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 M (1), Basali T (2), Hartmann S (3), de Boniface J (4,5), Gentilini OD (6,7), Stickeler E (8), Untch M (9), Ruf F (1), Fröhlich S (3), Gasparri ML (10), Thill M (11), Lux MP (12), Peintinger F (13), Karadeniz Cakmak G (14), Rubio IT (15), Kontos M (16), Di Micco R (6), Murawa D (17), Schlichting E (18), Aktas Sezen B (19), Rody A (1), Langanke D (20), Sanchez-Mendez JI (21), Bjelic-Radisic V (22), Solbach C (23), Cardenas Ovalle S (24), Mau C (8), Buchmann N (8), Riemer S (25), Hansen MH (26), Bauer L (27), Schnabel J (28), Von Abel E (29), Ditsch N (30), Kuehn T (31,32) 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.

MATERIALS AND 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 SaviScout

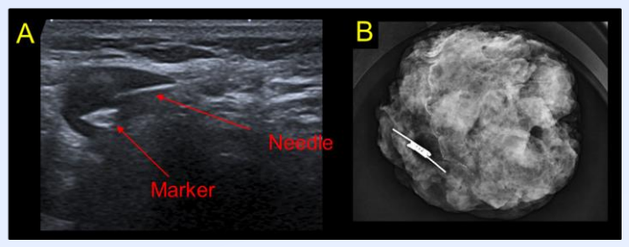

Fig. 2. A: Ultrasound imaging of a radar reflector in the TLN; B: Specimen radiography showing a radar reflector

RESULTS

A TLN was marked using a radar reflector in 137 patients prior to NACT. All patients were female. 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). In 61 patients (44.5%) lymph nodes were suspicious upon palpation and in 136 (99.3%) upon ultrasound. Most patients (51.8%) had one suspicious node at time of diagnosis (Fig. 3). 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%).

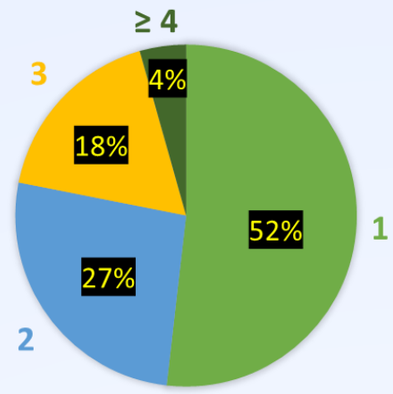

Fig. 3. Number of suspicious nodes

All patients		117 (100%) *
ypT stage	ypT0	45 (38.5%)
	ypTis	8 (6.8%)
	ypT1-4	64 (54.7%)
ypN stage	ypN0	67 (57.3%)
	ypN0 (i+)	3 (2.6%)
	ypN1mi	12 (10.2%)
	ypN1-3	35 (29.9%)
Pathological response		
	ypT0 ypN0	41 (35.0%)
	ypTis ypN0	5 (4.3%)
	Residual invasive tumor	71 (60.7%)

* 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 converted to ycN0. Most patients had undergone a TAD (106; 89.1%), followed by upfront ALND in 8.4% of patients.
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.

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.

Affiliations: 1) Department of Obstetrics and Gynecology, University Hospital of Schleswig Holstein, Campus Lübeck, Lübeck, Germany, 2) Department of Gynecology and Obstetrics, Klinikum Esslingen, Esslingen, Germany, 3) Department of Gynecology and Obstetrics, University Hospital Rostock, Rostock, Germany, 4) Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden, 5) Department of Surgery, Capio St. Göran's Hospital, Stockholm, Sweden, 6) Breast Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy, 7) Università Vita-Salute San Raffaele, Milan, Italy, 8) Department of Gynecology and Obstetrics, University Hospital Aachen, Aachen, Germany, 9) Breast Cancer Center, Clinic for Gynecology and Obstetrics, Helios Klinikum Berlin-Buch, Berlin, Germany, 10) Department of Gynecology and Obstetrics, Ospedale Regionale di Lugano EOC, 6900 Lugano, Switzerland; Centro di Senologia della Svizzera Italiana (CSSI), Ente Ospedaliero Cantonale, via Pietro Capelli 1, 6900 Lugano, Switzerland; Faculty of Biomedical Sciences, Università della Svizzera Italiana (USI), via Giuseppe Buffi 13, 6900 Lugano, Switzerland, 11) Department of Gynecology and Gynecological Oncology, AGAPLESION Markus Krankenhaus, Frankfurt am Main, Germany, 12) Klinik für Gynäkologie und Geburtshilfe, Frauenklinik St. Louise, Paderborn, Frauenklinik St. Josefs-Krankenhaus, Salzkotten, St. Vincenz Kliniken, Paderborn, Germany, 13) Universitätsklinik für Frauenheilkunde und Geburtshilfe, Graz & Institut für Pathologie, Med. Univ Graz, Austria, 14) Zonguldak BEUN The School of Medicine, General Surgery Department, Breast and Endocrine Unit, Kozlu/Zonguldak 67600, Turkey, 15) Breast Surgical Unit, Clínica Universidad de Navarra, Madrid, Spain, 16) 1st Department of Surgery, Laiko Hospital, National and Kapodistrian University of Athens, Athens, Greece, 17) Department of General Surgery and Surgical Oncology, Collegium Medicum, University of Zielona Góra, Zielona Góra, Poland, 18) Oslo University Hospital, Oslo, Norway, 19) EUBREAST e.V., Esslingen, Germany, 20) St. Elisabeth KH Leipzig-Brustzentrum, Leipzig, Germany, 21) Breast Unit - Hospital Universitario La Paz - Madrid, Spain, 22) Breast Unit, Helios University Hospital, Wuppertal, University Witten/Herdecke, Germany, 23) Breast Center, University Hospital, Goethe-University Frankfurt, Frankfurt, Germany, 24) Ev. Waldkrankenhaus Spandau, Berlin, Germany, 25) St. Joseph Stift Bremen, Bremen, Germany, 26) University Hospital of North Norway, Tromsoe, Norway, 27) GRN Klinikum Weinheim, Weinheim, Germany, 28) DRK Krankenhaus Chemnitz Rabenstein, Chemnitz, Germany, 29) Stauferklinikum Mutlangen, Mutlangen, Germany, 30) Breast Cancer Center, University Hospital Augsburg, Augsburg, Germany, 31) Department of Gynecology and Obstetrics, Die Filderklinik, Filderstadt-Bonlanden, Germany, 32) Department of Gynecology and Obstetrics, University of Ulm, Germany