# Reliability of Optical Coherence Tomography Angiography for Identifying Choroidal Neovascular Membranes: A Masked Study

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## Background

- Optical coherence tomography angiography (OCT-A) is a non-invasive , faster alternative to fluorescein angiography (FA), allowing three-dimensional imaging of the chorio-retinal circulation without the risk of side effects including anaphylaxis.
- Here we report on the sensitivity and specificity of the Heidelberg Spectralis ® OCT-A for the identification of CNV in patients with neovascular age-related macular degeneration (nAMD). All data was collected in a 'real-world' clinical setting.
- We additionally report on the sensitivity and specificity of two surrogate markers of nAMD, the 'double layer sign' (DLS) and 'sub-retinal hyper-reflective material' (SHRM).

## Methods

- 43 eyes from 26 treatment-naïve patients were included and retrospectively analysed.
- Spectral domain optical coherence tomography (SD-OCT) and OCT-A scans were obtained using the Heidelberg Spectralis at their baseline visit, in addition to fluorescein angiography (FA).
- Three masked clinicians then viewed each patient's images and graded them as per the following protocol:

1. **Decide if CNV is present using the built-in 'avascular complex' automated slab tool to view the OCT-A image**
2. **Decide if CNV is present by manually scrolling through the OCT-A image using a slab of 40µm (see Figure 1) and then 100µm thickness**
3. **Decide if CNV is present by reviewing the OCT-A images in conjunction with SD-OCT, and additionally record the presence/absence of a double layer sign (DLS) and sub-retinal hyper-reflective material (SHRM).**

- After all OCT-A images had been graded, the FA results were assessed for the presence/absence of CNV.
- To obtain group data, any disagreements between clinicians were resolved by a majority decision.

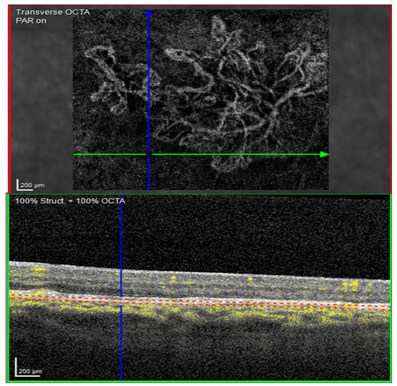



**Figure 1:** En face view of CNV (top) using a manual 40µm slab. Dashed red lines represent the slab position on the SD-OCT scan.

## Results

- 58% of eyes had active CNV confirmed on FA.
- Combined across all three clinicians, the average sensitivity of OCT-A across all three segmentation methods was 88% with specificity of 96%. When analysed separately, sensitivity was highest for the manual segmentation and specificity was highest for the automated segmentation.
- For individual clinicians the sensitivity and specificity were best for combined SD-OCT and OCT-A (88-92% and 78-94% respectively – see Table 1), suggesting the addition of SD-OCT can be useful in improving sensitivity when clinicians are working independently.
- The level of agreement between clinicians, calculated using a free-marginal multi-rater kappa statistic, ranged from 0.59 – 0.65 for the OCT-A image analysis.
- Sensitivity and specificity of the DLS was 96% and 78% respectively, and for SHRM was 92% and 94% respectively, in the detection of CNV.
- DLS was present in 28% and SHRM was present in 6% of eyes with no CNV.
- 40% of false negative cases were classified as Type 3 CNV, suggesting OCT-A may not be ideal for identifying these lesions.
- Type 1 lesions may be missed with automated segmentation as the software does not include regions posterior to Bruch's membrane.

| | Automated OCT-A | Manual OCT-A | SD-OCT and OCT-A |
|---|---|---|---|
| **True positive** | 21 | 23 | 22 |
| **True negative** | 18 | 17 | 17 |
| **False positive** | 0 | 1 | 1 |
| **False negative** | 4 | 2 | 3 |
| **Sensitivity (%)** | 84 | 92 | 88 |
| **Specificity (%)** | 100 | 94 | 94 |
| **Positive predictive value (%)** | 100 | 96 | 96 |
| **Negative predictive value (%)** | 82 | 89 | 85 |
| ***Individual Data*** | | | |
| *FDG Sensitivity (%)* | *64* | *76* | *88* |
| *FDG Specificity (%)* | *89* | *83* | *89* |
| *ZM Sensitivity (%)* | *88* | *92* | *92* |
| *ZM Specificity (%)* | *83* | *78* | *78* |
| *CF Sensitivity (%)* | *76* | *84* | *88* |
| *CF Specificity (%)* | *100* | *94* | *94* |

**Table 1:** Individual and mean sensitivity and specificity data for the three grading methods.

## Conclusion

- OCT-A is a reliable tool for detecting CNV in treatment naïve nAMD patients.
- If no lesion is found using automated segmentation, and there is an absence of SHRM, it is highly likely that CNV is not present.
- SD-OCT images and SHRM can provide useful additional clinical markers when used in conjunction with OCT-A.