Standardized evaluation of Tumor-Infiltating Lymphocytes (TIL) in Breast Cancer for daily clinical and research practice or clinical trial setting

A tutorial prepared by the International Working Group for TIL in breast cancer - 2014

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Aim of this tutorial

- To provide a guideline to pathologists for the standardized evaluation of tumor-infiltrating lymphocytes based on H&E slides of core biopsies or tumor resections.

- Please consult the manuscript for more specific details.

Step 1: Define area for TIL evaluation

- Only TILs within the borders of the invasive tumors are evaluated
- The invasive edge is included in the evaluation, but not reported separately
- Immune infiltrates outside of the tumor borders, e.g. in adjacent normal tissue or DCIS are not included
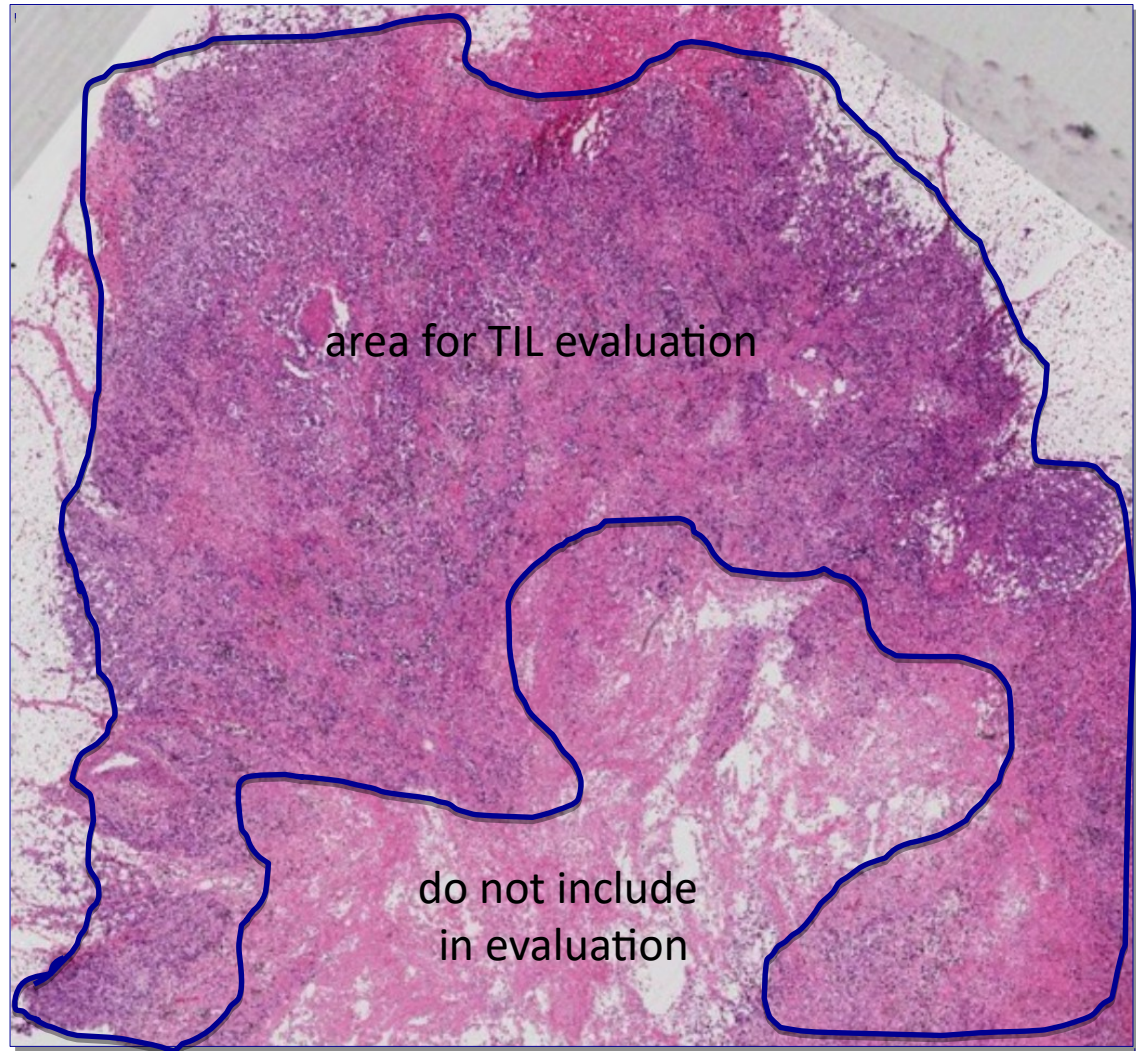
do not include immune infiltrate outside of the tumor

TLS

area within tumor borders

area within tumor borders
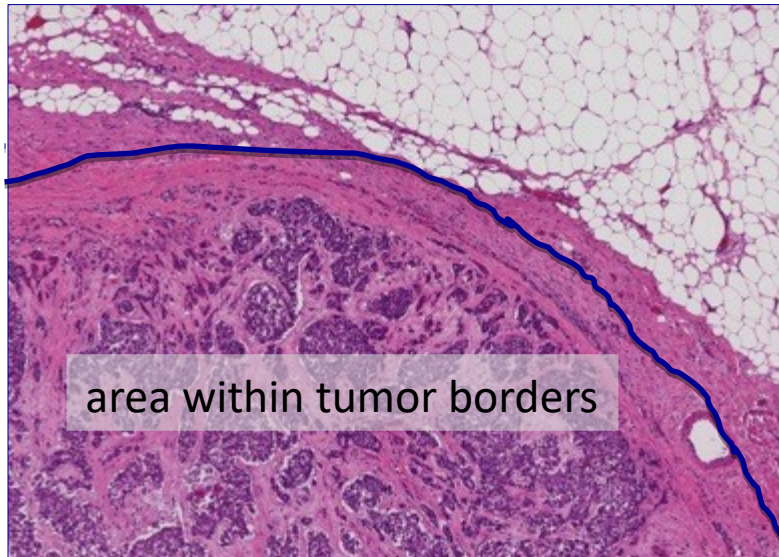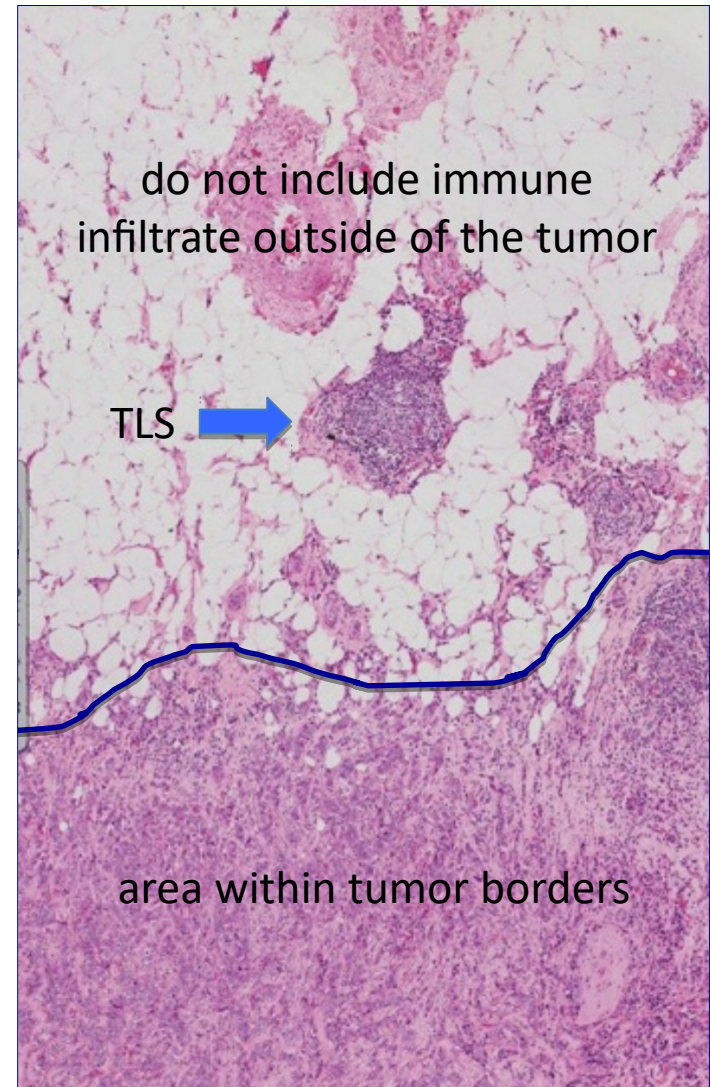
Example 1

Example 2

Step 1: Define area for TIL evaluation

- Large areas of central necrosis or fibrosis are not included in the evaluation
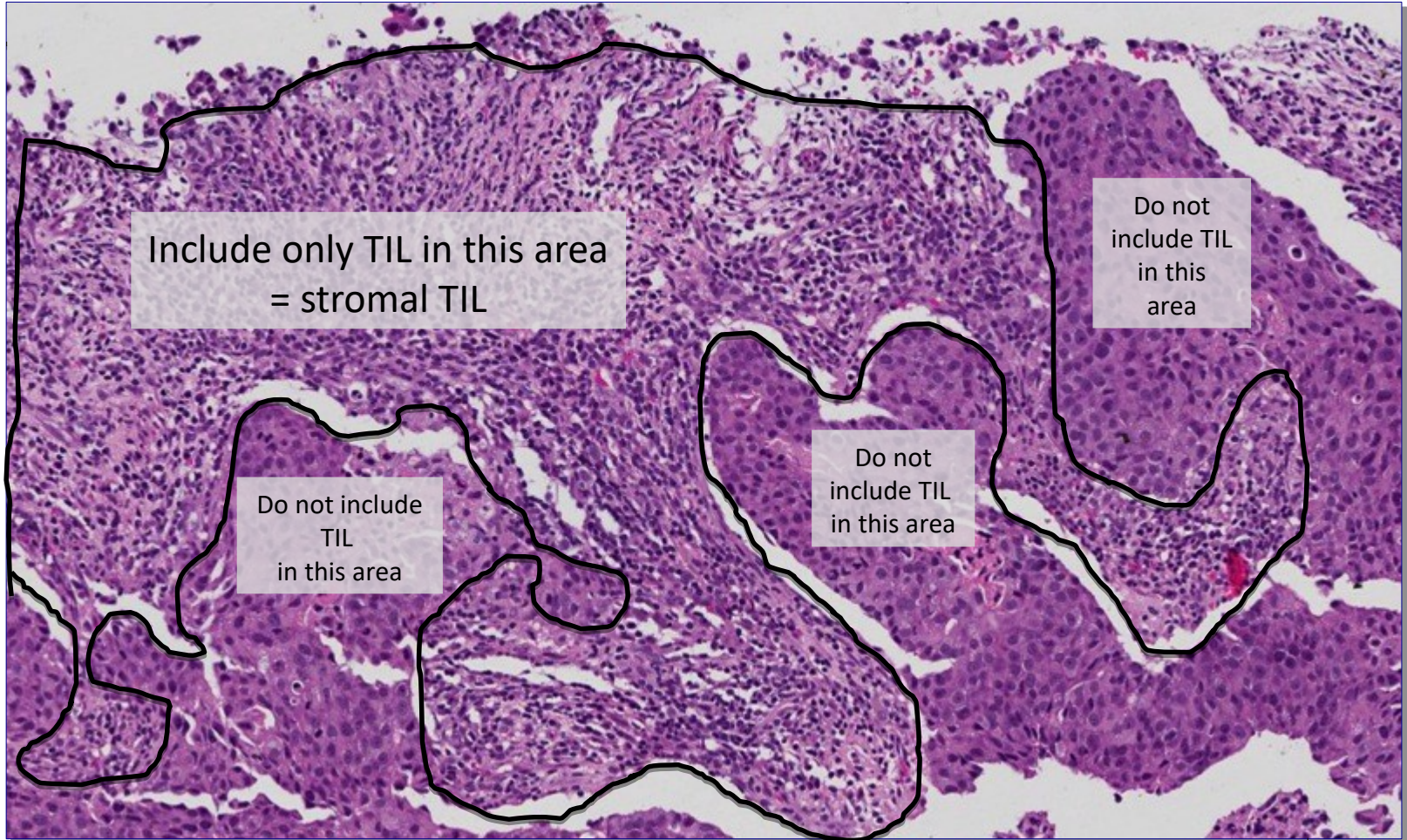

area for TIL evaluation

do not include in evaluation

Example 3

Step 2: Focus on stromal TIL

- In the diagnostic setting, only stromal TILs are relevant

Do not include TILs in this area

Include only TILs in this area = stromal TILs
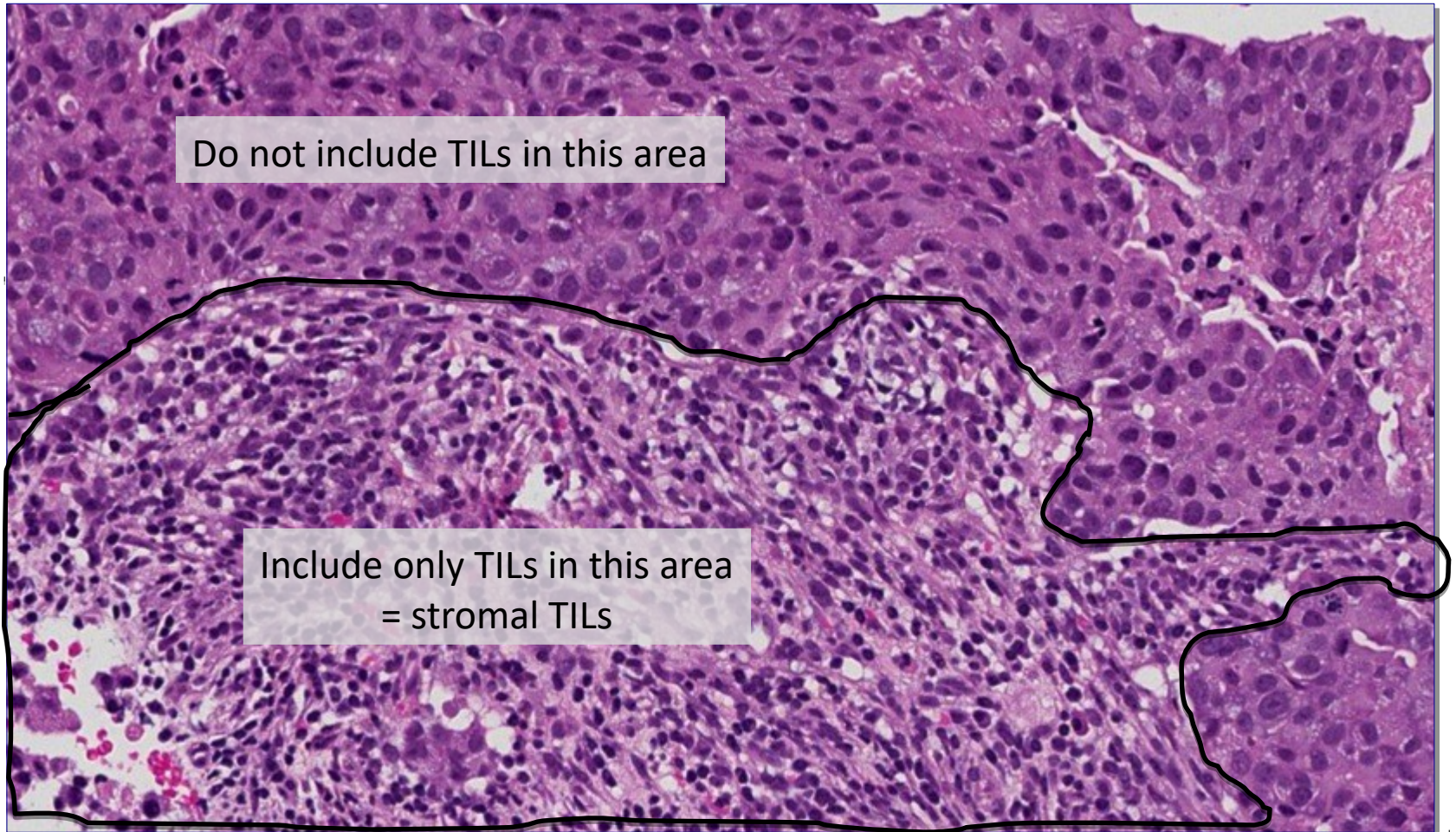
Example 4

Step 2: Focus on stromal TIL

- in the diagnostic setting, only stromal TIL are relevant

Include only TIL in this area = stromal TIL

Do not include TIL in this area

Do not include TIL in this area

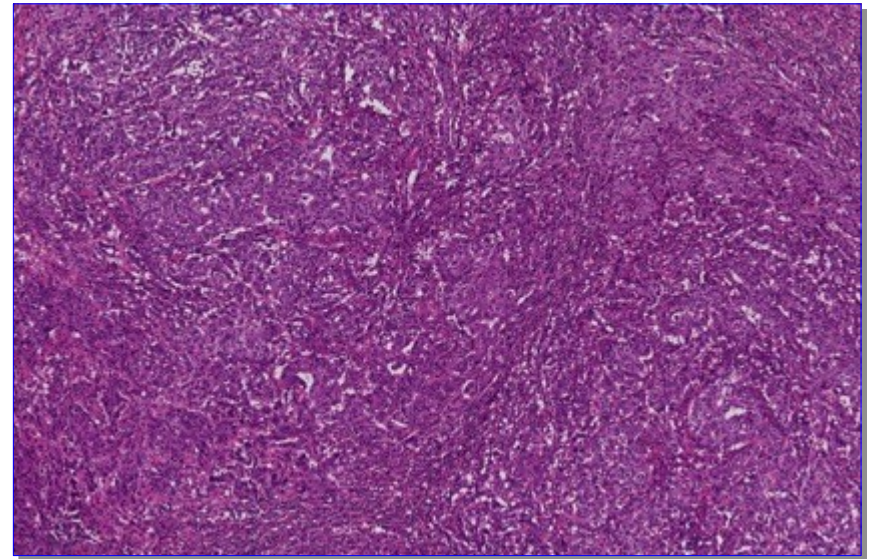Do not include TIL in this area

Example 5

Step 2: Scan tumor at low magnification – focus on the tumor stroma

- Stroma contains predominantly collagenous tissue, few round cells

- Stroma contains predominantly round cell infiltrate, collagenous tissue difficult to recognize
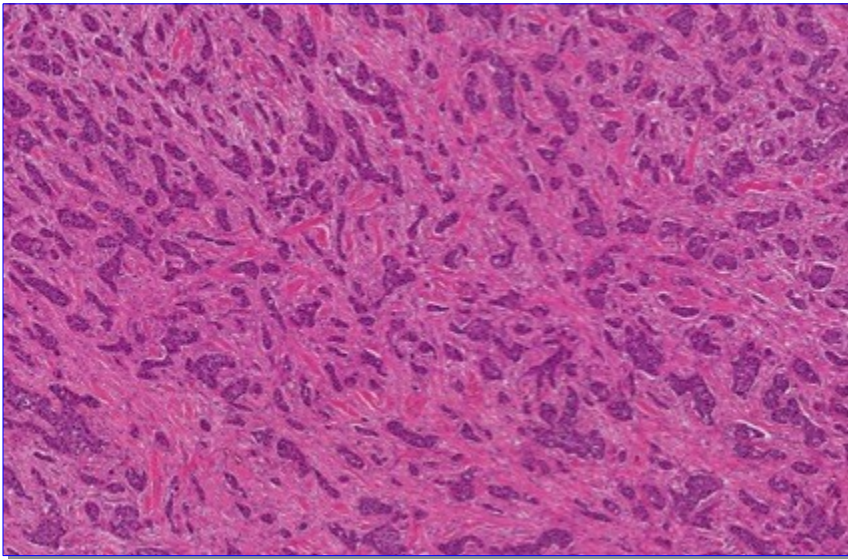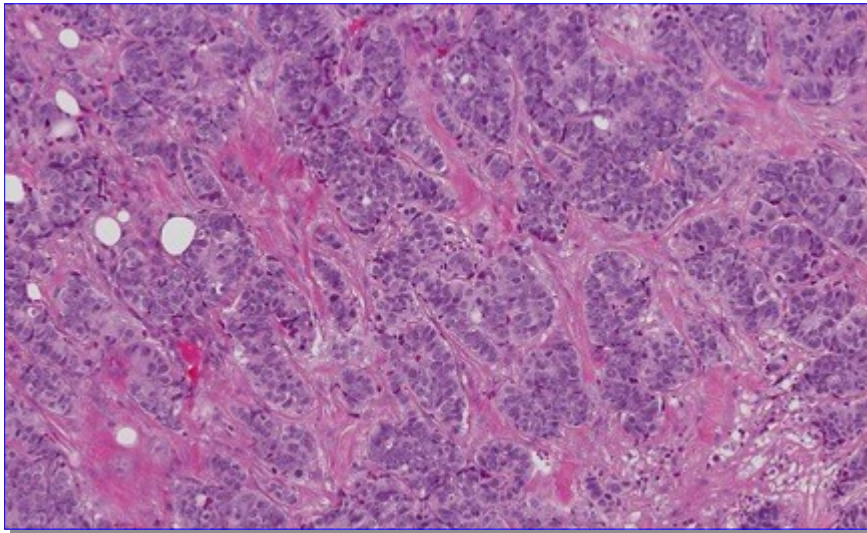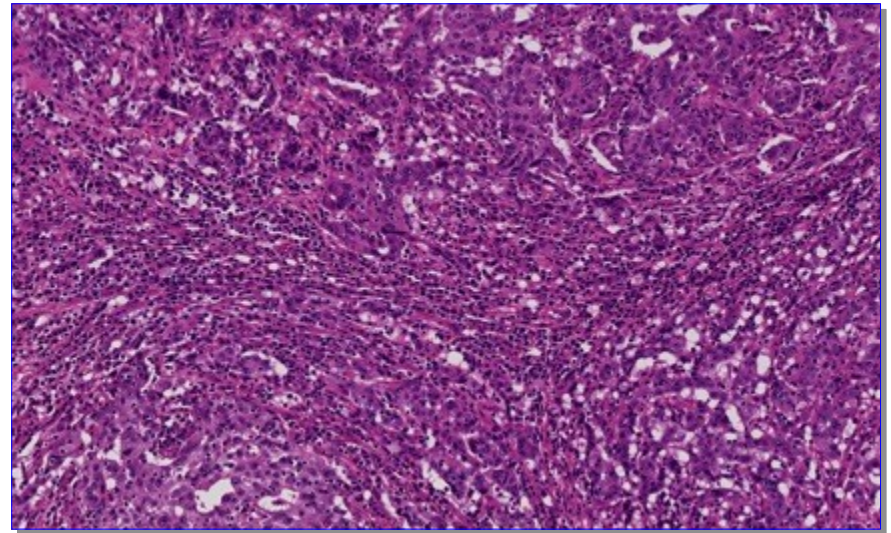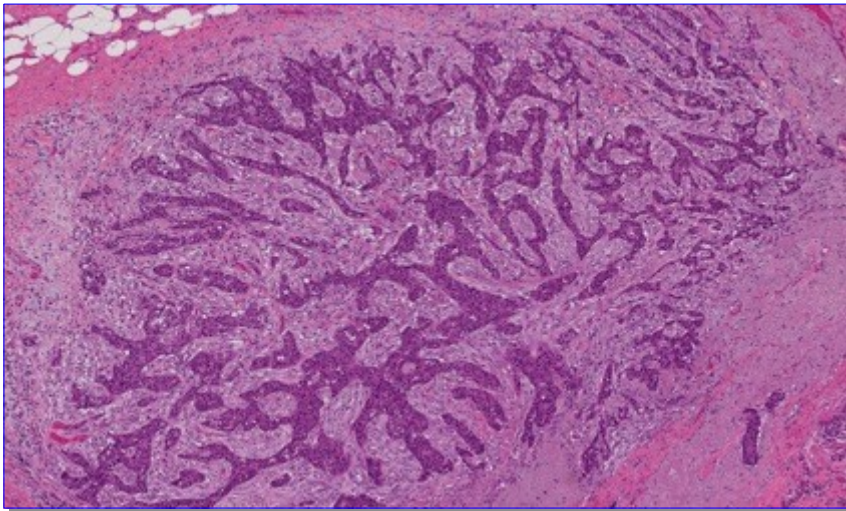

Example 6

Example 6

Step 2: Scan tumor at low magnification – focus on the tumor stroma

- Stroma contains predominantly collagenous tissue, few round cells

Example 8

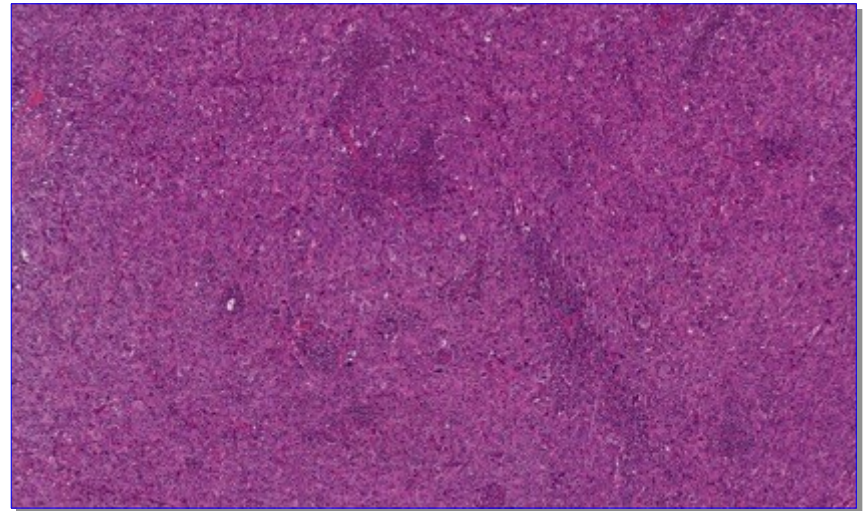- Stroma contains predominantly round cell infiltrate, collagenous tissue difficult to recognize

Example 9

Step 2: Scan tumor at low magnification – focus on the tumor stroma

- Stroma contains predominantly collagenous tissue, few round cells

Example 10

- Stroma contains predominantly round cell infiltrate, collagenous tissue difficult to recognize
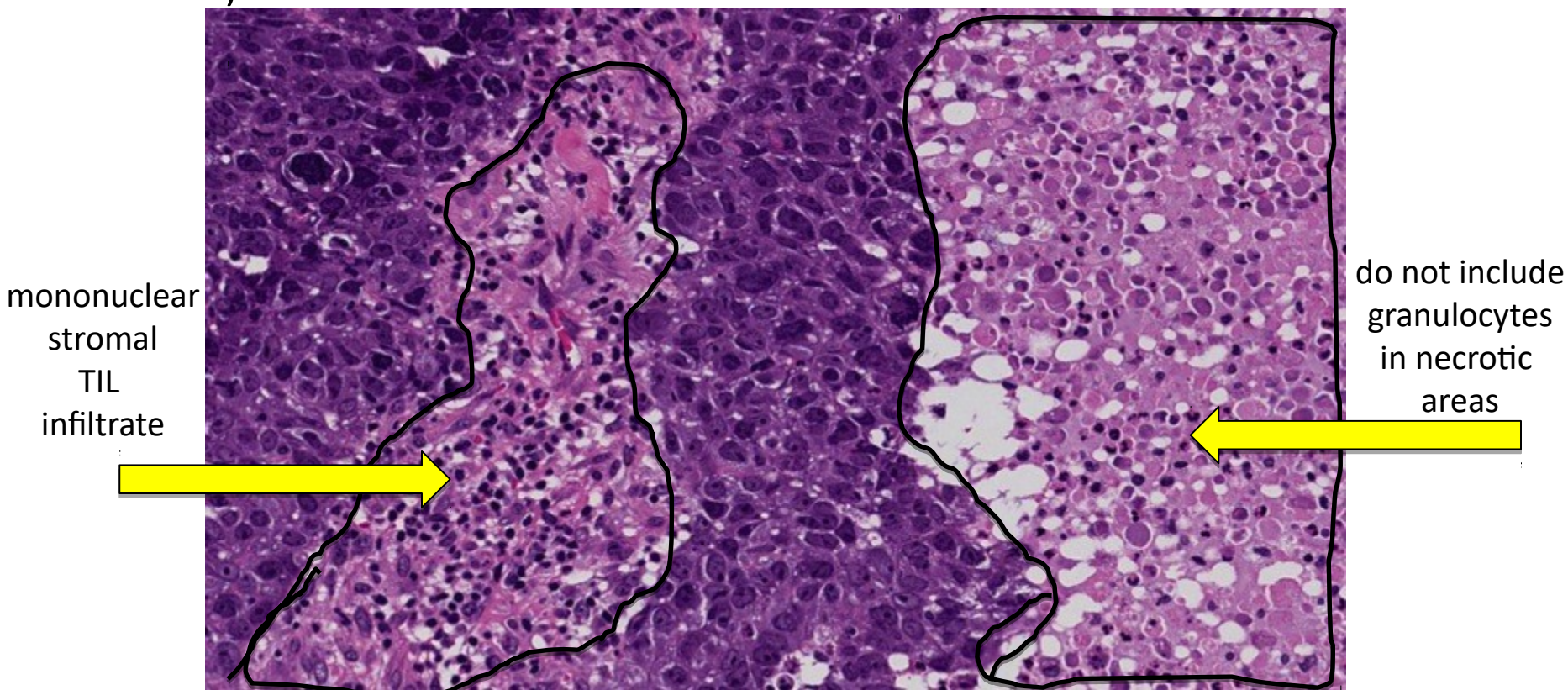

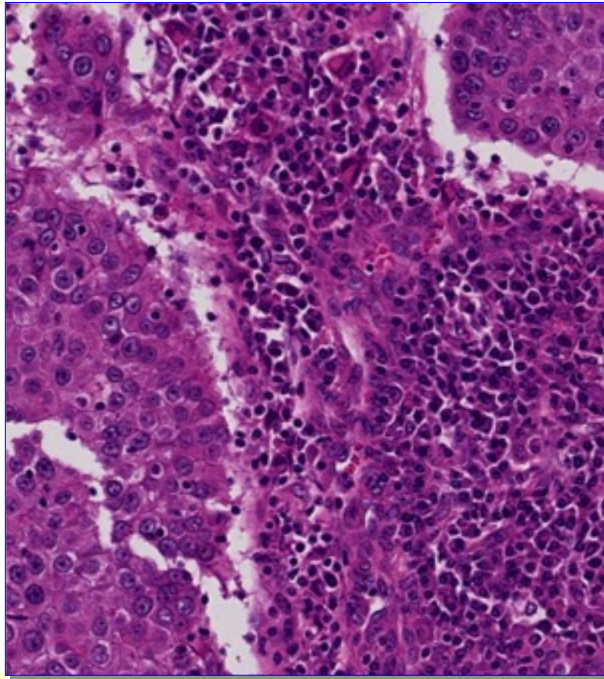Example 11

Step 3: Determine type of inflammatory infiltrate

- Include only mononuclear infiltrate (lymphocytes & plasma cells)

- Do not include granulocytic infiltrate in areas of tumor necrosis
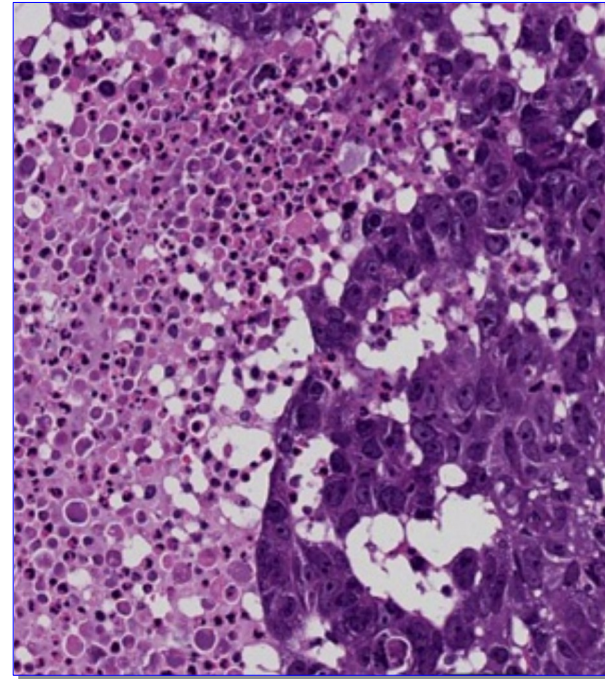

mononuclear stromal TIL infiltrate

do not include granulocytes in necrotic areas

Example 12

Step 3: Determine type of inflammatory infiltrate

- Include only mononuclear infiltrate (lymphocytes & plasma cells)

Example 13

- do not include granulocytic infiltrate in areas of tumor necrosis

Example 14

Step 4: As a first approach, include tumor in one of three groups based on low magnification and assess % stromal TILs (continue with Step 5 for percentage)

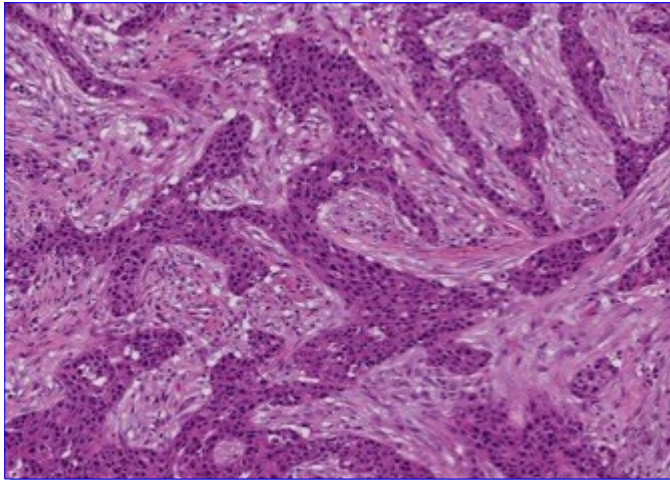**Group A: tumor with no/minimal immune cells**

Group B: tumor with intermediate / heterogeneous infiltrate

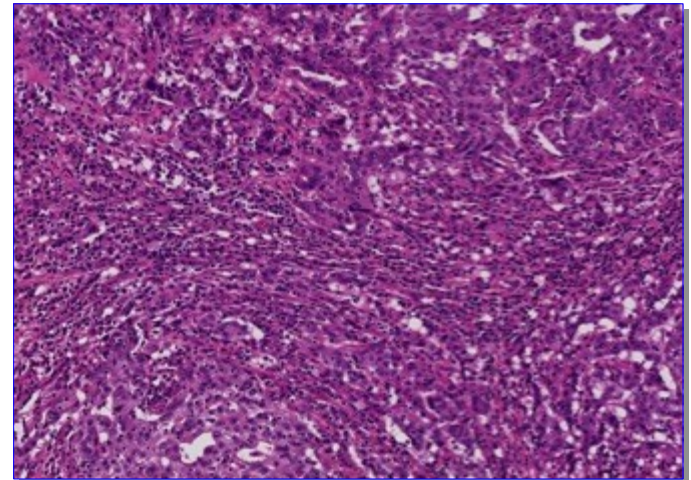**Group C: tumor with high immune infiltrate**

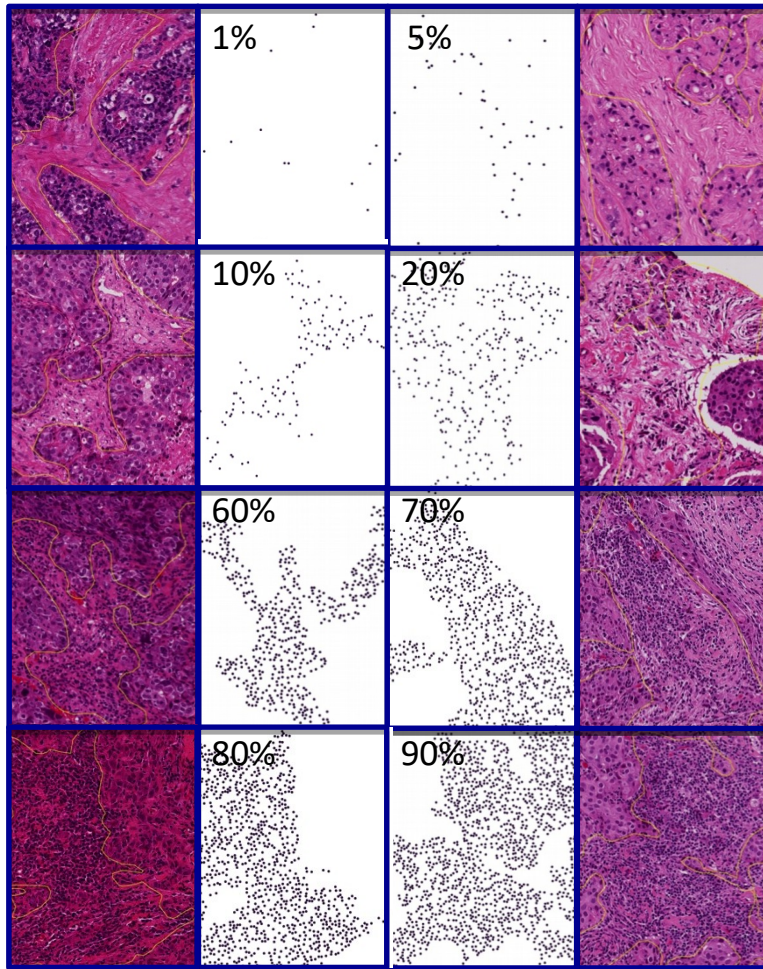| 0-10% stromal TILs	10-40% stromal TILs	40-90% stromal TILs

For this intermediate group evaluate different areas at higher magnification.

Example 15

Example 16

Step 5: Report percentage of stromal lymphocytes

- Report the average of the stromal area, do not focus on hot spots.

- For intermediate group evaluate different areas at higher magnification.

- Please note that lymphocytes to not form solid aggregates, therefore even with 90-100% stromal TILs there will still be some space between the individual lymphocytes.

Please send any questions or comments to:

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