## Three-blind validation of a Deep Learning model to obtain the dense tissue area in digital mammographies.

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## Abstract

Breast Cancer (BC) is the most frequent in women worldwide. Although mortality has significantly decreased in recent years, the incidence continues to increase, making screening programs crucial. In these programs, mammograms are collected from women over 40-45 years of age, which are then assessed by radiologists. The most relevant image biomarker of the risk of developing BC is the dense tissue [1], but its evaluation is time-consuming [2] and has a subjective component (inter and intra-observer) [3]. Approaches based on Machine Learning (ML) would reduce the analysis time; still, the subjective component challenges automatic methods to deal with the imperfect supervision problem. Moreover, different mammographic devices and acquisition protocols may influence the image and its analysis. In such a way, a conscious validation of automated technologies becomes critical.

We have trained an ML (Deep Learning) model, CM-YNET [4], to infer the dense tissue region in digital mammographies automatically. We used a dataset of images (1407 women, 2814 mammographies) from 11 centers ascribed to the Valencian screening program. Two experienced radiologists (R1 and R2) segmented the dense tissue in each mammography. The model demonstrated robustness against image sources and promising performance results (overall CM-YNET DICE 0.82, overall R1 vs. R2 DICE 0.77). We also tested CM-YNET in a longitudinal (2011 – 2021) dataset of 320 mammographies from  $Hospital \ del \ Mar$  (Barcelona), where acquisition devices were updated during this period, and then, the image quality changed. The same two radiologists segmented the mammographies. The results suggested the model generalization capability since the CM-YNET performance was comparable to the radiologists' (old devices, R1 vs. R2 DICE 0.71 and CM-YNET DICE 0.76; new devices, R1 vs. R2 DICE 0.76 and CM-YNET DICE 0.86).

After the extraction of a new set of 500 mammographies from Hospital del Mar, which were labeled by two radiologists (L1 and L2), we developed the three-blind validation: (1) the images were also labeled by applying CM-YNET (L3) (obtaining 1500 labeled images), (2) from each labeler we randomly duplicated 100 segmented mammograms (1800 labeled images), (3) a third radiologist (R) assessed its agreement or disagreement with the 1800 labeled images randomlyshowed. The experiment allowed us to measure the intraobserver variability of R, inconsistent in a total of 23/300 (7.67%) images, and check if CM-YNET behavior is as good as a specialist behavior for such a task (imperfect supervision). Preliminary analysis of the results shows that CM-YNET has an agreement with R (95.72%) as good as L1 (96.50%) and L2 (95.72%) have in the most current devices (those that are nowadays in clinical practice), meanwhile in older devices a slightly worse trend is observed (L1 72.42%, L2 73.66%, and CM-YNET 60.49%) due to the brightness of the images where the pectoral muscle appear.

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These results suggest that CM-YNET could be a powerful support decision tool for BC screening programs. Future work covers the application of preprocessing stages to remove undesired artifacts, such as pectoral muscle, and the repetition of the experiment to analyze the improvement of the agreement ratio observed in this study.

## References

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