## The More Likely Etiology Behind Suboptimal Results From Corneal Inlays

We read with great interest the article "Corneal Inlays for Presbyopia Explanted Due to Corneal Haze" by Ong et al. in the May 2018 issue.[1] We agree with the decision to explant the corneal inlay implantation (KAMRA; AcuFocus, Inc., Irvine, CA) secondary to postoperative stromal haze and hyperopic shifts. However, there is an important item that remains unclear concerning the implantation and possible cause of the suboptimal outcome. Specifically, we were curious in regard to the depth of inlay implantation. We assume it was implanted at a depth of 175 to 180 µm based on the thickness of the flap.

Although AcuFocus guidelines for implantation suggest an ideal depth of 200 to 250 µm,[2] recent studies have shown ideal placement of the KAMRA inlay to be 250 to 350 µm[3] while maintaining a residual stromal bed of 250 µm because it leads to less chance of an inflammatory response, hyperopic shift, and visual unpredictability. Keratocyte density has been shown to be greater in the anterior 10% of the stroma, increasing the risk of an inflammatory response and fibrosis the more anterior the implantation takes place.[4] Additionally, the use of the KAMRA inlay underneath the flap has become obsolete secondary to the reasons mentioned above. The manufacturer now endorses implantation only via pockets.[2] This has been shown to produce superior visual outcomes with fewer complications.

We believe the hyperopic shift, haze, and accompanying visual disturbances that were observed are most likely due to a shallower depth of implantation underneath a LASIK flap instead of using the recommended corneal pocket with a deeper depth of implantation. Thus, we would recommend this method of implantation hereafter. We commend the authors for their fine contribution concerning a potentially reversible complication of corneal inlay implantation.

### REFERENCES


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**Reply**

We thank Dr. Moshirfar and colleagues for their interest in our published article.[1] We acknowledge that the implantation of KAMRA inlays (AcuFocus, Inc., Irvine, CA) underneath corneal flaps is now no longer standard practice.[2] The current standard practice is indeed that KAMRA inlays are to be implanted using stromal pockets. Advantages of stromal pockets over flaps include stronger corneal biomechanics[3] and the fact that stromal pockets tend to be less neurotrophic; the latter is evidenced by a dose-dependent interaction between nerve regeneration and the density of activated keratocytes.[4]

However, all three patients described in our article were recruited as part of an initial U.S. Food and Drug Administration (FDA) clinical trial at a time when KAMRA inlays were first introduced into clinical practice in 2009. When the original multi-centered FDA clinical trials were conducted, KAMRA inlays were implanted underneath stromal flaps or in pockets created with target depths of 180 µm or greater.[5] Hence, there will be a significant number of individuals who would have had KAMRA inlays implanted underneath stromal flaps in the past and are still undergoing follow-up. As reported, our patients developed visual symptoms from corneal haze and hyperopic shifts 3 to 6 years following implantation; the time from initial implantation to inlay explantation ranged from 6 to 7 years. Our case series thus aimed to illustrate such late complications of KAMRA inlays. We propose that long-term monitoring of patients who had undergone KAMRA inlay implantation is recommended.

Currently, as per the manufacturer's recommendations,[2] our institution implants KAMRA inlays using intrastromal pockets created by femtosecond laser. We aim for depths of between 200 and 250 µm. We note that Moshirfar et al. reported preliminary data showing hyperopic shifts when KAMRA inlays are implanted at depths of 200 to 249 µm, but not when they are

implanted at depths of 250 µm or greater.[6] However, to maintain a safe residual stromal bed of 250 µm, the preoperative corneal thickness would need to be between 550 and 600 µm, to be able to place inlays at depths of 250 to 350 µm as advocated. Corneal thicknesses vary between different ethnicities, with Asians generally having thinner corneas.[7,8] Because our institution serves a predominantly Asian population, we do not regularly encounter patients with corneal thicknesses greater than 550 µm in most patients with emmetropia. Furthermore, KAMRA inlays are indicated for implantation into eyes with refractions close to emmetropia (plano to -0.75 diopters).[2] Patients seeking KAMRA inlays are often ametropic and require laser refractive surgeries prior to inlay implantation to achieve such near emmetropic refractions. Such procedures leave even thinner pre-implantation corneal thickness, making the prospect of allowing safe residual depths of 250 µm while placing inlays at depths of greater than 250 µm even less likely.

Finally, Moshirfar et al. quoted a study by Patel et al.[9] reporting greater keratocyte density in the anterior 10% of the stroma detected on in vivo confocal microscopy. In this study, keratocyte density was found to be highest adjacent to Bowman's membrane, then decreased significantly through the first 10% of the anterior stroma.[9] From then on, the reduction in keratocyte density was only marginal throughout the remaining depth of the stroma, with no significant differences in keratocyte densities between the mid and posterior stroma. Moshirfar et al. postulate that placing KAMRA inlays more anteriorly in the stroma increases the risk of an inflammatory response and fibrosis. However, for an average corneal thickness of 500 to 550 µm, the anterior 10% of the stroma refers to depths of between 50 and 55 µm. As discussed above, typical KAMRA inlays are placed in positions beyond these depths. Because there are no significant differences in keratocyte densities between mid and posterior stroma, Patel et al.'s findings do not explain the absence of hyperopic shifts when KAMRA inlays are implanted at depths of greater than 250 µm compared to when they are implanted at depths of 200 to 250 µm.[6] Moreover, there is currently insufficient evidence to ascertain whether stromal keratocyte density indeed correlates with late keratocyte activation or with differentiation of myofibroblasts, factors associated with corneal haze after inlay implantation. Further studies are needed to evaluate this.

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