Computational pathology reveals the association of collagen fiber architecture in both peritumoral and stromal areas with clinically relevant outcomes in high-grade serous ovarian carcinomas

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Background
Qualitative research suggests that collagen fiber architecture is associated with the prognosis of high-grade serous ovarian carcinomas (HGSOC), which account for the majority of ovarian malignancies and have a five-year overall survival (OS) rate of less than 50%. Here, we utilize computational techniques to develop a quantitative biomarker of collagen fiber architecture and evaluate its association with OS in patients undergoing primary debulking surgery.

Methods
Hematoxylin and Eosin (H&E) slides were obtained from 220 surgically-resected HGSOC cases from The Cancer Genome Atlas (TCGA) and University of Pittsburgh Medical Center (UPMC). These slides were divided into a training set (St, TCGA, n=102) and a validation set (Sv, UPMC, n=118). Each slide was divided into tumor neighborhoods, and a derivative-of-Gaussian-based model was used to detect fiber orientations within peritumoral and stromal regions. For each tumor neighborhood, we constructed an orientation co-occurrence matrix based on the identified fiber orientations. We computed the quantitative measurement of Collagen Fiber Orientation Disorder in the Peritumoral and Stromal regions using entropy theory from this matrix. First-order statistics (mean and maximum) were then extracted from feature maps for three different tumor neighborhood sizes, resulting in 12 features per patient. A Cox regression model was trained on St using these features to predict patient survival. Patients were stratified into low or high-risk groups based on the 33rd percentile risk score threshold established in St.

Results
These features were found to be associated with OS in both cohorts (St, HR= 2.16, 95% CI=1.35-3.45, p= 0.002 and Sv, HR= 1.56, 95% CI= 1.02-2.42, p= 0.04). Multivariable analysis controlling for prognostic clinical variables (Optimal debulking (Yes/No), HRD status (Yes/No), BRCA mutation status (Yes/No)) showed image-based features (HR=1.73, CI=1.09-2.7, p=0.02) were independently associated with OS in Sv.

Conclusion
Our findings indicate that the collagen fiber architecture is more ordered in patients with poorer OS. Validating these results across multiple sites independently could facilitate its use as a prognostic tool to support decision-making in managing patients with HGSOC.