Radar reflectors for marking of target lymph nodes in initially node-positive patients receiving neoadjuvant chemotherapy for breast cancer —a subgroup analysis of the prospective AXSANA (EUBREAST-03) trial

Maggie Banys-Paluchowski, Steffi Hartmann, Timo Basali, Maria Luisa Gasparri, Jana de Boniface, Oreste Davide Gentilini, Güldeniz Karadeniz Cakmak, Nina Ditsch, Elmar Stickeler, Ellen Schlichting, Isabel Rubio, Florentia Peintinger, Michael Untch, Christine Mau, Frederike Klaassen Federspiel, Susanne Bucher, Kerstin Ramaker, Peter Paluchowski, Lelia Bauer, Sabine Riemer, Dagmar Langanke, Tanja Durpektova Leuf, Jens Schnabel, Ekkehard von Abel, Christine Solbach, Sonja Cáradenas Ovalle, Kerstin Hilmer, Vesna Bjelic-Radisic, Nicole Stahl, Jose I. Sanchez-Mendez, Vibeke Hagen, Marit Helene Hansen, Natalia Krawczyk, Bilge Aktas Sezen, Katharina Jursik, Marc Thill, Hans-Christian Kolberg, Toralf Reimer, Franziska Ruf, Kristina Wihlfahrt, Angelika Rief, Tomasz Berger, Esther Schmidt, Nikolas Tauber, Sarah Fröhlich, Thorsten Kühn

Angaben zur Veröffentlichung / Publication details:

Banys-Paluchowski, Maggie, Steffi Hartmann, Timo Basali, Maria Luisa Gasparri, Jana de Boniface, Oreste Davide Gentilini, Güldeniz Karadeniz Cakmak, et al. 2025. "Radar reflectors for marking of target lymph nodes in initially node-positive patients receiving neoadjuvant chemotherapy for breast cancer —a subgroup analysis of the prospective AXSANA (EUBREAST-03) trial." *Breast Cancer Research and Treatment* 211 (1): 203–11. https://doi.org/10.1007/s10549-025-07635-4.

Radar reflectors for marking of target lymph nodes in initially node-positive patients receiving neoadjuvant chemotherapy for breast cancer—a subgroup analysis of the prospective AXSANA (EUBREAST-03) trial

Maggie Banys-Paluchowski · Steffi Hartmann · Timo Basali · Maria Luisa Gasparri · Jana de Boniface · Oreste Davide Gentilini, et al. ***[full author details at the end of the article]***

Abstract

Background Surgical staging procedures of the axilla in initially clinically node-positive (cN+) breast cancer patients receiving neoadjuvant chemotherapy (NACT) vary across countries. Different procedures such as axillary lymph node dissection, sentinel lymph node biopsy, target lymph node biopsy and targeted axillary dissection are currently in use. To date, data on radar reflectors as a non-wire and non-radioactive technique for marking target lymph nodes are limited. The present study aims at examining the detection rate, the rate of lost markers, and magnetic resonance imaging artifacts after TLN marking using a radar reflector before NACT in the largest available cohort of breast cancer patients enrolled in the international prospective AXSANA study.

Methods AXSANA (EUBREAST-03) is an international prospective cohort study including cN + patients managed with different surgical axillary staging techniques after NACT. Eligible patients have cT1-4c cN + breast cancer and receive neoadjuvant chemotherapy. Patients are followed up for 5 years. In the present subgroup analysis, only patients with a TLN marked by a radar reflector were included.

Results A TLN was marked by radar reflector insertion in 158 patients prior to NACT. Of these, 136 had final surgery results available at the time of analysis, and in 135 out of these 136 patients, localization of TLN was attempted. All radar markers were successfully removed. While lymphoid tissue corresponding to the TLN was identified in 132 patients (97.8%), no lymphoid tissue was detected on histopathology in three patients. It remains unclear whether the TLN was excised in these cases or not. In 1 out of 27 patients (3.7%) who underwent preoperative MRI, image assessment was compromised due to artifacts after radar marker placement.

Conclusion To the best of our knowledge, this is the largest prospective series of patients receiving a radar reflector for the marking of a TLN prior to NACT for breast cancer. Our data demonstrate that radar reflectors are a reliable tool for marking target lymph nodes before neoadjuvant treatment.

Trial registration number: NCT04373655 (date of registration May 4, 2020).

Keywords Breast cancer · Neoadjuvant chemotherapy · Targeted axillary dissection · Radar reflector · Target lymph node · Recurrence

Introduction

The optimal surgical management of the axilla after neoadjuvant chemotherapy (NACT) in patients with breast cancer (BC) has been controversially discussed over the last two decades [1, 2]. While axillary lymph node dissection (ALND) has been recommended as gold standard for all initially node-positive patients for many years, studies have shown that the removal of selected lymph nodes, such as sentinel lymph node biopsy (SLNB) or targeted axillary dissection (TAD), may sufficiently stage the axilla and allow surgical de-escalation [3–10]. However, it remains unclear which patients may safely be offered de-escalation and how

Maggie Banys-Paluchowski and Steffi Hartmann have contributed equally to this manuscript.

different staging strategies affect oncological outcomes, arm morbidity, and health-related quality of life (HRQoL). This uncertainty results in heterogeneous recommendations from national and international societies [1].

In TAD, the most suspicious biopsy-confirmed metastatic lymph node is defined as the target lymph node (TLN), marked before and removed after NACT along with a SLNB [1, 11–14]. This procedure can reliably reduce the false negative rate (FNR) from 12 to 14% for SLNB alone to 2–9%, which is lower than the generally accepted cut-off of 10% [1, 9, 11–14]. To ensure detection and removal of the TLN, the marking technique must allow its reliable identification after NACT even in patients achieving complete clinical and radiological response in the axilla. Currently, available techniques include placement of metallic clips and coils [9, 15], carbon particles allowing direct visualization during exploration of the axilla [13, 14, 16], or markers suitable for intraoperative probe-guided detection, e.g., radioactive iodine seeds [11], magnetic seeds [17], radar reflectors [18] or radiofrequency identification tags. Clips and coils usually require a separate preoperative localization procedure, e.g., using a wire placement, which may lead to logistic challenges and discomfort for the patient, or localization failure if the clip/coil is not reliably visible upon imaging. In contrast, carbon and probe-guided detection markers allow the patient to directly proceed to surgery following NACT without any further intervention. Detection rates of different marking techniques vary from 70 to 80% in case of clips/coils to over 90% in case of radioactive seeds, carbon ink, and magnetic seeds [9, 11, 13, 17]. The optimal marking technique, however, has not been unanimously identified yet, and data on oncological outcomes and complication rates among different methods are not available.

Radar reflector localization (RRL) includes the insertion of a 12 × 1.6 mm electromagnetic wave reflector under ultrasound guidance, using a sterile 16-gauge introducer needle system (SAVI SCOUT®, Merit Medical, CA, USA). Intraoperatively, the reflector is activated by infrared light from the probe, reflecting an electromagnetic wave signal back to the detection probe. The surgeon is guided by the acoustic signal, and the distance between probe tip and marker is shown on the console. The reflectors are transcutaneously detectable up to a penetration depth of 6 cm and approved for implantation in soft tissue, including lymph nodes, for an unlimited preoperative period. While RRL is commonly used for localization of non-palpable breast lesions, the evidence on its use for the marking of TLNs in the neoadjuvant setting is limited. In studies on RRL of lymph nodes, TLNs were first marked with a clip before NACT, and then marked using a radar reflector in a second procedure shortly before surgery [15, 18, 19]. However, this two-stage approach does not address the limitation of the relatively low detection rate of clips in BC patients responding well to NACT.

The present study aimed at examining the detection rate, the rate of lost markers and magnetic resonance imaging (MRI) artifacts after TLN marking using a radar reflector before NACT in the largest available cohort of BC patients enrolled in the international prospective AXSANA study.

Materials and methods

The design of the ongoing AXSANA study (NCT04373655, www.eubreast.org/axsana) has been described elsewhere [1, 17, 20]. Briefly, AXSANA is an international, multicenter, prospective cohort study initiated by the European Breast Cancer Research Association of Surgical Trialists (EUBREAST e.V.). Patients with initially cN + BC who receive at least four cycles of NACT and convert to ycN0 are eligible. Axillary staging is performed according to institutional and national standards and may include ALND, SLNB, TAD, or target lymph node biopsy (TLNB). Co-primary endpoints are invasive disease-free survival, axillary recurrence rate, HRQoL, and arm morbidity. Enrollment started in June 2020. The trial has high-quality standards with 100% of the datasets being monitored by expert surgeons. Performance of different marking techniques, MRI artifacts, dislocation and localization failure rates, and lost marker rates are secondary endpoints of the study. All currently available marking techniques for the TLN are allowed.

The current subgroup analysis included patients who had TLN marking with a radar reflector before NACT and who had undergone axillary surgery by September 30th, 2024. At surgery, the marker was identified using the SAVI SCOUT® handheld probe (Fig. 1). Node status at diagnosis and after NACT was assessed clinically according to institutional standards without study-specific imaging requirements. Pathological complete response (pCR) was defined as the absence of invasive tumor cells in the breast and axilla. Thus, the presence of isolated tumor cells in lymph nodes (ypN0[i +]) was defined as non-pCR for the purpose of this analysis.

For descriptive analysis, absolute frequencies and proportions were reported for qualitative parameters and means ± standard deviations (SD) for quantitative parameters. Detection rate was defined as the proportion of patients with successful perioperative identification of at least one lymph node marked with a radar reflector out of all included cases. The rate of lost markers was determined from the proportion of all unsuccessfully removed reflectors out of all initially inserted ones. Statistical analysis was performed using SPSS® version 27 (IBM, Armonk, New York, USA).

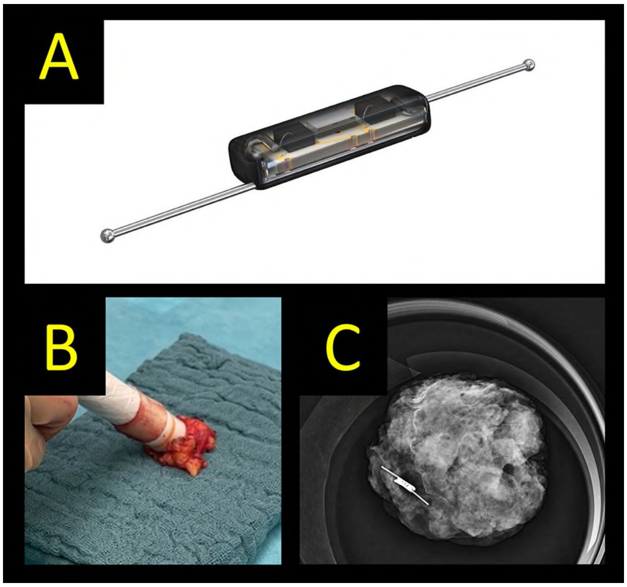

Fig. 1 Radar reflector localization: **A** Radar reflector, **B** Intraoperative confirmation of the presence of the reflector in the removed specimen, **C** Specimen radiography showing radar reflector in the tissue

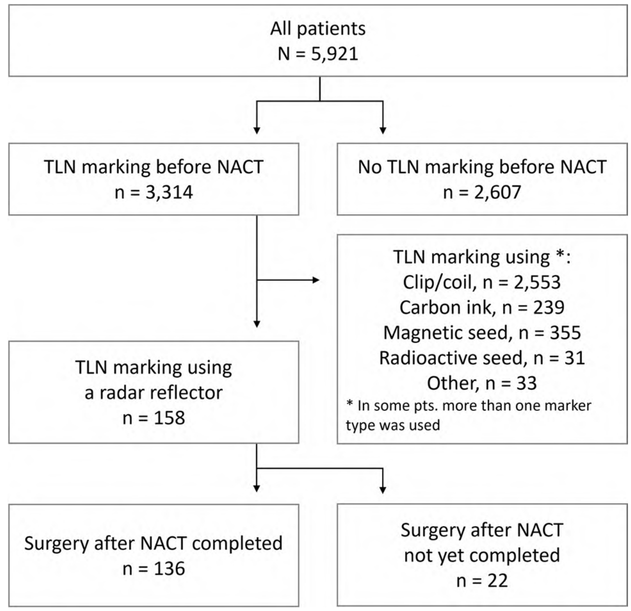

Fig. 2 Flowchart of AXSANA study cohort included until September 30th, 2024

Results

Five thousand nine hundred twenty-one patients from 27 countries and 291 study sites had been enrolled in the AXSANA study until data cut-off (September 30th 2024). In 3314 out of 5921 patients (56.0%), the TLN had been marked before NACT, and among these, a radar marker had been inserted in 158 cases (4.8%). 136 out of these 158 patients (86.1%) in whom surgery had been performed and documented by September 30th, 2024, were included in the present analysis (Fig. 2). These patients were recruited at 24 study sites in 5 countries. Clinicopathologic characteristics are shown in Table 1.

Radar marker placement

In all patients, radar markers were placed before NACT. One lymph node was marked in 128 (94.1%) patients, two lymph nodes in six cases (4.4%), and three in two patients (1.5%). In 135 patients (99.3%), TLN marking was conducted under ultrasound guidance. The mean size of the largest marked lymph node was 18.1 mm ± 7.1 mm (6–37 mm). In 66 patients (48.5%), the lymph node marking was performed immediately after the core biopsy. In the remaining 70 patients, node marking took place as a separate procedure, with a mean time between core biopsy and TLN labeling of 25.5 days (±21.8). The mean time between TLN marking and surgical removal was 178.9 ± 50.1 days. Clinical conversion from cN + to ycN0 was achieved in 108 patients (79.4%) and 69 patients (50.7%) achieved clinical complete response of the primary tumor (ycT0; Table 2).

Radar markers and magnetic resonance imaging

A breast MRI was performed in 27 patients between TLN marking and surgery. MRI artifacts caused by radar markers were described in five out of these 27 patients (18.5%). In one of these five patients, the radiologist described an impairment of the interpretation of the MRI due to artifacts caused by the radar marker (Fig. 3) resulting in a rate of 3.7% (one out of 27 patients) for patients receiving MRI.

Surgical staging

Targeted axillary dissection was planned as staging technique in 116 patients (85.3%). Axillary lymph node dissection as first surgery was scheduled in nine cases (6.6%) and target lymph node biopsy in two patients (1.5%). Other staging techniques were planned in nine (6.6%) patients. In all 116 patients in whom a TAD was planned, information on experience with the radar marker technique for TLN localization was provided by the study site. In 62 cases (53.4%), more than 30 TLN labelings with a radar marker had already been performed at the sites to that date.

In 123 patients (90.4%), SLNB was attempted along with the TLNB. In 100 patients (81.3%), single-tracer technetium was used, followed by dual tracer (technetium + dye) in 16 patients (13.0%), ICG in 3 patients (2.4%), ICG + technetium in 2 patients (1.6%), SPIO + technetium in one patient

Table 1 Characteristics of patients included in the present analysis

	n (%)
Sex	
Female	135 (99.3%)
Male	1 (0.7%)
Age (years)[a]	50.6 ± 12.0 (25–77)
Body mass index (kg/m^2)[a]	26.8 ± 5.5 (17.2–47.3)
Clinical tumor stage at diagnosis	
cT1	31 (22.8%)
cT2	87 (64.0%)
cT3	17 (12.5%)
cT4	1 (0.7%)
Focality	
Unifocal tumor	117 (86.0%)
Bifocal tumor	12 (8.8%)
≥ 3 tumors	7 (5.1%)
Number of suspicious lymph nodes at diagnosis	
1	68 (50%)
2	39 (28.7%)
3	22 (16.2%)
≥ 4	7 (5.1%)
Histopathological tumor type	
Ductal	124 (91.2%)
Lobular	7 (5.1%)
Other	5 (3.7%)
Tumor subtype	
HR + HER2 −	45 (33.1%)
HR + HER2 +	31 (22.8%)
HR − HER2 +	14 (10.3%)
HR − HER2 −	46 (33.8%)
Proliferation index Ki67 (%)[a]	47.0 ± 26.5 (5–95)
Type of breast surgery	
Breast-conserving surgery	106 (77.9%)
Mastectomy	30 (22.1%)

HR hormone receptor, *HER2* human epidermal growth factor receptor 2

[a]Mean ± standard deviation (min–max)

Table 2 Clinical and histopathological response to neoadjuvant therapy

	n (%)
Clinical tumor stage after NACT	
ycT0	69 (50.7%)
ycT1	47 (34.6%)
ycT2	16 (11.8%)
ycT3	2 (1.5%)
ycT4	1 (0.7%)
Missing	1 (0.7%)
Clinical lymph node status after NACT	
ycN0	108 (79.4%)
ycN +	28 (20.6%)
Pathological tumor stage after NACT	
ypT0	52 (38.2%)
ypTis	11 (8.1%)
ypT1	44 (32.4%)
ypT2	19 (14.0%)
ypT3	7 (5.1%)
ypT4	2 (1.5%)
Missing	1 (0.7%)
Pathological lymph node status after NACT	
ypN0	79 (58.1%)
ypN0(i +)	3 (2.2%)
ypN1mi	12 (8.8%)
ypN1	27 (19.9%)
ypN2	11 (8.1%)
ypN3	3 (2.2%)
Missing	1 (0.7%)
Pathological complete response after NACT[a]	
Yes	56 (41.2%)
No	79 (58.1%)
Missing	1 (0.7)

NACT neoadjuvant chemotherapy

[a]ypT0/ypTis ypN0

(0.8%), and dye as single-tracer in one patient (0.8%). The SLN was detected and removed in 116 out of 123 cases (94.3%) and corresponded to the TLN in 75 (64.7%) of patients.

In one patient, primary ALND was conducted and the radar probe not used during surgery. In this case, 42 lymph nodes were removed, and no postoperative imaging was performed. Therefore, we can report on the removal status of radar reflectors in 135 cases. In 134 out of these patients, radar markers placed before NACT were unequivocally removed. In one case, the radar reflector was neither found in the TLN nor in the ALND specimen, but the removal was confirmed by a postoperative low-dose thoracic computed tomography. The removal rate of radar reflectors was thus 100%.

In three patients, the tissue specimen containing radar reflector consisted of fat tissue and no lymphatic tissue was identifiable, so it remains unclear whether the TLN was excised, or the reflector might have dislocated.

Discussion

To our knowledge, this study presents the first prospective, multicenter analysis of the feasibility of target lymph node removal with RRL. It analyzed the largest patient group to date and is the only study in which the radar marker was

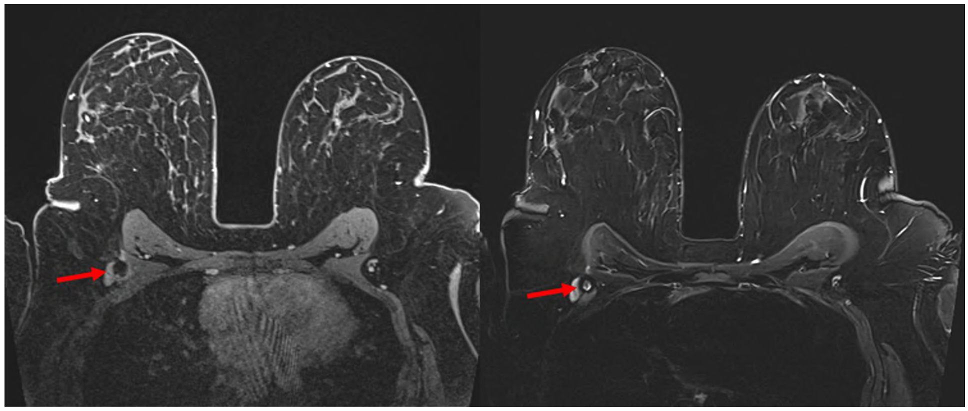

Fig. 3 MRI imaging in a patient with a radar reflector in the axilla; the minimal artifact did not impair radiological assessment in this case

inserted into the TLN exclusively before or at the beginning of NACT. In contrast, in six out of seven studies published to date, the radar marker was sometimes inserted into the clip-marked TLN before and sometimes after NACT [21–26]. Only Baker et al. marked the TLN exclusively before NACT in a small, prospective study [27]. This single-stage procedure avoids the difficulties of detecting clip-marked TLNs after NACT due to the limited sonographic visualization of the clips [9, 28]. Furthermore, the patient is spared an additional invasive localization procedure (e.g., wire placement) before surgery, usually necessary in case a clip is used for TLN marking. If a radar reflector is placed at the time of lymph node biopsy, no further axillary procedures are required until surgery. The present analysis confirms the high removal rate of radar markers after pre-NACT application reported by previous studies (Table 3).

However, for the first time, not only the rate of successfully removed markers but also the detection rate of the TLN is reported. Lymphatic tissue was detected in most, but not all TLN specimens. This may be due to either misplacement of the marker before NACT or intraoperatively, the dislocation of the marker into the perinodal tissue due to shrinkage of the TLN during NACT, or the absence of lymphatic tissue following complete response of a metastatic node. Ultimately, it is impossible to determine which of the three reasons is the causative factor. At 12 mm in length, the radar marker is quite large compared to other markers and it seems plausible that it may dislocate from a node that only measures a few millimeters after NACT. However, other studies have pointed out that the design of the radar marker with two antennae ensures very good adhesion in the surrounding tissue, and therefore, no migration is to be expected [18, 19, 27].

In general, all probe-guided markers used for labeling of TLNs have the advantage that the exact position of the TLN can be detected transcutaneously during surgery. In contrast to the method of carbon marking of the TLN, in which the TLN is detected intraoperatively but purely visually, this enables targeted localization even before the skin incision and thus minimal preparation effort. Whether this leads to lower arm morbidity compared to non-probe-assisted axillary surgical procedures is still unclear. Recently, a pooled analysis of all available wire-free, probe-based localizable markers showed a removal rate of 99% for these markers in 1355 TAD procedures. According to this analysis of 17 studies, all radar reflectors were successfully removed; the cases of unsuccessful marker removal concerned only magnetic seeds, radioactive seeds, and radiofrequency identification

Table 3 Studies reporting on the feasibility of axillary lymph node marking with radar reflectors before and/or during NACT

Study	Design	Number of patients with marked lymph nodes (*n*)	Number of radar reflectors placed before/during NACT (*n*)	Retrieval rate of radar reflector (%)
Our study	Prospective, multicenter	136	136	100
Coogan et al. [25]	Retrospective, unicentric	79	32	97
Baker et al. [27]	Prospective, unicentric	25	25	100
Balija et al. [22]	Retrospective, unicentric	57	22	100
Sun et al. [21]	Retrospective, unicentric	45	7	100
Easwaralingam et al. [26]	Prospective, unicentric	26	7	100
Weinfurtner et al. [24]	Retrospective, unicentric	105	n.a	97
Gallagher et al. [23]	Prospective, unicentric	86	n.a	100

NACT neoadjuvant chemotherapy, *TLN* target lymph node, *n.a.* not available tags (RFID) [29]. Compared to all other markers, radioactive seeds have the disadvantage that there are regulatory restrictions on their use due to their radioactivity, and in many countries, they may only be applied to axillary lymph nodes for a short time or not at all for radiation protection reasons [1]. Apart from radar markers, magnetic and paramagnetic markers, and RFIDs are used as probe-guided systems for TLN marking [22]. However, these markers may cause artifacts of 2–4 cm in MRI [18]. This can lead to an impairment of the assessment of breast MRI when it is performed to assess tumor response during NACT [17]. Radar markers, in contrast, cause minimal MRI artifacts (< 5 mm) [30]. The study presented here is the first to investigate the impairment of the assessment of breast MRI by radar reflectors located in the axilla and shows a low rate of only 3.7%. Therefore, impairment of MRI assessment is an important factor to be considered, when a TLN is marked before NACT. Further, the probe does not require recalibration for each application and has a penetration depth of 6 cm [18, 29]. In general, when using probe-supported marking systems, the targeted removal of marked lymph node requires a facility that is equipped with the corresponding probe system. Therefore, costs for the marker itself and the associated probe systems need to be considered [1, 22, 31]. Therefore, the dissemination of these modern guidance procedures may be challenging, particularly in countries with limited financial resources in the healthcare system.

Strengths of the current study are the comparatively large patient cohort and the prospective, multicenter study design. In addition, all datasets were monitored by experienced breast surgeons. We do not report on a direct comparison with other TLN marking procedures in terms of feasibility, postoperative complication rates, and quality of life, as recruitment in the AXSANA study is still ongoing. However, an evaluation of these endpoints is planned after completion of the study.

Conclusion

The use of radar reflectors for marking axillary TLNs in patients with initially node-positive breast cancer before NACT is associated with high detection rates for TLNs. This method represents a safe procedure for the targeted removal of initially metastatic axillary LNs after NACT. MRI assessment is rarely impaired by radar markers placed in the axilla. Future studies should evaluate all available TLN labeling methods not only in terms of applicability but also in terms of cost and postoperative morbidity and quality of life.

Acknowledgements The authors wish to thank Jessica Wagner, Jana Shabbir, Markus Höing, and Marina Mangold for the coordination of the AXSANA study and all participating study sites for their valuable contribution to this trial. The AXSANA study is supported by the AGO-B, the Claudia von Schilling Foundation for Breast Cancer Research, the Ehmann Foundation Savognin, AWOgyn, EndoMag, Merit Medical GmbH, Mammotome, German Breast Group Forschungs GmbH (GBG), and Nord-Ostdeutsche Gesellschaft für Gynäkologische Onkologie (NOGGO e.V.).

Author contributions All authors contributed to the study`s conception, design and data collection. Data analysis were performed by Maggie Banys-Paluchowski, Steffi Hartmann and Thorsten Kühn. The first draft of the manuscript was written by Maggie Banys-Paluchowski, Steffi Hartmann and Thorsten Kühn and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding This work was supported by the AGO Breast Study Group (AGO-B), the Claudia von Schilling Foundation for Breast Cancer Research, the Ehmann Foundation Savognin, Arbeitsgemeinschaft für ästhetische, plastische und wiederherstellende Operationsverfahren in der Gynäkologie e.V. (AWOgyn), EndoMag, Merit Medical, and Mammotome.

Data availability The dataset generated and analyzed during the current study is available from the corresponding author upon reasonable request.

Declarations

Competing interests Maggie Banys-Paluchowski: Honoraria for lectures and advisory role from: Roche, Novartis, Pfizer, pfm, Eli Lilly, Onkowissen, Seagen, AstraZeneca, Eisai, Amgen, Samsung, Canon, MSD, GSK, Daiichi Sankyo, Gilead, Sirius Medical, Syantra, resitu, Pierre Fabre, ExactSciences, Menarini Stemline; Study support: EndoMag, Mammotome, MeritMedical, Sirius Medical, Gilead, Hologic, ExactSciences, Claudia von Schilling Foundation for Breast Cancer Research, Ehmann-Stiftung Savognin; Travel reimbursement: Eli Lilly, ExactSciences, Pierre Fabre, Pfizer, Daiichi Sankyo, Roche Hans-Christian Kolberg: Honorare for lectures and advisory role from Pfizer, Seagen, Novartis, Roche, Genomic Health/Exact Sciences, Amgen, AstraZeneca, Riemser, Carl Zeiss Meditec, TEVA, Theraclion, Janssen-Cilag, GSK, LIV Pharma, Lilly, SurgVision, Onkowissen, Gilead, Daiichi Sankyo and MSD, Travel support from Carl Zeiss meditec, LIV Pharma, Novartis, Amgen, Pfizer, Daiichi Sankyo, Gilead, Roche, Onkowissen and Tesaro; Stock ofTheraclion SA. Jana de Boniface: Honoraria for lectures for Astra Zeneca, Lily and Novartis Nina Ditsch: Advisory Boards: Gilead, Lilly, MSD, Novartis, Pfizer, Roche, Seagen, Exact Sciences, Lectures: AstraZeneca, Daiichi-Sankyo, Exact Sciences, Pierre-Fabre, I-Med-Institute, Merit-Medical, pfm medical ag, Medi-Seminar GmbH, Roche, Lilly, Pfizer, Gilead, Novartis, Manuscript: pfm medical ag, Trial funding: Gilead, BZKF, Other: Onkowissen, Jörg Eickeler Kongress, if-Kongress Vesna Bjelic-Radisic: Honoraria for lectures and advisory role from: Roche, Novartis, Pfizer, pfm, Eli Lilly, AstraZeneca, Gilead, Sirius Medical, Pierre Fabre, Mammotome, Travel reimbursement: Pierre Fabre, Pfizer Maria Luisa Gasparri: Consultant for Merit Medical Nikolas Tauber: Honoraria for lectures and participation in advisory boards: Novartis, ExactSciences, Georg Thieme Verlag. Support for attending meetings from Astra Zeneca Marc Thill: Advisory Board: Agendia, Amgen, AstraZeneca, Aurikamed, Becton/Dickinson, Biom 'Up, ClearCut, Clovis, Daiichi Sankyo, Eisai, Exact Sciences, Gilead Science, Grünenthal, GSK, Lilly, MSD, Neodynamics, Novartis, Onkowissen, Organon, Pfizer, pfm Medical, Pierre-Fabre, Roche, Seagen, Sirius Medical, Sysmex; Manuscript support: Amgen, ClearCut, Clovis, Lilly, Organon, pfm medical, Roche, Servier; Travel expenses: Amgen, Art Tempi, AstraZeneca, Clearcut, Clovis, Connect Medica, Daiichi Sankyo, Eisai, Exact Sciences, Gilead, Hexal, I-Med-Institute, Lilly, MSD,

Neodynamics, Novartis, Pfizer, pfm Medical, Roche, RTI Surgical, Seagen, ZP Therapeutics; Congress support: Amgen, AstraZeneca, Celgene, Daiichi Sanyko, Gilead, Hexal, Lilly, Neodynamics, Novartis, Pfizer, Pierre Fabre, Roche, Sirius Medical; Lecture honoraria: Agendia, Amgen, Art Tempi, AstraZeneca, Clovis, Connect Medica, Eisai, Endomag, Exact Sciences, Gedeon Richter, Gilead Science, GSK, Hexal, I-Med-Institute, Jörg Eickeler, Laborarztpraxis Walther et al., Lilly, Medscape, MSD, Novartis, Onkowissen, Pfizer, pfm medical, Roche, Seagen, StreamedUp, Stemline, Sysmex, Vifor, Viatris, ZP Therapeutics; Trial Funding: Endomag, Exact Sciences; Trial honoraria: AstraZeneca, Biom'Up, CairnSurgical, Clearcut, Neodynamics, Novartis, pfm medical, Roche, RTI Surgical. Other authors declare no competing interests.

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University Aachen, Germany (Date: April 28, 2020, Number: EK 013/20).

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Banys-Paluchowski M, Gasparri ML, de Boniface J, Gentilini O, Stickeler E, Hartmann S, Thill M, Rubio IT, Di Micco R, Bonci EA et al (2021) 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 13(7):1565
2. Banys-Paluchowski M, Rubio IT, Ditsch N, Krug D, Gentilini OD, Kuhn T (2023) Real de-escalation or escalation in disguise? Breast 69:249–257
3. Kuehn T, Bauerfeind I, Fehm T, Fleige B, Hausschild M, Helms G, Lebeau A, Liedtke C, von Minckwitz G, Nekljudova V et al (2013) Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study. Lancet Oncol 14(7):609–618
4. Boughey JC, Suman VJ, Mittendorf EA, Ahrendt GM, Wilke LG, Taback B, Leitch AM, Kuerer HM, Bowling M, Flippo-Morton TS et al (2013) Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial. JAMA 310(14):1455–1461
5. Classe JM, Loaec C, Gimbergues P, Alran S, de Lara CT, Dupre PF, Rouzier R, Faure C, Paillocher N, Chauvet MP et al (2019) Sentinel lymph node biopsy without axillary lymphadenectomy after neoadjuvant chemotherapy is accurate and safe for selected patients: the GANEA 2 study. Breast Cancer Res Treat 173(2):343–352
6. El Hage CH, Headon H, El Tokhy O, Heeney J, Kasem A, Mokbel K (2016) Is sentinel lymph node biopsy a viable alternative to complete axillary dissection following neoadjuvant chemotherapy in women with node-positive breast cancer at diagnosis? An updated meta-analysis involving 3398 patients. Am J Surg 212(5):969–981
7. Kahler-Ribeiro-Fontana S, Pagan E, Magnoni F, Vicini E, Morigi C, Corso G, Intra M, Canegallo F, Ratini S, Leonardi MC et al (2021) Long-term standard sentinel node biopsy after neoadjuvant treatment in breast cancer: a single institution ten-year follow-up. Eur J Surg Oncol 47(4):804–812
8. Caudle AS, Yang WT, Krishnamurthy S, Mittendorf EA, Black DM, Gilcrease MZ, Bedrosian I, Hobbs BP, DeSnyder SM, Hwang RF et al (2016) 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 34(10):1072–1078
9. Kuemmel S, Heil J, Rueland A, Seiberling C, Harrach H, Schindowski D, Lubitz J, Hellerhoff K, Ankel C, Grasshoff ST et al (2022) A prospective, multicenter registry study to evaluate the clinical feasibility of targeted axillary dissection (TAD) in node-positive breast cancer patients. Ann Surg 276(5):e553–e562
10. Montagna G, Mrdutt MM, Sun SX, Hlavin C, Diego EJ, Wong SM, Barrio AV, van den Bruele AB, Cabioglu N, Sevilimedu V et al (2024) Omission of axillary dissection following nodal downstaging with neoadjuvant chemotherapy. JAMA Oncol 10(6):793–798
11. Simons JM, van Nijnatten TJA, van der Pol CC, van Diest PJ, Jager A, van Klaveren D, Kam BLR, Lobbes MBI, de Boer M, Verhoef C et al (2022) 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 157(11):991–999
12. Banys-Paluchowski M, Thill M, Kühn T, Ditsch N, Heil J, Wöckel A, Fallenberg E, Friedrich M, Kümmel S, Müller V, Janni W (2023) AGO-Empfehlungen zur operativen Therapie des Mammakarzinoms: update 2022. Senologie-Zeitschrift für Mammadiagnostik und-therapie 20(01):81–93
13. de Boniface J, Frisell J, Kuhn T, Wiklander-Brakenhielm I, Dembrower K, Nyman P, Zouzos A, Gerber B, Reimer T, Hartmann S (2022) 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 193(3):589–595
14. Hartmann S, Kuhn T, de Boniface J, Stachs A, Winckelmann A, Frisell J, Wiklander-Brakenhielm I, Stubert J, Gerber B, Reimer T (2021) Carbon tattooing for targeted lymph node biopsy after primary systemic therapy in breast cancer: prospective multicentre TATTOO trial. Br J Surg 108(3):302–307
15. Banys-Paluchowski M, de Boniface J (2023) Axillary staging in node-positive breast cancer converting to node negativity through neoadjuvant chemotherapy: current evidence and perspectives. Scand J Surg 112(2):117–125
16 Hartmann S, Stachs A, Schultek G, Gerber B, Reimer T (2021) The clinical relevance of target lymph node biopsy after primary systemic therapy in initially node-positive breast cancer patients. Cancers 13(11):2620
17. Hartmann S, Banys-Paluchowski M, Stickeler E, de Boniface J, Gentilini OD, Kontos M, Seitz S, Kaltenecker G, Warnberg F, Zetterlund LH et al (2023) 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 202(3):497–504
18. Wazir U, Michell MJ, Alamoodi M, Mokbel K (2024) Evaluating radar reflector localisation in targeted axillary dissection in patients undergoing neoadjuvant systemic therapy for node-positive early breast cancer: a systematic review and pooled analysis. Cancers 16(7):1345
19. Kasem I, Mokbel K (2020) Savi Scout(R) radar localisation of non-palpable breast lesions: systematic review and pooled analysis of 842 cases. Anticancer Res 40(7):3633–3643
20. Hartmann S, Kuhn T, Hauptmann M, Stickeler E, Thill M, Lux MP, Frohlich S, Ruf F, Loibl S, Blohmer JU et al (2022) Axillary staging after neoadjuvant chemotherapy for initially node-positive breast carcinoma in Germany: initial data from the AXSANA study. Geburtshilfe Frauenheilkd 82(9):932–940
21. Sun J, Henry DA, Carr MJ, Yazdankhahkenary A, Laronga C, Lee MC, Hoover SJ, Sun W, Czerniecki BJ, Khakpour N et al (2020) Feasibility of axillary lymph node localization and excision using

radar reflector localization. Clin Breast Cancer. https://doi.org/10.1016/j.clbc.2020.08.001
22. Balija TM, Braz D, Hyman S, Montgomery LL (2021) 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 189(1):121–130
23. Gallagher KK, Iles K, Kuzmiak C, Louie R, McGuire KP, Ollila DW (2022) Prospective evaluation of radar-localized reflector-directed targeted axillary dissection in node-positive breast cancer patients after neoadjuvant systemic therapy. J Am Coll Surg 234(4):538–545
24. Weinfurtner RJ, Leon A, Calvert A, Lee MC (2022) Ultrasound-guided radar reflector localization of axillary lymph nodes facilitates targeted axillary dissection. Clin Imaging 90:19–25
25. Coogan AC, Lunt LG, O'Donoghue C, Keshwani SS, Madrigrano A (2024) Efficacy of targeted axillary dissection with radar reflector localization before neoadjuvant chemotherapy. J Surg Res 295:597–602
26. Easwaralingam N, Nguyen CL, Ali F, Chan B, Graham S, Azimi F, Mak C, Warrier S (2024) Radar localization of breast and axillary lesions with SCOUT: a prospective single institution pilot study. ANZ J Surg 94(6):1083–1089
27. Baker JL, Haji F, Kusske AM, Fischer CP, Hoyt AC, Thompson CK, Lee MK, Attai D, DiNome ML (2022) SAVI SCOUT(R) localization of metastatic axillary lymph node prior to neoadjuvant chemotherapy for targeted axillary dissection: a pilot study. Breast Cancer Res Treat 191(1):107–114
28. Hartmann S, Reimer T, Gerber B, Stubert J, Stengel B, Stachs A (2018) Wire localization of clip-marked axillary lymph nodes in breast cancer patients treated with primary systemic therapy. Eur J Surg Oncol 44(9):1307–1311
29. Varghese J, Patani N, Wazir U, Novintan S, Michell MJ, Malhotra A, Mokbel K, Mokbel K (2024) Wire-free targeted axillary dissection: a pooled analysis of 1300+ cases post-neoadjuvant systemic therapy in node-positive early breast cancer. Cancers 16(12):2172
30. Hayes MK (2017) Update on preoperative breast localization. Radiol Clin North Am 55(3):591–603
31. Hartmann S, Stachs A, Kuhn T, de Boniface J, Banys-Paluchowski M, Reimer T (2021) Targeted removal of axillary lymph nodes after carbon marking in patients with breast cancer treated with primary chemotherapy. Geburtshilfe Frauenheilkd 81(10):1121–1127

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Authors and Affiliations

Maggie Banys-Paluchowski[1] · Steffi Hartmann[2] · Timo Basali[3] · Maria Luisa Gasparri[4,5] · Jana de Boniface[6,7] · Oreste Davide Gentilini[8,9] · Güldeniz Karadeniz Cakmak[10] · Nina Ditsch[11] · Elmar Stickeler[12,13] · Ellen Schlichting[14] · Isabel Rubio[15] · Florentia Peintinger[16,17] · Michael Untch[18] · Christine Mau[18] · Frederike Klaassen Federspiel[19] · Susanne Bucher[20] · Kerstin Ramaker[21] · Peter Paluchowski[21] · Lelia Bauer[22] · Sabine Riemer[23] · Dagmar Langanke[24] · Tanja Durpektova Leuf[25] · Jens Schnabel[26] · Ekkehard von Abel[27] · Christine Solbach[28] · Sonja Cáradenas Ovalle[29] · Kerstin Hilmer[30] · Vesna Bjelic-Radisic[31,32] · Nicole Stahl[33] · Jose I. Sanchez-Mendez[34] · Vibeke Hagen[35] · Marit Helene Hansen[36] · Natalia Krawczyk[37] · Bilge Aktas Sezen[38] · Katharina Jursik[38] · Marc Thill[39] · Hans-Christian Kolberg[40] · Toralf Reimer[2] · Franziska Ruf[1] · Kristina Wihlfahrt[41] · Angelika Rief[42] · Tomasz Berger[43] · Esther Schmidt[2] · Nikolas Tauber[1] · Sarah Fröhlich[2] · Thorsten Kühn[44,45]

✉ Maggie Banys-Paluchowski
Maggie.Banys-Paluchowski@uksh.de

1 Department of Obstetrics and Gynecology, University Hospital of Schleswig-Holstein, Campus Lübeck, Lubeck, Germany

2 Department of Gynecology and Obstetrics, University Hospital Rostock, Rostock, Germany

3 Department of Gynecology and Obstetrics, Hospital Esslingen, Esslingen, Germany

4 Department of Gynecology and Obstetrics, Ospedale Regionale di Lugano, Ente Ospedaliero Cantonale, Lugano, Switzerland

5 Faculty of Biomedicine, University of the Italian Switzerland (USI), Lugano, Switzerland

6 Department of Surgery, Breast Center, Capio St. Göran's Hospital, Stockholm, Sweden

7 Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

8 Breast Surgery Unit, Universita Vita-Salute San Raffaele, Milan, Italy

9 Breast Surgery Unit, IRCCS Ospedale San Raffaele, Milan, Italy

10 Breast and Endocrine Unit, General Surgery Department, Zonguldak BEUN The School of Medicine, Zonguldak, Turkey

11 Gynecology, Obstetrics and Senology, Faculty of Medicine, University Hospital Augsburg, University of Augsburg, Augsburg, Germany

12 Department of Gynecology and Obstetrics, University Hospital Aachen, Aachen, Germany

13 Center for Integrated Oncology Aachen Bonn Cologne Düsseldorf (CIO ABCD), Bonn, Germany

14 Department of Oncology, Oslo University Hospital, Oslo, Norway

15 Breast Surgical Unit, Clínica Universidad de Navarra, Madrid, Spain

[16] Department of Gynecology and Obstetrics, University Hospital Graz, Graz, Austria

[17] Institute of Pathology, Medical University of Graz, Graz, Austria

[18] Department of Obstetrics and Gynecology, Helios Hospital Berlin-Buch, Buch, Berlin, Germany

[19] Department of Senology, University Hospital Salzburg, Paracelsus Medical University, Salzburg, Austria

[20] Breast Center, Cantonal Hospital Luzern, Lucerne, Switzerland

[21] Breast Center Pinneberg, Regio Hospitals, Pinneberg, Germany

[22] Department of Obstetrics and Gynecology, GRN Hospital Weinheim, Weinheim, Germany

[23] Department of Obstetrics and Gynecology, St. Joseph Stift Bremen, Bremen, Germany

[24] Department of Senology and Breast Center, St. Elisabeth Hospital, Leipzig, Germany

[25] Department of Gynecology and Breast Center, Asklepios Hospital, Weissenfels, Germany

[26] Department of Obstetrics and Gynecology, DRK Hospital Chemnitz Rabenstein, Chemnitz, Germany

[27] Department of Obstetrics and Gynecology, Staufer Hospital Mutlangen, Mutlangen, Germany

[28] Department of Obstetrics and Gynecology, University Hospital Frankfurt, Frankfurt, Germany

[29] Department of Gynecology, Protestant Forest Hospital Spandau, Spandau, Germany

[30] Department of Obstetrics and Gynecology, Helios Hospital Gifhorn GmbH, Gifhorn, Germany

[31] Breast Center, Helios University Hospital, Wuppertal, Germany

[32] University Witten/Herdecke, Herdecke, Witten, Germany

[33] Breast Center, Helios Hospital Schwerin, Schwerin, Germany

[34] Department of Gynecology, Hospital Universitario La Paz, Madrid, Spain

[35] Department of Gynecology, St. Olavs Hospital, Trondheim, Norway

[36] Department of Breast and Endocrine Surgery, The Arctic University of Norway, Tromsoe, Norway

[37] Department of Obstetrics and Gynecology, University Hospital Düsseldorf, Dusseldorf, Germany

[38] EUBREAST e.V., Esslingen, Germany

[39] Department of Gynecology and Gynecological Oncology, Agaplesion Markus Hospital, Frankfurt, Germany

[40] Department of Gynecology and Obstetrics, Marienhospital Bottrop, Bottrop, Germany

[41] Practice for Gynecology and Obstetrics Wihlfahrt, Kiel, Germany

[42] Department of Gynecology and Obstetrics, Medical University of Graz, Graz, Austria

[43] Department of Gynecology and Obstetrics, Müritz-Klinikum Waren, Waren, Germany

[44] Department of Gynecology and Obstetrics, University of Ulm, Ulm, Germany

[45] Breast Center, Die Filderklinik, Filderstadt, Germany