genius AI®
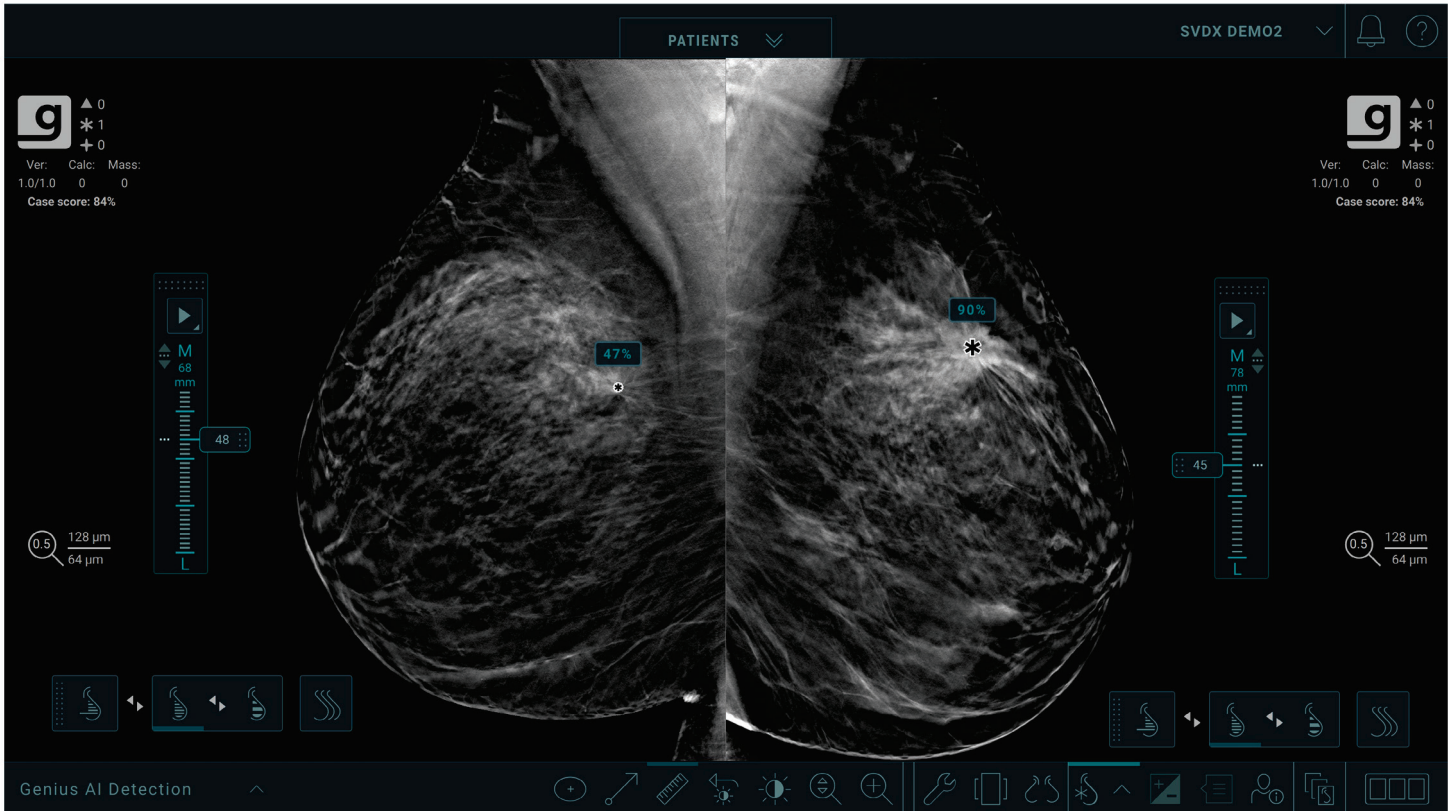## DETECTION

Genius AI Detection Software Physician User Guide
Version 1.0
MAN-10562-002 Revision 001

HOLOGIC®

Genius AI® Detection

Software

Physician User Guide

For Software Version 1.0

Part Number MAN-10562-002
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HOLOGIC®

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Chapter 1 Introduction

Genius AI® Detection software is a software module intended to identify suspicious breast lesions appearing as soft-tissue densities (masses, architectural distortions, and asymmetries) or calcification clusters in breast tomosynthesis images. Genius AI Detection software analyzes each slice of each view from a Hologic 3D Mammography™ exam to identify such lesions using deep learning neural networks. For each identified lesion, Genius AI Detection software produces the following CAD findings:

- Location of the lesion.
- Outline of the lesion.
- Confidence score of the lesion.

In addition, Genius AI Detection software produces a case score for the entire breast tomosynthesis exam representing the confidence that the exam contains a malignant lesion.

Genius AI Detection software stores all properties of these CAD findings into a DICOM Mammography CAD SR object for storage and display on DICOM-compliant review workstations and archive systems. An option to create a DICOM Secondary Capture Image object is available when the review workstations cannot interpret DICOM Mammography CAD SR objects.

The information in this manual is intended to serve as a reference for interpreting physicians and other clinicians who may need to understand how Genius AI Detection software can be integrated into their practices.

Note
The 3D Mammography™ exam is only available on the Hologic Selenia® Dimensions® and 3Dimensions™ systems.

1.1   Intended Use

R̲x Only   Caution: United States federal law restricts this device to sale by or on the order of a physician.

Genius AI Detection is a computer-aided detection and diagnosis (CADe/CADx) software device intended to be used with compatible digital breast tomosynthesis (DBT) systems to identify and mark regions of interest including soft tissue densities (masses, architectural distortions, and asymmetries) and calcifications in DBT exams from compatible DBT systems and provide confidence scores that offer assessment for Certainty of Findings and a Case Score. The device intends to aid in the interpretation of digital breast tomosynthesis exams in a concurrent fashion, where the interpreting physician confirms or dismisses the findings during the reading of the exam.

Intended user population

Intended users of Genius AI Detection are MQSA qualified interpreting physicians. For users of Hologic review workstations, training on image review tools related to Genius AI Detection is provided in the workstation User Guide. For other workstations, the user is expected to be trained based on materials provided by the workstation vendor.

Intended patient population

The device is intended to be used in the population of patients undergoing screening mammography.

1.1.1 Contraindications

There are no known contraindications for Genius AI Detection software. However, the diagnostic performance of Genius AI Detection software has not been evaluated for mammograms from patients with breast implants and partial views (for example, "mosaic" views).

1.2 Using This Manual

This manual is organized as follows:

- *Introduction* on page 1 provides an overview of Genius AI Detection software including features, benefits, and precautions for use.
- *Image Processing and Workflow* on page 9 explains how information flows through systems with Genius AI Detection software, the supported breast tomosynthesis views, and how to manage workflow.
- *Performance Validation* on page 21 describes how the Genius AI Detection algorithm analyzes tomosynthesis images.

This manual uses the following conventions to provide technical and safety information of special interest.

⚠ **WARNING!**
An instruction that, if not followed, can result in a hazardous condition.

⚠ **Caution:**
An instruction that, if not followed, can result in damage to the system.

✔ **Important**
An instruction provided to ensure correct results and optimal performance, or to clarify limitations of the device.

✔ **Note**
Information provided to clarify a particular step or procedure.

1.3   Resources Available

In addition to this User Guide, the following resources are available to assist you.

- **Training:** Training is available for interpreting physicians using Hologic review workstations. Contact your Hologic representative for more information.
- **Website:** The Hologic website (*www.hologic.com*) provides access to electronic versions of User Guides. For printed copies, contact your Hologic representative.
- **Technical Support and Service:** For contact information, see the copyright page of this guide.

1.4   Warnings and Precautions

Note

For Warnings and Precautions related to the installation, operation, and maintenance of the Selenia Dimensions and 3Dimensions breast tomosynthesis systems, refer to the respective Selenia Dimensions or 3Dimensions system *User Guide*.

Important

Before reviewing images processed with Genius AI Detection software, observe the following instructions that are provided to ensure correct results and optimal performance, or to clarify limitations of the algorithm.

- The interpreting physician should base interpretation only on diagnostic-quality images and should not solely depend on Genius AI Detection marks for determining clinical disposition.
- Genius AI Detection software is an aid to be used by interpreting physicians concurrently while interpreting Hologic 3D Mammography™ image sets.
- Genius AI Detection software does not enhance what the user sees; rather, it helps to identify regions on 3D™ mammograms that should be examined.
- Workstations that implement the Hologic recommended schema to overlay marks generated by Genius AI Detection software will use consistent overlay symbols for different types of marks. Typically, calcification findings identified by Genius AI Detection software are marked with triangles (Calc marks) and soft tissue findings are marked with asterisks (Mass marks). If mass and calcification findings occur at the same location on the image, then the workstation identifies the findings with marks shaped like the four points of a compass (Malc™ marks). These findings may or may not represent cancer, and the skill of the user is still required for proper interpretation of the marked areas.
- Workstations that offer variable-size marks (EmphaSize™ marks) will display marks where the size of a Calc, Mass, or Malc mark is proportional to the confidence score (Certainty of Finding) for each mark. The marked findings may or may not represent cancer, and the skill of the user is still required for proper interpretation of areas marked by the device.

Important

Genius AI Detection software has not been evaluated and may not operate at expected performance level for patients with the following:

- Abnormality with symptomatic and palpable lesions
- Breast implants.
- Pacemakers in the mammography field of view
- Skin markers
- Motion during imaging
- Cut-off anatomy
- Prior surgery and/or presence of biopsy clips visible in imaging
- Studies with missing standard views or report exclusions

Important

The safety and effectiveness of the system has not been established in patients with biopsy proven malignant primary breast cancers that were not visible mammographically on 2D or DBT images but were detected based on ultrasound or MRI findings.

Important

The safety and effectiveness of the system has not been established in patients with mammographically visible malignant lymph nodes but no mammographically visible primary breast cancer.

Important

The safety and effectiveness of the system has not been established in images with evidence of previous surgery (for example, surgical clips or breast reduction).

Important

Certainty of Finding and Case Scores are not intended to be the clinically used "probability of malignancy". Certainty of Finding and Case Scores are not calibrated to the prevalence in the intended use population, and consequently, the Certainty of Finding and Case Scores are in general higher than the actual probability of malignancy in an intended use population with less than 50% prevalence of cancer. These scores represent a relative level of concern or level of suspicion because they do not represent an absolute clinical probability of malignancy.

Important

The interpreting physician must still use diagnostic skills and any necessary additional workup to differentiate benign from malignant lesions. Therefore, the physician's workup decision should not be altered if the system fails to detect an area that the physician has detected and has decided requires further workup. Nor should the decision be affected if the system detects an area that the physician decides is not suspicious enough to warrant further workup.

> **Important**
>
> Only images from a supported digital breast tomosynthesis system as defined in *Digital Breast Tomosynthesis Systems* on page 9 of this manual should be used with Genius AI Detection software.

> **Important**
>
> The product will detect false positives and may increase the false-positive rates as determined by the interpreting physician for both screening and diagnostic mammography. Increased false positives may lead to unnecessary additional imaging radiation exposure, biopsy, patient anxiety, etc.

> **Important**
>
> - For routine interpretation of 3D™ mammograms with Genius AI Detection software, Hologic recommends use of a mammography workstation that has been FDA approved, recently calibrated, and employs Hologic CAD marking schema.
> - Genius AI Detection software does not identify all areas that are suspicious for cancer.
> - The device may not mark all cancerous lesions. A user should not be dissuaded from working up an actionable finding if the device fails to mark that site.
> - The device is not currently designed to follow changes from prior mammograms.
> - The device is not designed to detect skin thickening, nipple retractions, asymmetric breast tissue, or tubular density/solitary dilated duct.
> - Individual practice patterns may influence results obtained when using Genius AI Detection software. Therefore, each facility and interpreting physician should carefully monitor the results that the device has on their practice of mammography to optimize its effectiveness.

> **Important**
>
> Genius AI Detection software uses raw tomosynthesis projections as input. Future reprocessing of a case is not possible unless the site stores raw projections. Alternatively, if a site would like to access the CAD results at a later time, the CAD output needs to be stored in PACS as DICOM Mammography CAD SR or DICOM Secondary Capture Image.

> **Note**
>
> Genius AI Detection software does not process images that include the following DICOM view modifiers (with Systematized Nomenclature of Medicine (SNOMED) RT codes):
>
> - Cleavage (R-102D2)
> - Spot Compression (R-102D7)

> **Note**
>
> The diagnostic performance of Genius AI Detection software has not been characterized for mammograms from patients with:
>
> - Breast implants
> - Partial views (for example, "mosaic" views)

1.5   Overview of Genius AI Detection Software

Genius AI Detection is a tool to help identify visually perceptible and potentially cancerous regions of interest. These regions of interest can include clusters of calcifications and soft tissue lesions such as masses, architectural distortions, and asymmetries in digital tomosynthesis images. The marked areas are presented as overlays on images concurrently as a interpreting physician assesses the images on a review workstation for determining clinical disposition. The overlays can be toggled on or off using the review workstation display tools.

Genius AI Detection software utilizes Artificial Intelligence (AI), specifically complex neural networks. It employs the cutting edge technology of "Deep Learning" that has revolutionized the field of Artificial Intelligence over the last decade. Deep Learning is a sub-specialty of Machine Learning that utilizes the advanced computational power offered by GPUs (Graphical Processing Units) to train very complex statistical models containing hundreds of layers of parameters hence the description as "deep learning".

1.6   Benefits of Genius AI Detection Software

Tomosynthesis is becoming a more accessible modality, replacing conventional mammography due to its ability to enhance rate of cancer detection and reduce false recalls. As a result, instead of dealing with four standard images captured in conventional mammography, the interpreting physician needs to scroll through hundreds of tomosynthesis reconstructed slices. The interpreting physician also must balance the need for accurate detection of cancer with limiting the number of unnecessary call-backs. The combination of viewing a large number of slices per study, interpreting physician fatigue, the complex image of the breast structure, and the subtle nature of certain observable characteristics of the disease can result in false-negative readings, especially in dense breasts.

Genius AI Detection software functions like an additional pair of eyes on tomosynthesis images that can be used concurrently during the image review. Genius AI Detection software is designed to assist interpreting physicians while they review tomosynthesis slices by overlaying marks on top of potential abnormalities on the tomosynthesis slices. The concurrent use of Genius AI Detection software for interpretation of tomosynthesis images has proven to enhance diagnostic accuracy of interpreting physicians as described in *Performance Validation* on page 21.

Depending on capabilities of review workstation, results of Genius AI Detection software including marks representing potential lesions can be displayed automatically as part of a configured hanging protocol or enabled at any time based on toolbar button. The interpreting physician is responsible for reviewing the findings in combination with image review and confirming or dismissing the findings as part of the final interpretation.

1.7   Warranty Statement

Except as otherwise expressly stated in the Agreement: i) Equipment manufactured by Hologic is warranted to the original Customer to perform substantially in accordance with published product specifications for one (1) year starting from the date of shipment, or if Installation is required, from the date of Installation ("Warranty Period"); ii) digital imaging mammography x-ray tubes are warranted for twenty-four (24) months, during which the x-ray tubes are fully warranted for the first twelve (12) months and are warranted on a straight-line prorated basis during months 13-24; iii) replacement parts and remanufactured items are warranted for the remainder of the Warranty Period or ninety (90) days from shipment, whichever is longer; iv) consumable Supplies are warranted to conform to published specifications for a period ending on the expiration date shown on their respective packages; v) licensed Software is warranted to operate in accordance with published specifications; vi) Services are warranted to be supplied in a workman-like manner; vii) non-Hologic Manufactured Equipment is warranted through its manufacturer and such manufacturer's warranties shall extend to Hologic's customers, to the extent permitted by the manufacturer of such non-Hologic Manufactured Equipment. Hologic does not warrant that use of Products will be uninterrupted or error-free, or that Products will operate with non-Hologic authorized third-party products. These warranties do not apply to any item that is: (a) repaired, moved, or altered other than by Hologic authorized service personnel; (b) subjected to physical (including thermal or electrical) abuse, stress, or misuse; (c) stored, maintained, or operated in any manner inconsistent with applicable Hologic specifications or instructions, including Customer's refusal to allow Hologic recommended Software upgrades; or (d) designated as supplied subject to a non-Hologic warranty or on a pre-release or "as-is" basis.

Chapter 2 Image Processing and Workflow

This chapter explains how information flows through systems with Genius AI Detection software, supported tomosynthesis views, and how to manage workflow.

2.1 Digital Breast Tomosynthesis Systems

Genius AI Detection software is only able to process raw projections from the following 3D Mammography™ systems:

- Hologic Selenia Dimensions system supporting either standard resolution or high resolution tomosynthesis acquisition modes.
- Hologic 3Dimensions system supporting either standard resolution or high resolution tomosynthesis acquisition modes.

Genius AI Detection software does not process 6-mm SmartSlices from 3DQuorum® volumes. Instead, after Genius AI Detection software processes the corresponding 1-mm tomosynthesis volume, the Acquisition Workstation converts the 1-mm tomosynthesis slice references of each detected lesion to 6-mm SmartSlice references. The conversion is a simple mapping exercise from the 1-mm tomosynthesis volume to the 3DQuorum volume.

As the 6-mm SmartSlices are generated following a known and normal pattern of combining six 1-mm slices into one 6-mm SmartSlice while advancing 3 mm at a time maintaining a 3-mm overlap, remapping of the CAD findings from one 3D volume to the next becomes a counting exercise. For example, the Acquisition Workstation determines that a calcification cluster identified at slice #22 within the 1-mm 3D volume corresponds to SmartSlice #8 of the 3DQuorum volume.

The Acquisition Workstation creates up to four different DICOM Mammography CAD SR objects, one referencing the 1-mm tomosynthesis volume, one referencing the 6-mm SmartSlices, one referencing the corresponding synthesized 2D images of a TomoHD or ComboHD procedure, and one referencing the corresponding conventional 2D images of a Combo or ComboHD procedure. Downstream review workstations associate the corresponding CAD SR object with the types of images available for display on the review workstation (that is, l-mm tomosynthesis slices, 6-mm SmartSlices, synthesized 2D images, or conventional 2D images). Thus, the single set of CAD findings resulting from Genius AI Detection software can be applied equally to both created 3D volumes and the corresponding synthesized 2D or conventional 2D images.

Important
Genius AI Detection software does not support processing of digital breast tomosynthesis images from non-Hologic digital breast tomosynthesis systems.

Important
Genius AI Detection software uses raw tomosynthesis projections as input. Future reprocessing of a case is not possible unless the site stores raw projections. Alternatively, if a site would like to access the CAD results at a later time, the CAD output needs to be stored in PACS as DICOM Mammography CAD SR or DICOM Secondary Capture Image.

2.2 Image Types and AI Output Formats

This section describes the different types of images involved in processing or display with Genius AI Detection software. A typical screening exam acquired with Hologic Selenia Dimensions and 3Dimensions systems produces the following types of images for a tomosynthesis imaging protocol:

- Raw Projection images, which are a set of unprocessed individual projection images of the breast acquired at multiple angles and used to reconstruct the 3D tomosynthesis volume for review

- Processed Projection images, which are a set of individual projection images of the breast acquired at multiple angles processed for display on compatible review workstations

- Tomosynthesis Reconstructed Slices, which are reconstructed slices of the breast with focal planes at 1 mm intervals and are used as primary diagnostic images. Tomosynthesis Reconstructed Slices come in standard resolution and high resolution (otherwise known as Hologic Clarity HD® images).

- 3DQuorum image sets and SmartSlices, the first being synthesized slabbed volumes of the breast with SmartSlices being individual slices of the breast with a thickness of 6 mm and an overlap of 3 mm used as primary diagnostic images in place of 1-mm Tomosynthesis Reconstructed Slices

- C-View™ and Intelligent 2D™ images, the first being the synthesized 2D image from standard resolution Tomosynthesis Reconstructed Slices and the latter being the synthesized 2D image from high resolution Tomosynthesis Reconstructed Slices. C-View and Intelligent 2D images are used in conjunction with Tomosynthesis Reconstructed Slices or 3DQuorum volumes.

- Conventional 2D images that are acquired in combination with tomosynthesis projection images under the same breast compression, that are used in conjunction with Tomosynthesis Reconstructed Slices, 3DQuorum volumes, or synthesized 2D images.

Genius AI Detection software uses Raw Projection images as input, processes the corresponding Tomosynthesis Reconstructed Slices, and outputs CAD information. The CAD information is packaged into a DICOM Mammography CAD SR object for distribution and display on DICOM compliant review workstations. An option to create a DICOM Secondary Capture Image object is also available when review workstations cannot interpret DICOM Mammography CAD SR objects.

Both 6-mm SmartSlices and synthesized 2D images are generated from combining the same 1-mm tomosynthesis volume into either thicker slices or a single slice. The nature of the recombination is such that all x-y pixel spatial relationships are maintained between the original 1-mm tomosynthesis slices and the resulting 6-mm SmartSlices or synthesized 2D image. Thus, x-y locations of either 6-mm SmartSlices or synthesized 2D images coincide exactly to the x-y locations within each tomosynthesis slice.

In addition, the 6-mm SmartSlices are generated following a regular pattern of combining six 1-mm slices into one 6-mm SmartSlice while advancing 3 mm at a time maintaining a 3 mm overlap. As a result, the z location of a 1-mm tomosynthesis volume is accurately predicted to a z' location within the 3DQuorum volume. Remapping of the z coordinate from one 3D volume to the next becomes a simple counting exercise. For example, a calcification cluster identified at slice #22 within the 1-mm 3D volume corresponds to SmartSlice #8 of the 3DQuorum volume, as predicted by the regularity of the pattern used to generate the continuum of SmartSlices within the 3DQuorum volume.

Conventional 2D images that are acquired under the same compression as Hologic Clarity HD tomosynthesis projection images have the same x-y spatial relationships and pixel matrices. Thus, x-y locations of the conventional 2D images coincide exactly to the x-y locations within each tomosynthesis slice. Conventional 2D images that are acquired under the same compression as standard resolution tomosynthesis projection images have the same x-y spatial relationships but a different pixel matrix. Remapping the x and y coordinates of the findings from the 1-mm tomosynthesis volume to the conventional 2D image uses a mathematical ratio of the pixel matrices.

2.3   Image Processing Sequence

1. When the technologist accepts an eligible tomosynthesis view on the Acquisition Workstation, Genius AI Detection software processes the view and passes the CAD information to the Acquisition Workstation.

2. When the technologist closes a procedure as "completed" on the Acquisition Workstation, the Acquisition Workstation provides the CAD information for all processed views and identification of the views selected for case processing to Genius AI Detection software. Genius AI Detection software then performs case processing and passes the CAD information for each view and the tomosynthesis exam to the Acquisition Workstation.

3. The Acquisition Workstation packages the received CAD information into a DICOM Mammography CAD SR object including CAD marks, lesion outlines, location of individual calcifications, lesion scores, and case score. In the case of a DICOM Secondary Capture Image object, the Acquisition Workstation creates a mosaic of synthesized 2D images or conventional 2D images with overlaid CAD marks, lesion scores, and case score.

4. After all processing is complete, the DICOM CAD SR and/or CAD SC objects are sent to review workstations along with the processed tomosynthesis images.

5. For each 3D Mammography™ exam, a review workstation may overlay the Genius AI Detection CAD information on any or all of the following images as applicable:
    a) digital tomosynthesis reconstructed slices; b) 3DQuorum SmartSlices,
    c) synthesized 2D images, and d) conventional 2D images.

    At the review workstation, the interpreting physician has the option to utilize the Genius AI Detection CAD information concurrently with image review. The CAD information may be toggled on or off as desired.

Note

The display of Genius AI Detection information depends on the capabilities of the review workstation to interpret the information. Some review workstations may only display a subset of Genius AI Detection information, depending on their implementation.

2.4   Supported Views

Genius AI Detection software analyzes standard screening tomosynthesis views.

Table 1: Supported DICOM Views

Supported DICOM Views and View Modifiers		ACR MQCM 1999* View Label
Screening Views	Cranio-Caudal	CC
	Medio-Lateral Oblique	MLO

2.5   Image and Case Processing

Genius AI Detection software processes individual images (called "Image Processing") in a study and then also processes information from images that have been grouped by study for a single patient (called "Case Processing"). There is no specified limit to the number of images that can be included in a study or case. However, for many patients, a study consists of the four screening views:

- LCC – Left Cranio-Caudal
- LMLO – Left Medio-Lateral Oblique
- RCC – Right Cranio-Caudal
- RMLO – Right Medio-Lateral Oblique

2.5.1   Image Processing

During Image Processing, Genius AI Detection software analyzes each received tomosynthesis view, if the view is supported by the device as prescribed in *Supported Views* on page 12. The device searches for regions of interest such as calcification clusters and soft-tissue densities (masses, architectural distortions and asymmetries), which are suspect of malignancy. The device then characterizes each finding to assign a confidence score called "Certainty of Finding" to each region of interest identified in each view. The algorithm determines and saves the location information and certainty of finding to each suspected lesion identified in each view.

2.5.2   Case Processing

When a study includes two or more views, the Acquisition Workstation selects up to four eligible views and provides to Genius AI Detection software all the information that was derived from Image Processing as input to a process known as Case Processing. Case Processing analyzes the location and confidence information of each finding and assigns a case score to each study.

2.5.3   Image Selection for Case Processing

Genius AI Detection software uses the following criteria to determine which images Case Processing will use for its analysis:

- If a study includes one image for each of the four standard screening views (typical), Case Processing processes all four standard views.
- If a study includes multiple images of the same view and laterality (for example, two RCC views), the image that the Acquisition Workstation selects for Case Processing can be configured as a user selected view, the newest of the duplicate views, or the oldest of the duplicate views.

2.6 Managing Workflow

There are no special considerations to the order in which views were acquired when a study consists solely of the four screening views (LCC, RCC, LMLO, and RMLO). For studies that include just the four screening views, the acquisition time does not play any role in processing or results.

2.6.1 Multiple Instances of the Same View

Whenever a study includes multiple instances of the same view and laterality (for example, two RCC views), Genius AI Detection software results may be minimally affected by view the Acquisition Workstation selects for Case Processing. The Acquisition Workstation can be configured to select which image to use for case processing in the following ways:

- Always use the view with the newest time stamp.
- Always use the view with the oldest time stamp.
- Allow the technologist to select the view to use for Case Processing.

2.6.2 Images with Partial Views

Some studies require segmented breast views; that is, multiple images of the same view and laterality. In such cases, if the views cannot be ordered consistently so that the view with the most clinical significance is taken either first or last in the sequence, it is advised to configure user selection of the views to identify for Case Processing. For example, if the study requires three RCC views, if the most glandular region of the breast can be imaged first or last consistently, the Acquisiion Workstation configuration to select either the first or last view will automatically identify the view with the most glandular tissue for optimized Case Processing. This will ensure that the views with the most clinical significance will be included for Case Processing.

2.7 Certainty of Finding and Case Score

The Image Processing function assigns a relative score to each detected lesion. The relative score represents the confidence of Image Processing that a suspicious lesion is malignant.

Relative scores are normalized to a Certainty of Finding. The normalization process used a data set of consecutively collected biopsy malignant lesions. Relative scores from those lesions were ranked in an ascending order. A lookup table was then created, which mapped the relative score of each lesion to the percent of lesions that had a lower relative score within the data set. That percent becomes the Certainty of Finding. Thus, a lesion with a Certainty of Finding of 80%, for example, means that the deep learning network assigned a relative score to that lesion that was higher than 80% of similar lesions, hence very suspicious for malignancy. A lesion with a Certainty of Finding of 20% means that it ranked within the 20th percentile of the representative data set, hence less suspicious for malignancy. The Certainty of Finding is available for display next to each suspicious lesion during image review.

Case Processing function assigns a relative score to the entire 3D Mammography™ exam, which represents the confidence of Case Processing that the tomosynthesis exam contains a malignant lesion.

Case Processing normalizes its relative score to a Case Score using a data set of consecutively collected biopsy malignant cases, similar to the way Certainty of Finding is normalized. As a result, a 3D Mammography™ exam with a Case Score of 80% means that the exam ranks within the 80th percentile compared to other exams with a confirmed malignant lesion. As the Case Score is a normalization of the relative score that the case overall, and not a specific suspicious lesion, is malignant, the Case Score does not have a direct relationship to the Certainty of Finding of any suspicious lesion in the tomosynthesis exam. A Case Score of 0% is assigned to exams with zero findings.

Both Certainty of Finding and Case Score are provided to the interpreting physician to aid them in evaluating if a suspicious finding requires follow-up. Neither score represents an absolute probability of malignancy; they simply prompt the interpreting physician to a level of suspicion compared to malignant lesions or cases.

2.8 Genius AI Detection Software Mark Display on Hologic Diagnostic Review Workstations

The display of Genius AI Detection marks on a review workstation depends on the implementation details followed by each workstation vendor. The contents of the DICOM Mammography CAD SR can be rendered in different ways in order to generate an overlay to indicate regions of interest identified by Genius AI Detection software. This section illustrates some schema of markings that Hologic recommends and are implemented on Hologic review workstations.

It is important to note that the Genius AI Detection marks can be overlaid on tomosynthesis reconstructed slices, 3DQuorum SmartSlices, synthesized 2D images (C-View or Intelligent 2D images), and co-registered conventional 2D images, as applicable.

2.8.1 RightOn Marks

Workstations using Hologic proposed schema provide three types of Genius AI Detection marks, known as RightOn™ marks. Each mark indicates the centroid of a region of interest for the interpreting physician to review. RightOn marks include two basic types of marks plus a composite mark:

Mass – Identifies regions suggestive of densities (masses, architectural distortions, and asymmetries)

Calc – Identifies regions suggestive of calcifications

Malc – Composite mark that indicates Calc and Mass marks occurring in the same location on the image

The following figures show typical examples of the regions flagged by each type of RightOn Mark. Each set also shows the region with and without the RightOn overlay.
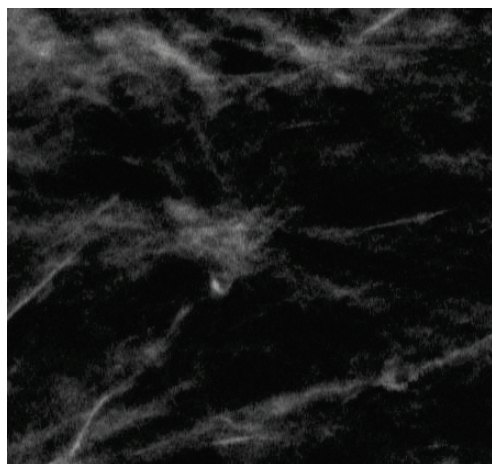
Figure 1: Region without RightOn Mass Mark
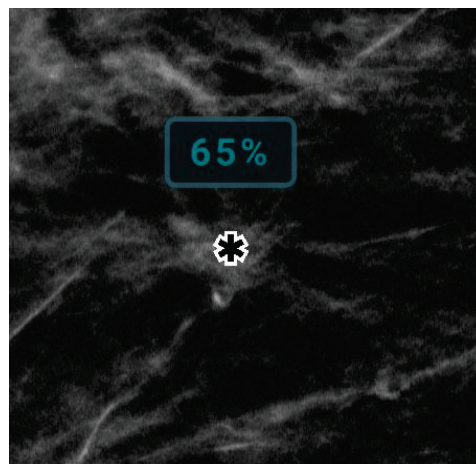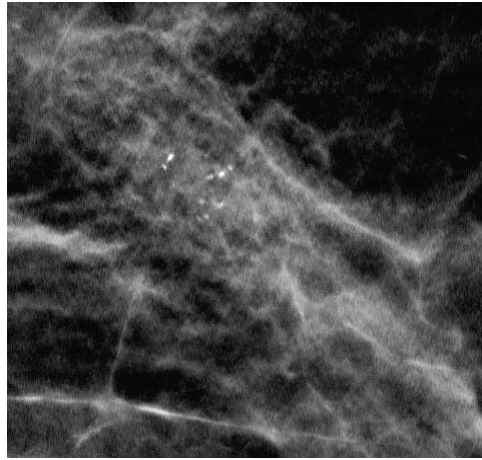

Figure 2: Region with RightOn Mass Mark

Figure 3: Region without RightOn Calcification Mark
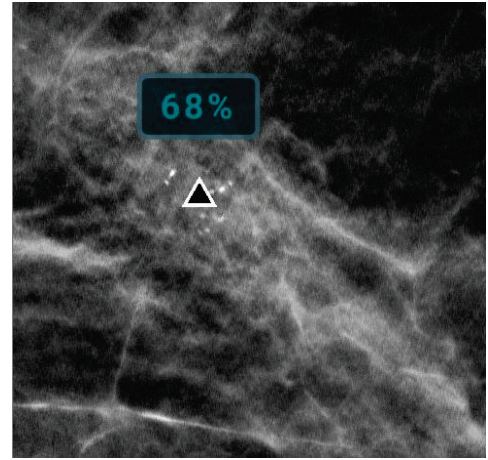

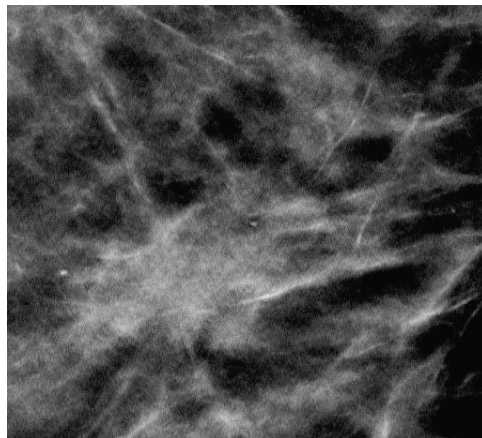*Figure 4: Region with RightOn Calcification Mark*

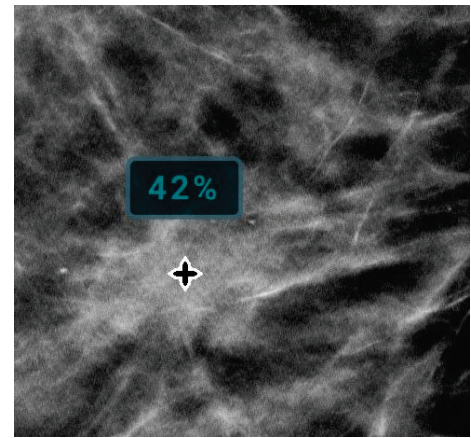*Figure 5: Region without RightOn Malc Mark*

Figure 6: Region with RightOn Malc Mark

Note

Not all mammography workstations can display Malc marks. Consult with your workstation vendor concerning availability and integration of Genius AI Detection software features with your workstation.

2.8.2　EmphaSize Marks

EmphaSize™ marks is an optional feature that provides variable-size Genius AI Detection marks that scale according to the Certainty of Finding. When Genius AI Detection software considers a region to be more significant, certain review workstations can be configured to increase the size of the corresponding Genius AI Detection mark. The size of the mark does not correlate to the size of the lesion but to the Certainty of Finding of the corresponding lesion.

Normally the review workstation displays all Genius AI Detection marks at the same size, regardless of ranking. If your site has enabled the EmphaSize feature and configured the review workstation to use it, the workstation can adjust the size of each mark according to its ranking. The EmphaSize feature can be disabled if you do not want to use it.
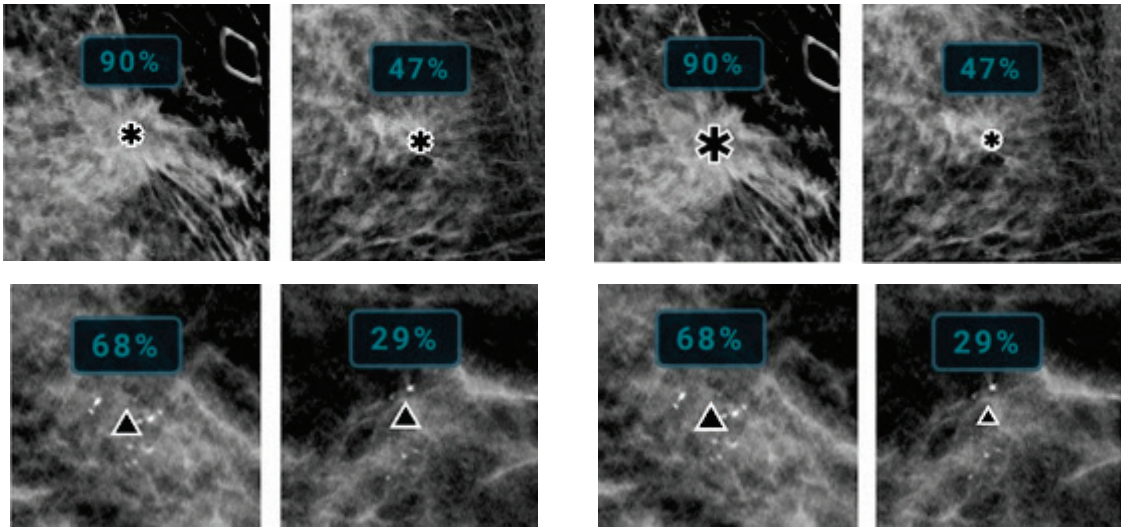
Figure 7: Regions Showing Marks with the EmphaSize Feature Disabled

Figure 8: Regions Showing Marks with the EmphaSize Feature Enabled

Note

Not all mammography workstations can display EmphaSize marks. Consult your workstation vendor concerning availability and integration of Genius AI Detection software features with your workstation.

2.8.3 PeerView Marks

PeerView™ marks is a feature designed to help interpreting physicians better understand the extent of a region of interest that was marked. At the review workstation, the interpreting physician can use the PeerView feature to highlight regions of interest detected by Genius AI Detection software.

- **Masses** – The PeerView feature defines and outlines the region of most significant central density of the soft tissue lesion. The interpreting physician can then evaluate the overall extent of the identified region and evaluate the margin, shape, and interior characteristics of the identified soft tissue lesion.
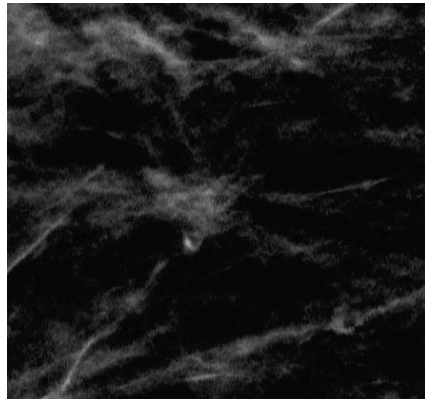
Figure 9: Region without a PeerView Mass Mark
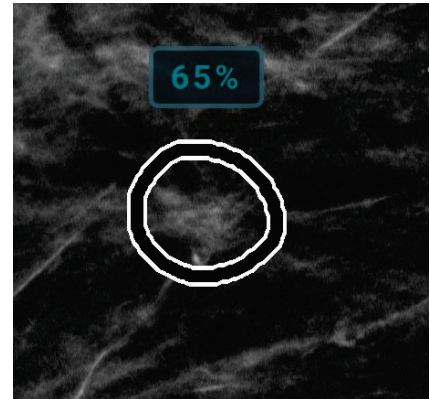
Figure 10: Region with a PeerView Mass Mark

- **Calcifications** – The PeerView feature outlines individual calcifications and the calcification cluster.

Note

The PeerView feature may not outline all the calcifications in a cluster, and it may show findings suggestive of calcifications that are not calcifications. The PeerView marks are dependent upon which elements of the cluster were identified by Genius AI Detection software.
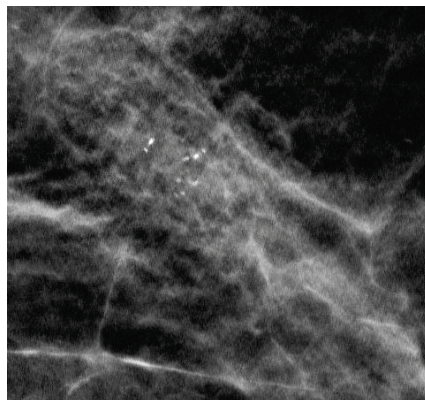

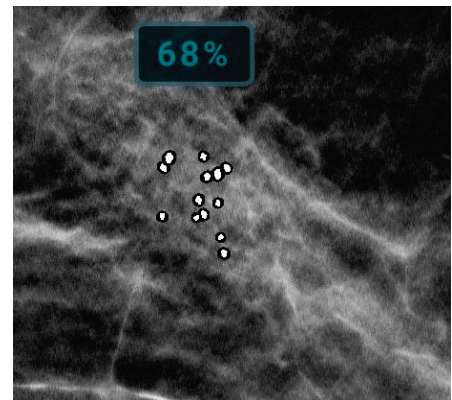*Figure 11: Region without a PeerView Calc Mark*

Figure 12: Region with a PeerView Calc Mark

- **Masses with Calcifications** – Composite Malc marks indicate that one or more Mass and Calc marks occur at the same location on the image. The PeerView feature highlights the individual calcifications in an identified cluster and also outlines the central region of the soft tissue lesion found by Genius AI Detection software.
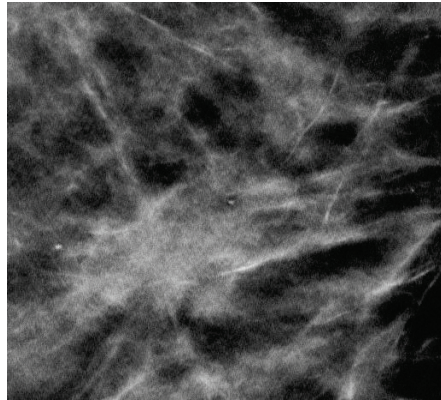

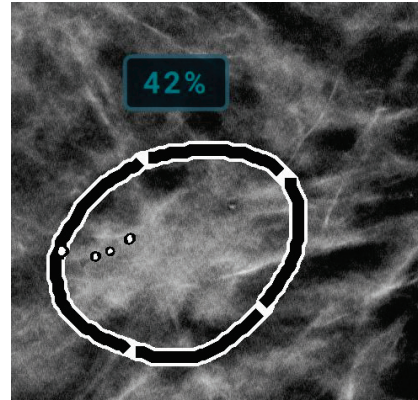*Figure 13: Region without a PeerView Malc Mark*

Figure 14: Region with a PeerView Malc Mark

Note

Not all mammography workstations can display PeerView highlights. Consult your workstation vendor concerning availability and integration of Genius AI Detection software features with your workstation.

Chapter 3 Performance Validation

In order to demonstrate that Genius AI Detection software is safe and effective for its intended use, clinical performance assessment was done as per the guidelines set by US FDA. This chapter outlines the design and results of its performance assessment.

3.1 Clinical Study Design and Case Set

Hologic performed a multi-reader, multi-case (MRMC) study to establish safety and effectiveness of the performance of interpreting physicians when interpreting Hologic tomosynthesis images concurrently with the marks generated by the Genius AI Detection algorithm. The goal of the study was to compare the diagnostic performance of interpreting physicians to read a set of cases with and without the use of Genius AI Detection software results. The study included a total of 390 tomosynthesis cases including 160 negative, 27 recall, 97 benign, and 106 biopsy proven cancer cases. Each case was read by 17 readers with and without use of Genius AI Detection software with a minimum 4 weeks washout period between the reads in a fully-crossed design. For each case, the interpreting physicians recorded initial BIRADS, forced BIRADS, and a probability of malignancy (POM) score. This same data set was used to establish equivalence of performance between Standard resolution and High Resolution images.

The images used in the reader study for Genius AI Detection software were subject to the following exclusion criteria:

- Abnormality with symptomatic and palpable lesions
- Breast Implants
- Patient with pacemakers in the mammography field of view
- Skin markers
- Motion during imaging
- Cut-off anatomy
- Prior surgery and/or presence of biopsy clips visible in imaging
- Studies missing standard views

3.2 Safety and Effectiveness Results

ROC analysis was performed using a interpreting physician-assigned POM score to calculate ROC Area Under the Curve (AUC) with and without use of Genius AI Detection software. In addition, cancer detection sensitivity was estimated by determining the recall rate on cancer cases using initial BI-RADS™ scores with and without the use of Genius AI Detection software. In a similar manner, recall rate on negative cases was also compared with and without the use of Genius AI Detection software. This section summarizes the most significant outcomes of this study.

The following table shows the ROC area under the curve for each reader participating in the study with and without the use of Genius AI Detection software. The average difference in the AUC over all readers and all cases was +0.031 in favor of the concurrent Genius AI Detection software display reading condition (95% CI: 0.012, 0.051; p-value=0.002).

Table 2: AUC Performance by Reader
based on whether Genius AI Detection software information was or was not available for
diagnostic consideration when interpreting a case

Reader Number	ROC AUC		Difference
	Without Genius AI Detection software	**With Genius AI Detection software**	
1	0.719	0.773	0.054
2	0.680	0.742	0.063
3	0.702	0.725	0.023
4	0.783	0.789	0.006
5	0.882	0.881	-0.001
6	0.880	0.888	0.009
7	0.873	0.896	0.023
8	0.705	0.766	0.061
9	0.753	0.810	0.056
10	0.754	0.808	0.053
11	0.840	0.880	0.040
12	0.843	0.878	0.036
13	0.851	0.885	0.034
14	0.742	0.756	0.014
15	0.820	0.842	0.023
16	0.797	0.808	0.011
17	0.871	0.893	0.022
Mean	0.794	0.825	0.031
p-value			0.002
Standard Error			0.010
Degrees of Freedom			243.76
95% two-sided CI			(0.012, 0.051)

The following figure shows a comparison of pooled ROC curve plots demonstrating average reader performance when interpreting 3D Mammography™ exams with and without Genius AI Detection software across the 17 participant readers. The green curve shows the average reader performance with Genius AI Detection software. The red curve

shows the average reader performance without Genius AI Detection software. The black curve shows the standalone performance of Genius AI Detection software operating on these same cases.
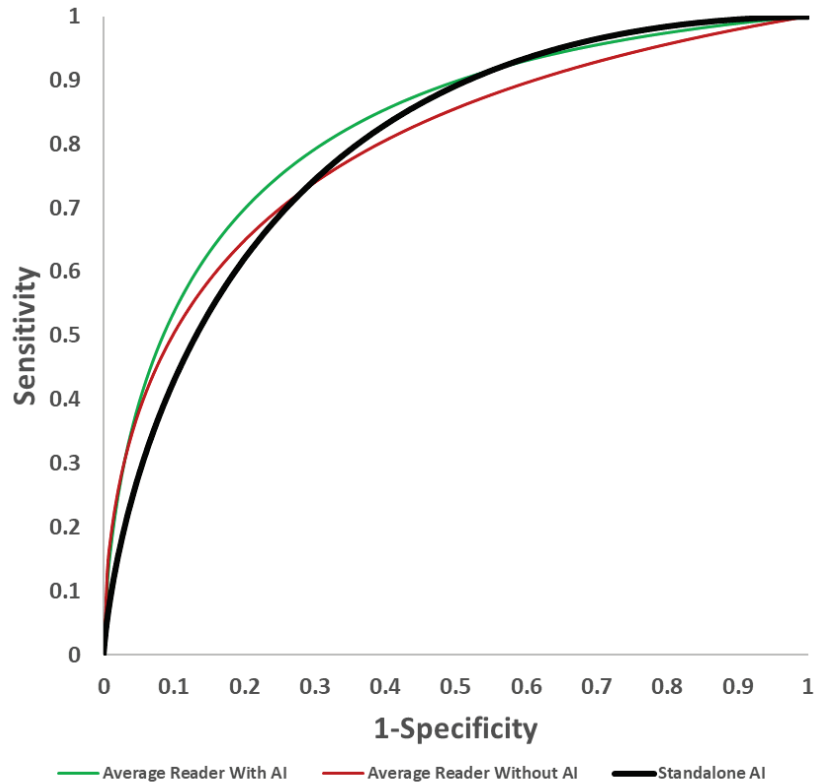

Figure 15: Average ROC Curves of the Genius AI Detection Software Study

This study also demonstrated that the interpreting physicians accurately recalled 9% more malignant cancers (CI 6%-12%, p<0.001) while reading along with Genius AI Detection software than while reading without it. This gain in sensitivity to detect malignant cases attributed to the use of Genius AI Detection software did not significantly affect the recall rate of the interpreting physicians for negative cases.

3.3 Comparison of Genius AI Detection Software to Readers' Average

To compare the Overall Standalone AUC Performance of Genius AI Detection software to the panel of readers participating in this study, the public domain iMRMC software (version 4.0.3, Division of Imaging, Diagnostics, and Software Reliability, OSEL/CDRH/FDA, Silver Spring, MD) was used. Following such analysis, it was observed that the Genius AI Detection AUC was equivalent to reader AUCs on average, with the Genius AI Detection AUC having an average +0.01 difference higher AUC across all readers (95% CI: +0.0584, -0.0380; SE:0.0246; p=0.677).

3.4 Support for Hologic's Standard Resolution Tomosynthesis Acquisition Mode

The MRMC reader study summarized in *Clinical Study Design and Case Set* on page 21 was performed using Hologic Clarity HD images acquired using Hologic's high resolution tomosynthesis acquisition mode. However, Genius AI Detection software can run equally effectively on images acquired using Hologic's standard resolution tomosynthesis acquisition mode. This section summarizes the results of a standalone study, which was conducted to establish equivalence of Genius AI Detection software performance on Hologic's standard resolution tomosynthesis acquisition mode compared to Hologic's high resolution acquisition mode. The standalone study was conducted on paired high resolution and standard resolution 3D data sets, where each high resolution reconstructed 3D volume had a counterpart standard resolution 3D volume, both acquired from a single exposure and under the same compression. Such pairing of the two 3D data sets adds extra value to the standalone study by eliminating biases such as those that may be observed due to breast positioning, breast compression, radiation dose, radiographic techniques, equipment used, and order of acquisition.

The Genius AI Detection software results from the two types of acquisition modes were compared using fROC analysis, ROC analysis, and the key performance metrics at the operating point of the product. The location specific fROC analysis was conducted using lesion score. The ROC analysis was conducted using Case Score for each study.

The following figures show the outcomes of the comparison of Genius AI Detection software results on standard resolution and high resolution tomosynthesis acquisition modes. It is evident that the curves for standard resolution and high resolution modes follow each other very closely. This indicates that the overall performance of Genius AI Detection software is equivalent for both Hologic's standard resolution and high resolution tomosynthesis acquisition modes.

There is a small difference of 0.08 false positive marks per view between the standard resolution and high resolution modes. This is a result of Genius AI Detection software having a single operating point for both standard resolution and high resolution modes, while the model was trained with a mix of cases, which included tomosynthesis images from both standard resolution and high resolution modes. This small difference may be a result of the unbalanced number of cases used from standard resolution and high resolution modes during training. However, as the difference is very small and the false marks are below one per view for either mode, this small difference is considered of no concern. The extension of the false positive marks per view on the standard resolution acquisition mode produces effectively a one percent (0.94%) increase in sensitivity, which balances the increase of 0.08 false positives per view.
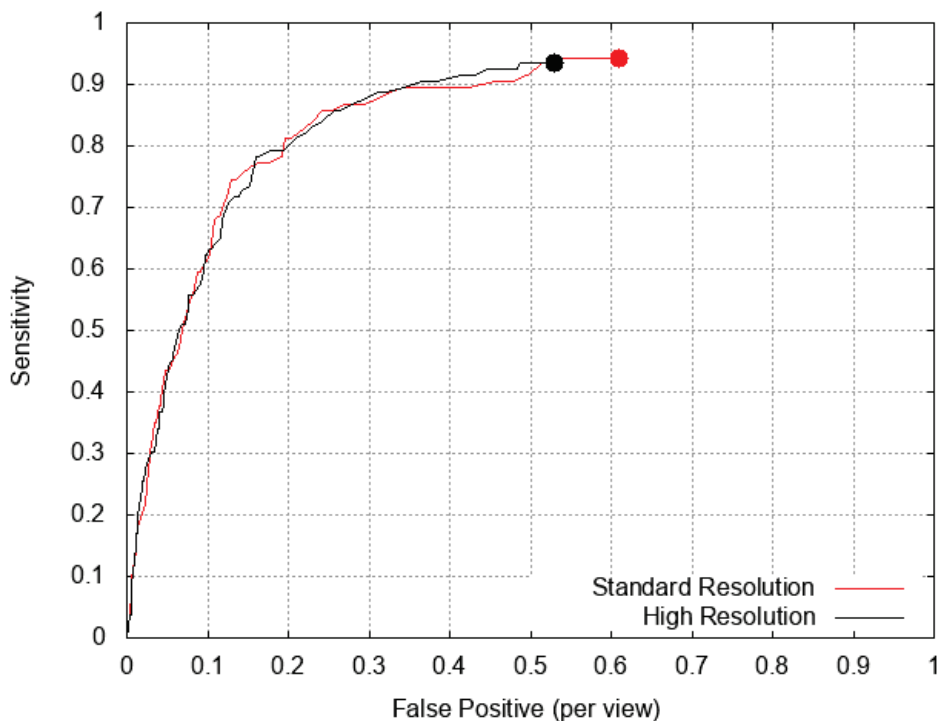
Figure 16: Comparison of FROC between Standard Resolution and High Resolution Images -- based on a dataset of 106 cancers and 658 non-cancer cases
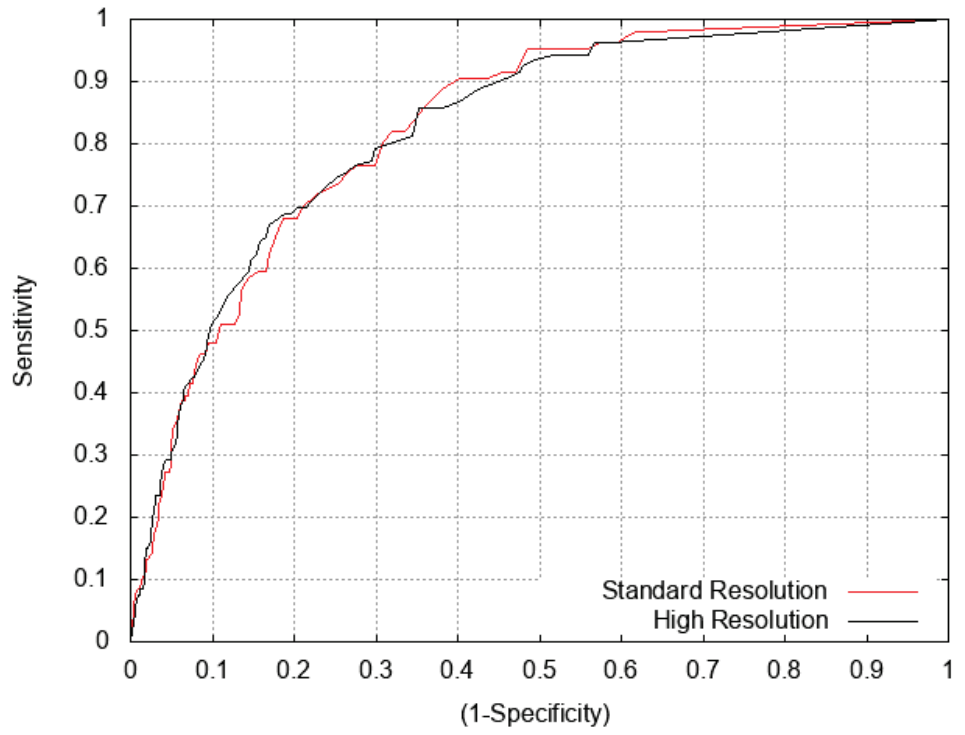
Figure 17: Comparison of ROC between Standard Resolution and High Resolution Images

The following tables list the performance metrics at the product operating point. The unbalanced number of cases used from standard resolution and high resolution acquisition modes during training also results in the following minor differences:

- a higher number of false positive count by 0.08 per view on the standard resolution acquisition mode
- a lower specificity on the standard resolution acquisition mode by 4.8%
- a higher sensitivity on the standard resolution acquisition mode by 0.94%

The confidence intervals indicated in the tables are calculated based on bootstrapping method with 1,000 iterations.

Table 1 shows the standalone Genius AI Detection software sensitivity. Tables 2 and 3 show the Specificity on Non-Cancer cases with and without biopsied benign cases. Similarly, Tables 4 and 5 show the false marks per view by Genius AI Detection software on Non-Cancer cases with and without biopsied benign cases. The false positives generated by Genius AI Detection software on biopsied benign cases is always a higher percentage of the overall non-cancer cases used in the reader study. This is because biopsied cases incorporate actionable lesions. Therefore, the specificity and false positive rate metrics are calculated first using all non-cancer cases then using only screening normal and recall cases that never went to biopsy. In other words, the metrics are also calculated on a subset of the database that excludes biopsied benign cases. This gives a fair understanding of the false marks generated by Genius AI Detection software.

These key performance metrics indicate equivalent performance of Genius AI Detection software on Hologic's standard resolution and high resolution tomosynthesis acquisition modes.

Key Performance Metrics

Table 1: Case Level Sensitivity (Percentage number of cancers accurately marked by Genius AI Detection software)

Number of Cancers = 106	Standard Resolution	High Resolution
Sensitivity (%)	94.34	93.40
Confidence Interval	(89.87, 98.83)	(88.30, 98.25)

Table 2: Case Level Specificity on All Non-Cancers (Percentage number of negative cases with no Genius AI Detection marks)

Number of Non-Cancers = 658	Standard Resolution	High Resolution
Specificity (%)	36.63	41.33
Bootstrapped Confidence Interval	(33.05, 40.26)	(37.60, 45.14)

Table 3: Case Level Specificity on BIRADS 0, 1, and 2 Cases Only (Percentage number of negative cases with no Genius AI Detection marks)

Number of Neg, Recall = 561	Standard Resolution	High Resolution
Specificity (%)	41.18	45.99
Bootstrapped Confidence Interval	(37.02, 45.35)	(41.78, 50.16)

Table 4: False Marks per View

Number of Non-Cancers = 658	Standard Resolution	High Resolution
FP/view	0.61	0.53
Bootstrapped Confidence Interval	(0.55,0.66)	(0.49,0.59)

Table 5: False Marks per View on BIRADS 0, 1, and 2 Cases

Number of Neg, Recall = 561	Standard Resolution	High Resolution
FP/view	0.53	0.47
Bootstrapped Confidence Interval	(0.47,0.59)	(0.41,0.52)

3.5 Conclusion

The studies conducted to assess safety and effectiveness concluded that the use of Genius AI Detection software can bring the following clinical benefits when used concurrently with tomosynthesis images. Based on analyses that do not control type I error and therefore cannot be generalized to specific comparisons outside this particular study, in this study:

- The average observed AUC was 0.825 (95% CI: 0.783, 0.867) with CAD and 0.794 (95% CI: 0.748, 0.840) without CAD. The difference in observed AUC was +0.031 (95% CI: 0.012, 0.051).

- The average observed reader sensitivity for cancer cases was 75.9% with CAD and 66.8% without CAD. The difference in observed sensitivity was +9.0% (99% CI: 6.0%, 12.1%).

- The average observed recall rate for non-cancer cases was 25.8% with CAD and 23.4% without CAD. The observed difference in negative recall rate was +2.4% (99% CI: 0.7%, 4.2%).

- The average observed case read-time was 52.0s with CAD and 46.3s without CAD. The observed difference in read-time was 5.7s (95% CI: 4.9s to 6.4s).

These performance characteristics persisted in the specific subgroup analyses for breast density (fatty and dense) and lesion types (mass and calcs).

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