Explainable AI (xAI) in Computational Pathology

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In the past 12 months, I have had a significant financial interest or other relationship with the manufacturer(s) of the following product(s) or provider(s) of the following service(s) that will be discussed in my presentation.

SpIntellx, Inc. (co-founder with equity)
Objectives

• What is xAI
• Why is xAI important
• How to achieve xAI
• xAI-driven applications
Manual Digital Pathology

- Present manual approach is inefficient and is error prone
- High degree of discordance between pathologists
- Inefficient case triaging
Evolution of Digital Pathology to Intelligent Pathologist Assistants

Digital Pathology Imaging Platforms

Simple Image Analytics

Computational Pathology

Spatial Analytics, xAI and Computational Guides

Explainable AI (xAI) can explain its decisions in ways that people can understand
For Deep Learning, opening the black box is ... ‘far from trivial’ – Geoffrey Hinton (New Yorker, AI vs MD 2017, S Mukherjee)
Trust with Explainable AI (xAI)

- Why did you do that?
- Why not something else?
- When do you succeed?
- When do you fail?
- When can I trust you?
- How do I correct an error?

- I understand why
- I understand why not
- I know when you succeed
- I know when you fail
- I know when to trust you
- I know why you erred
xAI can address:

- Bias – catastrophic failures related to occult AI flaws
- Transparency – on-demand supervision
- Safety – result of the above in real-time, on individuals’ cases
- Causality – potential to understand and learn about underlying pathological basis of disease mechanisms
- Efficiency – improvement to manual microscopy
- Accuracy – guidance to pathologists’ diagnoses
- Trust – access to all information needed to make best diagnosis
xAI - HOW
Computational Pathology Pipeline

(A) Color normalization
- Source
- Target
- Matching color stats
- Normalized

(B) Ductal ROI segmentation
- Original image
- Superpixel decomposition
- Segmentation result

(C) Cytological phenotyping
- Masked segmented ROI
- Segmented nuclei masks
- Cytological phenotypes

(D) Architectural phenotyping
- Spatial network
- Architectural phenotypes

H&E Breast WSIs
Classifying benign lesions
High Risk
Low Risk
Computational Pathology Pipeline
xAI platform for Atypical Ductal Hyperplasia
Atypical Ductal Hyperplasia

Key Findings

- Strong Rigid Architecture
- Non-Hyperplastic
- Very high stromal density

**xAI interface for Pathologists – “Why?” button**
xAI Features with Pathologist-Friendly labels
xAI feedback display for transparency

**HistoMapr Suggested Label:** Atypical Ductal Hyperplasia (ADH)

**Confidence Level:** 0.5

**Justification:** Ambiguous but favor Atypical (Click for Consult)

Rigid Architecture: Mild

Monomorphic: Mixed Pattern Hi/Lo

Atypical Stroma: Low

Mixed pattern: Mostly Usual Ductal Hyperplasia (UDH)
EXAMPLE xAI APPLICATIONS
Bridge App: Difficulty-based Specimen Triage

1. **HistoMapr Preview of a Case**
   - **Critical Finding?**
     - **Yes** → Forward Case to STAT/Rush Pathologist
     - **No** → **Confidence Level Indicates Difficult Case?**
       - **Yes** → Forward Case to Subspecialist Expert
       - **No** → Assign Workload Estimate Score

2. **Load Balanced Pool of Pathologists**
Example: Content Based Image Retrieval, matched for Difficulty/Content

Key Findings
- Strong Rigid Architecture
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- Very high stromal density

Reference ROIs
- ROIs from previous cases that carry similar features with ROI in question.

ADH

ADH

Why?

ADH

Agree  Disagree  Not Sure  Finalize
**xAI - Numerous Applications in Pathology**

**ROI Quantification:**
- ROI Detection
- ROI Segmentation
- Spatial Statistics
- Cell and Structure Phenotyping

- Explainable Feature Extraction
- ROI Classification
- ROI Labeling
- ROI & Feature Matching

**Explainable Interface**
Suggested Diagnosis Label and Confidence Score

**Content-based Activities**
Decision Support with Similar ROIs

**Quality Assurance**
Standardized Terminology for Diagnosis Labels & Patient Safety with Realtime Diagnostic Surveillance
Spatial Intelligence Guides Clinical Decisions and Informs Therapeutic Strategies

Current State of the Art
Hyperplexed Image Analytics

A. Patient Cohort

B. Hyperplexed Fluorescence Imaging

1 mm
TMA / Whole Slide Images

C. Simple Analytics (Count / Measure)

Imaging modalities including but not limited to
- Transmitted Light (H&E + IHC)
- Fluorescence
- Mass-Spectrometry
- Spatial Transcriptomics
TumorMapr with xAI Enables Precision Oncology

D. Identify Tumor Microdomains

E. Infer Tumor Microdomain Network Biology

F. Develop Diagnostics / Prognostics
CRC Cohort
Stages I – III
N = 432 chemo-naïve

G. Inform Therapeutic Strategies
xAI Conclusions

• Computational Pathology is here and it can help pathologists
• Steep Trust Curve must be climbed
• Initially, xAI is a powerful method to build trust, triage cases and ensure safety through bridge applications
• In the Future is the potential to guide to pathologists’ diagnoses
• xAI will also enable more powerful advanced analytics via hyperplexed image data sets
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Links and References

Pipelines
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Nguyen L, et al – ISBI 2017 PMID

Computer assisted diagnosis (pCAD)
Farahani N, et al – Arch Pathol Lab Med 2017 PMID
FINE JL – J Pathol Inform 2016 PMID

xAI
Whitepaper on SpIntellx website (spintellx.com)