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Systematic Review

Systematic review of targeted axillary dissection in node-positive breast cancer treated with neoadjuvant systemic therapy: variation in type of marker and timing of placement

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Abstract

Background: In node-positive (cN+) breast cancer treated with neoadjuvant systemic therapy, combining sentinel lymph node biopsy and targeted lymph node excision, that is targeted axillary dissection, increases accuracy. Targeted axillary dissection procedures differ in terms of the targeted lymph node excision technique. This systematic review aimed to provide an overview of targeted axillary dissection procedures regarding definitive marker type and timing of placement: before neoadjuvant systemic therapy (1-step procedure) or after neoadjuvant systemic therapy adjacent to a clip placed before the neoadjuvant therapy (2-step procedure).

Methods: PubMed and Embase were searched, to 4 July 2023, for RCTs, cohort studies, and case–control studies with at least 25 patients. Studies of targeted lymph node excision only (without sentinel lymph node biopsy), or where intraoperative localization of the targeted lymph node was not attempted, were excluded. For qualitative synthesis, studies were grouped by definitive marker and timing of placement. The targeted lymph node identification rate was reported. Study quality was assessed using a National Institutes of Health quality assessment tool.

Results: Of 277 unique records, 51 studies with a total of 4512 patients were included. Six definitive markers were identified: wire, ^{125}I-labelled seed, ^{99m}Tc, (electro)magnetic/radiofrequency markers, black ink, and a clip. Fifteen studies evaluated one-step procedures, with the identification rate of the targeted lymph node at surgery varying from 8 of 13 to 47 of 47. Forty-one studies evaluated two-step procedures, with the identification rate of the clipped targeted lymph node on imaging after neoadjuvant systemic therapy varying from 49 to 100%, and the identification rate of the targeted lymph node at surgery from 17 of 24 to 100%. Most studies (40 of 51) were rated as being of fair quality.

Conclusion: Various targeted axillary dissection procedures are used in clinical practice. Owing to study heterogeneity, the optimal targeted lymph node excision technique in terms of identification rate and feasibility could not be determined. Two-step procedures are at risk of not identifying the clipped targeted lymph node on imaging after neoadjuvant systemic therapy.

Introduction

In clinically node-positive (cN+) breast cancer, axillary lymph node dissection (ALND) is associated with substantial morbidity[1,2], but used to be standard of care. At present, patients with cN+ disease often receive neoadjuvant systemic therapy (NST). After NST, approximately one-third of patients achieve an axillary pCR[3–6], which is associated with improved prognosis compared with having residual axillary disease[7–10]. Less invasive axillary staging procedures were therefore proposed in an effort to enable response-guided treatment, by identifying an axillary pCR so that ALND could be omitted in such patients. Currently, several less invasive axillary staging procedures are being performed worldwide.

Several studies have assessed the diagnostic accuracy of these less invasive axillary staging procedures compared with ALND in patients with cN+ disease. Trials[6,11–13] such as SENTINA, SN FNAC, and ACOZOG Z1071 have shown that performing sentinel lymph node biopsy (SLNB) after NST results in false-negative

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rates (FNRs) of 14.2, 13.3, and 12.6% respectively, and a negative predictive value (NPV) that does not exceed 86%. Using dual tracers, immunohistochemistry, and excising at least three sentinel lymph nodes (SLNs) can improve the FNR[6]. The median number of SLNs detected is two[14], and so recommending removal of three or more SLNs may result in node-picking, whereby non-SLNs are also removed. An alternative to SLNB is to specifically target a metastatic axillary lymph node by placing a marker inside it before NST. After NST, this targeted lymph node (TLN) is localized using visual inspection, imaging, or probe-guided methods, and subsequently excised. For example, when the marking the axilla with radioactive iodine (MARI) procedure is undertaken[15], a radioactive iodine-labelled seed (^{125}I seed) is placed before NST, followed by excision of the TLN after NST under the guidance of a hand-held γ probe. The MARI procedure, first described in 2010[16], has an FNR of 7% and NPV of 83.3%. This is comparable to the NPV of SLNB. Lastly, SLNB and excision of a TLN can be combined in the procedure called targeted axillary dissection (TAD)[17].

In a subanalysis of the Z1071 trial[18], published in 2016, a clip was placed in a metastatic axillary lymph node before NST in 170 patients. Intraoperative localization of the clipped lymph node was not attempted, yet reporting whether it was located in either the SLNB or ALND specimen was encouraged. In 29 of 170 patients (24.1%), the clipped lymph node was reported to be found in the ALND specimen, suggesting that performing TAD improves diagnostic accuracy by removing additional relevant lymph nodes[18]. Three studies[17,19,20] assessing TAD in 35–85 patients reported an FNR that varied from 2 to 4%, and an NPV that ranged from 92 to 97%. In 2022, a Dutch prospective multicentre trial[21] investigating radioactive iodine seed localization in the axilla with the sentinel node procedure reported an FNR of 3.5% and an NPV of 92.8% among 212 patients, confirming the superior diagnostic accuracy of TAD. Studies of oncological outcomes, and especially impact on quality of life, of response-guided axillary treatment based on less invasive axillary staging techniques remain limited[22–24].

Meanwhile, a wide variety of TAD procedures are being incorporated into clinical practice, with variation in the type of definitive marker used (for example, magnetic marker, black ink, wire, clip)[20,25–27], as well as the timing of definitive marker placement (before or after NST). The technique used may affect ability to identify the TLN. The aim of this systematic review was to provide an overview of studies reporting on TAD in cN+ breast cancer treated with NST, focusing on types of marker used for TLN excision, timing of marker placement, and ability to identify the TLN.

Methods

Inclusion criteria

The PRISMA checklist was used for this systematic review[28]. A systematic literature search was made for RCTs, cohort studies, and case–control studies with a minimum of 25 included patients describing experience with TAD in cN+ breast cancer treated with NST. Study protocols, conference abstracts, case reports, editorials, commentaries, and reviews were excluded, as were studies for which the full text was not available in English. Pathological confirmation of nodal positivity was not required, as the focus was on the surgical technique and the identification rate (IR) of the TLN, rather than on diagnostic accuracy. Studies in which the suspicious or pathologically proven metastatic axillary lymph node was marked only after NST, that is without clip placement before initiation of treatment, were excluded as this was not in agreement with the definition of TAD[17]. Studies that evaluated only excision of a TLN without SLNB were also excluded, as were those in which intraoperative localization of the TLN was not attempted (for example, only an X-ray was used to check whether the TLN was present in the surgical specimen). Studies that also included patients with clinically node-negative breast cancer or those who underwent primary surgery were excluded if it was not possible to identify the results specifically for patients with cN+ disease treated with NST. If more than one study reported on (part of) the same cohort, only that describing the largest cohort was included.

For qualitative synthesis, studies were grouped by type of definitive marker used and by timing of definitive marker placement. In one-step procedures, the definitive marker was placed before NST, followed by excision of the TLN during surgery. In two-step procedures, a clip was first placed before NST, followed by placement of a definitive marker adjacent to the clip after NST to enable subsequent excision of the TLN during surgery. In clinical practice, a wide variety of clips is used. When assessing the included studies, the specific type of clip used was not taken into account.

Identification of studies

PubMed and Embase were searched until 4 July 2023, without restriction on language or date of publication. The search strategies for both databases (*Appendix S1*) were checked by a librarian specialized in health sciences. The reference lists of included studies were checked for additional relevant studies, as were existing reviews.

Selection of studies

Reference management software (Endnote® version 20.5, Philadelphia, PA, USA) was used to identify and remove duplicate references. The title and abstract of all remaining references, and subsequently the full text of potentially eligible studies, were evaluated independently by two authors. Disagreements regarding eligibility of studies were resolved in a consensus meeting.

Data extraction and analysis

The following variables were extracted from each included study: first author, year of publication, study design, sample size, percentage of patients with cN+ disease in whom nodal positivity at diagnosis was verified by pathology, type of tracer used for SLNB, type of definitive marker used for intraoperative excision of TLN, whether this marker was placed before or after NST, IR of the clipped TLN on imaging after NST (if applicable), IR of the TLN during surgery, percentage of patients who underwent ALND, proportion of SLNB and TLN being the same node (concordance), number of excised lymph nodes (mean or median), and whether immunohistochemistry was used for the assessment of excised lymph nodes. A second author was consulted in case of uncertainty.

The random-effects model for meta-analysis in the metaprop command in Stata® SE16.1 (StataCorp, College Station, TX, USA) was employed to calculate the overall pooled estimate of the IR of the TLN during surgery for both one- and two-step procedures. Effect sizes with 95% confidence intervals and weights were provided in forest plots visualized by type of marker and for the whole group. The variability of IR estimates owing to heterogeneity among included studies was quantified using the I^2 index. The χ^2 test was used to assess statistical heterogeneity. The test was two-sided, and $P < 0.050$ was considered statistically significant.

Quality assessment

One author assessed the quality of the included studies, including the risk of bias, using the National Institutes of Health (NIH) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, which consists of 14 questions[29]. All questions could be answered with yes, no, cannot determine, not applicable, or not reported. Based on these responses, studies were rated as having good, fair, or poor quality. A second author was consulted in the event of uncertainty.

Results

Study selection

The literature search identified 460 articles. After removal of duplicates, 277 titles and abstracts were screened, followed by full-text evaluation of 89 articles. Eventually, 51 studies with a total of 4512 patients were included in the qualitative synthesis (*Fig. 1*).

Study characteristics

Characteristics of the included studies, sorted by type of definitive marker, are listed in *Table S1*. In 42 of 51 studies (82%), nodal positivity at diagnosis was proven by pathology in all patients. In 18 of 51 studies (35%), dual tracer (consisting of blue dye and radioisotope) was used routinely during SLNB. The percentage of patients who underwent ALND was available in 42 of 51 studies (82%), and varied from 22 to 100%. In 8 of 42 studies, all patients underwent ALND.

Type of definitive marker

Six definitive markers were used to mark the TLN, all in combination with SLNB. In 17 studies[17,19,27,30–43], on the day of surgery a wire was placed after NST in the clipped TLN. In 12 studies[17,21,41,42,44–51], the clipped TLN was marked with a ^{125}I seed, either before or after NST, and in 5 studies[52–56], a form of ^{99m}Tc was used to localize and excise the clipped TLN. In three of five studies[52–54], the clipped TLN was injected with ^{99m}Tc-labelled macroaggregated albumin under ultrasound guidance 1 day before surgery. In the other two[55,56], either ^{99m}Tc-labelled Nanoscan tracer or ^{99m}Tc-labelled nanocolloid was injected (peritumorally or periareolarly) to localize the SLN by single-photon emission CT (SPECT)/CT on the day of surgery or 1 day before, and to determine whether the clipped TLN was an SLN. If not, either ^{99m}Tc-labelled Nanoscan tracer was injected into the clipped TLN, or a wire was placed under ultrasound guidance to enable excision of the clipped TLN. In both ^{125}I and ^{99m}Tc marking, a hand-held γ probe was used to localize and subsequently excise the TLN during surgery. In 10 studies, the clipped TLN was marked with a magnetic marker[25,57–61], radiofrequency identification (RFID) tag[57], or an electromagnetic reflector[43,57,62–64], either before or after NST. At surgery, the TLN was localized using a hand-held probe based on magnetic fields, radiowave signalling, or radar/infrared technology respectively. In nine studies[26,65–72], the clipped TLN was tattooed with black ink (carbon, charcoal, or 4% carbon microparticle suspension), either before or after NST. Subsequently, it was excised under visual guidance during surgery. In two studies[73,74], the clipped TLN was localized and excised under intraoperative ultrasound (IOUS) guidance.

Timing of marker placement

Five studies assessed both one- and two-step procedures, whereas the remainder evaluated either a one- or two-step procedure. *Tables 1* and *2* provide detailed information for one-step (15 studies) and two-step (41 studies) procedures respectively.

Studies using a one-step procedure

Fifteen studies described a 1-step procedure, with a total of 1321 patients. In all studies, the definitive marker was placed in the metastatic or suspicious TLN before NST, followed by surgical excision after NST. The marking technique comprised the use of either a ^{125}I seed (4 studies), magnetic marker (2 studies), black ink (7 studies), or a clip combined with IOUS-guided localization (2 studies). Overall, the IR of the TLN at surgery varied from 8 of 13 to 47 of 47. When grouped by type of definitive marker, the IR ranged from 93.0 to 99.3, 98 to 44 of 44, 8 of 13 to 47 of 47, and 30 of 37 to 96.2% for ^{125}I seed, magnetic marker, black ink, and clip with IOUS-guided localization respectively. The overall pooled IR at surgery was 96 (95% c.i. 93 to 98)% (*Fig. S1*). Statistically significant heterogeneity was present between studies ($I^2 = 73.2\%$, $P < 0.001$). The concordance rate between the TLN and SLN ranged between 47.9 and 100%.

Studies using a two-step procedure

Forty-one studies described a 2-step procedure, with a total of 3191 patients. In all studies, a clip was placed in the metastatic or suspicious TLN before NST. After NST, the clipped TLN was localized with imaging (ultrasonography in the vast majority), and was subsequently marked with either a wire (17 studies), ^{125}I seed (10 studies), ^{99m}Tc (5 studies), (electro)magnetic/radiofrequency marker (11 studies), or black ink (3 studies). The IR of the clipped TLN on imaging was reported in 23 of 41 studies, ranging from 49 to 100%. In 18 of 41 studies, the IR of the clipped TLN could not be determined on imaging (only an overall IR was provided in 3 studies), or it was not reported (15 studies; mostly because patients were excluded from analyses in the event of unsuccessful localization of the clipped TLN on imaging). Overall, the IR of the TLN at surgery varied from 17 of 24 to 100%. When grouped by type of marker, the IR at surgery ranged from 17 of 24 to 100, 11 of 12 to 29 of 29, 27 of 30 to 98, 76 to 100, and 82 to 27 of 28% respectively for wire, ^{125}I seed, ^{99m}Tc, (electro)magnetic/radiofrequency markers, and black ink. The IR at surgery could either not be determined or was not reported in six studies. The overall pooled IR was 97 (95% c.i. 95 to 98)%. Statistically significant heterogeneity was present between studies ($I^2 = 69.3\%$, $P < 0.001$) (*Fig. S2*). The concordance rate between the TLN and SLN was reported in 28 studies and ranged from 35.7 to 91.0%.

Quality assessment

Assessed using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, 8 studies were rated as being of good quality, 40 of fair quality, and 3 of poor quality (*Table S2*).

Discussion

Worldwide, several different surgical procedures are being used in clinical practice for axillary staging after NST in cN+ breast cancer. Most institutions now prefer less invasive staging procedures, including SLNB alone, excision of a TLN, or the TAD procedure, with the aim of enabling response-guided axillary

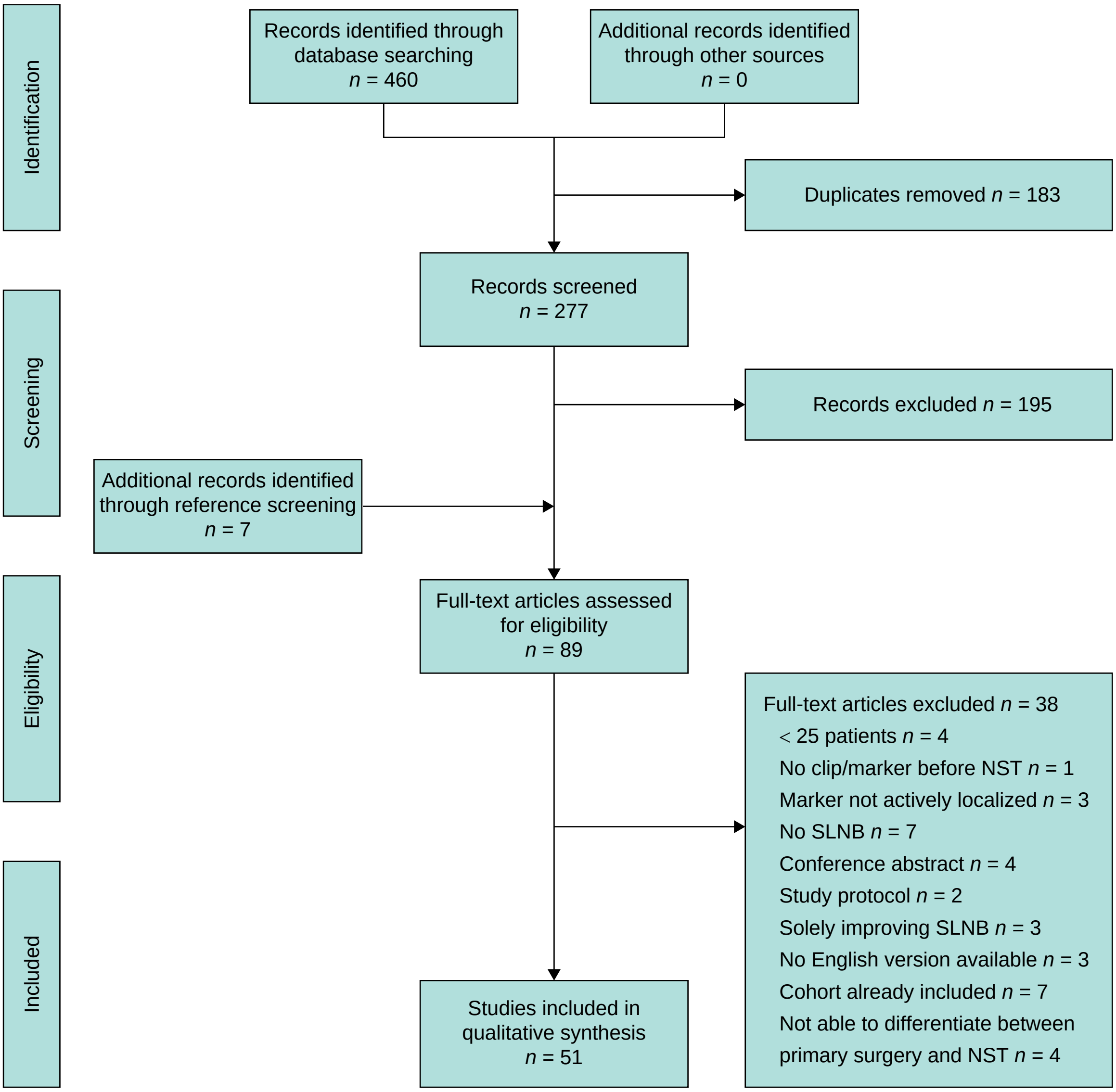

Fig. 1 Flow chart showing selection of studies for review

NST, neoadjuvant systemic therapy; SLNB, sentinel lymph node biopsy.

treatment after NST[75–78]. This systematic review included 51 studies of TAD with a total of 4512 patients, and a wide range of TLN excision techniques were identified. Six definitive markers were recognized: wire, ^{125}I seed, ^{99m}Tc, (electro)magnetic/radiofrequency markers, black ink, and clips (with IOUS-guided localization and excision). Apart from this, variations in timing of definitive marker placement were assessed.

The use of wire-guided localization is both accessible and inexpensive[79]. The wire, however, needs to be placed 1 day before operation or on the day of surgery, which requires adequate planning. Furthermore, the wire may dislocate in the event of patient movement or manipulation during surgery, which can complicate retrieval of the clipped TLN[32]. The wire may be also be uncomfortable for the patient. A ^{125}I seed does not have to be placed on the day of surgery, and can even be placed before NST. In addition, the use of a hand-held γ probe facilitates identification of the TLN[16]. A downside is that the use of ^{125}I seeds is strictly regulated, making widespread application difficult because many countries do not allow them to be used for diagnostic purposes, or only allow them if the ^{125}I seed is placed after NST[79]. An alternative would be to mark the TLN with ^{99m}Tc, which is inexpensive, already widely applied for diagnostic purposes, and the use of a hand-held γ probe facilitates localization of the TLN during surgery[52–54]. A downside is its short half-life of 6 h, so it has to be injected just before surgery[52–54]. If ^{99m}Tc is not injected into the TLN itself, but peritumorally or periareolarly (as is already part of routine SLNB), and the clipped TLN is an SLN on SPECT/CT, an additional procedure, for example injecting ^{99m}Tc-labelled Nanoscan tracer into the clipped non-SLN to enable excision, is not needed. Magnetic markers, RFID tags, and electromagnetic reflectors are promising non-radioactive alternatives, which can all be placed before the start of NST, and are localized with a hand-held probe to facilitate intraoperative excision of the TLN[25,43,57–64]. In the case of the RFID tag and electromagnetic reflector, the probe also displays the distance from the tip of the probe to the marker[80]. As these three markers are not radioactive, there are no regulatory issues, but they are more expensive and require purchase of additional instruments, such as the localization device[79]. In addition, the magnetic marker

Table 1 Studies describing a one-step procedure

Reference	Sample size	Type of definitive marker	IR at surgery (%)
Simons et al.[42]	68	^{125}I seed	93
Rebollo Aguirre et al.[48]	6*	^{125}I seed	97†
Simons et al.[21]	238	^{125}I seed	94.1
Munck et al.[51]	142	^{125}I seed	99.3
Martinez et al.[60]	44	Magnetic marker	44 of 44
Barry et al.[61]	54	Magnetic marker	98
Patel et al.[66]	47	Carbon ink	47 of 47
Natsiopoulos et al.[26]	75	Carbon ink	95
Allweis et al.[67]	63	Carbon ink	95
Dostalek et al.[68]	27	Carbon ink	22 of 27
de Boniface et al.[69]	149	Carbon ink	94.6
Pinto et al.[70]	13*	Carbon ink	8 of 13
Spautz et al.[72]	123	4% CMS	98.3
Pinto et al.[73]	37	Clip (IOUS)	30 of 37
Siso et al.[74]	235	Clip (IOUS)	96.2

*Included as the total study comprised 25 patients or more. †Both one- and two-step procedures were assessed; an overall outcome was provided. IR, identification rate; CMS, carbon microparticle suspension; IOUS, intraoperative ultrasonography.

and RFID tag both create an artefact on MRI[25,81], complicating response evaluation, especially when the primary tumour is located in the lateral upper quadrant. Employing a magnetic marker also requires use of non-magnetic equipment during surgery. The electromagnetic marker may also create minimal artefacts[81]. Currently, the magnetic marker is being updated, in an effort to reduce MRI artefacts and to avoid the need for non-magnetic equipment[82]. Another non-radioactive and inexpensive technique is to tattoo the TLN with black ink. As this technique lacks a detection probe and the ink cannot be visualized on imaging, it is more difficult to localize the TLN during surgery, and the IR for this type of marker was reported to be as low as 61.5%. Moreover, studies[26,79] have described spontaneous migration of black ink, but also deliberate distribution of black ink around the TLN to increase the IR[65,66]. In both instances, this can result in unnecessary excision of additional lymph nodes[26,66], increasing the risk of postoperative morbidity. Finally, IOUS-guided excision of the clipped TLN is possible, which is inexpensive and does not require additional markers or the purchase of new instruments. It does require an ultrasound machine in the operating room, and a specialist qualified to perform IOUS[79].

As a result of the abovementioned benefits and drawbacks of the different techniques, institutions and/or specialists each have their own TAD preferences, resulting in a wide variety of techniques used in daily practice. As the included studies are very heterogeneous with a broad range of reported IRs, it is not possible to conclude which technique is superior in identifying the TLN. This systematic review, however, does show an important drawback of two-step procedures that breast cancer specialists need to take into consideration. The TLN needs to be localized twice, not only at surgery, but also after NST in order to place the definitive marker. The ability to localize the clipped TLN on imaging after NST varied from 49 to 100%. Importantly, 18 of 41 studies did not report any data regarding localization of the clipped TLN. The wide variation in ability to localize the clipped TLN on imaging may be explained by the diverse range of clips used in clinical practice. In addition, it may be influenced by the level of experience of the specialist performing the localization, and whether or not this is done by a dedicated breast cancer specialist. Furthermore, the inability to identify the TLN on imaging after NST is possibly explained to the fact that the visibility of clips decreases with time[83]. When a hyperechogenic clip is placed in the hypoechogenic cortex, regression of the cortex in the event of response to NST can also affect the visibility of the clip or cause the clip to dislocate[84]. This is in accordance with the multivariable analyses of Kuemmel *et al.*[19], in which an axillary pCR on imaging was also associated with inability to identify the TLN at surgery. Hence, it is important to use a clip with good visibility on ultrasonography.

A large number of studies describing experiences with marking techniques for TLN excision were identified in this systematic review. Although it is of great importance that these studies are performed to share experiences, the included studies also had some limitations. Most had a relatively small sample size, with study populations ranging from 25 to 543 patients. Twenty-four studies had fewer than 60 patients. For example, in the study of Pinto *et al.*[70], which assessed both one- and two-step procedures with carbon ink in a prospective cohort, the IR of the TLN at surgery was 61.5% for the one-step procedure. This was, however, based on a small subgroup of the study population (8 of 13 patients). Another limitation was the retrospective (45% of studies) or single-centre (80%) study design. Moreover, the definition of IR was not always clear and, for two-step procedures, the IR of the clipped TLN on imaging was not provided in 18 of 41 studies. Because of these limitations and study heterogeneity, the results of the random-effects model should be interpreted with caution. Finally, it was not considered whether, at the time of diagnosis, the definitive marker (in a 1-step procedure) or clip (in a 2-step procedure) was placed directly after fine-needle aspiration cytology or core needle biopsy of the suspicious axillary lymph node, or if this was done after the lymph node had been shown to be metastatic by pathology. Along this line, the assessment did not include the different types of clip used for marking the TLN before NST, which also likely varies between, and even within, institutions.

High-quality prospective studies are thus needed that evaluate both one- and two-step procedures, provide a clear definition of IR, and take into account the results of clip identification on imaging in two-step procedures. Currently, the Magellan trial (NCT03796559) is recruiting patients in a prospective study evaluating a magnetic marker in a one-step procedure. In addition, Hartmann *et al.*[85] recently published results regarding the applicability of a magnetic marker in one-step procedure in a multicentre cohort of 151 patients. The TLN was removed successfully in 146 patients, which resulted in an IR of 96.0%. Response assessment with MRI was reported to be compromised in 15 of 151 patients (9.9%). Furthermore, in the prospective IMTAD study[86], which included 189 patients, marking with a ^{125}I seed (135 patients), magnetic marker (30), or carbon suspension (24) after NST in a clipped TLN are being compared. Recently published results demonstrated comparable complication rates regarding marker placement and localization, and marker dislodgement.

In the meantime, while TAD and other less invasive axillary staging procedures are being performed in daily practice worldwide, limited but increasing evidence is available regarding the oncological outcomes of response-guided treatment based on less invasive axillary staging procedures. Interestingly, although these procedures were initially introduced to omit ALND in the event of an axillary pCR, ALND

Table 2 Studies describing a two-step procedure

Reference	Sample size	Type of definitive marker	IR on imaging after NST (%)	IR at surgery (%)
Plecha *et al.*[30]	73	Wire	n.r.	97
Dashevsky *et al.*[31]	28	Wire	28 of 28	26 of 28
Hartmann *et al.*[32]	30	Wire	24 of 30	17 of 24
Balasubramanian *et al.*[27]	25	Wire	25 of 25	23 of 25
Alarcon *et al.*[33]	28	Wire	28 of 28	28 of 28
Flores-Funes *et al.*[34]	60	Wire	97	97
Garcia-Novoa *et al.*[35]	42	Wire	42 of 42	42 of 42
Gurleyik *et al.*[36]	64	Wire	98	100
Sierra *et al.*[37]	51	Wire	n.r.	96
Kuemmel *et al.*[19]	423	Wire	c.d.	77.8*
Acea-Figueira *et al.*[38]	81	Wire	100	99
Sargent *et al.*[39]	62	Wire	n.r.	n.r.
Wu *et al.*[40]	239	Wire	c.d.	94.1*
Munck *et al.*[41]	543	Wire (263)	79.4†	90.1
		^{125}I seed (103)		96.1
		Ink on skin (62)		82
		Magnetic marker (3)		3 of 3
Caudle *et al.*[17]	96	^{125}I seed (94)	n.r.	n.r.
		Wire (2)		
Diego *et al.*[44]	30	^{125}I seed	29 of 30	29 of 29
Nguyen *et al.*[45]	25	^{125}I seed	20 of 25	20 of 20
Beniey *et al.*[46]	35	^{125}I seed	34 of 35	34 of 35
Simons *et al.*[42]	70	^{125}I seed (12)	n.r.	11 of 12
		Wire (58)		95
Aragon-Sanchez *et al.*[47]	32	^{125}I seed	29 of 32	31 of 32‡
Rebollo Aguirre *et al.*[48]	44	^{125}I seed	n.r.	97§
Weiss *et al.*[49]	78	^{125}I seed	c.d.	c.d.
Clark *et al.*[50]	77	^{125}I seed	n.r.	97
Fuertes Manuel *et al.*[52]	30	^{99m}Tc	30 of 30	27 of 30
del Castillo *et al.*[53]	54	^{99m}Tc	n.r.	98
ella *et al.*[54]	77	^{99m}Tc	94	97
Winder *et al.*[55]	38	^{99m}Tc	n.r.	37 of 38
Dilege *et al.*[56]	61	^{99m}Tc	93	97
Laws *et al.*[57]	56	RFID tag (43)	95†	93†
		Magnetic marker (12)		
		Electromagnetic reflector (1)		
Sun *et al.*[62]	45	Electromagnetic reflector	n.r.	45 of 45
Balija *et al.*[43]	99	Electromagnetic reflector (57)¶	84	100¶
		Wire (42)	35 of 42	79†
Weinfurtner *et al.*[63]	105	Electromagnetic reflector	n.r.	100.0
Taj *et al.*[64]	80	Electromagnetic reflector	49	n.r.
Mariscal Martinez *et al.*[58]	30	Magnetic marker	30 of 30	30 of 30
Reitsamer *et al.*[25]	40#	Magnetic marker	40 of 40	40 of 40
Simons *et al.*[59]	51	Magnetic marker	98	100
Martinez *et al.*[60]	37	Magnetic marker	n.r.	37 of 37
Barry *et al.*[61]	74	Magnetic marker	98	76
Kim *et al.*[65]	28	Charcoal	n.r.	27 of 28
Pinto *et al.*[70]	18**	Carbon ink	n.r.	17 of 18
Porpiglia *et al.*[71]	32	Carbon ink	n.r.	27 of 32

*An overall identification rate (IR) was provided (on imaging and during surgery combined). †More than one marking technique was assessed; an overall outcome was provided. ‡Three of 32 patients underwent stereotactic wire localization with mammography to enable excision. §Both one- and two-step procedures were assessed; an overall outcome was provided. ¶In 22 patients, the marker was placed in the clipped axillary lymph node before or during neoadjuvant systemic therapy (NST). #In two patients, the marker was placed directly before NST. **Included as the total study comprised 25 patients or more. n.r., Not reported; c.d., cannot determine.

is now also being omitted in selected patients with residual disease[75]. Van Loevezijn *et al.*[23] recently published 3-year follow-up results of the MARI protocol, in which axillary treatment decisions were made based on the findings of [^{18}F] fluorodeoxyglucose PET–CT in combination with the outcome of the MARI procedure. ALND was omitted in 217 of 272 patients (80.0%) and replaced by axillary radiotherapy in 161 (74.2%) in this single-centre study, with a 3-year axillary recurrence-free survival rate of 98.0 (95% c.i. 96.0 to 100)%. NSABP-B51/RTOG 1304 and ATNEC (NCT01872975 and NCT04109079 respectively) are ongoing RCTs evaluating ALND and/or locoregional radiotherapy in patients with cN+ breast cancer treated with NST, and are including patients with ypN0 disease, whereas Alliance A011202 and TAXIS (NCT01901094 and NCT03513614 respectively) are including patients with ypN+ disease. Together with registry studies such as MINIMAX and AXSANA[83,87], these trials will provide more evidence about appropriate locoregional treatment strategies for cN+ disease in terms of long-term prognosis, in order to prevent overtreatment as well as undertreatment. In addition, these trials may help determine the optimal procedure for axillary staging in such patients, not only in terms of IR and feasibility but also oncological safety and quality of life. With regard to quality of life, the number of excised lymph nodes should also be taken into account, as this can affect arm morbidity. For instance, excision of three or more SLNs may be required when SLNB alone is performed (to improve the FNR), whereas TAD may involve the removal of a single lymph node.

The present systematic review has underlined the scarcity of high-quality studies, rendering it impossible to determine the optimal procedure in terms of IR and feasibility. Each TLN excision technique, however, has its own benefits and drawbacks that should be taken into consideration when performing TAD in clinical practice.

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Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS* online.

Data availability

No new data were generated or analysed in this manuscript.

References

1. Mansel RE, Fallowfield L, Kissin M, Goyal A, Newcombe RG, Dixon JM *et al.* Randomized multicenter trial of sentinel node biopsy *versus* standard axillary treatment in operable breast cancer: the ALMANAC trial. *J Natl Cancer Inst* 2006;**98**:599–609
2. Lucci A, McCall LM, Beitsch PD, Whitworth PW, Reintgen DS, Blumencranz PW *et al.* Surgical complications associated with sentinel lymph node dissection (SLND) plus axillary lymph node dissection compared with SLND alone in the American College of Surgeons Oncology Group trial Z0011. *J Clin Oncol* 2007;**25**:3657–3663
3. Boughey JC, McCall LM, Ballman KV, Mittendorf EA, Ahrendt GM, Wilke LG *et al.* Tumor biology correlates with rates of breast-conserving surgery and pathologic complete response after neoadjuvant chemotherapy for breast cancer: findings from the ACOSOG Z1071 (alliance) prospective multicenter clinical trial. *Ann Surg* 2014;**260**:608–614; discussion 614–606
4. Samiei S, Simons JM, Engelen SME, Beets-Tan RGH, Classe JM, Smidt ML *et al.* Axillary pathologic complete response after neoadjuvant systemic therapy by breast cancer subtype in patients with initially clinically node-positive disease: a systematic review and meta-analysis. *JAMA Surg* 2021;**156**: e210891
5. Dominici LS, Negron Gonzalez VM, Buzdar AU, Lucci A, Mittendorf EA, Le-Petross HT *et al.* Cytologically proven axillary lymph node metastases are eradicated in patients receiving preoperative chemotherapy with concurrent trastuzumab for HER2-positive breast cancer. *Cancer* 2010;**116**:2884–2889
6. Simons JM, van Nijnatten TJA, van der Pol CC, Luiten EJT, Koppert LB, Smidt ML. Diagnostic accuracy of different surgical procedures for axillary staging after neoadjuvant systemic therapy in node-positive breast cancer: a systematic review and meta-analysis. *Ann Surg* 2019;**269**:432–442
7. Cortazar P, Zhang L, Untch M, Mehta K, Costantino JP, Wolmark N *et al.* Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. *Lancet* 2014;**384**:164–172
8. von Minckwitz G, Untch M, Blohmer JU, Costa SD, Eidtmann H, Fasching PA *et al.* Definition and impact of pathologic complete response on prognosis after neoadjuvant chemotherapy in various intrinsic breast cancer subtypes. *J Clin Oncol* 2012;**30**:1796–1804
9. Mougalian SS, Hernandez M, Lei X, Lynch S, Kuerer HM, Symmans WF *et al.* Ten-year outcomes of patients with breast cancer with cytologically confirmed axillary lymph node metastases and pathologic complete response after primary systemic chemotherapy. *JAMA Oncol* 2016;**2**:508–516
10. Fayanju OM, Ren Y, Thomas SM, Greenup RA, Plichta JK, Rosenberger LH *et al.* The clinical significance of breast-only and node-only pathologic complete response (pCR) after neoadjuvant chemotherapy (NACT): a review of 20 000 breast cancer patients in the National Cancer Data Base (NCDB). *Ann Surg* 2018;**268**:591–601
11. Kuehn T, Bauerfeind I, Fehm T, Fleige B, Hausschild M, Helms G *et al.* Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study. *Lancet Oncol* 2013;**14**: 609–618
12. Boughey JC, Suman VJ, Mittendorf EA, Ahrendt GM, Wilke LG, Taback B *et al.* Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial. *JAMA* 2013;**310**: 1455–1461
13. Boileau JF, Poirier B, Basik M, Holloway CM, Gaboury L, Sideris L *et al.* Sentinel node biopsy after neoadjuvant chemotherapy in biopsy-proven node-positive breast cancer: the SN FNAC study. *J Clin Oncol* 2015;**33**:258–264
14. Krag DN, Anderson SJ, Julian TB, Brown AM, Harlow SP, Ashikaga T *et al.* Technical outcomes of sentinel-lymph-node resection and conventional axillary-lymph-node dissection in patients with clinically node-negative breast cancer: results from the NSABP B-32 randomised phase III trial. *Lancet Oncol* 2007;**8**:881–888
15. Straver ME, Loo CE, Alderliesten T, Rutgers EJ, Vrancken Peeters MT. Marking the axilla with radioactive iodine seeds (MARI procedure) may reduce the need for axillary dissection after neoadjuvant chemotherapy for breast cancer. *Br J Surg* 2010; **97**:1226–1231
16. Donker M, Straver ME, Wesseling J, Loo CE, Schot M, Drukker CA *et al.* Marking axillary lymph nodes with radioactive iodine seeds

for axillary staging after neoadjuvant systemic treatment in breast cancer patients: the MARI procedure. *Ann Surg* 2015; **261**:378–382

17. Caudle AS, Yang WT, Krishnamurthy S, Mittendorf EA, Black DM, Gilcrease MZ *et al*. Improved axillary evaluation following neoadjuvant therapy for patients with node-positive breast cancer using selective evaluation of clipped nodes: implementation of targeted axillary dissection. *J Clin Oncol* 2016;**34**:1072–1078
18. Boughey JC, Ballman KV, Le-Petross HT, McCall LM, Mittendorf EA, Ahrendt GM *et al*. Identification and resection of clipped node decreases the false-negative rate of sentinel lymph node surgery in patients presenting with node-positive breast cancer (T0–T4, N1–N2) who receive neoadjuvant chemotherapy: results from ACO SOG Z107 1 (Alliance). *Ann Surg* 2016;**263**:802–807
19. Kuemmel S, Heil J, Rueland A, Seiberling C, Harrach H, Schindowski D *et al*. A prospective, multicenter registry study to evaluate the clinical feasibility of targeted axillary dissection (TAD) in node-positive breast cancer patients. *Ann Surg* 2022;**276**:e553–e562
20. Siso C, de Torres J, Esgueva-Colmenarejo A, Espinosa-Bravo M, Rus N, Cordoba O *et al*. Intraoperative ultrasound-guided excision of axillary clip in patients with node-positive breast cancer treated with neoadjuvant therapy (ILINA trial) : a new tool to guide the excision of the clipped node after neoadjuvant treatment. *Ann Surg Oncol* 2018;**25**:784–791
21. Simons JM, van Nijnatten TJA, van der Pol CC, van Diest PJ, Jager A, van Klaveren D *et al*. Diagnostic accuracy of radioactive iodine seed placement in the axilla with sentinel lymph node biopsy after neoadjuvant chemotherapy in node-positive breast cancer. *JAMA Surg* 2022;**157**:991–999
22. Galimberti V, Ribeiro Fontana SK, Maisonneuve P, Steccanella F, Vento AR, Intra M *et al*. Sentinel node biopsy after neoadjuvant treatment in breast cancer: five-year follow-up of patients with clinically node-negative or node-positive disease before treatment. *Eur J Surg Oncol* 2016;**42**:361–368
23. van Loevezijn AA, van der Noordaa MEM, Stokkel MPM, van Werkhoven ED, Groen EJ, Loo CE *et al*. Three-year follow-up of de-escalated axillary treatment after neoadjuvant systemic therapy in clinically node-positive breast cancer: the MARI-protocol. *Breast Cancer Res Treat* 2022;**193**:37–48
24. Galimberti V, Ribeiro Fontana SK, Vicini E, Morigi C, Sargenti M, Corso G *et al*. This house believes that: sentinel node biopsy alone is better than TAD after NACT for cN+ patients. *Breast* 2023;**67**:21–25
25. Reitsamer R, Peintinger F, Forsthuber E, Sir A. The applicability of Magseed® for targeted axillary dissection in breast cancer patients treated with neoadjuvant chemotherapy. *Breast* 2021; **57**:113–117
26. Natsiopoulos I, Intzes S, Liappis T, Zarampoukas K, Zarampoukas T, Zacharopoulou V *et al*. Axillary lymph node tattooing and targeted axillary dissection in breast cancer patients who presented as cN+ before neoadjuvant chemotherapy and became cN0 after treatment. *Clin Breast Cancer* 2019;**19**:208–215
27. Balasubramanian R, Morgan C, Shaari E, Kovacs T, Pinder SE, Hamed H *et al*. Wire guided localisation for targeted axillary node dissection is accurate in axillary staging in node positive breast cancer following neoadjuvant chemotherapy. *Eur J Surg Oncol* 2020;**46**:1028–1033
28. PRISMA. *PRISMA Checklist 2020*. http://prisma-statement.org/prismastatement/checklist.aspx (accessed 27 October 2023)
29. NIH. *Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies*. https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools (accessed 1 July 2023)
30. Plecha D, Bai S, Patterson H, Thompson C, Shenk R. Improving the accuracy of axillary lymph node surgery in breast cancer with ultrasound-guided wire localization of biopsy proven metastatic lymph nodes. *Ann Surg Oncol* 2015;**22**:4241–4246
31. Dashevsky BZ, Altman A, Abe H, Jaskowiak N, Bao J, Schacht DV *et al*. Lymph node wire localization post-chemotherapy: towards improving the false negative sentinel lymph node biopsy rate in breast cancer patients. *Clin Imaging* 2018;**48**:69–73
32. Hartmann S, Reimer T, Gerber B, Stubert J, Stengel B, Stachs A. Wire localization of clip-marked axillary lymph nodes in breast cancer patients treated with primary systemic therapy. *Eur J Surg Oncol* 2018;**44**:1307–1311
33. Alarcon M, Buch E, Julve A, Hernandorena M, Tajahuerce M, Rodriguez H *et al*. Sentinel lymph node BIOPSY after neoadjuvant therapy in breast cancer patients with lymph node involvement at diagnosis. Could wire localization of clipped node improve our results? *Surgeon* 2021;**19**:344–350
34. Flores-Funes D, Aguilar-Jimenez J, Martinez-Galvez M, Ibanez-Ibanez MJ, Carrasco-Gonzalez L, Gil-Izquierdo JI *et al*. Feasibility and validation of the targeted axillary dissection technique in the axillary staging of breast cancer after neoadjuvant therapy: definitive results. *Surg Oncol* 2021;**38**: 101636
35. Garcia-Novoa A, Acea-Nebril B, Diaz Carballada C, Bouzon Alejandro A, Conde C, Cereijo Garea C *et al*. Combining wire localization of clipped nodes with sentinel lymph node biopsy after neoadjuvant chemotherapy in node-positive breast cancer: preliminary results from a prospective study. *Ann Surg Oncol* 2021;**28**:958–967
36. Gurleyik G, Aksu SA, Aker F, Tekyol KK, Tanrikulu E, Gurleyik E. Targeted axillary biopsy and sentinel lymph node biopsy for axillary restaging after neoadjuvant chemotherapy. *Ann Surg Treat Res* 2021;**100**:305–312
37. Sierra JN, Cuesta PR, Salguero FJV, Romera AE, Gómez IV. Evaluation of axillary response to neoadjuvant systemic therapy with sentinel node biopsy and axillary wire in node-positive breast cancer. *Eur J Gynaecol Oncol* 2021;**42**: 1291–1299
38. Acea-Figueira E, Garcia-Novoa A, Diaz Carballada C, Bouzon Alejandro A, Conde C, Santiago Freijanes P *et al*. Lymph node staging after primary systemic therapy in women with breast cancer and lymph node involvement at diagnosis. *Cir Esp (Engl Ed)* 2023;**101**:417–425
39. Sargent RE, Siegel E, Ito F, Kramme K, Kraft E, Hendrix V *et al*. Axillary lymph node recurrence following wire-directed sentinel lymph node dissection for breast cancer patients with biopsy-proven axillary metastases prior to neoadjuvant chemotherapy at a safety net medical center. *J Surg Oncol* 2023; **128**:9–15
40. Wu SY, Li JW, Wang YJ, Jin KR, Yang BL, Li JJ *et al*. Clinical feasibility and oncological safety of non-radioactive targeted axillary dissection after neoadjuvant chemotherapy in biopsy-proven node-positive breast cancer: a prospective diagnostic and prognostic study. *Int J Surg* 2023;**109**:1863–1870
41. Munck F, Jepsen P, Zeuthen P, Carstensen L, Hauerslev K, Paaskesen CK *et al*. Comparing methods for targeted axillary dissection in breast cancer patients: a nationwide, retrospective study. *Ann Surg Oncol* 2023;**30**:6361–6369
42. Simons JM, van Pelt M, Marinelli A, Straver ME, Zeillemaker AM, Pereira Arias-Bouda LM *et al*. Excision of both pretreatment

marked positive nodes and sentinel nodes improves axillary staging after neoadjuvant systemic therapy in breast cancer. *Br J Surg* 2019;**106**:1632–1639

43. Balija TM, Braz D, Hyman S, Montgomery LL. Early reflector localization improves the accuracy of localization and excision of a previously positive axillary lymph node following neoadjuvant chemotherapy in patients with breast cancer. *Breast Cancer Res Treat* 2021;**189**:121–130
44. Diego EJ, McAuliffe PF, Soran A, McGuire KP, Johnson RR, Bonaventura M *et al.* Axillary staging after neoadjuvant chemotherapy for breast cancer: a pilot study combining sentinel lymph node biopsy with radioactive seed localization of pre-treatment positive axillary lymph nodes. *Ann Surg Oncol* 2016;**23**:1549–1553
45. Nguyen TT, Hieken TJ, Glazebrook KN, Boughey JC. Localizing the clipped node in patients with node-positive breast cancer treated with neoadjuvant chemotherapy: early learning experience and challenges. *Ann Surg Oncol* 2017;**24**:3011–3016
46. Beniey M, Boulva K, Rodriguez-Qizilbash S, Kaviani A, Younan R, Patocskai E. Targeted axillary dissection in node-positive breast cancer: a retrospective study and cost analysis. *Cureus* 2021;**13**: e14610
47. Aragon-Sanchez S, Ciruelos-Gil E, Lopez-Marin L, Galindo A, Tabuenca-Mateos MJ, Jimenez-Arranz S *et al.* Feasibility of targeted axillary dissection for de-escalation of surgical treatment after neoadjuvant chemotherapy in breast cancer. *Surg Oncol* 2022;**44**:101823
48. Rebollo Aguirre AC, Fernandez Fernandez J, Sanchez Sanchez R, Mendoza Arnau I, Rivas Navas DJ, Martinez Meca S. Radioguided surgery with iodine-125 seeds in breast cancer patients treated with neoadjuvant chemotherapy. *Rev Esp Med Nucl Imagen Mol (Engl Ed)* 2022;**41**:71–77
49. Weiss A, King C, Grossmith S, Portnow L, Raza S, Nakhlis F *et al.* How often does retrieval of a clipped lymph node change adjuvant therapy recommendations? A prospective, consecutive, patient cohort study. *Ann Surg Oncol* 2022;**29**: 3764–3771
50. Clark BZ, Johnson RR, Berg WA, McAuliffe P, Bhargava R. Response in axillary lymph nodes to neoadjuvant chemotherapy for breast cancers: correlation with breast response, pathologic features, and accuracy of radioactive seed localization. *Breast Cancer Res Treat* 2023;**200**:363–373
51. Munck F, Andersen IS, Vejborg I, Gerlach MK, Lanng C, Kroman NT *et al.* Targeted axillary dissection with ^{125}I seed placement before neoadjuvant chemotherapy in a Danish multicenter cohort. *Ann Surg Oncol* 2023;**30**:4135–4142
52. Fuertes Manuel J, Kohan S, Jorda Sole M, Mateu Hidalgo I, Miralles Curto M, Aguilo Sagrista O *et al.* Patients with initial nodal involvement due to breast cancer who have received neoadjuvant chemotherapy: combined sentinel node-radioguided surgery of the pathological node. *Rev Esp Med Nucl Imagen Mol (Engl Ed)* 2022;**41**:284–291
53. Del Castillo A, Gomez-Modet S, Mata JM, Tejedor L. Targeted axillary dissection using radioguided occult lesion localization technique in the clinically negative marked lymph node after neoadjuvant treatment in breast cancer patients. *Eur J Surg Oncol* 2023;**49**:1184–1188
54. Rella R, Conti M, Bufi E, Trombadori CML, Di Leone A, Terribile D *et al.* Selective axillary dissection after neoadjuvant chemotherapy in patients with lymph-node-positive breast cancer (CLYP study): the radio-guided occult lesion localization technique for biopsy-proven metastatic lymph nodes. *Cancers (Basel)* 2023;**15**:2046
55. Winder AA, Spillane AJ, Sood S, McKessar M, Cohn D, Snook K. Radio-isotope occult lesion localization (ROLL) techniques to identify the clipped node for targeted axillary dissection (TAD) in breast cancer. *ANZ J Surg* 2022;**92**:3017–3021
56. Dilege E, Celik B, Falay O, Boge M, Sucu S, Toprak S *et al.* SPECT/CT lymphoscintigraphy accurately localizes clipped and sentinel nodes after neoadjuvant chemotherapy in node-positive breast cancer. *Clin Nucl Med* 2023;**48**:594–599
57. Laws A, Dillon K, Kelly BN, Kantor O, Hughes KS, Gadd MA *et al.* Node-positive patients treated with neoadjuvant chemotherapy can be spared axillary lymph node dissection with wireless non-radioactive localizers. *Ann Surg Oncol* 2020;**27**:4819–4827
58. Mariscal Martinez A, Vives Rosello I, Salazar Gomez A, Catanese A, Perez Molina M, Sola Suarez M *et al.* Advantages of preoperative localization and surgical resection of metastatic axillary lymph nodes using magnetic seeds after neoadjuvant chemotherapy in breast cancer. *Surg Oncol* 2021;**36**:28–33
59. Simons JM, Scoggins ME, Kuerer HM, Krishnamurthy S, Yang WT, Sahin AA *et al.* Prospective registry trial assessing the use of magnetic seeds to locate clipped nodes after neoadjuvant chemotherapy for breast cancer patients. *Ann Surg Oncol* 2021; **28**:4277–4283
60. Martinez M, Jimenez S, Guzman F, Fernandez M, Arizaga E, Sanz C. Evaluation of axillary lymph node marking with Magseed® before and after neoadjuvant systemic therapy in breast cancer patients: MAGNET study. *Breast J* 2022;**2022**:6111907
61. Barry PA, Harborough K, Sinnett V, Heeney A, St John ER, Gagliardi T *et al.* Clinical utility of axillary nodal markers in breast cancer. *Eur J Surg Oncol* 2023;**49**:709–715
62. Sun J, Henry DA, Carr MJ, Yazdankhahkenary A, Laronga C, Lee MC *et al.* Feasibility of axillary lymph node localization and excision using radar reflector localization. *Clin Breast Cancer* 2020;**21**:E189–E193
63. Weinfurtner RJ, Leon A, Calvert A, Lee MC. Ultrasound-guided radar reflector localization of axillary lymph nodes facilitates targeted axillary dissection. *Clin Imaging* 2022;**90**:19–25
64. Taj R, Chung SH, Goldhaber NH, Louie BH, Marganski JG, Grewal NS *et al.* Localizing positive axillary lymph nodes in breast cancer patients post neoadjuvant therapy. *J Surg Res* 2023;**283**: 288–295
65. Kim WH, Kim HJ, Kim SH, Jung JH, Park HY, Lee J *et al.* Ultrasound-guided dual-localization for axillary nodes before and after neoadjuvant chemotherapy with clip and activated charcoal in breast cancer patients: a feasibility study. *BMC Cancer* 2019;**19**:859
66. Patel R, MacKerricher W, Tsai J, Choy N, Lipson J, Ikeda D *et al.* Pretreatment tattoo marking of suspicious axillary lymph nodes: reliability and correlation with sentinel lymph node. *Ann Surg Oncol* 2019;**26**:2452–2458
67. Allweis TM, Menes T, Rotbart N, Rapson Y, Cernik H, Bokov I *et al.* Ultrasound guided tattooing of axillary lymph nodes in breast cancer patients prior to neoadjuvant therapy, and identification of tattooed nodes at the time of surgery. *Eur J Surg Oncol* 2020;**46**:1041–1045
68. Dostalek L, Cerny A, Saskova P, Pavlista D. Selective extirpation of tattooed lymph node in combination with sentinel lymph node biopsy in the management of node-positive breast cancer patients after neoadjuvant systemic therapy. *Breast Care (Basel)* 2021;**16**:623–629
69. de Boniface J, Frisell J, Kuhn T, Wiklander-Brakenhielm I, Dembrower K, Nyman P *et al.* False-negative rate in the extended prospective TATTOO trial evaluating targeted axillary dissection by carbon tattooing in clinically

node-positive breast cancer patients receiving neoadjuvant systemic therapy. *Breast Cancer Res Treat* 2022;**193**:589–595

70. Pinto D, Batista E, Gouveia P, Mavioso C, Anacleto J, Ribeiro J *et al.* Targeted axillary dissection after chemotherapy: feasibility study with clip and carbon dye tattoo—Neotarget trial. *Breast Care (Basel)* 2022;**17**:166–171
71. Porpiglia M, Borella F, Chieppa P, Brino C, Ala A, Marra V *et al.* Carbon tattooing of axillary lymph nodes in breast cancer patients before neoadjuvant chemotherapy: a retrospective analysis. *Tumori* 2023;**109**:301–306
72. Spautz CC, Schunemann Junior E, Budel LR, Cavalcanti TCS, Louveira MH, Junior PG *et al.* Marking axillary nodes with 4% carbon microparticle suspension before neoadjuvant chemotherapy improves sentinel node identification rate and axillary staging. *J Surg Oncol* 2020;**122**:164–169
73. Pinto CS, Peleteiro B, Pinto CA, Osorio F, Costa S, Magalhaes A *et al.* Initial experience with targeted axillary dissection after neoadjuvant therapy in breast cancer patients. *Breast Cancer* 2022;**29**:709–719
74. Siso C, Esgueva A, Rivero J, Morales C, Miranda I, Peg V *et al.* Feasibility and safety of targeted axillary dissection guided by intraoperative ultrasound after neoadjuvant treatment. *Eur J Surg Oncol* 2023;**49**:106938
75. Simons JM, Koppert LB, Luiten EJT, van der Pol CC, Samiei S, de Wilt JHW *et al.* De-escalation of axillary surgery in breast cancer patients treated in the neoadjuvant setting: a Dutch population-based study. *Breast Cancer Res Treat* 2020;**180**:725–733
76. Simons JM, Maaskant-Braat AJG, Luiten EJT, Leidenius MHK, van Nijnatten TJA, Boelens PG *et al.* Patterns of axillary staging and management in clinically node positive breast cancer patients treated with neoadjuvant systemic therapy: results of a survey amongst breast cancer specialists. *Eur J Surg Oncol* 2020;**46**:53–58
77. Caudle AS, Bedrosian I, Milton DR, DeSnyder SM, Kuerer HM, Hunt KK *et al.* Use of sentinel lymph node dissection after neoadjuvant chemotherapy in patients with node-positive breast cancer at diagnosis: practice patterns of American Society of Breast Surgeons members. *Ann Surg Oncol* 2017;**24**: 2925–2934
78. Nguyen TT, Hoskin TL, Day CN, Degnim AC, Jakub JW, Hieken TJ *et al.* Decreasing use of axillary dissection in node-positive breast cancer patients treated with neoadjuvant chemotherapy. *Ann Surg Oncol* 2018;**25**:2596–2602
79. Murthy V, Young J, Tokumaru Y, Quinn M, Edge SB, Takabe K. Options to determine pathological response of axillary lymph node metastasis after neoadjuvant chemotherapy in advanced breast cancer. *Cancers (Basel)* 2021;**13**:4167
80. Lee MK, Sanaiha Y, Kusske AM, Thompson CK, Attai DJ, Baker JL *et al.* A comparison of two non-radioactive alternatives to wire for the localization of non-palpable breast cancers. *Breast Cancer Res Treat* 2020;**182**:299–303
81. Hayes MK. Update on preoperative breast localization. *Radiol Clin North Am* 2017;**55**:591–603
82. Wärnberg F, Obondo C, Chin K. The magnetic technique—a novel and promising method to improve axillary staging localisation from a Swedish perspective. *Medicina (B Aires)* 2023;**59**:1727
83. Banys-Paluchowski M, Gasparri ML, de Boniface J, Gentilini O, Stickeler E, Hartmann S *et al.* Surgical management of the axilla in clinically node-positive breast cancer patients converting to clinical node negativity through neoadjuvant chemotherapy: current status, knowledge gaps, and rationale for the EUBREAST-03 AXSANA study. *Cancers (Basel)* 2021;**13**: 1565
84. Dialani V, Dogan B, Dodelzon K, Dontchos BN, Modi N, Grimm L. Axillary imaging following a new invasive breast cancer diagnosis—a radiologist's dilemma. *Journal of Breast Imaging* 2021;**3**:645–658
85. Hartmann S, Banys-Paluchowski M, Stickeler E, de Boniface J, Gentilini OD, Kontos M *et al.* Applicability of magnetic seeds for target lymph node biopsy after neoadjuvant chemotherapy in initially node-positive breast cancer patients: data from the AXSANA study. *Breast Cancer Res Treat* 2023;**202**:497–504
86. Zatecky J, Coufal O, Zapletal O, Kubala O, Kepicova M, Faridova A *et al.* Ideal marker for targeted axillary dissection (IMTAD): a prospective multicentre trial. *World J Surg Oncol* 2023;**21**:252
87. de Wild SR, Simons JM, Vrancken Peeters M, Smidt ML, Koppert LB, MINIMAX Group. MINImal *vs.* MAXimal invasive axillary staging and treatment after neoadjuvant systemic therapy in node positive breast cancer: protocol of a Dutch multicenter registry study (MINIMAX). *Clin Breast Cancer* 2022;**22**:e59–e64