An estimated 18 million individuals in the United States are affected by diabetes mellitus, approximately 4% of whom also have diabetic macular edema (DME). This equates to about 700,000 individuals with DME. The Diabetes Control and Complications Trial reported that slightly more than one-fourth of type 1 diabetic patients developed DME within 9 years of disease onset. Those with type 2 diabetes have a similarly high rate, with 28% of individuals developing DME by 20 years after diagnosis.

Although the mechanisms of DME development are complex, the end result is a breakdown of the inner blood-retina barrier (tight junctions between retinal vascular endothelial cells), which ultimately allows accumulation of mostly extracellular fluid in the retina. Once initiated, this process is typically chronic, resulting in potential long-term central vision loss.

IMAGING OPTIONS

In the era before optical coherence tomography (OCT) imaging, the indication to treat macular edema via focal laser was based on a clearly defined standard established in the ETDRS, termed clinically significant macular edema. Since the time of the ETDRS, treatment modalities have expanded to include anti-VEGF therapy, steroids, and pars plana vitrectomy. In addition to the expansion of treatment options, the imaging technologies that complement the diagnosis and management of DME are now a critical component of the optimal approach to DME. An understanding of these imaging technologies is critical to delivering optimal care in the management of DME.

Fundus Photography

This established imaging modality provides important objective information regarding the severity of diabetic retinopathy (DR) and disease progression. It is also helpful for communication between physicians. Fundus photography can also serve as a useful tool for counseling patients on the extent of their retinopathy.
Additionally, nonmydriatic ultra-widefield fundus photography provides excellent photos that can document disease severity throughout the posterior segment (Figure 1), and the introduction of this modality has improved detection of DR relative to standard fundus photography.\(^5\) As it pertains to DME, however, fundus photography is less useful for diagnosing and monitoring retinal thickening or macular edema.

**OCT**

OCT has emerged as the most critical imaging test for DME as well as vitreoretinal interface disorders associated with DR. This sensitive imaging modality allows detailed evaluation of the retinal anatomy, the vitreoretinal interface, and the presence of retinal thickening, edema, or subretinal fluid. Although there is still no official classification of OCT-based DME, a number of informal classification schemes have been devised.\(^{16-19}\) OCT documents both qualitative and quantitative parameters, including the following:

- Retinal thickness at the fovea and parafoveal regions;
- Retinal morphology, such as sponge-like thickening (Figure 2A), diabetic cystoid macular edema (Figure 2B), serous retinal detachment without posterior hyaloidal traction (PHT; Figure 2C), and DME with associated PHT (Figure 2D);
- Retinal topography across the macular cube; and

**Figure 2.** OCT patterns in DME. Sponge-like thickening (A), cystoid macular edema (B), serous retinal detachment and intraretinal fluid in the absence of PHT (C), DME with PHT (D).

- Presence or absence of vitreomacular adhesion or traction.
- Additional OCT features that have been described to correlate with visual acuity and treatment response include the presence of an intact ellipsoid zone and external limiting membrane.\(^{20,21}\)

The application of segmentation algorithms to OCT images allows accurate measurement of retinal thickness within the macular cube (Figure 3). Increased retinal thickness has been demonstrated to correlate with clinical biomicroscopic edema\(^22\) and fluorescein leakage.

**Figure 3.** Retinal thickness map in a patient with DME.
There is also a modest correlation between visual acuity and increased retinal thickness. With the application of eye tracking software and retinal vessel recognition, retinal thickness maps can be compared across visits, and a change analysis can be generated (Figure 4). This information is helpful in assessing disease progression and treatment efficacy. Additionally, it may serve as an educational tool when patients are counseled on interval changes in their retinal status.

OCT also provides excellent resolution of the vitreoretinal interface and can identify DME with comorbid PHT (Figure 5). This condition, occurring in a distinct subgroup of patients, is often overlooked on biomicroscopic exam alone. These patients are often more resistant to medical therapy and may benefit from earlier surgical intervention to optimize visual outcomes.

A novel use of OCT, particularly in patients with comorbid PHT or tractional retinal detachments, is as a guide for intraoperative decision-making. The technology may help facilitate the identification of surgical planes, define membrane relationships, and localize the presence of small full thickness breaks. Although it did not directly address diabetic surgery exclusively, the PIONEER study demonstrated that the use of intraoperative OCT potentially affected posterior segment surgical decision-making in a significant number of eyes.

Fluorescein Angiography

Although studies have attempted to correlate OCT changes in patients with enlarged foveal avascular zones, a shortcoming of conventional OCT imaging is its inability to evaluate the presence or extent of macular ischemia. As a result, fluorescein angiography remains an essential part of the imaging armamentarium in DR for assessing the leakage pattern (focal or diffuse) contributing to DME. Variations in leakage may alter the treatment paradigm. For example, focal laser may be a beneficial treatment for extrafoveal focal leakage, while pharmacologic therapy with intravitreal anti-VEGF agents or steroids may be more effective in diffuse macular edema. Fluorescein angiography is also important in evaluating the extent of ischemia.

Ultra-widefield fluorescein angiography confers the additional advantage of not only detecting macular leakage and ischemia, but also providing simultaneous evaluation of the extent of peripheral nonperfusion and occult peripheral neovascularization (Figure 6). Through the utilization of this technology, our understandings of the interconnections between peripheral nonperfusion, severity of DR, and responsiveness of macular edema are continuously evolving.

Using ultra-widefield fluorescein angiography, Wessel et al demonstrated a correlation between peripheral retinal ischemia and DME. Patients with retinal ischemia were 3.75 times more likely to develop DME.
relative to patients without retinal ischemia. Another study reported a correlation between recalcitrant DME and larger areas of peripheral nonperfusion, which suggests that targeted laser photocoagulation to the area of peripheral ischemia may serve as an adjunctive treatment for the management of DME. This is an area of active research and investigation.

**OCT Angiography**

This emerging imaging modality provides novel information compared with both conventional OCT and fluorescein angiography. OCT angiography (OCTA) utilizes an OCT scanner and a unique algorithm to identify areas of motion that correlate with vascular flow. It is a noninvasive, no-dye technique that captures the motion of particles (eg, red blood cells) within tissues. The motion signals can then be aggregated to provide a 3-D view of both the retinal and choroidal vasculature. Although OCTA does not provide leakage information, it reconstructs vascular flow patterns with detail that exceeds the imaging resolution of fluorescein angiography. Additionally, it can detail with precision the extent of microaneurysms (Figure 7A), the disruption of the foveal avascular zone (Figure 7B), and the extent of vascular remodeling (Figure 7C). This noninvasive modality is still in its infancy, and its specific role in the management of DME remains unclear. However, the high-quality image detail and noninvasive nature of OCTA makes it particularly attractive for assessing retinal vascular disorders such as DR.

**CONCLUSION**

Ophthalmologists and retina specialists have entered an exciting era of retinal imaging that provides accurate and highly reproducible information on retinal vascular leakage, retinal edema, and ischemia. Several multicenter randomized clinical trials have already implemented treatment and retreatment criteria based on imaging results that provide the clinician a framework to extrapolate into practice. OCT-guided therapy has become the gold standard to enable individualized treatment of conditions with multiple management options.

As clinicians become increasingly familiar with emerging technologies such as intraoperative OCT, ultra-widefield angiography, and OCTA, treatment paradigms will become more precise and tailored to each patient to yield the best possible outcomes. This is an exciting time in the evolution of our understanding of DME, and clinical studies are ongoing to determine the contribution of these new imaging modalities to improving outcomes.

“As clinicians become increasingly familiar with emerging technologies ... treatment paradigms will become more precise and tailored to each patient to yield the best possible outcomes.”

**Figure 7. OCTA demonstrating microaneurysms with associated nonperfusion (A), foveal avascular zone irregularity and enlargement (B), and capillary nonperfusion and vascular remodeling (C).**

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