MammoWave clinical trials within RadioSpin project: results obtained using microwave images' features approaches with thresholds

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***Abstract*—In this paper, we present preliminary outcomes derived from a prospective multicentric clinical trial focusing on microwave breast imaging involving 336 women. This investigation was conducted as part of the RadioSpin project. Our primary objective was to evaluate the prospective performance of MammoWave, our microwave imaging device, in differentiating between breasts with and without radiological findings, utilizing specific microwave images features' thresholds. Beyond this primary assessment, we explored the use of individual frequency sub-bands to categorize breasts into two groups: healthy (without findings or with benign findings) and non-healthy (malignant findings), drawing on features identified in a previous clinical trial. Our findings reveal a sensitivity of 72% in detecting radiological findings and a noteworthy 78% in identifying non-healthy (cancerous) breasts.**

I. Introduction

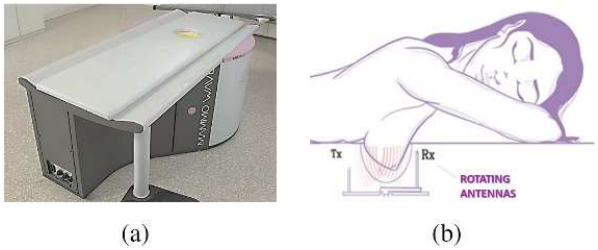
Microwave imaging techniques have attracted significant attention in the field of medical imaging due to their potential to identify abnormalities in the human body, stemming from variations in dielectric properties among different tissues. Within this domain, microwave breast imaging has become a focal point, with numerous research groups advancing to clinical trial stages [1]. Notably, breast tumors exhibit increased dielectric properties compared to surrounding tissues, positioning microwave imaging as a promising alternative to established conventional technologies such as mammography, MRI, and ultrasound [2].

MammoWave, a radar-based microwave imaging prototype developed by UBT Srl, has undergone multiple rounds of clinical trials in European hospitals [3]. This paper presents preliminary results from a recently completed clinical trial in the framework of the European RadioSpin project. To achieve this, we calculated and selected five optimal microwave image parameters (features) for quantifying the non-homogeneous characteristics of images. These features enabled the differentiation between breasts with radiological findings (WF), including benign or malignant lesions, and breasts without radiological findings (NF). The prospective selection of these five features was based on investigations conducted in our prior clinical trial [4]. Moreover, we explored the efficacy of these features in distinguishing between healthy (H) and non-healthy (NH) breasts. In this classification, NH breasts denote those with malignant findings, while H breasts encompass those without any findings or those with benign findings. As part of a further investigation, we also examined the impact of individual 1 GHz sub-bands on MammoWave's performance in distinguishing between H and NH breasts.

II. MammoWave Description

MammoWave, as depicted in Fig. 1(a), is configured with two antennas, one for transmission and the other for reception. Positioned at the same height, these antennas operate in the air within a frequency range of 1-9 GHz, thereby eliminating the need for a matching liquid or medium [4]. The hub, taking on a cylindrical shape and housing the antennas, incorporates a cup situated within cavity where the patient's breast comfortably rests in a prone position (Fig. 1(b)). The azimuthal rotation of both antennas enables an 8-minute-long multi-bistatic scan in the frequency domain. Subsequently, the received signals undergo post-processing utilizing our imaging algorithm based on the Huygens' principle, leading to the formation of an image through internal field reconstruction.

For measurement purposes, a vector network analyzer is connected to the antennas, capturing S21 signals that represent the backscattered electromagnetic signal.



(a) (b)

Fig. 1. (a) MammoWave prototype, (b) MammoWave's scanning configuration sketch, depicting the breast holder cup and antenna positions.

III. Clinical Trials Description

The clinical trials conducted in this study were part of a use case within the EU-funded FET H2020 RadioSpin project [5]. The trials, registered under ClinicalTrials.gov Identifier NCT05300464, took place in three hospitals—two in Italy (Ospedale San Giovanni Battista—USL Umbria 2 in Foligno and Azienda Ospedaliera Universitaria IRCCS San Martino in Genova) and one in Spain (Complejo Hospitalario Universitario de Toledo. The clinical study adhered to the accepted protocol and principles outlined in current version of the Declaration of Helsinki, the guidelines of Good Clinical Practice issued by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, European Directive on medical devices 93/42/EEC, ISO Norms 14155 and 14971, European Law, and regulatory requirements of Italian and Spanish authorities.

As a reference standard, radiologic study conducted within the last month and integrated with histological studies if deemed necessary by the responsible investigator and when available, were used to categorize breasts into NF and WF groups. The classification followed the American College of Radiology recommendations using their BI-RADS system. Specifically, breasts with a BI-RADS assessment of 1 were categorized as NF, while those with final BI-RADS assessments of 2 for benign findings, 3 for follow-up findings, or 6 for confirmed carcinoma were classified as WF. Each breast underwent MammoWave scanning, resulting in microwave images computed both using the full frequency (1-9 GHz) and the eight 1 GHz bandwidths. From the raw S21 output of MammoWave, microwave images were produced using Huygens' algorithm, representing 2D homogeneity maps of dielectric properties in azimuthal plane. Subsequently, various image parameters (features) were extracted, such as maximum intensity. A dedicated software, based on predefined and preselected features and thresholds [3,4], was employed to classify breasts into the respective groups. Finally, the results from MammoWave's classification were compared with the reference standard.

In addition, a retrospective analysis quantified the capability of these features in allowing distinction between NH (malignant findings, BI-RADS 6) and H breasts (without findings or with benign findings, all other BI-RADS).

IV. Results and Discussions

The clinical protocol for this study is detailed in [6]. From January 2022 to December 2023, a total of 336 subjects were enrolled, with a mean age of 52 years ± 12 [SD] (ranging from 19 to 87 years old). Hospital distribution included 100 subjects from hospital 1 (Foligno, Italy), 130 from hospital 2 (Genoa, Italy), and 106 from hospital 3 (Toledo, Spain). MammoWave exams were conducted on both breasts for the majority of women, while for a few, only one breast was examined, resulting in a total analysis of 651 breasts. Based on the radiologist study review, 233 NF and 348 WF breasts were analyzed. For the remaining 70, the radiologist study review was not yet available at the paper submission date, and thus, these breasts were excluded from the NF/WF analysis. Lesions' final assessment categorized 89 breasts as NH (confirmed BI-RADS 6) and 554 as H. For the remaining 8, the lesions' final assessment was not yet available and hence not considered for H/NH analysis.

The prospective sensitivity of MammoWave in detecting WF was found to be 72%, aligning with the primary objective of the study [6]. Table I instead provides the performance results achieved in the evaluation of features within different frequency sub-bands for classifying between H/NH breasts. The highest sensitivities were achieved in the 1-2 GHz (75%), 2-3 GHz (78%) and 7-8 GHz (70%) sub-bands. It's important to note that sensitivity and specificity values depend on chosen thresholds; in this case, slightly lower specificities than 50% were expected since thresholds were preselected using values higher than the median of the H breasts group.

Future steps include the evaluation of specificity and sensitivity of MammoWave against the reference standard when retrospectively using MammoWave data from the RadioSpin technology simulator/artificial intelligence (AI) algorithms.

MammoWave, as a promising new device in breast imaging, offers a non-invasive and radiation-free approach, utilizing low-power radio-frequency signals (<1mW) without breast compression. Over the next three years, larger-scale clinical trials involving ten thousand volunteers will be conducted. During this period, MammoWave will be equipped with dedicated AI algorithms, tested and optimized using data collected from the RadioSpin clinical trial presented here.

Table I. Performace for Individual Sub-bands to Classify H/NH.

Sub-band (GHz)	Sensitivity (%)	Specificity (%)
1-2	75	47
2-3	78	37
3-4	65	41
4-5	65	40
5-6	69	37
6-7	65	38
7-8	70	37
8-9	60	45

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