



A Comparative Efficacy Evaluation of Recombinant Topical Thrombin (RECOTHROM[®]) With A Gelatin Sponge Carrier Versus Topical Oxidized Regenerated Cellulose (TABOTAMP[®]/SURGICEL[®]) In A Porcine Liver Bleeding Model

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A Comparative Efficacy Evaluation of Recombinant Topical Thrombin (RECOTHROM[®]) With A Gelatin Sponge Carrier Versus Topical Oxidized Regenerated Cellulose (TABOTAMP[®]/SURGICEL[®]) In A Porcine Liver Bleeding Model

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ABSTRACT

Purpose: Topical hemostatic agents can be classified as active or passive. This study compared the hemostatic efficacy of an active agent, recombinant thrombin (RECOTHROM[®] [rT]) plus gelatin sponge carrier versus a passive agent, oxidized regenerated cellulose (TABOTAMP[®]/SURGICEL[®] [ORC]), in a porcine liver abrasion model.

Materials and Methods: Eight pigs were used, four of them were heparinized. A total of 80 liver lesions were created, 40 of them in heparinized pigs. Lesions were treated with rT plus gelatin sponge or ORC. Bleeding rate was quantified before treatment by applying pre-weighed gauze. Time to hemostasis was assessed visually for 10 minutes.

Results: Seven of the 80 lesions were excluded for having initial bleeding rates exceeding the target of 10 g/min. Sixteen and 20 lesions were treated with rT plus gelatin sponge and 19 and 18 lesions were treated with ORC, in non-heparinized and heparinized animals, respectively. Time to hemostasis (median [IQR]) was significantly shorter with rT plus gelatin sponge (30 [30,30] seconds) in heparinized and non-heparinized animals versus ORC in non-heparinized (180 [120,210] seconds) and heparinized animals (215 [135,345] seconds); $P < 0.0001$ for both comparisons. In heparinized animals, ORC took longer to achieve hemostasis, with treatment failure in 2/18 lesions. Time to hemostasis with ORC was longer for lesions in heparinized animals with initial bleeding rates of >5 – 10 g/min (285 [225,394] seconds) versus ≤ 5 g/min (175 [108,290] seconds).

Conclusions: In this model, rT plus gelatin sponge carrier (active) was a more effective hemostat than ORC (passive) in both heparinized and non-heparinized animals.

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Animal model; hemostasis; Recothrom; surgical bleeding; Tabotamp Original; Surgicel Original

Introduction

Management of bleeding during surgery is important for reducing the risk of complications which can lead to increased morbidity and mortality.¹ Major bleeding often necessitates blood product transfusion which is associated with potential adverse events and significant costs.^{2–4} Incidence and severity of surgical bleeding can be minimized to some degree by optimizing the surgical technique used.^{5,6} However, patients with coagulopathy (either prior to, or developed during surgery) are at much greater risk of experiencing bleeding complications, regardless of surgical technique.^{7,8}

Topical hemostatic agents can be used to supplement coagulation and prevent or control bleeding. Time to hemostasis is an important efficacy measure for hemostatic agents, as shorter times not only result in better clinical outcomes^{4,9} but also save hospital resources in terms of reduced blood product use,⁴ reduced operating times,¹⁰ shorter duration of

hospital stay⁹ and reduced likelihood of needing to apply additional hemostatic agents.⁴ A variety of hemostatic agents are available, with oxidized regenerated cellulose (ORC) being one of the most widely used.¹¹ However, the efficacy of ORC is reduced in patients with coagulopathy and may therefore be an inappropriate choice of hemostat when treating these patients.¹²

Hemostatic agents can be broadly characterized as active or passive based on their mechanism of action (MoA). Active hemostatic agents, such as thrombin (stand-alone or combined with gelatin), fibrin sealants and advanced patches act biologically at the end of the coagulation cascade, accelerating the natural clotting process, and are effective regardless of whether patients have received anticoagulants or antiplatelet therapies, or not.^{13–15} This is due to their MoA, which is effective independently of the state of the coagulation cascade. Active hemostatic agents are also effective over a broader range of bleeding rates than passive agents.¹⁴ As a

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Table 1. The validated intraoperative bleeding scale (ViBe SCALE).

Grade	Visual presentation	Anatomic appearance	Qualitative description	Visually estimated rate of blood loss (mL/min)
0	No bleeding	No bleeding	No bleeding	≤1.0
1	Ooze or intermittent flow	Capillary-like bleeding	Mild	>1.0–5.0
2	Continuous flow	Venule and arteriolar-like bleeding	Moderate	>5.0–10.0
3	Controllable spurting and/or overwhelming flow	Noncentral venous- and arterial-like bleeding	Severe	>10.0–50.0
4	Unidentified or inaccessible spurting or gush	Central arterial- or venous-like bleeding	Life threatening*	>50.0

*Systemic resuscitation is required (e.g., volume expanders, vasopressors, blood products, etc.).

The scale is designed and validated for use in clinical studies to generate labeling claims. The scale is a Likert-type scale, in which the user assigns a grade based on the overall agreement of the items listed.

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result of this broad range of efficacy, active hemostatic agents can be a more cost-effective option in some patients by lowering risk of requiring additional treatment due to hemostatic failure and shorter operative and recovery times.^{4,14} Passive hemostatic agents, such as collagens, cellulose, gelatins and polysaccharide sphere powder work via contact activation and promote platelet aggregation by providing a structure to assist platelet aggregation and clot formation.^{13–16} As their MoA is dependent on an intact or functioning coagulation cascade, the efficacy of passive agents is reduced in patients treated with anticoagulant or antiplatelet medications, or in those with other coagulation disorders.

Comparison of the efficacy of hemostatic agents used in routine surgery is important for providing evidence to guide clinical practice. The Validated Intraoperative Bleeding Scale (ViBe SCALE)¹⁷ has been developed for studies of hemostatic agents, and can also be used to assess the severity of bleeding during surgery and guide the choice of hemostatic technique or agent. This scale classifies bleeding into 5 grades (ranging from 0: No bleed, to 4: Life threatening) and aligns the rate of blood flow with the appearance of the bleed, as shown in Table 1. Active hemostatic agents are effective in a wider range of bleeding grades than passive agents, with passive agents being limited to mild or moderate bleeding rates.^{13,14} The aim of this study was to compare an active hemostatic agent, recombinant thrombin (rT; RECOTHROM[®]), with a passive agent, oxidized regenerated cellulose (ORC; TABOTAMP[®]/SURGICEL[®]) for ViBe SCALE grade 1–2 bleeds using a porcine liver abrasion model.

Materials and methods

The porcine liver abrasion model was chosen as it is an established method for assessing the efficacy of hemostats on mild to moderate (ViBe SCALE grade 1–2) bleeds.^{18,19} An animal experiment permit was issued by the municipal government of Vienna and all experimental methods are consistent with the Guide for the Care and Use of Laboratory Animals of the National Institute of Health.²⁰

Two treatment arms were investigated. The rT (active treatment) used was RECOTHROM[®]; Baxter Healthcare Corporation, Deerfield, IL, USA, with a gelatin sponge carrier (SPONGOSTANTM; Ethicon, Norderstedt, Germany). The ORC (passive treatment) used was TABOTAMP[®]

Original/SURGICEL[®] Original; Ethicon, Norderstedt, Germany. Treatments were tested in 8 male pigs weighing approximately 35 kg, with a target of 15 applications per animal. Premedication and anesthesia were performed as previously described.²¹ Briefly, animals were premedicated with a combination of tiletamine and zolazepam intramuscularly, followed by inhalation anesthesia with isoflurane. Upon completion of the experiment, animals were humanely euthanized under deep anesthesia with a lethal intravenous dose of thiopental sodium and embutramide/mebezonium iodine/tetracaine hydrochloride.

Surgical procedure

Animals were placed in dorsal recumbency. After surgical preparation of the carotid artery and jugular vein, these vessels were cannulated for blood pressure monitoring and intravenous access. A urinary catheter was inserted into the bladder after preparation. A median laparotomy was performed and the liver was exposed. Half of the animals (N=4) were heparinized with 1000 IU/mL sodium heparin (Gilvasan Pharma, Vienna, Austria) to obtain an activated clotting time 1.5–2.5 fold of the initial measurement. These animals were heparinized for the duration of the investigation and activated clotting time was measured approximately every 60 minutes, with heparin being re-administered as needed.

Circular lesions of about 1.8 cm in diameter and 2 mm in depth were created on the liver surface using a grinding disc. Initial blood loss was quantified as described below, and lesions were excluded from the study if the bleeding rate was >10 mL/min. Treatments were allocated to lesions in an alternating pattern in each animal (ABAB, etc.), with 20 applications in heparinized plus 20 applications in non-heparinized animals per treatment. The rT plus gelatin sponge carrier and ORC treatments were prepared and applied according to the Prescribing Information²² or Instructions for Use.^{23,24} Each sheet of gelatin sponge carrier (supplied as 7 × 5 cm) was cut to approximately 3.5 × 3.5 cm before treating with rT solution. Each sheet of ORC (supplied as 7.5 × 5 cm) was cut to approximately 4 × 4 cm and an additional layer of ORC was added after every evaluation of hemostatic effect, up to a maximum of 3 layers or until hemostasis was achieved.

Table 2. Initial bleeding rates in non-heparinized and heparinized animals.

All lesions with initial bleeding rates ≤ 10 g/min	Without heparin		With heparin	
	rT + gelatin sponge carrier	ORC	rT + gelatin sponge carrier	ORC
Mean \pm standard deviation	3.069 \pm 1.928	3.140 \pm 2.236	3.649 \pm 1.810	4.326 \pm 1.885
Median [interquartile range]	2.66 [1.90–3.44]	2.60 [1.72–4.04]	3.03 [2.46–4.42]	4.19 [2.57–5.99]
Number of valid applications (n)	16	19	20	18

ORC, oxidized regenerated cellulose; rT, recombinant thrombin.

All data are g/min unless specified otherwise. Bleeding rates >10 g/min were excluded.

Assessment of bleeding and quantification of blood loss

Initial bleeding rates were assessed by measuring the amount of blood absorbed by a pre-weighed gauze (measuring 5×5 cm) in 6 seconds, and the bleeding rate in grams of blood per minute was calculated. Initial bleeding grades were also visually assessed using the VIBe SCALE (Table 1). All lesions with initial bleeding rates greater than the target of 10 g/min (i.e., $>$ grade 2 VIBe SCALE) were excluded from the study.

Once the hemostatic agent had been applied to the lesion, residual bleeding rates and time to hemostasis were assessed by application of fresh dry gauze over the hemostatic agent for 30 seconds followed by careful removal of the gauze and visual assessment of bleeding through and around the hemostatic agent for up to 1 minute. Hemostasis was defined as the absence of observable active bleeding or the absence of sustained soaking of blood into the hemostatic material within the observation period of 1 minute. In the case of bleeding during that period, fresh gauze was re-applied immediately for 30 seconds followed by another minute of observation. This was repeated for up to 10 minutes, or until hemostasis was achieved, whichever came first. A treatment was regarded as a failure if hemostasis was not achieved within 10 minutes.

Histology

Samples were prepared and stained as described previously.²¹ Briefly, tissue samples were harvested *postmortem*, fixed in formalin and stained with Martius, Scarlet and Blue (MSB) for microscopic assessment.

Statistics

Bleeding rates were reported as median values with interquartile range (IQR) and mean values with standard deviation (SD). For consistency with the VIBe SCALE, all bleeding rates were reported in g/min which corresponds to mL/min due to the close similarity in the density of blood and water.²⁵ All statistical comparisons were performed using the Mann-Whitney test. GraphPad Prism (version 8.2.0 for Windows, GraphPad Software, San Diego, CA, USA) was used to conduct the statistical analyses.

Results

Initial bleeding rates

The mean initial bleeding rate was 3.485 ± 2.388 g/min in the non-heparinized animals and 3.975 ± 1.865 g/min in the

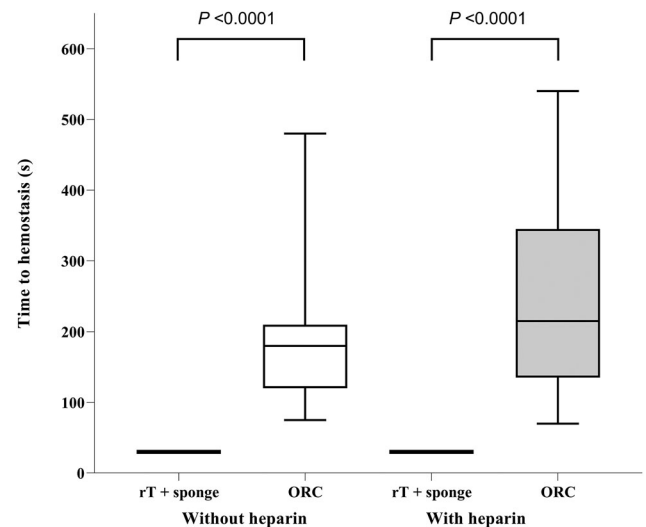


Figure 1. Comparison of time to hemostasis – all initial bleeding rates within intended range (≤ 10 g/min).

ORC, oxidized regenerated cellulose; rT, recombinant thrombin. Horizontal line and box represent the median and interquartile ranges; error bars represent maximum/minimum values.

heparinized animals. Initial bleeding rates by treatment group and heparin status are shown in Table 2. There was no significant difference in initial bleeding rates between treatment groups or heparinization status. A total of 7 out of 80 lesions were excluded as they had an initial bleeding rate >10 g/min (i.e., $>$ grade 2 VIBe SCALE).

Time to hemostasis

All lesions with initial bleeding rates within intended range (≤ 10 g/min)

Time to hemostasis for all included lesions is shown in Figure 1 and Table 3. In lesions treated with rT and gelatin sponge carrier, all bleeding stopped within the first 30 seconds in both non-heparinized and heparinized animals (16 and 20 applications, respectively), with no treatment failures. With ORC, hemostasis was achieved in all non-heparinized lesions but there were 2 failures out of 18 ORC-treated lesions (11.1%) in heparinized animals (Table 3). The 2 failed applications were not accounted for in the time to hemostasis for ORC in heparinized animals.

The mean time to hemostasis in the ORC treatment group was 200 ± 107 seconds (median 180 [120, 210] seconds) in non-heparinized animals (19 applications) and mean 248 ± 145 (median 215 [135, 345] seconds) in heparinized animals (16 applications). Time to hemostasis was significantly shorter with rT plus gelatin sponge carrier (median 30 [30, 30] seconds) versus the ORC group, both in heparinized and

Table 3. Time to hemostasis and number of applications by treatment in non-heparinized and heparinized animals.

	Without heparin		With heparin	
	rT + gelatin sponge carrier	ORC	rT + gelatin sponge carrier	ORC
All lesions with initial bleeding rates ≤ 10 g/min				
Mean \pm standard deviation	30 \pm 0	200 \pm 107	30 \pm 0	248 \pm 145
Median [interquartile range]	30 [30, 30]	180 [120, 210]	30 [30, 30]	215 [135, 345]
Number of effective applications (n)	16	19	20	16
Number of failures (n)	0	0	0	2
Sub-set of lesions with initial bleeding rates ≤ 5 g/min				
Mean \pm standard deviation	30 \pm 0	203 \pm 117	30 \pm 0	215 \pm 156
Median [interquartile range]	30 [30–30]	188 [105–263]	30 [30–30]	175 [108–290]
Number of effective applications (n)	15	16	17	10
Number of failures (n)	0	0	0	1
Sub-set of lesions with initial bleeding rates >5 –10 g/min				
Mean \pm standard deviation	30	185 \pm 9	30 \pm 0	304 \pm 116
Median [interquartile range]	– [180–195]	180 [30–30]	30 [225–394]	285
Number of effective applications (n)	1	3	3	6
Number of failures (n)	0	0	0	1

ORC, oxidized regenerated cellulose; rT, recombinant thrombin.

All data are time in seconds unless specified otherwise.

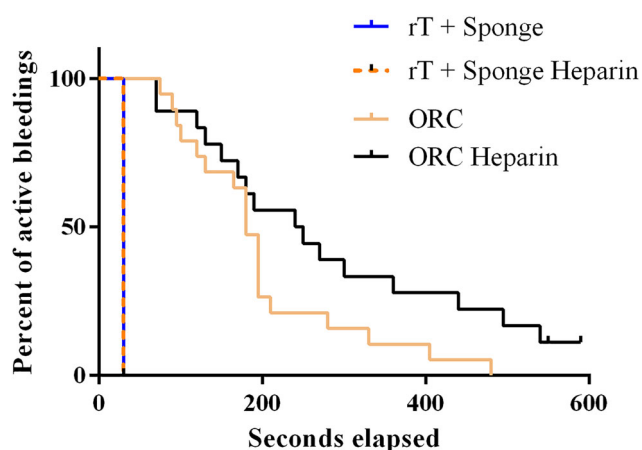


Figure 2. Proportion of active bleeding events over time – all initial bleeding rates within intended range (≤ 10 g/min).

ORC, oxidized regenerated cellulose; rT, recombinant thrombin.

non-heparinized animals ($P < 0.0001$ for both comparisons). For lesions where hemostasis was achieved with ORC, an average of 3 layers was required. Heparinization did not significantly affect time to hemostasis in either treatment group versus non-heparinized lesions in successful applications of ORC. However, as mentioned above, the 2 failed applications with ORC in heparinized animals were not included when calculating time to hemostasis.

The proportion of active bleeding events over time for each treatment group is shown in Figure 2. The plots for rT plus gelatin sponge carrier are identical regardless of whether the applications were in heparinized or non-heparinized animals. Conversely in the ORC group, there is a clear reduction in efficacy in heparinized animals, where more than 50% of lesions still had active bleeding at 200 seconds compared with approximately 25% of lesions in non-heparinized animals.

Lesions with initial bleeding rates ≤ 5 g/min (VIBe SCALE grade 1) versus >5 –10 g/min (VIBe SCALE grade 2)

A sub-analysis distinguished between an initial bleeding rate ≤ 5 g/min (VIBe SCALE grade 1) and an initial bleeding rate

>5 –10 g/min (VIBe SCALE grade 2). Hemostasis was achieved within 30 seconds regardless of initial bleeding rate or presence or absence of heparin for all lesions treated with rT and gelatin sponge carrier (Figures 3A and 3B). In the ORC group, time to hemostasis in non-heparinized animals with initial bleeding rates ≤ 5 g/min (VIBe SCALE grade 1; 16 applications) was comparable with non-heparinized animals with initial bleeding rates >5 –10 g/min (VIBe SCALE grade 2; 3 applications); durations of 203 ± 117 and 185 ± 9 seconds, respectively; $P = 0.9742$. In heparinized animals, however, mean time to hemostasis with ORC was numerically longer for lesions with initial bleeding rates of >5 –10 g/min (304 ± 116 seconds; 6 applications) versus ≤ 5 g/min (215 ± 156 seconds; 10 applications), although this difference did not reach statistical significance ($P = 0.1130$). The mean number of layers of ORC required to achieve hemostasis was increased non-significantly from 2.6 to 3 in lesions with initial bleeding rates ≤ 5 g/min versus >5 –10 g/min.

Visual and histologic observations

A representative photograph of each treatment post-application is shown in Figure 4. Representative samples of rT plus gelatin sponge carrier and ORC stained for fibrin, erythrocytes, and connective tissue are shown in Figure 5.

Discussion

In this bleeding model study, hemostasis was achieved fastest in the rT plus gelatin sponge carrier (active) group, occurring consistently within 30 seconds regardless of heparinization status or initial bleeding intensity tested (VIBe SCALE grades 1 and 2). There were no treatment failures in the rT plus gelatin sponge carrier group. It is important to note that due to the experimental design, the minimum time that could be recorded for hemostasis was 30 seconds, so hemostasis may have been achieved in < 30 seconds. In the ORC group, hemostasis was achieved in all applications in non-heparinized animals, but there were a clinically

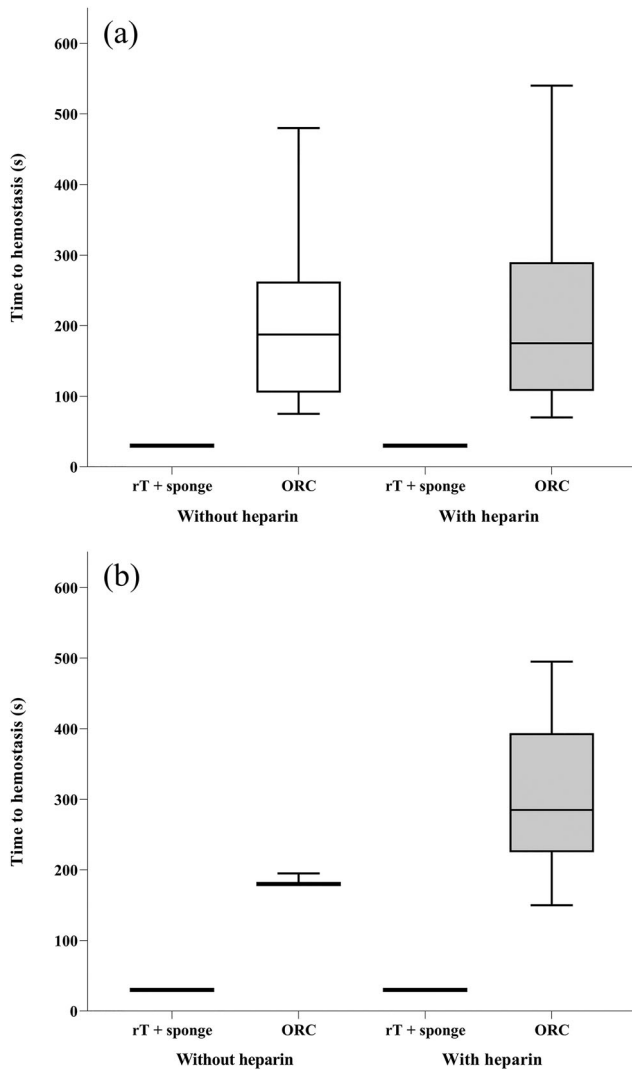


Figure 3. Comparison of time to hemostasis – A. Initial bleeding rates ≤ 5 g/min (Vibe SCALE grade 1), and B. Initial bleeding rates $>5-10$ g/min (Vibe SCALE grade 2). A. B. ORC, oxidized regenerated cellulose; rT, recombinant thrombin. Horizontal line and box represent the median and interquartile ranges; error bars represent maximum/minimum values.

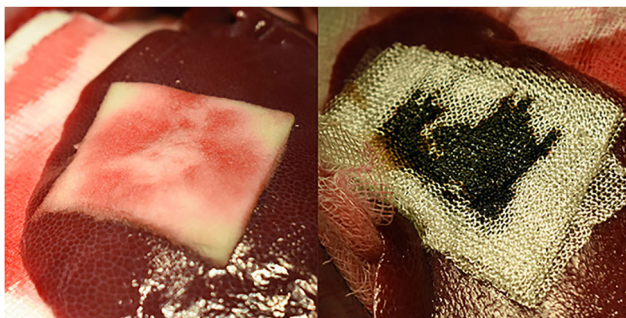


Figure 4. Test samples post application. ORC, oxidized regenerated cellulose; rT, recombinant thrombin plus gelatin sponge on the left, ORC on the right, after 3 layers have been applied.

relevant number of failures under heparinized conditions (2/18). When hemostasis was achieved with ORC, it was at a significantly later time (an average of 200 seconds in non-heparinized animals and 248 seconds in heparinized animals) than with rT plus gelatin sponge carrier. It is also important

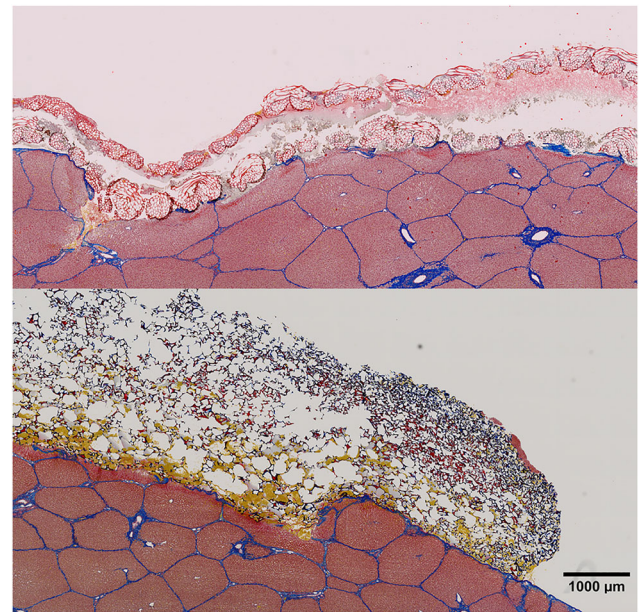


Figure 5. Martius, Scarlet and Blue staining of ORC (top) and rT plus gelatin sponge carrier (bottom). ORC, oxidized regenerated cellulose; rT, recombinant thrombin. Orange-yellow coloring represents fresh fibrin, red represents mature fibrin, erythrocytes are stained yellow, and connective tissue is shown in blue. Liver tissue can be seen in the lower part of each picture with the patch material covering the superficial organ defect on top. Note the spongy structure of the gelatin sponge carrier that has been partially penetrated with blood in the lower regions, whereas ORC shows significant amounts of coagulated blood between the individual layers and blood penetration throughout the top layer.

to note that the lesions that failed to reach hemostasis in the ORC group are not included in these values.

Initial bleeding rates in this study for the rT plus gelatin sponge carrier treatment group in non-heparinized animals (93.75% mild; 6.25% moderate) were similar to those reported in a previous porcine liver abrasion study (95% of lesions had mild bleeding).¹⁹ The performance of rT plus gelatin sponge carrier is in agreement with a phase 2 study that suggested that rT plus gelatin sponge had greater clinically meaningful efficacy versus a control gelatin sponge in a variety of surgical indications.²⁶ Furthermore, the presence of heparin did not reduce the hemostatic efficacy of rT plus gelatin sponge carrier, in line with previous findings in a rabbit model of vascular bleeding.²⁷ Treatment with ORC was generally effective in non-heparinized animals, although 3 layers of ORC (cut from separate sheets) were required to achieve hemostasis in the majority of cases (potentially conflicting with recommendations to use the minimum amount of material)^{13,23} and hemostasis was significantly slower than with rT plus gelatin sponge carrier. Although there was no significant increase in time to hemostasis with ORC in heparinized versus non-heparinized conditions in successful applications, the failure of 2 out of 18 ORC applications in heparinized conditions (which is not reflected in the time to hemostasis) is clinically relevant and represents a key finding of this study. Hemostatic agent failure is associated with increased blood loss and the corresponding greater likelihood of blood product transfusion, longer operative times, and greater use of surgical consumables, which result in poorer patient outcomes and higher economic costs.^{4,9,10,12} When the time to hemostasis of all ORC

applications was examined, there was an apparent reduction in efficacy in heparinized animals. These results demonstrate the importance of using an appropriate hemostat for the individual patient, with active hemostatic agents (in this case rT plus gelatin sponge carrier) performing reliably in both intact and impaired coagulation settings due to their biological action that is independent of the coagulation cascade.^{13,15} Passive agents (in this case ORC) on the other hand, rely on contact activation and are only suitable for patients with a fully functioning coagulation cascade,¹³ a factor which may not be immediately apparent in a traumatic clinical situation. This study adds to previous evidence^{15,28,29} that active agents such as rT plus gelatin sponge carrier have higher hemostatic success rates than passive agents such as ORC across a range of bleeding rates and patient coagulation profiles. Additionally, as an active hemostatic agent, rT plus gelatin sponge carrier meets more of the criteria for an 'ideal' hemostatic agent (which include rapid, effective hemostasis and reliability for different types of bleeding) than ORC, a passive agent.¹³ Therefore rT plus gelatin sponge carrier is appropriate for treating a wider range of patients and lesion types than ORC.

In heparinized test conditions, ORC showed a non-significant trend for better results with VIBe SCALE grade 1 bleeding events compared with grade 2 bleeding events, but comparable efficacy under non-heparinized test conditions for grade 1 and 2 bleeding. This investigation was not powered to identify a difference between bleeding grades and therefore the low number of lesions with an initial bleeding grade of 2 (≤ 7 per treatment/heparinized group) may explain the trend of poorer performance of ORC in heparinized conditions not reaching statistical significance. However, a previous study has shown greater hemostatic efficacy with active agents versus passive agents in moderate-to-severe bleeds.¹³ Therefore passive hemostatic agents such as ORC may be inappropriate for use in patients with grade 2 bleeds and impaired coagulation, and active agents such as rT may be a preferred choice. The instructions for use for ORC indicate that although ORC is absorbable, care should be taken to avoid excess material when used for wounds which are surgically sealed, to minimize risk of foreign body reactions, and that all ORC material should be removed once hemostasis is achieved when applied to open wounds, the spinal cord, the optic nerve and chiasm, or in proximity of bone.²³ Furthermore, it has been recommended to remove ORC after hemostasis due to serious adverse events when left in place.¹³ Adverse events resulting from ORC may be due to incomplete absorption,¹³ or swelling of the material.²³ Foreign-body reactions have been documented with ORC, where it has led to a granuloma-like presentation in several patients.^{30–33} Swelling of ORC due to its hygroscopic nature has been attributed to compression of luminal tissue when used in cardiac surgery³⁴ and compression of nerves after use in spinal surgery.^{35,36} Granuloma has been reported with gelatin sponge when used in neurosurgery.³⁷ The Instructions for Use for gelatin sponge also recommend removal once hemostasis is achieved to avoid possible dislodgment or compression of surrounding

tissues.²⁴ Gelatin sponge has led to spinal cord compression due to swelling of the material^{38,39} and the Instructions for Use therefore specify that it should be removed after use on or near the spine, bone or optic nerve.²⁴ Swelling of hemostatic material has also been observed with gelatin-thrombin hemostatic matrices,^{40,41} but to a lesser degree than ORC or gelatin sponge. Removal of hemostatic material may lead to rebleeding, which requires additional treatment, longer operative times and/or hospital stays, and consumption of expensive blood products in severe cases.^{4,14} Adverse events reported with rT in clinical trials include thromboembolic adverse reactions (6% of patients) and antibody formation to rT (<1% of patients).²²

A limitation of this study was the low number of lesions with initial bleed rates of VIBe SCALE grade 2, making it difficult to compare efficacy in lesions with less severe initial bleeds. Furthermore, the experimental design limited the minimum possible time to observation of hemostasis to 30 seconds, so hemostasis that occurred in <30 seconds could not be more precisely assessed.

In conclusion, rT plus gelatin sponge carrier demonstrated superior hemostatic properties compared with ORC, regardless of coagulation status or initial bleeding rate. When the consistent efficacy of rT plus gelatin sponge carrier resulting from its active hemostasis properties is considered, together with the compromised efficacy of ORC in heparinized conditions, multiple layers of ORC required in every application, and the risk of adverse events when left in place, this study suggests that an active hemostatic agent such as rT (plus gelatin sponge carrier) may be a preferable first choice of hemostatic agent versus a passive agent such as ORC for all mild and moderate bleeds.

Disclosure statement

The authors report conflicts of interest. PS is CEO of Trauma Care Consult GmbH, the organization that received the funding to conduct the study. DL and HG are full-time employees of Baxter Medical Products GmbH. The studies reported here were designed and performed using established scientific methods with impartial data collection and analysis. The authors are responsible for the content of the article. Meridian Health Comms Ltd provided writing assistance, which was paid for by Baxter Healthcare Corporation.

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