Minimally Invasive Ultrasound-guided Synovial Biopsy Using SuperCore Biopsy Instrument

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**Background:** To develop a new method for synovial biopsy with ultrasound (US) guidance and a semiautomatic SuperCore biopsy instrument.

**Patients and methods:** Twenty-two patients [8 men and 14 women, median age: 57 years (range: 22–79 years)] with active arthritis or tenosynovitis were enrolled from April 2012 to October 2012. Each patient had one joint or tendon biopsied. US examination was performed to determine the optimal synovial site for biopsy. After skin disinfection and local anesthesia, a portal was established using a trephine needle as needed. An 18-gauge SuperCore biopsy needle was placed into the target synovial site via the portal or just percutaneously under US guidance using the freehand technique. Repeated needle passes and cuts were made to obtain 3-10 pieces of synovial tissues in each joint. The success of biopsy was defined as the identification of the synovium on histological examination.

**Results:** The synovium of 21 joints (10 knees, 6 wrists, 3 ankles, 1 elbow, and 1 metacarpophalangeal joint) were biopsied. One patient had biopsy of the flexor digitorum tendon sheath. All biopsies obtained adequate amounts of synovial tissues for histologic reading with a success rate of 100%. The synovial lining was identified in 18 (85.7%) of 21 joints. All patients tolerated the procedures well, and no complication was observed during the 2-week follow-up period.

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Introduction

Synovial hypertrophy and synovitis are the main characteristics of inflammatory arthritis. Synovium is usually the area where disease pathogeneses take place, for example, in cases of rheumatoid arthritis (RA). Thus synovial histology provides diagnostic clues and aids in assessment of disease activity and therapeutic response [1]. In gout and pseudogout, crystal deposition in the synovium appears as punctiform hyperechoic spots, namely, bright stippled foci, on the ultrasound (US) image [2]. In infectious arthritis, the microscopic examination of the synovium may be valuable in the detection of causal pathogens, especially for mycobacteria, fungi, and varicella-zoster virus. Synovial histology also provides diagnostic clues for sarcoidosis, amyloidosis, and hemochromatosis [1].

However, current synovial biopsy methods such as arthroscopy and blind needle biopsy are not optimal because of the complex procedure and higher cost in the former and sampling error in the latter [3]. Ultrasonography has been used for assessing both the synovium and tendon lesions in patients with joint pain and/or swelling [4]. US could be applied for guiding needle aspiration and injection [5]. US-guided synovial biopsy has been proposed as a feasible method for obtaining synovial samples [6–8]. The instruments used in the former US-guided synovial biopsies are Tru-cut needles [6,7] or “portal and forceps” [8]. In this study, we report our experience of an alternative method for synovial biopsy method under US guidance using a semiautomatic SuperCore biopsy instrument.

Patients and methods

This study was approved by our Institutional Review Board. Twenty-two patients (8 men and 14 women) with active arthritis or tenosynovitis were enrolled from April 2012 to October 2012. The patients’ median age was 57 years (range: 22–79 years). Sixteen (72.7%) of them were outpatients and the rest were inpatients. The prebiopsy clinical diagnoses included rheumatoid arthritis (RA; n = 11), septic arthritis (n = 4), systemic lupus erythematosus (SLE, n = 2), adult-onset Still’s disease (AOSD, n = 1), idiopathic arthritis (n = 3), and hand flexor tenosynovitis (n = 1). The patients with RA, SLE, AOSD, and idiopathic arthritis were monoarthritis. The median disease duration was 12 months (range: 0.25–120 months). The diagnosis of RA was made on the basis of 2010 American College of Rheumatology (ACR)/European League Against Rheumatism criteria for the classification of RA [9]. The diagnosis of AOSD was made on the basis of the classification criteria proposed by Yamaguchi in 1992 [10]. The diagnosis of SLE was made on the basis of the 1997 ACR revised criteria for the classification of SLE [11]. The indications of synovial biopsy in the patients with RA, SLE, and AOSD were assessing disease activity and excluding the possibility of concomitant joint infection and amyloidosis. The indication of synovial biopsy in the patients with septic arthritis was identifying the causal pathogens because the initial synovial fluid cultures failed to yield pathogens. In patients with idiopathic arthritis and tenosynovitis, synovial biopsies were performed for diagnosis. Each patient had one joint or tendon biopsy. The contraindications were skin infection, bleeding tendency, xylocaine allergy, and uncooperative patients.

The ultrasonic assessments of joints and the US-guided synovial biopsies were performed with a General Electric LOGIC 500 unit (GE, Milwaukee, Wisconsin, USA) using a 6-13-MHz linear array transducer. The ultrasonic assessments of joints were performed prior to synovial biopsies in order to determine the optimal areas of the synovium for histologic reading. In principle, the most hypertrophied area of the synovium was the target for biopsy. The scanning techniques used while performing biopsies were dorsal longitudinal approach in the metacarpophalangeal (MCP) joint, elbow, and ankle, dorsal longitudinal or transverse approach in the wrist, and longitudinal lateral or suprapatellar transverse approach in the knee. The probe position was longitudinal while performing tendon sheath biopsy.

All biopsies were performed by the author (Lai K-L) who had an eight-year US experience. A trained nurse or technician was required for assistance. The operator wore sterile gloves and a mask. The US probe was covered with a sterile plastic sleeve. No sedation was used. Skin disinfection was performed with tincture iodine and 70% alcohol. A sterile cloth with a hole was placed on the area interested. Sterile gel was applied to the skin. Local anesthesia with 110 ml of 2% xylocaine was injected into the involved skin, subcutaneous tissue, and joint cavity or tendon sheath without air bubbles in the syringe to avoid US artifacts. A portal was established using a trephine needle (Medical Device Technologies, Inc., USA) under US guidance in patients who needed repetitive needle passes to obtain more than three specimens. An 18-gauge semi-automatic SuperCore biopsy instrument (Medical Device Technologies, Inc., USA), with a needle length of 9 cm, was used to obtain synovial tissues via the portal (or directly percutaneous puncture if no portal was established) under US guidance with the freehand technique (Fig. 1). The operating skills of this instrument followed the manufacturer’s instructions. Needle passes and cuts were repeated to obtain 3-10 pieces of synovial tissues in each joint (Figs. 2 and 3) and in the case of tenosynovitis, three pieces of tendon sheath (Fig. 4). The optimal amount of synovial specimens was determined by both the type of synovial research and joint size. After biopsy, the puncture site was compressed with a sterile gauze and elastic band, and kept dry until the next

**Conclusion:** US-guided synovial biopsy using SuperCore biopsy instrument is a promising method for synovial research. It has the advantages of being a simple method with mini-invasiveness and high success rate. The complications are rare.

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day. Patients were asked to immobilize the joint within the initial 2 hours and avoid heavy physical activities with the involved joint for 3 days. All patients were followed for 2 weeks to observe any possible complication such as skin and joint infection, hematoma, and deep vein thrombosis.

The biopsied specimens were immediately fixed in 4% formaldehyde for up to 24 hours and embedded in paraffin. Tissue sections were stained with hematoxylin and eosin and assessed by the same histopathologist. The biopsy procedure was rated as successful if the synovial tissue was identified on histological examination. Besides, the lining layer of the synovium was checked. We also evaluated the feasibility of obtaining the synovial lining using this biopsy method by calculating the ratio of synovial lining-positive joints to total biopsied joints.

Results

The synovium of 21 joints including the knee (n = 10), wrist (n = 6), ankle (n = 3), elbow (n = 1), and MCP joint were assessed.

Fig. 1  SuperCore biopsy instrument. (A) A semiautomatic biopsy needle with an 18-gauge diameter and 9-cm length. The specimen notch (1.2 cm or 2.2 cm) is exposed when the sonographer advances the stylet (left lower). (B) A 17-gauge trephine needle (upper) with matching stylet (lower) is used to establish a portal. (C) Biopsy of the knee synovium via a portal under ultrasound guidance with the freehand technique.

Fig. 2  A 30-year-old woman with rheumatoid arthritis. (A) Right knee suprapatellar transverse ultrasonic scan shows prominent synovial hypertrophy. (B) A SuperCore biopsy needle is placed into the synovium via a portal under ultrasound guidance. The tip of the biopsy needle (arrow 1), the extent of the specimen notch (between arrows 2 and 3), and the tip of the trephine needle (arrow 4) are indirectly visualized.
Fig. 3  A 59-year-old man with idiopathic arthritis of the left wrist. (A) Dorsal transverse grayscale (left) and power Doppler (right) scans show synovial hypertrophy with increased vascularity. (B) A SuperCore biopsy needle is percutaneously placed into the synovium under ultrasound guidance. The tip of the biopsy needle (arrow 1) and the extent of the specimen notch (between arrows 2 and 3) are indirectly visualized. No trephine needle is used in this case.

Fig. 4  A 51-year-old woman with right hand flexor tenosynovitis. (A) Longitudinal ultrasound scan of the third flexor digitorum tendon shows prominent tendon sheath hypertrophy. (B) A SuperCore biopsy needle is percutaneously placed into the hypertrophied tendon sheath under ultrasound guidance. The extent of the specimen notch (between arrows 1 and 2) is indirectly visualized. MC = metacarpal bone.
adequate amount of specimens for histologic reading with a success rate of 100% (Fig. 5). Synovial linings were identified in the specimens from 18 joints with an availability of 85.7%. We took 25–40 minutes to complete a synovial biopsy procedure per case. All patients tolerated the biopsy procedures well and did not feel pain due to the filling of xylocaine in the joint cavity or tendon sheath. The blood loss during biopsy procedure was minimal (less than one gauze). No procedure-related complication such as skin and joint infection, hematoma, and deep vein thrombosis was observed during the 2-week follow-up period.

We had encountered some technical difficulties in this study. As the US beam is two dimensional and narrow, it was difficult to visualize the needle by US imaging using the freehand technique in the first cases. Although we had practiced more, the needle position could be easily and indirectly visualized in the other cases. The accuracy of needle positioning using the freehand technique was operator dependent and would be improved by more practice. Besides, the ability to indirectly visualize the needle was decreased when the needle direction was more parallel to the US beam and when the depth of needle position increased.

Discussion

The histological analysis of synovial biopsies may provide diagnostic clues for idiopathic arthritis and is valuable in an early diagnosis of RA [1]. Some studies have documented the role of synovial pathologies in the assessment of disease activity and prediction of the response to biologics in RA [12–14]. There are three methods proposed for synovial biopsy. The first method is a blind needle technique that uses a simplified biopsy needle designed by Parker and Pearson in 1963 [15]. The second is arthroscopy, and the third is US-guided biopsy using Tru-cut needle [6,7] or portal and forceps [8]. The major disadvantage of the blind needle technique is the sampling error. Synovial sites adjacent to cartilage cannot be easily biopsied by a blind procedure [1]. Usually the application of blind needle technique is limited to the knee joint. Arthroscopy remains the gold standard method for synovial biopsy. It has the advantage of direct visualization of the synovium and could harvest a large amount of synovial tissues. The disadvantages of arthroscopy include higher costs and the need for two portals into a joint [1]. Arthroscopy has been mostly applied to the knee joint.

As more and more rheumatologists used musculoskeletal US for management of arthritis in the past decade, US-guided interventional procedures have been developed in order to perform accurate aspiration and injection. New methods of synovial biopsy with US guidance have also been developed. US-guided synovial biopsy using a Tru-cut needle with a diameter of 18 gauge equipped with an automated gun had been proposed by van Vugt et al [6] in 1997, with a success rate of 100% in seven wrist joints and there was no complication. In 2006, Marin et al [7] reported their experience in US-guided synovial biopsy using Tru-cut needle in 83 patients with monoarthritis of unknown etiology. Synovial tissues were obtained in 78 patients (successful rate 94%) from several joint sites, including shoulder, elbow, wrist, hip, knee, and ankle. No procedure-related complication occurred.

In 2005, Koski and Helle [8] reported the utility of US-guided synovial biopsy using portal and forceps, a set of device borrowed from angiology and gastroenterology, in 37 outpatients with mono- or polyarthritis. Biopsy samples were taken from small and large joints, bursae, and tendon sheaths. Representative synovial tissue in adequate amounts for histopathological evaluation was obtained in 33 out of 37 cases (successful rate 89%). The biopsy procedures were well tolerated, but a complication of skin infection was encountered [8].

In this study we use a semi-automatic SuperCore biopsy instrument for synovial sampling. It is a variant of Tru-cut needle and has been clinically used for biopsies of liver, breast tumor, and pleura in Taiwan, but to the best of our knowledge, it has not been reported for the biopsy of the synovium yet. Thus, we tried to evaluate the utility of SuperCore biopsy instrument with US guidance in synovial biopsy. The manufacturer provides SuperCore biopsy needles with varied diameter (14–20 gauge) and length (9 cm or 15 cm). Our experience shows that a needle with a diameter of 18 gauge and a length of 9 cm is suitable for most joint sites, from small joint such as the MCP joint to large joints such as the knee. An exclusive trephine needle is commercially available from the manufacturer. We establish a portal using a trephine needle in order to repeat biopsies if more than three pieces of synovial tissues are required. Our study demonstrates that US-guided synovial biopsy using SuperCore biopsy instrument has a success rate of 100% in 22 patients with active arthritis or tenosynovitis. It also has a high success rate (85.7%) in obtaining the synovial lining, which is an important target for RA research. No procedure-related complication is encountered.

The SuperCore biopsy needle has some advantages on synovial biopsy. It is easier to approach deep synovial areas adjacent to bone or cartilage where the rheumatoid pannus is often present. When the sonographer moves the plunger to advance the stylet, exposing the specimen notch, the target synovial lesion located at the specimen notch could be indirectly visualized. The lining layer of the synovium,

![Fig. 5](image-url)

Histological image of the corresponding case in Fig. 2. The synovial lining is hyperplastic. Chronic inflammation with apparent plasma cell infiltration and fibrosis in the synovial sublining are seen (hematoxylin and eosin stain, ×400).
an important synovial site for molecule biologic study of RA, can also be obtained using this biopsy technique. The SuperCore biopsy needle is a semiautomatic device; hence, the sonographer can hold the US probe with one hand and operate the needle with the other hand simultaneously. The needle is disposable; therefore, there is no risk of transmission of the infectious disease. US-guided synovial biopsy using the SuperCore biopsy instrument is a simple and safe procedure with minimal invasiveness. The puncture wound is minimal. It can be used in outpatients and is well tolerated by patients. It is applicable to both small and large joints as well as to the tendon sheath.

This study may have some limitations. First, the utility of US-guided synovial biopsy using the SuperCore biopsy instrument in larger joints—hip and shoulder—are not clarified in this study although it is theoretically applicable. Further study is needed to clarify its utility in the hip and shoulder. Second, this biopsy needle may not be applicable to smaller joints, such as the proximal interphalangeal joint, because the specimen notch is relatively too long. Third, this technique may not work well in the biopsy of unhydroptic synovium.

In conclusion, US-guided synovial biopsy using a semi-automatic SuperCore biopsy instrument is a promising method for synovial research. It is a simple method with mini-invasiveness and a high success rate. Complications are rare. We hope that this simplified synovial biopsy method could be widely used by rheumatologists in turn to promote synovial researches to discover the pathogenesis of early RA and to predict therapeutic response to biologics. In the future, an individualized treatment could be tailored according to the synovial histology.

References


