AMERICAN UNIVERSITY OF BEIRUT

PANCREATIC AND KIDNEY PHANTOMS FOR THE EVALUATION OF ELECTROMAGNETIC SENSORS IN MONITORING THE COMPLICATIONS OF DIABETES AT 3.9 – 5.8 GHZ FREQUENCY RANGE

by
REEM ALI JOUNI

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for the degree of Master of Science
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ABSTRACT

OF THE THESIS OF

Reem Ali Jouni for Master of Science
Major: Biomedical Engineering

Title: Pancreatic and Kidney Phantoms for The Evaluation of Electromagnetic Sensors in Monitoring the Complications of Diabetes at 3.9 – 5.8 GHz Frequency Range

Diabetes is a metabolic disease characterized by elevated blood glucose levels due to impaired insulin secretions, action, or both. According to the International Diabetes Federation "IDF", diabetes affects almost 537milion adults aging between 20 and 79 years by the year 2021 with the highest prevalence in the Middle East and North Africa. Such metabolic disease can affect all body organs and lead to death if left untreated, but several treatments and precautions could be taken to render the development of such disease in the human body. The effectiveness of such actions is closely dependent on how early the disease is detected. Consequently, both devices designated to either treat or detect this disease are broadly developed and investigated and are referred to as biomedical devices. The fabrication of such devices has been greatly correlated with the utilization of electromagnetic technology. In other words, biomedical devices that require the recruitment of electromagnetic waves applied and/or received from the human body are facilitating and improving the detection and treatment of various diseases. Hence, the interest in studying the interaction of electromagnetic fields with biological tissues has been elevated leading to the need for models that can simulate the electrical properties of actual tissues. These simulated biological models are known as "phantoms" and aim to speed up and ease the process of verification and validation of biomedical devices. Diverse phantoms have been developed using different materials and targeting several tissues such as skin, muscle, fat, and breast tissues.

This research is mainly concerned with the electromagnetic interaction between the various organs such as pancreas and kidneys with electromagnetic sensors. Since there is a lack in data studying the behavior of these two specific organs, electrical characterization (dielectric constant and loss tangent) and measurements of the latter are carried out. The data collected were compared and analyzed based on relevant information presented in literature. Following that, and according to what have been established, various attempts to develop pancreas and kidney phantoms are proposed within a frequency range of 3.9-5.8GHz. This report discusses the characteristics of, to our knowledge, first of its kind, fabricated phantoms that realized electrical properties equivalent to the actual either human or animal pancreas and kidney tissues. These phantoms are prepared in a semi-solid form using simple off-the-shelf materials that require simple procedures including, sunflower oil, deionized water, NaCl, dishwashing soap, and gelatin. In the present phantoms, relative permittivity and loss tangent almost equal to those of the biological tissues are realized over the frequency range of 3.9 GHz to 5.8 GHz. Furthermore, several samples for each successful phantom candidate were

fabricated, so the reproducibility of the proposed methodology, as well as the electrical properties maintenance of the proposed tissue-mimicking materials was investigated. Hence, projects that require actual pancreas or kidney organs for electromagnetic-based systems verification and design validation could simply use the proposed phantoms at their corresponding frequencies. On the other hand, even by simple adjustment in the composition of the several proposed models would allow simulating the dielectric properties of any other tissue type as a function of formulation across a frequency range.

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ABBREVIATIONS

- International Diabetes Federation: IDF
- Diabetes mellitus: DM
- complex permittivity: ε_r'
- loss tangent: ε_r''
- Gigahertz: GHz
- The number of moles per liter: mol/l
- Medical Implant Communications Service frequency band: MICS: 402–405 MHz
- Industrial, Scientific, and Medical frequency band: ISM: 2.4–2.48 GHz
- Megahertz: MHz
- Cerebrospinal fluid: CSF
- Magnetic Resonance Imaging-derived 3 dimensional study: MRI-derived 3D
- Waveguide Rectangular with the number next to it reflects the waveguide dimensions' inner width in hundredths of an inch: WR187
- Phosphate-buffered saline: PBS
- Sodiumchlodride: NaCl

CHAPTER 1

INTRODUCTION

Considered one of the top 10 mortality-causing diseases (Lin, 2020), diabetes, which is also referred to as Diabetes mellitus “DM”, is a metabolic disease characterized by elevated blood glucose levels due to impaired insulin secretions, action, or both. According to the International Diabetes Federation “IDF”, diabetes affects almost 537milion adults aging between 20 and 79 years by the year 2021 with the highest prevalence in the Middle East and North Africa. Moreover, Chronic hyperglycemia results in a reduction in insulin-secreting pancreatic beta cells’ mass or function, and consequently the progression of the latter leads to organ damage such as the kidney referred to as “nephropathy”. Nephropathy, on the other hand, induces increased levels of serum creatinine. Then, in a way to limit the prevalence of diabetes, continuous efforts are done to develop several biomedical devices that can accelerate and facilitate either the detection of the disease or its treatment. Recently, technologies requiring the recruitment of biomedical devices that utilize electromagnetic emissions to monitor health parameters of the human body have been extensively expanded and developed. Such devices include the integration of body/wearable sensors/antennas into the body, and consequently, expose various biological tissues to electromagnetic radiations. Thus, the interaction of various biological tissues with electromagnetic fields has been investigated and studied. Ideally, these electrical biomedical devices should be designed and evaluated based on their intended media, the actual human being, to confirm their incrimination is coherent with the expected design. As a matter of fact, the bulk of the fabrication process is carried out on the basis of computer-aided simulations, in a way to save time and minimize costs (Lau, 2019). In addition, human testing introduces several challenges such as delays in the development cycle of the sensor, financial attribution, and ethical and logistic concerns. Hence, instead of human testing, system characterization is carried out based on synthetic simulating media that mimic the actual human environments, “tissues”, known as phantoms. Such synthetic testing complements any existing animal or human testing that is planned for a later stage in the design of a medical device.

1.1. Phantoms’ definition and different types

Tissue phantoms are artificially generated environments that aim to mimic the behavior of their respective targeted tissues stimulated by the applied electromagnetic radiations. Using phantoms, the preclinical ex-vivo testing and certification are made much easier, feasible, and reproducible. Generally, materials used for phantom fabrication are preferably characterized by being low-cost, off-the-shelf, and ensuring prolonged storage time. For instance, materials that are water-soluble are preferred to develop phantoms as no complex mixing or harmful additives are required. There are mainly four types of phantoms based on their physical and physiological states: liquid, hydrogel, or semi-solid, solid, and animal phantoms (Vardaki, 2020). Liquid tissue phantoms require uncomplicated and rapid synthetic procedures resulting in the most flexible type in terms of the fabrication process as well as system characterization. On the other hand, the semisolid models that are hydrogel-based phantoms consist of either agarose or gelatin solutions. Both latter materials have been mainly utilized in the field of imaging and are characterized for biocompatibility. This type of phantom largely consists of water, so they are prone to solvent evaporation and consequently lack reproducibility within a short duration. Moreover, the solid phantoms are made of bulk matrices such as polymers, silicone, and wax and thus require a time-consuming and inflexible fabrication process. The most realistic phantom types are the animal phantoms as they specifically exhibit the heterogeneity and consistency of human tissue, but are also restricted by ethical, feasibility, and reproducibility concerns.

1.2. Electromagnetic behavior and dielectric parameters

Furthermore, it is not applicable to generate the whole properties of the human body with the complexity it exhibits, so, generally, phantoms are fabricated according to the specific biomedical application. Then, for electromagnetic field-based biomedical devices, the electrical properties of the actual tissue should be simulated by the generated phantom. In fact, the interaction of electromagnetic waves with biological tissues is defined by what is known as relative complex permittivity, which defines the interaction of a certain material with an electromagnetic wave (Balanis, 2012). This complex permittivity is composed of a real part (ε_r'), which is referred to as the dielectric constant and reflects how easily a material can get polarized by the application of an electromagnetic field. On the other hand, absorption in lossy media, particularly in biological tissue, is governed by the imaginary part (ε_r'') which in turn is usually represented by the loss tangent. The latter indicates to what extent a medium of electromagnetic propagation is lossy.

1.3. High and low- water content tissues

The discussed dielectric parameters are mainly influenced by the water content at the level of biological tissues, and accordingly, the human tissues are categorized into two types: high water content such as blood, muscle, and internal organs and low water content such as fat and bone (Stauffer, 2003). High water content tissues are characterized by higher dielectric constant and loss tangent in comparison with that of lower water content (S. Gabriel, 1996). Consequently, materials that exhibit both high dielectric constant and high loss tangent are used for the fabrication of tissue-mimicking phantoms (Tamura, 1997). Most of such materials were used to fabricate phantoms that mimic, for instant, the skin and muscle tissues.

1.4. Pancreas and kidney phantoms

Most of the efforts done to electrically characterize the various human tissues took place up to the year 2000. Almost all these attempts were collected and analyzed in one literature survey written by Gabriel et al. (Gabriel C. G., 1996). The presented data includes the dielectric parameters of about 13 different tissue types over a frequency band extending from 10Hz to 100GHz. The measurements of these parameters were conducted by several scientists and on different samples. The samples could be extracted from either animals or humans, and their dielectric characterization was done either in in-vivo or ex-vivo. Following the survey, Gabriel broadened the data electrically characterizing biological tissues (Gabriel S. L., 1996), so in addition to the tissues which were already characterized, 7 new tissues were placed under investigation. Collectively, the electromagnetic behavior of 20 different tissues was established. Based on all the information obtained, a parametric model was proven to enable the prediction of the dielectric properties of tissues as a function of frequency (S. Gabriel, 1996). Hence, almost all of the research projects that involve the interaction of electromagnetic fields with tissues as well as the fabrication of phantoms refer to Gabriel's work as a reference. Despite the tremendous work done to electrically characterize the biological tissues, and to our knowledge, there is no data collected that examines the dielectric properties of actual pancreatic tissue, so the only information presented in this regard is a prediction of the electromagnetic behavior of this organ based on the parametric equation developed by Gabriel et al. (S. Gabriel, 1996). This scarcity might explain as well the lack of attempts to fabricate a pancreas phantom. On the other hand, even though, the electrical characterization of actual kidney tissue is almost well-established, experiments carried out to mimic these characteristics are inadequate. Thus, to our knowledge, there are no attempts to simulate the pancreas nor the kidney within the frequency range of 3.9- 5.8GHz, despite the fact that both of the organs are major effectors in diabetes, one of the top 10 mortality-causing diseases (Lin, 2020).

1.5. Main Objective

Diabetes is characterized by being a disease associated with a group of metabolic disorders resulting mainly in hyperglycemia due to abnormalities either in insulin secretion, insulin effect, or both. This hyperglycemic state induces complications at the level of various tissues such as the pancreas and kidneys. Hence, creating phantoms that allow us to mimic the electromagnetic behavior of the latter tissues would facilitate and accelerate the development assessment and translation processes of electromagnetic-based biomedical devices. Such devices are designed to detect, monitor, and treat the metabolic disorders associated with diabetes. Since, as per mentioned earlier, the literature lacks enough data regarding the interaction between electromagnetic fields and the corresponding two tissues, the information collected regarding muscle and blood mimicking materials and phantoms are utilized in a way to pave the path to developing pancreas and kidney phantoms. This is since all 4 tissues are categorized as high-water content tissues with close dielectric properties, especially within the range of 3.9 GHz till 5.8GHz.

Moreover, the materials utilized for the fabrication of tissue phantom are managed to be categorized as simple and off-shelf constituents. Then, the results obtained not only provide readily prepared and optimized phantoms that can mimic the actual pancreas and kidney through simple and cheap procedures, but also allow further characterization of the proposed materials over the frequency band of interest. This, in turn, would facilitate the generation of other different models based on the targeted dielectric parameters and through simple interpolation of composition as a function of the frequency applied. Regarding the validation of the results that are obtained, animal testing was conducted, and together, with the data proposed in literature a fair comparison and analysis is done. The animal testing of pancreas and kidney tissues, as well, will strongly contribute to the depiction of a standard reference to which corresponding phantoms and solutions could be analyzed and validated.

CHAPTER 2

LITERATURE REVIEW

In this chapter, a chronological representation and synthesis of different attempts mentioned in the literature is presented.

In 2006, Zhou et.al (Jian Zhou, 2006) proposed a liquid phantom to mimic the dielectric properties of the biological environment mainly the muscular layers of the human arm and torso within a frequency band of 3.1-10GHz. The dielectric properties of solutions of sucrose concentrations were measured using an open-ended coaxial probe and represented. It was shown that as the sucrose concentration increases, the dielectric constant of the solutions decreases. Furthermore, Zhou et. al claimed that a 1mol/l sucrose solution is optimal to be utilized and so compared its electromagnetic responses to antennas and electromagnetic waves' propagation with that of actual human subjects. Even though, the dielectric properties of the 1mol/l liquid phantom were not able to accurately match with that of human (it was based on an inaccurate assumption as per the author's claim), the responses of both the phantom and human subjects were correlated with the applied electromagnetic field.

In 2007, another muscle mimicking phantom was suggested by Takimoto et.al (Takimoto, 2007). The phantom was an agar-based semi-solid dedicated to simulating the dielectric properties of muscle tissue at frequencies between 3 – 6 GHz, however, Takimoto et.al measured and represented the dielectric properties of the phantom over a bandwidth of 900MHz - 10GHz. The percent error was calculated, and it is defined as:

Error = (actual value observed – expected value)/ expected value

Percent error= Error*100

The measured percent error showed elevations at frequencies below 3GHz and above 6GHz, but this increase did not substantially affect the antenna input impedance (the measure of the opposition to current/impedance into the load network/ tissue that is external to the electrical source/antenna), radiation efficiency, and radiation directivity.

Then in 2008, the interest in body-implantable electromagnetic systems elevated and similarly, to the efforts settled to fabricate skin-mimicking phantoms. In this regard, two specific frequency bands: the medical implant communications service (MICS) (402–405 MHz) and the industrial, scientific, and medical (ISM) (2.4–2.48 GHz) band are defined. First, Karacolak et.al (Karacolak, 2008) studied different solutions of sucrose and salt over the 300MHz- 3GHz frequency range using Agilent's 85070E dielectric probe kit and an HP8753D network analyzer. Secondly, two different phantom recipes for MICS and ISM were concluded based on the targeted dielectric constant. The phantom model correlates with the reference dielectric properties for the MICS band, but this is not the case for that the ISM band. Therefore, Yilmaz et.al (Yilmaz T. K., 2008) used another type of material to simulate the skin over the ISM band solely and was able to achieve a close correlation between the dielectric properties of the proposed materials and that of the reference human tissue.

In 2009, the delight in simulating cancerous breast tissue emerged with the increased interest in detecting and treating breast cancer. Hence, Croteau et al. (J. Croteau, 2009) and Ostadrahimi et.al (Ostadrahimi, 2009) tried developing a breast phantom with discrete layers resembling the structure of actual breast tissue as well as in a similar overall concave anatomy. The generated phantoms were based on oil-in-gelatin recipes with different constituents' ratios concluded from the measurement done by Lazebnik et al. (Lazebnik, 2005) according to the targeted tissue to mimic. Croteau's breast phantom was subjected to dielectric measurement within the range of 50MHz to 13.51GHz, and the obtained values were represented but not compared with any reference. The phantom being able to maintain a realistic anatomical shape like an actual breast tissue was the main concern of the author. On the other hand, Ostadrahimi's proposed phantom showed a correlation with that of reference in terms of dielectric properties over 50MHz – 7.5GHz, but the obtained results are not based on measurement of percent error.

Breast phantoms continue to be of interest in 2010, and the same oil-in-gelatin materials mentioned earlier were used by Porter et.al (Porter, 2010). The breast phantom fabricated included mixtures for fat, skin, gland, and tumor tissues that are proposed to mimic their corresponding target between 200MHz and 6GHz. However, the correlation in dielectric properties was observed only between the skin mimicking phantom and that of the reference; the other mixtures failed to simulate their corresponding tissue. Nevertheless, Porter claimed that this difference is tolerable as the dielectric properties of actual breast tissue are subjected to intrinsic variation within the breast and between different patients. On the other hand, using different types of tissue-mimicking materials but in liquid form, Romoe et.al (Romeo, 2011) claimed that a non-ionic detergent, Triton X-100, shows a promising ability to mimic the normal and malignant breast tissues as a whole in the 0.5-12GHz frequency band.

In 2011, Mashal et.al (Mashal, 2011) proposed another attempt to fabricate a phantom based on Lazebnik's materials that could mimic the complexity and heterogeneity of a breast tissue. In a way to address the intrinsic variations mentioned by Porter, the reference data used were represented in 25^{th}, 50^{th}, and 75^{th} percentiles of the breast tissue data groups. The phantoms' measured properties within 1 – 6 GHz band fall within the range of the 25^{th} and 75^{th} percentile of the corresponding breast tissue group, except for the skin tissue phantom which showed decreased lossy properties compared to that of reference. Other than breast tissue, Lopez-Haro et.al (Lopez-Haro, 2011) tried to develop tumor tissue in the liver over one MHz frequency range (200-300). The obtained dielectric properties of the developed phantom were claimed to agree with the range of values for tumor cells presented in the literature with less than 10% error. Additionally, different types of tissue phantoms were developed by Arunachalam et.al (Arunachalam, 2011) with each one targeted to imitate either urine, kidney, muscle, or fat tissues at 1.375GHz. Unfortunately, the liquid nature of kidney and muscle tissue phantoms renders their application in electromagnetic system evaluation and validation.

In 2012, multiple phantom designs were presented by Yuan et.al (Yuan, 2012) that were able to mimic the human thigh biological environment with tumor tissue. Oil-in-gelatin emulsions were designed for the muscle, fat, bone, bone marrow, and tumor tissues, and their dielectric characterization was given. The data obtained were claimed to model the dielectric properties of the targeted group of tissues at a frequency range of 80-500MHz. Also in 2012, Chahat et.al (Chahat, 2012) claimed to propose the first skin equivalent phantom for implantable antenna characterization at millimeter waves at a frequency of 60GHz.

Other than building phantoms, the field of phantom fabrication also includes the addition of new constituents to already proposed mixtures to enhance their simulating ability; this is like what had been done by Yamamoto et.al (Yamamoto, 2013) 2013. Both adding new constituents, the carbon micro coil, and varying the concentration of already utilized material, the NaCl, were proposed to enable the already built muscle equivalent phantom in 1998 (K. Ito, 2001) to resemble the dielectric properties at frequencies below 30MHz. Even though these attempts failed to fulfill the purpose at frequencies below

30MHz, it was revealed that they couldn’t deviate and change the dielectric properties of the conventional phantom at frequencies above 300MHz.

In 2014, Garrett et.al (Garrett, 2014) aimed to study the ability of different solutions to mimic both high and low water content tissues in general as a function of variation of either graphite, carbon black, or both. The obtained results did not define an accurate path to follow using such tissue-mimicking materials in the 1-10GHz band, but the former could be utilized for further assessment and utilization in more specific applications. Besides, a human head model was fabricated by Mobashsher et.al (Mobashsher, 2014) by developing phantoms mimicking the gray matter, white matter, blood, Dura, CSF (cerebrospinal fluid), cerebellum, spinal cord, and eyes tissues. Together with the dielectric correlation of the phantoms with the targeted tissues and the MRI-derived 3D printed molds, the model can be used for experimental validation of systems operating from 0.5GHz to 4GHz.

Most of the mentioned developed phantoms and models were then readily utilized by other researchers to validate and verify their proposed biomedical device or concept. Despite the achievement and development presented of various tissue-mimicking phantoms, there are no attempts to fabricate pancreas equivalent phantom, as well as kidney phantom in the range of 3.9 - 5.8 GHz. Hence, this paper aims to study the electromagnetic behavior of either the actual pancreas and kidney or their corresponding generated phantoms.

CHAPTER 3

THE EXPERIMENTAL APPROACH

3.1. Dielectric Characterization of Mice Pancreatic and Kidney Tissues Between 3.9 GHz and 5.8 GHz

To validate our dielectric characterization methods and to provide reference data for both the pancreas and kidney-equivalent phantoms, we studied the electromagnetic behavior of the mice's actual pancreas and kidneys. The study was carried out by using a rectangular waveguide characterization method (Chen, 2004). In this method, a WR187 waveguide is used as shown in Fig.1 (H. Shwaykani, 2021)f, where the material under test is sandwiched between two rectangular waveguide sections. It is important to mention that the harvested pancreatic tissues were placed in a 47.5mm x 22.1mm x 2mm material holder, while the collected pairs of kidneys were placed in a 47.5mm x 22.1mm x 3mm material holder, and then both were covered using nylon sheets at both sides as depicted in Figure 2. When placed within the holder, air gaps were removed between the volume of material and that of the holder, in order to ensure the accuracy of the results. Consequently, nine mice were sacrificed to extract their pancreas and kidneys. The extracted organs (Pancreas & Kidneys) are washed with phosphate-buffered saline solution (PBS), then dried with paper towels, and aligned as presented in Figure 2. Since kidneys have a rigid well-defined bean-like shape, their alignment next to each other in the material holder presented many gaps that affect the measurement's accuracy. Consequently, the extracted kidneys were smashed as gently as possible in a way to remove any air gaps while maintaining the structure of the kidney tissue. The dielectric characterization of the corresponding aligned organs was done within less than an hour from the moment the mice were sacrificed to make sure their original properties are preserved. Then the obtained results were validated by reference values of human tissues presented in the literature (S. Gabriel, 1996). Furthermore, together the harvested electrical properties of mice pancreas and kidney tissues with that established in the literature for the human tissues (S. Gabriel, 1996) were used as references for comparison and evaluation of the proposed phantoms.

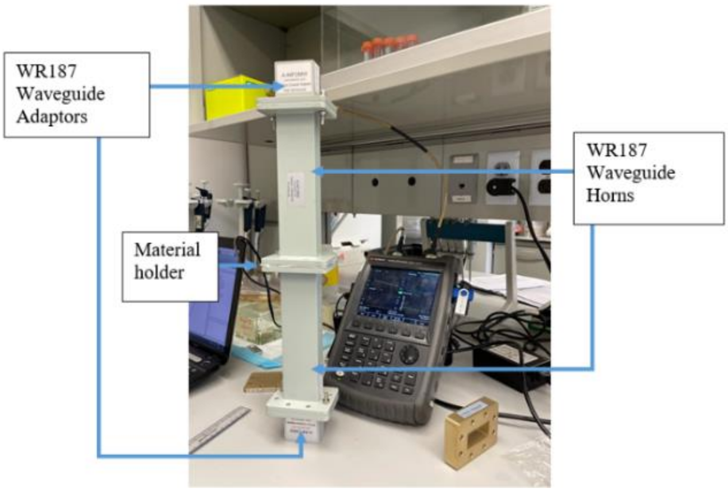


Figure 1. The rectangular waveguide set up used for dielectric characterization at frequencies between 3.95 – 5.85GHz

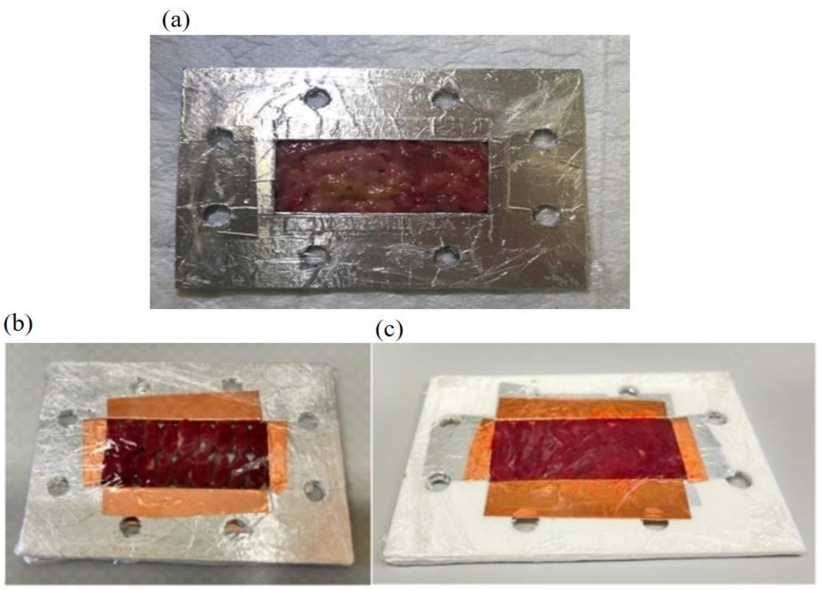
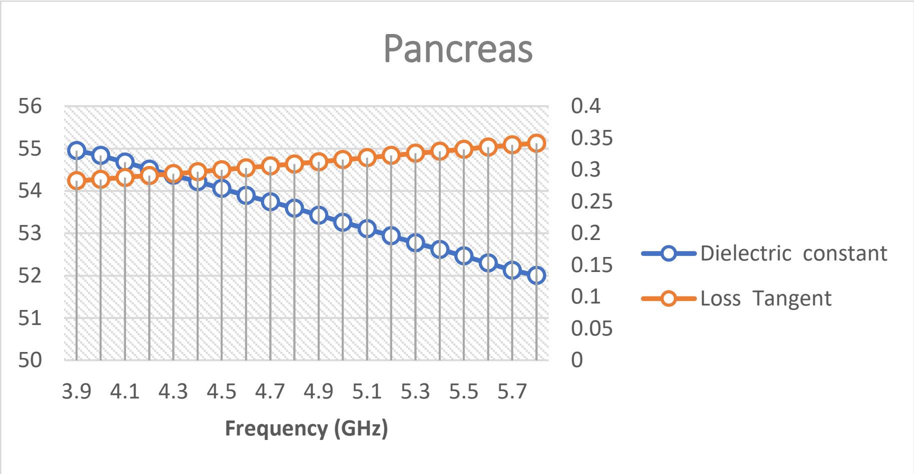


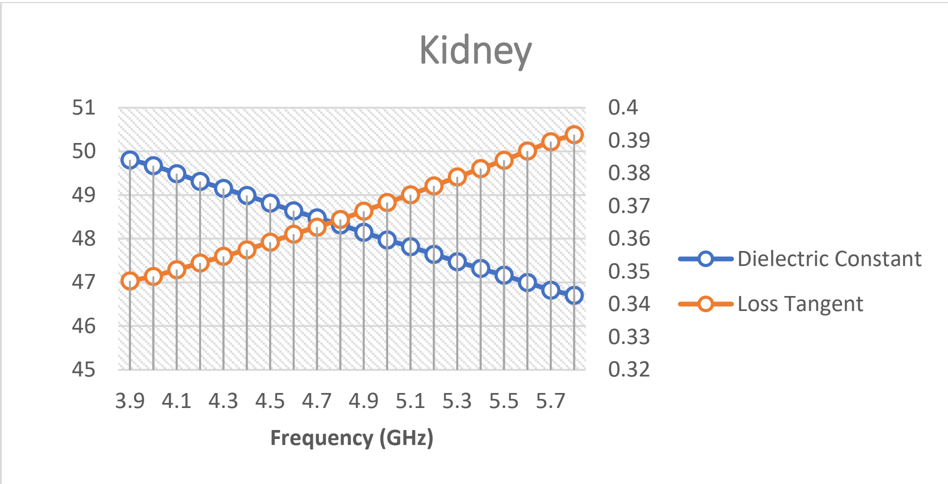
Figure 2. (a) The pancreases of 9 mice are placed next to each other in a 2mm material holder. (b) The kidneys of 9 mice are placed next to each other in a 3mm material holder. (c) The kidneys are then smashed gently to ensure the lack of air gaps.

3.2. Creating several recipes for pancreas and kidney phantoms within our frequency range of interest based on relevant data presented in literature

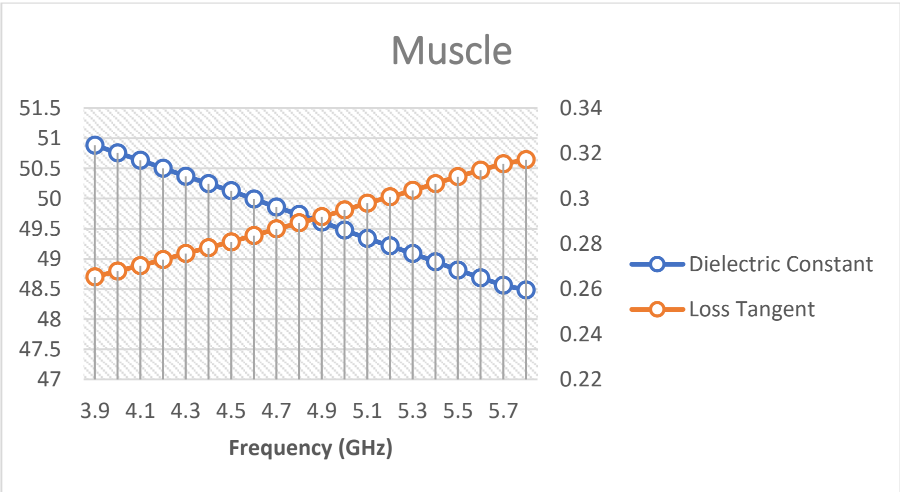
As presented earlier, no pancreatic phantom has been realized so far. Even as well, for the kidney phantoms, the efforts are scarce specially in the frequency band of 3.9-5.8GHz. Luckily, Gabriel et.al (Gabriel C. G., 1996) (Gabriel S. L., 1996) collected all the data in literature discussing the interaction of electromagnetic fields with biological tissues and performed measurements as well on actual tissues from dead bodies. Based on the obtained information, it was possible to produce a parametric equation that enables the prediction of the dielectric properties of almost all tissue types of the human body starting from a frequency of 10Hz to 100GHz (D.Andreuccetti, 1997). Hence, Figure 3(a) and 3(b) shows the dielectric parameters of actual pancreas and kidney over the range 3.9-5.8GHz. Comparing the features with that of actual blood and muscle tissues (Figure 3(c) and 3(d)), we can conclude that these tissues exhibit tissue equivalent electromagnetic behavior. For instance, the dielectric constant over the dictated frequency range decreases in a) blood: from 55.5 to 52.5, b) muscle: from 51 to 48, c) kidney: from 50 to 46.5, and d) pancreas: from 55 to 52. However, the conductivity increases in a) blood: from 4 S/m to 6.5 S/m, b) muscle: from 3 S/m to 5 S/m, c) kidney: from 4 S/m to 6 S/m and d) pancreas: from 4 S/m to 6 S/m.


Pancreas
56
55
54
53
52
51
50
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
3.9 4.1 4.3 4.5 4.7 4.9 5.1 5.3 5.5 5.7
Frequency (GHz)
Dielectric constant
Loss Tangent

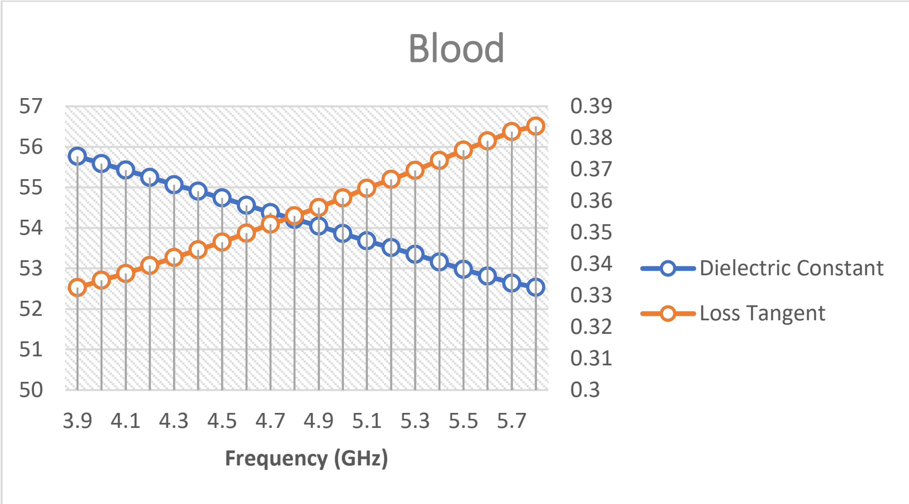
(a)


Kidney
51
50
49
48
47
46
45
0.4
0.39
0.38
0.37
0.36
0.35
0.34
0.33
0.32
3.9 4.1 4.3 4.5 4.7 4.9 5.1 5.3 5.5 5.7
Frequency (GHz)
Dielectric Constant
Loss Tangent

(b)


Muscle
51.5
51
50.5
50
49.5
49
48.5
48
47.5
47
0.34
0.32
0.3
0.28
0.26
0.24
0.22
3.9 4.1 4.3 4.5 4.7 4.9 5.1 5.3 5.5 5.7
Frequency (GHz)
Dielectric Constant
Loss Tangent

(c)



(d)

Figure 3. The variation of the dielectric constant and loss tangent of: (a) actual human pancreas (according to the parametric equation provided by Gabriel et.al (Gabriel S. L., 1996), (b) actual kidney tissue, (c) actual muscle tissue, and (d) actual blood tissue based on data presented in literature.

Recall that the values presented for the pancreas specifically are based on calculations derived from the parametric equation (S. Gabriel, 1996). Thus, we can utilize the already electrically characterized muscle and blood phantoms found in literature to build up recipes for pancreas and kidney phantoms. This is further facilitated by knowing the electromagnetic influence of tissue- mimicking materials. In other words, it is possible to estimate the dielectric properties (effective dielectric constant and equivalent loss tangent) of tissue mimicking phantom models as a function of formulation over specific frequency range. The estimation uses the data obtained from the dielectric characterization of a set of tissue mimicking materials which established known parameters across certain frequency bands at certain concentration. Additionally, an ideal phantom should be made of cheap and easily available constituents and exhibits ease of fabrication in standard research labs with minimal harm to the human body. These conditions are fulfilled using oil-in-gelatin semisolid phantoms. Thus, our hypothesis considers the recruitment of already characterized gelatinous muscle and blood phantoms to develop pancreatic and kidney tissue- mimicking phantoms, and by varying the constituents' concentration based on their dielectric effects, we report the dielectric properties of the newly developed phantoms. For this purpose, the recipes are like the most recent well-characterized semisolid fabricated muscle and blood phantoms by Yilmaz et.al (Yilmaz T. F., 2014) which were further optimized by Costanzo et.al (Costanzo, 2021). Table 1 shows the materials and their corresponding weight percent previously adopted by Yilmaz and Costanzo.

Reference	Yilmaz T. F., 2014		Costanzo, 2021	
Phantom Type	Muscle	Blood	Muscle	Blood
Materials	Weight percent			
Deionized Water	67.33%	71.80%	30%	70%
Vegetable Oil	10.25%	4.68%	60%	7%
NaCl	0.35%	0.37%		1%
Detergent	11.71%	12.49%	4%	12%
Gelatin	9.98%	10.65%	6%	10%

Table 1. The amount in weight percent used for each constituent to generate the 2 different phantoms by Yilmaz et.al and Costanzo et.al.

Knowing the dielectric characterization of NaCl, oil, and deionized water, variations at the level of these influencers would enable the generation of several phantom candidates. These variations are dictated by the fact that increasing the concentration of NaCl does not affect the reduction pattern of the dielectric constant with frequency, but it does increase the dielectric loss tangent of the solution in particularly at frequency bands of 0.5 to 5GHz (Castello-Palacios, 2017). Regarding the dielectric effect of oil, it is well known that increasing oil weight percent in phantom models reflects the dielectric properties of low-water content biological tissues (Lazebnik, 2005) and mainly the dielectric constant of such tissues. So, contrary to water's electromagnetic behavior, oil incrimination decreases the dielectric constant of the solution. Furthermore, based on the data presented for the 2014 phantoms, the behavior of blood phantom's dielectric constant mimics that of actual pancreas. However, the trend of elevation of conductivity for the muscle phantom shows close correlation with that of pancreas. Thus, several pancreas phantom candidates were generated including water and oil content similar to that of the blood phantom, but with NaCl (the main effector on loss tangent and conductivity) content close to that in muscle phantom. For the kidney models, both the decrease and increase in dielectric constant and conductivity respectively of the muscle phantom correlates with that of an actual kidney (Figure 4). Utilizing both phantoms and increasing the water content while decreasing that of NaCl, three different kidney models are proposed. Table 2 summarizes the composition of the proposed phantom candidates for each tissue.

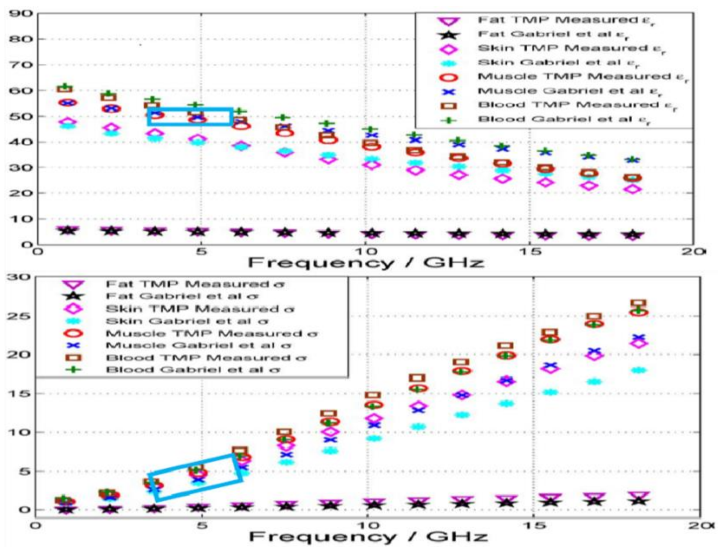


Figure 4. The graph at the top refers to the variation of dielectric constant of the represented templates as a function of frequency in GHz, and the below graph refers to that of conductivity. The graphs are replicated from the paper of (Yilmaz T. F., 2014). The added blue boxes are to highlight the frequency zone of interest in this research.

Tissue Targeted	Phantoms	Weight Percent Of Constituents				
		Deionized Water	Oil	NaCl	Soap	Gelatin
Pancreas	(1)	72%	4.50%	0.35%	12.50%	10.65%
	(2)	72%	4.50%	0.30%	12.50%	10.70%
	(3)	72%	4.50%	0.27%	12.50%	10.73%
	(4)	72%	4.50%	0.25%	12.50%	10.75%
	(5)	72%	4.50%	0.20%	12.50%	10.80%
	(6)	72%	5%	0.20%	13%	9.80%
Kidney	(1)	72.80%	4.60%	0.20%	12.40%	10%
	(2)	72.90%	4.60%	0.10%	12.40%	10%
	(3)	67.50%	10.25%	0.35%	12%	10%

Table 2. The composition by constituent for all the proposed phantom candidates based on the work of Yilmaz et.al (Yilmaz T. F., 2014).

On the other hand, another set of models are proposed based on the work of Costanzo et al. From the data provided (Figure 5), the dielectric constant's values of actual pancreas are greater than that of the muscle phantom, so either decreasing %oil or increasing %water. But the elevation in conductivity of the muscle phantom is lower than that of actual pancreas, so %NaCl could be elevated. Therefore, the added amount of NaCl was subtracted from oil content. Moreover, the fabricated muscle phantom showed slight increase in the dielectric constant's values in comparison with that of actual tissue contrary to conductivity when compared to the actual kidney tissue. Then, the increase in %NaCl was deducted from the %water. Table 3 shows the suggested recipes based on Costanzo's phantom.

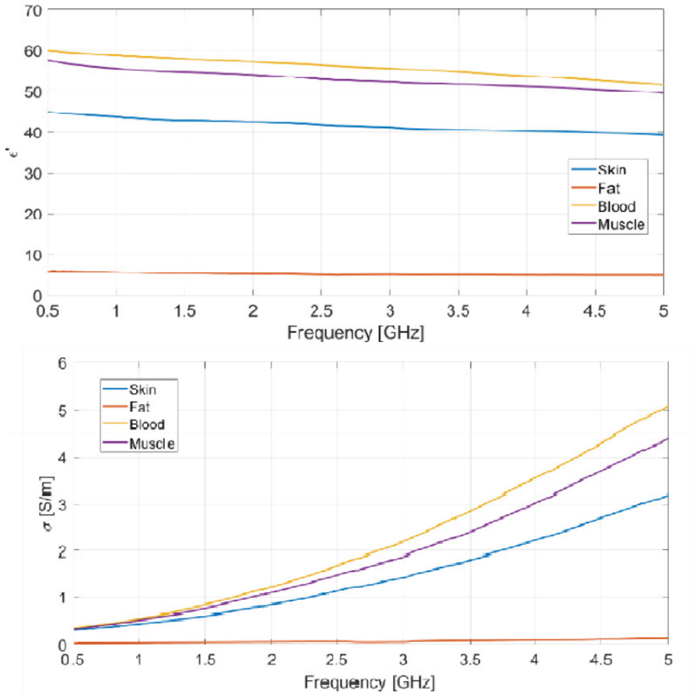


Figure 5. The measured dielectric constant variation as a function of frequency in GHz in the top graph and that of conductivity in S/m in the bottom graph. The figures are replicated from the paper of (Costanzo, 2021).

Tissue Targeted	Phantoms	Weight Percent Of Constituents				
		Deionized Water	Oil	NaCl	Soap	Gelatin
Pancreas	(1)	30%	58.50%	1.50%	4%	6%
	(2)	30%	59%	1%	4%	6%
	(3)	30%	59.50%	0.50%	4%	6%
	(4)	30%	59.80%	0.20%	4%	6%
Kidney	(1)	27.50%	60%	2.50%	4%	6%
	(2)	28%	60%	2%	4%	6%
	(3)	28.50%	60%	1.50%	4%	6%
	(4)	29%	60%	1%	4%	6%

Table 3. The proposed phantoms whose constituents' concentration distribution is contingent on (Costanzo, 2021).

3.3. Fabrication Procedure and Dielectric Characterization of the Phantom Candidates

To initiate the fabrication process, we first, started by weighing the constituents, then we added the gelatin pieces to the distilled water in a 100ml beaker covered with aluminum foil and placed it in a hot boiling bath maintained at 80°C. Once the gelatin was completely dissolved in water, we stirred the mixture gently using a vertically aligned spatula, then covered it and placed it in the hot bath again for a few minutes. Secondly, once the mixture was cooled down to a temperature of 60°C, the NaCl content was added, and placed the solution on a magnetic stirrer maintained at a rate that provides the maximum gentle stirring effect without causing air bubbles formation. Following that, and while the content in the beaker are still mixed on the magnetic stirrer, the soap content was added using a syringe to ensure that all the amount is poured, and when the mixture cooled down to room temperature, we poured the oil content gradually i.e., 1ml of the weighed oil amount successively should be added while ensuring that each added ml is completely dissolved in the solution. Consequently, the continuous stirring of the solution would lead to the formation of a white homogenous oil-in-water emulsion which in turn was poured into the desired airtight container. The container should be lined with a nylon sheet for easy handling after solidification. Finally, we should tap and hit the container at the bench counter to remove all possibly formed air bubbles and enhance the linearity of the surface and then place the container in the fridge to allow the solidification of the emulsion overnight. It is important to note that it is easy to cut the dimensions of the solidified mold, except for the height, so it is preferable to pour the mold into the desired height where the width and length can be easily managed after solidification, i.e., the container's dimension may or may not match the required dimensions of the phantom except for the height/thickness. After solidification, the phantoms must be handled with care as their surface will become adhesive. Touching the material with the naked hand is not recommended as it may lead to additional external disturbing factors.

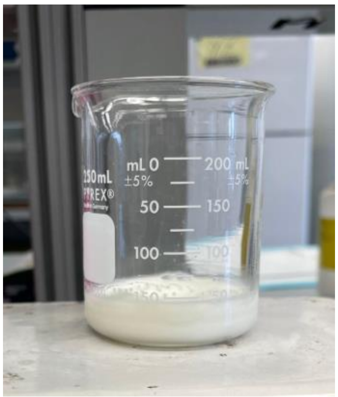


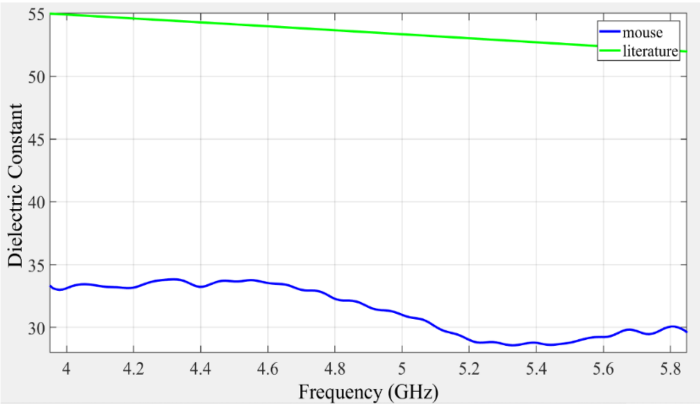
Figure 6. The state of the homogenous oil-in-water emulsion generated.

The setup explained in section 3.1 was adopted to perform the dielectric characterization of each phantom model. After solidification in the fridge overnight, each model was then placed in the material holder with care to prevent environmental or external factors that may affect the measurement’s results. Consequently, the evaluation and validation of these values obtained were carried out based on the harvested mice properties and the reference models in the literature. Moreover, another set of dielectric characterization measurements was performed to study the variations of the dielectric parameters within each sample.

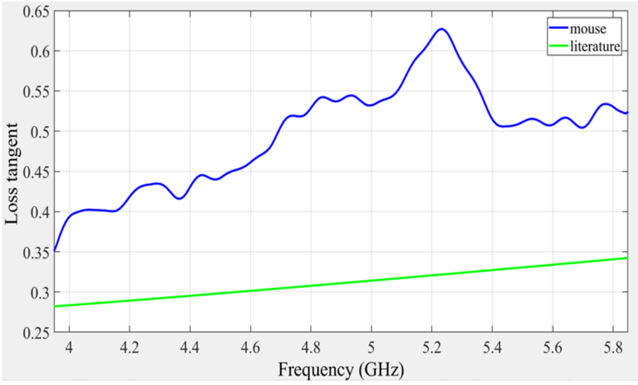
CHAPTER 4

RESULTS

The measured dielectric parameters of the mice's pancreas and kidney tissues are collected and presented in Figures 7 and 8, and then compared with that estimated by the parametric equation generated in literature (Gabriel C. G., 1996), (Gabriel S. L., 1996), (S. Gabriel, 1996), and (D.Andreuccetti, 1997). This comparison between calculated mice and estimated human electrical properties showed point value dispersions but similar overall behavior, as the dielectric constant decreases and loss tangent increases with frequency. The dispersion illustrated between human and mouse tissues is logical and expected since the dielectric properties show intrinsic variations within the populations, as well as in the same individual at different states or positions. Moreover, regarding the mice kidney tissue, the measured dielectric parameters of intact tissue differ from that obtained for smashed tissue. Consequently, a standard should be set up for each tissue type to be utilized as a reference for phantom evaluation.

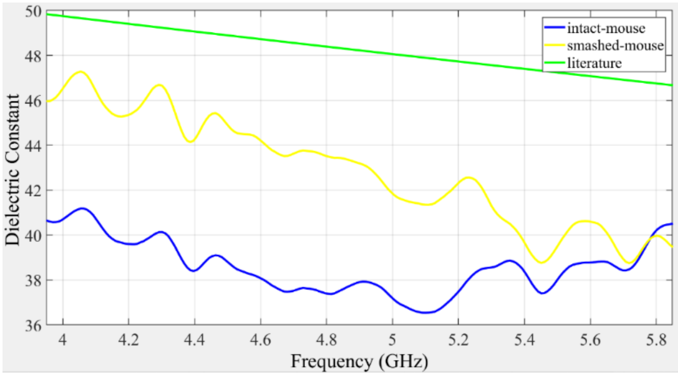


(a)

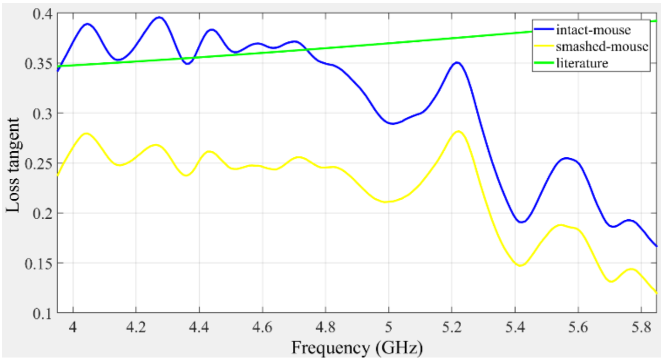


(b)

Figure 7. The curves show the variation of the: (a) dielectric constant and (b) loss tangent, of the tested pancreatic tissue in comparison with the data presented in literature as a function of frequency in GHz.



(a)



(b)

Figure 8. (a) The curves show the variation of the: (a) dielectric constant and (b) loss tangent, of the tested kidney tissue (both intact and smashed) in comparison with the data presented in literature as a function of frequency in GHz.

Since the electrical properties of human biological tissues are based on a parametric equation, the collected measurements for each phantom candidate are compared to both, the calculated mice tissue properties and those estimated in the literature. Based on the latter comparison, all correlations can be summarized in Table 4, in which the percent difference between the expected value (of targeted tissues) and the phantoms' characteristics is below 15%.

Phantom's composition		**Targeted Tissue**	**Dielectric parameter**	**Frequency Range**
1	30% deionized water + 6% gelatin + 59.8% oil + 4% soap + 0.2% NaCl	Pancreas Human	Loss Tangent	3.9 – 5.8
2	30% deionized water + 6% gelatin + 58.5% oil + 4% soap + 1.5% NaCl	Pancreas Mouse	Loss Tangent	5.1 – 5.3
3	72.8% deionized water + 10% gelatin + 0.2 % NaCl + 4.6% oil + 12.4 % soap	Kidney Mouse	Permittivity	5.1 – 5.8
			Loss Tangent	4
		Kidney Human	Permittivity	3.9 – 4.9
			Loss Tangent	3.9 – 5.3
4	72% deionized water + 5% oil + 13% soap + 0.2% NaCl+ 9.8% gelatin	Kidney Mouse	Permittivity	3.9 – 5.8
			Loss Tangent	3.9 – 5.5
		Kidney Human	Permittivity	3.9 – 4.5
5	72% deionized water + 4.5% oil + 12.5% soap + 0.2% NaCl + 10.8% gelatin	Kidney Mouse	Permittivity	3.9 – 5
			Loss Tangent	5.1 – 5.8
		Kidney Human	Loss Tangent	3.9 – 4.8
		Pancreas Mouse	Loss Tangent	3.9 – 4.2
		Pancreas Human	Loss Tangent	4.4 - 5.1
6	72% deionized water + 4.5% oil + 12.5% soap + 0.25% NaCl + 10.75% gelatin	Kidney Mouse	Permittivity	4.7 – 5.8
			Loss Tangent	3.9 – 5.3
		Kidney Human	Permittivity	3.9 _ 5.8
		Pancreas Human	Permittivity	3.9 – 5.5
			Loss Tangent	3.9 – 4.4
7	72% deionized water + 4.5% oil + 12.5% soap + 0.27% NaCl + 10.73% gelatin	Kidney Mouse	Permittivity	3.9 – 5.4
		Kidney Human	Permittivity	3.9 – 4.4

8	72% deionized water + 4.5% oil + 12.5% soap +0.3% NaCl + 10.7% gelatin	Kidney Mouse	Loss Tangent	5.5 – 5.8

Table 4. the frequency ranges in GHz in which the difference between the dielectric parameters of the phantom models and that of the reference is less than 15% error.

Noticing that several phantoms succeeded to mimic each of the animal and human pancreas and kidney tissues over several frequencies, some models simulated one parameter over the other in certain frequencies, however, others were able to mimic both parameters for each tissue at specific frequencies. Hence, the appropriate phantom is selected based on the type of tissue to be simulated, the frequency of interest, and the dielectric property of concern. However, Table 4 shows that three phantom models (phantom models designated by: (3), (4), and (6), in the Table) succeeded to simulate both parameters with that of the targeted tissues over a specific frequency range. Thus, to ensure the reproducibility of these three phantoms and that the obtained results are not affected by external factors or environmental interventions, an additional set of measurements was done. For this further evaluation, three replicates for each phantom model designated by numbers (3), (4), and (6) in Table 4 were developed and electrically characterized by the rectangular waveguide characterization method described in chapter 3. The obtained values for the dielectric constant and loss tangent were analyzed. The analysis includes calculating the average of N=3 values corresponding to the replicates of each model, and therefore the external factors which could affect the readings are minimized. The average of each parameter for each set of replicates was then compared with the targeted tissue originally successfully simulated by the chosen phantom model and the corresponding percent error was calculated.

Figures 9, 10, and 11 highlight the variation of the percent error between the averages calculated and the reference values selected. Accordingly, the behavior of the calculated values average with respect to the targeted reference tissue indicates that when generating several replicates for each model, the progression of the dielectric parameters over frequency was clearer with the decreased effect of external noise. Consequently, the percent error depicted in Figures 9(a), 10(a), and 11(a) indicates that the selected phantoms exhibit a dielectric constant that closely matches the targeted tissue over the chosen frequency range. However, the measurements of the loss tangent resulted in an increase in the percent error at certain frequencies. In other words, the percent error increased from 15% to 20% at certain frequencies within the range assigned in Table 4 for the three selected candidates. Accordingly, this variation in percent error resulted in a slight decrease in the original frequency range of correlation of the chosen phantom models. As a result, the obtained observations confirm that the selected three phantoms models have promising applications in simulating the electromagnetic behavior of the targeted pancreatic and kidney tissues.

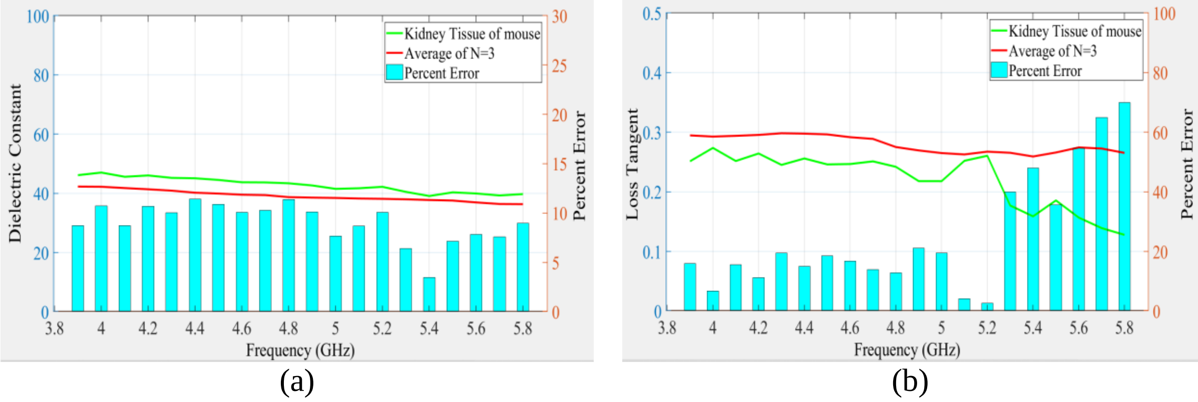
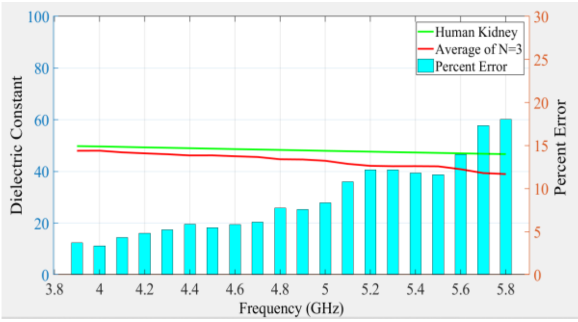
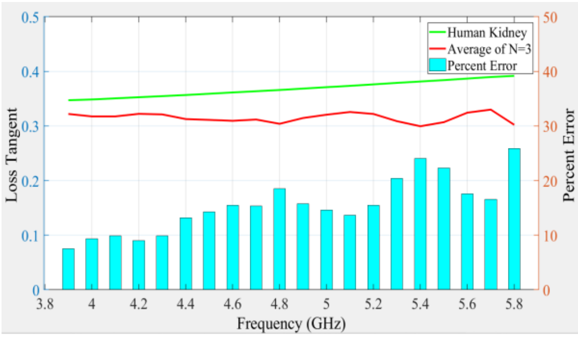


Figure 9. (a) Dielectric constant and (b) loss tangent of the tested mouse kidney tissue (smashed) vs the average of the three phantom samples of (4) as a function of frequency in GHz, with the bars reflecting the percent error generated from their difference.

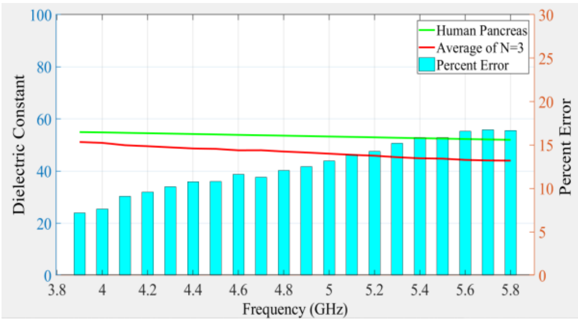


(a)

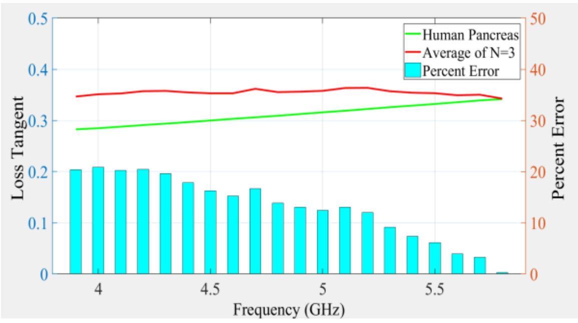


(b)

Figure 10. (a)Dielectric constant and (b) loss tangent of the human kidney tissue vs the average of the three phantom samples of (3) as a function of frequency in GHz, with the bars reflecting the percent error generated from their difference.



(a)



(b)

Figure 11. (a) Dielectric constant and loss tangent of the human pancreatic tissue vs the average of the three phantom samples of (6) as a function of frequency in GHz, with the bars reflecting the percent error generated from their difference.

CHAPTER 5

CONCLUSION

The proposed work has led to the development of the first kidney and pancreas phantoms that are able to mimic and replicate both the dielectric properties of actual human kidney and pancreatic tissues in the 3.9-5.8GHz frequency range using low-cost and easy-to-obtain materials such as water, oil, salt, soap, and gelatin. These materials have the potential to simulate various biological tissues so that a simple adjustment in the composition of the proposed models would allow the simulation of the dielectric properties of any other tissue. Using the same constituents, a kidney phantom that mimics the dielectric properties of a mouse's kidney over a 3.9 GHz to 5.8 GHz frequency range was successfully generated. Moreover, and based on the measured dielectric properties, an optimal phantom can be selected depending upon which specific tissue needs to be mimicked, as well as which electrical property is of interest (loss tangent or dielectric constant), in addition to the frequency range of interest.

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