Tissue Adhesives for a Sutureless Fadenoperation: An Experimental Study in a Rabbit Model

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Purpose. To use tissue adhesives for a sutureless Fadenoperation to eliminate perioperative risks related to the sutures.

Methods. In an in vivo procedure, 120 superior recti muscles in New Zealand White rabbits were subjected to the posterior fixation procedure, at a distance of 6 mm from the insertion point of the muscle. They were divided into four groups of 30 muscles, according to the material used to perform a myopexy: group 1 (control): nonabsorbable 5-0 polyester sutures; group 2: *n*-butyl-2-cyanoacrylate adhesive; group 3: fibrin glue; group 4: gelatin-resorcin-formaldehyde-glutaraldehyde (GRFG) adhesive. The animals were examined at 1, 7, 14, and 21 days after surgery. Afterward, they were killed, and their eyes were enucleated to measure the distance between the myopexy and the anatomic insertion point and to assure the strength of the bond with a dynamometer. Finally, a histologic examination was performed.

Results. Almost all eyes were clear after the third week, although group 4 presented the most intense inflammatory reaction. In histologic examination, groups 1 and 2 showed a chronic inflammatory reaction of the foreign-body type, with similar intensity. Fibrin glue induced minimal inflammation, but GRFG adhesive produced a pronounced reaction. Concerning the distance of the myopexy, groups 1 and 2 presented measures close to the expected distance of 6 mm, whereas groups 3 and 4 showed a greater variability. All groups performed well in the strength test, with no statistically significant differences among them.

Conclusions. *n*-Butyl-2-cyanoacrylate adhesive performed best in the sutureless Fadenoperation, characterized by precision in the expected distance of myopexy, sufficient resistance to separation, and acceptable inflammatory reaction. (*Invest Ophthalmol Vis Sci.* 2004;45:4340–4345) DOI:10.1167/iovs.04-0049

The Fadenoperation, a modification proposed by Cüppers[1] of Peter's operation for shortening the arc of contact,[2] is a strabismus surgery with a German name that means "thread operation." Such a technique involves some risks, including bulbar perforation with retinal detachment or vitreous hemorrhage, attributable to accidents related to the sutures.[3–5] To intensify the modification of the arc of contact, these sutures are placed in an awkward posterior location—retroequatorial—with a significant degree of difficulty.[6] Seeking to make this surgery easier and safer, in a rabbit model, we evaluated three different kinds of tissue adhesives (cyanoacrylate, fibrin and gelatin-resorcin-formaldehyde-glutaraldehyde [GRFG]) as substitutes for the traditional sutures in the Fadenoperation.

The literature provides few and sporadic reports on the use of tissue adhesives in strabismus surgery. Most of them are experimental studies in animals. Ellis and Levine[7] introduced the theme, mentioning the reinsertion of eight recti muscles of rabbits with methyl 2-cyanoacrylate adhesive; in 1969, Dunlap et al.[8] were the first researchers to measure the tensile strength of rabbit muscles reattached with cyanoacrylates. Their report, discouraging the use of these substances in humans because of inadequate bond strength observed during the first days after surgery, may have influenced North American investigators, who have not published a single paper on this subject since then. Other researchers throughout the world have explored the topic. Munton[9] asserted that cyanoacrylates would be satisfactory for squint operations, based on his experience with the gluing of pig and rabbit muscles. Although Flick and Tauchert[10] reported insufficient tensile strength of rabbit muscles reattached with cyanoacrylate, Jung and Chang[11] considered the outcome of glued muscles in the rabbit favorable, comparable to results in sutured muscles. Aichmair et al.[12] were pioneers in using fibrin sealants for muscle surgery in rabbits and in recommending such a technique in humans. After them, other researchers experimented with fibrin adhesive for reattachment of rabbit muscles in different experimental designs (Erbil et al.,[13] Spierer et al.,[14] and Moreira et al.,[15]). Finally, investigators in Mexico (Villaseñor-Solares and Aguirre-Aquino[16]) reported good results with the use of cyanoacrylate in strabismus surgeries in 10 patients, and in Italy Ricci et al.[17] experimented with octyl 2-cyanoacrylate to reattach rabbit muscles.

Nevertheless, only one study about the use of glue in the Fadenoperation has been reported. Flick[18] described an experimental posterior fixation procedure with cyanoacrylate tissue adhesive in a group of 12 superior recti muscles of rabbits (four muscles for each period of follow-up). A case report on the use of such a technique in seven patients complemented his description. In this same article, the author mentioned 35 other surgeries in humans in which poor preliminary clinical results were achieved. Considering that such an experiment was accomplished with a single type of adhesive, without a control group or any objective analysis, we assumed that this subject was deserving of further evaluation.

Methods

This experimental study was supported by the Departamento de Oftalmologia da Universidade Federal de Minas Gerais (UFMG; Belo Horizonte, State of Minas Gerais, Brazil) and was conducted in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

Sixty male New Zealand White rabbits (*Oryctolagus cuniculus*) were selected, with a healthy appearance and weight ranging from 1500 to 2500 g. The superior rectus muscles in both eyes were subjected to the Fadenoperation, in a randomized distribution among four groups of 30 muscles, classified according to the material used in the posterior fixation procedure: group 1 (control), two U-shaped

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FIGURE 1. *Left*: Histoacryl blau (B. Braun, AG) ampoule; *right*: application of the adhesive.

nonabsorbable 5-0 polyester sutures (Mersilene; Ethicon, Piscataway, NJ); group 2, *n*-butyl-2-cyanoacrylate tissue adhesive (Histoacryl Blau; B. Braun AG, Melsungen, Germany); group 3, fibrin glue (Tissucol; Baxter AG, Vienna, Austria); and group 4, gelatin-resorcin-formaldehyde-glutaraldehyde (GRFG) biological adhesive (Colagel; Cirumédica SA, São Paulo, Brazil). Samples of these materials were generously provided by local distributors, in whose products the authors have no financial interest.

The surgical procedure was performed under optical microscopy with ×10 magnification. The animals were anesthetized with an intramuscular combination of 5 mg/kg xylazine and 35 mg/kg ketamine. Immediately before surgery, a topical anesthetic (proxymetacaine 0.5%) was instilled in both eyes.

The conjunctiva was approached by limbic incision, exposing the superior rectus muscle and the reflex portion of the superior oblique tendon, which was resected. A cotton tip was applied beneath the superior rectus muscle to absorb the dampness. Then, with a Castroviejo caliper, two points were marked 6 mm distant from the insertion site, which was left untouched. This distance reached the equatorial region, sufficiently posterior to reproduce the usual difficulties characteristic of this surgery. The retroequatorial region was avoided due to the location of the retractor bulbi muscle insertion point.[19] At the points marked, the posterior fixation procedure was accomplished in each of the four groups.

Group 1

Two U-shaped nonabsorbable 5-0 polyester sutures (Mersilene; Ethicon), covering the muscular fibers of both the nasal and temporal thirds, were used.

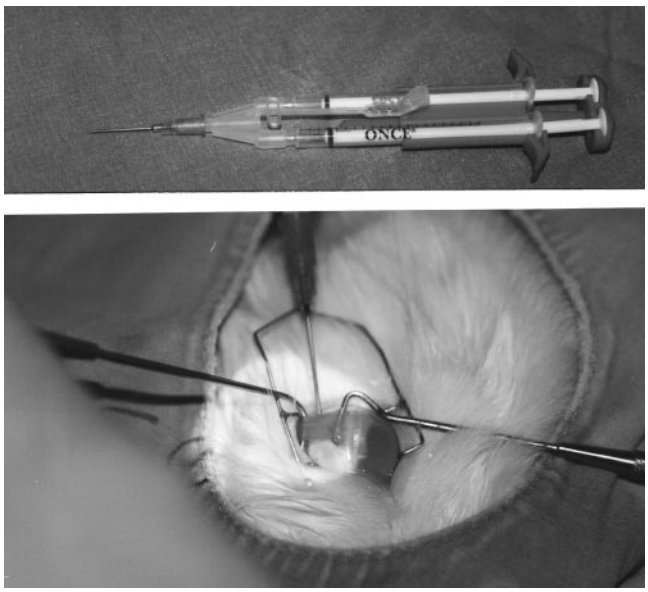

FIGURE 2. *Top*: Duploject (Baxter, AG); *bottom*: application of Tissucol (Baxter, AG).

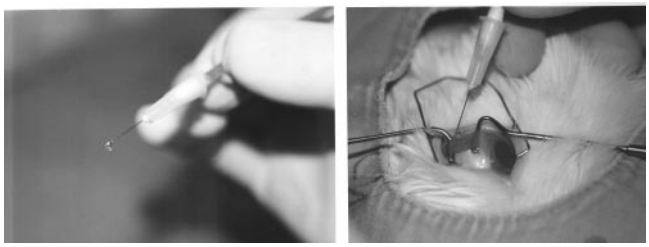

FIGURE 3. *Left*: a drop of Colagel (Cirumédica SA) adhering to the end of the needle; *right*: application of the adhesive.

Group 2

Histoacryl blau (B. Braun AG) is presented in plastic ampoules containing 0.5 g *n*-butyl-2-cyanacrylate, blue stained. The ampoules have a tubular end that permits direct dropping (Fig. 1).

Group 3

Tissucol (Baxter AG) consists of two components: the adhesive solution, containing human fibrinogen and bovine aprotinin, and the catalyzer solution, comprising thrombin and calcium chloride. Simultaneous application of these components was achieved by the use of a double syringe (Duploject; Baxter AG; Fig. 2, top). A human thrombin solution with a concentration of 500 IU/mL was used to ensure a faster fibrin formation (within a few seconds).

Group 4

Colagel (Cirumédica SA) is composed of two components, gelatin-resorcin polymerized by formaldehyde-glutaraldehyde (an aldehyde solution). Once the components were combined on a glass lamina, a drop of the resultant biological glue was transported with a 13 × 0.35-mm needle to the marked points in the sclera, taking advantage of its greater viscosity. This method enabled the most precise application among the three tissue adhesives (Fig. 3).

After surgery, all eyes had the conjunctiva closed with a 7-0 polygalactin suture, and an ophthalmic ointment containing chloramphenicol was applied to the superior conjunctiva fornix.

The animals were observed for 21 days, and a clinical examination under optical microscopy was performed at 1, 7, 14, and 21 days after surgery. At these time points, the conjunctiva's inflammatory reaction was clinically graded from 1+ to 4+. On the 21st day after surgery, the rabbits were killed with an intracardiac pentobarbital sodium injection, after anesthesia was induced as already described. Afterward, their eyes were carefully enucleated, keeping the posterior myopexy intact. The distance of myopexy was measured with the Castroviejo caliper,

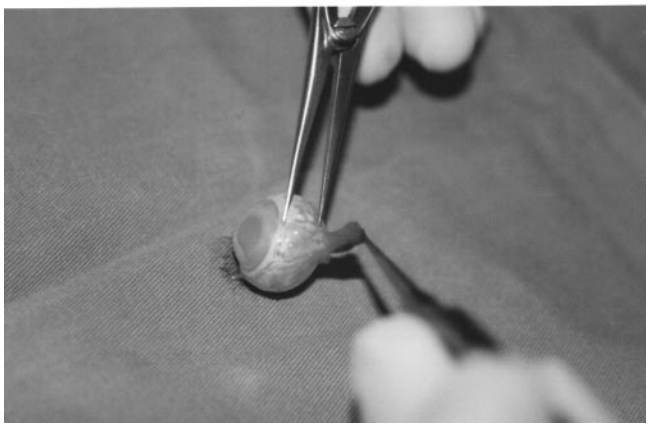

FIGURE 4. Measurement of the distance between the myopexy and the anatomic insertion with a caliper.

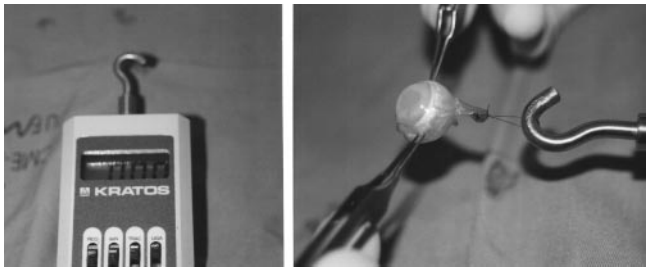

FIGURE 5. *Left*: digital dynamometer; *right*: the strength test.

from the original insertion to the most posterior point of gluing, at both margins of the superior rectus muscle (Fig. 4).

Finally, a test was undertaken to check the tensile strength of adhesion. A loop of polygalactin was sutured to the stump of the superior rectus muscle, and this loop was adapted to the hook of a digital dynamometer (model DDK2; Kratos, São Paulo, Brazil), which can be used to take constant measures of the traction force at 1 gram force (gf) intervals. Adhesion that constantly resisted a perpendicular traction of 100 gf, administered three times for 1 second each, was considered to be adequate (Fig. 5). The adopted pattern was based on studies that had stipulated between 60 to 95 g, the maximum active force of human extraocular muscles,[20–24] achieving 100 g in a saccadic movement.[25] It is interesting to note that the same force in the rabbit is estimated to be approximately one tenth of these values,[26] making indispensable the use of a dynamometer to reproduce an adequate test force.

After each procedure, histologic sections were prepared and stained with hematoxylin-eosin (HE) and the results recorded.

The aspects statistically assessed were (1) differences between inflammatory reactions clinically observed (the Kruskal-Wallis and Friedman tests), (2) distances from the myopexy to the anatomic insertion (Kruskal-Wallis test), and (3) resistance to the strength test (Fisher exact test).

RESULTS

Based on clinical examinations, all groups showed an acceptable and progressively lesser inflammatory reaction, and most eyes were clear and stable after the third week of follow-up. In the group with GRFG adhesive (group 4), the reaction was persistently more intense, as disclosed by the Kruskal-Wallis' test, in a transverse comparative analysis.

Regarding the distance of the posterior fixation, it was observed that groups 1 and 2 had the best results, achieving the expected distance of 6 mm in both sides of the muscle, without significant deviation. Groups 3 and 4 showed a greater variability, and the distances observed were more frequently less than expected (Tables 1, 2). It is interesting to point out that the whole arc of contact of the operated-on muscles was noted to adhere to the sclera in all eyes of the four groups under study.

Concerning the bond strength, it was observed that most of the operated-on muscles adhered sufficiently to the sclera. Only 10 of the 120 muscles were not resistant to the traction applied: four in group 2, four in group 3, and two in group 4. These differences were not statistically significant; thus, it was assumed that all groups performed well in the strength test (Fig. 6).

The histologic examination showed a foreign-body reaction of similar intensity in groups 1 and 2, limited to the sclera and muscle involved in the area of gluing. In group 3, the tissues were almost undisturbed, characterizing a histologic reaction consistently less intense than that observed in all other groups, with a tiny infiltrate of mononuclear cells. On the contrary, group 4 produced the worst histologic picture, characterized by excessive inflammatory reaction of the foreign-body type that reached the choroids and culminated with diffuse fibrosis and calcification (Fig. 7).

DISCUSSION

The use of tissue adhesives for sutureless strabismus surgery has been a matter of interest for more than 40 years, although few reports on this subject have been produced.

Among the adhesives available for medical use, cyanoacrylates have been extensively investigated in most surgical specialties. They have also been examined experimentally in different fields of ophthalmology: corneal surgery, glaucoma filtering surgery, conjunctiva synthesis, oculoplastics, and orbital and posterior segment surgeries. Their best performance, however, was established in the treatment of small corneal perforations and descemetoceles.[27] Since the first studies about their toxicity were performed, it has been known that cyanoacrylates with longer chains, such as butyl- or octyl-cyanoacrylates, were shown to have better tolerance.[28–30] This fact is related to the velocity of polymer degradation—the slower its degradation, the lower its toxicity. Moreover, long-term studies on the use of cyanoacrylates in dogs, rats, mice,[31] and chimpanzees[29] have failed to reveal any evidence of carcinogenicity, contrasting with other acrylic nonabsorbable substances.[32] In experimental studies on the use of cyanoacrylates for muscle surgery, their toxicity, once detected, has not been reported as a limiting factor.[8–11,17,18] When used for squint operation in humans, observations have shown good tolerance that was inversely proportional to the amount of adhesive applied.[16]

Fibrin glue, however, has been pointed to as the most biocompatible adhesive, but it is not at all devoid of disadvantages. The great concern about this sealant is its potential risk of being a vehicle for blood-transmitted diseases, because it is composed of blood derivatives. The possibility of obtaining its components from a single selected donor[33,34] or, preferably, from the patient,[35,36] may resolve this problem. Nevertheless, the fibrin sealants commercially available to date are obtained from pools of donors, which calls for rigorous donor selection, reliable serologic tests, and well-established methods for sterilization. Furthermore, the literature provides reports of fatal reactions secondary to the use of fibrin adhesives.[37–39] Today, with the substitution of bovine thrombin for human thrombin

TABLE 1. Distance of Adhesion in the Nasal Muscular Border

Group	*n*	Minimum	Maximum	Median	Mean	Deviation
1 (suture)	30	5.0	6.0	6.0	6.0	0.2
2 (Histoacryl)	30	4.5	7.5	6.0	5.8	0.7
3 (Tissucol)	30	3.0	7.0	5.0	5.1	1.0
4 (Colagel)	30	4.0	7.0	5.0	5.3	0.9

Conclusion: $(1 = 2) > (4 = 3)$; $P < 0.001$ through the Kruskal-Wallis test. Distance data are in millimeters.

TABLE 2. Distance of Adhesion in the Temporal Muscular Border

Group	*n*	Minimum	Maximum	Median	Mean	Deviation
1 (suture)	30	5.0	6.0	6.0	5.9	0.2
2 (Histoacryl)	30	4.5	7.5	6.0	5.8	0.7
3 (Tissucol)	30	3.0	7.0	5.0	5.0	1.0
4 (Colagel)	30	4.0	7.0	5.0	5.4	0.8

Conclusion, data expression, and probability are as in Table 1.

in the fibrin glue's makeup, these rare accidents may be avoided. However, the mechanisms of such serious or even fatal reactions are not completely understood, and anaphylaxis related to aprotininemia has also been reported.[40] Fibrin sealants, although studied for use in surgery since 1940,[41] were first used experimentally in muscles operations only in 1988.[12] Among four experimental studies on this subject,[12–15]two had promising results,[12,15] and the other two had discouraging outcomes.[13,14]

GRFG adhesive is the least studied in ophthalmology. To our knowledge, a single experimental study[42] on its use has been reported, and significant toxicity was observed at the site of application (rabbit sclera). This biological glue has been used in cardiovascular surgery, although late complications secondary to its use have been reported.[43]

These data suggest a well-defined field for research. The possibility of using glue in a sutureless Fadenoperation has been poorly explored; moreover, this technique, among other surgical methods for strabismus, seems to be the one that would most benefit from the use of sealants, due to its particularities. This subject demands investigation of all common tissue adhesives available, since their potentials and usefulness in strabismus surgery has not been definitely established.

The present study is a pioneer in assessing the posterior myopexy with tissue adhesives through an analysis of objective parameters, notably the expected position of gluing and its tensile strength. Concerning the former, *n*-butyl-2-cyanoacrylate produced adherence at the expected distance, with a performance comparable to the control group of sutures. The other substances showed inadequate results, as the adherences between muscle bellies and sclera were found at lesser distances than were intended. Data in the literature poorly describe such aspects. When used in other strabismus surgeries, cyanoacrylate adhesives are reported to produce an imprecise final position of reinserted rabbit muscle, because of the growth of muscle fibers anterior to the point of gluing.[8] Other investigators have asserted that rabbit muscles recessed with cyanoacrylate adhesives were found "approximately" at the distance expected,[17] whereas significant slippage of the muscles occurred in recessions inferior to 6 mm[14] when fibrin glue was used. It has been postulated that the insufficient distances observed in the groups of fibrin and GRFG adhesives is due to a partial slippage of the myopexy that occurred during the period before the third week. If this hypothesis is correct, it means there was an insufficient bond strength in these groups, probably during the first days after surgery.

An unexpected result was the complete adherence of the whole arc of contact in all eyes from all groups observed, a fact that had already been verified in traditional Fadenoperations performed on rabbit muscles.[44,45] It is well known that rabbits possess a strong "healing nature," notably evidenced in intraocular surgeries, when intense tissue organization may occur, related to the existence of fibrinogen in the aqueous humor. Nevertheless, no adhesions were reported in rabbit muscles that have been simply manipulated, but not sutured (control group for the traditional Fadenoperation).[45] Hence, such a tendency for robust healing, alone, seems not to be sufficient to amplify the muscle scaring in this technique. In group 1, it was speculated that extended adherence resulted from ultrastructural changes in the muscle fibers, induced by the sutures themselves, which could be responsible for innervational and/or ischemic alterations, as reported elsewhere.[45] In groups 2 and 3, however, this fact could be explained by the spread of adhesives beneath the arc of contact, by capillarity, considering that these substances are liquid. In group 4, this wide adherence could be due to the intense fibrosis produced by the GRFG adhesive.

As for the strength of the bond, all groups showed firm adhesion at the third week after surgery. This fact has been shown to be in accordance with reports on reattachments of rabbit muscles with cyanoacrylates[11,17] and fibrin glue,[15] at this point in the follow-up.

These three classes of tissue adhesives have never been compared before in ophthalmology. Histologic examination showed that *n*-butyl-2-cyanoacrylate adhesive induced an inflammatory reaction of a type and intensity similar to that in the

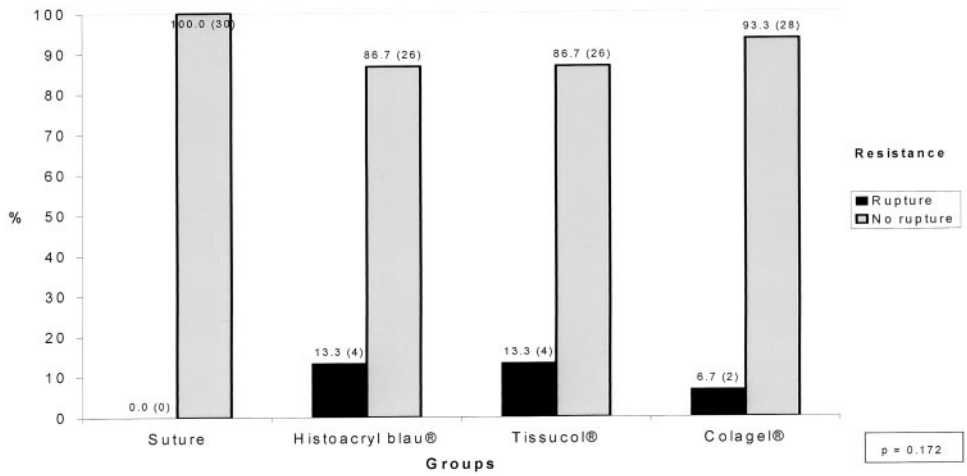

FIGURE 6. Percentage of resistance to the traction of 100 gf for 1 second: distribution per group. The probability was obtained with the Fisher exact test.

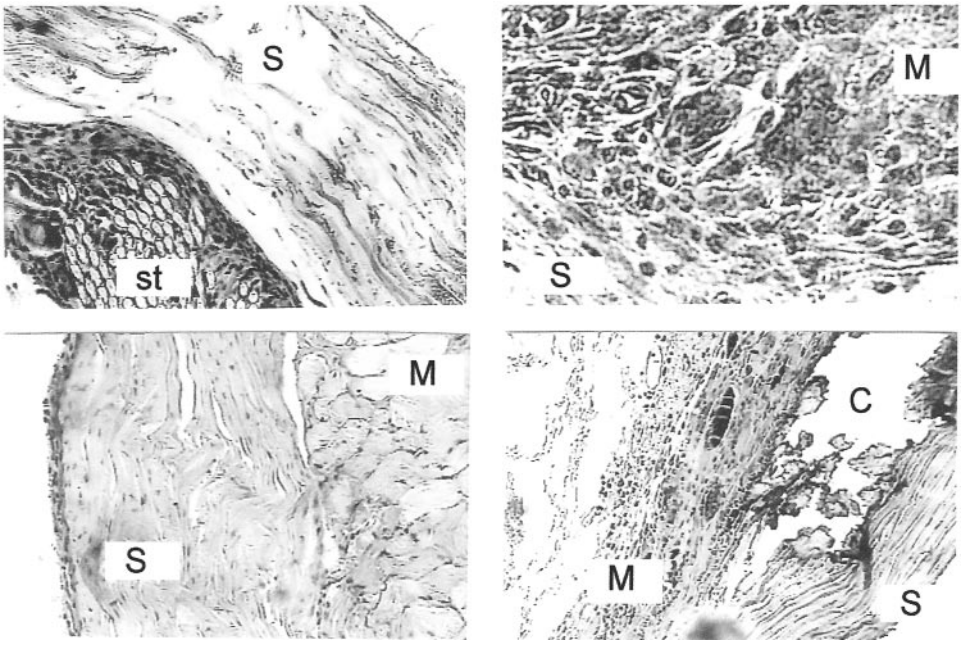

FIGURE 7. *Top left*: Mersilene (Ethicon) suture (st) within the sclera, causing in a mononuclear foreign-body reaction. *Top right*: (Histoacryl blau; B. Braum, AG): site of adhesion infiltrated by mononuclear and foreign-body giant cells. *Bottom left* (Tissucol, Baxter, AG): tiny infiltrate of mononuclear cells at the site of adhesion. *Bottom right* (Colagel, Cirumédica SA): calcification (C) distorting the sclera; fibrosis with neovascularization at the muscle. S, sclera; M, muscle. HE staining; magnification: *top left*, *bottom left*, and *right*, ×100; *top right*, ×400.

suture group. The fibrin adhesive showed the best tissue performance, confirming that it is the adhesive with the best biocompatibility. The GRFG adhesive produced an excessive inflammatory response, affecting grossly the sclera up to the choroid, a fact that had already been observed in another experimental study in rabbits.[42] Hence, the use of GRFG in the Fadenoperation or any other strabismus surgery should be discouraged.

Through analysis of the findings mentioned herein, we may conclude that the *n*-butyl-2-cyanoacrylate adhesive showed the best performance in a sutureless Fadenoperation in a rabbit model, characterized by precision in the expected distance of the myopexy, sufficient resistance to the effects of tension, and an acceptable inflammatory reaction. Although the conclusions drawn from such a model cannot be directly applied to humans because of anatomic differences, these observations could guide further studies to recommend this technique in the surgical treatment of strabismus. The reproduction of this experiment in human eyes that are scheduled for enucleation (for instance, atrophic eyes) would provide a good experimental setup for future investigations. Besides avoiding the risks related to the traditional posterior fixation procedure, another great advantage of testing adhesives for sutureless Fadenoperation is the impossibility of losing a muscle, as would occur if glue were used for reinsertions. Hence, such an experiment should also represent a preliminary step in the investigations into the use of tissue adhesives for other strabismus surgery.

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References

1. Cüppers C. The so called "Fadenoperation": (surgical corrections by well defined changes of the arc of contact). Proceedings of the 2nd Congress of International Strabismological Association; May 20–25, 1974; Marseille, France. Paris-Marseille: Diffussion Generale de Librairie; 1974:395–400.
2. Peter LC. *The extra-ocular Muscles: a Clinical Study of Normal and Abnormal Ocular Motility.* 2nd ed. Philadelphia: Lea & Febiger; 1936:296–297.
3. Spielmann A. The Fadenoperation: personal approach. In: Barbosa PH, ed. *Estrabismo.* Rio de Janeiro: Cultura Médica; 1997:224–235.
4. Shuckett EP, Hiles DA, Biglan AW, Evans DE. Posterior fixation suture operation (Fadenoperation). *Ophthalmic Surg.* 1981;12:578–585.
5. Curi RLN. A mioescleropexia posterior ("Fadenoperation") e seus efeitos sobre os ângulos de desvio das esotropias adquiridas não acomodativas (dissertation). Belo Horizonte, Brazil: Faculdade de Medicina, Universidade Federal de Minas Gerais; 1985.
6. Hugonnier R. L'opération du fil: opération facile ou difficile? *J Fr Ophtalmol.* 1978;1:671–673.
7. Ellis RA, Levine AM. Experimental sutureless ocular surgery. *Am J Ophthalmol.* 1963;55:733–741.
8. Dunlap EA, Dunn M, Rossomondo R. Adhesives for sutureless muscle surgery. *Arch Ophthalmol.* 1969;82:751–755.
9. Munton CGF. Tissue adhesive in ocular surgery: a prospective study. *Exp Eye Res.* 1971;11:1–6.
10. Flick H, Tauchert A. Gewebekleber in der Augenmuskelchirurgie. *Ber Zusammenkunft Dtsch Ophthalmol Ges.* 1978;75:500–503.
11. Jung YC, Chang BL. Experimental strabismus surgery using n-butyl-2-cyanoacrylate (Histoacryl®). *Korean J Ophthalmol.* 1988;2:57–61.
12. Aichmair MW, Aichmair H, Lintner F. Fibrinklebung an äusseren Augenmuskeln: expermentelle Anwendung am Kaninchen. *Klin Monatsbl Augenheilkd.* 1988;193:499–503.
13. Erbil H, Sinav S, Süllü Y, Kandemir B. An experimental study on the use of fibrin sealants in strabismus surgery. *Turk J Pediatr.* 1991;33:111–116.
14. Spierer A, Barequet I, Rosner M, Solomon AS, Martinowitz U. Reattachment of extraocular muscles using fibrin glue in a rabbit model. *Invest Ophthalmol Vis Sci.* 1997;38:543–546.
15. Moreira ATR, Torres LFB, Scarpi MJ, Moreira Júnior CA, Miranda SP, Matsumoto LH. Uso do adesivo biológico de fibrina para reinserção de músculos retos superiores em coelhos: I. estudo clínico. *Rev Bras Oftal.* 1998;57:501–512.
16. Villaseñor-Solares J, Aguirre-Aquino BI. Uso de adhesivos tisulares en cirugía de estrabismo. *Rev Bras Oftal.* 1998;57:273–277.
17. Ricci B, Ricci F, Bianchi PE. Octyl 2-cyanoacrylate in sutureless surgery of extraocular muscles: an experimental study in the rabbit model. *Graefes Arch Clin Exp Ophthalmol.* 2000;238:454–458.

18. Flick H. Myopexia posterior mit Gewebekleber: Fadenoperation nach Cüppers ohne Faden. *Klin Monatsbl Augenheilkd*. 1981;178: 193–196.
19. Prince JH, Eglitis I. Extraocular muscles. In: Prince JH, ed. *The Rabbit in Eye Research.* Springfield, IL: Charles C. Thomas Publisher; 1964: 57–71.
20. Madroszkiewicz M. Okulomyodynamometr. Nowy przyrzad do pomiarów siły miœêsni ocznych. *Klin Oczna*. 1954;24:407–410.
21. Scott AB, Collins CC, O'Meara DM. A forceps to measure strabismus forces. *Arch Ophthalmol*. 1988;88:330–333.
22. Collins CC, Carlson M, Scott AB, Jampolsky A. Extraocular muscle forces in normal human subjects. *Invest Ophthalmol Vis Sci*. 1981;20:652–664.
23. Robinson DA. The mechanics of human saccadic eye movement. *J Physiol*. 1964;174:245–264.
24. Childress DS, Jones RW. Mechanics of horizontal movement of the human eye. *J Physiol*. 1967;188:273–284.
25. Scott AB, Collins CC, O'Meara DM. *Extraocular Muscle Forces in Strabismus.* Proceedings of the 1st Congress of International Strabismological Association; 1971; St. Louis, MO. St. Louis: CV Mosby; 1971: 125–136.
26. Barmack NH. Measurements of stiffness of extraocular muscles of the rabbit. *J Neurophysiol*. 1976;39:1009–1019.
27. Werner LP, Legeais JM. Les colles chirurgicales en ophtalmologie. *J Fr Ophtalmol*. 1997;20:146–159.
28. Woodwards SC, Herrmann JB, Cameron JL, Brandes G, Pulaski E, Leonard F. Histotoxicity of cyanoacrylate tissue adhesive in the rat. *Ann Surg*. 1965;162:113–122.
29. Lehman RAW, Hayes GJ, Leonard F. Toxicity of alkyl 2-cyanoacrylates. *Arch Surg*. 1966;93:441–446.
30. Refojo MF, Dohlman CH, Koliopoulos J. Adhesives in ophthalmology: a review. *Surv Ophthalmol*. 1971;15:217–236.
31. Matsumoto T, Heisterkamp CA. Long-term study of aerosol cyanoacrylate tissue adhesive spray: carcinogenicity and other untoward effects. *Am Surg*. 1969;35:825–827.
32. Oppenheimer BS, Oppenheimer ET, Stout AP, Willhite M, Danishefsky I. The latent period in carcinogenesis by plastics in rats and its relation to the presarcomatous stage. *Cancer*. 1958;11: 204–213.
33. Dresdale A, Rose EA, Jeevanandam V, et al. Preparation of fibrin glue from single-donor fresh frozen plasma. *Surgery*. 1985;97: 750–755.
34. Spotinitz WD, Mintz PD, Nancy Avery MT, et al. Fibrin glue from stored human plasma: an inexpensive and efficient method for local blood bank preparation. *Am Surg*. 1987;53:460–462.
35. Siedentop KH, Harris DM, Sanchez B, et al. Autologous fibrin tissue adhesive. *Laryngoscope*. 1985;95:1074–1076.
36. Durham LH, Willatt DJ, Yung MW, et al. A method for preparation of fibrin glue. *J Laryngol Otol*. 1987;101:1182–1186.
37. Flaherty MJ, Henderson R, Wener MH, et al. Iatrogenic immunization with bovine thrombin: a mechanism for prolonged thrombin times after surgery. *Ann Intern Med*. 1989;11:631–634.
38. Berguer R, Staerkel RL, Moore EE, et al. Warning: fatal reaction to the use of fibrin glue in deep hepatic wounds: case reports. *J Trauma*. 1991;31:408–411.
39. Berruyer M, Amiral J, French P, et al. Immunization by bovine thrombin used with fibrin glue during cardiovascular operations: development of thrombin and factor V inhibitors. *J Thorac Cardiovasc Surg*. 1993;105:892–897.
40. Oswald AM, Joly LM, Gury C, Disdet M, Leduc V, Kanny G. Fatal intraoperative anaphylaxis related to aprotinin after local application of fibrin glue. *Anesthesiology*. 2003;99:762–763.
41. Young JZ, Medawar PB. Fibrin suture of peripheral nerves: measurement of the rate of regeneration. *Lancet*. 1940;2:126–128.
42. Spera CA, Schellini SA, Silva MRBM, Marques MEA, Rahal SC. Uso da colagel na cirurgia da conjuntiva: estudo experimental. *Arq Bras Oftalmol*. 1998;61:152–158.
43. Bingley JA, Gardner MA, Stafford EG, et al. Late complications of tissue glues in aortic surgery. *Ann Thorac Surg*. 2000;69:1764–1768.
44. Goldstein JH, Kopelowitz N. Tissue response to the Fadenoperation. *Br J Ophthalmol*. 1979;63:684–686.
45. Alió JL, Vives A, Chacon M, et al. Muscular structural changes following Fadenoperation. *J Pediatr Ophthalmol Strabismus*. 1984;21:102–109.