STREAMLoc- Streamlined Localization using SCOUT® at Biopsy: An analysis of process improvement, cost savings and enhanced patient experience.

STREAMLoc SCOUT Registry

Registry Plan

Protocol Number: SCOUT2021

Sponsor:
Merit Medical Canada Ltd.
1 Valleywood Drive,
Unit 4 and 5
Markham, ON L3R 5L9

Coordinating Investigators:
Dr. Christine Desbiens
CHU de Québec, Hôpital St-Sacrement

Dr. Isabelle Trop
Centre hospitalier de l'Université de Montréal (CHUM)

Version 3.0 (CA)
21 February 2023
(amendment to V2.0, 16JUN2021)

CONFIDENTIAL

Protocol Signature Page – Site Principal Investigator

Protocol Title: STREAMLoc- Streamlined Localization using SCOUT® at Biopsy: An analysis of process improvement, cost savings and enhanced patient experience.

Protocol number: SCOUT2021
Protocol version: v3.0 (CA)
Protocol version date: 21FEB2023

I have read this protocol, amendments (if any) and appendices, and agree to adhere to the requirements therein.
I will provide copies of this Protocol and all pertinent information to the study personnel under my supervision and to the Research Ethics Board/ Institutional Review Board. I will discuss this material with them and ensure they are fully informed regarding the device and the conduct of the study.

I will conduct the study in accordance with the protocol and the International Conference on Harmonization Good Clinical Practice (ICH GCP), ISO 14155:2020, national and local laws of the appropriate regulatory authorities, and the Declaration of Helsinki, and 21 CFR Parts 50, 54, and 56 (as applicable).

I, the undersigned, have read and approved the protocol specified above, and agree upon the contents:

Site Name_____ Principal Investigator Name _____

Principal Investigator (signature)_____ Date _____

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List of Abbreviations

ADE	Adverse Device Effect
AE	Adverse Event
BCS	Breast conserving surgery
BI-RADS	Breast Imaging, Reporting and Data System
CAPA	Corrective and preventive actions
CADTH	Canadian Agency for Drugs and Technologies in Health
CFR	Code of Federal Regulations
CIP	Clinical Investigation Plan
CRF	Case Report Form
CV	Curriculum vitae
DCIS	Ductal carcinoma in situ
DD	Device Deficiency
eCRF	Electronic Case Report Form
EMR	Electronic Medical Record
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICH	International Conference on Harmonization
ICF	Informed Consent Form
ICMJE	International Committee of Medical Journal Editors
IFU	Instructions For Use
ISO	International Organization of Standardization
IR	Infrared
IRB	Institutional Review Board
ITT	Intention to treat
MRI	Magnetic Resonance Imaging
N	Number (typically refers to participants)
OR	Operating room
PP	Per protocol
REB	Research Ethics Board
RSL	Radioactive Seed Localization
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAS	Statistical Analysis System
SD	Standard Deviation
SDV	Source Data Verification
SM	Safety margins
STX	Stereotaxis
TOMO	Tomosynthesis
WL	Wire localization

KEY ROLES AND CONTACT INFORMATION

Coordinating Investigator:	Dr. C. Desbiens, Surgeon
Study Site:	CHU de Québec, Hôpital St-Sacrement
Coordinating Investigator:	Dr. I. Trop, Radiologist
Study Site:	CHUM
Sponsor:	Merit Medical Canada

AMENDMENT HISTORY

Protocol Version No.	Date Issued	Author(s) of Changes	Details of Changes Made
v1	5MAR2021	Linnea Aasen-Johnston	Original; pre-market registry
V2	16JUN2021	Linnea Aasen-Johnston	Change to post-market registry
V2.0 (US)	20SEP2022	Linnea Aasen-Johnston / Vicky Brunk	Country specific amendment for US sites only
V3.0 (CA)	21FEB2023	Linnea Aasen-Johnston	Canadian specific amendment to include US sites, add physician adjudication, include additional device models

REGISTRY SYNOPSIS

Sponsor:	Merit Medical Canada Ltd. 1 Valleywood Drive, Unit 4 and 5 Markham, ON L3R 5L9
Study Title:	**Streamlined Localization using SCOUT® at Biopsy: An analysis of process improvement, cost savings and enhanced patient experience.**
Short Title / Study ID:	**STREAMLoc**
Protocol Version and Date:	**Version 3.0 (CA) 21FEVB2023**
Trial Registration:	NCT04815291
Phase of Development:	Post-market registry (Canada & US)

Background and Rationale:	SCOUT® has been identified as an alternative to other localization options, providing maximum flexibility in patient visit scheduling. In the COVID-19 era, it would follow that improved efficiencies, leading to a decrease in patient visits to the breast center, as well as reduced contact with the technicians prior to surgery, is the preferred treatment option for patient and clinician safety and reduced logistical burden. Taveh et al.[1] showed that by deploying the SCOUT® Reflector at the time of tumor biopsy, the need for a second procedure to localize the tumor was eliminated, thus reducing the number of patient visits and potential COVID- 19 exposure. The authors demonstrated that wireless localization using the SCOUT® System was an effective and time-efficient alternative to wire localization, resulting in excellent physician and patient acceptance. Parkinson et al.[2] found insertion of the SCOUT®Reflector at biopsy resulted in at least one (1) less patient visit to the breast center. This post-market registry is intended to assess the utility of SCOUT® in the Canadian public and US healthcare systems with fixed resources and a conservative approach to patient and clinician exposure to harm (i.e., radiation, COVID-19 exposure, patient emotional trauma). By assessing the utility of reflector insertion at the time of biopsy, this study will be able to measure the impact on patient visits to the breast center for invasive procedures between biopsy and surgery, and quantify this value to the public healthcare system. The efficacy and safety of this system will be further assessed, as well as the acceptance of clinicians and patients.

Objective:	*Primary (Efficiency Endpoint):* To demonstrate the utility of the SCOUT® Surgical Guidance system to improve workflow and efficiency in centers treating breast cancer. *Secondary*: To further evaluate the safety and performance of the SCOUT® Surgical Guidance system in 500 consented BI-RADS 4C/5 patients according to the instructions for use.
Endpoints:	*Primary (Efficiency Endpoint):* The number of patient visits to the breast center for invasive procedures from the time of biopsy to surgery. *Secondary:* 1. Device success: percent successful localization, detection and retrieval; 2. Device safety: rate of device-related adverse events; 3. Procedural success: absence of close margins (DCIS: <2mm), positive margins (tumor on ink) or requirement for re-excision. 4. Duration (days) from assessment to surgery and biopsy to surgery; 5. Radiologist assessment: ease of placement; ability to position reflector in desired location; scheduling flexibility; visibility on ultrasound/ mammography (immediate and late); artifact (Tomo/MRI if applicable). 6. Surgeon assessment: ease of detection; ease of device retrieval. 7. Participant satisfaction questionnaire: anxiety; convenience; pain; overall experience compared to expectation 8. Process improvement with implementation of same-day biopsy and SCOUT® Reflector placement.
Study Design:	A single-arm, multicenter, non-randomized cohort study. The registry is divided into three periods: 1. Inclusion Period: from registry eligibility screening until reflector insertion; 2. Device Period: from reflector insertion at biopsy to removal at surgery; 3. Outcomes Period: from completion of surgery to pathology report of outcomes.
Inclusion / Exclusion Criteria:	**Inclusion Criteria:** 1. Woman ≥18 years and <80 years of age; 2. Classified as BI-RADS 4C or 5; 3. Lesion depth is ≤6 cm from skin surface; 4. Non-palpable lesions; 5. Informed consent obtained. **Exclusion Criteria:** 1. Multicentric breast cancer; 2. Pregnant or lactating patient; 3. Known or suspected nickel-titanium allergy.

Study Product / Intervention:	SCOUT® Reflector, SCOUT® Console, SCOUT® Handpiece -all components of the SCOUT® Surgical Guidance System.
Control Intervention (if applicable):	The primary endpoint of this cohort will be compared to historical standard of care.
Number of Participants:	Five hundred (500) BI-RADS 4C/5 patients undergoing biopsy of a breast lesion at a participating study center.
Study Duration:	12 -18 months
Study Schedule:	**Reflector Insertion**: Device (Reflector) will be inserted in eligible, consented participants at the time of biopsy as per the instructions for use. **Surgery:** Reflector will be detected and retrieved at the time of breast surgery. Reflector performance and safety will be assessed based on detection and retrieval success and the rate of adverse events. **Pathology report:** Results from the pathology report will be recorded. Procedural success defined as the absence of close margins (DCIS: <2mm), positive margins (tumor on ink) or requirement for re-excision. No post-operative participant follow-up will be required.

1. Study Purpose

The purpose of this post-market registry is to demonstrate the utility of the SCOUT® Surgical Guidance system to improve workflow and efficiency in Canadian and US centers treating breast cancer by reducing the number of patient visits for invasive procedures required from biopsy to surgery.

To further evaluate the safety and performance of the SCOUT® Surgical Guidance system in 500 consented Breast Imaging, Reporting and Data System (BI-RADS) 4C/5 patients according to the instructions for use (IFU).

Patient selection for biopsy will be performed according to current clinical practice at participating sites.

2. Background and Rationale

2.1 Breast Cancer: Clinical Background

Breast cancer continues to be a consequential disease posing a considerable burden on patients, families and the healthcare system. One in eight women are expected to develop breast cancer in their lifetime.[3,4] In Canada, it is estimated that 28,600 women will be diagnosed with breast cancer in 2022. In the United States (US), 281,550 new cases of breast cancer were estimated in 2021.[5]

Due to increased utilization of mammographic screening and improved imaging techniques, there has been a rapid increase in the detection of palpable and non-palpable breast lesions. This increased detection rate of non-palpable breast lesions has increased the need for imaging-guided localization before surgery. Localization plays an important role in conservative surgical excision, with or without neoadjuvant therapy.[6,7] The goal of breast conserving surgery (BCS) is to safely remove the target tissue with adequate surgical margins (SM), avoid unnecessary resection of healthy breast tissue, providing a good cosmetic outcome without compromising survival.[8] Re-excision rates in Canada have been previously reported as high as 23%[9] and in the US 22.6%.[10]

Currently lesions are classified based on the Breast Imaging, Reporting and Data System (BI-RADS, American College of Radiology). Lesion categorization provides an estimated risk of malignancy based on imaging findings. BI-RADS classification of 4C or 5 estimate risk of malignancy to be >50% and >95% respectively. These patients are considered highly likely to receive surgical intervention.[11]

Table 2. Risk of Breast Cancer.[a]

Indication	Risk of malignancy
BI-RADS 5	>95%
BI-RADS 4C	>50%-95%
BI-RADS 4B	>10%-50%
BI-RADS 4A	>2%-10%
New breast problem for diagnostic workup	2.5%-6.5%
BI-RADS 3	≤2%
High-risk screening	~1%
Intermediate risk screening	0.8%
Average risk screening	0.5%

Abbreviation: BI-RADS, Breast Imaging, Reporting & Data System.
[a]Breast biopsy of lesion: 30% to 40% overall risk of malignancy subdivided according to BI-RADS assessment.[46-48]

FIGURE 1: RISK OF BREAST CANCER: BI-RADS

2.2 Breast Cancer & Clinical Management

2.2.1 Wire Localization

The most common technique for pre-operative localization of breast lesions has historically been wire localization (WL). Under imaging guidance, and through a co-axial needle introducer, a thin 3-15 cm wire is guided through the skin to the lesion and the surgeon uses the wire to help guide the excision. This technique has several problematic features including: patient discomfort, vasovagal symptoms (in up to 7-10% of patients), wire rupture, wire migration or scheduling difficulties due to the necessity of prior-day or same-day insertion.

In response, wireless technologies have been developed to address the limitations of wire localization. Advantages of wireless devices include: avoiding wire dislodgement or migration, increased flexible with surgical scheduling, improved options for surgical access resulting in improved cosmesis.[8,12]

2.2.2 Radioactive Seed Localization

Radioactive seed localization (RSL) is an alternative to WL and was first described in 2001. RSL utilizes a small 5-mm titanium seed containing iodine-125 placed in the center of the breast lesion under ultrasound or mammographic guidance. The half- life of the I-125 seed is 59.4 days, and pre-operative localization can be performed several days before the surgical excision, which allows flexibility in scheduling operative procedures. A study reporting on RSL noted a mean time from RSL insertion to surgery of 4.0 $\pm$ 2.8 days (range 1-17 days).[13] Bloomquist et al.[14] reported a median duration of localization to surgery of 2 days (range 0-5 days). Importantly, the RSL cannot be placed in patients who may undergo neoadjuvant chemotherapy or patients whose surgery may be delayed more than 5 days. Therefore, it is not advisable to place it at the time of biopsy.

Overall, RSL has been reported as a more convenient and less painful option to WL[14] and has been purported to reduce operative time, increase surgeon and radiologist satisfaction and reduce excised tissue volume.[15] However, disadvantages include radiation exposure and related safety precautions. [7,8]

Zang et al.[12] performed a cost comparison analysis between RSL and WL and found that RSL was less costly than WL due to a reduction in operating room (OR) delays (RSL: WL=120 vs 254 min; $p < 0.001$) and fewer vasovagal reactions at insertion, allowing for more efficient use of radiology scheduling and shorter wait times for patients on their day of surgery.

2.2.3 SCOUT® Reflector

The SCOUT® System aids in the detection and excision of soft tissue lesions during various surgical procedures. The SCOUT® System is a sophisticated wide band radar-based technology. The technology consists of a Console, handheld Guide and the implantable Reflector. The Guide simultaneously transmits infrared (IR) light and Ultra-Wide Band Micro Impulse RADAR signal at 50 million pulses per second. IR light activates an electronic switch in the Reflector to create a unique, modulating signal. The Reflector "reflects" a unique RADAR ECHO back to the Guide. The Console receives the unique radar signal (Echo return), processes the data, and detects and locates the reflector in real-time based on the signal cadence. The SCOUT® Console provides an audible cadence signal and a visual representation of distance. During surgery, the surgeon uses the Guide, which emits pulses of radar and IR light. Upon the Guide contacting the skin, 50 million pulses per second are transmitted into the breast, allowing the system to directionally "lock in" on the exact location of the reflector within +/- 1mm of accuracy.

The SCOUT® Reflector is placed percutaneously at the time of or subsequent to biopsy to mark the lesion. Using imaging guidance (such as ultrasound, MRI or radiography) or aided by non-imaging guidance (SCOUT® System), the SCOUT® Reflector is located and surgically removed along with the target tissue. The SCOUT® System is required for the non-imaging detection and localization of the SCOUT® Reflector that has been inserted in a soft tissue biopsy site or a soft tissue site intended for surgical removal.

Studies comparing SCOUT® to RSL or WL have shown comparable clear margin rates and re-excision rates.[16,17,18]

Clinical investigation data has demonstrated the SCOUT® system is safe and effective for guiding the excision of palpable and non-palpable breast lesions and is a viable alternative to standard localization options.[18,19,20,21] Similar to RSL, SCOUT® allows flexibility in placing the reflector from any direction without impacting the surgical approach.[19] Further, use of SCOUT® has resulted in improved efficiencies in scheduling radiology and surgery independent of one another.[16,17,19] SCOUT® is an accurate, reliable method to localize and excise breast lesions with acceptable incidence of positive margins and re- excision rates.[18]

In a multisite study,[20] a surgeon survey on workflow including ability to start cases earlier, patient wait times and reduction in surgery schedule delays, the responses for SAVI SCOUT® were significantly better than WL.

2.3 Localization at Biopsy: Rationale for the Registry

The SCOUT® System has been identified as an alternative to other localization options, providing maximum flexibility in patient visit scheduling. In the COVID-19 era, it would follow that improved efficiencies, leading to a decrease in patient visits to the breast center, as well as reduced contact with the technician prior to surgery, is the preferred treatment option for patient and clinician safety and reduced logistical burden. Taveh et al.[1] showed that by deploying the SCOUT® Reflector at the time of tumor biopsy, the need for a second procedure to localize the tumor was eliminated, thus reducing the number of patient visits and potential COVID- 19 exposure. The authors demonstrated that wireless localization using the SCOUT® System is an effective and time-efficient alternative to WL, resulting in excellent physician and patient acceptance. Parkinson et al.[2] found insertion of the SCOUT® Reflector at biopsy resulted in at least one (1) less patient visit to the breast center. If the reflector is placed at the time of the diagnostic work-up, two (2) patient visits could be eliminated.

This post-market registry is intended to assess the utility of the SCOUT® System in the Canadian public and US healthcare system with fixed resources and a conservative approach to patient and clinician exposure to harm (i.e., radiation, COVID-19 exposure, patient emotional trauma). By assessing the utility of reflector insertion at the time of biopsy, this study will be able to measure the impact on patient visits to the breast center for invasive procedures between biopsy and surgery, and it will quantify this value to the healthcare system. The efficacy and safety of this system will be further assessed, as well as the acceptance of clinicians and patients.

3. Devices

3.1 Device Description and Indication

The SCOUT® Console, SCOUT® Guide, SCOUT® Handpiece and SCOUT® Reflector are components of the SCOUT® Surgical Guidance System (Merit Medical). This same system was previously marketed as the SAVI SCOUT® Surgical Guidance System. The SCOUT® Console is a medical device that provides control operations for detecting the presence of the SCOUT® Reflector within soft tissue during surgery. The SCOUT® Handpiece and SCOUT® Reflector are available separately. Inclusion of devices for use in this post-market registry are limited to those that are cleared/approved in the regions where the study is conducted.

The SCOUT® System employs micro-impulse radar and IR light technology to determine the location of the Reflector, which is placed into the soft tissue during a prior procedure. The Console provides the micro-impulse radar signal to the Handpiece along with power for the IR light sources. The Handpiece delivers the micro-impulse radar signal and IR light into the soft tissue and, in turn, receives signals reflected back from the Reflector. The Console processes the reflected radar signals to provide the surgeon with Reflector proximity and location information via audible and visual feedback.

The numeric display provides real-time distance between the Handpiece and Reflector. The audible feedback produced by the Console increases in cadence as Handpiece is placed in closer proximity to the Reflector. The Console provides a maximum detection range of 60mm from the Handpiece to the Reflector. Excision of the lesion is then performed using standard surgical techniques.

The Console and Guide are provided non-sterile. The Handpiece and Reflector (available separately) are provided as sterile.

The SCOUT® Reflector is intended to be placed percutaneously in soft tissue (>30 days) to mark a biopsy site or a soft tissue site intended for surgical removal. Using imaging guidance (such as ultrasound, MRI, or radiography) or aided by non-imaging guidance (SCOUT® System), the SCOUT® Reflector is located and surgically removed with the target tissue. The SCOUT® System is required for the non-imaging detection and localization of the SCOUT® Reflector that has been inserted in a soft tissue biopsy site or a soft tissue site intended for surgical removal.

3.2 SCOUT® Reflector

The SCOUT® Reflector is delivered via a delivery system to a pre-determined site in close proximity or within the identified tissue lesion. The Reflector is designed to be highly reflective to radio frequency (electromagnetic wave/micro- impulse radar) signals allowing it to be easily identified and located within soft tissue by the electromagnetic wave signal. The Reflector is delivered percutaneously. The SCOUT® Reflector is preloaded into either the SCOUT® Delivery Device or SCOUT® Bx Delivery Device. The standard SCOUT® Delivery Device contains a 16G introducer needle which retracts into the handle when a release button is actuated, thereby deploying the SCOUT® Reflector. The SCOUT® Bx Delivery Device consists of a plastic molded handle and a 15G rigid cannula, and it is designed for insertion through the biopsy introducer sheath utilized with the following biopsy devices (Hologic Eviva 0913-20; 1213-20 (STX), Hologic BREV09 (STX), ATEC ILS 0914-20 (MRI)). The SCOUT® Reflector is deployed by actuating a

deployment plunger. Availability of these different delivery device configurations within this post-market registry study is dependent upon regional regulatory licensing/clearance. The SCOUT® Reflector and delivery systems are provided as sterile single-use devices.

Part no.	Description
SSR05-01	SCOUT® 5cm Delivery Needle and Reflector
SSR75-01	SCOUT® 7.5cm Delivery Needle and Reflector
SSR75S-01	SCOUT® 7.5cm Delivery Needle and Reflector, Single-handed
SSR75SM-01	SCOUT® 7.5cm Delivery Needle and MINI Reflector, Single-handed
SSR10-01	SCOUT® 10cm Delivery Needle and Reflector
SSR13B-01	SCOUT® Bx Delivery System

TABLE 1: LISTING OF SCOUT® REFLECTOR AND DELIVERY SYSTEM MODELS

All future models that are regulatory licensed/cleared for the same indication in the region of the participating site will be allowed in this registry. Note: Please refer to the Instructions for Use of the device for complete information.

3.3 SCOUT® Guide and Control Unit

A handheld probe (SCOUT® Guide or Handpiece) is placed in direct contact with the skin overlying the target tissue, and is used to deliver the electromagnetic wave signal. It receives the return signal which is reflected back from the previously implanted marker.

A control unit (SCOUT® Surgical Guidance Console) processes the reflected electromagnetic wave signals, providing the surgeon with marker proximity information via audible and visual feedback.

Part no.	Description
SSC-01	SCOUT® Surgical Guidance Console
SSC-01L	SCOUT® Surgical Guidance Console, Loaner Unit
HPSU-01	SCOUT® Single-Use Handpiece
SG-01	SCOUT® Surgical Guide18mm
SG-02	SCOUT® Surgical Guide 12mm
CHK-01	SCOUT® Check Console with 1 handpiece
CHK-01L	SCOUT® Check Console with 1 handpiece, Loaner Unit
CHKHP-01	SCOUT® Check Handpiece
SH-01	Sterile Sheath for reusable handpieces

TABLE 2: LISTING OF SCOUT® GUIDE AND CONTROL UNIT MODELS

All future models that are regulatory licensed/cleared for the same indication in the region of the participating site will be allowed in this registry. *Note: Please refer to the Instructions for Use of the device for complete information.*

3.4 Labelling

The model number and lot number of the implantable reflector(s) will be identified and recorded on the participant case report form (CRF).

4. Registry Plan

4.1 Objectives

The primary objective of this registry is to demonstrate the utility of the SCOUT® Surgical Guidance system to improve workflow and efficiency in centers diagnosing and treating breast cancer. The secondary objective is to further evaluate the safety and performance of the SCOUT® Surgical Guidance system in 500 consented BI-RADS 4C/5 patients according to the IFU.

4.2 Endpoints

The primary endpoint is the number of patient visits to the breast center for invasive procedures from the time of biopsy to surgery. The primary endpoint will be compared to historical controls. It is expected that there will be a mean reduction of at least one (1) visit for invasive procedures.

The secondary endpoints are defined below:

1. Device success: percent successful localization, detection and retrieval.
2. Device safety: rate of device-related adverse events.
3. Procedural success: absence of close margins (<2mm), positive margins (tumor on ink) or requirement for re-excision.
4. Duration (days) from diagnosis to surgery and biopsy to surgery.
5. Radiologist assessment: ease of placement; ability to position reflector in desired location; scheduling flexibility; visibility on ultrasound/ mammography (immediate and late); artifact (Tomo/MRI if applicable).
6. Surgeon assessment: ease of detection; ease of device retrieval.
7. Participant satisfaction questionnaire: anxiety; convenience; pain; overall experience compared to expectation
8. Process improvement with implementation of same-day biopsy and SCOUT® Reflector placement.

4.3 Population

Five hundred (500) BI-RADS 4C/5 patients undergoing biopsy of a breast lesion at a participating study center.

It is expected that 3-7 centers will participate in this registry, so enrollment per center is estimated as approximately 100-150 per center.

4.4 Inclusion and Exclusion Criteria

The inclusion criteria are as follows:

1. Woman ≥18 years and < 80 years of age;
2. Classified as BI-RADS 4C or 5;
3. Lesion depth is ≤ 6 cm from skin surface;
4. Non-palpable lesions;
5. Informed consent obtained.

The exclusion criteria are as follows:

1. Multicentric breast cancer;
2. Pregnant or lactating;
3. Known or suspected nickel-titanium allergy.

4.5 Design

This is a single-arm, multicenter, non-randomized cohort study that will include five hundred (500) participants scheduled to undergo a biopsy of a breast lesion at participating Canadian and US study centers.

The expected duration of the trial is 12-18 months. Enrollment is expected to take approximately 12 months.

The primary endpoint of this cohort will be compared to historical controls (standard of care visits).

The registry is divided into three periods:

1. Inclusion Period: from registry eligibility screening until reflector insertion;
2. Device Period: from reflector insertion at biopsy to removal at surgery;
3. Outcomes Period: from completion of surgery to pathology report of outcomes.

4.6 Inclusion Period

Patients meeting all inclusion criteria and no exclusion criteria will be considered for inclusion into the registry. Each eligible patient will be informed about the registry by the Investigator or designate.

Prior to any data collection, the patient must be thoroughly informed about all aspects of the registry and must have signed the Research Ethics Board (REB) or Institutional Review Board (IRB) approved Informed Consent Form (ICF). Participants will be assigned a unique identifier for the registry upon enrollment.

No patient data, including adverse events will be collected in this period. A patient will be considered enrolled in the registry at the time of reflector insertion.

4.6.1 Informed Consent Process

Written Informed Consent with the REB/IRB approved consent form will be obtained for all subjects prior to conducting any study-related assessments and prior to administration of any pre-procedure medications or sedation. The principal investigator, or qualified designee, will explain to each patient all aspects of the clinical study that are relevant to the patient's decision to participate in the clinical study including, but not limited to, the following: purpose and nature of the study, study procedures, expected study duration, available alternative therapies, the benefits and risks involved with study participation and the potential treatment. The principal investigator, or qualified designee, shall avoid any coercion or undue improper influence on, or inducement of, the patient to participate and will not waive or appear to waive the patient's legal rights. Patients will be given a copy of the informed consent form and will be provided ample time to read and understand the document and be given the opportunity to ask questions. Patients will be informed of their right to withdraw from the study at any time without prejudice; consent forms will use non-technical language and be provided in a language understandable to the patient. After this explanation, and before any study-specific procedures have been performed, the patient and the principal investigator, or qualified designee, responsible for conducting the informed consent process will voluntarily sign and personally date the ICF. The patient will receive a copy of the signed and dated written informed consent.

The informed consent process may be completed during an in-person meeting or through remote consent procedures. All procedures of remote consent must be in compliance with institutional requirements for remote consent.

The principal investigator or qualified designee will document in the medical records on the informed consent document the informed consent process, including the date of consent and name of the person conducting the consent process. Documentation of the time of consent is required if the informed consent process occurs on the same day as the index procedure. The principal investigator or qualified designee shall ensure important new information is provided to new and existing participants throughout the clinical investigation.

4.7 Device Period

Insertion of the SCOUT® Reflector shall be conducted according to the IFU at the time of biopsy. The physician will follow regular clinical practice before and during the biopsy procedure.

SCOUT® Reflector may be inserted in a soft tissue biopsy site or a soft tissue site intended for surgical removal as per IFU and clinician decision. Additionally, as per clinician decision, more than one (1) SCOUT® Reflector may be inserted in a participant (bracketing) ensuring a minimum distance of 25 mm between Reflectors.

The data collected during the biopsy and reflector insertion will consist of the following:

- Patient demographic: age, weight, height and diagnosis
- Date of assessment
- Date of biopsy and insertion
- Reflector insertion data: success, deployment within lesion or distance from lesion, depth of reflector, type of guidance used, number of reflectors used, type of lesion
- Lot number(s) and model of the SCOUT® Reflector

- Reflector detection (if performed)
- Adverse events (if applicable)

The data collected during the surgery will consist of the following:

- Date of surgery
- Neoadjuvant therapy (if applicable): start and stop date
- Reflector detection: success before or after incision
- Reflector retrieval data: success, identification and retrieval duration
- Operative time: Time from beginning the detection to the time the lesion is removed from the breast.
- Participant satisfaction questionnaire:[1] this may be completed by/collected from the participant up to 2 weeks after the surgery.
- Adverse events (if applicable)

4.8 Final Outcomes

The assessment of procedure success is determined by the pathology report. This will not require an additional participant visit for the purposes of the registry. Participation will be considered complete following collection of the final outcomes and Participant satisfaction questionnaire.

The following data points will be recorded from the report:

- Excised tissue information
- Specimen size
- Margins: (positive, close, negative)
- Re-excision required (after surgery)
- Radiologist assessment (collected once per radiologist at completion of study)
- Surgeon assessment (collected once per surgeon at completion of study)

[1] Romanoff A, Schmidt H, McMurray M, et al. Physician preference and patient satisfaction with radioactive seed versus wire localization. J Surg Res. 2017; 210: 177-180.

4.9 Assessments

All assessments will be conducted according to the standard practice applicable at each participating site. Assessments to be collected during the registry are found below:

Schedule of Assessments

	Consent*	Biopsy**	Surgery	Final Outcomes***
Patient Data				
Informed Consent	X			
Demographic information (age, height, weight, diagnosis)		X		
Neoadjuvant therapy (start and stop date)			X	
Device and Procedural Data				
Reflector insertion data (success, deployment within lesion or distance from lesion, depth of reflector, type of guidance used, number of reflectors used, type of lesion, reflector detection)		X		
Reflector detection (before incision or after incision)		X[i]	X	
Reflector retrieval (success, identification and retrieval duration)			X	
Operative time			X	
Adverse events (including device deficiencies)		X	X	
Scheduling Data				
Date of assessment		X		
Date of biopsy and insertion		X		
Date of surgery			X	
Satisfaction Assessments				
Radiologist assessment: ease of placement; ability to position reflector in desired location; scheduling flexibility; visibility on ultrasound/mammography; artifact (Tomo/MRI if applicable)				X[ii]
Surgeon assessment: ease of detection; ease of reflector removal				X[ii]
Participant satisfaction questionnaire			X[iii]	

Pathology Report data				
Margins (positive; close <2mm; negative >2mm)				X
Re-excision required (after surgery)				X
Excised tissue information				X

[*]Performed prior to biopsy
[**]Reflector insertion performed at time of biopsy
[***]No additional participant visit; data recorded from pathology report
[i] If performed
[ii] Collected once per clinician at completion of registry
[iii] Window up to 2 weeks post-surgery (remote completion)

4.10 Participating Centers

Participating centers will be selected by the Sponsor. All required approvals will be confirmed by the Sponsor prior to initiation of a participating site [i.e., REB/IRB, ISO 14155:2020 requirements and 21 CFR Parts 50, 54 and 56 requirements (US centers only)].

It is anticipated that there will be 3-7 centers participating in this registry.

4.11 Sponsor responsibilities

Merit Medical Canada has the overall responsibility for the conduct of the study, including assurance that the study satisfies international standards and the regulatory requirements of the relevant regulatory authorities.

The Sponsor will be responsible for:

- Selection of clinical investigators and sites: The Sponsor will select qualified investigators and facilities which have adequate study population to meet the requirements of the investigation.
- Training of investigators and site personnel and site monitoring: The training of the Investigator and clinical site personnel will be the responsibility of the Sponsor, or designee, and may be conducted during an investigator meeting, a site initiation visit, or other training sessions. Periodic monitoring visits will be conducted frequently enough to ensure that all clinical participant data are properly documented and that the study is properly conducted.
- Documentation: The Sponsor will collect, store, guard and ensure completion of all study relevant documents by the relevant parties.
    - Signed and dated CRFs
    - Records of any Serious Adverse Events (SAEs) reported to the Sponsor during the clinical investigation
- Any statistical analyses and underlying supporting data
- Final report of the clinical investigation
- Submitting Reports

- Maintaining Records: The Sponsor will maintain copies of correspondence, data, SAEs and other records related to the clinical study according to requirements set forth by ISO 14155:2020 and regulations.
- Monitoring: The Sponsor is responsible for monitoring the study to ensure compliance with ISO 14155:2020 and regulatory requirements.

4.12 Investigator responsibilities

- Protocol acceptance: Prior to starting enrolment of participants, the Investigator must read and understand this study protocol, and must sign and date the Protocol Signature page. The Site Agreement documents agreement to all conditions of the study protocol and agreement to conduct the study accordingly. This study will be conducted in accordance the Declaration of Helsinki and other applicable regulatory requirements and standards, and any conditions of approval imposed by the REB/IRB or regulatory authorities.
- Required documents: The following documents must be submitted to the Sponsor, or designee prior to participant enrolment:

    1. Signed Protocol Signature Page
    2. Recent (≤ 2 years old) signed and dated English Curriculum Vitae (CV) of the Principal Investigator and co-investigators of the clinical site. The CV should clearly show the Investigator/co-investigators' qualifications and experience.
    3. Copy of the written confirmation of the REB/IRB regarding approval of the protocol including version number and date, ICF (including version and date) and other adjunctive participant material.
    4. List of voting REB/IRB members
    5. Signed Clinical Trial Agreement

- REB/IRB approvals and notifications: According to the local requirements, the Investigator must have all necessary approvals, including written approval from the REB/IRB of the clinical site prior to enrolling participants in the study. A copy of the written approval must be provided to the Sponsor.
    - Serious Adverse Event (SAE) reports as well as annual and final reports will be submitted to the REB/IRB as required.
- Obtaining informed consent: The Principal Investigator, or qualified designee, will obtain informed consent in accordance with the procedure described in this study protocol and the requirements of the REB/IRB.
- Medical care of participants
- Reporting requirements
- Audits / Inspections: In the event that audits/inspections are initiated by the Sponsor (or its designee) or national/international regulatory authorities, the Investigator must allow access to

the original medical records and must provide all requested information. In the event that audits are initiated by regulatory authorities, the Investigator will immediately notify the Sponsor.

5. Data Analysis & Statistics

5.1 Sample Size Calculation

No formal sample size calculation has been performed. Five hundred (500) participants will be included in this registry. This sample size has been selected to adequately support a multi-center experience reflective of the Canadian and US healthcare system and associated workflow.

Further, the Canadian Agency for Drugs and Technologies in Health (CADTH) assessed the evidence of a competitive device and noted the requirement for a cohort size greater than 200 in order to draw conclusions of effectiveness.[22] It is estimated that this sample size will result in a robust data set.

5.2 Point of Inclusion

A patient is considered enrolled in the registry as soon as they:

1. Have provided signed consent agreeing to be part of this registry; and
2. Undergo the insertion of the SCOUT® Reflector at the time of biopsy

Note- If a patient has given consent but the Reflector is not inserted at biopsy, the patient will not receive a participant number and will not be considered as enrolled in the registry. No patient data will be collected.

The intent-to-treat (ITT) population includes all participants in whom the SCOUT® Reflector has been inserted. Any participants who have a reflector inserted and do not undergo surgery will be exited from the registry using a study completion form. The occurrence of this scenario is expected to be low ($\leq$ 10%). Reasons may include:

1. Benign concordant biopsy results.
2. Participant death prior to surgery due to metastases.
3. Lesion is metastatic from another location.
4. Participant declines surgery.
5. Participant is ineligible for surgery.

The per protocol (PP) population will include all participants in whom a SCOUT® Reflector has been inserted and who subsequently undergo breast surgery.

Participation in the registry will be considered complete after surgery, documentation of surgical outcomes and completion of the Participant Assessment Questionnaire. This will be documented on a study completion form. It is expected the duration of each participant will be approximately <7 months and will vary based on each participant's treatment plan.

5.3 Analysis of Clinical Data

This registry is not hypothesis driven. The limitation of the design for this registry is that there are no pass/fail criteria from a statistical hypothesis testing.

Descriptive statistics will be generated for all endpoints using a 1-sided 95% confidence interval. Participant data will be quantified. For quantitative parameters, descriptive statistics will be reported: number, mean, standard deviation (SD), minimum, median and maximum values. For categorical variables, frequency and percentage will be reported. The primary endpoint will be compared to historical data using one-way analysis of variance.

Subset analysis may be performed for participants who have undergone neoadjuvant therapy.

Endpoint analysis will be performed on the PP analysis set. Descriptive data and adverse event analysis will be performed on the ITT analysis set.

Full analysis will be described in the statistical analysis plan and specified in the final report. No interim analysis is planned.

The Sponsor will perform data management and statistical analysis. Statistical analyses will be performed using the Statistical Analysis System (SAS) or other widely accepted statistical software.

5.4 Missing, Unused & Spurious Data

Attempts will be made to complete any missing data. In addition, the means and ranges of all variable distributions and outlying data or improbable combinations of variables will be examined before analysis is undertaken. Queries will be sent to investigators for inconsistent or missing data. Endpoint analysis will be performed with and without using imputation of missing data (where applicable) to estimate the effect of missing data on ITT and PP population. Differences between their results will be summarized and discussed.

6. Data Collection & Reporting

6.1 Method of Data Collection & Documentation

The Sponsor will provide the center with the Registry Plan, electronic Case Report Forms (eCRF) and all other necessary documentation to perform the registry.

6.2 Protocol Deviations

Investigators may not deviate from the registry plan, unless to protect the health and safety of a participant. Any deviations from the protocol must be reported to the Sponsor as soon as possible and no later than 10 calendar days. Deviations will be assessed by the Sponsor and corrective and preventive action plans (CAPA) may be implemented to avoid future deviations. Deviations will be reported to the REB/IRB according to reporting guidelines.

6.3 Electronic Case Report Form (eCRF)

Registry data will be documented on a web-based eCRF. The eCRF is provided by the Sponsor and will be used to record data that are integral to the registry and subsequent reports. The Sponsor will obtain

evidence of verification, validation and security of the eCRF platform. All collected data will be de-identified and reside in Canada.

The eCRF must be accurate and complete. All participant data entered onto the eCRF should be supported by source documents (e.g., medical records). The eCRFs are completed for each enrolled participant and signed by the Investigator.

Because of the potential for errors, inaccuracies, and illegibility in transcribing data onto eCRF, originals of all relevant procedural records and reports, post-procedural examinations, laboratory and other test results should be kept on file in each participant's medical file as permissible by each site's record keeping policy. The eCRF must be kept current to reflect participant's status during the course of the registry.

The Sponsor will train each participating center in this registry on the proper use of the eCRF.

6.4 Data Management

The Investigator shall enter all participant data into a web-based registry database. Only de-identified participant data will be collected to ensure and maintain participant privacy. The database will be maintained within Canada and will comply to all relevant privacy laws.

6.5 Data Quality Control & Assurance

Data entry will be reviewed on a regular basis. Quality control audits of all key performance and safety data in the database will be made after the sites complete enrollment and prior to database lock.

The Sponsor (or delegate) will oversee all aspects of data quality. The data will be monitored according to the Monitoring Plan through central and remote monitoring strategies. Outlier data will be queried and remote access to electronic medical records (EMR) may be requested for source data verification (SDV).

Each clinical site will be monitored according to the study monitoring plan to ensure to verify that:

- The rights and well-being of the participants are protected
- The reported study data are accurate, complete and verifiable from source documents
- The conduct of the study is in compliance with the currently approved Clinical Investigation Plan (CIP)/ amendment(s), ICH GCP, ISO 14155:2020, 21 CFR parts 50, 54 and 56, and applicable requirements of the REB/IRB
- There is adequate participant enrollment

6.6 Registry Records Retention

It is the responsibility of the investigator to maintain a comprehensive and centralized filing system of all relevant study documentation. Investigators will be instructed to retain all study records required by the Sponsor in a secure and safe facility with limited access for one of the following time periods based on sponsor notification:

- A period of at least two years after completion of the registry
- Or longer as required by local regulations

The investigator will be instructed to consult with the Sponsor before disposal of any study records and to provide written notification to the Sponsor of any change in the location, disposition, or custody of the registry documentation.

7. Safety

7.1 Definition and assessment of safety related events

Information on safety related events will be collected during the Device Period of the registry by the investigators or their designate. Classification of events is based on ISO 14155:2020.[23]

- Adverse Event (AE): any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in participants, users or other persons, whether or not related to the device. This definition includes events related to the procedures involved.
- Serious Adverse Events (SAE): An adverse event that led to death or led to serious deterioration in the health of the participant, that either resulted in:
    - Death
    - A life-threatening illness of injury, or
    - A permanent impairment of a body structure of a body function, or
    - In-patient or prolonged hospitalization, or
    - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, or
    - Fetal distress, fetal death or a congenital abnormality of birth defect.

  Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigation plan without serious deterioration in health, is not considered a serious adverse event.
- Adverse Device Effect (ADE): An adverse event related to the use of the device. This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation or operation, or any malfunction of the device. This definition includes any event resulting from use error or from intentional misuse of the medical device.
- Serious Adverse Device Effect (SADE): Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
- Device Deficiency (DD): inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance. Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling.

7.2 Reportable Events

For the purpose of this post market registry and per the study AE CRF, the following adverse events of interest and device deficiencies will be collected:

- Adverse reaction to material

- Device Migration
- Inaccurate location detection
- Inaccurate deployment
- Infection
- Tissue/vascular trauma
- Other: any AE that, in the opinion of the investigator, has a causal relationship (probable or definite) to the device or procedure, or any device deficiency, whether or not associated with an adverse event.

7.3 Reporting of safety related events

Adverse events and DD will be collected from the time the reflector is inserted into the participant (at biopsy) to the time the reflector is removed at surgery (Device Period) or until a study completion form is completed. Any AE in this period, either serious, non-serious, whether deemed device-related or not, must be reported to the Sponsor immediately after the investigator or coordinator has become aware of its occurrence. Reporting of an AE or DD to the Sponsor should take place within 24 hours upon becoming aware of the event, but not later than 3 calendar days. All AE (serious or non-serious) and DD will be documented in the eCRF. The AE/DD eCRF page should be submitted to the Sponsor within 24 hours even if all of the information is not available at the time of the initial contact. Sponsor contact for reporting: .

The investigator will evaluate (S)AEs with regard to causality and seriousness.

Reporting of serious incidents to the regulatory authorities will be reported per local regulations:

- Incident means any malfunction or deterioration in the characteristics and/or performance of the SCOUT® Surgical Guidance system, including use-error due to ergonomic features, any inadequacy in the information supplied by the manufacturer and any undesirable side-effect.
- Serious incident means any incident that directly or indirectly led, might have led or might lead to any of the following:
    - Death of a participant, user or other person,
    - Temporary or permanent serious deterioration of the participant's, user's or other person's state of health,
    - Serious public health threat;

Safety related events, which require preventive or corrective measurements intended to protect participants, may have to be reported to the local REBs/IRBs. The Sponsor will notify all other involved sites to report to their respective REBs/IRBs according to their requirements. The Sponsor will report any (S)ADEs and DD(s) to Health Canada and US FDA as required and within stipulated timelines.

7.3.1 Severity Definition

- Mild: Generally transient & not interfering with daily activities;
- Moderate: Sufficiently discomforting to interfere with usual activities;
- Severe: AE that prevents normal daily activities.

The investigator will document their assessment of the relationship of the AE to the device using the criteria outlined below.

7.3.2 Causality or Relationship to the Device and/or Procedure

- Unrelated: The AE has no temporal relationship to the device or to the procedure, and/or there is evidence of alternative cause such as concurrent medication or illness;
- Possibly related: A temporal relationship with the device or the procedure is not clear, alternative causes are also possible;
- Reasonable Causal Related: The AE is associated with the device or with procedures beyond reasonable doubt when:
    - The event is a known side effect of the product category the device belongs to or of similar devices and procedures;
    - The event has a temporal relationship with the device use/application or procedures;
    - The event involves a body-site or organ that the device or procedures have an effect on;
    - The AE follows a known response pattern to the medical device (if the response pattern is previously known);
    - The discontinuation of 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 of another device, drug or treatment) have been adequately ruled out;
    - Harm to the participant 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 the AE.

7.4 Independent Physician Adjudicator

An independent Physician Adjudicator (IPA) will be responsible for review and adjudication of all serious and potentially device-related adverse events, at minimum. Other events may be reviewed as defined in the IPA Charter.

In order to enhance objectivity and reduce the potential for bias, the IPA shall be independent of the Sponsor as well as the investigational sites and investigators. The methodology for performing these responsibilities shall be developed and outlined in the IPA Charter. Operational provisions shall be established to minimize potential bias.

8. Measures to Minimize Bias

The following measures will be implemented to minimize the potential for bias in this single arm Registry:

- Sites are requested to screen and enroll consecutive subjects, as far as possible, and enrollment activities will be documented in a screening/enrollment log.
- Multiple sites will be included to ensure a representative sample of physicians performing the procedure and to provide a reasonable enrollment period.
- Site selection will be performed using predefined parameters to ensure Investigators are appropriately qualified to conduct registry.
- Site training will be performed to assure full understanding and engagement to comply with the study design and all protocol requirements.
- A sample of adverse events will be reviewed and assessed by an independent Physician.
- Any known or foreseeable factors that may compromise the outcome of the Registry or the interpretation of results are covered by the Inclusion and Exclusion criteria.
- Financial disclosures will be collected from all investigators to document any potential for bias or conflict of interest.

9. Risks and Benefits

9.1 Risk Analysis

Risks associated with the SCOUT® Surgical Guidance System are managed in accordance with ISO 14971, Medical Devices- Application of risk management to medical devices. Risks associated with localization devices are well-understood and have been documented in the risk analysis, published clinical literature,[19,20,22,24,25] as well as post-market surveillance data available for the benchmark devices. The nature of the SCOUT® System procedure carries the same clinical risks to the intended patient population as other localization technologies.[19,20,21,24,25,26] The risk analyses for these devices included objective reviews of published and available unpublished medical and scientific data. The sections below provide an overview of residual risks identified in the risk management reports and anticipated benefits of the medical device.

The safety and performance aspects of the SCOUT® System have been evaluated using risk analysis techniques. The risks associated with the use of the SCOUT® System are considered reasonable in comparison to the anticipated benefits to patients. There were no reports of morbidity/mortality attributable to use of the SCOUT® System in any study.[2,18,19,20,24,25]

The risks associated with the SCOUT® System are the same as existing benchmark localization technologies used in the intended patient population, as such the SCOUT® System poses an acceptable level of risk for its intended use.[25,26]

9.2 Anticipated Clinical Benefits

All information supplied with the SCOUT® System clearly indicates the intended purpose of the device, namely use as a localization system for the identification of a soft tissue biopsy site or soft tissue site intended for surgical removal. The intended clinical benefit of use of a localization system is to facilitate identification (e.g., location) of target tissue in patients medically indicated for excision of soft tissue due to suspected or confirmed carcinoma.

These same benefits were assessed for the SCOUT® device where the investigators concluded that the SCOUT® System is safe and effective for guiding the excision of palpable and non-palpable breast lesions and a viable alternative to standard localization options.[18,19,22,26,27]

While there is no guaranteed clinical benefit associated with participation in this registry, it is expected that participants will have similar benefits as other commercially available localization systems. Compared to other available localization systems, registry participants may benefit from a streamlined clinical pathway resulting in reduced number of invasive procedures.

9.3 Anticipated Adverse Events and Adverse Device Effects

The nature of the SCOUT® System procedure carries the same clinical risks to the intended patient population as other localization technologies. Namely anticipated ADEs included:

- infection- there have been no instances of reported infection from the reflector. Incidence of infection from other localization systems have been reported between 1.56-4.61%.[25]
- adverse reaction to materials- Using the highest values (worst case observed), a total of approximately 0.0075 µg of nickel was released, from each device, over a 30-day period. This translates to about 0.00025 µg per day released per reflector . Nickel potentially released from the reflector is less than 0.0004% of nickel absorbed by adults during the normal course of each day. Complaint rates range from 0-0.02% annually with no adverse events associated.[25]
- tissue/vascular trauma- Complaint rates ranges from 0-0.08% annually in the global market. [25]
- inaccurate location detection- Complaint rates range from 0-0.48% annually in the global market. [25]
- inaccurate deployment- complaint rates range from 0-0.22% annually in the global market. [25]
- device migration-complaint rates range from 0-0.02% annually in the global market. [25]

Risks associated with the SCOUT® System and localization procedure, together with their likely incidence, are described in the IFU.

There may be risks related to the device under investigation that are unknown at present. Likewise, the exact frequency of the risk may be unknown. However, the SCOUT® System has been commercially available and utilized extensively in the US market since 2014 (K141318) and Europe since 2020. The risks associated with the use of the SCOUT® System are considered reasonable in comparison to the anticipated benefits to patients. There were no reports of morbidity/mortality attributable to use of the SCOUT® System in any study.[2,18,19,20,24,25]

Possible risks associated with participating in this registry are not anticipated to be any different from risks associated with undergoing procedures with the commercially available SCOUT® System (globally). Protocol required assessments are aligned with standard of care for treating non-palpable breast lesions using localization and as such do not pose any additional risks.

9.4 Steps Taken to Control or Mitigate Risks

In-depth recommendations, special precautions and instructions regarding patient selection, device handling, and device placement are included in the IFU for the SCOUT® System. It is also stated in the IFU

that the devices can only be used by physicians who have received appropriate training on how to use the device. Physician users are expected to be aware of the known and foreseeable safety risks associated with the use of the device including the surgical and/or non-surgical treatment of these conditions.

Risks associated with the use of the device under investigation are minimized through device design, investigator selection and training, pre-specified participant eligibility requirements, and risk-based monitoring to ensure adherence to the protocol. All AEs will be reported to the Sponsor as summarized in Section 7.3 and will be monitored internally for safety surveillance purposes.

10. Quality Control & Quality Assurance

10.1 Training

Sponsor will ensure that Investigators and site staff are trained in the study protocol, including consent requirements and data collection procedures. Training may be completed by on-site visit or remote/web-based training. No additional device training or case support is required for Study Participation, device training will be in accordance with Merit requirements for commercial use applicable to the country where site is located.

Canadian sites are required to complete the Merit Medical Canada Training plan. Prior to use of the device, radiologists and surgeons will complete didactic and hands-on product training. Clinicians will complete proctor sign-off prior to enrolling participants in this registry.

US sites will be selected from established device users and no additional device training is required.

The Principal Investigator will be responsible for ensuring that all subsequent personnel involved in the study are trained and receive proctor sign-off, where applicable.

10.2 Quality Assurance

The Sponsor will implement and maintain quality systems defined by written procedures to ensure that study is conducted and data are generated, documented and reported in compliance with this CIP, Good Clinical Practices (ISO 14155:2020) and the applicable regulatory requirements. Included in these procedures will be quality control measures to ensure that all data are reliable and have been processed correctly at each stage of handling.

The Sponsor will secure agreement with the Investigator to ensure direct access to the site and source data/documents and reports, for the purpose of monitoring and auditing by the Sponsor and/or regulatory authorities and/or REBs/IRBs.

10.3 Regulatory Inspections/ Audits

The registry may be inspected by regulatory agencies or audited by the Sponsor. These inspections may take place at any time during or after the registry. In the event that audits are initiated by the Sponsor (or its designee) or national/international regulatory authorities, the Investigator must allow access to the original medical records and must provide all requested information. In the event that audits are initiated by a regulatory authority, the Investigator will immediately notify the Sponsor.

10.4 Suspension or premature termination of the registry

In the case that the registry must be suspended or prematurely terminated, investigational sites will be notified and arrangements will be made with the highest regard for participant safety.

11. Publication

The registry will be registered in a publicly accessible database prior to participant inclusion, and the results of the registry will be made publicly available upon conclusion in accordance with the Declaration of Helsinki. At the conclusion of the registry, a report will be prepared for presentation and for publication. Authorship is based on the ICMJE (International Committee of Medical Journal Editors) guidelines.

All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest must be declared in the publication.

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