situ in porcine knees were conducted in the current study. For clinical applications, further test on cartilage samples in vivo should be conducted. When the probe with further improvement meets the general standards of operation on human subjects such as easy disinfection, biological compatibility and reliable measurement, such in vivo tests can be arranged and then the utility of the probe can be demonstrated, which is the objective of future study.

V. Conclusion

It was feasible to develop an arthroscopic water-jet ultrasound indentation probe for the purpose of quantitative assessment of articular cartilage conditions in an intra-articular operation. The simulated cartilage degeneration induced by proteoglycan digestion could be detected by the developed probe. Therefore, the developed probe was demonstrated to be a potential tool for future clinical assessment of cartilage degeneration in vivo.

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