



## Editorial

## Tumor infiltrating lymphocytes in breast cancer

Lakshmi Agarwal<sup>1\*</sup> <sup>1</sup>Dept. of Pathology, Government Medical College, Kota, Rajasthan, India

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Breast cancer's complexity lies in its heterogeneous nature, driven by genetic alterations. It consists of different type of immune cells, mesenchymal cells and cancer cells. Recent data have shown TIL (Tumor infiltrating lymphocytes) density to be both a positive prognostic marker for disease-free and overall survival and a predictive marker for pathologic complete response (pCR) to neoadjuvant chemotherapy. TILs infiltrating into the tumor and stromal regions as a host immune response, enhances the anti-tumor effects of the therapy. TILs represent the immune system's frontline defense: a heterogeneous mix of T-cells, B-cells, and natural killer (NK) cells that infiltrate tumor tissue. Their presence often signals an ongoing immune response against the tumor, and higher levels of TILs have been associated with improved outcomes in several breast cancer subtypes. In triple-negative breast cancer (TNBC), for instance, multiple studies have demonstrated a consistent link between high TIL levels and better disease-free and overall survival. This association has also been observed in HER2-positive disease, where TILs may predict response to anti-HER2 therapies such as trastuzumab.

All mononuclear cells including lymphocytes and plasma cells should be scored (granulocytes and other polymorphonuclear leukocytes are excluded). The quantitative assessment of other mononuclear cells such as dendritic cells and macrophages is currently not recommended. There are two types of TIL. Intra tumoral TILs are defined as lymphocytes in tumor nests having cell-to-cell contact with no intervening stroma and directly interacting with carcinoma cells, while stromal TILs are

located dispersed in the stroma between the carcinoma cells and do not directly contact carcinoma cells. Both the categories represent true TILs. TILs is the area of stromal tissue (i.e. Area occupied by mononuclear inflammatory cells over total intra tumoral stromal area), not the number of stromal cells. TILs should be evaluated within the borders of the invasive tumor. TILs outside of the tumor border and around DCIS and normal lobules, necrotic areas, crush artifacts are excluded. One section (4–5µm, magnification×200–400) per patient is currently considered to be sufficient. Full sections are preferred over biopsies whenever possible. Cores can be used in the pretherapeutic neoadjuvant setting.

TILs in breast cancer are more than histological curiosities; they are dynamic players in the tumor immune ecosystem. As we continue to redefine cancer treatment through the lens of immunotherapy, it is imperative to harness the predictive and therapeutic potential of TILs. The future of personalized oncology may well depend on how effectively we can turn the immune system from a bystander into a weapon.

## Conflict of Interest

None.

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\*Corresponding author: Lakshmi Agarwal  
Email: [dr.laxmiagarwal@gmail.com](mailto:dr.laxmiagarwal@gmail.com)