

Diagnosics of immune exclusion: Focus on histopathology

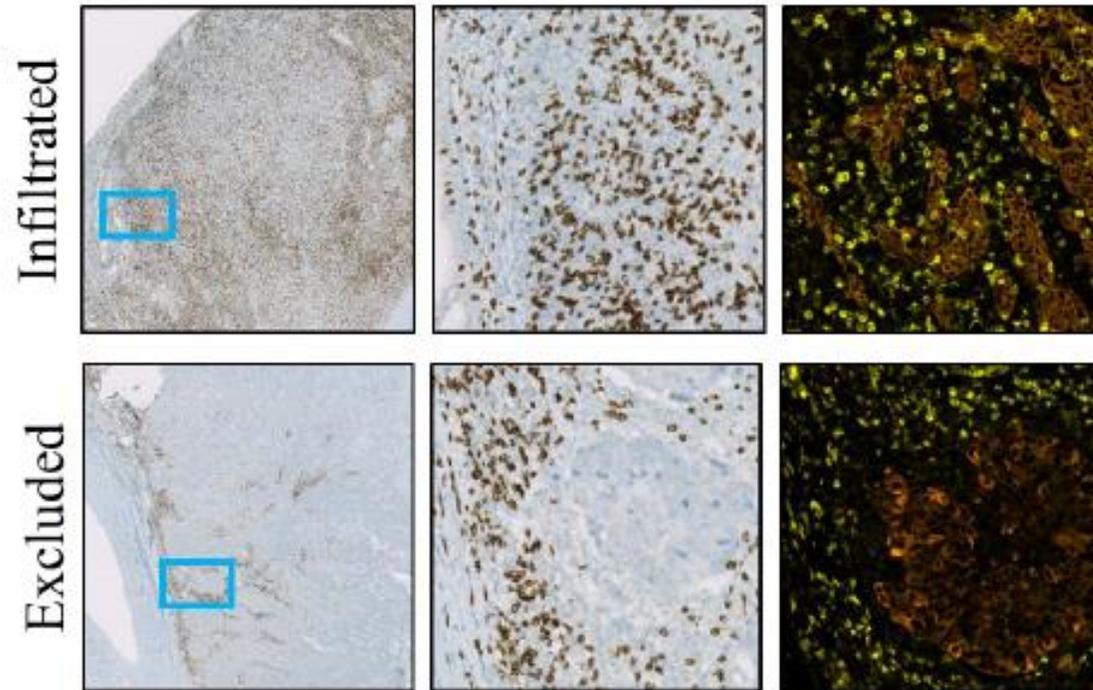
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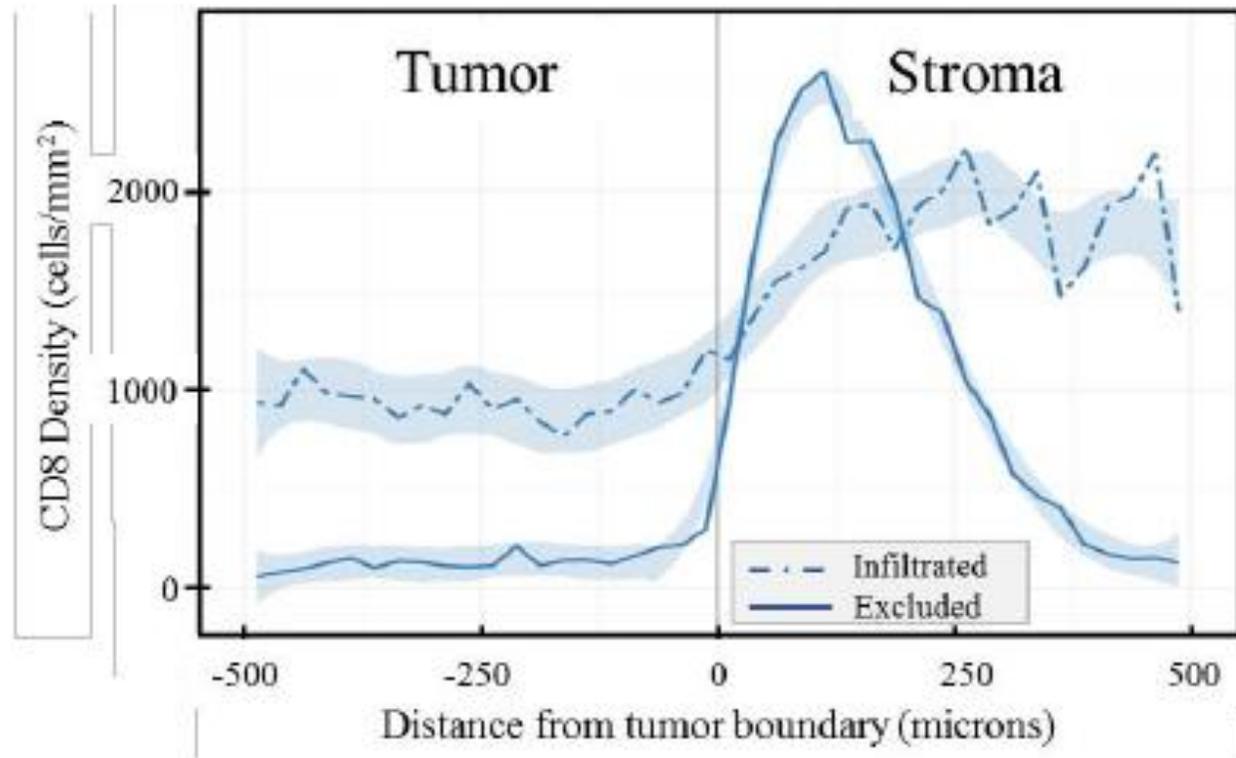
Immune infiltration and immune exclusion (two post-treatment tumor nodules from same NSCLC patient)

CD8 immunohistochemistry
(brown) highlights pattern of
infiltration vs. exclusion



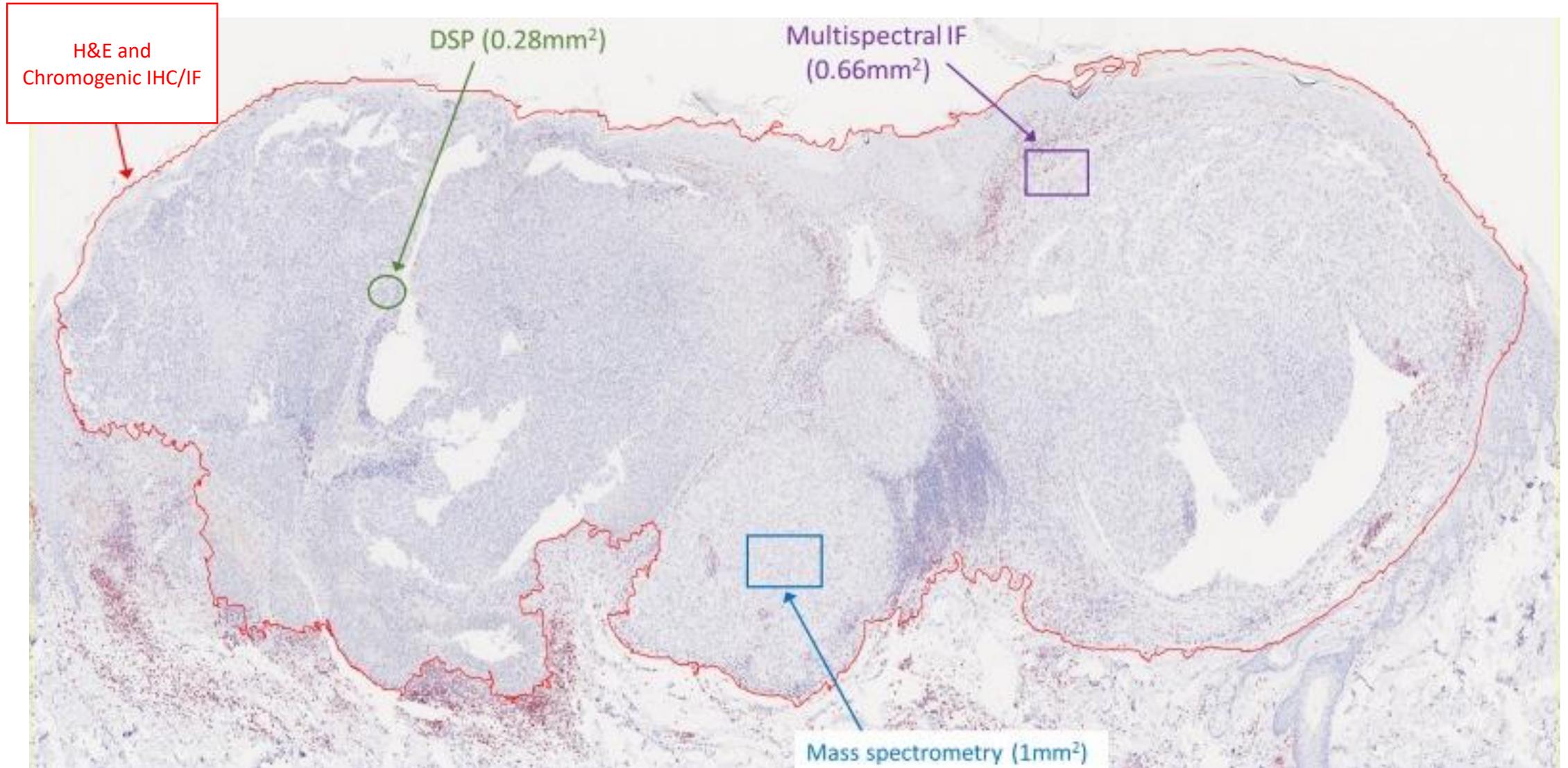
CD8 immunofluorescence
(yellow; tumor is orange)
highlights pattern of infiltration
vs. exclusion

Spatially-resolved digital quantification shows paucity of intratumoral CD8+ T-cells in the immune excluded tumor

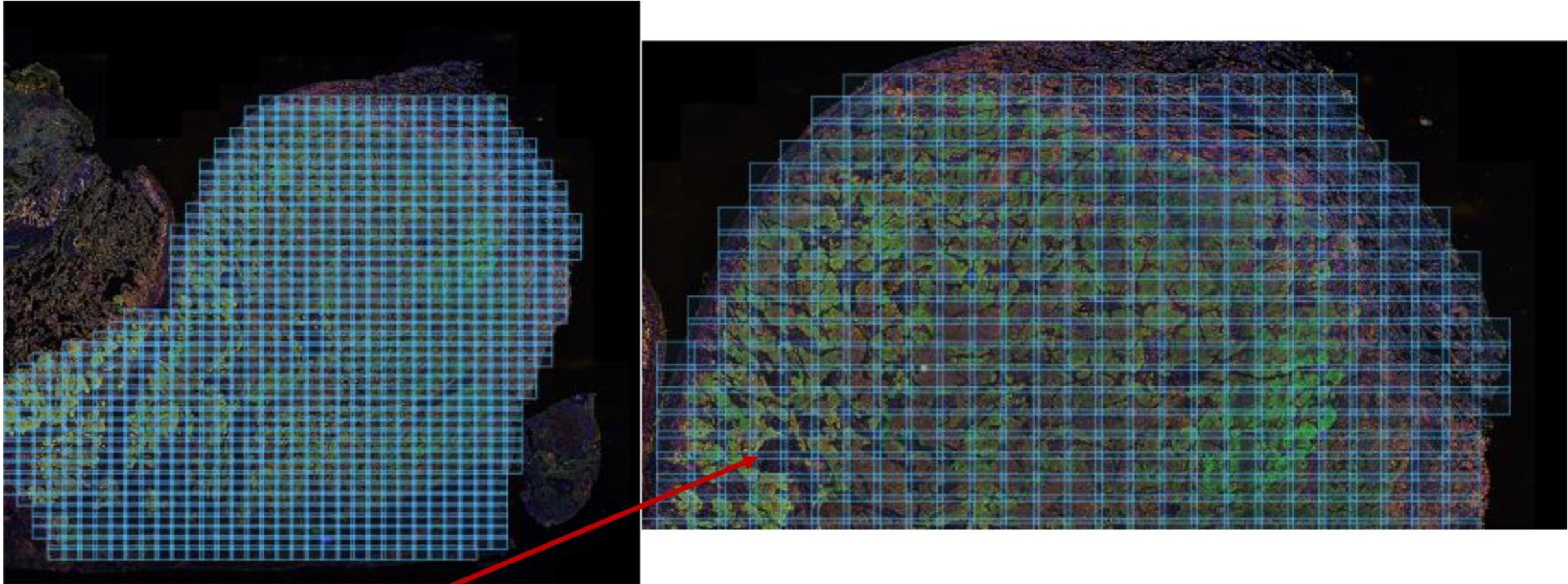


- Possibilities include a ratio, e.g. 10x difference between peritumoral CD8+ (or other cell type) densities and intratumoral densities
- Some studies have used samples characterized by IHC analysis to develop gene expression-based classifiers

Whole slide characterization is likely superior as consensus definitions are established

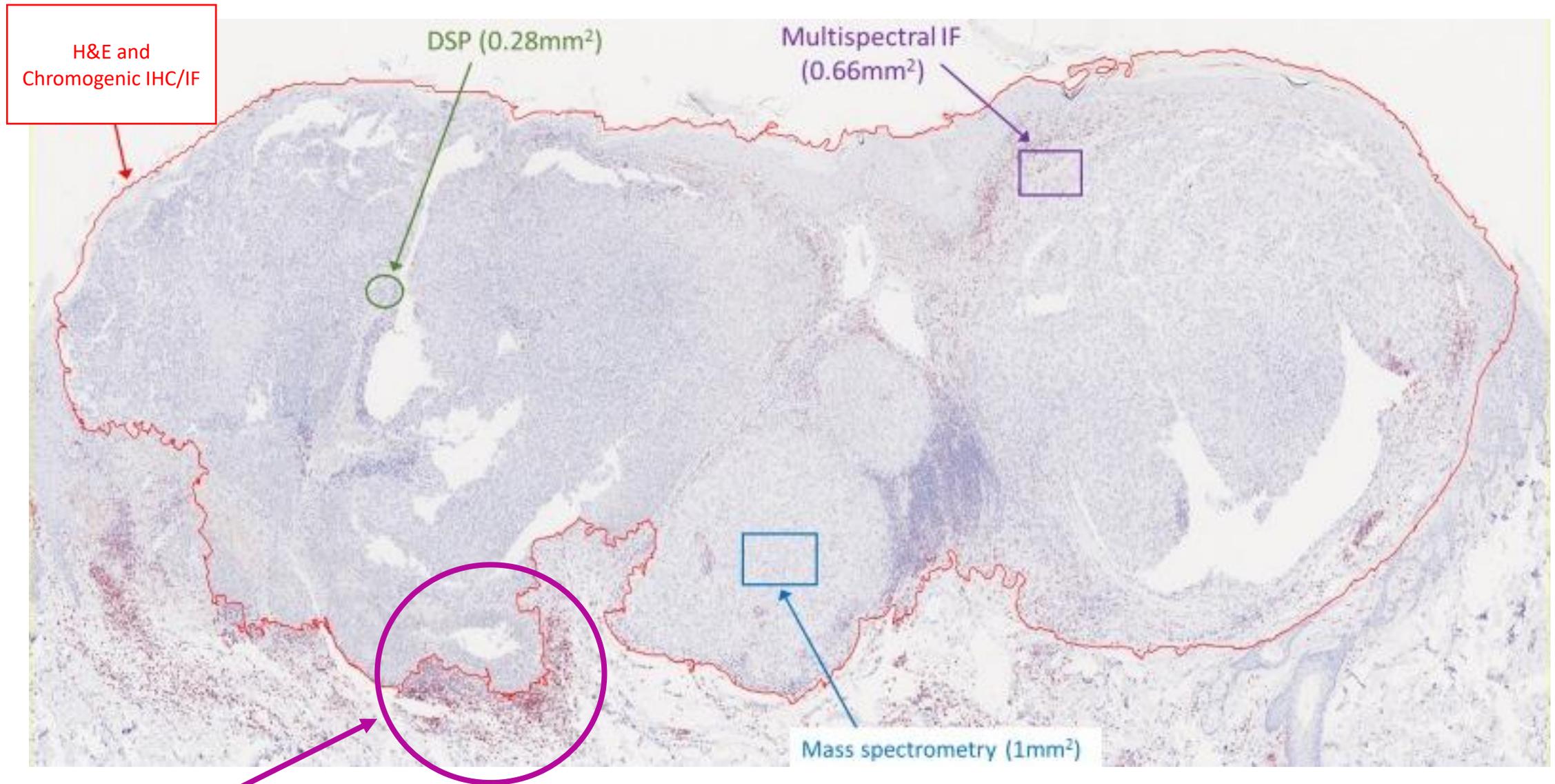


Whole slide imaging may be achieved through mIF, but mIF often does not equate to whole slide imaging (especially for higher plex technologies)



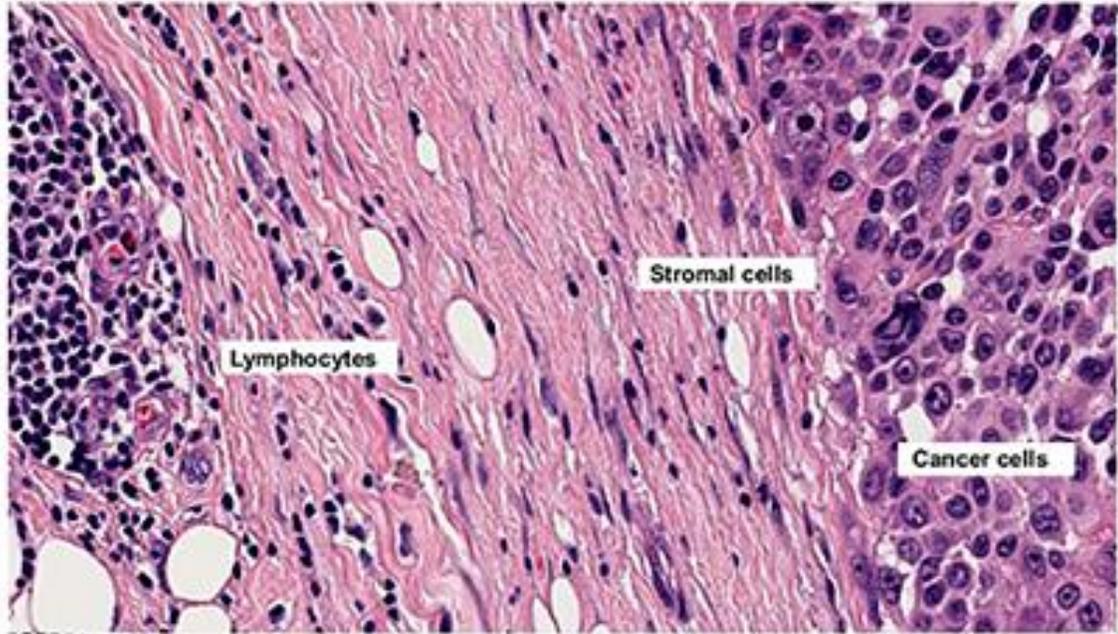
Each square= 1 HPF*

Whole slide characterization is likely superior as consensus definitions are established



Focus of immune exclusion

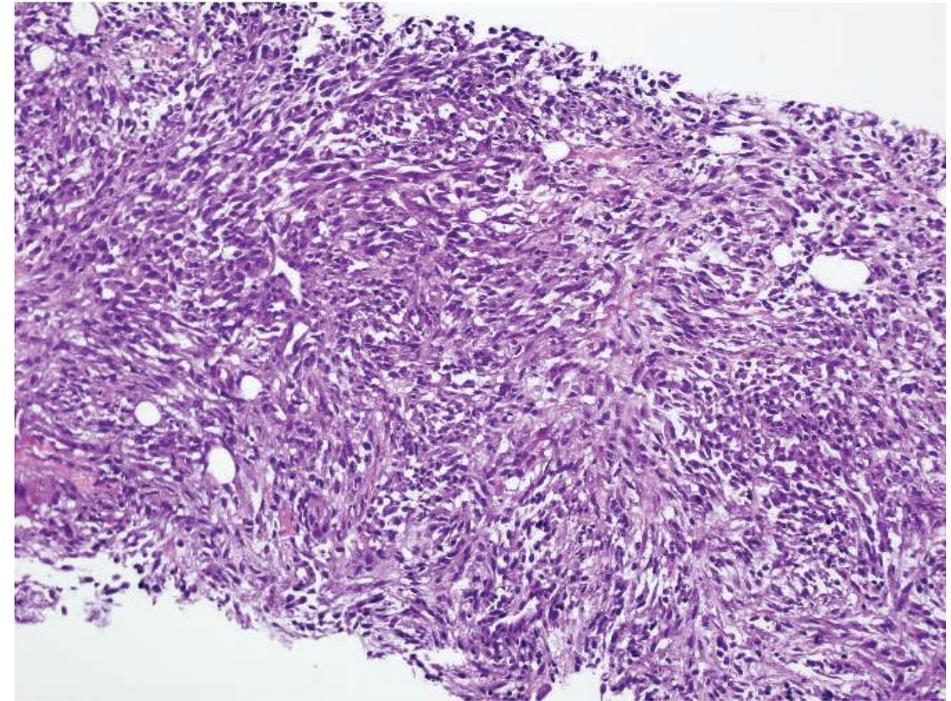
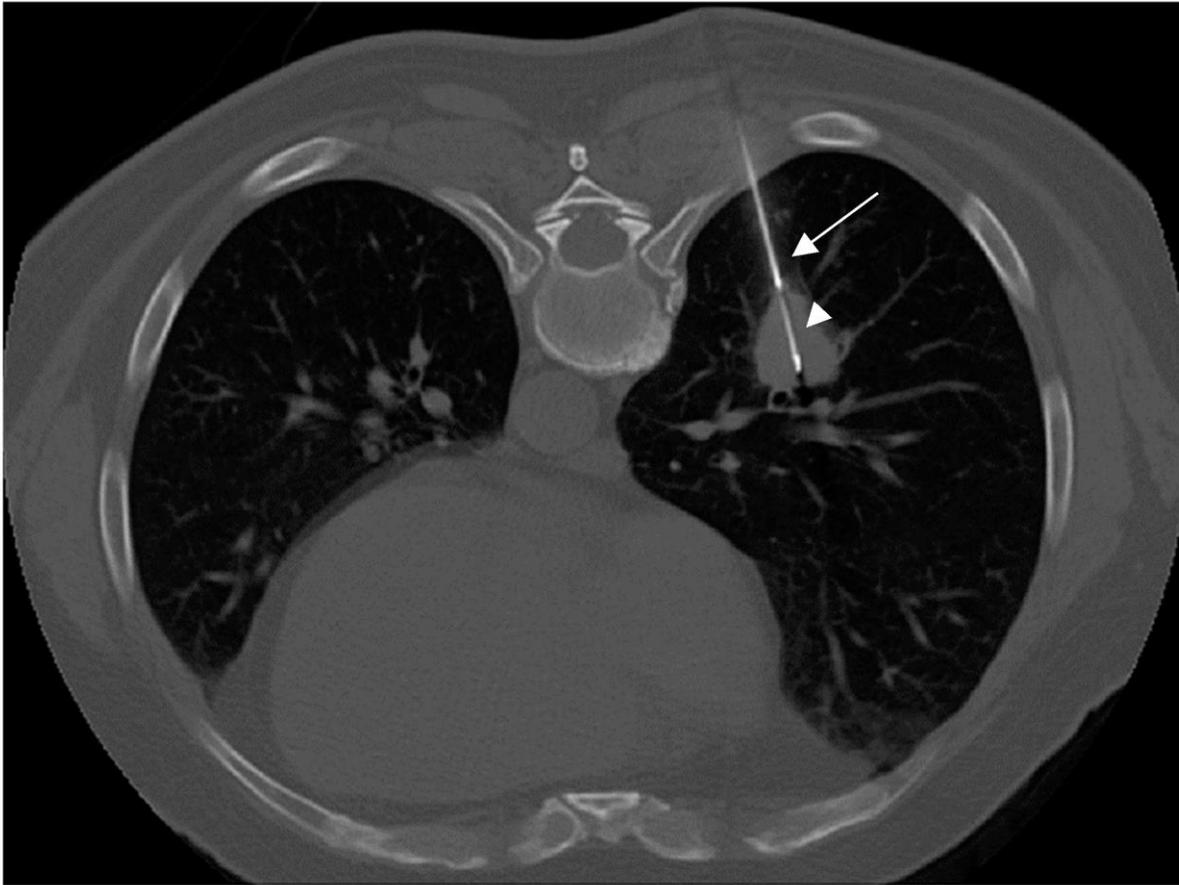
Classification may potentially be performed on H&E slides alone



1. Failmezger H, et al. *Cancer Res* 2020

- H&E stains are widely available and poised for inclusion in routine surgical pathology workflows.
- H&E analysis can be used to help differentiate between potential tumor-type specific patterns of immune exclusion.
- Automated morphologic cell classification on H&E sections: example showing a fibrotic stromal 'barrier' to lymphocyte infiltration.¹

Sampling – Core needle biopsies do not always capture the interface of tumor-peritumoral stroma



- Central aspect of tumor, with no interface with surrounding tissue
- Not immune infiltrated, but can not distinguish between immune desert vs. immune excluded

Deliberate sampling of this interface can be performed

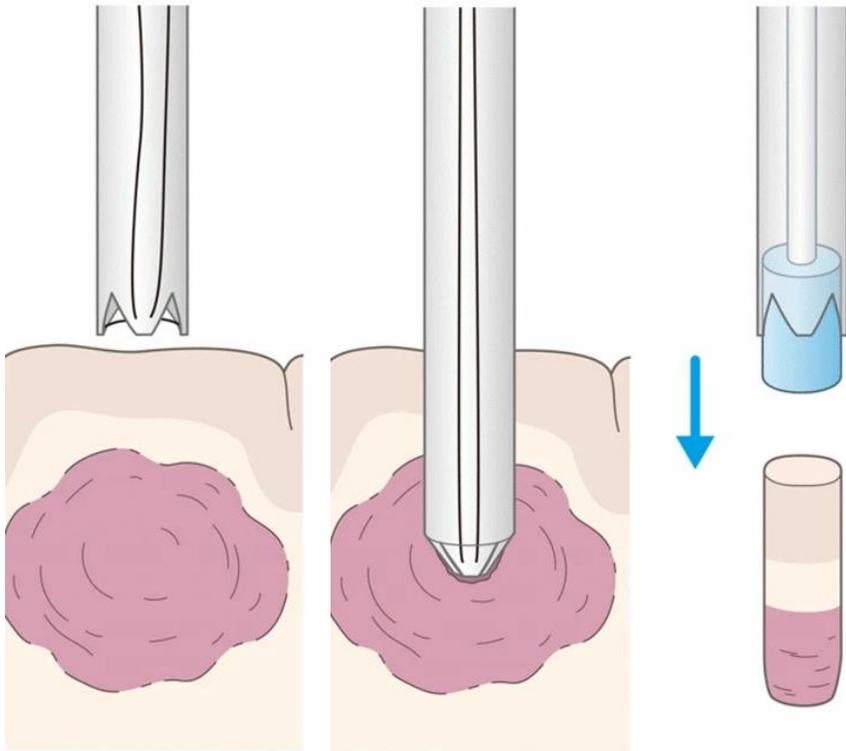
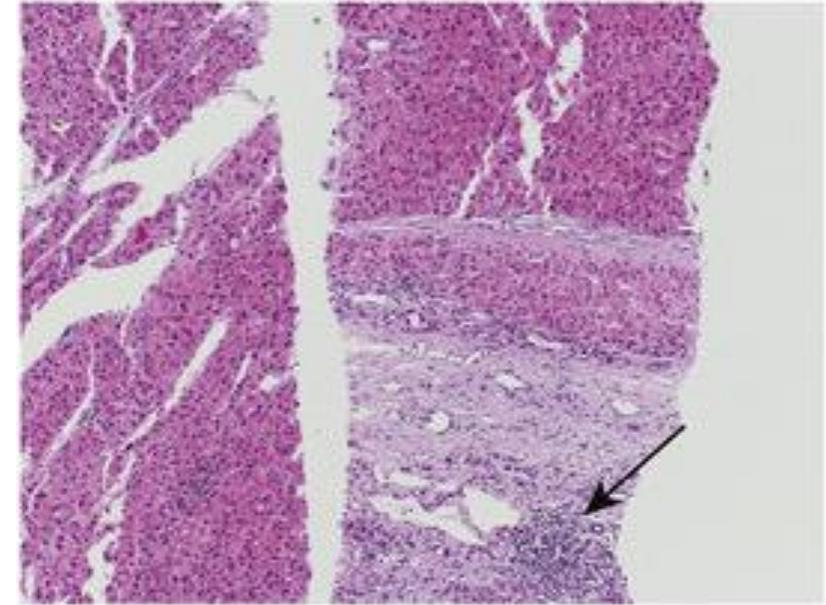


Figure modified from Ogiwara T, et al.
Sci Reports, 2022



Blasi DD, *Cell Mol Gastroenterol Hepatol*, 2020

- Discussions with teams performing biopsies may help ensure access to appropriate specimens to study
- For pre-existing material, histopathologic review of H&Es is recommended prior to bulk analysis of samples