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A THREE-PHASE INDUCTIVE SENSOR FOR *IN VIVO* MEASUREMENT OF ELECTRICAL ANISOTROPY OF BIOLOGICAL TISSUES

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Abstract: Biological tissue will have anisotropy in electrical conductivity, due to the orientation of muscular fibers or neural axons as well as the distribution of large size blood vessels. Thus, the *in vivo* measurement of electrical conductivity anisotropy can be used to detect deep-seated vessels in large organs such as the liver during surgeries. For diagnostic applications, decrease of anisotropy may indicate the existence of cancer in anisotropic tissues such as the white matter of the brain or the mammary gland in the breast.

In this paper, we will introduce a new tri-phase induction method to drive rotating high-frequency electrical current in the tissue for the measurement of electrical conductivity anisotropy. In the measurement, three electromagnets are symmetrically placed on the tissue surface and driven by high-frequency alternative currents of 0 kHz, modulated with 1 kHz 3-phase signals. In the center area of three magnets, magnetic fields are superimposed to produce a rotating induction current. This current produces electrical potentials among circularly arranged electrodes to be used to find the conductivity in each direction determined by the electrode pairs. To find the horizontal and vertical signal components, the measured potentials are amplified by a 2ch lock-in amplifier phase-locked with the 1 kHz reference signal. The superimposed current in the tissue was typically 45 micro Amperes when we applied 150 micro Tesla of magnetic field. We showed the validity of our method by conducting *in vitro* measurements with respect to artificially formed anisotropic materials and preliminary *in vivo* measurements on the pig's liver.

Compared to diffusion tensor MRI method, our anisotropy sensor is compact and advantageous for use during surgical operations because our method does not require strong magnetic field that may disturb ongoing surgical operations.

Keywords: conductivity anisotropy, biological tissue, three-phase magnetic field, induction current.

1. INTRODUCTION

Biological tissue in general will have anisotropy of mechanical, optical or electrical properties [1], depending on the fine structure of bones, muscular fibers [2], bundles of neural axons in the white matter of the brain [3] and blood vessels. Generally speaking, mechanical and optical anisotropic properties might be determined through anatomical knowledge as well as visual observation. However, electrical anisotropic properties of deep-seated tissues cannot be estimated just by visual superficial observations.

From the diagnostic point of view, a decrease of anisotropy may indicate the existence of cancer in anisotropic tissues such as the white matter of the brain [4], or the mammary gland in the breast [5]. This anisotropy can be detected by Diffusion Tensor Imaging using MR equipment. If we can obtain an anisotropic profile of biological tissues without using expensive equipment such as MR, we may be able to detect deeply seated cancerous tissues at small clinics even in the surgical circumstances for therapeutic applications, while the detection of the blood vessels may assist surgical operation of large organs such as the liver.

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For measuring the electrical impedance of biological tissue, the 4-dekectraode method is popularly used [1,3]. In that method, a pair of detection electrodes is used together with another pair of electrodes arranged on a line for driving the constant current in the tissue. If we use the conventional 4-electrode method to find anisotropy, we have to change the position of driving electrodes for every direction, which involves time-consuming procedures. In the actual in-vivo tissue, impedance and anisotropy may change rapidly mainly due to the blood-flow change. Thus for accurate measurement, it is desirable to complete the anisotropy measurement within a short time period. To realize the fast measurement, one may prepare many pairs of electrode in different directions to be switched automatically. Even in that method, it is difficult to place many electrodes on uniform conditions within a limited area for the observation.

In this paper we propose a three-phase electromagnetic sensing device for easy measuring of biological anisotropy. The three-phase sensor consists of three electrical magnets arranged in triangle, and two pairs of detection electrodes placed orthogonally. The three magnets are driven by symmetrical three-phase alternative current. By superimposing the magnetic fields, a rotating eddy current yields at the center of the triangle. This rotating current can be used to produce differential voltages across the horizontally arranged electrodes as well as for the vertically arranged pair of electrodes. From the differential voltages that appear across the pair of electrodes, we can estimate anisotropic conductivity for each direction. We show the experimental results on an anisotropic phantom as well as on biological tissues.

2. METHOD

In our method, as shown in Figure 1(a) and (b), three electromagnets M_1-M_3 of high-frequency specification are placed in each top of the equilateral triangle, i.e. they are placed in order to respectively make an angle of 120 degrees on the concentric circle, on the surface of biological tissue. These electromagnets are supplied with the current of each phase of the symmetrical three-phase alternative current. By the magnetic fields produced by these electromagnets, a set of eddy currents will be produced, in the middle of electromagnets M_1-M_3., as shown in (1),

$$\begin{aligned} \boldsymbol{J}_1 &= k_1\boldsymbol{h}_1 I_0 \cos(\omega_s t) \\ \boldsymbol{J}_2 &= k_2\boldsymbol{h}_2 I_0 \cos\{(\omega_s t) - (2\pi/3)\} \\ \boldsymbol{J}_3 &= k_3\boldsymbol{h}_3 I_0 \cos\{(\omega_s t) - (4\pi/3)\}, \end{aligned} \tag{1}$$

where, $\boldsymbol{h}_1$, $\boldsymbol{h}_2$, $\boldsymbol{h}_3$ denote the unit direction vectors depicted in Figure 1(b) respectively, k_1 through k_3 are constants determined by the shape of magnets, the number of coil turns, as well as the relative position of magnets and the observatory position. When we consider the superimposed eddy currents, at the center of electromagnets, the current can be expressed as (2), with parameters $k_1$through k_3 equal and described by “k”.

$$\boldsymbol{J}_{total} = kI_0[\boldsymbol{h}_1\cos(\omega_s t) + \boldsymbol{h}_2\cos\{(\omega_s t) - (2\pi/3)\} + \boldsymbol{h}_3\cos\{(\omega_s t) - (4\pi/3)\}] \tag{2}$$

When we express the above current in x and y components, we get,

$$\begin{aligned} Jx &= -\,1.5\,k\,I_0 \sin(\omega_s t) \\ Jy &= 1.5\,k\,I_0 \cos(\omega_s t)\,. \end{aligned} \tag{3}$$

This expresses the existence of a rotating current produced in the biological tissue.

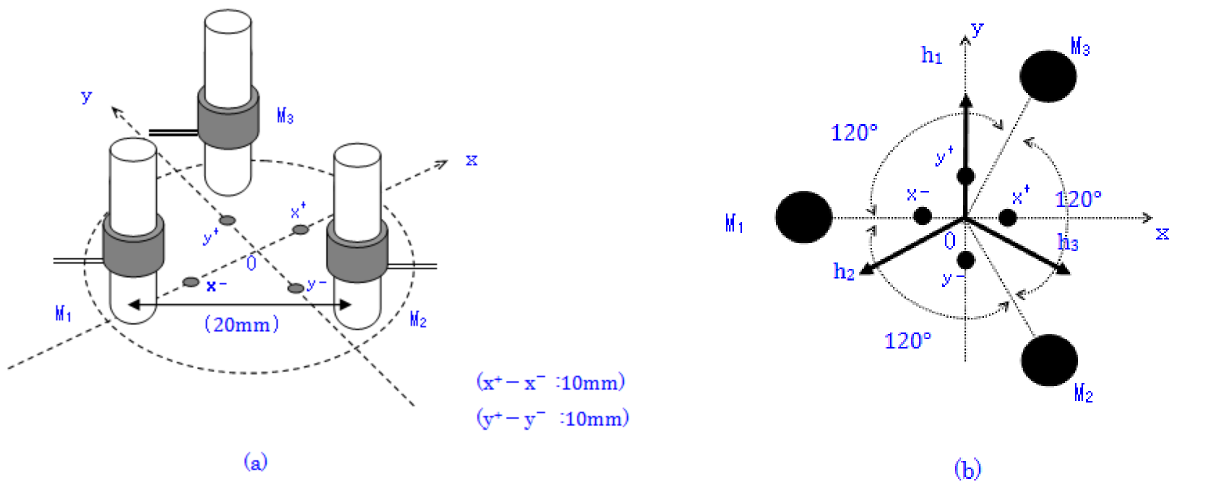


Figure 1. (a) The sensing head; (b) Arrangement of each part of the sensing head (M_1, M_2, M_3; electromagnet, x^-, x^+; electrode on the x-axis, y^-, y^+; electrode on the y-axis, h_1, h_2, h_3; unit vector)

In Figure 2 (a), individual eddy currents of (1) are shown and the superimposed rotating current is shown in Figure 2 (b). In Figure 2 the direction of superimposed current at time O-A of the figure (a) refers to the one flowing from the sensing head (O) towards A of the figure (b). With the progress of time, the superimposed current flows in the direction of O-B, O-C and so on, to yield a rotation during one period of alternating current.

When we place horizontal pair x^+, x^- and vertical pair y^+, y^- of electrodes, as shown in Figure 1 on the surface of the tissue, we can measure differential voltages Vx and Vy accompanied with the rotational eddy current. From the above measurement, the resistivity along the orientation of rotating current can be estimated. That is, the voltages along the current can be calculated as the root of squared sum of the horizontal and vertical voltages as,

$$V = (Vx^2 + Vy^2)^{1/2} \quad (4)$$

with the orientation of,

$$\theta = \arctan (Vy/Vx). \quad (5)$$

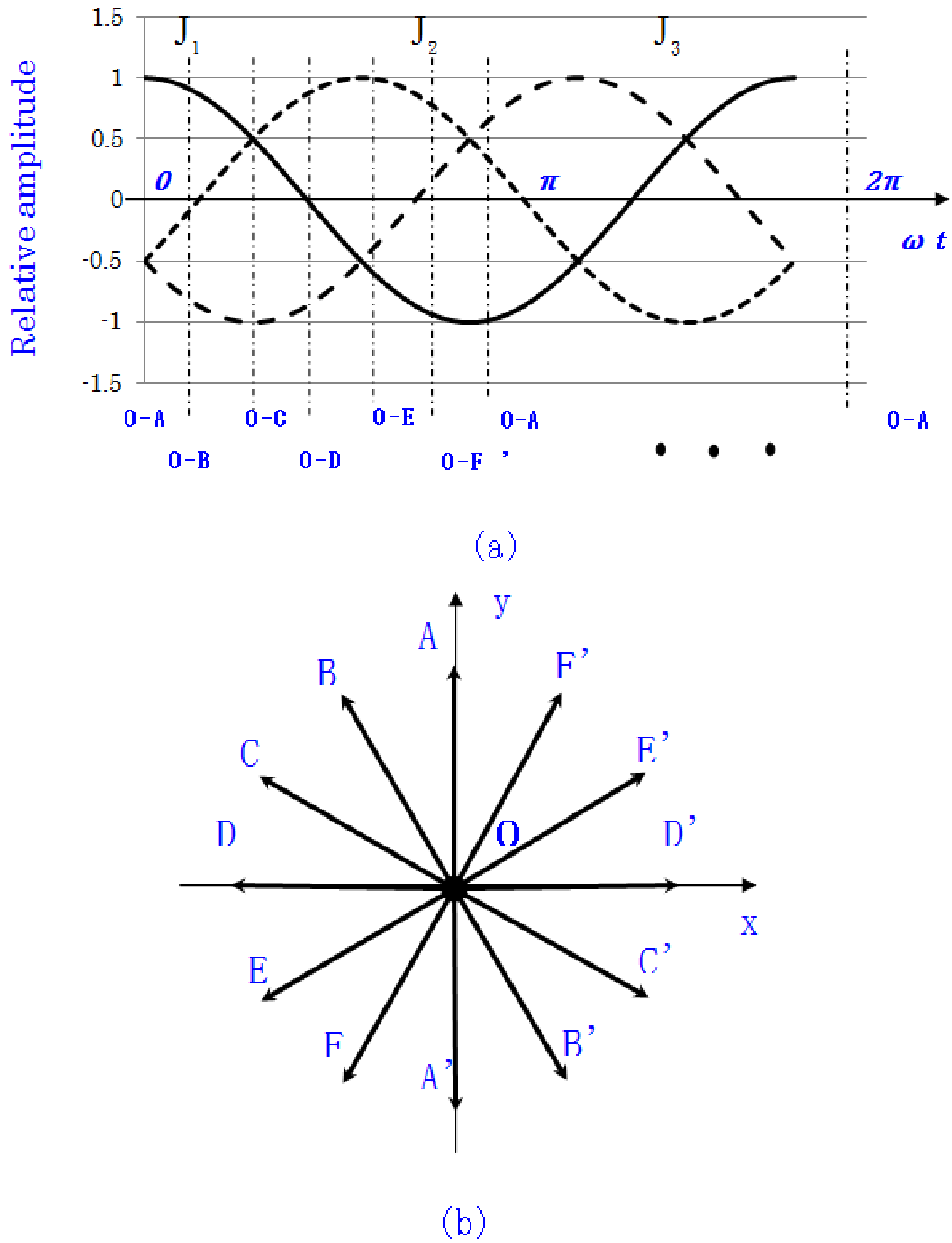


Figure 2. (a) Three phase alternative currents; (b) Directions of synthetic current

3. EXPERIMENTAL SET-UP

When we want to realize the measuring equipment directly based on the principle proposed in the above section, the superimposed current will rotate at the rate of high frequency current applied to the magnet, which may cause instability in the measurement. To overcome this difficulty, as shown in Figure 3, we adopted a modulation method. In this method, we used a high-frequency carrier signal of angular frequency ω_c, together with a stepwise modulation signal to control the amplitude of high-frequency carrier given to the electromagnets. With this stepwise amplitude modulation, stable voltage measurement can be realized, because the superimposed current will flow to a fixed direction during a certain period of time. As an experimental setup, we segmented the period into 6 sections; i. e. the same amplitude is maintained for 30 degrees of time shown as A-A', B-B' and so on in Figure 3. In this case, x and y components of the superimposed eddy-current at the center of the sensing head are given by,

$$Jx = -1.5\, k\, I_0 \sin\gamma \cos(\omega_s t)$$
$$Jy = 1.5\, k\, I_0 \cos\gamma \cos(\omega_s t) \quad (6)$$

where γ is 0, 30, 60, 90, 120 or 150 degrees, corresponding to the orientation of the superimposed current as shown in Figure 3. In this case, the weight coefficients of the driving voltage of the electromagnet, depending on the orientations are summarized in Table 1. In this modulation method, the measurement direction is different from the one-side area as O to A in Figure 2 (b); both side area as A-A'in the figure is scanned in the measurement. If there is no non-linearity in the tissue, the measured result will not be different from the one explained for non-modulation case. Whereas, the parameter θ in (5) corresponds to γ in (6), however it is not the same one as shown in the model experiment in the next section.

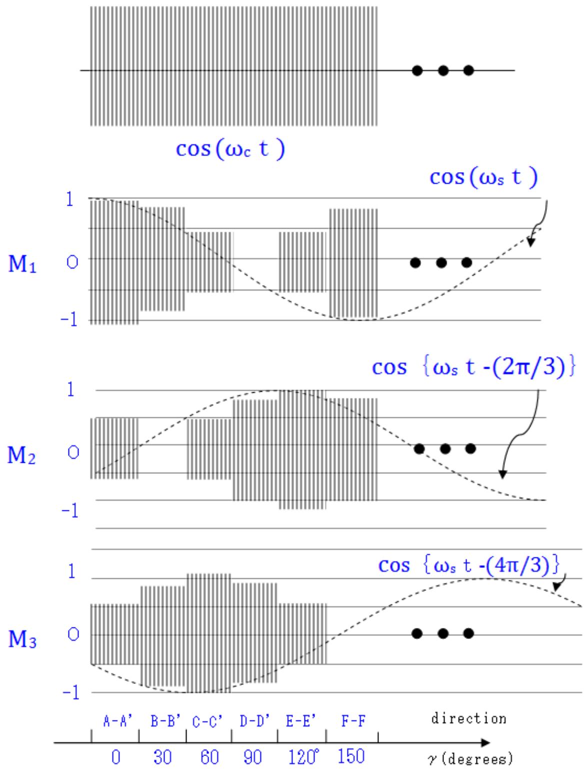


Figure 3. Current waveform of each coil of electromagnet M_1, M_2, M_3

The mechanical size of the sensing head is, as shown in Figure 1, three electromagnets of 3mm diameter, 40mm long are placed on each top of the equilateral triangle, 20 mm apart to each other. Also, a pair of electrodes 10mm apart are placed in x direction and y direction to measure the horizontal and vertical components of electrical potential difference evoked by the eddy current. Each electromagnet is composed of an 80-turns coil and a ferrite core HF70 (TDK Co. Ltd) and each electrode is made of silver rod of the 2mm diameter.

The driving circuit of the magnets is shown in Figure 4. The high-frequency sinusoidal three-phase signal of 50 kHz is modulated with the weight coefficients assigned in Table 1, and applied to the electromagnets via switching circuits and the power amplifiers. In the switching circuit, the direction of the superimposed eddy current can be continuously changed one after another, or fixed at a particular direction. The maximum repetitive frequency of the switching signal was set at 1 kHz. The electrical circuit for differential voltage measurement is shown in Figure 5, where each differential voltage is smoothed by LPF, after the product with the reference voltage is taken. In this case, the reference signal is determined in order for the product result to agree with each quadrant defined by x-y plane of Figure 2(b), because we want to know the direction of the superimposed current in the measurement. By this circuit arrangement, on-line measurements of (4) (5) are possible with Lissajous indication on the oscilloscope. The carrier signal frequency was set at 50 kHz, the maximum magnetic field is about 150 μTesla (1.5 Gauss), which produced the synthesized current of about 45 μA p-p in the saline water of the 100Ωcm resistivity with 10 mm depth.

Table 1. Weighting coefficients of the driving voltage of the electromagnet and setting direction (γ)

Weighting	$\gamma^{(°)}$					
	0	30	60	90	120	150
C_1	1	0.86	0.5	0	−0.5	−0.86
C_2	−0.5	0	0.5	0.86	1	0.86
C_3	−0.5	−0.86	−1	−0.86	−0.5	0

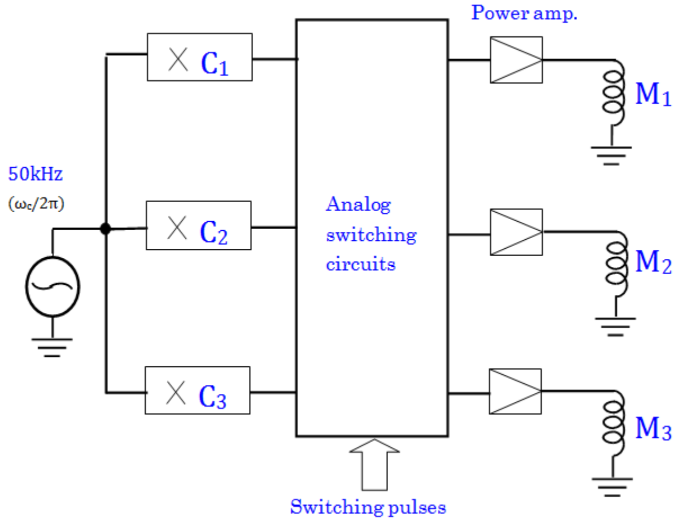


Figure 4. Driving circuit of each electromagnet M_1, M_2, M_3

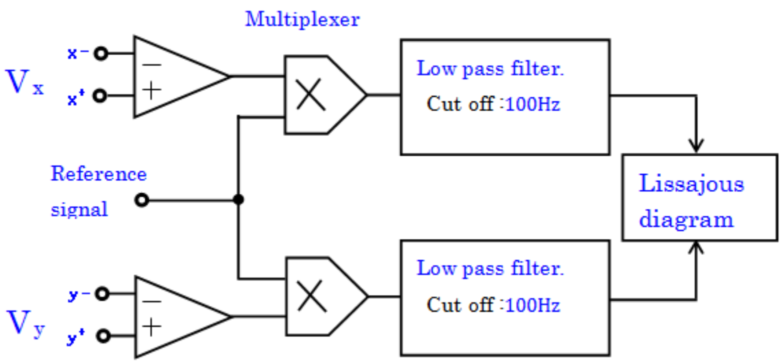


Figure 5. Observation circuit of V_x-V_y Lissajous diagram

4. RESULTS AND DISCUSSION

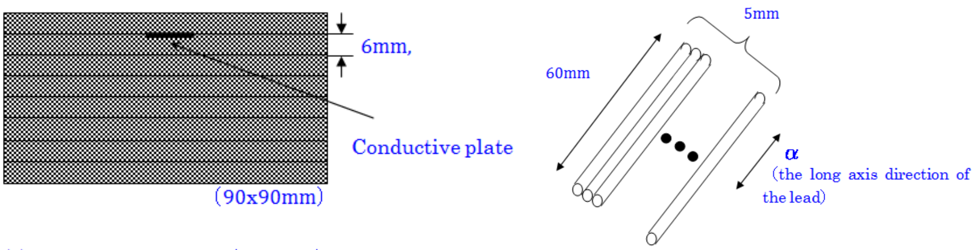
4.1 Phantom Experiment

An isotropic phantom, as shown in Figure 6(a), consists of 8 sheets of 6mm-thick rubber sponge immersed with saline water to yield 100 Ωcm of resistivity, whereas a conductive sheet consisting of ten HB pencil rods of 0.5 mm diameter and 60mm length, sandwiched with isotropic rubber sponges comprise an anisotropic phantom as shown in Figure 6(b). In the measurement, the conductive sheet placed at 6 mm depth was step-wisely rotated by 30-degrees pitch, starting with an initial point that the high conductivity orientation is aligned to A-A’ direction of Figure 2, ends with F-F’ direction. For each of 6 orientations, horizontal and vertical voltage differences were measured and substituted to (4) to yield the output voltage profile dependent on the orientation of the high-conductivity direction as shown in Figure 8. Also, the depth of the conductive sheet was changed as 6, 12, 18 and 36mm depth, and plotted as the function of the high-conductivity direction as shown in Figure 9. In all cases, the output voltage had the minimum value, when the eddy current direction is set at the same direction of high-conductivity orientation in the conducting sheet. For the depth dependence experiment of Figure 9, it is clear that output voltage is maximum at d=6mm and gradually decreased for deeper cases.

In Figure 10 (a)-(c), Lissajous figures are plotted for the case of isotropic phantom, phantom with the conductive plate inserted in direction A-A’ and for the conductive plate inserted in direction D-D’ respectively. As shown in Figure 10(a), in the case of isotropic phantom, the diameter of Lissajous is constant for every current direction, while for the case of (b), it shows minimum radius for A-A’ direction, and in case (c) it took minimum at D-D’ direction; the minimum radius direction agrees with conducting plate insertion direction, while it has maximum radius in the direction perpendicular to the insertion direction. However, for other directions, the current direction does not coincide with that of plate insertion. The reason is explained with the aid of Figure11. Figure 11(a) shows the Lissajous for the case that the conductive sheet with high conductivity along C-C’ direction was inserted at 6mm depth. As shown in this figure, for the assigned direction C-C’ and that for F-F’ which is perpendicular to C-C’, Lissajous indication and the assigned direction agree, while for other directions Lissajous indication does not agree with the assigned direction.

The differential voltage along the direction C-C’, caused by magnet M_3, will be reduced due to the existence of the anisotropic conduction sheet, while the influence of the conductive sheet to the differential voltages along A-A’ and E-E’, produced by magnets M_1 and M_2 respectively, tended to be small to yield orientation of the synthesized eddy current is a little bit small angle, comparing to the A-A’ direction as shown in Figure 11(b); this theoretical result agrees with that of experimentally obtained Lissajous of Figure 11(a).

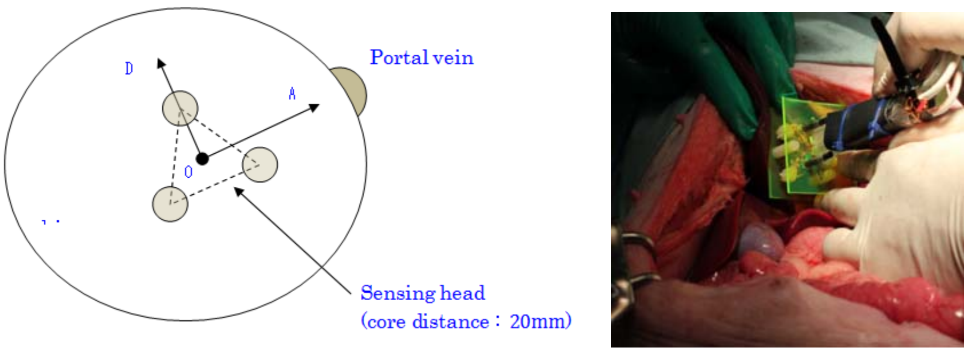
This Lissajous expression facilitates short time measurement of tissue anisotropy, e.g. in the experimental setup, a hundred times of measurement can be done in a second; this allows to make a dynamic observation of swift changes of anisotropy accompanied with pulsatile changes of the blood flow in the artery. Also, this high-speed response of the observation system facilitates to scan over the tissue with a handheld sensor head.



(a) Eight sponge sheets (250Ωcm) soaked in salt solution (100Ωcm)

(b) Conductive plate using ten leads of the eversharp pencil (HB: ϕ=0.5 mm)

Figure 6. Experimental model



(a) Position of the sensing head *(b) Measurement of the liver of pig*

Figure 7. Measurement of the liver of pig

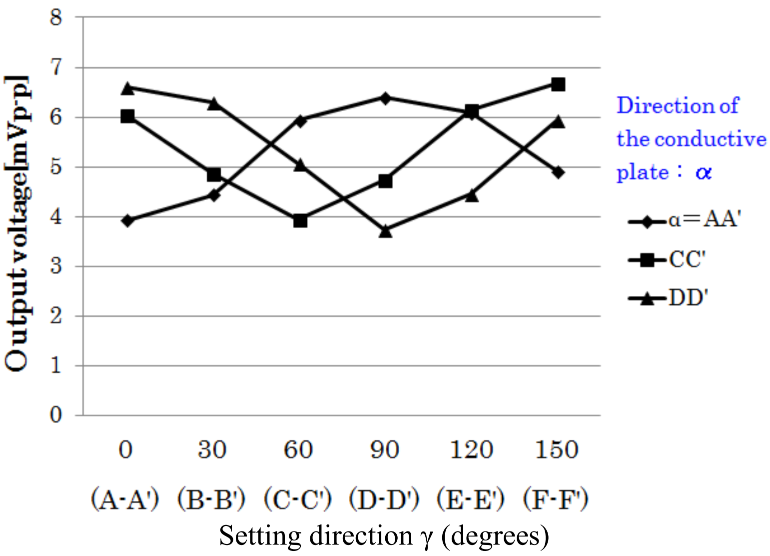


Figure 8. Results of measurements for the model (6 directions) − (inserting depth of the conductive plate: d = 6 mm)

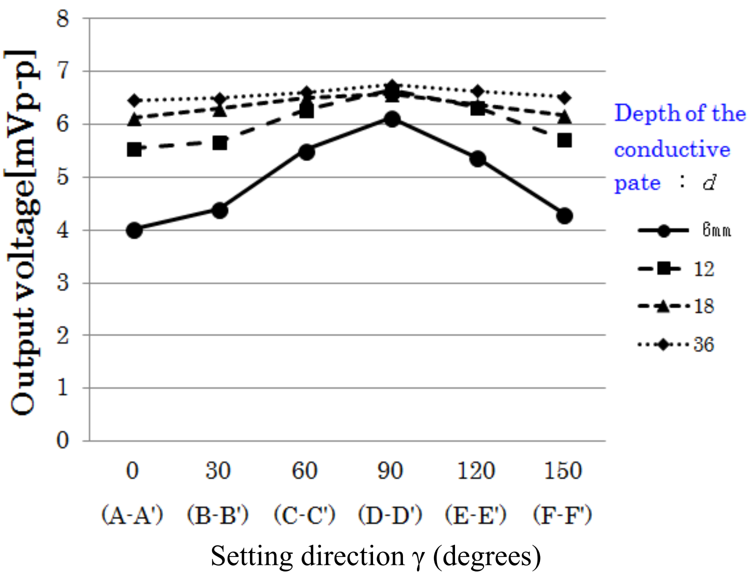


Figure 9. Results of measurements for the model (inserting direction of the conductive plate: A-A')

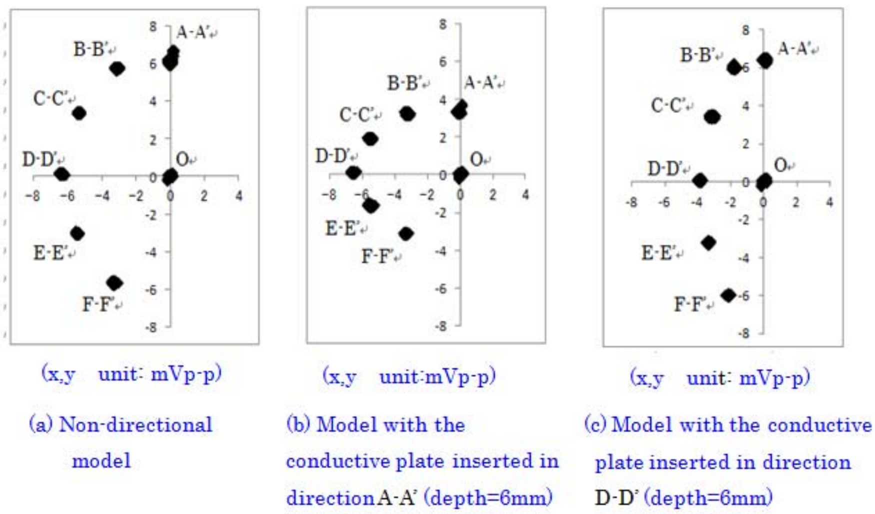


Figure 10. Lissajous figure (x,y unit:mVp-p)

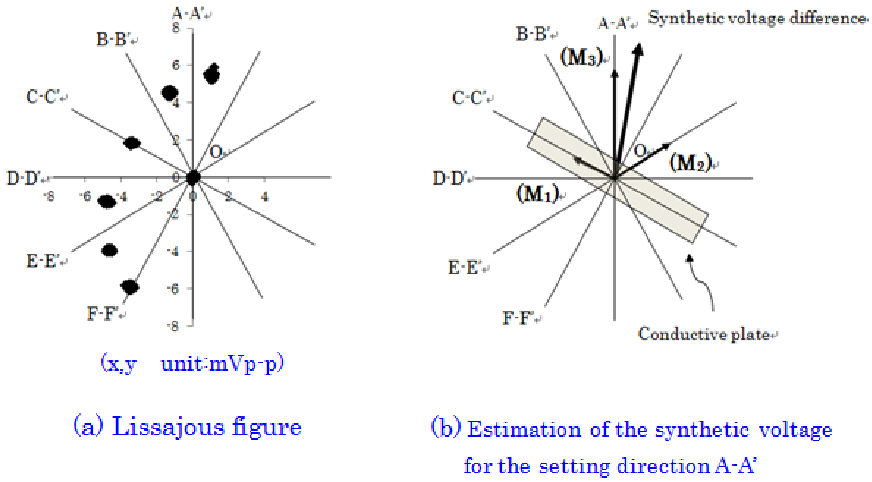


Figure 11. Results of measurements for the model with the conductive plate inserted in the direction C-C' and in the depth of 6mm

4.2. *In vivo* experiment

We have conducted an *in vivo* experiment on an anesthetized pig's liver. The electric impedance of the liver of pig is shown for the direction along with the portal vein, as well as for the perpendicular angle to the direction of the portal vein is shown in Table 2. As shown in the Table, the electrical impedance along with the portal vein is about 20% less than that of orthogonal direction to the body. The differential voltages given by (4) are plotted in Figure 12 as a function of setting directions γ, similarly to the expression of Figure 8. From this plot, it can be recognized that the differential voltage is minimum for near the direction F-F' along with the portal vein, while it becomes maximum for the D-D' which is orthogonal to the vein flow, which is consistent with the one shown in Table 2, obtained by the conventional 4-Electrode method.

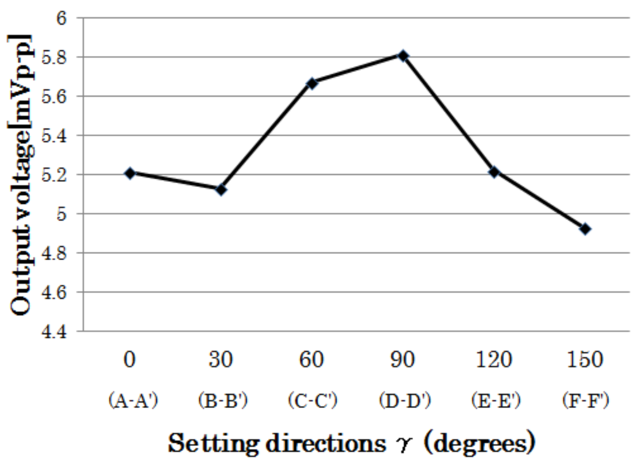


Figure 12. Results of measurement for the liver of pig

Table 2. Electric impedance on the liver of pig

Measurement direction	Mean ± SD (Ω)	Number of determinations
Direction to the portal vein	75.5 ± 11.6	11
Direction at right angle to the direction to the portal vein	77.7 ± 11	11

5. CONCLUSION

We propose a three-phase electromagnetic sensing device for measuring biological anisotropy and the effectiveness is confirmed in the phantom experiment as well as *in vivo* experiment on the pig's liver. In our method, it is not necessary to change the attachment position of the electrodes for changing the measurement direction.

It is possible to make a real-time *in vivo* measurement of tissue anisotropy, just by lightly putting the applicator on the surface of the body. Therefore, during emergent cases in surgical operations, information on the blood vessel orientation in large organs can be obtained. Also, this method may facilitate the evaluation of tumor malignancy in anisotropic part of the body, without using large scale MR observation systems.

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ТРОФАЗНИ ИНДУКТИВНИ СЕНЗОР ЗА *IN VIVO* МЈЕРЕЊЕ ЕЛЕКТРИЧНЕ АНИЗОТРОПИЈЕ БИОЛОШКИХ ТКИВА

Сажетак: Биолошко ткиво ће имати анизотропију електропроводљивости због оријентације мишићних влакана или нервних аксона, као и због распореда великих крвних судова. Тако се *in vivo* мјерење анизотропије електричне проводљивости може употријебити да би се открили дубоко смјештени крвни судови у великим органима, као што је јетра, током операција. У дијагностичке сврхе, смањење анизотропије може указати на постојање карцинома у анизотропским ткивима, као што је бијела твар у мозгу или млијечна жлијезда у дојци.

У овом раду уводимо нову методу трофазне индукције, како бисмо увели ротирајућу високофреквентну електричну струју у ткиво ради мјерења анизотропије електричне проводљивости. Приликом мјерења на површину ткива симетрично се стављају три електромагнета која покреће високофреквентна наизмјенична струја од 50 kHz, модулирана трофазним сигналима од 1 kHz. У централном подручју три магнета, магнетна поља су постављена један изнад другог како би произвела ротирајућу индуктивну струју. Ова струја производи електрични потенцијал међу кружно постављеним електродама које се користе за проналажење проводљивости у сваком смјеру одређеном паровима електрода. Како би се нашле хоризонталне и вертикалне компоненте сигнала, мјерени потенцијали се појачавају помоћу два наизмјенична фазна појачала, фазно затворена, са референтним сигналом од 1 kHz. Струја постављена на ткиво је била типично 45 μA када смо примијенили магнетно поље од 150 μT. Доказали смо да је наша метода ваљана тако што смо спровели *in vitro* мјерења на вјештачки креиране анизотропне материјале као и прелиминарна *in vivo* мјерења на јетри свиње.

У поређењу са дифузионом тензор МРИ методом, наш сензор анизотропије је компактан и његова предност је у томе што може да се користи током хируршких операција будући да за наш метод није потребно јако магнентно поље које може пореметити ток хируршких операција.

Кључне ријечи: анизотропија проводљивости, биолошко ткиво, трофазно магнетно поље, индуктивна струја.