

Redefining Thyroid Cytology with AlxTHY: Improved Accuracy and Efficiency in FNAC Interpretation

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Disclosure

- Consultant to AlxMed Inc



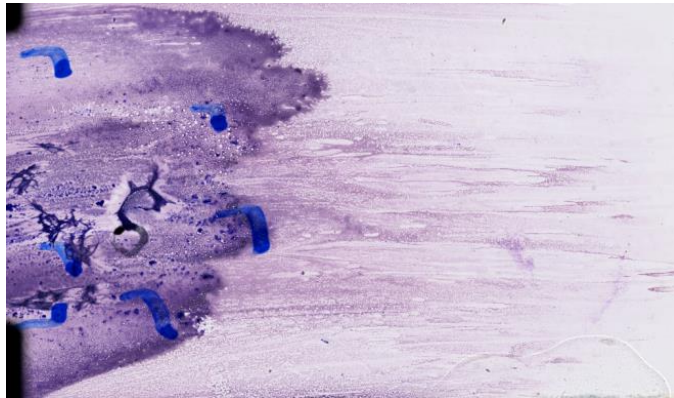
Outline

- Thyroid cytology digital perspective
- TBS= The Bethesda system for reporting thyroid cytology
- Role of AI for thyroid cytology
- Summary of our study

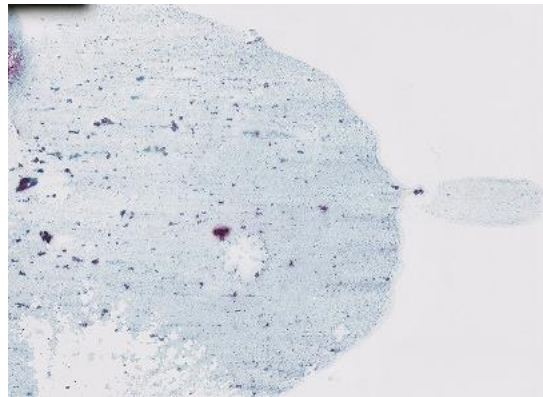


Thyroid Cytology: Digital Perspective

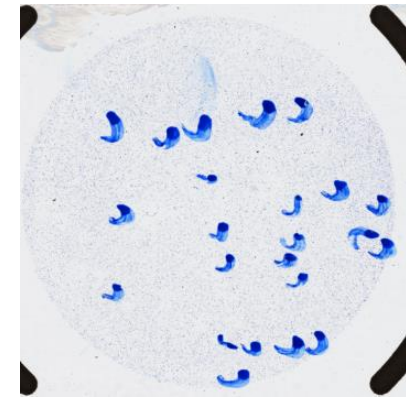
Preparation types: Smears and LBC (liquid-based cytology) or LBC only +/- cell-block



Smear: Diff Quik stain



Smear: Pap stain



LBC: Pap stain

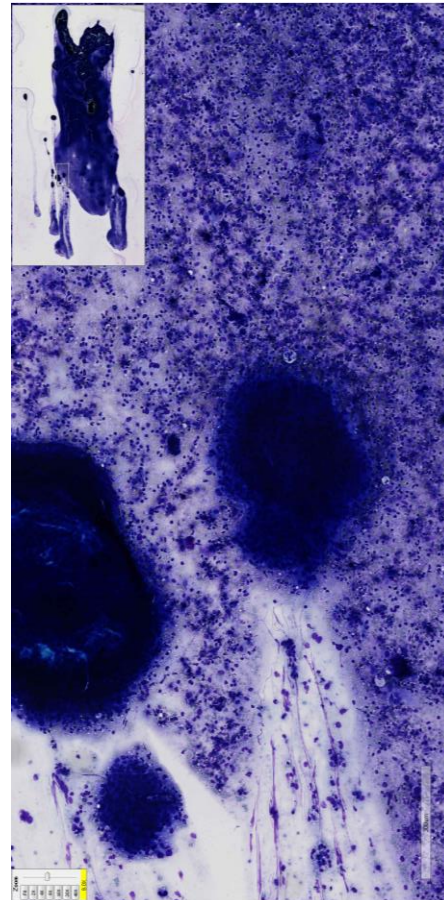
Issues for digitization: 3-D clusters, variable thickness of smears, thick smears etc.

Digitization Issues: Cytology vs Surgical Path

	Cytology	Surgical pathology
Specimen types	Exfoliative, abrasive, fine needle aspiration	Biopsy, resections
Preparation types	Smears, LBC, cytopsin, touch preparation, cell-blocks	Formalin fixation and paraffin embedded tissue
Commonly used Stains	Diff-Quik, Pap, H&E, IHC	H&E, IHC
Differences in procured material	3-D clusters, uneven distribution of cells, material extending beyond cover slips, frequent scant cellularity,	Uniform thickness of tissue sections on a glass slide and simple topography
Case level differences	Single cases can have multiple preparation types such as smears and cell-block for FNA cases and cytopsin and cell-blocks for effusion specimens etc.	NA
Workflow	All specimens are screened by cytologists and areas of interest are marked using colored markers	No screening
Automated barcode	Only subset of cases	Yes, all cases



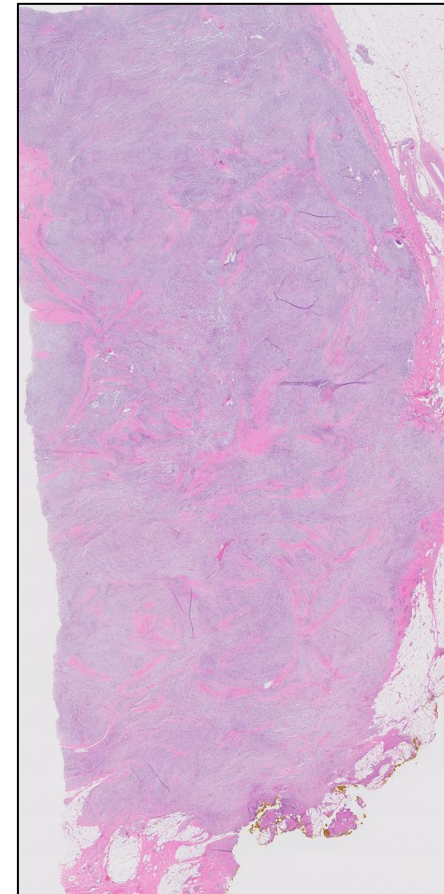
Cytology Smear



3-D clusters

Thick smear

Surgical section



Simple topography



Scanning Cytology Slides: Z-layer

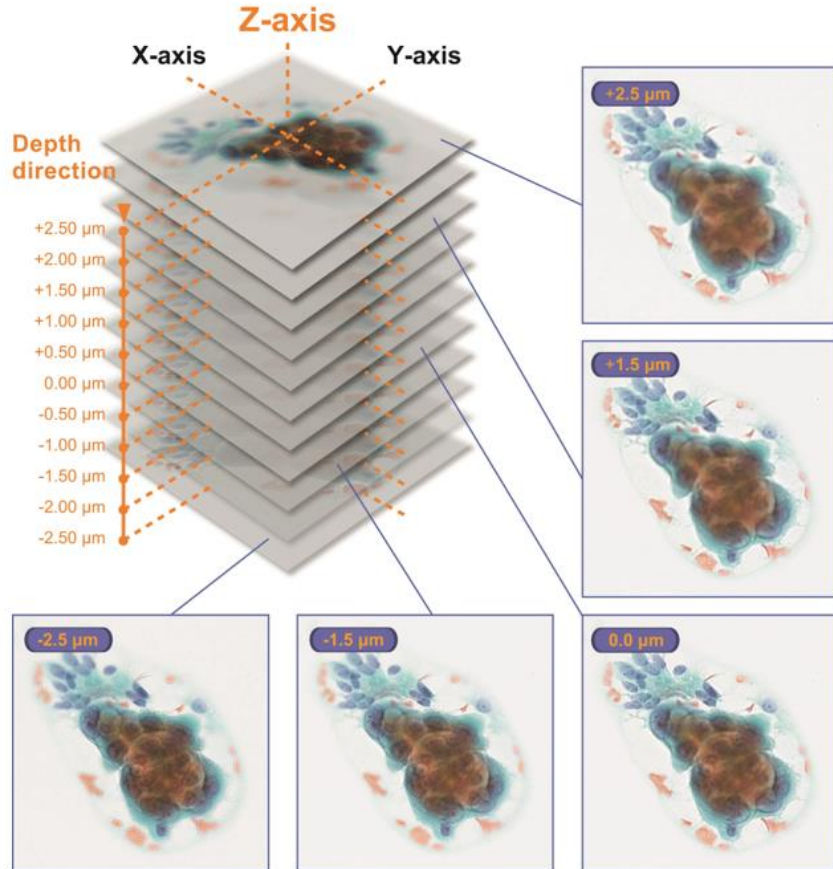
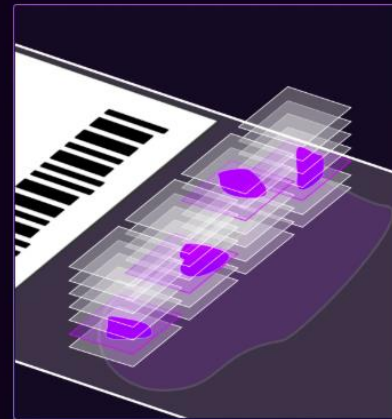
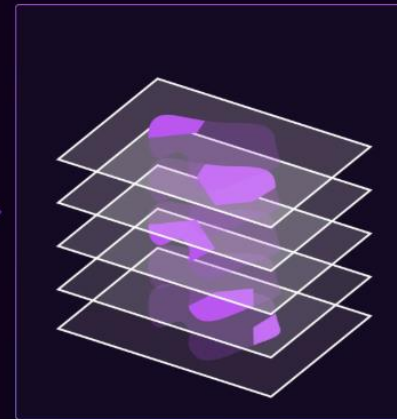


Image Source: Pramana website

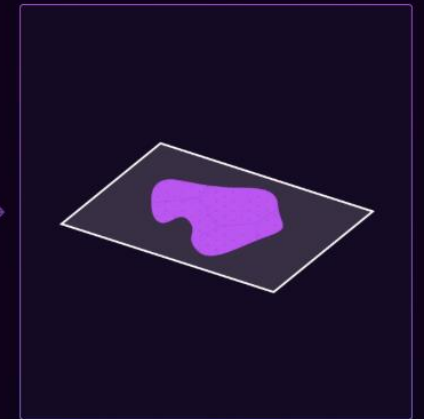
Volumetric Imaging



Volumetric scanning at each field of view



Fusion of Z-stacks and stitching



Fully focused image

Cytology Slides: Z-layer Stacking

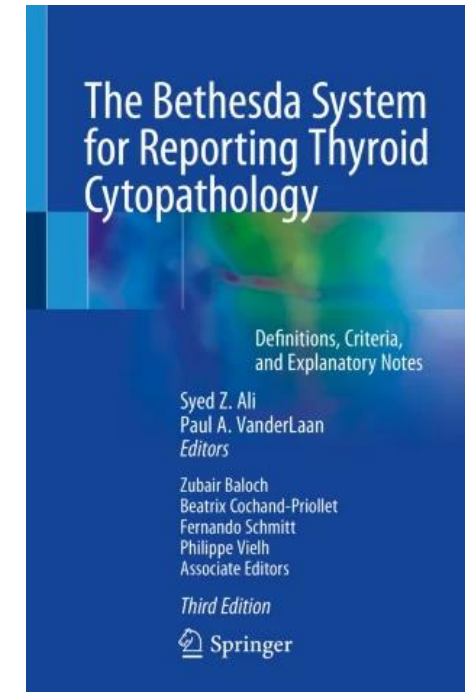
- Z-stacking = Focus fusion
- The exact number of z planes and the distance between z planes for digitizing cytology slides have not yet been standardized
- LBC preparations needs less z-layers as compared to smears
- **Increase scanning time**
- **Increase file size**
- **Needs better bandwidth for data transmission**
- **More costly**



The Bethesda System (TBS) for Reporting Thyroid Cytopathology

TBS Categories and Terminology:

- I Non-diagnostic
- II Benign
- III Atypia of undetermined significance
- IV Follicular neoplasm
- V Suspicious for malignancy
- VI Malignant

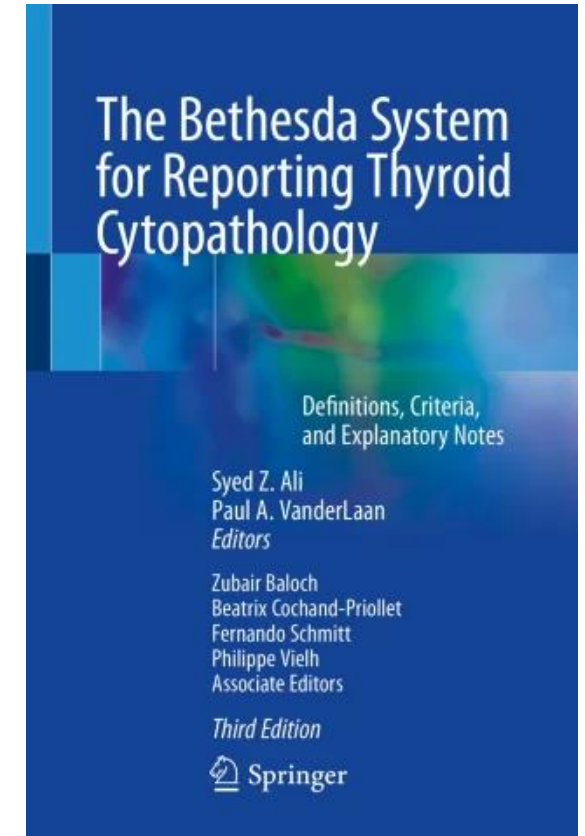


Interobserver subjectivity remains an issue; specially for AUS, FN, SFM categories



The Bethesda System (TBS): ROM

- ROM for thyroid FNA (excluding NIFTP)
 - TBS II (Benign) = 2%
 - TBS III (Atypia of undetermined significance) = 16%
 - TBS IV (Follicular neoplasm) = 23%
 - TBS V (Suspicious for malignancy) = 65%
 - TBS VI (Malignant) = 94%
- Diagnostic lobectomy is considered at TBS III and above



Is thyroid cytology amenable to AI development?

Yes! AI development and application possible

- Majority lesions are benign
- PTC is most common malignancy

TBS Categories, Terminology and AI perspective:

Adequacy: Quantitative (60 cells)

I Non-diagnostic: Detect cellularity, quantify, identify artifacts, QC etc.

II Benign: Feature extraction: Identification of colloid, follicular cell architecture

III Atypia of undetermined significance (nuclear vs other): Nuclear atypia, quantitation, architecture

IV Follicular neoplasm: Feature extraction micro-follicles, quantitation

V Suspicious for malignancy: PTC vs other

VI Malignant: PTC vs other



AixTHY Platform

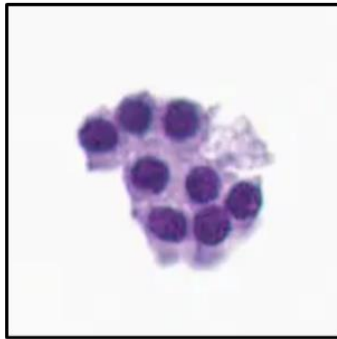
- AI platform applicable to WSIs of thyroid cytology LBC
- Assist (cytologists and cytopathologists) during thyroid cytology review, enhance efficiency and end-user experience
- Reduce turn-around-time

All candidate “hot-spot” cells detected by the algorithm are displayed as clickable thumbnails and are automatically grouped according to the AI-predicted TBS category.

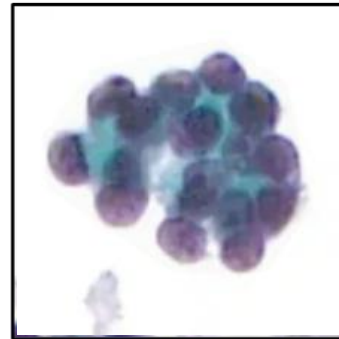


Representative Candidate-Cell Tiles Identified by AlxTHY

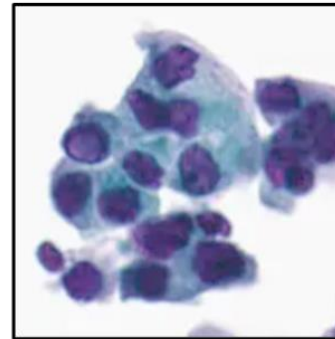
A. Benign FC



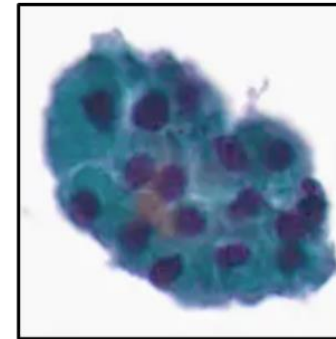
B. FN



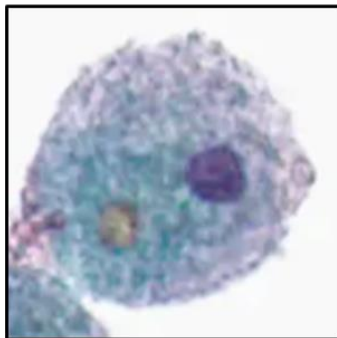
C. PTC



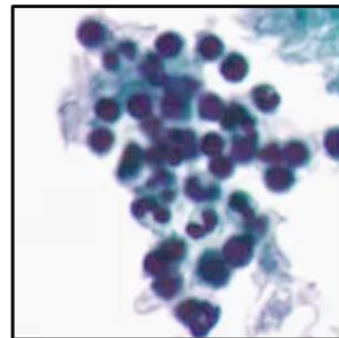
D. Hurthle cells



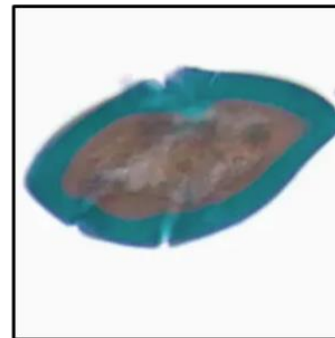
E. Histiocyte



F. Lymphocytes



G. Colloid



FC: Follicular-cell cluster

FN: Follicular neoplasm

PTC: Papillary thyroid carcinoma

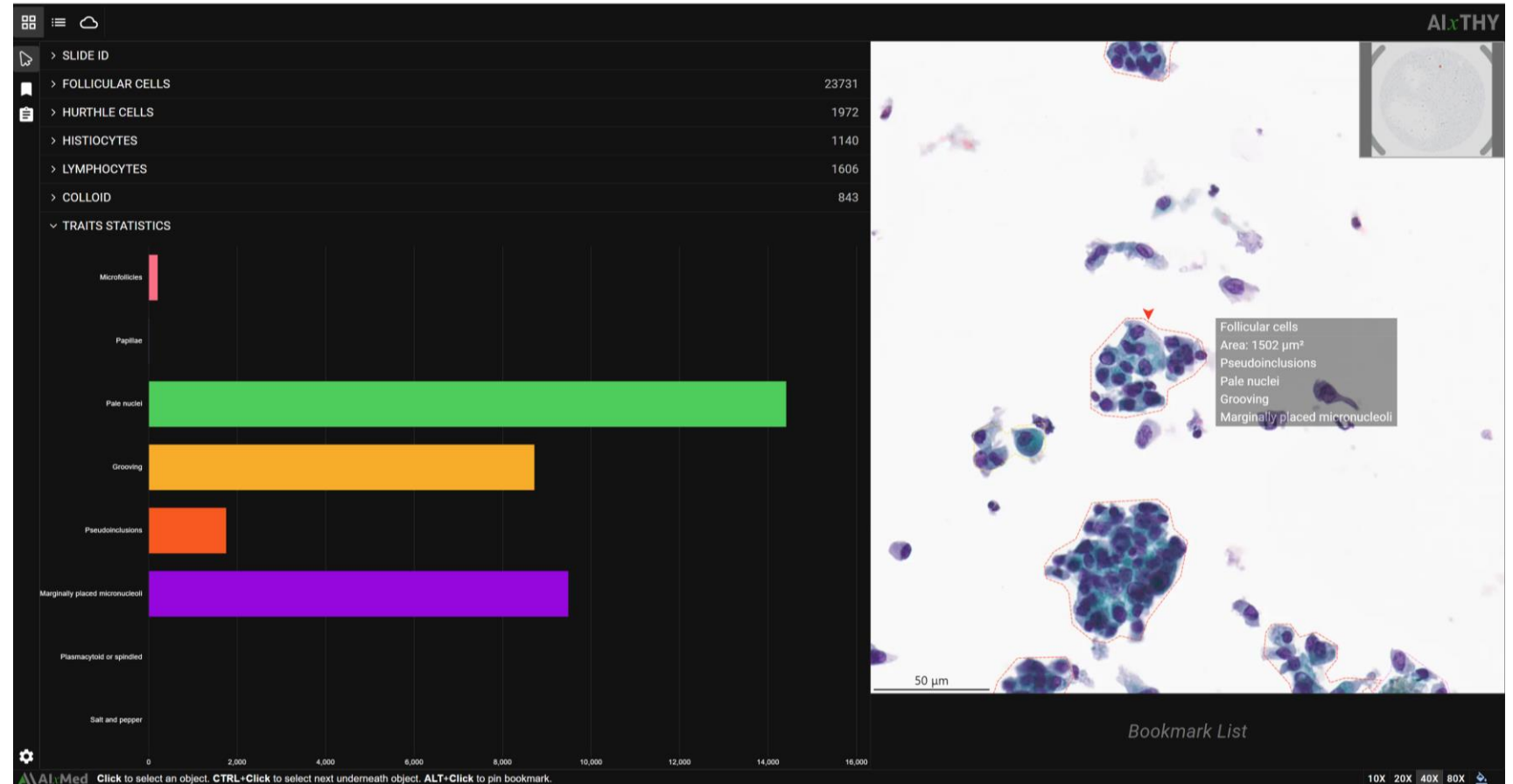
AIxTHY User Interface/Dashboard: AI-assisted Thyroid Cytology

The screenshot displays the AIxTHY User Interface/Dashboard. The interface is divided into several sections:

- Top Bar:** Contains the AIxTHY logo and a navigation menu.
- Slide ID:** Displays the slide ID "024" and the label barcode "23731".
- Follicular Cells:** A grid of 24 microscopic images showing various thyroid cell clusters. The first two images in the top row have green checkmarks.
- Cell Type Counts:** A list of cell types and their counts:
 - > FOLLICULAR CELLS: 23731
 - > HURTHLE CELLS: 1972
 - > HISTIOCYTES: 1140
 - > LYMPHOCYTES: 1606
 - > COLLOID: 843
 - > TRAITS STATISTICS
- Large View:** A large microscopic image of a selected cell cluster. A red arrow points to a specific cell. A tooltip box lists the following traits:
 - Follicular cells
 - Area: 1502 μm^2
 - Pseudo-inclusions
 - Pale nuclei
 - Grooving
 - Marginally placed micronucleoli
- Bookmark List:** A section at the bottom right for managing bookmarks.
- Bottom Bar:** Contains the AIxMed logo, a legend for selection (Click to select an object, CTRL+Click to select next underneath object, ALT+Click to pin bookmark), and a zoom control (10X 20X 40X 80X).

AIxTHY User Interface for AI-assisted Thyroid Cytology Review: Quantitative-Traits Panel

- Papillae
- Pale nuclei
- Grooving
- Intra-nuclear pseudoinclusions
- Marginally placed micronucleoli
- Micro-follicles, lack of colloid
- Plasmacytoid or spindled
- Salt and pepper chromatin





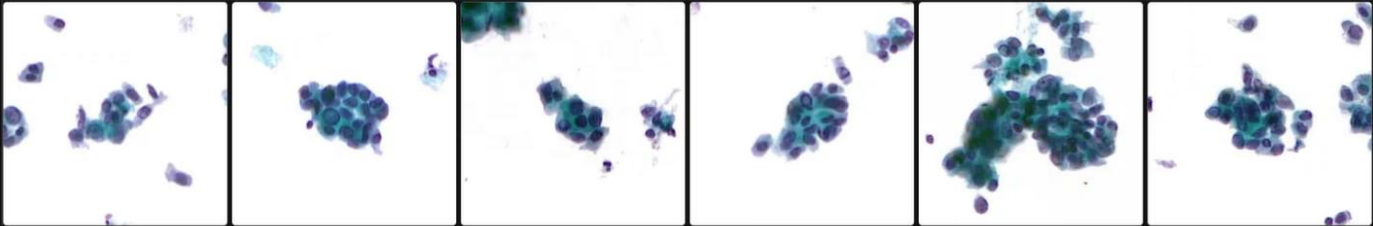
SLIDE ID

FILE NAME LABEL BARCODE

VTC-024

FOLLICULAR CELLS

24907



HURTHLE CELLS

1542

HISTIOCYTES

788

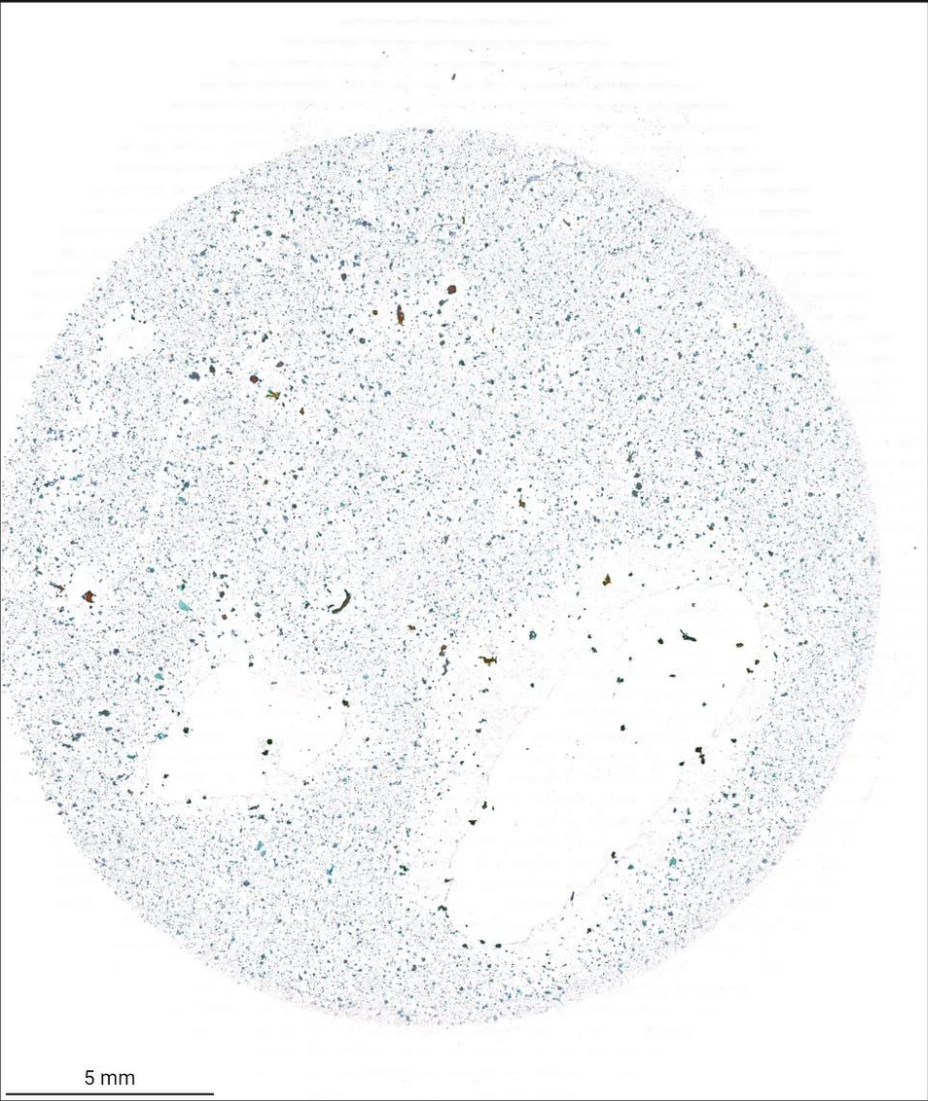
LYMPHOCYTES

663

COLLOID

1473

TRAITS STATISTICS



Bookmark List



Study Objectives

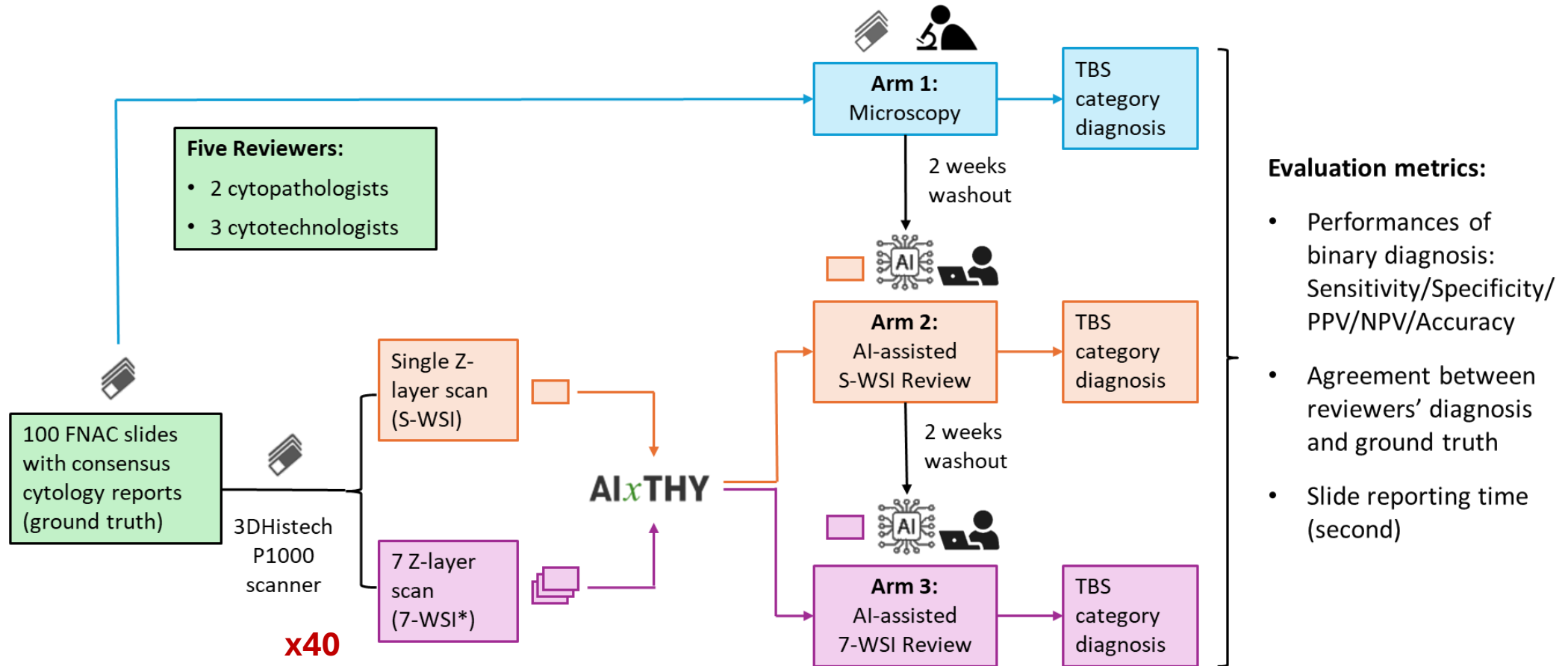
- AI platform applicable to WSIs of thyroid cytology to assist diagnosis
- Single-layer issues: 3-D clusters, visualization of nuclear features, uneven smears
- Multi-Z-layer scanning has the potential to improve visual clarity and diagnostic performance.

Objectives:

1. To evaluate performance with AI-assisted review versus manual review
2. To evaluate AIxTHY's performance: Single-layer versus 7-Z-layer WSIs of thyroid FNA (Conventional microscopy as the benchmark)



Study Design



FNAC: Fine needle aspiration cytology; TBS: The Bethesda System for Reporting Thyroid Cytopathology; *7-layer-stacking whole-slide image

100 Cases Dataset: Thyroid FNA ThinPrep Cytology Slides with Consensus Cytology Reports (Ground Truth)

		TBS Category	Number
Binary Diagnosis	Excluded	I- Non-Diagnostic	5
	Negative	II- Benign	35
		III- Atypia of Undetermined Significance	15
	Positive	IV- Follicular Neoplasm	15
		VI- Malignant	30
		Total Number	100

Binary Diagnosis Results: Microscopy vs AIxTHY-Assisted Review

Modality	Arm 1 Microscopy	Arm 2 AIxTHY-S-WSI	Arm 3 AIxTHY-7-WSI
Sensitivity	0.687 (0.631 ~ 0.739)	0.813 (0.765 ~ 0.856)	0.83 (0.783 ~ 0.871)
	p<0.001		p=0.522
Specificity	0.731 (0.659 ~ 0.796)	0.68 (0.605 ~ 0.748)	0.657 (0.582 ~ 0.727)
	p=0.176		p=0.522
PPV*	0.916 (0.529 ~ 0.664)	0.853 (0.621 ~ 0.764)	0.838 (0.633 ~ 0.778)
NPV*	0.598 (0.529 ~ 0.664)	0.696 (0.621 ~ 0.764)	0.71 (0.633 ~ 0.778)
Accuracy	0.703 (0.66 ~ 0.744)	0.764 (0.723 ~ 0.802)	0.766 (0.726 ~ 0.804)
	p=0.004		p=1.000
	P=0.004		

Binary diagnosis:

Negative: TBS-II

Positive: TBS-III~VI

* Exclude diagnosis of TBS I category from calculation of PPV and NPV results.

Reviewer–Ground Truth Agreement by TBS Category

TBS Category	Arm 1 Microscopy	Arm 2 AIxTHY-S-WSI	Arm 3 AIxTHY-7-WSI
I- NonDx	18/25 72.0%	14/25 56.0% ↓	12/25 48.0% ↓
II- Benign	128/175 73.1%	119/175 68.0% ↓	115/175 65.7% ↓
III- AUC	19/75 25.3%	40/75 53.3% ↑	33/75 44.0% ↑
IV- FN	31/75 41.3%	29/75 38.7%	31/75 41.3%
VI- Malignant	71/150 47.3%	56/150 37.3%	75/150 50.0%
Total	267/500 53.4%	258/500 51.6%	266/500 53.2%

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Two cytopathologists' reads N = 190



Conclusion

AlxTHY vs manual review of thyroid cytology:

- Increased sensitivity
- Improved agreement in indeterminate (TBS-III, AUC) cases, only a modest trade-off in specificity
- Improved diagnostic accuracy

AI-assisted 7-layer vs 1-layer WSI review:

Sensitivity (slight gain) and reduction in nondiagnostic calls

Reduced review time (30-37%)

- AI-assisted digital thyroid cytopathology shows strong potential to streamline thyroid FNAC workflows and improve diagnostic efficiency.



Thank You!!

**PATHOLOGY
VISIONS 25**

