Clinically applicable deep learning for diagnosis and referral in retinal disease

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Presented by Ming
27-08-2018

Outline

- Background of the study
- Study design / methods
- Results
- Summary

Background - goal

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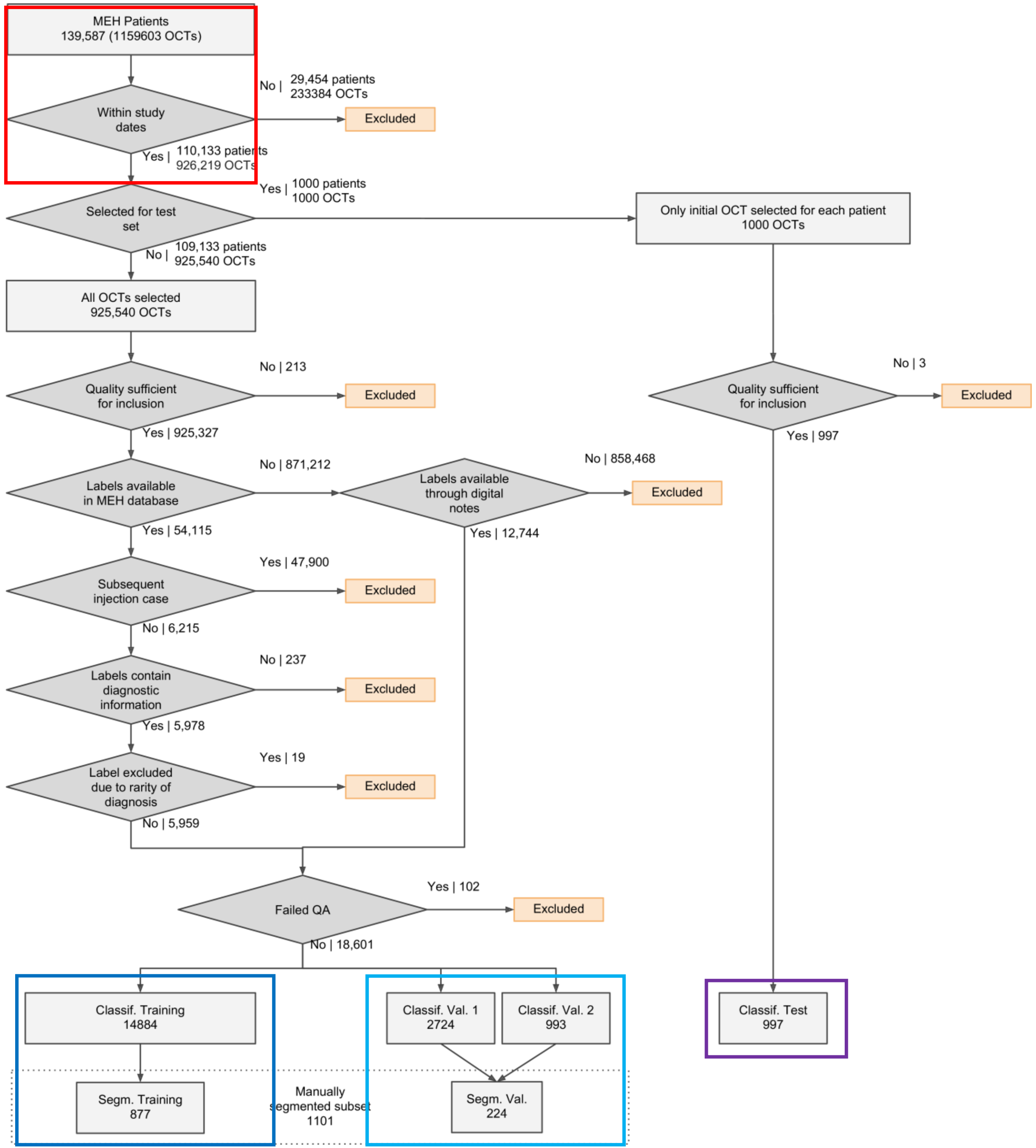
- to **produce automated diagnosis** that reach **performance of expert clinicians**
  - Referral decisions
  - Classification of 9 retinal pathologies
- on three-dimensional diagnostic scans of the retina

Background - dataset

- A retrospective cohort of patients who
  - attended Moorfields Eye Hospital between 1 June 2012 and 31 January 2017,
  - received OCT imaging as part of their routine clinical care
- Training set (n= 14884 /877)
  - Train the networks in the framework
- Validation set (993/224)
  - Fine-tune hyperparameters
- Test set (997)
  - Compare performance of the framework with human experts



Supp. Fig. 11, Fauw *et al.* (2018) *Nat. Med.*

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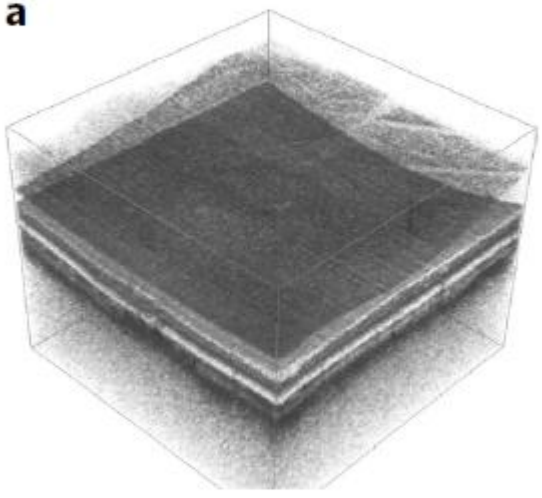
Optical coherence tomography (OCT) image

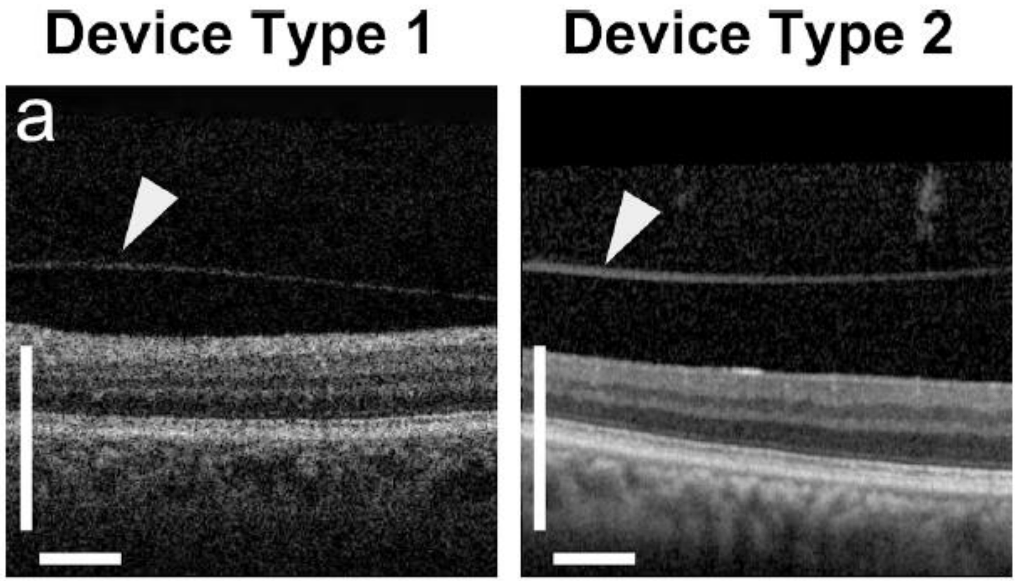
- 3-D medical imaging technique
- Analogous to 3-D ultrasonography (near-infrared light instead of sound waves)
- Resolution: ~5 μ m



Digital OCT scan

Image credit : Fauw *et al.* (2018) *Nat. Med.* Midwest City Eye Care Associates

Challenge I - technical variability



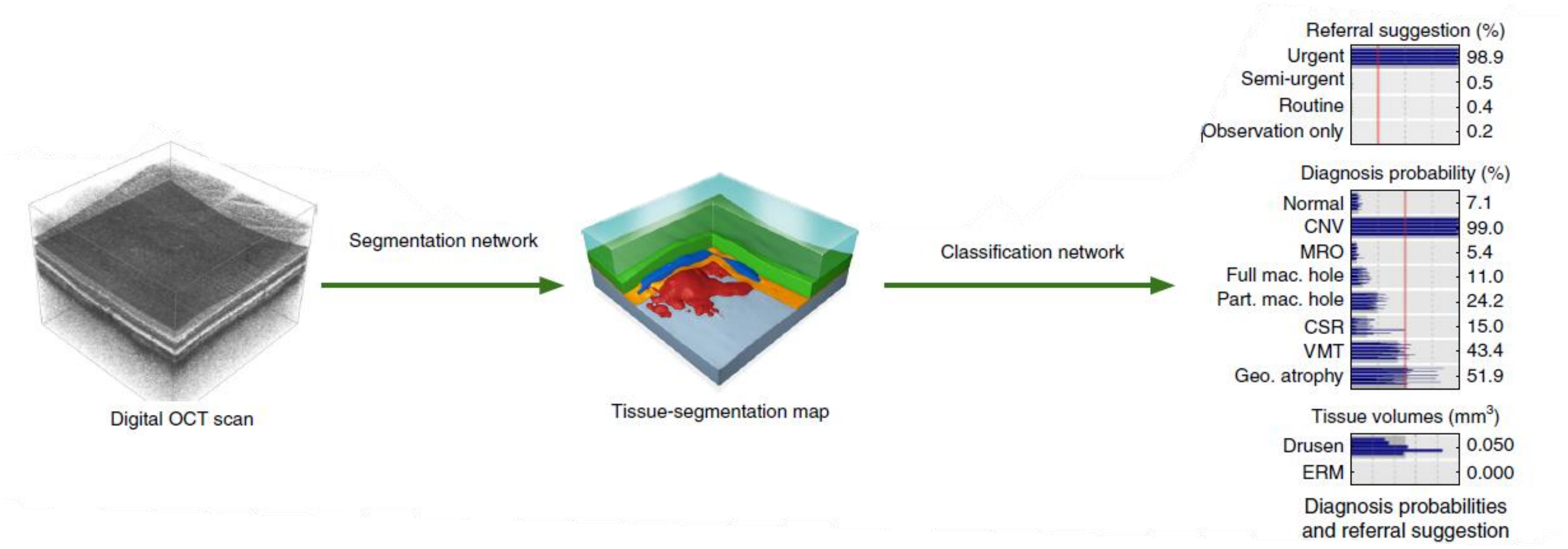
Topcon 3D OCT

Heidelberg Spectralis

- Model trained on images from one device may perform poorly on images from the other

Modified from Supp. Fig. 9, Fauw *et al.* (2018) *Nat. Med.*

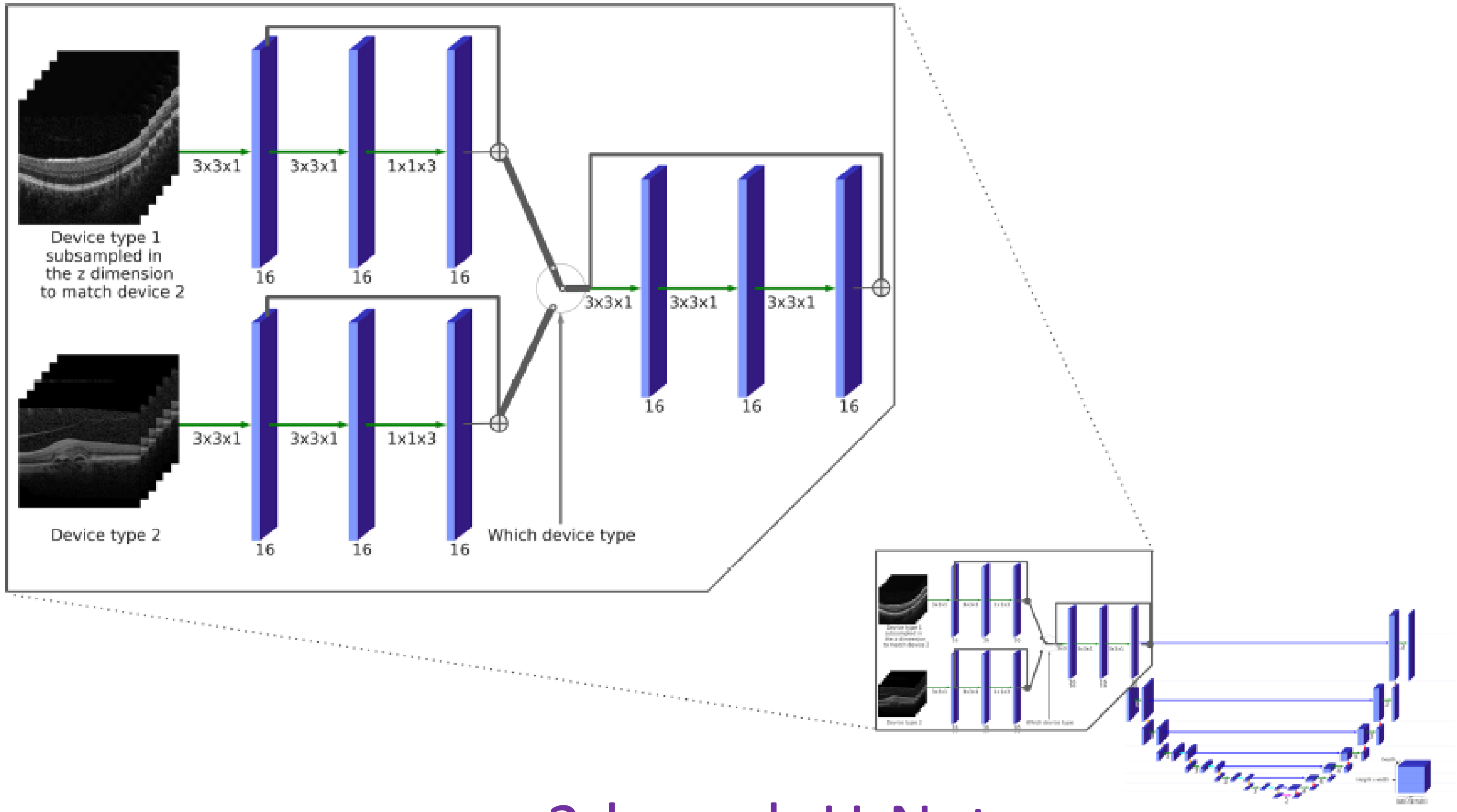
Method - proposed 2-stage framework



1. Creates device independent segmentation map
2. Prediction of referral decision and retinal morphologies

Modified from Fig. 1, Fauw *et al.* (2018) *Nat. Med.*

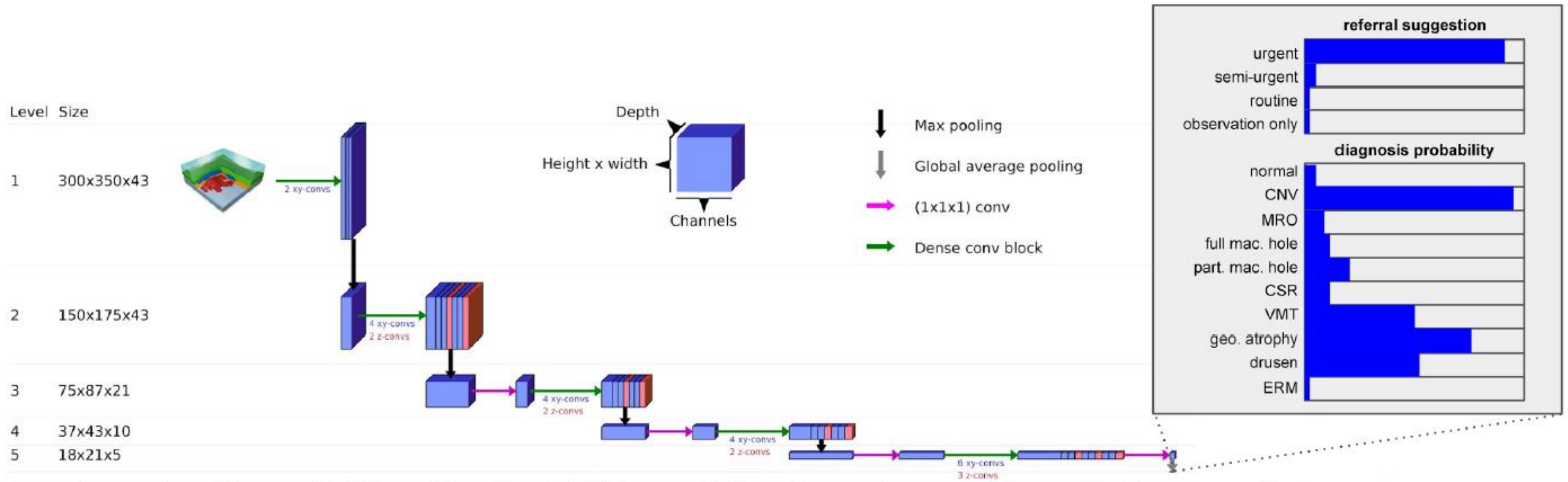
Architecture of the segmentation network



2-branch U-Net

Supp. Fig. 15, Fauw *et al.* (2018) *Nat. Med.*

Architecture of the classification network

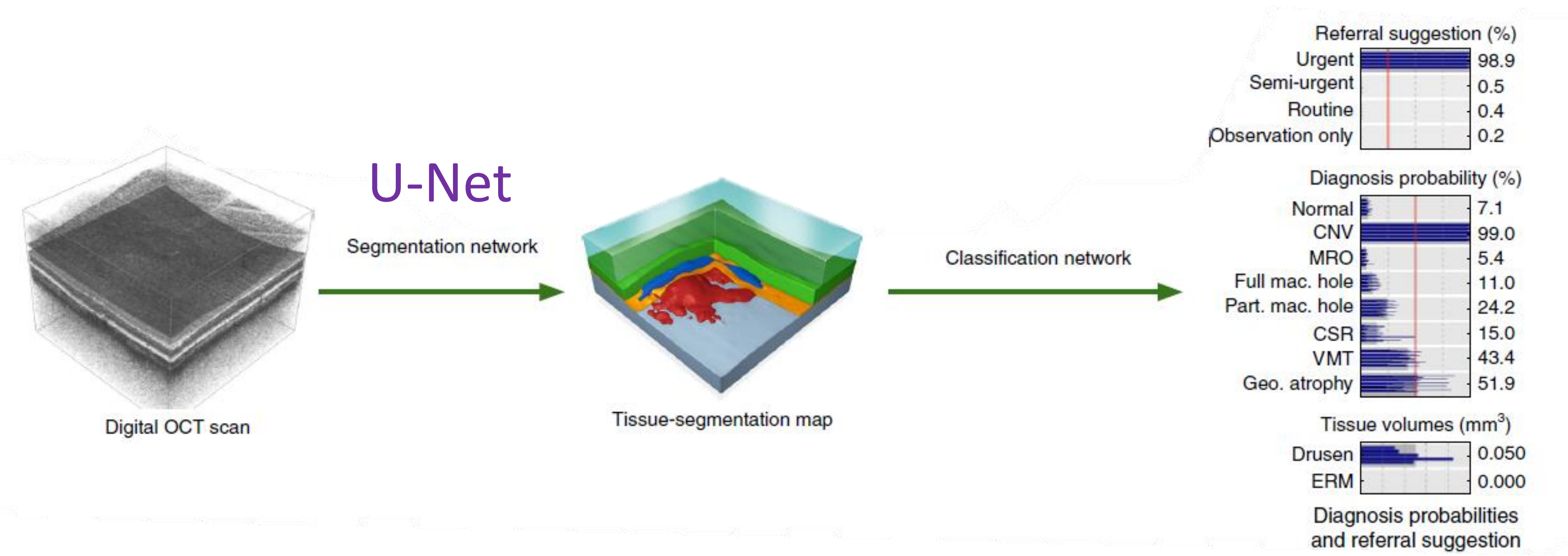


Supplementary Figure 16 | Classification CNN (convolutional neural network) used in the second stage of our approach. Blue and red boxes illustrate the 4D activation maps. Blue boxes are the result of a (3x3x1) convolution, while red boxes are the result of a (1x1x3) convolution.

Supp. Fig. 16, Fauw *et al.* (2018) *Nat. Med.*

Challenge II - Annotation

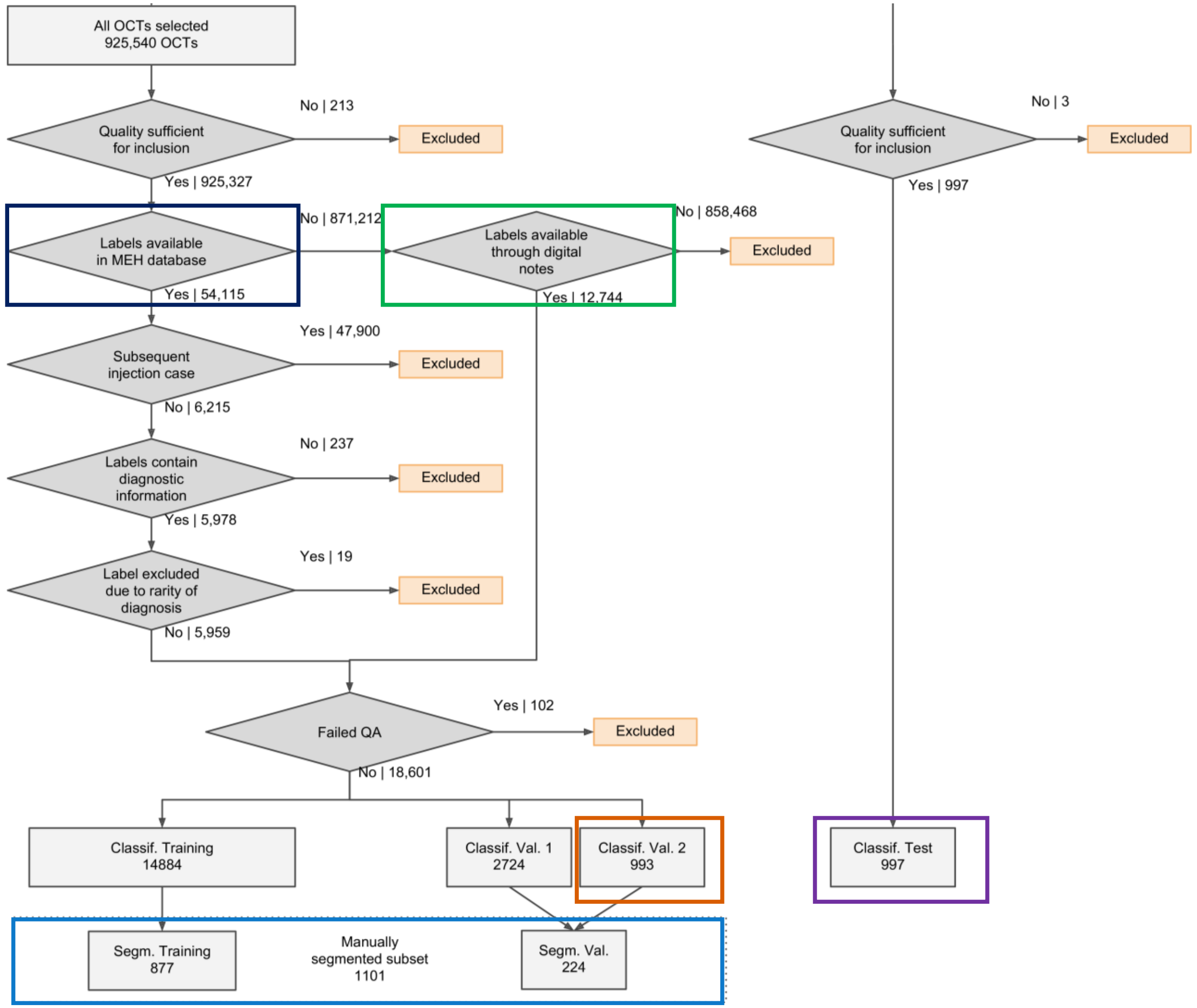
- Deep learning typically requires a large amount of data
- Many data are without label
- Unrealistic to annotate all images



Modified from Fig. 1, Fauw *et al.* (2018) *Nat. Med.*

Method - annotations scheme

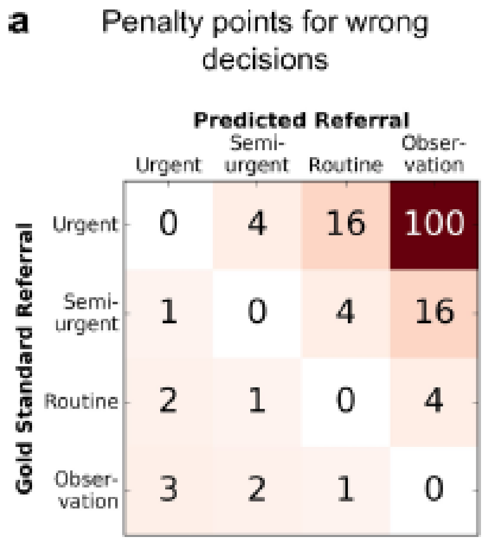
1. Referral decision
   - Electronic health record
   - 4 junior + 4 senior experts
2. Retinal pathologies
   - Automated notes search + manual review of the OCT scans
   - Manual annotation by 3 junior graders by 1 senior
   - 4 junior + 4 senior experts
3. Segmentation map
   - Manual annotations **on 3-5 out of 128 slices per OCT** with review by 1 senior



Modified from Supp. Fig. 11, Fauw *et al.* (2018) *Nat. Med.*

Penalty score

- Scale the penalty to the severity of adverse consequences for each misdiagnosis



Modified from Supp. Fig. 6, Fauw *et al.* (2018) *Nat. Med.*

The framework

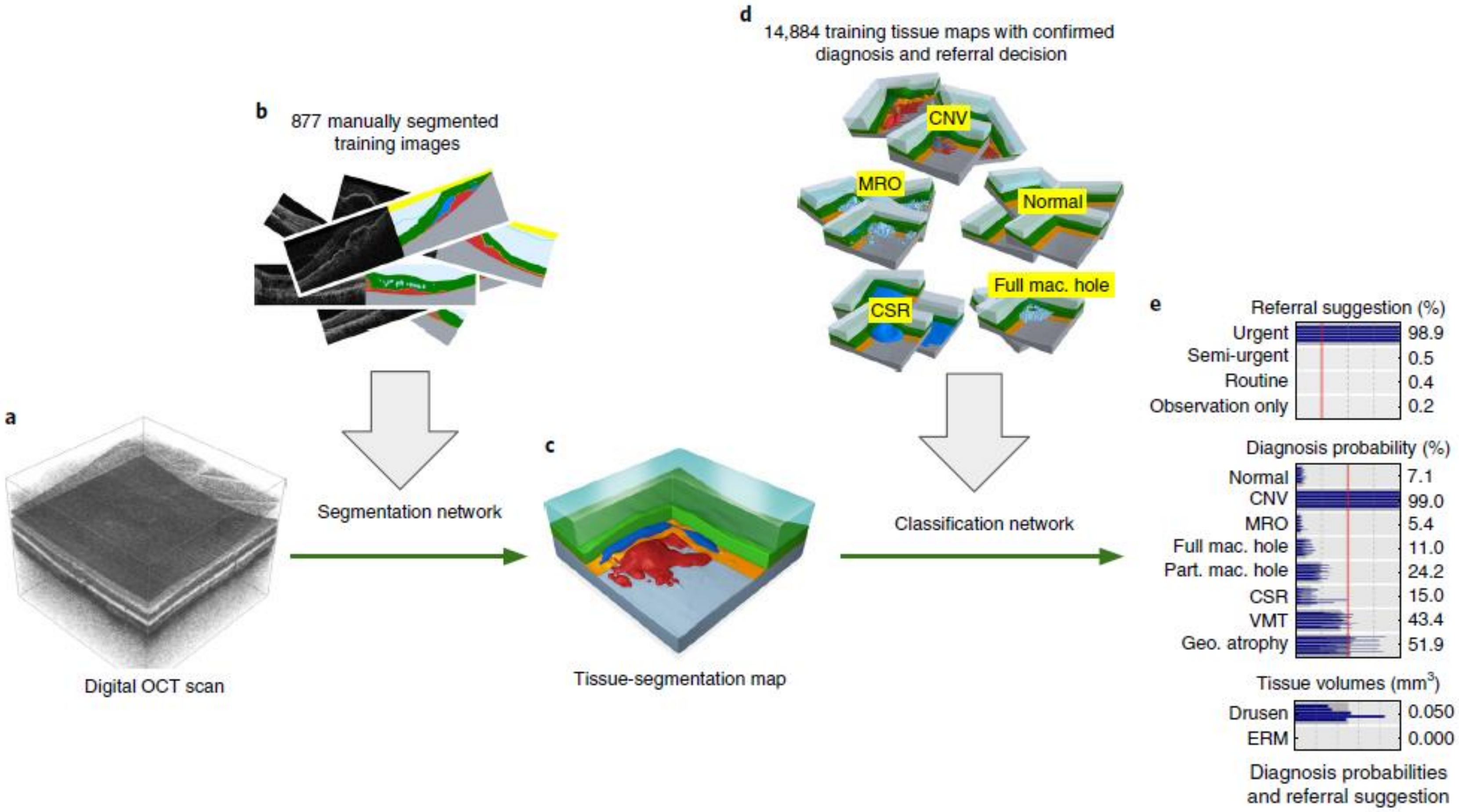
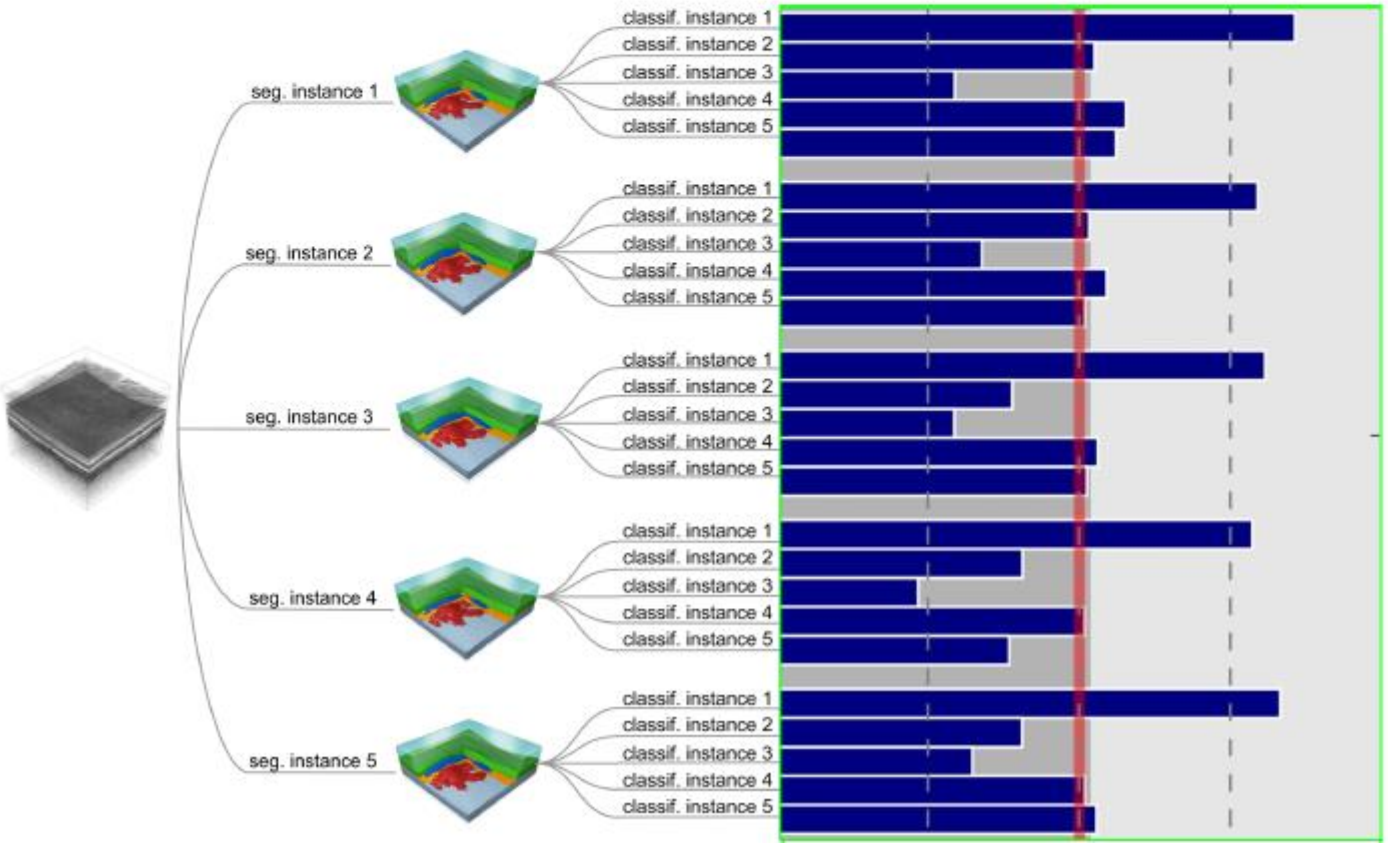


Fig. 1 | Our proposed AI framework. a, Raw retinal OCT scan ($6 \times 6 \times 2.3\,mm^3$ around the macula). **b**, Deep segmentation network, trained with manually segmented OCT scans. **c**, Resulting tissue segmentation map. **d**, Deep classification network, trained with tissue maps with confirmed diagnoses and optimal referral decisions. **e**, Predicted diagnosis probabilities and referral suggestions.

Fauw *et al.* (2018) *Nat. Med.*

Method – ensemble output

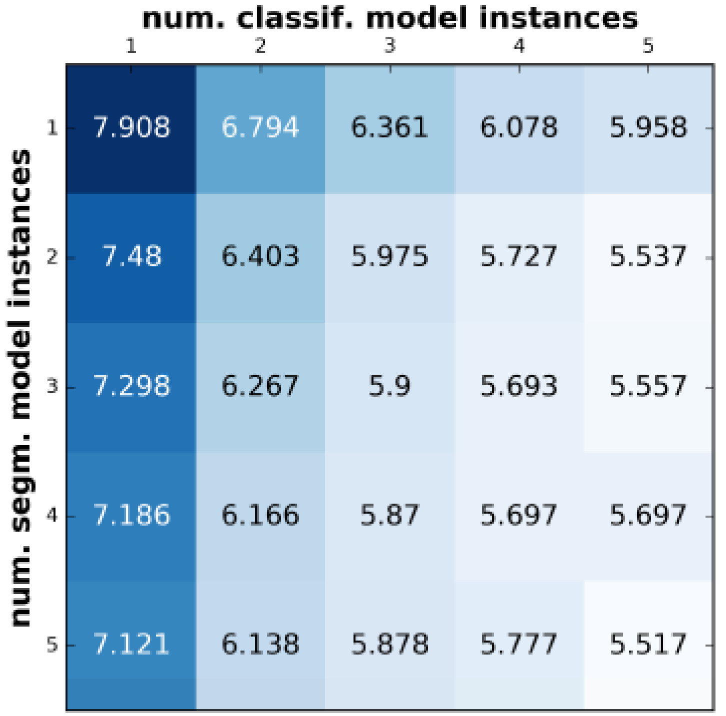
- 5 segmentation network instance x 5 classification network instances
- Averaging the probabilities of 25 outputs



Modified from Supp. Fig. 1 , Fauw *et al.* (2018) *Nat. Med.*

Error rate with different number of instances

Error rate [percent]



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Result - segmentation

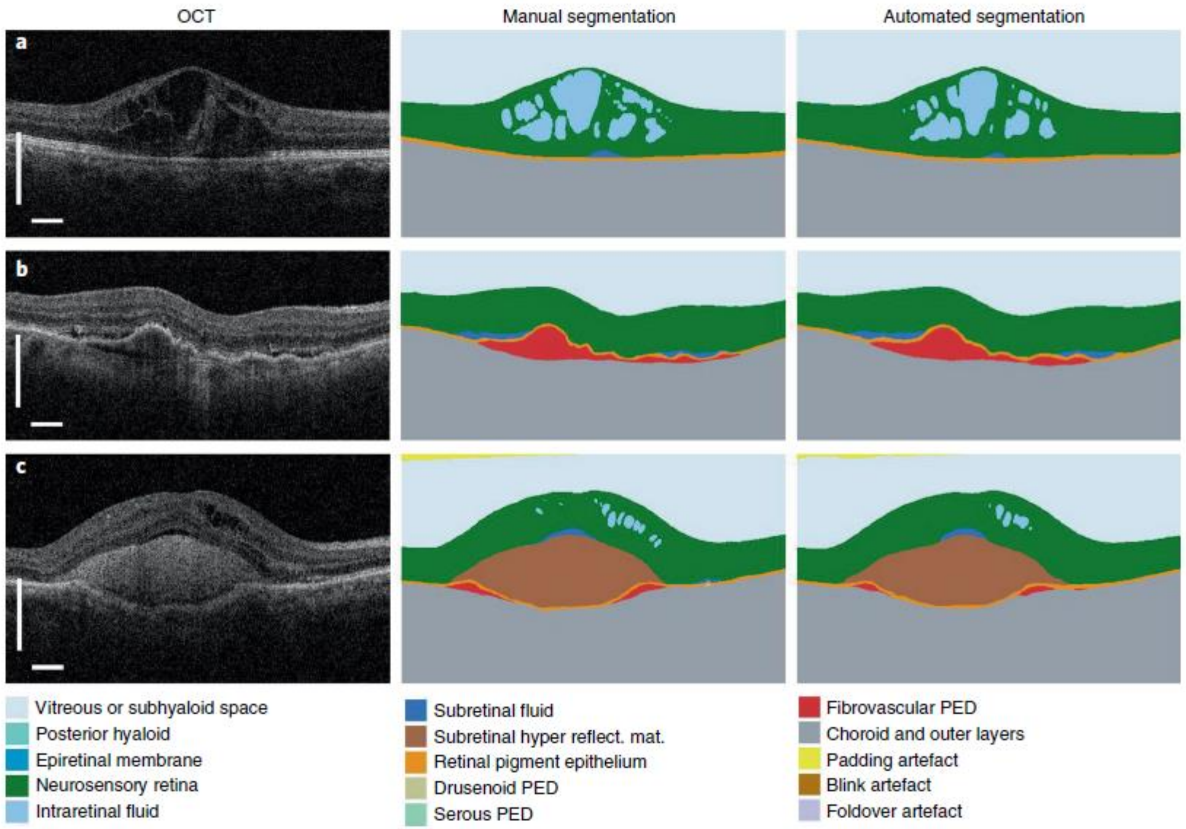


Fig. 2 | Results of the segmentation network. Three selected two-dimensional slices from the $n = 224$ OCT scans in the segmentation test set (left) with manual segmentation (middle) and automated segmentation (right; detailed color legend in Supplementary Table 2). **a**, A patient with diabetic

Fauw *et al.* (2018) *Nat. Med.*

Result – performance on referral decision I

- Framework vs 8 clinical experts
- Empty markers: expert performance using OCT, fundus image and summary notes
- Filled: using only OCT

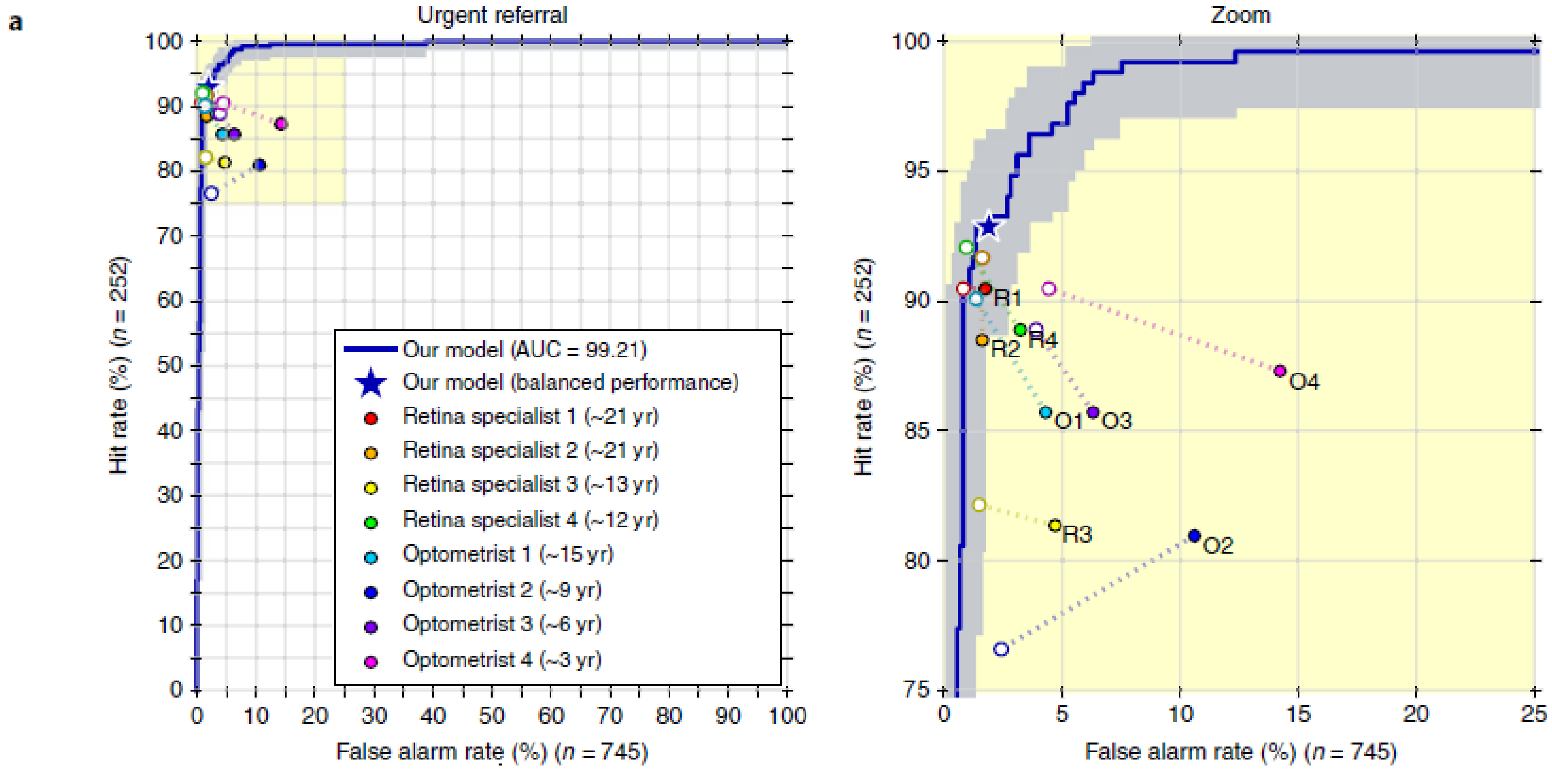


Fig. 3, Fauw *et al.* (2018) *Nat. Med.*

Result – performance on referral decision II

- Framework vs 2 senior experts

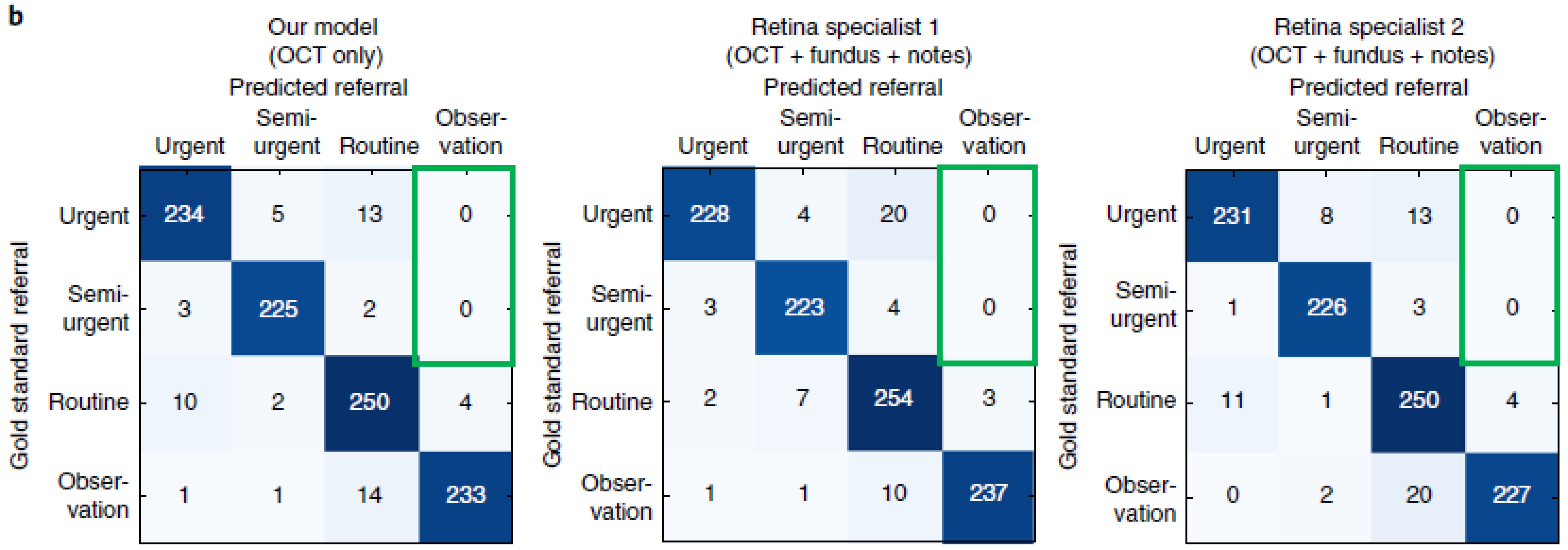
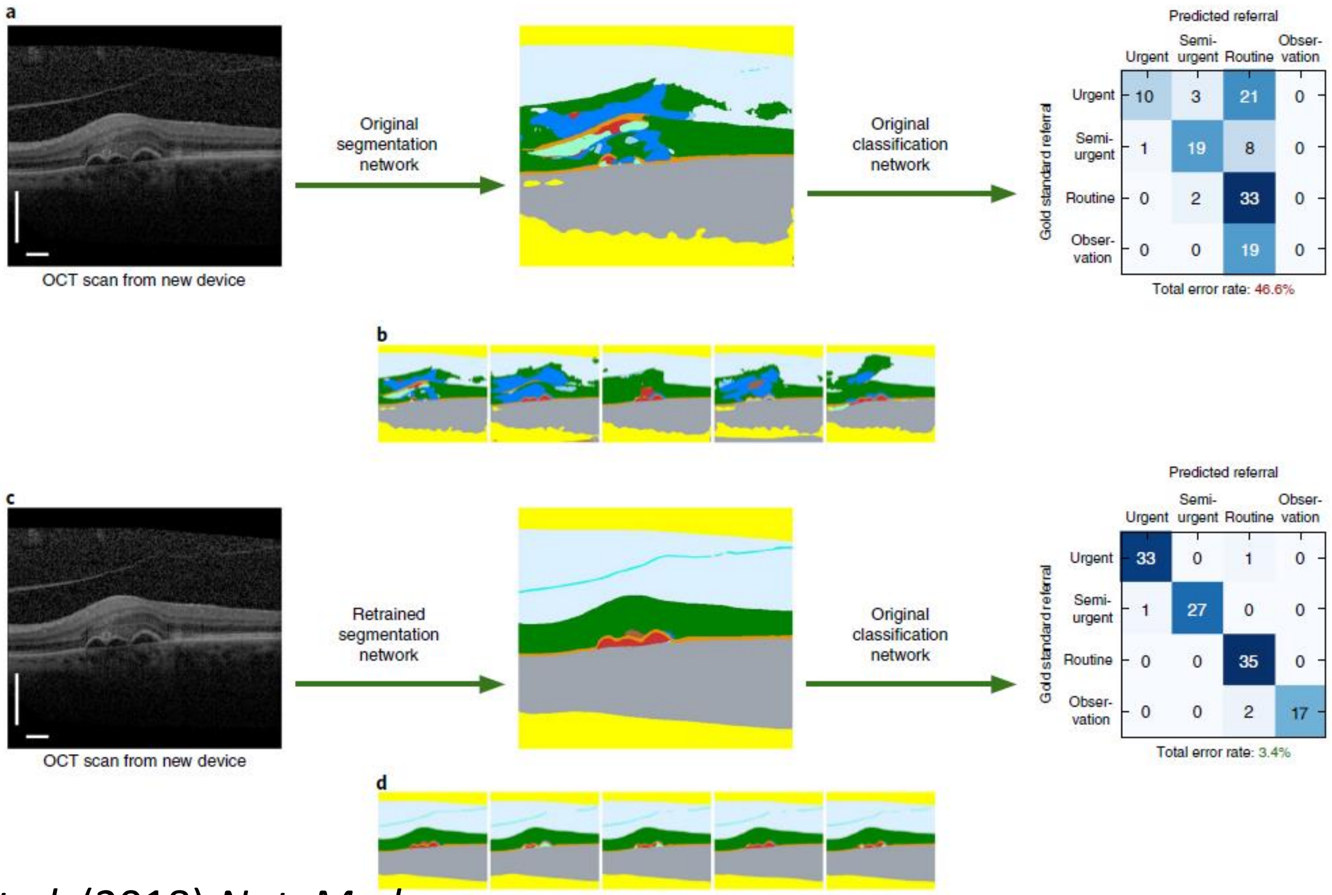


Fig. 3, Fauw *et al.* (2018) *Nat. Med.*

Result – generalization to a new device type

- High error rate likely due to erroneous segmentation



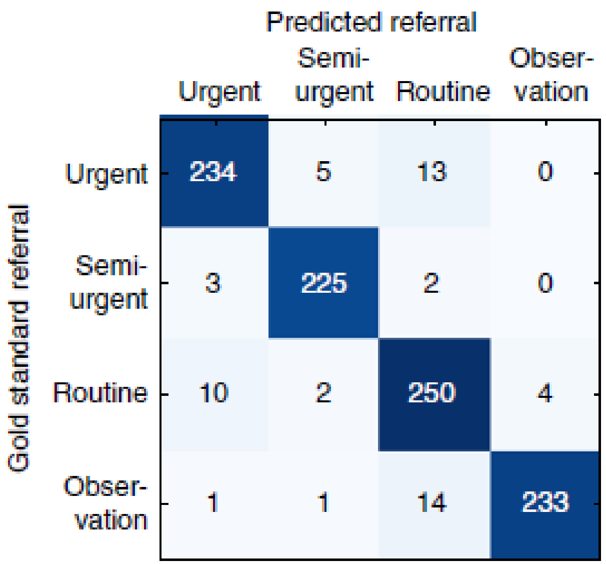
With original U-Net
for segmentation
Error rate: 46.6 %

With 2-branch U-Net
Error rate: 3.4 %

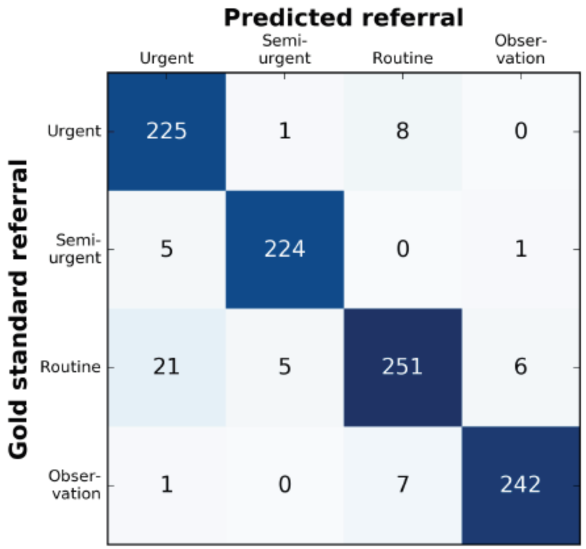
Fig. 4, Fauw *et al.* (2018) *Nat. Med.*

Result – 2-stage vs end-to-end approach

- The same classification network architecture trained on 14884 raw images instead of segmentation map
- Error rate: 5.5% both



2-stage approach



end-to-end approach

Note:
All images are from device type 1 !
Performance on device type 2 unknown.

Fig. 3 & Supp. Fig. 7 , Fauw *et al.* (2018) *Nat. Med.*

Summary

- New architecture
  - 2-stage approach
    - Reduced training data requirement
- Penalty customized to reflect consequence of error
- Generalizability
  - Wide coverage on pathologies
  - Images collected using 37 devices (2 types) at 32 different clinical sites
- The ensemble output had **performance comparable to top clinical expert**