Author's response to reviews

Title: Customized pachymetric guided epithelial debridement for corneal collagen cross linking

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Author's response to reviews: see over
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Ms No. 2061028657220805 BMC Ophthalmology,
“Customized pachymetric guided epithelial debridement for corneal collagen cross linking”

Heraklion, 11th December 2008

Dear Rikki Graham,

All the authors that participated in this work would like to take this opportunity to thank you for sending the manuscript for an external peer-review and the referees for reading and commenting on the manuscript. We found the comments from the reviewers very helpful. We have responded carefully to each point in turn and modified the m/s accordingly.

We include a short response to reviewer’s main comments, which clarifies some issues. Our responses (A) to each comment (Q) can be summarized as follows:

Reviewer #1
Q: Since 2 years, the currently existing protocol has been modified for the treatment of thin corneas by using hypoosmolar riboflavin solution (Hafezi et al, JCRS, in press). The use of riboflavin solution enables the surgeon to treat corneas down to a thickness of only 320 microns without the epithelium which is thinner than the method described here would allow.

A: The authors are aware of the hypo-osmolar riboflavin which enables surgeons to perform corneal cross linking treatments (CXL) in thin corneas. The technique proposed by our manuscript is based on a different principle and examines the intra-operative preservation of an anatomical structure (epithelium) on post CXL outcomes with concern on potential corneal toxicity. We believe that even though the existing used protocol for thin corneas (hypo-osmolar riboflavin) overcomes the corneal pachymetric limitations for CXL treatments; our proposed technique can be also used as an alternative solution for patients with localized thin cornea.

Q: Furthermore, there simply is no cross-linking effect in a non-deepithelialized area. This has clearly been demonstrated by Mazotta et al (Mazotta et al, JCRS, in press) and has been shown at the 3rd CXL congress in Switzerland in 2007. The adjacent cornea is cross-linked but the steepest area is not. The swelling approach where the entire cornea is treated is clearly preferable.

A: The technique which preserves the entire epithelial layer intact when performing CXL treatment has demonstrated no CXL effects; in our study we only preserved a small area of epithelium (approximately 1x1 mm) at cone apex area (thinnest corneal area). This enabled riboflavin to penetrate the corneal stroma in a sufficient manner (area under intact epithelium was soaked with riboflavin), thus CXL treatment was not influenced by this customized epithelial preservation.

Q: The authors state that the currently used cross-linking protocol involves the use of BSS drops during the irradiation and that this might lead to corneal swelling during the time of irradiation. This is prevented using the customized approach described here. This statement is false: the currently widely accepted protocol uses riboflavin not only for the saturation of the cornea before the irradiation but also during the irradiation. Since
the osmolarity of the riboflavin solution used and the corneal stroma are almost identical, no swelling is observed during the illumination. This has been demonstrated already five years ago.

A: The use of BSS during treatment prevented corneal dehydration during the 30 minutes treatment but it did not significantly swell the cornea since has the same osmolarity as the corneal stroma.

Q: Minor orthographical errors: Introduction: corneal ec(s)tatic diseases.

A: All the pointed out errors in English usage, spelling and grammar have been corrected. Proof reading and corrections were made by a native speaker throughout the manuscript.

Reviewer #2
Q: The prevention of endothelial cell damage in the thinnest area may be the result of two effects. First, the remaining epithelium has a protective effect. Second, the application of riboflavin and balanced salt solution acts like hypoosmolar solution and cause a swelling of the cornea. Unfortunately, the thickness was not measured during CXL and the two different effects cannot be separated. These two possibilities should be discussed.

A: Pachymetric evaluation of the corneas was conducted several times during CXL procedure, the use of BSS prevented excessive corneal dehydration. Since the corneas were denuded and the corneal stroma was exposed to the environment for a long period of time (over 30 minutes), dehydration and decrease in corneal pachymetry is expected. The use of BSS during treatment prevented corneal dehydration but it did not significantly swell the cornea. We believe that in this study the preservation of the epithelium at the area of the conus (thinnest area) was the factor that prevented the toxic effects due to CXL treatment. The current protocol which uses hypoosmolar riboflavin may offer the same effect in respect with preventing dehydration.
Q: Page 4, line 17: The company which produce the UVX-system version 1000 should be included.
A: The name of the company was included as suggested.

Q: What was the diameter of the irradiated area at the cornea?
A: The diameter of the irradiated corneal area was 8mm, this was included in the manuscript, surgical technique section, page 4, paragraph 2, line 13.

Q: Was the irradiation homogenous?
A: The irradiation was homogenous; the UVA lamp was placed above the cornea according to the manufactures protocol in order to achieve homogenous irradiation.

We hope that you will find our answers and m/s modifications sufficient, and you will conceder our study for publication.

Sincerely,

Vasilios F. Diakonis M.D.