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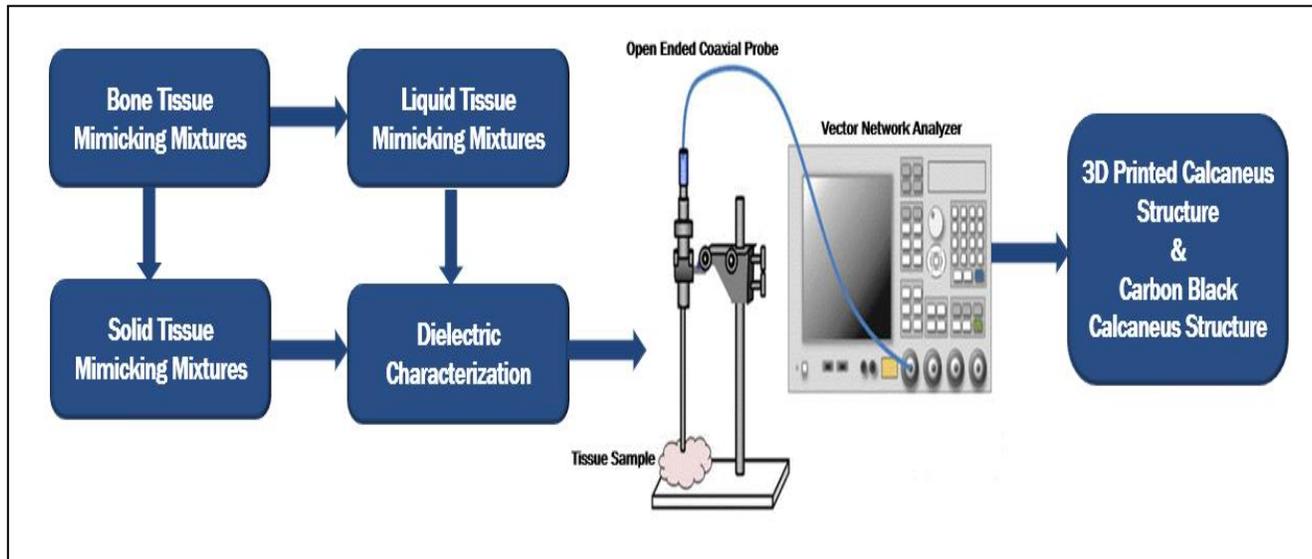
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Anthropomorphic Calcaneus Phantom for Microwave Bone Imaging Applications

Bilal Amin, Atif Shahzad, Daniel Kelly, Martin O'Halloran, and Muhammad Adnan Elahi



Tissue-Mimicking Mixtures and Anthropomorphic Calcaneus Phantom for Bone Imaging Applications

Take-Home Messages

- This work presents tissue-mimicking mixtures to mimic the dielectric properties of skin, muscle, cortical bone, and trabecular bone.
- Anatomically realistic phantoms must be considered as preclinical testing of the microwave imaging system.
- The tissue-mimicking mixtures and the 3D-printed structures presented in this work can be used as a valuable test platform for a microwave imaging system for bone health monitoring.
- The recipe of tissue-mimicking mixtures for cortical bone and trabecular bone is presented separately.
- This study has proposed separate tissue-mimicking mixtures for cortical bone and trabecular bone.

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Abstract: Recent studies have found a significant dielectric contrast between healthy and osteoporotic human trabecular bones. This dielectric contrast can be exploited by microwave imaging for monitoring human bone health. The tissue-mimicking phantoms play a vital role in preclinical testing of the microwave imaging system. This paper presents anatomically realistic multi-layered 3D-printed and carbon black-based human calcaneus structure. The liquid and solid based tissue-mimicking mixtures are also proposed to mimic the dielectric properties of skin, muscle, cortical bone, and trabecular bone. The liquid tissue-mimicking mixtures are composed of Triton X-100, water, and salt, whereas the solid tissue-mimicking mixtures are composed of carbon black, graphite, polyurethane, and isopropanol. The dielectric properties of the tissue-mimicking mixtures were measured using an open-ended coaxial probe measurement technique across 0.5 – 8.5 GHz. The average percentage difference between the relative permittivity and conductivity of reference data and proposed liquid tissue-mimicking mixtures was found to be 7.8% and 9.6% for skin, 0.38% and 14% for muscle, 9.6% and 5% for cortical bone, and 3.4% and 2.4 % for trabecular bone, respectively, across 0.5 – 8.5 GHz. For solid tissue-mimicking mixtures, this difference was found to be 3.93% and 0.64% for skin, 6.13% and 9.21% for cortical bone, and 10.66% and 41.82% for trabecular bone, respectively for relative permittivity and conductivity. The proposed tissue-mimicking mixtures along with 3D-printed structures can be used as a valuable test platform for microwave bone imaging system development.

Keywords — Bone health, dielectric properties, microwave imaging, phantoms, tissue-mimicking mixtures

I. INTRODUCTION¹

MICROWAVE imaging (MWI) is an emerging diagnostic technology being investigated for a range of medical applications. MWI relies on the contrast of dielectric properties of biological tissues, namely relative permittivity (ϵ_r) and conductivity (σ (S/m)), of target anatomical site in the human body [1]. The key advantages of MWI over the other clinical imaging modalities are safety (non-ionizing radiations), portability, and low cost [2]. These advantages make MWI a safe alternative to existing imaging technologies for diagnosing and monitoring various diseases such as breast cancer detection and diagnosing brain stroke [3],[4],[5]. Several recent studies have investigated the feasibility of using MWI for osteoporosis monitoring [6],[11], which are based on a notable contrast between the dielectric properties of different diseased bones [10]. The current standard modalities for osteoporosis diagnosis and monitoring are Dual-energy X-ray Absorptiometry (DXA) and Computed Tomography (CT). Both DXA and CT use ionizing radiations, therefore, these are not suitable for frequent scans [6],[9]. The associated clinical advantages of MWI and contrast of dielectric properties between healthy

and diseased bones make MWI a potential routine imaging modality for monitoring bone health in comparison to the DXA and CT [11].

The experimental evaluation of the MWI prototype helps to examine the prototype in a controlled real-world scenario. To this end, tissue-mimicking phantoms play a vital role in the evaluation of repeatability, stability, imaging quality, and imaging resolution of an MWI system. Moreover, the performance of the imaging algorithms in the presence of external noise and system interference can be well assessed from experimental evaluation [12]. The tissue-mimicking phantoms emulate the dielectric properties and anatomy of various human body parts. Ideally, the reference phantoms should be anatomically and dielectrically accurate whilst being mechanically and dielectrically stable over time and easily produced [13]. The tissue-mimicking mixtures (TMMs) used in phantoms can be either liquid-based, such as oil-in-gelatin and Triton X-100 mixtures, or solid based, such as polyurethane-based TMMs [14]. Oil-in-gelatin TMMs have been widely used to emulate breast tissues and are attractive due to their ease of fabrication and their ability to simulate the dielectric properties of a wide range of tissues [15]. One major limitation of oil-in-gelatin TMMs is their sensitivity to environmental exposure, which causes desiccation over time [13]. Among liquid-based TMMs, Triton X-100 appears to be an excellent candidate due to its better relative heat stability (allowing to perform experiments at the room as well as the human body temperature) and because its dielectric properties are stable for up to a year [13]. The liquid nature of Triton X-100 solutions ensures that complex three-dimensional (3D)-structures can be filled by avoiding air bubbles in these structures. Various studies have used this approach to mimic

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the dielectric properties of head and breast tissues [13],[25]. The limitation in this approach is that the 3D-printed shells have not been dielectrically characterized and this can potentially affect the quality of reconstructed images [18]. Alternatively, the polyurethane can be used as a potential solid TMM. In the polyurethane TMMs, the dielectric properties are controlled by adding carbon black and graphite powders to the rubber mixture [19]. Due to flexibility, dielectric stability, and mechanical strength, the polyurethane mixtures outperform the liquid TMMs [20]. Moreover, the solid TMMs does not involve any additional and unwanted 3D-printed structures, thus minimizing the effect on reconstructed microwave images [19]. However, these TMMs are hard to reconfigure to account for changes associated with the shape of the anatomical lesion compared to liquid-based TMMs [13]. There has been a limited development on bone mimicking phantoms with only simplified homogeneous structures reported for head models [13],[21]. However, to the best of authors' knowledge, no study has ever reported TMMs for cortical and trabecular bones separately for the application of bone imaging.

Recent advancements in manufacturing technologies have enabled building complex and relatively easily reproducible 3D-printed structures for use in solid phantom development. One drawback of 3D-printed moulds is the limited choice of fabrication substrates. Acrylonitrile butadiene styrene (ABS) is a commonly used substrate for 3D-printed phantom moulds despite its electrical permittivity and conductivity being far from the dielectric properties of the biological tissues. At a frequency of 2.45 GHz, the dielectric contrast in terms of the average percentage difference between ABS and trabecular bone is 144% and 195% for ϵ_r and σ , respectively. This significant dielectric contrast creates a mismatch between the biological tissues and the ABS layers in the 3D-printed structures referred to as "electrical perturbation". The previous studies have experimentally [18] shown that due to the high dielectric contrast with respect to the various biological tissues, the ABS walls perturb the field significantly even with wall thickness as low as 1.5mm [13].

This paper presents an anthropomorphic multi-layered human calcaneus phantom for MWI system evaluation. A full 3D model of a human foot was altered to obtain a multi-layered human calcaneus structure. The major tissue layers considered for developing the calcaneus phantom are skin, muscle, cortical bone, and trabecular bone. The human calcaneus bone is shown in Fig. 1. The peripheral location of human calcaneus bone as can be seen in Fig. 1, makes it the most suitable location for MWI. Our preliminary study has reported Triton X-100 based TMMs to mimic the dielectric properties of skin, muscle, cortical bone, and trabecular bone over 0.5 – 8.5 GHz frequency range [14]. These TMMs are used in 3D-printed structures that hold the liquid TMMs. While phantoms based on these TMMs and 3D-printed structures are useful for preliminary experiments, there is significant unwanted electromagnetic (EM) field perturbation due to the presence of 3D-printed substrate [13]. To avoid this unwanted EM field perturbation, this study proposes carbon black-based anatomical phantoms that

mimic the dielectric properties of skin, cortical bone, and trabecular bone over 0.5 – 8.5 GHz frequency range. Most of the microwave tomography (MWT) imaging systems operate below 3 GHz [8]. Gilmore *et al.* [22] has reconstructed the human forearms bones by MWT. The optimal results were found at 0.8 GHz and 1 GHz. Scapatucci *et al.* [5] found that the penetration of electromagnetic (EM) waves in human biological tissues reduce as a function of frequency. Therefore, considering frequencies above 3 GHz for microwave bone imaging application would not be feasible due to the low penetration of EM waves. However, the wideband imaging systems particularly the radar-based imaging techniques use higher frequencies [4]. Therefore, the liquid and carbon black-based TMMs are characterized over a wide frequency range (0.5 – 8.5 GHz). These TMMs can be used for both the tomographic and radar-based imaging techniques. The 3D-printed moulds and counter-moulds were designed to develop the realistic carbon black-based calcaneus phantom. The outer layer of the calcaneus phantom mimics the dielectric properties of the skin. The interior of the calcaneus phantom mimics the calcaneus bone. The calcaneus bone has a carbon black-based layer mimicking dielectric properties of the cortical bone, and a cavity to contain the trabecular bone mimicking material. This trabecular bone cavity is filled with trabecular bone mimicking liquid. The flexibility of using liquid TMM for trabecular bone in the proposed phantom allows for mimicking natural variation of trabecular bone dielectric properties. Moreover, the trabecular bone cavity can be filled with TMM of diseased trabecular bone. The carbon black based phantoms will reduce the artefacts in images which would be otherwise present in the plastic phantoms. However, the liquid TMMs based phantoms are still useful for preliminary experiments for evaluation of the prototype and imaging algorithms due to ease of preparation.

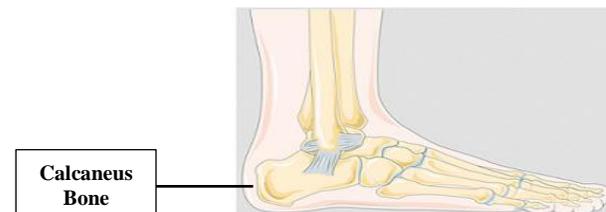


Fig. 1. Human calcaneus bone.

The remainder of the paper is organized as follows: Section II discusses the methodology including the preparation of liquid and solid TMMs, design of 3D-printed structures, and dielectric characterization of the phantoms. Section III presents the results and discussion on dielectric properties of liquid and solid TMMs, design of 3D-printed structures, and carbon black based phantoms. Finally, conclusions are drawn in Section IV.

II. METHODOLOGY

A. 3D-Printed Structures

The design and fabrication complexity of the anatomical structure primarily depends upon the corresponding details of the anatomical site. Moreover, the accuracy and precision to replicate any anatomical site in the human body highly

dependent upon the application to be investigated [23]. In this study two types of human bone structures were modelled: 1) a two-layered hollow cylinder was designed to represent the cortical and trabecular bones; and 2) a 3D model of the human foot was used to develop anatomically realistic human calcaneus phantom. The model was designed as a three-layered human calcaneus structure. These three layers were filled with liquid TMMs for skin, cortical bone, and trabecular bone. The human calcaneus was chosen as the target anatomical site due to the proximity of the calcaneus bone to the skin, and the ratio of cortical to the trabecular bone is also similar to that found in the femoral head and lumbar spine [24],[25], which are primary targets for standard osteoporosis monitoring technologies. A 3D-modelling software (Autodesk Fusion 3D) was used to produce all 3D models. These models were then printed with Ultimaker 2+ Extended 3D printer at 200 °C using a polylactic acid (PLA) filament. The thickness of walls was kept to 2mm to prevent leakage of liquid TMMs and to avoid potential low field perturbation. Finally, these 3D-printed structures were filled with liquid TMMs for Triton X-100 based phantoms. Moreover, similar 3D models were developed as moulds for carbon black-based phantoms.

B. Liquid Tissue Mimicking Mixtures Preparation

The liquid TMMs were composed of Triton X-100, water, and salt (NaCl). The preparation of TMMs was based on the guidelines outlined in [13],[26]. The solution of Triton X-100, water, and salt was put in a glass beaker and was thoroughly mixed until the disappearance of air bubbles. The percentage of salt was varied following the difference between the conductivity of reference tissue and the conductivity of the proposed TMM. The higher concentrations of salt were used for tissues having high conductivity values, however, higher concentrations of Triton X-100 were used to lower both the conductivity and permittivity of the solutions. As described in [13], TMM solutions that contain 45-55% of Triton X-100 become highly viscous, however, none of the Triton X-100 solutions except skin fell in that range. In this study, we have proposed liquid TMMs for skin, cortical bone, and trabecular bone. The composition of constituents was adjusted until the dielectric properties of TMMs were close to the reference values reported by Gabriel *et al.* [27].

C. Solid Tissue Mimicking Mixtures Preparation

The solid TMMs were composed of carbon black, graphite, polyurethane, and isopropanol. Since this TMM provides enough flexibility for recreating the target dielectric properties of various biological tissues [28]. A similar procedure has been adopted for the preparation of TMMs as outlined in [23]. Firstly, a polyurethane base was prepared by mixing equal masses of two liquid precursors to polyurethane as per the manufacturer's instructions (VytaFlex 20, Smooth-On, Easton, PA, USA). Once the polyurethane base was ready, the graphite powder and carbon black powder were mixed. To get the desired dielectric properties of TMMs, the mixture of carbon black, graphite, and polyurethane was thoroughly mixed. It has

been observed in [16] that polyurethane provides a mechanically strong base while the relative permittivity and conductivity of various biological tissues can be achieved by varying proportions of graphite and carbon black. It was observed that the values of dielectric properties increase as the mass percentage of carbon black and graphite powder increases. However, the blended mixture gets thicker and extremely difficult to mix as the mass percentage of carbon black and graphite powder is increased. To achieve the uniformity of mixture and higher dielectric properties, a small amount of isopropanol was added as a thinning agent. For optimal dielectric properties of the final phantom, rectangular cuboids $50 \times 20 \times 20 \text{ mm}^3$ were designed as reference samples and their dielectric properties were measured. The 3D-printed moulds were developed to shape the solid TMMs into anatomically realistic carbon black based phantoms. This study has proposed the composition of solid TMMs for skin, cortical bone, and trabecular bone.

D. Dielectric Properties Measurement

The dielectric properties of liquid and solid TMMs were measured by employing an open-ended coaxial probe (OECL) technique. The measurements were recorded in the frequency range of 0.5 – 8.5 GHz over 101 linearly spaced frequency points. The dielectric measurements were performed by Keysight slim form probe 85070E connected directly to the Keysight E5063A vector network analyzer (VNA) [29]. The temperature of liquids for calibration and validation was measured using a digital thermometer (HI98509-1) from Hanna Instruments. The VNA was used to measure the reflection coefficient (S_{11}) at 101 linearly spaced frequency points, and a commercially available software suite (Keysight N1500A) was used to convert the S_{11} parameters to real (ϵ') and imaginary (ϵ'') parts of complex permittivity [1].

A standard three-load one-port calibration (Air, Short, and Deionized water) was used to calibrate the measurement equipment before the measurement of dielectric properties. The calibration of the measurement equipment was verified by measuring dielectric properties of 0.1 M NaCl solution (saline) at 22 °C [30]. A total of 6 validation measurements were performed. The uncertainty of the equipment's accuracy is reported in Table I. The uncertainty in accuracy in terms of percentage is defined as:

$$UC_{ACC}(f) = \left(\frac{x_{meas}(f) - x_{ref}(f)}{x_{ref}(f)} \right) \times 100 \quad (1)$$

where x_{meas} represents measured dielectric properties of 0.1 M NaCl and x_{ref} represents standard dielectric properties of 0.1 M NaCl [30] at the measured temperature. The repeatability of measurements is also reported in Table I, and defined as:

$$UC_{REP}(f) = \left(\frac{x_{meas}(f) - x_{mean}(f)}{x_{mean}(f)} \right) \times 100 \quad (2)$$

where x_{mean} represents the mean of the measured dielectric properties. To compute the uncertainties, the measurements were recorded in the frequency range of 0.5-8.5 GHz over 101 linearly spaced frequency points. The reported values of UC_{ACC} and UC_{REP} are averaged over the measured frequency range (0.5-8.5 GHz). The combined uncertainty is the sum

of UC_{ACC} and UC_{REP} both for relative permittivity and conductivity. The uncertainty analysis was based on previous studies [1],[30]. The total combined uncertainty is reported in Table I.

TABLE I
 PERCENT UNCERTAINTY IN ACCURACY AND REPEATABILITY OF MEASUREMENTS

Parameter	ϵ_r (%)	σ (S/m) (%)
UC_{ACC}	0.04	2.75
UC_{REP}	0.07	0.75
Combined	0.11	3.50

The reported values of UC_{ACC} and UC_{REP} are averaged over the measured frequency range (0.5-8.5 GHz).

III. RESULTS AND DISCUSSION

A. 3D-Printed Structures

The 3D-printed structures were developed to hold the liquid TMMs for each tissue. Fig. 2 (a) and (b) shows the two-layered cylindrical bone phantom, and Fig. 2 (c) and (d) shows the anatomically realistic three-layered calcaneus phantom. The cylindrical structure only incorporates the cortical bone and trabecular bone. The cylindrical structure was printed as an initial simplistic test case for the MWI system. As the calcaneus bone, in general, resembles an irregular shaped cylinder, therefore for initial imaging purposes, the cylindrical structure can be used. The anatomically realistic 3D calcaneus structure was designed to simulate a more realistic imaging scenario. To avoid problems such as leakage, trapped air, and weakness of the structure, the thickness of the walls was chosen to be 2mm, which is a compromise between mechanical stability and electrical perturbation. The authors have tested ABS structures of 1.5 mm thickness and 2 mm thickness. The thickness of 2 mm for ABS structures ensured that the liquid TMMs do not leak to adjacent layers in a multi-layered 3D-printed structure and provides good mechanical stability.

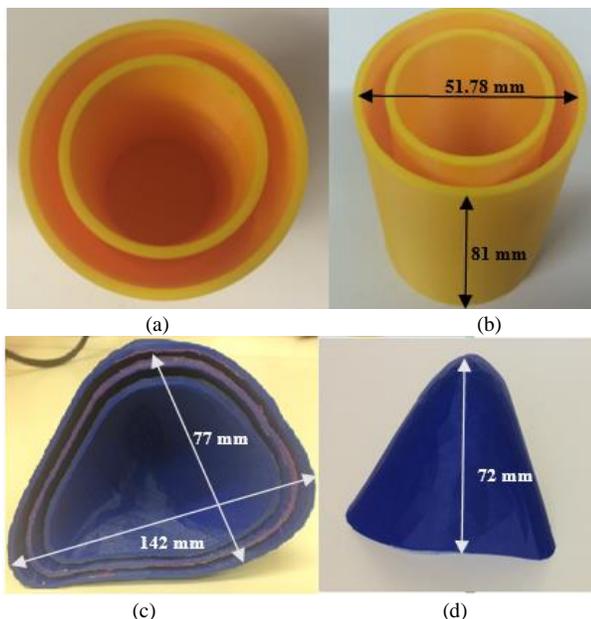


Fig. 2. 3D-printed two-layered cylindrical bone phantom (a) Top View (b) Side View and anatomically accurate human calcaneus structure (c) Interior View (d) Exterior View.

B. Liquid Tissue Mimicking Mixtures

To mimic the dielectric properties of skin, muscle, cortical bone, and trabecular bone, several TMMs containing Triton X-100, water, and salt were made. The percentage of Triton X-100 was varied from 90% to 24%, whereas, the percentage of water was varied from 10% to 76%. The dielectric properties of all TMMs were analyzed and the composition of each TMM was varied to match the target tissue. Among all TMMs, four solutions were selected that mimic the dielectric properties of skin, muscle, cortical bone, and trabecular bone. The recipe for muscle tissue-mimicking material was obtained from [13], whereas the dielectric properties of skin, cortical bone, and trabecular bone were achieved by varying the composition of TMMs. The composition of TMMs that mimic the dielectric properties of each target tissue is given in Table II.

TABLE II
 COMPOSITION OF LIQUID TMMs

Target Tissue	Triton X-100 (vol %)	Deionized water (vol %)	NaCl (g/L)
Skin	40	60	5.2
Muscle [13]	24	76	5
Cortical Bone	77	23	0.8
Trabecular Bone	69.5	30.5	0.8

While the recipe of muscle is taken from [13], the recipes for skin, cortical bone, and trabecular bone are proposed in this study. NaCl is expressed in terms of grams/liter(g/L).

The measured dielectric properties of liquid TMMs of target tissues (solid plots) and the reference dielectric data (dashed plots) are shown in Fig. 3. Each solid curve in Fig. 3 indicates the mean value of six measurements taken at 101 linearly spaced frequency points between 0.5 – 8.5 GHz. The measurements were obtained at multiple sites in the liquid. The dashed plots represent the corresponding tissue's reference dielectric data taken from a large scale study conducted by Gabriel *et al.* [27]. It can be observed from Fig. 3 (a) and (b), that the mean dielectric properties of TMMs are well aligned with the reference dielectric properties of modelled tissues. The average percentage difference was calculated between relative permittivity and conductivity values of reference tissues from Gabriel *et al.* [27] and the relative permittivity and conductivity values of proposed TMMs over 0.5 – 8.5 GHz and is presented in Table III. This difference was found to be less at lower frequencies compared to higher frequencies. The average percentage difference between the dielectric properties of TMM and its respective tissue is found to be less than $\pm 10\%$, which is within the expected variance in biological tissue [31]. The variations observed in results are in agreement with literature reporting TMMs for human biological tissues [13],[23],[32].

TABLE III
 AVERAGE PERCENTAGE DIFFERENCE BETWEEN TMM AND REFERENCE TISSUE DIELECTRIC DATA

Target Tissue	ϵ_r (%)	σ (S/m) (%)
Skin	7.8	9.6
Muscle	0.38	14
Cortical Bone	9.6	5
Trabecular Bone	3.4	2.4

Table V
 AVERAGE PERCENTAGE DIFFERENCE BETWEEN TMM AND
 REFERENCE TISSUE DIELECTRIC DATA

Target Tissue	ϵ_r (%)	σ (S/m) (%)
Skin	3.93	0.64
Cortical Bone	6.13	9.21
Trabecular Bone	10.66	41.82

The average percentage difference between the dielectric properties of each TMM and corresponding reference values was found to be less for lower frequencies compared to higher frequencies for solid TMMs as observed in liquid TMMs. The average percentage difference in relative permittivity profiles of the bone TMMs and corresponding tissues are smaller compared to the average percentage difference in conductivity profiles.

Fig. 5 (a) and (b) show side and top views of cylindrical shaped solid calcaneus phantom. As discussed earlier the cylindrical-shaped phantoms were designed as initial test cases for the MWI system. The outer layer of the phantom mimics the dielectric properties of cortical bone and the inner layer was filled with trabecular bone's liquid TMM.

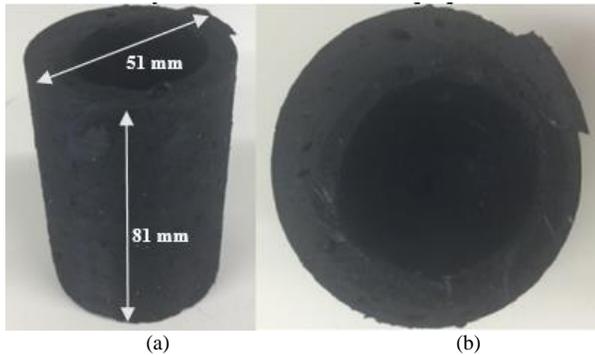


Fig. 5. Cylindrical shaped calcaneus bone phantom (a) Side view (b) Top View.

An anatomically realistic solid calcaneus phantom was also developed as shown in Fig. 6 (a) and (b). Fig. 6 (a) and (b) shows the interior and exterior views of a realistic calcaneus phantom. The phantom is composed of a solid single layer having an interior cavity, where the external and internal layers mimic the dielectric properties of the skin.

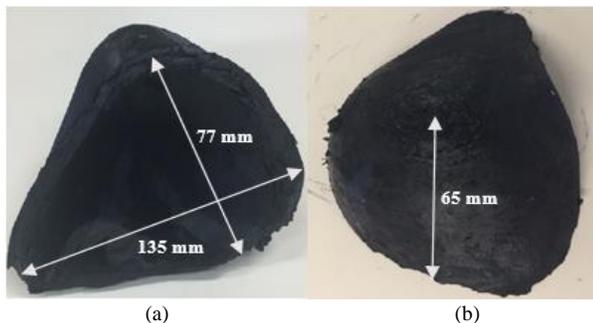


Fig. 6. Anatomically realistic calcaneus phantom (a) Interior view (b) Exterior View.

Fig. 7 (a) and (b) shows the exterior and interior views of a realistic calcaneus bone phantom. The outer layer mimics the dielectric properties of cortical bone and the inner layer constitutes the liquid TMM of trabecular bone. The calcaneus bone phantom was then placed into the calcaneus phantom. The empty spaces left between the skin layer and

the outer layer of calcaneus bone phantom were filled with liquid TMM of muscle.

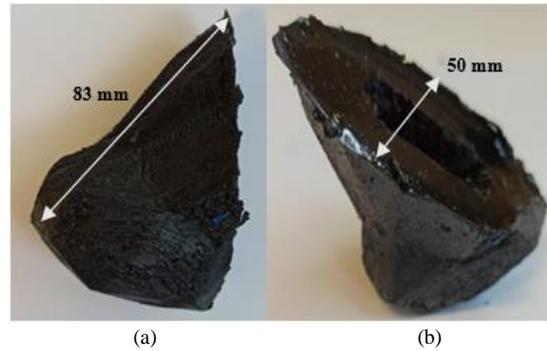


Fig. 7. Anatomically realistic calcaneus bone phantom (a) Exterior View (b) Interior view.

IV. CONCLUSION

Phantoms play a vital role in assessing the data acquisition, pre-processing signal evaluation, and repeatability of measurements in a controlled realistic scenario for an MWI system. In this study, two types of MWI phantoms were developed: 1) liquid-based TMMs to provide the flexibility of varying dielectric properties to mimic the tissue behaviors such as the growth of cancer or degradation of bone tissue; 2) solid TMMs for more realistic, stable and anatomically accurate phantoms. The liquid TMMs for skin, muscle, cortical bone, and trabecular bone were developed using mixtures of Triton X-100, water, and salt. These liquid TMMs can be used with 3D-printed structures to mimic anatomical calcaneus bone for imaging applications. The solid TMMs for skin, cortical bone, and trabecular bone were developed using carbon black, graphite, polyurethane, and isopropanol. The solid TMMs are easily mouldable, relatively inexpensive, mechanically, and dielectrically stable over time. The dielectric properties of TMMs developed in this study aligns well with the reference dielectric data. The combined average percentage difference between dielectric properties of liquid TMMs and the reference data is found to be less than 10% for target tissues. Similar findings are observed for solid TMMs, except for the conductivity of trabecular bone that significantly deviated from reference data at higher frequencies. The objective of the study was to propose liquid and solid based TMMs within an acceptable error range of dielectric properties and hence to maintain a contrast between target tissues of the considered anatomical site. The variations observed in dielectric properties of TMMs are in agreement with the literature reporting TMMs for human biological tissues. Future studies will focus on developing more realistic replication of human calcaneus that should also involve trabecular bone microarchitecture along with bone marrow for experimental investigation of bone models for monitoring bone health.

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