Editorial

Where do we draw the line?—micrometastases and complete axillary lymph node dissection

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In breast cancer patients, a sentinel lymph node biopsy is an important component of staging and determining prognosis. It is generally agreed that macrometastases in the axillary lymph nodes, defined as tumor deposits that measure 2 mm or more, warrants a complete axillary lymph node dissection (ALND) (1). For micrometastases, defined as tumor deposits between 0.2 to 2 mm, it is common to not pursue ALND. The 2013 multicenter, randomized, controlled phase III trial by Galimberti *et al.* clarified this standard by showing that there was no significant improvement in 5- and 10-year disease-free survival of patients with micrometastasis who undergone ALND (2,3).

In the study by Galimberti *et al.*, there was an average disease-free survival of 76.8% in the no axillary dissection group and 74.9% in the axillary dissection group, which begs the question if the quarter of patients who had disease recurrence could be isolated for additional treatment. As the involvement of non-sentinel lymph nodes may be the key modulator of the survival of these patients with micrometastases, this is an area of keen interest. Fortunately, a new study from Chauhan *et al.* titled "*In patients with micrometastases in sentinel lymph node biopsies, involvement of the non-sentinel lymph nodes cannot be predicted by clinicopathological variables*" elucidates this particular issue in detail (4).

As the title suggests, Chauhan *et al.* could not identify any clinicopathological variables that predicted non-sentinel lymph node involvement in patients with micrometastases in their thorough investigation. They retrospectively analyzed 1,152 breast cancer patients who undergone sentinel lymph node biopsies between 2008 and 2013 at their institution. From the 1,152 patients, 224 patients were positive for sentinel lymph node involvement of the tumor, and of the 224 patients with sentinel lymph node involvement, 72 patients were positive for micrometastases. Of the 72 patients with micrometastases, complete ALND was not done in 10 patients due to concerns for fitness of anesthesia.

With the 62 patients with sentinel lymph node micrometastases who undergone complete ALND, the presence of positive non-sentinel lymph nodes was not predicted by tumor grade, size of the primary breast tumor, nor number of positive sentinel lymph nodes biopsied. They also saw that the age of the patients, under 50 *vs.* over 50, nor the presence of lymphovascular invasion were associated with the presence of positive non-sentinel lymph nodes in these patients.

Whilst there were no predictive variables found, this study by Chauhan *et al.* exceptionally clarifies areas of additional exploration and research. Through their investigation, they have found that 14.5% of their patients with micrometastases on sentinel lymph node biopsies had non-sentinel lymph node involvement of the tumor. Although this is not a novel discovery as it was seen in other studies at similar percentages around 16–18%, it reinforces the study's validity (5-7). Although it may not seem significant, the 14.5% of patients with non-sentinel lymph node involvement may represent the quarter of patients with disease recurrence in Galimberti *et al.* (2,3). If so, this raises the possibility that the non-ALND group

and the ALND group of patients in Galimberti *et al.* had similar numbers of disease recurrence because no additional treatment or action was taken after non-sentinel lymph node micrometastases were identified on complete ALND.

Currently, the standard of care for micrometastases may not be capitalizing on the prognostic value of non-sentinel lymph node involvement. Further research is needed to clarify if the patients with non-sentinel lymph node involvement may benefit from additional interventions that result in longer disease-free survival. For this to be of clinical benefit, two key points need to be addressed. First, as Chauhan *et al.* investigated, an effective way to predict non-sentinel lymph node involvement without ALND has to be discovered. Furthermore, the prognostic value of non-sentinel lymph node involvement has to be firmly established. If these two points are addressed, there may be a chance to provide patients with breast cancer micrometastases to lymph nodes a significantly better chance at disease-free survival in the future. In summary, Chauhan *et al.*'s study raises an interesting point that highlights the value of non-sentinel lymph node status and provokes the need for studies that utilize this information for the betterment of patient outcomes.

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