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Ex-vivo Dielectric Properties of Tissues in Athymic Nude Mice

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Abstract

Measuring and reporting the dielectric properties of tissues remains a key area for microwave imaging and sensing, providing solid foundation for biomedical research in the field. In this study, the dielectric properties of tissues in athymic nude mice were evaluated. Measurements were conducted on liver, skin, muscle, and fat tissues using the co-axial probe technique within the microwave range between 500MHz–4GHz. The results demonstrate the distinct profiles for specific tissues as well as the variation that can be observed between individual animals. Notably, we evaluated fat samples from two distinct locations: from the abdomen and fat in close proximity to the tumour. It was observed that the location of the fat tissue can have an impact on the measured dielectric properties.

1. Introduction

Microwave imaging and sensing systems show promise in providing a low-cost alternative for tumour detection without the use of ionising radiation. Central to the technology is the innate difference in dielectric properties observed between surrounding and target tissues. In some applications such as breast cancer, however, contrast between healthy and malignant tissues has been noted to be as low as 10% [1], [2] varying individual to individual. With this in mind, accurate understanding of the dielectric properties of tissues continues to be an essential element in this research area.

Early studies exploring dielectric characterisation formed the foundation for the wide knowledge base now available[3]–[7]. More recent work now encompasses an even wider range of measurement techniques and technologies across a number of model organisms. Detailed studies have covered a broad spectrum of tissues including the heart [8], brain [9], [10] and liver [11]–[13], amongst many others.

Inconsistency in reported values has been a challenge in the field, with several previous studies having explored the factors leading to variability in published dielectric tissue measurements. In addition to this, many studies use excised tissues, with some authors raising the question of whether these are comparable to the *in-situ* properties [14]. Conversely, in 2016 Farrugia *et al.* correlated the *in vivo* and *ex vivo* measurements conducted on rat liver, concluding that hydration and temperature are key parameters in ensuring that *ex vivo* data provides a true reflection of *in vivo* values [12]. Furthermore, Shahzad *et al.* reported liver measurements from BALB/c nude mice over a time period of 3.5 hours post-excision, noting the decrease in dielectric constant over time [13]. This again was concluded to be the result of dehydration, emphasising the need for careful timing and measurement protocols.

In this study, we present the results of *ex-vivo* measurements of excised tissues from athymic nude mice using the open-ended co-axial probe technique. Measurements were taken between 500MHz and 4GHz on samples of liver, skin, muscle, and fat. Results were evaluated to examine the distinct profiles observed from individual tissues as well as any differences seen between individual animals. In characterising these tissues, we seek to provide a foundation for further work, with dielectric values specific to this model and measurement style. We also highlight the known variability in contrast between tumour and surrounding tissues, and how this can vary between individuals.

2. Materials and Methods

2.1 Dielectric Characterization Equipment

Dielectric characterization was conducted using the well-established open-ended coaxial probe technique. A Keysight P9372A two-port network analyser was used directly connected to a Keysight 200mm probe (85070-20037). Before use, the slim-form probe was calibrated using Keysight's E-Cal module and three known dielectric materials: air, shorting block, and deionized water.

2.2 Animal Studies

All animal procedures were conducted under the U.K. Home Office regulations and the Guidance for the Operation of Animals (Scientific Procedures) Act (1986).

Liver, skin, muscle, and fat tissues were excised from 6 female athymic nude mice immediately after euthanasia. Bilateral tumours on the dorsal haunch had been induced via subcutaneous injection of the triple-negative breast cancer cell line MDA-MB-231. Studies were conducted in parallel with other experiments in order to uphold the 3Rs principles for humane research with animals.

2.3 Tissue Measurements

Measurements were conducted over a frequency range of 500 MHz – 4 GHz. Ten consecutive surface measurements were taken for each individual sample while keeping the probe in the same position, and an average was subsequently calculated. Samples were elevated towards the probe to minimize any disruption to measurements and to ensure full sample contact with the co-axial probe. All measurements were taken within 1-2 minutes from excision to minimise tissue evaporation. Due to the nature of the experiments, the number of samples for each tissue varies: liver (n=2), abdominal fat (n=6), muscle (n=6), skin (n=2). In this context, each sample (n) is derived from an individual animal. Tumour proximal fat measurements were taken from 2 individual animals, to give a total of 3 samples.

3. Results and Discussion

The measured dielectric properties of liver, leg muscle, skin, and abdominal fat are illustrated across Fig. 1-4 respectively, with dielectric constant displayed on the *y*-axis over a scale of 0-90, and frequency (GHz) on the *x*-axis over a range of 0.5-4GHz. Effective conductivity is presented over the same frequency range plotted between

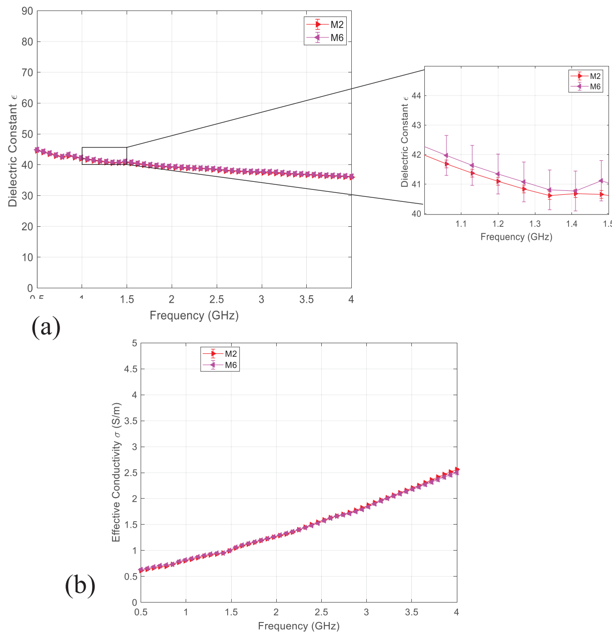

Figure 1. Measured dielectric properties of two individual liver samples across a 0.5–4 GHz frequency range: (a) dielectric constant, (b) effective conductivity.

0 and 5. Each coloured line represents a distinct sample from an individual mouse, with the plot representing the average of the 10 consecutive surface measurements. Each dielectric constant plot contains a zoomed portion over a frequency range of 1-1.5GHz for comparison of the measured properties between samples.

The measured dielectric properties of the excised liver are shown in Figure 1. As can be seen, there is minimal variation between the two individual samples measured, with both samples showing an average dielectric constant of approximately 42 at 1GHz. These values are higher than those measured for fat and skin which can be attributed to both the strong blood supply and fluid content of the liver. These values are similar to those reported in previous literature on the dielectric properties of the liver [9], [12], [15].

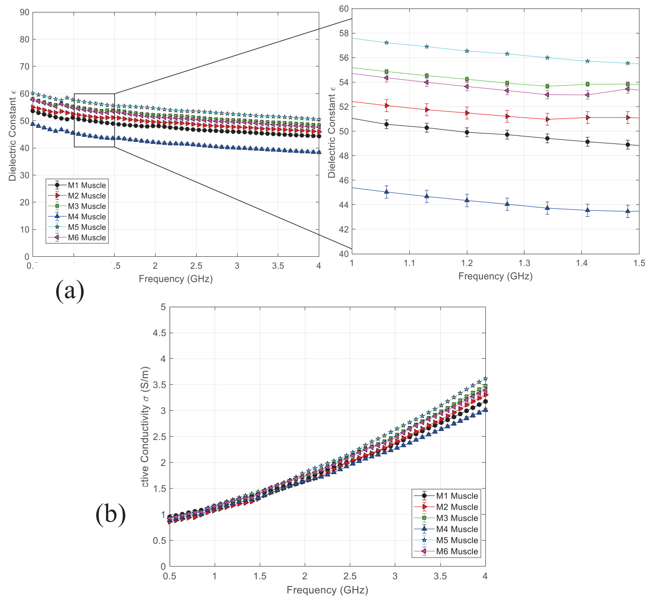

Figure 2. Measured dielectric properties of six individual leg muscle samples across a 0.5–4 GHz frequency range: (a) dielectric constant, (b) effective conductivity.

Muscle is a highly vasuclar tissue, as is demonstrated in Figure 2. Here we can see the 6 individual samples show dielectric constant over a range of 45-58 at 1GHz, which is the largest variation we observed over any of the measured tissues. Muscle tissue is known to be highly heterogenous, which may account for this variability. This observed profile however, is in line with an *in vivo* study conducted by Cho *et al.* in 2006 [15] which the relative permitivity of skeletal muscle in athmyic nude mice was measured using a planar-tip probe, giving an average of 48.5.

Both liver and musle measurements showed increasing conductivity over the frequency range. This is in contrast to skin and fat measurements, which while demonstrating an increase, was observed to be much smaller.

Excised skin samples presented more of a challenge to excise and measure, particularly due to the thickness of the samples. This again may account for some of the variation

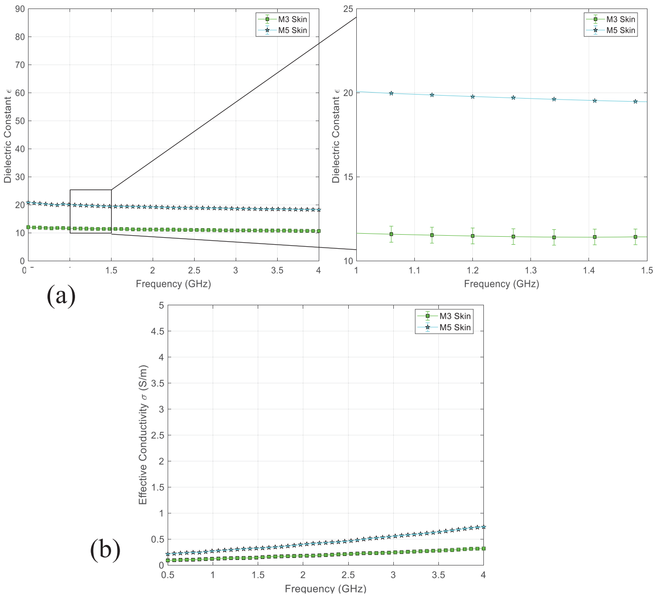

Figure 3. Measured dielectric properties of two individual skin samples across a 0.5–4 GHz frequency range: (a) dielectric constant, (b) effective conductivity.

observed in Figure 3, with a dielectric constant ranging from 11-20 at 1GHz. Nevertheless, these values are low compared with muscle and liver samples, which is to be expected given the lesser blood supply and water content.

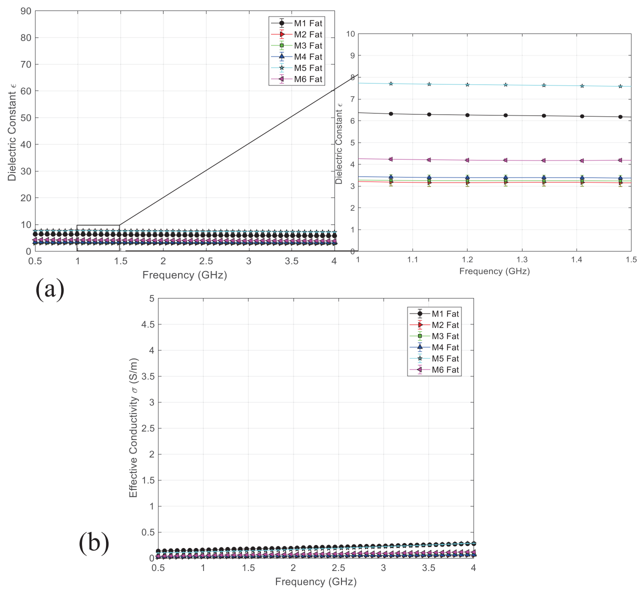

Figure 4. Measured dielectric properties of six individual abdominal fat samples across a 0.5–4 GHz frequency range: (a) dielectric constant, (b) effective conductivity.

Six fat samples from the abdomen were measured as illustrated in Figure 4. This data set showed lower variability than that of the more vascular tissues, with a measured dielectric constant of between 3 and 8 at 1GHz.

Figure 5 illustrates four plots comparing excised abominal fat with fat excised in close proximity to the tumour. Dielectric constant is displayed on the y-axis over a scale of 0-35, and frequency (GHz) is on the x-axis over a range of 0.5-4GHz. Graphs presenting the conductivity values have a y-axis scale of 0 to 5. It should be noted that the tumour proximal fat sample size is small, with a total of 3 samples from 2 individual animals and was collected based on the availability of suitable deposits near the tumour site. For both animals, we can see an increase in the measured dielectric constant for the tumour proximal fat, when compared with the abdominal fat. The observed effect is particularly prominent in plot (a), where both tumour proximal fat samples show a large dielectric constant increase. In plot (b), the effect is less pronounced, but nonetheless observed, rising from an average of 3.2 to 10 at 1GHz. The increase could be due to increased tumour vasculature, which is typically abnormal, having an impact on the surrounding tissue. The difference is also observed in conductivity values, with increases in measurements taken from tumour proximal fat.

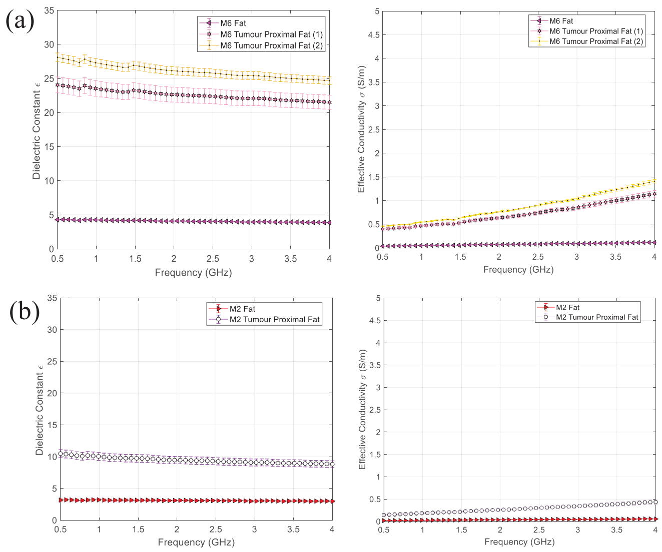

Figure 5. Measured dielectric properties of two individual abdominal fat samples across a 0.5–4 GHz frequency range compared with tumour proximal fat excised from the same animal. Graphs (a) and (b) show dielectric constant and conductivity values for two indidvual animals.

Comparing the dielectric constant values highlights the variance in normal tissue's dielectric properties near cancerous tissue, even with tumours of the same origin and in a similar location. This has long been a key issue in microwave imaging/sensing, where tumour identification is based on the contrast between the cancerous and surrounding tissues and reinforces the potential of contrast enhancers or even reference tissues within an individual to circumvent this challenge.

4. Conclusion

Liver, skin, muscle, and fat tissues excised from athymic nude mice were evaluated for their dielectric properties. The results echo experiments performed on similar models, highlighting the unique dielectric profiles of individual tissues, as well as the variance that can exist between individuals. We also demonstrate that fat sampled in close proximity to tumours showed a higher measured dielectric constant than abdominal fat excised from the same animal. This is hypothesised to be due to the impact of tumour angiogenesis on the surrounding tissue and is an important consideration for microwave imaging and sensing systems based on dielectric contrast.

5. Acknowledgements

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