

OCT Biomarkers Redefining Macular Edema Diagnosis and Management

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DESCRIPTION

Macular edema remains one of the most significant causes of visual impairment across a spectrum of retinal diseases, including diabetic retinopathy, retinal vein occlusion, uveitis, and postoperative complications. Historically, its diagnosis relied heavily on clinical examination and fluorescein angiography, which, although valuable, lacked the structural precision required for nuanced interpretation. The advent of Optical Coherence Tomography (OCT) revolutionized the understanding of retinal architecture by offering high-resolution, cross-sectional views of macular pathology. As OCT technology matured from time-domain to spectral-domain and now swept-source imaging its utility expanded beyond visualization into the realm of biomarker identification. These OCT biomarkers provide quantifiable, reproducible insights into disease severity, treatment response, and prognosis, ultimately reshaping the diagnostic and management algorithms for macular edema. This commentary explores the evolving role of OCT biomarkers, highlighting their importance in clinical decision-making and their potential to elevate precision medicine in retinal care.

The Recognition of intraretinal Fluid (IRF) as a primary OCT biomarker has significantly influenced the understanding of macular edema pathophysiology. IRF is typically observed as hyporeflective cystoid spaces located within the inner nuclear and outer plexiform layers. Its presence correlates strongly with retinal vascular leakage, hallmark features of Diabetic Macular Edema (DME) and Retinal Vein Occlusion (RVO). Importantly, IRF serves as both a diagnostic indicator and a therapeutic guide, as persistent intraretinal cysts are often associated with poorer visual outcomes. Studies suggest that eyes with chronic IRF exhibit structural disorganization, including disruption of the photoreceptor layers and external limiting membrane. As a biomarker, IRF highlights the active disease state and helps clinicians evaluate the urgency of intervention and the anticipated response to anti-VEGF or corticosteroid therapies.

Equally critical is the identification of Sub Retinal Fluid (SRF), a distinguishing OCT biomarker that represents fluid accumulation between the neurosensory retina and Retinal Pigment Epithelium (RPE). Unlike IRF, SRF has a more variable

prognostic significance depending on the underlying pathology. In diabetic macular edema, SRF has been associated with a more reversible course and better visual response to treatment compared to IRF. Conversely, in uveitic macular edema or postoperative states, SRF can indicate ongoing inflammation or impaired fluid transport across the RPE. The presence and volume of SRF inform treatment choices, particularly in determining whether a patient may benefit more from anti-inflammatory agents, anti-VEGF therapy, or laser intervention. Therefore, SRF serves as a dynamic biomarker that reflects both disease activity and therapeutic potential.

Hyper Reflective Foci (HRF) have emerged as one of the most intriguing and clinically relevant biomarkers in OCT-based assessment of macular edema. These small, punctate, reflective lesions scattered throughout the retinal layers are believed to represent activated microglia, lipid extravasation, or degenerative cellular debris. Their presence is strongly correlated with inflammation, retinal ischemia, and chronic edema. In diabetic retinopathy, HRF are associated with higher levels of inflammatory cytokines and can predict a suboptimal response to anti-VEGF therapy. As a result, their detection may prompt clinicians to consider corticosteroids or combination therapy earlier in the treatment course. HRF are also prognostic markers for outer retinal damage, indicating potential risk of photoreceptor loss. Their distribution, density, and persistence provide critical insights into the chronicity of macular pathology and help tailor individualized treatment plans.

Disorganization of Retinal Inner Layers (DRIL) is another pivotal OCT biomarker recognized for its strong association with visual acuity outcomes. DRIL refers to the loss of distinct boundaries among the ganglion cell layer, inner plexiform layer, and inner nuclear layer. It is considered a marker of neuroretinal injury rather than mere fluid accumulation. DRIL has been consistently linked to visual dysfunction in diabetic macular edema and retinal vein occlusion, and its improvement over time is correlated with visual recovery. Unlike fluid biomarkers that may fluctuate rapidly with treatment, DRIL often reflects long-term structural damage and is therefore essential for prognostication. Its assessment guides clinicians in setting realistic expectations for visual improvement and helps

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Received: 04-February-2025, Manuscript No. JECO-25-39279; **Editor assigned:** 07-February-2025, PreQC No JECO-25-39279 (PQ); **Reviewed:** 21-February-2025, QC No. JECO-25-39279; **Revised:** 28-February-2025, Manuscript No. JECO-25-39279 (R); **Published:** 10-March-2025, DOI: 10.35248/2155-9570.25.16.1004

Citation: Turner M (2025). OCT Biomarkers Redefining Macular Edema Diagnosis and Management. Clin Exp Ophthalmol. 16:1004.

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determine which patients may require more aggressive or prolonged therapy.

Another integral biomarker, the integrity of the Ellipsoid Zone (EZ), represents functional health of the photoreceptors. Damage to the EZ appears as focal disruptions or attenuation on OCT imaging and directly correlates with visual acuity. In macular edema, prolonged fluid accumulation can disrupt the photoreceptor structure, resulting in long-term visual impairment. Restoration of the EZ following treatment often signifies meaningful visual recovery. Therefore, monitoring EZ integrity offers invaluable information about disease severity, treatment efficacy, and long-term prognosis. It underscores the importance of early intervention in macular edema to preserve photoreceptor health before irreversible damage occurs.

Central Subfield Thickness (CST), although one of the earliest OCT-derived quantitative biomarkers, remains fundamental in monitoring macular edema. CST provides an objective measure of retinal swelling and is widely used in clinical trials and routine care to evaluate treatment response. However, reliance on CST alone is now recognized as insufficient, as structural thickness does not always correlate with visual function. The emergence of additional OCT biomarkers has enhanced the interpretation of CST by providing context regarding the type and location of fluid, photoreceptor involvement, and inflammatory burden. Nevertheless, CST continues to serve as a valuable metric for tracking disease progression and guiding injection intervals in anti-VEGF therapy.

CONCLUSION

OCT biomarkers have fundamentally redefined the diagnostic and therapeutic landscape of macular edema. What was once approached primarily through clinical examination and dye-based angiography is now understood through high-resolution structural and vascular imaging that reveals microscopic details of retinal pathology. Biomarkers such as intraretinal fluid, subretinal fluid, hyperreflective foci, DRIL, and EZ integrity have become indispensable tools for evaluating disease activity, predicting visual outcomes, and tailoring treatment strategies. Together, these biomarkers illuminate the multifactorial nature of macular edema, distinguishing vascular leakage from inflammatory processes, acute swelling from chronic damage, and reversible changes from permanent injury.

As retinal diseases become increasingly prevalent worldwide, the ability to diagnose and manage macular edema precisely is more important than ever. The integration of OCT biomarkers into routine practice enhances clinical decision-making, supports individualized therapy, and improves prognostic accuracy. With continuing advancements in imaging technology, artificial intelligence-based analysis, and multimodal integration, OCT biomarkers are poised to evolve even further, driving the next era of personalized retinal medicine. The journey from simple visualization to biomarker-guided management marks a transformative leap in ophthalmology one that continues to shape how clinicians understand, treat, and ultimately preserve vision in patients with macular edema.