THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

AIxTHY Digital Cytopathology Platform Improves Diagnostic Accuracy and Reduces Nondiagnostic Interpretations in Thyroid Fine-Needle Aspiration Cytology

PRESENTED BY

Swati Satturwar, MD

Associate Professor, Department of Pathology, The Ohio State University

Swati.Satturwar@osumc.edu; x handle@SatturwarSwati

USCAP 115TH ANNUAL MEETING
MAKING CONNECTIONS
USCAP Advancing Pathology Together

Disclosure

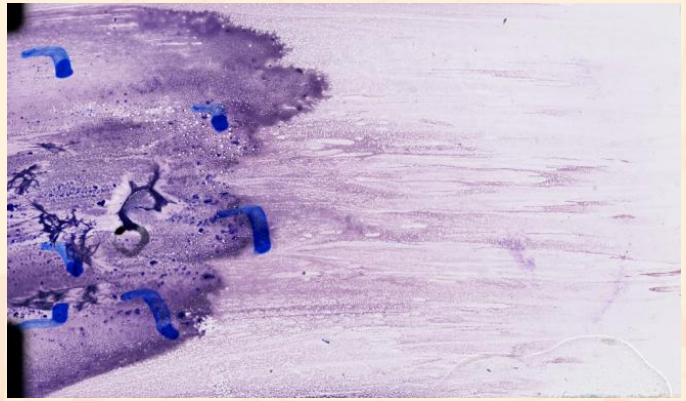
- Consultant to AIxMed Inc.

Outline

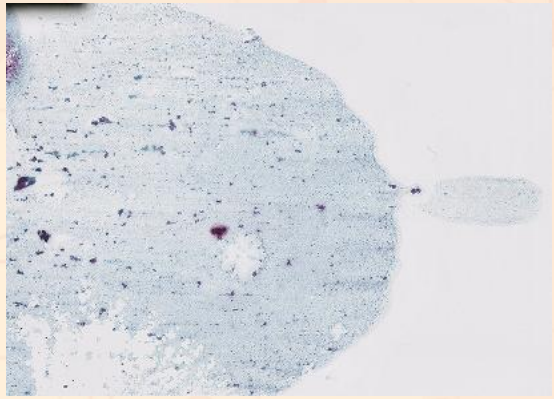
- Thyroid cytology digital and AI perspective
- TBS= The Bethesda system for reporting thyroid cytology and AIxTHY platform
- Summary of our study

Thyroid Cytology: Digital Perspective

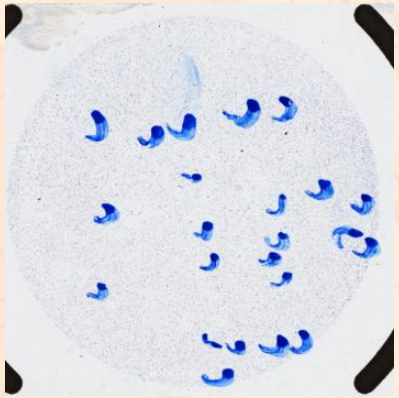
Preparation types: Smears and LBC (liquid-based cytology) or LBC only +/- cell-block



Smear: Diff Quik stain



Smear: Pap stain



LBC: Pap stain

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

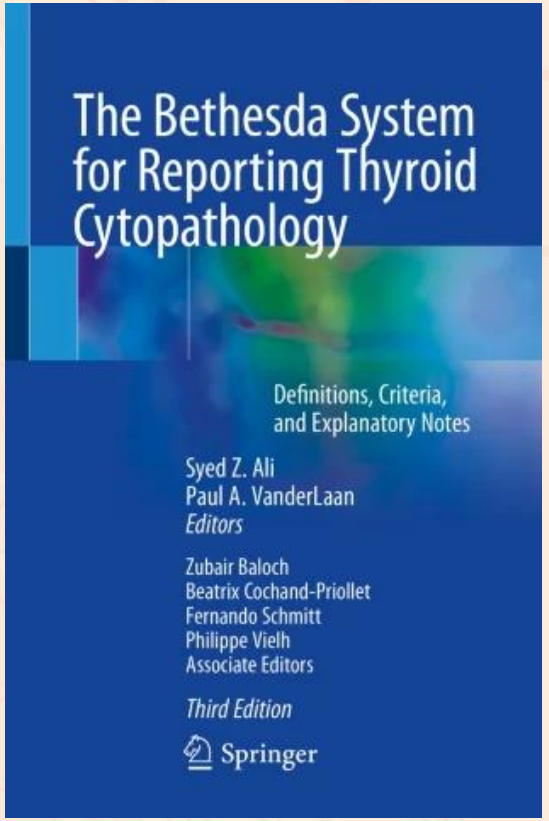
For this study we chose LBC only approach for AI development

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

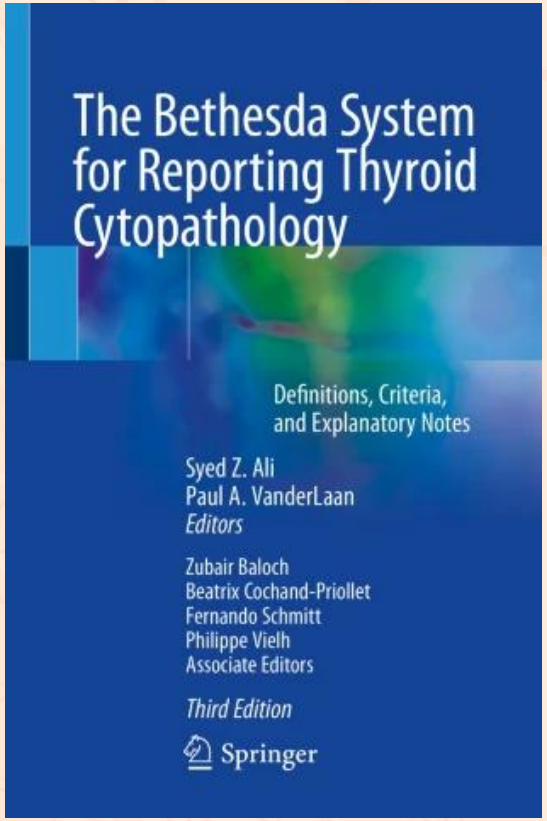
Interobserver subjectivity remains an issue; specially for AUS, FN, SFM categories



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

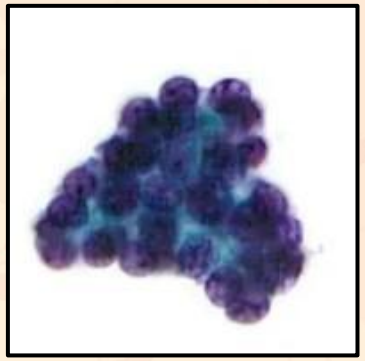
- AI platform applicable to WSIs LBC of thyroid cytology
- Assist (cytologists and cytopathologists) during thyroid cytology review, enhance efficiency and end-user experience
- Reduce turn-around-time

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.

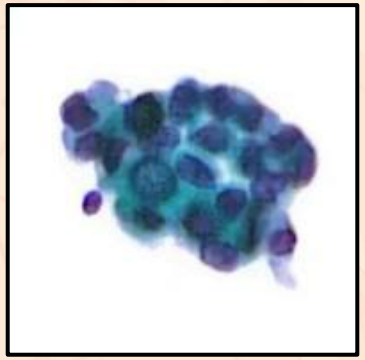
Representative Candidate-Cell Tiles Identified by AIxTHY

Benign Follicular-cell cluster

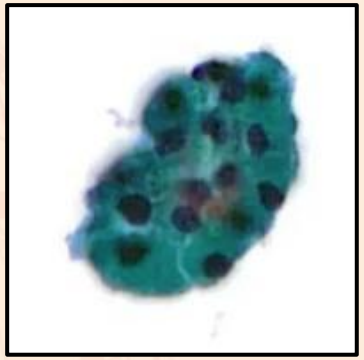
Follicular Neoplasm



Papillary Thyroid Carcinoma

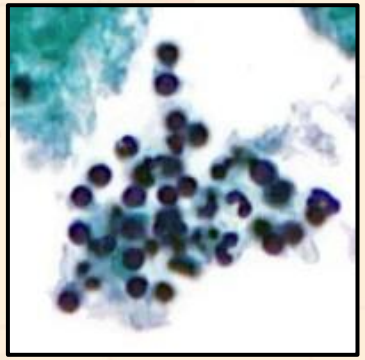


Hurthle Cells



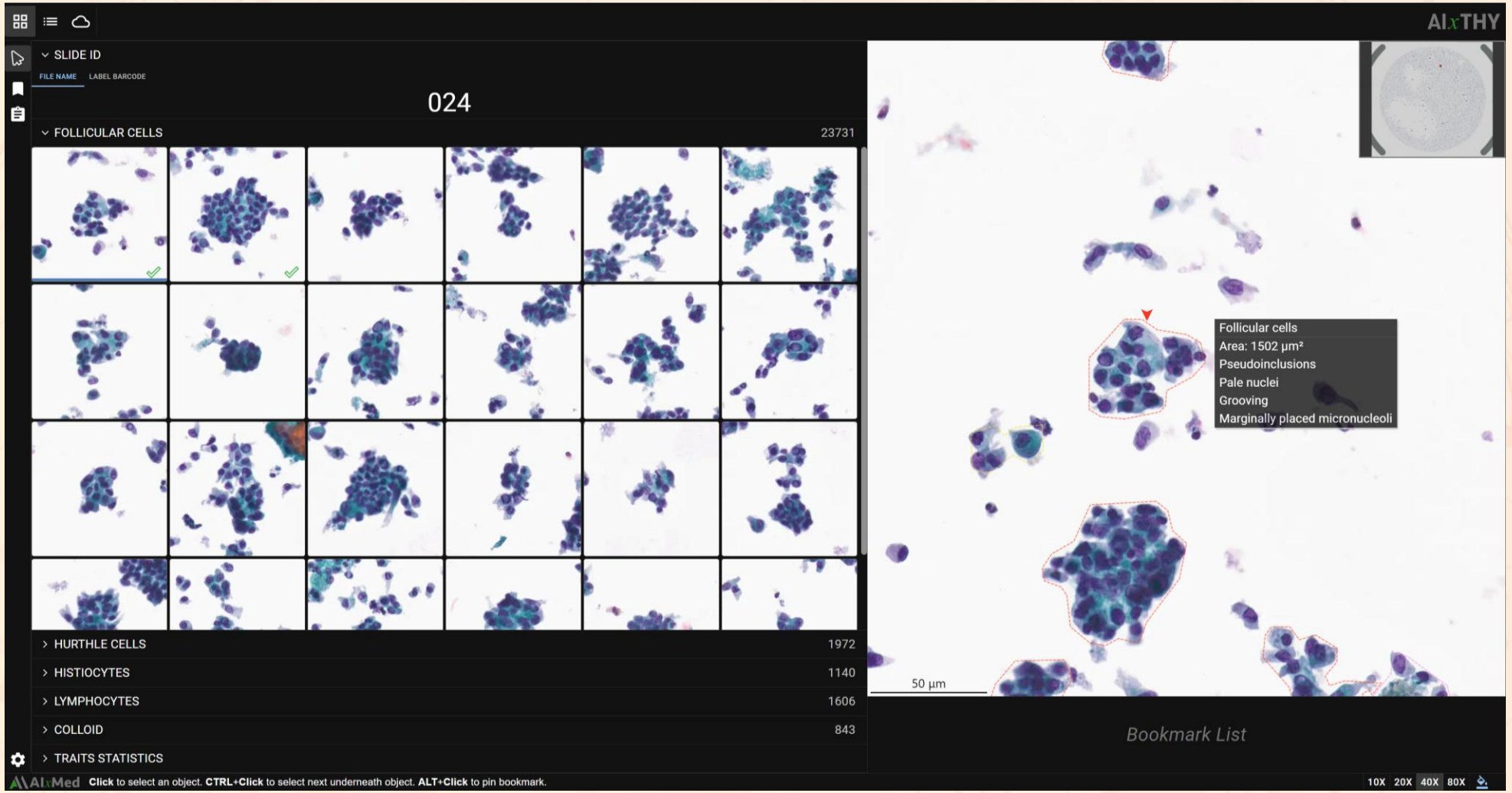
Histiocytes

Lymphocytes



Colloid

AIxTHY User Interface/Dashboard: AI-assisted Thyroid Cytology

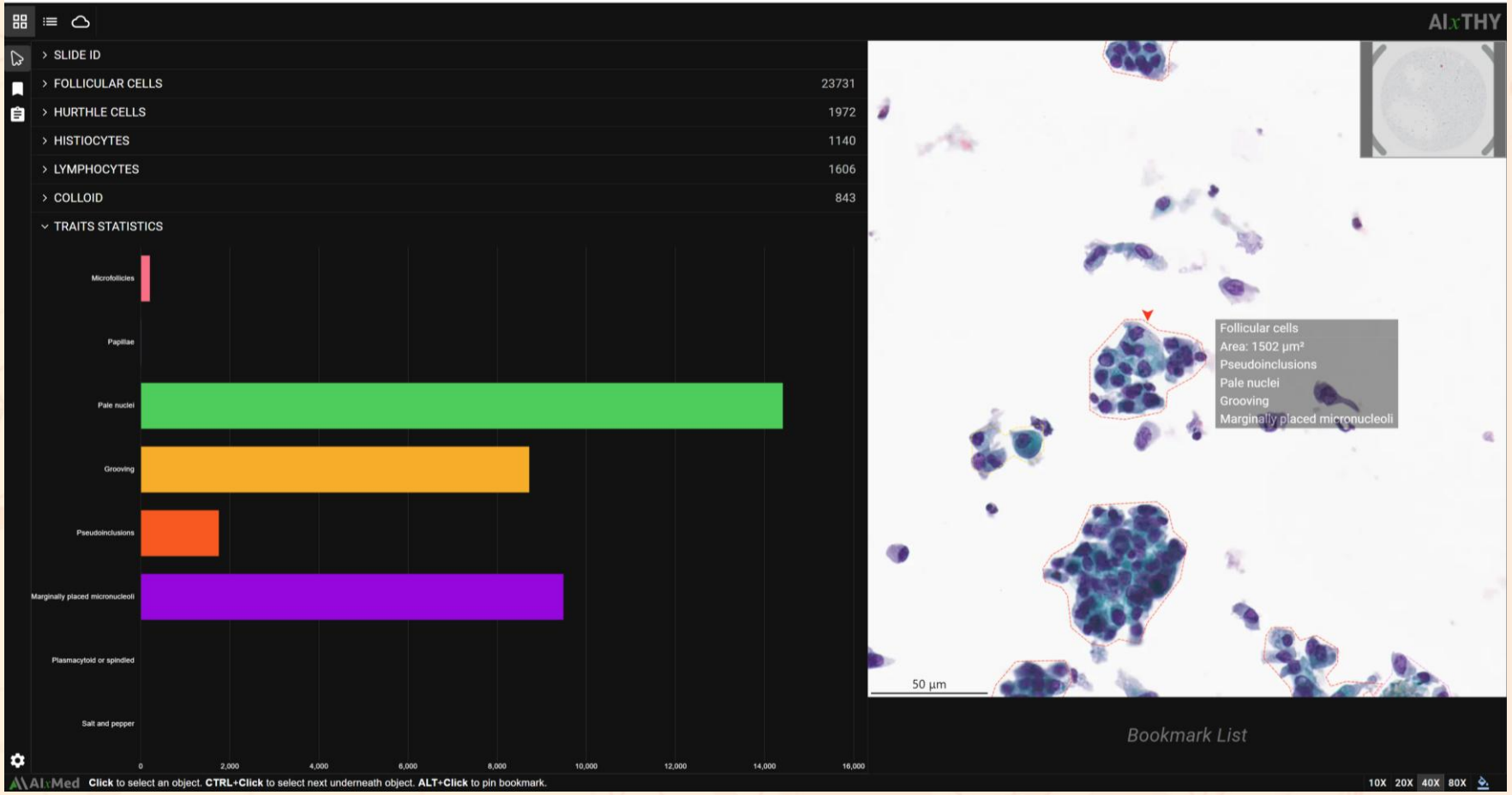


AIxTHY User Interface for AI-assisted Thyroid Cytology Review: Quantitative-Traits Panel

- Papillae
- Pale nuclei
- Grooving
- Intra-nuclear pseudoinclusions
- Marginally placed micronucleoli

- Micro-follicles, lack of colloid

- Plasmacytoid or spindled
- Salt and pepper chromatin



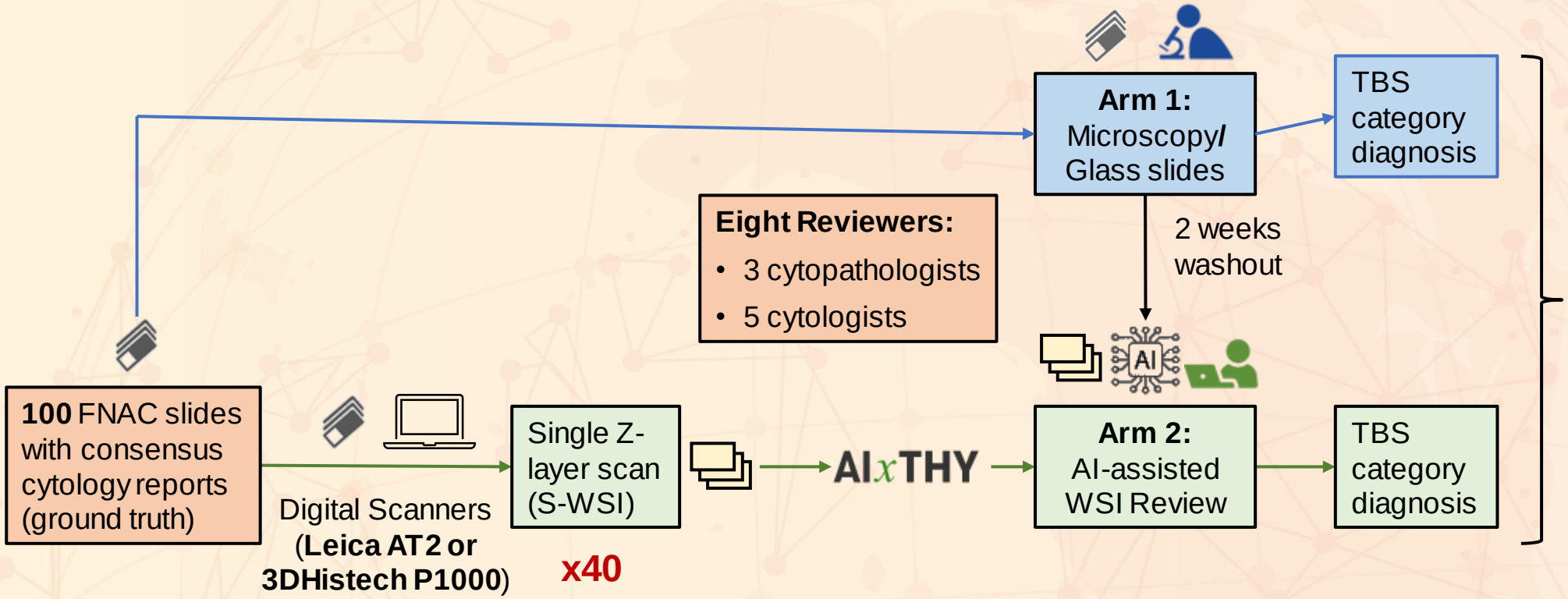
Study Objectives

- To analyze **nondiagnostic** (Bethesda I) interpretations in thyroid FNAC in depth
- To compare **nondiagnostic** rates between conventional microscopy and AI-assisted review (AIxTHY)

- To assess how often **Bethesda I cases are reclassified** into more actionable Bethesda categories with AI assistance
- To evaluate the impact of this reclassification on diagnostic **performance**, including sensitivity, specificity, and accuracy

- To explore possible explanations and **clinical implications** of the unexpected findings in nondiagnostic cases

Study Design



FNAC: Fine needle aspiration cytology; TBS: The Bethesda System for Reporting Thyroid Cytopathology

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

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

Reviewer–Ground Truth Agreement by TBS Category and NonDx reads between Microscopy and AI-assisted Review

TBS Category	Arm 1 Microscopy	Arm 2 AI-assisted Review
I- NonDx	32/40 **80.0%**	23/40 **57.5%** ↓
II- Benign	209/280 **74.6%**	194/280 **69.3%** ↓
III- AUS	35/120 **29.2%**	56/120 **46.7%** ↑
IV- FN	35 **29.2%**	34/120 **28.3%**
VI- Malignant	119/240 **49.6%**	91/240 **37.9%**
Total	430/800 **53.8%**	398/800 **49.8%** ↓
Modality	**Microscopy**	**AI-assisted Review**
NonDx reads/total reads	80/800 **10.0%**	54/800 **6.8%** ↓

Reviewer–Consensus Agreement for Microscopic Thyroid FNAC Diagnoses

Agreement to Cytology Consensus Reports (N=800)	Reviewers' Diagnosis in Microscopy (Arm 1)						
	NonDx	Benign	AUS	FN	SFM	Malig	Total
NonDx	32 (80.0%)	7	0	0	1	0	40 (5.0%)
Benign	38	209 (74.6%)	26	7	0	0	280 (35.0%)
AUS	4	69	35 (29.2%)	5	2	5	120 (15.0%)
FN	5	35	42	35 (29.2%)	2	1	120 (15.0%)
Malig	1	25	31	13	51	119 (49.6%)	240 (30.0%)
Total	80 (10.0%)	345 (43.1%)	134 (16.8%)	60 (7.5%)	56 (7.0%)	125 (15.6%)	800 (100.0%)

Reviewer–Consensus Agreement for AI-assisted Thyroid FNAC Diagnoses

Agreement to Cytology Consensus Reports (N=800)	Reviewers' Diagnosis in AI-assisted Review (Arm 2)						
	NonDx	Benign	AUS	FN	SFM	Malig	Total
NonDx	23 (57.5%)	17	0	0	0	0	40 (5.0%)
Benign	24	194 (69.3%)	45	12	5	0	280 (35.0%)
AUS	0	56	56 (46.7%)	3	5	0	120 (15.0%)
FN	7	35	41	34 (28.3%)	3	0	120 (15.0%)
Malig	0	9	28	35	77	91 (37.9%)	240 (30.0%)
Total	54 (6.8%)	311 (38.9%)	170 (21.3%)	84 (10.5%)	90 (11.3%)	91 (11.4%)	800 (100.0%)

Binary Diagnosis Results: Microscopy vs AIxTHY-Assisted Review

Modality	Arm 1 Microscopy	Arm 2 AI-assisted Review
Sensitivity	**68.7%**	**81.3%**
95% C.I.	(63.1% ~ 73.9%)	(76.5% ~ 85.6%)
p value	<0.001	
Specificity	**73.1%**	**68.0%**
95% C.I.	(65.9% ~ 79.6%)	(60.5% ~ 74.8%)
p value	0.176	
PPV*	**91.6%**	**85.3%**
95% C.I.	(86.7% ~ 94.4%)	(81.1% ~ 90.2%)
NPV*	**59.8%**	**69.6%**
95% C.I.	(52.9% ~ 66.4%)	(62.1% ~ 76.4%)
Accuracy	**70.3%**	**76.4%**
95% C.I.	(66.0% ~ 74.4%)	(72.3% ~ 80.2%)
p value	0.004	

- **Reviewers:**

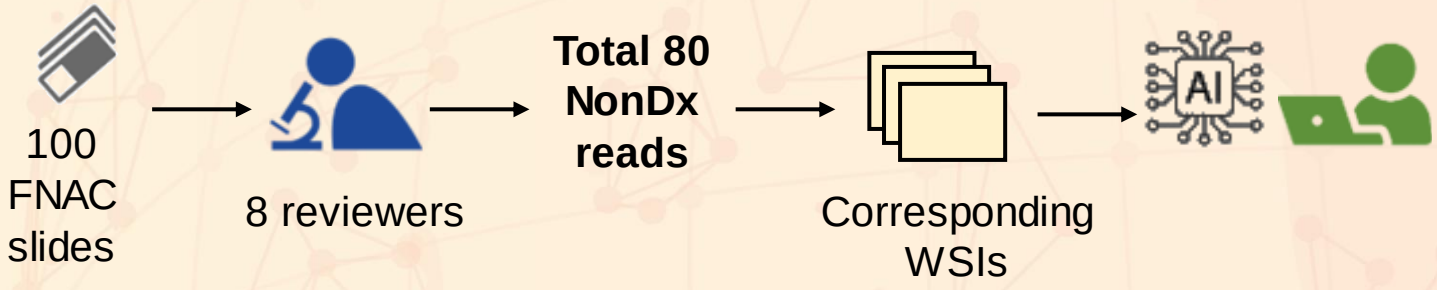
  2 Cytopathologists + 3 Cytologists
- WSI scanned by 3DHistech imageer
- **Binary diagnosis:**

  Negative: TBS-II

  Positive: TBS-III~VI

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

Impact of AIxTHY Assistance on Diagnostic Performance in Non-diagnostic Microscopy Reads



Ground Truth	AI-assisted Review: Reviewers' Read	AI-assisted Review: Agreement
NonDx (TBS-I) N= 32	NonDx n= 21	65.7%
	Negative n= 11	
	Positive n= 0	
Negative (TBS-II) N= 38	NonDx n= 19	
	Negative n= 12	31.6%
	Positive n= 7	
Positive (TBS-III~VI) N= 10	NonDx n= 4	
	Negative n= 2	
	Positive n= 4	40.0%

Binary outcome **(Negative – Benign):** additional **31.6%** improvement of negative diagnosis

Binary outcome **(Positive – AUS and above):** additional **40%** improvement of positive diagnosis

Reclassification of Microscopy-Categorized Nondiagnostic Cases Using AIxTHY

Agreement to Cytology Consensus Reports (N=80)	Reviewers' Diagnosis in AI-assisted Review (Arm 2)						
	NonDx	Benign	AUS	FN	SFM	Malig	Total
NonDx	21 (65.7%)	11	0	0	0	0	32
Benign	19	12 (31.6%)	5	2	0	0	38
AUS	0	2	2 (50.0%)	0	0	0	4
FN	4	0	1	0 (0.0%)	0	0	5
Malig	0	0	0	0	0	1 (100.0%)	1
Total	44	25	8	2	0	1	80

Conclusion: Using AIxTHY Platform

- **Reduced nondiagnostic interpretations** in thyroid FNAC compared with conventional microscopy
- **Improved overall diagnostic accuracy**, particularly in challenging and previously indeterminate cases
- **Reclassification of nondiagnostic** cases into actionable Bethesda categories increased both specificity and sensitivity
- By enabling more definitive benign or malignant interpretation, AIxTHY may expedite clinical decision-making and patient care
- This a promising adjunct to digital thyroid cytology workflows, enhancing interpretive reliability and efficiency

Acknowledgement

- AIxMed team and all study participants

Thank You!!