Stable classification of diabetic structures from incorrectly labeled OCTA enface images using multiple instance learning

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Poster # 1087 - C0181

PURPOSE

- Diabetic retinopathy (DR) is one of the leading vision impairments in working-aged adults
- DR progression can be controlled when diagnosed early
- Early signs of lesions start occurring in the periphery of the retina – widefield OCT angiography (wOCTA) en face images provide this information
- We propose a novel multiple instance learning (MIL)-based CNN classifier for classifying DR in wOCTA en face images with weakly (binary) labeled data

METHODS

- wOCTA images cover a field of view (FoV) of 65°
- Used a database consisting of 354 wOCTA en face images
- 257 en face images of diabetic patients and 97 images of healthy volunteers, split into:
  - Training (211/64)
  - Validation (24/24)
  - Testing (22/8)
- Image dimensions are 1536 x 2048 x 2048 samples for every volume, covering 6 x 18 x 18 mm^3 (Figure 1 (c))
- Figure 1 shows the concept of MIL:
  - A bag is a collection of sub-structures/features, so-called instances (Figure 1 (a))
  - Information is assumed to be held at the instance level
  - Only binary bag labels available for the entire dataset – whether it's from a diabetic or not (Figure 1 (b))
- MIL-processing requires image normalization and creation of 10 x 10 instances per bag (Figure 2)
- We benchmarked our network, MIL-ResNet14, against proven capable DR-classifiers: ResNet14 & VGG16

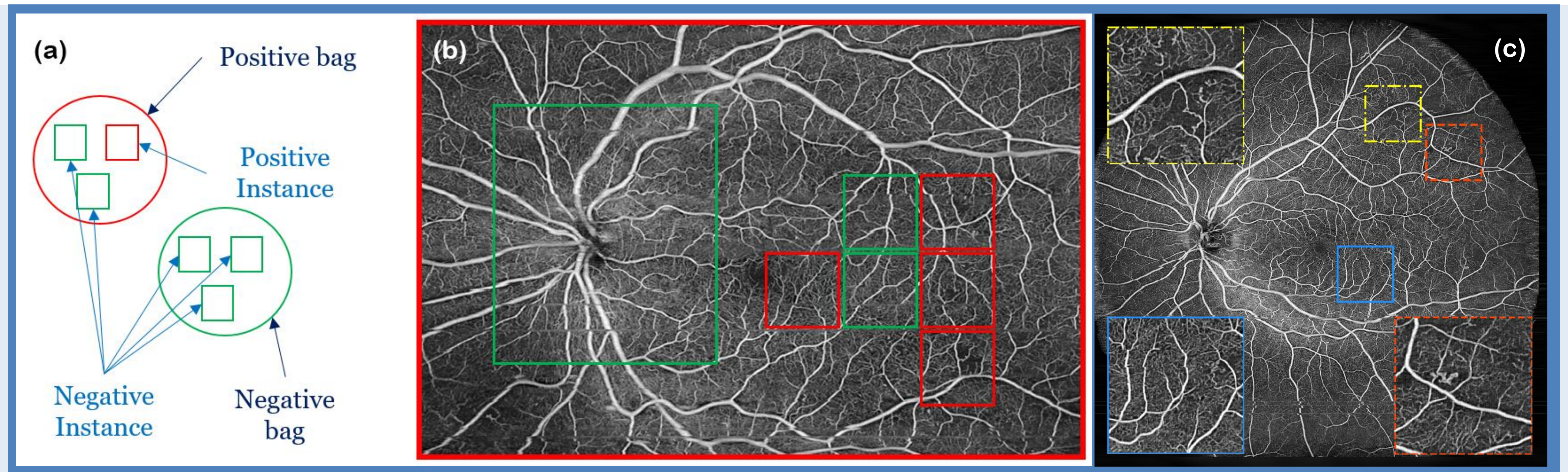

Figure 1. (a) Conceptual visualization of instances and bags in MIL. (b) Example of instances in a wOCTA en face image. (c) Categories of lesions on wOCTA en face images of a patient with slight signs of DR.

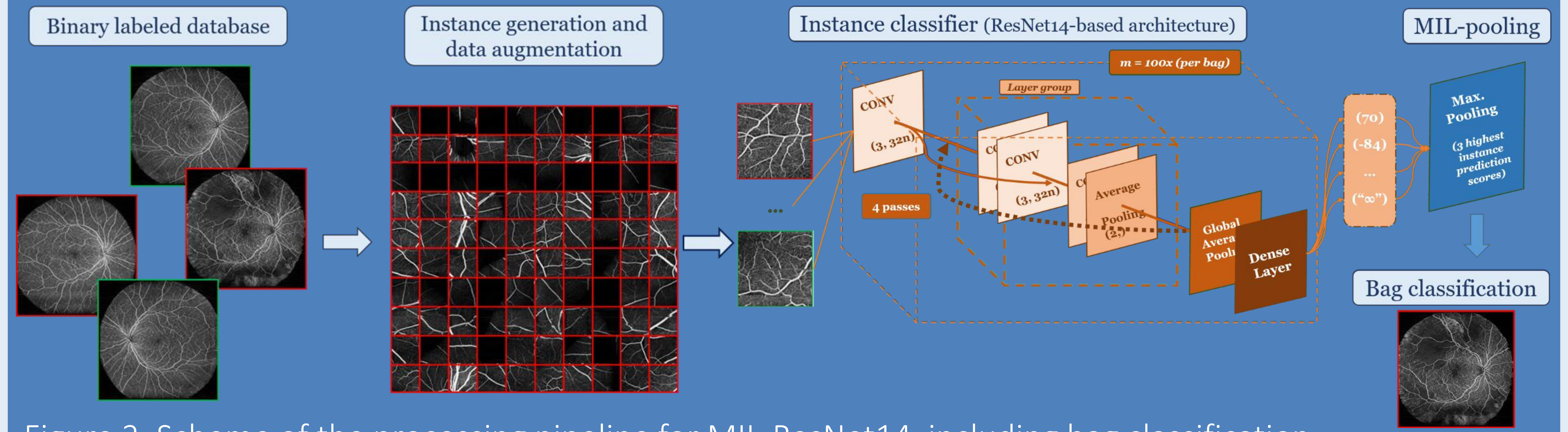

Figure 2. Scheme of the processing pipeline for MIL-ResNet14, including bag classification.

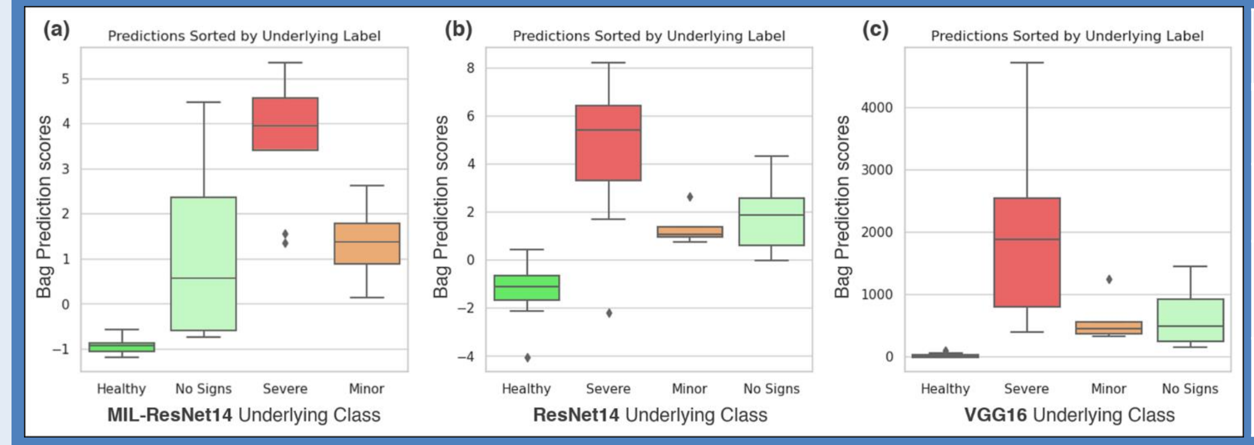

Figure 3. Predictions after underlying classes of (a) MIL-ResNet14, (b) ResNet14 and (c) VGG16.

Metric	VGG16	ResNet14	MIL-ResNet14
F1-score	0.857	0.909	0.950
ROC-AUC	1.000	0.942	0.973
Instance Accuracy	-	-	0.541
Instance Precision	-	-	0.993

Table 1. Classification metrics of the benchmarked classifiers on test dataset.

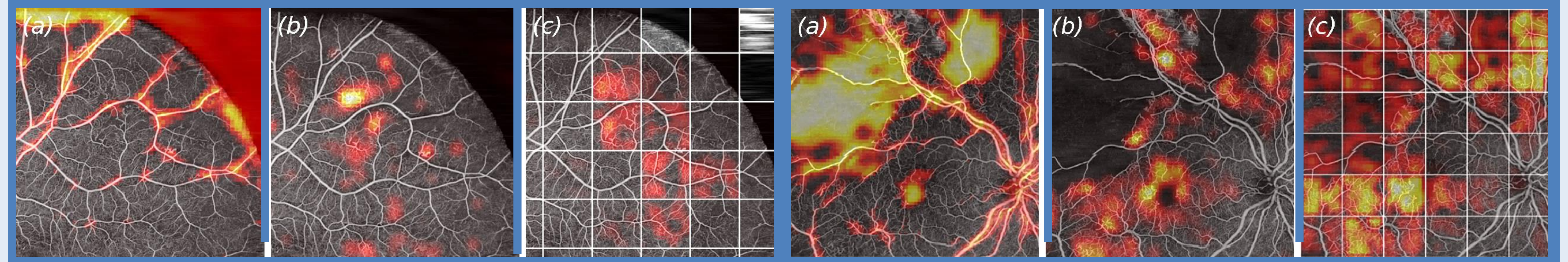

Figure 4. Grad-CAM overlays onto two different eyes with mild DR signs (left) and severe signs (right).

- We created Grad-CAM overlays to show feature activation heatmaps of all different networks (Figure 4 (a)-(c) left & right)

RESULTS

- Figure 3 shows the classification results of carefully put together test dataset, containing the entire spectrum of severity of DR in our dataset
- Table 1 shows MIL-ResNet14 reached an F1-score (harmonic mean of precision and recall) of 0.95 and outperformed ResNet14 and VGG16 (Table 1)
- MIL-ResNet14 was trained until the AUC-accuracy didn't improve anymore
- MIL-ResNet14 generalized better during training while ResNet14 and VGG16 required careful hyperparameter tuning
- We created Grad-CAM overlays for all corresponding original wOCTA en face – MIL-ResNet14 "paid closer attention" to all relevant biomarkers/lesions

CONCLUSIONS

- We developed a multiple instance learning-based classifier which outperformed state-of-the-art DR-Classifiers, ResNet14 and VGG16
- Grad-CAM images give a good idea of which parts of the image were deemed important but should not be mistaken with semantic annotations/segmentations
- MIL-ResNet14 has potential to be used as a clinical support tool for decision making and early detection of DR

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Disclosures: PM, JS, TS, JN, WD, RAL (C)(i), HS (N), TS (E)(i), WD, RAL (F)(i) AP (F)(i,iii) (C)(ii,iii,iv,v)

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