

## Technical note

# Reconstruction of the sellar floor using Bioglue following transsphenoidal procedures

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**Summary Objective.** Cerebrospinal fluid rhinorrhea, pneumocephalus and meningitis are serious complications following transsphenoidal excision of sellar, suprasellar and parasellar lesions. This study evaluates the use of a new bioadhesive, Bioglue as an adjunct in reconstructing the sellar floor and preventing CSF fistula and investigates the possible complications associated with its use. **Methods.** In thirty-two patients (31 pituitary adenomas and 1 meningioma) Bioglue was used to help reconstruct the sellar floor after endonasal transsphenoidal procedures between January 2001 and April 2002 at the Royal Melbourne Hospital. **Results.** There were no post-operative CSF rhinorrhea, allergic rhinitis, meningitis, pneumocranium, granulomas or other complications associated with the use of Bioglue. **Conclusion.** This technique of reconstruction of sellar floor using Bioglue is simple and time efficient in preventing CSF fistula formation following transsphenoidal procedures for sellar region lesions.

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**Keywords:** bioglue, transsphenoidal resection, sellar floor reconstruction, cerebrospinal fluid leak

## INTRODUCTION

Initial attempts at transcranial resection of pituitary lesions in the late 1800s and early 1900s resulted in unacceptable morbidity and mortality. Consequently in 1906, Schloffer suggested and later reported the first successful transsphenoidal resection of a pituitary tumour. Over subsequent decades this procedure was adopted by interested surgeons and underwent a number of important modifications, most notably by Halstead, Cushing, Dott, Guiot and Hardy.<sup>24</sup> With the introduction of fluoroscopy screening, the operating microscope and selective adenectomy, the transsphenoidal approach, with its low mortality and morbidity, became the accepted and preferred route for the removal of pituitary tumours.

Cerebrospinal fluid (CSF) fistula is potentially the most frequent serious complication of transsphenoidal surgery with a reported incidence of between 2.7% and 6.4%.<sup>1,2,4,21,23,25</sup> CSF fistulae are frequently seen intraoperatively, particularly during transsphenoidal resection of tumours with suprasellar extensions. There are diverse and well-described techniques for repairing these fistulae,<sup>8,13,14,18,19</sup> including intrasellar and sphenoid sinus packing with autologous fat, muscle and fascia<sup>5,19</sup> and reconstruction of the sellar floor with fragments of sphenoid bone. These can be deployed both with and without the assistance of lumbar CSF diversion.<sup>9,10</sup> Other variations of sellar floor reconstruction include the use of titanium plates, dermal grafts, special suture tying techniques, fascia lata, lyophilised dura mater, fibrin glue and collagen sponge.<sup>11,14,19,22</sup> If an intraoperative iatrogenic CSF fistula is not appreciated and properly repaired, it may persist and become complicated by meningitis and/or pneumocranium<sup>12</sup> with serious consequences.

There is no universal consensus of the best technique for repairing transsphenoidal CSF fistula or for reconstructing the sellar floor. In this paper we describe our technique that utilises a new

tissue glue – Bioglue<sup>®</sup> Surgical Adhesive (Cryolife, Inc., Kenesaw, GA, USA) which in a technically undemanding manner both secures and supports the bone graft reforming the sellar floor while at the same time forming a watertight seal. Our clinical experience with the technique is presented.

## MATERIALS AND METHODS

A prospective study of the use of Bioglue in sellar floor reconstruction following transsphenoidal surgery, was conducted over a period of sixteen months (January 2001–April 2002), at the Royal Melbourne Hospital. Thirty-two consecutive patients were recruited into the study. Their ages ranged from 22 to 86 years (mean 54.2 years). There were 21 male patients and 11 females. Sixteen patients (50%) had tumours with suprasellar extension. The various tumour types are shown in Table 1. All the patients had similar selection criteria, pre-operative evaluation, surgical technique and post-operative management. CSF diversion via a lumbar spinal drain was used post-operatively in nine cases (where CSF was seen at surgery) for a period of up to 48 h. Duration of hospitalisation ranged from 4 to 9 days (mean 6.4 days) and the amount of Bioglue used ranged from 5.0 to 10 ml (mean 6.45 ml per patient). Post-operatively all the patients received antibiotics for 2–5 days (mean 2.46 days). Post-operatively all nasal discharges possibly suggestive of CSF rhinorrhea were analysed for the presence of  $\beta$ -2-transferrin. Results were analysed in order to evaluate the effectiveness of Bioglue in sellar floor reconstruction and in sealing CSF fistulae.

## Technique

All 32 patients underwent endonasal transseptal submucosal transsphenoidal resection of sellar region tumours using microsurgical techniques. A subarachnoid lumbar drain was inserted preoperatively in selected cases with macroadenomas extending into the suprasellar cisterns to assist intraoperative descent of the diaphragma sellae. The drain was removed at the end of procedure if a defect was not identified in the arachnoid during the procedure. However, if a CSF leak was observed during tumour resection, lumbar CSF diversion was continued for 24–72 h post-operatively.

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**Table 1** Pathological diagnoses of 32 patients where Biogluce was used for sellar floor reconstruction

Diagnosis	No. of patients (%)
Null cell adenoma	15 (46.7)
GH secreting adenoma	7 (27.9)
ACTH secreting adenoma	3 (9.4)
Prolactin secreting adenoma	2 (6.3)
Gonadotroph cell adenoma	1 (3.2)
FSH secreting adenoma	1 (3.2)
Meningioma	1 (3.2)
Null cell adenoma with haemorrhagic infarct	2 (6.3)

In all cases, regardless of whether a CSF leak was identified, the resection cavity was packed with autologous abdominal fat graft. The anterior wall of the pituitary fossa was then reconstructed with a customised fragment of bone taken from the sphenoid. While this fragment was being held in position with a bayonet forceps against the defect in the floor of the pituitary fossa, from within the sphenoid sinus, it was reinforced and secured in place with Biogluce. This was introduced via a malleable plastic 10 cm extender tip under direct vision, incrementally and as required once the mixing tip had been primed ensuring the Biogluce components had been appropriately mixed. The quantity of Biogluce used varied between 5 and 10 ml. The nasal cavity was then packed with iodine impregnated ribbon gauze (BIPP), that was removed after 48 h.

Patients were followed up by the authors in outpatients at 3 months, 6 months and thereafter at yearly intervals with follow-up imaging.

## RESULTS

No patient developed CSF rhinorrhea, allergic rhinitis, meningitis or pneumocranium during the post-operative period. No patient required reoperation. No granuloma formation or gadolinium enhancement was observed on follow-up radiological investigation. Follow-up ranged from 90 to 485 days with a median of 298 days.

## DISCUSSION

Biogluce is an admixture of bovine serum albumin (45% w/v) and glutaraldehyde (10% w/v). The bovine serum comes from United States and Canadian cattle-herds which are free of transmissible bovine spongiform encephalopathy. It is purified by heat precipitation, chromatography and  $\gamma$ -irradiation. Two solutions are dispensed in a predefined ratio and mixed in a special applicator through to a tip where cross linkage begins. The glutaraldehyde molecules covalently bond the bovine serum albumin molecules to each other and to the cell surface protein and extracellular matrix protein. The albumin provides an extensive flexible network of bonds. This reaction is spontaneous and independent of the coagulation state of the patient. When applied to the repair site it forms a mechanical seal. It begins to polymerise in 20–30 s and reaches bonding strength in 2 min. It also adheres to synthetic graft materials. A wet surgical field may impair adhesion. It does not engender a chronic inflammatory response and does not enhance on gadolinium injection.

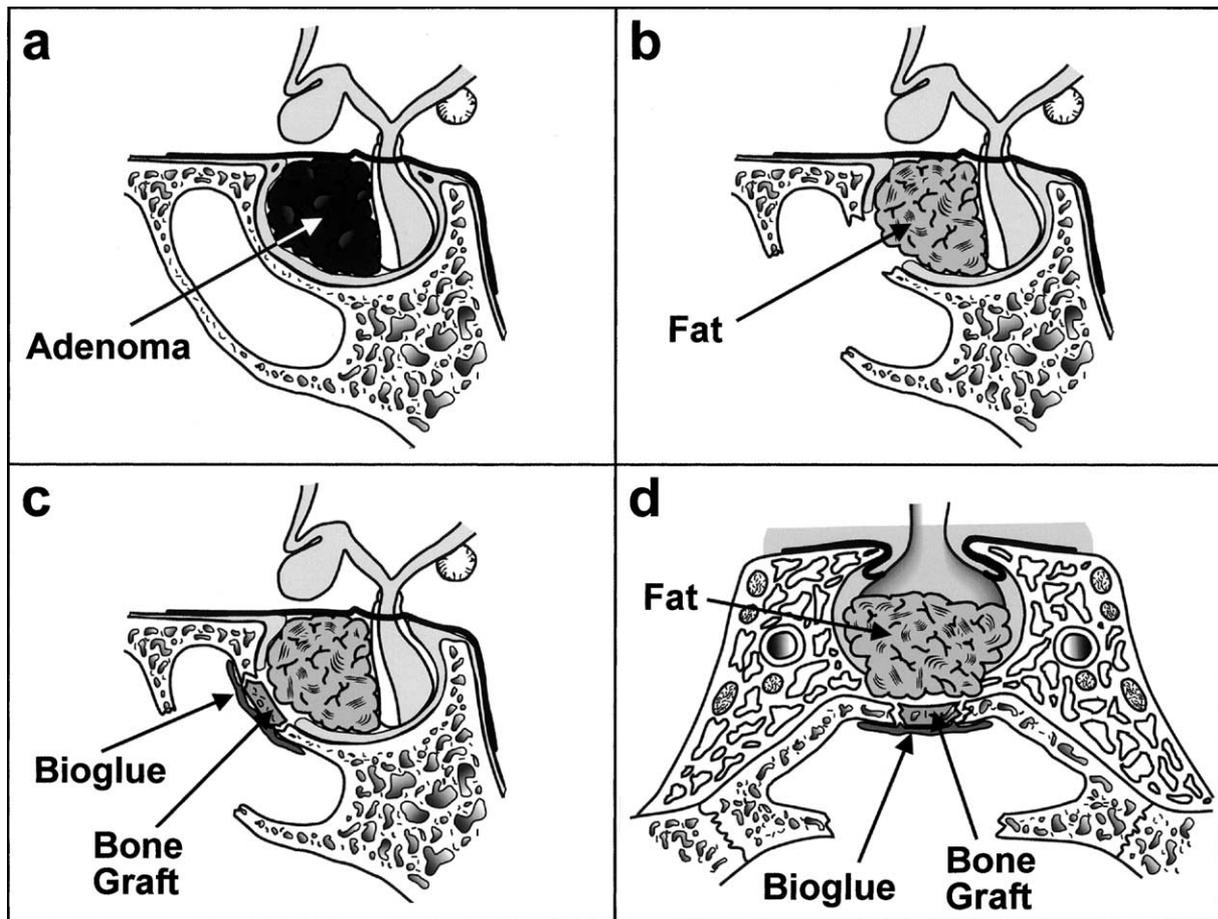
To date studies utilising Biogluce have concentrated on its use as an adjunct for vascular surgical anastomoses.<sup>15–17</sup> In this role tissue explanted from animal studies up to 2 months post-operatively have demonstrated a paucity of prominent inflammatory response.<sup>16</sup> Rarely specimens showed chronic granulomatous inflammation as a typical foreign body response but with no fibrosis

nor the presence of multinucleate giant cells. This correlated with our follow-up radiological observations.

The transsphenoidal route to sellar region tumours is now accepted as the optimal approach and is considered safe in expert hands, having a perioperative mortality of 0.9%.<sup>2</sup> CSF leakage following this procedure is the most frequent serious complication, the incidence varying between 2.7% and 6.4%.<sup>1,2,4,20,25</sup> If the arachnoid is breached and CSF observed various techniques are employed to avoid post-operative CSF rhinorrhea. The most commonly accepted technique was popularised by Hardy<sup>5</sup> who used nasal septal cartilage to support the sella-floor after packing with autologous fat. Freidberg et al. recommended the use of stainless steel minifragment three hole plates to support the intradural fat pack.<sup>6</sup> These plates are tissue compatible but they interfere with interpretation of subsequent CT/MRI studies. Muscle is also sometimes used for packing the resection cavity in order to prevent CSF rhinorrhea and chiasmal descent. However, revascularization of muscle can also hinder radiological interpretation of tumour recurrence post-operatively.<sup>19</sup> Cappabianca et al. recommended the use of a bent sheet of polyester-silicone dural substitute placed into the sella after removal of the lesion followed by autologous fat graft and then a layer of dural substitute and fibrin glue.<sup>14</sup> In this report no mention is made about post-operative migration of the dural substitute or inflammatory changes due to its use. Kobayashi et al. advocated the use of alumina ceramica for sellar floor reconstruction but it may cause a foreign body reaction.<sup>18</sup> Guity and Young recommended the watertight closure of the dura following transsphenoidal procedures using specially designed suture-tying instruments and needle, but this is technically very demanding<sup>8</sup> and not always practicable. Spaziante et al. practice a method of multiple plugging to occlude the sella including intradural and extradural packing and anchored intradural packing and using cartilage.<sup>3</sup> Kelly et al. proposed the use of a two-layered collagen sponge and titanium mesh for small CSF leaks but this method fails where a large defect in the arachnoid is identified. An alternative method of sellar repair proposed by Citardi et al. was to use intrasellar extradural acellular dermal allograft followed by bony floor reconstruction.<sup>7</sup> Fibrin sealant, which is concentrated fibrinogen from a single donor (screened for Hep B surface antigen and HIV antibody) combined with topical bovine thrombin, has also been widely used for dural sealing. However in order to increase the clot stability, fibrin sealants frequently contain antifibrinolytic substances such as aprotinin or synthetic Tranexamic acid (tAMCA) which have been implicated in seizures following topical applications.<sup>22</sup>

Our rationale for routinely reconstructing the sella floor is firstly to restore the normal anatomy. This is always advantageous, facilitating more accurate post-operative radiological evaluation, easier and safer redo transsphenoidal surgery and also minimises the risk of CSF fistula if the patient concerned subsequently requires a transcranial procedure. Reconstructing the floor also provides a barrier to infection and provides a strut to support the fat seal against the arachnoid defect. The intrasellar fat held in place by a bone strut also minimises the possibility of the optic apparatus prolapsing into the sella with consequent visual deterioration.

The technique of supporting the position of the bone graft against the floor of the pituitary fossa from within the sphenoid sinus makes the repair simple, safe and quick. The technique avoids having to wedge the bone fragment within the fossa extradurally as this invariably precipitates bleeding. Often with macroadenomas it is difficult to find edges to support the graft. The Biogluce furthermore has a haemostatic effect. As yet we have not had to reoperate on any patients in whom Biogluce was applied



**Fig. 1** Sketch diagram of an intact sella turcica with the pituitary adenoma still in situ (a). In (b) the adenoma has been resected and the resection cavity packed with subcutaneous abdominal fat. (c) (Sagittal) and (d) (coronal) shows the bone graft, a fragment of sphenoid bone, in place across the resected sellar floor, strutting the fat graft and secured in position with a layer of Bioglué.

and are thus not able to comment on the impact it has on facilitating such surgery (see Fig. 1).

## CONCLUSION

In our series of 32 patients, we used Bioglué following transsphenoidal procedures for sellar floor reconstruction. This series includes nine cases in which CSF fistula was observed intraoperatively. The Bioglué has been found to be biocompatible and does not cause any post-operative CT/MRI artefact. None of our patients developed CSF fistula, allergic rhinitis, meningitis, pneumocranium or granulomas. Bioglué is a valuable adjunct in both the reconstruction of the sellar floor and in sealing CSF fistula.

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## REFERENCES

- Black PMcL, Zervas NT, Candia G. Incidence and management of complications of transsphenoidal operation for pituitary adenomas. *Neurosurgery* 1987; 20: 920–924.
- Ivan Ciric, Ragin et al. Complications of transsphenoidal surgery: results of a national survey, review of literature, and personal experience. *Neurosurgery* 1997; 40: 225–238.
- Spaziante R, de Divitiis E, Cappabianca P. Reconstruction of the pituitary fossa in transsphenoidal surgery: an experience of 140 cases. *Neurosurgery* 1985; 17: 453–458.
- Laws Jr ER, Kern EB. Complications of transsphenoidal surgery. *Clin Neurosurg* 1976; 23: 401–416.
- Hardy J. Transsphenoidal hypophysectomy. *J Neurosurg* 1971; 34: 582–594.
- Freidberg SR, Hybel RL, Bohigian RK. Closure of CSF leakage after transsphenoidal surgery. *Neurosurgery* 1994; 35(1): 159–161.
- Citardi, Cox AJ III, Bucholz RD et al. Acellular dermal allograft for sellar reconstruction after transsphenoidal hypophysectomy. *Am J Rhinol* 2000; 14(1): 69–73.
- Guity A, Young PH. A new technique for closure of the dura following transsphenoidal transclival operation. *J Neurosurg* 1990; 72(5): 824–828.
- Shapiro SA, Scully T. Closed continuous drainage of cerebrospinal fluid via a lumbar subarachnoid catheter for treatment or prevention of cranial/spinal cerebrospinal fluid fistula. *Neurosurgery* 1992; 30(2): 241–245.
- Raquet F, Mann WJ. Lumbar cerebrospinal fluid drainage for prevention of CSF fistula. *H.N.O* 1993; 41(7): 335–338.
- Kelly DF, Oskouiian RJ et al. Collagen sponge repair of small CSF leaks obviates tissue graft and CSF diversion after pituitary surgery. *Neurosurgery* 2001; 49(4): 885–890.
- Haran RP, Chandy MJ. Symptomatic pneumocephalus following transsphenoidal surgery. *Surg Neurol* 1997; 48(6): 575–578.
- Costantino PD et al. Sphenoethmoidal cerebrospinal fluid leak repair with hydroxyapatite cement. *Arch Otolaryngol Head Neck Surg* 2001; 127(5): 588–593.
- Cappabianca P, Cavallo LM et al. Easy sellar reconstruction in endoscopic endonasal transsphenoidal surgery with polyester silicone dural substitute and fibrin glue. *Neurosurgery* 2001; 49(2): 473–475.
- Raanaani E, Latter DA, Errett LE, Bonneau DB, Leclerc Y, Salasidis GC. Use of “Bioglué” in aortic surgical repair. *Ann Thor Surg* 2001; 72: 638–640.

16. Hewitt CW, Marra SW, Kann BR, Tran HS, Puc MM, Chrzanowski FA, Tran JLV, Lenz SD, Cilley JH, Simonetti VA, DelRossi AJ. Biogluce surgical adhesive for thoracic aortic repair during coagulopathy: efficacy and histopathology. *Ann Thor Surg* 2001; 71: 609–612.
17. Westaby S, Saito S, Katsumata T. Acute type a dissection: conservative methods provide consistently low mortality. *Ann Thor Surg* 2002; 73: 707–713.
18. Kobayashi S, Sugita K, Matsuo K, Inoue T. Reconstruction of the sellar floor during transsphenoidal operations using alumina ceramica. *Surg Neurol* 1980; 15: 196–197.
19. Hudgin WR, Raney LA, Young SW. Sachson: Failure of intrasellar muscle implant to prevent recurrent downwards migration of the optic chiasm. *Neurosurgery* 1981; 8: 231–232.
20. Garcia-Uria J, Carrillo R, Serrano P, Bravo G. Empty sella and rhinorrhea: a report of eight treated cases. *J Neurosurg* 1979; 50: 466–471.
21. Cabezudo JM, Carrillo R, Vaquero J, Areitio E, Martinez R. Intracavernous aneurysm of the carotid artery following transsphenoidal surgery. *J Neurosurg* 1981; 54: 118–121.
22. Schlag MG, Hopf R, Redl H. Convulsive seizure following subdural application of fibrin sealant containing tranexamic acid in a rat model. *Neurosurgery* 2000; 47: 1463–1467.
23. Wilkins RH, Rengachary SS. *Neurosurgery: Complications of Trans-sphenoidal Surgery for Acromegaly*, pp. 1319; *Nonsecretory Pituitary Adenomas – Complications of Surgery*, pp. 1325, Second edn. Vol. 1.
24. Welbourn: Evolution of trans-sphenoidal microsurgery. *Surgery* 1986; 100: 1185–1190.
25. Wilson CB, Dempsey LC. Transsphenoidal microsurgical removal of 250 pituitary adenomas. *J Neurosurg* 1978; 48: 13–22.