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RESEARCH

Internal Mammary Sentinel Node Biopsy in Breast Cancer. Is it Indicated?

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Abstract Axillary sentinel node (A-SN) biopsy is a standard procedure in breast cancer surgery. Sampling of intenal mammary sentinel nodes (IM-SN) is not performed routinly, although it is also considered an important prognostic factor of breast cancer. The role of this latter procedure was investigated in cases of IM-SN visualized on lymphoscintigraphy. Between January 2001 and June 2012 1542 patients with clinically node negative operable primary breast cancer had sentinel node biopsy (SNB). Both axillary and IM-SN were sampled (whenever detected), based on lymphoscintigraphy, intraoperative gamma probe detection and blu dye mapping. Lymphoscintigraphy showed IM-SN in 83 cases. IM-SN biopsy (IM-SNB) was succesfull in 77 patients (93 %). A total of 86 IM-SNs were removed. IM-SN involvement was identified in 14 cases, representing 18 % of patients who underwent IM-SNB. This included macrometastases (MAC) in 5 cases, micrometastases (MIC) in 2 cases, isolated tumor cells (ITC) in 7 cases. No significant differences were found between patients with and without IM-SN involvement in terms of age, tumor location, tumor size, axillary involvement, tumor grade or estrogen receptor status. The IM-SN involvement has lead to new therapeutic indications in 2 cases (2.6 %), both of them due to MAC in the IM-SN: in 1 case change in chemotherapy and in 1 case change in radiotherapy, with the addition of iradiation of the internal mammary chain. Based on this series and information from the literature, we conclude that the indication for an IM-SNB procedure is very limited and its routine use should not be recommended.

Keywords Breast cancer · Internal mammary nodes · Sentinel node biopsy

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Introduction

The sentinel lymph node (SN) procedure has become the standard of care for staging clinically node-negative patients with breast cancer. [1–3] The two main nodal regions of the breast are the axillary and the parasternal or internal mammary (IM), the latter consisting of approximately 8 lymph nodes. Although studies of lymphatic drainage patterns report internal mammary chain (IMC) involvement in 13–35 %, the value of an SN procedure for the IMC is still controversial. [4–8] Most authors do not perform internal mammary sentinel node biopsy (IM-SNB), because the clinical importance and therapeutical implications of IM lymph node metastases are unclear.

Tumor location within the breast may influence the prevalence of IM nodal metastases. Medial tumors may have internal mammary drainage somewhat more often than breast tumors at other locations, but tumor location alone has not

been found to be a good predictor of IM-SN involvement. [9] Whether the site of the primary breast tumor should be considered when deciding about IM-SNB can also be a matter of debate.

In addition to the axillary lymph node status, the IM lymph node status also provides prognostic information in breast cancer patients. [10] If positive, prognosis is less favorable. The worse prognosis can be expected in patients with involvement of both nodal regions, whereas patients with involvement of either region alone seem to have similar prognosis. [9]

The aim of our retrospective study was to investigate in what percentage lymphoscintigraphy visualized IM-SNs during the axillary SNB (A-SNB) operations performed in patients with invasive, clinically node-negative breast cancer. Furthermore, we analyzed in what proportion the IM-SNB was succesful in these patients, what was the rate of metastatic IM-SNs and what were the factors influencing the presence of metastatic involvement. We have also assessed to what extent the IM-SN involvement has lead to a change in treatement.

Patients and Methods

Selective axillary lymph node dissection based on A-SNB results was introduced in our hospital with the approval of the local ethical committe. From January 2001 to June 2012, 1542 patients with clinically node-negative operable primary breast cancer gave an informed consent and underwent SNB. Except for pregnancy and T4-tumors, no patients were excluded. The preoperative diagnosis of breast cancer was established by mammography, ultrasonography and fine-needle aspiration or core biopsy in all patients. Prior to surgery, ultrasound of the axilla was performed routinely and if suspicious lymph nodes were identified, fine needle aspiration was also done. [11–13] When this revealed an axillary lymph node metastasis axillary lymph node dissection (ALND) was performed, whereas in case of negative cytology findings, A-SNB was the staging procedure done.

Our technique of SNB involved intraparenchymal administration (intra- and/or peritumoral injection in 3–4 depots) of 60–90 MBq 99mTc-labelled colloids the day before surgery: either 200–600 nm particle size SENTISCINT (Medi-Radiopharma Kft., Érd, Hungary) or 40–80 nm particle size colloids Nanoalbumon (Medi-Radiopharma Kft., Érd, Hungary) or Nanocoll (Gipharma, Saluggia, Italy). From January 2006, we introduced superficial, periareolar injection of the radiocolloid according to the localization of the quadrant harboring the tumor as preferred method. However, in case of non-palpable tumors, the radioactive tracer was injected intraparenchymally, into and around the tumor, with ultrasound guidance to permit Radioguided Occult Lesion Localisation (ROLL). [14] Lymphoscintigraphy was generally performed 2 h after the administration of the radioactive tracer and was often repeated the next day, shortly before surgery. Lymphoscintigraphic images were obtained in three standard positions: anterior, anterior oblique and lateral. The location of the non palpable tumors, A-SNs and IM-SNs was marked on the skin. Two ml Patent Blue V dye (Laboratoire Guerbet, France) was injected intraparenchymally above the tumor after the induction of general anaesthesia, 10–15 min before the incision. Harvesting both axillary and IM-SNs was attempted in all patients, as visualized on lymphoscintigraphy (Fig. 1). A-SNB was performed before the removal of the primary carcinoma and A-SNs sliced at about 2 mm intervals were subjected to imprint cytology as a means of intraoperative evaluation, to allow immediate ALND in patients with metastasis. The primary breast tumor was removed next by either breast conserving methods or by mastectomy, according to the tumor and patient characteristics. This was followed by IM-SNB whenever lymphoscintigraphy highlighted IMC drainage.

The IM-SNB technique, based on the IM lymph node biopsy method described by Haagensen, can usually be performed using the mastectomy incision. In breast conserving operations, a small additional horizontal incision (2.5–3 cm) over the desired interspace was used to sample IM-SNs. It is usually preferable that this incision does not cross the midline, because of cosmetic reasons. The pectoral major muscle was exposed for 2 to 3 cm directly over the desired interspace. The muscle fibers were then separetad to expose the posterior intercostal space. The external and internal intercostal muscles are divided transversely from the sternal border in a lateral direction for 3 to 4 cm. In cutting the internal intercostal muscle, particular care must be taken to avoid injury to the inferior parietal pleura or the internal mammary artery (Fig. 2). In case of multiple IM hotspots on the lymphoscintigraphy, the IM lymph nodes were mostly retrieved through the same incision. Intraoperative identification of the A-SNs and IM-SNs was based both on blue dye mapping and gamma probe detection (C-Trak Surgical Guidence System, Care Wise Medical Products Corporation, Morgan Hill, CA, USA). IM-SNs were not subjected to intraoperative assessment.

The final pathological evaluation of all SNs included formaline fixation, paraffin embedding and step sectioning at 250 μm intervals of all slices or unsliced lymph nodes smaller than 6 mm with hematoxylin and eosin staining of all, and cytokeratin immunohistochemistry of several levels. [15] Metastases in the A-SLNs discovered only in the permanent sections also generally resulted in axillary lymph node dissection with the exception of a few patients.

As the largest part of the study period used the 6th edition of the TNM classification of malignant tumors, this edition was used for staging purposes and the discrimination of metastases, micrometastases and isolated tumor cells (ITC). [16]

Statistical analysis for the comparisons included the chi-square test for categorical variables and the student t test for continuous variables. The significance level was set at $p<0.05$.

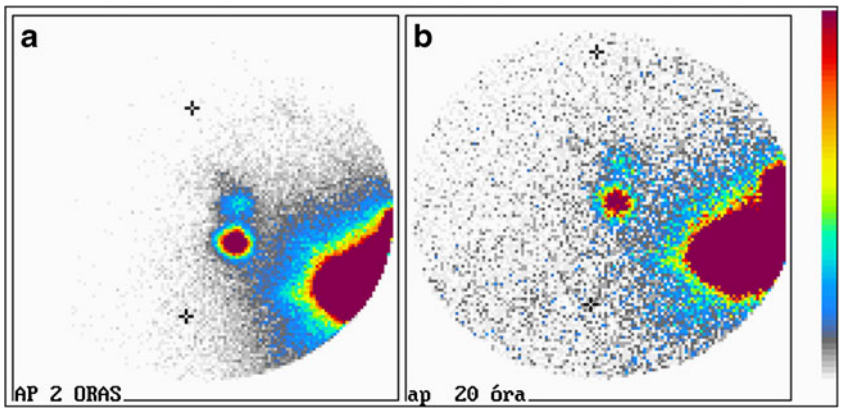

Fig. 1 The hotspot of internal mammary sentinel node (IM-SN) on lymphoscintigraphy (antero-posterior view). Description: The IM-SN hotspot was visualized on lymphoscintigraphy in the parasternal location after 2 h (**a**) and after 20 h (**b**)

Results

A total of 1542 consecutive breast cancer patients with an attempted A-SNB between January 2001 and June 2012 were included in this review. All, but 13 patients were women. The A-SNB was successful in 1485 cases, 96 % of the patients. At least one A-SN was involved in 606 cases, i.e. 41 % of the patients.

Only the data of the 77 patients who had IM-SNB were analyzed in details. The histological type of the tumors was as follows: invasive carcinoma of no special type (n=54), invasive lobular (n=11), mixed ductal and lobular (n=2), tubular (n=5), medullary, micropapillary, tubulolobular, metaplastic and mucinous carcinoma (n=1 each). The operations performed are summarized in Table 1.

IM-SNs were visualized on preoperative lymphoscintigraphy in 83 of the 1542 patients (5.4 %), IM-SNB was succesfull in 77 cases (93 %). Of the 6 failed attempts to remove an IM-SN, the uptake of the SN was low in one case: although the IM-SN was visualized the day before surgery, it vanished by the next day. The gamma-probe went wrong during the operation in a second case. The mean age of patients with successful IM-SN mapping was 56.5 years (range: 33–77). The median tumor size was 1.45 cm. IM-SNs were mostly found in the second or third interspace. This node was tipically smaller (0.5–2 mm) than the A-SN. The IM-SN stained blue in only 11 patients (14 %). A total of 86 IM-SNs were dissected (mean 1.11). IM-SN involvement was identified in 14 cases, which represents 18 % of patients who underwent IM-SNB. This included macrometastases (MAC) in 5 cases, micrometastases (MIC) in 2 cases, isolated tumor cells (ITC) in 7 cases. In the IM-SNB group, we removed 114 A-SNs (average 1.84). Axillary involvement was found in 16 cases (20 % of the 77 patients) and consisted of ITC in 3 cases, MIC in 6 and MAC in 7 (Fig. 3).

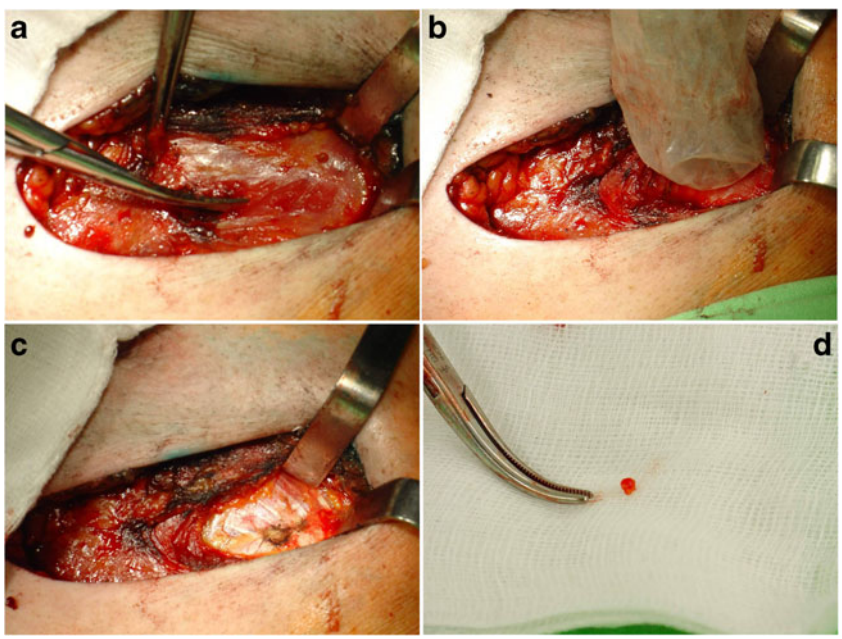

Fig. 2 The technique of internal mammary sentinel node (IM-SN) biopsy: step by step. **a** The fibers of the pectoral major muscle are separetad to expose the posterior intercostal space. **b** Intraoperative identification of the IM-SN hotspot with the help of the gamma probe. **c** The intercostal muscles were separated from the lower rib to expose the fatty tissue along the internal mammary vessels on the surface of the parietal pleura. D: The harvested IM-SN, which is tipically smaller (0,5–2 mm) than the axillary sentinel node and rarely stains blue

Table 1 Summary of different types of operation in patient with successful IM-SNB

Characteristic	IM-SN- (n=63)	IM-SN+(n=14)
Type of the operation		
ROLL+A-SNB+IM-SNB	31	5
ROLL+A-SNB+ALND+IM-SNB	5	3
BCS+A-SNB+IM-SNB	21	4
BCS+A-SNB+ALND+IM-SNB	3	0
Mastectomy+A-SNB+IM-SNB	3	1
Mastectomy+A-SNB+ALND+IM-SNB	0	1

ALND axillary lymphe node dissection; *A-SNB* axillary sentinel node biopsy; *BCS* breast conserving surgery; *IM-SNB* internal mammary sentinel node biopsy; n: number; *ROLL* Radioguided Occult Lesion Localisation

No significant differences were found between patients with and without IM-SN involvement in terms of age, tumor location, tumor size, axillary involvement, tumor grade or estrogen receptor status (Table 2).

Specific features of patients with IM-SN involvement and their disease are shown in Table 3. In 10 cases (13 % of the IM-SNB patients) the IM-SN was involved without A-SN involvement. Out of these patients, the IM-SN involvement has lead to new therapeutical indications in 2 cases (3 % of all IM-SNB patients), both of them due to MAC in the IM-SN. One patient had a change in chemotherapy and one had a change in radiotherapy with the addition of locoregional iradiation of the IMC (Fig. 4).

Table 2 Characteristics of patients with successful IM-SNB

Characteristic	IM-SN- (n=63)	IM-SN+(n=14)	P-value
Age			0.47
≤50	21	3	
51–70	36	9	
>70	6	2	
Tumor location			0.41
Lateral	39	7	
Medial or Central	24	7	
Tumor size			
≤20 mm	47	12	0.37
>20 mm	16	2	
Axillary nodal status			
Negative	49	8	0.41
Positive	14	4	
Tumor Grade			0.14
I	16	6	
II	30	4	
III	17	4	
Estrogen receptor status			0.15
Negative	8	0	
Positive	55	14	

IM-SN internal mammary sentinel node; *IM-SNB* internal mammary sentinel node biopsy

The patients who had undergone succesful IM-SNB were followed until June 2012, their follow-up included axillary ultrasound; no evidence of loco-regional recurrence was noted.

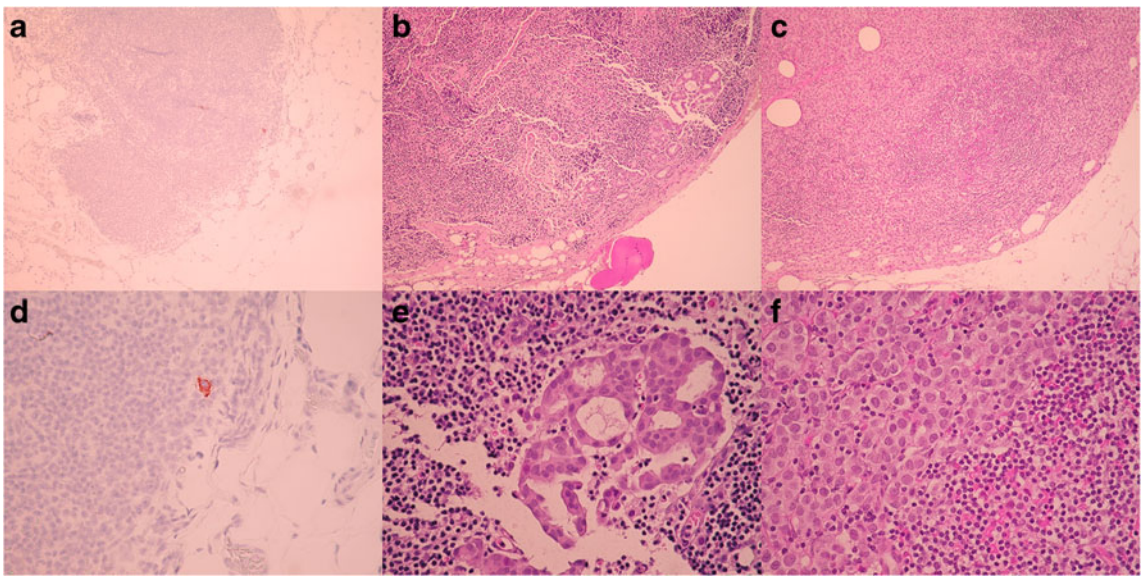

Fig. 3 Different types of IM-SN involvement. Isolated tumor cell (**a**, **d**), micrometastasis (**b**, **e**) and macrometastasis (**c**, **f**) at medium power (x100, **a**, **b**, **c**) and high power (x400, **d**, **e**, **f**) as detected by cytokeratin immunohistochemistry (**a**, **d**) and hematoxylin and eosin stain (**b**, **c**, **e**, **f**). Microscopy of three representative cases

Table 3 Details and main conclusions of larger IM-SNB studies

Reference	Number of patients	IM hot nodes %	Number of IM-SNB patients	% of IM metastases	% IM metastases without axillary metastases	Predictors of IMC positivity	Opinion
Nathan J (21)	577	18	90	22	18	age<35 Grade 3 LVI	IM-SNB allows for improved staging, potential improvements in regional control, and the potential to increase long term survival and the identification of patients who may benefit from IMC radiation.
E.M Heuts (20)	1008	20	139	22	29	tumor location	Patients with IM hotspots have a substantial risk (22 %) of IM SN metastases. True IM node negative patients can be spared the morbidity associated with adjuvant radiotherapy.
Eve Madsen (23)	499	17	85	24	1	axillary metastases	IM-SNB is recommended when SNs are visualized by preoperative lymphoscintigraphy.
E.M Heuts [40]	764	22	115	24	25		Routine IM SNB is recommended and treatment of proven IM metastases accordingly.
E.L. Postma [41]	493	24	107	13	7		Since the adjustment rate of systemic treatment based on the finding of this procedure is minimal and there is no sufficient ground for adjustment of RT, IM SNB should not be performed routinely.
M.H.K.Leidenius [42]	984	14	138	13	2		IM SNB results in upstaging in 2 % of all breast cancer patients who undergo SNB. The clinical value of the procedure seems insignificant, although it may influence the adjuvant treatment regimen in some patients.

IM Internal mammary; *IMC* internal mammary chain; *IM-SN* internal mammary sentinel node; *IM-SNB* internal mammary sentinel node biopsy;.*LVI* lymphovascular invasion; *RT* radiotherapy; *SN* sentinel node; *SNB* sentinel node biopsy

Median follow-up time was 46 month (range:2–121 month). Three of the 77 patients in this study died, one of distant metastases of breast cancer in the liver, and two of unrelated causes (rectal cancer and cardiorespiratory insufficiency).

IM-SNB had few complications. Out of the 83 patients in whom IM-SNB was attempted, minor complications were seen in 8 cases (9.6 %). Pleural lesions occurred in 5 patients (none of them needed thoracic drainage), the injury of the IM artery occurred in 2 cases and the injury of a minor thoracic vein in 1 case, all three vascular lesions were solved by ligation of the respective artery or vein, with no additional incision. There was also one major complication (1.2 %): a major retrocostal leak of the IM artery requiring partial resection of two adjacent ribs to allow its restauration . The latter patient is well and alive with no evidence of disease after 12 months of follow up at the time of writing.

Discussion

The SN is the first lymph node to receive lymphatic drainage from a tumor, and SNB is a minimally invasive diagnostic modality for diagnosing axillary lymph nodes metastases in breast cancer. Many studies on lymphatic drainage of the breast have confirmed the importance of the IM basin as a second draining route in breast cancer. [17, 18] As a consequence, IM lymph node dissection was part of the standard surgical treatment in some centers in the 1950s and 1960s. This radical surgical procedure was abandoned in the 1970s because patient outcome studies showed that radical dissection did not improve survival. [19] However, these studies have clearly shown that patients with documented IM metastases, who did not receive adjuvant therapy, had a worse prognosis. [19] Veronesi et al. found in their analysis of 1119 patients that survival was significantly affected by the presence of positive IMC nodes. Ten-year survival varied from 80 % in patients with axillary and IMC negative nodes, 55 % in axillary positive and IMC negative nodes, 53 % in IMC positive and axillary negative patients and 30 % in patients with both axillary and IMC positive nodes. [20] Since the introduction of SNB there has been a renewed interest in the IM-SNs. As a consequence, IM-SNB can refine staging in breast cancer patients and offers the possibility of providing tailored treatment in case of proven metastases to the IMC.

Some authors have found a correlation between the location of the tumor and the visualized IM-SN. The proportion of patients in whom the IM-SN could be visualized was found to be higher in patients with a tumor in the medial or central part

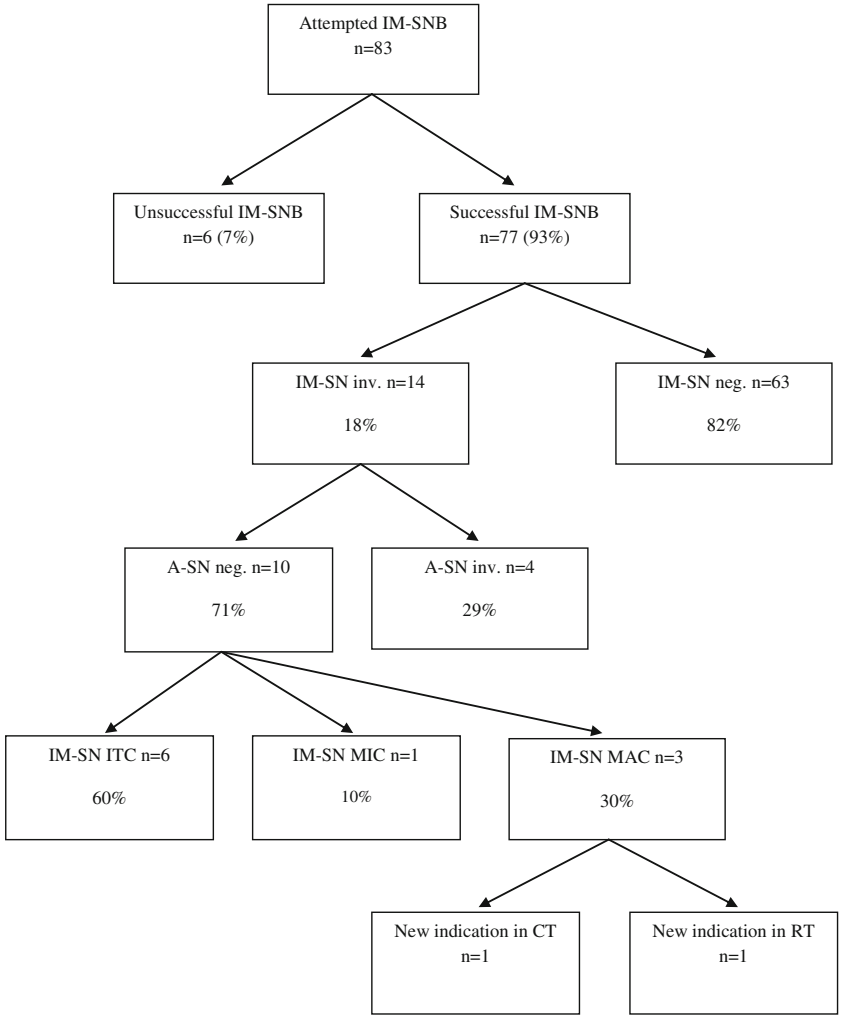

Fig. 4 Changes in post-operative adjuvant therapy of patients with IM-SNB. ASN: axillary sentinel node; CT: chemoterapy; IM-SN: internal mammary sentinel node ; IM-SNB: internal mammary sentinel node biopsy; ITC: isolated tumor cells; inv: involvement; MAC: macrometastases; MIC: micrometastases; *n*=number; neg: negative; RT: radiotherapy

of the breast, compared to those with a tumor in the lateral part of the breast. [6, 19, 20] Other authors have not found such an association. [21, 22] In keeping with the unpredictabilty of lymphatic drainage on the basis of tumor location, this series demonstrated IM drainage in more lateral tumors than medial or central tumors. The higher rate of IM drainage in medial tumors may reflect their lower overall frequency compared to lateral tumors.

The rate of identification of SNs in the IM region is lower than in the case of A-SNB. [9] The success rate of A-SNB in the literature is between 94–97 %, compared to the success rate of 63–88 % of IM-SNB. [19, 20, 22] There are two main reasons for this. Firstly, IM-SNB is not performed routinely, as opposed to A-SNB, because many breast surgeons have concerns about the rate of complications of the procedure, due to the lack of technical expertise and familiarity with the route of access. Secondly, it is difficult to compare the results of the different studies. Ultrasound-guided intra- or peritumoral tracer administration followed by lymphoscintigraphy (draining via the perforating lymphatic system) has a higher rate of IMC drainage than subareolar or subdermal injections using the superficial lymphatic system [23]. It may also be hypothesized that a peritumoral injection more accurately demonstrates the true lymphatic drainage of the tumor than an injection given away from the tumor site in the skin or around the areola [23], despite the fact that most of the time the breast can be and is viewed as a single organ with a unique drainage independently of tumor location [24]. Because of these issues, the reported rates of IMC drainage on lymphoscintigraphy vary greatly, from <2 % to 38 % of all breast tumors. [25] The proportion of patients with IMC drainage reported here (5.4 %) is also an underestimate of all patients with this phenomenon, because the universal intraparenchymal radiotracer administration used in the first part of the study period was replaced by the use of this adminstration route only for non-palpable tumors having a smaller chance of nodal involvement. This caveat should be kept in mind, but the data did not allow a better approach of the rate of IMC drainage, and the study concentrated more on the IM-SNB and its implications in patients with a visualized drainage to this region, rather than the drainage itself.

In our series the success rate of A-SNB was 96 % and that of IM-SNB was 93 %. The latter high result might be a consequence of the fact that the procedure was first introduced by a breast and thoracic surgeon (G.B.), and the operations were performed by experienced breast surgeons.

The number of axillary nodes involved is also an important prognostic information [26] and this may hold true for the number of metastatic IMC lymph nodes too. The overall risk of IM lymph node metastasis in breast cancer patients is well known and reported to be 18–33 %. Metastases exclusively situated in the IM node, without concurrent axillary metastases, occur in 2–11 % of patients. [27] A larger axillary metastatic load may represent a higher risk of IMC metastasis [19], and the total number of involved nodes in the two regions together may likewise be important from a prognostic aspect, but this is currently very difficult to assess, as IMC lymph node dissection is not part of the standard treatment of breast carcinoma. [9] In our study no significant differences were found between patients with and without IM-SN involvement in terms of age, tumor location, tumor size, axillary involvement, tumor grade or estrogen receptor status.

A possible role of nodal positivity detected by IM-SNB may be the indication of more aggressive systemic treatment in axillary node-positive patients. Adjuvant locoregional radiation therapy has proven to be beneficial after mastectomy [28–30], but the contribution of radiation to the IMC to improve survival and recurrence rates is still unclear. [31–34] Although radiation therapy of the parasternal region does not seem to improve the survival [35], the value of this treatment in IM-SN-positive patients detected by IM-SNB should also be assessed in future studies. [9] The EORTC 22922/10925 trial has been devised to investigate the potential survival benefit and toxicity of elective irradiation of the internal mammary and medial supraclavicular (IM-MS) nodes. It is currently evaluating the impact of IM-MS irradiation on longterm disease-free and overall survival in breast cancer patients with centrally or medially located tumors. Only lung (fibrosis; dyspnoea; pneumonitis; any lung toxicities) but not cardiac toxicity increased significantly with IM-MS treatment. IM-MS irradiation seems well tolerated and does not significantly impair WHO performance status at 3 years. A follow-up period of at least 10 years is needed to determine whether cardiac toxicity is increased after such radiotherapy. [36] As for today, there is insufficient data to determine a positive effect of parasternal radiotherapy on survival in patients with proven IM metastases. Axillary adjuvant radiotherapy is beneficial in terms of locoregional control in high-risk subgroups, such as patients with more than 3 axillary metastases,. [36] As a consequence, by extrapolation, it could be reasonable to add parasternal radiotherapy to the treatment regimen in patients with tumor-positive IM-SNs, if their metastatic volume is higher, e.g. in case of MAC or multiple nodal involvement.

In contrast to adjuvant radiotherapy to the IMC, systemic treatment of high-risk breast cancer patients has a proven survival benefit. [37] Its administration is based on a set of prognostic and predictive factors, of which nodal status is only one, even if considered among the most important ones. The systemic treatment strategy was rarely influenced by IM metastases in this series of patients. Due to axillary metastases and unfavorable primary tumor characteristics, a lot of patients would have already received adjuvant chemotherapy and even more of them would have had adjuvant hormonal therapy. In the remaining patients, old age and negative estrogen receptor status further limited the proportion of patients who would have received adjuvant systemic therapy based on IM-SN metastases. Dutch national guidelines on the treatment of breast cancer do not recommend routine biopsy of the IM-SLNs. Adjuvant chemotherapeutic treatment and IMC irradiation is however indicated when a tumor-positive IMC lymph node is found. [38]

IM-SNB may be associated with some additional morbidity in about 3–10 % of the cases, according to the literature: pleural lesions or injury of the IM artery. [6, 19, 20] Recovery is usually uneventful in the case of pleural lesions, after simple vacuum drainage. The injury of the IM artery poses more serious challenges. In our study we recognized minor complications in 8 cases (9.6 %) and one major complication (1.2 %) also occurred. Recovery was uneventful in both the minor and the major complication group.

The literature is rather inconclusive as concerns the recommendation of IM-SNB. Table 3 shows details and main conclusions of larger IM-SNB studies. On the basis of recent publications, arguments for performing IM-SNB are the follwing:

It helps the correct staging of patients with breast cancer [9].

IM-SN involvement is a prognostic factor [9] and an adverse prognostic indicator of increased distant metastases and reduced survival, even in the absence of axillary disease [20].

In case of IM-SN-positive patients, the treatment can be altered (chemo- or radiotherapy). [9] Studies evaluating the effect of the IM-SNB on the treatment strategy in patients with an IMC drainage pattern report a change of treatment in 2–9 %. [36, 39] Since adjuvant systemic treatment in this small but substantial patient group is likely to improve prognosis, authors of these studies recommend routine biopsy of IM-SNs.

There are also arguments against IM-SNB, and these are listed as follows:

IM-SN metastases occur only in a small propotion of patients undergoing SNB (1.4–4.6 %) [9, 39], (although they have a higher rate of occurrence (18–33 %) [16] in patients having IMC drainaged and IM-SNB.

IM-SNB is not performed routinely, as opposed to A-SNB because many breast surgeons have concerns about the rate of complications of the procedure, due to the lack of technical expertise and familiarity with the route of access.

Ultrasound-guided intra- or peritumoral tracer administration demonstrates a higher rate of IMC drainage than subareolar or subdermal injections which are often used for A-SNB.

Overall, isolated IMN involvement is rare (2–9 %). [9, 36, 39]

If the A-SNs are negative, then IM-SNs are also negative in 41,2 %–56,6 %. [9]

Although there could be new indications for IMC radiotherapy if both A-SNs and IM-SNs are positive (13.2–22.7 %) [9] and for chemotherapy if A-SNs are negative but an IM-SN is positive (2.1–9 %) the IM node status resulted in a change of the adjuvant treatment plans in only 3.4 % of the patients. [19]

Some authors have found predictive factors of IMC positivity, including age<35 years, grade III histology and lymphatic vascular invasion [20], that would make IM-SNB less important.

The impact of IM-SN biopsy on altering adjuvant systemic therapy was relatively small in our series. We have found IM-SN involvement in 14 cases, which represents 18 % of the patients who underwent IM-SNB, but in 7 cases, only ITC were found, and these are not considered metastasis at present [43]. Neither ITC, nor MIC nor MAC of the IM-SN has lead to further surgical therapy. Micrometastases in A-SNs or IM-SNs were not an indication for adjuvant chemotherapy. In our series, only 1 patient received radiotherapy to the IMC, and a new indication for chemotherapy was also established in only 1 patient because of MAC of the IM-SN. Therefore in our series consisting of 77 patients, only 2 of the IM-SNB patients (2.6 %) had therapeutic consequences. As for today, there are insufficient data to determine a positive effect of parasternal radiotherapy on survival in patients with proven IM metastases. On the other hand, IM-SNB may be associated with some additional morbidity: pleural lesions or injury of the IM artery. Based on our own series and information from the literature, we conclude that the indication for an IM-SNB procedure is very limited, and its routine use should not be recommended—wich is also in agreement with the latest Hungarian guidelines. [44] A failure to identify an A-SN is an indication for ALND in general, but it is felt that if there is no lymphatic drainage towards the axilla on lymphoscintigraphy, and even vital dye guided A-SNB fails to identify an A-SN, but an IM-SN is visualized on the scintigram, IM-SNB could be considered for nodal staging, and the omission of ALND could also be envisaged. In the studied setting, the data point more to abandoning routine IM-SNB in patients with IMC drainage and potentially restricting its use to a very small subset of patients.

Conflict of Interest Statement None declared

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