3^{rd} URSI AT-AP-RASC, Gran Canaria, 29 May – 3 June 2022

Bi-modal tissue-mimicking breast phantoms: comparison between the performance of agar- and gelatin-based phantoms

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Abstract

Tissue-mimicking phantoms represent a key point for the development of biomedical systems for diagnostic imaging. In this paper, new recipes for tissue-mimicking breast phantoms are proposed and tested, both dielectrically and mechanically. Phantoms mimicking human breast neoplastic tissues are considered, as they are anatomically stiffer than the surrounding healthy tissues. In our recipes, only cheap, easy-to-manage and safe components are involved, and the performance of two solidifying agents (i.e., gelatin and agar) are evaluated both from a dielectric and a mechanical point of view. Dielectric measurements are performed from 500 MHz to 40 GHz, and mechanical tests are performed with the unconfined compression approach, using a preload of 0.2 N and a test speed of 0.5 mm/min. This analysis shows that agar is more suitable for the fabrication of stiffer phantoms as compared to gelatin.

1. Introduction

Breast cancer is one of the most diagnosed diseases among women worldwide. Early detection can increase the survival chances and several imaging techniques are currently available. However, their limitations are pushing the interest toward new complementary or supplementary approaches. Microwave imaging is gaining increasingly interest in the biomedical community, as it represents a safe and low-cost alternative to the current imaging methods, which relies on the dielectric contrast between healthy and neoplastic breast tissues [1-4]. Several prototypes working in the microwave and millimeter wave regimes have been proposed and tested on phantoms and/or *in vivo*, and very promising results were achieved in high contrast scenarios [5-8]. However, the most challenging configuration is represented by breasts with tumors embedded in high-density fibro-glandular tissues, where, due to the similar dielectric properties, the electromagnetic scattering from the target may be confused with that from healthy tissues, leading to a misdiagnosis. A possible solution to this problem relies on the use of combined information about the dielectric and mechanical properties of tissues. Indeed, it has been demonstrated that pathological conditions are associated to increased tissue stiffness, and several experimental campaigns on mechanical characterization of both tissues and materials for tissue-mimicking breast phantoms have been performed to quantify this difference [9-15]. In our research group, we are focusing on the design and testing of bi-modal phantoms, able to mimic both dielectric and mechanical properties of all breast tissues, both healthy and malignant. In particular, starting from recipes previously proposed for electromagnetic imaging [16], we extended our analysis by measuring their mechanical properties [17]. All our recipes are based on cheap, safe and easy-to-manage components (i.e., deionized water, sunflower oil, common dishwashing liquid, and gelatin or agar), and we demonstrated that a slight increase of gelatin volume percentage has not a significant impact on the dielectric properties of the produced phantoms [16]. In [17], we presented the mechanical properties of these recipes, but we showed that the mixtures presented in [16] are not able to well mimic the mechanical properties of breast tissues. Thus, we tried to considerably increase the percentage of gelatin, and we found recipes able to mimic both the dielectric and mechanical properties of all categories of human healthy tissues. However, if on one hand we were able to obtain the mechanical properties of healthy tissues by changing only the percentage of gelatin in the mixtures produced, on the other hand, this modification alone was not sufficient to mimic the mechanical properties of neoplastic tissues, which are generally much stiffer than healthy ones. The results of this study will be published in a paper currently in preparation.

To further address this aspect, in this work, we propose modified recipes in which we changed the solidifying agent, from gelatin to agar, evaluating its impact on the mechanical properties of the produced phantoms. In particular, we present the comparison between the dielectric and mechanical properties (i.e., the dielectric permittivity and Young's modulus) of phantoms where the same percentages of the two solidifying agents are used in exactly the same mixtures.

This paper is organized as follows. In Section 2, the proposed mixtures are presented. In Section 3 and Section 4, the setup for both dielectric and mechanical measurements of phantoms are shown together with the characterization results. Then, some discussions and conclusions are derived.

2. Phantom Recipes

The mixture components used in this paper were derived from [16]. In particular, in the present work we focused on the comparison between the impact of agar and gelatin on both dielectric and mechanical properties of phantoms mimicking malignant tissues. The analyzed recipes are summarized in Table I. From each phantom, we derived four samples for mechanical measurements.

Phantom	Deionized water (ml)	Sunflower Oil (ml)	Dishwashing liquid (ml)	Agar (g)	Gelatin (g)
A6O5	95	5	3	6	
A6O15	85	15	3	6	
A6O20	80	20	3	6	
G6O5	95	5	3		6
G6O15	85	15	3		6
G6O20	80	20	3		6

The acronym in the first column of Table I indicates the volume percentage of agar (A) or gelatin (G), and volume percentage of oil (O) in the phantom, respectively. In the computation of the volume percentages, we considered only the sum of the deionized water and sunflower oil amount; in all cases, it was 100 ml.
The procedure for phantom realization is the same presented in [16], and it is not repeated in this paper.

3. Dielectric characterization of phantoms

The experimental setup used for the dielectric characterization of the produced phantoms involved:

- A vector network analyzer (ENA Network Analyzer E5080B) able to perform reliable measurements from 100 kHz to 44 GHz;
- An open-ended coaxial probe (Keysight 85070E Dielectric Probe Kit);
- A mechanical positioner for the probe;
- A mechanical mover to put in contact the phantom with the tip of the probe, without moving the probe.

A photo of the experimental setup is shown in Figure 1.

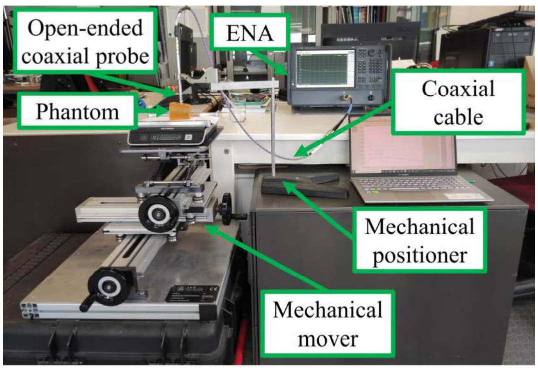

Figure 1. Experimental setup for dielectric measurements.

All measurements were acquired from 500 MHz to 40 GHz. A minimum pressure on the sample under test was applied, to ensure a perfect contact between the tip of the probe and the sample itself, avoiding any leakage of liquids from the phantom. For each phantom, three independent measurements were performed to assess the mixture homogeneity. Both real and imaginary part of the complex dielectric permittivity were measured and compared to those of human breast *ex vivo* malignant tissues [4]. The dielectric properties of the phantoms involving oil percentages from 15% to 20% fall within one standard deviation from the mean values obtained for human breast *ex vivo* malignant tissues, both for the real and imaginary part of the dielectric permittivity, as shown in Figure 2 a) and b), respectively. In these figures, only the average values for all phantom samples are shown.

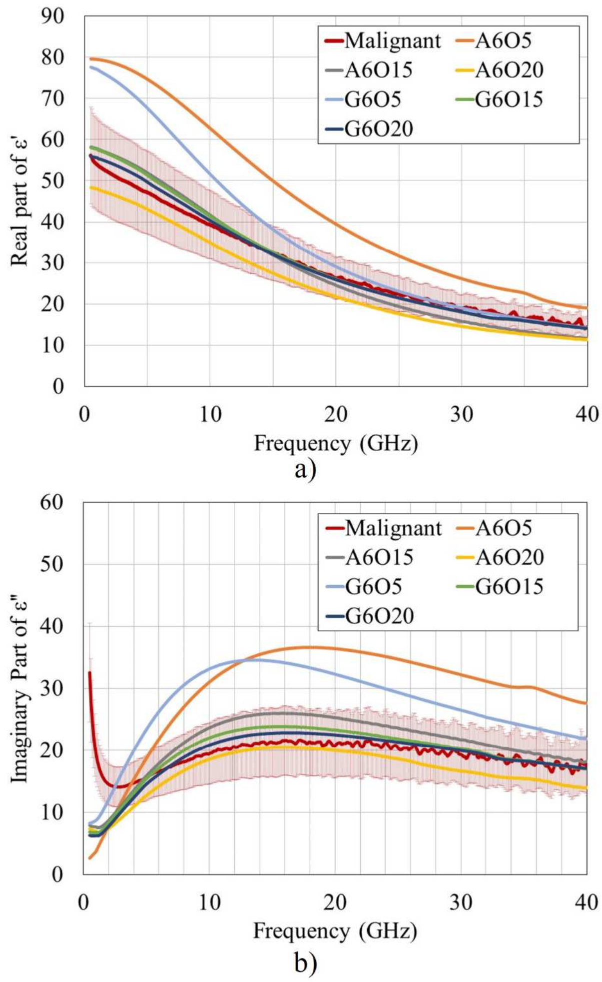

Figure 2. Comparison between the average dielectric properties of the produced phantoms and those of human breast *ex vivo* malignant tissues for a) real and b) imaginary part of the dielectic permittivity. Shaded region indicates ± one standard deviation for human breast *ex vivo* malignant tissues [4].

4. Mechanical characterization of phantoms

After the dielectric characterization, four different samples from each phantom were derived and prepared for mechanical compression testing. This technique is the one that better represents the real test scenario. The experimental setup for mechanical measurements involved:

- A MTS Insight 10 electromechanical traction/compression machine with precision guide columns (MTS Insight 10, MTS System Corporation);
- a load cell of 250 N maximum capacity (MTS Load Cell);
- a digital controller for the crosshead position tuning;
- two aluminum compression plates;
- a computer to monitor the compression test in real time with the TestWorks software;

A photo of the experimental setup for mechanical measurements is shown in Figure 3.
A standard 1-cm high mold with a diameter of 2.8 cm was used for sample preparation, and a photo of the samples is shown in Figure 4.

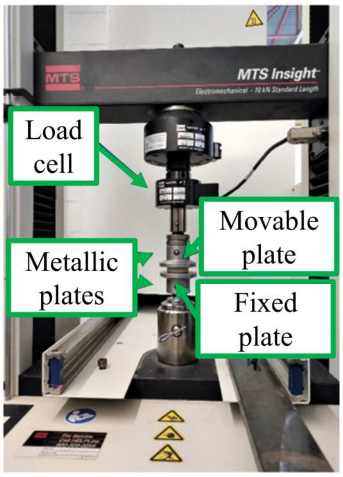

Figure 3. Experimental setup for mechanical measurements.

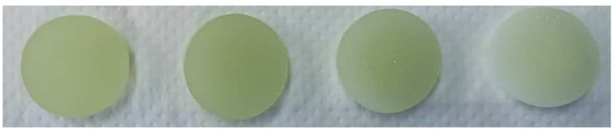

Figure 4. Photo of the samples to be mechanically tested.

According to [11], a preload of 0.2 N and a test speed of 0.5 mm/min were chosen for mechanical measurements. The stress-strain curves of each phantom were measured under these experimental conditions up to the sample breakage. In Figure 5, the comparison between the average Young's moduli of all the produced mixtures, both with agar and with gelatin, are shown as a function of the percentage of oil at 5 % of strain.
In [11], mixtures involving similar components (i.e., agar and gelatin) at the same strain level and under the same experimental conditions were characterized, and values higher than 80 kPa were achieved in both cases.
As it can be seen from this figure, phantoms using agar as solidifying agent are stiffer than those based on gelatin, even if their Young's moduli are still lower than those reported in the literature [11]. In addition, differently from gelatin-based phantoms, the increase of oil percentage (which is necessary to match the dielectric properties to those of *ex vivo* tissues, as shown in Figure 2) in agar-based mixtures is responsible of a decrease of the phantom stiffness. Thus, further research is required to approach the reference values.

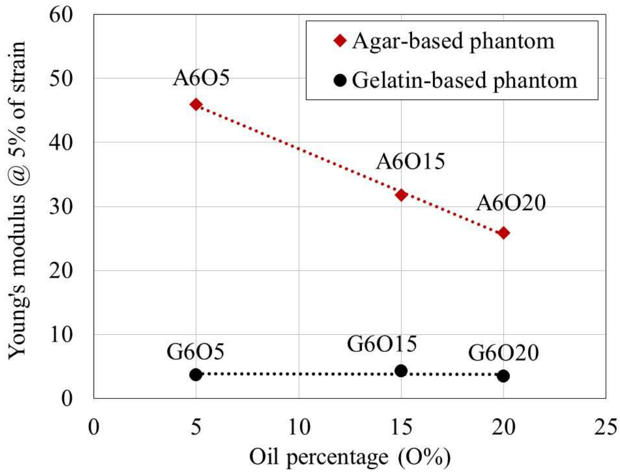

Figure 5. Comparison between the average Young's moduli of the produced phantoms based on agar and gelatin, as a function of the oil volume percentage at 5% of strain. For all phantoms, the average Young's modulus measured on the four samples derived from each mixture is shown.

5. Discussion and conclusion

In this paper, new recipes for tissue-mimicking breast phantoms are proposed. This activity inserts in a broader framework whose goal is to design phantoms mimicking not only the dielectric but also the mechanical properties of human tissues, possibly suitable for testing new multi-modal imaging techniques.
Recently we have proposed several recipes to mimic the dielectric properties of all categories of human breast tissues based on cheap, easy-to-manage and safe components (i.e., deionized water, sunflower oil, dishwashing liquid and gelatin).
For healthy-tissue-like phantoms, we have shown that, by increasing the amount of gelatin in our recipes, the mechanical properties of human tissues can be also mimicked. However, we proved that this increase in gelatin is not enough to mimic the higher stiffness of tumor tissues. For this reason, in the present work, we tried to change the solidifying agent, while leaving the other ingredients in the recipes unchanged, and compared the performance of gelatin- and agar-based phantoms both from a dielectric and a mechanical point of view. Specifically, 6% gelatin

and 6% agar were used. Dielectric measurements were performed in a broad frequency range, from 500 MHz to 40 GHz. Mechanical measurements were performed with a compression machine with a preload of 0.2 N and a test speed of 0.5 mm/min. The results show that, from a dielectric point of view, mixtures with oil percentages from 15% to 20% are able to mimic the dielectric properties of malignant breast tissues in all the investigated bandwidth, regardless of the solidifying agent; while, from a mechanical point of view, agar allows to produce stiffer phantoms than gelatin. However, the stiffness of the agar-based phantoms decreases as the oil percentage increases, making it necessary to minimize the amount of oil in the mixture in order to obtain Young's moduli values similar to those reported in the literature for malignant phantoms. Nevertheless, this would lead to phantoms no longer able to mimic the dielectric properties of human neoplastic tissues. On the other hand, increasing the percentage of agar only would lead to mixtures not able to solidify (indeed, we tried unsuccessfully to produce phantoms with 7% of agar).
Therefore, in this paper we demonstrated that stiffer phantoms are achievable when agar is involved in the recipes instead of gelatin, but a further investigation is needed to design mixtures able to mimic at the same time dielectric and mechanical properties of human breast malignant tissues. Further tests will involve e.g. a finer tuning of the recipe ingredients, the combined use of agar and gelatin, and of different solidifying agents.

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