NONINVASIVE IMAGING FOR TISSUE CHARACTERIZATION AND HYPERTHERMIA THERMOMETRY

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ABSTRACT. We extend volume-integral eddy-current models that have been developed for conventional nondestructive evaluation (NDE) to tissue characterization and hyperthermia thermometry. Hyperthermia is a method of cancer treatment in which the tumor is selectively heated electromagnetically relative to the surrounding tissue. The problem is to noninvasively measure the temperature of the tumor, so that the treatment can be properly handled. In past research we have reported on inverse methods in eddy-current NDE, and we demonstrate how these inversion algorithms can be applied to solve this problem.

INTRODUCTION

Heating cancer tumors facilitates their treatment by conventional means. The treatment of tumors by raising their temperatures in called hyperthermia, and can be accomplished by using microwaves if the antennas in Figure 1 are excited with such phases and amplitudes that the resulting field is focused within the body. This allows selected regions of the body to be heated (at least more than the surrounding tissue).

As part of the planning stage for hyperthermia, the patient is scanned by a CT system, which produces a very precise map of his innards, with a resolution of fractions of a millimeter. Thus, the location of the tumor is precisely known, which then allows a precise computation of the excitation of each of the antennas, so that the tumor is irradiated. Of course, the nearby tissue will also be heated, but it is the duty of the designer of the antenna control system to minimize this heating. Hence, the 'forward' problem is an interesting optimization problem. The forward problem is made more interesting, because it requires the joint solution of an electromagnetic and bio-thermal problem.

It is desired to run the hyperthermia system as a closed loop system, in which the temperature is sensed, and then fed-back to the applicator. At the present time, the only way to measure the temperature of the tissue is to insert six to ten thermocouples that are mounted on the ends of optical fibers. This is invasive; what is needed in the industry is a noninvasive method of measuring the temperature, and that’s the basis for this study.1

1 Magnetic resonance imaging (MRI) is being studied for noninvasive thermometry, but this technique is likely to be slow and expensive.
Noninvasive Thermometry by Microwave Inversion

We are going to apply a nonlinear parameter estimation inversion algorithm to a phantom shown in Figure 2. This three-dimensional phantom was designed by the Center for Devices and Radiological Health (CDRH) Division of the United States Food and Drug Administration (FDA). It comprises a truncated elliptical cylinder, whose length is 57 cm, major axis 32 cm, and minor axis 22 cm, with a fatty layer of 1 cm thickness. The tumor is modeled as a sphere whose radius is 2 cm.

The parameter estimation algorithm is limited to estimating a few parameters, perhaps ten, which is roughly the number of thermocouples currently used in hyperthermia. In order to apply the algorithm, we assume that we know the electromagnetic parameters of the tissue that surrounds the measurement points, and the job is to estimate the parameters (conductivity and dielectric constant) at these points. Of course, this means that we must know the thermal state of the system, because this determines the electromagnetic state (indeed, that is our premise; we can determine the temperature by estimating the conductivities and dielectric constants).

We will assume that the system (the phantom) is excited by a single probe coil that induces eddy-currents into the tissue. (We will leave the more realistic assumption of probing by dipole antennas to a later study.) As the probe is scanned past the phantom, an 'impedance signature' is obtained. If we perform a scan of the phantom with the tumor at one temperature, and a second scan of the phantom with the tumor at an elevated temperature, we can subtract the two impedance signatures. The result of this 'digital subtraction' then, is an impedance signature for the change in tumor temperature, which
FIGURE 2. Cross-section of the CDRH phantom, comprising an elliptical cylinder. The major axis is 32 cm, the minor axis 22 cm, and the depth is 57 cm. The fatty layer is 2 cm thick, and the tumor is spherical, with a 2 cm radius.

can be presented to the parameter estimator algorithm for inversion. The output will be the change in conductivity of the tumor, which can then be translated into the temperature elevation of the tumor.

To illustrate the signal-to-background ratio, we will show in the following examples the impedance signature of the phantom with no tumor (called the ‘host’), and the impedance signature of each scan with this ‘background’ signal subtracted. We will also assume that we have a reference scan, for which we know the tumor temperature and conductivity. This allows us to present absolute temperatures for the tumors, rather than temperature elevations.

Example 1. Digital Subtraction

In the phantom of Figure 2 let the conductivity of the fat be 0.07 S/m, and the muscle 0.74 S/m. The coil contains 10,000 turns, has an inner radius of 25 mm, and outer radius of 35 mm, and a height of 10 mm. It is excited at 100 kHz, and is canned from –250 mm to +250 mm across the midpoint of the phantom in 51 steps. The impedance signature of the phantom without a tumor (‘host only’) is shown in Figure 3.

Next, we center the tumor in the phantom, and let it have a conductivity of 0.70 S/m.² This corresponds to the tumor at normal body temperature (37°C). When the tumor is heated to 43°C, its conductivity falls to 0.63 S/m. When we take the impedance signature of the complete phantom, with the tumor at each temperature, and then subtract the host impedance signature shown in Figure 3 from both of the ‘loaded-phantom’ signatures, we get the impedance signature of each tumor, alone. These are shown in Figure 4. The apparent ‘noise’ in these signatures is entirely numeric, and is due to digital

² At 100 kHz the dielectric constant is unimportant when compared to this value of conductivity.
FIGURE 3. Impedance signature of the host-only phantom: resistance (left), reactance (right).

subtraction. These signatures are important in determining system hardware and software requirements for inversion.

Note that the signature of the tumor whose conductivity is 0.70 S/m is smaller than that of the second tumor. This follows because the background host conductivity of the muscle, 0.74 S/m, is closer to the first tumor, than to the second. These results suggest that it should be relatively simple to distinguish tumors whose temperatures differ by the extreme temperatures of hypothermia. We can do better, however, as demonstrated in the next example.

**Example 2. Reconstruction of a Two-Layer Tumor**

Imagine, next, that the centered-tumor is nonuniformly heated, resulting in the upper-hemisphere having a conductivity of 0.67 S/m, and the bottom-hemisphere having a conductivity of 0.65 S/m, as in Figure 5.

When the impedance data of the split tumor are presented to the nonlinear parameter estimation inversion algorithm, we get the results shown in Table 1.

If the conductivity of the tumor varies from 0.7 S/m to 0.63 S/m over a six degree Centigrade rise in temperature, then a change in tumor temperature of one-half degree Centigrade corresponds to a change of 0.00583 S/m. From Table 1, therefore, we conclude that even with additive noise of ten percent (which is huge), we are still able to resolve temperatures within one-half degree Centigrade, which is a requirement for hypothermia.

**Example 3. Reconstruction of a Four-Layer Tumor**

Let the tumor now comprise the four layers shown in Figure 6.

Each layer is one centimeter high, so we are going to determine if we can reconstruct tumors with a spatial resolution of one centimeter, while maintaining an accuracy of one-half degree Centigrade. These are the requirements of hypothermia.
FIGURE 4. Impedance signatures of two tumors, one whose conductivity is 0.70 S/m, and one whose conductivity is 0.63 S/m: resistance (left), reactance (right). The top views are of unsmoothed data, and the bottom of Bezier-smoothed data.
FIGURE 5. A nonuniformly heated tumor, resulting in a conductivity of the top of 0.67 S/m, and of the bottom of 0.65 S/m.

TABLE 1. Results for the split tumor.

<table>
<thead>
<tr>
<th>% Noise in Data</th>
<th>Result (top, bottom)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>(0.6681, 0.6553)</td>
</tr>
<tr>
<td>1</td>
<td>(0.6685, 0.6536)</td>
</tr>
<tr>
<td>10</td>
<td>(0.6698, 0.6447)</td>
</tr>
</tbody>
</table>

FIGURE 6. A four-layer tumor; each layer is one centimeter high.
Upon taking data, as before, and inverting it, using the nonlinear parameter estimation algorithm, we get the results of Table 2.

Once again, we note that we are able to accurately reconstruct the temperatures, while meeting the one-centimeter spatial resolution requirement, even when the noise reaches ten percent, which is quite large. Breakdown occurs in \( \sigma_4 \), which is the layer that is most shielded from the source by the other layers, as shown in Figure 6. If we had scanned the body from below, as well as above, we would have gotten a better, more stable, reconstruction of the bottom layer of the two-layer and four-layer tumors.

**Example 4. Reconstruction of a Complex Tumor**

Consider the complex tumor of Figure 7, in which a spherical portion, at one temperature, lies within a cube at another temperature. The sphere has a radius of 2 centimeter, as before, and the cube has 4 centimeter edges. The results are shown in Table 3, from which we see that we can meet the temperature accuracy requirement, even with ten percent noise.

**TABLE 2. Results for the four-layer tumor.**

<table>
<thead>
<tr>
<th>% Noise in Data</th>
<th>Result ((\sigma_1, \sigma_2, \sigma_3, \sigma_4))</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>(0.6511, 0.6595, 0.6707, 0.6799)</td>
</tr>
<tr>
<td>1</td>
<td>(0.6545, 0.6602, 0.6711, 0.6697)</td>
</tr>
<tr>
<td>10</td>
<td>(0.6546, 0.6596, 0.6706, 0.6695)</td>
</tr>
</tbody>
</table>

**FIGURE 7.** A complex tumor, comprising a sphere nested within a cube.
**TABLE 3.** Results for the complex tumor.

<table>
<thead>
<tr>
<th>% Noise in Data</th>
<th>Result ((\sigma_1, \sigma_2))</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>((0.6315, 0.6986))</td>
</tr>
<tr>
<td>1</td>
<td>((0.6295, 0.7007))</td>
</tr>
<tr>
<td>10</td>
<td>((0.6306, 0.6971))</td>
</tr>
</tbody>
</table>