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
Histology Examination
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
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
Soft labels

Step 1: Compute $\bar{s}$

Step 2: Assigning soft labels to tissue slices without ROI

Compute $d$-dimensional singular values $s$ using SVD

Compute mean singular value

Concatenate $C$-dimensional soft label

Dot-product

Softmax
## Soft labels

**Invasive T1a Skin Biopsy Image (or Class 3)**

| Hard Label (one-hot encoding)       | Label smoothing (smoothing=0.1)       |
|-------------------------------------|--------------------------------------|
| TS 1: 0 0 1 0                      | TS 1: 0.033 0.033 0.9 0.033           |
| TS 2: 0 0 1 0                      | TS 2: 0.033 0.033 0.9 0.033           |
| TS 3: 0 0 1 0                      | TS 3: 0.033 0.033 0.9 0.033           |

| Constrained label smoothing         | Soft labels (ours)                    |
|-------------------------------------|--------------------------------------|
| TS 1: 0.5 0.5 0 0                  | TS 1: 0.54 0.46 0 0                  |
| TS 2: 0 0 1 0                      | TS 2: 0 0 1 0                        |
| TS 3: 0.5 0.5 0 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

| Diagnostic Category | MMD | MIS | pT1a | pT1b |
|---------------------|-----|-----|------|------|
| Accuracy            |     |     |      |      |
| ChikonMIL           |     |     |      |      |
| MS-DA-MIL (MSC)     |     |     |      |      |
| Ours (7.5x + 10x)   |     |     |      |      |
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  |
|--------------|----------|----|-------------|-------------|------|
| 7.5x         | 0.55     | 0.55 | 0.55        | 0.85        | 0.75 |
| 10x          | 0.60     | 0.60 | 0.60        | 0.87        | 0.77 |
| 12.5x        | 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 Category | Accuracy | F1 | Sensitivity | Specificity |
|---------------------|----------|----|-------------|-------------|
|                     | 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
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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