White Paper

Breast Mass Analyzer (BMA)

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Background

Breast cancer represents the most common oncological disease in women worldwide, and a multimodality imaging approach is becoming increasingly important to detect and monitor early-stage cancer and to initiate timely and appropriate treatment in order to reduce mortality. According to WHO data, in 2020, there were 2.3 million women diagnosed with breast cancer and 685,000 deaths globally[1].

Technological developments over recent years have made breast ultrasound (US) an essential component for the breast cancer care, together with mammography/ tomosynthesis and magnetic resonance imaging (MRI). Mammography is the gold standard screening technique for breast cancer[2]. Ultrasound is not typically used at this stage but appears to be especially helpful in mass characterization where mammogram performance is limited and can be difficult to see abnormal features, as well as when a better look at a suspicious area, previously identified on mammography, is required[3].
Other advantages of US include its wide availability, good tolerance by patients, lack of ionizing radiation and relative low cost[4].

Moreover, US provides an optimal, cheap, and comfortable guidance for performing percutaneous needle biopsy, and, in particular, large-core needle biopsy (US-LCNB), the gold standard in diagnosis in case of suspect of breast cancer. This safe and cost-effective procedure has almost entirely replaced surgical biopsy, thus limiting costs, patients discomfort and possible complications[5]. However, it remains a semi-invasive procedure associated with an anticipatory emotional distress which could be avoided, where not necessary.

BI-RADS® (Breast Imaging-Reporting and Data System) provides a widely accepted reporting schema for imaging of the breast and characterization of findings. This system is designed to standardize breast imaging reporting and to reduce confusion in breast imaging interpretation, thus facilitating outcome monitoring and quality assessment. Results are sorted into categories numbered 0 through 6, by increasing the order of likelihood of findings [6,7].

Category		Management	Likelihood of cancer
0	Need additional imaging or prior examinations	Recall for additional imaging and/or await prior examinations	N/A
1	Negative	Routine screening	Essentially 0%
2	Benign	Routine screening	Essentially 0%
3	Probably Benign	Short interval-follow-up (6 months) or continued	>0% but ≤2%
4	Suspicious	Tissue sampling	4a. low suspicion for malignancy (>2% to ≤10%); 4b. moderate suspicion for malignancy (>10% to ≤50%); 4c. high suspicion for malignancy (>50% to <95%)
5	Highly suggestive of malignancy	Tissue sampling	≥95%
6	Known biopsy-proven	Surgical excision when clinical appropriate	N/A

Table 1: BI-RADS® final assessment category.

BI-RADS® category 3 represents a finding with a very low (>0% but ≤2%) probability of being cancer, that is not expected to change over time. A follow-up with repeat imaging in 3 to 6 months and regularly after that until the finding is known to be stable (usually at least 2 years) is usually prescribed. Studies aiming at reducing the US-guided biopsy rate should take particular attention to this category.

US images contain a high number of quantitative features, known as radiomics, which can be associated with a higher or lower probability of malignancy and may thus help to better characterize breast lesions[8-10]. These features include not only shape, margins, and spatial orientation of lesions, but also their signal intensity and heterogeneity, the quantification of which is difficult for the human reader. Recent technological advances in the field of artificial intelligence applied to image analysis allow the development of machine learning models predicting different class of risks based on the wide spectrum of information found in a US image[11-12].

TRACE4BUS is a machine learning model based on radiomics features belonging to different families, such as morphology, intensity-based statistics, intensity histogram, grey-level co-occurrence matrix, grey-level run length matrix, grey-level size zone matrix [13-14], neighborhood grey tone difference matrix, grey-level distance zone matrix, and neighboring grey-level dependence matrix. Their definition, computation, and nomenclature are compliant with the International Biomarker Standardization Initiative (IBSI) guidelines[15].

Rank	Feature Family	Feature Name
1	Morphology	Perimeter-to-area ratio **
2	Morphology	Maximum diameter **
3	Morphology	Compactness **
4	Morphology	Acircularity **
5	Morphology	Perimeter **
6	Morphology	Area **
7	Morphology	Center of mass shift **
8	Morphology	Circularity *
9	Neighborhood grey tone difference matrix	Strength **
10	Neighborhood grey tone difference matrix	Coarseness **
11	Neighborhood grey tone difference matrix	Contrast
12	Neighborhood grey tone difference matrix	Busyness *
13	Grey-level size zone matrix	Zone size non-uniformity **
14	Grey-level size zone matrix	Grey-level non-uniformity glszm **
15	Neighboring grey-level dependence matrix	Dependence count non-uniformity **
16	Neighboring grey-level dependence matrix	Low-dependence low-grey-level emphasis
17	Grey-level run length matrix	Grey-level non-uniformity
18	Grey-level run length matrix	Run length non-uniformity
19	Intensity-based statistics	Minimum
20	Intensity-based statistics	Energy
21	Intensity-based statistics	Variance
22	Intensity-based statistics	Quartile coefficient
23	Intensity-based statistics	10th percentile
24	Intensity histogram	10th percentile
25	Grey-level co-occurrence matrix	First measure of information correlation

* Denotes statistical significance at 0.05 (adjusted with Bonferroni–Holm correction).
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Table 2: Top 25 most relevant predictors sorted in descending order of relevance.

TRACE4BUS: clinical validation

The development and the clinical validation of TRACE4BUS is described in detail in the paper by Interlenghi M. et al. "A Machine Learning Ensemble Based on Radiomics to Predict BI-RADS® Category and Reduce the Biopsy Rate of Ultrasound-Detected Suspicious Breast Masses"[12].
Esaote systems were part of the pool of ultrasound devices that were used for the development and validation of the algorithm.

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Article

A Machine Learning Ensemble Based on Radiomics to Predict BI-RADS Category and Reduce the Biopsy Rate of Ultrasound-Detected Suspicious Breast Masses

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Abstract: We developed a machine learning model based on radiomics to predict the BI-RADS category of ultrasound-detected suspicious breast lesions and support medical decision-making towards short-interval follow-up versus tissue sampling. From a retrospective 2015–2019 series of ultrasound-guided core needle biopsies performed by four board-certified breast radiologists using six ultrasound systems from three vendors, we collected 821 images of 834 suspicious breast masses from 819 patients, 404 malignant and 430 benign according to histopathology. A balanced image set of biopsy-proven benign (n = 299) and malignant (n = 299) lesions was used for training and cross-validation of ensembles of machine learning algorithms supervised during learning by histopathological diagnosis as a reference standard. Based on a majority vote (over 80% of the votes to have a valid prediction of benign lesion), an ensemble of support vector machines showed an ability to reduce the biopsy rate of benign lesions by 15% to 18%, always keeping a sensitivity over 94%, when externally tested on 236 images from two image sets: (1) 123 lesions (51 malignant and 72 benign) obtained from two ultrasound systems used for training and from a different one, resulting in a positive predictive value (PPV) of 45.9% (95% confidence interval 36.3–55.7%) versus a radiologists' PPV of 41.5% ($p < 0.005$), combined with a 98.0% sensitivity (89.6–99.9%); (2) 113 lesions (54 malignant and 59 benign) obtained from two ultrasound systems from vendors different from those used for training, resulting into a 50.5% PPV (40.4–60.6%) versus a radiologists' PPV of 47.8% ($p < 0.005$), combined with a 94.4% sensitivity (84.6–98.8%). Errors in BI-RADS 3 category (i.e., assigned by the model as BI-RADS 4) were 0.8% and 2.7% in the *Testing set I* and *II*, respectively. The board-certified breast radiologist accepted the BI-RADS classes assigned by the model in 114 masses (92.7%) and modified the BI-RADS classes of 9 breast masses (7.3%). In six of nine cases, the model performed better than the radiologist did, since it assigned a BI-RADS 3 classification to histopathology-confirmed benign masses that were classified as BI-RADS 4 by the radiologist.

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Fig. 1: Clinical study front page.

Augmented Insight™, an Esaote smart solution applied to breast ultrasound imaging

Augmented Insight™ embeds all the solutions powered by Artificial Intelligence, developed by the Research & Development department at Esaote according to a multidisciplinary approach, across different modalities such as Ultrasound, MRI and Ebit. Based on data-driven machine learning, Augmented Insight™ is designed to simplify the workflow in repetitive gestures, complex procedures, measurements, or lesions analysis.
Esaote, particularly active in the breast imaging field and in constant search of innovative solutions, has recently developed many Augmented Insight™ solutions specifically for breast US imaging, including BreastNav™MRI, eDetect and Breast Mass Analyzer technologies.

Esaote Breast Mass Analyzer Technology

Esaote Breast Mass Analyzer (BMA) has embedded the TRACE4BUS software by Deep Trace Technologies.
BMA Augmented Insight™ technology is a radiomics-based machine learning model to predict the BI-RADS® category of ultrasound-detected suspicious breast lesions and support medical decision-making towards BI-RADS® 3 versus BI-RADS® 4-5.
Therefore, this technology is indicated for all physicians with experience in breast ultrasound seeking support for reporting ultrasound-detected suspicious breast masses, assigning the diagnostic category to such masses according to BI-RADS® classification, and, consequently, making an informed decision whether or not to send such masses for ultrasound-guided needle biopsy.
During the ultrasound examination, as soon as the user identifies a suspected lesion, freezes the image and manually contours the mass using the trackball.
The software, supported by A.I., automatically processes the mass, and within a few seconds provides its characteristics (i.e. shape and orientation) and BI-RADS® category (BI-RADS® category calculated by BMA is on 3 levels: 3, 4 and 5).
The user can subsequently accept the proposed value, modify, or refine it on categories 4a, 4b and 4c, directly from the touchscreen. If approved, all the information are automatically included in the worksheet environment and in the report.

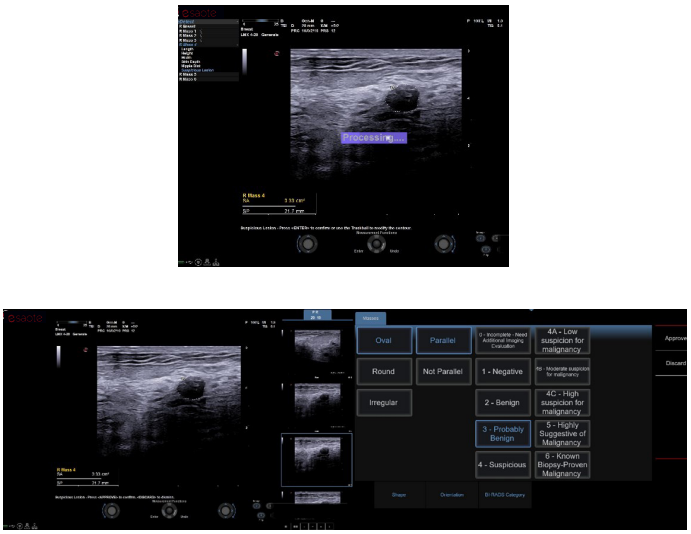

Fig. 2: BMA procedure: step 1 – mass processing; step 2 – BI-RADS® categorization.

The report, a dedicated template (that can be edited directly from the touchscreen) produced according to the BI-RADS® scoring and categorization, provides information on the localization of the lesion, with a dedicated body mark to visually locate the lesion in the correct quadrant, as well as details on the mass itself (shape, orientation, and echo pattern) and its margins (circumscribed, lobulated and spiculated).

To enhance the quality of lesion characterization, additional technologies such as microV, the Esaote tool for microvascularization visualization, and QElaXto 2D, the Esaote 2D shear wave technique for stiffness evaluation of the breast tissue, are available on the system.

Breast					
R Mass			L Mass		
R Mass 1			**L Mass 1**		
Length	6.8	mm	Length	3.3	mm
Height	8.6	mm	Height	6.7	mm
Width	10.7	mm	Width	1.9	mm
Volume	0.328	ml	Volume	0.022	ml
Skin Depth	5.8	mm	Skin Depth	20.7	mm
Nipple Dist	10.0	mm	Nipple Dist	23.0	mm
Location			Location		
O'clock		---	O'clock		---
Region		Nipple	Region		Areolar
Quadrants		Upper Inner	Quadrants		Upper Outer
Profile		Posterior	Profile		Middle
Probe Angle		60	Probe Angle		120
Masses			Masses		
Shape		Oval	Shape		Oval
Orientation		Parallel	Orientation		Parallel
Echo Pattern		Anechoic	Echo Pattern		Hypoechoic
Posterior Features		No posterior features	Posterior Features		No posterior features
Margin			Margin		
Circumscribed		Yes	Circumscribed		Yes
Not circumscribed - Indistinct		No	Not circumscribed - Indistinct		No
Not circumscribed - Angular		No	Not circumscribed - Angular		No
Not circumscribed - Microlobulated		No	Not circumscribed - Microlobulated		No
Not circumscribed - Spiculated		No	Not circumscribed - Spiculated		No
Elasticity Assess		---	Elasticity Assess		---
BI-RADS Category		**3 - Probably Benign**	**BI-RADS Category**		**3 - Probably Benign**

Fig. 3: BI-RADS® report.

Innovation and research

This innovative BMA tool further expands the scope of the company's breast ultrasound technologies dedicated to the breast. It has proved its viability as a second opinion on BI-RADS® classification as well as its potential clinical value in reducing the biopsy rate.
The underlying philosophy of research and development in Esaote is based on open innovation involving external expertise in a valuable co-operative network that includes research centers and highly experienced physicians and their patients.

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Notes

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