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Electrical characterization of bolus material as phantom for use in electrical impedance and computed tomography fusion imaging

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Abstract

Phantoms are widely used in medical imaging to predict image quality prior to clinical imaging. This paper discusses the possible use of bolus material, as a conductivity phantom, for validation and interpretation of electrical impedance tomography (EIT) images. Bolus is commonly used in radiation therapy to mimic tissue. When irradiated, it has radiological characteristics similar to tissue. With increased research interest in CT/EIT fusion imaging there is a need to find a material which has both the absorption coefficient and electrical conductivity similar to biological tissues. In the present study the electrical properties, specifically resistivity, of various commercially available bolus materials were characterized by comparing their frequency response with that of *in-vivo* connective adipose tissue. It was determined that the resistivity of Gelatin Bolus is similar to *in-vivo* tissue in the frequency range 10 kHz to 1MHz and therefore has potential to be used in EIT/CT fusion imaging studies.

Keywords: Bolus, Electrical Impedance Tomography, CT, Tissue Electrical Properties

Introduction

Electrical impedance tomography (EIT) is a rapidly emerging field in medical imaging. Recently, studies have been conducted on fusing EIT with other imaging modalities like ultrasound [1], computed tomography (CT) [2] etc. The search for a material to be used during testing as phantom is becoming increasingly important, particularly for EIT/CT fusion studies. The required phantom should have electrical conductivity and x-ray absorption coefficient similar to those of *in-vivo* tissue.

Various studies have been conducted in an attempt to create or improve phantoms to mimic electrical properties of diverse biological tissues at different frequencies [3-5].

Studies have also been done on evaluating new phantom materials specific to an imaging technique [9] and for different fused imaging techniques [2,10].

A potential phantom material for both CT and EIT is the bolus material, a material widely used for compensating missing tissue as well as modifying radiation doses for skin surface treatment in radiation therapy. Efforts have been made to design bolus materials with mechanical strength and dosimetric properties close to water over diagnostic and therapeutic ranges [6] and to study the function of different materials in dose distribution when used as bolus [7] with recommendation of paraffin for clinical use [8]. The most commonly used standard bolus material is the commercially available bolus with the trade name Superflab [11]. The radiation absorption characteristics of Superflab are equivalent (+/- 2%) to human soft tissue and the density is close to water. However, Gelatin Bolus is also popular as it can be readily prepared at low cost. It has also been tested for density changes overtime and has shown no significant changes, leading to its common use as bolus material. Further, the dielectric properties of gelatin phantoms have been used to simulate biological tissue [12], making it a promising phantom for EIT imaging.

Commonly used phantoms for impedance measurement can be either biological (banana, cucumber) or non-biological (inorganic). As the impedance of biological tissues changes with time, they are not suitable for long-term EIT studies [13]. Further, shape complexity and size variation in biological objects prevents them from being used as suitable phantoms for testing imaging methods. On the other hand inorganic phantoms (Superflab and gelatin) show long-term stability and standardized conductivity [12]. However, both gelatin and Superflab do not show complex impedances as shown by biological tissue. Therefore, these materials can be used as phantoms only in studies based on the resistive component of complex impedance.

Before bolus materials with conductivities similar to biological tissues can be used as phantoms in studies involving fusion of imaging technologies with EIT, the conductive properties of these materials need to be characterized to verify their similarity with *in-vivo* tissue.

In this paper, we present the conductive characterization of commercially available bolus material Superflab and in-house prepared bolus material, Gelatin Bolus, in frequencies from 10 kHz to 1 MHz. Further, its comparison to *in-vivo* connective adipose tissue is made and its application in fused EIT/CT imaging is also discussed.

Materials and methods

Bolus material

Two types of bolus materials used in radiation therapy were considered in the present study. The first sample, Sample 1, was the commercially available material Superflab made of 100% Akton® viscoelastic polymer; it is a low cost, well conforming material with a tissue equivalent dose absorption properties and density of 1.03 g/cc. The second sample, Sample 2, was an in-house developed material Gelatin Bolus made of gelatin (Benson Foods Ltd., Gelatine 175 Bloom). The gelatin is manufactured using pig skin and has 2% sodium by weight. Ten sub-samples of each sample were used for cross validation of results and detecting the homogeneity and variability of the material. All sub-samples had a diameter of 10.40 mm and a thickness of 3.18 mm. The diameter of the samples has been matched to the diameter of the electrodes, used for injecting current and measuring voltage.

Gelatin Bolus preparation procedure

Sample 2 was prepared using a standard recipe used in radiation therapy. To create a sheet of 45 cm x 30 cm x 0.5 cm bolus material, 500 mL of cold distilled water is heated with 125 g of gelatin (without sugar, flavoring or coloring). After liquification of gelatin, 250 mL of glycerin is added and stirred until mixed thoroughly. Then the mixture is poured into a mold. The sample takes around 60 minutes to set. After solidifying it is carefully removed from the mold and wrapped in saran wrap to avoid sample shrinkage. The sample is refrigerated for storage.

Experimental Set Up

The electrical impedance was measured at 50 different frequencies from 10 kHz to 1 MHz. An impedance spectroscope HF2IS from Zurich Instruments [14] was used to collect the data. The amplitude of the signal was controlled at one volt such that the 1 mA safe current limit was never exceeded, in accordance with the American National Standard: Safe current limits for electromedical apparatus guidelines [15]. The highest impedance variability at low frequencies coming from "stratum corneum" was compensated by use of pre-gelled Ag/AgCl electrodes with conductive adhesive hydrogel from Kendall™ that were non-polarizable and generate less than 10µV noise, hence preferred for skin surface measurements. Prior skin preparation was done as the quality of contact is reduced by a factor of 10 without proper preparation.

The impedance can be measured using two methodologies: two-electrode configuration or the four-electrode configuration. In the present study two-electrode configuration was considered as represented in Figure 1. The HF2IS generated an output signal of amplitude V_Z. A reference electrode was attached to this output of the HF2IS. A second, measuring electrode, was used to measure the output signal that was modified due to the tissue/sample properties based upon the transfer function of the sample.

One volt amplitude V_z (generated by the impedance spectroscope) was applied to the sample through the reference and the measuring electrode. The current, I_z, flowed through the sample was measured with the measuring electrode. The measuring electrode was virtually grounded. Thus the voltage that is applied to the sample was V_z and the current passing through the sample was I_z, hence impedance spectrum of the tissue is calculated as follows:

$$Z = \frac{V_Z}{I_Z} \quad (1)$$

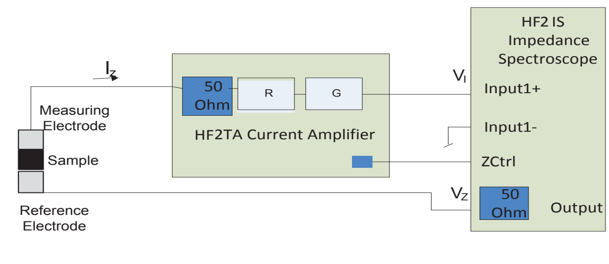

Fig. 1: Measurement set-up

The experimental procedure consists of placing the sample in between the reference and measuring electrodes with a pressure just enough to prevent the sample from falling out. Further, the collected data is analyzed using algorithms in MATLAB®.

In-vivo electrical impedance measurement set up

EIT measurements require the calculation of the complex impedance (Z) of tissue. The electrical properties of *in-vitro* tissue show a decrease in both conductivity and permittivity compared to *in-vivo* tissue [16]. Therefore the conductive properties of the bolus material need to be compared with *in-vivo* tissue. In the present study, we compared bolus samples to *in-vivo* data collected from an earlobe, which consists of mostly adipose connective tissue. The measurement was done by attaching the measuring and reference electrode on both sides of the earlobe. The size of the electrode was smaller than the earlobe and therefore poor contact or air between skin and electrode was avoided.

Computed Tomography (CT) Scan

CT scans of the samples were done to compare the electron densities of the samples, using a Philips Big Bore CT. The parameters were 120 KVP at 350 mAS, with a thickness of 3 mm.

Electrode contact impedance:

As two-electrode configuration was used in this study, it was important to assess the electrode impedance throughout the applied frequency range. This was accomplished by getting frequency sweep data without the sample present between the measuring and the reference electrode.

Results

The electrode impedance without the sample, over the frequency range 10 kHz to 1 MHz is shown in Figure 2.

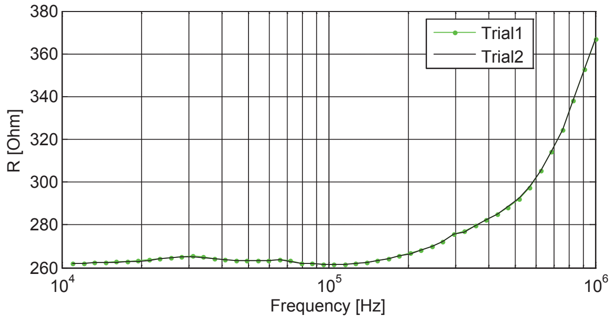

Fig. 2: Electrode impedance without any sample

Figure 3 shows the frequency response of the resistance component of Sample 1: Superflab. The 10 sub-samples were collected from different parts of the same sheet. Frequency response from each sample is represented by an individual trace on the plot.

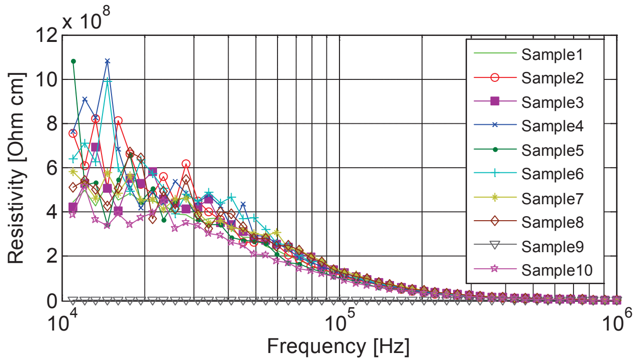

Fig.3: Frequency Response from 10 samples of superflab from 10 kHz to 1 MHz

The mean and standard deviation of the resistance component over the frequency range were calculated, as shown in Figure 4. The x-axis denotes the frequency and the y-axis denotes the mean resistance (bar plot) and standard deviation (line plot) for 10 samples at a 50 different frequencies.

The frequency response for Sample 2 is shown in Figure 5. Ten samples were also tested to verify phantom homogeneity. Mean and standard deviation of the data are shown in Figure 6.

Similarly, the frequency response for *in-vivo* tissue with mean and standard deviation is shown in Figures 7 and 8.

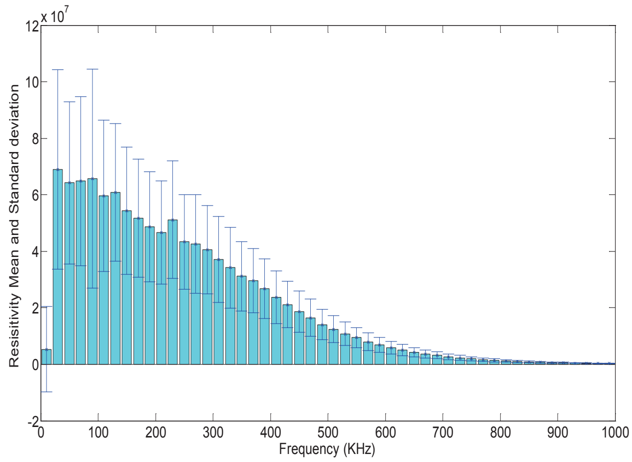

Fig. 4: Mean and standard deviation for Superflab from 10 kHz to 1 MHz

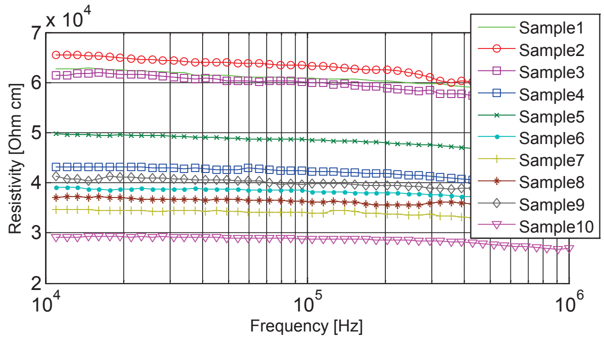

Fig. 5: Frequency response of gelatin bolus material from 10 kHz to 1 MHz

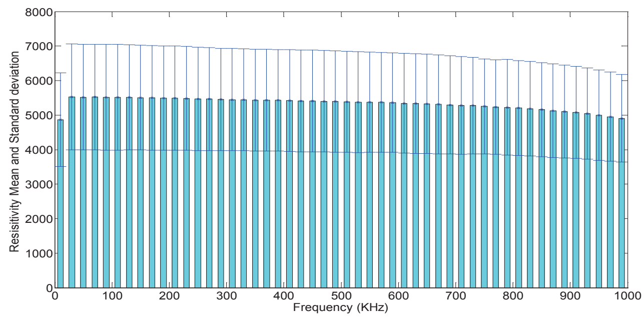

Fig. 6: Mean and standard deviation for gelatin bolus material from 10 kHz to 1 MHz

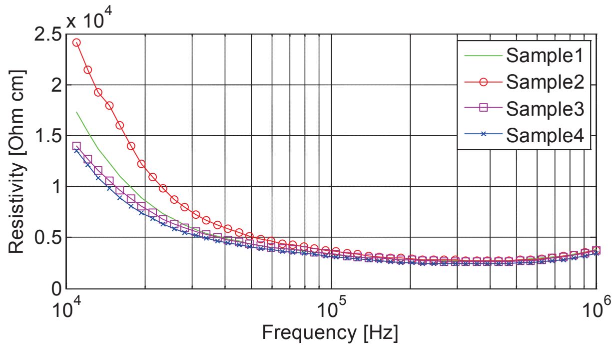

Fig. 7: *In-Vivo* Frequency response of human ear lobe from 10 KHz to 1MHz

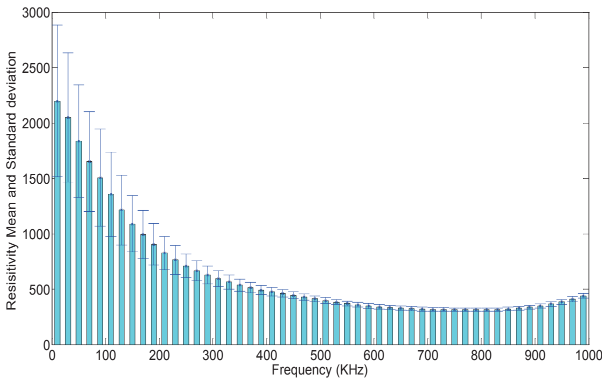

Fig. 8: Mean and standard deviation for *in vivo* ear lobe from 10 kHz to 1 MHz

For further comparison, the mean resistivity of Superflab, gelatin, and *in-vivo* data were plotted simultaneously against frequency sweep, as shown in Figure 9. The x-axis represents the frequency sweep, and the y-axis represents the mean resistivity in ohm cm represented in logarithmic scale.

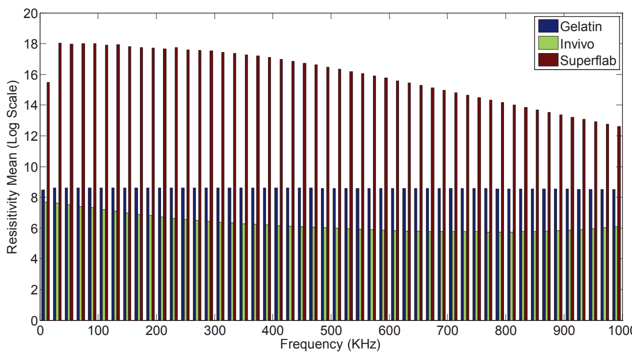

Fig. 9: Mean resistivity of Superflab, gelatin and *in-vivo* earlobe from 10 kHz to 1 MHz

As the density of the Gelatin Bolus material does not change over time, though it does experience shrinkage in size due to the evaporation of water molecules, it can be used over long periods of time following proper storage procedures. The procedure consists of storing the material wrapped in saran wrap in a refrigerator. Similarly, the conductive properties of the gelatin bolus have been studied over a time period of 12 months, to verify its usability for EIT based multi-modality imaging over such a long period of time. Figure 9 shows the impedance response of the Gelatin Bolus over time. Three samples of same size have been considered for comparison. All samples were created six months apart. One sample was only one day old and considered freshly prepared.

The effect of temperature on the conductivity of the phantom was also studied from 20ºC to 26ºC temperature. Previously, all the readings were taken at room temperature (20ºC) for all the samples, whereas the tissue from which *in-vivo* data was collected had a higher temperature close to 37ºC (body temperature).

The Gelatin Bolus temperature was increased above room temperature to 26ºC (beyond this temperature the bolus melts). It was found that no significant change occurred in response to increased temperature.

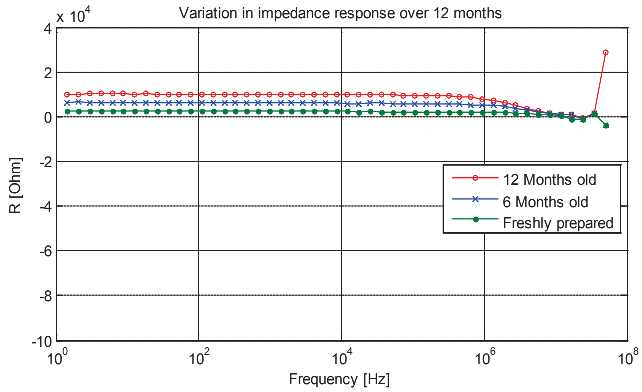

Fig. 10: Impedance difference *in-vivo* data and sample 2&3 data from 1 Hz to 50MHz

Discussion

Electrical impedance measurements are based upon tissue specific electric field distribution and the measurability of currents or potentials on the surface of the region of interest. At low frequencies the current is mostly extracellular, whereas with increasing frequencies intracellular contributions become increasingly significant, and the observations become more cell specific [17]. Thus, the tissue impedance is frequency dependent. Tissue electrical impedance is different at different frequencies depending upon the tissue classification. Therefore, phantoms to be used in EIT should show frequency dependent impedance behavior similar to *in-vivo* tissue.

Comparative studies, over biological (banana, cucumber) and non-biological phantoms (homogenous saline phantom with acrylic plastic, stainless steel), show that the complex conductivities of biological objects change more with time and therefore cannot be reused as imaging objects for EIT based studies [13]. Further, biological objects are also not good as phantoms for CT imaging due to their irregular shapes and sizes. Therefore, the required EIT phantoms should show long-term stability and standardized conductivity over a frequency range to be useful for comparative experimental studies.

Interestingly, the non biological phantom made with gelatin, simulates biological tissue well in terms of dielectric properties and is also popular for electrical impedance imaging studies [12]. Gelatin consists of mobile ions: Amino, hydroxyl, and thiol groups are present with multitude of hydrogen ions and the small chain fragments can readily migrate through the gel under the influence of a small field [18].

Superflab and Gelatin Bolus are both recommended for use in radiological applications. For CT-EIT fusion imaging, specifically, the frequency dependant impedance of the sample needs to be compared with *in-vivo* collected data. Few constraints need to be added to overcome the effect of high impedance of skin that is observed below the

1000 Hz range and the effect of electrode polarization at low frequencies [19]. Keeping these constraints in mind the comparative frequency range considered in the present study was from 10 kHz to 1 MHz. Electrode impedance without sample present was also collected over the entire frequency range. Figure 2 depicts a resistance of 260 Ω from 10 kHz to 100 kHz, and thereafter it starts increasing. Therefore, the most suitable frequency range to use for comparative study was from 10 kHz to 100 kHz.

Unfortunately, gelatin based phantoms do not show complex impedance whereas biological tissue show complex impedance. Consequently, the present study is capable of comparing only the real part of the complex impedance of biological tissue to bolus material. In the future, complex impedance behavior materials need to be studied for better representation of *in-vivo* tissue in terms of complex electrical properties.

Sample 1 (Superflab) showed a lot of inhomogenity and variability in the real impedance value throughout the range of frequencies tested, as shown in Figure 3. Therefore, though Superflab is one of the most popular materials to be used as bolus material in radiation imaging, it is not suitable for phantom development in multi-modality imaging involving EIT. Figure 4 is very useful in further elaborating the variability and inconsistency of the sample, as observed the standard deviation is very high. The difference between *in-vivo* tissue resistivity and superflab sample is quite high (Figure 9) making the sample unsuitable as a phantom for validation in EIT.

The frequency response obtained using Sample 2 (Gelatin Bolus) was very consistent, as shown in Figure 5 and 6, showing much smaller standard deviation compared to Superflab. As shown in Figure 9, though the frequency response of the Gelatin Bolus is similar to *in-vivo* collected data, the resistivity of Gelatin Bolus is higher. The conductivity of the Gelatin Bolus can further be increased by addition of conducting ions e.g. NaCl. This may lead to a much closer response to the *in-vivo* tissue response. Therefore, Gelatin Bolus can be used in multi-modality imaging involving EIT in the frequency range from 10 kHz to 1 MHz. It also has the advantage of being easily prepared in-house.

With passage of time the resistance of Gelatin Bolus decreases due to loss of water molecules, as shown in Figure 10. Freshly prepared gelatin bolus has response closest to *in-vivo* data.

The CT images showed a CT number with mean 17.2 and standard deviation of 12 for sample 1 (Superflab) and mean of 116.7 and standard deviation of 5 for sample 2.

Conclusion

Gelatin Bolus has similar frequency response but lower conductivity compared to *in-vivo* adipose connective tissue at frequencies from 10 kHz to 1 MHz. A freshly prepared Gelatin Bolus has much closer response to *in-vivo* tissue as compared to samples stored over 6 months. After heating the same sample to 26ºC we observed no significant change in electrical properties compared to sample stored at room temperature. Superflab bolus is not recommended for EIT/CT fusion studies as its electrical properties are quite different from biological tissue. Therefore, freshly prepared gelatin bolus shows the closest similarity to *in-vivo* tissue in the 10 kHz to 1 MHz frequency range.

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