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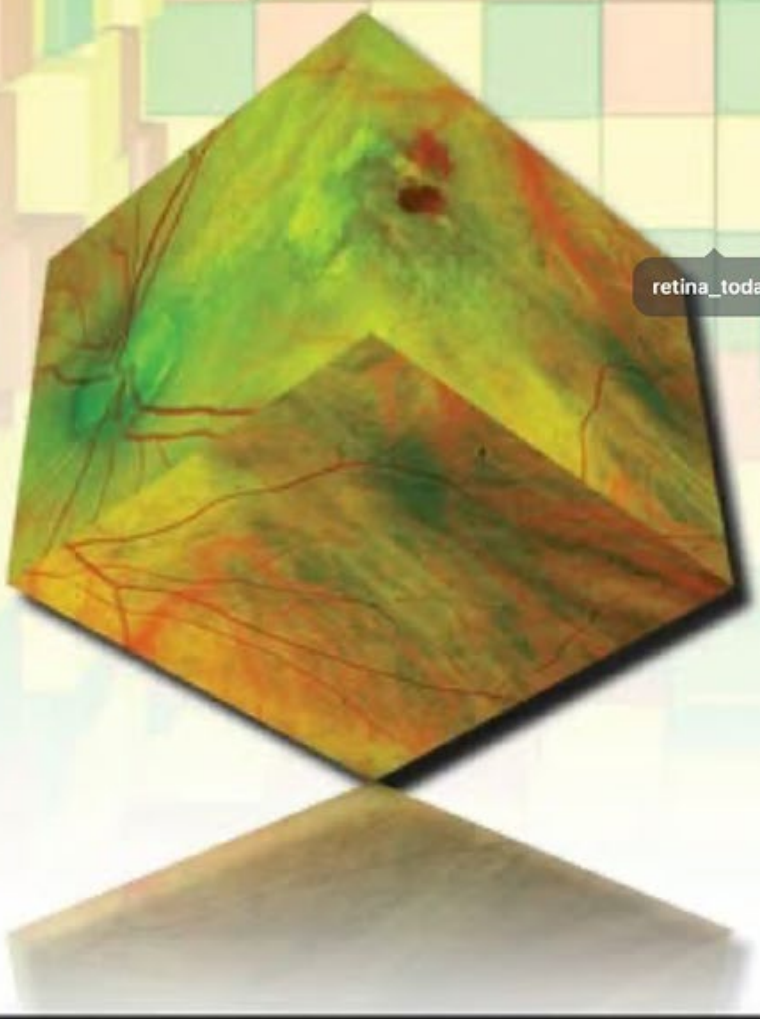

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Beyond One-Size-Fits-All: The Move Toward Personalized Vitreoretinal Therapy

By calculating the vitreous volume exact, clinicians can treat eyes with greater precision.

Andreas F. Borkenstein, MD

KEY TAKEAWAYS

- Because the vitreous cavity is not a uniform 4- to 5-mL reservoir, the author advocates for the use of the vitreous volume exact (VIVEX) to personalize intravitreal therapeutics.
- Using VIVEX-derived vitreous volumes of 2.98 mL, 5.12 mL, and 11.76 mL for small, emmetropic, and large eyes, the author's model predicted an approximately fourfold difference in initial intravitreal concentration despite identical dosing.
- The vitreous cavity is a dynamic therapeutic compartment with meaningful biomechanical and pharmacokinetic properties.

When the vitreous volume exact (VIVEX) concept was first introduced,[1] its central message was simple: The vitreous cavity is not a uniform 4- to 5-mL reservoir, and intravitreal therapy is therefore not delivered into a standard compartment in every patient.

We now know that vitreous volume varies substantially with axial length, ranging from approximately 2 mL in short hyperopic eyes to more than 10 mL in highly myopic eyes. If concentration is determined by dose divided by volume, identical intravitreal doses must inevitably produce different intraocular concentrations in different eyes.

Since my 2024 article in Retina Today, this idea has moved from concept toward validation. In a first real-world clinical case series, VIVEX-predicted vitreous volumes were compared with intraoperatively measured volumes in 27 eyes undergoing vitreoretinal surgery. The correlation was strong (R = 0.961), the mean absolute error was 0.48 mL, and 89% of estimates were

within ±1.0 mL of the measured volume. Most importantly, this study showed that individualized vitreous volume estimation is not only mathematically plausible but clinically usable. It also clarified where caution is needed: Oil-filled eyes remain more difficult because axial length measurements can be distorted and residual oil may influence the apparent intraoperative reference volume.[2]

MOUNTING EVIDENCE

Other groups have found similar results. A Brazilian study of 144 vitrectomized eyes demonstrated a strong correlation between axial length and the volume of the vitrectomized space and proposed a practical axial-length–based guideline for estimating this volume in routine surgery.[3] Another paper then translated those anatomical differences directly into pharmacologic consequences.4 Under fixed dosing conditions, a standard intravitreal dose was calculated to produce about 135% of the intended concentration in small eyes, about 75% in large eyes, and less than 60% in extra-large eyes. On that basis, the authors proposed dose reductions for small eyes and dose increases for large and extra-large eyes.[4]

Taken together, these studies indicate that personalization is no longer a theoretical concept but an emerging clinical reality. Whether treating patients with intravitreal drugs or performing vitreoretinal surgery, the evidence increasingly supports accounting for individual ocular anatomy rather than relying on uniform assumptions and fixed-volume paradigms.

A recent Korean study of endophthalmitis using intravitreal 0.625% povidone-iodine calculated the final intravitreal concentration on the basis of an assumed 5-mL vitreous volume, illustrating how deeply fixed-volume thinking remains embedded in clinical practice.[5] However, the authors themselves acknowledged that vitreous volume varies substantially between individuals and suggested future intravitreal treatment strategies move toward individualized concentration-based approaches rather than relying on a uniform volumetric assumption. In addition, when de Smet and colleagues analyzed intravitreal methotrexate for vitreoretinal lymphoma, they noted that a fixed 400-µg dose may expose small eyes to unnecessarily high concentrations while underdosing large eyes, because vitreous volume may

vary from roughly 3 mL to 10 mL.[6] He therefore argued that ocular treatment protocols should move toward fixed initial concentrations rather than fixed doses.

PERSONALIZED DOSING IN THE CLINIC AND OR

Recent theoretical pharmacokinetic analysis further quantifies what this means in practical terms. Using VIVEX-derived vitreous volumes of 2.98 mL, 5.12 mL, and 11.76 mL for small, emmetropic, and large eyes, the model predicted an approximately fourfold difference in initial intravitreal concentration despite identical dosing.[7] For triamcinolone acetonide, the modeled duration above the therapeutic threshold fell from 67.4 days in a small eye to 31.8 days in a large eye. For vancomycin, it fell from 9.1 to 6.1 days. At the same time, the predicted immediate IOP rise after injection was higher in small eyes versus in large eyes.[7]

Importantly, this geometry-driven effect is not limited to intravitreal pharmacology. Gas behavior and surgical fluidics such as silicone oil appear to follow the same logic. In a Brazilian case series of pseudophakic eyes undergoing pars plana vitrectomy with a fixed 0.7-mL pure C_3F_8 gas injection, axial length showed a strong inverse correlation with gas duration, and shorter eyes also exhibited greater acute postoperative IOP elevation.8 Similarly, a recent real-world study of silicone oil removal found that extraction time correlated with axial length and calculated vitreous volume.[9] These studies reinforce the idea that ocular geometry influences not only drug concentration but also tamponade dynamics, operative efficiency, and possibly safety margins during vitreoretinal surgery.

At the same time, novel retinal therapies such as gene therapies using a “biofactory” model may make anatomical personalization even more relevant. Researchers emphasize that interindividual variability, route-dependent biodistribution, and compartmental anatomy remain central to exposure, durability, and future model-informed personalization.[10] Likewise, the renewed interest in hydrogels and vitreous substitutes reflects a broader understanding that the vitreous cavity is a dynamic therapeutic compartment with meaningful biomechanical and pharmacokinetic properties.[11]

Even ocular oncology is beginning to reflect the same principle. In retinoblastoma, a recent high-throughput screening study identified

gemcitabine plus carboplatin as a promising synergistic combination and explicitly used vitreous-volume scaling when translating the intravitreal gemcitabine dose from mouse experiments to a human-equivalent estimate.[12] Thus, geometry-aware dosing is influencing areas that were previously driven mainly by empirical protocols and fixed regimens.

VITREOUS VOLUME CONSIDERATIONS

Taken together, these developments suggest we are now in a genuine conceptual shift. The earlier question was whether individualized vitreous volume mattered. The newer question may be where it does not. Across anti-infective therapy, corticosteroids, methotrexate, gas tamponades, silicone oil handling, sustained-delivery systems, gene therapy, and ocular oncology, the same message continues to reappear: One-size-fits-all intravitreal therapy is convenient, but the anatomy of the eye is not uniform.

Within 2 years of the original publication, researchers from different regions of the world and from diverse areas of vitreoretinal research have cited our original work and explored related questions. Although their scientific focus varies, their findings collectively support the need to move beyond uniform assumptions and toward a more individualized approach that acknowledges patient-specific ocular anatomy.

This growing body of evidence also highlights an important opportunity for future research. With the availability of the VIVEX formula, individualized vitreous volume estimation can now be performed rapidly and reproducibly in routine clinical settings. This may facilitate the design of well-defined studies with larger patient cohorts, ultimately providing the robust evidence needed to establish anatomy-based treatment strategies on a broader clinical scale.

VIEW REFERENCES

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