Bioimpedance spectroscopy tensor probe for anisotropic measurements

H. Kwon, H. Wi, B. Karki, E.J. Lee, A. McEwan, E.J. Woo, B. Harrach, J.K. Seo and T.I. Oh

The tetrapolar electrode configuration used in bioimpedance suffers from negative sensitivity and is confounded by anisotropic tissue such as blood vessels or muscle and nerve fibres. We propose a circular array of electrodes to focus current directly underneath the probe and provide anisotropy information. We show that an implementation using 16 miniature electrodes is able to outperform the tetrapolar method in sensitivity and impedance estimation. The proposed method can also recover anisotropic conductivity tensors from experiments for the first time.

Introduction: The bioimpedance spectra of tissues can provide information to estimate physiological and pathological conditions of tissue in-vivo and ex-vivo, providing diagnostic medical information as well as expanding our understanding of bioelectromagnetic phenomena [1, 2, 3]. In bioimpedance an induced voltage is measured in response to a small bioelectrical current. Conventionally, tissues are extracted from the body (ex-vivo) and measured in a vessel with large surface electrodes so that a uniform current is injected and the average tissue conductivity can be measured in a known geometry [4].

In-vivo measurement is preferred as tissues change following biopsy [2]. The four terminal electrode (tetrapolar) measurement is typically used for surface bioimpedance because it can reduce the non-ideal effects of the electrode polarization impedance. However tetrapolar measurements include errors from electrode placement and negative sensitivity regions within the typical region of interest beneath the electrodes [4].

Many tissues of interest are not homogenous but composed layers of cells, leading to further errors in tetrapolar measurements due to anisotropic impedance where the conductivity is much greater in one direction, (such as along a nerve fibre for the conduction of action potentials). In this paper, we propose a probe design with multiple electrodes and a localized electrical energy concentration method for measuring bioimpedance. We focus on the region of interest under the probe using a sensitivity analysis to minimize the effect of geometrical errors. We directly compare an implementation of the new method using 16 electrodes against the tetrapolar measurement with the same electrodes in agar phantoms with homogenous and anisotropic conductivity, fig. 1.

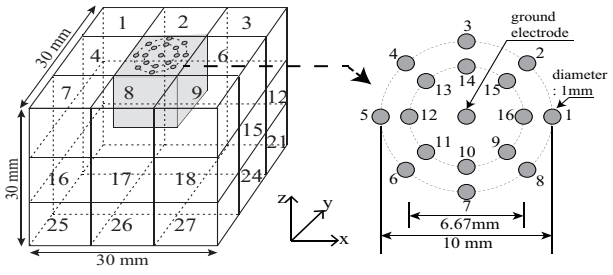

Fig. 1 *The proposed multiple electrode configuration of 16 electrodes with central ground electrode. The conventional tetrapolar setup is compared by using four of the 16 electrodes in the x direction. The test object is an agar or saline phantom setup with 27 interchangeable blocks to test the probe. The probe is located directly above blocks 5 which is the region of interest.*

Methods: Each measurement uses 4 electrodes; the current is driven between the i-th and the j-th electrode and the voltage is measured between the k-th and the l-th electrode. We fix the injection current to be $I = 1$ mA operated at 10 kHz and denote the recorded voltage U_{ij}^{kl}. Let $\gamma = \sigma + i\omega\epsilon$ denote complex conductivity distribution in an imaging object occupying 3D domain Ω. The recorded voltage U_{ij}^{kl} is determined by the formula

$$U_{ij}^{kl} = \int_\Omega \gamma(\mathbf{r}) \nabla u_\gamma^{kl}(\mathbf{r}) \cdot \nabla u_\gamma^{ij}(\mathbf{r})\, d\mathbf{r} \tag{1}$$

where $u_\gamma^{ij}(\mathbf{r})$ denotes the induced potential at position $\mathbf{r} = (x, y, z)$ due to the injection current using i-th and j-th electrodes. Here, u_γ^{ij} satisfies $\nabla \cdot (\gamma \nabla u_\gamma^{ij}) = 0$ in Ω. One complete measurement consists of M measurements and is denoted by the column vector $\mathbf{U}^{\mathrm{meas}}$.

We first consider the case when γ is isotropic. We discretize the domain Ω into N subregions as $\Omega = \cup_{n=1}^{N} T_n$ as shown in fig. 1. We set T_5 to be the block underneath the probe. Assume that γ is a constant in each T_n, and denote $\Upsilon = (\gamma_1^{-1}, \gamma_2^{-1}, \cdots, \gamma_N^{-1})^t$ with $\gamma|_{T_n} = \gamma_n$. Then the goal is to recover only γ_5 from the data $\mathbf{U}^{\mathrm{meas}}$.

The proposed local conductivity identification method is based on a careful analysis of the well-known system with the sensitivity matrix

$$\mathbf{S}\Upsilon = \mathbf{U}^{\mathrm{meas}} \tag{2}$$

where the rows of the sensitivity matrix $\mathbf{S}$ are of the form $[\int_{T_1} \nabla u_1^{kl} \cdot \nabla u_1^{ij} d\mathbf{r},\ \int_{T_2} \nabla u_1^{kl} \cdot \nabla u_1^{ij} d\mathbf{r},\ \cdots]$ and u_1^{ij} is a corresponding solution to u_γ^{ij} with γ replaced by 1. The system (2) is based on the approximation $\gamma \nabla u_\gamma \approx \nabla u_1$ and the formula (1) which lead to

$$U_{ij}^{kl} \approx I^{-1} \int_\Omega \gamma^{-1} \nabla u_1^{kl} \cdot \nabla u_1^{ij}\, d\mathbf{r}. \tag{3}$$

By multiplying a suitably chosen local focusing matrix Q to (2), we can recover γ_5 via the following approximation

$$\gamma_5^{-1} \approx \text{5-th component of } ((Q\mathbf{S})^{-1} Q \mathbf{U}^{\mathrm{meas}}) \tag{4}$$

Next, we consider the anisotropy case $\boldsymbol{\gamma}$. Based on Ohm's law $\gamma\mathbf{E} = \mathbf{J}$, we derive the following approximation

$$\begin{bmatrix} & & & \vdots & & \\ a_{xx}^{ijkl} & a_{xy}^{ijkl} & a_{yy}^{ijkl} & a_{zz}^{ijkl} & a_{xz}^{ijkl} & a_{yz}^{ijkl} \\ & & & \vdots & & \end{bmatrix} \begin{bmatrix} b_1 \\ b_2 \\ \vdots \\ b_6 \end{bmatrix} = \mathbf{U}^{meas}$$

where $\boldsymbol{\gamma}^{-1} = \begin{pmatrix} b_1 & b_2 & b_4 \\ b_2 & b_3 & b_5 \\ b_4 & b_5 & b_6 \end{pmatrix}$ and $a_{xx}^{ijkl} = \int_\Omega \partial_x u_1^{kl} \partial_x u_1^{ij}$, $a_{xy}^{ijkl} = \int_\Omega (\partial_x u_1^{kl} \partial_y u_1^{ij} + \partial_y u_1^{kl} \partial_x u_1^{ij})$, $a_{yy}^{ijkl} = \int_\Omega \partial_y u_1^{kl} \partial_y u_1^{ij}$, and so on. Since only difference surface voltage are available, the useful information can be obtained by observing γ_{11}, γ_{12} and γ_{22} when γ_{mn} is mn-component of $\boldsymbol{\gamma}$. Particularly, we focus on the conductivity $\sigma_{mn} = \mathrm{Re}(\gamma_{mn})$. We can determine eigenvectors $\mathbf{v}_1, \mathbf{v}_2$ and the corresponding eignevalues λ_1, λ_2 from the well-known relation

$$\begin{bmatrix} \sigma_{11} & \sigma_{12} \\ \sigma_{12} & \sigma_{22} \end{bmatrix} [\mathbf{v}_1\ \mathbf{v}_2] = [\mathbf{v}_1\ \mathbf{v}_2] \begin{bmatrix} \lambda_1 & 0 \\ 0 & \lambda_2 \end{bmatrix}. \tag{5}$$

If the ratio $r_\lambda = \lambda_1/\lambda_2$ is close to one, then we can conclude the material underneath the probe is homogeneous. However, if $r_\lambda \gg 1$ or $r_\lambda \ll 1$ then there is an anisotropy underneath the probe. For example, the case with $\lambda_1 \gg \lambda_2$ can be interpreted as a high resistance in $\mathbf{v}_2$-direction which implies the anisotropy lies parallel to $\mathbf{v}_1$-direction, because of the orthogonality of $\mathbf{v}_1$ and $\mathbf{v}_2$.

We simulated the sensitivity distribution of the tetrapolar system and the localized electrical energy concentration method using the circular array multi-electrode after [4]. For a fair comparison, we obtained the same number of datasets ($M(=28)$) with different angles using the tetrapolar electrode configuration to obtain the sensitivity distribution.

We built the test electrode setup shown in fig. 1 and assessed the accuracy of tetrapolar and multi-electrode probes by measuring the conductivity of four 27000 mm^3 homogeneous agar phantoms with different conductivity using by a commercial impedance spectrometer (1260A, AMETEK Inc., UK). The sensitivity to conductivity contrasts was measured using the testing phantom shown in fig. 1 filled with saline of 0.6 S/m and an agar block of 0.16 S/m at various locations. Conductivity tensor measurements of anisotropic objects were measured by inserting two thin polystyrene layers of 14 μm at 0, 45, 90 and 135° referred to the x-direction into an agar object of 0.3 S/m.

Results: Fig. 2 shows that the ratio of negative sensitivity and positive sensitivity for the tetrapolar method with 28 measurements (1.0489) is smaller than one of the localized electrical energy concentration method using multi-electrode (3.3626). It explained that the new method was more sensitive of conductivity in the region of interest than the tetrapolar method. We estimated the conductivity of four different homogenous agar phantoms with fixed volume. Table 1 shows the results for each measurement using both methods. The results from the localized electrical energy concentration method were closed to the correct values.The coefficient of determination, R^2, for new method and tetrapolar measurement were 0.99 and 0.95 against reference conductivity.

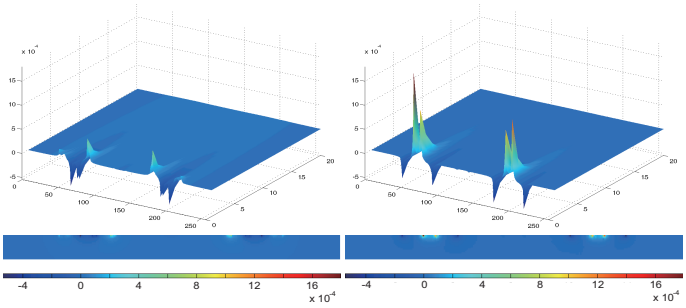

Fig. 2 *(a) Sensitivity distribution of the tetrapolar electrode and (b) sensitivity matrix of localized electrical energy concentration method using 16 electrodes.*

Table 1: Estimated conductivity of four different isotropic homogeneous phantoms using both methods.

True value [S/m]	0.13	0.27	0.6	0.9
Tetrapolar Meas. [S/m]	0.155	0.244	0.702	0.992
Multi-elec. Meas. [S/m]	0.143	0.265	0.639	0.864

Without any anomaly, both methods measured similar conductivity as fig. 3. Conductivity was estimated correctly using new method when different conductivity object was placed underneath the probe. However, conventional tetrapolar electrode measured underestimated value influenced by surrounding material of different conductivity. In anisotropy experiments, the conductivity values in each case were estimated as 0.2807 ± 0.0019, 0.2639 ± 0.0046, 0.2882 ± 0.0106, and 0.2737 ± 0.0026 using the new method on a phantom, respectively. Conductivity tensor of anisotropic object was displayed by arrows in fig. 4(b).

Discussion and conclusion: The proposed tensor probe and localized electrical energy concentration method was found to be an improvement over the conventional tetrapolar electrode in recovering conductivity in homogenous and inhomogeneous models over a range of conductivities. It was found to be more sensitive to the typical region of interest under the probe (fig. 3) and able to detect the anisotropic tensor (fig. 4).

To the best of our knowledge this is the first time anisotropic conductivity has been recovered from bioimpedance measurements using tetrapolar or any other electrode configurations. The direction of the conductivity tensor was approximately 4 degrees different to the intended model and the error in estimated conductivity increased at 45 and 135^o. We have not yet determined if this is due to the novel model setup using polystyrene layers or if it is a technical or algorithmic limitation. However the recovery of anisotropy is vitally important in many bioimpedance applications such as electrical stimulation or electrosurgical planning where the presence of fibre bundles or blood vessels could shunt away considerable current.

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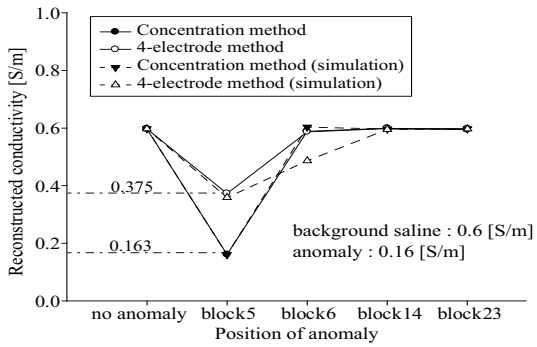

Fig. 3 *Region of interest (block5) sensitivity comparison. The target was to measure an anomaly of 0.16 S/m at the position of block 5 in a homogenous background of 0.6 S/m. With reference to fig. 1 block 6 represents a single shift in the x-direction, block 14 and block 23 in the z-direction.*

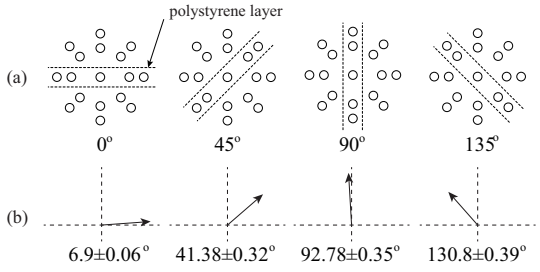

Fig. 4 *(a) Examples of conductivity tensor reconstruction from an agar phantom with anisotropy simulated by two thin polystyrene layers of thickness $14\mu m$ introduced at different angles (0, 45, 90, and 135^o). (b) Results of anisotropic direction (mean±std)*

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