Therapixel
% Ms. Cindy Domecus
Principal
Domecus Consulting Services LLC
1171 Barroihet Drive
HILLSBOROUGH CA 94010

March 25, 2020

Re: K192854
Trade/Device Name: MammoScreen
Regulation Number: 21 CFR 892.2090
Regulation Name: Radiological computer assisted detection and diagnosis software
Regulatory Class: Class II
Product Code: QDQ
Dated: February 10, 2020
Received: February 11, 2020

Dear Ms. Domecus:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR

803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

For

Thalia T. Mills, Ph.D.
Director
Division of Radiological Health
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
*See PRA Statement below.*

510(k) Number *(if known)*
K192854

Device Name
MammoScreen

Indications for Use *(Describe)*
MammoScreen™ is intended for use as a concurrent reading aid for interpreting physicians, to help identify findings on screening FFDM acquired with compatible mammography systems and assess their level of suspicion. Output of the device includes marks placed on findings on the mammogram and level of suspicion scores. The findings could be soft tissue lesions or calcifications. The level of suspicion score is expressed at the finding level, for each breast and overall for the mammogram. Patient management decisions should not be made solely on the basis of analysis by MammoScreen™.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

**CONTINUE ON A SEPARATE PAGE IF NEEDED.**

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# 510(k) Summary
# K192854

This 510(k) summary of safety and effectiveness information is prepared in accordance with the requirements of 21 CFR § 807.92.

**Applicant Information:**

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Date Summary Prepared: March 18th, 2020

**Device Information**:

| | |
|---|---|
| Trade Name: | MammoScreen |
| Common Name: | Computer-Assisted Detection Device |
| Device Classification Name: | Radiological Computer Assisted Detection/Diagnosis Software For Lesions Suspicious For Cancer |
| Regulation Number: | 892.2090 |
| Regulation Class: | Class II |
| Product Code: | QDQ |
| Submission type | Traditional 510(k) |

**Predicate Device**:

The predicate device is Transpara™, cleared under K181704.

**Device Description:**

MammoScreen is a software-only device for aiding interpreting physicians in identifying focal findings suspicious for breast cancer in screening FFDM (full-field digital mammography) acquired with compatible mammography systems. The product consists of a processing server and a web interface. The software applies algorithms for recognition of suspicious calcifications and soft tissue lesions. These algorithms have been trained on large databases of biopsy proven examples of breast cancer, benign lesions and normal tissue.

MammoScreen automatically processes FFDM and the output of the device can be used by radiologists concurrently with the reading of mammograms. The user interface of MammoScreen has several functions:

a) Activation of computer aided detection (CAD) marks to highlight locations, known as findings, where the device detected calcifications or soft tissue lesions suspicious for cancer.

b) Association of findings with a score, known as the MammoScreen Score, which characterizes findings on a 1-10 scale, with increasing level of suspicion. Only the most suspicious findings (with a MammoScreen score equal or greater than 5) are initially marked to limit the number of findings to review. The user shall also review findings with score of 4 or lower.

c) Indication, with matching markers, when findings corresponding to the same findings are detected in multiple views of the FFDM.

MammoScreen is configured as a DICOM Web compliant node in a network and receives its input images from another DICOM node, called "the DICOM Web Server". The MammoScreen output will be displayed on the screen of a personal computer compliant with requirements specified in the User Manual.

The image analysis unit includes machine learning components trained to detect positive findings (calcifications and soft tissue lesions).

**Indication for Use:**

**MammoScreen™** is intended for use as a concurrent reading aid for interpreting physicians, to help identify findings on screening FFDM acquired with compatible mammography systems and assess their level of suspicion. Output of the device includes marks placed on findings on the mammogram and level of suspicion scores. The findings could be soft tissue lesions or calcifications. The level of suspicion score is expressed at the finding level, for each breast and overall for the mammogram. Patient management decisions should not be made solely on the basis of analysis by **MammoScreen™**.

Intended patient population

The device is intended to be used in the population of women undergoing screening FFDM.

Warnings and precautions

Patient management decisions should not be made solely on the basis of analysis by MammoScreen.

**Predicate and Subject Device Comparison:**

| | **Subject Device**<br>**MammoScreen** | **Predicate Device**<br>**Transpara™**<br>**K181704** | **Substantially Equivalent?** |
|---|---|---|---|
| **Classification Regulation** | 21 CFR 892.2090<br>Radiological Computer Assisted Detection And Diagnosis Software | SAME | Yes, identical. |
| **Medical Device Classification** | Class II | SAME | Yes, identical. |
| **Product Code** | QDQ | SAME | Yes, identical. |
| **Level of Concern** | Moderate | SAME | Yes, identical. |
| **Intended Use** | A concurrent reading aid for physicians interpreting screening FFDM acquired with compatible mammography systems, to identify findings and assess their level of suspicion. | SAME | Yes, identical. |
| **Target patient population** | Women undergoing FFDM screening mammography | SAME | Yes, identical |

| | **Subject Device**<br>**MammoScreen** | **Predicate Device**<br>**Transpara™**<br>**K181704** | **Substantially Equivalent?** |
|---|---|---|---|
| **Target user population** | Physicians interpreting FFDM screening mammograms | SAME | Yes, identical |
| **Design** | Software-only device | SAME | Yes, identical |
| **Indication for Use** | MammoScreen™ is intended for use as a concurrent reading aid for interpreting physicians, to help identify findings on screening FFDM acquired with compatible mammography systems and assess their level of suspicion. Output of the device includes marks placed on findings on the mammogram and level of suspicion scores. The findings could be soft tissue lesions or calcifications. The level of suspicion score is expressed at the finding level, for each breast and overall for the mammogram. Patient management decisions should not be made solely on the basis of analysis by MammoScreen™. | The ScreenPoint Transpara™ system is intended for use as a concurrent reading aid for physicians interpreting screening mammograms, to identify regions suspicious for breast cancer and assess their likelihood of malignancy.<br>Output of the device includes marks placed on suspicious soft tissue lesions and suspicious calcifications; region-based scores, displayed upon the physician's query, indicating the likelihood that cancer is present in specific regions; and an overall score indicating the likelihood that cancer is present on the mammogram.<br>Patient management decisions should not be made solely on the basis of analysis by Transpara™. | Yes, identical |

| | **Subject Device**<br>**MammoScreen** | **Predicate Device**<br>**Transpara™**<br>**K181704** | **Substantially Equivalent?** |
|---|---|---|---|
| **Score** | Finding level:<br>10-point scale score indicating the level of suspicion of malignancy (from low suspicion to high suspicion).<br><br>Breast level:<br>The same 10-point scale score as finding level. The score of a breast is equal to the maximum score of the findings detected in this breast.<br><br>Exam level:<br>Exam-level of suspicion resulting directly from the maximum score of both breasts (1-to-1 mapping between the score and the exam-level of suspicion). | Finding level:<br>Continuous score 1-100 indicating the level of suspicion of malignancy (from low suspicion to high suspicion).<br><br>Breast level:<br>None<br><br>Exam level:<br>10-point scale score indicative of higher frequency of cancer positive | Both scores are substantially equivalent.<br>Both scores increase with the level of suspicion. The minimum (resp. the maximum) of the both scores describes the same status.<br>At the Exam level, both scores have a 10-point scale. |
| **Finding discovery** | Findings are by-default displayed when score is equal or higher to 5.<br>Upon user request for findings of score equal or less to 4. | Upon user request by clicking in a position of the image also detected by Transpara™. | Both are the demonstration of the same intention: reducing the number of findings the user has to review. In this sense, both are equivalent. |

| | **Subject Device**<br>**MammoScreen** | **Predicate Device**<br>**Transpara™**<br>**K181704** | **Substantially Equivalent?** |
|---|---|---|---|
| **Performances** | Reader study:<br>- 240 cases<br>- 14 radiologists<br><br>Reading time (two sessions mean):<br>- 57,67 seconds (unaided session)<br>- 64, 13 seconds (with MammoScreen)<br><br>AUC:<br>- radiologists AUC (unaided) = 0,769<br>- standalone AUC = 0,786 | Reader study:<br>- 240 cases<br>- 14 radiologists<br><br>Reading time:<br>- 146 seconds (unaided session)<br>- 149 seconds (with Transpara™)<br><br>AUC:<br>- radiologists AUC (unaided) = 0,866<br>- standalone AUC = 0,887 | Despite a slightly higher performance of MammoScreen compared to Transpara™, gains are still comparable and do not raise new questions regarding safety and effectiveness of the device. |
| **Features** | Distinguishes two types of suspicious findings (calcifications and soft tissue lesions).<br><br>The CAD output provided by the server includes the location and the outline of findings.<br><br>MammoScreen processing server is a standalone system WITH a user interface. | Distinguishes two types of suspicious findings (calcifications and soft tissue lesions).<br><br>The CAD output provided by the server includes the location and the outline of findings.<br><br>Transpara™ processing server is a standalone system WITHOUT a user interface. | Despite some differences between the predicate device and MammoScreen, features are still comparable and do not raise new questions regarding safety and effectiveness of the device. |
| **Imaging Modality** | FFDM | SAME | Yes, identical |

| | Subject Device<br>MammoScreen | Predicate Device<br>Transpara™<br>K181704 | Substantially Equivalent? |
|---|---|---|---|
| **Fundamental scientific technology** | In MammoScreen, a range of medical image processing and machine learning techniques are implemented. The system includes 'deep learning' modules for recognition of suspicious calcifications and soft tissue lesions. These modules are trained with very large databases of biopsy-proven examples of breast cancer and normal tissue. | SAME | Yes, identical |

*Table 7.1 Comparison between subject and predicate device*

Discussion:

The indication for use of MammoScreen is very similar to that of the predicate device. Both devices are intended to be used by clinicians interpreting digital mammogram images, to help them with localizing and characterizing suspicious findings. The devices are both intended to be used concurrently with the reading of images and are not intended as a replacement for the review of a clinician or their clinical judgement. Both devices target the same findings, the same patient and user populations and use the same imaging modality. Also, both devices have a Moderate Level of Concern.

Both devices give a score. The scoring system is not the same, but is based on similar principles: providing users with a level of suspicion for malignancy from low (score 1) to high (score 10 or 100). Transpara™ exhibits some minor differences though:

- at the finding level, Transpara™ uses a 1-100 score of Transpara™ while the MammoScreen score has a 10-point scale. Indeed, Therapixel believes, based on questionnaire submitted to 15 radiologists, that interpretability of less granular scale is easier for users (how shall a difference between a score of 41 and 43 be interpreted for instance?)
- at the breast level, Transpara™ does not provide a score. Therapixel considers that this level is required for better interpretability at exam level, scores are equivalent. However, using Transpara™, the user cannot determine with precision to which of the breast (if not both), and where in the breast(s) this overall score applies. On the contrary, Therapixel's score (and the indication of the exam-level of suspicion that directly results from it) is directly connected to one of the breasts (or both) and indicated as such, and exactly where in the breast (finding) thanks to the scoring consistency (a breast inherits from the maximum score of its findings, and the exam inherits from the maximum score of both breasts). Doing so makes the algorithm decision more explicit, and easier to interpret from a user point of view.

Both scores increase with the level of suspicion. The minimum (resp. the maximum) of the both scores describes the same status. At the Exam level, both scores have a 10-point scale.

Both scores are substantially equivalent, the minor differences do not raise further or different questions of performance or safety.

In conclusion, these differences do not raise different questions of safety and effectiveness of the device when used as labeled. The overall design of MammoScreen is very similar to that of the predicate device. Both devices have the same intended use, very similar indications for use, and minor differences between MammoScreen and the predicate device do not raise different questions of safety and effectiveness which are equivalent.

**Non-clinical Testing**

MammoScreen is a software-only device. The level of concern for the device is determined as Moderate Level of Concern.

Tests have been performed in compliance with the following recognized consensus standards:

- IEC 62304 Edition 1.1 2015-06 - Medical device software - Software life-cycle processes
- IEC 62366-1 Edition 1.0 2015-02 - Medical devices - Application of usability engineering to medical devices.

MammoScreen has successfully completed integration and verification testing and beta validation. In addition, potential hazards have been evaluated and mitigated, and have acceptable levels.

**Standalone Performance Testing**

Standalone performance testing of MammoScreen assesses the performance of MammoScreen–algorithms in the absence of a clinician and includes mammograms of women acquired with devices from two manufacturers: Hologic® and GE®.

The following graph shows the ratio of positive cases over all cases processed by both GE® and Hologic® devices that fall into each score:

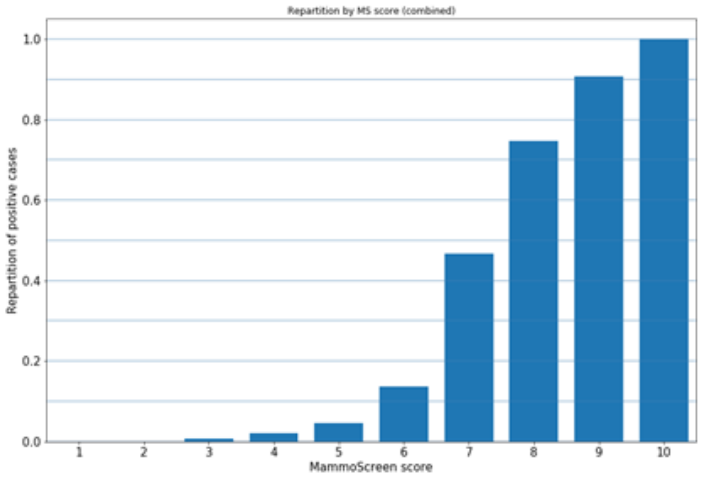


*Figure 7.2.-Repartition of positive cases per MammoScreen scores for Hologic® and GE® combined*

**Mammogram level**

Standalone performance of the MammoScreen-AI algorithm in characterizing positive and negative US FFDM acquired on Hologic® devices, and performance comparison with FFDM acquired on GE® devices, are given in the table below:

| | **Hologic®** | **GE®** | **Combined** | **$FOM_{GE}$-$FOM_{HOL}$** |
|---|---|---|---|---|
| **ROC AUC** | 0.868 (0.851, 0.885) | 0.887 (0.875, 0.898) | 0.883 (0.873, 0.892) | 0.018 (-0.002, 0.039) |

| | | | | |
|---|---|---|---|---|
| **Sensitivity** | 0.844 (0.815, 0.872) | 0.849 (0.827, 0.871) | 0.847 (0.829, 0.864) | 0.005 (-0.032, 0.042)[1] |
| **Specificity** | 0.705 (0.689, 0.722) | 0.738 (0.728, 0.747) | 0.729 (0.721, 0.737) | 0.032 (0.014, 0.051) |

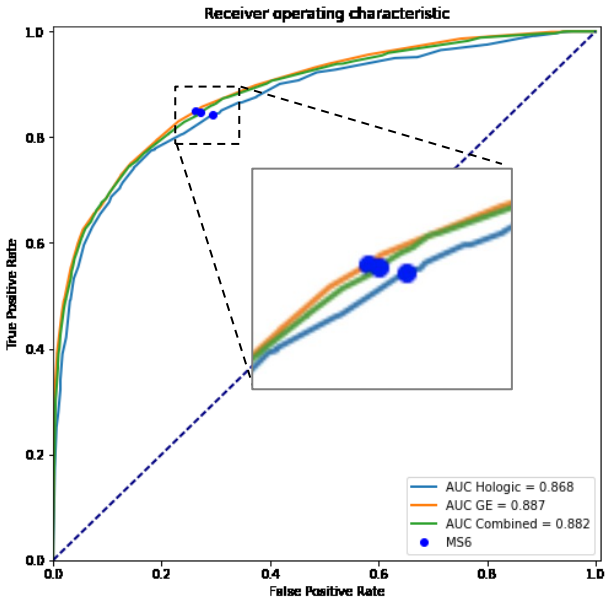


*Figure 7.3: ROC curves of MammoScreen-AI algorithm at **mammogram** level on US Hologic® FFDM (blue), GE® FFDM (orange), and on both types combined (green). Sensitivity and specificity at the chosen standalone regime (MS6) are shown with a blue dot for each case.*

### Breast level

Standalone performance of the MammoScreen-AI algorithm in characterizing positive and negative breasts on US FFDM acquired on acquired on Hologic® devices, and performance comparison with FFDM acquired on GE® devices, are given in the table below:

| | **Hologic®** | **GE®** | **Combined** | **$FOM_{GE}$-$FOM_{HOL}$** |
|---|---|---|---|---|
| **ROC AUC** | 0.901 (0.886, 0.915) | 0.916 (0.906, 0.926) | 0.911 (0.902, 0.919) | 0.015 (-0.002, 0.033) |
| **Sensitivity** | 0.813 (0.781, 0.843) | 0.830 (0.808, 0.853) | 0.823 (0.805, 0.841) | 0.017 (-0.023, 0.056) |
| **Specificity** | 0.840 (0.831, 0.848) | 0.846 (0.840, 0.851) | 0.844 (0.839, 0.849) | 0.006 (-0.004, 0.016) |

[1] Due to the lower bound of the 95% CI being close to the non-inferiority margin (-0.03), 10,000 bootstrap replicates were used instead of 2,000.

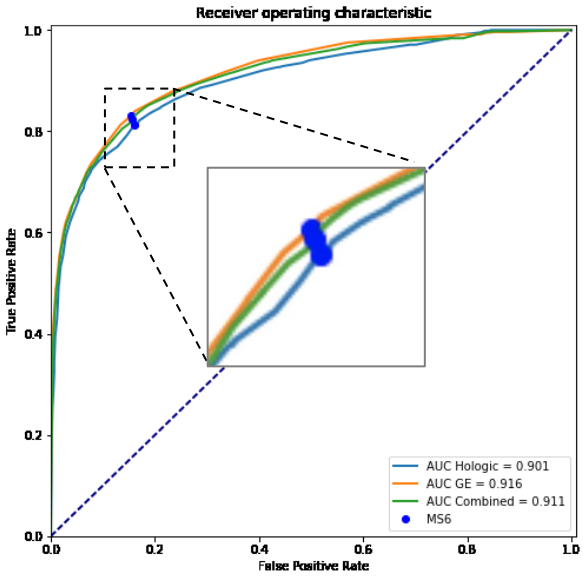


*Figure 7.4: ROC curves of MammoScreen-AI algorithm at **breast** level on US Hologic® FFDM (blue), GE® FFDM (orange), and on both types combined (green). Sensitivity and specificity at the chosen standalone regime (MS6) are shown with a blue dot for each case.*

### Finding level

Standalone performance of the MammoScreen-AI algorithm in detecting and characterizing positive findings (soft tissue lesions and calcifications) on FFDM acquired on Hologic® devices, and comparison with FFDM acquired on GE® devices, are given in the tables below.

Two characteristics are considered: The Free-Response ROC (FROC) and the Localized ROC (LROC).

FROC curve shows the sensitivity of finding detection and characterization as a function of the average number of false marks per image. It illustrates how performant an algorithm is at detecting and characterizing positive findings while keeping the number of false marks as low as possible. The drawback of FROC curves is that the x-axis has virtually no limit and that the curve area is not bound to unit square. Therefore, no simple unique measure (such as the AUC) may be derived from FROC curves to compare between several of such curves. However, it is still valuable information as it accounts for the average number of false marks per image.

LROC curves are generally used when only one positive finding per case shall be localized. It shows the sensitivity of correctly marking a positive case (a case is considered as correctly marked

if the algorithm placed a mark at a reasonable distance from the ground truth location – here in a 15mm radius from the ground truth) as a function of the false positive rate (a negative case is considered a false positive if the algorithm has placed one or more marks on it). LROC curve areas are bound to unit square, allowing to derive single measures to describe them such as AUC.

For MammoScreen, LROC curves at the breast level are used. This allows to measure how performant the algorithm is at marking the correct finding within a breast (in either of the 2 views of the breast) as a function of the false positive breast rate (i.e., rate of placing false marks in either of the 2 views of a negative breast).

In addition to FROC and LROC analysis, the performance of four detection Operating Points (OP) is reported. Those correspond to the three OP made corresponding to visualization levels made available to users via the MammoScreen user interface, using the Filtering slider (refer to section 5.3.1.1 Filtering of findings) and corresponding to MammoScreen scores 1, 3 and 5 respectively.

| MammoScreen Score | MS1 | MS3 | MS5 |
|---|---|---|---|
| Filtering slider position | Left (Lowest Suspicion shown) | Middle (Lowest Suspicion hidden) | Right (Low Suspicion hidden) |

| **Soft tissue lesions** | | | | | |
|---|---|---|---|---|---|
| | | **Hologic®** | **GE®** | **Combined** | **$FOM_{GE}$-$FOM_{HOL}$** |
| **LROC** | **AUC (primary)** | 0.837 (0.811, 0.861) | 0.900 (0.884, 0.916) | 0.877 (0.862, 0.890) | 0.064 (0.034, 0.095) |
| | **Sensitivity @ MS1** | 0.942 (0.921, 0.963) | 0.976 (0.964, 0.987) | 0.962 (0.951, 0.973) | 0.034 (0.010, 0.060) |
| | **Sensitivity @ MS3** | 0.926 (0.902, 0.949) | 0.966 (0.951, 0.978) | 0.950 (0.937, 0.963) | 0.039 (0.012, 0.067) |
| | **Sensitivity @ MS5** | 0.774 (0.735, 0.811) | 0.852 (0.824, 0.879) | 0.822 (0.799, 0.843) | 0.080 (0.032, 0.128) |
| | | | | | |
| | **Specificity @ MS1** | 0.109 (0.102, 0.116) | 0.166 (0.161, 0.172) | 0.150 (0.146, 0.155) | 0.058 (0.048, 0.067) |
| | **Specificity @ MS3** | 0.233 (0.222, 0.242) | 0.222 (0.216, 0.228) | 0.225 (0.219, 0.230) | -0.011 (-0.022, 0.002) |
| | **Specificity @ MS5** | 0.780 (0.771, 0.791) | 0.801 (0.795, 0.807) | 0.795 (0.790, 0.800) | 0.021 (0.010, 0.032) |
| | | | | | |
| **FROC** | **Sensitivity @ MS1** | 0.895 (0.872, 0.915) | 0.952 (0.940, 0.963) | 0.930 (0.918, 0.940) | 0.057 (0.033, 0.081) |
| | **Sensitivity @ MS3** | 0.878 (0.854, 0.901) | 0.943 (0.930, 0.955) | 0.918 (0.906, 0.929) | 0.064 (0.038, 0.090) |
| | **Sensitivity @ MS5** | 0.750 (0.718, 0.782) | 0.835 (0.814, 0.855) | 0.802 (0.784, 0.819) | 0.084 (0.047, 0.121) |
| | | | | | |
| | **Avg false marks @ MS1** | 1.819 (1.815, 1.824) | 1.268 (1.266, 1.270) | 1.424 (1.422, 1.426) | NA |
| | **Avg false marks @ MS3** | 1.182 (1.171, 1.193) | 1.026 (1.021, 1.031) | 1.070 (1.066, 1.075) | NA |
| | **Avg false marks @ MS5** | 0.294 (0.286, 0.302) | 0.218 (0.214, 0.222) | 0.239 (0.235, 0.243) | NA |

| Calcifications | | | | | |
|---|---|---|---|---|---|
| | | **Hologic®** | **GE®** | **Combined** | **FOMGE-FOMHOL** |
| **LROC** | **AUC (primary)** | 0.974 (0.959, 0.985) | 0.930 (0.912, 0.948) | 0.942 (0.928, 0.954) | -0.044 (-0.067, -0.021) |
| | **Sensitivity @ MS1** | 0.994 (0.979, 1.000) | 0.971 (0.953, 0.987) | 0.978 (0.964, 0.989) | -0.023 (-0.043, -0.001) |
| | **Sensitivity @ MS3** | 0.994 (0.979, 1.000) | 0.971 (0.953, 0.987) | 0.978 (0.964, 0.989) | -0.023 (-0.043, -0.001) |
| | **Sensitivity @ MS5** | 0.962 (0.930, 0.988) | 0.804 (0.764, 0.844) | 0.851 (0.820, 0.879) | -0.158 (-0.209, -0.108) |
| | | | | | |
| | **Specificity @ MS1** | 0.549 (0.537, 0.561) | 0.645 (0.638, 0.652) | 0.619 (0.613, 0.625) | 0.096 (0.083, 0.110) |
| | **Specificity @ MS3** | 0.584 (0.573, 0.597) | 0.658 (0.652, 0.665) | 0.638 (0.632, 0.644) | 0.074 (0.061, 0.088) |
| | **Specificity @ MS5** | 0.869 (0.861, 0.878) | 0.909 (0.905, 0.913) | 0.898 (0.894, 0.901) | 0.040 (0.031, 0.048) |
| | | | | | |
| **FROC** | **Sensitivity @ MS1** | 0.994 (0.984, 1.000) | 0.941 (0.923, 0.956) | 0.957 (0.944, 0.969) | -0.052 (-0.072, -0.033) |
| | **Sensitivity @ MS3** | 0.994 (0.984, 1.000) | 0.938 (0.920, 0.955) | 0.955 (0.941, 0.968) | -0.055 (-0.075, -0.036) |
| | **Sensitivity @ MS5** | 0.942 (0.916, 0.968) | 0.779 (0.747, 0.809) | 0.828 (0.805, 0.851) | -0.163 (-0.202, -0.124) |
| | | | | | |
| | **Avg false marks @ MS1** | 0.870 (0.867, 0.873) | 0.531 (0.529, 0.532) | 0.627 (0.625, 0.628) | NA |
| | **Avg false marks @ MS3** | 0.753 (0.748, 0.759) | 0.479 (0.477, 0.482) | 0.557 (0.554, 0.559) | NA |
| | **Avg false marks @ MS5** | 0.238 (0.232, 0.245) | 0.122 (0.119, 0.125) | 0.155 (0.152, 0.158) | NA |

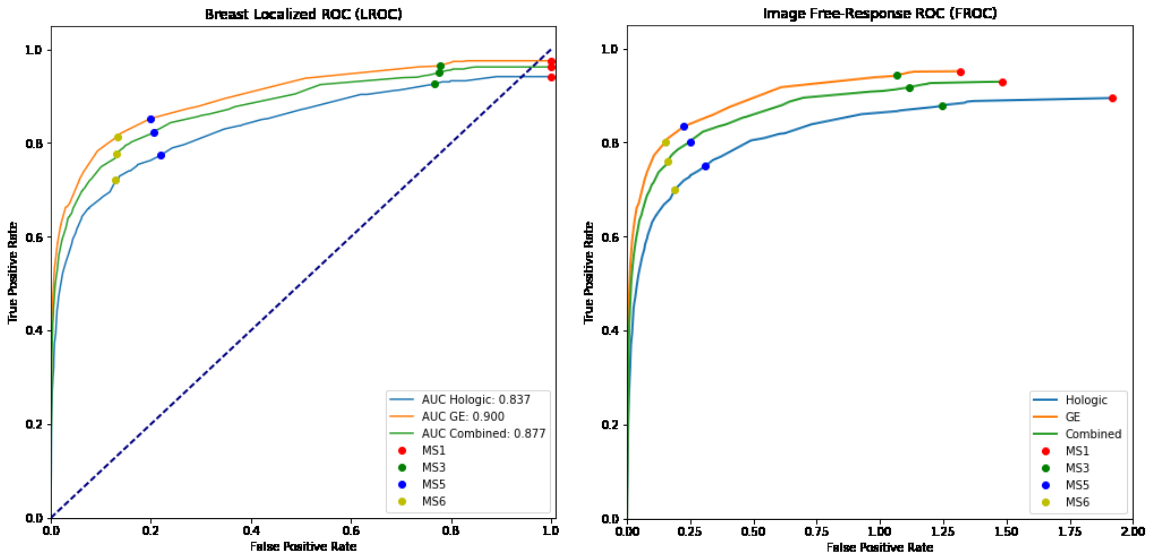


*Figure 7.5: LROC (left) and FROC (right) curves on US soft tissue lesions only.*

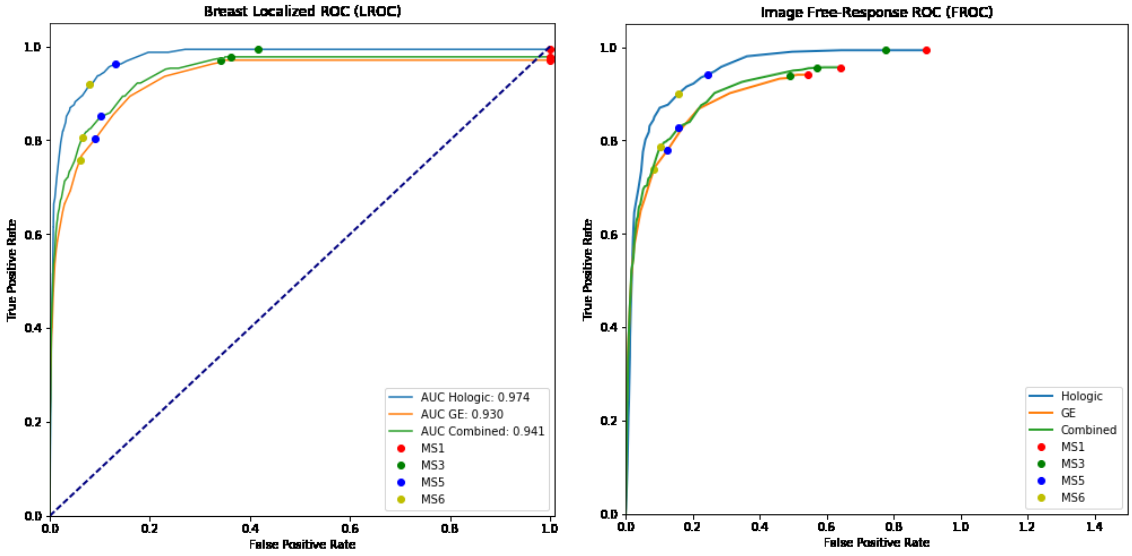


*Figure 7.6: LROC (left) and FROC (right) curves on US calcifications only.*

## Per-MammoScreen score analysis

*Mammogram level*

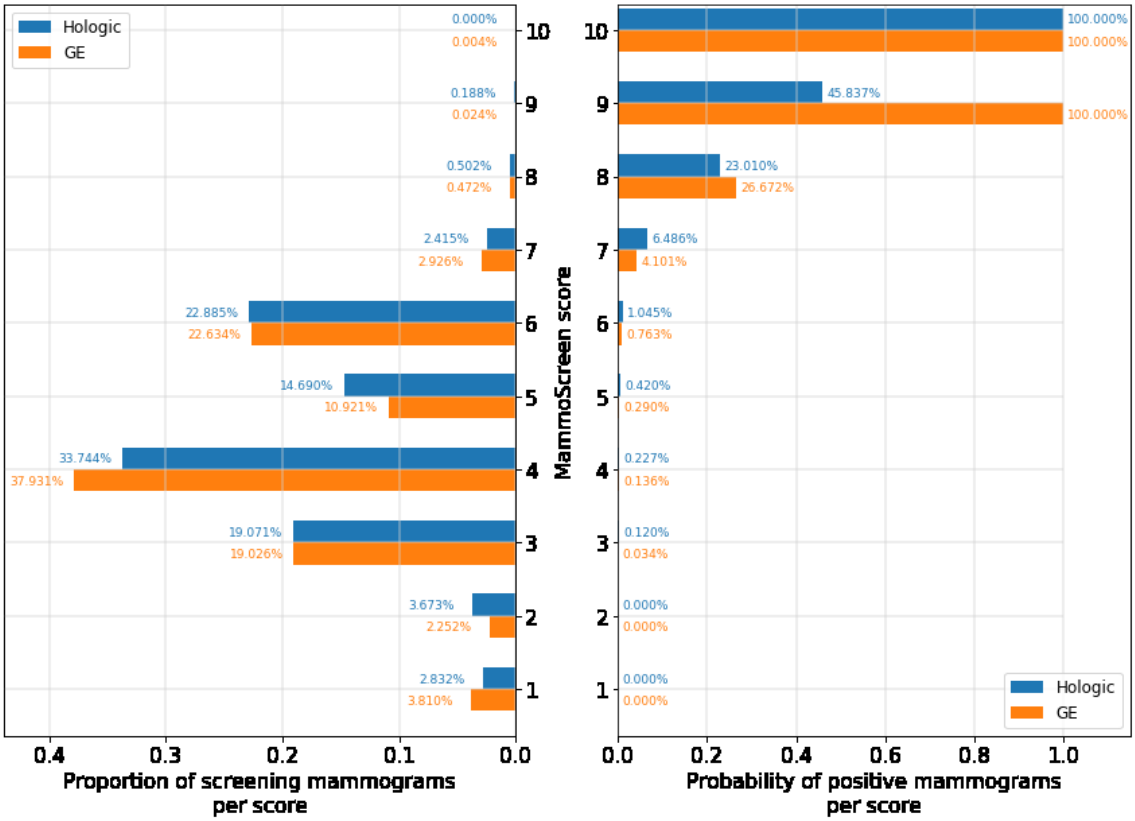


*Figure 7.8 : Repartition of screening FFDM per MammoScreen™ score at **mammogram** level.*
*Left: Repartition of screening FFDM per score for Hologic® and GE® manufacturers.*
*Right: Probability of discovering a positive FFDM per score.*

*Breast level*

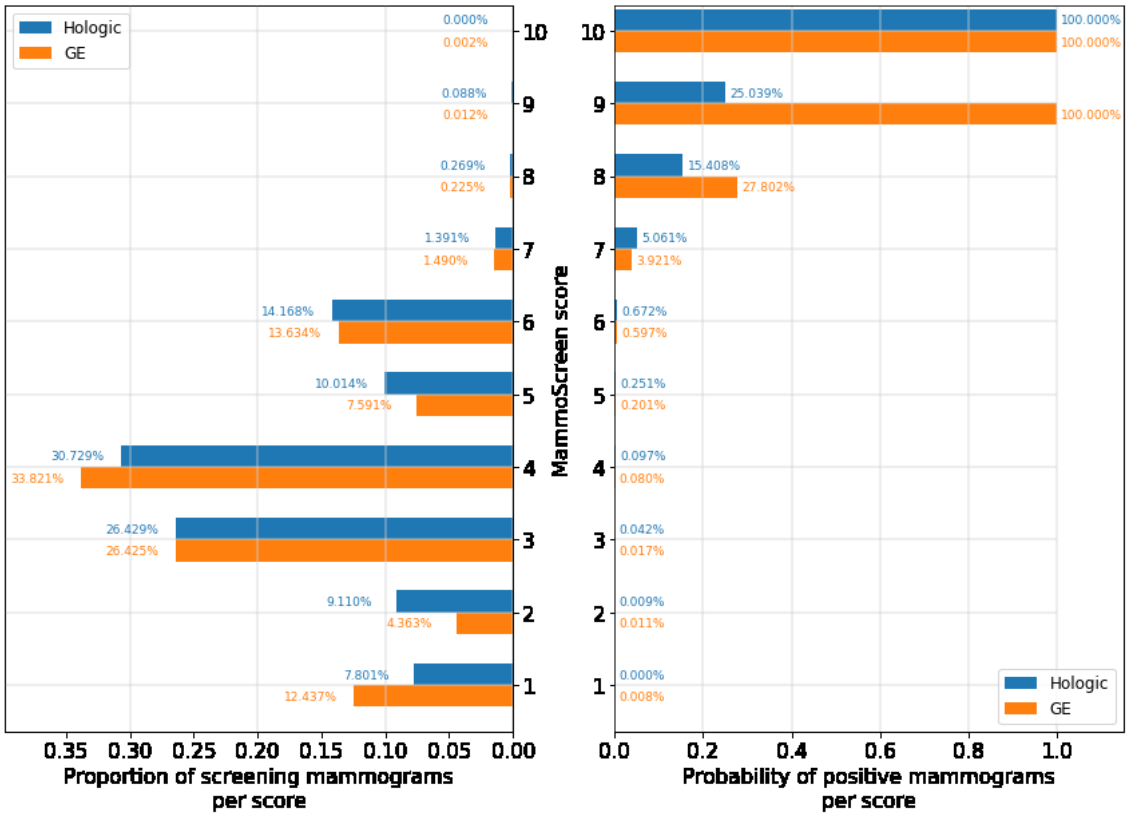


*Figure 7.9: Repartition of screening FFDM per MammoScreen™ score at **breast** level.*
*Left: Repartition of screening FFDM per score for Hologic® and GE® manufacturers.*
*Right: Probability of discovering a positive FFDM per score.*

*Table 7.2: NPV, specificity, NPV, sensitivity at **mammogram** level for each of the MammoScreen™ scores on a simulated screening distribution (95% confidence interval in brackets).*

## Hologic®

| FOM | MS1 | MS2 | MS3 | MS4 | MS5 | MS6 | MS7 | MS8 | MS9 | MS10 |
|---|---|---|---|---|---|---|---|---|---|---|
| **NPV** | 1.0000 (1.0000 - 1.0000) | 1.0000 (1.0000 - 1.0000) | 0.9991 (0.9987 - 0.9995) | 0.9984 (0.9977 - 0.9991) | 0.9979 (0.9970 - 0.9987) | 0.9956 (0.9946 - 0.9964) | 0.9939 (0.9927 - 0.9948) | 0.9928 (0.9916 - 0.9938) | 0.9922 (0.9911 - 0.9932) | 0.9922 (0.9911 - 0.9932) |
| **Specificity** | 0.0162 (0.0129 - 0.0196) | 0.0460 (0.0390 - 0.0533) | 0.2175 (0.2051 - 0.2309) | 0.5632 (0.5424 - 0.5805) | 0.7185 (0.7015 - 0.7332) | 0.9690 (0.9627 - 0.9739) | 0.9942 (0.9922 - 0.9968) | 0.9987 (0.9968 - 0.9998) | 1.0000 (1.0000 - 1.0000) | 1.0000 (1.0000 - 1.0000) |
| **PPV** | 0.0078 (0.0068 - 0.0089) | 0.0079 (0.0069 - 0.0091) | 0.0082 (0.0071 - 0.0094) | 0.0097 (0.0084 - 0.0111) | 0.0158 (0.0134 - 0.0180) | 0.0221 (0.0185 - 0.0250) | 0.1049 (0.0863 - 0.1267) | 0.2443 (0.1804 - 0.3734) | 0.3788 (0.1662 - 0.7885) | 1.0000 (1.0000 - 1.0000) |
| **Sensitivity** | 1.0000 (1.0000 - 1.0000) | 1.0000 (1.0000 - 1.0000) | 1.0000 (1.0000 - 1.0000) | 0.9764 (0.9617 - 0.9862) | 0.8882 (0.8397 - 0.9302) | 0.8073 (0.7331 - 0.8737) | 0.4584 (0.4040 - 0.5177) | 0.2294 (0.1956 - 0.2693) | 0.0844 (0.0643 - 0.1036) | 0.0000 (0.0000 - 0.0000) |

## GE®

| FOM | MS1 | MS2 | MS3 | MS4 | MS5 | MS6 | MS7 | MS8 | MS9 | MS10 |
|---|---|---|---|---|---|---|---|---|---|---|
| **NPV** | 1.0000 (1.0000 - 1.0000) | 1.0000 (1.0000 - 1.0000) | 0.9996 (0.9994 - 0.9997) | 0.9992 (0.9987 - 0.9994) | 0.9988 (0.9982 - 0.9991) | 0.9973 (0.9969 - 0.9978) | 0.9965 (0.9960 - 0.9969) | 0.9955 (0.9950 - 0.9960) | 0.9953 (0.9947 - 0.9958) | 0.9952 (0.9947 - 0.9958) |
| **Specificity** | 0.0409 (0.0372 - 0.0448) | 0.0610 (0.0558 - 0.0655) | 0.4238 (0.4108 - 0.4338) | 0.6339 (0.6232 - 0.6442) | 0.7741 (0.7659 - 0.7822) | 0.9808 (0.9786 - 0.9838) | 0.9973 (0.9962 - 0.9982) | 1.0000 (1.0000 - 1.0000) | 1.0000 (1.0000 - 1.0000) | 1.0000 (1.0000 - 1.0000) |
| **PPV** | 0.0048 (0.0042 - 0.0053) | 0.0050 (0.0044 - 0.0055) | 0.0051 (0.0045 - 0.0056) | 0.0079 (0.0070 - 0.0088) | 0.0115 (0.0103 - 0.0127) | 0.0166 (0.0148 - 0.0184) | 0.1015 (0.0861 - 0.1235) | 0.3154 (0.2385 - 0.4166) | 1.0000 (1.0000 - 1.0000) | 1.0000 (1.0000 - 1.0000) |
| **Sensitivity** | 1.0000 (1.0000 - 1.0000) | 1.0000 (1.0000 - 1.0000) | 1.0000 (1.0000 - 1.0000) | 0.9626 (0.9529 - 0.9731) | 0.8936 (0.8288 - 0.9233) | 0.7992 (0.7325 - 0.8514) | 0.4513 (0.4054 - 0.5004) | 0.2579 (0.2236 - 0.2983) | 0.0516 (0.0398 - 0.0635) | 0.0078 (0.0035 - 0.0130) |

**Clinical Testing**

This investigation was a retrospective multi reader multi case study meant to compare cancer detection performance of radiologists reading with the aid of MammoScreen to the reading results of the same cohort of radiologists without any decision support.

The main objective of this investigation was to determine whether the radiologist performance when using MammoScreen is superior to unaided radiologist performance for interpretation of 2D Full Field Digital Screening Mammograms.

To do this, 240 mammographic screening images acquired at a US center have been collected. For each exam, the cancer status has been verified by either biopsy results (for all cancer positive cases and some of the negative cases) or an adequate follow-up (for negative cases only) and used as gold standard. The images have been read by 14 radiologists with and without the aid of MammoScreen, the interpretation of the standalone MammoScreen has been recorded as well. Finally, the algorithm's interpretation, the radiologist interpretation using the help of the algorithm and the unaided radiologist interpretation of every mammogram have been compared to the "gold standard". Those pairwise comparisons, have been used to numerically compute the primary and secondary endpoints (AUC under the ROC curve, Sensitivity and Specificity) to compare radiologist performance when using the system and without using it and standalone algorithm performance.

The performance characteristics of radiologists taking part to the clinical investigation was improved when using MammoScreen support, with the average AUC going from 0.77 to 0.8 (difference = 0.028; P = 0.035) (Figure 7.10.1). The AUC was higher with the aid of MammoScreen for 11 of the 14 radiologists (Figure 7.10.2).

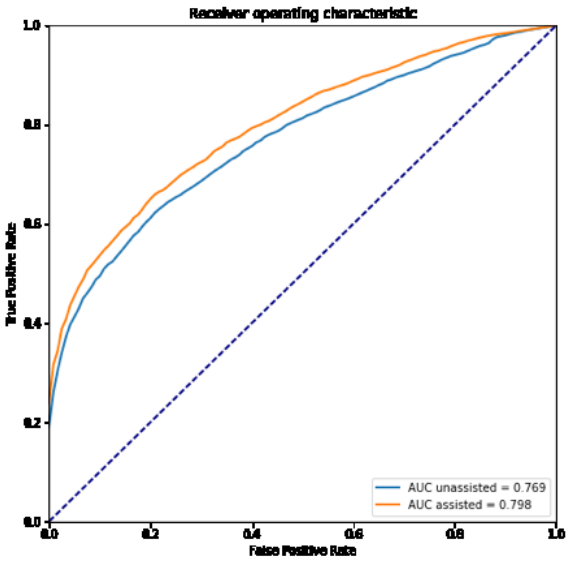


*Figure 7.10.1– Average ROC curves of all readers when unassisted (blue) and assisted (orange) with MammoScreen.*

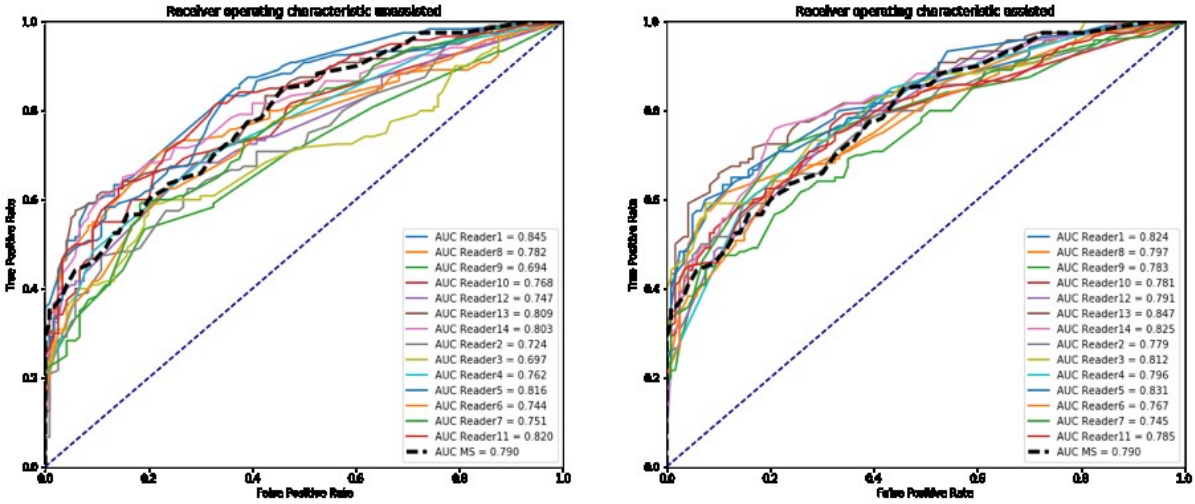


*Figure 7.10.2- Left: ROC curves of all readers when unassisted. Right: ROC curves of all readers when assisted with MammoScreen.*

Performances were also measured at breast and lesion level; the overall performance improvement was found to be statistically significant at both breast (in terms of AUC) and lesion (in terms of pAUC) level confirming the trend of the analysis at mammogram level (Figure 7.10.3).

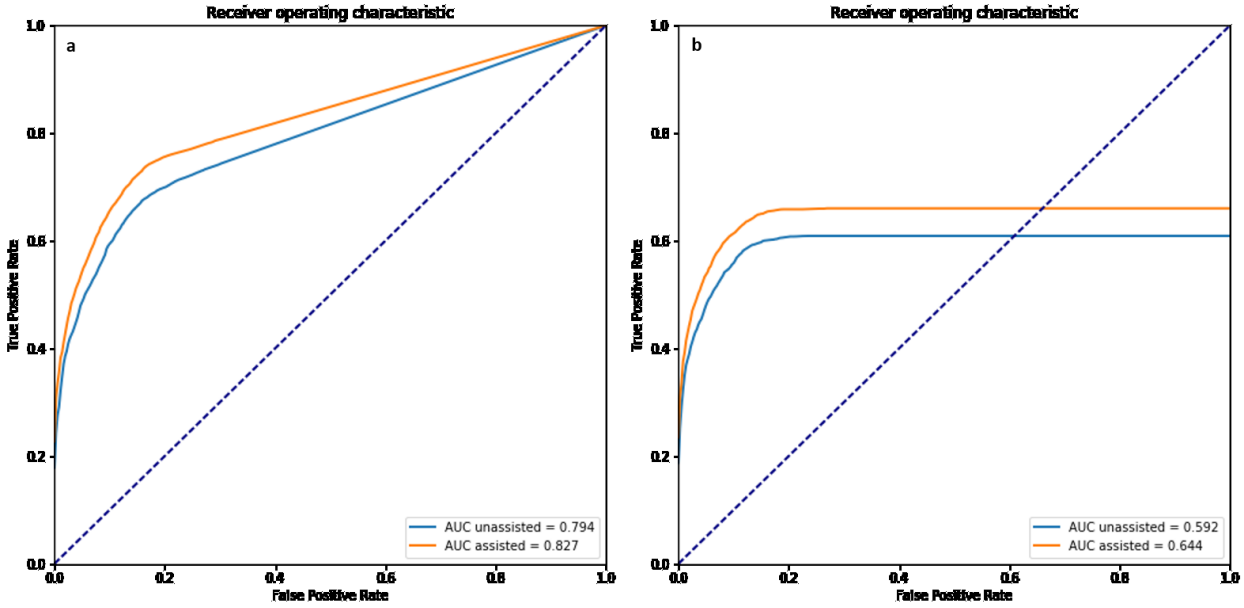


*Figure 7.10.3 – Average ROC curves of all readers when unassisted (blue) and assisted (orange) with MammoScreen at breast level (a) and lesion level (b).*

On average, reading time per case increased when using MammoScreen in both reading sessions. During the first session the average reading time was 60.82 seconds (95% confidence interval: 59.25 seconds, 62.39 seconds) for the unaided reading condition and 68.65 seconds (95% confidence interval: 66.92 seconds, 70.39 seconds) when using MammoScreen. For the second reading session the average time was lower with respect to the first session, 54.52 seconds (95% confidence interval: 52.97 seconds, 56.07 seconds) for the unaided reading condition and 59.61 seconds (95% confidence interval: 58.05 seconds, 61.17 seconds) when using MammoScreen. Differences in reading time with and without the use of MammoScreen changed as a function of the MammoScreen score ($P < 0.05$): for score equal or lower than 4 during the first reading session radiologists increased their reading time by 1% when using MammoScreen, while during the second reading session the use of MammoScreen made them decrease their reading time by 2%. For score higher than 4 in both reading sessions the use of MammoScreen increased the average reading time of about 14%, the maximum increase in reading time did not exceed 15s.

The standalone analysis of MammoScreen has shown that the algorithm exhibits performances comparable (non-inferior) to those of an experienced radiologist as confirmed by the absence of statistical effect ($p>0.05$) and by the lower confidence interval of the difference of AUC being equal or superior to the effect size (-0.03). Indeed, the performance of the standalone MammoScreen (AUC = 0.79) was found to be non-inferior to the average performance of unaided radiologists (AUC = 0.77) (Figure 7.10.4).

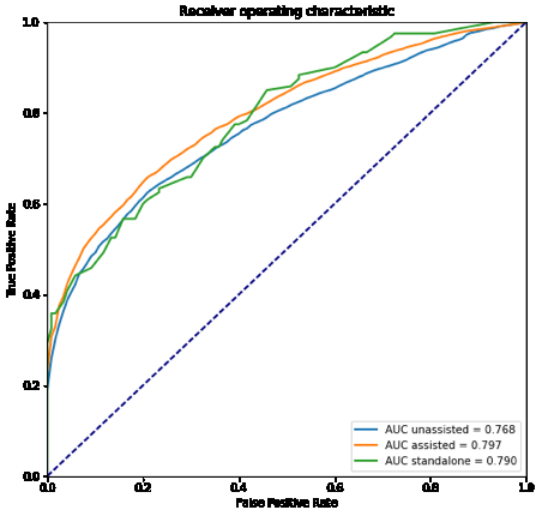


*Figure 7.10.4– Comparison of unassisted radiologists, assisted radiologists, and standalone MammoScreen ROC curve*

**Conclusions**

Non-clinical and clinical performance tests demonstrate that MammoScreen is safe and effective.

Results of the primary analysis of the clinical test demonstrate that use of MammoScreen improves detection of breast cancer in mammograms. Descriptively, improvement was observed to depend negligibly on lesion type and the total reading time was not observed to increase with the use of MammoScreen. In addition, the sensitivity of the readers tended to increase with the use of MammoScreen without decreasing specificity.

Radiologists improved their diagnostic performance in the detection of breast cancer with 2D FFDM (Full-Field Digital Mammography) by using MammoScreen. The overall conclusion of this clinical investigation is that the MammoScreen improves the diagnostic performance of radiologists in the detection of breast cancer without slowing down their average reading time. Finally, in standalone testing, MammoScreen breast cancer detection performance was observed to approach the average performance of the clinical study radiologists when reading mammograms unaided.

Based on the Intended Use, Indications for Use, product technical information, performance evaluation, and standards compliance provided in this premarket notification, MammoScreen has been shown to be substantially equivalent to the cited predicate device.