Inverse Problems in Medical Imaging: Electromagnetic and Mechanical Property Imaging

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ABSTRACT

Last two decades, much researches in biomedical imaging area deal with electromagnetic or mechanical property imaging instead of anatomical imaging since they manifest structural and pathological conditions of the tissue providing valuable diagnostic information. The corresponding objectives are in visualizing cross-sectional image reconstructions of admittivity, susceptibility, shear modulus distributions inside the human body. These electromagnetic or mechanical property imaging modalities belong to interdisciplinary research areas incorporating mathematical theories (PDEs, harmonic analysis, micro-local analysis), inverse problems and image reconstruction algorithms, image processing (denoising, segmentation, compressed sensing), numerical analysis and error estimates, MR physics and experimental techniques. To achieve these objectives, we need to set up a mathematical framework using the constitutive relation, related physical principles (electromagnetism, elasticity), and available measurement techniques, and it must be taken into account the well-posedness (uniqueness, existence, stability) and uncertainties in boundary conditions and material characterizations. It is often necessary to make various simplifications of reality with sacrificing physical details so that the simplified model is manageable and holds key information to be aimed. In this talk, we discuss these subjects from its mathematical framework to most recent outcomes. We present future directions and challenging issues in mathematics.

1 INTRODUCTION

Computerized tomography (CT) and magnetic resonance imaging (MRI) are the well established medical imaging technologies providing three dimensional detailed images of anatomical structures of the body in which computer based mathematical methods are used for image reconstructions. Lately, much researches in biomedical imaging deal with a new imaging techniques providing knowledge of physiologic functions and pathological conditions instead of anatomical image. Electromagnetic or mechanical property imaging are one of such attempts since they reveal physiological and pathological conditions of body tissues and organs. Over the past decade, there has been marked progress in magnetic resonance(MR)-based electromagnetic or mechanical property imaging techniques where cross-sectional image reconstructions of admittivity, susceptibility, shear modulus distributions inside the human body are pursued.

At the frequency range of tens of Hz to several hundred MHz, the electrical properties of a biological tissue change with ion concentrations in extra- and intra-cellular fluids, cellular structure and density, molecular composition, membrane characteristics, and other factors. Indeed, cell membranes separating intracellular and extracellular fluid compartments behave as capacitors when exposed a sinusoidal current, while extracellular space and body fat
behave as resistors. Consequently, they reflect structural, functional and pathological conditions of the tissue and can provide valuable diagnostic information. Hence, cross-sectional imaging of electrical conductivity and permittivity distributions within the human body has been an important research topic in the field of medical imaging. Electrical property imaging technique includes EIT(electrical impedance tomography), MREIT(magnetic resonance EIT), MREPT(MR-electrical property tomography), MIT(magnetic induction tomography), micro-EIT, and so on. [2,13,1,7]

Evaluating mechanical property of tissue such as tissue stiffness by touch palpation is old clinical skill. Very recently, GE healthcare commercialized MR elastography(MRE) as a visual palpation technology that uses low frequency sound waves in combination with MRI to measure tissue elasticity. Richard Ehman who is the team leader of MR elastography Lab. at Mayo clinic said “Today we know that abnormal tissue stiffness can actually be a cause of some disease processes. However, many regions of the body are not accessible to palpation and conventional diagnostic imaging technologies do not allow physicians to assess tissue stiffness. The introduction of MRE is important as it will also allow physicians to explore new applications diagnostic imaging technology.” MRE is based on the fact that tissue stiffness is closely related to the velocity of wave, and the shear modulus (or modulus of rigidity) varies over a wide range differentiating various pathological states of tissues. Hence, the speed of the harmonic elastic wave provides quantitative information for describing malignant tissues that typically are known to be much stiffer than normal tissues. For MRE, we refer to [10,8] and reference therein.

The corresponding objectives are the followings: (1)Electrical property imaging aims to visualize the distribution of the admittivity \( \sigma(\mathbf{r}) + i\omega\epsilon(\mathbf{r}) \) which depends on position \( \mathbf{r} = (x, y, z) \) and angular frequency. (2) Mechanical property imaging aims to visualize shear modulus \( \mu(\mathbf{r}) \) (or Young modulus). To achieve these objectives, we need to set up the mathematical models using the constitutive relation, related physical principles, and available measurement techniques. When we set up a mathematical modeling for solving inverse problems, we should take account of well-posedness that was given by Hadamard. He believed that mathematical models, which transform a physical concept into a collection of mathematical expressions and data, should have the three properties: (i) Existence-at least one solution exists. (ii)Uniqueness-only one solution exists. (iii) Stability-solution depends continuously on the data. Taking into account the well-posedness and uncertainties in boundary conditions and material characterizations, we try to make various simplifications of reality with sacrificing physical details so that the simplified model is manageable and holds key information to be aimed.

Theoretical and technical progress in these medical imaging area requires a kind of unified
approach involving mathematical modeling and analysis, numerical analysis, algorithm development, experimental mathematics (validation), software implementation and program execution, and visualization of results with human experiments. This lecture includes the followings:

(1) Understanding underline physical phenomena. (2) Mathematical formulation of forward problems in such a way that we can deal with them systematically and quantitatively. (3) Data collection method-Practical limitations associated with measurement sensitivity and specificity, noise, artifact, interface between target object and instrument, data acquisition time. (4) Mathematical analysis explaining any interrelation between those qualities and measurable data. (5) Image reconstruction formula and sensitivity analysis. (5) Numerical implementation and human experiments. (6) Challenging problems and future research directions.

2 MATHEMATICAL FRAMEWORK

Electrical Property Imaging. Let the object to be imaged occupy a three-dimensional bounded domain $\Omega \subset \mathbb{R}^3$ with a smooth boundary $\partial \Omega$. For electrical property imaging, we should use Ohm’s law to evaluate the admittivity $\gamma(r) := \sigma(r) + i \omega \varepsilon(r)$:

$$
\mathbf{J}(r) = (\sigma(r) + i \omega \varepsilon(r)) \mathbf{E}(r) \quad (r \in \Omega)
$$

where $\mathbf{J}(r)$ and $\mathbf{E}(r)$ are time-harmonic electrical current density and electric field, respectively. The physical basis for electrical Property Imaging are

$$
\nabla \cdot (\gamma(r) \mathbf{E}(r)) = 0 \quad \text{in} \quad \Omega \tag{1}
$$

and

$$
-\nabla^2 \mathbf{H} = \frac{\nabla \gamma}{\gamma} \times (\nabla \times \mathbf{H}) - i \omega \mu_0 \gamma \mathbf{H} \quad \text{in} \quad \Omega. \tag{2}
$$

In order to simplify the problem, we will assume that the admittivity distribution $\gamma$ in $\Omega$ is isotropic.

- EIT uses surface electrodes attached on $\partial \Omega$ to inject a sinusoidal current (Neumann data) and measure the corresponding boundary voltage. The corresponding inverse problem is to recover $\sigma(r) + i \omega \varepsilon(r)$ from a set of current-to-voltage data, a rough knowledge of discrete NtD (Neumann-to-Dirichlet) data. In $L$-channel EIT system, we attach surface electrodes $\mathcal{E}_j$ for $j = 1, \cdots, L$ on $\partial \Omega$ and inject constant current of $I$ mA at an angular frequency of $\omega$ through an adjacent pair of electrodes. Assuming that the current source and sink are connected to electrodes $\mathcal{E}_j$ and $\mathcal{E}_{j-1}$, respectively, the resulting time-harmonic voltage, denoted by $u^{j,\omega}$, satisfies

$$
\begin{aligned}
\nabla \cdot (\gamma \omega \nabla u^{j,\omega}) &= 0 \quad \text{in} \quad \Omega \\
(u^{j,\omega} + z_k \gamma \omega \frac{\partial u^{j,\omega}}{\partial n})|_{\mathcal{E}_k} &= U^{j,\omega}_k, \quad k = 1, \cdots, L \\
\gamma \omega \frac{\partial u^{j,\omega}}{\partial n} &= 0 \quad \text{on} \quad \partial \Omega \setminus \bigcup_{k=1}^L \mathcal{E}_k \\
\int_{\mathcal{E}_k} \gamma \omega \frac{\partial u^{j,\omega}}{\partial n} \, ds &= I - \int_{\mathcal{E}_{j-1}} \gamma \omega \frac{\partial u^{j,\omega}}{\partial n} \, ds \\
\int_{\mathcal{E}_j} \gamma \omega \frac{\partial u^{j,\omega}}{\partial n} \, ds &= I - \int_{\mathcal{E}_{j-1}} \gamma \omega \frac{\partial u^{j,\omega}}{\partial n} \, ds
\end{aligned} \tag{3}
$$

where $z_k$ is the contact impedance of the $k$th electrode $\mathcal{E}_k$, $U^{j,\omega}_k$ is the potential on $\mathcal{E}_j$, $n$ is the outward unit normal vector on $\partial \Omega$ and $\gamma \omega = \sigma(r, \omega) + i \omega \varepsilon(r, \omega)$ is the complex conductivity which depends on the position $r = (x, y, z)$ and $\omega$. Setting a reference voltage having $\sum_{k=1}^L U_k^{j,\omega} = 0$, we can obtain a unique solution $u^{j,\omega}$ of (3)[18].
We assume that we have measured the boundary voltage \( f^j,\omega := \left(U^1_{j,\omega}, U^2_{j,\omega} - U^1_{j,\omega}, \ldots, U^j_{L,\omega} - U^j_{L-1,\omega}\right) \in \mathbb{C}^L \) where \( \mathbb{C} \) is the set of the complex number. Using the \( L\)-channel EIT system, we may inject \( L \) number of currents through adjacent pairs of electrodes and measure the following voltage data set:

\[
f_\omega = \left(f^1,\omega, f^2,\omega, \ldots, f^L,\omega\right) \in \mathbb{C}^L \times \mathbb{C}^L \times \cdots \times \mathbb{C}^L = \mathbb{C}^{L \times L}.
\]

The voltage data \( f^k,\omega(k - 1), f^k,\omega(k), f^k,\omega(k + 1) \) are influenced by the contact impedance whose value is unknown. From the reciprocity principle, \( f^k,\omega(j) = f^j,\omega(k) \). Therefore, using this kind of data collection scheme, \( f_\omega \) contains at most \( \frac{L(L-3)}{2} \) number of independent data, which becomes the maximum degree of freedom in the conductivity imaging problem. The inverse problem is to visualize \( \gamma \) by using the voltage data sets \( f_\omega \).

The amount of information in the measured NtD data is limited by the number of electrodes that is usually from 8 to 32. In practice, a cumbersome procedure to attach many electrodes is prone to increase measurement errors in addition to electronic noise and various systematic artifacts. Within a reasonable amount of cost and practical applicability, there always exist uncertainties in terms of electrode positions and boundary shape of the imaging subject. Due to the ill-posed nature of the inverse problem, it seems that measurable information is insufficient for robust reconstructions of high-resolution conductivity images in spite of novel theoretical results guaranteeing a unique identification of \( \sigma \) from the NtD data \([2,13,1,7]\). EIT has several merits such as its portability and high temporal resolution even though its spatial resolution is poor. Noting that common errors may cancel out each other by a data subtraction method, time-difference EIT imaging has shown its potential in clinical applications where monitoring temporal changes of a conductivity distribution is needed \([11,3,5]\). Frequency-difference EIT imaging can detect an anomaly such as bleeding and stroke in the brain and tumor tissue in the breast \([15]\).

- **MREIT** uses a pair of surface electrodes to inject low-frequency currents below a few kHz to induce extra \( B \), whose \( z\)-components are measured from MR phase images using an MRI scanner with its main field in the \( z \)-direction. The corresponding inverse problem is to recover \( \sigma(r) \) from the measured internal \( B_z \) data and the physical relation between \( \sigma \) and \( B_z \).

In 2001, a constructive \( B_z \)-based MREIT algorithm \([14]\) called the harmonic \( B_z \) algorithm was developed and its numerical simulations showed that high-resolution conductivity image reconstructions are possible. The harmonic \( B_z \) algorithm is to invert the map \( \Lambda : C^1_+ (\Omega) \rightarrow H^1(\Omega) \times H^1(\Omega) \times \mathbb{R} \) by

\[
\Lambda[\sigma](r) = \left(\frac{\omega}{4\pi} \int_{\Omega} \frac{(r-r') \cdot \sigma \nabla u_1[\sigma](r') \times \hat{z}}{|r-r'|^3} \, dr' \right) \quad r \in \Omega.
\]

where \( u_j[\sigma] \) is a solution of the following boundary value problem:

\[
\begin{aligned}
\nabla \cdot (\sigma \nabla u_j[\sigma]) &= 0 \quad \text{in} \Omega \\
I_j = \int_{\partial \Omega_j} \sigma \frac{\partial u_j[\sigma]}{\partial n} \, ds &= - \int_{\partial \Omega_j} \sigma \frac{\partial u_j[\sigma]}{\partial n} \, ds \\
\nabla u_j[\sigma] \times \hat{n} &= 0 \quad \text{on} \ \partial \Omega_j \cap \mathcal{E}_j^+ \\
\sigma \frac{\partial u_j[\sigma]}{\partial n} &= 0 \quad \text{on} \ \partial \Omega \setminus \bigcup_{j=1}^J (\mathcal{E}_j^- \cup \mathcal{E}_j^+).
\end{aligned}
\]

This novel algorithm is based on the key observation that the Laplacian \( \Delta B_z \) probes changes in log of the conductivity distribution along any equipotential curve having its tangent to the
Figure 2. Multi-slice MR magnitude images and MREIT images of a canine head (left). Multi-frequency EIT image using KHU Mark 1 (right).

vector field $\mathbf{J} \times (0, 0, 1)$ where $\mathbf{J} = (J_x, J_y, J_z)$ is the induced current density vector. Since then, imaging techniques in MREIT have been advanced rapidly and now reached the stage of in vivo animal and human experiments.

Future studies should overcome a few technical barriers to advance the method to the stage of routine clinical uses. The biggest hurdle at present is the amount of injection current that may stimulate muscle and nerve. Reducing it down to a level that does not produce undesirable side effects is the key to the success of this new bio-imaging modality. This demands innovative data processing methods based on rigorous mathematical analysis as well as improved measurement techniques to maximize SNRs for a given data collection time.

- **MREPT** utilizes $B_1$ maps that are influenced by the admittivity[4]. MREPT is fully compatible with a clinical MRI scanner without requiring any added hardware and provides admittivity images at only the Larmor frequency. Currently available practical MREPT methods [6] require an assumption of a locally homogeneous conductivity: Neglecting the term $\nabla \left( \sigma + i\omega\varepsilon \right) \times (\nabla \times \mathbf{H})$, we can extract an absolute admittivity from the relation

$$\nabla^2 \mathbf{H} \approx i\omega \mu_0 (\sigma + i\omega\varepsilon) \mathbf{H}. \quad (6)$$

Then, $\sigma + i\omega\varepsilon$ can be estimated by

$$\sigma(\mathbf{r}) + i\omega\varepsilon(\mathbf{r}) \approx \frac{\nabla^2 H_x(\mathbf{r})}{i\omega \mu_0 H_x(\mathbf{r})} \approx \frac{\nabla^2 H_y(\mathbf{r})}{i\omega \mu_0 H_y(\mathbf{r})}. \quad (7)$$

Most MREPT methods presently use only the positive rotating magnetic field $H^+ = \frac{1}{2}(H_x + iH_y)$ to compute the right side of (7) since the negative rotating magnetic field $H^-$ is not available at present. MREIT provides conductivity images at frequencies below a few kHz whereas MREPT produces both conductivity and permittivity images at the Larmor frequency which is about 128 MHz at 3 T, for example.

**Magnetic Resonance Elastography.** In order to produce harmonic mechanical displacements inside an elastic object to be imaged, we apply a time-harmonic excitation at a frequency $\frac{\omega}{2\pi}$ in the $50 \sim 200$Hz range through the surface of the object. Then, the induced internal time-harmonic displacement vector $\mathbf{u}$ is dictated by the following elasticity equation:

$$\nabla \cdot (\mu(\nabla \mathbf{u} + \nabla \mathbf{u}^t)) + \nabla (\lambda \nabla \cdot \mathbf{u}) + \omega^2 \rho \mathbf{u} = 0 \quad (8)$$

where $\nabla \mathbf{u}^t$ denotes the transpose of the matrix $\nabla \mathbf{u}$, the real part $\Re(\mu)$ the shear modulus with $\Re(\mu) = \frac{E}{2(1+\sigma)}$, $\Re(\lambda)$ the Lamé coefficient with $\Re(\lambda) = \frac{\sigma E}{(1-2\sigma)(1+\sigma)}$, $\rho$ the density of the mate-
Figure 3. In vivo human liver experiment results using MRE: MR image, displacement, reconstructed shear modulus images.

\[ \Im(\mu) \text{ the shear viscosity accounting for attenuation within the medium, and } \Im(\lambda) \text{ the viscosity of the compressible wave. Here, } E \text{ is Young’s modulus and } \sigma \text{ Poisson’s ratio. Although most of human tissue exhibit anisotropic, we assume that all elastic constants are isotropic in order to simplify the underlying problem. The most common algorithm in MRE would be the direct inversion method [12] which requires the locally homogeneous assumption on } \mu: \]

\[ \mu = \frac{\omega^2 \rho \ u}{\nabla^2 u} \quad (9) \]

Recently, Kwon et al [8,9] proposed the following hybrid one-step inversion formula

\[ \mu(r) = \mu^*(r) + \mu^{**}(r) = \frac{\nabla f(r) \cdot \nabla \bar{u}(r)}{\left| \nabla u(r) \right|^2} + \frac{\nabla \times W_h(r) \cdot \nabla \bar{u}(r)}{\left| \nabla u(r) \right|^2} \quad (10) \]

where

\[ W_h(r) = \int_{\Omega} \nabla \Phi(r - r') \times (\mu^*(r') + \bar{\mu}_d(r')) \nabla u(r') \, dr' \quad \text{ for } r \in \Omega \quad (11) \]

The hybrid one-step algorithm based on theoretical analysis: \( \mu^* \) reflecting \( \nabla \mu \cdot \nabla u \) and \( \mu_d \) reflecting \( \nabla \mu \times \nabla u \) play complementary non-overlapping roles. The hybrid method recovers the shear modulus \( \mu \) by decomposing it into two components: one is for capturing the main feature of \( \mu \) using a relatively noise-insensitive inversion method and the other is to correct the residual caused by the quantity \( \nabla \mu \times \nabla u \). Numerical simulations show that the proposed method significantly improves reconstructions without requiring boundary conditions.

In our future studies, we plan to investigate a stable algorithm to reconstruct anisotropic Lamé parameters without incompressibility assumptions.

REFERENCES


*Because of 6-page limitation, this article does not cite many important references and various key issues are skipped.*