Heterogeneity of tumor cells and metastases in breast cancer patients: cause or consequence?

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First of all, we would like to congratulate Sopik and colleague for their article [1] in which they tried to find out a relationship between tumor size, nodal status, and distant metastases. In this very comprehensive and detailed article, the authors concluded that the relationship between tumor size, lymph node status, and distant metastases in patients with invasive breast cancer is not linear. However, we would like to highlight our observation regarding this very important topic.

It is well known that the metastatic process is a multistep process, involving multiple genetic alterations affecting both tumor cells and the surrounding stroma, allowing spreading of metastases at distant sites. Tumor metastasis could be explained by two different models: linear progression model and parallel progression model, and this article is based on the first one. We could not neglect the fact that the release of tumor cells may happen also at early stages of the disease. Many studies confirmed that about 30–40% of patients in early stage of the disease may present occult metastasis derived from circulating tumor cells (CTCs). Contrary, data from preclinical animal studies have shown that less than 0.02% of circulating tumor cells can survive and have the capability to form metastatic lesion [2]. It is obvious that the heterogeneity of tumor cells rises during the tumors growth. We agree with authors that a smaller proportion of cells accessible to the vascular or lymphatic system in larger tumors because of lack of stable blood supply and further tumor necrosis. Undoubtedly that the tumor size is clinically and radiologically initial predictor of metastasis and prognosis, but heterogeneity of tumor cells in terms of genetic

alterations and the status of host's immune system is more predictable factor regarding metastases in breast cancer patients. Detailed histopathology and immunohistochemistry of primary tumor and affected lymph nodes or metastatic lesion could give precise information and determine further diagnostic procedures and therapy as well as prognosis [3].

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Compliance with ethical standards

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

Ethical approval This article complies with the ethical rules applicable for this journal.

Human and animal rights This article does not contain any studies with human participants or animals performed by any of the authors.

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