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Research

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Feasibility of *in vivo* Magnetic Induction Tomography in Rabbits

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Abstract

Background: As a non-contact, non-invasive medical imaging technique, magnetic induction tomography (MIT) can measure the conductivity distribution inside the human body. Numerical calculation and physical phantom tests have showed the accuracy of MIT in principle. However, very few human studies have limited the development and application. At the key stage before clinical trials, animal experiment will be an effective method to verify the feasibility of *in vivo* detection the conductivity variation inside of biological body.

Methods: An abdominal subcutaneous injection rabbit model was used to simulate the local conductivity perturbation by injecting a 0.9% NaCl solution along with *in vitro* heparinized blood step by step. An insulated and sliding operation console was built to carry out the animal tests. An improved 16-channel MIT data acquisition system was used to record the data at 13.56 MHz and 4 seconds per frame. A series of time-difference reconstructed images, relative to non-injection, were obtained by the regularized Newton-Raphson algorithm for every 3 mL of injection.

Results: 15 rabbits were divided by two groups. Six rabbits were injected with 0.9% NaCl solution and nine rabbits were injected with the *in vitro* heparinized blood. The target with an increased conductivity distribution can clearly be observed in all the reconstructed images. The maximum target value in each image increased with the injection dosage. The slopes of the regressive line for the mean of maximum target value in two groups were statistically different.

Conclusion: Local conductivity perturbation inside of the rabbits is able to be reconstructed. The position and conductivity difference relative to the surrounding tissue of the target can be reflected correctly. This preliminary rabbit test shows the feasibility of the *in vivo* application for MIT and will be the basis for further animal tests and clinical trials in the future.

Keywords: magnetic induction tomography, rabbit model, *in vivo* experiment, difference imaging

Background

Magnetic induction tomography (MIT) is a potential medical imaging method that can reconstruct the conductivity distribution of the subject by using eddy current responses with a contactless coil array [1-3]. The expected applications of MIT are mostly focused on edema and hemorrhages [4-6].

After performing several numerical simulations and physical phantom experiments [7-9], some experiments that involve biological species have been published. Brunner *et al.* reconstructed a series of images of a potato immersed in saline solution using a frequency-differential algorithm [10].

Maimaitijiang *et al.* obtained the images of an artificial peripheral hemorrhage cerebral stroke by inserting 10 mL of *in vitro* heparinized blood in a pig's intestine [11]. In these two studies, there is a big difference between the *in vivo* condition and its phantom. Watson *et al.* obtained *in vivo* conductivity and permittivity images, without an internal structure, of the human thigh [12].

Two types of techniques are used for detecting the conductivity of humans or animals when applying the eddy current response, in addition to MIT. The first technique is the magnetic induction phase shift (MIPS) and the second technique is volumetric impedance phase shift spectroscopy (VIPS). MIPS is used to detect the phase shift of the induced magnetic flux density from the excited flux density. This is achieved by one excitation coil and one detection coil, which denotes the average conductivity of the subject. Pan *et al.* obtained the MIPS curve with the injected autologous blood volumes in a rabbit brain [13]. Li *et al.* obtained the MIPS curve with time using epidural freeze-induced rabbit cerebral edema models [14]. VIPS is able to differentiate a severe stroke from minor strokes by applying bioimpedance asymmetry scores for the human brain. This is accomplished by using three coils, two transmitting coils placed on both sides of the back of the head and one receiving coil placed on the forehead, with varying frequencies for low energy radio waves [15]. Even though there were no images, these studies demonstrate the feasibility of magnetic induction for *in vivo* detection.

This investigation reconstructs a series of conductivity distribution images by performing an abdominal subcutaneous injection in rabbits using an improved MIT data acquisition system. The injected liquids consisted of 0.9% NaCl solution and *in vitro* heparinized blood, respectively. The dosage of injection increased several times using a volume of 3 mL. Besides the time-difference images, the trends of the reconstructed values of the object were analyzed.

Results

In this experiment, 15 rabbits were divided by two groups according to the statistical requirements. Six rabbits were injected with 0.9% NaCl solution. These rabbits were referred to as the NaCl solution group. Nine rabbits were injected with the *in vitro* heparinized blood. These rabbits were referred to as the blood group.

Reconstructed images of injection experiment

Before injecting any liquid, several measured data frames were obtained. One of the data frames before injection was set as a background data frame. Then, 3 mL of 0.9% NaCl solution was injected into the rabbit. A series of continuous measurement data frames were obtained; this generally consisted of more than 10 frames. One of the data frames after injecting 3 mL of liquid was used as the foreground data frame. Using equation (1), the conductivity change image was reconstructed as shown in Fig. 1. A red region indicates increased conductivity, green signifies that the conductivity is unchanged, and a blue region indicates that the conductivity has decreased. These colors are based on the maximum and minimum values of the reconstructed image. In Fig. 1, a red region near the No. 10 to No. 11 coils was observed. This corresponds with the 3 mL liquid injection because the conductivity of the 0.9% NaCl solution and the *in vitro* heparinized blood are higher than the skin. For all of the rabbits, similar images were reconstructed whether injecting 0.9% NaCl solution or *in vitro* heparinized blood.

This process was repeated for 10 injections with the 3 mL 0.9% NaCl solution unless if the rabbit died. In order to observe the varying process of the conductivity distribution in the reconstructed images, a reconstructed image was selected for every 3 mL injection. All of the images displayed based on the maximum and minimum values of the final image as shown in Fig. 2. For all of the rabbits, similar continuous images were reconstructed whether injecting 0.9% NaCl solution or *in vitro* heparinized blood.

Data analysis of the two groups of rabbits

From Fig. 1 and 2, the injected liquid, called the target, showed an increase in the local conductivity region in the reconstructed images. Each image was linearly interpolated from finite element triangular meshes. The maximum of the target triangular elements was selected as the expression of the target, which is the maximum target value. The first 10 frames, or all frames if the number of frames was less than 10, for each injection were used to reconstruct the difference images. The maximum target values

for each injection were used to observe the varying trends of the target. All of the maximum target values were normalized by the mean of the first 3 mL injected for the 15 rabbits. Fig. 3 and 4 illustrate the plots of the maximum target value with the data frame index of the 0.9% NaCl group and the *in vitro* heparinized blood, respectively. Fig. 5 depicts the mean in each group and its regressive line.

Using IBM SPSS Statistics 23 software, the equations for the regressive lines of the two groups were determined as follows:

0.9% NaCl solution group: $y = 0.099x + 0.794$, $r = 0.988$, $p < 0.001$.

Blood group: $y = 0.078x + 0.703$, $r = 0.991$, $p < 0.001$.

where r is the regression coefficient and p is the probability.

The results of the covariance analysis demonstrated that the slopes of the two regressive lines were statistically different ($p < 0.001$).

Discussion

The aim of using the abdominal subcutaneous injection rabbit model is to obtain the local conductivity perturbation target. One advantage of this model is that it is easy to specify the location of the target. Another advantage is that it is convenient to set the conductivity of the injected liquid. If the liquid is injected into the abdominal cavity, it is likely to spread. Therefore, it is difficult to obtain the local conductivity perturbation target.

The conductivity of the blood and skin at 13.56 MHz is about 1.12 S/m and 0.38 S/m [16], respectively, and that of the 0.9% NaCl solution is about 1.26 S/m [2]. For all of the abdominal subcutaneous injection rabbits, whether injecting 0.9% NaCl solution or the *in vitro* heparinized blood, the increased conductivity target was observed in the time-difference reconstructed images. Moreover, the size and the reconstructed value of the target in the time-difference images increased with an increase in the dosage of the liquid.

The plots of the maximum target value with the measured frame index expressed a strongly positive correlation. The regression coefficients of the regressive line of the mean of the maximum target value in the two groups are more than 0.98. In particular, the slopes of the regressive lines are statistically different. This may be due to the conductivity difference of the 0.9% NaCl solution and the blood.

Compared with a physical phantom experiment, the animal model experiment displays significant volatility. For the same rabbit, the plot of the maximum target value sometimes went up and then went down. This might be due to the random shaking of the rabbit or accidental external interference. On the

other hand, the plot sometimes remained stable and sometimes it rose. This might be related to the rabbit's strong or weak physiological activities (e.g. respiration). When the anesthesia is deeper, the curve is more stable. For a different rabbit in the same group, the standard deviation (SD) of the mean of the maximum target value is large. This could be attributed to the individual differences in the injection location, liquid distribution shape, rabbit size, weight, along with many other factors. However, the absolute value of the SD increases with an increase in the mean. The ratio between the mean and SD is relatively stable. The mean of the ratio for the SD/mean is 23% for the 0.9% NaCl solution group and 35% for the blood group, respectively.

Conclusion

To verify the feasibility of *in vivo* magnetic induction tomography, we conducted an abdominal subcutaneous injection animal test for 15 rabbits. These rabbits were divided into two groups: a 0.9% NaCl solution group and an *in vitro* heparinized blood group. This was achieved by using an improved data acquisition system and a time-difference reconstructed algorithm. In the reconstructed images, the conductivity perturbation target was observed. Moreover, the increasing trend of the target in the images, for the same rabbit, was related to the injection dosage. The data analysis of the maximum target value further verified this relationship. By contrast, the slope of the regressive line of the mean maximum target value may reflect the conductivity difference of the injected liquid. This preliminary animal test will be the basis for further animal tests or clinical trials in the future. Additionally, we intend to develop a non-local conductivity perturbation target, such as an abdomen cavity bleeding animal model. Moreover, the feasibility of detecting the deep body conductivity perturbation target also needs to be considered.

Methods

MIT System

The data was obtained by using an improved FMMU MIT data acquisition system as shown in Fig. 6. In comparison to the original system [9], there were three changes. First, the coil array consisted of 16 coils, whose centers were located on one circle 20 cm in diameter with equal angles. All of the coils are the same with 13 turns, an inner diameter of 18 mm, and an outer diameter of 22 mm. Every coil was multiplexed as an excitation coil or a receiver coil and was controlled by a circuit. Second, the time for data acquisition for one frame was about 4 s. This is significantly less than the original time of 1 min. Third, the supported cylinder was hollow. It was convenient to place the subject in the region surrounded by the coil array. All of the supports were insulated and the excitation frequency was set to 13.56 MHz.

Fig. 6 Improved FMMU MIT data acquisition system.

In order to evaluate the long term performance of the improved data acquisition system during the expected test period, continuous data frames without any subject in the coil array were measured using this system for one hour. Then, the coefficients of variation of each excitation coil and receiver coil combination except the same coil were calculated as shown in Fig. 7.

Fig. 7 Coefficient of variation of each excitation coil and receiver coil combination except the same coil.

Reconstruction algorithm

The time-difference regularized Newton–Raphson algorithm was adopted to reconstruct the conductivity distribution variation [9]. The conductivity change between the foreground and the background data frame can be expressed as:

$$\Delta\sigma_{21} = -H^{-1}J^T(V_{m1} - V_{m2}) \quad (1)$$

where H is the Hessian matrix; J is the Jacobian matrix; -1 is the inverse of the matrix; T is the transpose of the matrix; V_{m1} is the background data frame; and V_{m2} is the foreground data frame.

The eigenvalue threshold method (ETM) is used to regularize the Hessian matrix. The conditional number of the Hessian matrix was set to $ec=1.0\times 10^{-10}$.

During the continuous data acquisition process, the background data frame remained the same and the foreground data frame changed over time. The reconstructed images consisted of a series of images that displayed the difference in the conductivity distribution relative to the background data frame.

Rabbit model and console

An abdominal subcutaneous injection rabbit model was used to simulate the accumulating process. The subjects used in this experiment were healthy adult rabbits with a mass of 2.0 - 2.5 kg. These rabbits were provided by the animal experiment center of the FMMU. The animal experiment was approved by the ethics committee of the FMMU.

First, the rabbits were anesthetized with 3.5% pentobarbital (1 mL/kg dosage) by performing an ear vein injection. Then, the rabbit was put on the sliding plate while lying sideways. Next, an indwelling needle for the intravenous injection was inserted into the abdominal subcutaneous of the rabbit. Afterwards, the metallic portion of the needle was pulled out and the insulation part of the needle remained in the abdominal subcutaneous of the rabbit. Next, an infusion pipe was connected to the indwelling needle and a syringe was connected to the pipe. The needle and pipe were fixed to the rabbit using medical adhesive tape as shown in Fig. 8. Third, the rabbit slid until the indwelling needle located at the cross-section of the MIT coil array as shown in Fig. 9.

Fig. 8 Demo of the rabbit model before injection.

Fig. 9 Demo of the rabbit model inside the MIT coil array.

Fig. 10 Demo of the rabbit model after injection.

Two types of liquids were injected into the abdominal subcutaneous of the rabbit. These included the 0.9% NaCl solution and the *in vitro* heparinized blood from another rabbit. Before performing the injection, the liquid was heated to the rabbit's temperature by using a thermostatic water bath. Afterwards, the liquid was inhaled into the syringe. While carefully following the scale of the syringe, the dosage of the injection was controlled. In this experiment, each injection dosage was 3 mL. After several injections, an abdominal bulge in the rabbit was observed as shown in Fig. 10.

Abbreviations

MIT: magnetic induction tomography; MIPS: magnetic induction phase shift; VIPS: volumetric impedance phase shift spectroscopy; SD: standard deviation; ETM: eigenvalue threshold method.

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Authors' contributions

RGL contributed to the drafting and editing of this document. QHC designed experiments and completed the experimental data acquisition. RSL and CW contributed the reconstructed algorithm. All authors read and approved the final manuscript.

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Availability of data and materials

The authors agree to make all published data available.

Ethics approval and consent to participate

The animal experiment in the conducted research is approved by the ethics committee of the FMMU.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

Fig. 1 Reconstructed image of one rabbit after injecting 3 mL of 0.9% NaCl solution.

Figure 2

Reconstructed image of one rabbit after injecting 3 mL of 0.9% NaCl solution.

Figure 4

Continuous reconstructed images of one rabbit after 10 injections with 3 mL of 0.9% NaCl. **a** 3mL; **b** 6mL; **c** 9mL; **d** 12mL; **e** 15mL; **f** 18mL; **g** 21mL; **h** 24mL; **i** 27mL; **j** 3mL

Fig. 3 Maximum target value of the 0.9% NaCl group.

Figure 6

Maximum target value of the 0.9% NaCl group.

Fig. 4 Maximum target value of the blood group.

Figure 8

Maximum target value of the blood group.

Fig 5 Mean and linear regression lines of the two groups.

Figure 10

Mean and linear regression lines of the two groups.

Fig. 6 Improved FMMU MIT data acquisition system.

Figure 12

Improved FMMU MIT data acquisition system.

Fig. 7 Coefficient of variation of each excitation coil and receiver coil combination except the same coil.

Figure 14

Coefficient of variation of each excitation coil and receiver coil combination except the same coil.

Fig. 8 Demo of the rabbit model before injection.

Figure 16

Demo of the rabbit model before injection. Fig. 9

Fig. 9 Demo of the rabbit model inside the MIT coil array.

Figure 18

Demo of the rabbit model inside the MIT coil array.

Fig. 10 Demo of the rabbit model after injection.

Figure 20

Demo of the rabbit model after injection.