Impact of Histology Region Size on Measured Dielectric Properties 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. Both electromagnetic diagnostic and therapeutic techniques depend heavily on the dielectric properties of the tissues in the region of interest. These properties quantify the accuracy and efficacy of systems, and enable realistic modelling and simulation prior to clinical evaluation. Despite these strong needs, the dielectric properties reported in the literature have suffered from significant inconsistencies. These inconsistencies have mainly been attributed to clinical confounders that have not historically been well-controlled. In this work, the sensing depth of the dielectric probe, a key clinical confounder, is investigated using heterogenous biological samples composed of porcine muscle and fat. Complex heterogeneous samples can contain several different types of tissues, which are identified through histology. When measuring the dielectric properties, it is crucial to know which tissues contribute to the measurements. In order to achieve this, a histology region is used, which enables correspondence between complex tissue samples and the measured dielectric properties. The histology region is given by the sensing depth in the longitudinal direction, and the sensing radius in the radial direction. We perform dielectric measurements on heterogenous samples and calculate the sensing depth of the dielectric probe for this measurement scenario. We then examine how errors in the assumed sensing depth value affect quantification of the tissue composition. This study demonstrates that the sensing depth, and thus the histology region, has a significant impact on how we interpret the dielectric properties of a sample, indicating that this region must be defined and measured with extreme care. With an improved understanding of these parameters, more accurate and repeatable dielectric measurements will be possible, thus facilitating the development of electromagnetic medical devices.

1. INTRODUCTION

The dielectric properties of biological tissues determine the interaction of electromagnetic fields with the human body, including how fields will reflect, transmit, and be absorbed by the tissues. Knowledge of these properties is highly relevant in the design and application of both existing and novel electromagnetic medical devices. For diagnostic and therapeutic technologies such as microwave imaging, ablation, and hyperthermia, these properties determine the accuracy and efficacy of the device. The dielectric properties are also used for numerical modelling of the problem and optimizing design parameters prior to physical implementation. Dielectric properties in the microwave frequency range are typically measured with an open-ended coaxial probe placed in contact with the tissue. Although the measurement procedure seems quite straightforward, the dielectric properties reported in the literature for key tissues have been inconsistent [1]-[4]. This inconsistency is problematic for medical device researchers who cannot be sure of the true dielectric properties of the underlying tissue, which is an unsatisfactory foundation for medical device development. This uncertainty leads to reduced interest in this field; therefore, clarifying the dielectric properties could have a significant positive impact on electromagnetic medical device research.

Dielectric measurements of tissues are affected by two types of confounders (uncertainties): measurement (equipment) uncertainty and clinical confounders. Measurement uncertainties, for example due to measurement noise, drift, calibration, and cable movement, have been well-quantified and known control and compensation strategies now exist [5]. If measurement uncertainties are handled carefully, they can be minimized to the point where they are negligible for most applications. However, clinical confounders, such as probe-sample contact, sample temperature, tissue heterogeneity, and probe-sample pressure, remain poorly understood. These clinical confounders may be responsible for the majority of the total uncertainty in dielectric measurements of tissues and are likely responsible for the inconsistencies in reported dielectric measurements. 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 complex heterogeneous samples. To overcome this limitation, researchers conduct histology in order to quantify the proportion of the sample that corresponds to each represented tissue type. The region of the sample that is subject to histology is used to determine the correspondence between measured dielectric properties and tissues present (for example, a combination of 30% fat and 70% muscle tissue). Previously, studies have been conducted to determine the probe sensing depth [6], which may be taken as defining the longitudinal extent of the histology region. However, to date, the sensing depth has not been defined in a standard or rigorous way. Consequently, the size of the histology region has also not been consistently defined across works [3], [4].

Thus, in this study, we investigate how histology region size affects interpretation of the corresponding dielectric data. In particular, we perform dielectric measurements on heterogenous structures composed of two homogeneous layers: one of fatty tissue and one of muscle tissue. Different heterogenous structures are attained by varying the thickness of the topmost tissue layer. In this way, the heterogeneous tissue variations are restricted to the longitudinal direction; there are no heterogeneities that vary in the radial direction from the probe. We then determine the sensing depth for each experimental scenario, and use this value to define the histology region. We calculate the error that is introduced by different estimates of the histology region, and demonstrate that the histology region size has a significant impact on how we interpret the dielectric properties of a sample. This result indicates that the region must be defined with extreme care. With an improved understanding of these parameters, more accurate and repeatable dielectric measurements will be possible.

The organization of this paper is as follows. In Section 2, we present the experimental set-up, the sensing depth calculation, and the dielectric measurements. Next, in Section 3, the methodology for calculating the error introduced by inaccurate sensing depth values is described. Then, in Section 4, the results are presented and discussed. Finally, conclusions are drawn in Section 5.

2. MATERIALS AND MEASUREMENTS

In this study, dielectric measurements are taken using the Keysight slim form dielectric probe attached directly to the Keysight E5063A network analyser. In order to reduce measurement uncertainties, no cable is used to connect the probe to the analyser, and all measurements are performed immediately following calibration of the measurement equipment. We record measurements over the bandwidth of 300 MHz – 8.5 GHz. First, two tissues are measured individually: Tissue 1 is fatty tissue and Tissue 2 is porcine muscle tissue (as shown in Fig. 1). The relative permittivity of Tissue 1, ε_{r1}, is found to be 3.5 at 300 MHz and 3.0 at 8.5 GHz; while the relative permittivity of Tissue 2, ε_{r1}, is 56.5 at 300 MHz and 35.0 at 8.5 GHz.

Next, as illustrated in Fig. 1, the dielectric probe is immersed in a tank of fat (Tissue 1) with the porcine muscle tissue (Tissue 2) anchored to the bottom of the tank. In order to enable accurate and repeatable positioning of the tissue with respect to the dielectric probe, the tank is attached to a micrometer. This tank-based set-up, adapted from the study in [7], allows for measurements of heterogenous bulk samples composed of different thicknesses of fatty tissue backed by muscle. Thus, each bulk sample is composed of a combination of both tissues, in varying proportions.

For the initial measurement, the probe is placed solidly in contact with the muscle tissue. Then, the probe is moved away from the muscle in increments, increasing the thickness of fatty tissue (t_1) between the probe and the muscle. At each position a new measurement is taken. In this way, each new measurement distance is equivalent to a given thickness of fatty tissue, and defines a unique heterogenous sample.

Finally, the sensing depth d_s is measured based on the technique described in [6]. In this technique, measurements are taken as the probe is moved closer to the interface of the two materials (in our case, the interface of fat and muscle tissue). At a certain distance from the interface, the probe will begin to pick up the effect of the material interface, resulting in a change in the recorded dielectric data. The distance at which this occurs is called the sensing depth. In this way, we found the measured sensing depth of the probe to be 2.221 mm at 300 MHz and 2.249 mm at 8.5 GHz. We note that the sensing depth is expected to vary based on the material types that are present in the measurement scenario. 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 Fig. 2, if we only take into consideration the materials within the sensing depth, then the thickness of Tissue 1 (fat) is equal to t_1; however, the thickness of

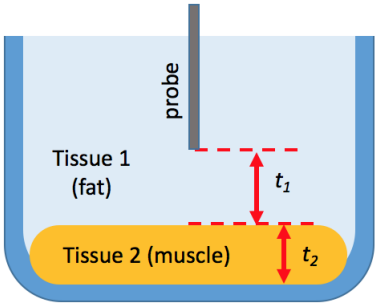

Figure 1: The dielectric measurement set-up, including both tissues inside a measurement tank and the dielectric probe. The thickness of the fatty tissue is given by t_1 and the thickness of the muscle tissue is given by t_2. When $t_1 = 0$ mm, the probe is in direct contact with the muscle and the measured permittivity is that of muscle alone.

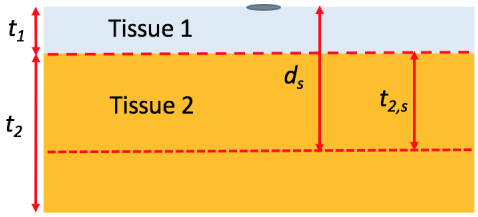

Figure 2: Diagram of the heterogenous sample, composed of the fatty Tissue 1 (top, blue) and the muscle Tissue 2 (bottom, yellow). The probe position is indicated by the grey oval. The sensing depth, d_s, and thicknesses of Tissue 1 (t_1) and Tissue 2 (t_2) are indicated. Also shown is $t_{2,s}$, the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

Tissue 2 (muscle) within this depth is given by $t_{2,s} = d_s - t_1$. The measured relative permittivity across the frequency range is plotted Fig. 3, for several instances of t_1. It is clear from the plot that changing the thickness of Tissue 1 has an extremely large affect on the measured dielectric properties, and that both materials contribute to the dielectric properties when the thickness of Tissue 1 is small but non-zero. However, as t_1 increases, eventually the impact of Tissue 2 is no longer seen in the dielectric data.

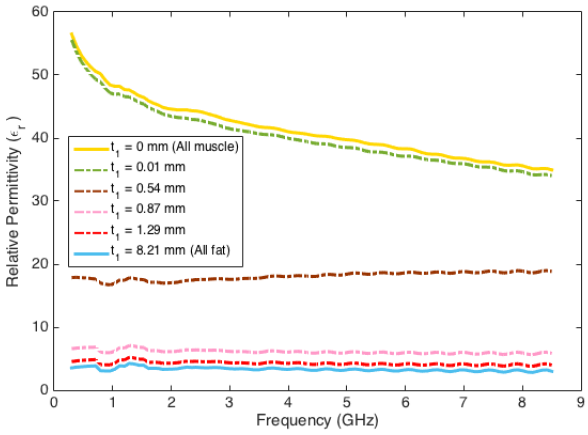

Figure 3: Measured relative permittivity for multiple Tissue 1 thicknesses, t_1. When $t_1 = 0$ mm, the probe is in direct contact with the muscle and the measured permittivity is that of muscle alone (i.e., it is equal to ε_{r2}), and when t_1 is large, in this case 8.21 mm, the probe is far enough away from the muscle that the measured permittivity is that of fat (i.e., is equal to ε_{r1}).

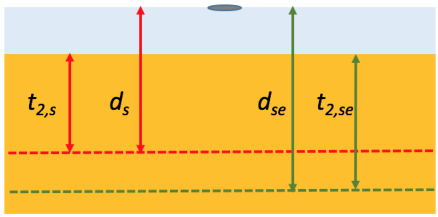

Figure 4: Diagram of the same heterogenous sample as shown in Fig. 3. Here, an example of how the sample composition changes when the assumed sensing depth is misestimated is illustrated with the green arrows. The assumed sensing depth, d_{se}, is given by the true sensing depth $d_s \pm e$, the error. The assumed thickness of Tissue 2 is also impacted by the error: the thickness within the assumed sensing depth is given by $t_{2,se}$.

3. METHODOLOGY

Based on the known tissue composition and the measured dielectric data, we then examine a situation in which error, e, is introduced into the sensing depth value. From this point on, the 'true' sensing depth will be used to denote the real, error-free sensing depth obtained in Section 2, and the 'assumed' sensing depth will be used to indicate the sensing depth values that are calculated with added error. The goal of this investigation is to determine how much of an impact an incorrect sensing depth value can have on interpretation of the dielectric data. This is of specific interest since it is not known if the technique used here, and in the literature in [3], [6], to calculate the true sensing depth is the optimal way to determine this value in complex heterogeneous samples; therefore error may be inadvertently introduced whenever heterogenous samples are investigated. The assumed sensing depth, with error added, is given by d_{se}. An error in the assumed sensing depth will also lead to an error in the assumed thickness of Tissue 2. The assumed thickness of Tissue 2, within d_{se}, is given by $t_{2,se}$. This thickness may be larger or smaller than $t_{2,s}$, depending on whether the error in the assumed sensing depth results in an overestimate or an underestimate of the true sensing depth value. While the thickness of Tissue 1 remains constant, the total volume of each tissue within the assumed sensing depth changes when error is introduced, and therefore so does the assumed percent volume occupied by both tissues.

In order to examine the impact of errors in the assumed sensing depth value, error is artificially introduced into the true sensing depth. The assumed sensing depth, d_{se}, i.e., the true sensing depth with error added, is calculated as:

$$d_{se} = d_s \pm e * d_s, \tag{1}$$

where e is the error. The error is introduced in increments, starting from zero percent error (equal to the true sensing depth), up to thirty percent error. Thus, a unique d_{se} is generated for each value:

$$e = [0, \pm 0.05, \pm 0.01, \pm 0.15, \pm 0.20, \pm 0.25, \pm 0.30]. \tag{2}$$

In this way, the effect of both small, minor errors, and large, significant errors can be examined. A diagram illustrating an example of d_{se} and its impact on the tissue composition is shown in Fig. 4. When an error is introduced into the assumed sensing depth, an error is also introduced into the assumed percent volume occupied by each tissue within the sample. In other words, if the assumed sensing depth is smaller than the true sensing depth, the assumed percent volume occupied by the fat tissue increases, and the assumed percent volume occupied by the muscle tissue decreases. Similarly, if the assumed sensing depth errs towards being larger than the true sensing depth, the assumed percent volume occupied by the fat tissue decreases, and the assumed percent volume occupied by the muscle tissue increases. Thus, errors in the assumed sensing depth lead to errors in the assumed sample composition, resulting in dielectric measurements that are attributed to the wrong sample composition. This poses a significant problem, as dielectric data is not meaningful without the knowledge of which tissues were present in the sample that generated that dielectric measurement.

4. RESULTS

First, we provide a summary of the known and measured values for two sample compositions. Both samples are composed of a top fatty tissue layer, backed by a layer of muscle tissue. The samples are defined by the thickness (t_1) of the top fat layer. The first sample is given by $t_1 = 0.54$ mm,

and the second sample by $t_1 = 0.87$ mm. For these samples, the true sensing depth, the thickness of the muscle, and the measured relative permittivity, are given in Tables 1 and 2, respectively. From these tables, it is clear that changing the thickness of the fatty top layer results in a change in the thickness of muscle that is within the true sensing depth. A larger t_1 results in a smaller $t_{2,s}$, since the true sensing depth is consistent across sample compositions. Further, the measured relative permittivity is quite different for the two sample compositions. As a result of the increased thickness of the fat in Table 2 ($t_1 = 0.87$ mm) relative to in Table 1 ($t_1 = 0.54$ mm), the measured relative permittivity is less impacted by the muscle tissue and more impacted by the fatty tissue. For example, in Table 1, the measured relative permittivity at 300 MHz is 17.87 (midway between the relative permittivity of fat and muscle, as seen in Fig. 2), whereas in Table 2 the measured relative permittivity at 300 MHz is only 6.58 (very close to the relative permittivity of fat only).

Table 1: Summary of known and measured data for $t_1 = 0.54$ mm.

f	d_s (mm)	$t_{2,s}$ (mm)	$(\varepsilon_r)_m$
300 MHz	2.221	1.681	17.87
8.5 GHz	2.249	1.709	18.83

Table 2: Summary of known and measured data for $t_1 = 0.87$ mm.

f	d_s (mm)	$t_{2,s}$ (mm)	$(\varepsilon_r)_m$
300 MHz	2.221	1.351	6.58
8.5 GHz	2.249	1.379	5.84

Next, we discuss the impact of error in the assumed sensing depth value. In Fig. 5, the percent of the bulk sample that is assumed occupied by each tissue type (muscle and fat) is plotted based on the true sensing depth value and for the assumed sensing depth with error added. The results are shown for two sample compositions, namely the sample given by a fat thickness $t_1 = 0.54$ mm (as in Table 1), and the sample given by fat thickness $t_1 = 0.87$ mm (as in Table 2). Within a small range of error (10%) in d_s, the error in the assumed percent volume of the sample that is occupied by each tissue remains small at <3% for $t_1 = 0.54$ mm and <5% for $t_1 = 0.87$ mm. This result indicates that introducing slight errors into the measurement or calculation of the sensing depth value is not likely to meaningfully affect the interpretation of the measured dielectric data. When the error in d_s increases to 30%, the error in the assumed percent volume occupied by each tissue increases as well: it is within 10% for $t_1 = 0.54$ mm, but reaches 17% for $t_1 = 0.87$ mm. For both sample compositions, the error introduced in the assumed percent volume occupied is higher if the sensing depth is underestimated (i.e., if $d_{se}/d_s < 1$).

Further, an important feature distinguishes the curves for the two sample compositions in Fig. 5. Specifically, for the sample given by $t_1 = 0.87$ mm, there is a cross-over in the assumed percent volume occupied for fat and muscle, when $d_{se}/d_s = 0.7$. At this level of error in d_s, the tissue that is assumed to occupy the majority of the sample volume is not correctly identified. Muscle tissue actually occupies the majority (61%) of the sample volume, but with the error it is calculated to occupy only 44% of the volume. Similarly, the fat tissue occupies only around one third of the sample volume, but it is calculated to occupy more than half. This result indicates that if the error in the assumed sensing depth is high, then it can have serious implications on the interpretation of the dielectric measurement. In this case, the relative permittivity for $t_1 = 0.87$ mm (given by the pink line in Fig. 3) is a result of the measurement of a sample that is 61% muscle and 39% fat. Here, if the assumed sensing depth was off by 30%, then we would obtain that this relative permittivity was the measured result from a sample of 56% fat and 44% muscle, completely changing our interpretation of the corresponding dielectric properties.

As the sensing depth value is taken to delimit the longitudinal extent of the histology region, errors in the assumed sensing depth will lead to errors in determining what tissue types are present in the sample and in what proportions. This study has demonstrated that accurate measurement of the sensing depth, and thus the histology region, is vital to achieving an accurate understanding of the measured dielectric properties of heterogeneous tissue samples.

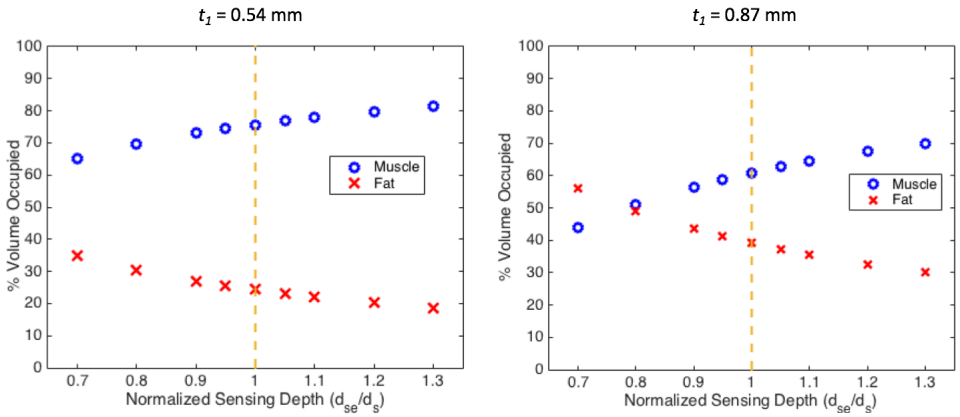

Figure 5: Assumed percent volume occupied in the bulk heterogeneous sample by each of the tissue constituents: fat tissue (red x's) and muscle tissue (blue circles). The results are shown at 300 MHz for $t_1 = 0.54$ mm (left plot) and $t_1 = 0.87$ mm (right plot). The assumed sensing depth with added error (d_{se}) is normalized to the true sensing depth (d_s), which is equal to 2.221 mm for both samples. The orange vertical dashed lines indicate the true sensing depth value (since $(d_{se})/(d_s) = 1$ when there is no error).

5. CONCLUSION

In this work, a key clinical confounder impacting the dielectric measurement of biological tissues was investigated. Specifically, the sensing depth of the probe, which defines the longitudinal extent of the histology region, was determined for heterogeneous tissue samples composed of fat and muscle tissue. The application of histology to heterogeneous samples is necessary in order to attribute the dielectric measurements to the tissues that they originated from. This study examined the influence of error in the sensing depth on the assumed sample composition. The results suggest that small errors in the sensing depth (within $\pm 10\%$) have only minor impacts on the determined percent volume that each tissue type occupies within the sample. However, as the error in the sensing depth increases, so does the error in the assumed percent volume occupied by the tissues. In extreme cases, it can also lead to misidentification of the tissue type that occupies the majority volume of the tissue sample. Incorrectly assuming the sensing depth, and thus the histology depth, leads to a mismatch between the measured dielectric properties and the material compositions that resulted in these properties. This study demonstrates that the sensing depth has a significant impact on how we interpret the dielectric properties of a sample, and as such, the depth must be defined and calculated with care in order to prevent the introduction of errors. With an improved understanding of these parameters, more accurate and repeatable dielectric measurements will be possible, thus facilitating the development of electromagnetic medical devices.

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