

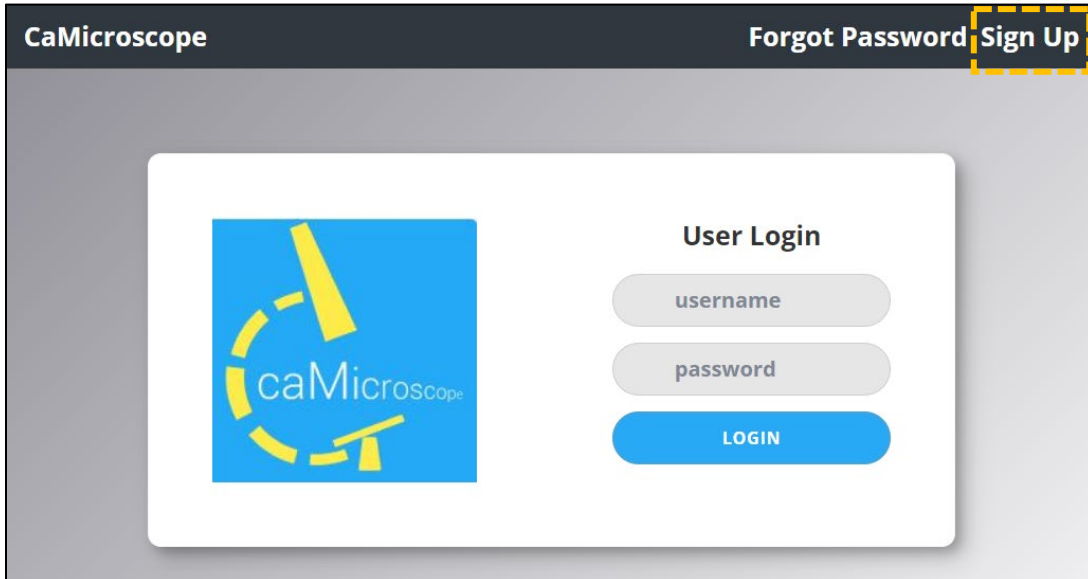
caMicroscope Process Guide

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Create your caMicroscope Account

1. In order to participate in Interactive sTILs Training, the HTT project studies, or ROI Selection on caMicroscope, you will first need to sign up for an account. Go to <https://wolf.cci.emory.edu/camic/htt/> and click "Sign Up."



CaMicroscope

Forgot Password **Sign Up**



User Login

username

password

LOGIN

2. Please read and accept the Consent Form.

Consent Form

The study does not involve any benefits beyond the advancement of science and public health.

Are there risks to me if I participate in this study?
The study does not involve any risks beyond normal working conditions.

My rights as a research participant
Participation in this study is voluntary. There is no compensation for your participation. You have the right to choose not to participate in this study. You may leave the study at any time. Deciding not to participate or choosing to leave the study will not result in any penalty or loss of benefits to which you are entitled.

Page 1 of 2


Confidentiality
All personally identifying information will be kept confidential but may be inspected by a federal entity or federal regulators. Upon enrollment, you will be assigned a participant ID that will link to your real name by a look-up table. This look-up table will only be used by the PI for follow-up purposes, and will otherwise be kept confidential by the PI. Participant consent may be collected electronically or by hard copy. Hard documents will be stored in locked cabinets by the PI through the end of the study. Deidentified data will be shared publicly. Any publications presenting data and results will not be linked to your identity.

What if I have questions?

I Accept The Terms of Consent Form

[Download Consent Form](#)

3. Please complete the Basic Information, Professional, and Certifications forms as appropriate for you. Once the required sections are filled, you can click “Next” and/or “Submit” to move onto the next screen. Screen shots provided below.
 - a. After entering all the information and hitting submit, the screen may remain unchanged, but the request is being processed. If you click the submit button a second time, you will get an error message because the account is already made.



1 **2** **3** **4**
Consent From Basic Info Professional Certifications

Basic Information

First Name *(required)*

Last Name *(required)*

Contact Email *(required)*

Phone Number

Previous **Next**

1 **2** **3** **4**

Consent From **Basic Info** **Professional** **Certifications**

Professional

Institution of Employment *(required)*

Role at your institution *(required)*

- Pathologist
- Resident
- Medical Director
- Other

1 **2** **3** **4**

Consent From **Basic Info** **Professional** **Certifications**

Certifications

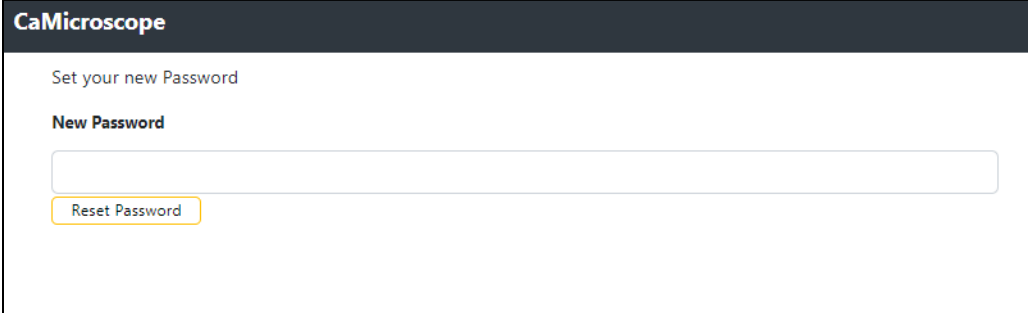
Board certifications and specialties or equivalent for your country (or enter NA) *(required)*

Board certification or residency organization and country (or enter NA) *(required)*

If you are a board-certified anatomic pathologist or the equivalent for your country, enter the number of years since your certification. (If you are not a board certified anatomic pathologist or equivalent, enter -1) *(required)*

If you are an anatomic pathology resident, how many years of residency have you had? (If you are not a anatomic pathology resident, enter -1) *(required)*

4. Within a few minutes, an email will be sent to the address you registered with (Subject: "caMicroscope : Welcome" from rbirmin@emory.edu). Please make sure to click the "Reset your password" link to be directed to a page to create a password for your account. The link will expire in one hour. In this case visit the login page and click "Forgot Password" in the top-right corner and another email with a link to reset your password will be sent.



CaMicroscope

Set your new Password

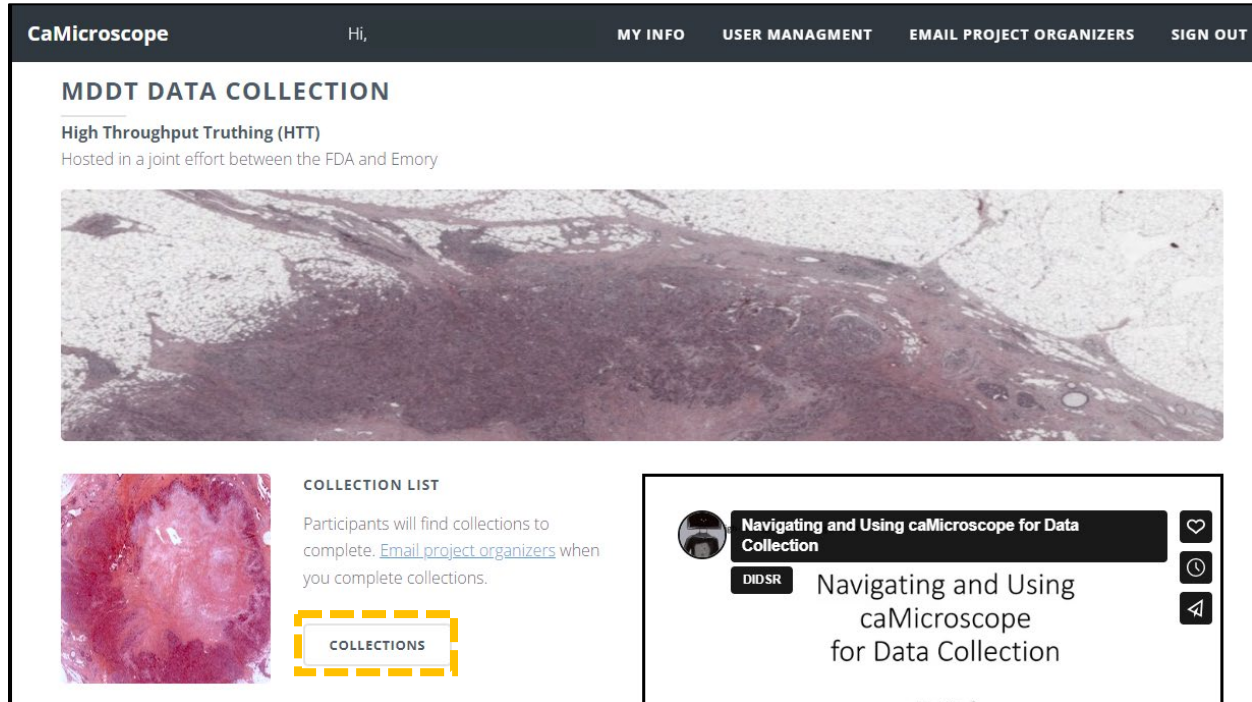
New Password

Reset Password

5. Once a password is created, you can return to <https://wolf.cci.emory.edu/camic/htt/> and log in with your credentials. Your username is your email address.
 - a. The platform starts empty. HTT project management needs to assign you collections.
 - b. Response time to your registration should be less than two days.
 - c. Please allow five business days for your registration to be processed by the HTT project management and for you to be sent further instructions.
 - d. If you haven't been contacted after five days, please email brandon.gallas@fda.hhs.gov.

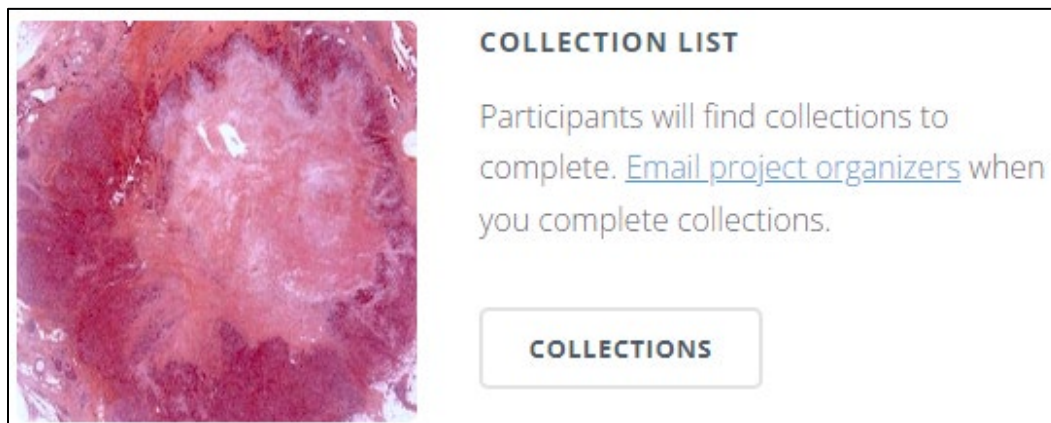
How to Access HTT Interactive Training & Pivotal Studies

1. Go to <https://wolf.cci.emory.edu/camic/htt/>. Login to your caMicroscope account with the email address and password you used to register. You will be brought to the landing page.



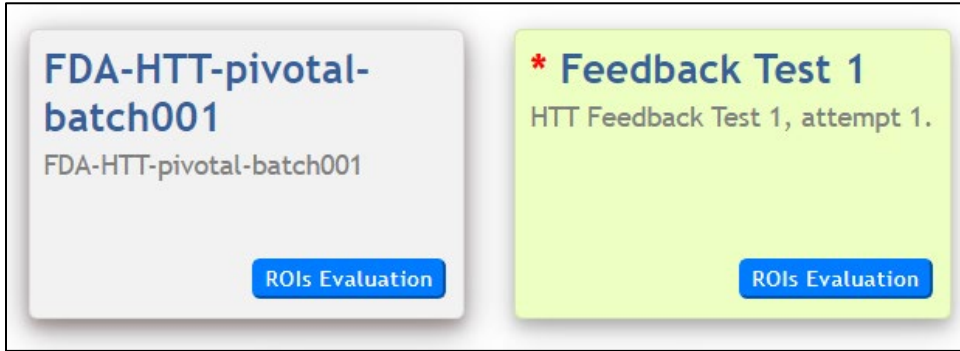
The screenshot shows the CaMicroscope website interface. At the top, there is a navigation bar with the text "CaMicroscope", "Hi,", "MY INFO", "USER MANAGMENT", "EMAIL PROJECT ORGANIZERS", and "SIGN OUT". Below this, the main heading is "MDDT DATA COLLECTION" followed by "High Throughput Truthing (HTT)" and "Hosted in a joint effort between the FDA and Emory". A large histological image is displayed. Below the image, there is a "COLLECTION LIST" section with a smaller histological image and the text: "Participants will find collections to complete. [Email project organizers](#) when you complete collections." A yellow dashed box highlights a "COLLECTIONS" button. To the right, there is a dark overlay with a user profile picture, the text "Navigating and Using caMicroscope for Data Collection", and a "DIDSR" label. Below this, another dark overlay contains the text "Navigating and Using caMicroscope for Data Collection" and a "COLLECTIONS" button.

2. Click **“Collections”** under the **“Collection List”** module to find the interactive training and pivotal study collections.



This is a close-up of the "COLLECTION LIST" module. It features a histological image on the left and the following text on the right: "COLLECTION LIST", "Participants will find collections to complete. [Email project organizers](#) when you complete collections.", and a button labeled "COLLECTIONS".

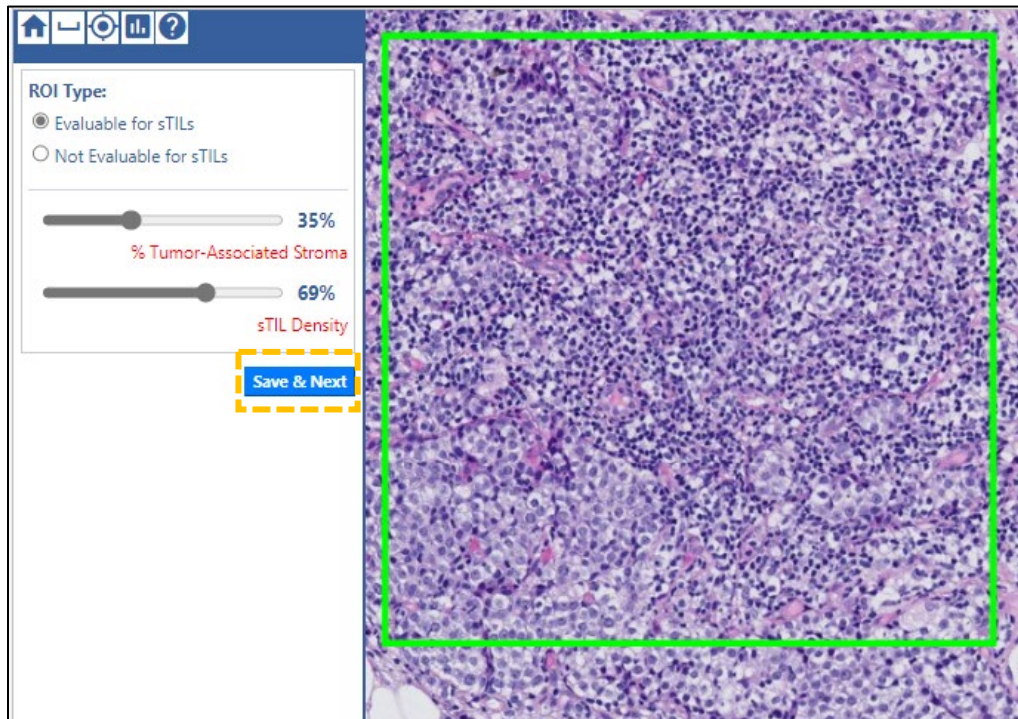
- Click the “ROIs Evaluation” to select the collection you would like to complete (example below: “HTT-pivotal-batch001” and “Feedback Test 1”).



- Once in the collection, click “Annotate” to begin the sTILs evaluation on the ROIs within a slide. The number of ROIs on a slide may vary and your “ROIs” column will update as you complete the task. To view the details about a WSI’s ROIs, click “Review”.

COLLECTION LIST				Hi, emma.gardecki@fda.hhs.gov	
n: FDA-HTT-pivotal-batch001 on: FDA-HTT-pivotal-batch001					
entries per page					Search...
	Name	MPP	ROIs	Annotate	Review
9c2f04001498f845	HTT-TILS-003-040	0.2525	0/10	Annotate	Review
9c2f04001498f846	HTT-TILS-003-043	0.2525	0/10	Annotate	Review
9c2f04001498f847	HTT-TILS-003-049	0.2525	0/10	Annotate	Review
9c2f04001498f848	HTT-TILS-003-052	0.2525	0/10	Annotate	Review
9c2f04001498f849	HTT-TILS-003-059	0.2525	0/10	Annotate	Review
9c2f04001498f84a	HTT-TILS-004-008	0.2525	0/10	Annotate	Review
9c2f04001498f84b	HTT-TILS-004-009	0.2525	0/10	Annotate	Review
9c2f04001498f84c	HTT-TILS-004-011	0.2525	0/10	Annotate	Review

5. Annotate the ROI presented, then click “Save & Next” to save your annotation and move to the next ROI. It may take a moment to move to the next ROI. When you finish annotating all ROIs for a WSI, you will return to the list of cases in step 4. Notes on the annotation:
- WSI Magnification:** We recommend that all annotations are made using **20x magnification**.
 - ROI Type:** If the ROI is within 1 mm of the tumor (500 μm of the tumor margin) and includes stroma, it is “Evaluable for sTILs”. Otherwise, it is not.
 - % Tumor-Associated Stroma:** The area of tumor-associated stroma divided by the area of the ROI.
 - sTILs Density:** The area of the tumor-infiltrating lymphocytes divided by the area of the tumor-associated stroma.



- e. If you are annotating the “Feedback Test”, you will see feedback from the experts (scores, comments, and pitfalls) before moving to the next ROI. Select “Next” to continue.

ROI Type:

Evaluable for sTILs
 Not Evaluable for sTILs

% Tumor-Associated Stroma: 39%

sTILs Density: 6%

Expert Panel Annotations:

ROI Type	% Tumor-Associated Stroma	% sTIL Density
Evaluable	25	0
Evaluable	12	5
Evaluable	25	5
Evaluable	25	0
Evaluable	40	0
Evaluable	50	2

Mean Percent Stroma: 29.5
Mean sTILs Density: 2

Comments: Adipocytes are excluded from tumor-associated stroma.
Pitfalls: Adipocytes are not considered part of the tumor-associated stroma for purposes of sTILs assessment.

Next (button highlighted with a yellow dashed box)

200 μm (scale bar)

Note:

To help resolve issues, please grab the url of the page that shows a problem. That will help us to find it quickly and investigate.

Overview of caMicroscope Icons



Icon functionality listed in order of left to right:

1. **Home:** Return to list of assigned WSIs and ROIs (Collection List)
2. **ROI Location:** Return to the center of the ROI
3. **TIL Sample:** View the TILs cheat sheet
4. **Tutorial:** View slides of a tutorial presentation on the sTILs assessment from the International Working Group for TIL in breast cancer (2014, adapted 2020)

Summary of the Five Steps of the sTILs Assessment

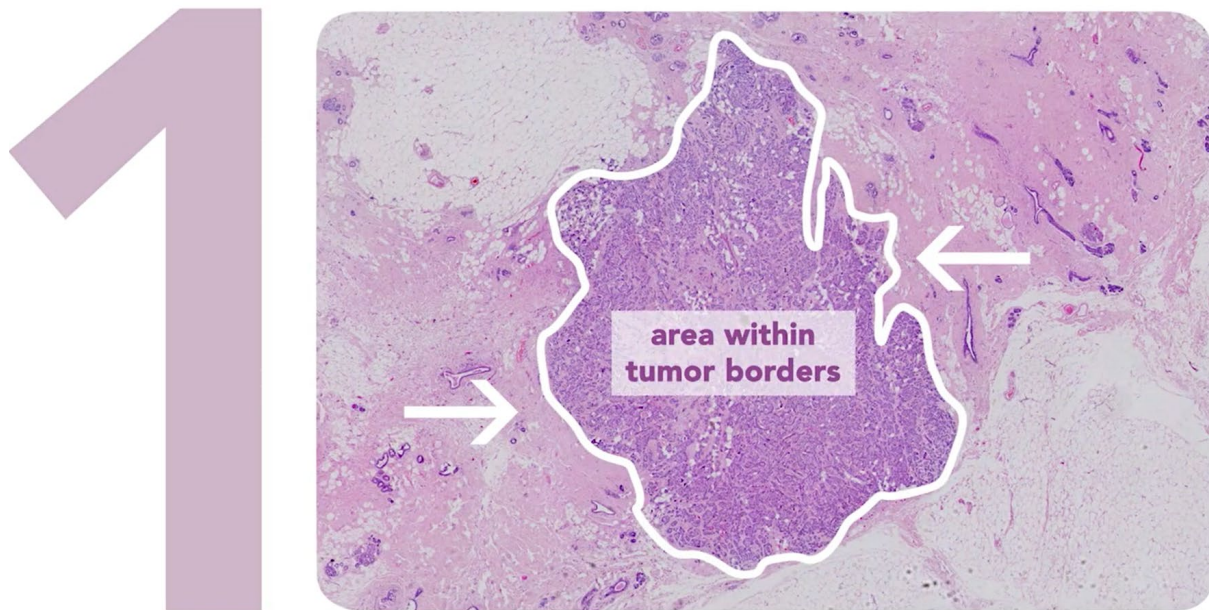
Below are screen shots from the training video that was part of the FDA CME course, "Assessment of Stromal Tumor-Infiltrating Lymphocytes."

- Link to the video on YouTube: <https://www.youtube.com/watch?v=aPa-pXIBBIU>

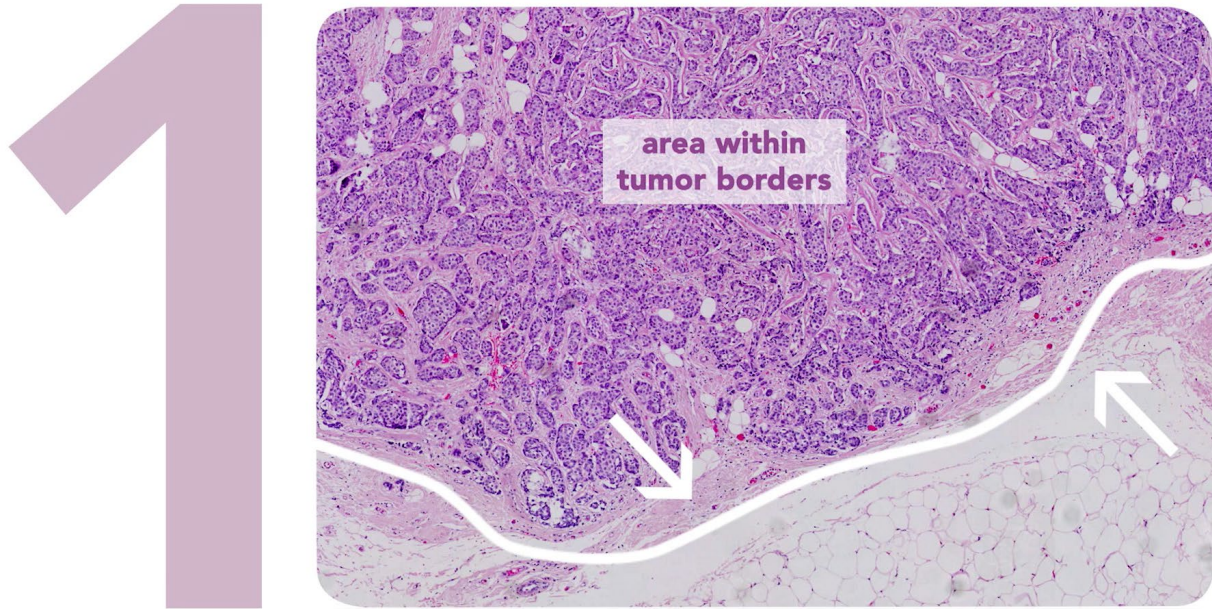
5 steps



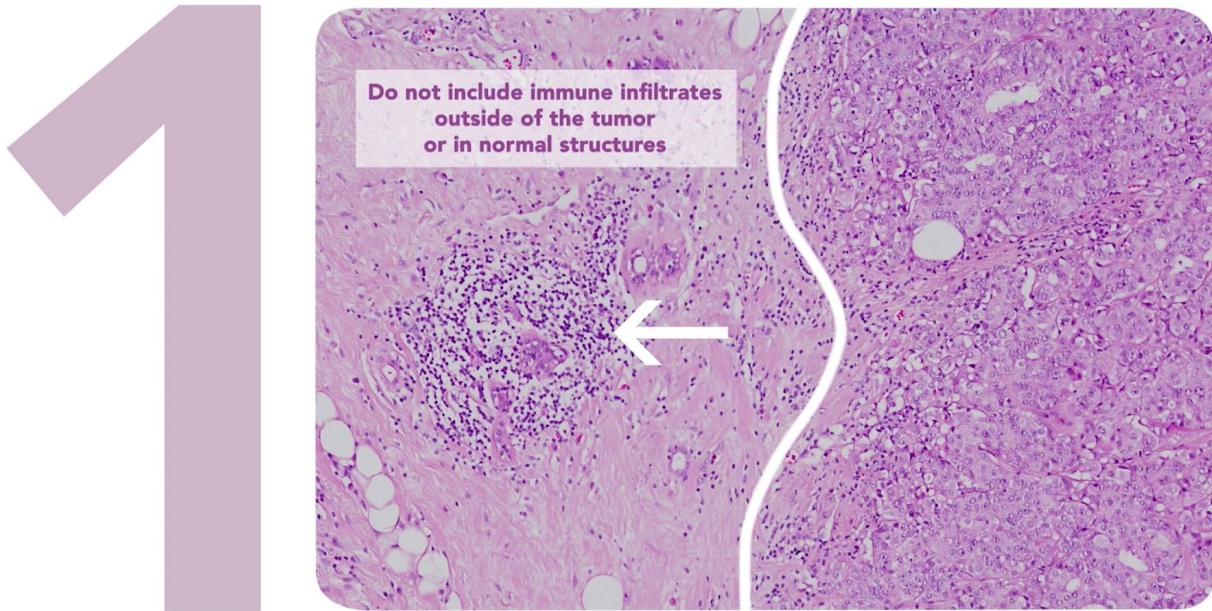
1. Define the areas for TILs evaluation
 - a. Only TILs within the borders of invasive tumors are evaluated



b. The invasive edge is included in the evaluation, but not reported separately

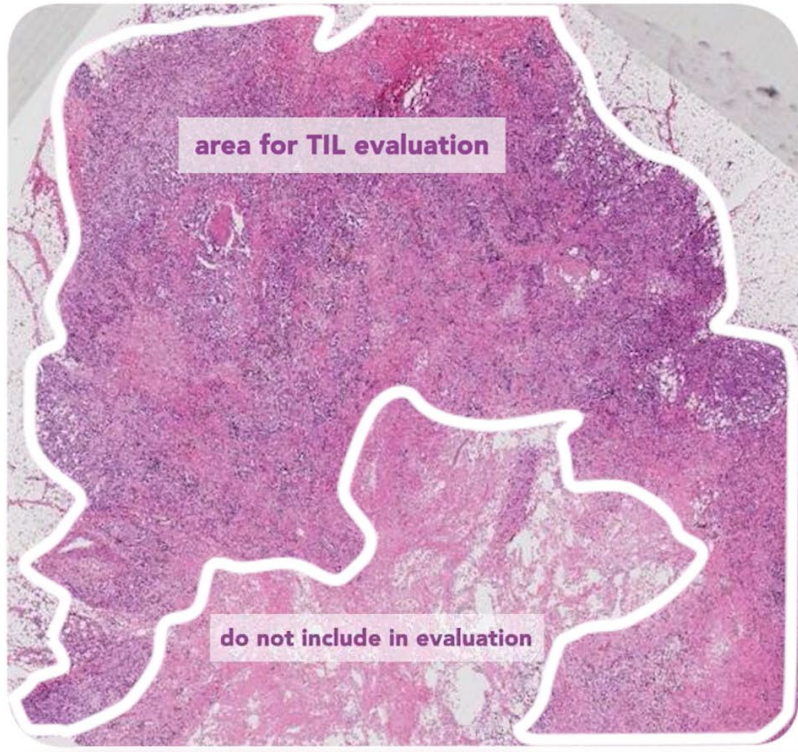


c. Immune infiltrates outside the tumor borders are not included



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

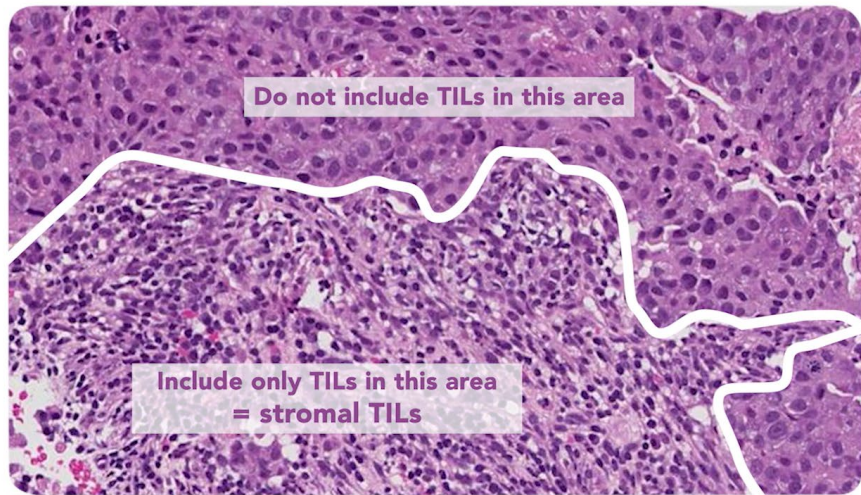
1



2. Focus on stromal TILs

- In the clinical setting, only stromal TILs are relevant.
- Scoring TILs in the intratumoral compartment is poorly reproducible between pathologists, that's why we only score TILs in the stromal area

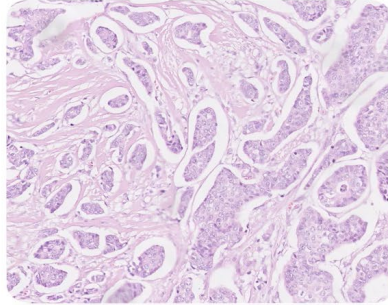
2



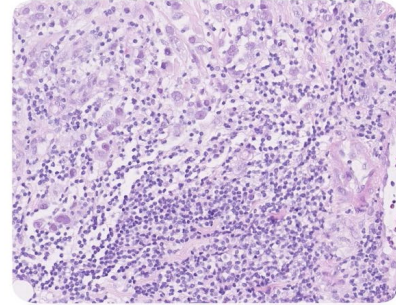
- Scan the tumor at low magnification and focus on tumor stroma

2

Stroma contains predominantly collagenous tissue, few immune cells



Stroma contains predominantly immune cell infiltrate, collagenous tissue difficult to recognize

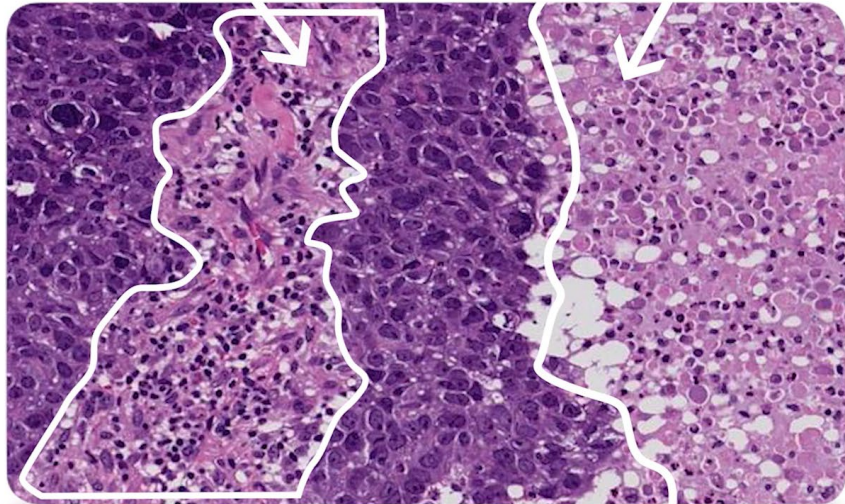


3. Determine the type of inflammatory infiltrate
 - a. Include only mononuclear cells, lymphocytes and plasmacytes.
 - b. Do not include granulocytes or immune cells in necrotic areas.

3

Mononuclear stromal TILs infiltrate

Do not include immune cells in necrotic areas



4. As a first approach, include tumor in one of three groups based on low magnifications and assess % stromal TILs
 - a. The denominator used to determine the percentage stromal TILs is the area of stromal tissue, not the number of stromal cells


4

Group A
tumor with no/minimal immune cells
0-10% stromal TILs

Group B
tumor with intermediate / heterogeneous infiltrate
10-40% stromal TILs

Group C
tumor with high immune infiltrate
40-90% stromal TILs

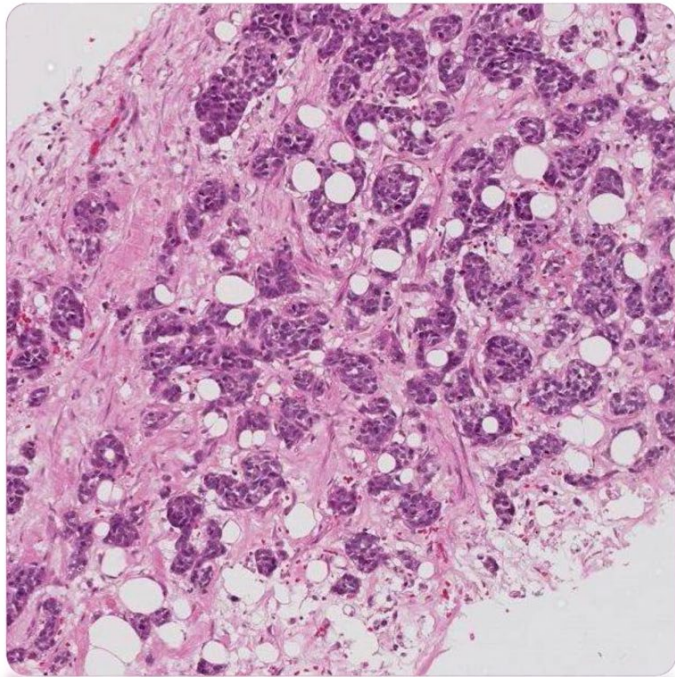
For this intermediate group evaluate different areas at higher magnification



5. Report the percentage of TILs
 - a. Report the average of the stromal areas you see, don't focus on hotspots

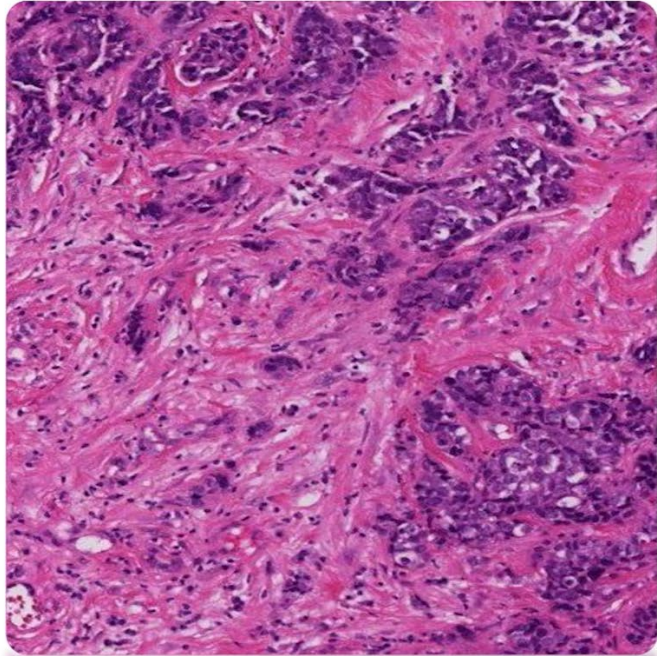
TILs score = 0 %

5



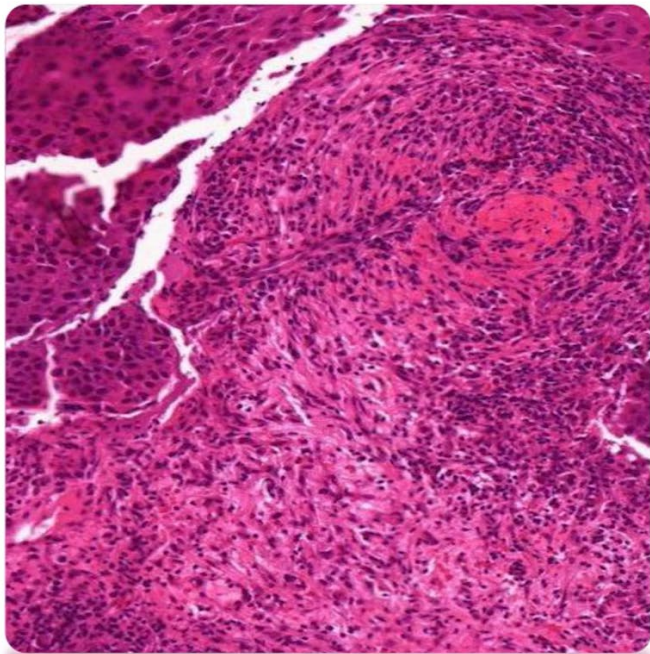
5

TILs score = around 10%



5

TILs score = around 50%



5

TILs score > 80%

