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Preliminary comparison up to 50 GHz between *in-vivo*, *in-loco*, and *ex-vivo* measurements for the dielectric permittivity of tissues with high water content

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Abstract

In this paper, preliminary results about the comparison between *in-vivo*, *in-loco* and *ex-vivo* dielectric properties of a limited colony of mice in the wide frequency range from 500 MHz to 50 GHz are shown. This is instrumental to the development of several applications that make use of microwaves and millimeter waves, including systems for breast cancer imaging.

1 Introduction

Breast cancer is one of the leading causes of death from cancer in women [1]. Nowadays, the most widely used diagnostic technique for breast imaging in post-menopausal women, as well as in screening campaigns, is mammography. However, women's exposure to ionizing radiation and the sub-optimal *Sensitivity* and *Specificity* of this method are critical aspects, which possibly call for new imaging modalities.

Among the most promising and most studied alternative techniques are those based on the use of microwaves. Various research groups around the world have proposed several prototypes in the microwave regime [2-7]. These systems are based on the detection of differences in the dielectric properties of breast tissues, particularly large between low water content (i.e., high fat content) tissues and neoplastic tissues. Some microwave systems have also reached a certain degree of maturity to the point of having been tested on a significant number of women. However, while these experimental tests have shown promising results, there are still many uncertainties and open questions about the practical capacity of this type of system for the early detection of breast cancer.

Among the most important factors, there are the lack of resolution, especially for breasts with low water content, and the real contrast between healthy and neoplastic tissues, which in *in-vivo* condition could be different from the data available from *ex-vivo* measurement, which is in turn the most common measurement modality for human tissues, due to obvious reasons [2], [8].

In this paper, a brief overview of the results achieved so far for a millimeter-wave imaging system, capable of solving the first problem, thus delivering a suitable resolution in breast with an high fat content, while maintaining a reasonable penetration, is provided [9-15]. Then, first preliminary results on an experimental campaign aimed at the identification of the differences, up to 50 GHz, in terms of dielectric permittivity, between *in-vivo*, *in-loco* and *ex-vivo* measurements, performed on a small colony of mice, are provided and discussed to partially address the second problem.

2 Overview of mm-waves for breast imaging

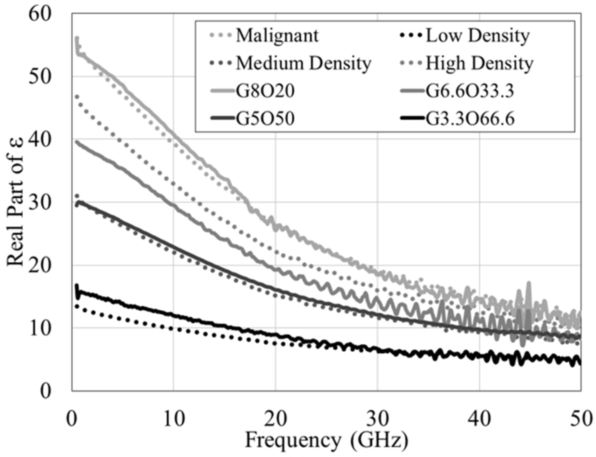
In 2014 and 2016, two experimental campaigns on healthy and neoplastic human breast *ex-vivo* tissues were carried out and 342 samples were measured (247 healthy and 95 neoplastic) taken from more than 100 women with different ages, spanning from 14 to 85 years old and a significant dielectric difference between healthy and diseased tissues was detected up to 50 GHz [9-10]. This confirmed, experimentally, the ground for using also millimeter waves for breast imaging.

In addition, the availability of such a large database allowed for determining that a large portion of *post*-menopausal women does exhibit, on average, breasts with high fat content, thus with dielectric permittivity values that could be in line with the use of millimeter waves [11]. Indeed, the comparatively low values for both the real and the imaginary part of the dielectric permittivity for these cases not only suggest that millimeter waves could provide the resolution microwaves cannot achieve, but also maintaining a reasonable penetration depth.

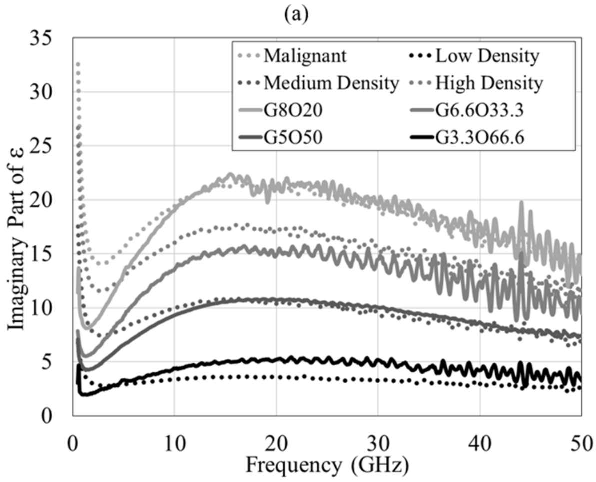
As of first validation of this, in a simulated scenario a 2-mm neoplastic-like target was detected at a depth of 40 mm [12], [13]. In addition, to move on with the required experimental validation, novel tissue-mimicking materials able to mimic the dielectric properties of human breast tissues up to 50 GHz were developed (Fig. 1), and a first heterogeneous phantom with inclusion was created (Fig. 2) [14]. Finally, some experimental images, obtained by testing an initial imaging prototype of these phantoms, have been generated (Fig. 3) [15].

3 Dielectric properties of *in-vivo* tissues

In order to validate the dielectric properties of *ex-vivo* tissues up to 50 GHz, taking into account the effect of blood perfusion as well as the different temperature, experimental campaign on mice involving *in-vivo* tissues have been evaluated. As a first preliminary preparatory work, two mice were measured to fine-tune the entire procedure. Indeed, even if the same experimental setup is similar to the one used for *ex-vivo* measures [9], [10], thus must be adjusted for *in-vivo* and *in-loco* measures.



(a)



(b)

Figure 1. Comparison between dielectric properties of the produced mixtures and the dielectric properties of human breast *ex-vivo* samples for a) real and b) imaginary part of the relative dielectric permittivity [14].

In particular, with *in-loco* we intend measures taken from 2 to 20 minutes after the sacrifice of the animal, but still at the places where *in-vivo* measures were taken, without any kind of artificial alteration of the measurement site. Thus, the main difference between *in-vivo* and *in-loco* measures is the presence, or lack, of the blood circulation, respectively. When possible, *ex-vivo* measurements were also taken, that is removing the tissue from the mouse. In all case, neoplastic tissues were taken into consideration during this preparatory work.

Measurements were made on two mice, one naked and one white (with hair). On the white mouse, all measurements were made by removing the skin, due to the presence of hair. At the same time, on the naked mouse both skin and skinless measurements were made to demonstrate the significant impact of the skin presence on the dielectric measurements. To this regard, it is worth observing that, despite the skin of mice normally exhibit a very poor content of water (which is just the opposite with respect to human skin), the impact on dielectric properties is significant.

Fig. 4 shows the real and imaginary part of the relative dielectric permittivity of the white mouse, while in Fig. 5 the same information is shown for the naked mouse.

(a)

(b)

Figure 2. a) Lateral photo of the produced phantom and b) photo of a piece of phantom in which is visible the inclusion [14].

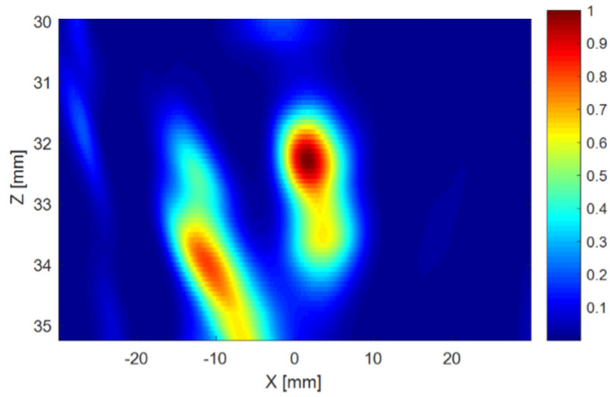


Figure 3. Preliminary draft experimental mm-wave image of a metallic sphere with diameter of 8 mm at a depth of 16 mm within a tissue-mimicking phantom with low losses [15] (ε'=3.67, ε''=0.13 @ 30 GHz), placed 18 mm far from the antenna array. The normalized amplitude of the reflection echo is shown, for a Z distance from 30 mm to 35 mm from the antenna array.

As it can be seen from the graphs, the measured dielectric properties do not change significantly between *in-vivo*, *in-loco* and *ex-vivo* measurements. This is valid for when all measurements are done with the skin, and when all measurements are done without the skin

Instead, the difference between skin and skinless measurements is significant. In particular, the values measured for the neoplastic tissues when the skin is not removed are significantly lower than when the skin is removed. On average, at 30 GHz, approximately from 25 to 18 (28%) for the real part of the dielectric permittivity, and from 24 to 15 (38%) for the imaginary part.

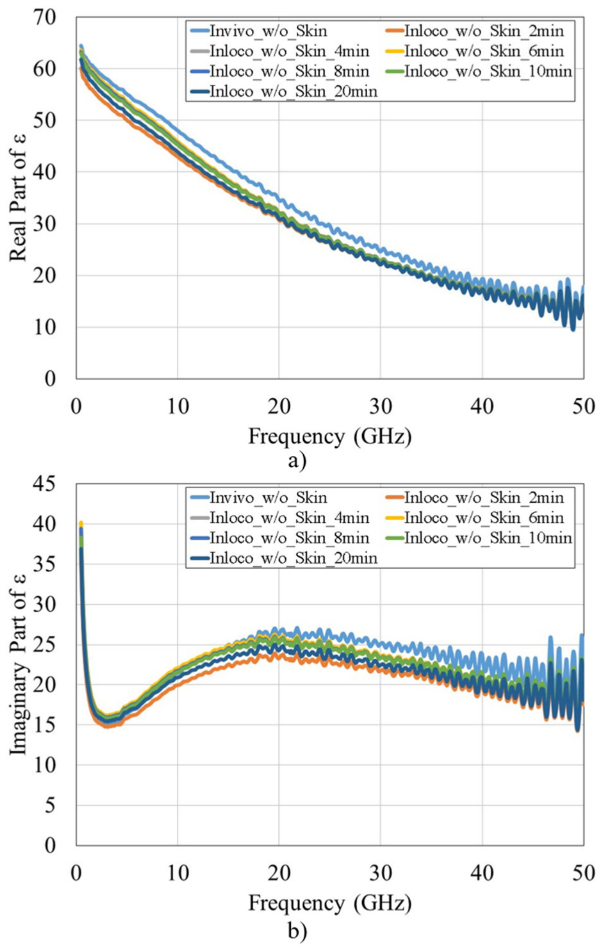


Figure 4. Comparison between *in-vivo* and *in-loco* dielectric measurements for the white mouse for a) real and b) imaginary part of the relative dielectric permittivity.

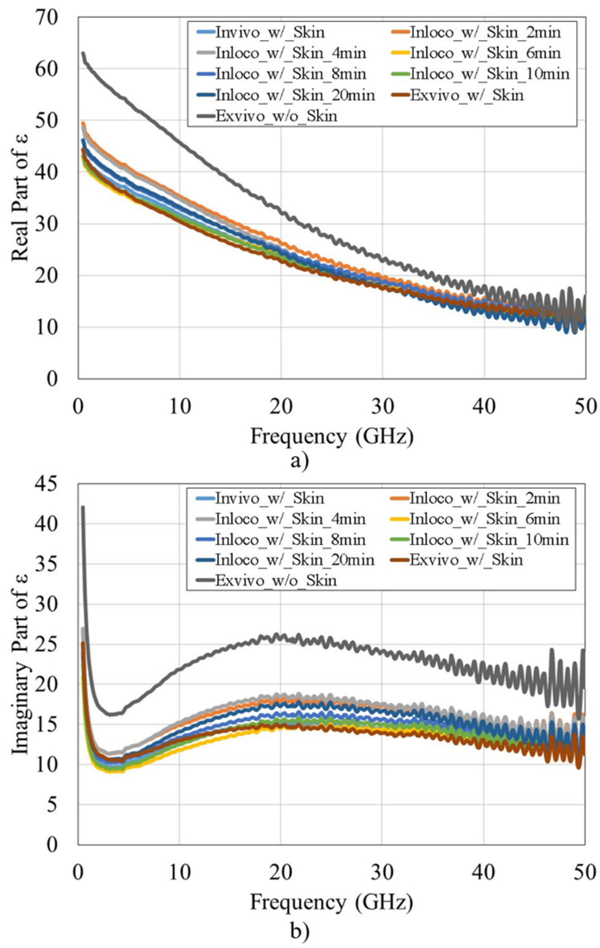


Figure 5. Comparison between *in*-vivo, *in-loco*, and *ex-vivo* dielectric measurements for the naked mouse for a) real and b) imaginary part of the relative dielectric permittivity.

4 Conclusions

In this paper, a first preliminary set of results about the comparison, in terms of dielectric permittivity, between *in-vivo*, *in-loco*, and *ex-vivo* measurements up to 50 GHz for neoplastic tissues in mice were presented.
This preparatory measurements, carried out on two mice, with the aim of a more extensive campaign, showed that they are very similar to each other. This suggests that *ex-vivo* measurements, which are easier to handle especially on humans, could be in good correlation with *in-vivo* conditions.
A complete validation of this aspect is important for the development of a large range of studies and applications, including millimeter-wave imaging systems for breast imaging, which was briefly outlined.

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