The role of OCT-A in retinal disease management

OCT-A, optical coherence tomography angiography.
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OCT-A, optical coherence tomography angiography.

Objectives

To examine the role of OCT-A in the management of nAMD	To outline the utility, limitations, and potential for clinical / research applications of OCT-A	To present the recommendations of the Vision Academy on this topic

The Vision Academy provides ophthalmic specialists with a forum to share existing skills and knowledge, build best practice, and lead the wider community in the drive towards optimized, compassionate patient care.

Through their collective expertise, the Vision Academy seeks to provide guidance for best clinical practice in the management of retinal disease, particularly in areas with insufficient conclusive evidence.

? **QUESTION**
Does OCT-A provide any benefit and should it be used in the management of retinal disease?

nAMD, neovascular age-related macular degeneration; OCT-A, optical coherence tomography angiography.

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The role of OCT-A in retinal disease management: Background

Imaging neovascular age-related macular degeneration

- nAMD requires ongoing assessment and long-term management

- Newer imaging techniques can help to better establish diagnosis, refine treatment, and enable accurate monitoring
  - The best approach involves multimodal imaging but this is probably only required in a subset of patients

- The identification of active nAMD largely depends on finding subretinal or intraretinal fluid and/or hemorrhage in a patient with some features of AMD

- Successful treatment of nAMD, based largely on anti-VEGF therapy, involves monitoring the response by imaging for fluid

- Monitoring is essentially performed with OCT and accuracy is improved with newer SD-OCT and SS-OCT, with higher resolution, better depth resolution, and eye tracking

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Approaches to identifying and monitoring nAMD

- Beyond OCT, current clinical evaluation of retinal disease activity is achieved with the help of multimodal imaging[1,2]

- FA is commonly used for detecting neovascularization and classifying it into subtypes (occult, minimally classic, and predominantly classic CNV); diagnosis is mainly based on patterns of fluorescein leakage[3]

- ICGA does not leak as much as FA and the infrared can penetrate the retinal pigment epithelium or hemorrhage to some extent[3]
  - ICGA is better at distinguishing polypoidal choroidal vasculopathy, retinal angiomatous proliferation, and occult CNV

- OCT-A is now used to image the macular blood vessels and detect nAMD[3]
  - In some cases, OCT-A detects nAMD earlier than conventional imaging and increasingly, as technology advances, it can be used to define lesion type
  - The current role of OCT-A is usually to complement OCT, FA, and ICGA

Imaging to define nAMD subtype

- As all types of nAMD can be treated with anti-VEGF, the exact subtype of neovascularization may not be critical; however, certain features may dictate treatment decisions and influence the likely prognosis

- Identifying the subtype may also inform the risk for the fellow eye and subsequently influence the monitoring strategy

Introducing OCT-A

- **OCT-A is a non-invasive, non-dye-based technique that uses motion contrast imaging, calculating differences in backscattered OCT signal intensity between sequential scans of the same area[1,2]**

- Axial bulk motion from patient movement is eliminated, so sites of motion between repeated OCT B-scans represent strictly erythrocyte movement in retinal blood vessels[1]

- OCT-A generates high-resolution angiographic images in a matter of seconds and offers the potential to enhance our understanding of retinal diseases; however, guidance is needed to effectively interpret results and improve its use and understanding[2]
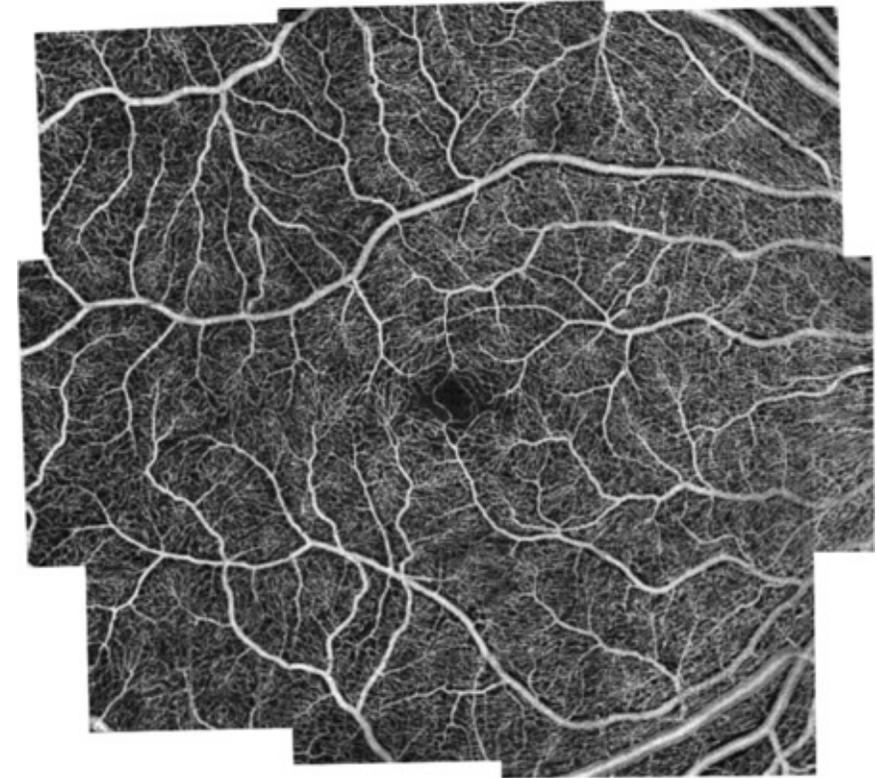

Image from de Carlo *et al.* 2015

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Overview of OCT-A technology

- OCT-A technology examines sequential B-scans taken at the same location of the retina to detect differences in amplitude, intensity, and phase variance

- The degree of decorrelation in signal is then calculated, which enables visualization of only the moving parts, assumed to be due to the movement of cells within the bloodstream and thus blood flow

- This process is repeated for different positions in the retina to achieve a 3D dataset

- Automated, objective, and quantitative measures (angio-analytics) of flow have been incorporated into many OCT-A platforms

When is OCT-A used?

Since the development of OCT, OCT-A uses the same technology to:[1]	OCT-A is used to visualize the microvasculature in diseases that affect the central macula, including:[2]	OCT-A can also be used to distinguish the features of other disorders, including:[2-4]
• Visualize retinal and choroidal vasculature • Resolve the distances between reflective structures within tissues • Produce high-resolution, cross-sectional scans of vascular flow in seconds	• AMD • Diabetic maculopathy • Retinal vascular occlusion • Macular telangiectasia type 2 • Microvasculature in optic nerve diseases • Microvasculature in glaucoma	• Polypoidal choroidal vasculopathy (not always detectable) • Paracentral acute middle maculopathy • Sickle cell retinopathy • Macular atrophy • Choroidal melanoma

How does OCT-A compare to FA and ICGA?

OCT-A	FA	ICGA
New technology	Gold standard for retinal imaging	Gold standard for choroidal imaging
Non-invasive, no need for dye	Invasive, need for dye, risk of anaphylaxis	Invasive, need for dye, risk of anaphylaxis
Quick to acquire	Time-consuming to perform	Time-consuming to perform
Interpretation may require more time	Image viewing may be faster	Image viewing may be faster
Provides depth information of both retinal and choroidal vasculature	Provides 2D image mostly of retinal features or 3D image with a stereo angiography	Provides 2D image of retinal and choroidal features or 3D image with a stereo angiography; choroidal features dominate
Able to image through blood (thickness-dependent)	Blockage due to blood	Able to image through blood
Potential for projection and motion artifacts	Fewer artifacts (not motion related)	Fewer artifacts (not motion related)
Detection of flow but not leakage	Detection of staining and leakage	Detection of flow, staining, and leakage in some diseases
High resolution (good contrast)	Intermediate resolution	Lower resolution (instrument-dependent). Detection of new vessels may be more difficult due to fluorescent background

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Challenge requiring Vision Academy guidance

- Unlike FA and ICGA, OCT-A has the ability to easily segment different layers of the retina, making it an exciting tool for developing our understanding of retinal diseases

- There is currently little consensus within the retinal specialist community on the appropriate place and use of OCT-A for diagnosis or monitoring

- Current treatment recommendations state that the use of OCT-A is not essential for good patient management

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CHALLENGE REQUIRING VISION ACADEMY GUIDANCE
**What is the role of OCT-A in retinal disease management?**

RECOMMENDATIONS

Opportunities and challenges with OCT-A

OCT-A, optical coherence tomography angiography.

OCT-based imaging biomarkers

- SD-OCT is a useful tool for monitoring disease activity and response to treatment in the identification of biomarkers
  - For example, the image on the right shows disruption of the external limiting membrane; this serves as a prediction of visual outcome in eyes with center-involving DME

- Identification of biomarkers is useful for diagnosis and predicting disease progression; they are also important clinical trial endpoints

- Increased use of OCT-A in clinical trials and clinical practice may have the potential to identify novel biomarkers for different retinal diseases
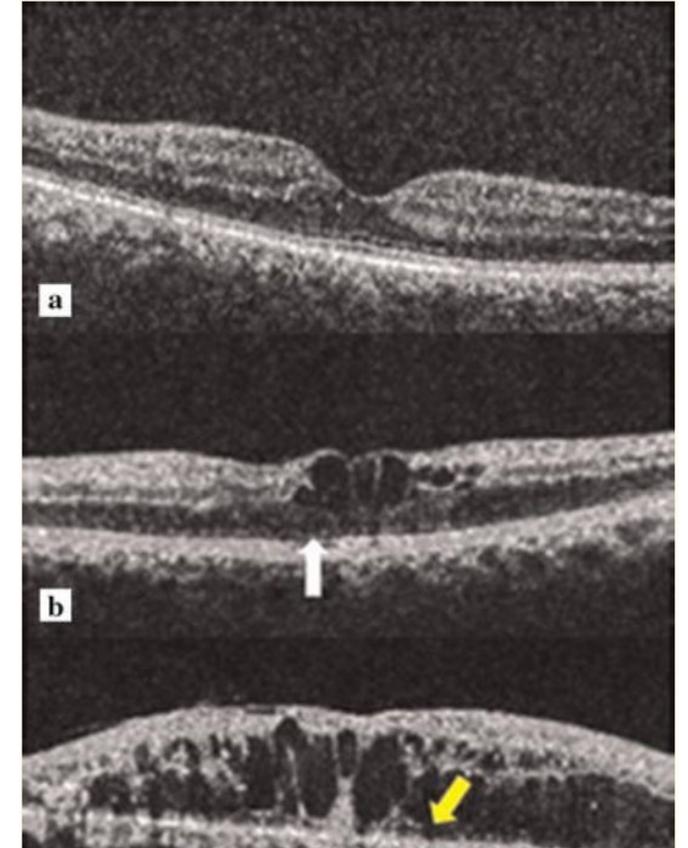
Other opportunities with OCT-A

As the nature of chronic central serous retinopathy is insufficiently understood, identification of the choroidal neovascular membrane within an area of subretinal fluid may provide insight into this condition

The deep-penetrating capabilities of OCT-A distinguish between deep and superficial blood vessels, which is not easy to do with FA alone

The non-invasive nature of OCT-A is suited to cases where dye-based techniques are not appropriate

Rapid nature of OCT-A may be preferable to methods such as FA or ICGA, which can be more time-consuming

OCT-A may be an important tool for the identification of deeper pathologies

Challenges with OCT-A

Click on a section

1 Increased potential for artifacts	**2** Lack of standardized protocols for image acquisition
3 Lack of official guidance for use	**4** Larger scan sizes may decrease image quality

OCT-A, optical coherence tomography angiography.

1. Projection artifacts with OCT-A

- Projection artifacts are caused by interference from superficial vessels during visualization of deeper tissue structures and are nearly always present in any structure that appears below the vasculature[1]

✓	A useful way to ascertain whether the flow signal seen is due to a projection artifact is by examining the cross-sectional OCT-A (or Angio B-scan), in which the linear signals can be traced to blood flow within a more superficial layer[2]

✕	There is concern that some of the information may be lost or new sets of image artifacts may be introduced, ultimately leading to misinterpretation by the physician[2]

Projection artifacts seen with OCT-A

Examples of projection artifacts:

RPE level **CC level** **Choroid level**
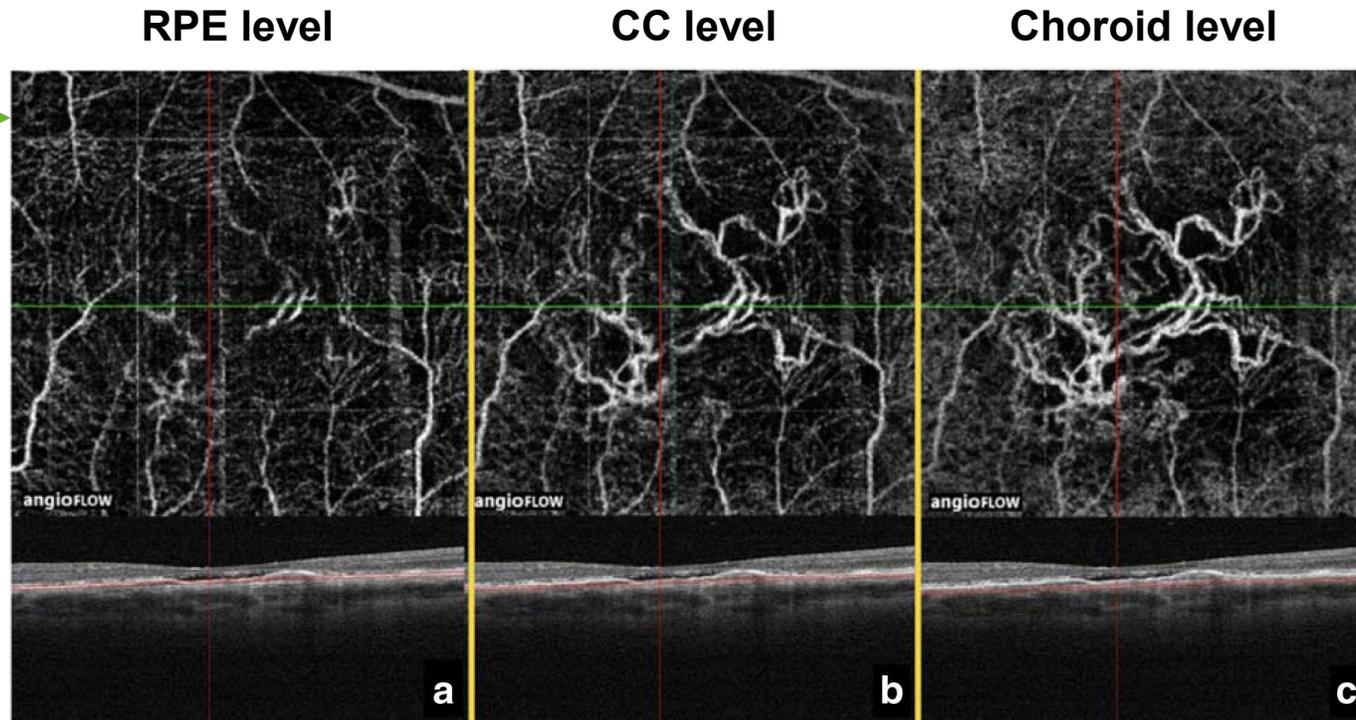
At the level of the RPE, retinal vessels are seen because of projection artifacts
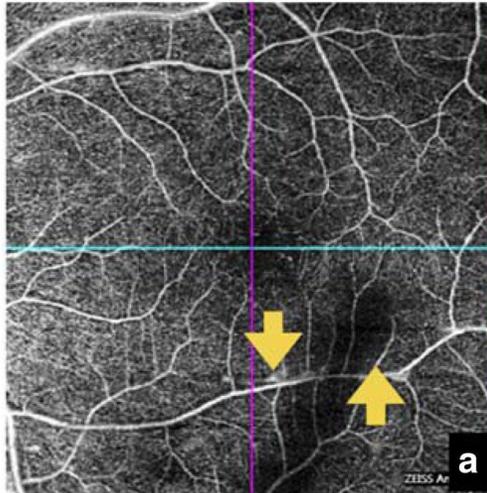
Scanning further back into the choroid reveals less projection of retinal vasculature

When scanning at the level of the choriocapillaris, the image is still dominated by retinal vasculature projection
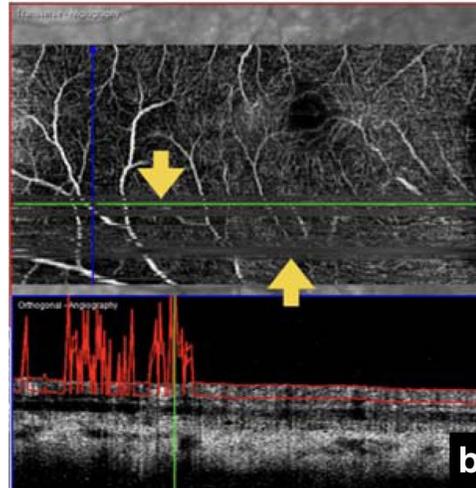
Other examples of artifacts using OCT-A

Ocular motion
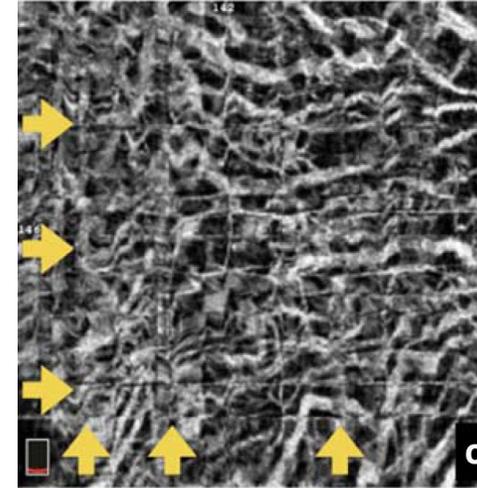Loss of detail despite high signal score, with apparent doubling of vessels

Segmentation failure
Visualization of vessels from different layers in one image that does not reflect anatomy
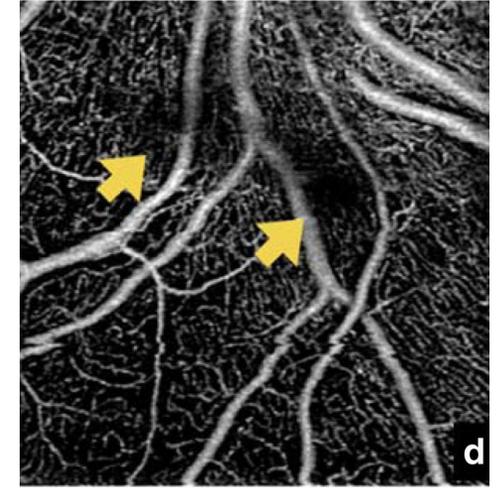
Criss-cross defects
Due to software-based motion correction to compensate for ocular motion artifacts

Intrinsic eye properties
E.g. vitreous "floaters", causing a loss of signal with media opacity

While software-based motion correction has been developed to manage image distortions such as those caused by ocular motion (a), this can still introduce criss-cross image defects (c)

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2. High number of OCT-A technologies available and lack of standardized protocols leads to inconsistencies in clinical practice

| OCT-A algorithm	Definition	Developer (OCT device)
OMAG	Optical microangiography	ZEISS / University of Washington (AngioPlex™)
CODAA	Complex OCT signal differential analysis angiography	NIDEK (AngioScan)
SSADA	Split-spectrum amplitude-decorrelation angiography	Optovue (AngioVue™)
FSADA	Full-spectrum amplitude-decorrelation angiography	Canon (Angio eXpert)
SPECTRALIS OCT-A	Full-spectrum probabilistic approach	Heidelberg Engineering (SPECTRALIS®)
OCTARA	OCT angiography ratio analysis	Topcon (Triton SS OCT Angio™)
PRD-OCT	Phase-resolved Doppler OCT	University of Amsterdam
PV-OCT	Phase-variance OCT	California Institute of Technology
UHS SS-OCT	Ultra-high-speed swept-source OCT with variable interscan time analysis	Massachusetts Institute of Technology

There is variation in imaging across the range of OCT-A technologies now available

- Images of the microvasculature of a healthy retina in the same patient, taken using a range of OCT-A technologies available on the market
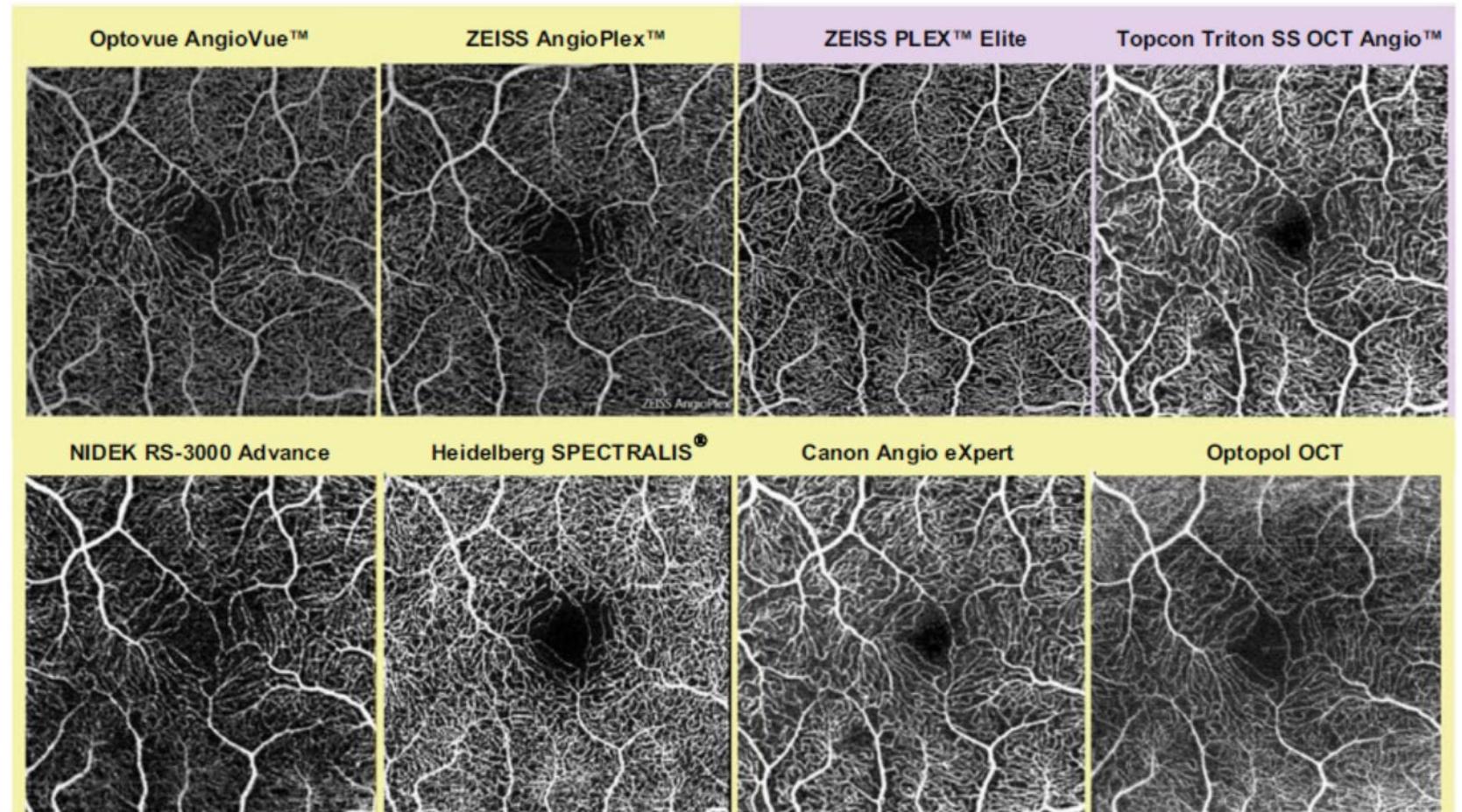
And different OCT-A technologies have different capabilities

- The images demonstrate the visual capabilities of the different OCT-A algorithms to resolve structures across multiple tissue levels

- Software relating to image processing and visualization is continuously being upgraded to improve the quality of these images

- However, variation in image quality further highlights the need for standardized protocols for imaging the different retinal layers in each disease

Rodríguez FJ *et al. Graefes Arch Clin Exp Ophthalmol* 2018; 256 (11): 2019–2026.
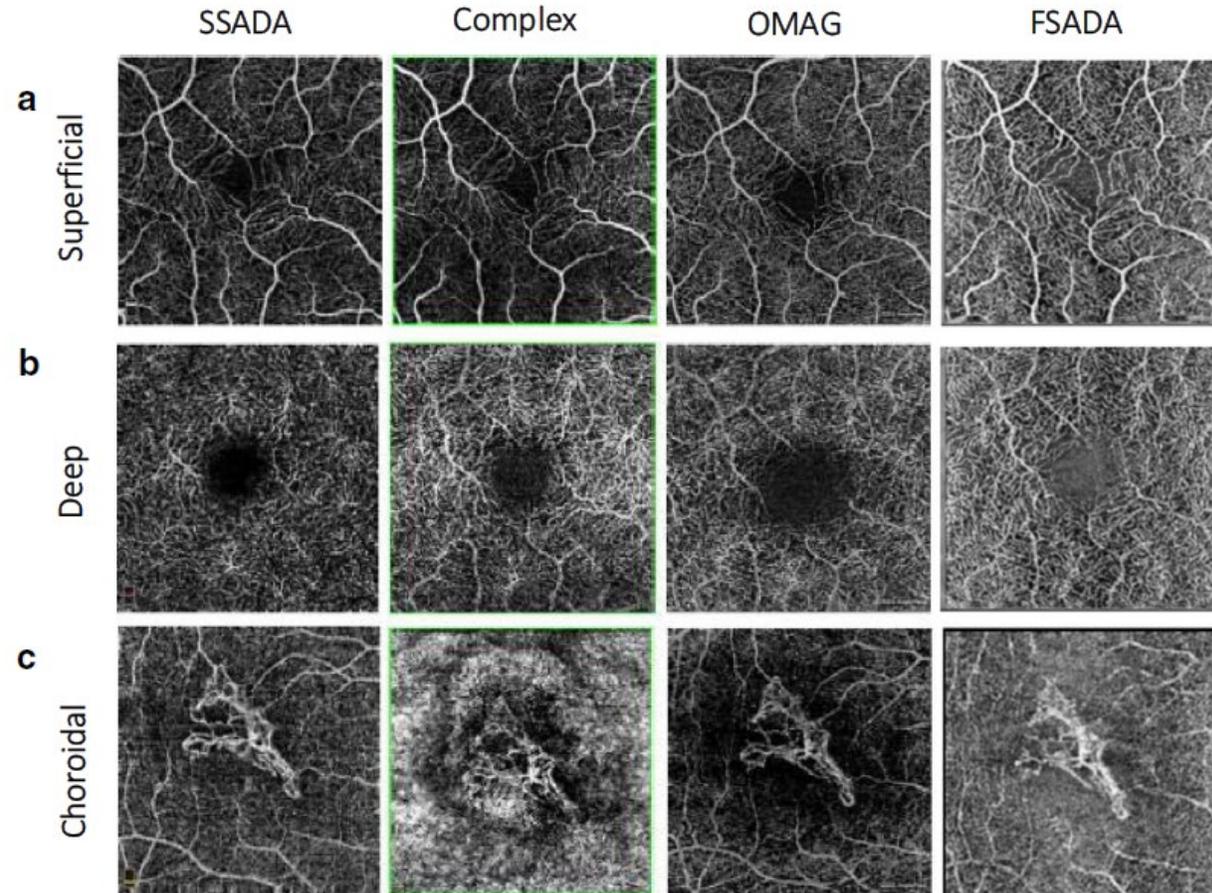
3. Lack of official guidance for use

- Despite only emerging in recent years, OCT-A is already widely used in clinical practice and is increasingly used as a diagnostic tool for retinal disease

- However, available OCT-A technology is advancing at a much faster rate than the ophthalmic community's experience

- Without official guidance for OCT-A use in retinal disease management, there remains a lack of clarity on the appropriate interpretation of disease characteristics, as well as a lack of understanding of "normal" OCT-A images from disease-free eyes for use as a reference point when making diagnoses and treatment decisions

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4. Larger scan sizes using OCT-A may decrease the image quality

- Smaller scan sizes, with a limited field of view, may limit the use of OCT-A for disease screening; however, larger scan sizes (e.g. 6 × 6 mm or 8 × 8 mm) may decrease image quality
  - This is due to specific software using the same number of B-scans across all scanning areas

- Use of montage techniques allows for a larger field of view, much like FA / ICGA, while maintaining this improved resolution
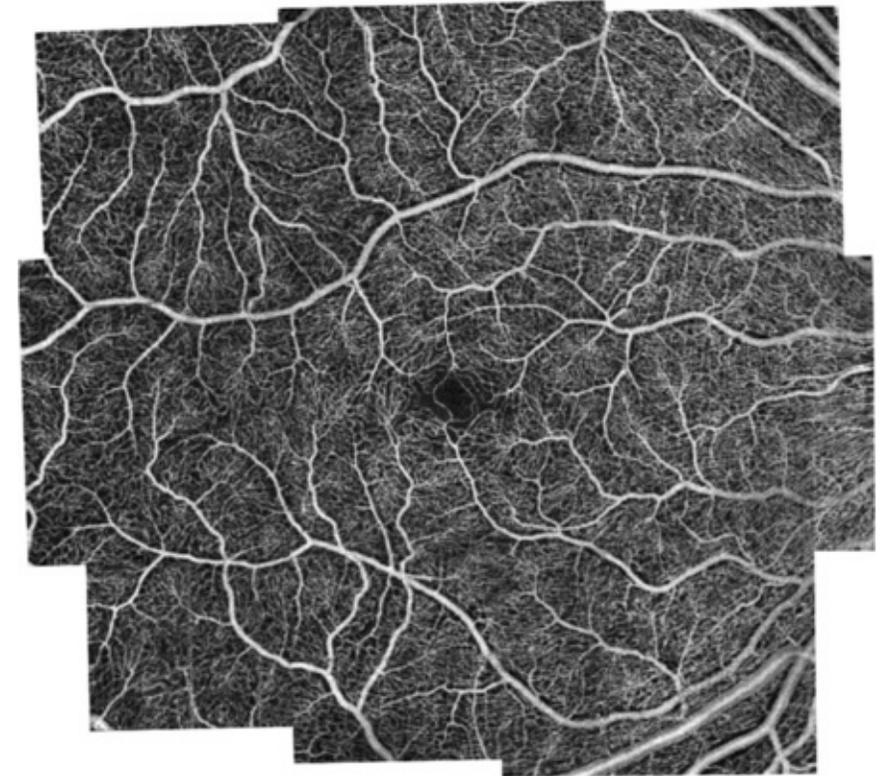
OCT-A wide-field montage of a normal eye

Image from de Carlo *et al.* 2015

Interpreting OCT-A

- After assessing the quality of the scan, consider the area and layer of interest

- Examine the cross-sectional OCT-A for abnormal vascular flow

- Assess the segmentation pattern that optimally visualizes the abnormal flow

- Manipulate the segmentation to optimize en face OCT-A image

- Correlate to other imaging modalities

- Watch out for artifacts!

Clinical challenges

Clinical challenges requiring guidance
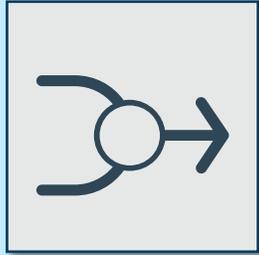
Opportunities for OCT-A

- What should OCT-A be used for?

Diagnostic tool

- Is OCT-A a reliable complementary diagnostic tool for macular complications associated with retinal disease?

Considerations for OCT-A

- What do retinal specialists need to know about OCT-A when interpreting its outputs?

Education

- What are the knowledge gaps that could improve community-wide understanding of OCT-A?

OCT-A, optical coherence tomography angiography.

Vision Academy recommendations

OCT-A should be considered a complementary diagnostic tool alongside already established imaging modalities

• The effectiveness of OCT-A has been demonstrated in principle for the diagnosis of CNV in patients with nAMD, and the technique has the potential to improve the accuracy of diagnosis in clinical practice[1]
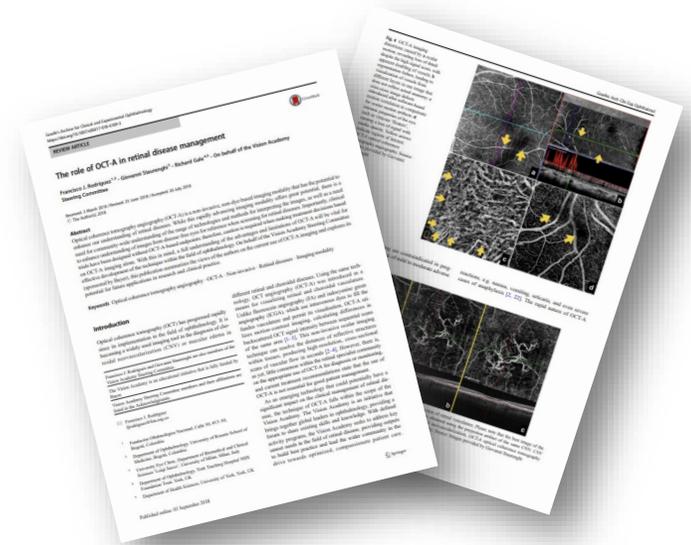
OCT-A, with structural OCT, is more effective than FA or OCT-A alone in evaluating macular complications associated with retinal disease[2]

OCT-A may also be useful where patients are unsuitable for dye-based techniques (e.g. allergy) or where accurate assessment may be difficult[3]
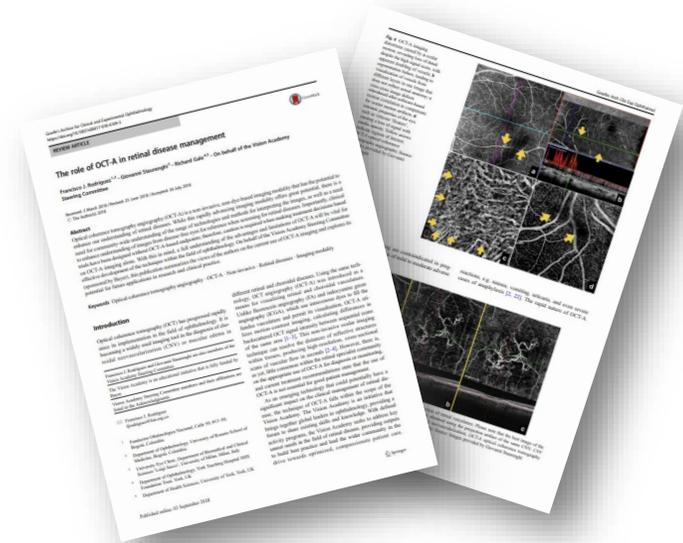
✓ General consensus

Imaging artifacts with OCT-A

✓
- Physicians should be aware of the multiple imaging artifacts that are possible with OCT-A

- An understanding of OCT-A image artifacts is essential for accurate assessment of retinal disease pathologies

OCT-A image artifacts can be caused by distortions resulting from errors in image processing and display or ocular motion

▶ While software-based motion-correction methods have been developed to manage image distortions caused by eye movement, these can introduce criss-cross image defects

✓ General consensus

OCT-A, optical coherence tomography angiography.
Rodríguez FJ *et al. Graefes Arch Clin Exp Ophthalmol* 2018; 256 (11): 2019–2026.

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Vision Academy recommendations for the role of OCT-A in nAMD

✓ OCT-A should be considered a complementary diagnostic tool alongside already established imaging modalities, with potential for use in special cases where invasive imaging techniques are inappropriate

✓ Further information is required on the accurate identification of image artifacts to reliably measure signals showing vascular perfusion

The Viewpoint "The role of OCT-A in retinal disease management" can be downloaded from:
https://www.visionacademy.org/resource-zone/resources/all

Further considerations

- The use of OCT-A is growing faster than the community's understanding and experience. There are a number of knowledge gaps that the Vision Academy believes need to be addressed:
  - Several methods of OCT-A image acquisition have been developed using a variety of technical protocols that have not yet been sufficiently validated
  - OCT-A may identify new biomarkers for different retinal diseases, which may provide a valuable tool for detecting the early stages and progression of ocular diseases
    - These could be used to monitor specific pathologies (e.g. subretinal hyperreflective material lesions) that may be helpful in monitoring disease activity and response to treatment. This, however, remains to be demonstrated
  - The need for standard protocols for image acquisition and interpretation should be a primary focus. As a new technology, further research is needed to define best practice for OCT-A in various retinal diseases

Further considerations

- While OCT-A has shown great potential for use in clinical practice as an additional tool for diagnosis, its use as a primary method in diagnosis and disease monitoring is yet to be established

- There is currently no consensus on whether OCT-A would be useful in all cases or in specific patient subgroups