The First AI Algorithm in Pathology

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INDUSTRY PERSPECTIVE
DECISION SUMMARY SCOPE AND GOAL

Decision Summary is a high-level output from a much larger submission effort:

- ~2000 pages of documentation submission throughout its review

Its main goal is to:

- Provide key details to the predicate device manufacturers to establish fundamentals, but also reserve specific details to encourage the industry to engage with the FDA to fine-tune device functionality and study designs etc. appropriate to the device indication/intended use

INDUSTRY PERSPECTIVE

DECISION SUMMARY KEY COMPONENTS

1. Intended Use/Indications for Use

- Locks the intended use, and requires device manufacturer to work with FDA to review for certain modifications
- In pathology, this is specifically true for the tissue type, device output, compatibility (scanner & image viewer), use setting (diagnostic aid).

2. Development Dataset Distribution and Its Diversity

Indications for use:

Paige Prostate is a software only device intended to assist pathologists in the detection of foci that are suspicious for cancer during the review of scanned whole slide images (WSI) from prostate needle biopsies prepared from hematoxylin & eosin (H&E) stained formalin-fixed paraffin embedded (FFPE) tissue. After initial diagnostic review of the WSI by the pathologist, if Paige Prostate detects tissue morphology suspicious for cancer, it provides coordinates (X,Y) on a single location on the image with the highest likelihood of having cancer for further review by the pathologist.

Paige Prostate is intended to be used with slide images digitized with Philips Ultra Fast Scanner and visualized with Paige FullFocus WSI viewing software.

Paige Prostate is an adjunctive computer-assisted methodology and its output should not be used as the primary diagnosis. Pathologists should only use Paige Prostate in conjunction with their complete standard of care evaluation of the slide image.

tissue

output

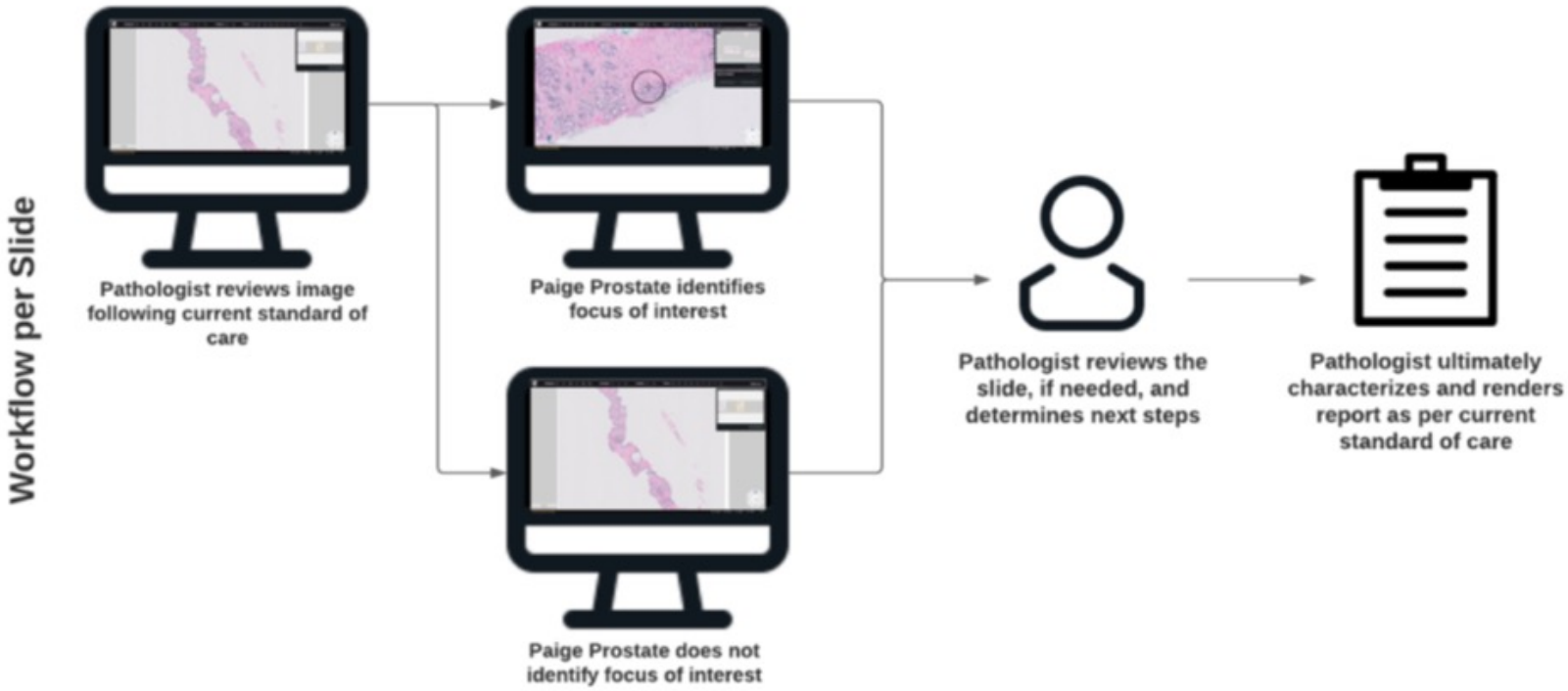
compatibility

use setting

INDUSTRY PERSPECTIVE

DECISION SUMMARY KEY COMPONENTS (CONTD.)

3. Mechanism of Action and Principles



Approved Clinical Workflow

INDUSTRY PERSPECTIVE

DECISION SUMMARY KEY COMPONENTS (CONTD.)

4. Performance Characteristics

- Study Data Characteristics and Its Diversity
- Analytical Performance Study Design Overview and Results (Accuracy, Localization, and Precision for Intra/Inter Scanner/Operator Variability)
- Clinical Performance Study Design Overview and Results (Reader Diagnostic Accuracy)

		Classification for unassisted read			
		Cancer	**Deferred**	**No Cancer**	**Total**
Classification for assisted read	**Cancer**	4.31 (1.2%)	1.12 (0.3%)	0.81 (0.2%)	6.25 (1.76%)
	Deferred	3.19 (0.9%)	22.75 (6.4%)	5.19 (1.5%)	31.12 (8.74%)
	No cancer	0.69 (0.2%)	9.06 (2.5%)	308.87 (86.8%)	318.62 (89.5%)
	Total	8.19 (2.3%)	32.94 (9.2%)	314.87 (88.45%)	356 (100%)

Numbers in grey colors are numbers of slide images with the same classification in assisted and unassisted reads. Numbers in green color, 0.69 (0.2%) and 9.06 (2.5%), present a reduction in the number of false positive results for the benign slide images because of use of the Paige Prostate device. Numbers in orange color, 0.81 (0.2%) and 5.19 (1.5%), present an increase in the number of false positive results because these benign slide images had "Cancer" assisted reads (0.2%) or "Deferred" assisted reads (1.5%) but had "No Cancer" for unassisted reads. Overall difference in the number of false positive slide images was 3.75 slides [=(0.69+9.06)-(0.81+5.19)] what is 1.05% (=3.75/356). Difference in the number of false positives slides of 1.1% with 95% CI: (-0.7%; 3.4%) was not statistically significant.

INDUSTRY PERSPECTIVE

DECISION SUMMARY KEY COMPONENTS (CONTD.)

5. Benefit/Risk Determination

- Discussion for favorable benefits when compared to its risks

Paige Prostate appears to provide a reasonable assurance of safety and effectiveness for diagnostic use by its intended users after taking into consideration the special controls. The clinical and analytical studies have shown that the risk of accuracy loss resulting in a false positive or false negative diagnosis, is minimal relative to the patient safety benefits, including new findings that would contribute to the correct diagnosis. This is contingent on the device being used according to the approved labeling, particularly that the end user must be fully aware of how to interpret and apply the device output.

The potential for false negative and false positive results is mitigated by special controls. Labeling requirements, which include certain device description information as well as certain limitations, ensure that users will employ all appropriate procedures and safeguards as specified, including use of the device as an adjunct rather than as the sole basis of making the diagnosis. In addition, design verification and validation includes data on software performance as supported by the underlying software design, as well as software algorithm training and validation within the limits of the specified intended use. This also includes analytical validation (including precision studies) and clinical validation (including user validation studies and performance studies) studies.

The probable clinical benefits outweigh the potential risks when the standard of care is followed by qualified users, and appropriate mitigation of the risks is provided for through implementation of and adherence to the special controls. The combination of the general controls and established special controls support the assertion that the probable benefits outweigh the probable risks.

INDUSTRY PERSPECTIVE

SPECIAL CONTROLS AND THEIR IMPORTANCE

Regulation is currently not published under Code of Federal Regulations (CFR) but is already available in Paige Prostate Reclassification Order document. Document provides key guidelines on:

- Intended Use
- Device Label
- Details about performance testing
- Device limitations
- Device verification and validation (analytical and clinical testing)