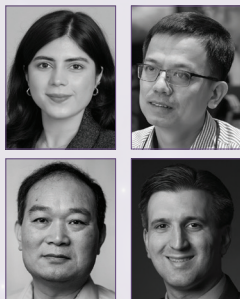


# The Value of OCTA in Retinal Vascular Disease

Measuring retinal blood flow is easier than ever before, with new tools under investigation to further improve our ability to assess changes in the retinal vasculature.

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OCT angiography (OCTA) has dramatically changed the landscape of retinal disease diagnosis because it allows clinicians to noninvasively evaluate early vascular changes at the capillary level in asymptomatic patients. This has significant clinical potential, as ischemic microangiopathies remain a leading cause of vision loss in developed countries.<sup>1</sup>

Here, we review the clinical utility of qualitative blood flow assessment in three major retinal diseases—diabetic retinopathy (DR), AMD, and central serous retinopathy (CSR)—and highlight evidence demonstrating the utility of additional blood flow quantification (Table).

## AN OVERVIEW OF OCTA

OCTA visualizes blood flow by detecting motion contrast of individual red blood cells. This technology has high axial resolution (ie, 5-10  $\mu\text{m}$  or better) and provides depth-resolved images of the retinal and choroidal vasculature at the capillary level, allowing clinicians to pinpoint the exact layer in which perfusion is present or absent.<sup>2</sup>

Currently, OCTA devices provide pseudocolor maps of retinal capillaries based on the presence or absence of red blood cell flow within a certain range of velocities (typically 0.3-3 mm/sec); they do not provide information about exact blood velocity in one region versus another. However, experimental OCT-based algorithms now allow quantification

of red blood cell velocity at the capillary level.<sup>3-5</sup> Known as *velocimetry*, these techniques take advantage of faster laser scanning speeds and more sophisticated scan patterns to understand disease onset and progression at a much more granular scale than standard OCTA (Figure). OCTA-based velocimetry has demonstrated that blood velocity varies across different retinal capillary beds, laying the foundation upon which abnormal blood flow—leading to diseases such as DR and others—can be categorized.<sup>3</sup>

## DIABETIC RETINOPATHY

DR is rooted in capillary nonperfusion, endothelial dysfunction, and autoregulatory failure.<sup>6,7</sup> Quantitative flow measurements have demonstrated a range of retinal blood flow alterations in patients with diabetes, even in the absence of overt retinopathy.<sup>8</sup> Doppler-based studies have demonstrated various changes in blood flow in the large retinal vessels among patients with diabetes but without retinopathy.<sup>9-12</sup> Other doppler-based studies have shown a reduction in retinal blood flow in eyes with severe nonproliferative DR (NPDR) and proliferative DR (PDR).<sup>13,14</sup> At the capillary level, OCTA studies show a decrease in vessel perfusion across the superficial and deep capillary plexuses correlating with disease severity and progression.<sup>15</sup> Even patients with minimal or no retinopathy demonstrate impaired capillary perfusion on OCTA.<sup>16,17</sup>

A recent study using OCTA-based second-generation variable interscan time analysis revealed an increase in the red blood cell velocity in the deep capillary plexus of

**TABLE. RETINAL BLOOD FLOW CHANGES IN RETINAL DISEASE**

Disease	Flow Changes	Potential Clinical Role
Diabetic Retinopathy	<ul style="list-style-type: none"> <li>• Early impaired capillary perfusion</li> <li>• Reduced capillary density, altered blood flow speed, and autoregulatory dysfunction in the deep capillary plexus</li> </ul>	<ul style="list-style-type: none"> <li>• Monitoring treatment response (anti-VEGF injection, panretinal photocoagulation)</li> <li>• Identifying preclinical high-risk eyes</li> </ul>
AMD	<ul style="list-style-type: none"> <li>• Choriocapillaris hypoperfusion in early/intermediate AMD, with reduced perfusion predicting progression to geographic atrophy</li> <li>• Altered macular neovascularization (MNV) hemodynamics in active vs quiescent lesions</li> </ul>	<ul style="list-style-type: none"> <li>• Early detection before visible atrophy</li> <li>• Potential prognostic marker for geographic atrophy progression</li> <li>• Evaluating treatment response and recurrence risk in MNV</li> </ul>
Central Serous Retinopathy (CSR)	<ul style="list-style-type: none"> <li>• Choroidal hyperperfusion and hyperpermeability in acute and chronic CSR, especially in the vortex venous system</li> <li>• Choroidal flow normalization after therapy</li> <li>• Detection of MNV</li> </ul>	<ul style="list-style-type: none"> <li>• Distinguishing acute vs chronic CSR</li> <li>• Persistent hyperperfusion as a biomarker for chronic CSR and risk of recurrence</li> <li>• Guiding choice of therapy with evidence of flow normalization with photodynamic or mineralocorticoid therapy</li> <li>• Tracking recovery</li> </ul>

patients with DR, which correlated with a decreased vessel density in patients with NPDR.<sup>18</sup> Longitudinal work also indicates that eyes with early flow deficits, especially in the deep retinal layer, are more likely to progress to vision-threatening stages of DR, including PDR.<sup>19-21</sup>

### Clinical Applications In DR

For clinicians, the most compelling potential of blood flow measurement in DR lies in its ability to guide both early diagnosis and personalized care. By identifying subtle flow deficits before retinopathy becomes apparent, clinicians can stratify which patients are at highest risk for progression, allowing more targeted surveillance and earlier intervention.

Beyond screening, new quantitative flow metrics from velocimetry-based algorithms will provide a useful biomarker of treatment response for novel early interventions. For example, flow changes measured after anti-VEGF therapy or panretinal photocoagulation have been shown to correlate with anatomic and functional improvement.<sup>22,23</sup>

Finally, offering patients a concrete demonstration of early microvascular dysfunction could motivate tighter systemic control of diabetes.

### MACULAR DEGENERATION

A central feature of early AMD is loss of choriocapillaris perfusion, which impairs metabolic support to the retinal pigment epithelium (RPE) and photoreceptors.<sup>24</sup> In wet AMD, aberrant macular neovascularization (MNV) reflects a maladaptive response to hypoxia and vascular insufficiency.<sup>25</sup>

Studies using OCTA have shown that choriocapillaris, choroidal, and retinal blood flow alterations are detectable in early and intermediate AMD, often preceding active MNV or atrophy.<sup>26-29</sup> In addition, reduced choriocapillaris perfusion is associated with faster progression to geographic atrophy (GA), suggesting it may serve as a

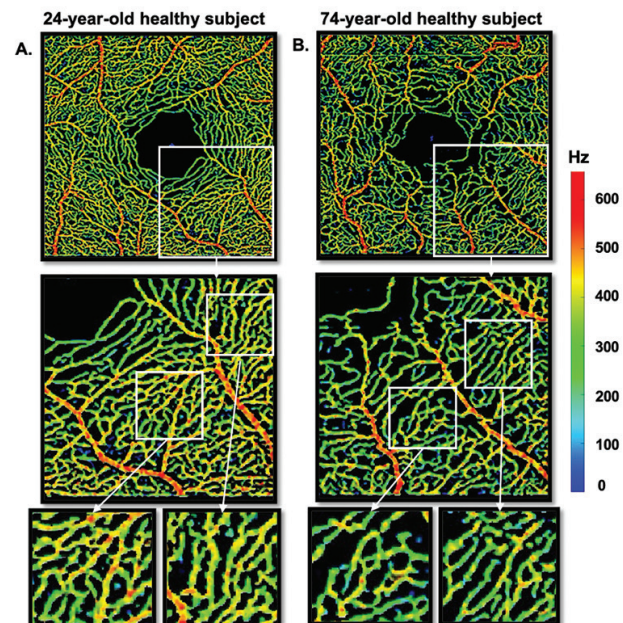


Figure. These pseudocolor flow velocity maps illustrate the age-related differences in retinal capillary flow within the superficial retinal layer. A 24-year-old healthy subject demonstrates higher capillary flow velocities, represented by higher color saturation (A), whereas a 74-year-old healthy subject shows lower overall flow (B), with differences most evident at the capillary level. Magnified views highlight the flow patterns within individual capillary networks. The color bar indicates mean frequency in Hertz (Hz), used as a surrogate measure of capillary flow velocity. Adapted with permission from Aman et al.<sup>3</sup>

valuable prognostic biomarker.<sup>30-32</sup> OCTA has been used to detect MNV before the presence of exudation in subjects with clinically apparent and intermediate AMD.<sup>33,34</sup> In wet AMD, OCTA provides unique insight into MNV hemodynamics, where flow patterns can distinguish potentially active lesions from quiescent subretinal fibrosis,<sup>35</sup> and where lower choroidal perfusion can serve as a risk factor for MNV development in the fellow eye of patients with

## KEY TAKEAWAYS

- ▶ Subclinical changes in retinal and choroidal blood flow are qualitatively detectable using commercially available OCT angiography (OCTA).
- ▶ Quantitative blood flow measurements obtained from non-FDA cleared research devices have demonstrated correlations with disease severity, progression, and treatment response in studies of diabetic retinopathy, geographic atrophy risk in AMD, and central serous retinopathy.
- ▶ OCTA-based velocimetry and variable interscan time analysis represent emerging strategies for quantitative assessment of capillary perfusion.

unilateral MNV.<sup>36</sup> Anti-VEGF therapy also alters MNV perfusion, and flow changes measured on OCTA correlate with treatment efficacy and recurrence risk.<sup>37-39</sup>

### Clinical Applications in AMD

Retinal blood flow measurement enables early detection of AMD by revealing subtle choriocapillaris flow deficits, which has the potential to flag high-risk eyes for closer monitoring of MNV or RPE loss.

In addition, flow mapping provides a functional biomarker of treatment response. By capturing MNV perfusion changes alongside structural OCT metrics, clinicians can make more refined decisions about retreatment and long-term management. Clinicians can also monitor patients with nonexudative MNV more closely for progression to active exudation.

Information about blood flow abnormalities holds value in prognostic counseling, as they correlate with rates of atrophy progression and visual decline. For example, reduced choriocapillaris flow deficits on OCTA predict faster GA enlargement,<sup>40</sup> and baseline OCTA parameters such as fractal dimension and blood flow surface area are associated with treatment burden in wet AMD.<sup>41</sup>

### CENTRAL SEROUS RETINOPATHY

CSR is thought to occur due to dysregulation of the choroidal circulation. The hallmark is a state of choroidal hyperperfusion and hyperpermeability, which leads to leakage through the RPE and subsequent accumulation of subretinal fluid.<sup>42-44</sup>

Laser speckle flowgraphy studies have consistently shown elevated choroidal blood flow in acute CSR compared with unaffected eyes, with levels that normalize following spontaneous resolution or treatment.<sup>45-47</sup> OCT and OCTA have further demonstrated evidence of choroidal vascular

dysregulation, with dilated choroidal vessels and focal zones of hyperperfusion in both acute and chronic cases.<sup>43,48-51</sup>

Adaptive optics (AO) imaging has helped clarify regional alterations in choroidal perfusion, with evidence of significant RPE changes.<sup>52</sup> OCT has also demonstrated evidence of an asymmetric vortex venous system in CSR eyes, with relative hyperperfusion in all vortex veins.<sup>53</sup> Importantly, persistent hyperperfusion is associated with disease chronicity and a higher risk of recurrence.<sup>45</sup>

Lastly, OCTA is probably the most useful tool to assess the presence of MNV in chronic CSR lesions, while fluorescein angiography and ICG angiography often show diffuse areas of non-specific staining.

### Clinical Applications in CSR

Blood flow assessment in CSR may aid in distinguishing acute from chronic disease, and quantitative flow measures could guide treatment selection. For example, normalization of choroidal hyperperfusion following photodynamic therapy has been observed, reinforcing its role in restoring hemodynamic balance.<sup>54-56</sup> This dynamic biomarker could allow physicians to monitor therapeutic response more directly than structural OCT alone. Flow abnormalities could serve as prognostic indicators, identifying patients more likely to experience recurrent or persistent subretinal fluid, and thereby guiding closer follow-up. In the future, integrating choroidal flow assessment into CSR care may provide a more tailored, patient-specific approach to what has historically been a challenging condition to manage.

### BARRIERS TO CLINICAL INTEGRATION

Despite significant progress in imaging technologies, the clinical adoption of quantitative retinal blood flow measurement remains limited. A major barrier is inter-device variability, with various devices differing in acquisition principles, algorithms, output parameters, and measurement sensitivity. This makes it difficult to compare results across platforms or establish standardized clinical cutoffs.

Other challenging caveats include the lack of robust normative databases and the need for standardized metrics. For example, studies use a variety of parameters, such as vessel density, perfusion density, capillary flux, red blood cell velocity, and mean blur rate, all of which are often defined differently between research groups. Such heterogeneity has led to conflicting results in the literature.

To see a listing of current devices, their field of view, availability, and advantages and limitations, read this article online at [retinatoday.com](http://retinatoday.com).



## THE BENEFITS OF OCTA IN THE CLINIC

OCTA (and its velocity-based extensions) is reaching a level of maturity that allows reliable, reproducible data collection in clinical settings. Still, challenges remain. Inter-device variability, a lack of normative databases, and workflow integration are significant barriers to adoption.

Despite these limitations, clinical trials incorporating flow endpoints, AI-driven image analysis, and growing interest in multimodal integration are all accelerating the pathway to clinical translation. ■

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