DRIL: A ROBUST IMAGING BIOMARKER IN DME

Here's why you should be on the lookout for disorganization of retinal inner layers on OCT.

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Diabetic retinopathy (DR) is a major complication of diabetes mellitus, a chronic condition with widespread effect due to its high rates of morbidity and mortality.[1] Diabetic macular edema (DME) is the leading cause of vision loss among individuals with DR, particularly affecting working-age adults.[2] Despite advances in treatments such as intravitreal injections of anti-VEGF agents and corticosteroids, predicting visual outcomes in patients with DME remains challenging. This limitation has spurred research into reliable biomarkers that could better assess treatment efficacy and predict changes in visual acuity.

One promising biomarker is disorganization of retinal inner layers (DRIL), which has shown potential as a noninvasive indicator of visual prognosis in patients with DME. DRIL, observed through spectral-domain OCT (SD-OCT), reveals structural changes in the retina that correlate with decreased visual acuity. Its ease of measurement and noninvasive nature make DRIL a practical tool for tracking DME progression.[2-4]

A PREDICTIVE INDICATOR OF VISUAL ACUITY

After reviewing seven studies that included DRIL as a biomarker, we found that the presence and extent of DRIL consistently correlated with reduced visual acuity in patients with DME.[5] DRIL is defined as the horizontal extent where the boundaries between retinal inner layers (ie, ganglion cell-inner plexiform layer, inner nuclear layer, and outer plexiform layer) become indistinct (Figures 1 and 2).[2] The seven studies showed that an increased extent of DRIL was linked to worse baseline visual acuity and a decline in visual acuity over time. For example, research by Sun et al demonstrated that every 100 µm increase in DRIL corresponded with a reduction of approximately 4.6 ETDRS letters in visual acuity.[2] Similarly, Das et al observed that a greater horizontal DRIL extent significantly predicted poorer visual outcomes over time.[4]

Based on our review, patients with minimal or no DRIL at baseline showed a greater potential for visual acuity improvement, underscoring the importance of detecting DRIL in the early stages of DME. In studies by Radwan et al

AT A GLANCE

- Disorganization of retinal inner layers (DRIL) is defined as the horizontal extent where the boundaries between various retinal inner layers become indistinct.
- In one meta-analysis, the presence and extent of DRIL consistently correlated with reduced visual acuity in patients with diabetic macular edema.
- DRIL is a promising biomarker for clinical practice, especially as a predictor of visual outcomes in diabetic macular edema.

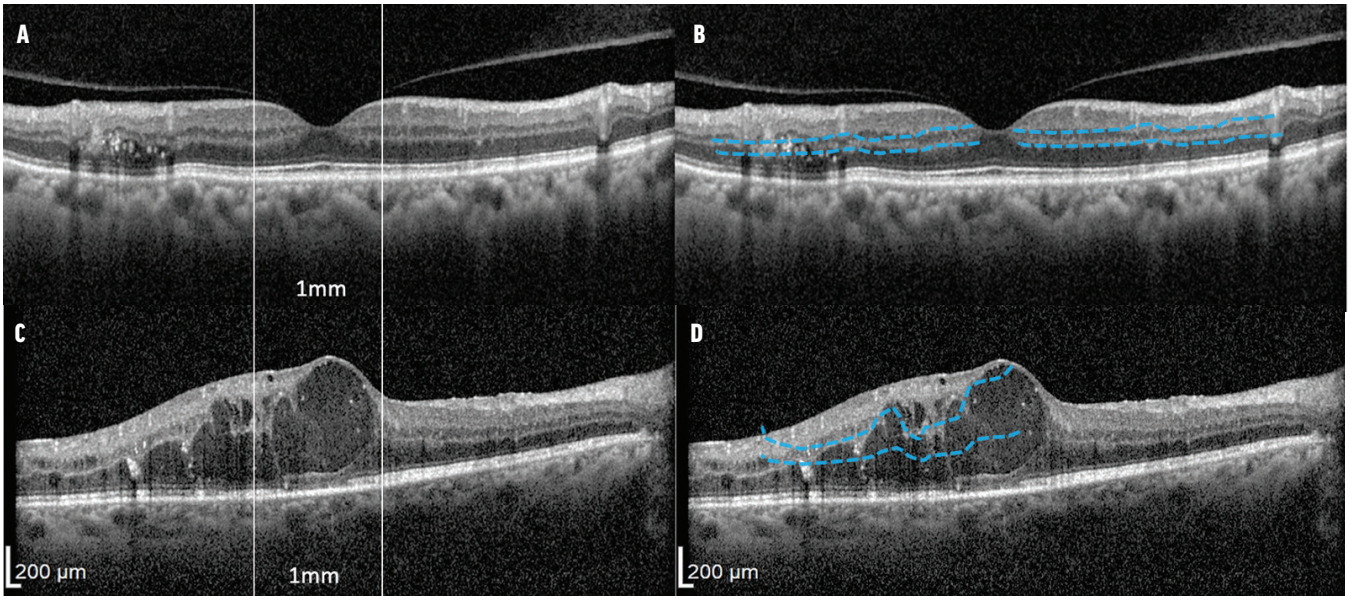

Figure 1. DRIL is evaluated within 1 mm centered on the fovea. In this SD-OCT image of the eye of a 58-year-old man (A), the boundaries of the inner nuclear layer are clearly identified (B, blue lines). Swept-source OCT imaging of the eye of a 61-year-old man (C) shows that the boundaries of the inner nuclear layer cannot be identified clearly (D, blue lines).

and Eraslan et al, patients lacking DRIL at baseline experienced significantly better visual outcomes, while those with existing DRIL saw minimal or no improvement in visual acuity.[6,7] This pattern suggests that DRIL may indicate structural damage to the retina that, once established, could limit the efficacy of DME treatment options.

ASSOCIATION WITH OTHER RETINAL BIOMARKERS

Within these studies, DRIL often appeared alongside other structural and functional abnormalities in the retina. Several studies reported a connection between DRIL and increased retinal thickness, the presence of intraretinal cysts, and reduced vessel density in the superficial capillary plexus (SCP) and deep capillary plexus (DCP).[4] These concomitant factors suggest that DRIL may be part of a broader set of pathological changes in the retinal microstructure. Cennamo et al, for example, found that DRIL was associated with lower vessel density in both the SCP and DCP, suggesting that retinal ischemia and reduced blood flow may contribute to DRIL formation and progression.[8]

Furthermore, DRIL was frequently associated with disruptions in other retinal layers, such as the external limiting membrane (ELM) and ellipsoid zone (EZ). The presence of DRIL alongside ELM and EZ disruptions was found to significantly worsen visual outcomes, as noted by Das et al and Lee et al.[4-9] These disruptions likely reflect damage to essential cellular structures within the retina, including the photoreceptor and bipolar cells, which are critical for transmitting visual information. Consequently, DRIL may serve as an indicator not only of visual acuity loss but also of broader structural deterioration within the retina.

TREATMENT IMPLICATIONS

Our review also examined the effect of DME treatments on DRIL and visual outcomes. Although anti-VEGF injections and corticosteroids have been shown to reduce retinal swelling and, in some cases, improve visual acuity, Sun et al and Zur et al reported their limited effect on reversing DRIL.[4-8] This suggests that once DRIL is established, it may represent irreversible retinal damage, making early detection crucial to managing DME more effectively.

Patients with lower baseline levels of DRIL were more likely to experience visual improvement with treatment; thus, identifying DRIL early could help tailor treatment. Additionally, the presence of DRIL could inform clinicians about the potential limits of visual recovery in patients with advanced DME, supporting realistic patient expectations and guiding decisions on treatment intensity and frequency.

POTENTIAL FOR PERSONALIZED MEDICINE AND AI

As a noninvasive and reproducible SD-OCT measurement, DRIL is a promising biomarker for clinical practice, especially as a predictor of visual outcomes in DME. Given its strong association with poor visual acuity and limited recovery potential, DRIL could become a valuable tool in personalized treatment planning for DR patients. By assessing DRIL early in DME, clinicians could potentially identify patients who are less likely to respond favorably to standard treatments, allowing for more customized and proactive care.[5]

Furthermore, DRIL holds potential for integration into AI and machine learning models that analyze retinal imaging data. DRIL could serve as a key data point for algorithms designed to predict DME progression and treatment

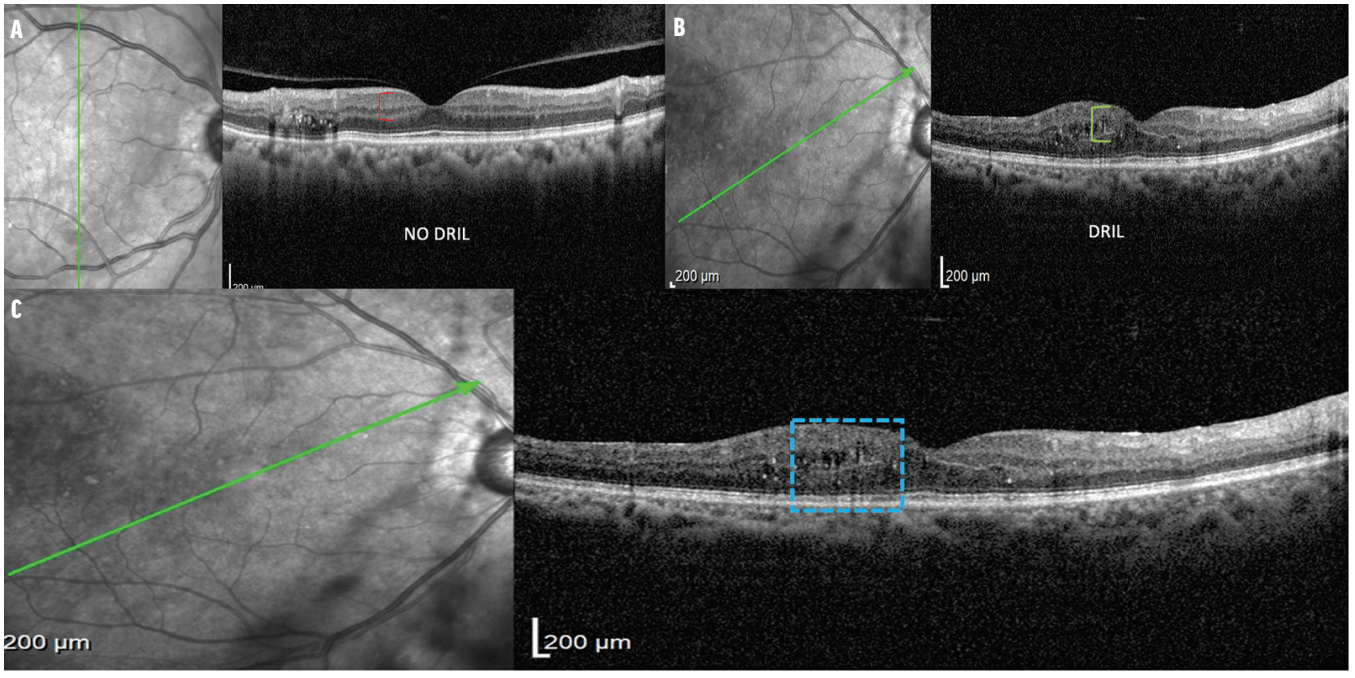

Figure 2. The red bracket in this OCT image shows no DRIL (A). In another OCT, the green bracket (B) and blue rectangle (C) show the lack of definition between the ganglion cell layer, inner plexiform layer, and outer plexiform layer.

response. Standardizing DRIL assessments across OCT devices and enhancing the accuracy of AI-driven interpretations could further improve its clinical utility, reducing variability and improving DME diagnosis and monitoring.[5]

USING DRIL IN YOUR PRACTICE

These findings underscore DRIL's role as a biomarker for assessing visual outcomes in DME patients. Its correlation with poorer baseline visual acuity, limited improvement potential, and association with other retinal pathologies position DRIL as a useful tool for guiding treatment decisions. Early detection and monitoring of DRIL could facilitate more effective, individualized treatment strategies, potentially slowing DME progression.

While further research is needed to clarify the underlying mechanisms of DRIL and standardize its measurement across devices, these findings support DRIL's integration into clinical practice and future AI-driven diagnostic platforms for DR. ■

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