ACE BRIEF FOR NEW AND EMERGING HEALTH TECHNOLOGIES

MagTrace and SentiMag for Locating Sentinel Lymph Node in Patients with Breast Cancer

Document Number: HSB-M 02/2023

Date: March 2023

ACE agency for care effectiveness

Summary of Key Points

- Breast cancer is the most diagnosed cancer in females worldwide.
- Sentinel lymph node biopsy (SLNB) guided by Tc-99m, blue dye or both (dual technique) is the current gold standard for determining if cancer cells have spread from the primary site. However, Tc-99m is weakly radioactive and blue dye is known to sometimes cause allergic reactions, which limits current use.
- Magtrace is a superparamagnetic iron oxide solution that can be used with a magnetic probe from Sentimag to locate sentinel lymph nodes (SLNs). Magtrace is non-radioactive and non-toxic, and can be an alternative technology to current standard care.
- Magtrace and Sentimag have been found to be safe and accurate in localising SLNs for patients with breast cancer undergoing SLNB.
    - No serious adverse events were reported. The main adverse outcomes would be staining of the skin and presence of MRI artefacts for up to 5 years post injection.
    - Magtrace was demonstrated to be non-inferior in localising SLNs compared to standard care. From the evidence base, the SLN detection rate for Magtrace was 89.7% to 100%, compared to 70% to 100% for standard care (Tc-99m, blue dye and dual technique), with a high concordance rate between Magtrace and standard care.
    - The number of SLNs retrieved is similar between Magtrace and standard care, ranging from 1 to 3 and 1 to 3.29 respectively.
- The healthcare system benefit of Magtrace is that the logistics required to store, prepare and use Magtrace are less compared to Tc-99m, which requires specialised preparation, facilities for storage and protocol for use. Hence Magtrace may minimise disruptions in operating theatre time.
- Key limitations of the evidence include the lack of utility studies on patient outcomes with the use of Magtrace.
- NICE's decision-tree model comparing Magtrace and Sentimag to dual technique found that Magtrace and Sentimag could be cost saving but it would depend on whether the opportunity cost of additional SLNB procedures can be realised. Different case scenarios produced a range of results from cost savings of £78.90 to cost incurring of £58.17. The cost-effectiveness of Magtrace and Sentimag in the local context remains uncertain.
- Key implementation considerations would be the need to train clinicians and establish a proper protocol for the use of Magtrace to minimise skin staining. In addition, the use of costly plastic instruments, instead of the standard metal ones, to be compatible with the Sentimag magnetic probe remains a limiting factor.
- Clinician feedback indicated the vendor pulled out of the Singapore market after a local trial, presumably due to low utilisation.

I. Background

Breast cancer was the most diagnosed cancer worldwide in 2020, with over 2.3 million new cases diagnosed and 685,000 deaths reported.[1] Locally, breast cancer is the most common cancer among Singaporean women accounting for 29.7% of all female cancers. The incidence rate is 54.9 per 100,000 person per year in Singapore.[2] Roughly 1,100 new cases are diagnosed locally and 270 women die each year from breast cancer.

The earliest form of breast cancer is ductal carcinoma in situ (DCIS), where abnormal cells begin to form within the milk ducts in the breast. Breast cancer can also begin in the glandular tissue called lobules (known as invasive lobular carcinoma) or any other cells or tissue within the breast[3]. The sentinel nodes are the first lymph nodes where a cancer spreads to from the primary site. A sentinel lymph node biopsy (SLNB) determines if a cancer has started to spread. The procedure involves removing the sentinel lymph nodes (SLNs) surgically and examining them for cancer.

SLNB is done by injecting a weakly radioactive solution (technetium-99m, Tc-99m) or a blue dye (isosulfan blue), or both together (also known as dual technique), near the cancer site to locate the SLNs. The solution and/or dye is transported to the SLNs via the lymphatic system. The current gold standard for breast cancer SLNB is the dual technique.

The use of radioactive Tc-99m may increase risks associated with radioactive exposure for both patients and clinicians.[5] The use of blue dye might also lead to allergic reactions that could be minor reactions or life-threatening anaphylaxis.[6] Hence, there is a clinical need for an alternative tracer that is non-toxic and does not have potential radiation risks. Locally, the blue dye is the most used tracer, as not all public health institutions have easy access to nuclear medicine. (Personal communication: Senior Consultant from Sengkang General Hospital, 8 February 2023)

II. Technology

The Magtrace/Sentimag system (Endomagnetics Ltd) (Figure 1) comprises the Magtrace magnetic tracer and Sentimag handheld magnetic probe to detect for SLN. Magtrace, previously known as Sienna XP is a dark brown liquid containing a magnetic substance called superparamagnetic iron oxide (SPIO). The solution is injected beneath the areola or into tissue near the cancer site between 30 days to 20 minutes before the SLNB procedure.[7,8] The injected solution travels though the lymphatic system and localise to the SLNs. The Sentimag handheld probe is then used to locate the Magtrace particles and hence the location of the SLNs. The colour of the Magtrace solution also allows SLNs to be visually identified if the injection is given preoperatively.

Figure 1: Vial containing the brown Magtrace solution (bottom left) and the Sentimag system with the probe to detect for magnetised SPIO particles (centre). Image adapted from: *https://www.endomag.com/magtrace/overview/*

A key benefit of the Magtrace is that it is non-radioactive. This eliminates any potential side effects associated with the use of radioactive tracer. It is also claimed to be non-toxic. Another benefit is the flexible injection timing before an SLNB procedure for Magtrace compared to radioactive Tc-99m and blue dye which have specific timing. This flexibility means Magtrace can be injected 20 minutes before the procedure, after a patient has been anesthetised, to help reduce any pain associated with the injection.[7]

III. Regulatory and Subsidy Status

Magtrace and the Sentimag system were approved by the United States Food and Drug Administration FDA in July 2018, to assist in localising lymph nodes draining a tumour site, as part of a SLNB procedure for peoples with breast cancer (P160053).[9] In Europe, Magtrace received the Conformité Européenne (CE) mark in November 2012 and the Sentimag system received the CE mark in December 2010.

IV. Stage of Development in Singapore

A local trial has compared the technology with standard care for SLNB in patients with breast cancer.[10] However, one of the clinicians from the pilot trial has reported that the vendor has pulled out of the Singapore market after the trial presumably due to low utilisation. (Personal communication: Senior Consultant from Sengkang General Hospital, 8 February 2023)

☐	Yet to emerge	☐	Established
☒	Investigational / Experimental (subject of clinical trials or deviate from standard practice and not routinely used)	☐	Established *but* modification in indication or technique
☐	Nearly established	☐	Established *but* should consider for reassessment (due to perceived no/low value)

V. Treatment Pathway

People suspected to have breast cancer undergo diagnostic tests such as breast ultrasound scans, magnetic resonance imaging (MRI) and tomosynthesis[11] to detect potential tumours. If a tumour or suspicious growth is confirmed as cancer, a SLNB is done to determine if, and to what extent, the breast cancer has spread. This is done as SLNs are the first lymph nodes that cancer cells will spread to.[12] If cancer cells are present, downstream lymph nodes will also be removed for analysis to better determine how far the cancer has spread. NICE's guideline on the diagnosis and management of early and locally advanced breast cancer recommends SLNB using the dual technique for people with invasive breast cancer and no evidence of lymph node involvement on ultrasound or a negative ultrasound-guided needle biopsy.[13] NICE's guideline also recommends SLNB be offered to people with DCIS, the earliest form of breast cancer, who are undergoing mastectomy.[13]

The introduction of Magtrace/Sentimag into the local healthcare setting would provide an alternative tracer for the SLNB procedure, especially in healthcare institutions without easy access to radiopharmacy. This could lead to an increase in SLNB procedures done, a potential increase in the early detection of metastasised breast cancer and improved clinical outcomes for patients with breast cancer in Singapore.

VI. Summary of Evidence

This assessment was conducted using the Population, Intervention, Comparator and Outcome (PICO) criteria (Table 1). Literature searches was performed in Cochrane, Pubmed, Embase and International Network of Agencies for Health Technology Assessment (INAHTA) databases.

Similar to the HTA guidance report by NICE, studies that used the previous name of Magtrace (i.e., Sienna XP) or the previous version of Magtrace (i.e., Sienna+) were also deemed relevant and included in the evidence base for this brief. The only difference between the previous (Sienna+) and current generation of tracer (Magtrace) is the particle diameter. Magtrace particles are smaller than Sienna+, which allows for faster migration to the SLN and potentially requires lower dosage.[14]

The evidence base consists of a HTA report[8] from NICE (including 36 studies), and three additional comparative studies.[15-17] These additional studies compared SLN detection rates

between Magtrace and blue dye[16] or Tc-99m with or without blue dye,[17] and the postoperative complication between Magtrace and Tc-99m.[15] Appendix A summarises the evidence base for this brief.

Table 1: PICO criteria

Population	Patients with known breast cancer
Intervention	Magtrace and Sentimag System
Comparator	Other tracers used in SLNB, including radioactive isotope technetium-99m, blue dye or a combination of both (dual technique)
Outcomes	Safety, clinical- and cost-effectiveness
Abbreviation: SLNB, Sentinel lymph node biopsy.	

Safety

Overall, there were no major safety concerns associated with the use of Magtrace for SLNB. Common adverse events include skin staining, although NICE reported this was not a major issue and patients prefer the brown staining of Magtrace compared to the blue staining associated with blue dye. In addition, staining can be minimised with proper and established clinical guidelines for the tracer injection. Besides skin staining, six studies reviewed by NICE also reported that Magtrace may interfere with MRI, leading to imaging artefacts for up to 5 years after the tracer injection. One of the six studies found that all patients had compromised MRI image quality after a Magtrace injection and that MRI results were non-diagnostic in 5 out of 16 patients.[8] In another study where MRI was performed 42 months after a Magtrace injection, compromised images were reported for 10 out of 25 patients and 3 out of 25 images could not be interpreted at all.[8]

One additional study by Lorek et al (2022) reported similar rates of postoperative complications between the Sentimag and radiotracer methods Complications were all minor.[15]

Effectiveness

Detection Rates

The NICE HTA guidance[8] and two additional studies[16,17] reported on SLN detection rate. Detection rate is defined as the percentage of the patient population where at least one SLN was found and removed during the SLNB procedure.[18] Overall, the Magtrace/ Sentimag system showed non-inferiority to current tracers in terms of SLN detection rates. Similar SLN detection rates have been reported for Magtrace (89.7% to 100%) compared to: the dual technique; Tc-99m with or without blue dye; and blue dye alone (70% to 100%) (Table 2). Specifically for studies that compared Magtrace with the gold standard (dual technique), overall SLN detection rates ranged from 99.3% to 100.0% for Magtrace and 83.3% to 100.0% for dual technique. The concordance rate (where reported) is also high between Magtrace/Sentimag and comparators, ranging from 89.7% to 100%. More details on individual studies are found in Appendix B.

In patients with malignant lymph nodes, detection rates were similar between Magtrace/Sentimag and dual technique or Tc-99m with or without blue dye, ranging from 91.7% to 100% and 88.3% to 100% respectively. The reported detection rate for malignant

lymph nodes was the same between Magtrace and dual technique (95.5%). Concordance between Magtrace and comparators for the detection of malignant lymph nodes was also high, ranging from 90.5% to 100.0%.[18]

Table 2: SLN and Malignant Lymph Node Detection Rates

Study	Population (N)	Comparator	Detection rate (%)		Concordance (%)
			Magtrace	Comparator	
SLN Detection Rate					
NICE (2022)	169	Tc-99m + blue dye (dual technique) exclusively	99.3 – 100.0	83.3 – 100.0	100.0
	1115	Combination of Tc-99m and/or blue dye	91.9 – 97.6	95.0 – 97.8	90.5 – 99.0
	973	Tc-99m only	89.7 – 100.0	85.2 – 100.0	89.7 - 100.0
Vidya et al. (2022)	107	Tc-99m ± blue dye	98.1	96.3	98.1
Yilmaz and Vural (2022)	54	blue dye only	96.3	70.0	NR
Malignant Lymph Node Detection Rate					
NICE (2022)	22	Tc-99m + blue dye (dual technique) exclusively	95.5	95.5	100.0
	160	Combination of Tc-99m and/or blue dye	91.7 – 97.8	88.3 – 98.1	97.7 – 98.1
	148	Tc-99m only	94.4 – 100.0	90.5 – 98.3	90.5 – 100.0

Abbreviations: NICE, National Institute for Health and Care Excellence; Tc-99m, Technetium 99m radioisotope; NR, Not reported

Note: For detailed information, refer to Tables B1 and B2 in Appendix B.

Number of SLN retrieved

Although retrieving more SLNs may reduce the false negative rate of SLNB19, removal of more than four to five SLNs has minimal improvement in the accuracy of SLNB.20 The NICE HTA report and two other studies quantified the number of SLNs retrieved. The overall number of nodes retrieved was 1 to 3 for Magtrace and 1 to 3.29 for the comparators. Most studies did not report whether the difference was statistically significant, although three studies included in the NICE guidance reported that the median number of SLN retrieved using Magtrace were slightly higher compared to Tc-99m only. The summary of number of SLN retrieval can be found in Table 3.

Table 3: Number of SLNs Retrieved

Study	Total Number of Patients	Comparator	Number of Nodes Retrieved*		P value
			Magtrace	Comparator	
NICE Guidance Evidence Base					
Alvarado et al. (2019)	146	Tc-99m + Blue Dye (dual technique) Exclusively	2.4 (1.34)	2.4 (1.19)	NR
Karakatsanis et al. (2018)	12		1 [1-3]	1 [1-2]	NR
Pouw et al. (2015)	11		2.00 (NR)	1.73 (NR)	NR
Karakatsanis et al. (2018)	12	Combination of Tc-99m and/or Blue Dye	1 [1-2]	1 [1-2]	NR
Douek et al. (2013)	347		1.83 (NR)	1.80 (NR)	NR
Douek et al. (2014)	160		2.02 (NR)	1.86 (NR)	NR
Sukumar et al. (2020)	113		1.75	1.79	NR
Pelc et al. (2022)	124	Tc-99m Only	3 [2-4]	2 [2-2]	<0.0001
Rubio et al. (2015)	120		2.2 [NR]	1.9 [NR]	0.001
Shams et al. (2021)	59		1 [1-7]	1 [1-1]	<0.0001
Thill et al. (2014)	150		1.9 {1-9}[21]	1.8 {1-9}	NR
Other Evidence Base					
Vidya et al. (2022)	107	Tc-99m ± Blue Dye	1.76 {1-4}	1.82 {1-4}	NR
Lorek et al. (2022)	345	Tc-99m Only	1.83 (NR) / 1.5 {1-3}	3.29 (NR) / 2.5 {1-8}	NR

* Reported as Mean (SD), Median [IQR] or {Median Range}

Abbreviations: NICE, National Institute for Health and Care Excellence; Tc-99m, Technetium 99m radioisotope; NR, Not reported

Impact on Public Healthcare System

Additionally, the use of Magtrace may lead to improvements in the efficiency of the healthcare system[18] as there is reduced waste of clinical time due to delays or cancellation of SLNB procedures associated with the use of radioisotopes. This may arise from multiple logistical concerns with the use of Tc-99m as it is hard to obtain, requires specialist facilities to store and requires specialised staff to prepare.[22] Hence, any disruptions in the supply chain could lead to delays in patient going for SLNB as well when using radioisotopes. Magtrace is easier to source and can be kept at room temperature without the need for specialised facilities to store and handle.

Cost Effectiveness

A decision-tree model from NICE to compare Magtrace and Sentimag to dual technique in patients with breast cancer undergoing SLNB procedure showed that Magtrace/Sentimag

resulted in a cost savings of £78.90 (S$128)[a] per patient. Cost savings remained even after assuming 1% of the population are unable to use Magtrace due to contraindications (£78.11), or 1% of population require future MRI and 5% of those people have an MRI image compromised due to Magtrace leading to additional gadolinium-enhanced MRI required (£78.82).

However, NICE indicated that there was uncertainty on cost saving, as it was contingent on whether the opportunity cost related to one additional SLNB procedure performed each week could be realised in clinical practice. If no additional procedure was realised, Magtrace/Sentimag would be cost incurring by £58.17. The opportunity cost model was affected by multiple factors, including the amount of additional SLNB procedures done, the number of clinics that can do additional SLNB procedures, the duration for intraoperative injection of Magtrace, and clinic access to and practise with radiopharmacy. In the local setting, cost effectiveness of Magtrace/Sentimag might be questionable, as clinician feedback has indicated the use of Magtrace/Sentimag would not change the number of SLNB procedures performed. (Personal communication: Senior Consultant from Sengkang General Hospital, 8 February 2023)

Ongoing Clinical Trials

There are currently two ongoing studies investigating Magtrace for breast cancer identified from the ScanMedicine database (NIHR Innovation Observatory; Table 4). One feasibility trial seeks to investigate the impact of using a lower Magtrace dosage for SLN detection rate compared to Tc-99m with blue dye. Another trial compares the efficacy of Magtrace as a tracer with Tc-99m. Both trials are currently recruiting and are estimated to finish by April 2023 and December 2023 respectively.

Table 4: Ongoing Clinical Trials

Study name (Trial ID)	Estimated Enrolment	Aim of Trial	Estimated Study Completion Date
Sentinel Node Localization and Staging With Low Dose Superparamagnetic Iron Oxide (MAGSNOW) (NCT05359783)[23]	30	The aim of this study was to determine if SLN detection using ultra-low dose SPIO is feasible.	30 April 2023
Magseed and Magtrace Localization for Breast Cancer (NCT05161507)[24]	70	The aim of this single-centre prospective study is to compare the efficacy of the Sentimag localisation system and its tracer Magtrace, as a tracer in sentinel node biopsy in breast cancer with Tc-99m. It also aims to follow skin discoloration after Magtrace injection and describe when and how it resolves. The Magtrace will be injected preoperatively. Sentinel node biopsy will be performed, and detection rates will be recorded for both methods	31 December 2023
Abbreviations: SLN, sentinel lymph node; SPIO, superparamagnetic iron oxide; Tc-99m, Technetium 99m radioisotope			

[a] Based on the Monetary Authority of Singapore exchange rate as of 10 January 2023: £1=S$1.6197. Figures were rounded to the nearest dollar.

Summary

In summary, the Magtrace/Sentimag system was found to be generally safe and non-inferior to current standards with cost savings reported. In terms of safety, Magtrace was generally safe to use, without any serious adverse events reported. The main complication reported in trails was staining of the skin at the injection site. Another potential adverse effect is possible interference from a Magtrace injection with MRI scans performed near the injected region, which could last for up to 5 years. Magtrace/Sentimag was found to be non-inferior to dual technique for SLNB in terms of detection rates for SLNs and the number of SLNs removed. Healthcare system benefits would be that storage and supply of Magtrace is easier and more stable than Tc-99m, and there is less chance for delays in SLNB procedures due to supply chain disruptions. Based on the NICE report, use of Magtrace/Sentimag may result in cost savings of £78.90. However, it could also result in cost incurring of £58.17, if the opportunity costs of additional SLNB cannot be realised.

There is a lack of studies on how the use of the Magtrace /Sentimag system impacts patient outcomes.

VII. Estimated Costs

Based on NICE's HTA report, the cost of Magtrace is £226 (S$366)[a] per unit, while a single reusable Sentimag probe costs £24,900 (S$40,331)[a].

VIII. Implementation Considerations

There may be a considerable learning curve for clinicians to adopt the technology. The manufacturer suggests a minimum of 5 procedures to build familiarity with Magtrace and the Sentimag system, and a minimum of 50 procedures or 2 years of experience to be fully competent.[8] Of note, a local pilot trial of Magtrace/Sentimag for SLNB for breast cancer diagnosis found that the Magtrace performs equally well as the standard techniques with high detection rates.[10] The pilot study also reported that most surgeons found it easy to use Magtrace/Sentimag. However, the technology was withdrawn from the Singapore market, presumably due to low utilisation. (Personal communication: Senior Consultant from Sengkang General Hospital, 8 February 2023)

Another factor to consider is that use of other metallic or magnetic materials during the procedure will interfere with the Sentimag probe. Therefore, it is advised that surgeons use either plastic or titanium tools when using Magtrace and Sentimag. This may need considerations in clinical operating protocols for SLNB when using Magtrace, including an initial familiarisation phase for surgeons with the new tools. However NICE agreed that after familiarisation, it should not impact significantly on the procedure.[8] The local pilot study authors also noted some inconvenience with the use of costly plastic instruments and the need to re-equilibrate the Sentimag's magnetic probe repeatedly.[10]

IX. Concurrent Developments

Rizobist® is an alternative SPIO tracer that also use magnetic particles to detect SLNs. Rizobist® was used in a study to determine if the dosage of SPIO affects SLN detection in SLNB. This tracer has shown similar detection rates when compared to Tc-99m and blue dye but has

not received FDA approval or CE mark.[25] Another tracer currently being tested for SLNB is indocyanine green. This fluorescent tracer has shown superiority to blue dye alone in terms of safety and accuracy of localising SLNs.[21,26] Table 5 provides a brief summary of both of these tracers.

Table 5: Concurrent Developments

Tracer	Brief Description	Status
Ferucarbotran (Rizobist®)	Ferucarbotran (Resovist; Kyowa CritiCare, Tokyo, Japan) is another magnetic tracer. The particles are iron oxide covered with carboxydextran. The average hydrodynamic diameter of each particle is about 57nm.	No approval from FDA No CE Mark
Indocyanine Green	Indocyanine green is a low toxicity medical dye able to emit fluorescence after excitation by near-infrared light. Indocyanine green has been used for other medical diagnostics like determining cardiac output, hepatic function, liver and gastric blood flow and ophthalmic angiography.	Indocyanine green has been approved for medical applications since 1959.[27]
Abbreviations: FDA, United States Food and Drug Administration; CE, Conformité Européenne.		

X. Additional Information

NICE recommends Magtrace and Sentimag as an alternative for locating SLNs for breast cancer in hospitals with limited or no access to radiopharmacy.[8]

The Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) analysed the SentiMag/Sienna+ for SLN localisation in breast cancer. The group acknowledged the potentially significant impact of this technology for SLNB for patients with breast cancer and recommended the monitoring of this technology.[28]

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Appendix

Appendix A: Studies included and study design

Table A1: List of included studies

Type of Study	Number of studies included
NICE Guidance Report	1
Published studies	3

Note:

1. Inclusion criteria
   a. Studies that fulfil the PICO criteria listed in Table 1.
2. Exclusion criteria
   a. Studies only available in abstract form.
   b. Duplicate studies.

Table A2: Information on the included studies

Author (Year)	Type of Study	Interventions	Number of Participants	Summary of Results
NICE (2022)	HTA Guidance Report	Magtrace & Sentimag; Tc-99m; blue dye; Tc-99m with blue dye	4,202 (18 studies)	• Sentinel and malignant lymph node detection rate was non-inferior for SentiMag compared with standard care. • Magtrace administration may cause artefacts in future MRI of the injection and drainage sites. • Skin staining is the main adverse event associated with Magtrace. • Magtrace and Sentimag are cost savings compared to dual technique.
Lorek et al. (2022)	Retrospective, Comparative Study	Sienna+ & Sentimag; Tc-99m	345	• Sensation disorders in the arm were the most common complications found. • Both interventions are comparable diagnostic methods for SLNB, with a low risk of complications.
Vidya et al. (2022)	Prospective, Comparative Study	Sienna+ & Sentimag; Tc-99m with or without blue dye	109	• The identification rate of the magnetic technique is not inferior to the standard technique in SLNB. • Sentimag is a suitable alternative that avoids the complexities of nuclear medicine, hazards of radiation and the anaphylaxis risk of blue dye.
Yilmaz and Vural (2022)	Retrospective, Comparative Study	Sienna+ & Sentimag; blue dye	54	• Sentimag is an accurate alternative for SLNB in patients after neoadjuvant chemotherapy. • Sentimag is also safe, easy to perform with minimal adverse effects and is a

				viable alternative if nuclear medicine is not available.
Abbreviations: HTA, health technology assessment; NICE, National Institute for Health and Care Excellence; Tc-99m, Technetium 99m radioisotope; MRI, Magnetic resonance imaging; SLNB, sentinel lymph node biopsy.				

Appendix B: Individual SLN and Malignant Lymph Node Detection Rates

Table B1: Per Patient SLN Detection Rates

Study	N	Comparator	Detection rate (%)		Concordance (%)
			Magtrace	Comparator	
NICE Guidance Evidence Base					
Alvarado et al. (2019)	146	Tc-99m + blue dye (dual technique) exclusively	99.3	98.6	100.0
Karakatsanis et al. (2018)	12		100.0	83.3	100.0
Pouw et al. (2015)	11		100.0	100.0	100.0
Douek et al. (2013)	347	Combination of Tc-99m and/or blue dye	91.9	96.3	90.5
Douek et al. (2014)	160		94.4	95.0	93.1
Houpeau et al. (2016)	108		97.2	95.4	99.0
Karakatsanis et al. (2016)	206		97.6	97.1	98.0
Pinero-Madrona et al. (2015)	181		97.2	97.8	98.3
Sukumar et al. (2020)	113		97.2	97.2	NR
Alvarado et al. (2019)	146	Tc-99m only	99.3	95.9	100.0
Castillo-Berrio et al. (2015)	22		95.4	100.0	NR
Ghili et al. (2017)	193		97.9	99.0	97.9
Gimenez-Climent et al. (2021)	89		97.8	97.8	100.0
Granados et al. (2015)	29		89.7	100.0	89.7
Munawwar et al. (2021)	55		96.6	85.2	NR
Pelc et al. (2022)	124		100.0	100.0	100.0
Rubio et al. (2015)	120		98.3	95.7	98.2
Rubio et al. (2020) (Cohort 3)	45		100.0	100.0	100.0
Thill et al. (2014)	150		98.0	97.3	99.3
Other Evidence Base					
Vidya et al. (2022)	107	Tc-99m ± blue dye	98.1	96.3	98.1
Yilmaz and Vural (2022)	54	blue dye only	96.3	70.0	NR

Abbreviations: NICE, National Institute for Health and Care Excellence; Tc-99m, Technetium 99m radioisotope; NR, Not reported; SLN, sentinel lymph node

Table B2: Per Patient Malignant Lymph Node Detection Rates

Study	Total Number of Positive Patients (% of total patients)	Comparator	Detection rate (%)		Concordance (%)
			Magtrace	Comparator	
NICE Guidance Evidence Base					
Alvarado et al. (2019)	22 (15.1%)	Tc-99m + blue dye (dual technique) exclusively	95.5	95.5	100.0
Houpeau et al. (2016)	46 (42.6%)	Combination of Tc-99m and/or blue dye	97.8	95.7	97.7
Karakatsanis et al. (2016)	54 (26.2%)		96.3	98.1	98.1
Pinero-Madrona et al. (2015)	60 (33.1%)		91.7	88.3	98.1
Ghili et al. (2017)	57 (29.5%)	Tc-99m only	96.5	98.3	96.4

Gimenez-Climent et al. (2021)	21 (23.6%)		100.0	90.5	90.5
Rubio et al. (2015)	36 (30.5%)		94.4	91.7	97.0
Thill et al. (2014)	34 (22.7%)		97.1	91.2	100.0
Abbreviations: NICE, National Institute for Health and Care Excellence; Tc-99m, Technetium 99m radioisotope					