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Non-destructive electromechanical assessment (Arthro-BST) of human articular cartilage correlates with histological scores and biomechanical properties

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SUMMARY

Objective: The hand-held Arthro-BST™ device is used to map electromechanical properties of articular cartilage. The purpose of the study was to evaluate correlation of electromechanical properties with histological, biochemical and biomechanical properties of cartilage.
Method: Electromechanical properties (quantitative parameter (QP)) of eight human distal femurs were mapped manually *ex vivo* using the Arthro-BST (1 measure/site, 5 s/measure, 3209 sites). Osteochondral cores were then harvested from different areas on the femurs and assessed with the Mankin histological score. Prior to histoprocessing, cores were tested in unconfined compression. A subset of the cores was analyzed with polarized light microscopy (PLM) to assess collagen structure. Biochemical assays were done on additional cores to obtain water content and glycosaminoglycan (GAG) content. The QP corresponding to each core was calculated by averaging all QPs collected within 6 mm of the core center.
Results: The electromechanical QP correlated strongly with both the Mankin score and the PLM score ($r = 0.73$, $P < 0.0001$ and $r = -0.70$, $P < 0.0001$ respectively) thus accurately reflecting tissue quality and collagen architecture. Electromechanical QP also correlated strongly with biomechanical properties including fibril modulus ($r = -0.76$, $P < 0.0001$), matrix modulus ($r = -0.69$, $P < 0.0001$), and log of permeability ($r = 0.72$, $P < 0.0001$). The QP correlated weakly with GAG per wet weight and with water content ($r = -0.50$, $P < 0.0003$ and $r = 0.39$, $P < 0.006$ respectively).
Conclusion: Non-destructive electromechanical QP measurements correlate strongly with histological scores and biomechanical parameters providing a rapid and reliable assessment of articular cartilage quality.

Introduction

The deterioration of articular cartilage is a hallmark of degenerative joint diseases such as osteoarthritis which affects 8.9% of the adult population with 40% prevalence above the age of 70[1]. Currently, joint health and function are diagnosed at a late stage by methods including physical examination, X-ray and magnetic resonance imaging of joint space or visual arthroscopy with a blunt probe. None of these techniques are able to provide diagnostic information early in the disease process.

Multiple research groups have invented devices to assess cartilage function during arthroscopic surgery[2–6]. Methods involving ultrasound biomicroscopy[7], arthroscopic ultrasound imaging[8], optical reflection spectroscopy[9], pulsed laser irradiation[10] or near-infrared spectroscopy[11] have been proposed. Two devices obtained FDA regulatory clearance (Artscan™ 200 Arthroscopic Cartilage Stiffness Tester and Actaeon™ Probe), while the Artscan

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was only briefly commercialized. The reasons for limited clinical acceptance may be related to challenges in ease of use and difficult sensor orientation relative to cartilage surface as well as the need for repeated indentations at a controlled level of force[12]. There is an enduring demand in Orthopedics for an objective and reliable technique to evaluate articular cartilage tissue health[13].

Streaming potentials are compression-induced electric potentials that have been shown to reflect the structural and functional integrity of cartilage[14–19]. Streaming potential are generated by fluid-solid phase interactions in the loaded extracellular matrix[20], given that proteoglycans are negatively charged and entrapped within the collagen network, while an excess of mobile positive ions exists in the interstitial fluid. Thus, under equilibrium conditions, with no load applied, there is no net macroscopic electric field present since mobile cations are symmetrically arranged around negatively charged proteoglycan[21]. However, when the cartilage is compressed, the flow of the interstitial fluid entrains motion of the positive mobile ions relatively to the fixed negatively charges of the solid phase, generating measurable streaming potentials[22,23].

The Arthro-BST™ measures streaming potentials in articular cartilage on 37 microelectrodes located on its spherical indenter[24] during a gentle and instantaneous compression (<1 s). The contact between the indenter and the cartilage is tracked during measurement through the use of a non-planar microelectrode array to measure streaming potentials[25] without the need to control the force used by the surgeon to compress the cartilage. The calculation of the quantitative parameter (QP) is independent of the velocity of indentation or device orientation[26] since the software discards measurements when the loading time is outside the predefined limits, corresponding to high and low velocity, in order to minimize the effect of loading velocity on measurements. This device was previously used to assess degenerative changes on equine cartilage subjected *ex vivo* to high levels of mechanical impact and showed high reliability and excellent agreement between and within users' electromechanical measurements[18].

Histological scoring, biochemical analyses and biomechanical testing offer precise and specific measurements of cartilage structure and function (more so than MRI and X-ray) but involve destructive processing of tissue, and do not represent the entire joint surface. The objective of this study was to map electromechanical properties of cartilage across entire articular surfaces non-destructively with the hand-held Arthro-BST™ and to relate these maps with histological, biochemical and biomechanical properties of cartilage. Since the structure and composition of articular cartilage are reflected by its electromechanical properties[20–23], we hypothesized that the Arthro-BST QP correlates directly with histological, biochemical and biomechanical properties of cartilage. A secondary hypothesis was that the Arthro-BST can precisely assess cartilage quality non-destructively and rapidly. To test these hypotheses, the electromechanical properties of articular surfaces of eight human distal femurs were measured *ex vivo* with the Arthro-BST and osteochondral cores were then harvested to obtain histological, biochemical and biomechanical properties of cartilage.

Method

Sample source and preparation

Frozen cadaveric human distal femurs from research donors ($n = 8$; −80°C; age range 35–43 years old; three females and five males; four left joints and four right joints) were provided by a tissue bank (RTI Surgical, Florida, USA). The articular surfaces were thawed in a plastic bag overnight at 4°C. The distal femur was cut through a horizontal plane with a band saw at the appropriate orientation to permit mounting in a chamber for electromechanical mapping [Fig. 1(A)]. Distal femurs were fixed onto a cylindrical platform (D = 85 mm) [Fig. 1(B)] and the platform with the attached femur was then fixed to a testing chamber (D = 190 mm, H = 100 mm) equipped with a camera (1280 × 960 pixels) and a positioning software (Mapping Toolbox software, Biomomentum Inc.) [Fig. 2(A)]. The testing chamber was filled with phosphate buffered saline (pH 7.4) and a minimum of 15 min was allowed for equilibration prior to electromechanical mapping of the trochlea and anterior/central condyles (details below). Following core extraction, the central/posterior condyles were removed with a second band saw cut [Fig. 1(C)]. The central/posterior condyles block was then fixed onto the cylindrical platform [Fig. 1(D)] and the platform to the testing chamber for mapping of the central/posterior condyles followed by core extraction (details below). None of the donors had documented joint pathologies, however shallow focal cartilage lesions were observed on the articular surfaces of four out of eight femurs [see trochlear lesion in Fig. 1(E)].

Arthro-BST mapping

The Arthro-BST™ (Biomomentum Inc.) measures streaming potentials generated during a rapid compression of the articular cartilage with an array of microelectrodes lying on a semi-spherical indenter (effective radius of the tip = 3.18 mm, 5 microelectrodes/mm^2). The device calculates a quantitative parameter (QP, arbitrary units) of cartilage electromechanical activity corresponding to the number of microelectrodes in contact with the cartilage when the sum of their streaming potential reaches 100 mV. A high QP therefore indicates weak electromechanical properties and poor load-bearing capacity and low QP indicates strong electromechanical properties and high load-bearing capacity. Using the bench top version of the Arthro-BST, a positioning software overlays a 25 columns × 19 rows position grid (corresponding to ~9 sites per cm^2 on the articular surface) on the live video feed to help measurement registration and create a uniform mapping. The spherical indenter of the Arthro-BST was manually compressed onto the cartilage surface [Fig. 2(B)] for about 1 s at each position of the grid and the device displayed and recorded the corresponding QP.

Core extraction

Following a macroscopic visual assessment of the articular surfaces, a total of 163 osteochondral cores were harvested from non-lesional and also from lesional regions in triplicate (histology, biomechanics and biochemistry). Lesional areas appeared only sporadically in the age range examined here (35–43 years) so most of the cores were from non-lesional regions. Osteochondral cores (length > 10 mm) were harvested using Smith and Nephew tubular chisels of 4.5 mm diameter (for histology) and 3.5 mm diameter (for biomechanical and biochemical analyses). Cores for histology were fixed in 10% neutral buffered formalin. After coring, the condyles and trochlea were placed back onto the testing chamber, visually repositioned and oriented as per the initial position and a second image was acquired to precisely (~1 mm) document the location of each core relative to the position grid used for Arthro-BST measurements [Fig. 1(E and F)]. The Arthro-BST's electromechanical QP corresponding to the cored site was calculated as the average of all QPs measured within 6 mm from the core center location and was between 1 to a maximum of 4 QP measures. In total, 59 cores were isolated for histological assessment only, 53 cores for biochemical analysis and 51 cores for biomechanical testing followed by histology.