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

S. Di Meo(1), and M. Pasian(1)
(1) Department of Electrical, Computer and Biomedical Engineering, University of Pavia, Pavia, Italy, simona.dimeo01@universitadipavia.it

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 being able to mimic the dielectric properties of human breast tissues up to 50 GHz [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. 3) [15]. Finally, some experimental images, obtained by testing an initial imaging prototype of these phantoms, have been generated (Fig. 3) [15].

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.
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.
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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