Reader Study on multi-head microscope: Counting and Classifying Mitoses

# Objectives

Our objectives are to collect counts of mitoses and classifications from multiple readers simultaneously using a multi-headed microscope. An expert will also discuss classification decisions, as training the participants is another objective. We do not have a hypothesis for the results. However, the data that we will collect will be used to train or test a mitosis detection algorithm. It will also inform us on reader variability in this task.

# Slides and FOVs Same as Ongoing Single-Head Study

4 readers have been counting mitoses from 40 ROIs on 4 slides using WSI and using a single-head microscope. An ROI is the region of interest, the evaluation area. The ROIs in this study are 200 um x 200 um, which is equivalent to 800 x 800 pixels of a WSI with a scanning resolution of 0.25 um/pixel. This size was selected to fit within most digital displays without panning or zooming. We use a reticle in the microscope eyepiece to outline the ROI.

The slides and ROIs from this single-head study will be the slides and ROIs for the high-throughput study.

# Candidate Mitoses

For each FOV, we will pre-select 5-10 candidate mitoses. The candidate mitoses include consensus mitoses (8 or better out of 10 pathologists expected to call positive), 2-3 border-line mitoses (2 to 8 out of 10 pathologists expected to call positive), and 2 -3 candidates that are unlikely to be mitoses (2 or fewer out of 10 pathologist call positive).

## Ongoing Single-Head Study

Some readers of the single-head study have also recorded the locations of the detected mitoses. These detected mitoses will be candidates in the high-throughput classification study.

## Mitosis detection algorithm

If a mitosis detection algorithm is available, this will be used to increase the number of candidate mitoses.

# Data Collection

Data collection will use a 14-head microscope. If reticle can be inserted in optical path, ROI will be visible to all participants. If reticle cannot be inserted in optical path, ROI will be visible on the paper CRF.

For each FOV:

* Readers count independently. They record their count and mark locations of mitoses on paper CRF. Number the locations according to confidence in consensus.
* For each (pre-determined) candidate mitosis in the ROI:
  + Readers determine if candidate is one he or she detected during counting.
  + Readers independently classify candidate as a mitosis or not.
  + Readers score candidate 0-100; 50 is cutoff for binary decision.
  + Group discussion of current candidate is led by expert, and a consensus binary decision and score is determined.
* Readers propose any additional candidates.

Possible layout of CRF.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| C:\000_whole_slides\halseyPilotImages\annotationsHE-ROIs-MSKCC\tempROI.tif | ROI:  # of mitoses:  Classification scores of mitosis candidates   |  |  | | --- | --- | | 1. | 6. | | 2. | 7. | | 3. | 8. | | 4. | 9. | | 5. | 10. | |
| C:\000_whole_slides\halseyPilotImages\annotationsHE-ROIs-MSKCC\tempROI.tif | ROI:  # of mitoses:  Classification scores of mitosis candidates   |  |  | | --- | --- | | 1. | 6. | | 2. | 7. | | 3. | 8. | | 4. | 9. | | 5. | 10. | |
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Possible layout of CRF where we are showing full FOV containing the ROI.

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| C:\000_whole_slides\halseyPilotImages\annotationsHE-ROIs-MSKCC\temp.tif | ROI:  # of mitoses:  Classification scores of mitosis candidates   |  |  | | --- | --- | | 1. | 6. | | 2. | 7. | | 3. | 8. | | 4. | 9. | | 5. | 10. | |
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