Recommendations for assessing tumor-infiltrating lymphocytes (TILs) in breast carcinoma in situ

Guidelines for TILs assessment from the «International Immuno-Oncology Biomarker Working Group»

Authors: Nina Radosevic-Robin, Maria Vittoria Dieci, Roberto Salgado
These recommendations are valid for both ductal and lobular carcinoma in situ.

Ductal carcinoma in situ (DCIS) is used as an example.

- TILs in DCIS should be assessed **on surgical specimens** whenever possible; H&E slides representing the entire specimen should be submitted for TIL assessment (especially valid for multicentric studies); TILs should be assessed **on the entire surgical specimen**.

- These recommendations are related to the assessment of TILs on hematoxyllin-and-eosin (H&E)-stained sections of formalin-fixed, paraffin-embedded DCIS tissue; the sections should be 4-5 µm thick.
1. Identifying the area for TIL evaluation

- TILs in DCIS should be assessed **within the specialized tumor stroma**; as specialized tumor stroma is considered the area limited by the external borders of the tumor (DCIS) nests, extended for 2 High-Power Fields (HPFs, 40x) towards the tumor-adjacent stroma.
2. Areas to be excluded from TIL evaluation

- **ASSESS ONLY** the TILs **WITHIN THE STROMA →**
  → do not assess the intraepithelial TILs (within the tumor nests)

- **DO NOT ASSESS:**
  - TILs in the invasive tumor areas, whatever the size
    (micro-invasion or bigger)
  - TILs in the necrotic areas or the areas with artefacts
  - TILs in the hyalinisation areas
  - TILs around normal mammary structures
3. Cells to and not to assess

- **TILs are:**
  - small mature lymphocytes
  - « activated » lymphocytes (« lymphoblastoid », like in some infections)
  - lymphoplasmocytoid cells
  - plasmocytes

- **TILs are not:**
  - stromal mesenchymal cells
  - macrophages
  - neutrophils
  - mastocytes
  - altered tumor cells (apoptotic, the cells altered by tissue processing etc.)
4. How to assess TILs in DCIS

- **DO THIS** ON EACH SLIDE

- **DETERMINE THE PERCENTAGE (%) OF THE STROMAL SURFACE OCCUPIED BY TILs, ON EACH AREA DELINEATED FOR TIL ASSESSMENT**

- **DERIVE THE AVERAGE % FOR ALL THE AREAS EVALUATED**

This is the **TIL SCORE** of a DCIS

**DO NOT FOCUS ON THE « HOT SPOTS »** (the areas with the densest TILs)
5. Assess TILs % as continuous parameter

- Report TIL scores as a continuous parameter (0-100%)

- In case of DCIS associated to a micro-invasive carcinoma (µCa) report the TIL score of the µCa but do not include it when deriving the DCIS TIL score

- Examples of TILs scores in DCIS are given on the next page
EXAMPLES of TIL SCORES in DCIS (1)

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EXAMPLES of TIL SCORES in DCIS (2)

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For questions please contact:

nina.radosevic.robin@gmail.com
mariavittoria.dieci@unipd.it
roberto@salgado.be