



Retinal Imaging Biomarkers for Predicting Outcomes after Vitreoretinal Surgery

Muhammad Qasim^{1*}, Almas Tabassum¹, Areeb Muhammad Qasim¹, Muhammad Hamza¹, Muhammad Taha¹

¹Independent Researcher

*Corresponding Author

Muhammad Qasim

Independent Researcher

Article History

Received: 14.06.2026

Accepted: 06.08.2026

Published: 14.08.2026

Abstract: Vitreoretinal surgery often achieves anatomical success; however, functional recovery differs markedly among eyes with similar disease presentations. Retinal imaging biomarkers help reduce this uncertainty by characterizing tissue composition, photoreceptor integrity, traction, perfusion, inflammation, and postoperative remodeling before these changes are evident in visual acuity. This structured review compiles evidence from 2020 to 2025 regarding optical coherence tomography, optical coherence tomography angiography, wide-field imaging, fundus autofluorescence, and emerging computational evaluations for predicting outcomes after surgery for epiretinal membrane, macular hole, rhegmatogenous retinal detachment, and tractional diabetic retinal disease. A translational framework is used, distinguishing preoperative risk stratification, intraoperative confirmation, early postoperative assessment, and longitudinal recovery. Across indications, the most consistent favorable prognostic indicators include preserved ellipsoid-zone and external-limiting-membrane continuity, limited inner retinal disorganization, reduced chronicity-related tissue deformation, smaller or more favorable lesion geometry, and early restoration of normal foveal architecture. In contrast, ectopic inner foveal layers, extensive disorganization of retinal inner layers, persistent subretinal fluid, outer retinal corrugation, hyperreflective inflammatory deposits, severe macular ischemia, and segmentation-unstable edema are associated with slower or incomplete recovery. No single metric demonstrates sufficient robustness across diseases, devices, and surgical techniques. The most effective prognostic approach merges with structural condition, lesion geometry, perfusion, symptom-relevant function, and temporal change. Standardized acquisition, masked grading, artifact reporting, external validation, and outcome definitions extending beyond distance acuity are necessary before imaging-derived scores can independently guide consent, timing, or individualized follow-up.

Keywords: Vitreoretinal Surgery, Optical Coherence Tomography, Imaging Biomarkers, Epiretinal Membrane, Macular Hole, Retinal Detachment, Visual Outcome.

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1. INTRODUCTION

Pars plana vitrectomy, membrane peeling, internal limiting membrane manipulation, tamponade, drainage, and retinopexy can restore

anatomical structure in conditions that previously resulted in inevitable visual loss. However, anatomical success does not guarantee visual success. Two eyes may achieve complete retinal

Citation: Muhammad Qasim, Almas Tabassum, Areeb Muhammad Qasim, Muhammad Hamza, Muhammad Taha (2026). Retinal Imaging Biomarkers for Predicting Outcomes after Vitreoretinal Surgery. *Glob Acad J Med Sci*; Vol-8, Iss-3 pp- 113-123.

reattachment or macular-hole closure yet differ markedly in reading speed, metamorphopsia, contrast sensitivity, or final best-corrected visual acuity. This variation occurs because surgery addresses a mechanical issue at a single point in time, while visual performance depends on the cumulative status of photoreceptors, Müller cells, inner retinal circuitry, retinal pigment epithelium, capillary supply, and cortical adaptation. High-resolution scans provides a practical means to assess this biological reserve.

Contemporary optical coherence tomography (OCT) allows detailed visualization of the vitreoretinal interface, retinal layers, cystic changes, subretinal material, photoreceptor bands, and postoperative remodeling. Swept-source platforms enhance penetration and field of view, while OCT angiography (OCTA) provides dye-free mapping of vascular flow. En face reconstruction and volumetric analysis reveal spatial patterns that may be missed by a single central B-scan. Intraoperative OCT allows immediate confirmation of membrane removal, hole configuration, and retinal apposition. Consequently, recent studies increasingly regard images not solely as documentation but as sources of candidate biomarkers capable of estimating the probability, speed, and extent of recovery (Chatziralli *et al.*, 2020; Mahmoudzadeh *et al.*, 2022; Lee *et al.*, 2024).

This review intends to identify which retinal imaging biomarkers reported between 2020 and 2025 are most effective for predicting anatomical and functional outcomes following vitreoretinal surgery. The objectives differ from those of a technology-focused review. First, biomarkers are compared across four major surgical contexts instead than a single disease. Second, the review distinguishes predictors of anatomical success from those of patient-experienced visual recovery. Third, it assesses whether postoperative trajectories offer more prognostic value than isolated baseline measurements. Fourth, it proposes a reporting framework appropriate for high-impact ophthalmology journals and prospective multicenter validation. The central premise is that prognosis should be based on convergent evidence rather than a single thickness measurement or categorical OCT sign.

2. REVIEW METHODOLOGY

A structured narrative review was undertaken because the literature contains heterogeneous diseases, devices, surgical techniques, scan protocols, and outcome definitions that do not support a single pooled effect estimate. PubMed-indexed and publisher-indexed human studies

published from January 2020 through December 2025 were considered. Search concepts combined vitreoretinal surgery, pars plana vitrectomy, epiretinal membrane, macular hole, rhegmatogenous retinal detachment, tractional retinal detachment, diabetic vitrectomy, OCT, OCTA, imaging biomarker, ellipsoid zone, external limiting membrane, disorganization of retinal inner layers, ectopic inner foveal layers, retinal folds, subretinal fluid, and visual outcome. Recent reviews were used for backward reference checking, while individual clinical cohorts were prioritized for disease-specific interpretation.

Eligible evidence included prospective and retrospective surgical cohorts, secondary analyses of clinical data sets, reproducibility studies, systematic reviews, and algorithm-validation studies. Studies were included when imaging was obtained preoperatively, intraoperatively, or postoperatively and was related to visual acuity, metamorphopsia, reading function, retinal sensitivity, anatomical closure, retinal reattachment, recurrence, postoperative edema, or need for further intervention. Case reports, nonhuman studies, purely technical simulations, and studies published outside the requested evidence window were excluded from the core reference list. When a study used both eyes, appropriate statistical handling was considered during interpretation.

Methodological quality was appraised through clarity of eligibility criteria, consecutive recruitment, sample size, masking of image graders, prespecified definitions, control of baseline acuity and symptom duration, treatment consistency, artifact handling, and completeness of follow-up. Particular caution was applied to automatically generated metrics when segmentation correction was not described. The review organizes findings by clinical decision: estimation of preoperative reserve, prediction of anatomical success, prediction of functional recovery, identification of complications, and monitoring of longitudinal remodeling. This approach replicates clinical workflow and reduces the risk of presenting statistically significant but clinically disconnected image features.

The term biomarker is used here in a restricted sense. A candidate sign must be objectively observable, biologically plausible, reasonably repeatable, and linked to an outcome that matters. Association alone does not establish readiness for care. A variable may correlate with final acuity because it reflects baseline severity, not because it adds independent prognostic information. Accordingly, emphasis is placed on multivariable studies, longitudinal change, external validation, and

incremental value beyond age, baseline acuity, disease duration, lens status, and surgical method.

3. Imaging Platforms and Biomarker Classes

Structural spectral-domain OCT remains the principal source of surgical biomarkers because it combines micrometer-scale axial resolution with rapid, noninvasive acquisition. Cross-sectional scans show membrane-induced distortion, foveal contour, cysts, schisis, subretinal fluid, photoreceptor bands, and retinal pigment epithelial relationships. Thickness maps summarize macular deformation but can conceal focal defects; therefore, raw B-scans must be reviewed. En face OCT adds topographic information and is particularly useful for mapping retinal folds, membrane contraction, and ellipsoid-zone loss.

Swept-source OCT increases scan speed, depth, and field. In retinal detachment, wider volumes may capture the transition between attached and detached retina and characterize outer retinal corrugation beyond the central scan. In diabetic traction, deeper penetration can improve visualization beneath hemorrhage or fibrovascular tissue, although dense media opacity remains limiting. OCTA contributes capillary density, foveal avascular zone geometry, nonperfusion, and postoperative vascular remodeling. It is attractive for repeated follow-up but does not display leakage and remains vulnerable to slow-flow loss, projection, motion, and segmentation artifacts.

Fundus autofluorescence reflects fluorophore distribution and retinal pigment epithelial stress. Its role is less standardized than OCT, but abnormal macular autofluorescence may contextualize chronic photoreceptor-retinal pigment epithelial dysfunction after detachment or longstanding interface disease. Ultra-widefield color imaging and fluorescein angiography remain important when peripheral breaks, untreated ischemia, proliferative disease, or leakage will change management. Imaging modalities should therefore be complementary rather than ranked as substitutes.

Candidate biomarkers fall into five classes. Geometric biomarkers describe lesion dimensions, including macular-hole minimum diameter, base diameter, height, and derived indices. Layer-integrity biomarkers describe the ellipsoid zone, external limiting membrane, cone interdigitation zone, and inner retinal organization. Mechanical biomarkers describe traction, ectopic inner foveal layers, retinal folds, and residual membranes. Fluid and inflammatory biomarkers include intraretinal cysts, subretinal fluid, hyperreflective foci, and postoperative cystoid edema. Perfusion biomarkers include vessel density, nonperfusion, and foveal avascular zone distortion. Figure 1 illustrates why extraction alone is insufficient: every proposed measure must survive technical validation and demonstrate outcome relevance.

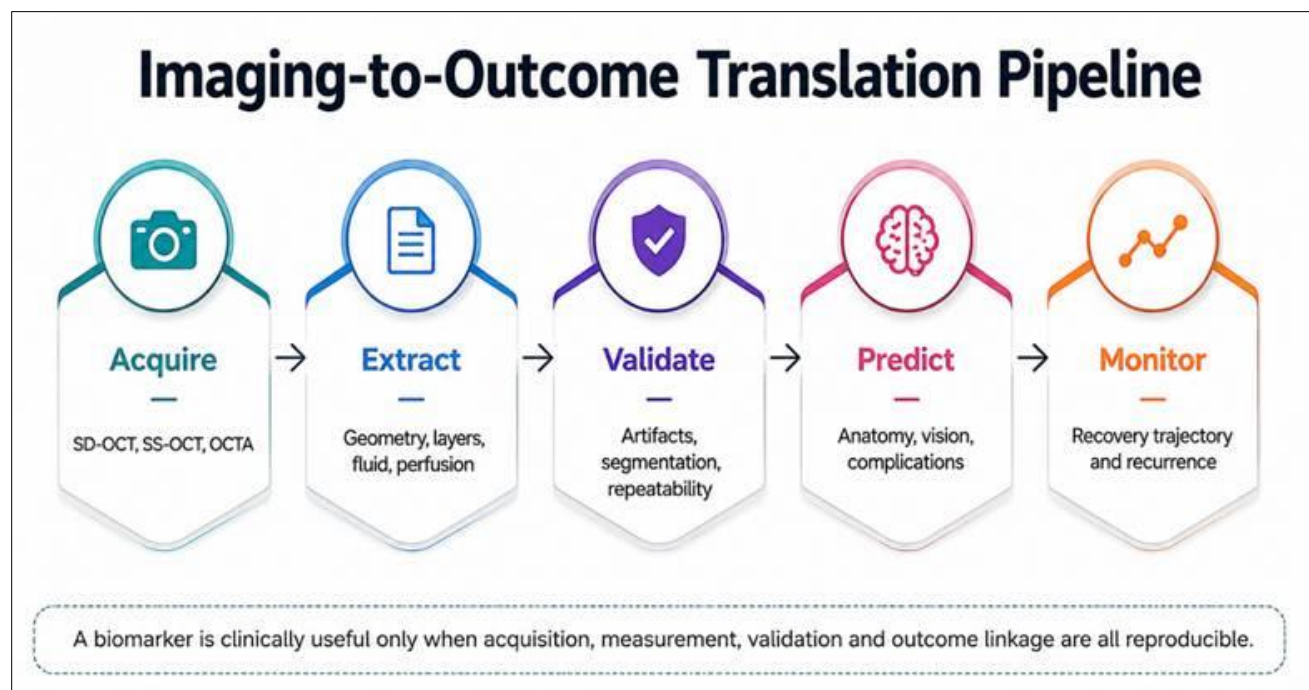


Figure 1: Imaging-to-outcome translation pipeline for surgical retinal biomarkers. Original conceptual illustration created for this review

Table 1: Major imaging biomarker domains in vitreoretinal surgery

Biomarker domain	Examples	Primary outcome	Main advantage	Key limitation
Geometry	Hole diameter, height, detachment height	Closure or reattachment	Directly reflects surgical anatomy	Orientation and scan-density dependent
Outer retina	EZ, ELM, interdigitation zone	Visual recovery ceiling	Biologically linked to photoreceptors	Binary grading oversimplifies partial loss
Inner retina	EIFL, DRIL, layer thickness	Acuity, distortion, reading	Captures chronic tractional remodeling	Affected by edema and segmentation
Fluid/inflammation	IRF, SRF, HRF, CME	Recovery speed and complications	Useful for longitudinal monitoring	Nonspecific and time dependent
Perfusion	Vessel density, FAZ, nonperfusion	Functional reserve	Adds vascular context	Artifacts and device dependence

4. Epiretinal Membrane Surgery

Idiopathic epiretinal membrane (ERM) provides a clear model of chronic tangential traction. Preoperative central retinal thickness is easy to measure but is an inconsistent independent predictor because thickening can represent reversible distortion, edema, or irreversible tissue remodeling. More informative signs describe how deeply traction has reorganized the fovea. Ectopic inner foveal layers (EIFL), disorganization of retinal inner layers (DRIL), inner nuclear layer thickening, and loss of a normal foveal pit indicate advanced structural remodeling. Studies published during the review window have associated these features with poorer baseline function and a lower or slower postoperative visual gain (Chatziralli *et al.*, 2020; Karasavvidou *et al.*, 2021; Mahmoudzadeh *et al.*, 2022).

The EIFL staging concept is clinically useful because it converts a complex OCT phenotype into an ordinal description of tractional remodeling. Eyes lacking continuous ectopic inner layers generally retain greater structural reversibility, whereas advanced stages may show persistent inner retinal tissue across the foveal center after successful peeling. Nevertheless, staging should not be used as a deterministic rule. Some advanced eyes improve meaningfully, particularly when symptoms are recent and outer retinal integrity stays preserved. Prognosis is strengthened when EIFL is interpreted alongside baseline acuity, metamorphopsia, ellipsoid-zone continuity, and duration.

Outer retinal biomarkers estimate photoreceptor reserve. A continuous ellipsoid zone and external limiting membrane before surgery generally support better visual potential. Disruption may result from chronic traction, edema, or coexisting disease. Postoperative restoration can occur gradually, so an early defect does not necessarily imply permanent limitation. Quantitative reflectivity and mapped defect area may be more

sensitive than a binary intact/disrupted grade, but such methods are not yet standardized across devices. Automated analysis in 2025 further suggested that combined quantitative features can improve prediction, although external validation and transparent segmentation continue to be necessary (Ferro Desideri *et al.*, 2025).

Functional outcomes should go beyond distance acuity. ERM often impairs near vision, reading speed, stereopsis, and metamorphopsia disproportionately. A patient can gain only a few acuity letters yet show considerable improvement in distortion. Recent work stresses near visual performance and symptom-relevant testing, which should be paired with OCT changes rather than treated as secondary observations (Gelormini *et al.*, 2025). This distinction affects biomarker evaluation: inner retinal disorganization may relate differently to metamorphopsia than photoreceptor integrity relates to acuity.

Postoperative imaging should assess residual membrane, foveal contour normalization, inner retinal relaxation, cystic change, and outer retinal recovery. Early thickening or transient cysts may occur without treatment failure. Persistent or increasing cystoid change, recurrent traction, or progressive ellipsoid-zone loss warrants closer evaluation. The most informative pattern is a trajectory: reduction of tangential distortion, gradual thinning toward a stable plateau, improved layer definition, and preserved photoreceptor bands. A single postoperative scan cannot distinguish delayed recovery from an unfavorable endpoint.

5. Macular Hole Surgery

For full-thickness macular hole surgery, baseline geometry has long been used to estimate closure probability and visual prognosis. Minimum linear diameter, base diameter, hole height, macular hole index, tractional hole index, diameter hole index,

and hole form factor capture different aspects of tissue separation. Larger minimum and base diameters generally indicate greater tissue displacement and a more demanding closure environment. However, measurement is sensitive to scan orientation; a radial volume centered on the hole is preferable to dependence on one horizontal B-scan.

Outer retinal integrity is central to functional prognosis. The ellipsoid zone represents mitochondria-rich photoreceptor inner segments and serves as an accessible marker of photoreceptor alignment and health. Longitudinal studies show that visual recovery can continue as ellipsoid-zone defects contract after successful closure (Sevgi *et al.*, 2021). Mapping the area of ellipsoid loss may provide more information than measuring one linear gap, particularly when the defect is irregular (Mehta *et al.*, 2021). Reflectivity-based measures also suggest that photoreceptor recovery is gradual and biologically meaningful (Tuğan *et al.*, 2020).

The external limiting membrane often restores before or alongside the ellipsoid zone and may indicate a scaffold for photoreceptor recovery. Closure configuration matters: a continuous neurosensory bridge without exposed retinal pigment epithelium is favorable, whereas persistent outer foveal defects, large cavitation, or a flat-open configuration limit function. Intraoperative OCT can document edge configuration after internal limiting membrane peeling and fluid-air exchange, but the prognostic meaning of immediate intraoperative changes remains under investigation.

Postoperative OCT should separate anatomical closure from tissue quality. A hole may be closed while the ellipsoid zone remains discontinuous, explaining limited early acuity. Conversely, a residual photoreceptor defect can improve for months. Singh *et al.*, proposed a structured ellipsoid-zone grading approach in 2025, strengthening the value of standardized outer retinal assessment after successful surgery (Singh *et al.*, 2025). Dynamic change may outperform a baseline-only model because the speed of restoration indicates both initial injury and postoperative healing capacity.

Lamellar macular holes need distinct interpretation. Volumetric parameters, residual foveal tissue, epiretinal proliferation, and outer retinal defects can influence outcome after selected surgery. Recent volumetric work suggests that three-dimensional characterization may better represent irregular cavities than conventional diameters (Lipperra *et al.*, 2024). Nevertheless, surgical indication remains individualized because some lamellar holes are stable and because postoperative

benefit depends on phenotype, symptoms, and associated traction.

No geometry index should be used alone for consent. Age, symptom duration, baseline acuity, lens status, hole chronicity, high myopia, and surgical technique modify outcome. A clinically responsible estimate combines hole dimensions, photoreceptor integrity, retinal pigment epithelial appearance, and expected ability to posture or tolerate tamponade. Imaging supports probabilistic counseling; it does not guarantee closure or a specific visual endpoint.

6. Rhegmatogenous Retinal Detachment Repair

In macula-off rhegmatogenous retinal detachment (RRD), preoperative OCT can explain why anatomically successful reattachment produces variable vision. Duration and height of detachment remain important, but imaging directly displays the condition of the detached macula. Ellipsoid-zone and external-limiting-membrane disruption, outer retinal corrugations, intraretinal cysts, hyperreflective dots, and subretinal deposits indicate differing degrees of photoreceptor stress and inflammatory response. Preserved outer retinal architecture is generally associated with better recovery, although severe detachment can make segmentation unreliable.

Outer retinal corrugation describes undulating photoreceptor layers in detached retina and may reflect mechanical buckling and chronicity. Hyperreflective dots have been associated with greater detachment extent, duration, height, reduced visual acuity, and postoperative cystoid macular edema (Jhaveri *et al.*, 2023). Their biological identity is uncertain and may include inflammatory cells, proteinaceous material, or degenerating photoreceptor components. They should therefore be treated as a composite stress marker rather than a disease-specific lesion.

Preoperative intraretinal cysts and disrupted layer boundaries may indicate more advanced injury. Subretinal fluid composition and the retinal pigment epithelium-photoreceptor relationship likewise influence recovery. Yet preoperative imaging may be technically difficult when the macula is highly elevated, fixation is poor, or the scan does not capture the deepest point. Studies should report imageability and exclusions because a biomarker derived only from easily imaged detachments may not generalize to severe cases.

Postoperative persistent subretinal fluid is common after some repair techniques and does not always signify surgical failure. Its prognostic meaning depends on amount, location, trend, and symptoms. Small pockets can resolve slowly while acuity

improves. Persistent fluid accompanied by photoreceptor disruption, retinal folds, or increasing symptoms deserves closer assessment. Outer retinal folds and full-thickness retinal folds are particularly important because they can produce metamorphopsia and may require early recognition. En face OCT can improve appreciation of their extent.

A multicenter study in 2024 evaluated imaging predictors of functional outcomes after primary RRD repair, illustrating the shift toward multivariable prognostic assessment (Lee *et al.*, 2024). Reviews published in 2025 similarly emphasize photoreceptor-layer integrity, macular microstructure, and postoperative remodeling (Zaidi *et al.*, 2025; Chereji *et al.*, 2025). Across studies, the strongest recurring message is that reattachment status is only the first endpoint. Visual prognosis depends on how much viable outer retina remains and how coherently it restores contact with the retinal pigment epithelium.

OCTA may reveal reduced macular perfusion after repair, but interpretation is challenging because segmentation and signal are altered by residual fluid and tissue displacement. Perfusion abnormalities may reflect preexisting vascular compromise, detachment-related injury, or postoperative change. Until device-independent thresholds are established, OCTA is best used as complementary evidence when structural recovery and visual performance diverge.

7. Diabetic Tractional Disease and Complex Vitrectomy

Tractional diabetic retinal disease combines mechanical distortion, ischemia, edema, hemorrhage, and neurodegeneration. Imaging prognosis is therefore more complex than in isolated idiopathic interface disease. Structural OCT can identify vitreomacular traction, tractional schisis, shallow tractional detachment, DRIL, ellipsoid-zone disruption, intraretinal fluid, and subretinal fluid. OCTA can estimate macular perfusion when image quality permits, while fluorescein angiography and wide-field imaging continue to be essential for peripheral ischemia and proliferative activity.

Preoperative macular ischemia limits visual potential even when traction is relieved. A relatively preserved foveal avascular zone and capillary network may support better recovery, whereas severe nonperfusion, extensive DRIL, and outer retinal disruption indicate reduced neural reserve. Edema can create segmentation failure and apparent flow loss, so vascular metrics must be interpreted with co-registered B-scans. Dense hemorrhage may prevent meaningful preoperative OCT, creating selection bias in published cohorts.

Surgical anatomy is also relevant. Broad adherent fibrovascular plaques, anteroposterior traction, combined tractional-rhegmatogenous detachment, and long-standing macular elevation increase operative complexity and the risk of iatrogenic breaks. Intraoperative OCT can confirm whether residual traction remains and can visualize retinal apposition after membrane dissection. However, the technique should support, not distract from, safe surgery; image acquisition must be rapid and targeted to a defined question.

Postoperative OCT distinguishes residual traction from edema, recurrent proliferation, ischemic thinning, and expected remodeling. Reduction in thickness is not always synonymous with improvement because thinning can represent resolution of fluid or loss of neural tissue. Conversely, some persistent fluid may coexist with functional gain. A composite interpretation should include layer organization, photoreceptor continuity, perfusion, and the direction of change. Systemic glycemic control, renal disease, blood pressure, and prior anti-vascular endothelial growth factor exposure can modify both anatomy and recovery and should be reported in prognostic studies.

8. Intraoperative OCT and Perioperative Decision Support

Intraoperative OCT converts imaging into a preoperative planning tool into a real-time surgical instrument. In membrane surgery it can identify residual tissue, reveal changes in foveal contour after peeling, and detect occult full-thickness defects. During macular-hole repair it can show edge relaxation, tissue configuration after internal limiting membrane manipulation, and the effect of fluid-air exchange. During retinal detachment repair it can demonstrate retinal apposition, subretinal fluid, and macular folds.

The principal advantage is confirmation of a specific surgical objective. The principal risk is overinterpretation. Immediate tissue deformation may not predict long-term biology, and metallic instruments, motion, shadowing, and limited scan access can degrade images. Intraoperative biomarkers should therefore be defined prospectively and linked to postoperative outcomes rather than selected retrospectively from visually striking scans. Current reviews describe expanding applications but also stress workflow, image acquisition, and evidence gaps (Horie *et al.*, 2025).

A useful perioperative framework asks three questions: Was the mechanical target achieved? Was new structural injury created? Does the immediate configuration justify modifying the planned

procedure? Examples include additional membrane peeling when a clear residual sheet remains, avoiding unnecessary manipulation when the target is complete, or correcting a macular fold before

concluding surgery. The value of intraoperative imaging should ultimately be measured by fewer complications, improved outcomes, or reduced operative time, not by image availability alone.

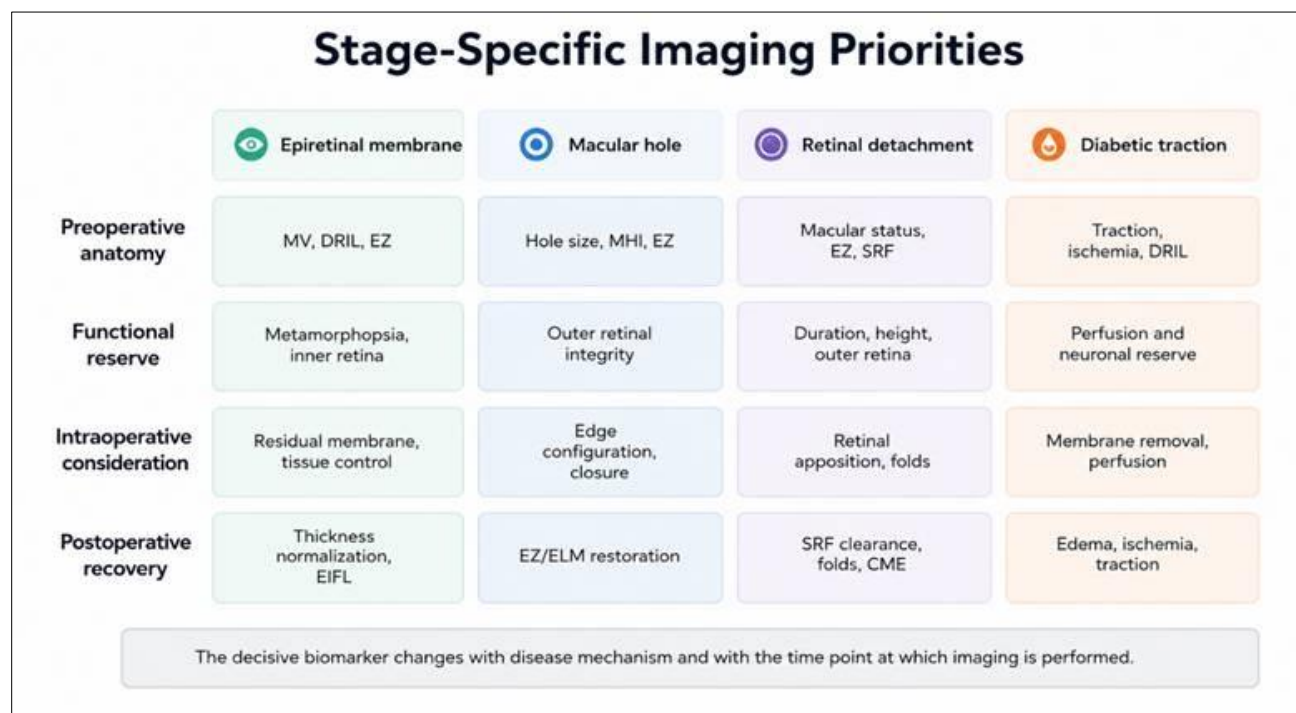


Figure 2: Stage-specific imaging priorities throughout common vitreoretinal surgical indications. Original conceptual illustration created for this review

9. Artificial Intelligence and Quantitative Prediction

Artificial intelligence can analyze entire OCT volumes, quantify irregular defects, and combine imaging with clinical variables. This is attractive because manual grading of ellipsoid-zone area, DRIL, retinal folds, and lesion geometry is time-consuming and reader dependent. Deep-learning segmentation can convert descriptive observations into continuous variables, while multimodal models can integrate baseline acuity, age, disease duration, surgical technique, and imaging features.

Recent ERM studies show the direction of travel. Automated systems have been used to quantify retinal biomarkers and predict postoperative acuity, with promising internal performance (Ferro Desideri *et al.*, 2025; Mariotti *et al.*, 2025). Yet model predictive accuracy can be inflated by small datasets, single-center imaging, inconsistent outcome timing, and leakage of postoperative information into training. External assessment on different devices and populations is essential. Calibration is equally important: a model

that ranks patients correctly may still provide misleading absolute probabilities.

Explainability should display the image regions and quantified features that add to a prediction. Attention maps alone are insufficient because they do not prove causal reasoning. Clinically deployable models must flag poor image quality, segmentation uncertainty, and out-of-distribution cases. They should also report confidence intervals and compare performance with simple baselines such as baseline acuity plus ellipsoid-zone status. The relevant question is not whether AI can fit the dataset, but whether it adds reliable, auditable information that changes counseling or subsequent follow-up.

Dynamic models may be notably valuable. Recovery is a process, and serial OCT can measure the rate of ellipsoid-zone restoration, thickness normalization, fluid clearance, and reduction of deformation. A model updated after the first postoperative scan may outperform a fixed preoperative estimate. Such tools could identify eyes recovering normally, eyes needing closer observation, and eyes in which unexpected anatomy warrants intervention.

Table 2: Clinical integration of imaging biomarkers by surgical question

Clinical question	Most informative imaging features	Suggested timing	Complementary outcome	Safeguard
ERM visual gain	EIFL, DRIL, EZ/ELM, deformation	Baseline and 3–6 months	Metamorphopsia and near vision	Adjust for baseline acuity and cataract
Macular-hole closure	3D geometry, edge configuration	Baseline and early postoperative	Primary closure and final acuity	Use radial scans centered on hole
RRD functional recovery	Macular status, outer retina, folds, HRD	Preoperative and serial postoperative	Acuity and distortion	Report duration and imageability
Diabetic traction outcome	Traction, DRIL, EZ, perfusion	Baseline and after edema stabilizes	Vision and reoperation	Inspect segmentation and ischemia
Unexpected recovery	Dynamic layer restoration and fluid trend	Repeated identical protocol	Patient-reported function	Distinguish change from measurement noise

10. Standardization, Limitations, and Future Research

The largest barrier to clinical translation is heterogeneity. Devices differ in wavelength, axial resolution, scan density, averaging, segmentation, and image enhancement. Studies define ellipsoid-zone disruption, DRIL, persistent subretinal fluid, and anatomical success differently. Outcome timing ranges from weeks to years. Surgical technique, tamponade, combined cataract surgery, and postoperative positioning vary. These differences can convert the same biological feature into apparently inconsistent evidence.

A minimum imaging dataset should report device and software version, scan protocol, number of averaged frames, scan orientation, signal-strength threshold, segmentation correction, grader masking, and reasons for image exclusion. Biomarker definitions should include diagrams or reproducible measurement rules. For geometric lesions, radial scans and three-dimensional measurements are preferable. For perfusion metrics, slab boundaries, projection removal, and motion correction must be disclosed. Repeatability should be measured across visits, not only within one session.

Outcome reporting should include baseline and final distance acuity in logMAR units but should not stop there. Metamorphopsia, reading speed, contrast sensitivity, retinal sensitivity, patient-reported visual function, and time to functional stability can be more relevant to daily life. Anatomical endpoints should distinguish primary closure or reattachment, final success after additional surgery, and tissue-quality outcomes such as photoreceptor restoration or persistent folds. Complications, reoperations, and missing follow-up must be transparent.

Prognostic models require adequate sample size and prespecified analysis. Baseline acuity is a

powerful confounder and must be included. Nonlinear relationships and interactions are plausible; for example, a large macular hole with preserved outer retinal tissue may behave differently from a smaller chronic hole with severe photoreceptor loss. Internal validation by bootstrapping is preferable to a single train-test split, and external validation is mandatory before clinical use. Decision-curve analysis can show whether a model improves decisions rather than merely increasing an accuracy statistic.

Future studies should test whether biomarker-guided pathways improve care. One trial could compare standard ERM counseling with counseling supported by a validated multimodal score. Another could evaluate whether an early postoperative healing trajectory safely reduces visits after uncomplicated macular-hole surgery. In RRD, a prospective registry could link preoperative macular microstructure and symptom duration to standardized visual and patient-reported outcomes. In diabetic traction, studies should integrate systemic status and wide-field ischemic burden.

Equity and access also require attention. Algorithms developed on high-quality scans from tertiary centers may underperform in eyes with dense cataract, hemorrhage, high myopia, or unstable fixation. These are often the eyes in which prognosis is most uncertain. Portable or lower-cost OCT may broaden access, but reduced scan quality must be incorporated into validation. The goal is not maximal technological complexity; it is dependable information that improves informed consent, timing, and follow-up across ordinary clinical settings.

Clinical interpretation must also preserve uncertainty because a mildly abnormal measurement may reflect biological variation acquisition noise or temporary postoperative change. Repeated scans obtained with the same device and protocol are more

informative than isolated comparisons with a normative database. Reports should distinguish observed change from change exceeding test-retest variability and should document treatment timing, lens status, media clarity, fixation quality, and concurrent retinal disease. This discipline prevents false exactness and supports communication between surgeons, optometrists, researchers, and patients. A staged validation pathway should move from analytical repeatability to biological coherence, longitudinal prediction, workflow testing, and outcome evaluation. Investigators should retain raw and processed images so that segmentation errors can be traced. They should calculate minimum detectable change for each metric and report the frequency and consequence of manual correction. Biomarkers should show coherent relationships with independent functional indices rather than only with another image variable. Prospective cohorts should evaluate incident complications, delayed recovery, reoperation, and patient-reported benefit. Pragmatic studies should measure technician time, reading burden, referral consequences, anxiety created by uncertain findings, and cost-effectiveness. A compact clinical report could present current status change from the prior visit; repeatability limits confidence in image quality and the specific features responsible for the prognostic category. Patient communication deserves equal care. OCT images are visually persuasive but color maps and magnification can exaggerate small differences. Clinicians should explain that a biomarker changes probability rather than establishing certainty. Shared decisions should integrate occupational needs, fellow-eye status, driving requirements, treatment burden, and willingness to accept the risks of observation or surgery. These safeguards keep sophisticated imaging connected to the purpose of vitreoretinal care: preserving useful visual function and quality of life. Clinical interpretation must also preserve uncertainty because a mildly abnormal measurement may reflect biological variation, acquisition noise, or temporary postoperative change. Repeated scans obtained with the same device and protocol are more informative than isolated comparisons with a normative database. Reports should distinguish

11. Clinical Integration and Conclusion

A practical prognostic report should begin with the surgical diagnosis and the outcome being estimated. For ERM, the report should describe tractional stage, EIFL, DRIL, outer retinal integrity, cystic change, and symptom-relevant function. For macular hole, it should record three-dimensional geometry, closure-related tissue configuration, and photoreceptor bands. For RRD, it should document macular status, duration when known, detachment morphology, outer retinal integrity, inflammatory

dots, folds, and postoperative fluid trajectory. For diabetic traction, it should integrate mechanical anatomy with ischemia and neural reserve.

The evidence from 2020 to 2025 supports several recurring principles. Preserved ellipsoid-zone and external-limiting-membrane continuity indicate stronger photoreceptor reserve. Severe inner retinal remodeling, chronic deformation, and macular ischemia reduce the expected functional ceiling. Lesion geometry helps estimate anatomical difficulty, but tissue condition better explains vision after anatomical success. Serial change often provides more useful information than a baseline snapshot. Imaging findings are strongest when they converge with symptoms, visual testing, and clinical context.

No current biomarker can independently determine whether surgery should be offered or predict an exact visual result. Measurements are device dependent, artifacts are common, and many studies remain retrospective. Imaging should therefore support probabilistic counseling. A patient can be told that certain features are favorable or unfavorable, that recovery may continue for months, and that anatomical success does not guarantee complete functional normalization.

The next advance is likely to be a standardized multimodal score that remains interpretable at the B-scan level. Such a score should combine geometry, inner and outer retinal integrity, perfusion, and early postoperative dynamics, while reporting uncertainty. Until multicenter validation is available, the most defensible approach is careful qualitative and quantitative synthesis by the surgeon. Retinal imaging biomarkers can meaningfully improve prediction after vitreoretinal surgery, but their clinical value depends on disciplined acquisition, transparent definitions, longitudinal interpretation, and outcomes that reflect how patients actually see.

REFERENCES

- Chatziralli I, et al. Optical coherence tomography biomarkers as predictive factors for postoperative visual acuity in patients with idiopathic epiretinal membrane. *Diagnostics (Basel)*. 2021;11(2):213. PMID: PMC7852424.
- Tuğan BY, et al. Correlation of visual recovery and increased ellipsoid zone reflectivity after macular hole surgery. 2020. PMID: PMC7610054.
- Mehta N, et al. Assessing the ability of preoperative quantitative spectral-domain optical coherence tomography characteristics to predict visual outcome in idiopathic macular hole

- surgery. *Retina*. 2021;41(1):29–36. doi:10.1097/IAE.0000000000002797. PMID: 32251240; PMCID: PMC7529763.
- Sevgi DD, Yee PS, Srivastava SK, et al. Longitudinal ellipsoid zone dynamics after macular hole repair in the DISCOVER Study: structure-function assessment. *Retina*. 2021;41(5):915–920. doi:10.1097/IAE.0000000000002983. PMID: 33887747; PMCID: PMC8074992
- Karasavvidou EM, Panos GD, Koronis S, Kozobolis VP, Tranos PG. Optical coherence tomography biomarkers for visual acuity in patients with idiopathic epiretinal membrane. *European Journal of Ophthalmology*. 2021;31(6):3203–3213. doi:10.1177/1120672120980951. PMID: 33307784.
- Guan I, Gupta MP, Papakostas T, et al. Role of optical coherence tomography for predicting postoperative visual outcomes after repair of macula-off rhegmatogenous retinal detachment. *Retina*. 2021;41(10):2017–2025. doi:10.1097/IAE.0000000000003162. PMID: 33734189
- Mahmoudzadeh R, Israilevich R, Salabati M, et al. Pars plana vitrectomy for idiopathic epiretinal membrane: OCT biomarkers of visual outcomes in 322 eyes. *Ophthalmology Retina*. 2022;6(4):308–317. doi:10.1016/j.oret.2021.10.008. PMID: 34718218.
- Yang X, et al. Effects of ectopic inner foveal layers on foveal configuration and visual function after idiopathic epiretinal membrane surgery. *Retina*. 2022;42(8):1472–1478. doi:10.1097/IAE.0000000000003495. PMID: 35502976
- Yanagida K, Wakabayashi Y, Usui Y, et al. Ectopic inner foveal layer as a factor associated with metamorphopsia after vitrectomy for epiretinal membrane. *Acta Ophthalmologica*. 2022;100(7):775–780. doi:10.1111/aos.15092. PMID: 35076169.
- Jhaveri A, Martins Melo I, Pecaku A, et al. Outer retinal hyperreflective dots: a potential imaging biomarker in rhegmatogenous retinal detachment. *Ophthalmology Retina*. 2023;7(12):1087–1096. doi:10.1016/j.oret.2023.07.016. PMID: 37481035
- Jong JLZ, et al. Surgical outcomes of pars plana vitrectomy in complex vitreoretinal disease. 2023. PMID: 37418640.
- Iwasaki M, Ando R, Aoki S, Miyamoto H. Restoration process of the outer retinal layers after surgical macular hole closure. *Retina*. 2022;42(2):313–320. doi:10.1097/IAE.0000000000003323. PMID: 34723901.
- Chang YH, Tan GSW, Chou HD, Tsai ASH. Reshaping vitreoretinal surgery: intraoperative optical coherence tomography as a tool for enhancing surgical decision-making in complex cases. *Taiwan Journal of Ophthalmology*. 2025. doi: 10.4103/tjo.TJO-D-24-00060. PMID: 39803398; PMCID: PMC11717328.
- Lee WW, Francisconi CLM, Marafon SB, et al. Imaging predictors of functional outcomes after rhegmatogenous retinal detachment repair. *Retina*. 2024;44(10):1758–1765. doi:10.1097/IAE.0000000000004172. PMID: 39287538
- Lippera M, et al. Volumetric biomarkers of visual outcome after surgical treatment of lamellar macular holes. *Journal of Personalized Medicine*. 2024; 14:755.
- Chaturvedi S, Paul A, Singh S, Akduman L, Saxena S. The ellipsoid zone is a structural biomarker for visual outcomes in diabetic macular edema and macular hole management. *Vision (Basel)*. 2025. PMID: 39846620; PMCID: PMC11755456.
- Singh S, Saxena S, Meyer CH, Chandra A, Akduman L. Retinal photoreceptor ellipsoid zone is a structural biomarker for visual outcome after successful macular hole surgery: a novel grading system-based study. *Indian J Ophthalmol*. 2025;73(Suppl 1):S126–S131. doi:10.4103/IJO.IJO_1031_24. PMID: 39141486; PMCID: PMC11834914.
- Ferro Desideri L, Hinrichsen L, Eldridge N, et al. Artificial intelligence analysis of OCT biomarkers to predict visual outcomes following vitrectomy for epiretinal membrane. *International Journal of Retina and Vitreous*. 2025;11(1):106. doi:10.1186/s40942-025-00735-9. PMID: 41088490.
- Chu X, et al. Baseline structural OCT biomarkers for visual outcomes following epiretinal membrane surgery. 2025. PMCID: PMC12707667.
- Gelormini F, et al. Visual performance and predictive OCT biomarkers in idiopathic epiretinal membrane. 2025. PMCID: PMC11734757.
- Mansilla R, et al. Spectral-domain optical coherence tomography assessment of structural changes in idiopathic epiretinal membrane. 2025. PMID: 39173025.
- Lin HL, Tseng PC, Hsu MH, Peng SJ. Using a deep learning model to predict postoperative visual outcomes of idiopathic epiretinal membrane surgery. *American Journal of Ophthalmology*. 2025; 272:67–78. doi: 10.1016/j.ajo.2025.01.003. PMID: 39814096.

- Horie S, et al. Current topics in OCT applications in vitreoretinal surgery. 2025. PMID: PMC12467528.
- Zaidi H, et al. Optical coherence tomography in retinal detachment: current applications and prognostic biomarkers. *Diagnostics*. 2025; 15:871.
- Chereji G, et al. Prognostic factors for visual postsurgical outcome in rhegmatogenous retinal detachment. 2025. PMID: PMC11943250.
- Carlà MM, et al. Preoperative OCT biomarkers predicting visual outcomes after macula-off retinal detachment surgery: systematic review and meta-analysis. 2025. PMID: 41106581.
- Patel R, Delhiwala K, Khamar B. Indistinct retinal outer layers in the walls of the idiopathic full-thickness macular hole—a potential predictive biomarker for surgical outcomes. *Indian Journal of Ophthalmology*. 2022;70(12):4383–4389. doi: 10.4103/ijo.IJO_1215_22. PMID: 36453349; PMID: PMC9940550.
- Baumann C, Iannetta D, Sultan Z, et al. Predictive association of pre-operative defect areas in the outer retinal layers with visual acuity in macular hole surgery. *Transl Vis Sci Technol*. 2021;10(4):7. doi:10.1167/tvst.10.4.7. PMID: 34003987; PMID: PMC8054630.
- Lin HL, et al. Predicting visual outcome after surgery in patients with idiopathic epiretinal membrane using a novel convolutional neural network. *Retina*. 2023. PMID: 36727822.
- Kamnig R, Robatsch N, Hillenmayer A, et al. A neural network for the prediction of the visual acuity gained from vitrectomy and peeling for epiretinal membrane. *Ophthalmology Science*. 2025;5(4):100762. doi: 10.1016/j.xops.2025.100762. PMID: 40291394; PMID: PMC12022697.