our DMEK patients and therefore did not have ASOCT data available for the study.

It has been mentioned by Dr. Singhal and Dr. Maharana that the theory of high subclinical postoperative inflammation in the F-DMEK group contributing to graft adherence might have produced an increased endothelial cell loss rate in F-DMEK. This indeed could be true, but, as mentioned before, our study was not designed to investigate etiologic factors.

Last, Dr. Singhal and Dr. Maharana commented that the fact that the visual outcome was found to be comparable in both groups should have been highlighted in the Conclusion as well. We would like to point out that although there were no statistically significant differences in visual acuity between the groups at any time point, this does not prove that visual acuity was similar between the groups, given the size of the cohort.

We reinforce the conclusion made by Dr. Singhal and Dr. Maharana and in previous publications, that F-DMEK is a safe and effective alternative to M-DMEK and that the lower graft detachment, rebubbling, and endothelial cell loss rates found in F-DMEK require further prospective controlled randomized research.

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Re: "Deep Anterior Lamellar Keratoplasty in Eyes With Intrastromal Corneal Ring Segments"

To the Editor:

Cannula insertion at a correct stromal depth[1] is key for the successful achievement of big-bubble formation using the big-bubble deep anterior lamellar keratoplasty technique. In a recent article, Ravera et al[2] described the advantage of using intracorneal ring segments (ICRSs), previously implanted, to gauge the depth of the cannula insertion into the stroma to accomplish big-bubble formation. In all 4 patients in whom this maneuver was attempted, big-bubble formation occurred. Using anterior segment optical coherence tomography, the cannula for air injection was introduced under the ICRS where the underlying stroma measured less than 150 μm. In a previous article,[3] we described the use of the big-bubble deep anterior lamellar keratoplasty technique in a series of patients with ICRSs previously implanted, where a 27-gauge needle was inserted into the stroma from the temporal quadrant using the gap between ICR segments. To perform this, the surgeon has to sit at the temporal side of the patient instead of assuming the more conventional position at the head of the table. Using the technique described by Ravera et al, it is not clear where the surgeon had to position himself to approach the targeted point for cannula insertion. In particular, we would like to know if the lower ICRS may be used, instead of the upper one, for reference, should the anterior segment optical coherence tomography measurements indicate that the lower ICRS is the more appropriate among the 2 implanted segments. In this case, we believe that the surgeon should assume an uncomfortable position to reach the targeted point.

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Reply:

We thank Dr. Fontana and coworkers for their interest in our work[1] and their valuable comments.

In all cases included in our series, the surgeon operated while sitting at the 12 o'clock position. The analysis of the location of the superior intracorneal ring segment (ICRS) obtained by means of anterior segment optical coherence tomography allowed us in all eyes to quantify the thickness of the stroma underlying the ICRS along its whole length. We could then select an appropriate location for cannula insertion below the ICRS and air injection at a level deep enough (±100 μm from the endothelial surface) to allow successful pneumatic dissection.

However, should the placement of the superior ICRS be too superficial or should only an inferior ICRS be present (single implant for low-degree ectasia or previous removal of the superior segment), a temporal surgical approach may be more comfortable at least for the initial steps of the procedure (including insertion of the cannula under the inferior ICRS), which could be then completed with the surgeon moving to the 12 o'clock position as soon as the bubble is obtained.

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What Causes Heterogeneity in the Pooled Effect of Omega-3 on Dry Eye Symptom Score? Countries or Measurements?

To the Editor:

We read the study by Giannaccare et al[1] (2019) with great interest. The study had no restriction on etiology, and synthesized 17 randomized clinical trials on omega-3 supplements for patients with dry eye. Although this largest systematic review involving 3363 patients with dry eye showed the effects of omega-3 supplements on dry eye and the impact of country on the effects of omega-3 for treating dry eye, there is a need for discussing the dry eye symptom score because of conceptual heterogeneity of measurements among trials. The systematic review seems to successfully reduce the statistical heterogeneity in the outcome of the dry eye symptom score through meta-regression using country, but the measurement in the trials from India differed from the measurement in trials from other countries. The trials in India measured dry eye symptoms by using the Dry Eye Scoring System (DESS), and the other trials used other common scales including the Ocular Surface Disease Index (OSDI). The systematic review would like to solve the problem about different scales through standardized mean differences. However, standardized mean difference is a way to solve the different units of measurement, and it cannot appropriately overcome the conceptual heterogeneity. To understand the conceptual heterogeneity between the scales, it is necessary to review the content of the scales.

Regarding the DESS, it was developed in India,[2] and the scale consists of 6 items covering itching or burning, sandy or gritty sensation, redness, blurring of vision, ocular fatigue, and excessive blinking. On the other hand, the OSDI is a 12-item scale evaluating not only ocular symptoms but also the functional limitations and the discomforts related to the environment.[3] The OSDI investigates more aspects than the DESS scale. Table 1 shows relevant information of the tools. They have similar subscales for symptom, but the OSDI has two more subscales for visual function and environmental trigger. The nature of the items for each of these instruments is quite different. In other words, they were not only different in units of measurement but also different in concept. Thus, it is not surprising to find high heterogeneity in the meta-analysis of the dry eye symptom score.

TABLE 1. Comparison of OSDI and DESS

Information	OSDI	DESS
Point range	0–4 points*	0–3 points†
No. items	12 items	6 items
Scoring	$\frac{\text{Sum of scores} \times 25}{\text{Of questions answered}}$	Sum of scores
Judgment	Mild: 13–22 points	Mild: 0–6 points
	Moderate: 23–32 points	Moderate: 6.1–12 points
	Severe: 33–100 points	Severe: 12.1–18 points
Symptom	Yes‡	Yes§
Visual function	Yes‖	No
Environmental trigger	Yes¶	No

*0: None of the time, 1: some of the time, 2: half of the time, 3: most of the time, 4: all of the time.
†0: absent, 1: sometimes, 2: frequent, 3: always.
‡Sensitive to light, feel gritty, pain or soreness, blurred vision, poor vision.
§Itching or burning, sandy or gritty, redness, blurring of vision, ocular fatigue, excessive blinking.
‖Reading, driving at night, working with a computer, watching TV.
¶Windy conditions, areas with low humidity, air conditioned area.

To our knowledge, country difference is a potential factor that may result in high heterogeneity because of different diet practices between India and other countries.[4] Nevertheless, based on the understanding of the conceptual heterogeneity in measurements among trials, the highly statistical heterogeneity in the dry eye symptom score cannot be easily explained by country difference because all the trials from India used the DESS for dry eye symptom. There is no way to separate the influences of country difference from the measurement difference. The co-contribution of country difference and measurement difference limits the explanation of heterogeneity. Therefore, we think that measurement difference may be another important source of heterogeneity, and we suggest that future studies should compare the 2 scales.

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