Premarket study to assess safety and performance of the Orion Magnetic Localization System for breast cancer

Published: 09-05-2019
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The primary objective is to show that the ORION SYSTEM is safe and performs as intended.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON48270

Source
ToetsingOnline

Brief title
Orion-1

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer, ductal carcinoma in situ, invasive ductal carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Sirius Medical Systems B.V
Source(s) of monetary or material Support: Sirius Medical Systems B.V.

Intervention

Keyword: breast cancer, magnetic, surgical localization

Outcome measures

Primary outcome

1) Performance. Number and percentage of procedures in which ORION SEEDS is present on post-operative specimen X-ray and only the ORION detector is used during surgery [=>95%]

2) Safety. Adverse events as assessed by MedDRA.Number and percentage of patients who experienced a device-related adverse event. [No SADEs]

Secondary outcome

In situ time Days between implantation and surgery [all cases <30 days]

Accuracy of placement - Average distance between centre of SEED and centre of lesion measured on two-way mammography in mm [descriptive]

Sonographic Tumour depth - Minimum distance between skin and tumour border on ultrasound imaging (mm) [descriptive]

Sonographic Tumour size - Shortest and longest axis of tumour on ultrasound (mm) [descriptive]

Radiologist Satisfaction - Satisfaction as measured on a questionnaire [see Appendix A]

Operative time - Minutes from first incision until excision of specimen [descriptive]

Transcutaneous detection - Number and percentage of procedures in which a reliable signal is measured on the intact skin preoperatively.

Also note the value. [*95% of cases]

Seed Confirmation - Seed detected in excised specimen using ORION detector

[descriptive]

Surgeon Satisfaction - Satisfaction as measured on a questionnaire

Patient Convenience - Patient convenience reported measured using a single

quesiton

Margin Status - Margin status defined per NABON Dutch national guidelines

[descriptive]

Reoperation - Second, separate surgical procedure of same lesion or area

indicated after multidisciplinary discussion [descriptive]

Study description

Background summary

The introduction of population-wide mammographic screening programmes for breast cancer has led to an increase in the incidence of screen-detected, non-palpable breast cancer. Breast conserving surgery (BCS) is the treatment of choice for these lesions [1], but this can be challenging and often requires pre-operative radiological localization to guide the surgeon towards the tumour location.
Wire guided localization (WGL) has been the gold standard for tumour localization since its first description in the 1970s [2]. In WGL, a metal anchor wire is placed in the tumour generally on the day of surgery. During surgery, the surgeon follows this wire from the skin to resect the tissue surrounding the tip.
Unfortunately, WGL is associated with disadvantages for all involved stakeholders: Surgeons have limited guidance towards the lesion as they are forced to follow the wire trajectory from the skin leading to undesirable incision locations and extensive dissection of healthy tissue[3]. Moreover, the wire may displace prior to or during surgery [4]. Hospitals are faced with logistical issues as patients need to visit the radiological department for wire placement prior to, but on the same day of surgery [5]. Coupling these schedules frequently leads to delays[3]. Patients need to undergo two stressful procedures on the day of surgery and have a wire protruding from their breast while awake which is painful [6].

Due to these well described disadvantages, radio guided technologies such as Radioactive Seed Localization (RSL) have been introduced as a challenging alternative to WGL and over the past decade found traction in the market.

In RSL, a tiny radioactive iodine-125 seed is preoperatively implanted into the lesion and removed during surgery using a handheld radioactive (gamma) detector)[5]. As such, RSL allows for surgical flexibility as surgeons can assess and reassess their approach independently; it decouples radiology and surgical schedules as the seed can be placed well in advance of surgery which improves logistics [7] and eliminates the need for two stressful procedures on the operative day which is preferred by patients [6].

However, the use of radioactive seeds is associated with its own set of limitations. Regulations regarding the safe procurement, use and disposal of these seeds are very strict and the penalties for example when losing a seed are severe, which hampers wide-spread uptake. Moreover, radioactive isotopes are scarce and according to the European Commission *there is a need to further explore possibilities for alternatives to radiopharmaceuticals in the EU* [8].

Sirius Medical Systems is a spin-out from the University of Twente (UTwente; Enschede, NL) and the Netherlands Cancer Institute * Antoni van Leeuwenhoek Hospital (NKI-AvL; Amsterdam, NL). At the NKI, a novel localization technology was developed that uses the principle of magnetism, rather than radioactivity [9]. Clinical investigations with a predecessor device and a commercially available magnetic detector have been performed and published [10].

However, this detector was limited by a detection depth of 3cm, provides relative count values only, requires the use of plastic surgical instruments as the signal is heavily influenced by conducting metal and needs frequent (re)calibration.
Sirius has further refined NKI*s magnetic technology, and developed an improved magnetic seed and detector that together provide an improved detection distance of 5 cm, absolute distance measurement towards the seed in mm, is not influenced by surgical steel and does not need recalibration during the procedure. The system is called ORION .

The objective of the current study is to show that this novel technology is safe and performs as intended for localization of early-stage (non-palpable) breast cancer. The results of this study will be used to obtain CE mark for this device.

[1] U. Veronesi et al., *Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer.,* N. Engl. J. Med., vol. 347, no. 16, pp. 1227*32, Oct. 2002.
[2] H. A. Frank, F. M. Hall, and M. L. Steer, *Preoperative Localization of Nonpalpable Breast Lesions Demonstrated by Mammography,* N. Engl. J. Med., vol. 295, no. 5, pp. 259*260, Jul. 1976.

[3] L. J. McGhan et al., *Radioactive seed localization for nonpalpable breast lesions: review of 1,000 consecutive procedures at a single institution.,* Ann. Surg. Oncol., vol. 18, no. 11, pp. 3096*101, Oct. 2011.
[4] P. J. Lovrics et al., *A multicentered, randomized, controlled trial comparing radioguided seed localization to standard wire localization for nonpalpable, invasive and in situ breast carcinomas.,* Ann. Surg. Oncol., vol. 18, no. 12, pp. 3407*14, Nov. 2011.
[5] R. J. Gray et al., *Randomized prospective evaluation of a novel technique for biopsy or lumpectomy of nonpalpable breast lesions: radioactive seed versus wire localization.,* Ann. Surg. Oncol., vol. 8, no. 9, pp. 711*5, Oct. 2001.
[6] J. S. L. Ong et al., *Patient satisfaction with Radioguided Occult Lesion Localisation using iodine-125 seeds ('ROLLIS*) versus conventional hookwire localisation,* Eur. J. Surg. Oncol., vol. 43, no. 12, pp. 2261*2269, 2017.
[7] L. Langhans et al., *Radioactive Seed Localization or Wire-guided Localization of Nonpalpable Invasive and In Situ Breast Cancer: A Randomized, Multicenter, Open-label Trial.,* Ann. Surg., vol. 266, no. 1, p. 1, 2017.
[8] European Commission, *Preliminary Report on Supply of Radioisotopes for Medical Use and Current Developments in Nuclear Medicine,* 2009.
[9] B. Schermers, ten H. Bennie, S. Muller, J. A. van der Hage, and T. J. M. Ruers, *Optimization of an implantable magnetic marker for surgical localization of breast cancer,* Biomed. Phys. Eng. Express, vol. 4, no. 6, 2018.
[10] B. Schermers et al., *Feasibility of magnetic marker localisation for non-palpable breast cancer,* The Breast, vol. 33, pp. 50*56, 2017.

Study objective

The primary objective is to show that the ORION SYSTEM is safe and performs as intended.

Study design

Premarket, open label, single-centre, prospective clinical interventional trial

Intervention

In the training phase, patients will receive both the standard treatment (radioactive seed localization) and the investigational treatment (magnetic seed localization). This means one additional puncture at the department of radiology during a standard treatment session.

In the study phase, patients will receive only the investigational treatment (magnetic seed localization). The activities pertaining to the standard treatment (implantation of a radioactive seed; surgery using a radioactive detector) will be replaced by comparable activities for the investigational treatmen (implantation of a magnetic seed; surgery using a magnetic detector).

Study burden and risks

Burden for training cases (combination of standard treatment and investigational treatment); additional puncture at the department of radiology during a routine procedure; answering a single question.

Burden for study patients: answering a single question

Risks associated with participation are risks that generally belong to placing a tiny radiological implant:
* Local hematoma after implantation
* Local seroma after implantation
* local infection after implantation
* Pain

Contacts

Public
Sirius Medical Systems B.V

High Tech Campus 41
Eindhoven 5656AE
NL
Scientific
Sirius Medical Systems B.V

High Tech Campus 41
Eindhoven 5656AE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

1. Patient is willing and able to provide informed consent for the investigation and to comply to the schedule of assessments of the clinical investigation
2. Patient is female
3. Patient is at least 18 years of age
4. Patient is diagnosed with a single, pathologically confirmed unifocal breast tumour (DCIS or invasive)
5. Tumour is ultrasound visible
6. Patient is indicated for primary breast conserving surgery
7. Patient is indicated for preoperative localization using a single (radioactive) seed

Exclusion criteria

1. Patient is pregnant;
2. Patient is receiving neo-adjuvant chemotherapy
3. Patient has and ICD or other active implant such as a pacemaker less than 5cm away from the intended target location
4. Patient has a proven infection or hematoma at or close to the intended target location
5. Patient is scheduled for immediate breast reconstruction (within the same surgical procedure)
6. Patient is currently participating in, or has recently exited from, or plans to be enrolled in another clinical investigation which may affect the outcomes of the current clinical investigation, as assessed by the discretion of the investigator
7. Patient is expected to require an MRI scan of the breast area in the period between implantation and surgery
8. The expected time between placement of ORION SEED and surgery exceeds 30 days

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-07-2019
Enrollment:	33
Type:	Actual

Medical products/devices used

Generic name:	Orion Magnetic Localization System
Registration:	No

Ethics review

Approved WMO Date:	09-05-2019
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-10-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 24152
Source: Nationaal Trial Register

Title:

In other registers

Register	ID
CCMO	NL69460.028.19
Other	NL7630
OMON	NL-OMON24152