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**Abstract citation ID: vdaf236.007**

**10189-CB-6**

## RAPID RAMAN DISCRIMINATION OF GLIOBLASTOMA EDEMA, INFILTRATION, AND ENHANCEMENT VIA SINGLE-CELL AND SPATIAL OMICS

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**Introduction:** In glioblastoma(GBM), extending resection beyond the contrast-enhancing margins on MRI to include infiltrative regions improves patients prognosis. However, objective biomarker to delineate tumor infiltration remain lacking. Raman spectroscopy rapidly provides label-free molecular information, making it a promising tool for intraoperative tumor boundary assessment. We investigated whether Raman spectra could distinguish edematous, infiltrative, and contrast-enhancing GBM regions and integrated single-cell Raman spectroscopy with spatial transcriptomics (Xenium) to elucidate molecular mechanisms of spectral variations. **Methods:** Seventeen GBM patients undergoing resection from June 2023 to March 2025 were enrolled. Navigation guided stereotactic sampling based on MRI yielded specimens from each areas; normal white matter from epilepsy surgery served as control. Tissue samples were analyzed using a Raman microscope with 532nm excitation, and spectral classification was performed via PCA and XGBoost. Single-cell suspensions were also prepared for Raman measurement and clustering. Spatial transcriptomic analysis (Xenium) was performed to validate the spectral findings. **Results:** We obtained 17 enhancing, 8 infiltrative, 7 edematous, and 11 control samples. Tissue-level spectra showed a significant increase in carotenoid peaks(1156, 1514cm-1) and a decrease in lipid peaks(1440, 1654cm-1) along the gradient from edema to infiltration to enhancement ($p < 0.05$). Five-fold cross-validation yielded classification accuracies of 96.7%(normal), 71.5%(edema), 81.5%(infiltration), and 93.0%(enhancement). Single-cell Raman analyses identified three major clusters: normal cells, tumor cells, and tumor-associated macrophages (TAMs). TAMs exhibited unique spectral profiles and contributed to tissue-level spectral differences. Spatial transcriptomics confirmed upregulation of lipid transport-related genes in TAMs, corroborating the spectroscopic findings. **Conclusion:** Raman spectroscopy enables accurate discrimination of edematous, infiltrative, and contrast-enhancing GBM regions at both tissue and single-cell levels. Integration with spatial transcriptomics revealed that TAM-mediated lipid metabolism underlies the observed spectral changes. This approach may facilitate intraoperative delineation of tumor margins and provides novel insights into the mechanisms of GBM infiltration.