

Peer Review File

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First Round of Peer Review

Reviewer A

Overview: Congenital ectopia lentis (CEL) can cause vision loss in young patients unless addressed with complex and delicate surgery. Because CEL overwhelmingly needs to be addressed surgically in young patients (<18 yo), these surgeries must be comfortable to avoid eye rubbing which can be a major issue in younger patients) and extremely durable to last for the life of the patient. Achieving these dual goals has proven a major challenge for the relatively small group of highly specialized and skilled physicians who perform these surgeries. I commend these authors for testing different sutures and knot configurations ex vivo prior to attempting in patients. This is a clearly written paper with a few issues that are listed below.

Comment 1: What is the position of this suture within the actual surgery? An illustration would be helpful – potentially as another panel in Figure 1

Reply 1: Thank you for your suggestion.

In the actual operation, the entry point of the suture is located 2.0mm behind the limbus, and the suture shuttles between the scleral layers, with a depth of about 1/2 of sclera thickness. In order to avoid the extraocular muscle, the sutures are often chosen on the meridians of 4 o'clock and 10 o'clock.

We have provided the schematic diagram as part of Figure 1 according to your suggestion.

Changes in the text: Figure 1 (Page 7, line 2-3)

Comment 2: The traction force for suture loosening? How did you determine when the suture loosened?

Reply 2: We thank the comments from the reviewer.

The minimum traction force required when the suture is loose or ruptured was determined based on the sudden drop in the force-displacement curve as a previous study reported. [Reference : Khorjestan SM et al. An investigation of the effects of suture patterns on the mechanical strength of intestinal anastomosis: an experimental study. *Biomedizinische Technik Biomedical Engineering* 2017;62:429-37.]

Changes in the text: “Methods” section (Page 7, line 15-17)

Comment 3: Page 9 line 3 – “rapture” should be rupture

• Page 9 line 20 – please

Reply 3: Thank you for the comment. We have revised accordingly.

Changes in the text: Page 9, line 4 and Page 9, line 21

Reviewer B

Comment 1: The experiments were all performed on pigs' eyes which, although share many similarities with human eyes, they behave in a different way compared with alive eyes. Authors have included this as a limitation but they need to discuss in more detail.

Reply 1: Thank you for the suggestions from the reviewer.

We agree with the reviewer that there are many differences between pig eyes and human eyes. For example, scleras from pigs' eyes are thicker, have a lower permeability coefficient, and lower light transmission than that in humans. However, the human and porcine sclera has similar water content, histology, and collagen bundle organization. Therefore, the porcine sclera is a relatively ideal material for such an experiment as previous studies reported. [References:1. Nicoli S, et al. Porcine sclera as a model of human sclera for in vitro transport experiments: histology, SEM, and comparative permeability. *Molecular Vision* 2009;15:259-66. 2. Olsen TW, Sanderson S, Feng X, et al. Porcine sclera: thickness and surface area. *Investigative Ophthalmology & Visual Science* 2002;43:2529-32. 3. Vogel A, Dlugos C, Nuffer R, et al. Optical properties of human sclera, and their consequences for transscleral laser applications. *Lasers In Surgery and Medicine* 1991;11:331-40.]

Changes in the text: "Discussion" section. (Page 12, line 18 to Page 13, line 1)

Comment 2: Introduction. Authors state "However, considering the continued growth of the eyeball in children and rougher and more sudden movements of children, this technique may not be suitable for children. Transscleral suture fixation of IOL, as a classic surgical technology, may still be a preferable option in children with ectopia lentis." Citations are missing. I would strongly recommend that authors read a recent review article published a few months ago by Karasavvidou and colleagues on the "Surgical Management of Paediatric Aphakia in the Absence of Sufficient Capsular Support" (PMID 34904056)

Reply 2: Thank you for your suggestion.

We have revised the “Introduction” section accordingly and added the above reference, and now it reads:

Surgery is currently effective treatment for CEL. However, there is still no consensus on the best surgical method for these patients and the operation still needs to be further improved.

Changes in the text : Page 5, line 6-7.

Comment 3: The techniques described are a bit confusing. I would recommend that authors include videos as supplement material.

Reply 3 : Thank you for the suggestion.

We have added panel A and B in figure 1 in order to clearly illustrate our surgical methods.

Changes in the text : Page 7, line 2-17. *Figure 1*

Comment 4: The statistical analysis is flawed. How many observations were included in each group? Is the assumption of independence of observations violated? Why did the authors use parametric tests? Did they assess data distribution. Professional statistical advice is strongly recommended.

Reply 4 : After consulting our statistician, the experiments were re-conducted and the observation count was increased to 5 times per group. We have revised the contents in “Methods” section accordingly.

Changes in the text: Page 7, line 21. Page 8, line 4 and Page 8, line 11. Table 1

Second Round of Peer Review

Reviewer A:

Authors have sufficiently revised their manuscript; however, I am not convinced that the statistical analysis is properly done.

Comment 1: The number of observations per group is still small ($n=5$). Authors need to assess data distribution before applying any statistical tests, and since the number of observations is so small the traditional normality tests (Shapiro - Wilk, Kolmogorov - Smirnov etc) are not powerful enough to reject the null hypothesis. I would strongly recommend that they use plots (i.e. Q-Q plots) to assess data distribution and then parametric or non-parametric tests should be applied accordingly.

Comment 2: Another issue is that the assumption of independence of observations seems to be violated and therefore no traditional statistics can be applied. It is not clear if the authors included both eyes of the same subject and whether the observations included are values from different experiments in the same eye(s).

I would strongly recommend that authors seek professional statistical advice.