Author’s response to reviews

Title: Refractive corneal Inlay for presbyopia in emmetropic patients in Asia: 6-month clinical outcomes

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Version: 1 Date: 10 Jan 2019

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To editor

1. Title page, please make clear who affiliated to which institute.

The authors’ institute was stated more clearly.

2. Abstract and Methods section, please make clear when patients admitted to hospital and received surgery.

Operation date was added at Abstract and Method section.

3. Why you would consider your study as "retrospective interventional"? Could you please kindly make clear if surgical procedure was adopted at the discretion of the surgeons or at the discretion of patients? If it was at the discretion of patients, then this is a purely retrospective
study, please remove "interventional". Otherwise, this should be considered as "interventional", and should be considered and reported as clinical trial.

We agreed with your suggestion and deleted “interventional” from study category,

To reviewer 1

1. Under inclusion criteria, please specify what level of cylinder preoperatively was allowed to be included in this study?

Inclusion criteria of cylinder power was added at Method section.

2. Concerning the Pocket energy setting using the Femto LDV40, please provide the spot and line separation, energy and incision angle of entry.

Detailed parameters of the femtosecond laser included energy setting, spot/line separation, and incision angle were added as Table 1.

3. What level of discrepancy was allowed in terms of the distance between the purkinjie reflex and the center of the pupil? Do we have any inclusion/ exclusion criteria? What is upper limit of angle kappa?

We spotted at the first Purkinjie reflex and inserted the inlay then tried to align the central hole and visual axis in the operation. The discrepancy might be the problem but we haven’t experienced those kinds of issues. As far as there is no company’s instruction about this, surgeon’s effort to align the inlay’s center and visual axis is the only way to solve this problem.

4. One may argue that six-month is not enough time for impact of inlay on wound healing in terms of potential gradual hyperopic shift or gradual haze formation.

In previous study, there was report that haziness resolved early after operation but we found that it lasted somewhat longer than that so we thought this might be the racial difference and also might be the reason for lower visual acuity and lower satisfaction. That is the reason why the information was stated but we totally agreed to your opinion that it is too early to call about structural safety. Statement that observation for 6 months is insufficient was added in
manuscript. Also, we added our experience (not with data, just personal experience) about longer follow-up with no safety issue.

5. One may argue that epithelial thickness evaluation would have been useful?

13. Please state that lack epithelial map versus stromal map analysis over time is another disadvantage of their analysis.

Epithelial/stromal thickness analysis could be useful in this study for lower visual acuity. Unfortunately, we don’t have those data so the analysis is impossible for now. Lack of the analysis was added in manuscript as disadvantage.

6. 29% loss of two lines of CDVA is above the safety threshold for some health agency such as FDA.

14. Please state that until longer study there should be skepticism concerning the efficacy of inlay technology. Based on recent Raindrop discontinuation in USA and hyperopic shift and loss of efficacy after KAMRA after 36 months for many cases, I suggest author to simply reflect such thoughts indirectly in their manuscript.

We also concerned about relatively high percentage of loss of 2 line in operated eye. Upon recent corneal inlay problems, safety issue must be stated very carefully. We added concern about recent inlay problems and deleted word “safe” from conclusion.

7. What were the reason or cause for loss of two lines of CDVA?

Various analysis about patient who lost 2 lines in CDVA was done but nothing came out. The reasons of loss of visual acuity is assumed as decreased contrast sensitivity and induced aberration as stated in manuscript.

8. What percentage of eyes lost one line or more of CDVA?

12 patients (60%) lost 1 line or more CDVA, added to manuscript result section.

9. How do you explain only 0.75 diopter of myopic change when the average power of the inlay was 1.77D? Authors fail to provide a potential explanation?
We assumed the reason of discrepancy between myopic change and inlay power as inaccuracy of measuring manifest refraction. There is moderate scissoring phenomenon after inlay implantation. But since all previous study shows same discrepancy with same tendency, and the discrepancy gradually increased over time. In one study, even postoperative SE is not difference from preoperative SE at 3 years. We thought this was complicated problem.

10. Line 45-47, page 14, what then is the potential explanation beyond its presbyopic correction action.

The mechanism is assumed as the combination of refractive power effect and increased depth of focus by induced aberration. It was stated in manuscript before, but the sentence was ambiguous so we added clear statement.

11. I suggest authors avoid stating that this is safe and effective technology and simply state that although the results are somewhat satisfactory longer study and larger sample size is required.

12. As stated by the authors, their sample size is too small and the study was too short to draw any definite conclusion concerning the safety and efficacy of Flexivue Microlens.

We totally agree that sample size is too small and follow-up is too short to make the definite conclusion about safety and efficacy. Conclusion was modified to emphasize that this study showed 6 months follow-up results.

15. I congratulate the authors for their fine work.

We really appreciate for your comments.

To reviewer 2

Surgical techniques : The authors should mention detailed configuration of the pocket and the parameters of the laser (femto LDV Z4) used to create pocket and tunnel because the difference in configurations of pocket may affect the outcome of the surgery.

Detailed configuration of the femtosecond laser was added as Table 1.
Material and methods: The parameters of Flexivue microlens should be mentioned in the paper such as diameter of the inlay, diameter of the central hole and thickness at different parts of the inlay.

The detailed information of the inlay added to manuscript method section.

Results

The sample sizes of 21 eyes is sufficient. Ophthalmic examination and complete range of tests and corneal scans were done to check the compatibility, tissue responses and visual acuity and aberrations.

Discussion: The paper stated that there is no significant changes in central corneal thickness. Since Flexivue microlens has central hole, the CCT (central cornea thickness) is not expected to change significantly but how about peripheral corneal thickness? The quantitative assessment of peripheral corneal thickness will help detect changes in corneal structure.

As you mentioned it, regarding the inlay structure, peripheral corneal thickness can be more reasonable value to evaluate structural change after the inlay implantation. However, since inlay diameter is only 3.6mm and flat central part is 1.6mm, changes from thicker peripheral part will also affect central corneal thickness too, especially if the change of thickness comes from inflammation which is important for safety issue. The statement for the importance of peripheral thickness for this inlay implantation and our excuses for using central thickness was added at Discussion section.

We really appreciate for your comments.