5340 - Quantitative imaging and characterization of collagen patterns in high grade serous ovarian carcinoma (HGSOC)

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BACKGROUND

- HGSOC is known to demonstrate diverse molecular heterogeneity. It is unclear whether the tumor microenvironments such as the stromal components in the extracellular matrix (ECM) also exist heterogeneity.

METHODS

- As a proof-of concept study, characterization of collagen patterns was performed on 60 unstained formalin-fixed paraffin embedded (FFPE) HGSOC samples (three sections from each of the 20 patients).

- Each section with 5 micron thickness and a minimum tumour surface area of 40 mm2 were scanned by using a **multiphoton imaging system (Genesis 200, HistoIndex)** following deparaffinization.

- Parameters including Collagen Area Ratio (**CAR**), Collagen Fiber Density (**CFD**), Collagen Reticulation Index (**CRI**), Collagen Fiber Number (**CFN**), Collagen Fiber Thickness (**CFT**), and Collagen Fiber Length (**CFL**) were analysed (Clinnovate Health Pte Ltd). Unsupervised hierarchical clustering analysis was performed.
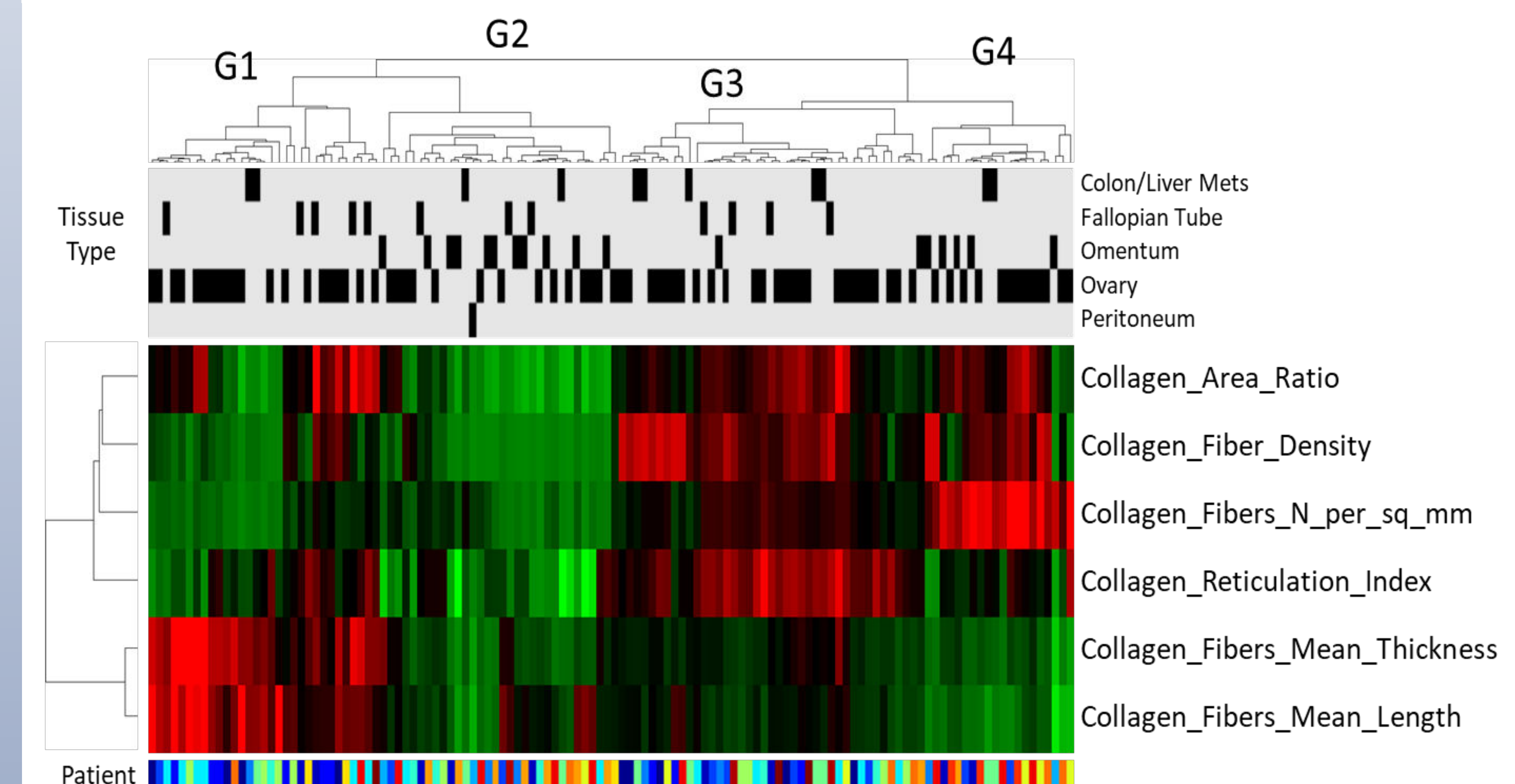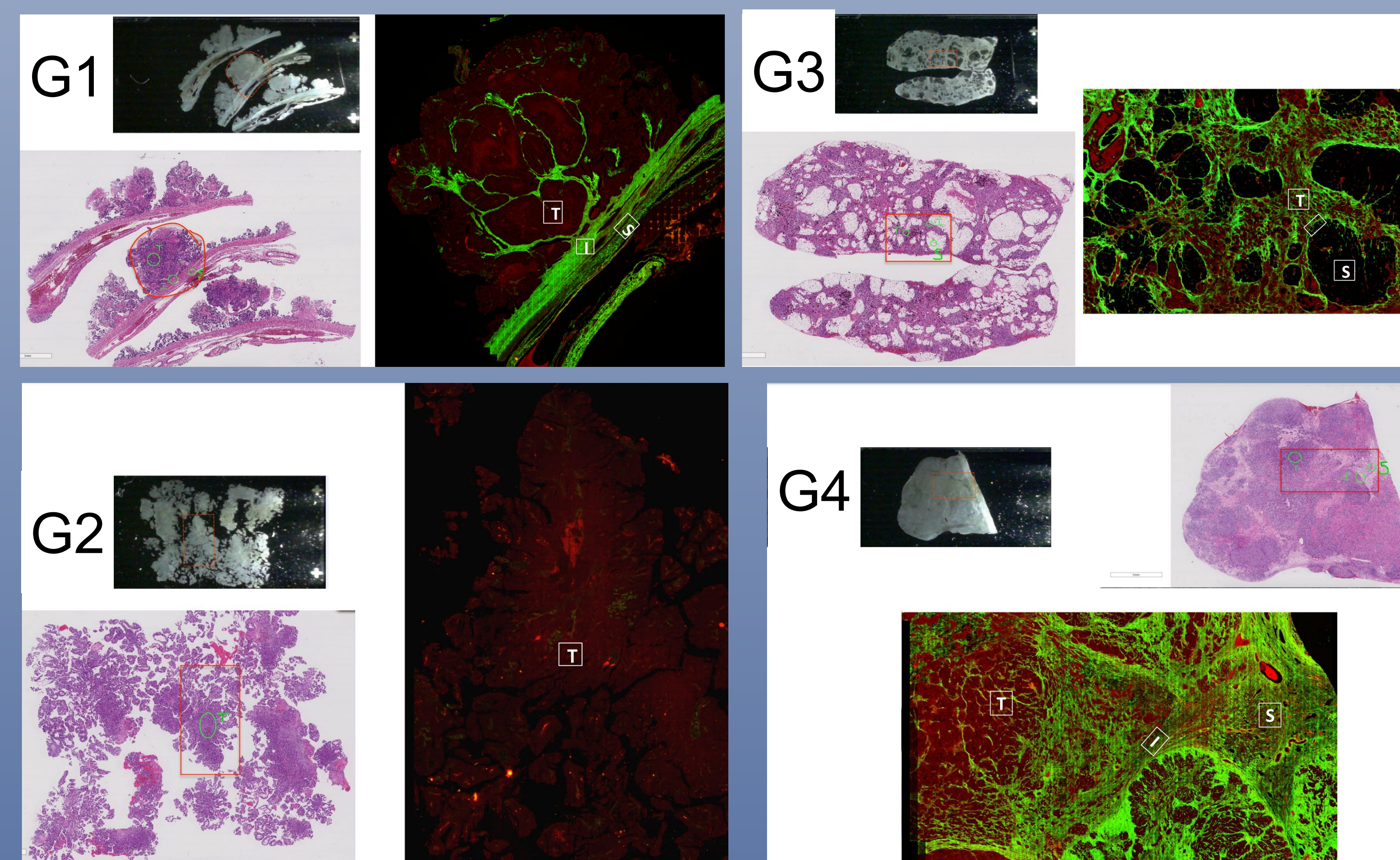
Unstained FFPE sections
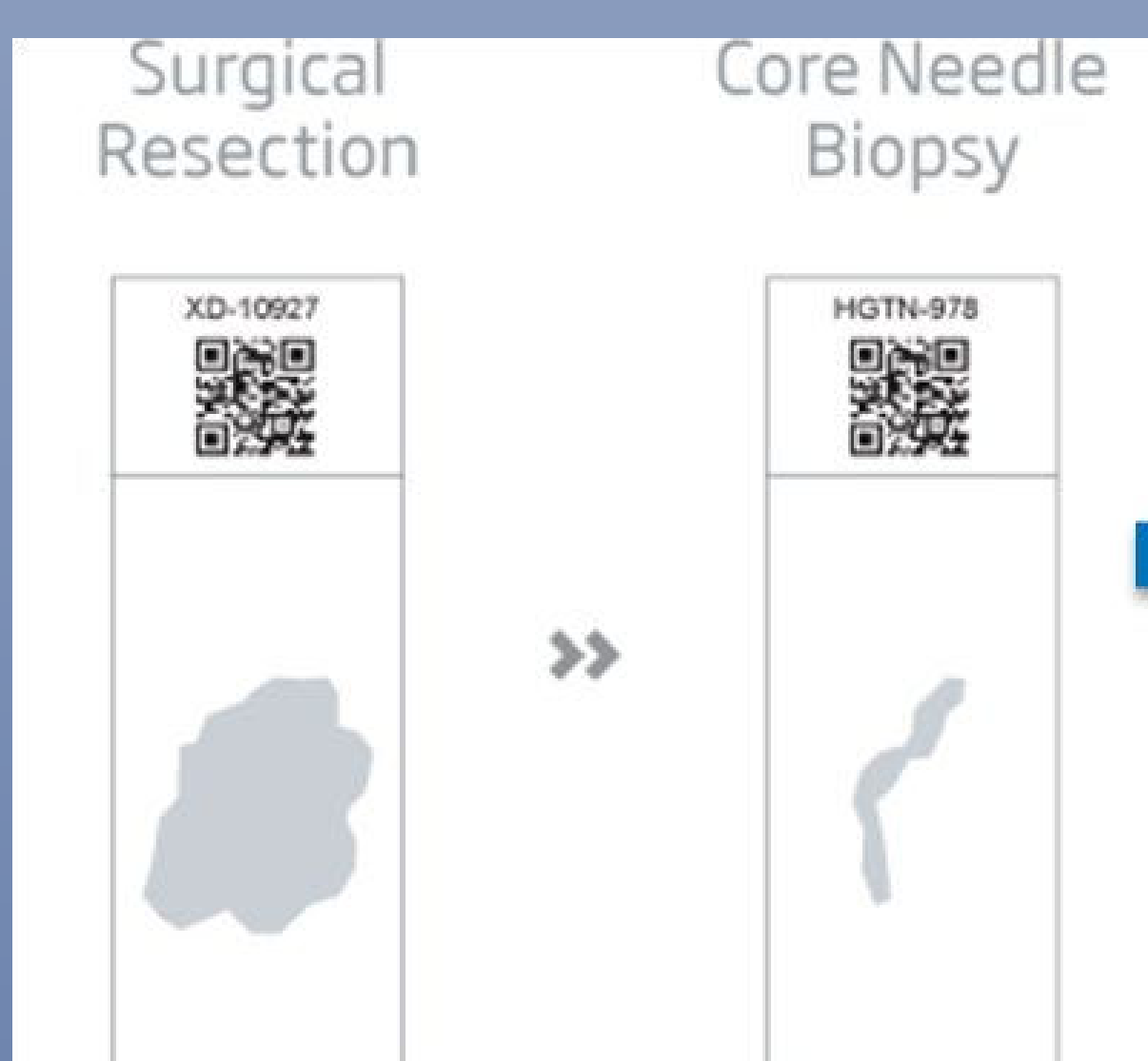
Stain-free ECM scanning

Image analysis

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RESULTS

Figure 1: Unsupervised Hierarchical Clustering

Heterogeneity in the collagen pattern within the ECM of HGSOC

- Unsupervised hierarchical clustering of the collagen parameters revealed **four distinct patterns** in HGSOC samples.

- G1 tumors consisted of long and thick collagen fibers with high CFT and CFL.

- G2 tumors were low in all the collagen parameters, suggesting a relatively "clean" stromal without collagen deposition.

- G3 tumors consisted of dense collagen fibers with high CRI suggestive of extensive cross alignment among the fibers.

- G4 tumors were high in CFN and low in CRI, CFT and CFL, suggesting a stroma loaded with high amount of thin and short collagen fibers without high cross alignment.

- The collagen patterns were not exclusive for specific organ sites (ovary, fallopian tube, other metastatic sites) except that the collagen pattern from the omental metastases were mainly G2 (10/18; 55.6%) and G4 (6/18; 33.3%).

CONCLUSION

- The stromal component in the ECM of HGSOC can be successfully quantitated by the multi-photon imaging technology on unstained FFPE sections. The collagen component exhibited significant heterogeneity in terms of the number, thickness, length, and reticulation patterns. The contribution of different collagen patterns to clinical outcomes and the correlation with known molecular subtypes in HGSOC warrants further investigation in larger cohorts.

ACKNOWLEDGEMENTS