

Instructions manual – E-learning

Important notes:

- Read these instructions and watch the [instruction video](#) of the scoring method
- The E-learning is mandatory and consists of a training set and a test set
- After completing the training set, your score will be calculated. If this kappa score is >0.7 , the test set will be made available (Figure 1)
- Save regularly, and save the final file before sending it to UNITED@lumc.nl
- The E-learning is finished if the test set is passed with a kappa of >0.7 as well
- A certificate is send after passing the E-learning, as confirmation for our Clinical Research Center to grant you access and rights for inclusion of patients (after the submission is approved and your center is participating).

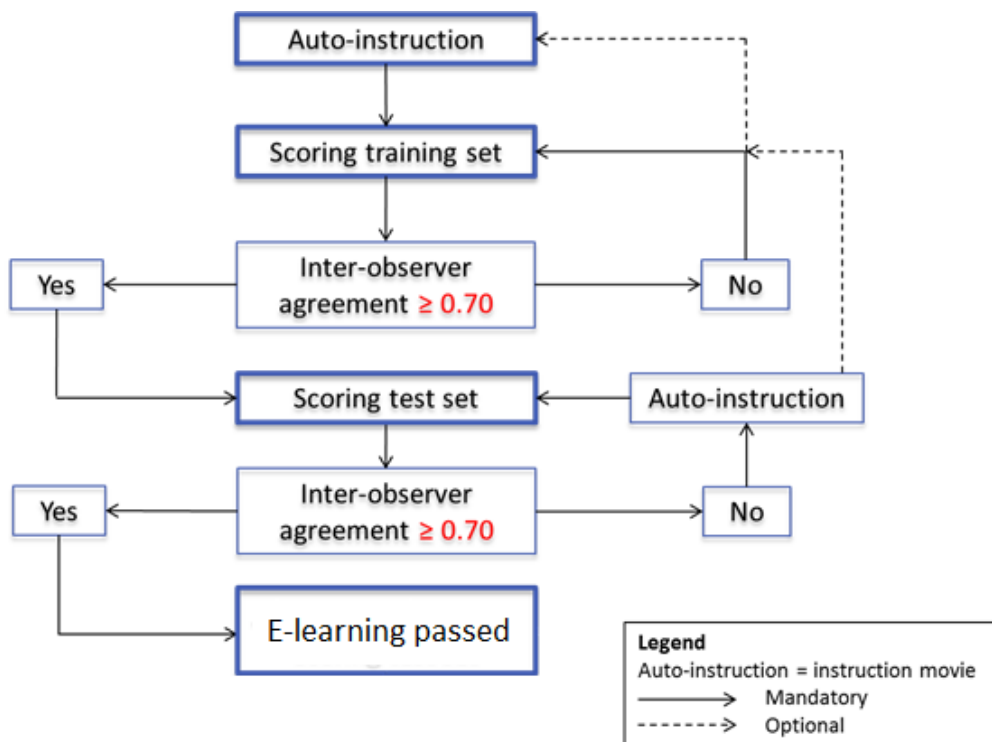


Figure 1. Workflow of the E-learning procedures.

Tumor-stroma ratio (TSR)

Scoring the TSR can be done in a few steps. First, the area of interest needs to be selected. Through conventional microscopy, this can be done by looking through the slide with the 2.5x or 5x magnification. If an area of interest is found, e.g. with the most amount of tumor-stroma, through a 10x magnification the TSR can be scored. Since the slide is used which is also used for determining the T-stage of the tumor, it is not necessary to look for the most invasive part anymore; the whole of the slide can be used (if it is tumor-stroma).

A scoring area should contain:

- Tumor epithelial cells on all four sides
- As much tumor-stroma possible on the whole of the slide

- No vessels, necrosis, erythrocytes, fatty and/or muscle tissue (or as least as possible)
- Mucus can be in the annotation, but needs to be excluded in scoring

First, you estimate in this field the percentage of stroma, in increments of 10%. This way, the carcinoma can be categorized as a stroma-low ($\leq 50\%$) or stroma-high ($> 50\%$) tumor.

The E-learning

Training set

The training set consists of three parts:

- Three general questions
- Five multiple choice cases, where you are asked to choose the best annotation and score the stromal percentage
- Thirty-five cases, where you place the annotation correctly and score the stromal percentage

Test set

The test set consists of forty cases, where you are asked to place the annotation correctly and score the stromal percentage.

General

The E-learning file is sent as an attachment in an mail alongside these instructions. Open and save the file locally, so changes can be made to the file.

The training set's general questions can be selected and/or written down (Figure 2). Please do this for our administration.

General questions

UNITED

What are you:

- Pathologist
- Resident pathology / Pathology trainee
- Other: ...

What is your specialty:

- Colorectal cancers
- Upper-GI cancers
- Breast cancers
- Other: ...

What country are you from:

- ...

Remove all options not relevant

Figure 2. The part of the training set with general questions.

The next five questions are training cases, in which a color can be selected in the 'menu' (by only leaving the correct color or only writing that color down). Next, score the stromal percentage by writing that in the 'menu'. If there are any remarks, e.g. that the case was difficult or any doubts, it can be written below in the 'menu' as well (Figure 3).

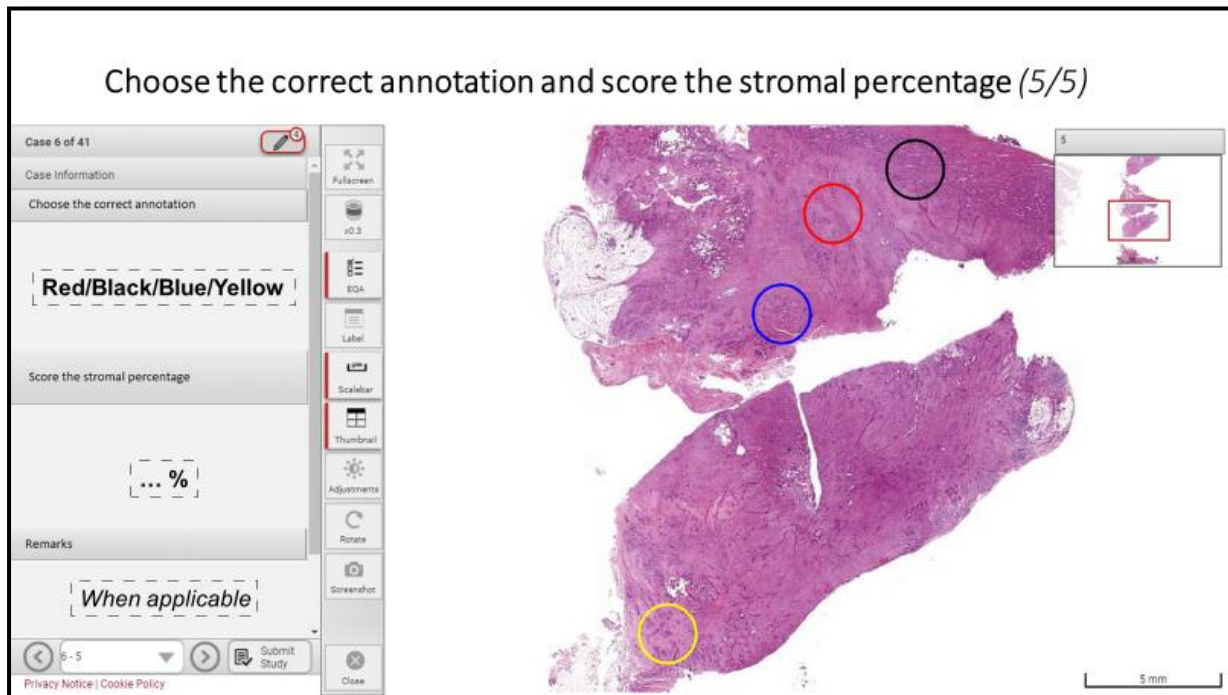


Figure 3. An example of the training cases of the training set.

After these five training cases, there are thirty-five regular cases in the training set and forty in the test set. The annotation in the 'menu' on the side is already in the correct size, and can be selected and dragged to the correct place in the tissue. After, the stromal percentage needs to be scored and when applicable, some notes can be written down (Figure 4).

Remember to save the file regularly!

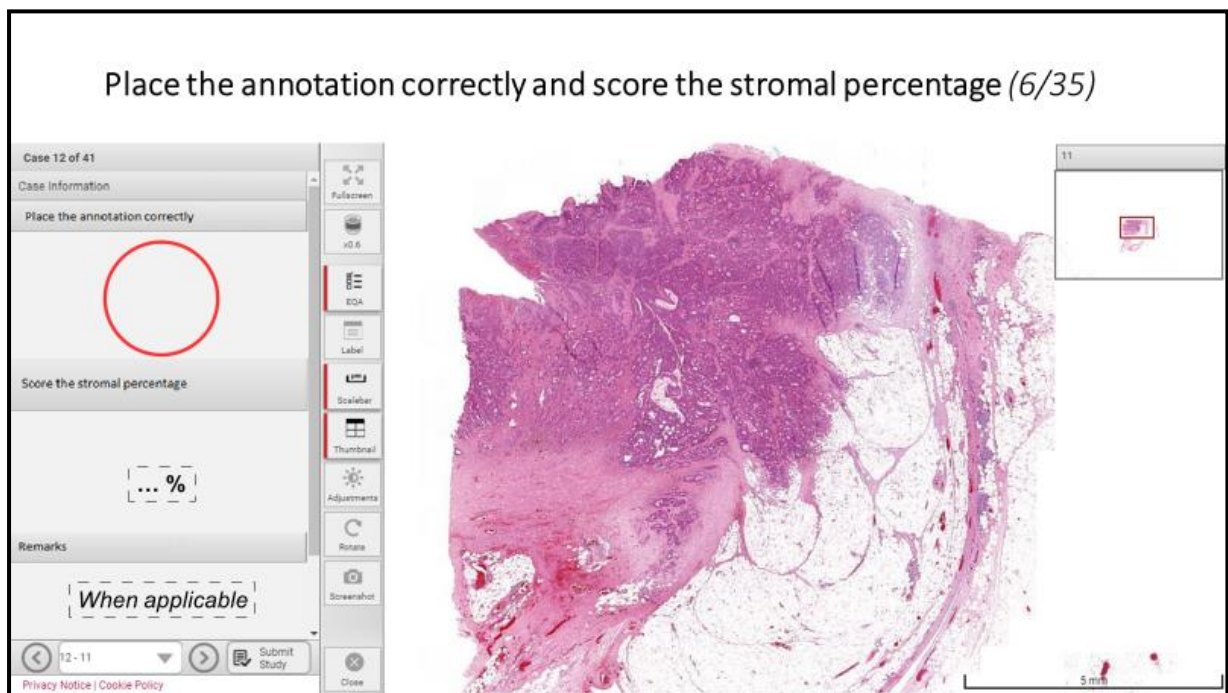


Figure 4. Example of the regular cases in the training and test set.

The rest of the buttons in the 'menu' are not useable. The image of the tissue has already been zoomed in to a useful format, and the annotation is already the right size to match the 10x magnification. Therefore, do not change these sizes! However, zooming in can be done by the general 'zoom in' button of Powerpoint (down below on the righthand). The file can be saved and thus paused if needed.

Final note

Submit study

After finishing all questions, save the last version of the file with the name of the set (training set or test set) and your name (e.g. Trainingset_MeaghanPolack). Then, submit the file by sending it in an attachment in an email to us at UNITED@lumc.nl. We will evaluate your answers and calculate a kappa. If your kappa is >0.7 , you pass the set. The E-learning is finished if both the training and test set are passed with a kappa of >0.7 , and a certificate is sent. However, if your score is <0.7 , then you will receive feedback on what errors were made and a request to redo some questions is made. This will be repeated until a score of >0.7 is reached.

Questions and/or problems

If you have any questions or experience problems, please contact us. You can send an email to drs. Meaghan Polack, PhD candidate at UNITED@lumc.nl or call us on +31 71 526 5130.