

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

Banys-Paluchowski Maggie (1), Basali Timo (2), Hartmann Steffi (3), de Boniface Jana (4,5), Gentilini Oreste Davide (6,7), Stickeler Elmar (8), Mau Christine (9), Ruf Franziska (1), Fröhlich Sarah (3), Gasparri Maria Luisa (10), Thill Marc (11), Peintinger Florentia (12), Karadeniz Cakmak Guldeniz (13), Rubio Isabel Teresa (14), Langanke Dagmar (15), Cardenas Ovalle Sonja (16), Riemer Sabine (17), Rody Achim (1), Ellen Schlichting (18), Kühn Thorsten (19,20) and the AXSANA Study Group

## Background

Surgical staging procedures of the axilla in breast cancer patients converting from a clinically positive to a clinically negative node status during neoadjuvant chemotherapy (NACT) vary across countries. Different surgical techniques are currently in use, such as axillary lymph node dissection (ALND), sentinel lymph node biopsy (SLNB), target lymph node biopsy (TLNB) and targeted axillary dissection (TAD). With regard to marking of the target lymph node (TLN), a variety of markers are available. Beyond clips/coils and ink, the use of new localization devices that allow for intraoperative probe-guided detection has increased in the last years. However, prospective evidence is still limited. In this subgroup analysis, we report on the largest prospective cohort of patients receiving a radar reflector for marking of the TLN prior to NACT.

## Methods

The AXSANA study is to date the largest prospective study on axillary management in patients converting from cN+ to ycN0 status through NACT. Primary outcomes are invasive disease-free survival, axillary recurrence rate and quality of life and arm morbidity. The comparison of marking techniques for the TLN is a secondary endpoint. In the present analysis, only patients with a TLN marked by a radar reflector (Fig. 1, 2) before NACT were included. We prospectively examined the retrieval rate of radar reflectors and the identification rate of the TLN (defined as unequivocal removal of the lymph node, i.e., the presence of lymphatic tissue in the TLN specimen and/or pathological confirmation of post-NACT changes typical for metastatic lymph nodes responding to treatment).

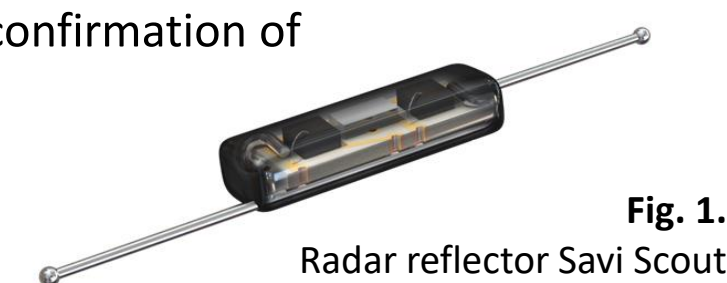
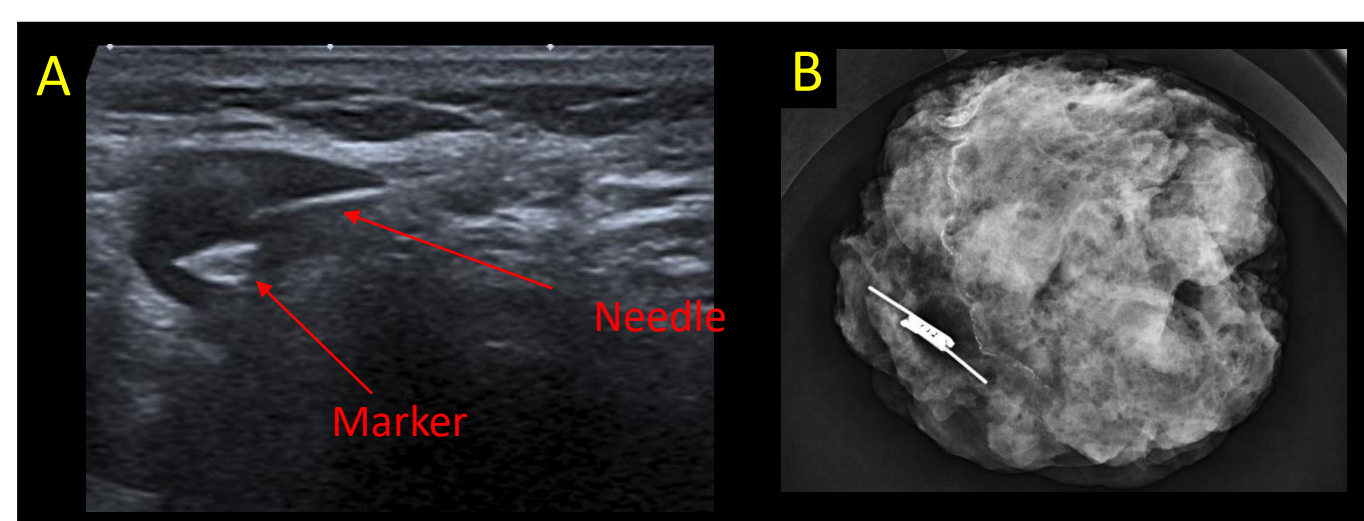


Fig. 1.

Radar reflector Savi Scout

Fig. 2.

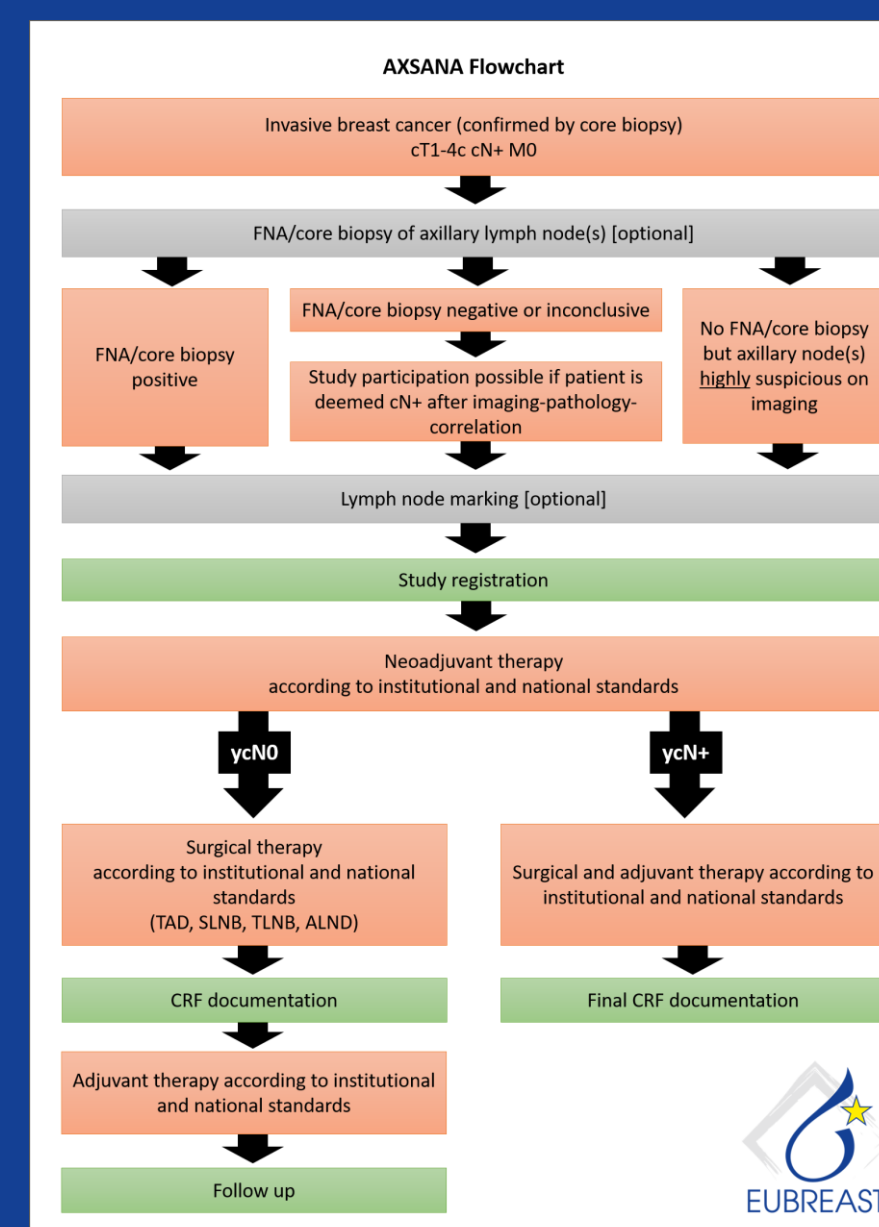
A: Ultrasound imaging of a radar reflector in the TLN after placement.  
B: Specimen radiography showing a radar reflector in the removed tissue.



## About the AXSANA study

AXSANA is an international prospective cohort study including cN+ patients converting to ycN0 status and treated with different axillary staging techniques according to the standard at their treating institution. The study was initiated by the EUBREAST network and started enrollment in August 2020. Eligible patients have cT1-4c tumors, initially present with axillary lymph node metastasis and receive neoadjuvant chemotherapy. Patients converting to ycN0 status are followed up for 5 years. The primary endpoints of the study are invasive disease-free survival, axillary recurrence rate and quality of life/arm morbidity.

**Enrollment status: 5514 patients**  
**27 participating countries**  
**290 open study sites**



## Financial support:

AWOgyn  
AGO-B  
Claudia von Schilling  
Foundation for Breast Cancer  
Research  
Ehmann Stiftung  
Merit Medical  
Endomaga  
Mammotome

For more information, visit:  
<http://eubreast.org/axsana>



## Results

A TLN was marked using a radar reflector in 137 patients prior to NACT. All patients were female. Most were enrolled in Germany (124; 90.5%), followed by Norway (6; 4.4%), Spain (3; 2.2%), Switzerland (3; 2.2%) and Austria (1; 0.7%). The median age was 51 years (range: 25-77). The most common subtype was no special type in 125 (91.2%) patients, followed by invasive lobular cancer (7; 5.1%), apocrine carcinoma (3; 2.2%) and metaplastic cancer (2; 1.4%). 120 (87.6%) patients had unifocal cancer, followed by 10 (7.3%) patients with bifocal cancer and 7 (5.1%) with 3 or more foci. Multicentric disease was documented in 10 (7.3%) cases. Most patients had a HER2-positive tumor (47; 34.3%), followed by triple-negative disease (46; 33.6%) (Table 1). Lymphovascular invasion was reported in 7 (5.1%) cases. In 61 patients (44.5%) lymph nodes were suspicious upon palpation and in 136 (99.3%) upon ultrasound. 36 patients received MRI of the axilla. Lymph nodes were suspicious in 32 out of these 36 patients (88.9%). Most patients (51.8%) had one suspicious node at time of diagnosis. The median size of the largest suspicious node was 17 mm (range: 6-39 mm). In most patients (130; 94.9%), only one node was marked. The TLN marking was performed under ultrasound guidance in all patients.

24 patients (17.5%) received breast MRI between marker placement and surgery. In 5 out of 24 cases (20.8%), MRI artifacts were described. However, the assessment of MRI was limited due to artifacts only in one out of these five patients (20%).

Table 2. Response to therapy and planned surgical staging.

All patients	119 (100%)
<b>ycT stage</b>	
ycT0	61 (51.3%)
ycT1	40 (33.6%)
ycT2	15 (12.6%)
ycT3	2 (1.7%)
ycT4	1 (0.8%)
<b>ycN stage</b>	
ycN0	96 (80.7%)
ycN+	23 (19.3%)
<b>Planned axillary surgical staging</b>	
ALND	10 (8.4%)
TAD	106 (89.1%)
TLNB	2 (1.7%)
Other *	1 (0.8%)
<b>ypT stage **</b>	
ypT0	45 (38.5%)
ypTis	8 (6.8%)
ypT1-4	64 (54.7%)
<b>ypN stage **</b>	
ypN0	67 (57.3%)
ypN0 (i+)	3 (2.6%)
ypN1mi	12 (10.2%)
ypN1-3	35 (29.9%)
<b>Pathological response **</b>	
ypT0 ypN0	41 (35.0%)
ypTis ypN0	5 (4.3%)
Residual invasive tumor	71 (60.7%)

\* Surgical procedure as in the TAXIS trial, i.e., removal of the TLN, the SLN as well as all palpably suspicious nodes  
\*\* Final histopathological report was available for 117 patients at time of the analysis

Out of the 137 patients with radar reflector marked TLN, 119 (86.9%) had undergone final surgery at the time of analysis and 18 (13.1%) are still under NACT. 80.7% of patients who received final surgery converted to ycN0 (Table 2). Most patients had undergone a TAD (106; 89.1%), followed by upfront ALND in 8.4% of patients. Technetium was used for sentinel lymph node marking in 102 out of 106 patients (96.2%), either as a single tracer (83; 78.3%) or in combination with superparamagnetic iron oxide (SPIO), indocyanine green (ICG) or dye (Table 3).

All radar reflectors were removed. In one patient, the radar reflector was neither in the TLN nor in the ALND specimen, but the removal was confirmed by postoperative low-dose computed tomography of the thorax. In 117 out of 119 patients (98.3%) the TLN was unequivocally identified and removed. In two 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. pCR defined as the absence of invasive or in situ residuum was reached in 35% of patients and pCR defined as the absence of invasive rest in 39% of patients (Table 2).

## Conclusion

To the best of our knowledge, this is the largest prospective series of patients receiving a radar reflector for the marking of target lymph node prior to neoadjuvant chemotherapy for breast cancer. The removal rate of the marker and the detection rate of the target node were very high. Our data demonstrate that radar reflectors are a reliable tool for marking of target lymph nodes before neoadjuvant treatment.

Table 1. Clinical-pathological characteristics of included patients.

All patients	137 (100%)
<b>T stage</b>	
cT1	34 (24.8%)
cT2	85 (62%)
cT3	18 (13.1%)
<b>Subtype</b>	
HR+ HER2-negative	44 (32.1%)
HR+ HER2-positive	31 (22.6%)
HR- HER2-positive	16 (11.7%)
Triple-negative	46 (33.6%)
<b>Number of suspicious nodes</b>	
1	71 (51.8%)
2	36 (27.3%)
3	24 (17.5%)
≥ 4	6 (4.4%)
<b>Minimally invasive biopsy of TLN</b>	
Core biopsy	115 (83.9%)
Fine needle aspiration	19 (13.9%)
None	3 (2.2%)
<b>Number of marked lymph nodes</b>	
1	130 (94.9%)
2 *	5 (3.6%)
≥ 3 *	2 (1.5%)

\* In most patients, only one node was marked with a radar reflector and further nodes with a clip

Table 3. Tracers used for sentinel node marking.

Sentinel lymph node tracer	106 (100%)
Technetium	83 (78.3%)
Technetium + SPIO	1 (0.9%)
Technetium + ICG	2 (1.9%)
Technetium + dye	16 (15.1%)
ICG	3 (2.8%)
Dye	1 (0.9%)