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ORIGINAL ARTICLE

Sentinel Lymph Node Biopsy in Locally Advanced Breast Cancer After Neoadjuvant Chemotherapy—an Indian Perspective

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Abstract

Sentinel lymph node biopsy (SLNB) alone in early breast cancer is an established standard of care. However, the same results have not been replicated in locally advanced breast cancer (LABC) after neoadjuvant chemotherapy (NACT). We aim to examine the feasibility of SLNB in LABC patients post NACT to determine identification rates (IR) and false negative rates (FNR). This was a single tertiary cancer center–based prospective study from February 2017 to November 2018. Forty-four patients with LABC (T3, T4 with N0 or N1) were studied and response after NACT was assessed. Only those patients who were N0 or who converted from N1 to N0 after NACT were included. Those patients who remained node positive after NACT directly proceeded with axillary dissection without SLNB and were excluded from the study. Demographic and clinical data is expressed in ratios and percentage and presented in table format. The median age at the time of study was 45.18 years. Most of the patients had T3 and above (97.7%) and N1 (86.3%) disease at the start of neoadjuvant therapy. The mean number of axillary lymph nodes dissected was 13.97. Dual method of sentinel lymph node mapping (methylene blue dye and radiolabeled colloid) was used in 26 (59.1%) patients. At least 1 SLN was identified in 86.4% patients with 100% identification in those patients in whom the dual method of SLN mapping was used. Median of 2 SLN was removed. Overall, false negative rate was 21.4%. FNR was high with the single method of SLN mapping (50% and 33.3% with methylene blue and radioactive colloid respectively) while it was considerably low when both were used simultaneously (11%). An average of 2 (range 0–4) SLN were identified and FNR were zero when 2 or more SLN were identified. Our study shows that SLNB in patients with LABC post NACT though viable cannot be recommended at present due to unacceptable high FNR. However, this should not dissuade us from exploring recurrence-free survival and overall survival associated with such IR and FNR albeit strictly under a clinical trial setting.

Keywords Sentinel lymph node biopsy · Locally advanced breast cancer · Neoadjuvant chemotherapy · Identification rate · False negative rate

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Introduction

Management of breast cancer has shifted from radical surgeries to more conservative approach since the results of NSABP-B06 were announced [1]. However, while the breast surgeons concentrated more on the conservation of breast, little attention was paid to the axilla. It was presumed that complete axillary lymph node dissection (ALND) should be the standard while breast conservation was the priority. Keeping in mind Halsted's principle of locoregional disease, even the node negative axilla underwent extirpation in the quest to clear as much microscopic disease as possible [2, 3]. While great cosmetic results were being obtained with breast conservation surgeries, the ugly appearance and morbidity of upper limb lymphedema and paresthesia became more apparent. The use of sentinel lymph node biopsy (SLNB) for axillary conservation was validated in 1994 by Guiliano et al. to stage the axilla in clinically node negative patients [4, 5]. Since then, the landmark trials—NSABP-B32, IBCSG 23-01, ACOSOG Z0011—revolutionized conservative management of sentinel node–negative, microscopic node–positive, and sentinel node–positive axilla respectively [6–8]. However, the same comfort has not been established in the management of axilla in locally advanced breast cancer after neoadjuvant chemotherapy. Due to abominably low identification rates (IR) and high false negative rates (FNR), conservative management of axilla in this group of patients has been controversial. There has been little data from Indian subcontinent regarding sentinel lymph node biopsy in locally advanced breast cancer (LABC) patients after neoadjuvant chemotherapy (NACT) where complete ALND still remains the gold standard. In this study, we have tried to evaluate feasibility of SLNB in patients with LABC post NACT to assess IR and FNR. Our secondary goal was to identify subgroup of patients with increased IR and decreased risk of FNR on SLNB after NAC.

Methodology

This was a single tertiary cancer center–based prospective study of cases of locally advanced breast carcinoma registered and operated in the Department of Surgical Oncology from February 2017 till November 2018. Forty-four patients with LABC (T3, T4 with cN0 or cN1) were studied and response after NACT was assessed. Axillary staging was performed by clinical examination and ultrasound of axilla both pre and post NACT. Only those patients who were cN0 or who converted from cN1 to cN0 after NACT were included. Those patients who had persistent nodes (cN1) directly proceeded with ALND without SLNB and were excluded from the study. Other exclusion criteria were pregnancy or lactating female, known allergy to methylene blue (MB) or radioactive colloid (RAC), previous breast or axillary surgery (excluding biopsy for primary cancer), patients not consenting for participation in study, inflammatory breast cancer, and cN2 or cN3 disease. The study was approved by the Institution's Scientific Review Board and Medical Ethics Committee (KMIO/MEC/007/24.Nov.2016). Written informed consent was taken from all patients for participation in the study.

On the operative day, perilesional intradermal injection of RAC was given before the surgery. Before starting the procedure, injection of 1 ml of blue dye (MB) was given intradermally after anesthesia just before surgery. Using gamma probe, biopsy of axillary lymph nodes with high radioactivity or blue nodes was taken as sentinel nodes. After sentinel lymph node biopsy, ALND was done to identify false negative rates.

Statistical Analysis

Data was entered in the Microsoft Excel and was analyzed using the same. Qualitative and quantitative data was represented with mean and standard deviation. Identification rates were calculated as ratio of at least one sentinel lymph node detected to the total number of SLNB attempted. False negative rate was calculated as the ratio of the number of patients with a negative sentinel lymph node to the number of patients with at least one involved lymph node among people in whom at least one sentinel node was detected.

Results

Between February 2017 and November 2018, 44 patients with clinical stages T2–T4, N0–1, and M0 who received neoadjuvant chemotherapy were enrolled in the study. Patient's, clinical, chemotherapy, and histopathological characteristics are presented in Table 1. Mean age was 45.18 years (SD ± 8.8) with majority of patients presenting with lump (90.9%) in upper outer quadrant (43.2%) with involvement of central quadrant in 59.1% patients. Majority of patients received 6 cycles of neoadjuvant chemotherapy (81.8%) with pathological complete response in 12 (27.3%) patients. Most of patients had T3 and above (97.7%) and N1 (86.3%) disease at the start of neoadjuvant therapy. The mean number of axillary lymph nodes dissected was 13.97 and majority of them had grade 3 tumor (59.1%). One patient (2.08%) had mild allergic reaction to MB in the form of rash which subsided with antihistaminic.

Identification Rates (Tables 2 and 3)

Dual method of sentinel lymph node mapping (MB + RAC) was used in 26 (59.1%). At least 1 SLN was identified in

Table 1 Patient, clinical, chemotherapy, and histopathological characteristics

	Number of patients		Number of patients
Age		cT stage before NACT	
Mean	45.18 ± 8.80 years	cT1	0
Median (range)	43.00 years	cT2	1 (2.3%)
Chief complaints		cT3	28 (63.6%)
Lump	40 (90.9%)	cT4b	13 (29.5%)
Lump + ulcer	4 (9.1%)	cT4c	2 (4.5%)
Tumor location		Number of lymph nodes dissected ALND	
Upper outer	19 (43.2%)	Mean	13.97
Lower outer	13 (29.5%)	Grading	
Upper inner	6 (13.6%)	G1	0
Lower inner	6 (13.6%)	G1	18 (40.9%)
Central quadrant	26(59.1%)	G3	26 (59.1%)
Pathological complete response		ER status	
Yes	12(27.3%)	Positive	20 (45.5%)
No	32 (72.7%)	Negative	24 (54.5)
Neoadjuvant regimen		Her2 status	
FEC	8 (18.2%)	Positive	16 (36.4%)
FEC + docetaxel	36 (81.8%)	Negative	28 (63.6%)
Number of cycles		Triple negative	
3	6 (13.6%)	Yes	18 (40.9%)
4	2 (4.5%)	No	26 (59.1%)
6	36 (81.8%)	Histological tumor type	
Methods of SLNB		Ductal	36 (81.8%)
MB	6 (13.6%)	Lobular	4 (9.1%)
RAC	12 (27.3%)	Others	4 (9.1%)
MB + RAC	26 (59.1%)		

ALND, axillary lymph node dissection; *ER*, estrogen receptor; *FEC*, 5FU, Adriamycin, cyclophosphamide; *MB*, methylene blue; *NACT*, neoadjuvant chemotherapy; *RAC*, radioactive colloid; *SLNB*, sentinel lymph node biopsy

86.4% patients with 100% identification in those patients in whom the dual method of SLN mapping was used. Median of 2 SLN was removed. Identification rates (IR) were dismal (66.7% each for MB and RAC alone) when only the single method of SLN mapping was performed. IR also decreased with addition of docetaxel (83.6% vs 100%) in the NACT regime as well as in patients who received 6 cycles of NACT (83.6% vs 100%) as compared with 4 or less cycles. IR decreased with increasing T stage of disease (T2, T3, T34—100%, 89.3%, 80% respectively) and was high for patients with ER-negative, Her2-negative, and triple-negative diseases (91.7%, 100%, 100% respectively).

False Negative Rates (Tables 2 and 3)

Overall, false negative rate was 21.4%. FNR was high with the single method of SLN mapping (50% and 33.3% with MB and RAC respectively) while it was considerably low when both were used simultaneously (11%). An average of 2 (range 0–4) SLN were identified and FNR were zero when 2 or more SLN were identified. Even though the IR were low in patients who received docetaxel-based NACT and those who completed 6 cycles, FNR fared better in these groups of patients (18.2% in 5-FU, Adriamycin, cyclophosphamide (FEC) + docetaxel vs 33.3% FEC alone and 100% in 4 cycles vs 18.2% in 6 cycles). FNR increased with increasing T stage and tumor grade (T3 18.8%, T4 27.3%; and G2 18.2%, G3 23.5%) while it was low in patients with ER-positive, Her2-negative, and non-triple-negative tumors (16.6%, 18.2%, and 14.3% respectively). Also, FNR was zero in patients who had competed pathological response.

Discussion

Axillary conservation in locally advanced breast cancer following neoadjuvant chemotherapy is debatable with trends still in favor of axillary dissection rather than SLNB alone. Results of GANEA 2 study seem misleading as it supports

Table 2 Identification rates and false negative rates based on methods of sentinel lymph node detection, neoadjuvant chemotherapy, and tumor location

	Identification rates	False negative rates
Overall (*n*, %)	38/44 (86.4%)	6/28 (21.4%)
Methods of SLNB		
MB	4/6 (66.7%)	2/4 (50.0%)
RAC	8/12 (66.7%)	2/6 (33.3%)
MB + RAC	26/26 (100%)	2/18 (11.1%)
Number of sentinel lymph nodes identified		
1	10/38 (26.3%)	6/10 (60.0%)
2	12/38 (31.57%)	0/8 (0.0%)
3	10/38 (26.3%)	0/8 (0.0%)
4	6/38 (15.78%)	0/2 (0.0%)
Neoadjuvant chemotherapy regimen		
FEC	8/8 (100.0%)	2/6 (33.3%)
FEC + docetaxel	30/36 (83.6%)	4/22 (18.2%)
Number of chemotherapy cycles		
3	6/6 (100%)	0/4 (0.0%)
4	2/2 (100%)	2/2 (100.0%)
6	30/36 (83.6%)	4/22 (18.2%)
Tumor location		
Upper outer	9/19 (47.4%)	3/13 (23.1%)
Lower outer	11/13 (84.6%)	1/7 (14.3%)
Upper inner	4/6 (66.7%)	0/4
Lower inner	6/6 (100.0%)	0/4
Central quadrant	22/26 (100.0%)	5/16 (31.2%)

FEC, 5FU, Adriamycin, cyclophosphamide; *MB*, methylene blue; *RAC*, radioactive colloid; *SLNB*, sentinel lymph node biopsy

Table 3 Identification rates and false negative rates based on histopathological characteristics

	Identification rates	False negative rates
cT stage before NACT		
cT1	0	0
cT2	1/1 (100.0%)	0/1 (0.0%)
cT3	25/28 (89.3%)	3/16 (18.8%)
cT4	12/15 (80.0%)	3/11 (27.3%)
Grading		
G1	0	0
G2	15/18 (83.3%)	2/11 (18.2%)
G3	23/26 (88.5%)	4/17 (23.5%)
ER status		
Positive	16/20 (80.0%)	2/12 (16.6%)
Negative	22/24 (91.7%)	4/16 (25.0%)
Her2 status		
Positive	10/16 (62.5%)	2/6 (33.3%)
Negative	28/28 (100.0%)	4/22 (18.2%)
Triple negative tumor		
Yes	18/18 (100.0%)	4/14 (28.6%)
No	20/26 (76.9%)	2/14 (14.3%)
Histological tumor type		
Ductal	30/36 (83.3%)	6/20 (30.0%)
Lobular	4/4 (100.0%)	0/4 (0.0%)
Others	4/4 (100.0%)	0/4 (0.0%)
Pathological complete response		
Yes	10/12 (83.3%)	0
No	28/32 (87.5%)	6/28 (21.4%)

ER, estrogen receptor; *NACT*, neoadjuvant chemotherapy; *SLNB*, sentinel lymph node biopsy

SLNB alone for those patients who have cN0 axilla prior to NACT and SLNB negative intraoperatively [9]. However, it fails to realize that 82% of patients in cN0 group had T2 and less primary disease in which case NACT is still not the standard of care and most of these patients would undergo primary surgery at most of the centers. The safety of SLNB alone without ALND in early breast cancer with primary surgery has already been established by NSABP-B32, IBCSG-23-01, AATRM-048, and ACOSOG Z0011 trials [6–8, 10].

Axillary nodal involvement increases with an increase in primary tumor size [11]. This is apparent in our study as more than three quarters of our patients were above T2 and node positive. Lymphatic drainage could be impaired due to NACT leading to decrease in SLN IR and increased FNR [12]. Almost all our patients (97.7%) were T3 and above disease and required NACT which explains the dismal rates of IR (86.4%) and high FNR (21.4%) in our study. Despite having 84% of patients with T1 and T2 disease in Cohort C of SENTINA study, the overall IR and FNR remained unacceptable at 80.1% and 14.2% respectively [13].Thus, advanced T stage and neoadjuvant chemotherapy (which is vital in these group of patients with LABC) are themselves perpetrators for poor IR and high FNR, a finding also experienced by Yagata et al. [14].

There are two major factors that improve the IR and accuracy (FNR)—dual method of sentinel lymph node mapping and more number of SLN harvested (two or more) as evident by SENTINA study. We found a similar trend in our study. However, more than one-third (36.36%) of our patients had less than 2 SLN detected. Hence, SLN only would be applicable to less than two-thirds of the patients, a finding seconded by SENTINA study [13]. Recently published ACOSOG Z1071 trial also reported high FNR (12.6%) even when two or more SLN were detected. This exceeded their prespecified threshold of 10%. The authors too concluded that changes in approach or patient selection would be necessary to support the use of SLNB in this setting [15].

Dual method of SLN mapping definitely improves IR as reported by multiple authors. However, in resource-limited country like ours having a dual method of SLN mapping can be challenging. Healthcare setup in India is more dependent

on out-of-pocket expenditure rather than insurance- or government-sponsored schemes. This is especially true in cancer treatment. Easy and timely access to radioactive colloid would not only require strong commitment on the part of hospital administration and government authorities but also depend on patient's affordability. A study from India showed methylene blue alone used for SLNB gives IR of 100% and FNR of 13.3%. However, we could not replicate this cost-effective method and our corresponding values were poor compared with the results obtained by Chintamani et al. (Tables 2 and 3) [16]. A novel method of low axillary sampling has shown similar results compared with SLNB with dual dye. Even though the study was performed in early breast cancers, it is an extremely cost-effective technique with lower morbidity and the results might be replicated in patients with LABC [17].

Most of the contemporary cohort studies have amassed vast data on IR and FNR; however, the recurrence-free survival (RFS) and overall survival (OS) are yet to be determined as conducting a trial with such low IR and high FNR will be ethically challenging. On the other hand, it is also imperative to confirm if low IR and high FNR bear any negative impact on RFS or OS of this group of patients with LABC. Experience from NSABP-B32 provides some evidence in which poor FNR (17.7%) did not translate into increased regional recurrence when only one SLN was detected [6].

A major push for SLNB patients of breast cancer comes from the development of arm lymphedema after ALND and that SLNB can help mitigate this irreversible complication. However, SLNB itself is not free of complications and has been associated with 0–6% risk of lymphedema. In addition to this, patients with locally advanced breast cancer would at some point in their treatment schedule receive radiotherapy which itself is associated with increased incidence of lymphedema [18]. To consider that both the risks would add up would not be correct, as recently reported meta-analysis by Shaitelman et al. did not find a significant risk of lymphedema in patients who underwent radical nodal irradiation after SLNB. Hence, the concept of SLNB in LABC should be viable subject to results of future trials [19].

A major drawback of this study is its small sample size. However, the study was designed as a feasibility study as there have been no major reports on this issue from Indian subcontinent except those by Chintamani et al. and Parmar et al. [16, 17]. Also, complex statistical analyses were avoided as study was only a feasibility study without any comparative arm and was not powered enough to reach any statistical significance between groups.

Future trials might determine the lowest and highest threshold of IR and FNR respectively that would not compromise the RFS and OS of patients with LABC who undergo SLNB post NACT. Hence, it is important for institutes to recognize their own IR and FNR in this setting. If SLNB becomes a standard in the future, then, institutes should be ready with their own IR and FNR so that they can improvise their technique of SLNB should they decide to offer such a treatment to patients with locally advanced breast cancer. However, at present, such low IR and high rates of FNR are unacceptable and should not be offered to patients with LABC except in the setting of a clinical trial.

Conclusion

Our study shows that the concept of SLNB in patients with LABC post NACT though viable cannot be recommended at present due to unacceptable high rates of FNR. However, this should not dissuade us from exploring RFS and OS associated with such IR and FNR albeit strictly under a clinical trial setting.

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Compliance with Ethical Standards

The study was approved by the Institution's Scientific Review Board and Medical Ethics Committee (KMIO/MEC/007/24.Nov.2016).

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Fisher B, Montague E, Redmond C, Barton B, Borland D, Fisher ER, Deutsch M, Schwarz G, Margolese R, Donegan W, Volk H, Konvolinka C, Gardner B, Cohn I Jr, Lesnick G, Cruz AB, Lawrence W, Nealon T, Butcher H, Lawton R (1977) Comparison of radical mastectomy with alternative treatments for primary breast cancer. A first report of results from a prospective randomized clinical trial. Cancer. 39:2827–2839
2. Halsted WS (1898) I: a clinical and histological study of certain adenocarcinomata of the breast: and a brief consideration of the supraclavicular operation and of the results of operations for cancer of the breast from 1889 to 1898 at the Johns Hopkins Hospital. Ann Surg 28(5):557–576
3. Halsted WS (1907) I: the results of radical operations for the cure of carcinoma of the breast. Ann Surg 46(1):1–19
4. Giuliano AE, Jones RC, Brennan M, Statman R (1997) Sentinel lymphadenectomy in breast cancer. J Clin Oncol 15(6):2345–2350
5. Giuliano AE, Kirgan DM, Guenther JM, Morton DL (1994) Lymphatic mapping and sentinel lymphadenectomy for breast cancer. Ann Surg 220(3):391–398 discussion 398–401)
6. Krag DN, Anderson SJ, Julian TB, Brown AM, Harlow SP, Costantino JP, Ashikaga T, Weaver DL, Mamounas EP, Jalovec LM, Frazier TG, Noyes RD, Robidoux A, Scarth HM, Wolmark N (2010) Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol 11(10): 927–933. https://doi.org/10.1016/S1470-2045(10)70207-2

7. Galimberti V, Cole BF, Zurrida S, Viale G, Luini A, Veronesi P, Baratella P, Chifu C, Sargenti M, Intra M, Gentilini O, Mastropasqua MG, Mazzarol G, Massarut S, Garbay JR, Zgajnar J, Galatius H, Recalcati A, Littlejohn D, Bamert M, Colleoni M, Price KN, Regan MM, Goldhirsch A, Coates AS, Gelber RD, Veronesi U, International Breast Cancer Study Group Trial 23-01 investigators (2013) Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial. Lancet Oncol 14(4):297–305. https://doi.org/10.1016/S1470-2045(13)70035-4
8. Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, Leitch AM, Saha S, McCall L, Morrow M (2011) Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. JAMA 305(6):569–575
9. Classe JM, Loaec C, Gimbergues P, Alran S, de Lara CT, Dupre PF, Rouzier R, Faure C, Paillocher N, Chauvet MP, Houvenaeghel G, Gutowski M, De Blay P, Verhaeghe JL, Barranger E, Lefebvre C, Ngo C, Ferron G, Palpacuer C, Campion L (2018) 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. https://doi.org/10.1007/s10549-018-5004-7
10. Solá M, Alberro JA, Fraile M et al (2012) Complete axillary lymph node dissection versus clinical follow-up in breast cancer patients with sentinel node micrometastasis: final results from the multicenter clinical trial AATRM 048/13/2000. Ann Surg Oncol 20:120–127. https://doi.org/10.1245/s10434-012-2569-y
11. Chung MJ, Lee JH, Kim SH, Suh YJ, Choi HJ (2016) Simple prediction model of axillary lymph node positivity after analyzing molecular and clinical factors in early breast cancer. Medicine (Baltimore) 95(20):e3689. https://doi.org/10.1097/MD.0000000000003689
12. Fisher ER, Wang J, Bryant J et al (2002) Pathobiology of preoperative chemotherapy: findings from the National Surgical Adjuvant Breast and Bowel (NSABP) protocol B-18. Cancer 95:681–695. https://doi.org/10.1002/cncr.10741
13. Kuehn T, Bauerfeind I, Fehm T 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. https://doi.org/10.1016/S1470-2045(13)70166-9
14. Yagata H, Yamauchi H, Tsugawa K, Hayashi N, Yoshida A, Kajiura Y, In R, Matsuda N, Nakamura S (2013 Dec) Sentinel node biopsy after neoadjuvant chemotherapy in cytologically proven node-positive breast cancer. Clin Breast Cancer 13(6):471–477. https://doi.org/10.1016/j.clbc.2013.08.014
15. Haffty BG, McCall LM, Ballman KV, McLaughlin S, Jagsi R, Ollila DW, Hunt KK, Buchholz TA, Boughey JC (2016) Patterns of local-regional management following neoadjuvant chemotherapy in breast cancer: results from ACOSOG Z1071 Allia. Int J Radiat Oncol Biol Phys 94(3):493–502. https://doi.org/10.1016/j.ijrobp.2015.11.005
16. Chintamani TM, Mishra A, Agarwal U, Saxena S (2011) Sentinel lymph node biopsy using dye alone method is reliable and accurate even after neo-adjuvant chemotherapy in locally advanced breast cancer–a prospective study. World J Surg Oncol 9:19. https://doi.org/10.1186/1477-7819-9-19
17. Parmar V, Hawaldar R, Nair NS, Shet T, Vanmali V, Desai S, Gupta S, Rangrajan V, Mittra I, Badwe RA (2013) Sentinel node biopsy versus low axillary sampling in women with clinically node negative operable breast cancer. Breast. 22(6):1081–1086. https://doi.org/10.1016/j.breast.2013.06.006
18. But-Hadzic J, Bilban-Jakopin C, Hadzic V (2010) The role of radiation therapy in locally advanced breast cancer. Breast J 16(2):183–188. https://doi.org/10.1111/j.1524-4741.2009.00885.x
19. Shaitelman SF, Chiang YJ, Griffin KD, DeSnyder SM, Smith BD, Schaverien MV, Woodward WA, Cormier JN (2017) Radiation therapy targets and the risk of breast cancer-related lymphedema: a systematic review and network meta-analysis. Breast Cancer Res Treat 162(2):201–215. https://doi.org/10.1007/s10549-016-4089-0 Review. Erratum in: Breast Cancer Res Treat. 2017 Apr;162(2):217