

# Could Nomograms Used to Identify Non-Sentinel Lymph Node Metastases May Be Valuable in Radiotherapy Planning?

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Surgery is the primary treatment modality employed in the majority of patients in early stage breast cancer. Axillary lymph node dissection (ALND) is a standard procedure that has been used for longer than a hundred year in the surgical treatment of breast cancer. However, there have been important advances in the assessment of axillary region (1, 2). In early 2000s, it was proven that sentinel lymph node biopsy (SLNB) was as reliable as dissection in patients with no axillary involvement in a clinical setting. Today, SLNB is being used with more than 95% reliability instead of ALND in routine practice for staging and treatment of early stage breast cancer in many centers (3, 4).

Patients with metastasis in SLNB have been routinely referred to axillary dissection; however, recent studies have identified a subset of patients who would not benefit from complementary axillary dissection. The review of data on SLNB from centers with high patient volume showed that there was no additional lymph node involvement in 40-70% of patients with metastasis on SLNB. Thus, it is thought that axillary dissection in such patients would not contribute to staging and therapy (2-4). Now, it has become important to predict this patient group. The idea to provide accurate and effective therapies with less invasive modalities has prompted us to predict the risk for metastasis in residual lymph nodes in patients with sentinel lymph node metastasis and to develop scoring systems for this purpose.

In recent years, many centers have assessed nomograms designed for this purpose. Memorial Sloan-Kettering Cancer Center (MSKCC) defined the first nomogram in 2005. In this nomogram without frozen examination, tumor diameter, estrogen receptor status, tumor histology and nuclear grade, lymphovascular invasion, multifocality variables are used. Methods for detecting SLN include the number of positive SLNs and the number of negative SLNs. The nomogram by Memorial Sloan-Kettering Cancer Center was followed by scoring systems from Stanford University, Cambridge University and Tenon Hospital. When the nomograms were examined, the tumor size and lymphovascular invasion was commonly used in nomograms in the MSKCC, Tenon and Stanford. Tumor grade MSKCC and Stanford nomograms showed positive SLN ratio are common variables in the nomograms Tenon. SLN metastasis size is only used in the nomograms by Stanford. Positive SLN number of negative SLN, SLN metastasis detection method, ER status, while multifocality was only used in the MSKCC nomogram; SLN micro-/macro-metastasis status is only used in the Tenon nomogram. There are no methods other than nomograms for the prediction of the likelihood of non-sentinel lymph node metastasis. However, there are some limitations for use of these nomograms. The major limitation is that the nomogram relies on the database of the center which created the nomogram; thus, the nomogram is reliable for use in that center; however, the validity and reliability analyses are recommended when using it in a different center (5).

There are 3 options in patients with metastasis on SLNB including follow-up, complementary axillary dissection and radiotherapy focused on the axillary region (1, 5-7). In radiation oncology, the general approach is to irradiate the axillary region via the addition of supraclavicular region in almost all patients who have metastasis on SLND but did not undergo complementary axillary dissection. However, there are differing opinions in this field, suggesting that tangential or high tangential irradiation may be administered to SLNB-positive patients according to risk groups (5-7).

The scoring system, which is used in prediction of non-SLNB involvement, may help us in decision making process regarding radiotherapy and field that will irradiated. Nomograms developed by using preoperative examination, radiological imaging and pathological data may provide radiotherapy treatment plans with distinct fields and doses.

In conclusion, there are distinct approaches in selection of optimal radiotherapy field in cases with metastasis on SLNB. This scoring system used in prediction of non-SLN involvement may be used to determine radiotherapy field. However, risk factors should be determined; and the relative risk should be estimated for SDLN metastasis by using multivariate analyses towards the aim of overcoming the limitations of

nomogram. All the steps of SLNB should be standardized and nomograms should be revised with multi-center or even international studies. However, rates of irradiation to smaller fields can be increased by improving understanding regarding cancer biology and behavior, and robust outcomes with nomograms.

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