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Significance of Heterogeneities in Accurate Dielectric Measurements of Biological Tissues

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Abstract

Accurate knowledge of the dielectric properties of biological tissues is necessary for the design and development of electromagnetic medical technologies; these properties quantify the accuracy and efficacy of system operations. Despite the pressing need, the dielectric properties reported in the literature have suffered from inconsistencies mainly attributed to differences in measurement procedures. In this work, a key source of uncertainty, heterogeneous tissue composition within the sensing region of the dielectric probe, is investigated for biological samples composed of porcine muscle and fat. In particular, the contribution of tissues within the sensing depth to measured dielectric data is quantified and the assumption of equal impact of all tissues within the sensing depth is examined. This study demonstrates quantitatively that tissues at different depths below the measurement site do not contribute proportionally to the measured properties, thus suggesting that new analysis methods need to be developed to account for heterogeneous tissue samples in dielectric measurement data. This improved understanding of how heterogeneous tissues within the sensing region affect dielectric measurements facilitates future studies to reduce uncertainty and improve the quality of collected dielectric data of biological tissues.

1. Introduction

Knowledge of the dielectric properties of biological tissues is of utmost importance for the design and application of electromagnetic medical devices. For technologies such as microwave imaging, hyperthermia and ablation, these properties determine the accuracy and efficacy of system operation, and impact the safety of the technology. Broadband dielectric properties are typically measured with an open-ended coaxial probe placed in contact with the tissue. Despite this seemingly straightforward measurement process, the reported properties for a selection of tissues have been inconsistent [1, 2]. This inconsistency is problematic for medical device developers who are unsure of the true dielectric properties of the underlying tissue, and it is no longer clear if the proposed devices are viable.

Dielectric measurements of tissues are affected by two types of uncertainties: measurement (equipment) uncertainty and clinical uncertainty. Measurement uncertainties have been well-quantified and known compensation strategies exist [3]. However, clinical uncertainties, such as probe-sample contact, sample temperature, tissue heterogeneity, and probe-sample pressure, remain poorly understood. These clinical uncertainties are likely responsible for the inconsistencies in reported dielectric measurements of tissues [3]. Therefore, in order to obtain more reliable dielectric data, these clinical effects must be thoroughly examined.

A key source of clinical uncertainty is the dielectric heterogeneity of the tissue. The coaxial probe is designed for homogeneous tissues; there is no clear procedure for measuring the properties of heterogeneous samples. To overcome this limitation, researchers conduct histology (microscopic investigation of tissues) in order to quantify the proportion of the sample that corresponds to each represented tissue type. The histology region is delimited by radial and longitudinal distances from the probe tip into the sample. Tissues within the histology region are assumed to be contributing to the collected dielectric data. For example, if histology indicates that the sample is composed of 40% fat and 60% glandular tissue, then the dielectric measurement is a result of a 40% fat and 60% gland composition. Studies have been conducted to determine the maximal probe sensing depth [4], which may be taken as defining the extent of the histology region. The sensing depth definitions used to date have been assumed to be constant across frequency and across samples regardless of their composition [1]. However, the sensing depth has not been standardly defined, nor has the histology region which varies across works [1, 2]. Furthermore, recent evidence suggests that tissues within the sensing depth may not contribute proportionally to the dielectric measurement [5]. Each of these factors must be addressed in order to achieve an accurate correspondence between tissue histology and tissue dielectric properties.

The importance of tissue heterogeneity and sensing depth is highlighted in Figure 1. Here, a histology slice clearly shows different tissue-types present in the tissue sample. If the sensing depth is taken to be d_1, then the material composition within the volume defined by that depth is vastly different than if it were taken to be d_2. If the sensing depth is d_2, the tissue composition is highly heterogeneous and would be poorly represented by a homogeneous assumption. Furthermore, it is unknown how different tissues within the sensing volume contribute to the total dielectric measurement. This presents a problem for medical device researchers, as oftentimes it is not clear which tissues have contributed to measured dielectric data, rendering the data error-prone when

information on specific tissues or regions is desired (as opposed to bulk information). If it is not clear which tissues have which dielectric properties, device developers face difficulties, for example, in being able to calculate how much power is needed to heat the region of interest in ablation or hyperthermia. The lack of transparent dielectric properties is a stumbling block in device development, making techniques less effective than they could be with more accurate knowledge of these properties.

For these reasons, in this study we investigate how heterogeneous tissue composition within the sensing depth affects the corresponding measured dielectric data. In particular, we measure the dielectric properties of controlled heterogeneous tissue structures made of porcine muscle and fat tissues, and then quantify the contribution of each tissue to the total relative permittivity. We also calculate the relative permittivity for each tissue structure based on the standard assumption of proportional representation (by volume occupied) of tissues within the sensing region. These two sets of results are compared in order to determine the validity of the proportionality assumption, enabling a better understanding of how heterogeneities within the sensing region affect interpretation of dielectric measurements.

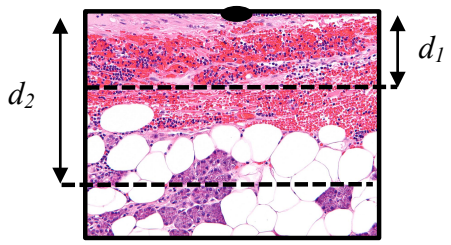

Figure 1. A histology slice containing a heterogeneous sample of tissues (histology from [6]). The dielectric probe measurement location is marked with the black oval. Two sensing depths, d_1 and d_2, show how significantly different the tissues counted as contributing to the dielectric property measurement may be, depending on the histology region used. This example underscores why tissue heterogeneity is important to take into consideration in dielectric measurements.

2. Materials and Measurements

In this study, dielectric measurements are taken using the Keysight slim form probe attached directly to the E5063A network analyser. Measurements are taken from 300 MHz – 8.5 GHz. As illustrated in Figure 2, the dielectric probe is immersed in a tank of liquid fat (Material 1). A slab of porcine muscle tissue (Material 2) is positioned at the bottom of the tank. The tank, attached to a micrometer, can move up and down enabling accurate positioning and repositioning of the probe with respect to the muscle tissue. We note that prior to conducting measurements on the heterogeneous structures of interest, the dielectric properties were also obtained individually for each material: for Material 1, ε_{r1} is 3.55 at 300 MHz and 2.99 at 8.5 GHz, and for Material 2, ε_{r2} is 56.5 at 300 MHz and 34.9 at 8.5 GHz.

This set-up enables measurements of layered samples composed of different thicknesses of Material 1 backed by Material 2. At each position, the thickness of Material 1 (t_1) is different, thus the bulk sample composition is different. The probe is initially placed in contact with Material 2 (t_1 = 0 mm), then moved away in increments. At each position a new measurement is taken.

In Figure 3, the measured data is plotted for several thicknesses t_1 (i.e., for several heterogeneous sample compositions). It is clear from the plot that changing the thickness of Material 1 has an extremely large effect on the measured dielectric properties, which is expected since this changes the sample composition. Further, both materials contribute to the dielectric properties within a range of thicknesses of Material 1.

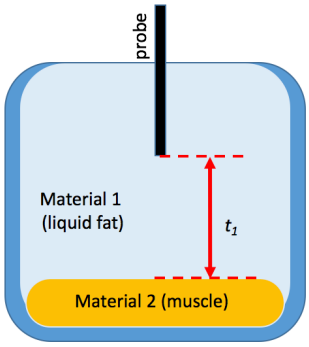

Figure 2. The dielectric measurement set-up showing Material 1 (fat, blue), Material 2 (muscle, yellow), and the dielectric probe. The thickness of the fat is given by t_1.

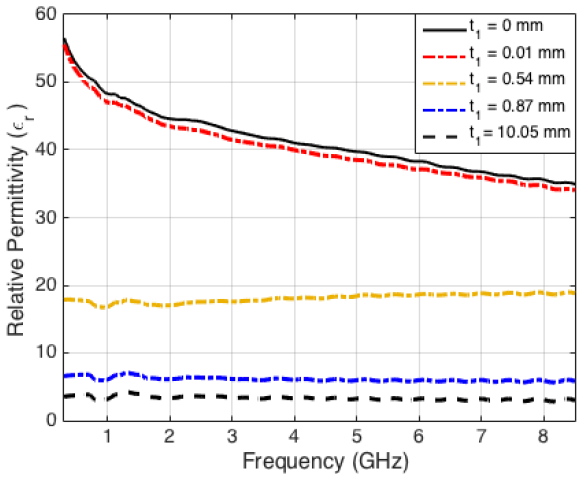

Figure 3. Measured relative permittivity, ε_r, versus frequency for multiple thicknesses (t_1) of Material 1. When t_1 = 0 mm, the probe is in direct contact with Material 2 and the measured permittivity is that of Material 2 alone (ε_{r2}). When t_1 = 10.05 mm, the probe is fully surrounded by Material 1 and the measured permittivity is equal to that of Material 1 alone (ε_{r1}).

3. Methodology

The sensing depth d_s is measured according to the technique described in [4], replacing deionized water with liquid fat and the glass beaker with the muscle tissue. The sensing depth is given by the distance away from a material at which that material ceases to be detectable (within 10% uncertainty) in the dielectric data. In this way, we measured the sensing depth of the probe to be 2.221 mm at 300 MHz and 2.249 mm at 8.5 GHz. The portion of the heterogeneous sample that is within the sensing depth is what is considered to make up the sample composition, as this is what contributes to the dielectric measurement. As shown in Figure 4, if we only take into consideration the materials within the sensing depth, then the thickness of Material 1 is equal to t_1; however, the thickness of Material 2 within this depth, $t_{2,s}$, is given by $d_s - t_1$. In the sample, heterogeneities are isolated to the longitudinal (depth) direction. As the width of the sample was ~10x larger than the sensing radius, the effect of sample edges or radial heterogeneities is not considered.

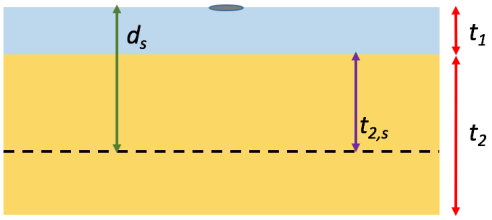

Figure 4. Diagram of the heterogeneous sample, composed of Material 1 (top, blue) and Material 2 (bottom, yellow). The probe position is indicated by the grey oval. The sensing depth, d_s, and thicknesses of Material 1 (t_1) and Material 2 (t_2) are indicated. Also shown is $t_{2,s}$, the thickness of Material 2 that is within the sensing depth.

In order to understand these measurements better, we perform two calculations. We calculate the weight of each material's contribution to the measured relative permittivity based on: i) the actual measurement result; and ii) the assumption that all materials within the sample contribute proportionally to the measured dielectric properties based on their respective volumes (or, here based on the depth since the width and length are constant). This assumption has been generally accepted in the literature to date [3]. The proportionality calculation is given by:

$$(\varepsilon_r)_c = (\omega_{M1})_c * \varepsilon_{r1} + (\omega_{M2})_c * \varepsilon_{r2} \quad (1)$$

where $(\varepsilon_r)_c$ is the calculated relative permittivity; ε_{r1} and ε_{r2} are the relative permittivities of Material 1 and Material 2 in isolation, respectively; and $(\omega_{M1})_c$ and $(\omega_{M2})_c$ are the calculated weights that Material 1 and 2, respectively, contribute to the relative permittivity. The weights are obtained based on the size of each material within the sensing region:

$$(\omega_{M1})_c = {}^{t_1}/_{d_s} \quad (2),$$

$$(\omega_{M2})_c = {}^{t_{2,s}}/_{d_s} \quad (3).$$

The sum of $(\omega_{M1})_c$ and $(\omega_{M2})_c$ is 1. After calculating the relative permittivity based on the proportionality assumption, we compare the actual and calculated results in order to verify the validity of this assumption. We note that the actual weights may be determined for the measured permittivity $(\varepsilon_r)_m$ in a similar manner to (1): the values $(\varepsilon_r)_m$, ε_{r1}, and ε_{r2} are known, and since $\omega_{M2} = \omega_{M1} - 1$, we are left with one equation with only ω_{M1} as a variable that can be solved for.

4. Results

The measured relative permittivity, $(\varepsilon_r)_m$, at 300 MHz for three different thicknesses of Material 1 is provided in Table 1. The table also shows the calculated relative permittivity $(\varepsilon_r)_c$, i.e., the value that the relative permittivity would be if Material 1 and Material 2 contributed proportionally (based on the portion of the sample that they respectively occupy) to the measurement. Further, the percent error between the calculated and measured values is also shown. Table 2 provides the same set of results for the highest measurement frequency, 8.5 GHz. From the results in these two tables it is seen that the measured relative permittivity matches well with the calculated one, to within 2.5%, when the thickness t_1 is small (0.010 mm). For example, at 300 MHz, the measured relative permittivity is 55.58 and the calculated relative permittivity is 56.25, indicating that the calculation represents the measurement well. However, as t_1 increases, the error increases significantly. Before t_1 is even 1 mm thick, the percent error is already on the order of several hundred, with 443% error at 300 MHz and 287% error at 8.5 GHz for t_1 = 0.870 mm. This result suggests that the assumption of proportional representation of both materials in the measured dielectric data may only be applicable in limited contexts. Furthermore, the data confirms the result in [5] that the top layer of tissue (that closest to the probe) contributes dominantly to the measured properties. Evidence of this dominance is given by the fact that the measured relative permittivity is always lower than the calculated relative permittivity. With the knowledge that Material 1 (fatty tissue) has a lower relative permittivity than Material 2 (the muscle tissue), a lower measured value than calculated would indicate that the Material 1 is contributing more than Material 2.

Next, in Table 3, the actual measured material weights $(\omega_{M1}, \omega_{M2})_m$ are compared to the weights $(\omega_{M1}, \omega_{M2})_c$ calculated based on the proportionality assumption. Values are presented for the lower and upper frequency limits of the measurement, for a Material 1 thickness of 0.540 mm. From the results in the table, it is evident that the calculated weights vary only marginally with frequency, whereas the measured weights change significantly. The reasons for this difference are apparent from Figure 2, where the yellow trace for t_1 = 0.540 mm falls approximately halfway between the curves for t_1 = 0 mm (when the measured permittivity is that of only

Material 2) and t_1 = 10.05 mm (measured permittivity is that of only Material 1) at 8.5 GHz, but falls only one third of the way between these delimiting traces at 300 MHz. This result provides a key insight: the effect of the material composition (i.e., the weights of the materials) is highly dependent on frequency.

Table 1. Measured relative permittivity $(\varepsilon_r)_m$ at 300 MHz for multiple sample compositions. The calculated relative permittivity $(\varepsilon_r)_c$ based on the assumption of proportional representation of materials within sensing depth is shown, along with the percent error between the calculated and measured values.

t_1 (mm)	$t_{2,s}$ (mm)	$(\varepsilon_r)_m$	$(\varepsilon_r)_c$	% error
0.010	2.211	55.58	56.25	1.20
0.540	1.681	17.87	43.61	144
0.870	1.351	6.59	35.75	443

Table 2. Measured relative permittivity $(\varepsilon_r)_m$ at 8.5 GHz for multiple sample compositions. The calculated relative permittivity $(\varepsilon_r)_c$ based on the assumption of proportional representation of materials within the sensing depth is shown, along with the percent error between the calculated and measured values.

t_1 (mm)	$t_{2,s}$ (mm)	$(\varepsilon_r)_m$	$(\varepsilon_r)_c$	% error
0.010	2.239	34.02	34.81	2.32
0.540	1.709	18.83	27.28	44.9
0.870	1.379	5.83	22.59	287

Table 3. Actual measured material weights $(\omega_{M1}, \omega_{M2})_m$ and weights calculated based on proportionality $(\omega_{M1}, \omega_{M2})_c$, for t_1 = 0.540 mm.

f	$(\varepsilon_r)_m$	$(w_{M1}, w_{M2})_m$	$(w_{M1}, w_{M2})_c$
300 MHz	17.87	(0.7295, 0.2705)	(0.2431, 0.7569)
8.5 GHz	18.83	(0.5046, 0.4954)	(0.2401, 0.7599)

These outcomes suggest a number of relevant points. Specifically, in order to accurately interpret the histology of a tissue sample for use in dielectric measurements:

- the extent of the histology region (equal to the sensing depth) should vary with measurement frequency;
- the contribution to the measurement of tissues within the histology region should not be weighted proportionally based on volume or area occupied by those tissues;
- the top layer of tissue (closest to the probe) should be taken as contributing dominantly to the measured data.

5. Conclusion

In this study, we have examined the role of tissue heterogeneities within the sensing region of the dielectric probe. An experimental setup enabling layers of muscle and fat tissue with varying thicknesses was developed, and multiple measurements were taken across a wide frequency band. The measured data was investigated by comparing the actual contribution that the tissues made to the dielectric properties, and the contribution that they would have made had they contributed proportionally based on their dimensions. These results demonstrate that tissues located at different depths into the tissue sample contribute disproportionately to the measured dielectric properties, and that the proportions of contribution change significantly with measurement frequency. This outcome is noteworthy as it confirms quantitatively for the first time that heterogeneous samples cannot be measured using the assumption that all tissues within the sensing region contribute proportionally to the measured data.

As accurate knowledge of the dielectric properties of tissues is vital for designing electromagnetic medical devices, future work will need to develop techniques for reliably measuring the properties of heterogeneous tissues. Specifically, future work will involve the development of algorithms to quantify the contribution of tissues based on their depth below the dielectric probe, and will examine how the contribution of heterogeneous tissues varies based on measurement frequency and on magnitude and contrast of the tissue dielectric properties.

6. Acknowledgements

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7. References

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