Author's response to reviews

Title: Two cases of biodegradable collagen matrix (ologenTM) implant and conjunctival autograft for scleral necrosis after pterygium excision

Authors:

Chan-Ho Cho (blitz527@naver.com)
Sang-Bumm Lee (sbummlee@ynu.ac.kr)
Eun-Young Cho (eyecho55@naver.com)

Version: 3 Date: 4 August 2015

Author's response to reviews: see over
Reviewer’s comments
For the article ‘Two cases of biodegradable collagen matrix (ologenTM) implant and conjunctival autograft for scleral necrosis after pterygium excision'

This research is about novel use of combined ologen collagen matrix and conjunctival autograft for management of extreme scleral ectasia following the use of mitomycin C for preventing recurrence in two cases of primary pterygium. Clinical course is evaluated for long term outcomes of the procedure following OCM and CAU grafting.

MMC induced scleral defects can be covered with autologous scleral grafts or by partial thickness scleral flap rotational procedures where in graft vs. host disease can be prevented. Authors should make it clear the disadvantages of using autologous scleral tissue use in these cases.

Answer: For example, preserved homologous sclera is a flexible avascular tissue that causes minimal immunologic reaction, infectious disease transmission.

Abstract-following points should be included to improve complete understanding of research theme

1. MMC concentration and applications duration-mention
   Answer: Two cases of marked scleral thinning after pterygium excision with 0.02% topical MMC for 2 weeks were included in this study.

2. Weather OCM was trimmed or scleral ectatic margin is trimmed by biopsy punch-mention
   Answer: To determine the boundary of conjunctivectomy, the size of scleral defect was measured and its margin was marked with a 3-mm diameter biopsy punch. The margin of the scleral thinning area was trimmed by Vannas scissors and the OCM was cut by using a circular-shaped biopsy punch of the same size (3-mm diatener) of scleral thinning area.

3. What suture material used and how many stitches used to anchor the grafts
   Answer: The OCM was sutured with a recipient scleral wall using 6 stitches of 10-0 nylon interrupted sutures. The CAU was carefully positioned over the previously sutured OCM bed and was anchored to the scleral wall and the healthy conjunctival margin through the OCM bed with 11 stitches of interrupted sutures of 10-0 nylon.

4. From where conjunctival autograft is prepared
   Answer: A 4-mm diameter, circular-shape free CAU was harvested from the superonasal bulbar conjunctiva with a biopsy punch 1 mm larger in diameter than that of the piece of OCM.

5. Weather interrupted sutures used for both OCM and CAU
   Answer: The OCM was sutured with a recipient scleral wall using 6 stitches of 10-0 nylon interrupted sutures. The CAU was carefully positioned over the previously sutured OCM bed and was anchored to the scleral wall and the healthy conjunctival margin through the OCM bed with 11 stitches of interrupted sutures of 10-0 nylon.

6. How the graft integrity was assessed during follow up-mention in detail
   Answer: Long-term follow-ups over two-year were performed on both patients by assessing graft thickness and surface vascularization using a slit-lamp biomicroscope. The entire graft site remained intact and provided a good healthy ocular surface with fluorescein stain negative intact epithelium and good vascularization of grafted conjunctiva.

7. Loss of ocular pain, loss of inflammation-correction needed
   Answer: All patients experienced loss of ocular discomfort and inflammation with rapidly
stabilized ocular surface.

8. Provide physical signs for good healthy ocular surface after grafting
   Answer: The entire graft site remained intact and provided a good healthy ocular surface with fluorescein stain negative intact epithelium and good vascularization of grafted conjunctiva. Recurrence of epithelial defects and scleral thinning were not observed in either patient for over the two-year follow-up period.

9. Weather follow up done for one year or two –clarity required
   Answer: Long-term follow-ups over two-year were performed on both patients by assessing graft thickness and surface vascularization using a slit-lamp biomicroscope.

Conclusion
1. What were the pre operative signs pointing towards MMC induced scleral melt-provide in Detail
   Answer: On slit-lamp examination, underlying sclera at the site of prior pterygium excision was necrotic and avascular, and showed marked thinning in the nasal portion of the left eye (Figure 1-A). The scleral bed appeared conjunctivalization over exposed ciliary body with no evidence of scleral perforation sign by Seidel test. On slit-lamp examination, focal epithelial defect at the site of prior pterygium excision and approximately 3 mm size scleral excavation with impending uveal exposure were observed (Figure 3-A).

2. What were the clinical healing markers for maintaining ocular surface to recommend for its clinical use-required
   Answer: Healthy ocular surface (no epithelial defect, normal vascularity of conjunctiva)
   Maintaining normal scleral thickness
   No sign of infection, necrotic tissue, and conjunctival defect

Long-term follow-ups over two-year were performed on both patients by assessing graft thickness and surface vascularization using a slit-lamp biomicroscope. The entire graft site remained intact and provided a good healthy ocular surface with fluorescein stain negative intact epithelium and good vascularization of grafted conjunctiva.

Keywords: Mitomycin C should be used as a keyword in this section
   Answer: Added in the revised manuscript.

Background-third paragraph
1. OCM application implant does not require donor tissue-what is the meaning
   Answer: Application of the OCM implant does not require donor preserved scleral tissue, the OCM is able to fill the space between the CAU and scleral bed easily, and it helps the ocular surface stay flat and regular.

2. Long term follow up- one year or two years-clarification needed
   Answer: Long-term follow-ups over two-year were performed on both patients by assessing graft thickness and surface vascularization using a slit-lamp biomicroscope.

Case 1
1. Was the patient normal 6 years previously without eye pain-clarify
   Answer: Few years after surgery, symptoms of intermittent ocular discomfort and mild ocular pain were developed, and then she had treated at local medical center.

2. Second Para-Fig 1 A shows conjunctivalization over exposed ciliary body or choroid-mostly it is ciliary body-clarify
   Answer: The scleral bed appeared conjunctivalization over exposed ciliary body with no evidence of scleral perforation sign by Seidel test.
a) Advantages of diamond burr over other traditional trephines-mention
   Answer: Using a diamond burr instead of knife can provide gentle polishing to obtain a flat and regular surface without damaging already much thinned scleral bed.

b) Was there hemorrhage during debridement if so how haemostasis is attained
   Answer: Conjunctival hemorrhage during debridement was controlled by ocular bovie and cotton swab compression.

c) Signs of healthy sclera bed-mention
   Answer: All necrotic scleral tissue was dissected away until a clean smooth and even scleral surface was obtained.

d) What were the dimensions of thinned out scleral bed and OCM implant
   Answer: To determine the boundary of conjunctivectomy, the size of scleral defect was measured and its margin was marked with a 3-mm diameter biopsy punch. The margin of the scleral thinning area was trimmed by Vannas scissors and the OCM was cut by using a circular-shaped biopsy punch of the same size (3-mm diatemer) of scleral thinning area.

e) From where the conjunctiva is harvested-measurements size and shape
   Answer: A 4-mm diameter, circular-shape free CAU was harvested from the superonasal bulbar conjunctiva with a biopsy punch 1mm larger in diameter than that of the piece of OCM.

f) What is donor OCM-earlier mentioned donor tissue is not required-clarify
   Answer: Application of the OCM implant does not require donor preserved scleral tissue, the OCM is able to fill the space between the CAU and scleral bed easily, and it helps the ocular surface stay flat and regular.

g) How many interrupted sutures- looks like 12 in the picture
   Answer: The OCM was sutured with a recipient scleral wall using 6 stitches of 10-0 nylon interrupted sutures. The CAU was carefully positioned over the previously sutured OCM bed and was anchored to the scleral wall and the healthy conjunctival margin through the OCM bed with 11 stitches of interrupted sutures of 10-0 nylon.

h) Advantage of larger conjunctival graft?
   Answer: A conjunctival graft that is larger than the scleral defect can achieve a stable, tension-free graft to avoid a wound dehiscence.

i) Figure 2D-OCM appears white after suturing to the sclera walls there is change in color-is it blood accumulation in the sclera bed
   Answer: The color of the OCM changed from white to red due to blood accumulation.

j) Where was CAU anchored-to OCM or scleral walls
   Answer: The CAU was carefully positioned over the previously sutured OCM bed and was anchored to the scleral wall and the healthy conjunctival margin through the OCM bed with 11 stitches of interrupted sutures of 10-0 nylon.

k) Post operatively what antibiotic and steroid used
   Answer: After surgery, the patient was given a patch dressing with a topical antibiotic ointment (Erythromycin, Ecolicin®, Taejoon Pharm., Seoul, Korea) and a steroid ointment (Dexamethasone, Maxitrol®, Alcon Laboratories Inc., Fort Worth, TX, USA) to be taken 4 times per day. After 5 days postoperative, the ointment patch dressing was replaced by topical antibiotics (0.5% levofloxacin, Cravit®, Taejoon Pharm, Seoul, Korea) and steroid (0.1%).
fluorometholone, Flarex®, Alcon Laboratories Inc., Fort Worth, TX, USA) eye drops to be taken 4 times a day.

l) Fluromethalone eye drops used after one month after removing sutures?
Answer: After 5 days postoperative, the ointment patch dressing was replaced by topical antibiotics and steroid.

m) Steroid ointment used for 5 days and between 5 days and one month was steroid therapy was not given-give reasons
Answer: After surgery, the patient was given a patch dressing with a topical antibiotic ointment (Erythromycin, Ecolicin®, Taejoon Pharm., Seoul, Korea) and a steroid ointment (Dexamethasone, Maxitrol®, Alcon Laboratories Inc., Fort Worth, TX, USA) to be taken 4 times per day. After 5 days postoperative, the ointment patch dressing was replaced by topical antibiotics (0.5% levofloxacin, Cravit®, Taejoon Pharm, Seoul, Korea) and steroid (0.1% fluorometholone, Flarex®, Alcon Laboratories Inc., Fort Worth, TX, USA) eye drops to be taken 4 times a day.

n) Step by step suture removal-clarify and give reasons
Answer: The conjunctival sutures were removed at intervals of 1 week to 1 month over the postoperative course.

o) Figure depiction is confusing-separate into preoperative figure, then procedural pictures and lastly pictures during follow up
Answer: Legends are corrected properly.

Case 2

1. Figures and legends proper arrangement-needed
Answer: Preoperative and postoperative slit-lamp photographs of Case 2, the left eye. A. Preoperative photography showing irregular scleral thinning and excavation with impending uveal exposure. B. First week after surgery. C. One month after surgery. D. Two years after surgery.

Conclusion

1. What is the advantage of CAU graft placed over the OCM implant-explain
Answer: Furthermore, we placed a conjunctival autograft over the OCM implant to avoid inflammation of the ocular surface and discomfort of the patient for the duration of the conjunctival epithelial margin in order to have complete epithelialization of the bare OCM surface. We expected the meticulous conjunctival autograft overlying the OCM implant to promote prompt epithelialization, vascularization, and wound remodeling of the conjunctival tissue.

2. Recommendations regarding RCT

Authors efficiently used OCM with CAU to maintained scleral integrity. OCM is mainly used in glaucoma filtering surgeries to have porous and spongy healing process through which aqueous could percolate. Tunica sclerosa is a tough walled structure-weather OCM provides sufficient integrity for sclera is questionable; nevertheless patients were free of irritative symptoms.

Answer: The authors believe that the OCM material cannot provide sufficient integrity such as a tough-walled tunica sclerosa if there is when large scleral thinning with an underlying uveal protruding ectatic surface change. However, in the case of a small scleral excavation without any underlying uveal ectatic change, the porous and spongy physical properties of OCM are able to provide enough space filler effect for the duration of the healing process of the wound with connective tissue replacement.

Lastly please mention limitations and strength of this research paper
Answer: 
Limitation:

- First, the quantitative measurement of postoperative scleral thickness and the integrity of the graft site using AS-OCT will be needed in further cases.
- Second, a larger number of enrolled participants will be required to assess the universality of the clinical usefulness of the OCM implant substitute for preserved sclera in scleral necrosis repair surgery.

Strength:

- This study provides a new surgical technique with the application of new materials to scleral necrosis surgery.
- The two-year follow-up period was sufficient to evaluate the outcome of the surgery.
- OCM is commercially available sterile material, which surgeons can use to provide prompt surface reconstruction.

Include patient perspective regarding OCM implant graft to complete this paper.

Answer: OCM is currently used mainly in filtration surgery of glaucoma. There will be various applications of OCM implants to ocular surface reconstruction such as scleral thinning, recurrent pterygium, and traumatic tissue defects.