

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

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

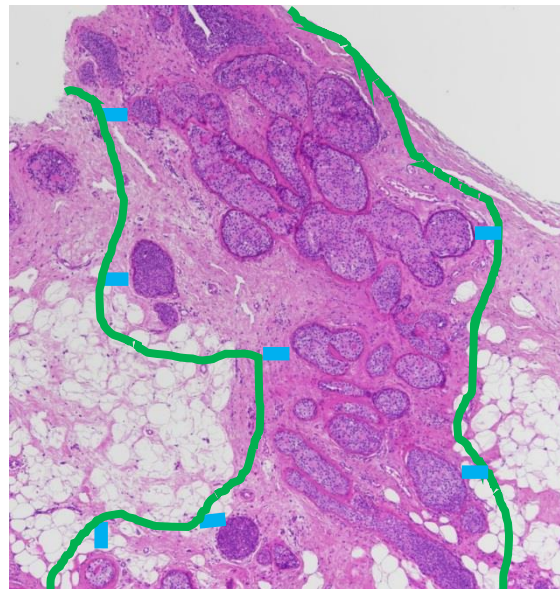
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These recommendations are valid for both ductal and lobular carcinoma in situ
Ductal carcinoma in situ (DCIS) is used as an example

- 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



- extension over 2 HPFs
- limits of the specialized stroma area to be considered for TIL assessment

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

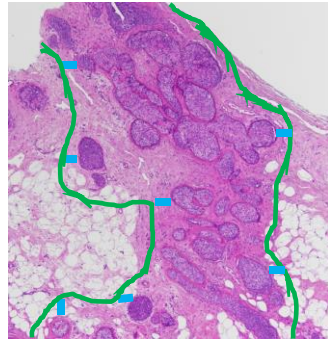
3. Cells to and not to assess

- **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

DO NOT FOCUS ON THE « HOT SPOTS »
(the areas with the densest TILs)

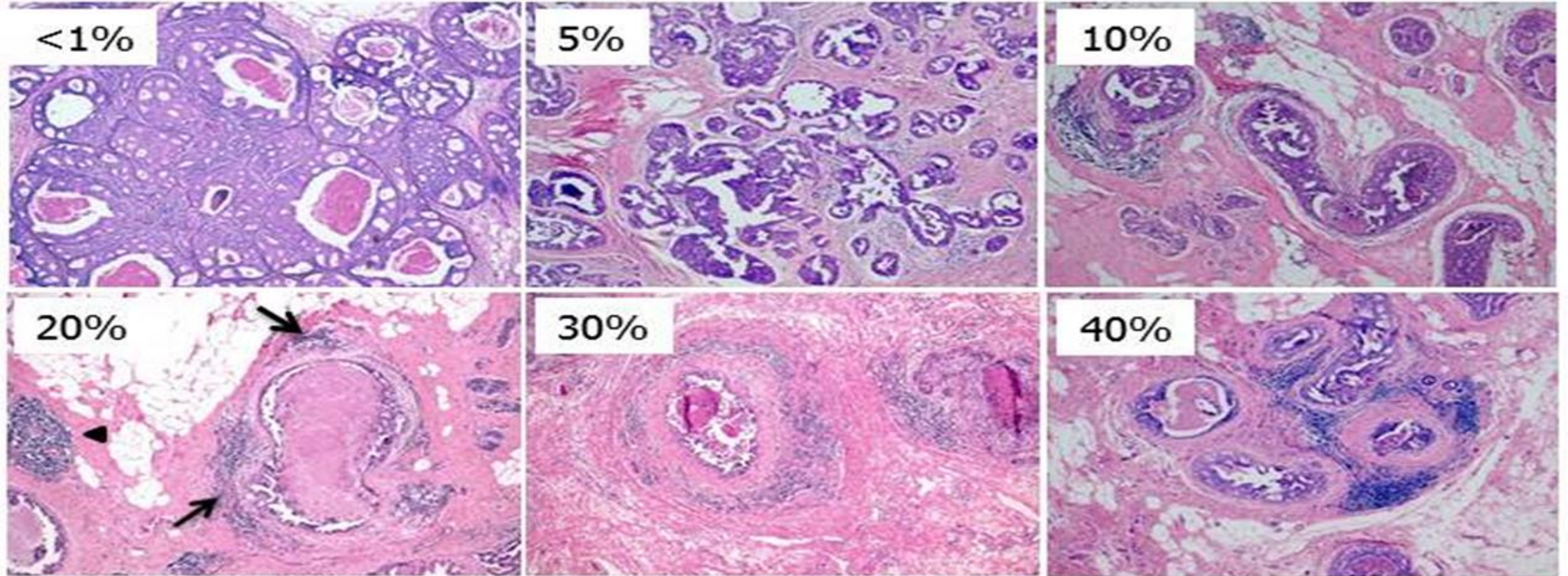
▪ DERIVE THE AVERAGE % FOR ALL THE AREAS EVALUATED

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

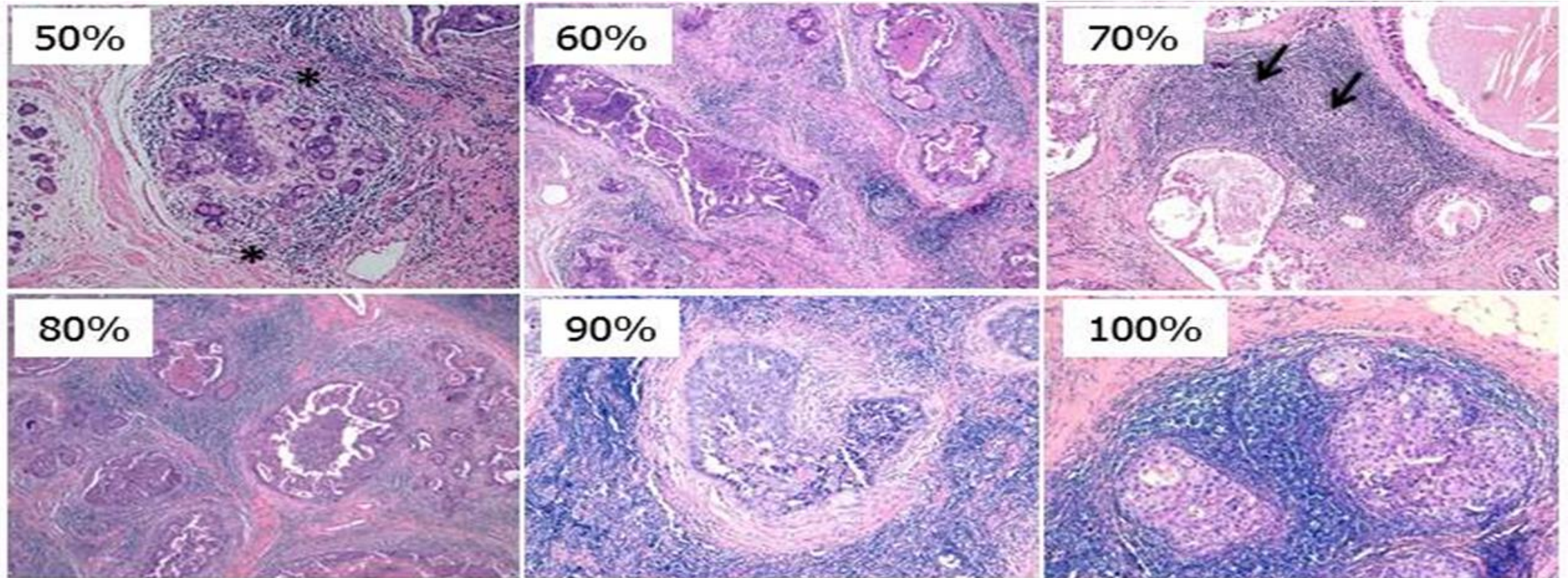
5. Assess TILs % as continuous parameter

- **Report TIL scores as a continuous parameter (0- 100%)**
- In case of DCIS associated to a micro-invasive carcinoma (μ Ca)
report the TIL score of the μ Ca 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)



EXAMPLES of TIL SCORES in DCIS (2)



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