Dielectric properties of bones for the monitoring of osteoporosis

Bilal Amin[1,2], Muhammad Adnan Elahi[1,2], Atif Shahzad[1,2], Emily Porter[2], Barry McDermott[1,2] and Martin O'Halloran[1,2]

[1]Department of Electrical and Electronic Engineering, National University of Ireland Galway, Ireland

[2]Translational Medical Device Lab, Lambe Institute for Translational Research & HRB Clinical Research Facility, University Hospital Galway

Address: Translational Medical Device Lab, Lambe Institute for Translational Research & HRB Clinical Research Facility, University Hospital Galway

Corresponding Author Email: b.amin2@nuigalway.ie

Corresponding Author Telephone: +35389-9802534

Corresponding Author Fax: N/A

Total number of words of the manuscript: 5682

Number of words of the abstract: 204

Number of figures: 10

Number of tables: 3

Abstract
Osteoporosis is one of the most common diseases that leads to bone fractures. Dual energy X-ray absorptiometry is currently employed to measure the bone mineral density and to diagnose osteoporosis. Alternatively, the dielectric properties of bones are found to be influenced by bone mineral density; hence dielectric properties of bones may potentially be used to diagnose osteoporosis. Microwave tomographic imaging is currently in development to potentially measure *in vivo* dielectric properties of bone. Therefore, the focus of this work is to summarize all available dielectric data of bone in the microwave frequency range, and analyse the confounders that may have resulted in variations in reported data. This study also compares the relationship between the dielectric properties and bone quality reported across different studies. The review suggests that variations exist in the dielectric properties of bone and the relationship between bone volume fraction and dielectric properties is in agreement across all studies. Conversely, the evidence of a relationship between bone mineral density and dielectric properties is inconsistent across the studies. This summary of dielectric data of bone along with a comparison of the relationship between the dielectric properties and bone quality will accelerate the development of microwave tomographic imaging devices for the monitoring of osteoporosis.

Key words: Bones, Osteoporosis, Bone mineral density, Dielectric Properties, Microwave Imaging.

1. Introduction

Osteoporosis, characterized as low bone mass, causes continuous systematic deterioration of the trabecular bone structure and leads to bone-fragility and fractures [34]. According to the Irish osteoporosis society guidelines published in 2012, approximately 300,000 Irish people aged above 50 years suffer from osteoporosis. If the same trends continue, then the expected cost for the treatment of osteoporosis will rise to €1,587- €2,043 million per annum by 2030 in Ireland. The report further states that in the EU, a hip fracture is reported every 30 seconds approximately, with about 1700 fractures reported per day; moreover, this number is expected to double by 2050. In the US, osteoporosis is considered the most commonly-encountered bone disease [14]. Almost 50% of American women and 25% of men over 50 years of age, have an osteoporosis-related bone fracture and around 43.6 million suffer from osteopenia, a precursor to osteoporosis [22]. Approximately two million osteoporotic fractures are reported in a year resulting into 432,000 hospital admissions in US [5].

From an anatomical perspective, bones typically have a hard, compact exterior layer called cortical bone and a less dense, spongy interior called trabecular bone, with the latter more prone to osteoporotic fractures as a result of this histological makeup and location [22]. The bone anatomy is shown in Figure 1. The majority of the fractures occur in the hip, with other sites including the spine and wrist. Hip fractures account for 72% of fracture costs [3] and 24% of the fracture related mortality rate [22]. Due to an aging population, the cost spent on osteoporosis by 2025 will be around $25.3 billion [2].

Demineralization of the bones is considered to be the major cause of osteoporosis [3]. Osteoporosis results from a continuous systematic loss of trabecular bone structure, making bones increasingly porous. Currently, bone mineral density (BMD) is used as the key clinical indicator for diagnosing osteoporosis [23]. Dual energy X-ray absorptiometry (DXA) is used as the standard modality used in clinics for the diagnosis of osteoporosis [16]. DXA calculates the BMD of central bone sites (hip, lumbar spine) and also peripheral sites (heel, distal forearm), and maps to a “T-score”, which is the difference between the BMD of the patient and the mean BMD of a healthy person with peak bone mass [5]. DXA offers an insight into BMD but does not provide information on the structure and biology of the trabecular bone pattern which are also considered key indicators for diagnosing osteoporosis; hence using bone mineral density solely for clinical care of overall fracture

risk has limitations [35]. The DXA scan uses standard X-ray doses, therefore frequent DXA scans are associated with long term health risks [17].

Alternative technologies include Quantitative Ultrasound (QUS) and Quantitative Computed Tomography (QCT). In QUS, the speed of sound and broadband attenuation in the patient's bone is observed, to estimate bone mass. The QUS technique was developed for bone imaging due to low health risks, since it is non-invasive technique and does not use ionizing radiation. However, this technique has not been well adopted by the clinicians because QUS is unable to penetrate through bone, and hence the bone mass was measured only by considering the outer bone surface [22]. The QCT measures volumetric bone mineral density (g/cm^3) and measures BMD of trabecular bones separately from cortical bone, and is therefore less prone to soft tissue errors [16]. QCT is rarely used in clinical practice settings due to the high intensity doses of X-ray required, expensive equipment, poor availability and cost of test [16].

Apart from BMD, the quality of bone and fracture risk can also be well characterized by bone volume fraction (BVF = Bone Volume/Total Sample Volume) [10]. BVF explains the micro-structure of bone and its relationship to biomechanic response. Since the strength of trabecular bone pattern is signifcantly effected by osteoporosis, BVF can be used to analyse the variation in bone strength [20]. Although BVF is clinically not considered for osteoporosis monitoring, a number of studies have suggested that BVF should be considered as a potential indicator of osteoporosis [10].

The dielectric properties (namely the relative permittivity and conductivity) of biological tissues characterise the interaction of electromagnetic (EM) waves with the tissue. Recent studies have suggested a significant correlation between the dielectric properties of bone and the corresponding BMD [9, 10, 12, 17, 18, 32]. Therefore, dielectric properties may be used to measure BMD for the diagnosis of osteoporosis. Dielectric properties are also important parameters in the development of novel EM diagnostic and therapeutic medical devices for various other diseases [26], such as time-domain microwave radar for breast health monitoring [25], microwave ablation for treating liver, lung, kidney, bone and adrenal tumours [1] and microwave hyperthermia for breast cancer treatment [21]. These dielectric properties of various biological tissues have been widely studied and reported in the literature, starting from early studies reported by [30] describing radio frequency (RF) field interactions with biological tissues. Comprehensive studies have been reported examining the behaviour of different biological tissues in relation to their dielectric properties [6, 29, 31]. Some studies have reported the dielectric properties of human tissues, while others have reported these dielectric properties for animal tissues. While dielectric data for majority of tissues is available, major variations are observed in dielectric data of key tissues such as breast. These variations are attributed to various confounders, and emphasize the challenge in measuring heterogeneous tissues. One of those challenging heterogeneous tissue is bone.

Fig. 1 Anatomical structure of bone

The human skeleton overall is composed of cortical and trabecular bone, in a ratio of 80:20 respectively [24]. The ratio of cortical and trabecular bone varies depending upon the anatomical site of body [4]. In Figure 1 the epiphysis (head) and start of the diaphysis (shaft) of a typical long bone is shown. Cortical bone has a dense and solid structure and forms the exterior of the bone. Trabecular bone with its characteristic honeycomb structure is prevalent in the epiphysis but does extend into the diaphysis underneath the cortex and surrounds the medullary (marrow) cavity. The metaphysis is the area between the head and shaft and contains the epiphyseal plate, which is the area where new bone tissues originate early in life with this area later ossifying. The structure of trabecular bone is weak, highly inhomogeneous and anisotropic as compared to cortical bone, and it is scattered in bone marrow [4, 33].

A number of studies have been performed to measure the dielectric properties of bones in both the low frequency range [3, 4, 8, 13, 19, 27, 28, 32, 36, 37] and in the microwave frequency range [6, 9, 10, 12, 15, 17, 18, 24]. While some of these studies only measured the dielectric properties of bone, some studies also investigated the relationship between the bone quality and dielectric properties. However, these studies are often limited in terms of number of bone samples and the range of BMD of bone samples examined, and do not provide a definite quantitative relationship between the BMD and dielectric properties. Additionally, these studies differ in terms of measurement techniques, location of bone sample source, type of bones, and bone sample preparation methods. Each of these factors can influence the measured dielectric properties. Despite the importance of the dielectric properties of the bone and their relationship to the bone quality for the diagnosis of osteoporosis, no comprehensive review has been reported in the literature that compares and contrasts various differences in these studies. The quantitative relationship between dielectric properties of bone and BMD can potentially be exploited to develop a microwave tomography based imaging device for the monitoring of osteoporosis. Microwave tomography imaging (MTI) has been previously used to measure *in vivo* dielectric properties of the breast, and it has been recently proposed to measure the dielectric properties of the calcaneus bone for monitoring of osteoporosis [7, 11, 17, 18]. However, the development of such a medical device requires reliable data that establishes a definitive correlation between dielectric properties and bone quality.

The objective of this study is to present a comprehensive review of historical studies that have investigated the dielectric properties of bone, and the relationship between the dielectric properties of bone and the bone quality in the microwave frequency range. This review includes a detailed analysis on all previous *in vitro* and *in vivo* dielectric studies of bones and a summary of evidence of a relationship between bone quality and dielectric properties. The comparison is performed across study type (*in vivo* or *in vitro*), frequency range, source of bone sample, bone type (cortical/ trabecular), and measurement technique.

The remainder of this paper is organized as follows: Section 2 presents the methods involved to review all studies on the dielectric properties of bone; Section 3 presents a summary of reported dielectric properties of bones and investigates the relationship between bone quality and dielectric properties; Section 4 presents a discussion on the comparison of results from different studies, analyses the variation in dielectric properties between different studies, and the variation of dielectric properties due to BMD and BVF; and finally, a conclusion is presented in Section 5.

2. Methods

Seven studies on dielectric properties of bone ranging from 1992-2014 are reviewed in this study. The inclusion criteria were based on studies evaluating dielectric properties of bones and the interrelationship between bone dielectric properties and bone quality across the microwave frequency range. Six of the studies investigated *in vitro* dielectric properties of bones and one study analysed *in vivo* dielectric properties of bones. The source of bone samples in all studies varied from each other. Two studies reported dielectric properties of bovine bone samples, three studies reported the same for porcine bone samples, and two studies reported these properties for human bone samples. The techniques employed to measure the dielectric properties of bones also varied across the different studies. Three studies used open-ended coaxial probes (OECL) along with a vector network analyser, two studies employed microwave tomography imaging system, and two studies used thin cell time domain spectroscopy in order to acquire dielectric properties. The study reference, study type, frequency range, source of bone sample, and measurement technique of each reviewed study are tabulated in Table 1.

Table 1. Comparative description of reported studies

ε = relative permittivity; σ = conductivity; IA=Impedance Analyser

3. Results

This section reviews all studies that have investigated the dielectric properties of bones in chronological order, along with studies that have examined the relationship between the dielectric properties and the bone quality (in terms of both BMD and BVF) in the microwave frequency range.

In 1992, Ivancich et al. examined the (*in vitro*) dielectric properties of water saturated cortical bone in both a natural (untreated) and demineralized state across the frequency range of 10 MHz-1.3 GHz using time domain spectroscopy [12]. The bone sample was taken from an adult bovine tibia and only one tibia was used for measurements. This study found that the relative permittivity for demineralized cortical bones is significantly higher than the relative permittivity of natural bones. Since the BMD of demineralized bone is less than that of natural bone, the study suggests a negative correlation between BMD and relative permittivity. The relative permittivity values are shown in Figure 2. This study did not report conductivity results and demineralization levels were not quantified in terms of the BMD.

Fig. 2 Permittivity for normal and demineralized bone samples [12]

Next, in 1996, Gabriel et al. examined the (*in vitro*) dielectric properties of cortical and trabecular bone across the frequency range of 10 Hz–20 GHz, with impedance and network analysers and OECL probes [6]. The bone samples were porcine in origin and the sample size was not specified in the paper. The permittivity and conductivity values are shown in Figure 3. It was observed in this study that the dielectric properties of trabecular bone are higher than those of cortical bone over the observed frequency range. This study only measured the dielectric properties of porcine cortical and trabecular bone samples and did not investigate relationship between dielectric properties and BMD.

Fig. 3 Permittivity and Conductivity for porcine cortical bone sample [6]. The dielectric properties of trabecular bone samples are higher than cortical bone samples

In 2009, Peyman et al. examined the (*in vitro*) dielectric properties of cortical bone samples across the frequency range of 50 MHz–20 GHz, using OECL probes and a network analyser. The bones were acquired from porcine models of three different ages (and therefore had an animal sample size of 3) [24]. This aim of the study was to examine the variation of dielectric properties of tissue with age. The dielectric properties were reported for only four frequency points (450 MHz, 900 MHz, 1800 MHz, and 2400 MHz) and are shown in Figure 4. Variations in dielectric properties with age were observed over the microwave frequency range, due to the reduction of water content in tissues [24]. The dielectric properties of porcine cortical bone decreased significantly as function the animals' age.

This result suggests a negative correlation between dielectric properties and aging. As BMD also decreases as function of age, a positive correlation between BMD and dielectric properties is suggested by this study.

Limitations of this study included that measurements were performed for only four frequency points, and the BMD of bone samples was not explicitly quantified within the study. The dielectric properties were reported against the normal demineralization process of aging; hence no quantitative relationship can be established between dielectric properties and BMD levels.

Fig. 4 Permittivity and conductivity of ageing porcine tissues at selected frequencies [24]. The dielectric properties reduce as the age increases

In 2011, Irastorza et al. examined the (*in vitro*) dielectric properties of fluid saturated trabecular and cortical bone from bovine animal models across the frequency range of 80 MHz–1 GHz, using time domain spectroscopy. The trabecular bone samples were acquired from the femoral condyle and femoral groove, whereas the cortical samples were acquired from the diaphysis of the femur. The number of samples examined was two [9]. The study was performed on natural and demineralized bone samples. It was observed from these measurements that the relative permittivity

for both trabecular and cortical bone samples was lower for natural bone samples compared to demineralized samples, as shown in Table 2.

Echoing the results of Ivancich et al., this study suggests a negative correlation between BMD and relative permittivity. The authors in this study did not report the exact BMD values of both natural and demineralized bone samples. The relative permittivity values for each sample in their natural and demineralized state is expressed at different frequencies also. No result was reported for the conductivity values of demineralized bone samples.

Table 2. Measurements on cortical and trabecular bone discs [9]

More recently, in 2012 Meaney et al. examined the (*ex vivo*) dielectric properties of trabecular bone submerged in a 0.9% saline solution over the frequency range of 900-1300 MHz, using a microwave tomography imaging (MTI) system. The bone sample was taken from a single porcine femur [18]. The study investigated the effect of bone demineralization on dielectric properties. The bone sample was demineralized between successive microwave scans using an acid treatment. The dielectric properties of the demineralized bones after each microwave scan were acquired from 2-D reconstructed microwave images, as shown in Figure 5. A decreasing trend of values was observed in both permittivity and conductivity plotted against BVF as shown in Figure 11. Once again, a negative correlation between bone mineralization and dielectric properties was observed, as shown in Figure 6. However, the study suggested that such experiments should be performed on *in vivo* or fresh bones to investigate the effect of blood vessels and marrow on dielectric properties that are found in the pores of bones. In this study, the variation in dielectric properties against the percentage change of mineralization level was presented, but again the BMD was not measured. Secondly, only one bone sample was considered for dielectric property measurement; hence the sample size was insufficient to draw any definite relationship between mineralization level of the bone sample and dielectric properties.

Fig. 5 Reconstructed permittivity images (left) of the **(a)** 1st, **(b)** 2nd, and **(c)** 5th microwave scan of a saline-saturated bone specimen in a test tube at 1100 MHz, respectively. The images on the right are the corresponding conductivity images (from [18]). The dielectric properties are increasing as the mineralization level of bones is decreasing after each microwave scan

Fig. 6 Relationship between the relative permittivity (top) and conductivity (bottom) with bone mineral density [18]. Negative correlation between dielectric properties and BMD

In 2012, Meaney et al. also examined the (*in vivo*) dielectric properties of the human calcaneus (heel) bone across the frequency range of 900-1700 MHz with a step size of 200 MHz, using the MTI system. The study was performed using two patients [17]. Figure 7(a, b) represent the soft-prior permittivity (top) and conductivity (bottom) reconstructed images for the first plane of the left and right heels of Patient 1 and Patient 2 respectively at 1300 MHz. The BMD values were acquired from quantitative ultrasound densitometry. It can be observed from Figures 7(a) and 7(b) that the dielectric properties of normal heel bone have lower values when compared to the values of affected heel bone.

Since the affected heel bone (with a low level of mineralization) has high dielectric properties relative to those of the normal heel bone (which has a high level of mineralization), a negative correlation between bone mineralization and dielectric properties was once again observed. The dielectric properties against BMD are tabulated in Table 3. The study only considered two patients and measurements were performed at only one frequency. Therefore, while it reinforces the results of a number of historical dielectric studies, again no definite correlation between dielectric properties and BMD can be established from these results and further studies are required.

Fig. 7(a) 1300 MHz relative permittivity (top) and conductivity (bottom) soft-prior images for the first plane of the left and right heels of patient 1, respectively, **(b)** 1300 MHz permittivity (top) and conductivity (bottom) soft-prior images for the first plane of the left and right heels of patient 2, respectively (from [17]). Affected heel bone has higher dielectric properties compared to normal heel bone. For Fig. 7, IEEE LICENSE received. License Number 4294280048384.

Table 3. Dielectric Properties against BMD values of two patients [17]

Patient	Foot	Ultrasound BMD	Relative Permittivity	% difference	Conductivity (S/m)	% difference
1	Affected	0.699	13.6	8.4%	0.84	45.2%
	Normal	0.773	12.5		0.53	
2	Affected	0.354	16.7	21.1%	0.92	13.9%
	Normal	0.311	13.5		0.80	

The %difference is between affected and normal feet values of relative permittivity and conductivity.

Irastorza et al. in 2014, examined the (*in vitro*) dielectric properties of trabecular bone across the frequency range of 100-1300 MHz, using OECL probes, a network analyser, and time domain reflectometer [10]. The bone samples were taken from the femoral heads of patients that had undergone total hip replacement, with the mean patient age being 80.7 years. The sample size was six, and therefore six femoral heads were obtained from surgeries. In this study, the authors found a negative correlation between BVF and the dielectric properties. Figure 8 represents permittivity and conductivity profiles for the trabecular bone samples. The results obtained both from experiments and simulations showed a significant linear negative correlation between BVF and dielectric properties. The higher the BVF, the lower the dielectric properties. However, the authors did not report any relationship between dielectric properties and BMD.

Fig. 8 Mean value of relative permittivity and conductivity [10]

4. Discussion

This section reviews; the variations in dielectric properties of bones for both trabecular and cortical bones samples, the relationship between bone dielectric properties and bone quality in terms of BMD and BVF in the microwave frequency range.

4.1 Variations in dielectric properties of bones

This section discusses the variation of dielectric properties across the microwave frequency range for all reported studies to date for both trabecular and cortical bone samples.

4.1.1 Variations in dielectric properties of trabecular bone

A comparison of the relative permittivity and conductivity of trabecular bone samples in microwave frequency range is shown in Figure 9 (a) and (b) respectively. The comparative analysis indicates that:

1. The dielectric properties of trabecular bone are of higher magnitude than those of cortical bone.

2. The dielectric properties of trabecular bone from human femoral heads are much higher than those of other species. The mean percent difference of relative permittivity between human and bovine trabecular bone is 51.57%.

3. Variations in dielectric properties are observed for bone samples acquired from different species: porcine, bovine, and human.

4. The conductivity profile of bones in the microwave frequency range also shows significant differences between values reported for samples of porcine, bovine and human origin.

4.1.2 Variations in the reported dielectric properties of cortical bone

A comparison of the relative permittivity and conductivity of cortical bone samples in the microwave frequency range is shown in Figure 9 (a) and (b) respectively. The comparative analysis suggests:

1. There is a significant variation in the dielectric properties of bovine and porcine cortical bone. However, this difference may be due to the bovine bone samples being saturated in water during measurments. The mean percent difference of relative permittivity values between bovine and porcine tissue is 17.46%.

2. Variations exist between the dielectric properties of porcine cortical bone reported in two different studies. The variation in dielectric properties of porcine cortical bones between [6] and [24] is likely due to the age difference of the porcine samples. The mean percent difference of relative permittivity between both studies is 32.59%.

Fig. 9 Comparison of relative permittivity and conductivity from reported studies. The reported studies exhibit variation in results; dielectric properties of trabecular bones are higher as compare to dielectric properties of cortical bones

4.2 Evidence of a Relationship between the Dielectric Properties of Bone and Bone Quality

This section examines the evidence of a link between bone dielectric properties and BMD and BVF, as a platform for new medical device development to potentially diagnose and monitor osteoporosis.

4.2.1 Dielectric Properties variation with respect to Bone Volume Fraction

The variation of dielectric properties with respect to BVF is reported only by Meaney et al. in [18] and Irastorza et al. in [10]. An analysis of these studies suggests the following:

1. There exists a negative correlation between BVF and dielectric properties (i.e., the higher the BVF, the lower the dielectric properties).

2. The relative permittivity values of human trabecular bones [10] across different levels of BVF are on average 38.25% higher than porcine trabecular bones [18].

3. In contrast to the relative permittivity, the conductivity values of porcine trabecular bones [18] across BVF are higher (at 900 MHz and 1100 MHz) when compared to human trabecular bones [10] . However, the trend is not consistent at 900 MHz, as the conductivity values of porcine trabecular bone dropped closer to conductivity values of human trabecular bones.

Fig. 10 Relationship between relative permittivity and conductivity against BVF [10, 18]. The black curves indicate dielectric properties of human and red curves indicate the same for porcine trabecular bones

4.2.2 Relationship between Dielectric Properties and Bone Mineral Density

A total of five studies reported relationship of BMD and dielectric properties, three of which involved animal bones and two involving human bones [9, 12, 17, 18, 24]. The comparative analysis indicates the following:

1. Dielectric properties of bone appear to vary consistently with BMD.

2. Since it is widely known that BMD varies with age, based on point 1 above, dielectric properties are also expected to vary with age.

3. Four of the five studies examined in this review reported a negative correlation between dielectric properties and BMD, while one reported a positive correlation.

To summarize, Peyman et al. in [24] found that the dielectric properties reduce as a function of age for porcine cortical bone samples. Since BMD also reduces as function of age, a positive correlation between BMD and dielectric properties can be inferred. Peyman's study did not report the absolute BMD values, and hence no definite conclusion can be drawn. Irastorza et al. in [9] found that the dielectric properties for both natural trabecular and cortical bone have lower values compared to the demineralized state; hence a negative correlation is suggested. Meaney et al. in [18] found negative correlation between mineralization levels and dielectric properties for a trabecular bone sample from a porcine femur (lower the mineralization level higher the dielectric properties). BMD values were not reported in this study and change of dielectric properties was expressed in terms of percentage change of mineralization. In a separate study Meaney et al. [17] found a negative correlation between BMD and dielectric properties for two human patients. As the sample size was small, a more comprehensive study is required over large frequency range in order to quantify this relationship. The relationship between BMD and dielectric properties for all frequency ranges is of paramount importance for characterization of osteoporosis.

5. Conclusion

This work has provided the first comprehensive review of the dielectric properties of bones over the microwave frequency range. The review has presented measurement techniques, variation of dielectric properties of bones among reported studies and the also examined the variation in dielectric properties with bone quality (BMD and BVF).

Based on review of all studies, the dielectric properties of trabecular bone samples are found to be higher than those of cortical bone samples. Variations are observed in the dielectric properties across all studies. All studies explaining variation of BVF against dielectric properties are well in agreement with each other in that there is a negative correlation between them. However, the magnitude of the variation between BVF and dielectric properties varies among these studies.

In contrast, the studies examining the relationship between BMD and dielectric properties found contradictory results. Four studies have reported a negative correlation between BMD and the dielectric properties; however, one study found a positive correlation. Hence, significant work is required to establish the relationship between BMD and dielectric properties over a wide frequency range; since BMD is considered as a key potential indicator for osteoporosis detection.

Acknowledgements

The research leading to these results has received funding from the European Research Council under the European Union's Horizon 2020 Programme/ ERC Grant Agreement BioElecPro n. 637780.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

1. Brace CL (2009) Radiofrequency and Microwave Ablation of the Liver, Lung, Kidney, and Bone: What Are the Differences? Curr Probl Diagn Radiol 38:135–143. doi: 10.1067/j.cpradiol.2007.10.001

2. Burge R, Dawson-Hughes B, Solomon DH et al (2007) Incidence and Economic Burden of Osteoporosis-Related Fractures in the United States, 2005-2025. J Bone Miner Res 22:465–475. doi: 10.1359/jbmr.061113

3. Chakkalakal DA, Johnson MW, Harper RA, Katz JL (1980) Dielectric Properties of Fluid-Saturated Bone. IEEE Trans Biomed Eng BME-27:95–100. doi: 10.1109/TBME.1980.326713

4. Clarke B (2008) Normal bone anatomy and physiology. Clin J Am Soc Nephrol 3 Suppl 3:1–16. doi: 10.2215/CJN.04151206

5. Cosman F, de Beur SJ, LeBoff MS et al (2014) Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int 25:2359–2381. doi: 10.1007/s00198-014-2794-2

6. Gabriel S, Lau RW, Gabriel C (1996) The dielectric properties of biological tissues .2.

Measurements in the frequency range 10 Hz to 20 GHz. Phys Med Biol 41:2251–2269. doi: 10.1088/0031-9155/41/11/002

7. Golnabi AH, Meaney PM, Geimer S et al (2011) Microwave tomography for bone imaging. Proc - Int Symp Biomed Imaging 9:956–959. doi: 10.1109/ISBI.2011.5872561

8. Haba Y, Wurm A, Köckerling M et al (2017) Characterization of human cancellous and subchondral bone with respect to electro physical properties and bone mineral density by means of impedance spectroscopy. Med Eng Phys 45:34–41. doi: 10.1016/j.medengphy.2017.04.002

9. Irastorza R, Mayosky M, Grigera R, Vericat F (2011) Dielectric properties of natural and demineralized collagen bone matrix. IEEE Trans Dielectr Electr Insul 18:320–328. doi: 10.1109/TDEI.2011.5704524

10. Irastorza RM, Blangino E, Carlevaro CM, Vericat F (2014) Modeling of the dielectric properties of trabecular bone samples at microwave frequency. Med Biol Eng Comput 52:439–447. doi: 10.1007/s11517-014-1145-y

11. Irastorza RM, Carlevaro CM, Vericat F (2013) Is there any information on micro-structure in microwave tomography of bone tissue? Med Eng Phys 35:1173–1180. doi: 10.1016/j.medengphy.2012.12.014

12. Ivancich A, Grigera JR, Muravchik C (1992) Electric behaviour of natural and demineralized bones. Dielectric properties up to 1 GHz. J Biol Phys 18:281–295. doi: 10.1007/BF00419425

13. Kosterich JD, Foster KR, Pollack SR (1983) Dielectric permittivity and electrical conductivity of fluid saturated bone. IEEE Trans Biomed Eng 30:81–86. doi: 10.1109/TBME.1983.325201

14. Laster AJ (2014) Dual-Energy X-Ray Absorptiometry: 75:132–136.

15. Liboff AR, Rinaldi RA, Lavine LS, Shamos MH (1975) On Electrical Conduction in Living Bone. Clin Orthop Relat Res 106:330–335.

16. Lochmüller E-M, Müller R, Kuhn V et al (2003) Can Novel Clinical Densitometric Techniques Replace or Improve DXA in Predicting Bone Strength in Osteoporosis at the Hip and Other Skeletal Sites? J Bone Miner Res 18:906–912. doi: 10.1359/jbmr.2003.18.5.906

17. Meaney PM, Goodwin D, Golnabi AH et al (2012) Clinical microwave tomographic imaging of the calcaneus: A first-in-human case study of two subjects. IEEE Trans Biomed Eng 59:3304–3313. doi: 10.1109/TBME.2012.2209202

18. Meaney PM, Zhou T, Goodwin D et al (2012) Bone dielectric property variation as a function of mineralization at microwave frequencies. Int J Biomed Imaging. doi: 10.1155/2012/649612

19. Mercato G De, Garcia Sanchez FJ (1992) Correlation Between Low-Frequency Electric Conductivity and Permittivity in the Diaphysis of Bovine Femoral Bone. IEEE Trans Biomed Eng 39:523–526. doi: 10.1109/10.135546

20. Nazarian A, Von Stechow D, Zurakowski D et al (2008) Bone volume fraction explains the variation in strength and stiffness of cancellous bone affected by metastatic cancer and osteoporosis. Calcif Tissue Int 83:368–379. doi: 10.1007/s00223-008-9174-x

21. Nguyen PT, Abbosh A, Crozier S (2015) Microwave hyperthermia for breast cancer treatment using electromagnetic and thermal focusing tested on realistic breast models and antenna arrays. IEEE Trans Antennas Propag 63:4426–4434. doi: 10.1109/TAP.2015.2463681

22. Office of the Surgeon General (2004) Bone Health and Osteoporosis - NCBI Bookshelf.

23. Organization WH (2004) WHO SCIENTIFIC GROUP ON THE ASSESSMENT OF OSTEOPOROSIS AT PRIMARY HEALTH Care Level. World Heal Organ May:5–7. doi:

10.1016/S0140-6736(02)08761-5

24. Peyman a., Gabriel C, Grant EH et al (2009) Variation of the dielectric properties of tissues with age: the effect on the values of SAR in children when exposed to walkie-talkie devices. Phys Med Biol 54:227–241. doi: 10.1088/0031-9155/55/17/5249

25. Porter E, Coates M, Popović M (2016) An Early Clinical Study of Time-Domain Microwave Radar for Breast Health Monitoring. IEEE Trans Biomed Eng 63:530–539. doi: 10.1109/TBME.2015.2465867

26. Porter E, OHalloran M (2017) Investigation of Histology Region in Dielectric Measurements of Heterogeneous Tissues. IEEE Trans Antennas Propag 1–1. doi: 10.1109/TAP.2017.2741026

27. Reddy GN, Saha S (1984) Electrical and Dielectric Properties of Wet Bone as a Function of Frequency. IEEE Trans Biomed Eng BME-31:296–303. doi: 10.1109/TBME.1984.325268

28. Saha S, Williams PA (1992) Electrical and dielectric properties of Wet Human Cancellous Bone as a Function of Frequency. IEEE Trans Biomed Eng 39:1298–1304. doi: 10.1109/TBME.1984.325268

29. Salahuddin S, Porter E, Krewer F, O' Halloran M (2017) Optimised analytical models of the dielectric properties of biological tissue. Med Eng Phys 43:103–111. doi: 10.1016/j.medengphy.2017.01.017

30. Schwan HP, Foster KR (1980) RF-Field Interactions with Biological Systems: Electrical Properties and Biophysical Mechanisms. Proc IEEE 68:104–113. doi: 10.1109/PROC.1980.11589

31. Shahzad A, Sonja K, Jones M et al (2017) Investigation of the effect of dehydration on tissue dielectric properties in ex vivo measurements. Biomed Phys Eng Express 3:1–9.

32. Sierpowska J, Töyräs J, Hakulinen MA, Saarakkala S, Jurvelin JS, Lappalainen R (2003) Electrical and dielectric properties of bovine trabecular bone -- relationships with mechanical properties and mineral density," Phys Med Biol 48:775–786.

33. Sierpowska J, Lammi MJ, Hakulinen MA et al (2007) Effect of human trabecular bone composition on its electrical properties. Med Eng Phys 29:845–852. doi: 10.1016/j.medengphy.2006.09.007

34. US Department of Health and Human Services (2004) Bone health and osteoporosis: a report of the Surgeon General. US Heal Hum Serv 437. doi: 10.2165/00002018-200932030-00004

35. Wilkie JR, Giger ML, Chinander MR et al (2004) Comparison of radiographic texture analysis from computed radiography and bone densitometry systems. Med Phys 31:882–891. doi: 10.1118/1.1650529

36. Williams PA, Saha S (1996) The electrical and dielectric properties of human bone tissue and their relationship with density and bone mineral content. Ann Biomed Eng 24:222–233. doi: 10.1007/BF02667351

Author biography

 Bilal Amin is pursuing his Ph.D. in Electrical and Electronics Engineering from National University of Ireland Galway. His Ph. D research, under the supervision of Dr. Martin O'Halloran at Translational Medical Device Lab., is on the application of Dielectric Metrology and Electromagnetic Medical systems for earlier diagnosis of Osteoporosis. His Ph. D program is being funded by European Research Council (ERC) scholarship. He did his BS in 2013, securing First Class, in Electrical Engineering from COMSATS Institute of Information Technology (CIIT) Lahore, Pakistan under the auspices of National ICT scholarship program. In 2015, he earned his Master's degree with distinction, in Electrical Engineering from COMSATS Institute of Information Technology (CIIT) Islamabad, Pakistan. Bilal has worked as Lecturer in Electrical Engineering Department CIIT Lahore, Pakistan and Bahria University Islamabad, Pakistan from 2015 to 2017. His current research interests are compressive sampling, optimization theory, microwave imaging, medical signal processing, dielectric metrology and electromagnetic medical systems.

 Muhammad Adnan Elahi is a postdoctoral researcher at Translational Medical Device Lab, NUI Galway. He holds M.Sc. in Embedded Digital Systems (Distinction) from University of Sussex, United Kingdom and BS in Computer Engineering (First Class) from COMSATS Institute of Information Technology (CIIT), Lahore, Pakistan. His PhD research was focused on investigation and development of novel signal processing algorithms to improve microwave imaging of the breast. His current research interests include development of novel electromagnetic medical imaging and therapeutic devices. He has previously worked as a visiting postgraduate researcher at University of Calgary, Canada; as a Research Associate at Computer Vision Research Group (COMVIS), Lahore, Pakistan and as a lecturer (2007-2012) at CIIT Lahore, Pakistan. He has received several national and international awards including IRC "New Foundations" Grant; SFI PhD Fellowship; and several EU COST Action grants for Short-term Scientific Missions and attending training schools. He is an active member of MiMed and EMF-MED EU Cost Actions.

 Atif Shahzad is a senior postdoctoral researcher and team lead ablation technologies at Translational Medical Device Lab, National University of Ireland, Galway. He received BSc (honors) in computer engineering from COMSATS Institute of Information

Technology, Pakistan, and MSc in electronics engineering from University of Leeds, United Kingdom. He is associated with NUI Galway since 2011, starting PhD in microwave imaging for medical applications. His research is focused on thermal ablation and sensing technologies, medical signal and image processing, applied electromagnetic, computational modelling, and dielectric spectroscopy. He worked as a lecturer at COMSTATS Institute of Informational Technology from 2006 to 2011, where he taught undergraduate courses to electronic and computer engineering students and supervised final year projects. He has also worked as research staff in Computer Vision research group at COMSATS, where he developed real time video processing techniques for vehicle recognition in forensic applications. He has received several national and international awards from Irish Research Council, Science Foundation Ireland, NUI Galway, and Ministry of Science and Technology Pakistan. He is also member of COST (European Cooperation in Science and Technology) Action MiMED and COST Action EMF-MED.

Dr Emily Porter is an EU Marie-Curie Research Fellow in the Translational Medical Device Lab at the National University of Ireland, Galway. She studied at McGill University, Canada, where she received her M.Eng. in 2010 and her Ph.D. in Applied Electromagnetics in 2015. Her current research is focused on novel medical applications of electromagnetics, with projects including bladder monitoring and stroke detection using electrical impedance tomography, microwave radar for breast cancer diagnosis and treatment, anatomically and electrically realistic phantoms, and standardized dielectric measurements of biological tissues. Dr. Porter is the recipient of several prestigious national and international awards, including the IEEE Antennas and Propagation Society Doctoral Research Award, the Irish Research Council (IRC) "New Foundations" Grant, the Royal Irish Academy (RIA) Charlemont Grant, the Natural Sciences and Engineering Research Council of Canada (NSERC) Postdoctoral Fellowship, Le Fonds de recherche du Québec – Nature et technologies (FRQNT) Fellowship (Research Fund of Quebec: Nature and Technologies), and the D.W. Ambridge Prize, awarded by McGill University for the most outstanding graduating doctoral student in Natural Sciences or Engineering.

Barry McDermott graduated with a 1st class honours B.E. (Electronic and Computer Engineering) degree from NUIG in 2016. He received the University Scholar Award from NUIG on 3 occasions as well as an ON Semiconductor Scholarship and Mature Student Scholarship from the university. He was awarded the James Hardiman Research Scholarship to pursue Ph.D. studies at NUIG as part of the Medical Device Research Group. As well as being an engineer, Barry holds professional qualifications in both Pharmacy and Veterinary Medicine. Barry qualified and worked professionally as a Pharmacist, graduating from The University of Dublin, Trinity College in 2003 with a 1st class honours B.Sc. (Pharm) degree and winning both a Gold Medal and the Antigen Prize for 1st place in Pharmaceutics & Pharmaceutical Technology. He received an honours MVB degree (DVM equivalent) from University College Dublin in 2009 in Veterinary Medicine as well as

the Veterinary Council of Ireland Freeman Memorial Medal for outstanding academic performance in a range of fields including animal husbandry, pathology, microbiology, parasitology and pharmacology.

Dr Martin O'Halloran is a European Research Council (ERC) and Science Foundation Ireland (SFI) Investigator at the National University of Ireland Galway. Reflecting the interdisciplinary nature of his research, he holds a joint affiliation with the College of Engineering and Informatics; and the College of Medicine, Nursing & Health Sciences, and leads the Translational Medical Device Laboratory in the Lambe Institute. Dr O'Halloran has received over 30 national and international research awards, and was recently awarded SFI's Early-Stage Researcher of the Year, Engineers Ireland Chartered Engineer of the Year, and the European Research Council's Starting Investigator Grant. He was a co-proposer of a European COST Action (entitled "MiMED"), and is now leading a network of over 180 medical device researchers from 24 countries, focused on the clinical evaluation and commercialisation of novel medical devices in Europe. Over the last 6 years, Dr O'Halloran has personally secured €5.6 million in direct research funding and has published more than 40 papers in peer-reviewed journals. Dr O'Halloran has been an invited chair and invited speaker at several major electromagnetics and translational medicine conferences/seminars. He is currently non-executive director of the BioInnovate programme, and co-lead of the Health Innovation Hub Ireland at NUI Galway.

Dielectric properties of bones for the monitoring of osteoporosis

Bilal Amin[1,2], Muhammad Adnan Elahi[1,2], Atif Shahzad[1,2], Emily Porter[2], Barry McDermott[1,2] and Martin O'Halloran[1,2]

[1]Department of Electrical and Electronic Engineering, National University of Ireland Galway, Ireland

[2]Translational Medical Device Lab, Lambe Institute for Translational Research & HRB Clinical Research Facility, University Hospital Galway

Address: Translational Medical Device Lab, Lambe Institute for Translational Research & HRB Clinical Research Facility, University Hospital Galway

Corresponding Author Email: b.amin2@nuigalway.ie

Corresponding Author Telephone: +35389-9802534

Corresponding Author Fax: N/A

Reference	Study Type	Frequency Range	Source	Measurement Technique	Dielectric Properties
Ivancich et al. [12]	*in vitro*	10 MHz-1.3 GHz	Adult bovine cortical and trabecular tibial bone	Thin cell time domain spectroscopy (TDS) HP (1815B) Sampler, HP (1801A) oscilloscope, SNA (HP8711A)	$\varepsilon = 9.64$ (demineralized bone, 238.49 MHz), $\varepsilon = 17.75$ (native bone, 414.85 MHz)
Gabriel et al. [6]	*in vitro*	10 Hz–20 GHz	Porcine cortical bone	OECL, IA (HP4192A) , IA(HP 8753C), IA(HP8720)	ε = 1.0E+3- 1.0E+1 σ (Sm^{-1}) = 1.0E-2- 1.0E+1
Peyman et al. [24]	*in vitro*	50 MHz–20 GHz	Porcine cortical bone	OECL, Network Analyser (Agilent 8720D)	$\varepsilon = 28.1 \pm 2.0$, σ (Sm^{-1}) = 0.34 ± 0.04 (10 Kg, 450 Hz)
Irastorza et al. [9]	*in vitro*	80 MHz–1 GHz	Bovine diaphysis femur cortical bone	OECL, HP (1815B) TDR/Sampler, HP (1801A) oscilloscope, SNA (HP8711A)	$\varepsilon = 14.8$ (natural bone) $\varepsilon = 27.5$ (demineralized bone) (80 MHz)
Meaney et al. [18]	*in vitro*	900-1300 MHz	Porcine trabecular femoral bone	MTI	$\varepsilon = 48$, $\sigma = 1.9$ (1100 MHz)
Meaney et al. [17]	*in vivo*	900-1700 MHz	Human trabecular calcaneus bone	MTI	$\varepsilon = 13.6$, σ =0.84 (1300 MHz)
Irastorza et al. [10]	*in vitro*	100-1300 MHz	Human trabecular femoral head bone	OECL, HP (1815B) TDR/Sampler, HP (1801A) oscilloscope, SNA (HP8711A)	$\varepsilon = 46.85$, $\sigma = 0.578$ (400 MHz)

Table 1

Parameters	Sample 1 (Natural)	Sample 1 (Demineralized)	Sample 2 (Natural)	Sample 2 (Demineralized)
ε_{mf}	14.8	27.5	16.0	42.6
$\Delta\varepsilon_{mf}$	2.1	1.8	1.8	2.3
f_r	452 MHz	247 MHz	580 MHz	264 MHz

Table 2

Patient	Foot	Ultrasound BMD	Relative Permittivity	% difference	Conductivity (S/m)	% difference
1	Affected	0.699	13.6	8.4%	0.84	45.2%
	Normal	0.773	12.5		0.53	
2	Affected	0.354	16.7	21.1%	0.92	13.9%
	Normal	0.311	13.5		0.80	

Table 3

Dielectric properties of bones for the monitoring of osteoporosis

Bilal Amin[1,2], Muhammad Adnan Elahi[1,2], Atif Shahzad[1,2], Emily Porter[2], Barry McDermott[1,2] and Martin O'Halloran[1,2]

[1]Department of Electrical and Electronic Engineering, National University of Ireland Galway, Ireland

[2]Translational Medical Device Lab, Lambe Institute for Translational Research & HRB Clinical Research Facility, University Hospital Galway

Address: Translational Medical Device Lab, Lambe Institute for Translational Research & HRB Clinical Research Facility, University Hospital Galway

Corresponding Author Email: b.amin2@nuigalway.ie

Corresponding Author Telephone: +35389-9802534

Corresponding Author Fax: N/A

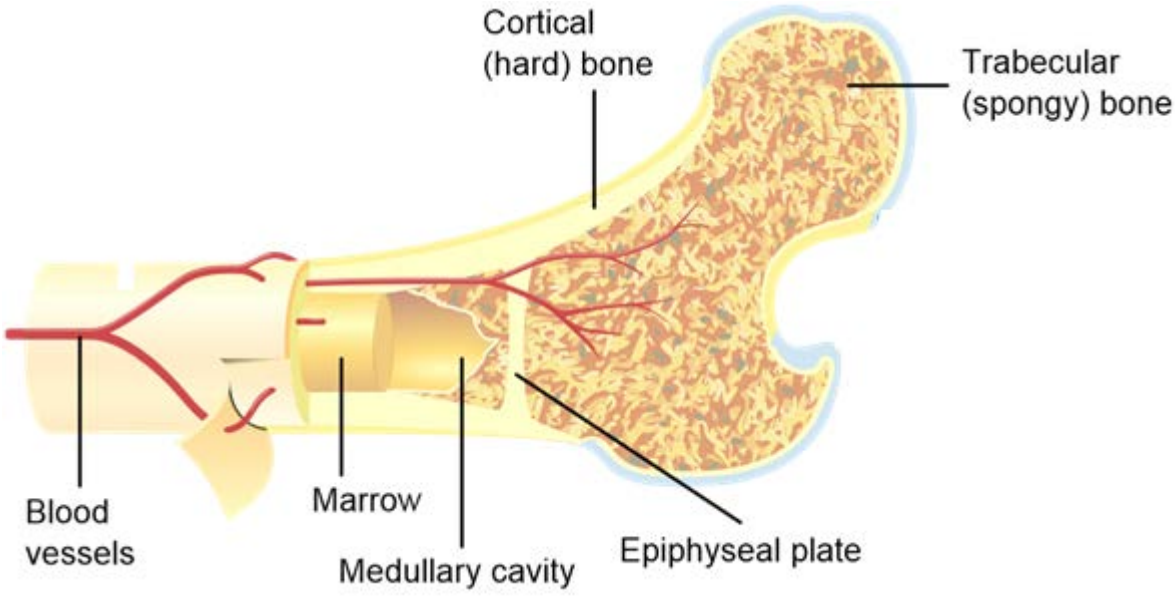

Cortical
(hard) bone
Trabecular
(spongy) bone
Blood
vessels
Marrow
Medullary cavity
Epiphyseal plate

Fig. 1

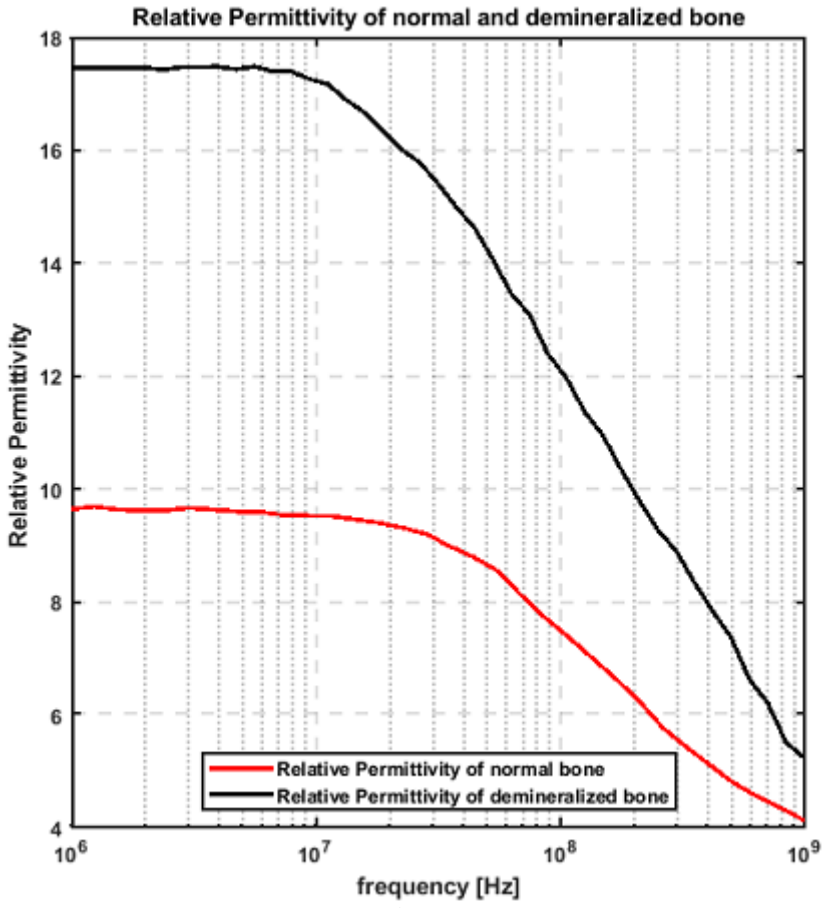
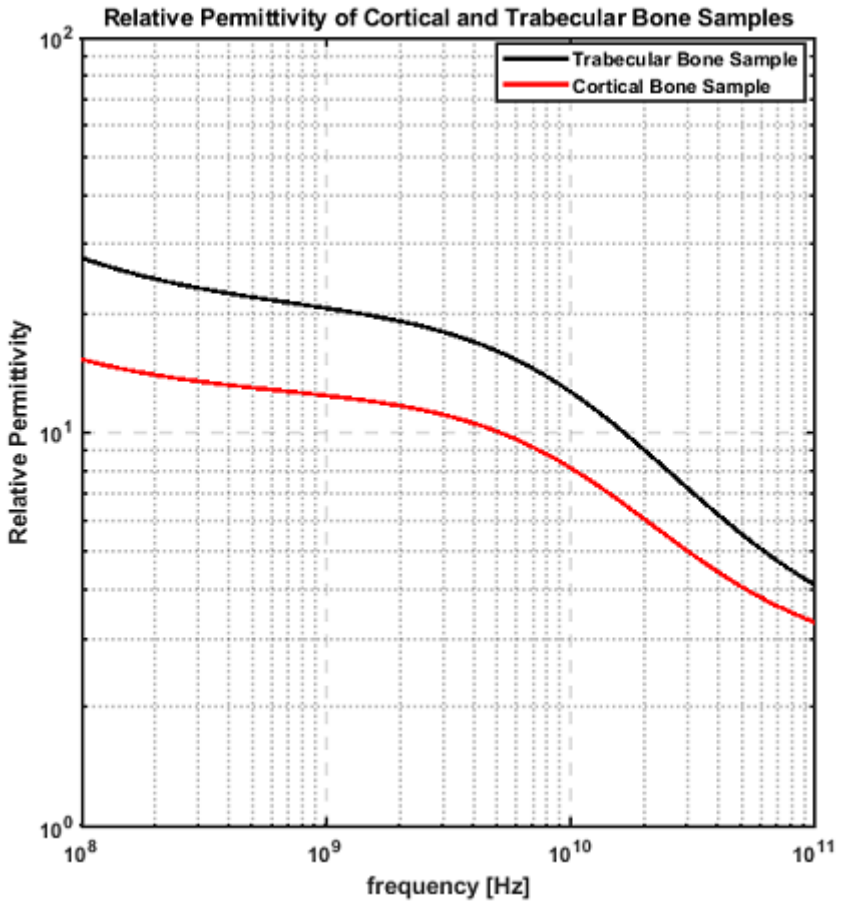

Relative Permittivity of normal and demineralized bone
Relative Permittivity
frequency [Hz]
Relative Permittivity of normal bone
Relative Permittivity of demineralized bone

Fig. 2


Relative Permittivity of Cortical and Trabecular Bone Samples
Trabecular Bone Sample
Cortical Bone Sample
Relative Permittivity
frequency [Hz]

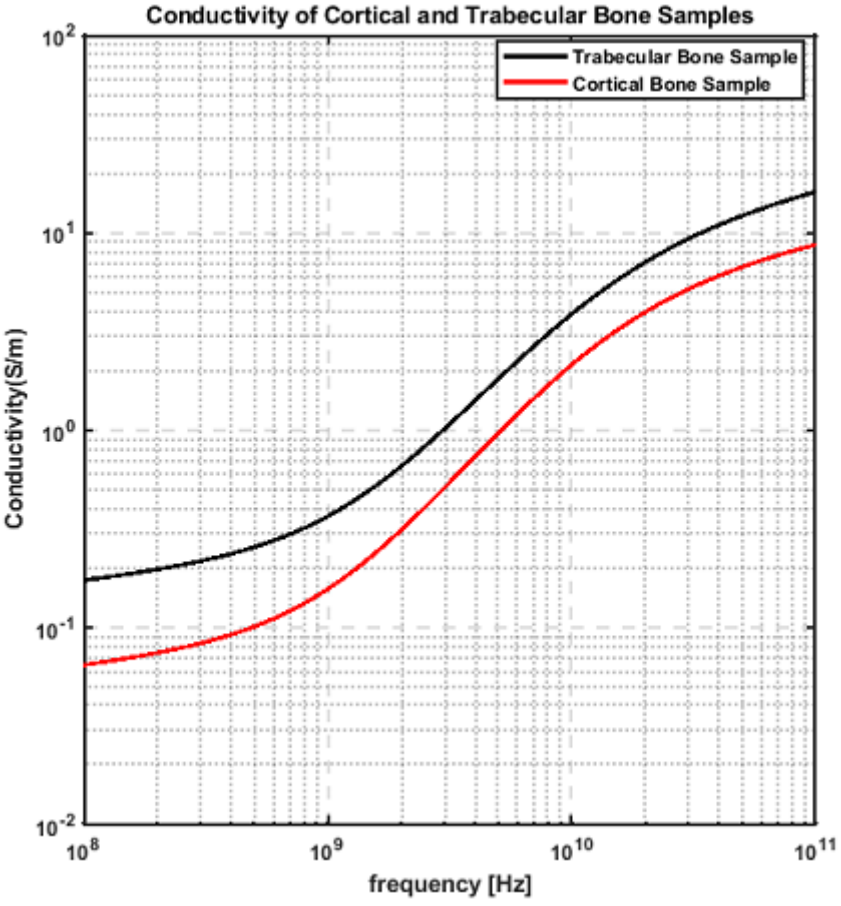
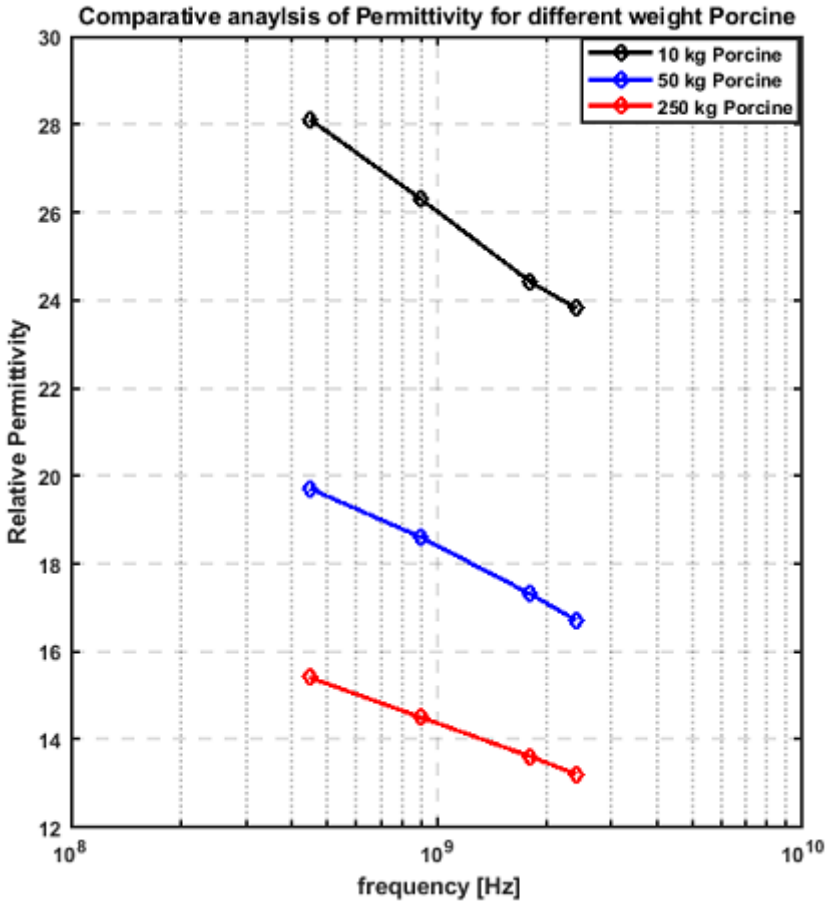

Conductivity of Cortical and Trabecular Bone Samples
Trabecular Bone Sample
Cortical Bone Sample
Conductivity(S/m)
frequency [Hz]

Fig. 3


Comparative anaylsis of Permittivity for different weight Porcine
10 kg Porcine
50 kg Porcine
250 kg Porcine
Relative Permittivity
frequency [Hz]

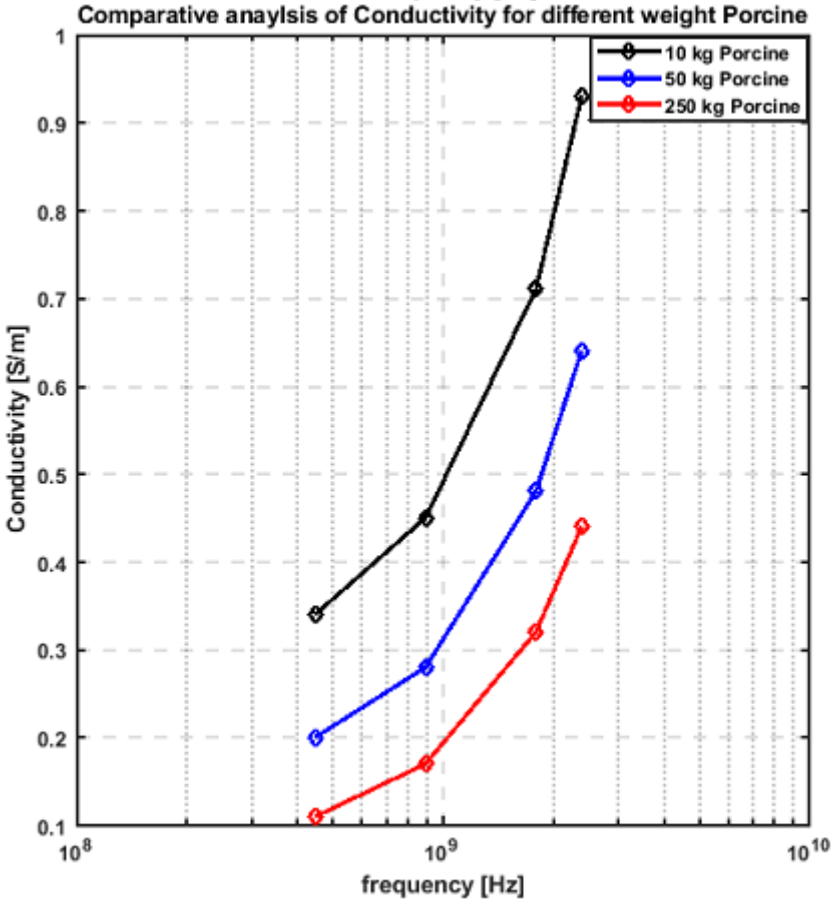

Comparative anaylsis of Conductivity for different weight Porcine
10 kg Porcine
50 kg Porcine
250 kg Porcine
Conductivity [S/m]
frequency [Hz]

Fig. 4

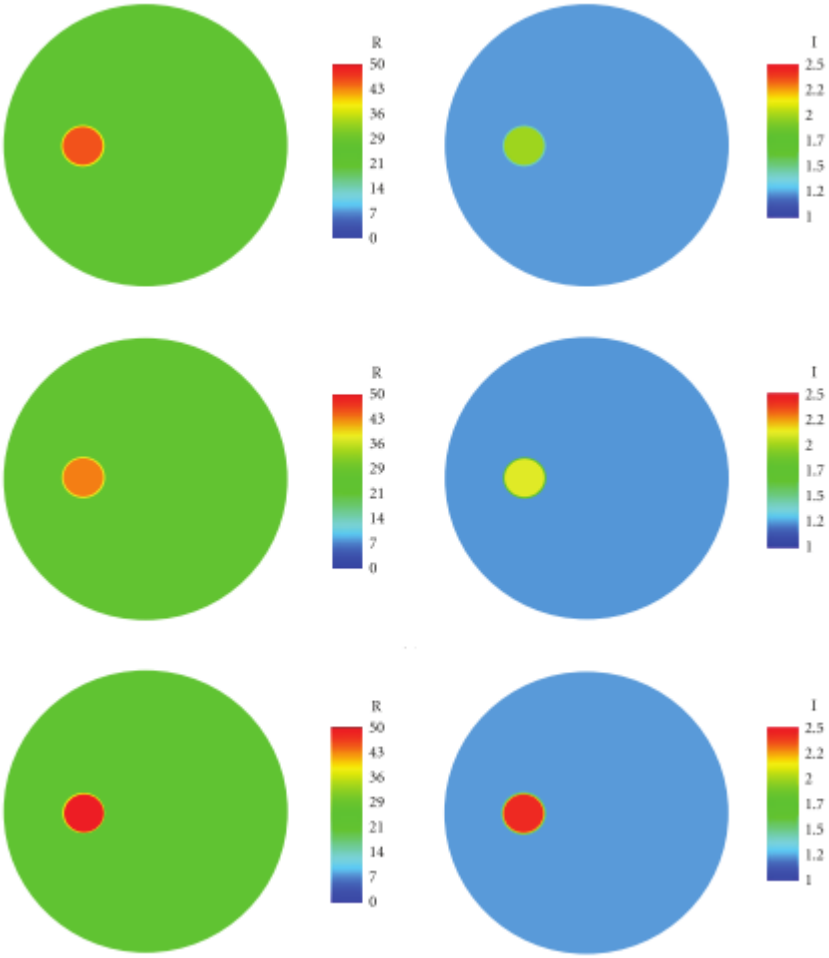

R
50
43
36
29
21
14
7
0
I
2.5
2.2
2
1.7
1.5
1.2
1
R
50
43
36
29
21
14
7
0
I
2.5
2.2
2
1.7
1.5
1.2
1
R
50
43
36
29
21
14
7
0
I
2.5
2.2
2
1.7
1.5
1.2
1

Fig. 5

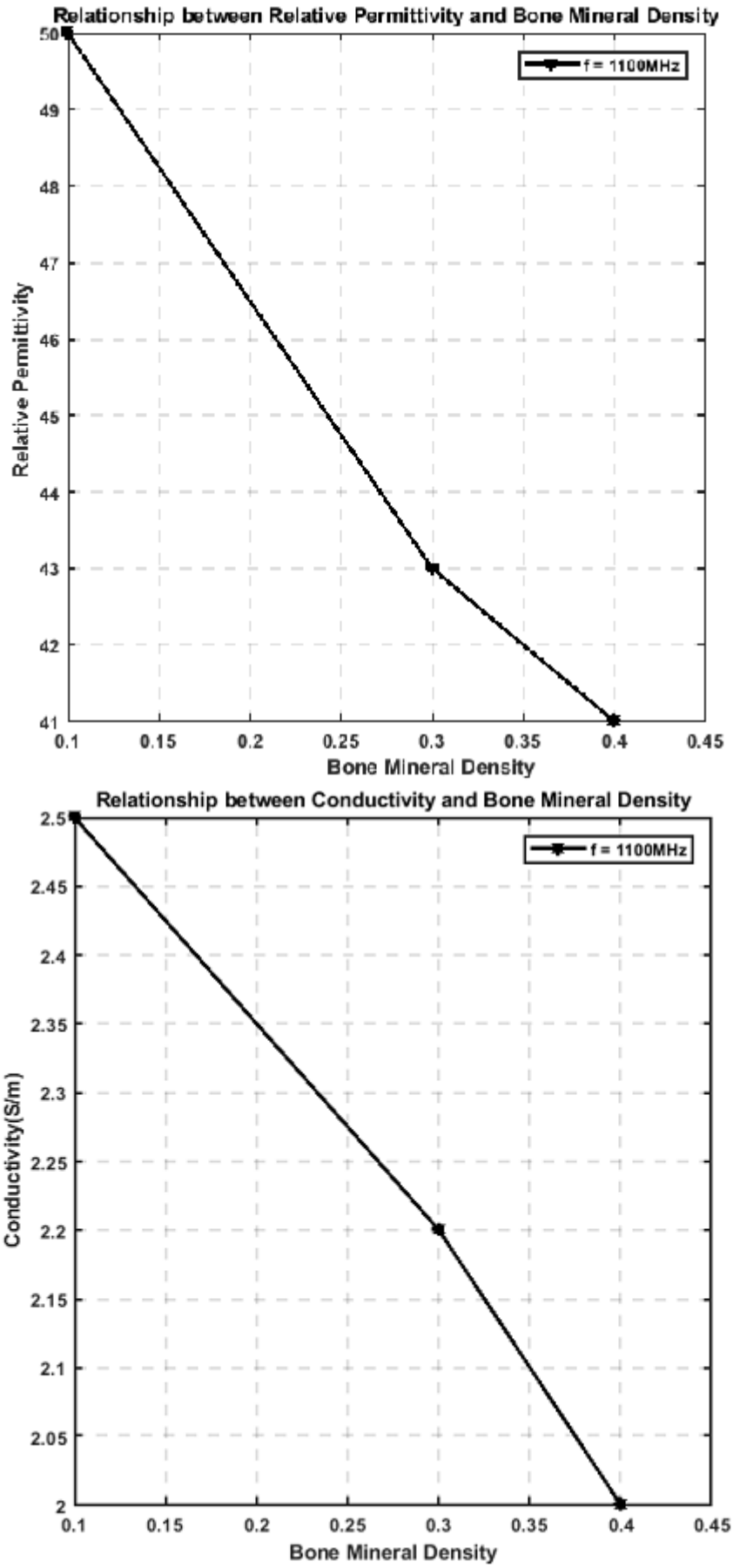

Relationship between Relative Permittivity and Bone Mineral Density
f = 1100MHz
Relative Permittivity
Bone Mineral Density
50
49
48
47
46
45
44
43
42
41
0.1
0.15
0.2
0.25
0.3
0.35
0.4
0.45
Relationship between Conductivity and Bone Mineral Density
f = 1100MHz
Conductivity(S/m)
Bone Mineral Density
2.5
2.45
2.4
2.35
2.3
2.25
2.2
2.15
2.1
2.05
2

Fig. 6

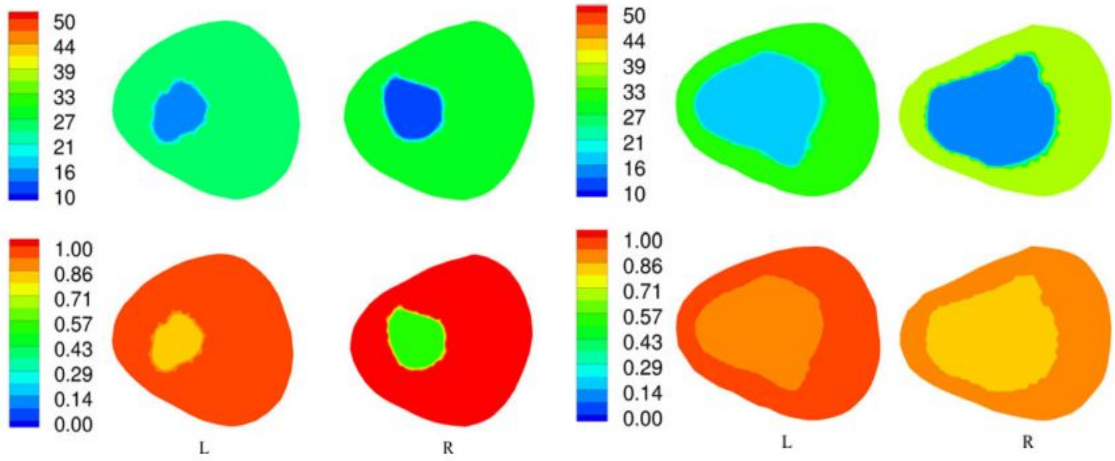

50
44
39
33
27
21
16
10
1.00
0.86
0.71
0.57
0.43
0.29
0.14
0.00
L
R
50
44
39
33
27
21
16
10
1.00
0.86
0.71
0.57
0.43
0.29
0.14
0.00
L
R

Fig. 7

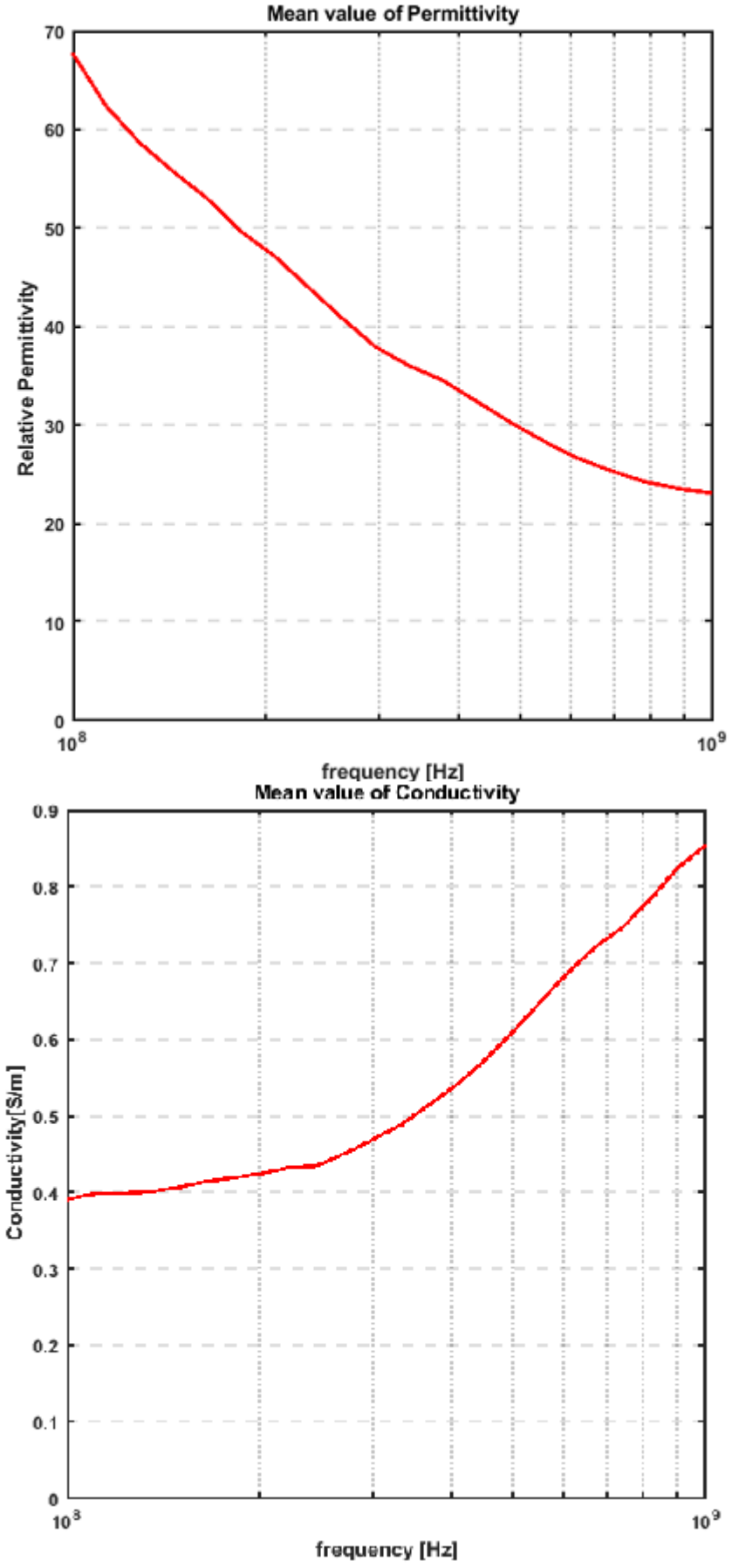

Mean value of Permittivity
Relative Permittivity
70
60
50
40
30
20
10
0
10^8
10^9
frequency [Hz]
Mean value of Conductivity
Conductivity[S/m]
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
10^8
10^9
frequency [Hz]

Fig. 8

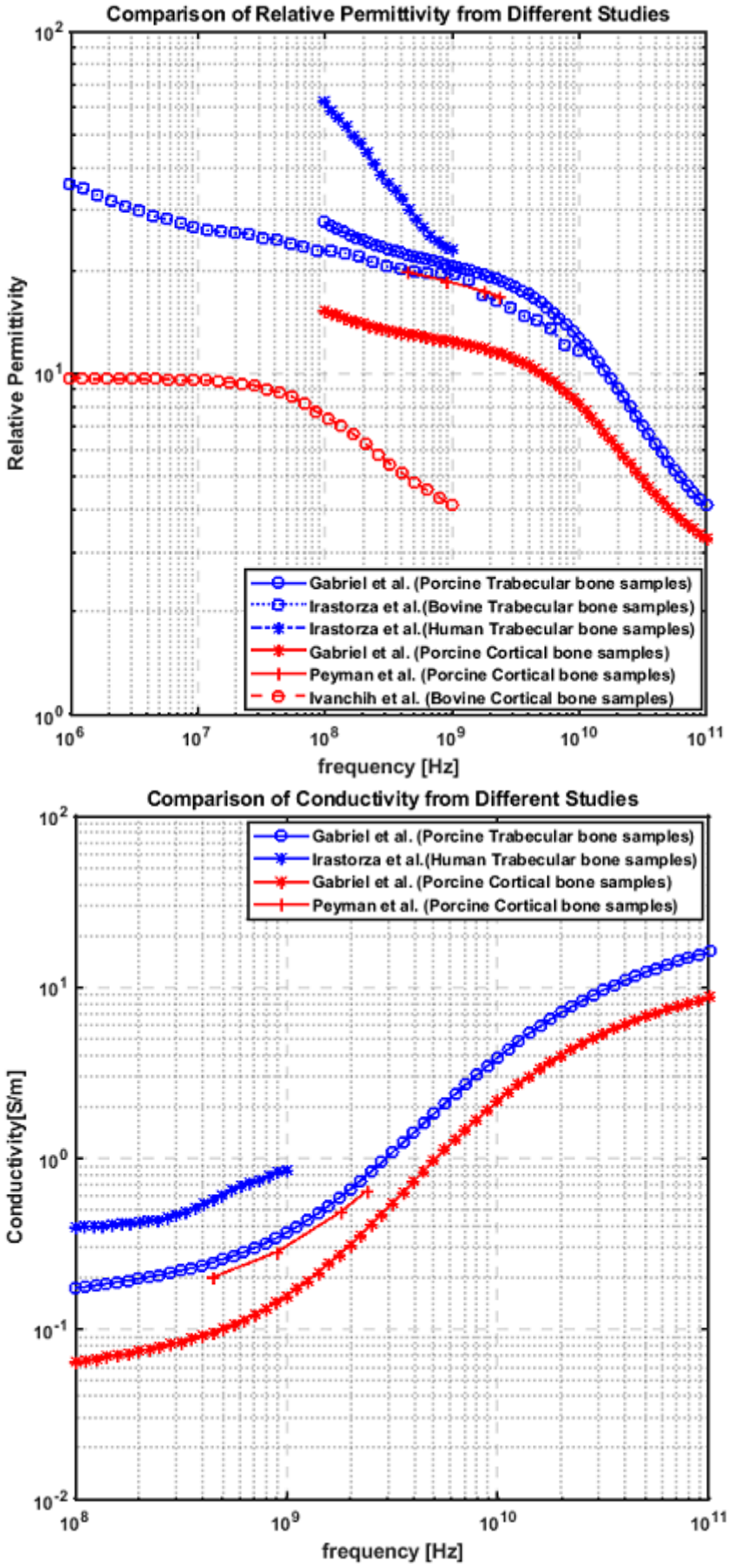

Comparison of Relative Permittivity from Different Studies
Relative Permittivity
frequency [Hz]
Gabriel et al. (Porcine Trabecular bone samples)
Irastorza et al.(Bovine Trabecular bone samples)
Irastorza et al.(Human Trabecular bone samples)
Gabriel et al. (Porcine Cortical bone samples)
Peyman et al. (Porcine Cortical bone samples)
Ivanchih et al. (Bovine Cortical bone samples)
Comparison of Conductivity from Different Studies
Conductivity[S/m]
frequency [Hz]
Gabriel et al. (Porcine Trabecular bone samples)
Irastorza et al.(Human Trabecular bone samples)
Gabriel et al. (Porcine Cortical bone samples)
Peyman et al. (Porcine Cortical bone samples)

Fig. 9

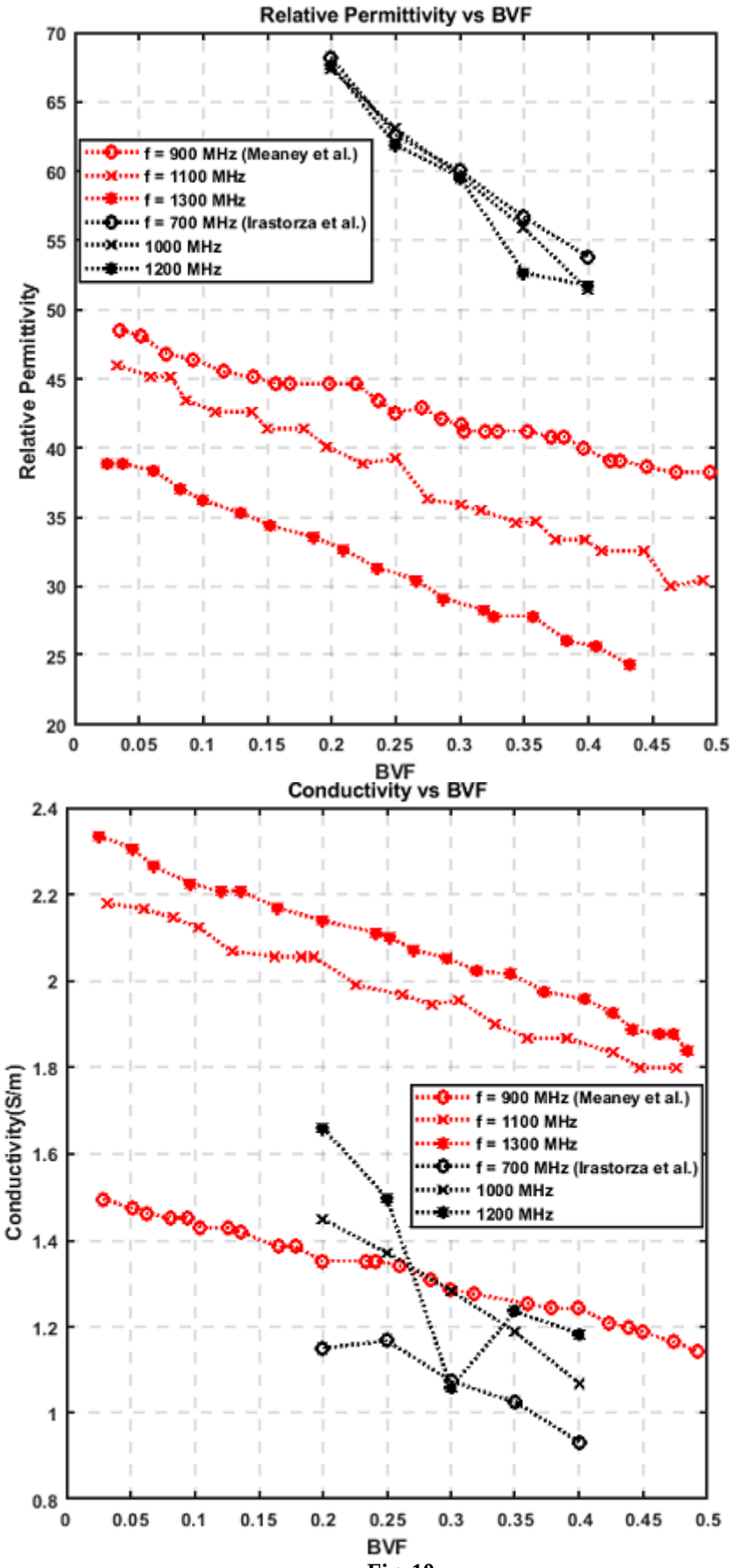

Relative Permittivity vs BVF
Relative Permittivity
BVF
f = 900 MHz (Meaney et al.)
f = 1100 MHz
f = 1300 MHz
f = 700 MHz (Irastorza et al.)
1000 MHz
1200 MHz
Conductivity vs BVF
Conductivity(S/m)
BVF
f = 900 MHz (Meaney et al.)
f = 1100 MHz
f = 1300 MHz
f = 700 MHz (Irastorza et al.)
1000 MHz
1200 MHz

Fig. 10