

Internal Mammary Sentinel Lymph Node Biopsy: Minimally Invasive Staging and Tailored Internal Mammary Radiotherapy

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Internal mammary lymph node (IMLN) metastasis has a similar prognostic importance as axillary lymph nodal involvement in breast cancer patients. Even though TNM staging has incorporated the internal mammary sentinel lymph node biopsy (IM-SLNB) concept since the 6th edition of the American Joint Committee on Cancer, IM-SLNB has not been performed routinely and has remained a subject of discussion. In fact, accurate staging could not be achieved by depending on the status of the axillary sentinel lymph node alone, which might lead to under-stage and under-treatment. The recent studies of Caudle et al.¹ and Gnerlich et al.² showed again that IM-SLNB was a minimally invasive technique for the efficient evaluation of the status of internal mammary sentinel lymph nodes (IM-SLN) with high safety and feasibility. Gnerlich et al.² reported no complications in their study, and Caudle et al.¹ found only two intraoperative surgical complications, but both were resolved smoothly. In our current study, there is no pneumothorax on postoperative chest radiography and no postoperative bleeding. IM-SLNB had made a more accurate lymph node staging and improved the decision making of the adjuvant radiotherapy of the IMLN, and even adjuvant systemic therapy in some cases.

Caudle et al.¹ suggested that IM-SLNB should be performed in patients who revealed IM-SLN drainage by

preoperative lymphoscintigraphy. Even though the success rate of IM-SLNB has reached 72–100 %, ^{3,4} the visualization rate of IM-SLN was low (mean 13 %; range 0–37 %), ^{3–5} which has been the restriction for both clinical study and daily practice of IM-SLNB to date. In the retrospective analysis of Caudle et al.,¹ only 71 cases (8.8 %) of 808 patients (from 1998 to 2011) underwent IM-SLNB according to preoperative lymphoscintigraphy. In order to improve the preoperative visualization rate of IM-SLN, we established a modified technology,⁵ which could significantly improve the preoperative visualization rate of the IM-SLN (70.2 %, 203/289, the latest data). With the combination of the intraoperative γ -probe, the detection rate of IM-SLN could reach 77.2 % (223/289; $p < 0.05$). The algorithm of our study is shown in Figs. 1 and 2. In the study, all patients who determined IMLN map + (hotspot on lymphoscintigraphy and/or detected intraoperative γ -probe) underwent IM-SLNB. We found the site of IM-SLNs concentrated in the second and third intercostal space (85.4 %, 176/206). The involvement rate of IM-SLN was 8.8 % (17/193) when the axillary lymph nodes (ALN) were negative, and 23.3 % when the ALN were positive. These results were in accordance with the form study of extended radical mastectomy,^{9,10} which could reflect the accuracy of IM-SLNB indirectly.

The IMLN metastases related significantly to the status of ALN. In the study of Veronesi et al.,¹¹ IMLN were positive in 29.1 % of patients with ALN metastases and only 9.1 % with negative ALN ($p < 0.001$). Gnerlich et al.² also confirmed that the number of the positive ALN was the only independent predictor of IM-SLN metastases. Similarly, Caudle et al.¹ showed that 91 % (10/11) of patients with IM-SLN metastases were ALN positive. Current research of SLNB (both axillary and internal mammary) was limited to patients with clinically negative ALN. As IMLN metastases are

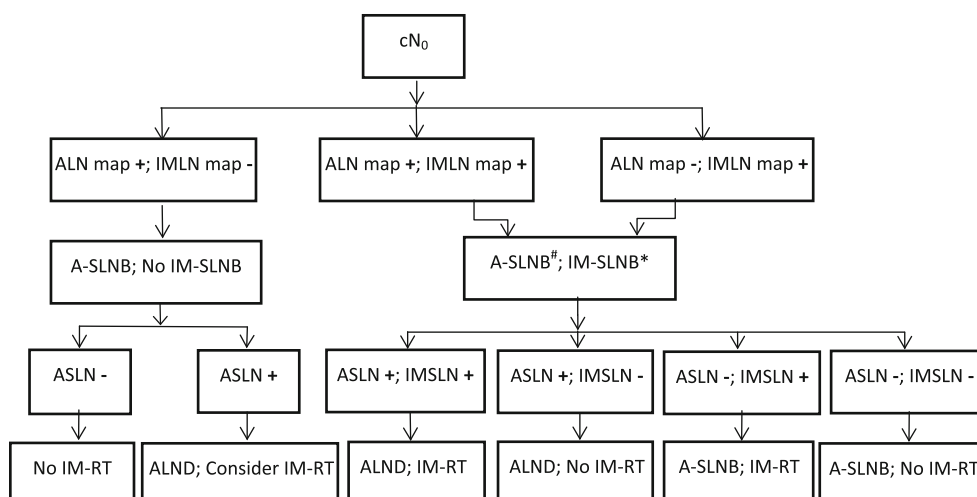


FIG. 1 Clinical N₀. Optional management of patients with negative nodes clinically. For the condition of ALN lymphatic mapping but not IMLN lymphatic mapping, if using an intraoperative γ -probe and the IMSLN could not be found, then perform A-SLNB but not IM-SLNB; however if the IMSLN is found, see the management of ALN lymphatic mapping and IMLN lymphatic mapping. If no ASLN metastasis is identified, do not perform IM-RT; however, if ASLN metastasis is identified then perform ALND. IM-RT should be considered in a high burden of disease. For the condition of ALN lymphatic mapping and IMLN lymphatic mapping, A-SLNB and IM-SLNB should be performed. If ASLN metastasis and IMSLN metastasis are identified, then perform ALND and IM-RT. If ASLN metastasis but no IMSLN metastasis is identified, then perform ALND but not IM-RT. If IMSLN metastasis is identified but not ASLN metastasis, then perform IM-RT. If no ASLN metastasis and no IMSLN metastasis is identified, do not perform IM-RT. For the condition of IMLN lymphatic mapping but not ALN lymphatic mapping, using an intraoperative γ -probe or combining with other tracers could identify the site of ASLN.⁶ Using a combination method

mostly found concomitantly with ALN metastases, patients with positive ALN would more likely benefit from IM-SLNB because of its impact to staging and accurate indication of radiation to the internal mammary area. Therefore, we recommend IM-SLNB should be performed in patients with clinically positive ALN; for patients with clinically negative ALN, IM-SLNB could be selectively performed for high-risk patients.¹²

Management of the IMLN has varied during the past decades. IMLN dissection with extended radical mastectomy has been abandoned since the 1970s due to its extra complications, longer operation time, and no survival benefit. Imaging techniques, such as positron emission tomography/computed tomography, ultrasound and magnetic resonance imaging, could only detect metastases lesions larger than 5 mm. Recently, at the 2013 European Cancer Congress, radiotherapy to the internal mammary and medial supraclavicular lymph nodes was reported

of radioisotope and blue dye, the ASLN was identified successfully in 98 % of patients, with no false negative results.^{7,8} In our institute, we could detect at least one ASLN by the combination method. Management of the condition is same to ALN and IMLN lymphatic mapping. *For the condition of IMLN map+, patients who receive mastectomy should perform IM-SLNB, while patients who receive breast conservative surgery and postoperative radiotherapy to the whole breast could consider not performing IM-SLNB. #ALN map⁻ does not mean there is no ASLN. We could use an intraoperative γ -probe or combine with other tracers to identify the site of ASLN and complete A-SLNB. ALN axillary lymph nodes, IMLN internal mammary lymph nodes, A-SLNB axillary sentinel lymph node biopsy, IM-SLNB internal mammary sentinel lymph node biopsy, ASLN axillary sentinel lymph node, IM-RT internal mammary radiotherapy, ALND axillary lymph node dissection, ALN map+ axillary lymph nodes hotspot on lymphoscintigraphy and/or detected intraoperative γ -probe, IMLN map+ internal mammary lymph nodes hotspot on lymphoscintigraphy and/or detected intraoperative γ -probe

to improve long-term breast cancer survival.¹³ This European Organisation for Research and Treatment of Cancer (EORTC) phase III trial 22922-10925 enrolled stage I–III breast cancer patients with high-risk IMLN metastases (positive ALN and/or medial/central primary tumor). These inclusion criteria might induce over- and under-treatment as high-risk did not mean IMLN metastases, while low-risk did not mean IMLN negative. Since radiotherapy of the IMLN chain carries increased cardiac and pulmonary side effects, the appropriate identification of patients who might benefit from adjuvant radiotherapy is essential and should be based on the tumor-positive results of IM-SLNB rather than the high-risk estimation only. Radiation therapy targeting the IMLN chain and/or additional systemic therapy should be tailored and balanced between the potential benefit and toxicity, and IM-SLNB-guided IMLN radiotherapy could achieve this goal.

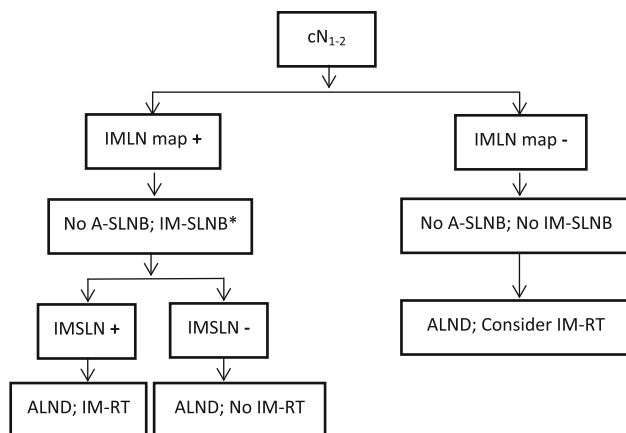


FIG. 2 Clinical N_{1-2} . Optional management of patients with clinical N_{1-2} . For the condition of IMLN lymphatic mapping, perform IM-SLNB. If IMSLN metastasis is identified, the patient should receive ALND and IM-RT. If no IMSLN metastasis is identified, then ALND but not IM-RT should be performed. For the condition of no IMLN lymphatic mapping, if using an intraoperative γ -probe could identify the site of IMSLN then execute the management of IMLN lymphatic mapping. If the IMSLN is not identified then perform ALND, IM-RT should be considered in high burden of disease. *For the condition of IMLN map+, patients who receive mastectomy should perform IM-SLNB, while patients who receive breast conservative surgery and postoperative radiotherapy to the whole breast could consider not performing IM-SLNB. IMLN internal mammary lymph nodes, A-SLNB axillary sentinel lymph node biopsy, IM-SLNB internal mammary sentinel lymph node biopsy, IM-RT internal mammary radiotherapy, ALND axillary lymph node dissection, IMLN map+ internal mammary lymph nodes hotspot on lymphoscintigraphy and/or detected intraoperative γ -probe, IMSLN internal mammary sentinel lymph nodes

CONFLICT OF INTEREST Bin-Bin Cong, Peng-Fei Qiu, and Yong-Sheng Wang have no conflicts of interest relating to this study.

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