The Forward Problem of Electroarthrography: Modeling Load-Induced Electrical Potentials at the Surface of the Knee

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Abstract—Electroarthrography (EAG) is a novel technology recently proposed to detect cartilage degradation. EAG consists of recording electrical potentials on the knee surface while the joint is undergoing compressive loading. Previous results show that these signals originating from streaming potentials in the cartilage reflect joint cartilage health. The aim of this study is to contribute to the understanding of the generation of the EAG signals and to the development of interpretation criteria using computer models of the human knee. The knee is modeled as a volume conductor composed of different regions characterized by specific electrical conductivities. The source of the EAG signal is the load-induced interstitial fluid flow that transports ions within the compressed cartilage. It is modeled as an impressed current density in different sections of the articular cartilage. The finite-element method is used to compute the potential distribution in two knee models with a realistic geometry. The simulated potential distributions correlate very well with previously measured potential values, which further supports the hypothesis that the EAG signals originate from compressed cartilage. Also, different localized cartilage defects simulated as a reduced impressed current density produce specific potential distributions that may be used to detect and localize cartilage degradation. In conclusion, given the structural and electrophysiological complexity of the knee, computer modeling constitutes an important tool to improve our understanding of the generation of EAG signals and of the various factors that affect the EAG signals so as to help develop the EAG technology as a useful clinical tool.

Index Terms—Arthritis, bioelectric phenomena, finite-element analysis, medical simulation.

I. INTRODUCTION

Articular cartilage is a conjunctive tissue which protects the subchondral bones from direct contact. This allows diarthrodial joints to absorb shock and reduce friction during movement. Osteoarthritis (OA), which is characterized by a degeneration of the articular cartilage, is the most prevalent form of joint disorders. It affects up to 10% of adults worldwide and is a leading cause of disability, which leads to an important economic burden that accentuates with an aging population [1]–[4].

This multifactorial joint disorder involves complex biochemical, enzymatic, and metabolic alterations associated with structural, morphological, and biomechanical changes. Appearing initially as superficial fibrillations on cartilage, OA can later spread into deeper zones until the denudation of subchondral bones [5], [6]. Treatments at this stage often require some form of partial or total prosthetic joint replacement [7], [8].

Current techniques that are employed by clinicians to assess joint function mainly include physical examination, imaging technologies, and marker-based evaluations. Medical imaging aims to visualize the morphologic changes of the cartilage using technologies such as radiography and magnetic resonance imaging [9], [10]. To date, none of these techniques provide specific diagnostic information early enough to prevent progression of the disease. By detecting biochemical and metabolic changes through blood, synovial fluid, or urine sample analyses, biomarkers may succeed to provide information on cartilage breakdown at a very early stage [11]–[13], however, without localizing the damaged area.

Experiments on bovine and on human cadavers showed that the breakdown of cartilage is correlated with its electromechanical characteristics [14], [15]. Articular cartilage comprises a solid phase consisting mainly of an extracellular matrix hydrate in a fluid phase containing electrolytes [16]. The matrix architecture is defined by a cross-linked network of collagen fibers (mainly type II with several minor collagen types) that immobilizes a high content of proteoglycans, primarily aggrecan, consisting of numerous glycosaminoglycan (GAG) chains branching off a core protein. Negatively charged sulfated and carboxyl groups in GAG attract cations in the electrolyte to maintain electrical neutrality. When a compressive force is exerted on articular cartilage, the cations and the synovial fluid are displaced away from fixed negatively charged GAGs by hydrodynamic drag and a mechanically derived electrical field arises along the flow direction. The electric potential associated with this field is known as streaming potentials [17]–[19]. Studies with animal models revealed that streaming potentials are highly sensitive to cartilage degradation, even at an early stage [15], [20]. This has led to the development of a novel technique called electroarthrography (EAG) where electrical potentials are recorded on the knee surface during mechanical loading of the joint (see Fig. 1).

A recent EAG study has shown that electrical potentials recorded on the knee surface were significantly higher in normal subjects than in patients with OA, whereas potentials recorded in patients with a total knee prosthesis were effectively null.
thus supporting the hypothesis that the EAG signals originate from compressed cartilage and that EAG could be used to detect articular cartilage degradation [15]. To further develop EAG as a noninvasive diagnostic tool for OA, some basic questions remain to be answered.

1) Can the spatial distribution of the potentials recorded on the knee surface be used to confirm that bioelectrical EAG sources are located within the region of compressed cartilage?
2) Even though in vitro experiments have shown that streaming potential amplitude is sensitive to cartilage deterioration, can EAG be used to detect and pinpoint lesions?
3) The knee being a highly heterogeneous structure, what are the factors that can affect the propagation of the EAG signals between the cartilage and the knee surface?

The aim of this study is to answer these questions by developing computer models that reproduce the geometrical and electrical properties of the human knee and by simulating the EAG potentials. By solving the forward problem of EAG using techniques commonly used in biophysical electrocardiography [22], we wish to improve the understanding of EAG signals and to contribute to the development of EAG interpretation criteria.

II. METHODS

A. Knee Geometry

To simulate accurate potential distributions on its surface, a realistic 3-D knee structure accounting for electrical properties but not mechanical properties was constructed. Rather than dealing with electromechanical events explicitly we will impose current sources consistent with their electromechanical generation. The knee model, which is delimited by a closed outer surface, consists of multiple internal regions with specific electrical conductivities. Four types of tissues are distinguished: muscle, bone, cartilage, and fat. For simplification, muscle is deemed as one bloc grouping all the muscular tissues around the articulation; also, the cartilage covering the femoral and the tibial condyles, as well as the menisci is treated as a single conducting region. Thereupon, the model geometry comprises seven regions: one muscular region; three bone regions (femur, tibia and patella); two cartilage regions with one covering the femorotibial joint and the other covering the interior facet of the patella; and finally one region of fat defined as the space between all the other regions and the outer knee surface.

In this study, two types of knee geometries are used: a simplified general geometry (GG) and a specific subject geometry (SG) (see Fig. 2). Both represent a healthy male subject’s right knee at full extension (zero degree of flexion). The GG model was created manually with a CAD toolkit using basic geometrical shapes and complying with averaged Caucasian male knee dimensions [23]–[28]. The SG model was based on data from the Visible Human Project (U.S. National library of Medicine). High-resolution photographs of cadaveric slices at 1-mm intervals in the transaxial plane were segmented individually and semimanually with respect to the tissue frontiers using a segmentation software (sliceOmatic v 4.3, Tomovision). The segmented images were then transformed into point clouds, assembled, and rendered into 3-D solid objects with the help of a 3-D CAD software (Catia V5, Dassault Systèmes).

The electrical sources are imposed in the load bearing areas where the streaming potentials occur in articular cartilage and menisci. Physiologically, two separate articular contact regions can be distinguished at the medial and lateral sides of the knee. Here, the cartilage contact regions are modeled as two cylindrical shapes joining the femoral condyles (medial and lateral) and the tibial plateau. These cylinders also include meniscal tissue since its conductivity is similar to cartilage. For the GG model, each contact region has a radius of 1.4 cm and a thickness of 4 mm which corresponds to the sum of femoral and tibial cartilage thicknesses, including the menisci. The dimensions of the GG model’s contact regions are based on measurements of the tibiofemoral weight-bearing areas [29]. The SG model has a variable thickness (3 to 7 mm) and a smaller area (1.2 cm radius) due to the single subject’s anatomy (Visible Human project).
B. Electrical Modeling

Streaming potentials are mechanically induced electrophysiological signals originating from compressed articular cartilage. Inside compressed cartilage, the flow of interstitial fluid created by a pressure gradient carries positively charged ions. This phenomenon constitutes the electrical source of streaming potentials for the intact knee and it can be represented as an impressed (or external) current density $\mathbf{J}_s$ within the compressed cartilage. For our study, the mechanical loading of the cartilage is achieved by the subject slowly shifting his weight from one leg to the other while standing. For such low frequency bioelectrical signals ($<5$ Hz), the capacitive and inductive effects are negligible and the quasi-static hypothesis is applicable. Thus, the electrical potential is governed by the following equation [22]:

$$\nabla \cdot (\sigma \nabla \phi - \mathbf{J}_s) = 0$$

(1)

where $\sigma$ is the local conductivity (S/m), $\phi$ is the electrical potential (V), and $\mathbf{J}_s$ is the impressed current density (A/m²). This impressed current density is zero in all regions except within the two load bearing regions described in the preceding section. At the interface between two homogeneous regions with different electrical conductivities or at the interface between compressed and uncompressed cartilage, the potential and the normal component of the current density are continuous. At the interface with air, on the outer surface of the model, the normal component of the current density is zero. The potential at the site of the reference electrode used in the experimental measurements and which is located over the tibia (see Fig. 2) is set to zero.

Inside compressed cartilage, the flow of interstitial fluid created by a pressure gradient carries positively charged ions. This convection current can be represented by the vector field $\mathbf{J}_s$ in a Cartesian coordinate system:

$$\mathbf{J}_s = (J_x, J_y, J_z).$$

(2)

The magnitude of each component depends on the fluid velocity along the same direction and on the concentration of charge carriers in the fluid phase. In this study, the following assumptions are applied.

1) Since the permeability of the bones (femoral condyles and tibial plateau) that compress the cartilage is negligible, there is no fluid flow and no impressed current density in the Z-direction within the two cylindrical shapes representing compressed cartilage.

2) The regions of compressed cartilage have isotropic hydraulic permeability.

3) The pressure gradient is oriented along the radius of a cylindrical shape representing compressed cartilage.

According to these assumptions, a simplified current source configuration is obtained:

$$\begin{align*}
J_x &= \frac{x - x_0}{\sqrt{(x - x_0)^2 + (y - y_0)^2}} \\
J_y &= \frac{y - y_0}{\sqrt{(x - x_0)^2 + (y - y_0)^2}} \\
J_z &= 0
\end{align*}$$

(3)
where $J_s$ is the scalar current magnitude of the subsource (either a quadrant or a cylinder), $x$ and $y$ are the coordinates of the impressed current source, and $x_0$ and $y_0$ are the coordinates of the center of the selected cylindrical shape representing compressed cartilage. The uniform impressed current density $\mathbf{J_s}$ is thus oriented radially within each cylindrical shape, from the center to the periphery. The values of $\mathbf{J_s}$ used in the simulations are obtained using the approach described in the D. Regression Method subsection.

C. Finite Element Method

The finite element method (FEM) was used for computing the potential distribution using the COMSOL Multiphysics simulation environment (version 3.5a, COMSOL, Inc., Burlington, MA, USA). The two knee models (GG and SG) were meshed with first-order tetrahedral elements with more than 200 000 elements for each geometry. The meshing technique was optimized as the cylindrical sources and the electrodes had higher mesh densities. The computations were carried out via iterated conjugated gradient for faster calculation speed and reduced memory requirements.

The two knee models were fashioned as multimcomponent volume conductors with sectionally homogeneous, constant conductivity distributions. The four types of tissue were attributed the following conductivities: $\sigma_{\text{muscle}} = 0.4$ S/m, $\sigma_{\text{bone}} = 0.035$ S/m, $\sigma_{\text{cartilage}} = 0.18$ S/m, $\sigma_{\text{fat}} = 0.04$ S/m. [30]–[34]. The electrode potentials were computed as the average of the node potentials inside the electrode zone.

D. Regression Method

The simulated potential distributions were fitted to the mean potential values measured at the eight electrode sites on 20 normal subjects [21] using the following procedure. The matrix representation of the simulated electrode potentials is

$$\mathbf{V_m} = \mathbf{A} \mathbf{J_s}$$  \hspace{1cm} (4)

where $\mathbf{V_m}$ is an $8 \times 1$ vector of electrode potentials, $\mathbf{A}$ is an $8 \times N$ transfer matrix which depends on both the geometry and conductivities of all the components of the knee structure, $\mathbf{J_s}$ is an $N \times 1$ vector of impressed current density, and $N$ can be 1 or 2 depending on the subsource configuration. The transfer matrix $\mathbf{A}$ was obtained by assigning unity to one subsource and zero to the others. The current density for the subsource $\mathbf{J_s}$ was estimated from the measured potentials $\mathbf{V_m}$ by using the least squares quadratic method with nonnegativity constraint (MATLAB).

III. RESULTS

Our initial hypothesis was that the EAG signals are generated by an impressed current density with a uniform value $J_s$ that is radially oriented within the two load bearing areas on the medial and lateral sides of the knee. By using the constrained regression method described in the preceding section, we found that the value $J_s = 0.173$ A/m$^2$ generated on the surface of the GG model a potential distribution that best reproduced in a least-squares sense, the mean potential values measured at eight electrode sites in 20 normal subjects [21]. These simulated potential values [see Fig. 3(b)] have higher amplitudes on the femorotibial joint level similar to the measured potentials. However, the simulated potentials are higher than the measured potentials on the lateral side and lower on the medial side. To compensate for this effect, we allowed the current density to differ in the lateral and medial regions (two-sub-source configuration). Permitting two separate subsources, the impressed current densities were estimated at $J_s = 0.062$ A/m$^2$ on the lateral side and $J_s = 0.180$ A/m$^2$ on the medial side. The simulated potentials, which are reduced on the lateral side and increased on the medial side, then accurately reproduce the measured potentials, with differences between the simulated and measured potentials smaller than 10 $\mu$V for the electrodes at the femorotibial joint level. However, the simulated potentials for both the single and double source configurations are much lower than the measured potential at the site of electrode 8.

The effect of the knee geometry of a specific subject was investigated with the SG model. The potential distribution on the entire knee surface is illustrated in Fig. 4 for both GG and SG models using the two previously determined impressed current densities (two-sub-source configuration). For both models, two local maximum potentials can be seen on both sides of the knee, with higher potentials on the medial side. The GG model has broader, more blurred, maximum, and minimum patterns than the SG model on both lateral and medial sides. The maximal potential values are higher for the GG model than for the SG model, with the medial maxima of 270 $\mu$V versus 234 $\mu$V, and the lateral maxima of 130 $\mu$V versus 90 $\mu$V. The minimal potential values are also more positive for the GG model than for the SG model, with the medial minima of $-20 \mu$V versus $-90 \mu$V, and the lateral minima of $-6 \mu$V versus $-25 \mu$V.

The current distribution inside the knee is illustrated in Fig. 5 for both GG and SG models. The current lines start from the side surfaces of the two cylindrical sources representing the load bearing regions, then spread sideways, either up or down, and finally rejoin the top or the bottom surfaces of the two cylinders. The current lines are concentrated around the articular joint, where the femoral condyles tend to be surrounded by a higher current density than the tibial plateau. There is little exchange of current between the medial and lateral sides. The current density drops greatly on the upper and lower parts of the knee.

To understand the relationship between the potential distribution on the knee surface and a localized defect in the articular cartilage, it is important to first characterize how the surface potential distribution reflects the activity of small, specific cartilage regions. Thus, Fig. 6(a) shows eight subsources that divide the lateral and medial cylinders into quadrants. The effect of an individual subsource on the surface potential distribution is obtained by assigning a radial impressed current density of 1 A/m$^2$ to a selected quadrant (this value is non-physiological and is simply used to visualize the transfer matrix), whilst by assigning a null impressed current density to the seven other quadrants and then computing the potential distribution. Fig. 6(b) shows that for the four external subsources (LPE, LAE, MPE, and MAE), a strong, well-localized maximum potential pattern is
recognizable when one of them is activated. Similarly, a strong but broader minimum potential pattern can be observed when any of the internal subsources are activated (LPI, LAI, MPI, and MAI). These observations clearly reflect the direction of the impressed current. When flowing toward the knee surface, it produces positive potentials on the nearest surface whereas it produces negative potentials when flowing toward the center of the knee. The distance between the sources and the knee surface is discernible in the equipotential maps: the maxima patterns are sharper and cover a smaller region for the external sources that are closer to the surface, whereas the minima patterns cover a broader region for the internal sources that are farther from the surface. Finally, the position of the sources is also discernible: the anterior subsources produce extrema that are more anterior on the maps than their posterior counterparts, whereas lateral subsources produce lateral extrema on the maps and medial subsources produce medial extrema.

To further contribute to the understanding of the relationship between the knee surface potentials and a localized defect in articular cartilage, Fig. 7(b) shows equipotential maps computed with the GG model after decreasing by 50% the impressed current density in one quadrant while maintaining the impressed current density in the seven other quadrants. For reference, Fig. 7(a) shows the map obtained with all eight quadrants active (their impressed current density corresponds to the medial and lateral densities estimated with the two-sub-source configuration). Overall, each subsource has a different effect on the potential distribution in the knee and the potential distributions on the knee surface. The most noticeable changes occur for the medial quadrants. The decrease of the current density in the external quadrants (MAE, MPE) produces a significant decrease
in the amplitude of the potential maximum, especially for the anterior one (MAE). Paradoxically, the decrease of the current density in the internal quadrants (MAI, MPI) produces an increase in the amplitude of the potential maximum. This increase can be attributed to an imbalance of the effects of impressed current flow between the external and internal quadrants. Impressed current from the internal quadrants produces negative extrema on the neighboring knee surface whereas impressed current from the external quadrants produces positive extrema (see Fig. 6). These potentials from the external quadrants are normally dominant when all the quadrants are active because the external sources are closer to the knee surface than the internal sources. A reduction of impressed current in the internal quadrants further contributes to the dominance of the positive potentials from the external quadrants. Similar changes can be observed for the lateral quadrants, but they are less discernible.

The fat layer under the skin of the knee constitutes an electrical barrier between the electrical sources and the knee surface that may have an effect on the knee surface potentials. To investigate this effect, the GG model was modified by increasing the thickness of the fat layer from 4 to 29 mm (to cover a large range), without changing the other structures in the knee. The potential at the electrode sites along the joint line (2, 3, 6, and 7) decreased, whereas the potential slightly increased or remained constant at the sites above and below the joint line (1, 4, 5, and 8). The X-axis corresponds to the thickness of the fat layer (mm) and the Y-axis indicates the electrode potential (μV).

Different approaches have been previously used to model articular cartilage. To understand its mechanical behavior under loading, the cartilage has been modeled as a biphasic linear medium [16], a poroviscoelastic medium [35], or a medium reinforced with collagen fibrils [36]. Given the complexity of realistic geometry and the governing differential equations, FEMs have often been used to investigate cartilage inhomogeneity [37], the presence of chondrocytes [38], or the effects of meniscectomy [39]. The electromechanical behavior of cartilage and the generation of streaming potentials have also been investigated with an electrokinetic model relating fluid flow and electrical current density to the pressure and electrical potential gradients [40], [41]. This study did not address the relationship between cartilage loading and streaming potentials, and focused instead on the propagation of the electrical signals between the cartilage sources and the knee surface.

Bioelectrical sources generate potential distributions on the body surface with spatial patterns that are specific to the location and orientation of the sources. Thus, these potential distributions can be used to localize the sources. The close fit between the measured and simulated potentials presented in Fig. 3 and in particular, the match between the site of maximum measured potential over the joint line and the site of maximum potential on the simulated potential distributions supports the hypothesis that the EAG electrical sources are located in the load bearing cartilage. For the rest of the knee surface shown in Figs. 4, 6, and 7 and which is not covered by the eight electrodes, the amplitude of the simulated potential is negligible, which corresponds to our preliminary measurements which were performed with 30 electrodes covering the entire knee surface [42].

Moreover, the higher potentials measured over the medial side versus the lateral side can be explained by the higher impressed current density in the medial compartment that was computed with our model. This higher impressed current density on the medial side is consistent with higher hydrostatic pressures in the medial compartment compared to the lateral compartment of the joint [39], [43], and by the relationship between the magnitude of the streaming potentials and the pressure gradient [40].

The potential distributions computed with the general knee geometry (GG model) and the specific SG (SG model) were consistent, and both conformed with the experimental data. The simulated potential distributions indicate that the positions of the electrodes applied on the knee surface are crucial and should concentrate on the medial and lateral joint lines.

A possible clinical application of EAG is the detection and localization of an underlying site of cartilage degradation. To investigate the relationship between the knee surface potentials and small, specific cartilage regions, the two cylindrical source regions were divided into eight quadrants, each having a specific radial impressed current density [see Fig. 6(a)]. Each quadrant represents a different functional area to which can be associated a specific abnormality [31], this division can discriminate between anterior and mid-anterior lesions as well as interior and exterior lesions of the tibiofemoral weight-bearing areas as in [44]. We found that the EAG signals reflect the direction of the impressed current, which generates positive potentials on

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**Fig. 8.** Effect of the thickness of the outer fat layer on the potentials computed at the eight electrode sites of the GG model. For the initial model, the medial and lateral sides have the same outer fat layer thickness. By increasing the circumference of the skin representing a thicker fat layer without changing the other structures in the knee, the potential at the electrode sites along the joint line (2, 3, 6, and 7) decreased, whereas the potential slightly increased or remained constant at the sites above and below the joint line (1, 4, 5, and 8). The X-axis corresponds to the thickness of the fat layer (mm) and the Y-axis indicates the electrode potential (μV).
the nearest surface when the current flows toward the surface, whereas it produces negative potentials when flowing toward the center of the knee (see Fig. 6(b)). Localized defects were simulated by decreasing by 50% the impressed current density in one quadrant while maintaining the impressed current elsewhere. This reduction can be interpreted as a reduction in either the thickness or the GAG concentration of the cartilage in that quadrant. As expected, a decrease of the current density in the external quadrants produced a decrease in the amplitude of the nearby potential maximum, but a decrease in the internal quadrants produced a paradoxical increase in the amplitude of the potential maximum (see Fig. 7). This last effect, which can be attributed to an imbalance of the impressed current flow, shows that the interpretation of the EAG signals may not be straightforward and that clinical studies are essential to determine rules for the EAG interpretation. At this point, it is difficult to determine the clinical importance of this effect since the more prevalent lesions tend to cover a large part of the condyles and are expected to result in an overall decrease in EAG signals. Similarly, even if the EAG changes were less discernible for reductions in the lateral quadrants with respect to the medial quadrants, the importance of this effect is unclear since medial lesions are more prevalent than lateral lesions [45].

Previous experimental results also showed variation in the amplitude of the EAG signals among different subjects. A range of factors can contribute to this variation such as age, sex, weight, Body Mass Index, alignment of the lower extremities (valgus, varus, hyperextension). We investigated specifically the effect of the fat layer thickness around the knee. As fat tissue has a low electrical conductivity, it can impede the electrical current flow. We found that the simulated potentials at the electrode sites along the joint line decreased significantly as a function of the fat layer thickness, whereas it is slightly increased or remains the same at sites above and below the joint line (see Fig. 8). On the corresponding knee surface equipotential maps (not shown), this effect corresponds to a smearing of the potential maximum pattern. A future clinical decision-making process could thus consider this factor for the interpretation of the EAG signals.

Since previous work has demonstrated that streaming potentials are sensitive to changes in the molecular structure of articular cartilage [14], [15], the noninvasive detection of streaming potentials with the EAG technique could provide critical information at early stages of disease that is currently not possible with imaging techniques that primarily detect changes in the geometry and thickness of the cartilage. The EAG technology thus appears to be a promising new technology that can complement the existing tools for the diagnosis of joint disease.

V. CONCLUSION

Computer modeling constitutes an important tool to improve, both qualitatively and quantitatively, our understanding of the generation of EAG signal. By using this approach, we were thus able to demonstrate that 1) the spatial distribution of the simulated potentials confirm that bioelectrical EAG sources are located within the region of compressed cartilage; 2) EAG has the potential to detect and localize articular cartilage lesions; and 3) the structure of the knee, such as the thickness of the subcutaneous fat layer can affect the propagation of the EAG signals between the cartilage and the knee surface.

REFERENCES


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