Osteoarthritis and Cartilage 21 (2013) 1731–1737

Osteoarthritis and Cartilage

Electroarthrography: a novel method to assess articular cartilage and diagnose osteoarthritis by non-invasive measurement of load-induced electrical potentials at the surface of the knee

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ARTICLE INFO

Article history:
Received 21 November 2012
Accepted 1 July 2013

Keywords:
Osteoarthritis
Rheumatoid Arthritis
Articular cartilage
Streaming potentials
Bioelectricity
Diagnostic
Biomarker
Joint imaging

SUMMARY

Objective: A new technique called electroarthrography (EAG) measures electrical potentials on the surface of the knee during joint loading. The objective of this study was to evaluate the effectiveness of EAG to assess joint cartilage degeneration.
Design: EAG recordings were performed on 20 asymptomatic subjects (Control group) and on 20 patients with bilateral knee osteoarthritis (OA) who had had a unilateral total knee replacement (TKR), both the TKR knee and the remaining knee were analyzed. EAG signals were recorded at eight electrode sites over one knee as the subjects shifted their weight from one leg to the other to achieve joint loading. The EAG signals were filtered, baseline-corrected and time-averaged.
Results: EAG repeatability was assessed with a test-retest protocol which showed statistically significant high intraclass correlation coefficients (ICC) for four electrode sites near the joint line. These sites also showed the highest mean EAG values. The mean EAG potentials of the Control group were significantly higher compared with the OA group for three sites overlying the joint line. The potentials overlying the TKR were statistically nul. In the Control group, no statistically significant correlation was found between the EAG amplitude and age, weight, height or body mass index (BMI); no statistical difference was found in mean EAG potentials between women and men.
Conclusions: This study indicates that EAG signals arise from the streaming potentials in compressed articular cartilage which are known sensitive indicators of joint cartilage health. EAG is a promising new technique for the non-invasive assessment of cartilage degeneration and arthritis.

Introduction

Degeneration of articular cartilage is a hallmark and common endpoint of joint disease that requires treatment, often in the form of prosthetic joint replacement. Our current inability to diagnose degeneration of articular cartilage at stages that are treatable, prior to necessitating joint replacement, has been a major impediment to the development of treatments to slow, stop, or reverse joint disease. Current methodologies to assess joint health and function include physical examination[1], synovial fluid analysis and imaging technologies such as X-rays, ultrasound, magnetic resonance imaging[2], and either planar[3] or computed tomography[4]. Although these techniques provide a wealth of information, none have been able to provide sensitive and specific diagnostic information early enough in the disease process to permit successful interventions or to assess outcome in clinical trials for the development of therapeutics that are effective prior to end-stage disease. Promising new diagnostic technologies are under development including biomarkers that reflect breakdown products of cartilage or bone[5], particular MRI methods that are partially specific to the molecular components of cartilage including collagen and proteoglycan[2], MRI imaging of cartilage repair[6], ultrasonography[7], delayed computed tomography

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1063-4584/$ – see front matter © 2013 Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International.
http://dx.doi.org/10.1016/j.joca.2013.07.003

arthrography[8], mechanical[9] and electromechanical[10] devices that can be used during arthroscopic surgery to directly contact articular cartilage and assess its function, and instruments for analyzing three-dimensional knee kinematics[11,12]. However, to date, there is no biomarker, or group of biomarkers, that has been identified to reliably reflect specific disease-related changes in joint structures. Although the new imaging methods represent significant improvements and additions to standard clinical imaging, the complexity of joint changes and the thinness of articular cartilage have to date precluded use of these methods as measures of outcomes for osteoarthritis (OA).

The extracellular matrix of articular cartilage is composed predominantly of collagen type II and the proteoglycan aggrecan. The latter is present at a concentration that endows articular cartilage with a very high concentration of charged glycosaminoglycans (GAG) via their sulfate and carboxyl groups[13]. This high level of fixed ionized charge groups on the extracellular matrix gives rise to the generation of electric fields, or streaming potentials, inside articular cartilage under load[14–16]. Essentially, load-induced interstitial fluid flow convects the excess of the sodium counterion that is present to balance the negatively charged glycosaminoglycan through the tissue, thereby generating a displacement of positive sodium relative to fixed negative sulfate and carboxyl groups on GAG to produce interstitial electric fields[17]. These streaming potentials in articular cartilage have been the subject of intense investigation since they may act as mechanobiological feedback signals to chondrocytes, informing cartilage cells of their load-bearing environment[18,19], and streaming potentials may be used as indicators of cartilage function and load-bearing capacity. With respect to the latter, several studies have shown that degradation of cartilage extracellular matrix results in reduced streaming potential amplitudes due to loss of proteoglycan and degradation of collagen and that these electromechanical signals are more sensitive to tissue changes than measurements of purely mechanical properties[20,21]. The high sensitivity of streaming potentials to cartilage degradation has led several groups to design arthroscopic instruments that can be inserted into the knee joint during arthroscopy to contact the cartilage surface and measure these electromechanical events in order to assess cartilage integrity[22,23]. The latter instrument[23] was shown to be able to detect changes in cartilage function immediately following an injurious impact load and also revealed greater sensitivity than mechanical property or histological changes, demonstrating the ability of load-induced electric fields in articular cartilage to sensitively and specifically identify regions of cartilage degeneration. However these devices are invasive, requiring arthroscopic surgery to access the articular cartilage.

In the current study we hypothesized that load-induced streaming potentials in cartilage can be detected non-invasively, using electrodes which contact the skin with a method called electroarthrography (EAG). We also hypothesized that, given the sensitivity of streaming potentials to cartilage degeneration, measured EAG potentials will decrease according to the degree of cartilage deterioration in OA.

Method

Study design

The study comprises: (1) a test-retest analysis on a subset of Control subjects; (2) a comparison of Control and experimental subjects, first control to OA knee, and then OA knee to OA knee after joint replacement; (3) an assessment of correlation between EAG and patient characteristics and, (4) a finite element model simulation.

Patients

EAG recordings were performed for three groups of knees from 20 asymptomatic subjects (Control group) and 20 patients diagnosed with bilateral knee OA who had a unilateral total knee replacement (TKR) (OA group and prosthesis group). The OA patients were recruited at Maisonneuve-Rosemont Hospital, whereas the Control subjects were recruited at École Polytechnique. All subjects signed an informed consent form and the study was approved by the ethic boards of both institutions.

All subjects underwent a detailed clinical history with particular attention to previous knee injury or surgery and a physical exam. The physical exam included assessment of body mass index (BMI), patellofemoral joint pathology (tenderness, alignment, tracking and crepitus), tibio-femoral joint pathology (tenderness, alignment, range of motion, ligament stability, crepitus, synovial thickening) and an evaluation of peri-articular structures (Bakers cysts, muscle atrophy, etc.).

The inclusion criteria in the OA group comprised patients with a unilateral total knee prosthesis (NexGen® Zimmer Inc., Warsaw, Indiana) implanted at least 6 weeks prior to the EAG recording and a diagnosis of contralateral knee OA. These patients underwent weight-bearing knee X-rays read by independent radiologists for diagnostic purposes. Knee OA was diagnosed according to the clinical and radiographic criteria defined by Altman R. *et al.*[24] and OA grading was based on the Kellgren–Lawrence scale[25]. OA patients with concomitant ankle or hip pathology, inflammatory arthritis and patients with neurological problems or any conditions that could impair their ability to perform EAG test were excluded. Control subjects were not radiographed for ethical reasons and were included after their clinical history and physical examination were found to be within normal limits.

EAG recording

The potentials were measured with eight electrodes placed over the knee of the strong leg for subjects from the Control group, and over both knees (contralateral and prosthesis) for the OA group. These electrode sites were selected so as to minimize electromyographic (EMG) interference after a preliminary study using 30 electrodes uniformly distributed over the knee. Skin preparation consisted of shaving for subjects with a high pilosity, and abrasion for all subjects (20 strokes with an abrasive pad) to reduce skin stretch artifacts[26]. Self-adhesive recessed ECG monitoring electrodes (Red Dot No. 2560, 3M) were used to reduce electrode movement artifacts[27]. The eight electrodes were placed with respect to anatomical landmarks (Fig. 1): two electrodes were positioned on the medial side over the joint line determined by palpation, then one electrode was placed above and another below; electrode placement was similar on the lateral side (lateral and medial joint lines heights may differ). A reference electrode was placed over the shin, at a site with little skin movement overlying the bone and at mid-level between the knee and the ankle. A ground electrode was placed below the reference electrode. The impedance of the electrodes was measured (MP36, Biopac Systems Inc., Goleta, California) to assure good contact ($Z < 100$ kΩ)[26]. The eight EAG signals were recorded with a wireless device (BioRadio 150, Clevemed Medical Inc., Cleveland, Ohio) attached to the waist of the subject with the following settings: DC coupling, 800 Hz sampling rate, 12 bit resolution, ±70 mV range. The signal from an embedded inclinometer was also recorded so as to synchronize the EAG signal processing with the loading cycles.

Joint loading was achieved by having the subjects slowly shift their weight from one leg to the other, approximately every 4 s. The subjects placed their feet at shoulder-width and kept their legs