

Graph Laplacian Transformer with Progressive Sampling for Prostate Cancer Grading

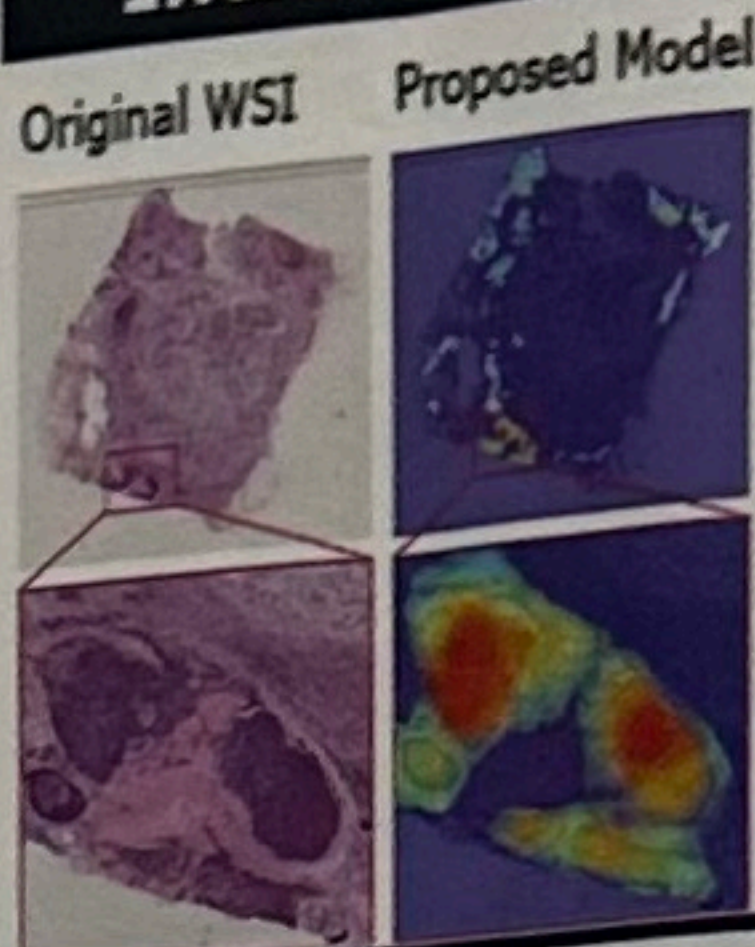
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Motivation and Challenges:

- Prostate cancer → 2nd leading cause of cancer deaths in men.
- Whole-Slide Images (WSIs) = high resolution but very large.
- Gleason grading → subjective & challenging due to:
- Tissue heterogeneity.
- Artifacts & staining variations.
- Disagreement between pathologists.

Goal: Build a robust, efficient, and spatially consistent WSI grading framework.

Introduction



Problem with Existing Approaches:

- Random/Static patch sampling → includes redundant or irrelevant regions.
- Attention-based MIL → struggles with non-informative patches.
- Correlation-based MIL → ignores spatial context → inconsistent grading.
- Graph-based models → computationally expensive, require high memory.
- Transformers → powerful, but discard critical tissue regions due to random patching.

Key Highlights:

- Patch Input: Whole-slide images (WSIs).
- Step 1 — IRM (Progressive Sampling):
 - Uses ResNet50 (Pretrained) + frozen foundation model (UNI).
 - Scores & iteratively refines patches → removes irrelevant regions.
- Step 2 — GLAT (Graph Laplacian Attention Transformer):
 - Models tissue-level connectivity using graph Laplacian constraints.
 - Preserves spatial coherence and histological structures.
- Step 3 — Convex Aggregation:
 - Learns dynamic patch weights → produces robust WSI-level embedding.
- Output: Accurate Gleason grade prediction.

Proposed Methods

Overview:

- Patch Extraction:** Divide WSIs into patches using CLAM + stain normalization.
- Iterative Refinement Module (IRM):** Start with all patches → score them → discard least relevant → refine selection.
- Graph Laplacian Attention Transformer (GLAT):** Captures spatial relationships among patches.
- Convex Aggregation:** Combines refined patch features into a WSI-level representation.
- Classification Head:** Predicts Gleason Grade.



Figure 1: Overview of the proposed prostate cancer grading model.

IRM

- Foundation Model (UNI, frozen) → assigns attention-based importance scores.
- Iterative Filtering → discard low-score patches → keep top M .
- Selected patches → forwarded to GLAT.

$$A_{ij} = \text{softmax} \left(\frac{Q_i K_j^T}{\sqrt{d_k}} \right),$$

$$Q_i = W_Q E_i, \quad K_j = W_K E_j$$

- A_{ij} : Attention score between patches i & j .
- Higher A_{ij} → prioritized in selection.
- Q_i, K_j : Query & key vectors derived from embeddings.
- W_Q, W_K : Learnable projection matrices.
- d_k : Key dimension for normalization.

- Selected patches from IRM → treated as graph nodes.
- Build graph edges based on patch similarity.
- Apply GLAT: Learns global context + enforces spatial coherence.
- Outputs refined embeddings → aggregated via Convex Aggregation → WSI-level representation.

GLAT

$$W_{ij} = \exp \left(- \frac{\|E'_i - E'_j\|^2}{2\sigma^2} \right)$$

$$A' = \text{softmax} \left(\frac{Q' K'^T + \lambda L_{\text{global}}}{\sqrt{d_k}} \right)$$

- W_{ij} : Similarity between patches i and j .
- E'_i, E'_j : Refined feature embeddings of patches.
- σ : Scaling parameter controlling sensitivity to distance.
- L_{global} : Graph-attention map, d_k : Dimension of key vectors.
- Q', K' : Query & key vectors after graph filtering.
- $L_{\text{global}} = D - W$: Graph Laplacian matrix.
- D : Degree matrix; and W : Adjacency matrix.
- λ : Weight controlling the contribution of spatial constraints.

Experimental Results

Dataset & Preprocessing

- Six datasets were used to validate the proposed method.
- Public (5): TCGA-PRAD, SICAPv2, GLEASON19, PANDA, and DiagSet.
- Private (1): 79 WSIs (UConn Health Center).
- Labels: ISUP grading (Grades 1-5; 1-2 ≈ normal, 3-5 malignant).
- Preprocessing:
 - CLAM pipeline for patching: stain normalization → tissue segmentation → patch extraction.
 - Patch size: 224x224; discard low-tissue patches; normalization to reduce staining variability.

Experimental Setup

- Hardware: NVIDIA RTX A6000 GPUs.
- Optimizer: Adam, LR = 1e-4, weight decay = 1e-5.
- Batch size: 16; 100 epochs max with early stopping (val-based).
- Augmentations: random flips & rotations.
- Metrics: AUC and Cohen's Kappa (CK).
- Reported as mean over 5-fold cross-validation for statistical reliability.
- Baselines reproduced from public code; hyperparameters aligned for fair comparison.

Results and Discussion

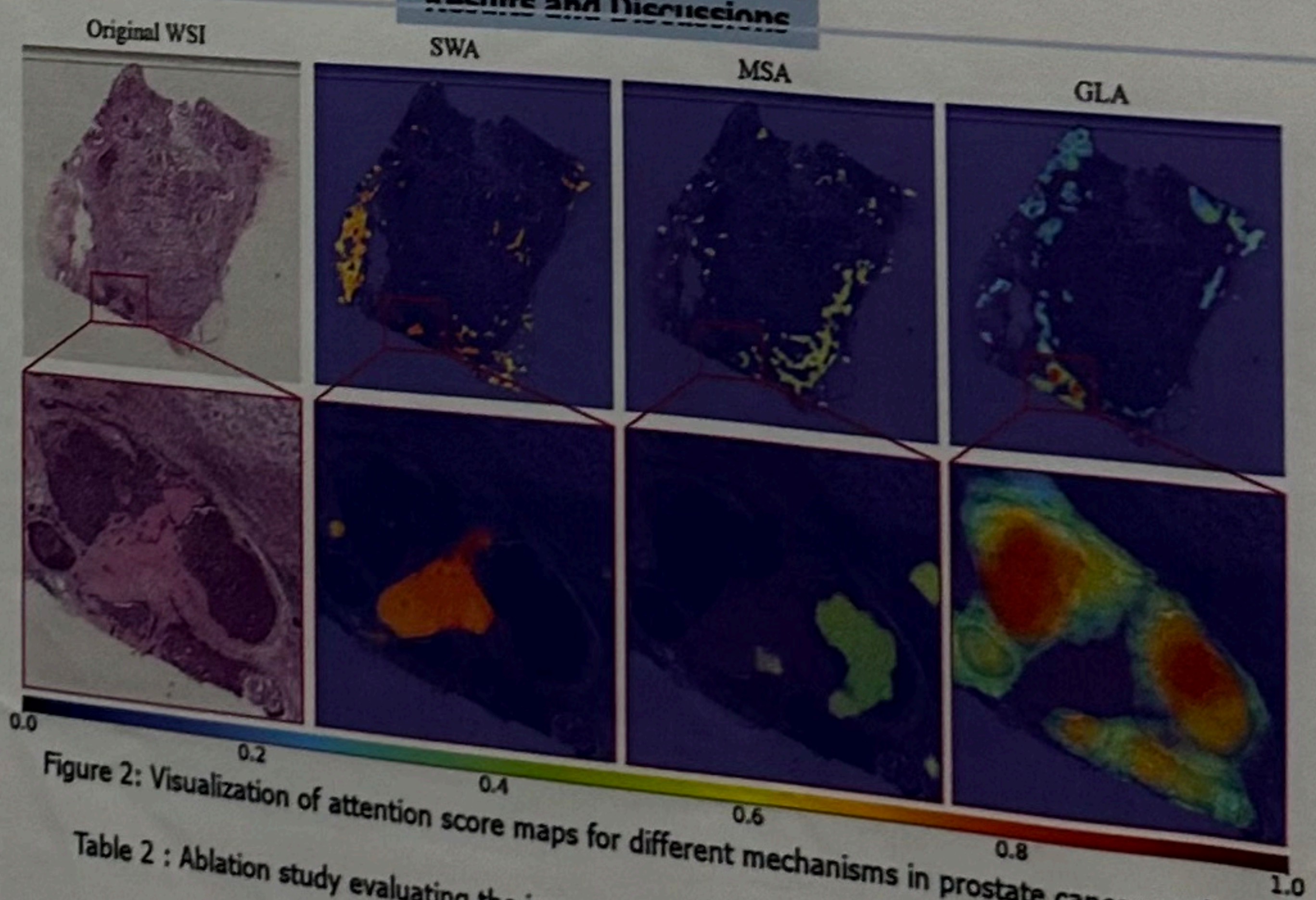


Figure 2: Visualization of attention score maps for different mechanisms in prostate cancer grading.

Table 1: Quantitative comparison of the proposed method against state-of-the-art approaches on six prostate cancer grading datasets. The best results are in bold, and the second-best results are underlined.

Dataset/Methods	SICAPv2		TCGA-PRAD		GLESON19		PANDA		Diagset		Private	
	AUC	CK	AUC	CK	AUC	CK	AUC	CK	AUC	CK	AUC	CK
ABMIL [20]	0.658	0.598	0.616	0.591	0.648	0.601	0.631	0.605	0.598	0.546	0.534	0.496
TranMIL [24]	0.593	0.567	0.587	0.538	0.612	0.582	0.605	0.580	0.535	0.486	0.481	0.437
MST [4]	0.918	0.796	0.863	0.792	0.839	0.810	0.895	0.851	0.720	0.679	0.679	0.609
DASML [5]	0.915	0.819	0.867	0.799	0.846	0.808	0.897	0.846	0.736	0.685	0.683	0.628
WSDMPC [2]	0.819	0.785	0.835	0.805	0.826	0.808	0.860	0.846	0.678	0.618	0.650	0.605
MaskIT [13]	0.938	0.868	0.909	0.856	0.887	0.853	0.922	0.901	0.785	0.724	0.746	0.701
SMAHM [14]	0.941	0.881	0.918	0.876	0.914	0.876	0.958	0.913	0.819	0.768	0.755	0.719
HEAT [6]	0.943	0.875	0.921	0.886	0.905	0.889	0.946	0.909	0.805	0.759	0.748	0.706
Proposed	0.951	0.892	0.923	0.885	0.913	0.892	0.963	0.936	0.836	0.791	0.781	0.731

Conclusions

- A novel approach combining iterative patch refinement and graph-aware transformers for accurate prostate cancer grading.
- IRM selects the most informative patches, while GLAT preserves spatial consistency and improves feature learning.
- Achieves superior AUC and Cohen's Kappa across six datasets, demonstrating strong generalization.

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