

## Reattachment of Recessed Superior Rectus Muscle Using Fibrin Glue Versus Vicryl: An Experimental Study in Rabbits

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### ABSTRACT

**Background:** During the reinsertion of extraocular muscle to the sclera, the risk of scleral perforation is possible. Endophthalmitis may also result in sequelae of scleral perforation. Reattachment of extraocular muscles using fibrin glue is an alternative option in muscle recession surgeries.

**Aim of the study:** to evaluate the efficacy of fibrin glue as an adhesive agent and to compare it with muscle suturing.

**Materials and methods:** In this prospective comparative experimental study, fifty-six eyes of twenty-eight rabbits of the same species (white New Zealand) weighing approximately 2.240 to three kg. All the superior rectus muscles (SRM) were disinserted and recessed 5 mm from the insertion and then reattached to the sclera either by fibrin glue (group 1) or sutures 6/0 vicryl (group 2).

**Results:** After two weeks, of surgical exploration of SRM in the glued group (28 eyes); 23 eyes (82.14%) the SRM was found in the same location of insertion (5mm recession). While the SRM in the remaining five eyes (17.86%) was slipped with posterior displacement of the muscle. on the other hand, surgical exploration of SRM in the control group was found in the same location of insertion. The correlation between inflammation and slippage was significant.

**Conclusion:** we concluded that fibrin glue was effective as an alternative to sutures to re-attach rectus muscles during recessions (even in small muscle recession) in strabismus surgery, however postoperative slippage of the muscles and inflammation are considerable complications.

**Keywords:** suture-less squint surgery; fibrin glue; muscle recession; muscle reattachment; vicryl

### INTRODUCTION

Scleral perforation may happen during the reinsertion of a muscle into the sclera. Incidence of scleral perforation is highly variable ranging from 0.3% to 7.8 % <sup>(1)</sup>. Such risk of scleral perforation during the recession would be much greater if the sclera is thinner <sup>(2)</sup>. Endophthalmitis may also result in sequelae of scleral perforation. Reattachment of extraocular muscles using fibrin glue is an alternative option in muscle recession surgeries.

Fibrin glue is a blood product that is easy to apply <sup>(3)</sup>. Fibrin glue was used instead of sutures in squint surgery during the closure of conjunctiva incisions <sup>(4)</sup>.

**Graham et al.** <sup>(5)</sup> reported that usage of fibrin glue (autologous= prepared from patient's blood) has proven to be an effective way compared to suturing in case of leaking from fornix-based conjunctiva incisions after subscleral trabeculectomy <sup>(5)</sup>. Fibrin glue was proven to be useful in the reinsertion of muscle recessions, but it was found that it was more effective in large-angle recessions than in small-angle recessions <sup>(6)</sup>.

In this study, we aimed to re-evaluate the reattachment of extraocular muscles in small muscle recession using fibrin glue in strabismus surgery, to detect its stability against contractile muscle strength and investigate whether it could replace the classic stitches, hence avoiding perforation of the globe and its complications.

### MATERIALS AND METHODS

This is a prospective comparative experimental study in rabbits that was reported following ARRIVE

guidelines (Animal Research: Reporting of In Vivo Experiments). All rabbits were middle-aged, white New Zealand, weighing approximately 2.250- 3.0 kg. The animal husbandry was in the experimental animal facility of the Research Institute of Ophthalmology, Giza, Egypt. The experiment was approved by the Memorial Institute of Ophthalmic Research Ethics Committee. All procedures followed the Institutional Guidelines and the Statement for the Use of Animals in Ophthalmology and Vision Research and observed the essential ARRIVE guidelines for animal research. Healthy litter cage animals were included and divided into single-cage animals which were provided with food, water, and veterinary supervision. Randomization and blinding were initially applied to minimize the confounder bias.

The experimental study was conducted on Fifty-six eyes of twenty-eight rabbits. They were divided into 2 groups: Group 1 (glued group): the recessed superior rectus muscle of the right eye of 28 rabbits is reattached using fibrin glue (consisting of twenty-eight eyes of twenty-eight rabbits). Group 2 (control group): the recessed superior rectus muscle of the left eye of 28 rabbits is reattached using 6/0 vicryl (consisting of 28 eyes of 28 rabbits); the sample size was decided based on the outcome measures.

### Procedure:

The animals were anesthetized with intramuscular ketamine (30mg/kg) and Xyla-Ject 20 mg/mL (xylazine hydrochloride). Xyla-Ject 20 mg/ml is a sedative and analgesic. It is administered /subcutaneously 1mL/ 20

lbs. body weight (1 mg/lb.). The dose was increased when needed. Respiratory rate and heart rate were monitored. Topical anesthesia 0.4% benoxinate hydrochloride was administered. Exposure of the superior temporal conjunctiva, and conjunctival incision. The superior rectus muscle was exposed and dissected from the surroundings. Two absorbable sutures were passed through the outer quarters of the tendon (partial-thickness and full-thickness). The muscle was then disinserted from the sclera. The value of recession (5mm) is measured and marked on the sclera with the caliper. The muscle was reattached to the sclera either via fibrin glue (in group 1- glued group-), or 6/0 vicryl suture (in group 2, the control group). Moreover, antibiotic eye drops (broad-spectrum) were instructed to the veterinary care personnel to be instilled three times per day for one week.

#### **Fibrin glue:**

Fibrin sealant is made from pooled human plasma. Fibrin glue is mainly composed of two components; fibrinogen and thrombin that are mixed using a two-syringe device. Thrombin splits the fibrinogen into fibrin monomers that polymerize to form an unstable fibrin clot. Factor XIII which is also present in the fibrinogen solution cross-links the clot to form a stable clot. The fibrinogen solution contains a fibrinolytic inhibitor to prevent early lysis of the clot by the fibrinolytic system. A high thrombin concentration of 500 IU/ml is used to achieve fast clotting.

The pre-filled syringe contains sealer protein solution: Total protein: 96 – 125 mg/mL; Aprotinin (Synthetic): 2250 – 3750 KIU/mL; Fibrinogen: 67 – 106 mg/mL. Thrombin Solution: Calcium Chloride: 36 – 44 µmol/mL, Thrombin (Human): 400 – 625 units/mL. The pre-filled syringe was placed into a water bath ensuring the pouches remain submerged. It is removed from the water bath after thawing and warming, and the syringe was maintained at 33-37°C until use.

Upon mixing Sealer Protein and Thrombin, soluble fibrinogen is transformed into fibrin, forming a rubber-like mass that adheres to the wound surface and achieves gluing of tissues. The glue was applied to the sclera after proper drying and around the muscle-cut edge. The application was sustained for 3 minutes to achieve sufficient polymerization- hardening of the glue-; the conjunctiva is replaced. Two weeks after surgery, the rabbits were anesthetized as described above. The superior rectus muscle in each eye was

exposed and hooked. The distance between the hooked muscle and the original muscle stump was measured using a caliper and then recorded. The primary goal was to detect slippage of EOM in small muscle recession.

#### **Ethics approval**

**The experiment was approved by the Memorial institute of ophthalmic research Ethics Committee. All procedures followed the Institutional Guidelines and the Statement for the Use of Animals in Ophthalmology and Vision. All experiments adhered to the Responsible Care and Use of Laboratory Animals (RCULA) guidelines.**

#### **Statistical methods**

Categorical data were presented as frequencies (No.) and percentages (%) and were analyzed using Fisher's exact test where the significance level was set at  $P = 0.05$ . Statistical analysis was performed using R statistical analysis software. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>.) Version 3.6.1. The bar chart was made using Microsoft Excel (2016) (Redmond, Washington, United States)

#### **RESULTS**

Postoperative exploration of the recessed muscles (two weeks postoperative) demonstrated that all recessed muscles in the glued group and control group were attached i.e. no lost muscles; which was statistically non-significant ( $p=1.000$ ), (OR=zero), 95%CI :( zero, Infinity).

However, in the surgical exploration of SRM in the glued group (28 eyes); 23 eyes (82.14%) the SRM was found in the same location of insertion (5mm recession).

While the SRM in the remaining five eyes (17.86%) was slipped with posterior displacement of the muscle from its new insertion of approximately 3 mm. On the other hand, surgical exploration of SRM in the control group (suture group) was found in the same location of insertion in all eyes (the muscle was 5mm from the insertion, and no slippage occurred). However, regarding muscle slippage, there was no significant difference between both groups ( $p=0.051$ ), (OR=Infinity), 95%CI :( 0.989, Infinity) as shown in **Table (1)**.

**Table (1):** Frequencies (n) and percentages (%) of muscle slippage in both groups

Slippage	Glued			Control			Total %(n)	P-value
	% r	% c	(n)	% r	%c	(n)		
No	45.10%	82.14%	(23)	100%	(28)	(28)	91.07% (51)	0.051ns
Yes	100%	17.86%	(5)	0%	(0)	(0)		
Total%(n)	50.00% (28)			50.00% (28)			100% (56)	

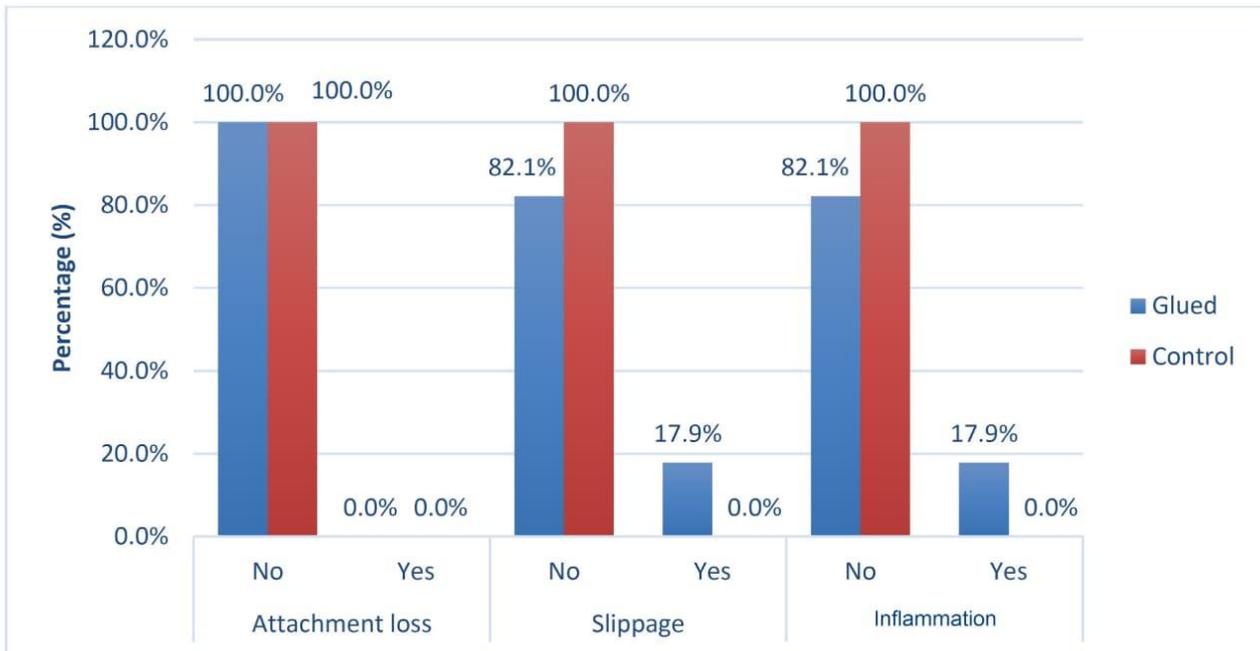
r : row percentage, c : column percentage\*; significant ( $p \leq 0.05$ ) ns; non-significant ( $p > 0.05$ )

Inflammation was detected later in the study as an association. Inflammation was detected in five eyes out of 56 eyes (8.93%) as shown in **Figure (1)**. The inflamed five eyes were the eyes in which the slippage of SRM occurred in the glued group. There was a significant association between inflammation and slippage ( $p < 0.001$ ), (OR= Infinity), 95%CI :( 27.33, Infinity) as demonstrated in **Table (2)**.

**Table (2):** Frequencies (n) and percentages (%) of the correlation between muscle slippage and inflammation

Slippage	Inflammation				Total%(n)	P-value
	No		Yes			
	%	(n)	%	(n)		
No	0%	(0)	100%	(5)	8.93% (5)	<b>P&lt;0.001*</b>
Yes	100%	(51)	0%	(0)	91.07% (51)	
Total%(n)	91.07% (51)		8.93% (5)		100% (56)	

\*; significant ( $p \leq 0.05$ ) vs ; non-significant ( $p > 0.05$ )



**Figure (1):** The percentage of post-operative attachment loss, slippage, and inflammation in reattachment and control.

## DISCUSSION

The present study demonstrated that reattachment of extraocular muscles during strabismus surgery in a rabbit model can be done successfully using fibrin glue instead of a 6/0 vicryl suture.

As such, the glue has been used for conjunctival closure following squint surgery, lamellar corneal grafting, closure of descemetocoeles and corneal perforations, amniotic membrane graft, management of leakage of the conjunctival incision after sub-scleral trabeculectomy, also in eyelid and lacrimal surgery<sup>(3)</sup>.

Adhesives have been used in squint surgery. They are two categories: biological (fibrin glue) and synthetic adhesives (n-butyl-2-cyanoacrylate)<sup>(7)</sup>. Also, Mulet ME et al concluded that adhesives with synthetic origin as (Adal-1) with a cyanoacrylate base, were efficient compared to vicryl 6/0 sutures in the recession of rectus muscle during squint surgery<sup>(8)</sup>. While in another study the cyanoacrylate has shown limited strength<sup>(9)</sup>.

In strabismus surgery, where muscular traction is important, the low tensile strength of fibrin glue is to be considered. **Tonelli et al.**<sup>(10)</sup> used fibrin glue in an experimental study in rabbits to study its adhesive property in squint surgery with the Faden technique, and minimal inflammation with fibrin glue was noted. Moreover, **Topiwala P and Bansal R,**<sup>(7)</sup> proved that fibrin glue is equally effective as cyanoacrylate glue during muscle reinsertion; but fibrin glue was proved to be better than cyanoacrylate in bio-tolerance. Fibrin glue was proven to be useful in the reinsertion of muscle recessions in rabbits by Abraham **Spiere et al.**<sup>(6)</sup> but it was found that it was more effective in large-angle recessions (6mm or more) than in small-angle recessions. However, in our study, it was effective in resisting the contractile strength of the muscle associated with small-angle recessions.

On the other hand, **Park et al.**<sup>(11)</sup> also used fibrin glue in an experimental study in rabbits to study its adhesive property in squint surgery with the hang-back technique. In the current study, we observed inflammatory reactions to fibrin glue clinically. This might be due to a reaction against fibrin glue as it was prepared from human blood derivatives. We also correlated slippage of the muscle with inflammation; however, the reason is unknown.

We explain this by the nature of fibrin glue as a blood derivative and there is a subsequent proliferation of fibroblasts and formation of granulation tissue within hours of clot polymerization. As a result, the fibrin clot degrades physiologically. However, there was no detached or lost muscle two weeks postoperatively.

Also, it is highly anticipated that the use of fibrin glue is likely to be more expensive than the use of Vicryl sutures although one vial can be used in up to five rabbits anesthetized and clustered at the same time.

In this study, reattaching the muscle with fibrin glue was found to be an alternative method in strabismus surgery which needs further evaluation for

postoperative complications. However, the study has faced some limitations such as the relatively small sample size. As the study was applied to both eyes of the rabbits, we observed the location of the muscle only after two weeks with no further observation (For ethical purposes).

## CONCLUSION

Our study provides evidence that supports the successful use of fibrin glue as an alternative to sutures to re-attach rectus muscles during small muscle recessions in strabismus surgery. However postoperative slippage of the muscles and inflammation are potential complications.

**Recommendation:** A large sample size is highly recommended for future research on the same subject to enable comparison between small and large muscle recessions, in addition to muscle resections. Human subjects instead of experimental models are recommended with autologous preparation of fibrin glue.

## DECLARATIONS

### Availability of data and materials

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials, and for further details on requests from the corresponding author.

### Competing interests

The authors declare that they have no competing interests.

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### Authors' contributions

ZAS contributed to the design, acquisition, and interpretation of data, and drafted the manuscript. AE, and EAM, contributed to the acquisition of data and edited the Manuscript; HAE anesthetized the animal for surgery and contributed to the critical revision of the manuscript. All authors read and approved the final manuscript.

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