

SenoClaire

GE Breast Tomosynthesis

Clinical and Non-Clinical Information

Supplement to Operator Manual



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Revision 1

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EN - ENGLISH

Supplement to Operator Manual

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Chapter 1 Publication presentation

1 Scope of this publication

SenoClaire (GE Breast Tomosynthesis) is an add-on to the existing, FDA-approved Senographe Essential Full Field Digital Mammography (FFDM) system that permits the acquisition and processing of Digital Breast Tomosynthesis (DBT) datasets. It is intended for screening and diagnostic mammography and can be used for many of the same clinical application as traditional mammographic systems. The output of SenoClaire is a DICOM dataset for display and archive on compatible DICOM devices.

The purpose of this document is to describe the results of the clinical and non-clinical studies designed to provide reasonable assurance of the safety and effectiveness of SenoClaire by comparing GE DBT to the conventional standard for screening and diagnostic imaging, FFDM.

Specifically, these studies tested the non-inferiority of DBT MLO + 2D CC to 2-view FFDM (2D CC + 2D MLO) in detecting breast cancer in initially asymptomatic women presenting for mammographic breast examinations.



United States Federal law restricts this device to use by or on the order of a physician.

2 Intended Use

SenoClaire is intended for screening and diagnostic mammography.

3 Indications for use

SenoClaire acquires 2D images and also acquires multiple projection views to produce 3D DBT images suitable for screening and diagnosis of breast cancer. SenoClaire can be used for the same clinical applications as traditional mammographic systems for screening mammograms.

A screening examination will consist of:

- a 2D image set consisting of a craniocaudal view and a mediolateral oblique view, or
- a 2D craniocaudal view and 3D DBT mediolateral oblique image set.

The SenoClaire Digital Breast Tomosynthesis (DBT) option for the Senographe Essential FFDM system may also be used for additional diagnostic workup of the breast.

4 Contraindications

There are no known contraindications.

5 Warnings and precautions

The warnings and precautions can be found in the SenoClaire Operator Manual.

6 Potential adverse effects

No serious adverse events were reported for the patients enrolled in the clinical study. However, potential adverse effects of any mammography system include:

- Excessive breast compression
- Excessive x-ray exposure
- Electrical shock

- Skin irritation, abrasion, or puncture wound
- Infection

7 Revision history

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File Name	DATE	REASON FOR CHANGE
5415896-1-899 rev 1	September, 2013	Initial release
5415896-2-199 rev 1	January, 2014	First draft update for FDA review
5415896-3-199 rev 1	July, 2014	Second draft for FDA review

Chapter 2 Clinical claims

These clinical claims are based on the results of clinical study reports and non-clinical study results that demonstrate the safety and effectiveness of GE Breast Tomosynthesis.

- An exam consisting of one Digital Breast Tomosynthesis (DBT) MLO view plus one 2D CC view is clinically non-inferior to a standard two-view digital mammography examination consisting of one 2D CC and one 2D MLO view, as measured by the area under the receiver operating characteristic (ROC) curve.
- The dose of a DBT view (e.g. MLO or CC) is equivalent to that of a 2D standard acquisition in the same view orientation.

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Chapter 3 Non-clinical studies

The data included below are included in response to guidance for the Class II Full Field Digital Mammography (FFDM), physical laboratory testing, where the physical testing results are applicable to Digital Breast Tomosynthesis (DBT). Some of the data included below involve new measurements where test results may be important to DBT, and are not currently included in standards or advised by guidance.

The non-clinical data include information on the following:

1. Image size
2. Apparent source size
3. Calcification artifact correction
4. Image uniformity
5. Signal-to-noise (SNR) transfer and noise analysis*
6. Automatic Exposure Control (AEC) performance and patient radiation dose *
7. Repeated exposure test*

*Part of Class II FFDM guidance

1 Image size

In conventional mammography, the conic projection of the volume results in coverage that varies with the height inside the object. Because of the source trajectory, the overall volume coverage in DBT is improved compared to that of conventional 2D mammography ([Illustration 1](#)).

Illustration 1 Front view of the imaging cone in 2D mammography (left) and of the multiple imaging cones in DBT (right). The maximum imaging area covered by DBT is larger than the 2D area.

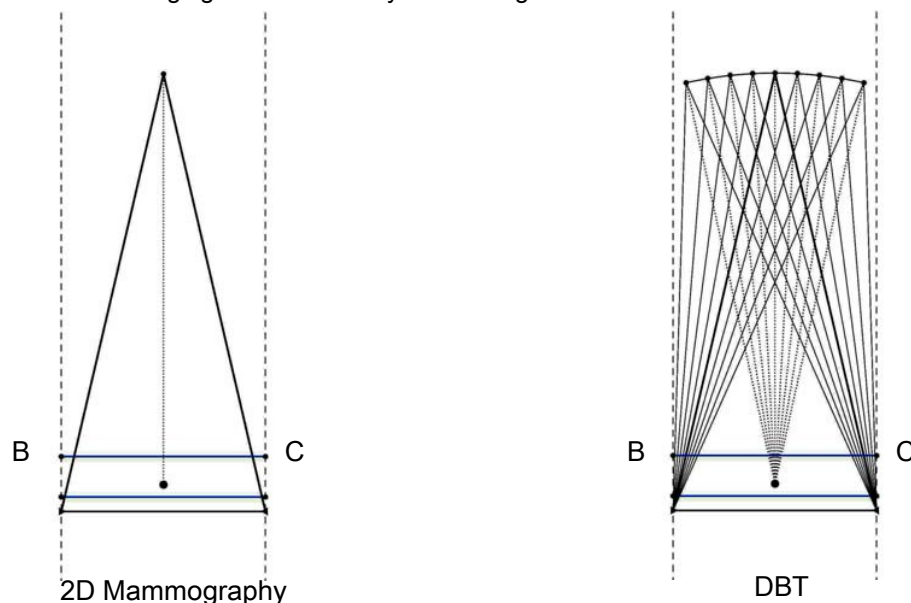


Table 1 2D and 3D effective imaging area at 40 mm height above the breast support.

	Area
Detector size	24.0 x 30.7 cm ²
Effective 2D imaging area	21.7 x 27.7 cm ²
Nominal 3D imaging area	21.7 x 27.6 cm ²
Optimal 3D imaging area	21.7 x 25.1 cm ²
Maximum 3D imaging area	21.7 x 28.0 cm ²

2 Apparent source size

Just as in 2D mammography, the capability of DBT to depict small objects such as micro calcifications depends on the apparent focal spot size.

The apparent focal spot size in DBT combines the actual physical extension of the focal spot during the exposure and the effect of back-projecting the projection data with limited angular accuracy. For both effects, the impact on the image is magnified with object height above the detector.

SenoClaire uses step-and-shoot rather than continuous motion of the source to minimize the impact of source motion during DBT data acquisition. The error due to angle inaccuracy in the back- projection was measured to be 0.0268°, which is geometrically equivalent to an apparent focal spot motion of 300 µm (0.3 mm).

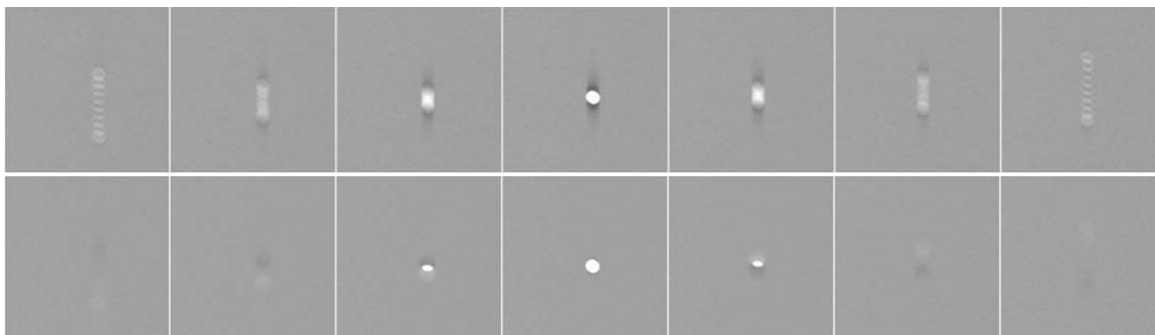
3 Calcification artifact correction

The artifact spread function (ASF) is the impulse response of the tomosynthesis system along the z-axis. It is sometimes used as a figure of merit for the assessment of out-of-plane artifacts.

When assessing out-of-plane artifacts in DBT, a linear response is not necessarily desirable. Highly attenuating objects such as macrocalcifications have a large out-of-focus “fan-beam” trace that can be distracting to the radiologist ([Illustration 2](#)). Using an iterative reconstruction scheme, including nonlinear processing of highly-absorbing objects, yields off-plane images much improved in terms of both in-plane and out-of-plane artifacts ([Illustration 2](#)).

Illustration 2 Sequence of tomographic planes (focal series) of a highly-absorbent object (a 1.75 mm diameter steel ball) using linear (top row) and nonlinear (bottom row) processing. The object plane is Z = 0 mm.

Z=-20 mm Z=-10 mm Z=-50 mm Z= 0 mm Z= 5 mm Z= 10 mm Z= 20 mm



4 Image uniformity

Signal uniformity and SNR uniformity are important image quality considerations in digital mammography and in DBT. Resolution uniformity (Modulation Transfer Function (MTF)) at 3 lp/mm was measured in reconstructed DBT planes. The area of interest was the field-of-view in 2D.

Signal and SNR uniformity were measured using a flat field phantom. Results are shown for SenoClaire on a reconstructed DBT plane located 3 cm above the breast support.

SenoClaire showed a signal non-uniformity of less than 2% over 95% of the 2D field-of-view, and less than 18% overall. SNR non-uniformity was less than 24% overall, and resolution non-uniformity was less than 20%.

5 Signal-to-noise (SNR) transfer and noise analysis

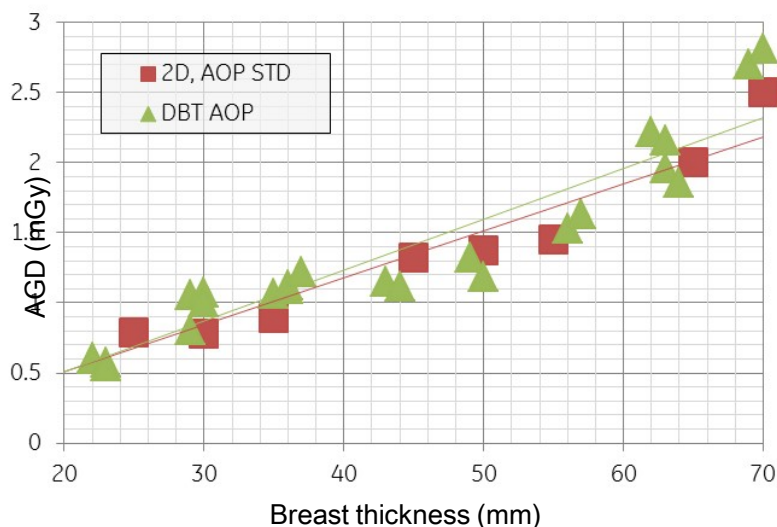
In radiological systems the Detective Quantum Efficiency (DQE), defined as the squared yield of the transfer of signal-to-noise by the imaging system: $DQE = (SNR_{out}/SNR_{in})^2$, measures imaging efficiency with varying doses. It is defined for projection views only.

At 0.5 lp/mm, the DQE in the projections used by the SenoClaire system to reconstruct the DBT planes was measured to be near 65%, or within 10 percentage points of the DQE in FFDM imaging conditions. The preservation of DQE, combined with the step-and-shoot acquisition, maintains good detectability of small test objects at the same total dose as single-view FFDM.

6 Automatic Exposure Control (AEC) performance and patient radiation dose

The automatic exposure level of SenoClaire in 3D is designed to deliver the same dose to the breast as the corresponding 2D view ([Illustration 3](#)). The Average Glandular Dose (AGD) was verified on PMMA plates of known thickness to offer maximum reproducibility. Actual results on individual patient images may differ depending on breast tissue overlaps affecting the automatic exposure control targets.

Illustration 3 AGD delivered by DBT view in automatic optimization parameters (AOP) compared to a 2D view of same object.



7 Repeated exposure test

The impact of ghosting between projections has been assessed following the procedure described in IEC 62220-1-2:2007, Annex A. Within a DBT sequence, the first projection is performed with a lead plate positioned to cover half of the field of view (FOV). This projection is called: "Light". After the first projection is done and before the second exposure, a lead plate is put on the detector covering the entire FOV, in order to acquire the next projection without incoming X-rays. This projection is called "Dark". The measured residual signal in the "Dark" projection is then computed as the ratio:

$$(ROI_1^{Dark} - ROI_2^{Dark}) / ROI_1^{Light}$$

where ROI_1^{Light} is the mean signal in a 10,000 pixel ROI, adjacent to, but not overlapping, the area covered by the lead plate in the "Light" projection, ROI_1^{Dark} is the mean signal in the same ROI in the "Dark" projection, and ROI_2^{Dark} is the mean signal in an ROI of the same size positioned in the area covered by the lead plate in the "Dark" projection.

For the Senographe Essential detector, the measured average residual signal from one projection to another was less than 0.6% and had no impact on the imaging.

8 Conclusion

The SenoClaire system offers dose efficiency comparable with FFDM over the full FFDM imaging area, while offering tomosynthesis imaging free of macrocalcification artifacts.

Chapter 4 Summary of clinical studies

Table 2 The pivotal reader study GE-190-004 provides data supporting safety and effectiveness of SenoClaire.

Clinical Study	Study Design	Objective	Number of Sites	Number of Subjects
Pivotal study: <ul style="list-style-type: none"> • Accrual: GE-190-001, -002, -003 • Reader study: GE-190-004-Blinded Image Evaluation (BIE) 	Prospective accrual studies and blinded reader study, randomized controlled clinical trial	<ul style="list-style-type: none"> • Evaluate the safety and effectiveness of the device • Primary endpoint: Comparison of DBT MLO + 2D CC to 2-view FFDM as measured by the area under the ROC Curve • Primary endpoint: Comparison of DBT MLO alone to 2-view FFDM as measured by the area under the ROC Curve 	<ul style="list-style-type: none"> • 6 enrollment sites • 7 readers 	753 patients were enrolled in the accrual studies. Number of cases evaluated: 444 <ul style="list-style-type: none"> • 67 cancers • 377 non-cancers
Continued assessment: GE-190-004-Feature Analysis (FA)	Subjective side-by-side lesion comparison	<ul style="list-style-type: none"> • Primary subjective comparison of DBT MLO to 2-view FFDM in terms of lesion conspicuity. • Secondary subjective comparison included other lesion features important in discriminating between benign and malignant lesions 	<ul style="list-style-type: none"> • 6 enrollment sites • 7 readers 	The subject data set for the feature analysis originated from the pivotal study. Number of cases evaluated: 70 <ul style="list-style-type: none"> • 33 cancers • 37 non-cancers

1 Patient accrual studies

1-1 Patient accrual

A total of 753 patients were enrolled from 5 United States clinical sites and 1 Canadian clinical site under 3 clinical protocols. Additional sources of DBT and FFDM mammography images were used for enrichment. Enrollment duration was approximately 1 year.

- Screening cohort: Subjects enrolled under protocol GE-190-001 (“A Multicenter Study to Test the Non-Inferiority of Digital Breast Tomosynthesis Compared to Full-Field Digital Mammography in Detecting Breast Cancer. Part 1 - Recruitment Plan for Asymptomatic Women Undergoing Screening Mammography”).
The total number of subjects enrolled in this screening cohort was 413.
- Diagnostic cohort: Subjects enrolled under protocol GE-190-002 (“A Multicenter Study to Test the Non-Inferiority of Digital Breast Tomosynthesis Compared to Full-Field Digital Mammography in Detecting Breast Cancer. Part 2 - Recruitment Plan for Asymptomatic Women Referred for Diagnostic Mammography”).
The total number of subjects enrolled in this diagnostic cohort was 238.
- Biopsy cohort: Subjects enrolled under protocol GE-190-003 (“A Multicenter Study to Test the Non-Inferiority of Digital Breast Tomosynthesis Compared to Full-Field Digital Mammography in Detecting Breast Cancer. Part 3 - Recruitment Plan for Asymptomatic Women Referred for Breast Biopsy”).
The total number of subjects enrolled in this biopsy cohort was 102.
- Enrichment data: Clinical data collected from separate clinical trials at the Massachusetts General Hospital and the University of Padua, Italy. The data included initially asymptomatic biopsy-confirmed cancer subjects that met all other criteria of GE’s prospective studies: GE-190-001, GE-190-002, and GE-190-003. 11 enrichment cancer cases were included in the BIE reader study.

1-2 Inclusion criteria

- Women 18 years or older, presenting for screening mammography
- Able and willing to comply with study procedures, and have signed and dated the informed consent form;
- The subject is either surgically sterile (has had a documented bilateral oophorectomy and/or documented hysterectomy), or postmenopausal (cessation of menses for more than 1 year); or, if of childbearing potential, the possibility of pregnancy is remote based on a negative patient history and, optionally, a negative urine pregnancy test (if subject requests one).

1-3 Exclusion criteria

- Pregnant or trying to become pregnant
- Has signs or symptoms of breast cancer
- Has been previously included in this study
- Has breast implants
- Has a history of breast cancer and is in active treatment. However, subjects with a prior lumpectomy who receive only routine screening mammography views can be included. Additionally, subjects with prior mastectomy currently not being treated can be included in the screening imaging of the unaffected breast
- Has undergone mammography for any purpose within approximately one year
- Has breasts too large to be adequately positioned on 19 x 23 cm FFDM digital receptor without anatomical cut-off during a DBT examination.

1-4 Imaging

- The subject had routine screening FFDM on a GE system with CC and MLO views (2-view FFDM), followed by diagnostic mammography also on a GE FFDM system (if applicable)
- The subject had DBT images obtained with MLO positioning (DBT MLO)

- The 2D FFDM images from screening mammography and/or diagnostic mammography and the DBT images were provided in digital format to GE.

1-5 Adverse Events (AE)

No Serious AEs occurred with the 753 women enrolled in the 3 accrual studies. AEs occurred in 2 subjects for an incidence rate of 0.3%. Both AEs occurred during DBT imaging and were mild and resolved.

Subject 003-1026 (randomized to be imaged with DBT first in the GE-190-001 study) reported pain in the left breast during the DBT procedure (before the compression paddle touched the breast) and asked to stop the study. Only one breast was imaged. The AE was resolved upon stopping the procedure. Relationship to the imaging procedure was not suspected. The subject withdrew from the study.

Subject 005-3004 (GE-190-003 study) presented with a rash during DBT imaging and, due to this, the compression applied to the breast caused the skin to tear. This AE was non-serious but was suspected to be related to the DBT imaging. The nurse gave the subject Bacitracin zinc with Polymoxin B sulfate ointment to prevent the tear from becoming infected. The AE was reported by the site as resolved.

2 Pivotal reader study (BIE)

2-1 Overall Study Design and Plan

The aim of the study was to compare the performance of DBT MLO alone, or DBT MLO + 2D CC compared to two-view (MLO + CC) FFDM for women undergoing mammography based on a Blinded Image Evaluation (BIE) reader study.

- Primary endpoints: The primary objective of this reader study was to test the hypotheses that DBT MLO alone, or DBT MLO + 2D CC, is non-inferior to 2-view FFDM for breast cancer detection. The endpoints for the primary analyses were comparison of area under the Receiver Operator Characteristic (ROC) curve (AUC) values. The ROC analyses compared the diagnostic outcome against a “standard of truth” (the clinical status of the subject) based on 1-year follow-up and histopathology outcomes.
- Secondary endpoints:
 - Sensitivity
 - Specificity
 - Recall rate
 - Reading time
 - Average Glandular Dose (AGD).

2-2 Case selection

482 subjects were randomly selected out of the 610 subjects available from the GE-190-001, -002, -003 and enrichment cohorts. The original randomization allowed for a 10% loss in subjects to achieve the necessary 450 evaluable subjects for the required Blinded Image Evaluation (BIE) power. This loss was planned because normal and benign subjects were selected for the BIE prior to completion of all of the 1-year follow-ups that confirmed a non-cancer truth status. Similarly, cancer cases were over-sampled by 10% to allow for loss of eligible cases due to poor image quality as ascertained by BIE study readers. Normal and biopsy-proven benign subjects were randomly selected from subjects in the GE-190-001, -002 and -003 studies.

All proven cancers from the accrual studies were included in the BIE reader study and supplemented by 11 additional cancers from enrichment cases.

2-3 Reader case presentation

The BIE study was conducted in 15 one-day sessions for each of the 7 readers. Approximately 90 cases were interpreted on each day's blinded reading session. Both FFDM and DBT image sets were presented without any medical history data, demographic information, prior image sets, or marks on the images suggestive or indicative of pathology. The sole exception to this was that blinded readers were notified of prior surgery and biopsy procedures so that scarring or other tissue abnormalities from these procedures were not confused with suspicious lesions.

The data sets to be evaluated by each reader included:

- Arm 1: 2-view FFDM image sets consisting of bilateral CC and MLO images of each subject. 13% of FFDM cases included additional CC and MLO views and exaggerated views, if obtained as part of the FFDM screening exam
- Arm 2: DBT MLO image sets consisting of planar tomographic reconstructed image sets. The readers had reconstructed DBT images of both planes (1 mm apart) and slabs (10 mm maximum intensity projections) over the full breast volume.
- Arm 3: DBT MLO + 2D CC including DBT MLO images along with corresponding 2D CC FFDM views of each breast.

2-4 Results for the BIE study

Table 3 Analysis of ROC AUC

	2-view FFDM	DBT MLO + 2D CC	DBT MLO
Area under ROC curve (std error)*	0.853 (0.027)	0.842 (0.028)	0.820 (0.033)
95% CI on AUC*	0.798, 0.908	0.786, 0.899	0.752, 0.888
Difference from FFDM in AUC (std error):			
DBM proper binormal analysis*		-0.0107 (0.019)	-0.0331 (0.019)
DBM Non-parametric analysis**		-0.0097 (0.016)	-0.0356 (0.016)
97.5% CI on AUC Difference:			
DBM proper binormal analysis*		-0.0541, 0.0326	-0.0764, 0.0103
DBM Non-parametric analysis**		-0.0473, 0.0279	-0.0731, 0.0020

* Based on DBM (Dorfman-Berbaum-Metz) MRMC (Multireader-Multicase) 2.32 build 3 Software ROC Analysis of Variance binormal analysis

** Based on DBM (Dorfman-Berbaum-Metz) MRMC (Multireader-Multicase) 2.32 build 3 Software ROC Analysis of Variance non-parametric analysis

- Primary endpoints (Table 3):
 - Readings of the DBT MLO + 2D CC image set were non-inferior to readings of the 2-view FFDM image set in terms of the malignancy scale assessment for suspicion of cancer. The lower end of the 97.5% CI on the difference in AUCs, -0.0473, was larger than the pre-specified non-inferiority criterion of -0.1 and the FDA-requested non-inferiority criterion of -0.05, which established the non-inferiority of DBT MLO + 2D CC to 2-view FFDM.
 - The lower end of the 97.5% CI of the AUC difference between DBT MLO and 2-view FFDM, -0.0731, was larger than the pre-specified non-inferiority criterion of -0.1 but lower than the FDA-requested non-inferiority criterion of -0.05.
- The average radiation dose to subjects was identical for DBT MLO compared to 2-view FFDM used

in the BIE, both 3.2 mGy (standard error 0.07 for DBT MLO and 0.05 for 2-view FFDM). On the final device, average radiation doses from DBT MLO + 2D CC are the same as those from 2-view FFDM.

- On average, interpretations times were 41% longer with DBT MLO + 2D CC than with the 2-view FFDM interpretations. This trend was consistent for malignant, benign and normal cases, with all modalities taking longer for malignant and benign cases than for normal cases.

The following results were secondary endpoints and were not accounted for in the multiple testing corrections, so the statistical significance of these findings cannot be assessed but we observed the following:

- Specificity based on screening BI-RADS was higher with DBT MLO + 2D CC than with 2-view FFDM.
- Recall rates based on screening BI-RADS were lower by 6.6% with DBT MLO + 2D CC than with 2-view FFDM. This represents a relative difference of 16.3% lower recall rate for DBT MLO + 2D CC than for 2-view FFDM.

2-5 Limitations of the BIE Clinical Study

There are two limitations of the BIE study:

- 1) there were device design changes after study completion, and
- 2) randomization of readings was not done for the DBT MLO + 2D CC arm.

Design changes after study completion are listed in the table below with a short description of the effect of each change:

Clinical study system features	Final design features	Effect
Non-motorized compression	Motorized compression	Simplifies breast positioning
Manual Exposure Technique Selection	<ul style="list-style-type: none"> o Automatic Exposure Management (AEM) o Reduction of average glandular dose (AGD) 	<ul style="list-style-type: none"> o Automates technique selection to control dose and improve consistency o Non-inferior Image quality with the same AGD per DBT view as an FFDM (2D)
19 x 23 cm Senographe DS detector	24 x 31 cm Senographe Essential detector	Accommodates larger breasts and provides better detector performance (higher DQE)
No grid	Includes a moving grid	Reduces scatter yielding better image quality
No artifact correction	Artifact correction algorithm	Improves image quality

Each of these design changes represents an improvement in the clinical device compared to the study device. Motorized breast compression increases the ease of breast positioning and compression for the technologist and patient, making positioning and breast compression with the clinical DBT device analogous to that on the Senographe Essential digital mammography system. The other four design differences represent improvements to equipment design that have either improved image quality, lowered radiation dose for comparable image quality, or both. Non-clinical data have been provided above in Chapter 3, Item 6 to demonstrate that automatic exposure management (AEM) on the final clinical device delivers automatically selected exposure parameters for the DBT exam that match dose to that of a single-view FFDM exam in automatic optimization of parameters (AOP) standard (STD) mode, providing improved exposure consistency compared to the clinical trial device. The replacement of the 19x23 cm Senographe DS detector in the clinical trial with the 24x31 cm Senographe Essential detector in the final design device permits DBT exams of larger breasts and benefits from the higher DQE performance of the Essential detector, especially at the low dose individual views collected and used to reconstruct DBT images. Non-clinical data confirm the improved detector performance of the final design device, leading to

equal or improved image quality at lower radiation doses. The inclusion of a moving grid in the final design device provides improved scatter rejection, with equal or improved image quality, especially for thicker breasts. The artifact correction algorithm in the final design device has improved image quality by eliminating artifacts from highly attenuating structures such as macrocalcifications or clips in the breast.

The lack of randomization of the DBT MLO + 2D CC arm of the BIE reader study has had little or no effect on BIE reader study outcome for the following reasons: 1) the long delay times between each arm of this study (average separations of 74 days between arms 1 and 2 and 73 days between arms 2 and 3, arm 3 being the DBT+2DCC arm, the large number of cases per reading session (98-110), and the randomization of cases within each reading block argue against case recall being a significant factor in this study, and 2) complementary analyses (based on Milliken GA, Johnson DE. *Analysis of Messy Data, Volume 1, Designed Experiments, 2nd Ed.*, Boca Raton, FL: Chapman & Hall/CRC Press, 2009) indicate that the lack of randomization of the DBT+2DCC arm is unlikely to have had an impact on study conclusions.

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3 Feature analysis reader study

3-1 Overall Study Design and Plan

In addition to the non-inferiority study used to demonstrate safety and effectiveness of the SenoClaire GE Breast Tomosynthesis option, a subjective user preference study was run to gather input on the reader's preference in terms of the ability to discern lesion features important in discriminating between malignant and benign lesions. Although the results of this analysis are subjective in nature, the results were evaluated for each feature compared. The primary objective of the feature analysis was to evaluate subjective preference of DBT MLO compared to 2-view FFDM in terms of the ability to discern lesion features important in discriminating between malignant and benign lesions. The primary goal of the feature analysis was a side-by-side comparison of lesion conspicuity.

A subjective side-by-side comparison of specific mammographic findings seen on both FFDM and DBT images was conducted to quantify the relative imaging performance attributes of each modality. Radiologist readers who evaluated feature analysis images were directed to the specific findings included in the feature analysis to ensure that the same lesion was compared between the two modalities by all readers. Feature analysis readers compared lesion features between 2-view FFDM (CC and MLO) and DBT MLO images, so it was not possible to blind readers to the modality being viewed. Each reader ranked the relative conspicuity of calcifications, masses and architectural distortions using a 5-point Likert scale ranging from -2 (FFDM significantly better) to +2 (DBT significantly better). These rankings were used to evaluate reader preference in this subjective observation study.

3-2 Selection of cases

The subject dataset for the feature analysis originated from the 3 prospective studies GE-190-001, GE-190-002, and GE-190-003, and the enrichment cohort. 70 cases from the BIE reader study were used, including 33 histologically-proven malignant cases and 37 proven benign cases, to comprise the dataset evaluated by the same 7 readers used in the BIE.

The feature analysis was conducted following the conclusion of the BIE to allow for the inclusion of some cases where significant discordance between FFDM and DBT image evaluations and readers existed.

The selection set was constrained as follows:

- Every effort was made to select lesions less than or equal to 1 cm in size and non-palpable
- All breast compositions were represented, with approximately:
 - 10% BI-RADS density scale 1
 - 40% BI-RADS density scale 2
 - 40% BI-RADS density scale 3
 - 10% BI-RADS density scale 4
- An even distribution of masses and clusters of microcalcifications, with some architectural distortions
- Every effort was made, where possible, to select at least:
 - 1 subareolar mass
 - 1 subareolar cluster of microcalcifications
 - 1 subareolar architectural distortion

Additionally, the dataset aimed to have at least 6 cases in each of the following categories based on the BIE screening BI-RADS assessment:

1. Concordant correct cases (cases in which FFDM and DBT image interpretations were both correct for at least 4 of the BIE readers, including true positive and true negative cases)
2. Concordant incorrect cases (cases in which FFDM and DBT image interpretations were both incorrect for at least 4 of the BIE readers, including false positive and false negative cases)
3. Discordant cases in which DBT was correct and FFDM was not for at least 4 of the BIE readers (including cases true positive and true negative by DBT)

4. Discordant cases in which FFDM was correct and DBT was not for at least 4 of the BIE readers (including cases that were true positive and true negative by FFDM).

Cases were not selected based on a visual comparison of lesions in DBT and FFDM images.

3-3 Results for the feature analysis reader study

- Relative conspicuity was perceived to be superior for DBT compared to FFDM in the subjective reader study. Relative conspicuity for DBT was also perceived to be superior to FFDM for both masses and calcifications, although slightly less so for calcifications. DBT superiority remained consistent in breast density, lesion size and lesion location subgroups. These results were consistent for both cancer and non-cancer cases.
- DBT MLO was perceived to be superior to 2-view FFDM in terms of image contrast, image sharpness, non-chest wall tissue visibility, discerning mass margins and discerning subtle irregularities in mass margin.

4 Conclusions drawn from the studies

The results of the image quality and clinical studies presented above demonstrate the safety and effectiveness of SenoClaire for screening and diagnosis of breast cancer.

SenoClaire DBT MLO + 2D CC has been shown to be non-inferior to 2-view FFDM in terms of overall diagnostic utility as measured by ROC analysis.

Clinical studies and non-clinical data demonstrate that the GE Senographe Essential-based SenoClaire system acquiring DBT MLO + 2D CC views has diagnostic accuracy non-inferior to that of conventional 2-view FFDM at comparable radiation doses.

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