

Micrometastatic Sentinel Lymph Node Disease: Do Patients Benefit or Suffer Harm from Axillary Lymph Node Dissection?

TO THE EDITORS:

The optimal treatment of early, node-negative breast cancer is controversial. Surgeons, pathologists, and oncologists are debating whether micrometastases in sentinel and nonsentinel axillary lymph node should be considered. Should this information regarding sentinel lymph node biopsy (SLNB) be included in decision-making for axillary lymph node dissection (ALND)? Does this micrometastatic nodal status in young women with early, estrogen-receptor (ER)-positive disease at low risk of distant metastases affect decision-making on adjuvant chemotherapy?

More recently, a paper in the *New England Journal of Medicine* addresses the problem of minimal disease in axillary lymph nodes. In this large study, retrospective analysis of 2,707 early breast cancer patients from The Netherlands was performed. Micrometastases or isolated tumor cells (ITCs) on sentinel lymph node biopsy were prognostic markers, and adjuvant chemotherapy in these women significantly improved disease-free survival. No conclusion on the benefits or harm of ALND could be made. However, in a critical comment, a series of limitations regarding the comparability of the two groups at baseline with or without micrometastases or ITCs was noted. Therefore, for evidence-based decisions, the results of phase III randomized trials, which are underway in the USA, should be awaited.¹

Awaiting such data from phase III trials, how should breast surgeons decide? ALND eliminates the risk of nodal recurrence but it is associated with a risk of lymphedema. A balance is needed, but how should one assess whether the risk of nodal recurrence is greater than the risk of lymphedema among women with micrometastases or ITCs in SLNB?

Insights into the clinical utility of considering minimal disease in SLNB are provided by the study by Langer et al. in the latest issue of *Annals of Surgical Oncology*.² In their

prospective study, the authors analyzed data on 236 SLN biopsies in 234 consecutive early-stage breast cancer patients (T1, T2 \leq 3 cm, cN0 M0) between 1998 and 2002. None of the patients with negative SLN or SLN micrometastases (International Union against Cancer classification, >0.2 mm to ≤ 2 mm) underwent completion ALND or radiation to the axilla. The SLN was negative in 55% of patients (123 of 224), but on the other hand SLN micrometastases were detected in 27 of 224 (12%) patients. After median follow-up of 77 months, neither locoregional recurrences nor distant metastases occurred in any of the 27 patients with SLN micrometastases. The authors conclude that completion level I and II ALND may be safely omitted in early-stage breast cancer patients with SLN micrometastases.

Although the study by Langer et al. is limited by its prospective nature without randomization and the very small number of women with SLN micrometastases ($n = 27$), it reveals how complex the problem is. The ongoing phase III trials may highlight the difficulties in the reliability of micrometastases or ITCs for decision-making. However, it is likely that they will have limitations and that the problem is much more complicated than we try to overcome with minimal nodal disease. Perhaps, molecular tests will be needed. Advances in genetics, cancer genome analysis, and systems approaches using next-generation DNA sequencing technology provide optimism for DNA-changes-based development of prognostic and predictive markers towards personalized surgical and adjuvant treatment of early breast cancer.^{3–10}

D. Ziogas, MD¹, and G. C. Zografos, MD²

¹Department of Surgery, School of Medicine, University of Ioannina, Ioannina, Greece;

²1st Department of Surgery, University of Athens, Athens, Greece

e-mail: deziogas@hotmail.com

Published Online: 25 November 2009

© Society of Surgical Oncology 2009

REFERENCES

1. Roukos DH. Isolated tumor cells in breast cancer. *N Engl J Med*. 2009;361:1994–5.
2. Langer I, Guller U, Viehl CT, Moch H, Wight E, Harder F, et al. Axillary lymph node dissection for sentinel lymph node micrometastases may be safely omitted in early-stage breast cancer

- patients: long-term outcomes of a prospective study. *Ann Surg Oncol.* 2009;September [Epub ahead of print].
3. Roukos DH. Breast cancer outcomes: the crucial role of the breast surgeon in the era of personal genetics and systems biology. *Ann Surg.* 2009;249(6):1067–8.
 4. Ziogas D, Roukos DH. Genetics and personal genomics for personalized breast cancer surgery: progress and challenges in research and clinical practice. *Ann Surg Oncol.* 2009;16(7):1771–82.
 5. Roukos DH. Personalized cancer diagnostics and therapeutics. *Expert Rev Mol Diagn.* 2009;9(3):227–9.
 6. Roukos DH. Mea Culpa with cancer-targeted therapy: new thinking and new agents design for novel, causal networks-based, personalized biomedicine. *Expert Rev Mol Diagn.* 2009;9(3): 217–21.
 7. Roukos DH. Genome-wide association studies: how predictable is a person's cancer risk? *Expert Rev Anticancer Ther.* 2009;9(4): 389–92.
 8. Roukos DH. Twenty-one-gene assay: challenges and promises in translating personal genomics and whole-genome scans into personalized treatment of breast cancer. *J Clin Oncol.* 2009; 27(8):1337–8.
 9. Roukos DH. Personal genomics and genome-wide association studies: novel discoveries but limitations for practical personalized medicine. *Ann Surg Oncol.* 2009;16(3):772–3.
 10. Roukos DH, Ziogas D. Human genetic and structural genomic variation: would genome-wide association studies be the solution for cancer complexity like Alexander the Great for the “Gordian Knot”? *Ann Surg Oncol.* 2009;16(3):774–5.