Collaborative Medical Vision for Precision Medicine: The Quest for Interpretable and Explainable ML Models

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AI-Informed Clinician

Clinician-Informed AI
Imperfect Data Scenarios where Clinician-AI collaboration is important

- Missing Modalities [MICCAI ’23, ICCV ’23]
- Costly Annotations [ICLR ’23, ECCV ’22, NeruIPS ’23]
- Scarcity of datasets [MICCAI ’23, IPMI ’23]
- Unpaired data [CVPR ’22]
- Complex Reasoning [CVPR ’24, MeDIA’24]
From purely data-driven models to...

Data-informed and domain-inspired models
Radiologist-in-the-Loop
Can Radiologists’ Eye Gaze Information Augment ML decisions?

Deep Learning based Analysis

Radiomic Analysis

Radiologist Eye-gaze maps

Shape
Texture
Tumor grading

COVID Normal
RadioTransformer: A Cascaded Global-Focal Transformer for Visual Attention–guided Disease Classification

Bhattacharya et al, MICCAI 2022, ECCV 2022
A global-focal transformer architecture to capture coarse-fine search behavior of radiologists.

Global module learns high-level coarse representations and the focal module learns low-level granular representations.
<table>
<thead>
<tr>
<th>Classification →</th>
<th>Pneumonia</th>
<th>COVID-19</th>
<th>14-Thoracic</th>
<th>COVID-19 (Test)</th>
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</thead>
<tbody>
<tr>
<td><strong>Dataset→</strong></td>
<td>F1</td>
<td>AUC</td>
<td>F1</td>
<td>AUC</td>
</tr>
<tr>
<td>R50 [18]</td>
<td>59.78</td>
<td>81.70</td>
<td>93.75</td>
<td>98.91</td>
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<td>R101 [18]</td>
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<td>91.97</td>
<td>98.57</td>
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<td>R50v2 [19]</td>
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<td>87.32</td>
<td>96.60</td>
<td>99.44</td>
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<td>R101v2 [19]</td>
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<td>71.23</td>
<td>96.39</td>
<td>99.33</td>
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<tr>
<td>R152v2 [19]</td>
<td>53.44</td>
<td>71.97</td>
<td>95.30</td>
<td>99.01</td>
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<td>88.86</td>
<td>95.60</td>
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<td>D201 [20]</td>
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<td>99.04</td>
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<td>ViT-B16 [12]</td>
<td>73.85</td>
<td>83.40</td>
<td>76.35</td>
<td>86.06</td>
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<td>90.74</td>
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<td>85.41</td>
<td>94.53</td>
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<td>87.07</td>
<td>69.32</td>
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<tr>
<td>CCT [17]</td>
<td>62.10</td>
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<td>80.60</td>
<td>92.04</td>
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<td>Swin0 [44]</td>
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<td>83.74</td>
<td>96.27</td>
<td>99.57</td>
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<td>Swin1 [44]</td>
<td>73.74</td>
<td>86.91</td>
<td>96.65</td>
<td>99.58</td>
</tr>
<tr>
<td><strong>RadT w/o (HVAT+VAL)</strong></td>
<td><strong>79.56</strong></td>
<td><strong>89.82</strong></td>
<td><strong>97.85</strong></td>
<td><strong>99.78</strong></td>
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<tr>
<td><strong>RadT</strong></td>
<td>77.40</td>
<td>88.80</td>
<td><strong>98.75</strong></td>
<td><strong>99.85</strong></td>
</tr>
</tbody>
</table>
Immunotherapy Response Prediction

Responder
N=139

Non-Responder
N=139

N=139
How do we use uncertainty estimation to efficiently obtain high fidelity segmentations?
Uncertainty estimation-driven interactive segmentation

Gupta et al., NeurIPS 2023
Pathologist-in-the-Loop
• Identifying salient regions in a WSI

• Several MIL methods provide the visualization of attention maps from the learned patch-level attention.

• Though useful, they may not offer an automated understanding of the model’s prediction due to a lack of user-friendly feature grounding.

• Also, these visualizations are hard and subjective for experts to interpret.
Whole slide image classification

Conventional MIL

Deep feature extractor

Morphometric and Spatial descriptors

Handcrafted features

SI-MIL

Handcrafted feature-level rationale

Tumor cellularity
Infiltration
Necrosis

class contribution

-ve
0
+ve
Proposed method – Self Interpretable Models

(a) WSI w/ heatmap
(b) Patch w/ nuclei map
(c) Feature-level interpretation
Contribution: $w_j \beta_j M_{ij}$
Distribution

1. $f_1$: Neoplastic cells: skewness of cells' intensity std
2. $f_2 & f_3$: Mixing of conn. cells in neoplastic cells' region
3. $f_4$: Skewness of cells' local max-entropy
4. $f_5$: Connective cells: skewness of cells' homogeneity
5. $f_6$: Graph modularity with cell types as community

Kapse et al, CVPR 2024
Text-conditioned image generation

Whole Slide Image

Patient Sample

Patches

VAE Encoder

VAE Decoder

U-Net denoiser

Cross Attention

CLIP Transformer

Embedding

GPT

Summary

Pathologist Report

Tumor classifier

High / Low Tumor

High / Low TIL

"high tumor; low tll, <summary>"

Yellapragada et al, WACV 2024
Extract information from breast pathology report. List the histological classification, i.e. type of cancer or DCIS, subtype, description of any necrosis, any mention of tumor infiltrating lymphocytes, histological grade, nuclear grade, lymphovascular invasion, calcification, receptor status, IHC and any other ancillary testing results. List out and expand the main points.

The report is:

Subtype LumA, Path No: Date Obtained: (Age: Date Received: F. See Addendum/Procedure. SPECIMEN: A: Lymph node, left axilla sentinel, biopsy. B: Breast, left, modified radical mastectomy. DIAGNOSIS(FS): A: Lymph node, left axilla sentinel, biopsy: ...
Metastatic carcinoma, following carcinoma of breast. B: Breast, left, modified radical mastectomy...

The breast pathology report indicates the following information:

1. Histological classification: The patient has Luminal A subtype breast cancer. The biopsy of the left axilla sentinel lymph node shows metastatic carcinoma following breast carcinoma.

2. Subtype: The invasive carcinoma is of the lobular type, poorly differentiated and multifocal, with extensive lymphatic permeation. Lobular neoplasia type B (pleomorphic), is widespread. The report also mentions fibrocystic disease, proliferative, with atypia.

3. Necrosis: No mention of necrosis.

4. Tumor infiltrating lymphocytes: The report mentions extensive lymphatic permeation but does not mention tumor infiltrating lymphocytes.

Please generate a succinct report in 75 words from the above information. Exclude any filler words or sentences. If something is not mentioned or specified, exclude it from the report. Low verbosity.

Report: Luminal A subtype breast cancer with metastatic carcinoma in axillary lymph nodes. Invasive carcinoma is of lobular type, poorly differentiated and multifocal, with extensive lymphatic permeation. Pleomorphic lobular neoplasia type B and cystic disease found. Nuclear grade 3, positive estrogen receptor and progesterone receptor expression with no Her-2/neu overexpression. Lymphovascular invasion present in lymphatics. No necrosis or tumor infiltrating lymphocytes mentioned.
Attention Diversity Matters!

Kapse et al. MedIA, 2024
Dataset Aggregation

<table>
<thead>
<tr>
<th>Clustering Output</th>
<th>Cluster 1</th>
<th>Cluster 2</th>
<th>Cluster 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>WSI ID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20%</td>
<td>45%</td>
<td>35%</td>
</tr>
<tr>
<td></td>
<td>5%</td>
<td>80%</td>
<td>15%</td>
</tr>
<tr>
<td></td>
<td>10%</td>
<td>10%</td>
<td>80%</td>
</tr>
</tbody>
</table>

- **WSI**
  - TCGA-S6-AB0Y-01Z-00-DX1
  - TCGA-CB-A1HH-02Z-00-DX1
  - TCGA-AC-ASX5-01Z-00-DX1

- **Baseline**
- **DiRL**

**ElasticNet_{CV15}**

- Survival Prediction
- Subtype Prediction
- Cluster Contribution

**Cluster interpretation**

**Patch Clustering**

**Patch Representation**

**Patch Quantification**
Pancreatic cancer - Basal

<table>
<thead>
<tr>
<th>Cluster</th>
<th>HR Beta</th>
<th>Subtype Beta</th>
<th>Description (Raj)</th>
<th>Parsed Description</th>
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</thead>
<tbody>
<tr>
<td>2</td>
<td>0.14</td>
<td>0.71</td>
<td>Stroma+Tumor</td>
<td>TME, Stroma+Tumor</td>
</tr>
<tr>
<td>13</td>
<td>0.11</td>
<td>0.29</td>
<td>Normal+Tumor</td>
<td>TME, Stroma+Tumor</td>
</tr>
<tr>
<td>4</td>
<td>0.07</td>
<td>0.25</td>
<td>Small dark nuclei</td>
<td>Small round black nuc</td>
</tr>
</tbody>
</table>
## Pancreatic cancer - Classical

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>0.06</td>
<td>-0.92</td>
<td>Desmoplastic stroma +/- tumor, TME, Stroma+Tumor</td>
</tr>
<tr>
<td>7</td>
<td>-0.03</td>
<td>-1.4</td>
<td>Bright pink</td>
</tr>
<tr>
<td>20</td>
<td>0.27</td>
<td>-2.93</td>
<td>Lymph</td>
</tr>
</tbody>
</table>

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ACKNOWLEDGEMENTS
Thank you

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