A Prospective, Multi-site Clinical Study to Collect User Feedback using Affirm® Contrast Biopsy

Sponsor:	Hologic, Inc. 250 Campus Dr. Marlborough, MA 01752 USA
Sponsor Contact:	ClinicalResearch@Hologic.com
Study Product:	Affirm® Contrast Biopsy
Protocol #:	#20-03
NCT #:	NCT04671329
Version:	3.0
Date:	11-February-2021

PROTOCOL SIGNATURE PAGE

The signature below constitutes the approval of this Protocol and the attachments and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable regulations. As an investigator on this study I commit to:

- Conduct the investigation in accordance with the signed agreement, the protocol, and other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB or FDA
- Supervise all testing of the device involving human subjects.
- Ensure that the requirements for obtaining informed consent are met.

Study Site Name: _____

Investigator Designation (please select as appropriate):

☐ Principal Investigator ☐ Sub-Investigator

Investigator Name (*Print*): _____

Investigator Signature: _____

Date of Signature: _____

Table of Contents

1. PROTOCOL SYNOPSIS

Sponsor:	Hologic, Inc.
Device(s):	The Hologic Selenia® Dimensions® or 3Dimension® Mammography System with: • Licensed I-View™ software for Contrast Enhanced Digital Mammography • Affirm® Breast Biopsy Guidance System (accessory) • Updated Affirm Contrast Biopsy Software
Design:	Post-market, prospective, multi-site clinical study
Planned Enrollment:	90 total subjects
Number of Sites:	Up to 3 sites in the United States
Population:	Women 40 years of age or older recommended for biopsy who have had a suspicious finding on previous contrast enhanced imaging or have lesions that may be occult under other modalities
Subject Follow-up:	No follow-up is required of subjects after the initial Affirm Contrast Biopsy procedure and associated data collection from the women and providers
Clinical Study Duration (Estimations):	6-10 months
Inclusion Criteria:	1) Females aged 40 years of age or older recommended for biopsy who have had a suspicious finding on previous contrast enhanced imaging or have lesions that may be occult under other modalities 2) Subject is able to read, understand, and sign the study specific informed consent form after the nature of the study has been fully explained to them
Exclusion Criteria:	1) Subjects who require a Legally Authorized Representative (LAR) for Informed Consent

2) Subjects who, based on the physician's judgement, may be at increased risk for complications associated with renal function, anticoagulant therapy, or bleeding disorders

3) Subjects who have had a previous allergic reaction to IV contrast agent

2. INTRODUCTION

Currently, if a radiologist finds a suspicious lesion seen only on a diagnostic Contrast Enhanced Digital Mammography (CEDM) exam requiring biopsy the biopsy procedure would likely be performed with MRI guidance because there are currently limited solutions to biopsy with CEDM guidance. Affirm Contrast Biopsy will provide an additional solution to biopsy/localize lesions found by using a CEDM imaging modality.

The bullets below highlight the devices which are commercially available which are involved in the Affirm Contrast Biopsy procedure.

- Gantry:
  - Selenia Dimensions Mammography System & 3Dimensions Mammography System (P080003)
- Software:
  - I-View Software (K123873)
- Accessory:
  - Affirm Breast Biopsy Guidance System (K122836, including Affirm Contrast Biopsy: K202294)
  - Optional - Affirm Lateral Arm Upright Biopsy Accessory (K161575)

As part of this study, a software upgrade will be made to the Selenia Dimensions/3Dimensons Mammography Systems which allows users to biopsy/localize lesions found by using a CEDM imaging modality. There are no other changes made to the hardware components of the gantries or accessories.

Even though the individual devices above are commercially available, the capability to biopsy with CEDM guidance required a 510k clearance (K202294) from the FDA for a software upgrade. This study is considered post-market study since the 510k clearance (K202294) has been received.

2.1 Device Description

Affirm Contrast Biopsy is used with Selenia Dimensions or 3Dimensions. The lesion will be localized by 2D stereotactic image acquisition based on visualization of the lesion enhancing after an IV injection of an iodinated contrast agent.
Safety Features include:

- Automatic detection of mounting, latching, and connection of biopsy guidance module
- C-arm motion disabled if biopsy guidance module is not locked in place
- Automatic compression release disabled when biopsy guidance module installed
- Motorized movement of biopsy device only under user control
- Audible alert if biopsy device motion could result in mechanical interference
- C-arm motion disabled when breast is under compression
- Lateral Arm: When system is in lateral approach biopsy mode, the system shall only allow exposures at C-arm position of 0 degrees

2.2 Device Accountability

The Hologic team will document the shipment & installation of the software to each clinical site and device accountability will be performed during monitoring visits as outlined in the study monitoring plan. The Principal Investigator or an authorized designee shall keep records documenting the type and use of devices during the course of this study.

2.3 Intended Use/Current Indication for Use

Affirm Contrast Biopsy is indicated as an optional accessory for the Selenia Dimensions 2D Full Field Digital Mammography System and 3Dimensions system. It is designed to allow the accurate location of lesions in the breast in three dimensions, using information extracted from stereotactic pairs of two-dimensional images. It is intended to provide guidance for interventional purposes (such as biopsy, pre-surgical localization or treatment devices).

Contrast Enhanced Digital Mammography (CEDM) is an extension of the existing indication for diagnostic mammography with the Selenia Dimensions system and 3Dimensions system. Biopsy targeting can be done on captured contrast enhanced images (scout and stereo pair). The CEDM application shall enable contrast enhanced breast imaging using a dual energy technique. This imaging technique can be used as an adjunct following mammography and/or ultrasound exams to localize a known or suspected lesion. Affirm Contrast Biopsy is intended for patients recommended for biopsy who have had a suspicious finding on previous contrast enhanced imaging or have lesions that may be occult under other modalities.

2.4 Device Procedure(s)/Training

Prior to use in clinical procedures, clinical site staff (e.g. technologists and radiologists) will be trained by a Hologic representative on the use of the devices and software (according to the Instructions for Use). This training will cover quality control procedures as well as training on the equipment. The sites selected for this study have previous experience with diagnostic imaging using the I-View software and performing breast biopsies using the Affirm Upright Breast Biopsy System.

3. POTENTIAL RISK/BENEFIT

3.1 Potential Clinical Benefit

The benefit of the device is to allow visualization and biopsy of suspicious lesions that may otherwise be occult or difficult to confidently target using other modalities. The main risks are the additional radiation dose and exposure to contrast agents.

The radiation dose is approximately 25% greater than performing FFDM stereotactic biopsy, and per exposure would be about the same as the reference device operating in 2D contrast enhanced imaging mode.

The exposure of the patient to the iodinated contrast agent presents another risk. Although the probability of occurrence is remote, the most significant additional risk to a patient during a contrast enhanced biopsy procedure relative to a stereotactic biopsy is an allergic reaction to the injected contrast agent which could potentially result in a life threatening aphylactic reaction. Recent estimates suggest that the rate of acute adverse events for low-osmolar contrast agents is approximately 0.2%–0.7%, with a severe acute reactions being approximately 0.04%. This risk is mitigated via procedural guidelines set up in hospitals which cover training, pre-screening of patients' kidney function (i.e.; glomerular filtration rate or GFR), and appropriate acute care readiness (e.g., "crash carts"), as may be expected to be in place for the reference device as well.

Furthermore, if the patient has had previous exposure to iodinated contrast agents safely with no adverse reaction, such as a contrast-enhanced digital mammography exam, then this risk will be additionally reduced. These additional radiation and contrast agent risks are therefore likely outweighed by the benefits of the device for patients recommended for biopsy who have had a suspicious finding on previous contrast enhanced imaging or have lesions that may be occult under other modalities.

The results from this study could help future subjects undergoing CEDM guided biopsy.

Subjects will still undergo a standard of care breast biopsy procedure (i.e. MRI) if they choose not to participate in this study.

3.2 Anticipated Adverse Device Effects

Common risks associated with the use of any commercial biopsy system:

- Bruising and swelling of the breast
- Infection or bleeding at the biopsy site
- Scar on the skin , depending on how much tissue is removed and how the breast heals
- Excessive pain following the procedure at the biopsy site.

  Although the probability of occurrence is remote, the most significant risk to a patient during a CEB procedure is an allergic reaction to the injected contrast agent which could potentially result in a life threatening anaphylactic reaction. This risk is mitigated via procedural guidelines set up in hospitals which cover training, pre-screening of patients' kidney function, and appropriate acute care readiness (e.g., "crash carts").

NOTE: To be eligible for participation in this study, the subject will have already undergone a previous contrast enhanced imaging exam which had identified a suspicious lesion and have been recommended to have a breast biopsy.

3.3 Risk Benefit Rationale

This clinical study is justified because Hologic and the clinical investigators believe that the potential benefits outweigh the potential risks of study participation.

4. STUDY DESIGN

4.1 Study Objectives

The objective of this study is to collect user and subject feedback on the design, use and operation of Affirm Contrast Biopsy.

4.2 Primary Endpoint

The primary endpoint of this study is to measure technical success and potential product failure mode rates of the system.

4.3 Secondary Endpoint

The secondary endpoint of this study is to obtain de-identified mammography and biopsy core sample images acquired using Affirm Contrast Biopsy.

4.4 Study Design

This is a post-market, multi-site, user and subject feedback study.

After obtaining informed consent, subjects will be considered enrolled once subject completes required pre-procedure testing (as applicable) and can proceed to the study procedure. If the subject is no longer recommended for the biopsy due to pre-procedure testing result, then the subject would be considered a screen failure. Once a subject has completed the Affirm Contrast Biopsy procedure, their direct participation in the study is concluded. There are no follow-up visits required for participation in this study.

Case Report Forms related to procedural data and surveys have been created in order to collect feedback from the radiologists, technologists, and subjects after each procedure using Affirm Contrast Biopsy. The surveys include questions that relate to the feel and aesthetic of the product as well as the performance of Affirm Contrast Biopsy.

4.5 Study Outcomes

Clinical data and the survey scores from radiologists, technologists, and subjects obtained directly after using Affirm Contrast Biopsy will be reviewed for overall performance.

4.6 Schedule of Assessment(s)

Table 1 – Schedule of Assessments

Assessment	Baseline	Procedure
Informed Consent	X	
Medical History*	X	
Procedure*		X
Questionnaires**		X
Adverse Event Evaluation	X	X

***Per standard-of-care
**To be completed by radiologist, technologist, and subjects

4.7 Subjects

This study will recruit up to 90 females 40 years of age or older with suspicious findings seen on prior contrast enhanced imaging.

4.7.1 Inclusion Criteria

1) Females aged 40 years of age or older recommended for biopsy who have had a suspicious finding on previous contrast enhanced imaging or have lesions that may be occult under other modalities.
2) Subject is able to understand, read and sign the study specific informed consent form after the nature of the study has been fully explained to them.

4.7.2 Exclusion Criteria

1) Subjects who require a Legally Authorized Representative (LAR) for Informed Consent.
2) Subjects who, based on the physician's judgement, may be at increased risk for complications associated with renal function, anticoagulant therapy, or bleeding disorders
3) Subjects who have had a previous allergic reaction to IV contrast agent

4.7.3 Informed Consent and Enrollment Procedures

Informed consent shall be obtained in writing from the subject and the process shall be documented before any procedure specific to the clinical study is performed

The general process for obtaining informed consent shall:

- ensure that the Principal Investigator or their authorized designee conducts the informed consent process;
- include all aspects of the clinical study that are relevant to the subject's decision to participate throughout the clinical study;
- avoid any coercion or undue improper influence on, or inducement of, the subjects to participate;
- not waive or appear to waive the subject's legal rights;
- use native non-technical language that is understandable to the subject;
- provide time for the subject to read and understand the informed consent form and to consider participation in the clinical study;
- include personally dated signatures of the subject and the principal investigator or an authorized designee responsible for conducting the informed consent process;
- provide the subject with a copy of the signed and dated informed consent form and any other written information; and,
- ensure the subject is aware that the de-identified case report forms and images are being sent to Hologic, Inc.

Upon signing the Informed Consent Form, the subject is considered enrolled in the study and will count towards the site's enrollment numbers.

4.7.4 Subject Withdrawal/Discontinuation

A subject will be discontinued from participation in the study if:

- The investigator feels that the subject can no longer fully comply with the requirements of the study or if any of the study procedures would not be in the best interest of the subject.
- The subject wishes to withdraw their consent for participation in the study.

5. STUDY PROCEDURES

5.1 Safety Events/Device Assessment

5.1.1 Adverse Events

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons whether or not related to the study medical device. Each AE is considered either anticipated or unanticipated as described below. The site is required to report all complications and adverse events, device related or not, to Hologic, Inc.

The time-period for the assessment of the occurrence of an AE will begin at the time of consent until the subject has left the breast care clinic/hospital and will be based on changes in the subject's physical examination, laboratory results and/or signs and symptoms. AEs are to be monitored until they are resolved or clearly determined to be a stable or chronic condition or due to an intercurrent illness. Medical care will be provided, as defined in the informed consent form, for any AE related to study participation.

Subjects who experience any untoward after effects are instructed to contact their Investigator or coordinator immediately. The Investigator must determine both the severity of the AE and the event's relationship to the breast biopsy system.

AE Severity Classification: Severity will be defined according to the following criteria:

- **Mild** – Awareness of event, but easily tolerated
- **Moderate** – Discomfort enough to cause some interference with activities of daily living (ADL).
- **Severe** – Incapacitating, with an inability to perform activities of daily living (ADL).

Life threatening events, events where the subject was at risk of death, are serious AEs and must be reported in accordance with the procedures and timelines in this protocol.

AE Relationship Classification: Relationship to study device & procedure use will be determined as follows:

- **Not Related** – relationship to the device or procedures can be excluded when:
    - The event is not a known side effect of the product category the device belongs to or of similar devices and procedures.
    - The event has no temporal relationship with the use of the device or the procedures.
    - The event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible.
    - The discontinuation of the medical device application or the reduction of the level of activation/exposure-when clinical feasible-and reintroduction of its use (or increase of the level of activation/exposure), does not impact the event.
    - The event involves a body-site, or an organ not expected to be affected by the device or procedure.
    - The event can be attributed to another cause (e.g. and underlying or concurrent illness/clinical condition, an effect or another device, drug, treatment or other risk factors).
    - The event does not depend on a false result given by the study device used for diagnosis when applicable.
    - Harms to the subject are not clearly due to use error.
    - In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.
- **Unlikely** – The relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
- **Possible** – The relationship with the use of the device is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/clinical condition/or and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.
- **Probable** – the relationship with the use of the study device seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.
- **Causal Relationship** – the serious event is associated with the device or with the procedures beyond reasonable doubt when:
    - The event is a known side effect or the product category the device belongs to or of similar devices and procedures
    - The event has a temporal relationship with the device application/use or procedures
    - The event involves the entire body, body-site or organ that:

- The device or procedures are applied to
- The device or procedures have an effect on
- The serious event follows a known response pattern to the medical device (if the response pattern is previously known)
- The discontinuation of the medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the serious event (when clinically feasible)
- Other possible causes (e.g. an underlying or concurrent illness/clinical condition or/and an effect or another device, drug or treatment) have been adequately ruled out
- Harm to the subject is due to error in use
- The event depends on a false result given by the device used for diagnosis, when applicable
- In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and serious event

AE Outcome Classification: Outcome of the event will be defined according to the following:

- **Resolved** – The event is resolved and is no longer present
- **Not resolved** – The event has not yet been resolved
- **Resolved with sequelae** – The event has resolved, but with an after affect possibly due to disease, injury, treatment or procedure
- **Fatal** – The event resulted in subject death

5.1.2 Serious Adverse Events (SAEs)

A SAE is any adverse event that:

- Led to death
- Let to a serious deterioration in heath that either:
  - Resulted in a life-threatening illness or injury, or
  - Resulted in a permanent impairment of a body structure or a body function, or
  - Required in-patient hospitalization or prolongation or existing hospitalization or
  - Resulted in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or body function
- Led to fetal distress, fetal death or a congenital abnormality or birth defect

5.1.3 Adverse Device Effect

An AE, which in the judgement of the Investigator, results from use of the study device.

5.1.4 Anticipated AEs/Adverse Device Effects

See section 3.2 above.

5.1.5 Unanticipated Adverse Device Effect

An Unanticipated Adverse Device Effect (UADE) is a serious adverse device effect, which by its nature, incidence, severity or outcome has not been identified, in the current version of the risk analysis report.

5.2 Reporting Procedures

5.2.1 Investigator Reporting

The Principal Investigator at each participating center is ultimately responsible for reporting applicable AEs to Hologic. Adverse events must be reported to Hologic (via entry in Electronic Data Capture (EDC) system) within 72 hours of occurrence. If the EDC system is not available, notification of adverse events can be communicated by other means (e.g. email, phone call, etc.). Serious adverse events must be reported to Hologic within 24 hours of occurrence.

The information to be reported on the AE case report form should include the start date of the AE, treatment, resolution, and assessment of both the seriousness, severity and the relationship to the device. The Investigator should report AEs to the IRB as required by the IRB's reporting requirements.

If there is a device malfunction or other observation (deficiency), the Investigator should notify Hologic within 72 hours of occurrence (via entry in EDC system). If the EDC system is not available, notification of adverse events can be communicated by other means (e.g. email, phone call, etc.) The investigator will indicate if the device malfunction or other observation resulted in an AE, and indicate if complications are related to the device, procedure or underlying disease.

In the event of a suspected observation or device problem, a field engineer may be dispatched to the site to resolve the problem. If the field engineer cannot resolve the problem, the device may be returned for analysis.

6. STUDY MONITORING

Representatives of Hologic (or designee) will verify subject informed consent/data and ensure compliance with clinical protocol, study monitoring plan, and any other study requirements, according to the guidelines set forth in the applicable monitoring Standard Operating Procedures (SOP) and ISO 14155 guidelines to be utilized for the study. As applicable, remote monitoring may be conducted according to the study monitoring plan.

6.1 Monitor Training

Hologic and/or designated monitors will be trained appropriately to monitor study progress as defined in the study monitoring plan.

6.2 Site/Investigator Training

Hologic and/or designee will be responsible for providing training to the Investigator and appropriate clinical site personnel as defined in the study monitoring plan.

6.3 Site Monitoring

Hologic and/or designee will conduct periodic compliance assessments at the study site(s) according to the study monitoring plan. Hologic and/or designee will request access to all study records including source documentation for inspection during monitoring visits. The Investigator and research coordinator must be available to respond to reasonable requests and queries made during the compliance assessment process.

6.4 Regulatory Agency Inspection

In the event that an investigator is contacted by a regulatory agency regarding this study, the Investigator will notify Hologic or its designee immediately (within 24 hours). The Investigator and research coordinator must be available to respond to reasonable requests and queries made during the inspection process. The investigator must provide Hologic or designee with copies of all correspondence that may affect review of the current study (e.g., Form FDA 483, Inspectional Observations and Warning Letters). Hologic may provide needed assistance in responding to regulatory audits.

7. STATISTICAL CONSIDERATIONS

A sample size of minimum 60 procedures was determined to achieve a 92% power to detect a non-inferiority proportion (P0) of 0.875 (87.5%, or 7 out 8 exams successful) using a one-sided exact test with a significance level (alpha) of 0.025 assuming a technical success rate of 98.3% (59 of 60 procedures successful) for procedures using the redesigned system. This sample size can be achieved through a multi-institutional study of up to 3 clinical study sites. For reference, with 60 subjects, a 100% technical success rate would result in a binomial exact 95% confidence interval of 94%-100%.

8. DATA HANDLING AND RECORD KEEPING

Each participating site will maintain appropriate medical and research records for this study, in compliance with regulatory and institutional requirements for the protection and confidentiality of subjects. As part of participating in this study, the site will permit authorized representatives of Hologic, Hologic's designee, and regulatory agencies to examine and copy de-identified study related clinical records and source data for the purposes of quality assurance reviews, audits, and evaluation of the study safety and progress.

Source data are all information, original records of clinical findings, observations, or other activities such as questionnaires and investigator assessments in a study necessary for the reconstruction and evaluation of the study.

The investigator is responsible to ensure the accuracy, completeness, legibility, traceability and timeliness of the data reported. All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. Dark ink is required to ensure clarity or reproduced copies. When making changes or corrections, cross out the original entry with a single line, and initial and date the change. Do not erase, overwrite, or use correction fluid or tape on the original.

Images will be anonymized before being collected by Hologic. Through this process, all PHI is removed from the images and the subject ID (unique clinical study ID) will remain to provide the linkage between the images and the applicable clinical study data.

8.1 Data Management Procedures/Electronic Data Capture System

This study will obtain informed consent and survey data for up to 90subjects. Monitoring will be conducted to ensure subject consent was obtained and data was accurately collected and recorded. Paper forms will be used to collect survey responses, which will serve as source data for the details of the procedure, and recorded in the applicable eCRFs in the EDC. Source documentation related to satisfaction of the inclusion/exclusion criteria should be maintained in the subject's study record and recorded in the applicable eCRFs within the EDC system.

Surveys will be reviewed for missing question responses/discordant answers and will be addressed as soon as missing points are noted.

Hologic will outsource the development, verification, and validation of the EDC system for the study. Sites will be trained on the use and responsible to enter data into the EDC System. The process details will be outlined in the study Data Management Plan.

8.2 Data Retention

Study documentation should be retained as required by local regulations. No records will be destroyed without the written consent of Hologic. It is the responsibility of Hologic to inform the investigator when these documents no longer need to be retained.

8.3 Investigator Records

Investigators will maintain completed, accurate and current study records. Records shall be maintained during the clinical study and for at least six years after the later of the date on which the study is terminated or completed, or the date the records are no longer required to support FDA clearance of the device. Investigator records shall include the following materials:

- **Correspondence**: Documentation of all verbal and written correspondence with Hologic, the Clinical Monitor, IRBs, the independent physician adjudicator, and other investigators regarding this clinical study or any subject enrolled therein.
- **Subject Records**: Signed informed consent forms, source document worksheets, and supporting documents and records of exposure of each subject to the device. Informed consent must comply with local regulations and ISO14155.
- **Clinical Study Plan/Protocol**: A current copy of the Clinical Study Protocol including Instructions for Use of the System and blank case report forms.
- **Institutional Review Board (IRB) Information**: All information pertaining to IRB review and approval of this clinical study including a copy of the IRB letter approving the clinical study, a blank informed consent form approved by the IRB, and certification from the IRB Chairman that the IRB complies with FDA and IRB regulations/regulatory body regulations.
- **Investigator Agreements**: All investigators (PI and Sub-I's) should provide and retain signed Protocol Signature Page/Investigator Agreement, CV (signed and dated within 2 years), copy of current Medical License and a completed Financial Disclosure Form.
- **Other**: Delegation of Authority Logs, Device Accountability Logs and supporting documentation, Subject ID Log and any other records that may be required by applicable state or federal laws.

8.4 Investigator Reports

The Investigator will prepare and submit the following reports and shall notify Hologic:

- **MDV**: Medical Device Vigilance Reporting of all events related to the device or device malfunctions.
- **Withdrawal of IRB Approval**: Withdrawal of approval shall be reported to Hologic or designee within five working days. The Investigator will provide a written report of the reason(s) approval was withdrawn.
- **Progress Reports**: Hologic shall provide to the Investigator progress reports on the completion of data as necessary. In addition, the Investigator may be asked to submit progress reports to Hologic or designee and the reviewing IRB that include the number of study subjects, a summary of follow-up data and complications and general description of the study progress.
- **Final Report**: Hologic shall provide to the Investigator a final report within three months of termination of completion of the study or that Investigator's participation in the study, to provide to the IRB.
- **Other Reports**: Upon the request of Regulatory Agency/FDA, the reviewing IRB, of Hologic or designee, the Investigator will provide accurate and timely information about any aspect of the clinical study.

9. QUALITY CONTROL AND ASSURANCE

9.1 Site and Investigator Selection

Hologic selects qualified investigators with appropriate experience at health care facilities with adequate resources to participate in this study. Study sites will be selected using combined current assessments of site and investigator qualifications.

9.2 Protocol Deviations

A protocol deviation is a failure to comply with the requirements specified within this clinical study protocol. An example of a protocol deviation may include enrollment of a study subject who does not meet all the inclusion/exclusion criteria specified in the protocol. Each investigator shall conduct this clinical study in accordance with this clinical study protocol, regulatory body regulations, ISO guidelines and any conditions of approval imposed by their IRB.

All deviations are reviewed and assessed for their impact on subject safety by Hologic or designee. The PI and study staff are responsible for knowing and adhering to their IRB reporting requirements.

The protocol deviations for this protocol consist of, but are not limited to the following:

- Failure to obtain subject's informed consent prior to any study-related activities;

- Failure to report procedure/device related AEs according to protocol requirements.

In the event of any deviation from the protocol, the Investigator will be notified of the site's non-compliance. Corrective actions will be required, if necessary. Continued protocol deviations, despite re-education of the study site personnel or persistent protocol deviations, may result in termination of the site's study participation. Subjects enrolled at these sites will continue to be followed per the clinical protocol.

9.3 Protocol Deviation Process

Investigators must report protocol deviations to Hologic within 72 business hours of the site's knowledge of the deviation by either entry of data into the EDC system or contacting Hologic and/or designee. Any protocol deviations that affect the rights, safety or well-being of the subject or the scientific integrity of the clinical study must be reported within 24 hours to Hologic and the IRB, if required by the IRB or national regulations.

9.4 Study Audit(s)

If required, the auditing of clinical study systems shall be conducted in accordance with Hologic's written procedures or specific plan on what to audit, how to audit and the form and content of audit reports. The audit results shall be documented and communicated to relevant parties, if applicable.

10. ETHICS/PROTECTION OF HUMAN SUBJECTS

10.1 Statements of Compliance

This clinical study shall be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, GCP/ICH Guidelines, International Standard Organization (ISO 14155:2011) and any regional or national regulations.

The clinical study shall not begin until the required approval/favorable opinion from the IRB or regulatory authority have been obtained, if appropriate.

Any additional requirements imposed by the IRB or regulatory authority shall be followed.

10.2 Institutional Review Board (IRB)

Each participating institution must provide for the review and approval of this protocol and the associated informed consent documents by an appropriate IRB. Any amendments to the protocol or consent materials must also be approved before they are placed into use.

10.3 Informed Consent Process

Informed Consent is a process that is initiated prior to the individual agreeing to participate in the study and continues throughout the individual's study participation. Extensive discussion of risks and possible benefits of this study will be provided to the subjects and their families. Consent forms describing in detail the study procedures, and risks are given to the subject and written documentation of informed consent is required prior to the study procedure.

Consent forms will be IRB-approved, and the subject will be asked to read and review the document. Upon reviewing the document, the investigator (or designee will explain the research study to the subject and answer any questions that may arise. The subject will sign the informed consent document prior to any procedures being done specifically for the study. The subject should have the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate, unless study timeframes do not allow for such discussions.

The subject may withdraw consent at any time throughout the course of the study. A copy of the informed consent document must be given to the subject for their records. The rights and welfare of the subjects will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

10.3.1 New Information

If new information becomes available that can significantly affect a subject's future health, medical care or willingness to participate in the study; that information shall be provided to the affected subject(s) in written form. If relevant, all affected subjects shall be asked to confirm their continuing informed consent in writing.

10.4 Subject Confidentiality

All parties involved in the clinical study shall always observe confidentiality of data. All data shall be secured against unauthorized access and all subject image data is anonymized prior to collection by Hologic.

The privacy of each subject and confidentiality of her/his information shall be preserved in reports and when publishing any data. The Principal Investigator or institution shall provide direct access to source data during and after the clinical study for monitoring, audits, IRB review and regulatory authority inspections.

11. PROTOCOL AMENDMENTS

The Protocol, informed consent form, or other clinical study documents shall be amended as needed throughout the clinical study, and a justification statement shall be included with each amended section of a document. Proposed amendments to the Protocol shall be agreed upon between Hologic and the Principal Investigator. The amendments to the Protocol or informed consent form shall be reviewed and approved by, the IRB and regulatory authorities, as required. For non-substantial changes [e.g. minor logistical or administrative changes, change of monitor(s), telephone numbers, renewal of insurance] not affecting the rights, safety and well-being of human subjects or not related to the clinical study objectives or endpoints, a simple notification to the IRB and, where appropriate, regulatory authorities can be sufficient. The version number and date of amendments shall be documented.

12. TERMINATION OF STUDY OR STUDY SITE PARTICIPATION

Hologic may terminate the study at any time. If the study is terminated prior to the completion of expected enrollment for any reason, all participating centers will be notified within five working days.

Hologic reserves the right to terminate study site participation and remove appropriate study materials at any time. Specific instances that may precipitate such termination include but are not limited to the following:

- Failure to meet minimum subject enrollment requirements
- Failure to comply with the protocol specified procedures and documentation

The site Investigator may also discontinue study participation with suitable written notice to Hologic as outlined in the study agreement.

Name and Clinic Number

Approval Date:
Not to be used after:

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: A Prospective, Multi-site Clinical Study to Collect User Feedback using Affirm® Contrast Biopsy

IRB#: ADD NUMBER

Principal Investigator: ADD NAME

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this research is to collect user and subject feedback on the design, use and operation of Affirm Contrast Biopsy system.
What's Involved	Study participation involves a questionnaire regarding your opinion and satisfaction after a clinical breast biopsy procedure using the Affirm Contrast Biopsy system. We will collect and de-identify images during the procedure and images of your biopsy sample as well from the procedure. The visit will take about 1 hour.
Key Information	You will not be paid for taking part in this research. Your alternative is to not participate in this research study. You may choose to have the procedure that you were scheduled for, using another commercially available breast biopsy system or this system. The goal of the study is to gather information; you will not directly benefit from participation.

Approval Date:
Not to be used after:

Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep.

For purposes of this form, ADD SITE NAME refers to ADD SITE NAME in ADD CITY, ADD STATE; and all owned and affiliated clinics, hospitals, and entities.

Name and Clinic Number

Approval Date:
Not to be used after:

Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** ADD NAME **Phone:** ADD NUMBER **Study Team Contact:** Study Coordinator **Phone:** ADD NUMBER **Institution Name and Address:** ADD INFORMATION
▪ Rights of a research participant	**ADD NAME of Institutional Review Board (IRB) Phone:** ADD NUMBER **Toll-Free:** ADD NUMBER
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Subject Advocate (RSA) (The RSA is independent of the Study Team) Phone:** ADD NUMBER **Toll-Free:** ADD NUMBER **E-mail:** ADD EMAIL
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** ADD NUMBER

Name and Clinic Number

Approval Date:
Not to be used after:

Why are you being asked to take part in this research study?

You are being asked to take part in this research study because you are having a breast biopsy procedure.

About 60 people will take part in this research study. The plan is to have about 30 people take part in this study at ADD SITE NAME.

Why is this research study being done?

The purpose of this research is to collect user and subject feedback on the design, use and operation of Affirm Contrast Biopsy.

This system is designed to allow the accurate location of lesions in the breast with enhanced imaging. The Affirm Contrast Biopsy is intended to provide guidance for interventional purposes such as biopsy. It may allow for identification of lesions that are difficult to see using other biopsy systems.

Information you should know

Who is Funding the Study?
Hologic, Inc. is funding the study. Hologic, Inc. will pay the institution to cover costs related to running the study.

Information Regarding Conflict of Interest:
Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation. If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

Name and Clinic Number

Approval Date:
Not to be used after:

How long will you be in this research study?

You will be in the study until you are discharged at the conclusion of your breast biopsy procedure. The procedure normally takes about one hour. There are no required follow-up visits.

What will happen to you while you are in this research study?

The Affirm contrast biopsy system will use contrast which might not be used in other types of biopsies. The contrast agent will be delivered to your system through IV injection.

If you agree to be in the study, you will be asked to participate in the following:

- Sign this consent form
- Complete one general procedure of a breast biopsy, which is consistent with the clinician's direction/standard of care, with the Affirm® Contrast Biopsy
    - Iodinated contrast (a non-metallic element used to improve pictures inside the body) will be used. It allows the radiologist to determine normal from abnormal conditions.
- Permit de-identified case report form data and images from your Affirm Contrast Biopsy procedure and images of your breast biopsy sample to be sent to Hologic. You will complete a patient questionnaire after the biopsy procedure.
    - The questionnaire asks about your opinion and satisfaction regarding the procedure. We hope that you will answer all the questions, but you can skip any questions you don't want to answer. The questionnaire will take about 5 minutes or less to complete.
- Report any adverse events including: bruising, bleeding, altered breast appearance, swelling or excessive pain following the procedure at the biopsy site prior to being discharged from the biopsy procedure.

If you take part in this research, you will be responsible to participate in the activities listed above.

Tests done as part of this study are performed regardless of whether or not you are participating in the study. The results are part of your clinical care and the results are important for research, too. The results of tests done with your information will be provided to you.

If the results indicate further medical testing or care is needed, those costs will be billed to you or your insurance.

What are the possible risks or discomforts from being in this research study?

Your doctor will discuss the risks of a stereotactic mammography as these tests and procedures are part of your standard clinical care.

The chance of having an allergic reaction to the injected contrast agent is low, but also the most significant risk to you during the Affirm Contrast Biopsy procedure. It could potentially result in a life-threatening allergic reaction. This risk is small since standard guidelines are set up in hospitals to be prepared if an event like this were to occur. These guidelines can include screening patients who may have had an allergic reaction in the past, review patient's kidney function, and be prepared to provide specific care if this event should occur. If you have had procedures using iodinated contrast agents done safely before, with no adverse reaction, then your chance of having an allergic reaction is already reduced.

The most common risks or discomforts associated with the use of any commercial biopsy system are limited to the region surrounding the biopsy site and include:

- Bruising and swelling of the breast.
- Infection or bleeding at the biopsy site.
- Scar on the skin, depending on how much tissue is removed and how the breast heals.
- Excessive pain following the procedure at the biopsy site.

There may be unknown risks to taking part in this study. This may include hurting a pregnancy or fetus in unknown ways. These may be minor or so severe as to cause death. It's important to speak with you doctor if you are or may be pregnant.

Your doctor will discuss the risks of mammography with contrast biopsy as these tests and procedures are part of your standard clinical care.

As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

Approval Date:
Not to be used after:

Are there reasons you might leave this research study early?

If you decide to leave the research, contact the Principal Investigator. You must notify the study him/her in writing. You will not be penalized or suffer a loss of benefits if you decide to leave the research study early. If you withdraw your permission, you will not be able to stay in this study.

You may decide to stop at any time. You should tell the Principal Investigator if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the Principal Investigator, the study sponsor, Hologic, Inc, or ADD SITE NAME may stop you from taking part in this study at any time:

- if it is in your best interest,
- if you don't follow the study procedures,
- if the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. ADD SITE NAME will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Approval Date:
Not to be used after:

Who will pay for the treatment of research related injuries:
The Sponsor Hologic, Inc. will offer to pay for medical treatment of research-related injuries directly resulting from the proper application of the study device/procedure. The Sponsor may not offer to pay for several reasons. The Sponsor may not offer to pay if the Sponsor concludes the injury happened because you did not follow the study directions, or the injury resulted from your actions. The Sponsor may not consider the worsening of an existing health condition to be a research-related injury. In the case of injury resulting from your participation in this study, you do not lose any of your legal rights to seek payment by signing this form. Contact the Principal Investigator, who can help you obtain this reimbursement.

If the Sponsor will pay for research-related injury costs and you are eligible for Medicare, federal law requires the Sponsor to inform the Centers for Medicare & Medicaid Services (the agency responsible for the Medicare program). Information, such as your name, date of birth, sex, and Medicare ID number (if you have one), may need to be shared with the Centers for Medicare & Medicaid Services.

What are the possible benefits from being in this research study?

You won't benefit from taking part in this research study. Others having a contrast biopsy may benefit in the future from what we learn in this research study.

What alternative do you have if you choose not to participate in this research study?

This study is only being done to gather information. You may choose not to take part in this study and proceed with a biopsy that is done standard of care.

What tests or procedures will you need to pay for if you take part in this research study?

You and/or your insurance will need to pay for the breast biopsy as it is considered standard of care. Standard of care means you would have this procedure done regardless of whether or not you were part of the study. Before you take part in this study, you should call your insurer to

find out if the cost of these tests and/or procedures will be covered. You will have to pay for any costs not covered by your insurance.

Taking part in this research study may lead to added costs to you. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance company to see what services will be covered and what you will be responsible to pay.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

You won't be paid for taking part in this study.

Will your information or samples be used for future research?

Your information collected for this study will not be used or shared for future research studies even if the identifiable information such as your name, ADD SITE NAME number or date of birth is removed.

How will your privacy and the confidentiality of your records be protected?

ADD SITE NAME is committed to protecting the confidentiality of information obtained about you in connection with this research study.

Your information will be safeguarded by coding data with numbers, storage of research materials in double locked cabinets, and password protected data on a computer.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this

research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to ADD SITE NAME.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- ADD SITE NAME research staff involved in this study.
- Other ADD SITE NAME staff involved in your clinical care.
- The sponsor(s) of this study and the people or groups hired by the sponsor(s) to help perform this research.
- The ADD SITE NAME Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you but does not include information that directly identifies you. This code will be used if your study information is sent outside of ADD SITE NAME. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed byADD SITE NAME may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at ADD SITE NAME or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from ADD SITE NAME.

Name and Clinic Number

Approval Date:
Not to be used after:

Is your health information protected after it has been shared with others?

ADD SITE NAME asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside ADD SITE NAME, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with ADD SITE NAME.

If you cancel your permission for ADD SITE NAME to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for ADD SITE NAME to use or share your health information at any time by sending a letter to the address below:

ADD SITE NAME
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
ADD ADDRESS

Alternatively, you may cancel your permission by emailing the ADD SITE NAME Research Subject Advocate at: ADD EMAIL.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for ADD SITE NAME to use and share your health information lasts until the end of this study, unless you cancel it. The study does not end until all data has been collected, checked

Approval Date:
Not to be used after:

(or audited), analyzed, and reported. Because research is an ongoing process, we cannot give you an exact date when the study will end. Sometimes this can be years after your study visits and/or activities have ended.

There is no expiration or end date related to the Sponsor's use of your health information received from ADD SITE NAME as part of this study.

Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature