Trace4BUS

PRODUCT SHEET

v2.0 14 January 2022

Deep Trace
TECHNOLOGIES

THE PROBLEM

Breast cancer (BC) is one the most frequent malignant neoplasms in women, with 2.3 million women newly diagnosed with this disease and 685 000 deaths worldwide in 2020, according to the World Health Organization.

Ultrasound imaging is a key tool in BC detection and diagnosis. However, benign breast abnormalities can mimic malignancies so that percutaneous needle biopsy is considered the best method for BC confirmation or exclusion to prevent unnecessary surgery, as recommended by the European Society of Breast Cancer Specialists (EUSOMA) and the European Commission Initiative on Breast Cancer.

As a consequence, to reliably exclude malignancy, breast radiologists perform biopsy not only of clearly malignant but also of probably benign lesions, unless they think that a given lesion in a given patient, also considering the patient-specific risk profile, has an extremely low probability of being malignant and that a six-month delayed diagnosis would not impact on patient's outcome.

This clinical behavior results in a huge number of needle biopsy performed every year for breast lesions that are finally revealed to be benign. Considering a rate of benign breast findings on the total number of breast needle biopsies being at least 60% and that at least a 70% of them are performed under ultrasound guidance, *every year about one million of ultrasound-guided breast biopsy of benign lesions are performed in the world, increasing the psychologic and economic cost of breast care*.

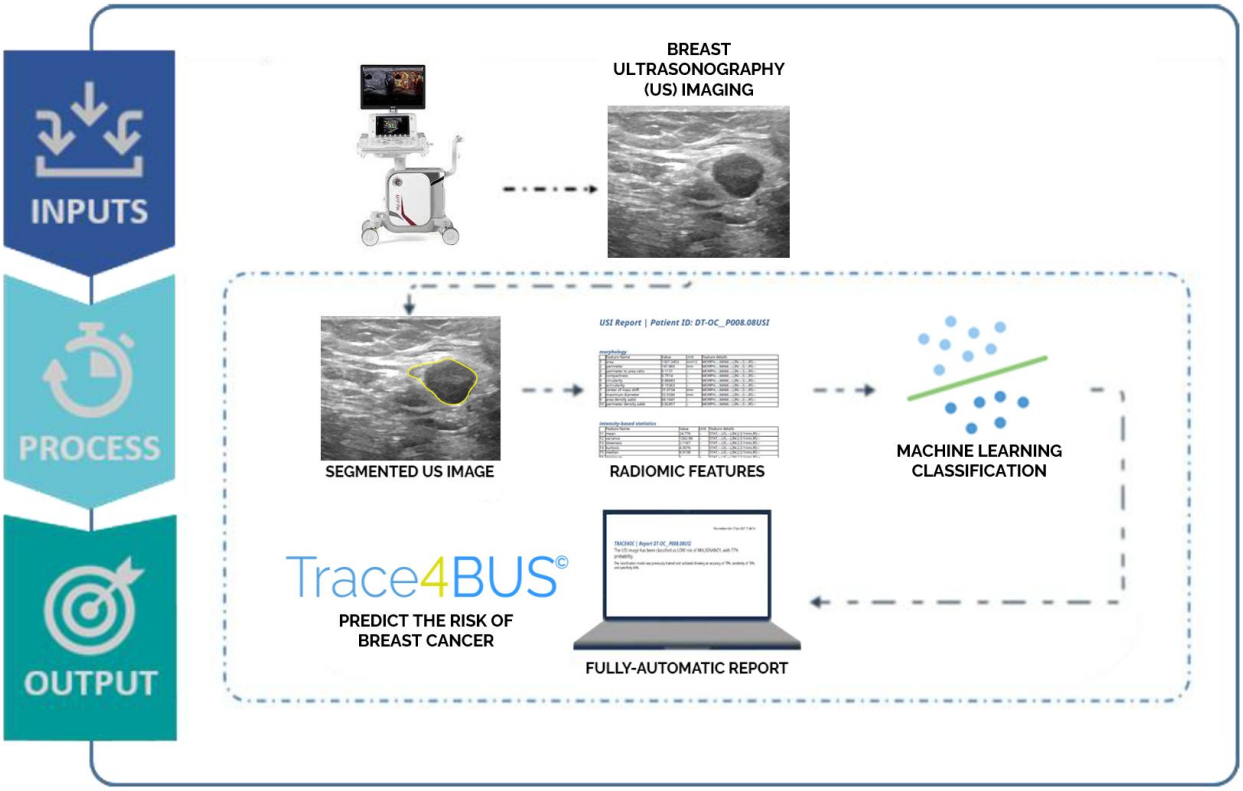
OUR SOLUTION: TRACE4BUS©

The breast masses appear to have characteristics at ultrasonography (US) that are helpful in the BC diagnosis to expert operators. However, Breast Imaging-Reporting and Data System (BI-RADS) guidelines developed so far by the American College of Radiation, are helpful in very low risk group discrimination (0% likelihood of malignancy, BI-RADS 2), while showing limits for masses assigned with an intermediate category (BI-RADS 3-4) and complex in some cases for masses assigned with BI-RADS 5, leading to high ratio of false positives.

TRACE4BUS is our proprietary licensed software that uses machine learning to deeply analyze US images of BC suspicious breast masses of subjects at risks to provide the breast mass BI-RADS category.

DESCRIPTION

TRACE4BUS provides the BI-RADS category of suspicious breast masses by analysing such masses on ultrasound images.



INDICATION OF USE of TRACE4BUS©

TRACE4BUS is indicated for women with breast masses detected at ultrasound imaging and considered suspicious for breast cancer by physicians with experience in breast ultrasound. Physicians with experience in breast ultrasound can use TRACE4BUS as a support for: reporting ultrasound-detected suspicious breast masses; assigning the diagnostic category to such masses according to the BI-RADS classification; and, as a consequence, making an informed decision to send such masses to ultrasound-guided needle biopsy or to short interval follow-up. Physicians with experience in breast ultrasound can use TRACE4BUS as a support for diagnosing and managing patients with ultrasound-detected suspicious breast masses. The TRACE4BUS software provides an assessment of suspicious breast masses at the date of the ultrasound examination in which such masses are detected.

It should be noted that DeepTrace Technologies S.R.L. considers TRACE4BUS as a support to physicians with experience in breast ultrasound for reporting, diagnosis and decision-making of suspicious breast masses. However, these medical professionals retain the ultimate decision-making responsibility.

HOW TRACE4BUS© PREDICTS BI-RADS CATEGORY OF BREAST MASSES SUSPICIOUS OF BREAST CANCER

TRACE4BUS is based on ultrasound (US) image analytics in the breast region, data mining and machine learning classifiers. The software computes a high number of image features representing the morphometric-echogenic pattern of a region of interest contouring a breast mass suspicious of breast cancer (BC) traced by the end-user on a 2-dimensional (2D) US breast image centered on the mass. Scientific evidence has shown that morphometric and echogenic features are different in malignant and benign breast masses and in their adjacent tissues.

The features of the morphometric and echogenic pattern of diagnosed breast masses from women are used to train, tune and test an artificial intelligence (AI) agent consisting into a machine learning model including hundreds of support vector machines to automatically associate the likelihood of malignancy of such masses (<2% likelihood of malignancy, 2%-95% likelihood of malignancy, >95% likelihood of malignancy). The machine learning training is supervised by the histological diagnosis of breast masses (malignant or benign disease) obtained following biopsy or definitive surgery from tissue samples of the breast mass.

When the US image of a BC suspicious breast mass is provided by the user as input to TRACE4BUS, the software uses the trained machine learning model (the AI agent of the software) to classify that breast mass into one of the three BI-RADS categories (BI-RADS 3 <2% likelihood of malignancy vs BI-RADS 4 2%-95% likelihood of malignancy vs > BI-RADS 5 95% likelihood of malignancy), representing a valid tool to support physicians in the reporting of ultrasound-detected suspicious breast masses.

PERFORMANCE

The machine learning model included in TRACE4BUS has been trained, tuned and tested on data reviewed by experts. The last machine learning model performance assessment was on 17 Dec 2021 on a set of US breast images obtained by US systems from different vendors from patients of a clinical study[1] including 806 women and 13 men with suspicious breast masses. TRACE4BUS was used to predict the BI-RADS category of suspicious breast masses based on the features computed from the manual contours of the breast masses. TRACE4BUS was proven effective in predicting BI-RADS 3, 4, and 5 categories and in providing 15-18% reduction of the biopsy rate of masses finally diagnosed as benign masses from biopsy or definite surgery, while still warranting very high sensitivity (94-98%). The features computed from the manual contouring provided by the end-user as input to the machine learning model are considered stable, showing an intra-class correlation coefficient > 0.75 among different users. Intra-observer agreement in the machine learning model classification of BI-RADS was 96%, with a mean DICE similarity coefficient of 89.7% ± 5.0%. Inter-observer agreement in the machine learning model classification of BI-RADS was 92%, with a mean DICE similarity coefficient of 87.0% ± 9.9% (The model design, performance and clinical validation is described in *Interlenghi M. et al., Diagnostics, 2022*).

Example of US image of a breast mass of a patient at risk of breast cancer, with highlighted the segmented region of interest of the breast mass analysed by TRACE4BUS.

SENSITIVITY > 94-98%

BIOPSY FALSE POSITIVES REDUCTION > 15-18%

The machine learning model has been trained and tested mostly from European Caucasian subjects. However, different performances in non Caucasian subjects are not expected since the ultrasound appearance of benign and malignant lesions should not be different, even for different structure of the breast (e.g., Asian women have breasts denser than Caucasian women). The machine learning model has been trained and tested on data mostly from women. TRACE4BUS should not be used to support the assignment of BI-RADS category in men due to the numerical limit of the currently tested men.

[1] Protocol SENORETRO IRCCS Policlinico San Donato (San Donato, Italy) v01/17 at the date of 16 December 2021.