



Application of a Thrombin-Gelatin Matrix in the Management of Intractable Hemorrhage During Stereotactic Biopsy

Cristian de Quintana-Schmidt, Andreas Leidinger, Joan Molet Teixidó, Gerardo Conesa Bertrán

■ **BACKGROUND:** Few studies have been published about percutaneous techniques for management of surgical bed hemorrhage during a stereotactic biopsy, a serious complication that may affect patient outcome. We describe the injection of a thrombin-gelatin matrix through the biopsy cannula as an effective method to arrest surgical bed bleeding that does not respond to conventional methods of hemostasis.

■ **METHODS:** We prospectively documented image-guided stereotactic brain biopsy procedures in 30 awake patients between July 2014 and July 2017 at our center. Among patients presenting with intractable surgical bed bleeding, a thrombin-gelatin matrix injection through the biopsy cannula was performed. Details of the injection technique, surgical outcome, and complications were recorded.

■ **RESULTS:** Among 30 documented stereotactic brain biopsies, 3 (10%) had intractable surgical bed bleeding during the procedure. In all 3 cases, thrombin-gelatin matrix was injected, and an immediate arrest of hemorrhage was achieved. None of the patients required a craniotomy or further invasive measure to achieve hemostasis. No postoperative complications were recorded.

■ **CONCLUSIONS:** Our preliminary results suggest that thrombin-gelatin matrix injection is a simple, safe, and effective stereotactic practice to manage persistent surgical bed bleeding that cannot be arrested by standard, conventional hemostatic methods.

INTRODUCTION

Hemorrhage of the surgical trajectory and surgical bed of a stereotactic brain biopsy (SBB) is clinically seen in 0.3%–8.6% of all cases, depending on the methodology chosen.^{1–4} Although this complication is frequently described, there is no gold standard concerning its intraoperative management. Traditionally, treatment of intraoperative bleeding during SBB includes irrigation with temperate saline solution through the biopsy cannula, favorable positioning of the headrest of the surgical table, and controlled intraoperative systemic hypotension. Intraoperative management of profuse arterial bleeding may be challenging during SBBs. The limited working channel and absence of direct visualization of the bleeding vessel often lead many neurosurgeons to convert the procedure to open craniotomy and coagulate the vessel under microscopic visualization and/or evacuate the associated hematoma. Some authors have described percutaneous techniques based on on-site compression or the use of hemostatic agents with favorable results.^{4–6} Their objectives were to describe effective techniques in the management of intractable bleeding during SBB that would avoid higher comorbidities associated with a higher surgical invasiveness and longer surgical times.

Thrombin-gelatin matrix (TGM) has been commonly used in general neurosurgical practice for several years,^{7,8} but, to our knowledge, no reports have been published concerning its use in management of surgical bed hemorrhage during SBB. The main objective of this study was to present our experience applying TGM injections through the biopsy cannula as an effective measure in the management of intractable surgical bed bleeding during SBB.

MATERIALS AND METHODS

We prospectively collected data from consecutive SBBs performed at our center from July 2014 until July 2017. All

Key words

- Complication
- Floseal
- Intractable hemorrhage
- Intraoperative hemorrhage
- Management hemorrhage
- Stereotactic brain biopsy
- Thrombin-gelatin matrix

Abbreviations and Acronyms

- CT:** Computed tomography
SBB: Stereotactic brain biopsy
TGM: Thrombin-gelatin matrix

Department of Neurosurgery, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

To whom correspondence should be addressed: Cristian de Quintana-Schmidt, M.D., Ph.D.
[E-mail: cquintana@santpau.cat]

Citation: *World Neurosurg.* (2019) 121:180–185.

<https://doi.org/10.1016/j.wneu.2018.10.053>

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

1878-8750/\$ - see front matter © 2018 Elsevier Inc. All rights reserved.

procedures were performed on awake patients. General demographic variables were collected. All complications were documented and tumor histology was assessed by a specialized pathologist at our center and recorded in our study.

Patient Selection

Among all patients who underwent awake SBB, patients presenting with intraoperative surgical bed bleeding were managed according to standardized recommendations: temperate saline solution was administered, relative hypotension was induced, and headrest was slightly elevated. Hemorrhages not responding to these measures were considered intractable, and TGM injection was applied through the biopsy cannula on all patients. No patient was excluded from the study.

Technique

All SBBs were performed by the main author (C.Q.-S.). All procedures were conducted on awake patients using a Sedan Side-Cutting 2.1-mm gauge biopsy cannula (Elekta AB, Stockholm, Sweden) with a 10-mm cutting window. All procedures were planned using StealthStation 7 Framelink software Version 5.4.1 (Medtronic, Minneapolis, Minnesota, USA) and were performed using a Leksell Stereotactic System (Elekta AB). All patients presenting with intractable hemorrhage received intraoperative TGM injection.

The description of the proposed technique is as follows: Without detaching the biopsy cannula from the trajectory stem and keeping the locking ring closed, the cutting stylet is removed. Profuse arterial bleeding may flow through the proximal end of the biopsy cannula during this phase. The cutting stylet is attached to a syringe of TGM (FloSeal; Baxter Healthcare Corp., Deerfield, Illinois, USA), and the TGM is pushed until reaching the cutting window (**Figure 1A**).

The cutting stylet is then reintroduced through the biopsy cannula. The cutting window is kept open, and up to 1–2 mL of TGM is injected into the surgical bed until significant

resistance is perceived by the surgeon (**Figure 1B**). It is important to consider the location of the biopsy because the infusion of TGM will cause a temporary increase in pressure in the zone (e.g., brainstem). The cutting window is closed, and the cutting stylet is kept inside the biopsy cannula for 5 minutes as per the manufacturer's recommendations. After 5 minutes, the cutting window is reopened, the stylet is removed from the biopsy cannula, and profuse irrigation with temperate saline solution is recommended until clear liquid without remnants of TGM.

The biopsy cannula is carefully removed from the surgical bed, and further irrigation is performed through the burr hole into the trajectory of the cannula. If the hemorrhage was successfully arrested, standard closure follows. We obtained an immediate control computed tomography (CT) scan in all patients presenting with hemorrhage who received a TGM injection during SBB.

Follow-Up

An early postoperative brain CT scan was obtained in all patients (within the first 24 hours after undergoing SBB). Neurologic status was recorded until discharge, and complications were recorded until the first monthly follow-up visit.

RESULTS

We prospectively collected data on 30 patients. Mean age was 61.8 ± 11.9 years, and 56.7% of patients were men and 43.3% were women. **Table 1** presents general demographics and clinical characteristics of all recorded patients.

During our study, 5 patients (16.7%) presented with intraoperative surgical bed bleeding, assessed by exit of blood through the proximal end of the biopsy cannula during the procedure. Two patients responded to irrigation with temperate saline solution and controlled hypotension achieving hemostasis within a few minutes. The 3 remaining patients (10% of all patients) presented with profuse arterial bleeding through the biopsy cannula, defined by the surgeon as intractable, and TGM

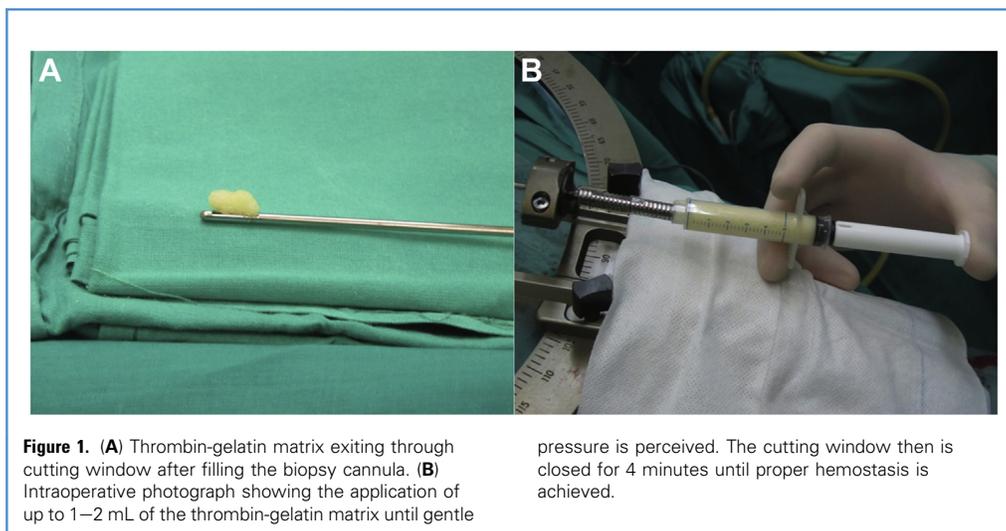


Table 1. General Characteristics and Demographics

Characteristic	Value
Total patients	30
Sex, M/F	17 (56.7%)/13 (43.3%)
Mean age, years (SD)	61.8 (11.9)
Risk factors	
Systemic hypertension	14 (46.6%)
Dyslipidemia	5 (16.6%)
Antiaggregant/anticoagulant treatment before intervention	4 (13%)
Type 2 diabetes	3 (10%)
Previous heart disease	3 (10%)
Human immunodeficiency virus	1 (3.3%)
Enolism	1 (3.3%)
Localization	
Left/right/bilateral	15 (50%)/9 (30%)/6 (20%)
Multilobar	12 (40%)
Basal ganglia	11 (36.7%)
Callosal (butterfly pattern)	5 (16.6%)
Insular	2 (6.7%)
Histologic diagnosis	
Grade IV glioma	20 (66.7%)
Diffuse glioma	5 (16.6%)
Grade III astrocytoma	2 (6.7%)
Lymphoma	2 (6.7%)
Reactive gliosis	1 (3.3%)
Complications	
Intraoperative seizures	1 (3.3%)
Intraoperative hemorrhage	5 (16.6%)
Intractable hemorrhage	3 (10%)

M, male; F, female.

injection was performed in all 3 patients. Immediate hemostasis was achieved in all 3 patients receiving TGM injection (100%). **Table 2** summarizes the 3 cases treated with TGM injection.

No immediate complications were reported after this technique. During the acute phase of intractable bleeding, 2 patients presented with a temporary decrease in consciousness level, which resolved after achieving hemostasis with complete recovery and no enduring consequences. All patients received immediate postoperative CT scans. Radiologic findings suggest arrest of surgical bed bleeding in all 3 cases (**Figures 2–4**). All patients were discharged within 48 hours after the control CT scan. At follow-up, no complications were associated with the use of TGM in the management of surgical bed bleeding.

DISCUSSION

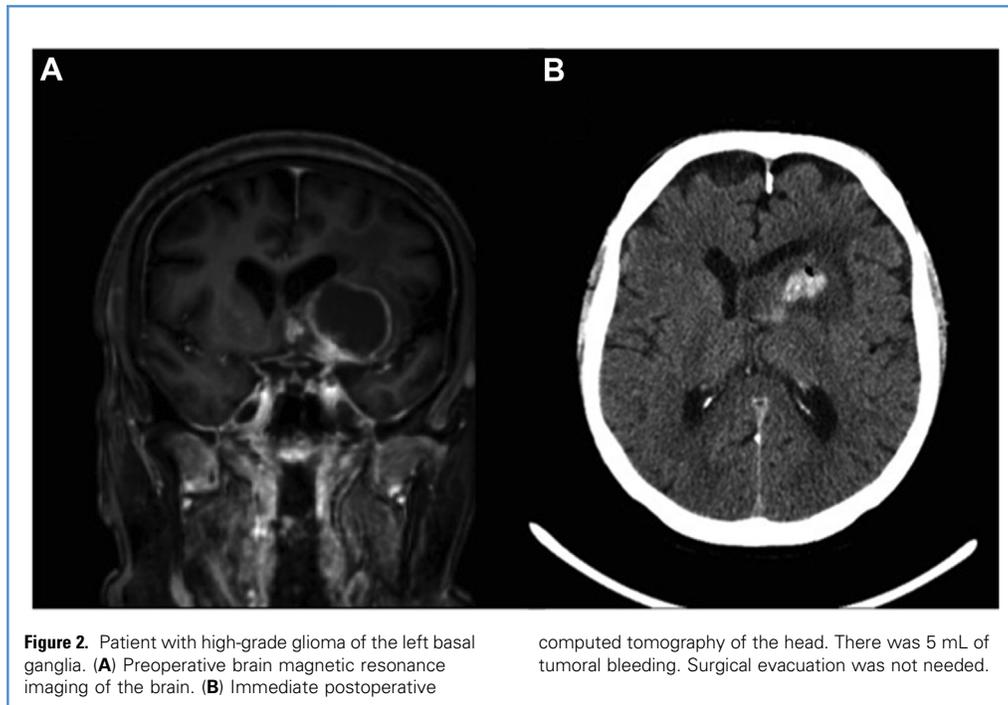
The prevalence of bleeding during SBB is 0.3%–8.6%,^{1-5,9,10} and achieving hemostasis requires an open craniotomy in 0.8%–2.7% of all patients.^{1,2} Classically, treatment of intraoperative bleeding during SBB includes irrigation with temperate saline solution through the biopsy cannula, favorable positioning of the headrest of the surgical table, and controlled intraoperative systemic hypotension. However, arterial bleeding may be difficult to manage during surgery, as hemostasis is difficult to attain with these methods, sometimes requiring craniotomy and coagulation of the bleeding vessel under direct visualization.¹¹ The need for an urgent craniotomy to control this type of intractable hemorrhage carries further risks, such as intracranial hypertension, unnecessary trauma and laceration of healthy brain parenchyma, increased infection rates, and prolonged hospital stay.^{6,11}

A few reports describe percutaneous techniques for controlling intraoperative arterial bleeding. Kutlay et al.⁴ described a fluoroscopically guided procedure consisting of a Fogarty catheter filled with contrast solution through the biopsy cannula to achieve mechanical control of any bleeding on the surgical site. Chimowitz et al.⁵ published 3 cases in which thrombin was injected through the biopsy cannula. Although bleeding stopped immediately in all 3 cases, 1 patient presented with diffuse vasospasm and bihemispheric cerebellar infarction 48 hours after the intervention with severe neurologic sequelae during follow-up. The authors concluded that the thrombin gel controlled the bleeding effectively, but that it could be associated with diffuse brain vasospasm.^{5,12}

Table 2. Patients Requiring Thrombin-Gelatin Matrix Injection (n = 3)

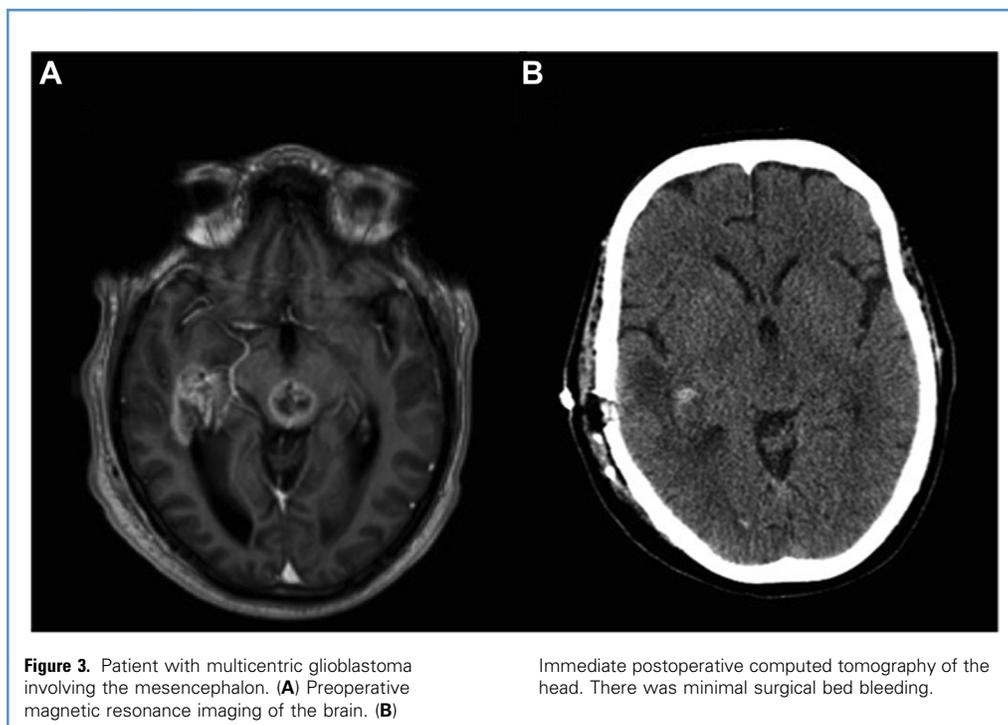
Case	Age (Years)/ Sex	Prior History	Biopsy Site	Histologic Diagnosis	Hemostasis After TGM	Complications After 48 Hours Follow-Up
1	57/M	Systemic hypertension	Left caudate nucleus	High-grade astrocytoma	Yes	None
2	50/M	Systemic hypertension, enolism	Bithalamic, mesencephalon, right temporal	Multicentric high-grade astrocytoma	Yes	None
3	79/M	None	Left temporal	High-grade astrocytoma	Yes	None

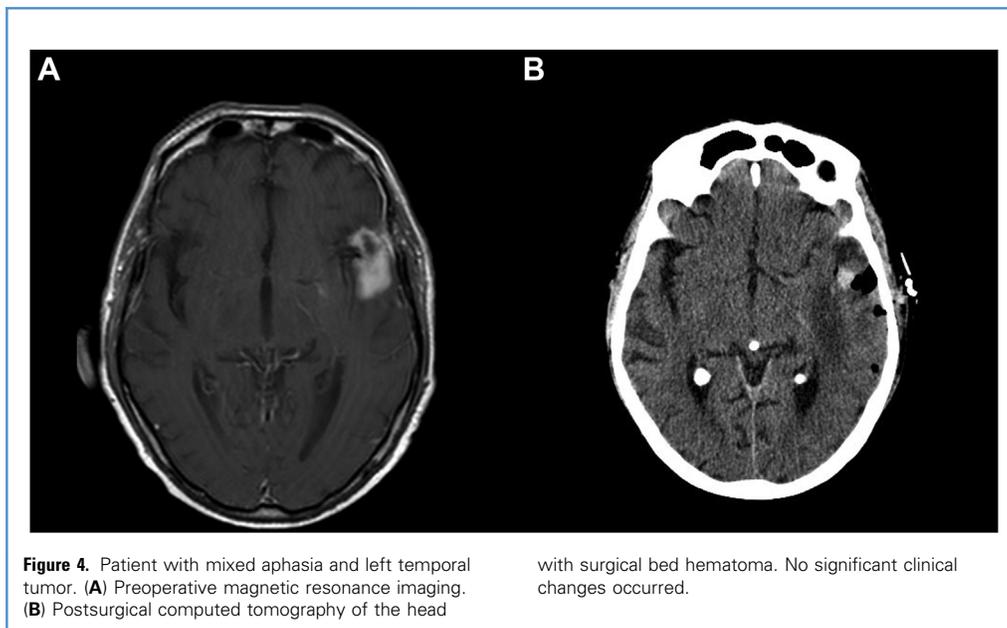
TGM, thrombin-gelatin matrix; M, male.



In contrast to thrombin gel injections, TGM (FloSeal) is a mixture of gelatin and bovine thrombin that is prepared intraoperatively. The gelatin matrix gains up to 20% of its original volume when in contact with body fluids and molds to fit the cavity where

injected.⁷ The clinical safety and biocompatibility of the direct application of TGM over diverse nervous tissues has been demonstrated in preclinical trials, and the U.S. Food and Drug Administration has approved its use. Its usefulness has been





described in spine surgery, craniotomies, and hypophyseal transsphenoidal surgery.^{7,8,13-15}

There are preclinical reports of the worsening of parenchymal edema after increasing the local concentration of thrombin.⁸ We believe that after achieving hemostasis, thorough rinsing may help decrease local concentrations of thrombin. In our experience, no patients experienced such a tissue reaction on postoperative CT scans or clinical assessment. Furthermore, to our knowledge, no reports have been published concerning vasospasm secondary to the use of TGMs.

We believe that the success of TGM injection is based on 2 factors. First, volume expansion of TGM within the surgical bed

plays a mechanical role in arresting the hemorrhage, as per the balloon compression method described by Kutlay et al.⁴ Second, the hemostatic effect of TGM, which promotes clot formation, contributes to achieving hemostasis. We think that the use of TGM may carry the benefits of both described techniques, with less associated morbidity.

CONCLUSIONS

In our experience, TGM injection is a simple, fast, and effective technique to control uncontrollable intraoperative bleeding during SBB. Further studies with larger sample sizes are needed to analyze the true effectiveness of this technique.

REFERENCES

1. Apuzzo MLJ, Chandrasoma PT, Cohen D, Zee CS, Zelman V. Computed imaging stereotaxy (experience and perspective related to 500 procedures applied to brain masses). *Neurosurgery*. 1987;20:930-937.
2. Ben-Haim S, Asaad WF, Gale JT, Eskandar EN. Risk factors for hemorrhage during microelectrode-guided deep brain stimulation and the introduction of an improved microelectrode design. *Neurosurgery*. 2009;64:754-763.
3. Binder DK, Rau GM, Starr PA. Risk factors for hemorrhage during microelectrode-guided deep brain stimulator implantation for movement disorders. *Neurosurgery*. 2005;56:722-732.
4. Kutlay M, Simşek H, Colak A, Demircan MN. Balloon compression technique in the management of persistent intraoperative intratumoral hemorrhage resulting from stereotactic biopsy: technical note. *Neurosurgery*. 2010;66(6 Suppl Operative):334-335.
5. Chimowitz MI, Barnett GH, Palmer J. Treatment of intractable arterial hemorrhage during stereotactic brain biopsy with thrombin. Report of three patients. *J Neurosurg*. 1991;74:301-303.
6. Zrinzo L, Foltyniec T, Limousin P, Hariz MI. Reducing hemorrhagic complications in functional neurosurgery: a large case series and systematic literature review. *J Neurosurg*. 2012;116:84-94.
7. Gazzeri R, Galarza M, Neroni M, Alfieri A, Giordano M. Hemostatic matrix sealant in neurosurgery: a clinical and imaging study. *Acta Neurochir (Wien)*. 2011;153:148-154 [discussion: 155].
8. Renkes KL, Payner TD, Leipzig TJ, Feuer H, Morone MA, Koers JM, et al. A multicenter, prospective, randomized trial evaluating a new hemostatic agent for spinal surgery. *Spine (Phila Pa 1976)*. 2001;26:15.
9. Bernstein M, Parrent AG. Complications of CT-guided stereotactic biopsy of intra-axial brain lesions. *J Neurosurg*. 1994;81:165-168.
10. Chan KH, Mann KS, Chan TK. The significance of thrombocytopenia in the development of postoperative intracranial hematoma. *J Neurosurg*. 1989;71:38-41.
11. Field M, Witham TF, Flickinger JC, Kondziolka D, Lunsford LD. Comprehensive assessment of hemorrhage risks and outcomes after stereotactic brain biopsy. *J Neurosurg*. 2001;94:545-551.
12. White RP, Robertson IT. Role of plasmin, thrombin, and antithrombin III as etiological

- factors in delayed cerebral vasospasm. *Neurosurgery*. 1985;16:27-35.
13. Lapierre F. Les agents hémostatiques locaux en neurochirurgie: note technique. *Neurochirurgie*. 2009;55:40-44.
 14. Ellegala DB, Maartens NF, Laws ER. Use of Floseal hemostatic sealant in transsphenoidal pituitary surgery: technical note. *Neurosurgery*. 2002; 51:513-516.
 15. Gazzeri R, Galarza M, Neroni M, Alfieri A, Esposito S. Minimal craniotomy and matrix hemostatic sealant for the treatment of spontaneous supratentorial intracerebral hemorrhage: technical note. *J Neurosurg*. 2009;110:939-942.

Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received 29 July 2018; accepted 7 October 2018

Citation: *World Neurosurg.* (2019) 121:180-185.
<https://doi.org/10.1016/j.wneu.2018.10.053>

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

1878-8750/\$ - see front matter © 2018 Elsevier Inc. All rights reserved.