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Optical Coherence Tomography Angiography (OCTA) Flow Speed Mapping Technology for Retinal Diseases

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Abstract

Introduction: Optical coherence tomography angiography (OCTA) is a noninvasive imaging modality for depth-resolved visualization of retinal vasculature. Angiographic data couples with structural data to generate a cube scan, from which en-face images of vasculature can be obtained at various axial positions. OCTA has expanded understanding of retinal vascular disorders and has primarily been used for qualitative analysis.

Areas Covered: Recent studies have explored the quantitative properties of OCTA, which would allow for objective assessment and follow-up of retinal pathologies. Various quantitative metrics have been developed, such as foveal avascular zone area and vessel density. However, quantitative assessment of the characteristics of retinal blood flow remains limited, as OCTA provides an image depicting either the presence or absence of flow at a particular region without information of relative velocities. The development of variable interscan time analysis (VISTA) overcomes this limitation. The VISTA algorithm generates a color-coded map of relative blood flow speeds. VISTA has already demonstrated utility in furthering our understanding of various retinal pathologies, such as geographic atrophy, choroidal neovascularization, aneurysmal type 1 neovascularization, and diabetic retinopathy.

Expert Commentary: VISTA, an OCTA flow speed mapping technique, may have a role in developing the utility of OCTA as a screening tool.

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Declaration of interest

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1.0 Introduction

1.1 Background of OCTA

Optical coherence tomography angiography (OCTA) is a noninvasive imaging technique that provides depth-resolved imaging of retinal vasculature. While fluorescein angiography (FA) has been the gold standard for the diagnosis of retinal and choroidal vasculopathies, OCTA is now able to provide most of the same information. FA and indocyanine green angiography (ICGA) allow for the visualization of chorioretinal vessels, but their procedures require the injection of a contrast agent. Dye-based angiography provides two-dimensional images and requires imaging of initial, intermediate, and late phases, extending over several minutes. Potential systemic adverse effects, such as nausea, vomiting, and anaphylaxis further limit the frequency with which FA/ICGA can be performed in a clinical setting. Kwan et al. found 132 adverse events from 11,898 FA injections, with nausea and vomiting being the most common[1]. However, despite these drawbacks, FA and ICGA currently offer certain advantages over OCTA, such as the ability to image a wider field, the visualization of vessel leakage, and the improved detection of microaneurysms and areas of slow flow[2–6].

OCTA emerged as an expansion of OCT. The first OCT developed in 1991 used the principle of time-domain, in which mechanical movement of the reference arm limited the imaging rate to 400 A-scans/second with an axial resolution of 10μm[7,8]. This slow imaging speed was not conducive to the acquisition of angiographic data. With the advent of spectral-domain (SD) OCT, scanning speeds improved to 68,000 A scans/second, with a higher axial resolution of ~5μm, allowing for the advent of OCT angiography[9,10]. In 2006, Makita et al used SD-OCT to compare sequential A-scans and demonstrated that it was possible to obtain three-dimensional angiograms of the retina and choroid and to analyze them by segmentation[11]. Currently, most OCTA devices use the principle of spectral-domain, while investigational devices use swept-source (SS) technology. SS-OCTA employs a different light source, a rapidly tunable laser which sweeps through frequencies. This technology allows for faster scanning speeds of 100,000–400,000 A-scans/second and utilizes a ~1050nm wavelength, which allows for increased depth penetration.

OCTA works by acquiring consecutive B-scans at the same location and comparing the decorrelation signal between them, consisting of differences in intensity and phase, to generate angiographic data. There are several ways to generate angiographic data from OCTs. Some algorithms use amplitude changes between scans to generate this data. Complex algorithms use both amplitude and phase information to generate angiographic data. Split-spectrum amplitude-decorrelation angiography (SSADA) and optical microangiography (OMAG) are currently used algorithms in commercially available OCTA devices in the US. SSADA is an amplitude-based algorithm in which the illumination beam

is first split into multiple spectral bands. This provides improved speckle contrast between the movement of erythrocytes and that of adjacent structures, enhancing flow signal and reducing background noise. Conversely, OMAG uses both magnitude and phase decorrelation data to generate angiographic images. Other algorithms use a ratio based approach (OCTARA) or a probabilistic approach to the generation of flow data[12]. Irrespective of algorithm, the acquired angiographic information is coupled with structural data to generate a volumetric cube scan that can be scrolled through to visualize vasculature at varying depths.

1.2 Limitations of OCTA

OCTA relies on the theory that in a static eye, movement only occurs from erythrocyte movement within blood vessels, and thus any observed decorrelation would ideally be from blood flow. However, there may be other sources of movement, such as bulk movement of the head or eye, microsaccades, and poor fixation. Some movement, especially limited bulk motion, may be compensated for, but overall, these movements give rise to motion artifacts. These artifacts appear as white lines on the en face image, representing decorrelation over the entire B-scan at that location[13]. To limit motion artifact, eye-tracking technology has been used in commercial OCTA devices. Additionally, certain devices use software based motion correction, such as co-registration of x-fast and y-fast scans for the same purpose.

OCTA is susceptible to other forms of artifact as well, such as projection artifact, in which superficial vessels may falsely appear in deeper layers, which could lead to inaccurate image interpretation[13]. To address these artifacts, projection artifact removal algorithms have been developed, such as one based on subtraction of superficial en face OCTA images from deeper en face OCTA slabs[14]. However, this technique may result in disconnected images. Projection-resolved OCTA has been suggested as a technique to remove projection artifacts while preserving image quality with density and continuity of the intermediate and deep retinal plexuses[15,16]. These algorithms may also be used to visualize the choriocapillaris and choroidal blood flow[17,18].

An additional limitation of OCTA is a restricted field-of-view. Currently available devices offer scan patterns ranging from 3×3mm to 12×12mm. Increasing field-of-view comes with a trade-off, as scanning density decreases with increasing scan area, in order to maintain reasonable patient scanning times. 3×3mm scans are of the highest quality, which then diminishes accordingly as scan area increases. Thus, the scanning speed of the device limits the field-of-view and lowers resolution in images with larger fields of view. Swept-source (SS) OCTA devices offer faster scanning speeds than spectral-domain (SD) OCTA devices. Faster scanning speeds allow for the acquisition of more B-scans within a given scan pattern in a comparable amount of time, thereby improving image quality in wider fields of view. Furthermore, scan patterns can be montaged to generate a composite OCTA image, with preservation of resolution, and field-of-view comparable to that of fluorescein angiography (FA). OCTA device manufacturers are employing such montaging algorithms as well in an effort to further develop widefield OCTA imaging.

Despite these limitations of OCTA, the technology offers excellent qualitative assessment of retinal and choroidal vasculature. OCTA images, in their currently commercialized form,

tend to show only flow or lack of flow in a certain area with no quantitative flow metrics, such as flow volume, velocity, flux, or tissue perfusion. However, secondary quantitative metrics derived from OCTA images are currently being investigated with great interest.

2.0 Quantitative Metrics in OCTA

OCTA has primarily been qualitatively analyzed. The image produced after an OCTA depicts either the presence or absence of flow in the area of interest. Looking at the scan, it is not possible to ascertain specific characteristics of the flow, such as speed, directionality, or volume, making quantification of OCTA difficult. However, quantification of OCTA would provide several benefits, such as more standardized patient follow-up on a specific OCTA device, comparability across different OCTA devices, threshold values to guide clinicians in diagnosis, and improved understanding of disease pathogenesis. Techniques are being developed to overcome this limitation and to develop ways to quantify vessel and flow metrics on OCTA.

2.1 Quantification of the foveal avascular zone

One such robust and reliable quantitative metric is foveal avascular zone (FAZ) area. Trends in FAZ size have been associated with various ocular pathologies, including diabetic retinopathy and branch retinal vein occlusion. Historically, FAZ size was measured via FA techniques. In 1984, Bresnick et al. found the longest FAZ diameters, greater than 1.0mm, to be in eyes with late-stage diabetic retinopathy, and determined FAZ size to be a strong predictor of the severity of retinal non-perfusion[19]. Subsequent studies have validated these results by confirming the predictive value of FAZ in determining extent of disease in patients with diabetic retinopathy[20–23].

More recently, OCTA has been used to quantify the FAZ, as it has proven to be a robust prognostic indicator. Vertical and horizontal FAZ diameter has been studied in healthy eyes and found to be statistically comparable in both eyes of a single subject[24]. When compared with healthy eyes, enlargement of FAZ area and FAZ remodeling has been demonstrated in eyes with diabetic retinopathy[25]. Furthermore, progressive enlargement of the FAZ has been shown to correlate with increased diabetic retinopathy severity[26–31]. Overall, OCTA was found to be successful in detecting microvascular changes in diabetic patients with no clinical signs of retinopathy. Enlargement of the FAZ, both in area and diameter, has also been noted in patients with retinal venous occlusions[32,33]. Further studies have also demonstrated the utility of OCTA in quantifying FAZ in other ocular pathologies as well[34,35].

2.2 Quantification of vessel density

Other methods of quantifying OCTA come from vessel density and its derivatives. The grayscale OCTA may be converted into a binary black-and-white image using third-party image-processing software, from which vessel density can be calculated as the area of flow over total image area. Further processing of these binarized images may yield skeletonization, in which vessels are reduced to a width of one pixel and can be used to calculate metrics, such as vessel length density or vessel skeleton density[36]. Other such

derivatives of vessel density include vessel diameter index, fractal dimension, vessel complexity index, intercapillary distance and vessel length, to name a few. While some OCTA device manufacturers have provided automated calculation of this metric, it is not uniform across devices, and thus clinical utility and overall accuracy and precision remain to be determined. Vessel density has been compared between retinal layers and in healthy eyes, was found to be greater in the deep capillary plexus as compared to the superficial plexus and to directly correlate with age and sex[37,38]. This difference was proposed to be due to the differing metabolic needs and roles of each retinal layer[39]. In terms of pathology, vessel density has been found to decrease with increased severity of diabetic retinopathy[31,35,37,39–42]. Analysis of trends in vessel density may help establish diagnosis, monitor disease progression, and understand the pathogenesis of various retinal vascular disorders.

2.3 Quantification of blood flow

As previously mentioned, OCTA provides an image that demonstrates either the presence or absence of flow. In an effort to understand flow velocity, various techniques have developed quantifying retinal blood flow, such as video fluorescein angiography and Doppler-based techniques. Fluorescein angiography may be used to measure arteriovenous passage time and mean dye-bolus velocity[43]. Laser Doppler velocimetry measures maximum velocity of blood flow in a single vessel at a time and may be used to determine total retinal blood flow with vessel caliber measurements[44,45]. Decreased retinal blood flow and flow speed were found in diabetic patients, both with and without retinopathy, and in patients with branched retinal artery or vein occlusions[45]. Color Doppler ultrasound can measure blood flow velocity and vascular resistance in the ophthalmic artery and other orbital vasculature, but not more specifically in retinal and choroidal vasculature[46]. Lastly, Doppler OCT can detect axial flow velocity and allow for computation of total retinal blood flow. However, this technique only measures blood flow in the plane perpendicular to the OCT beam and has been used to scan small volumes at the optic disc[47]. Overall, these aforementioned techniques provide valuable insight into retinal flow dynamics, although limited. Vessel flow speed may be quantified, but painstakingly in one vessel at a time, or only at the optic disc, or as a general perfusion measure overall. Therefore, a map of retinal flow speed in the macular region is difficult to generate from these techniques. However, through the development of variable interscan time analysis (VISTA), OCTA may be used to generate flow maps.

3.0 Variable Interscan Time Analysis (VISTA)

OCTA flow speed mapping is an initial step to developing a quantitative metric for retinal blood flow velocities that may be easily used in a clinical setting. VISTA is an imaging technique that scales the slowest detectable flow and the fastest detectable flow to produce a decorrelation signal that overcomes the grayscale limitations of normal OCTA[48].

As mentioned, OCTA acquires B-scans in rapid succession at specific locations and uses the decorrelation signal between them to generate the angiographic data. The fixed interscan time between successive B-scans on normal spectral-domain OCTA devices is ~5 ms. If the

flow within a particular vessel is slow so that the change in the blood vessel is not detected by consecutive B-scans, then the B-scans acquired at that location would display no differences, and thus the flow would not be detected. Similarly, fast flow above a certain threshold cannot be differentiated, causing all flow speeds to appear the same, because the image becomes saturated. VISTA is employed on the swept-source OCTA prototype device that offers increased scanning speeds (~400,000 A-scans per second), as compared to spectral-domain OCTA. The interscan time on this vertical cavity surface emitting laser (VCSEL) prototype is ~1.5ms. Faster scanning speed allows the device to capture more B-scans in rapid succession at a particular location without substantially increasing imaging time. With more B-scans available at a particular location, non-consecutive B-scans can be compared. VISTA assesses the decorrelation signal between consecutive B-scans (~1.5ms), as well as between alternative B-scans, with an interscan time of ~3ms. Changing the interscan time allows for differentiation between vessels that have a higher speed of blood flow and those that have a slower speed of blood flow. Increasing the interscan time varies the decorrelation signal and allows for improved differentiation between flow speeds [48].

VISTA analysis allows for the color-coded mapping of relative blood flow speeds[49]. The images are initially partitioned into two different parallel phases, one of which computes pixel brightness while the other computes hue of the pixels. This information is then used to generate a color map in which slow blood flow speeds are blue and faster blood flow speeds are red[49] (Figure 1). It is important to note that VISTA en face images display relative blood flow speeds, as opposed to depicting quantified speeds themselves. However, future advancements in this technology may even allow for quantification of retinal and choroidal blood flow velocities.

4.0 VISTA in various retinal pathologies

VISTA has been used to analyze changes in retinal and choroidal blood flow in various vascular pathologies. In patients with geographic atrophy (GA), choriocapillaris flow impairment has been visualized within the GA lesion[49]. Choriocapillaris changes were found in regions of nascent GA and drusen-associated GA[50,51]. Standard OCTA images had previously demonstrated decreased overall choriocapillaris flow in these areas of atrophy, depicting several areas with lack of flow. Interestingly, after the application of VISTA, certain vessels become newly visible in the choriocapillaris under regions of GA. This observation suggests that GA involves both flow impairment in some vessels and complete loss of flow in others. Furthermore, choriocapillaris flow alterations were noted to extend beyond the margin of atrophy, suggesting that perhaps choriocapillaris alterations precede retinal pigment epithelium (RPE) loss in the development of GA[48,50]. These studies have acknowledged the need for analyzing B-scans with even longer interscan times in order to further improve sensitivity by reducing the slowest detectable flow[48,52].

In addition to dry age-related macular degeneration (AMD), VISTA has also been used to analyze flow alterations in wet AMD. Longitudinal VISTA analysis of choroidal neovascularization (CNV) demonstrated relatively higher flow speeds in the central, larger vessels and lower flow speeds in the smaller peripheral vessels. Trunk vessels, representing either feeder or draining vessels, consisted of higher flow speeds, while branches contained

relatively slower flow. Expanding regions within a CNV lesion demonstrated persistent faster flow speeds, with similar flow speeds seen in densifying regions. Following anti-VEGF treatment, vessels with slower flow speeds, often small vessels at the periphery, contracted, while the central vessels with faster flow speeds persisted and even matured in certain cases. Maturation of vessels was found in 80% of eyes chronically treated with anti-VEGF, and was hypothesized to be a result of reduction in the smaller peripheral vasculature of the CNV. It was hypothesized that these smaller vessels may have been more responsive to anti-VEGF treatment due to a lack of pericytes, which may be more abundant around the persistent high-speed trunk vessels[52]. Thus, this analysis of blow flow speeds within CNV lesions specifically offers further insight into the pathogenesis of wet AMD and hemodynamic response to standard treatment.

The VISTA algorithm has further been applied to other disease processes, such as aneurysmal type 1 NV. Analysis of retinal and choroidal vasculature in patients with aneurysmal type 1 NV demonstrated variable flow within the polyps. Flow speeds varied from relatively slower to relatively faster speeds between polyps in the same eye and between patients. A range of flow speeds was also noted within a single polyp itself. Faster flow speeds were found in the periphery of the polyps, with slower flow speeds found in their center, indicative of turbulent flow in the polyps. Compared to the gold standard of indocyanine green angiography (ICGA), OCTA has been reported to have limited sensitivity in detecting the polyps of aneurysmal type 1 NV. This has been hypothesized to be due to slower flow speeds within the neovascular complex, which may be below the detection threshold of current OCTA devices[53]. Due to its shorter interscan times (1.5 ms and 3 ms) as compared to standard OCTA interscan times (~5 ms), VISTA does not contribute to lowering the OCTA detection threshold of slow flow. However, the VISTA algorithm has demonstrated variable flow speeds within the polyps, including certain polyps with slow flow speeds, which may suggest the presence of certain polyps with even slower relative flow speeds below the current threshold of detection. Relatively slower flow was also seen in the branching vascular network (BVN). Trunk vessels of the BVN consisted of relatively faster speeds, with slower speeds noted in smaller vessels[54]. With additional improvements and comparisons, VISTA may be able to offer further insight into the debate of whether or not aneurysmal type 1 NV is a variant of AMD-related CNV.

Additionally, VISTA has also been employed to analyze vascular features of diabetic retinopathy. Analysis of a neovascular lesion in a patient with proliferative diabetic retinopathy demonstrated a system of low flow speed. Increasing interscan time from 1.5ms to 3ms further enhanced visualization of vasculature within the neovascular lesion. Additionally, in patients with nonproliferative diabetic retinopathy, slower flow speeds were also associated with capillary looping and microaneurysms[49]. Flow speed analysis of other features classically associated with diabetic retinopathy, such as intraretinal microvascular abnormalities, remains to be conducted.

5.0 Limitations of VISTA

Although VISTA continues to improve our understanding of retinal pathologies, it is not without its limitations. Currently, VISTA demonstrates relative blood flow speeds, as

opposed to absolute flow speeds. The algorithm is limited to comparison of whether the speed of blood flow in a particular vessel is faster or slower than the speed in another vessel. However, the relative flow speeds visualized have been consistent with physical flow principles and vascular flow relationships demonstrated in previous literature[49,55]. Additionally, dye-based angiography depicts dynamic flow over time with the acquisition of images of initial, intermediate, and late phases extending over several minutes. VISTA is an extension of OCTA, and therefore it is comparatively akin to a snapshot of retinal flow and unable to provide information about leakage patterns in retinal diseases such as diabetic macular edema or CNV. Furthermore, OCTA images are often affected by artifacts, such as shadowing, projection artifacts, and motion artifacts. To correct for motion on the swept-source VCSEL OCTA device, two orthogonally-acquired volumes (with x-fast and y-fast directionality) are merged. However, motion artifacts may appear as white horizontal or vertical lines on the generated OCTA image, which persist through to the VCSEL image, appearing as lines of low relative flow speeds (Figure 2). The appearance of other commonly-encountered OCTA artifacts on VISTA images remains to be explored. However, VISTA images have been shown to be repeatable, and therefore are reliable in their color-coded depiction of relative flow speeds[52].

6.0 Expert Commentary

Overall, VISTA has already provided valuable insight into various retinal vascular pathologies, such as exudative and non-exudative AMD, aneurysmal type 1 NV, and diabetic retinopathy. As it is coupled with swept-source OCTA, VISTA provides a quick, non-invasive method to analyze relative retinal and choroidal flow speeds, creating a flow speed map that can readily be interpreted. Distinguishing between no flow, slow flow, and faster flow will allow for further insight into disease pathogenesis.

It remains to be determined whether or not OCTA has the potential to become a key screening modality for various retinal pathologies. Its noninvasive nature, high resolution, depth-resolved capabilities, and rapid image acquisition make it an attractive modality to consider for screening purposes. One retinal pathology this may hold utility in is diabetic retinopathy (DR). The prevalence of diabetes mellitus is projected to increase to 592 million by the year 2035[56]. With such a high prevalence, it will become essential to have a screening tool for diabetic retinopathy, for which early detection and management is of the utmost importance. The current gold standard for diabetic retinopathy screening and assessment is color fundus photography, with standard fields assessed per the Early Treatment Diabetic Retinopathy Study (ETDRS)[57]. Fluorescein angiography has arguably allowed for better assessment of diabetic retinopathy, as it allows for fairly easy visualization of diabetic retinal microvascular changes associated with dye-leakage and local ischemia[58]. However, due to its invasive nature, fluorescein angiography comes with certain risks, such as anaphylaxis. Thus, the development of OCTA as a screening tool for this widespread disease would be a major advancement in the field of retina.

OCTA has already demonstrated quantitative and qualitative differences in eyes with diabetic retinopathy as compared to normal eyes. Vessel density, a measure of the area occupied by vessels on an OCTA en face image, is a metric of interest and its calculation has

even been employed on commercial device software by manufacturers. Compared to normal eyes, lower vessel density values have been observed in eyes with mild non-proliferative DR, and additionally in diabetic eyes without diabetic retinopathy[59]. Similarly, foveal avascular zone (FAZ) area is a robust repeatable, reproducible measurement[60]. Enlargement of the FAZ has been demonstrated in eyes with DR compared to normal eyes and diabetic eyes without retinopathy, and furthermore in diabetic eyes without retinopathy compared to normal eyes[25,27]. These findings suggest that OCTA may not only be able to identify DR in its earliest stages, but also detect DR even before it is advanced enough for clinical detection.

In addition to detecting the presence of DR, OCTA may also help in staging disease severity. Both vessel density and FAZ area have demonstrated trends with increasing severity of diabetic retinopathy, with vessel density decreasing and FAZ area increasing with disease progression[19,61]. These trends indicate increasing ischemia with disease advancement. This quantitative assessment of ischemia by OCTA may allow for the development of threshold values of metrics that can be applied to disease diagnosis. Qualitatively as well, OCTA has been shown to be superior than color fundus photography in detecting microvascular alterations of DR, such as intraretinal microvascular abnormalities (IRMA), a key feature distinguishing moderate from severe non-proliferative DR[62].

Despite these advancements in quantitative OCTA, limitations exist. Great variability exists among the methods used to compute these quantitative metrics. Sources of this variability may be image acquisition from different OCTA devices, the use of different thresholding algorithms, varying image quality, different imaging scan patterns, varying image export resolutions, and differences in slab segmentation. With such inconsistency in metric calculation, it has become difficult to establish numeric threshold values between normal eyes, eyes with DR, and varying stages of DR. Additionally, OCTA comes with qualitative limitations as well. For example, as previously mentioned, microaneurysms are more readily detectable on fluorescein angiography than on OCTA, on which they appear smaller and less prominent[61]. This may be due to the limited sensitivity of OCTA in detecting flow slower than its threshold.

As previously discussed, VISTA scales the slowest detectable flow, overcoming such limitations of normal OCTA. Currently, VISTA is being used to explore flow characteristics of the various microvascular alterations in diabetic retinopathy, including microaneurysms, IRMA, neovascularization, and venous beading/looping. It is these features that are used to identify DR and stage its severity. Microaneurysms have been described as systems of slow flow[63,64]. Appearing as such on a color-coded VISTA map of relative blood flow speeds may help increase their visibility and detection compared to normal OCTA. Furthermore, with further analysis of relative flow speeds with VISTA, specific flow patterns may emerge for these microvascular abnormalities, such as the slow flow speeds with capillary looping and neovascularization[49]. Thus, improved visualization and color-coded flow-speed pattern recognition may increase the capability of OCTA as a screening tool in a qualitative approach. Quantitatively as well, VISTA may be able to help with this purpose. Perhaps, with future advancements, VISTA may be able to offer quantitative, as opposed to relative, flow speeds. This may help establish numeric thresholds differentiating between normal

eyes, eyes with DR, and varying DR severities. Thus, the advent of VISTA strengthens the qualitative and quantitative properties of OCTA, giving it the potential to become a widely-utilized screening modality for retinal vascular pathologies.

7.0 Five-year View

VISTA contributes to OCTA eventually becoming an essential mainstay of clinical imaging. Currently, VISTA has only been employed on limited OCTA scan patterns, with a maximum size of 6×6 mm. Swept-source OCTA technology has allowed for the recent introduction of greater scan patterns, such as 12×12 mm and 15×9 mm. These scan patterns can further be montaged, either with device manufacturer or third-party software, to generate a field-of-view comparable to that of fluorescein angiography[65]. Although VISTA is not yet compatible with this extended field-of-view imaging, the future application of VISTA to these wider scan patterns would generate a widefield OCTA color-coded map of relative blood flow speeds. Since peripheral vascular changes are often the key to identifying the presence of early disease[66], such an advent has the potential to combine the advantages of normal OCTA and fluorescein angiography to create a revolutionary imaging technique that may be used for screening and monitoring of disease.

Furthermore, the quantification of VISTA may be in the near future as well. As discussed, quantification may help set numeric cut-off values for screening purposes, but also further our understanding of various retinal vascular pathologies. Quantified blood flow speeds would allow for comparison between different microvascular alterations, between different retinal plexuses, and between different vessels to differentiate arterial from venous flow. These comparisons would greatly contribute to our understanding of disease pathogenesis and even normal retinal physiology. Further studies of VISTA on a larger-scale may help in standardizing outcomes and creating a normogram for the purposes of screening or disease-management. Thus, in the near future, much remains to be explored and discovered in the field of retina using VISTA flow-speed mapping.

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Key Issues

- Optical coherence tomography angiography (OCTA) is a noninvasive imaging technique that allows for depth-resolved, high-resolution imaging of retinal and choroidal vasculature. Qualitative and quantitative analysis using OCTA has been essential in further understanding the pathogenesis and progression of various vascular pathologies, such as diabetic retinopathy.
- A limitation of OCTA is that it offers an image depicting either the presence or absence of flow, without information about flow velocities.
- Variable interscan time analysis (VISTA) overcomes the grayscale limitation of OCTA and provides a color-coded map of relative retinal blood flow speeds. VISTA has been used to further analyze retinal vascular diseases, such as age-related macular degeneration, including choroidal neovascularization and geographic atrophy, diabetic retinopathy, and aneurysmal type 1 neovascularization.
- Further development of VISTA and its flow speed mapping capabilities may allow OCTA to become an essential tool for screening purposes.

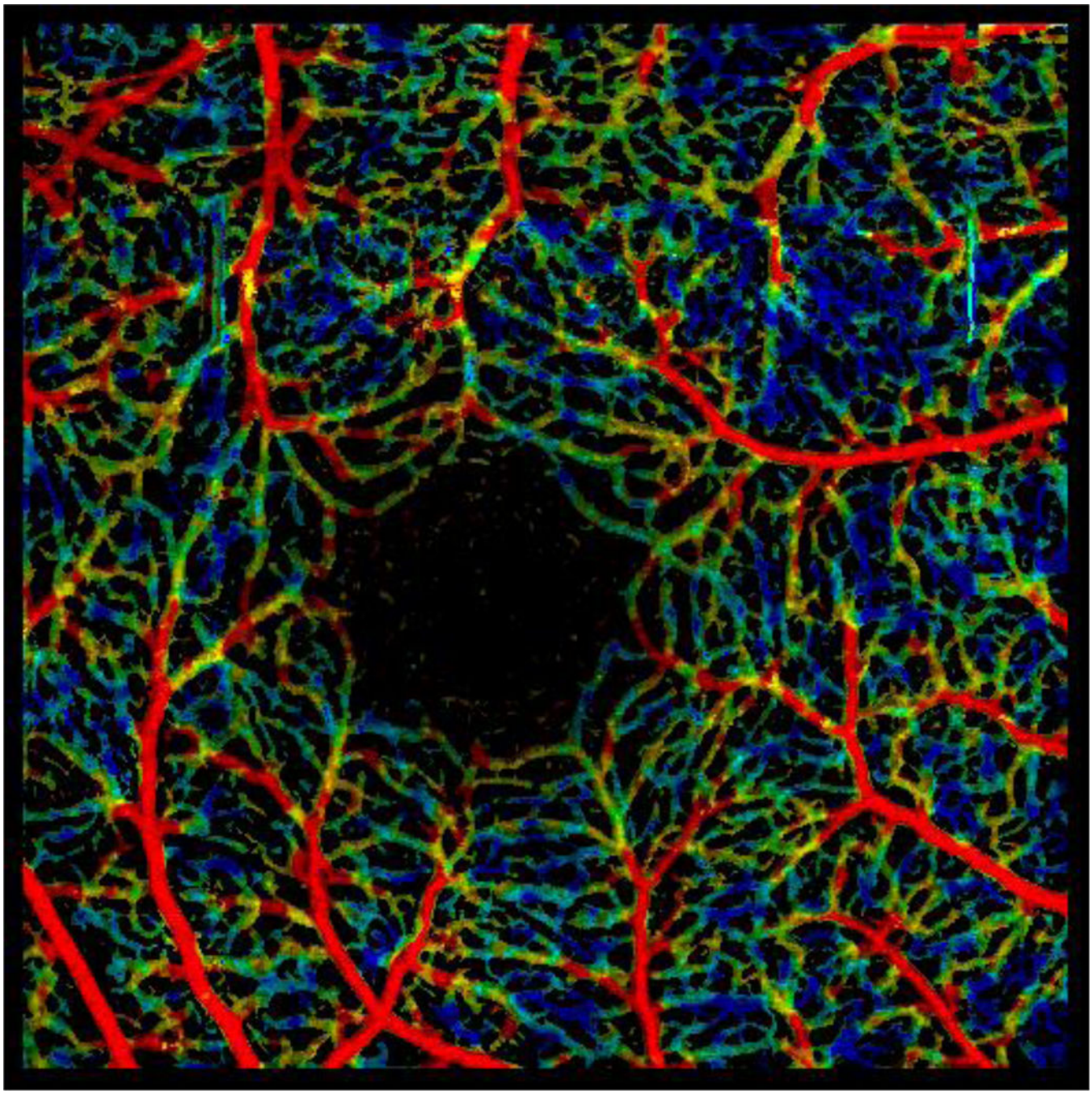

Figure 1:
VISTA-processed 3×3mm OCTA image of the full retina segmentation of a normal eye. The color-coded map depicts relative blood flow speeds, with faster flow speeds in red and slower flow speeds in blue.

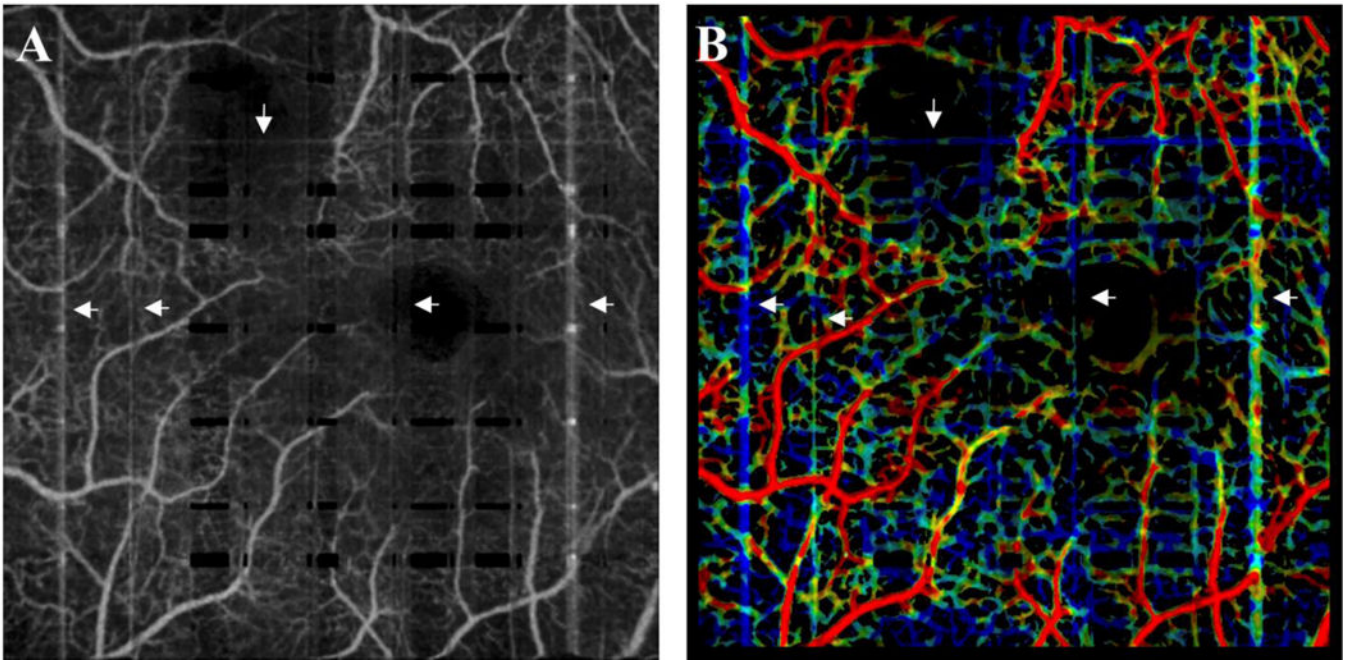

Figure 2:
Swept-source OCTA (A) and derived VISTA (B) images of a patient with moderate non-proliferative diabetic retinopathy. Motion artifacts (white arrows) are visible as white horizontal and vertical lines on the OCTA image and as lines of low relative flow speeds (predominantly blue color-coded) on the VISTA image.