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● *Original Contribution*

ULTRASOUND ASSESSMENT OF HUMAN MENISCUS

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Abstract—The aim of the present study was to evaluate the applicability of ultrasound imaging to quantitative assessment of human meniscus *in vitro*. Meniscus samples (n = 26) were harvested from 13 knee joints of non-arthritic human cadavers. Subsequently, three locations (anterior, center and posterior) from each meniscus were imaged with two ultrasound transducers (frequencies 9 and 40 MHz), and quantitative ultrasound parameters were determined. Furthermore, partial-least-squares regression analysis was applied for ultrasound signal to determine the relations between ultrasound scattering and meniscus integrity. Significant correlations between measured and predicted meniscus compositions and mechanical properties were obtained (R^2 = 0.38–0.69, $p < 0.05$). The relationship between conventional ultrasound parameters and integrity of the meniscus was weaker. To conclude, ultrasound imaging exhibited a potential for evaluation of meniscus integrity. Higher ultrasound frequency combined with multivariate analysis of ultrasound backscattering was found to be the most sensitive for evaluation of meniscus integrity. (E-mail: tuomas.viren@uef.fi) © 2017 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Quantitative ultrasound imaging, Osteoarthritis, Composition, Meniscus.**

INTRODUCTION

The menisci are two fibrocartilaginous crescent-shape discs located between femoral condyles and proximal tibia in the medial and lateral sides of the knee joint (Fox et al. 2012; Messner and Gao 1998). Menisci are composed mainly of water (60%–70%) and collagens (1%–25%, mainly type I) (Fox et al. 2012). Proteoglycans, non-collagenous proteins, glycoproteins and cells account for the remainder of meniscus weight (Fox et al. 2012). The meniscus has a highly organized structure, which gives the tissue its characteristic mechanical properties, such as high tensile stiffness and strength, low compression stiffness and low permeability (Fox et al. 2012; Masouros et al. 2008). The main functions of the meniscus are to stabilize the knee joint, distribute loads between the femur and tibia and participate in lubrication of the joint (McDermott et al. 2008). Changes in the structure and composition of the meniscus (caused by, *e.g.*, joint injury) may lead to deterioration of the mechanical function of the meniscus. This may subsequently lead to extensive loading of the articular cartilage and instability of the whole knee joint (McDermott and Amis 2006). Changes in knee joint function can initiate degeneration of the articulating surfaces, which eventually leads to the development of osteoarthritis (Englund and Lohmander 2004). Currently, meniscal injuries can be treated with surgical techniques, such as sutures and darts or, in the case of more severe injuries, meniscus allograft transplantation and partial or complete meniscectomy (Roos et al. 1998; Sihvonen et al. 2013; Van Der Straeten et al. 2016). Unfortunately, the effectiveness of current surgical techniques, especially meniscectomy, in the treatment of meniscus injuries is questionable (Roos et al. 1998; Sihvonen et al. 2013; Van Der Straeten et al. 2016). Quantitative tools capable of accurate determination of the extent and severity of meniscus injuries would be important when developing novel surgical techniques aimed at restoring meniscal function.

Currently, injuries and degeneration of the menisci are diagnosed using clinical examination, magnetic

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resonance imaging (MRI) and computed tomography (CT) arthrography and arthroscopy (Fox 2007; Huysse et al. 2008). However, current clinical MRI or CT techniques may not be optimal for quantitative assessment of the integrity of the menisci. The relatively low resolution, high cost and limited availability of clinical MRI; radiation exposure; and the need for contrast agents to improve the soft tissue contrast of clinical CT imaging hinder the potential of these techniques for the accurate evaluation of meniscal pathology. Furthermore, neither MRI nor CT imaging can be conducted during arthroscopic surgery. Thus, the final evaluation of the status of meniscal injuries during the repair operation is based on the arthroscopic evaluation. Arthroscopic assessment of the integrity of the joint consists of visual inspection and mechanical palpation of the articulating surfaces (Brittberg and Winalski 2003). However, this method is highly subjective, and the diagnosis is dependent on the experience of the operating surgeon (Spahn et al. 2009). Thus, novel quantitative arthroscopic imaging techniques are needed.

High-frequency external ultrasound imaging has been reported to be a sensitive method for evaluation of meniscal injuries and function (Akatsu et al. 2015; Rowland et al. 2016). In previous studies, ultrasound imaging was used to evaluate tears, cysts and mechanical function of the meniscus (Friedman et al. 2001; Nogueira-Barbosa et al. 2015; Rowland et al. 2016; Wareluk and Szopinski 2012). As ultrasound imaging is a tolerable and widely available technique, its use in screening meniscal damage after joint injuries might be possible. However, only limited areas of the meniscus are visible with external ultrasound, which decreases the diagnostic value of ultrasound investigation (Akatsu et al. 2015). Furthermore, ultrasound attenuation and scattering in the soft tissues surrounding the knee joint significantly complicate the interpretation and quantification of the ultrasound images (Friedman et al. 2001). Recently, ultrasound arthroscopy was introduced for high-resolution ultrasound imaging of the articular cartilage and subchondral bone during arthroscopic surgery (Kaleva et al. 2011; Liukkonen et al. 2013). Ultrasound arthroscopy technique has been reported to be sensitive to changes in the structure and composition of articular cartilage related to the development of osteoarthritis (Liukkonen et al. 2014; Virén et al. 2009). In previous studies, ultrasound arthroscopy was used to evaluate cartilage injuries in knee and shoulder joints *in vivo* (Kaleva et al. 2011; Liukkonen et al. 2014; Puhakka et al. 2016). However, the capability of ultrasound imaging to quantify compositional and structural changes related to meniscus degeneration is unknown. Furthermore, because of the highly organized layered structure of the meniscus, the quantitative ultrasound parameters related to bulk properties of the tissue may not reflect accurately the integrity of the complex tissue, and thus, more sophisticated techniques for analyzing depth-dependent ultrasound scattering are needed. In previous studies, multivariate partial-least-squares (PLS) regression analysis was applied for analysis of near-infrared spectroscopy and optical coherence tomography data for articular cartilage and meniscus (Afara et al. 2015; Ala-Myllymäki et al. 2016; Puhakka et al. 2015). PLS regression analysis is commonly used to detect relations between noisy predictor variables and one or more response variables. PLS analysis has also been used to correlate light backscattering with the composition and mechanical properties of cartilage and menisci (Ala-Myllymäki et al. 2016; Puhakka et al. 2015). However, the applicability of PLS regression analysis to ultrasound backscattering for the determination of structural and compositional parameters of the meniscus is unknown.

The aim of the present study was to evaluate the potential of ultrasound imaging for the assessment of meniscus degeneration and to introduce a multivariate technique for analysis of ultrasound backscattering in meniscus.

METHODS

Sample preparation

Lateral and medial meniscus samples ($n = 26$) were harvested from the left knee joints of human cadavers ($n = 13$, ages 24–76 y, 12 male, 1 female) with no history of joint disease (National Agency of Medicolegal Affairs, Helsinki, Finland; Permission 1781/32/200/01). Subsequently, menisci were wrapped in gauze soaked in physiologic phosphate-buffered saline (PBS, Euroclone, Paignton-Devon, UK) and stored at −25°C until the experiment. Before the ultrasound measurements, the menisci were thawed in a water bath at room temperature and immersed in PBS containing inhibitors of proteolytic enzymes (5 mM disodium EDTA and 5 mM benzamidine HCl).

Ultrasound measurements

A clinical ultrasound device (ClearView Ultra, Boston Scientific, San Jose, CA, USA) with two high-frequency (9 and 40 MHz; Ultra Ice and Atlantis Pro, respectively, Boston Scientific) intravascular ultrasound (IVUS) imaging catheters was used in the present study. The technical details of the imaging system have been described in our previous articles (Liukkonen et al. 2013; Virén et al. 2009). During measurements, the samples were kept in degassed PBS, which contained inhibitors of proteolytic enzymes (5 mM disodium