*Cutting-edge strategies for breast lesions detection through Radiomics in novel microwave imaging technologies: Features' extraction reliability on microwave images from MammoWave device*

Purpose.

This investigation aims to retrospectively test the use, for the first time, of radiomics approach from medical images obtained by a novel technique: microwave breast imaging (MBI). All medical images analyzed in this research have been collected using the microwave imaging system *MammoWave* (UBT Srl, Italy), in the framework of an international, multicentric study (Clinicaltrials.gov identifier NCT04253366).

Methods or Background.

Over the last years, microwave imaging has emerged as a safe and promising new technology in breast radiology [1], [2], based on the ability to discriminate between healthy tissues and tissues with lesions through the existing contrast in dielectric properties within the microwave frequency spectrum. One such microwave imaging device, named MammoWave, has been recently tested in a prospective clinical trial that was carried out as part of a European Horizon 2020 project, SME Instrument Phase 2 (Grant Agreement ID: 830265). After receiving approval from the corresponding Ethics Committee, three hospitals (two in Italy and one in Spain) were involved in the clinical trials to evaluate MammoWave’s ability in breast lesions’ detection.

MammoWave system is an X-Rays free technology that uses safe radiofrequency signals to determine the presence of a lesion inside the breast [3]. The device (Fig. 1) consists of an examination table, where the patient lies in prone positions with the breast introduced in a designed plexiglass cup. Two antennas (a transmitter and a receiver) azimuthally rotates around the cup, operating in air in the frequency band of 1 to 9 GHz. A vector network analyzer (Cobalt C1209, Copper Mountain, Indianapolis), is connected to both antennas and measures S21 signals (i.e., the backscattered electromagnetic signal) in a multi-bistatic fashion. Microwave signals are collected and sent to an external server for processing. Such processing involved images’ reconstruction by resorting Huygens’ Principle [3]. In the prospective study, a dedicated computerized decision support system (CDSS) was tested. This system automatically analyzed several images’ features (based on a rule-of-thumb proposed in [4]) and returned an output to MammoWave controlling PC station. For instance, this simple thresholding strategy based on some images' features was used to classify breasts without findings (NF) and breasts with any lesion (WF); then, a prospective comparative analysis was done using as gold standard the radiologic output from conventional imaging. Digital Breast Tomosynthesis and/or Digital Full-Field Mammography and/or echography and/or MRI conventional studies were used as reference. If deemed appropriate by the investigators, 1-year clinical follow-up and/or histology were included as relevant information to label each breast. BI-RADS assessment was used to label breasts and classify them in two groups: breasts with no radiological findings (NF), i.e., already assessed with BI-RADS 1 using conventional techniques, and breasts with radiological findings (F); i.e., with lesions that may be benign or malignant. Preliminary results of the prospective study are discussed in [5].

The potential of microwave imaging is still unknown and new approaches such as radiomics may open a world of possibilities. Radiomics concentrates on improvements of image analysis, using an automated throughput extraction of large amounts of features of medical images. Features’ extraction and analysis from conventional images (mammography, ultrasound, MRI) have been reported in literature, also when applying artificial intelligence methods, to overcome cancer detection limitations [6]–[8]; however, there is very limited or non-existent literature regarding the application of these approaches in microwave images. For instance, the retrospective analysis here presented involves the extraction of statistical and radiomic features on microwave images generated by MammoWave. Specifically, the S21 signals are processed through Huygens’ principle-based algorithm to generate microwave images [4], which are two-dimensional (2D) homogeneity maps of dielectric properties in the azimuthal plane. Microwave images are obtained using the 1-9 GHz frequency range plus, in addition, the 8 individual sub-bands of 1 GHz bandwidth. Images are 1mmx1mm isotropic, defined on 2D matrices with dimensions 141×141. For the original images, its derivatives and the wavelet filtered, the extracted feature classes are:

Global texture features (first-order gray-level statistics);

Gray-Level Co-occurence Matrix (GLCM) texture feature;

Gray-Level Run-Length Matrix (GLRLM) texture features;

Gray-Level Size Zone Matrix (GLSZM) texture features;Gray Level Dependence Matrix (GLDM) texture features;

Neighbourhood Gray-Tone Difference Matrix (NGTDM) texture features.

The redundant and highly correlated features have been discarded as described in the next section.

Results or Findings.

A dataset of 697 breasts from 353 women (enrolled in 2020-2021) was considered, of which: 376 WF and 321 NF breasts. Demographic details are given in Table 1

From the 9 images produced for each breast (see as examples Fig 3 and Fig 4), more than 3000 features were extracted. The redundant and highly correlated features (>0.9 Pearson coefficient) have been discarded from the analysis. For the remaining 300 features, a non-parametric analysis (Kruskal-Wallis H-test) was performed and the ROC was calculated for the two populations: NF and WF. As shown in Fig 5, several features were found with a p-value 0.65 and AUC>0.65.

Conclusion.

Microwave imaging is a promising new technology in breast radiology, avoiding discomfort and use of ionizing radiation. This study shows how radiomic features for microwave imaging contain useful information for breast classification. These features, together with the statistical features, form a large and descriptive set on which Artificial Intelligence (AI) algorithms may be applied, with the aim of improving the single feature performance [9]. Given the impact of radiomics in imaging, its reliability in the new field of microwave imaging enhances its innovative nature and extraordinary perspectives.

References.

[1] N. Nikolova, “Microwave Imaging for Breast Cancer,” *IEEE Microw Mag*, vol. 12, no. 7, pp. 78–94, Dec. 2011, doi: 10.1109/MMM.2011.942702.

[2] M. A. Aldhaeebi, K. Alzoubi, T. S. Almoneef, S. M. Bamatraf, H. Attia, and O. M. Ramahi, “Review of Microwaves Techniques for Breast Cancer Detection,” *Sensors*, vol. 20, no. 8, p. 2390, Apr. 2020, doi: 10.3390/s20082390.

[3] A. Vispa *et al.*, “UWB device for breast microwave imaging: phantom and clinical validations,” *Measurement*, vol. 146, pp. 582–589, Nov. 2019, doi: 10.1016/j.measurement.2019.05.109.

[4] L. Sani *et al.*, “Breast lesion detection through MammoWave device: Empirical detection capability assessment of microwave images’ parameters,” *PLoS One*, vol. 16, no. 4, p. e0250005, Apr. 2021, doi: 10.1371/journal.pone.0250005.

[5] D. Álvarez Sánchez-Bayuela *et al.*, “Introducing Microwave Breast Imaging via MammoWave into the clinical routine of a Reference Hospital. Results from a prospective, international clinical trial,” in *European Congress of Radiology*, 2023.

[6] P. Crivelli, R. E. Ledda, N. Parascandolo, A. Fara, D. Soro, and M. Conti, “A New Challenge for Radiologists: Radiomics in Breast Cancer,” *Biomed Res Int*, vol. 2018, pp. 1–10, Oct. 2018, doi: 10.1155/2018/6120703.

[7] V. S. Parekh and M. A. Jacobs, “Integrated radiomic framework for breast cancer and tumor biology using advanced machine learning and multiparametric MRI,” *NPJ Breast Cancer*, vol. 3, no. 1, p. 43, Nov. 2017, doi: 10.1038/s41523-017-0045-3.

[8] A. S. Tagliafico, M. Piana, D. Schenone, R. Lai, A. M. Massone, and N. Houssami, “Overview of radiomics in breast cancer diagnosis and prognostication,” *The Breast*, vol. 49, pp. 74–80, Feb. 2020, doi: 10.1016/j.breast.2019.10.018.

[9] L. Papini *et al.*, “Breast Cancer Detection using Machine Learning Approaches on Microwave-based Data,” *European Conference on Antennas and Propagation*, 2023.

Limitations. We did not consider patients pre-menstrual information.

Funding. This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreements No 830265, and 872752.

Ethics. This study involved human participants and was approved by the following Ethics Committee(s) or Institutional Board(s): (1) Comitato Etico Regionale della Liguria c/o Azienda Ospedaliera Universitaria S. Martino Di Genova Largo Rosanna Benzi 10, 16132 GENOVA (GE), Italy (ID: 262/2019); 2) Comitato Etico Indipendente dell’IRCCS Istituto Clinico Humanitas, Via Manzoni, 56, 20089 ROZZANO (Milano), Italy (ID: 2558); 3) CEIm Gerencia de Atención Especializada de Toledo, Antigua Escuela Enfermería de Toledo, C/ Alicante, s/n 45005 TOLEDO, Spain (ID: 760/19/EC).



  

