Explainable Artificial Intelligence (xAI) for Safe Breast Core Biopsy Diagnosis Support

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BACKGROUND

Computational pathology has great potential for augmenting the accuracy and efficiency of Pathologists. Explainable AI (xAI) is a new computational approach that can justify its results to pathologists, to promote safety, reliability and accountability of machine learning for critical pathology tasks. Ground truth data labeling is necessary for machine learning training but has historically been a bottleneck. The best-qualified pathologists are often busy with clinical work, and a major challenge has been creating efficient image annotation tools that they can easily use. Herein we report the initial phase of a validation study of a proprietary xAI platform for whole slide images (WSIs), HistoMapr-Breast (HMB) [1].

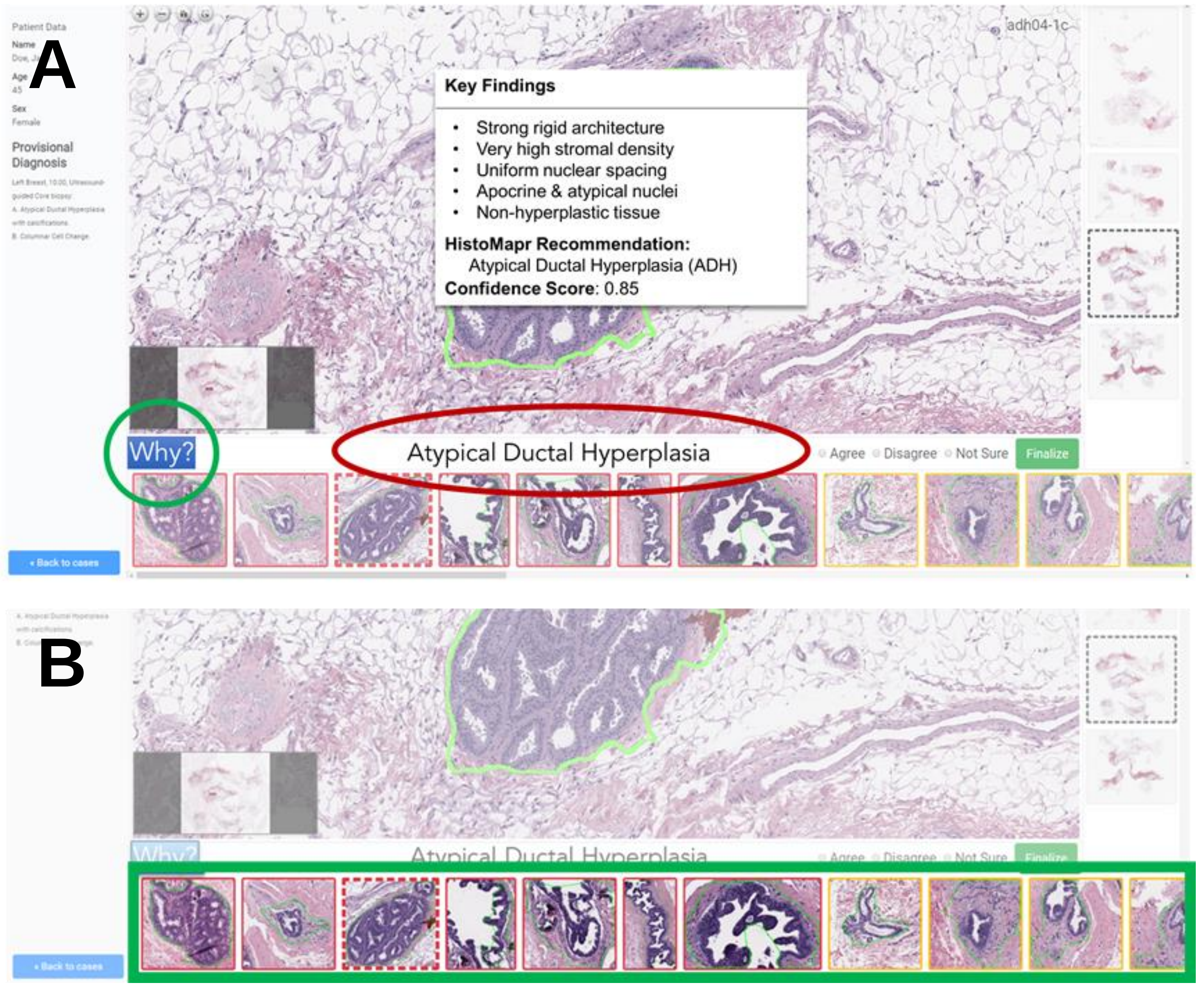
Table 1: Remapping diagnostic subcategories to 4 main diagnostic labels.

Invasive carcinoma	**Invasive/Infiltrating ductal carcinoma**
	Invasive/Infiltrating lobular carcinoma
	Invasive/Infiltrating mammary carcinoma
Ductal carcinoma in-situ (DCIS)	**Ductal carcinoma in-situ (DCIS)**
	Solid papillary carcinoma
	Encapsulated papillary carcinoma
High-risk	**Atypical ductal hyperplasia (ADH)**
	Atypical lobular hyperplasia (ALH)
	Lobular carcinoma in-situ (LCIS)
	Flat epithelial atypia (FEA)
	Atypical vascular lesion/proliferation
	Intraductal papilloma
	Radial scar
	Complex/radial sclerosing lesion
	Phyllodes
	Fibroepithelial
Low-risk/Benign	**Fibroadenoma**
	Fibrocystic changes
	Ductal epithelial hyperplasia
	Columnar cell changes and hyperplasia
	Sclerotic adenosis
	Pseudo angiomatous stromal hyperplasia (PASH)
	Apocrine metaplasia
	Benign / unremarkable / normal

This study was partially supported by NSF SBIR Phase I Award #1843825 to SpIntellx, Inc. in collaboration with the University of Pittsburgh.

DESIGN

With IRB approval, 1931 de-identified WSIs of breast core biopsies (n=862 cases) were scanned at 0.5 microns per pixel (ScanScope AT2, Leica Biosystems, Buffalo Grove IL). Breast duct regions of interest (ROIs) were spatially extracted from the WSIs using pointwise mutual information maps (~80,000 ROIs segmented). Further computational pipelines were used to generate diagnostically explainable features then classify the ducts into diagnostic categories: invasive carcinoma, ductal carcinoma in situ (DCIS), high-risk and low-risk (see Table 1). Three expert breast pathologists labeled 4500 ROIs using a novel annotation tool from SpIntellx (Figure 2).



Key Findings

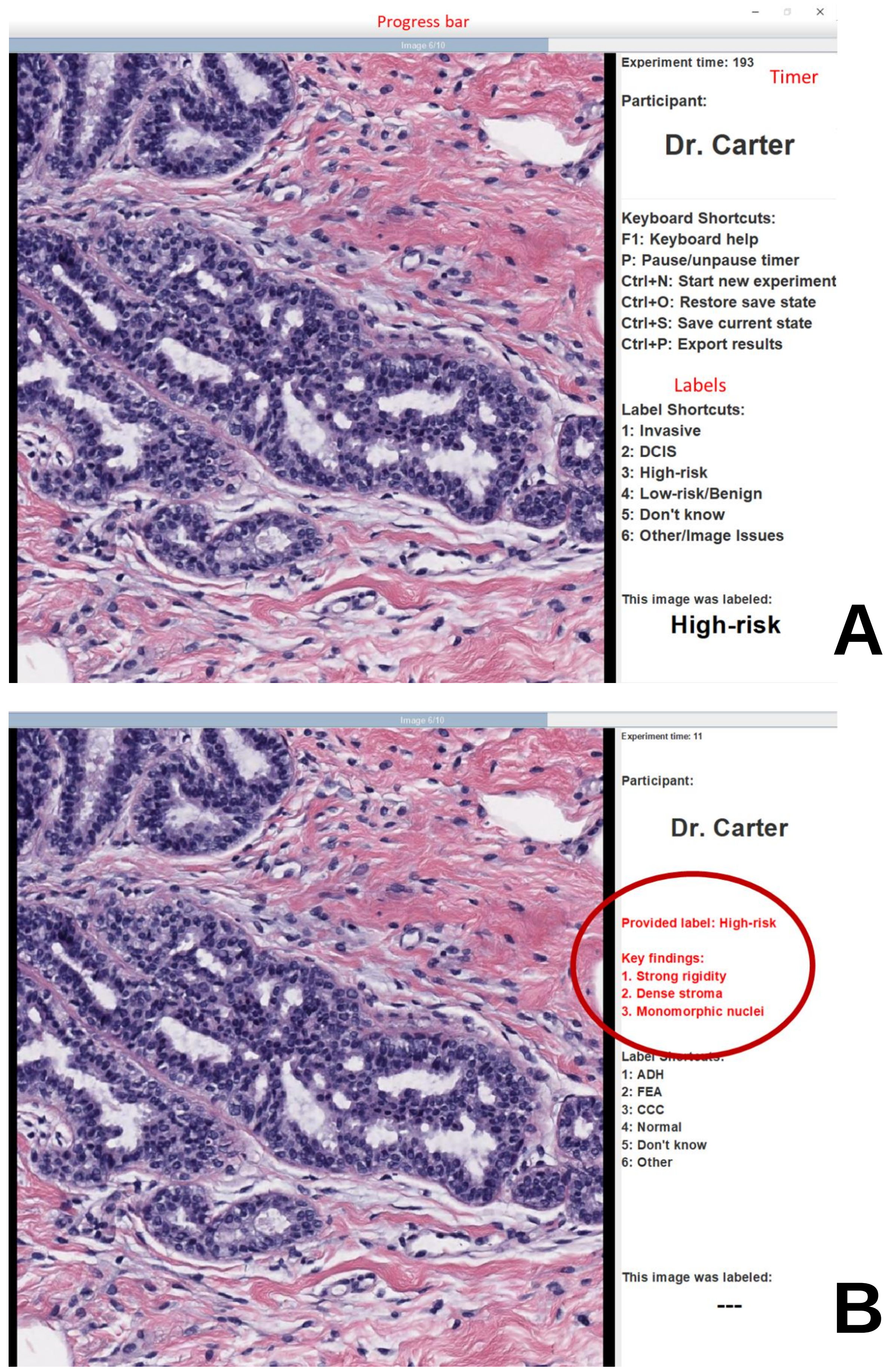
- Strong rigid architecture
- Very high stromal density
- Uniform nuclear spacing
- Apocrine & atypical nuclei
- Non-hyperplastic tissue

HistoMapr Recommendation: Atypical Ductal Hyperplasia (ADH)
Confidence Score: 0.85

Atypical Ductal Hyperplasia

Figure 1 – A) HMB xAI interface with **"Why?"** button. Left panel shows patient information and provisional diagnosis and the right panel has thumbnail images of the patient slides. **B)** ROIs are automatically detected and presented in the bottom panel, triaged based on diagnostic significance from left to right. In this example, HMB analyzed the slide and recommended the diagnosis of atypical ductal hyperplasia, which is a challenging call. Pathologist can hit the "Why?" button to let HMB display explanation as Key Findings that led to this recommendation.

xAI interface (HMB) designed to have a "Why?" button on the graphical user interface (GUI) to allow for the machine learning algorithm to present supporting evidence for the decisions made by HMB for any given ROI (Figure 1).



Experiment time: 193
Participant: Dr. Carter

Keyboard Shortcuts:
F1: Keyboard help
P: Pause/unpause timer
Ctrl+N: Start new experiment
Ctrl+O: Restore save state
Ctrl+S: Save current state
Ctrl+P: Export results

Label Shortcuts:
1: Invasive
2: DCIS
3: High-risk
4: Low-risk/Benign
5: Don't know
6: Other/Image Issues

This image was labeled: High-risk

Experiment time: 11
Participant: Dr. Carter

Provided label: High-risk

Key findings:
1. Strong rigidity
2. Dense stroma
3. Monomorphic nuclei

Label Shortcuts:
1: ADH
2: FEA
3: CCC
4: Normal
5: Don't know
6: Other

This image was labeled: ---

Figure 2 – A) Rapid annotation tool interface, allowing pathologists to go through HistoMapr detected ROIs and to label the ROI using keyboard shortcuts. The field of view in the interface is centered around the ROI. **B) xAI enhanced** annotator GUI for testing the effect of HMB's xAI outputs on improving diagnostic accuracy. HMB's provided label is given together with the key findings (explainable features) in right panel (circled in red), to assist the participant during annotation.

RESULTS

ROI labeling by experts was rapid and completed in 15-20 minute sessions each for 250 images (Figure 2A), yielding diagnostic labels for 4462 ROIs. There was complete concordance for 3172 ROIs (71%) among experts, including 650 invasive carcinomas, 132 DCIS, 200 High-risk and 2190 low-risk diagnoses. Fleiss' (overall) kappa for experts was K=0.6613, showing a substantial agreement. All 3 experts and 2 fellows were asked to label an additional 1,077 ROIs using a new xAI with enhanced annotator tool (Figure 2B). Expert concordance improved as the Fleiss' kappa increased to κ=0.75. The training fellows' performance significantly improved with the assistance of HMB xAI from 67% to 91% overall accuracy (see Table 2, note the improvement on high-risk benign assessments).

Table 2: Performance of clinical fellow (training) pathologists on diagnosing 1,077 ROIs (test set)

	Overall Accuracy (%)	Invasive Sensitivity (%)	DCIS Sensitivity (%)	High-risk Sensitivity (%)	Low-risk Sensitivity (%)
Mean ± Std dev. Not using HMB	66.6 ± 6.8	83.6 ± 12.5	76.3 ± 2.7	26.7 ± 22.5	72.0 ± 11.3
Mean ± Std dev. Using HMB	91.1 ± 3.6	96.7 ± 1.3	91.4 ± 0.5	78.5 ± 13.8	95.7 ± 1.5

CONCLUSION

Computational pathology can revolutionize pathology practice, enabling pathologists to make critical decisions that only they can make and delegating tasks that can be automated. xAI is an important new technology that gives pathologists unparalleled situational awareness, providing for trust and confidence. Building such systems requires user-friendly and high-throughput ground truth image annotation, as outlined in this study. The workflow developed here is similar to what can be used for computer-assisted diagnosis, and therefore is also useful for developing diagnostic xAI tools.

REFERENCES: [1] Tosun, A B.; Pullara, F; Becich, M.J.; Taylor, D.L; Fine, J.L.; Chennubhotla, S.C. "Explainable AI (xAI) for Anatomic Pathology", Advances in Anatomic Pathology, 2020, Accepted for Publication.