Automated Detection of Vascular Leakage on Fluorescein Angiography

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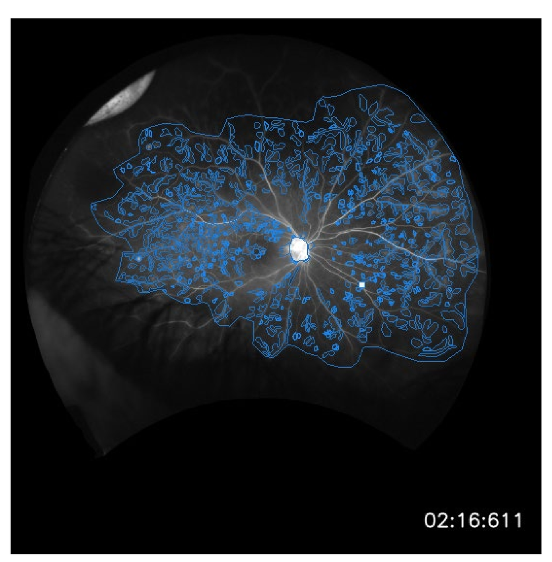
Background

Uveitis is a heterogeneous group of inflammatory eye diseases responsible for causing an estimated 10-15% of blindness in the United States[1]. Fluorescein angiography (FA) is the current gold standard for imaging retinal vasculature in uveitis. However, clinician interpretation of FAs can be subjective. We aimed to quantify variability of clinician FA segmentation. We also hypothesized that a deep learning algorithm can:

1. Segment FAs for vascular leakage, and
2. Detect clinically significant change in vascular leakage between FAs

Methods



Example of vascular leakage segmentation. All segmentations were performed in Adobe Photoshop

Ground Truth

200 uveitis patient FA images were obtained from a uveitis biobank with prospectively enrolled patients. A 2-clinician team annotated (segmented) images for vascular leakage. Before beginning, all graders met and discussed the definition of leakage, and agreed on a segmentation protocol defined by the senior clinician.

Algorithm

Deep Learning Algorithm with a modified U-net architecture was trained to segment leakage. 5-fold cross validation was used, each fold with 80% training and 20% testing

Statistics

The Dice Similarity Coefficient (DSC) was used to compare the algorithm's segmentation results to the ground truth segmentation (the DSC ranges from 0 to 1, 0 denotes no overlap between 2 segmentations and 1 denotes perfect overlap)

Interrater Variability

For interrater variability, 2 clinicians independently segmented 20 images and the average Dice Similarity Coefficient (DSC) was calculated.

Clinically Significant Change in Vascular Leakage

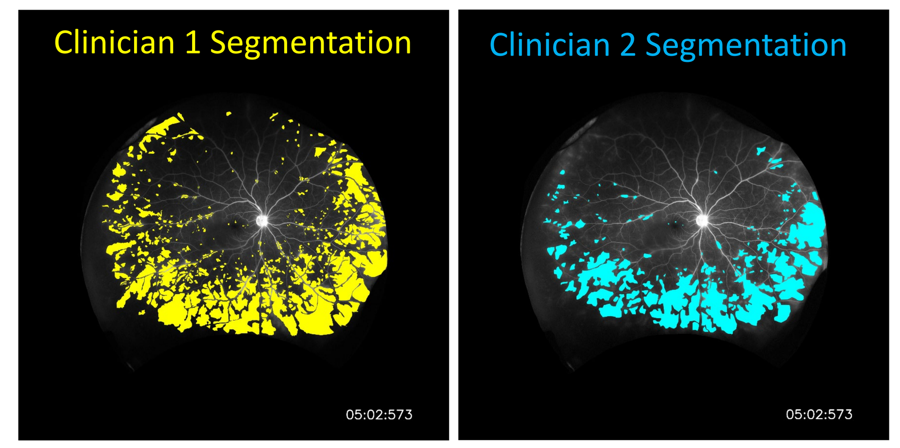
20 pairs of FA images were used to detect clinically significant changes in leakage (the gold standard being an expert uveitis specialist's assessment). For each pair, the difference in percentage of the image occupied by the algorithm's leakage segmentation was calculated and used to create a ROC curve and to determine a threshold for clinically significant change.

Results

Inter-rater variability was assessed with 2 clinicians each segmenting 20 images

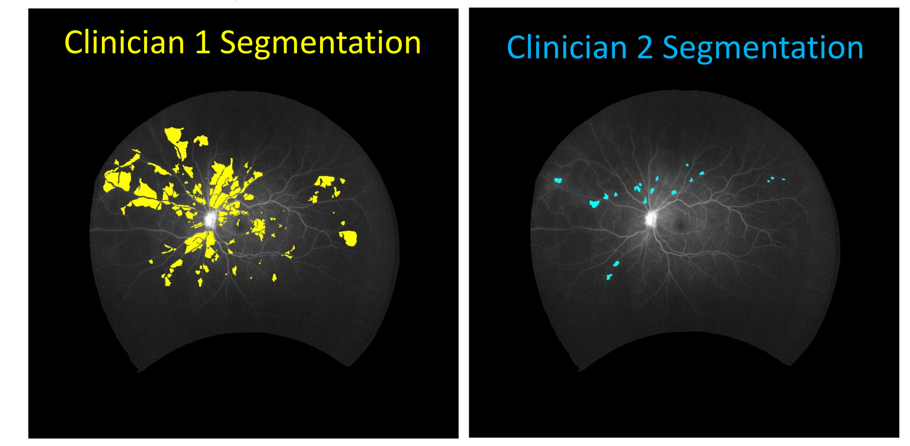
Example of good clinician concordance

Dice Similarity Coefficient: 0.642



Example of poor clinician concordance

Dice Similarity Coefficient: 0.095



	Average Dice Similarity Coefficient
Clinician 1 vs 2	**0.374**

Image characteristics of FAs used for algorithm training

Average FA timepoint	361 seconds
n, right eye	140/200 (60%)
Median images contributed (per patient)	2
Image date range	Mar 2016-Dec 2019

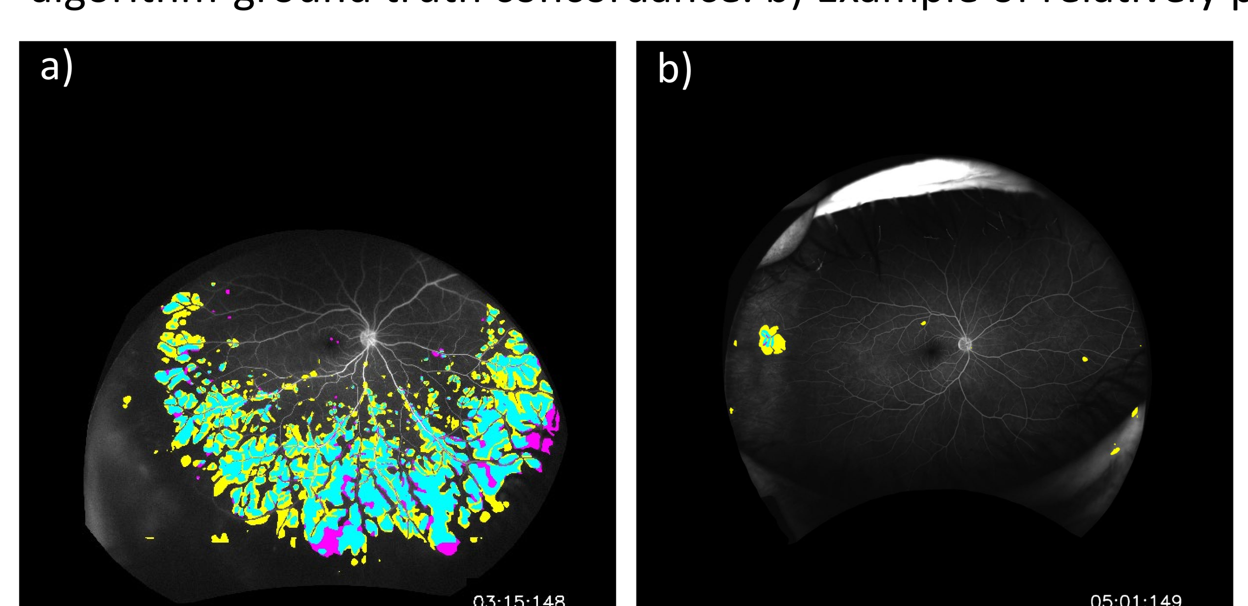
Patient characteristics of the photos (by anatomic location of uveitis)

Anatomic location	Patients, n
Anterior Uveitis	2
Intermediate Uveitis	24
Posterior/Panuveitis	31
Other	4

A variety of algorithm parameters were tested and algorithm performance measured. The best algorithm achieved an average DSC of 0.572

Crop Window Sizes	Loss Function	Image Enhancement	Epochs	Avg DSC
672×672	Binary Cross Entropy	No	20	0.482
672×672	Binary Cross Entropy	No	100	0.493
672×672	Dice Coefficient Loss	No	20	0.494
672×672	Binary Cross Entropy	No	50	0.528
672×672	**Dice Coefficient Loss**	**Yes**	**200**	**0.572**
1334×1334	Dice Coefficient Loss	Yes	50	0.505
1334×1334	Binary Cross Entropy	No	50	0.459
1334×1334	Dice Coefficient Loss	No	50	0.465
1792×1792	Binary Cross Entropy	No	100	0.471
1792×1792	Dice Coefficient Loss	No	100	0.455

Examples of algorithm and ground truth concordance. a) Example of relatively high algorithm-ground truth concordance. b) Example of relatively poor concordance



Dice Similarity Coefficient: 0.718

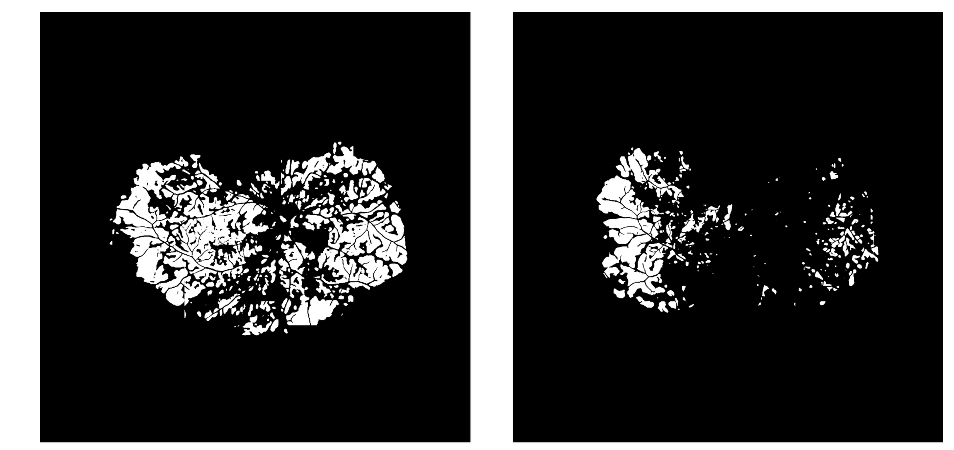
Dice Similarity Coefficient: 0.263

Figure Color Coding Legend

- Teal: denotes areas where algorithm and ground truth segmentation overlap
- Yellow: "false positive". Denotes areas where the ground truth segmentation did not detect vascular leakage, but the algorithm did
- Pink: "false negative". Denotes areas where the ground truth segmentation detected vascular leakage, but the algorithm did not

Results (continued)

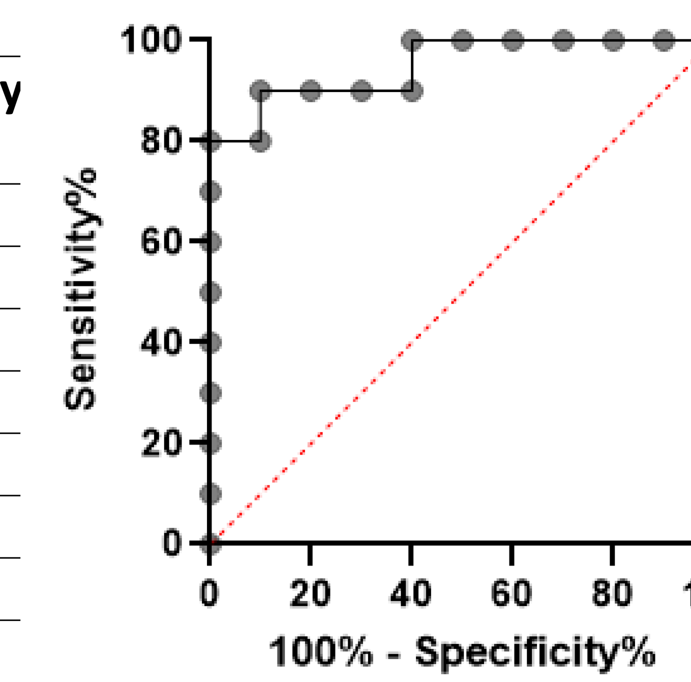
Algorithm-assisted automated detection of clinically significant changes in vascular leakage



Timepoint 1 Timepoint 2

Example of algorithm segmentation results of the same patient's eye at two different timepoints. 20 pairs were used

Threshold	Sensitivity %	Specificity %
>0.015	100	10
>0.150	100	40
>0.50	90	60
>0.635	90	70
>0.80	**90**	**90**
>2.50	60	100
>6.15	20	100



Area under the Curve: 0.95

Conclusions

FA leakage segmentation is a difficult computer vision problem to solve. In this project, we quantified variability between clinician segmentation of vascular leakage. We also developed a preliminary deep learning algorithm that was able to segment vascular leakage in the fluorescein angiograms of uveitis patients with modest results. However, the algorithm was able to determine clinically significant change in vascular leakage with high accuracy.

Future Directions

Efforts to develop an improved deep learning algorithm, training and testing on fluorescein angiograms from other institutions and testing the algorithm on non-uveitis causes of vascular leakage are underway.

References

1. Read R. General Approach to the Uveitis Patient and Treatment Strategies. In: Yanoff M, Duker J, eds. *Ophthalmology*. 5th ed. Elsevier; 2019.

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