Scale-Aware Transformers for Diagnosing Melanocytic Lesions

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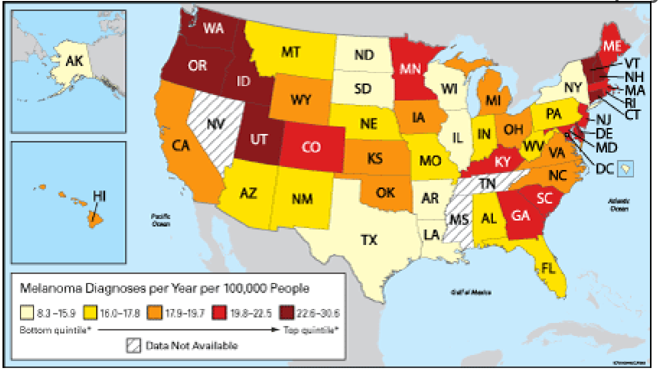
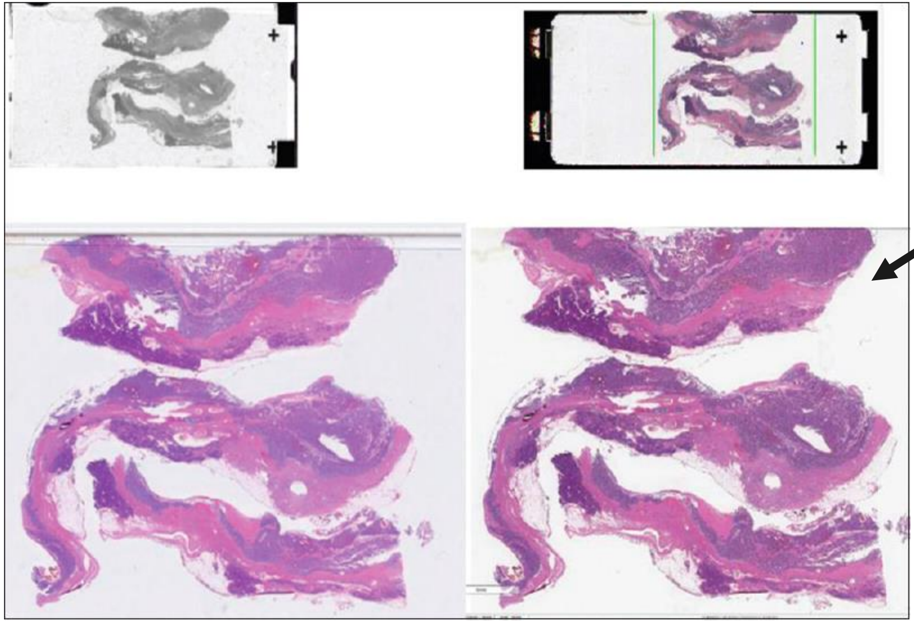
Melanoma

- Melanoma is the most aggressive type of skin cancer
- One of the most diagnosed cancers in the US
- Gold standard for diagnosis → visual assessment of skin biopsy by pathologists



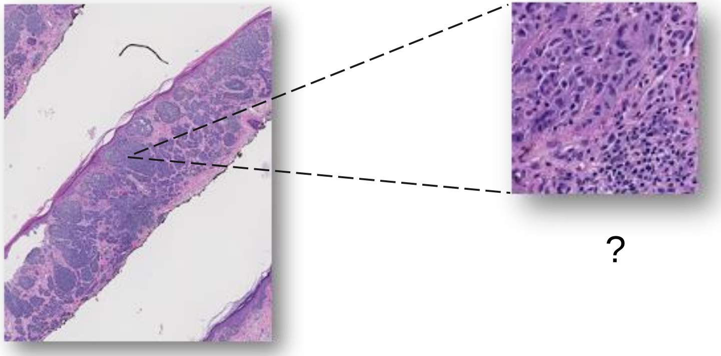
Digitized Whole slide Images (WSI)



Multiple tissues

Difficulties in diagnosis

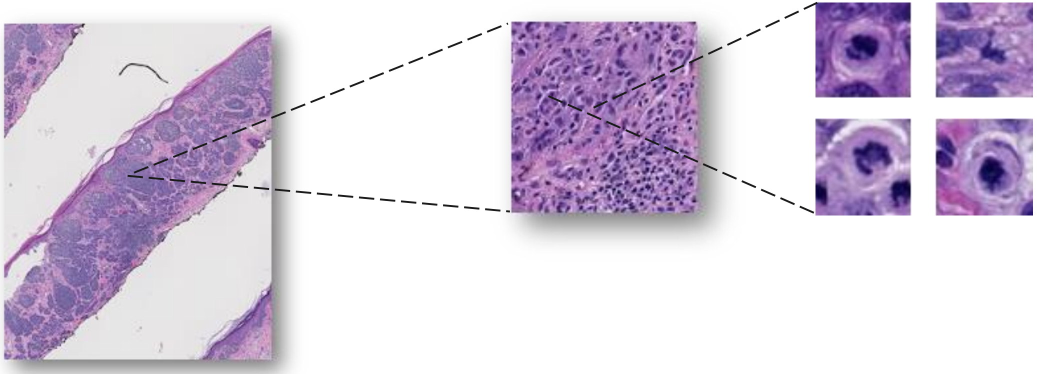
Mixed normal and cancerous tissue



Difficulties in learning to diagnose

Mixed normal and cancerous tissue

Feature is dependent on resolution



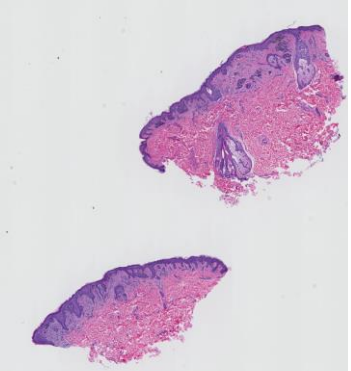
Difficulties in learning to diagnose

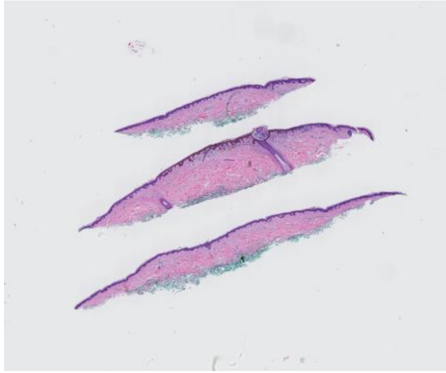
Mixed normal and cancerous tissue

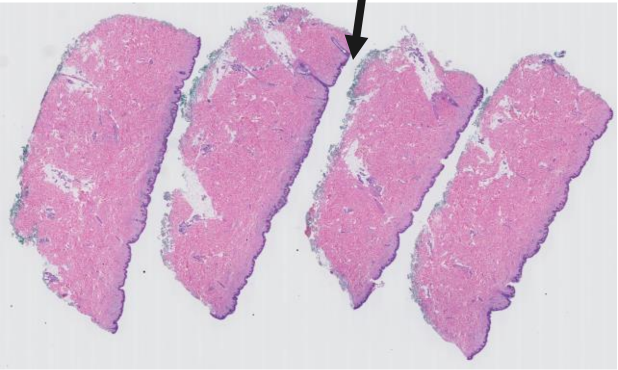
Feature is dependent on resolution

Dataset

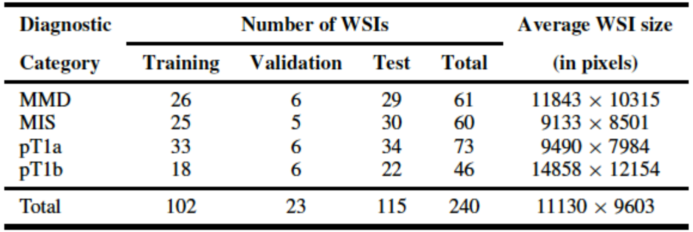
Dataset







Multiple tissues

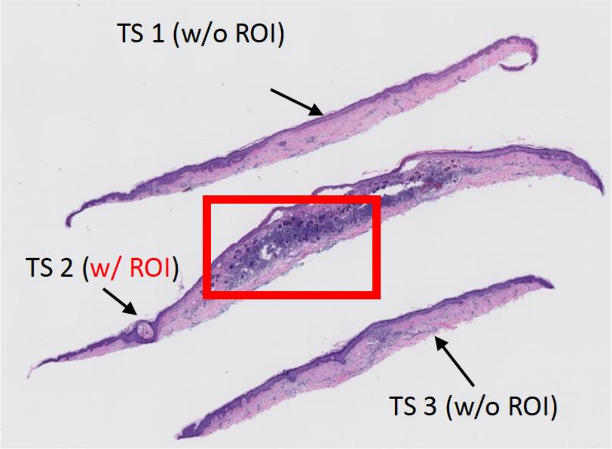


Diagnostic	Number of WSIs				Average WSI size
Category	Training	Validation	Test	Total	(in pixels)
MMD	26	6	29	61	11843 × 10315
MIS	25	5	30	60	9133 × 8501
pT1a	33	6	34	73	9490 × 7984
pT1b	18	6	22	46	14858 × 12154
Total	102	23	115	240	11130 × 9603

TABLE 1: Statistics of skin biopsy whole slide image (WSI) dataset. The average WSI size is computed at a magnification factor of x10. Diagnostic terms for the dataset used in this study are as follows: mild and moderate dysplastic nevi (MMD), melanoma in situ (MIS), invasive melanoma stage pT1a (pT1a), invasive melanoma stage ≥ pT1b (pT1b).

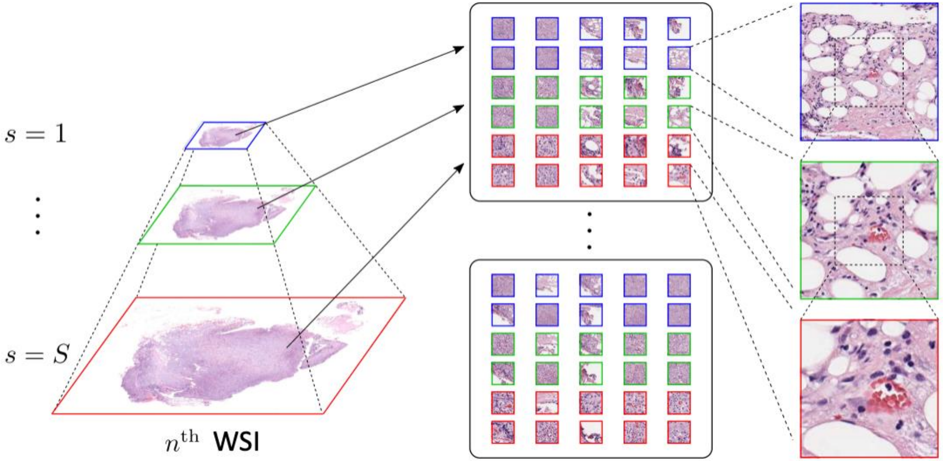
Dataset

Invasive T1a Skin Biopsy Image (or Class 3)

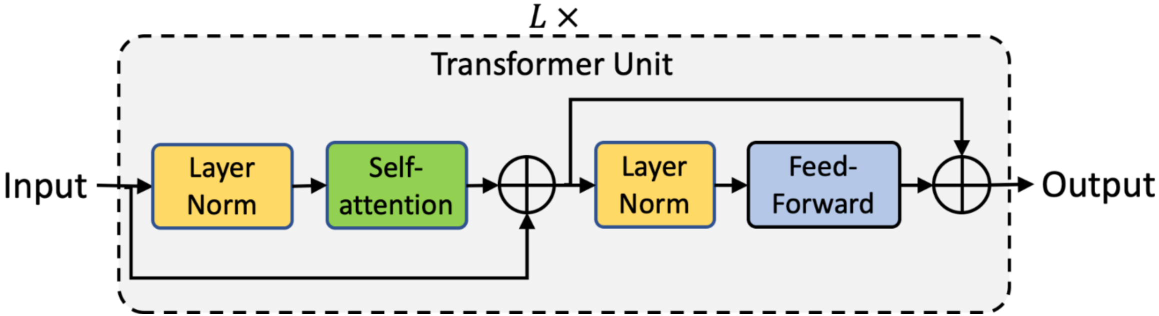


Key Idea

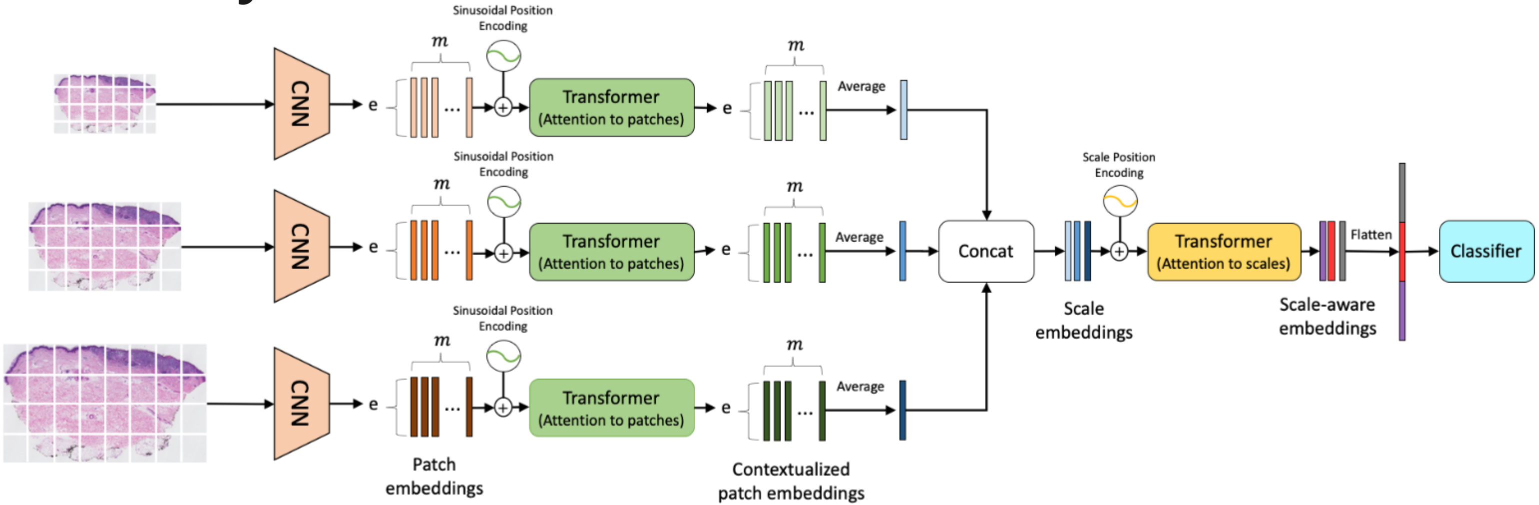
- Self-attention-based framework for classifying WSIs at multiple input scales
- A soft label assignment method to reduce ambiguities



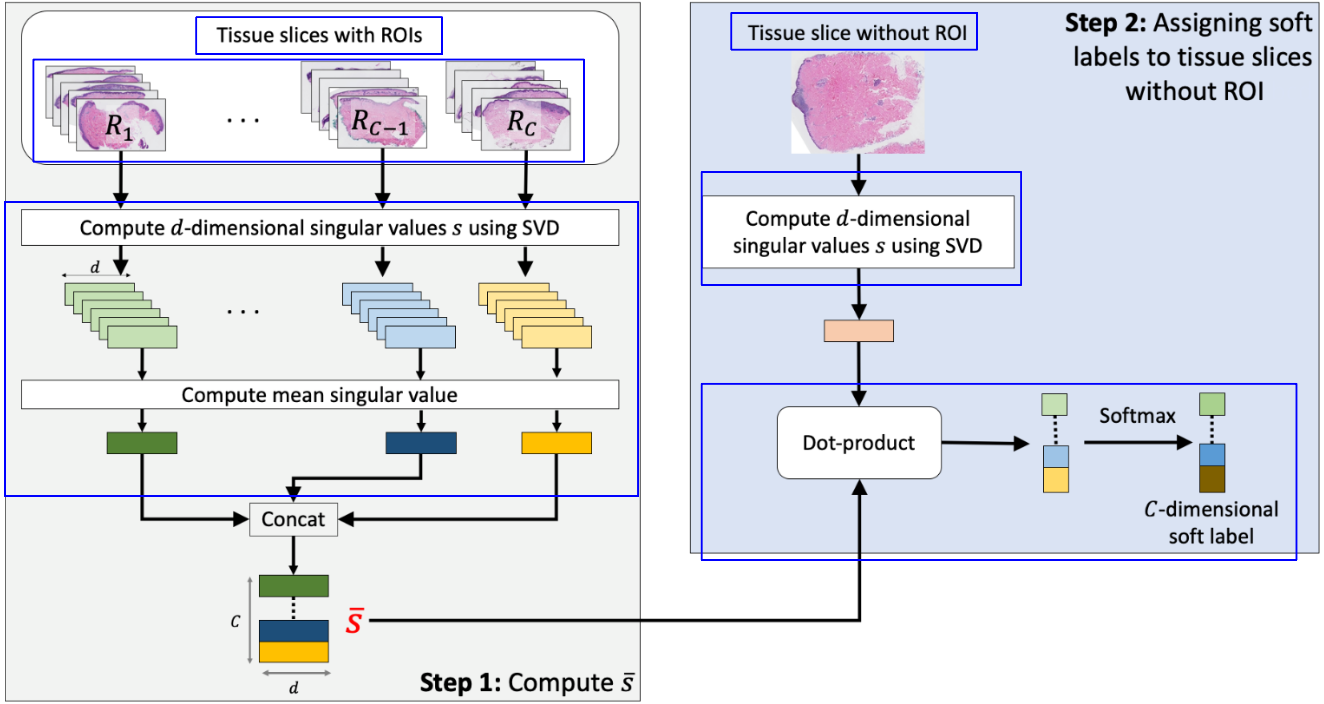
Transformer Unit



Scale-Aware Transformers for Diagnosing Melanocytic Lesions

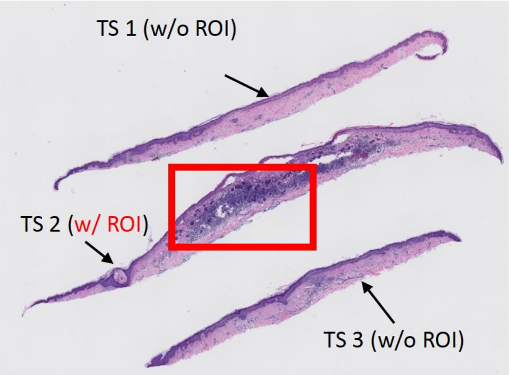

Sinusoidal Position Encoding
m
CNN
e
...
Transformer (Attention to patches)
Average
Concat
Scale Position Encoding
Transformer (Attention to scales)
Flatten
Classifier
Scale embeddings
Scale-aware embeddings
Patch embeddings
Contextualized patch embeddings

Soft labels


Tissue slices with ROIs
R_1
. . .
R_{C-1}
R_C
Compute d-dimensional singular values s using SVD
d
. . .
Compute mean singular value
Concat
C
$\bar{s}$
d
Step 1: Compute $\bar{s}$
Tissue slice without ROI
Step 2: Assigning soft labels to tissue slices without ROI
Compute d-dimensional singular values s using SVD
Dot-product
Softmax
C-dimensional soft label

Soft labels

Invasive T1a Skin Biopsy Image (or Class 3)



Hard Label (one-hot encoding)

TS 1	0	0	1	0
TS 2	0	0	1	0
TS 3	0	0	1	0

Label smoothing (smoothing=0.1)

TS 1	0.033	0.033	0.9	0.033
TS 2	0.033	0.033	0.9	0.033
TS 3	0.033	0.033	0.9	0.033

Constrained label smoothing

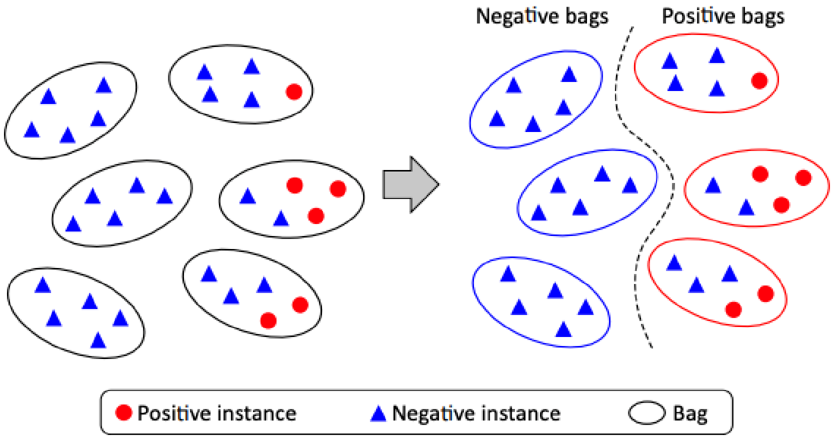
TS 1	0.5	0.5	0	0
TS 2	0	0	1	0
TS 3	0.5	0.5	0	0

Soft labels (ours)

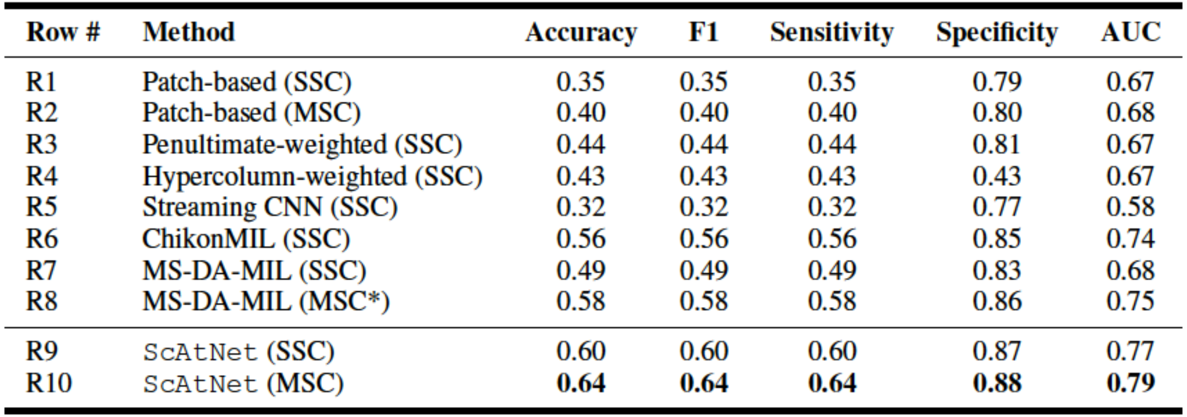
TS 1	0.54	0.46	0	0
TS 2	0	0	1	0
TS 3	0.28	0.72	0	0

Baseline Methods

- Patch-based classification
- Weighted feature aggregation
- ChikonMIL
- MS-DA-MIL
- Streaming CNN



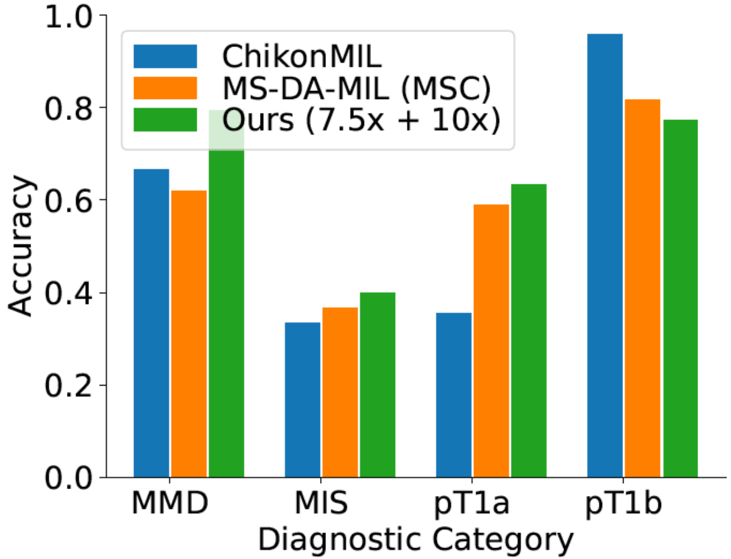
Experimental Result: baseline methods



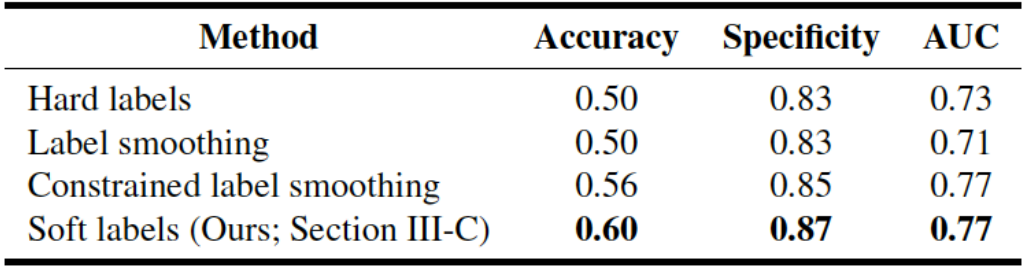
Row #	Method	Accuracy	F1	Sensitivity	Specificity	AUC
R1	Patch-based (SSC)	0.35	0.35	0.35	0.79	0.67
R2	Patch-based (MSC)	0.40	0.40	0.40	0.80	0.68
R3	Penultimate-weighted (SSC)	0.44	0.44	0.44	0.81	0.67
R4	Hypercolumn-weighted (SSC)	0.43	0.43	0.43	0.43	0.67
R5	Streaming CNN (SSC)	0.32	0.32	0.32	0.77	0.58
R6	ChikonMIL (SSC)	0.56	0.56	0.56	0.85	0.74
R7	MS-DA-MIL (SSC)	0.49	0.49	0.49	0.83	0.68
R8	MS-DA-MIL (MSC*)	0.58	0.58	0.58	0.86	0.75
R9	`ScAtNet` (SSC)	0.60	0.60	0.60	0.87	0.77
R10	`ScAtNet` (MSC)	**0.64**	**0.64**	**0.64**	**0.88**	**0.79**

TABLE 2: Comparison of overall performance with state-of-the-art WSI classification methods across different metrics on the test set. Here, SSC denotes single input scale (10×). MSC denotes multiple input scales (7.5×, 10×, 12.5×). MSC* denotes multiple input scales (10×, 20×)

Experimental Result: baseline methods



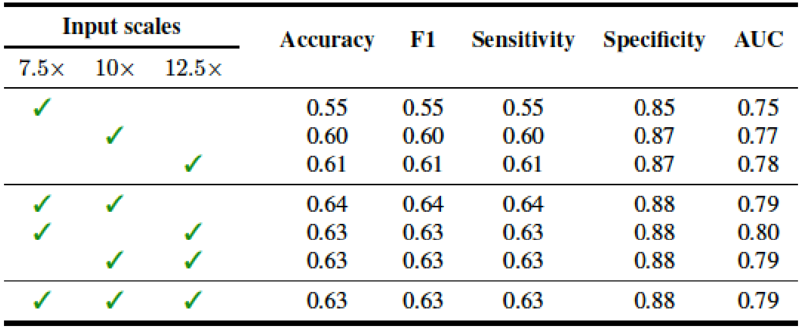
Experimental Result: soft label



Method	Accuracy	Specificity	AUC
Hard labels	0.50	0.83	0.73
Label smoothing	0.50	0.83	0.71
Constrained label smoothing	0.56	0.85	0.77
Soft labels (Ours; Section III-C)	**0.60**	**0.87**	**0.77**

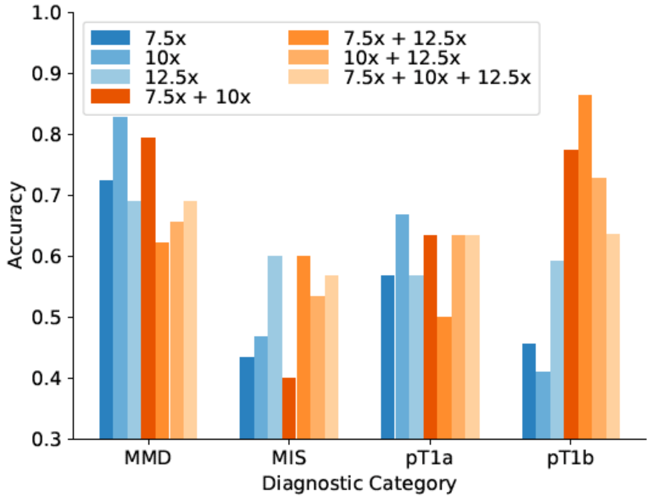
Comparison of the performance of different labeling methods.

Experimental Result: single vs. multiple input scales



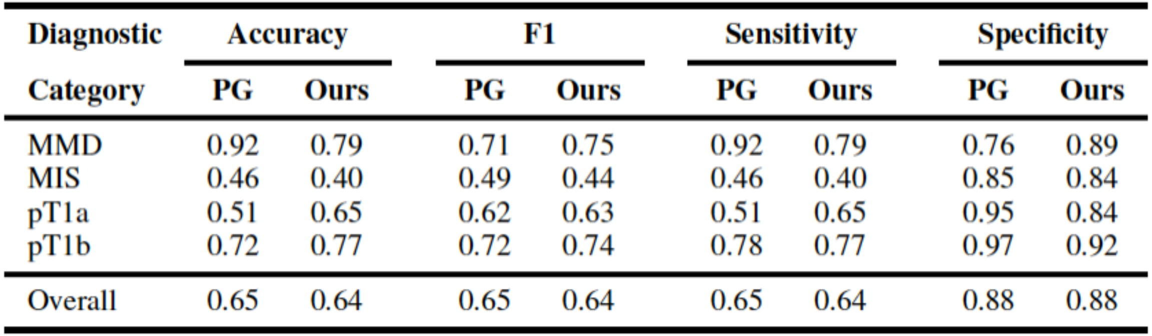
Input scales			Accuracy	F1	Sensitivity	Specificity	AUC
7.5×	10×	12.5×					
✓			0.55	0.55	0.55	0.85	0.75
	✓		0.60	0.60	0.60	0.87	0.77
		✓	0.61	0.61	0.61	0.87	0.78
✓	✓		0.64	0.64	0.64	0.88	0.79
✓		✓	0.63	0.63	0.63	0.88	0.80
	✓	✓	0.63	0.63	0.63	0.88	0.79
✓	✓	✓	0.63	0.63	0.63	0.88	0.79

(a) Overall performance of `ScAtNet`



(b) Class-wise accuracy of `ScAtNet`

Experimental Result: pathologists performance

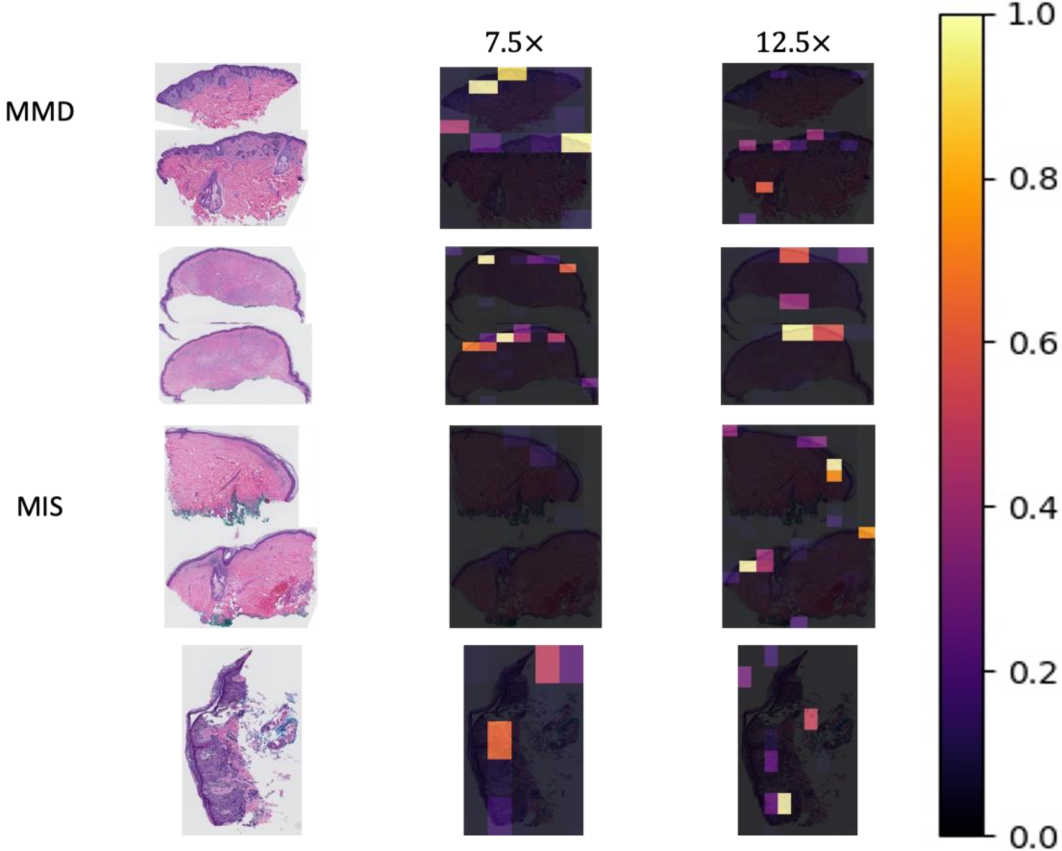


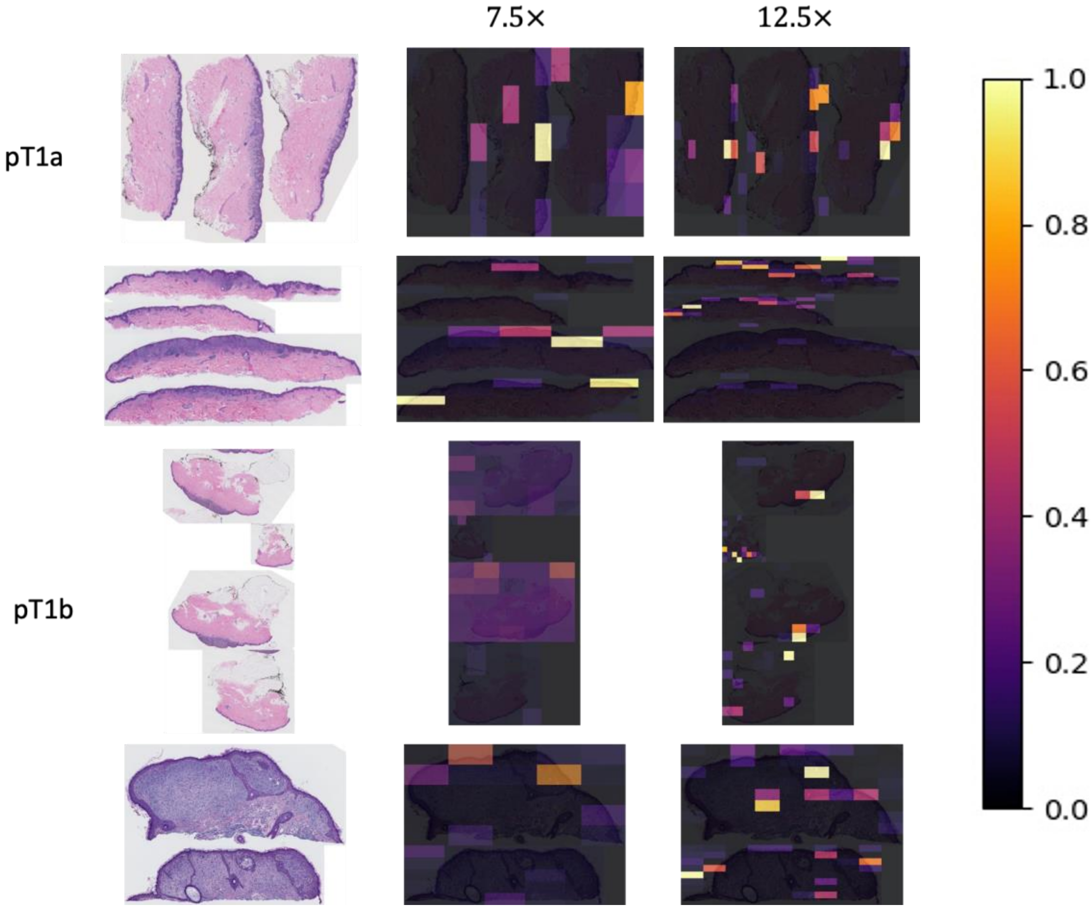
Diagnostic	Accuracy		F1		Sensitivity		Specificity	
Category	PG	Ours	PG	Ours	PG	Ours	PG	Ours
MMD	0.92	0.79	0.71	0.75	0.92	0.79	0.76	0.89
MIS	0.46	0.40	0.49	0.44	0.46	0.40	0.85	0.84
pT1a	0.51	0.65	0.62	0.63	0.51	0.65	0.95	0.84
pT1b	0.72	0.77	0.72	0.74	0.78	0.77	0.97	0.92
Overall	0.65	0.64	0.65	0.64	0.65	0.64	0.88	0.88

Comparison of ScAtNet with pathologists' (PG) performance.

Discussion

- Limited study on whole slide skin biopsy images (lack of public datasets)
- Limited in-house dataset size
- Mostly binary classification
    - This study covers the full spectrum of melanocytic skin biopsy
- Small test set
    - We have independent test set of 115 WSIs (50%)
- Saliency analysis shows that different input results in different attentions


7.5×
12.5×
MMD
MIS
1.0
0.8
0.6
0.4
0.2
0.0


7.5×
12.5×
pT1a
pT1b
1.0
0.8
0.6
0.4
0.2
0.0

Future Work

- Other types of image and cancer
- Learnable scale
- Wider range of scales
- Interpreting choice of scale, class and diagnosis accuracy
- Comparing viewing behavior with pathologists

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