rebubbling may not be because of retained tags and islands only. Because this is a retrospective nonrandomized study, it is difficult to suggest that both the groups were similar regarding anterior segment anatomy and posterior corneal irregularity, which might have contributed to a higher rate of graft detachment in the M-DMEK group.

Besides, other factors such as surgeon's inexperience, inadequate air tamponade, retained viscoelastic (all cases were triple procedures in this series), and noncompliance to positioning must have been considered too. The authors should have added the anterior segment optical coherence tomography images to verify the hypothesis of the retained Descemet tags to be the sole cause of such a high detachment rate in M-DMEK as compared to F-DMEK. These images could also help to compare the number of retained tags in the 2 groups. Moreover, removal of the retained tags during rebubbling could have been documented using ASOCT. This would have contributed to the fact that retained DM tags are important and the sole cause of graft detachment in M-DMEK. The authors have attributed high subclinical postoperative inflammation to better graft adherence in DMEK. However, increased postoperative inflammation could also lead to greater endothelial cell loss in the F-DMEK group, which is not reflected in endothelial cell loss rate. Last, the visual outcome was found to be comparable in both the groups; this should have been highlighted in the Conclusion as well.

Considering all of the above points, we believe that F-DMEK is a safe and effective alternative of M-DMEK, but the conclusion that graft detachment rate, endothelial cell loss, and rebubbling rate are high in M-DMEK requires a well-controlled randomized study.

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Reply:

We thank Dr. Singhal and Dr. Maharana for their interest in our work and research topic.[1] We also appreciate the comments made in their letter regarding our study.

In the letter, Dr. Singhal and Dr. Maharana commented that there may be additional causes for the reduced rates of detachment and rebubbling found in the femtosecond laser-assisted Descemet membrane endothelial keratoplasty (F-DMEK) group when compared with the manual DMEK (M-DMEK) group. We agree with this. It should be noted that our study was designed to compare the outcomes of the 2 techniques and was not designed to address this question. Future studies including histologic and anatomic data could help our understanding of the etiologic factors responsible for these differences.

Comments were also made regarding the retrospective nature of this study, not allowing control for differences in anterior segment anatomy and posterior corneal irregularity. Retrospective studies are indeed inherently flawed, and in an effort to try and control retrospectively for differences in anterior segment anatomy, we have excluded all eyes that had any sort of complicated anterior segments (presence of a glaucoma drainage device, history of trabeculectomy, extensive peripheral anterior synechiae, previous vitrectomy, previous keratoplasty, and any corneal opacity), as mentioned in the manuscript's Methods section. We recognize the fact that the optimal methodology to control for such differences would naturally be to conduct a prospective study and have concluded the manuscript with a call for further prospective research on this topic.

Dr. Singhal and Dr. Maharana also astutely pointed out that other potential factors for graft detachment and rebubbling such as surgeon's inexperience, inadequate air tamponade, retained viscoelastic, and noncompliance to positioning must have been considered too. We completely agree and tried to take into consideration in our analysis as many of these factors as was possible. To adjust for differences emanating from surgeon inexperience, we performed chronological matching of the groups (as detailed in the manuscript) so that M-DMEK and F-DMEK surgeries were performed during the same time period, thus minimizing the effect of the surgeon's learning curve. In addition, all procedures were not among the first 150 DMEK cases performed by our cornea surgeon (D.S.R.) or supervised by him. Moreover, we performed a univariate analysis which showed no difference between the M-DMEK and F-DMEK groups in the rate of inexperienced surgeons performing surgeries (Table 1). Last, we performed a multivariable analysis for factors which may be associated with graft detachment and found surgeon experience not to be a significant associated factor. We performed a similar statistical analysis for the type of tamponading agent used, which also showed no significant differences or associations with graft detachment. Quantification of retained viscoelastic and compliance to positioning is indeed extremely important, but hard to achieve in a retrospective and prospective setting.

In their letter, Dr. Singhal and Dr. Maharana suggested performing anterior segment optical coherence tomography (ASOCT) to examine the hypothesis of retained descemet tags being a cause of high detachment rate in M-DMEK compared with F-DMEK. They suggested that these images could also help to compare the number of retained tags in the 2 groups. We think this is an excellent study idea and intend on incorporating this into prospective comparative studies on F-DMEK and M-DMEK. Because patients were required to pay out of pocket for ASOCT in Canada during the study period, we did not routinely perform ASOCT on

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.