



Topic Exploration Report ¹

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

- Determine the quantity of evidence available for a technology of interest.
- Identify any gaps in the evidence.
- Inform decisions on topics that warrant fuller assessment by Health Technology Wales (HTW).

Topic exploration report number	TER530
Topic	Wire-Free, Nonradioactive Localisation Techniques to Guide Surgical Excision of Nonpalpable Breast Tumours
Summary of findings	<p>Health Technology Wales researchers identified one health technology assessment (HTA), one systematic review, and one primary study. The HTA by Ontario Health in 2023 concluded that wire-free nonradioactive localisation techniques could reduce the likelihood of additional surgery and carry the same risk as wire-guided and radioactive seed localisation. HTW researchers searched for any additional evidence since the search of the HTA.</p> <p>The systematic review reported on the effectiveness of indocyanine green fluorescence (ICG) for the identification of nonpalpable breast tumours which is a nonradioactive localisation technique. The review found the following outcomes: identification rate, clear resection margins, specimen volume, operative time, re-operation rate, adverse events, and complications. Overall, the review found all studies reported a 100% tumour identification rate with ICG, except for one study, with an identification rate of 87%. Only one study referenced in the review compared the intervention to wire localisation and many of the primary studies were non comparative.</p> <p>HTW researchers did not identify any additional cost effectiveness studies since May 2022. The HTA estimated that publicly funding these techniques over five years would cost an additional 7.73 million dollars. However, it would be unclear what the cost implications of implementing the intervention would be from a UK perspective, or what the cost effectiveness would be in comparison to standard care.</p> <p>Other areas of concern include a lack of comparative data in the systematic review identified and if this topic were to proceed to fuller appraisal, clarity about what is standard practice in Wales would be useful.</p>

¹ [Cyfieithu dogfennau HTW wedi'u cyhoeddi o'r Saesneg i'r Gymraeg](#)
[Translation of published technical HTW documents from English into Welsh](#)

Introduction and aims

Surgery is currently the standard treatment for nonpalpable breast tumours. Localisation techniques are needed to identify small nonpalpable breast tumours before surgically removing them. This includes implanting a marker inside the tumour using a mammogram or ultrasound guidance. Current localisation techniques include wire-guided localisation and radioactive seed localization, although these have limitations.

Ontario Health published an HTA on wire-free, nonradioactive localisation techniques to guide surgical excision of non-palpable breast tumours in 2023. HTW researchers searched for any additional evidence published since their search in May 2022.

Evidence overview

HTA Assessments and Guidance

The HTA (Ontario Health 2023) included 16 studies in the clinical evidence review, of which 15 were comparative prospective/retrospective studies and one was a single-arm study. Outcomes included re-excision rates, technical outcomes (i.e., successful device implantation, device dislodgement or migration, device detection issues, and device retrieval), operation time, post operative complications, and patient and clinician satisfaction

The HTA concluded that wire-free nonradioactive localisation techniques could reduce the risk of additional surgery and carries the same risk as wire-guided and radioactive seed localisation. They also concluded that the technical outcomes, postoperative complications, and operation time are similar to that of conventional localisation techniques (such as wired or radioactive). Overall, wire-free non-radioactive techniques were found to be safe and effective for the localisation of nonpalpable breast tumours.

Secondary Evidence

HTW researchers identified one systematic review published in September 2023.

Jansen et al. (2023) published a systematic review on the effectiveness of indocyanine green fluorescence (ICG) for the identification of nonpalpable breast tumours. ICG is a non-radioactive fluorescent dye, which in the context of breast cancer, is used for sentinel lymph node (SLN) mapping, replacing existing SLN mapping techniques. ICG is injected intratumorally or peritumorally (or intravenously) after general anaesthesia and is detected using a near-infrared fluorescence imaging system. Jansen et al. (2023) reported the following outcomes: identification rate, clear resection margins, specimen volume, operative time, re-operation rate, adverse events, and complications. Overall, the review found all studies reported a 100% tumour identification rate with ICG, except for one study, with an identification rate of 87%. Clear resection margins were found in 88-100% of all patients. The systematic review concluded that with ICG, reoperation rates ranged from 0.0 to 5.4% and no complications or adverse events related to ICG occurred, although the systematic review lacked direct prospective comparisons to wired and/or radioactive localisation techniques.

The review included 11 studies, two RCTs, three non-randomised comparative studies, four single-arm studies, and two case reports. However, six studies did not compare ICG with a control group, and only one study (Tong and Guo 2019) compared the intervention to wire

Evidence overview

localisation. Other comparators included activated charcoal and ultrasound guided skin marking.

Tong and Guo (2019) found ICG to have the same identification rate as wire localisation, although reported a higher clear resection margin for ICG compared with wire localisation (87.5% versus 63.3%, respectively) and a shorter mean duration of operation when compared to wire localisation (31.4 minutes versus 33.1 minutes, respectively).

Primary Evidence

Morgan et al. (2022) conducted a qualitative study exploring the feasibility and challenges associated with magnetic seed localisation versus wire localisation from the UK iBRA-NET breast cancer localisation study referenced in Ontario Health (2023). Between January 2019 and March 2020 and across 35 UK breast units, four focus groups were held including a total of 27 healthcare professionals, of which 24 were oncoplastic breast surgeons and three were breast radiologists. Clinician experience suggested magnetic seed index lesion identification was non-inferior to wire placement and improved the patient pathway in terms of scheduling and multi-site insertion. The study concluded that magnetic seed localisation offered additional non-clinical benefits over wire localisation, because it improved the efficiency of the patient pathway. The most common issues identified were percutaneous magnetic seed detection, instrument interference and potential seed or wire dislodgement.

Cost Effectiveness Studies

HTW researchers did not identify any additional cost effectiveness studies since May 2022.

Ontario Health (2023) were unable to report on the cost-effectiveness of wire-free, nonradioactive localisation techniques, although they identified one budget impact analysis and one cost-consequence analysis that compared wire-free, nonradioactive localisation techniques with wire-guided and radioactive seed localisation. The HTA estimated that publicly funding these techniques over five years would cost an additional 7.73 million dollars. However, it would be unclear what the cost implications of implementing the intervention would be from a UK perspective, or what the cost effectiveness would be in comparison to standard care.

Ongoing Research

HTW researchers did not identify any on-going research about wire-free, nonradioactive localisation techniques to guide surgical excision of nonpalpable breast tumours to be completed within the next 6-12 months.

Areas of uncertainty

HTW researchers identified one relevant systematic review since the HTA search, although this reported on one type of localisation technique, indocyanine green fluorescence (ICG). Many of the studies included in this review were not comparative (i.e., to wire localisation or radioactive techniques).

HTW researchers did not identify any additional cost effectiveness data since the Canadian HTA, and it is unclear how applicable these findings would be in the context of the NHS in the UK or

Areas of uncertainty

Wales. If this topic were to proceed to fuller appraisal, clarity about what is standard practice in Wales would be useful.

Literature search results

Health technology assessments and guidance

Ontario Health. (2023). Wire-Free, Nonradioactive Localization Techniques to Guide Surgical Excision of Nonpalpable Breast Tumours: A Health Technology Assessment. *Ont Health Technol Assess Ser.* 23(2): 1-139. Available at: <https://pubmed.ncbi.nlm.nih.gov/37284228/>

Evidence reviews and economic evaluations

Jansen BAM, Bargon CA, Huibers AE, et al. (2023). Efficacy of indocyanine green fluorescence for the identification of non-palpable breast tumours: systematic review. *BJS Open.* 7(5). doi: 10.1093/bjsopen/zrad092. Available at: <https://pubmed.ncbi.nlm.nih.gov/37751322/>

Individual studies

Morgan JL, Bromley HL, Dave RV, et al. (2022). Results of shared learning of a new magnetic seed localisation device - A UK iBRA-NET breast cancer localisation study. *European Journal of Surgical Oncology.* 48(12): 2408-13. doi: <https://doi.org/10.1016/j.ejso.2022.07.014>

Ongoing research

No evidence identified

Date of search	1 March 2024
Concepts used	“Wire-free, nonradioactive localization techniques” “wire-free localisation/localization techniques” “localisation/localization techniques” “Magnetic Seed” “Reflector-Guided localisation”

Proposed research question and evidence selection criteria (if selected)

Proposed Research question	What is the clinical effectiveness and cost effectiveness of wire-free, nonradioactive localisation techniques to guide surgical excision of nonpalpable breast tumours compared with wire-guided or radioactive seed localisation?
-----------------------------------	---

	Inclusion criteria	Exclusion criteria
Population	<p>Adult patients undergoing surgical excision of nonpalpable breast tumours (i.e., lumpectomy, partial or segmental mastectomy, quadrantectomy)</p> <p>Studies that included patients with nonpalpable and palpable tumours will be included if the proportion of palpable tumours is clearly stated and is 20% or less of the sample size</p>	Adult patients undergoing surgical excision of palpable breast tumours or surgical excision of axillary lymph nodes localised with localization devices
Intervention	Wire-free, nonradioactive localisation techniques (e.g., magnetic seed localisation systems, indocyanine green fluorescence, or the reflector-guided localisation system)	<ul style="list-style-type: none"> • Radio-opaque tumour marking techniques • Carbon nanoparticle suspension (CNS) • Cryo-assisted localization (CAL) • EnVisio Surgical Navigation System • Hematoma-directed ultrasound-guided localisation • Intraoperative ultrasound-guided surgery (IOUS) • Magnetic marker localisation (MaMaLoc) • Methylene blue • Radio-guided occult lesion localisation (ROLL) • Radiofrequency identification (RFID) tag system (LOCALizer) • Sirius Pintuition (navigational system)
Comparison/Comparators	<ul style="list-style-type: none"> • Wire-guided localisation • Radioactive seed localisation 	Techniques other than wire-guided and radioactive seed localization
Outcome measures	<ul style="list-style-type: none"> • Re-excision rate • Technical outcomes: <ul style="list-style-type: none"> • Successful placement of device in target tissue • Failure to implant the device • Failure to detect the device • Device dislodgement or migration • Operation time (duration of surgical procedure) • Postoperative complications • Patient and clinician satisfaction related to the use of a specific device • Quality of life • Economic outcomes 	

Proposed speciality	Cancer
----------------------------	--------