JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS 56 (2016) 106–119

Available online at www.sciencedirect.com

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Research paper

Towards Optical Coherence Tomography-based elastographic evaluation of human cartilage

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ARTICLE INFO

Article history:
Received 16 July 2015
Received in revised form
21 November 2015
Accepted 25 November 2015
Available online 4 December 2015

Keywords:
Cartilage
Optical Coherence Tomography
Indentation
Functional properties
Qualitative evaluation

ABSTRACT

Optical Coherence Tomography (OCT) is an imaging technique that allows the surface and subsurface evaluation of semitransparent tissues by generating microscopic cross-sectional images in real time, to millimetre depths and at micrometre resolutions. As the differentiation of cartilage degeneration remains diagnostically challenging to standard imaging modalities, an OCT- and MRI-compatible indentation device for the assessment of cartilage functional properties was developed and validated in the present study. After describing the system design and performing its comprehensive validation, macroscopically intact human cartilage samples ($n=5$) were indented under control of displacement ($\delta 1=202$ µm; $\delta 2=405$ µm; $\delta 3=607$ µm; $\delta 4=810$ µm) and simultaneous OCT imaging through a transparent indenter piston in direct contact with the sample; thus, 3-D OCT datasets from surface and subsurface areas were obtained. OCT-based evaluation of loading-induced changes included qualitative assessment of image morphology and signal characteristics. For inter-method cross referencing, the device's compatibility with MRI as well as qualitative morphology changes under analogous indentation loading conditions were evaluated by a series of T2 weighted gradient echo sequences. Cartilage thickness measurements were performed using the needle-probe technique prior to OCT and MRI imaging, and subsequently referenced to sample thickness as determined by MRI and histology. Dynamic indentation testing was performed to determine Young's modulus for biomechanical reference purposes. Distinct differences in sample thickness as well as corresponding strains were found; however, no significant differences in cartilage thickness were found between the used techniques. Qualitative assessment of OCT and MRI images revealed either distinct or absent sample-specific patterns of morphological changes in relation to indentation loading. For

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http://dx.doi.org/10.1016/j.jmbbm.2015.11.025
1751-6161/

OCT, the tissue area underneath the indenter piston could be qualitatively assessed and displayed in multiple reconstructions, while for MRI, T2 signal characteristics indicated the presence of water and related tissue pressurisation within the sample. In conclusion, the present indentation device has been developed, constructed and validated for qualitative assessment of human cartilage and its response to loading by OCT and MRI. Thereby, it may provide the basis for future quantitative approaches that measure loading-induced deformations within the tissue to generate maps of local tissue properties as well as investigate their relation to degeneration.

1. Introduction

Cartilage degenerative changes are a major cause of disability in humans. Their prevalence and socioeconomic impact is expected to further increase in our aging population (Uchio et al., 2002). In the clinical context, cartilage degeneration is the central hallmark of osteoarthritis (OA), a complex musculoskeletal disorder with numerous contributory genetic, constitutional and biomechanical factors. Early cartilage degeneration is marked by progressive extracellular matrix degeneration and decreased resistance to load deformation (Akizuki et al., 1987), while the macroscopic appearance of the tissue remains intact (Franz et al., 2001). The initial degenerative changes are reversible due to the tissue's limited intrinsic repair capabilities; however, the persistence of an unfavourable mechanical environment combined with tissue susceptibility leads to progressive and irreversible matrix degradation and structural damage in terms of fibrillation, fissuring and subsequent cartilage tissue loss (Johnson et al., 2012). Therefore, preventive interventions, including surgery or pharmaceutical agents, have to be initiated as long as the pathology is reversible (Bay-Jensen et al., 2010). The reliable detection of the very earliest evidence of cartilage degeneration is a prerequisite for such timely intervention. Current clinical imaging modalities such as radiography, arthroscopy and clinical routine Magnetic Resonance Imaging (MRI) are characterized by numerous limitations in resolution, sensitivity/specificity, inter-observer reliability, objectivity and cannot differentiate normal from early degenerative cartilage (Brismar et al., 2002; Marx et al., 2005; Palmer et al., 2013; Spahn et al., 2009). Furthermore, they do not properly assess mechanical properties, which may further limit these modalities' diagnostic performance as cartilage softening is regarded the first and most reliable sign of OA (Haapala et al., 2000).

Conventional biomechanical assessment of cartilage relies on the measurement of tissue deformation by indentation. In the past, arthroscopically available hand-held indentation devices have been developed and investigated for their clinical potential (Franz et al., 2001; Toyras et al., 2005). Amongst other reasons, their use has been restricted due to limited measurement accuracy: First, measurement of tissue thickness, an important parameter to calculate intrinsic biomechanical properties, was not possible using these devices. Second, reproducibility was low due to the difficult overall handling of the probe (Garcia-Seco et al., 2009). Also, these devices were not capable of assessing tissue structure or morphology.

Therefore, the comprehensive non-destructive microscale assessment of cartilage functional and structural properties with clinical potential remains elusive. Optical Coherence Tomography (OCT)-based imaging may provide a potential solution to this problem. As an imaging technique that has received considerable scientific and clinical attention since its first thorough description in 1991 (Huang et al., 1991), OCT is based on the measurement of near-infra-red light scattering and reflection and allows imaging of surface and subsurface tissue regions in real time and at high spatial resolution. High degrees of correlation between OCT and reference histology have been demonstrated (Chu et al., 2004; Nebelung et al., 2014). Although OCT-based parameterisation and quantification of morphological and optical parameters have been investigated recently, quantitative approaches so far cannot differentiate early disease stages (Nebelung et al., 2014; Saarakkala et al., 2009; Viren et al., 2012). Therefore, the present paper aims to evaluate whether loading-induced changes in human cartilage by means of OCT are to be assessed qualitatively. This feasibility study is thus meant to provide the basis for the comprehensive quantitative assessment of cartilage by Optical Coherence Elastography (OCE), which is classically used to determine tissue biomechanical properties by acquisition of tissue strain maps (i.e. elastograms) using OCT (Wang and Larin, 2015). Scientific evidence on OCE in the assessment of cartilage is sparse at present. Huang et al. (2011) pioneered the field in developing an OCT-based air-jet indentation system, which uses a pressurised air jet for standardized cartilage indentation. In comparison to alternative evaluation methods such as ultrasound elastography or magnetic resonance elastography, which allow spatial resolutions of hundred of micrometres and organ-size fields of view (Wang and Larin, 2015), OCE provides micrometre-scale resolution ($<15\ \mu m$) and millimetre-scale imaging depth of cartilage (Kennedy et al., 2014a; Wang and Larin, 2015). The exquisite displacement sensitivity may allow for the determination of very small changes in mechanical properties at the resolution of the OCT system (i.e. 5–20 μm) (Kennedy et al., 2013). Furthermore, high acquisition speeds in combination with real-time imaging make OCT-based approaches an interesting technique for cartilage evaluation.

Therefore, the present study introduces a new in vitro indentation device for the assessment of structural and