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Case Series

Assessment of the efficacy of a novel adhesive haemostat using real world, case series data collection

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ABSTRACT

Background: Post-operative haemorrhage can lead to significant complications and even mortality. These utilise scarce healthcare resources and increase hospital costs, as well as negatively impacting on patient's quality of life. Haemostats that exhibit additional adhesive properties can reduce the rate of bleeding complications. Standard gelatin sponges have been used safely in surgery for over 75 years but have almost no adhesive properties. This article reports the performance of a novel adhesive gelatin patch in human surgery for the first time.

Methods: A CE-marked gelatin foam patch (TenaTac®, Selentus Science, UK) has been created through a physical modification of the sponge surface, avoiding the need for the addition of blood-derived components or additional chemicals to stimulate adhesion. Real-world, post-approval clinical evaluations of the device were undertaken, and a structured data form was utilised to collect information on the device's performance during these procedures.

Results: In total, 63 evaluations were undertaken by 40 surgeons in 13 countries, covering 29 different surgical procedures. When assessing the adherence of TenaTac, 83 % (48/58) of the surgeons assessed the adhesion as very good or excellent. Both "haemostatic effect" and "time to haemostasis" achieved median scores of 4/5 (IQR 4–5), which equated to "very good" on the questionnaire. When surgeons were asked to compare their experience with TenaTac against their usual haemostat, 91.7 % (55/60) rated it as good, very good or excellent. When surgeons were asked if they would recommend the use of TenaTac, 96.5 % (55/57) of the surgeons responded positively to this question.

Conclusion: Real world evaluation of the novel adhesive patch, TenaTac, has confirmed that it exhibits very good adhesive and haemostatic qualities and could be considered for use by a wide variety of surgical specialities.

1. Introduction

The use of topical haemostats to control bleeding during surgical procedures is well established and these products contribute to improved clinical outcomes [1], reduced procedure times [2] and reduced usage of blood products [3]. In addition to controlling bleeding during a procedure it is necessary to consider the risk of post-operative re-bleeding [4,5] that might arise if, for example, the clotted site is disrupted by patient or organ movement. One approach to mitigating this risk is the use of adhesive and bioresorbable haemostats that stay in situ to coat or seal the clotted site and degrade within an acceptable time period.

Current haemostats with these properties are not ideal with respect to one or more criteria. For example, many leading products contain

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blood-derived thrombin and fibrinogen that carry a safety warning for blood-derived contaminants such as prions and viruses [6–8]. Since the main purpose of these ingredients is to form an adhesive layer rather than coagulate the patient's blood, the use of blood-derived materials to achieve this functionality is open to challenge. Other products contain materials such as oxidised cellulose for which there are reports of prolonged degradation and foreign body reactions [9,10]. For example, one study reported that a haemostat composed of oxidised cellulose had only degraded by 20 % after 30 weeks: considerably longer than the typical period of 4–8 weeks [10]. There are also many case reports implicating oxidised cellulose in the formation of masses requiring investigation [11].

Ease of use and speed of preparation are also important considerations for haemostats which may need to be deployed urgently. Current products such as liquid fibrin sealants require re-constitution or thawing. Finally, the high cost of adhesive, bioresorbable haemostats may be a hurdle for global adoption and the design of new products needs to accommodate this factor. Whilst the pharmacoeconomic case was made, for example, for a new haemostat (Evarrest ®) with a per patient cost of USD 1300 [12], in some countries, hospital budgets may simply not accommodate the upfront cost.

In this paper we report on a new adhesive, bioresorbable haemostat (TenaTac®). TenaTac is a novel haemostatic patch manufactured from gelatin which has a long history of safe use in haemostasis [13]. Normal gelatin sponges are not adhesive, whereas TenaTac has a precise physical modification in which the wound contact surface is divided into over 1000 miniature columns that create a highly adhesive product. The columns (Fig. 1) increase surface area over ten-fold; interdigitate with uneven surfaces and as the columns stretch and operate independently to resist the transmission of shear force. The purely physical modification, without the addition of active ingredients, is cost effective and free from blood products.

TenaTac has been demonstrated to exhibit superior adhesion and haemostatic efficacy to plain gelatin sponge and Tachosil in a rabbit liver biopsy model under independent testing (Fig. 2) (14). In a separate study, TenaTac was shown to be completely reabsorbed when implanted into porcine liver after just two weeks ([14]). To date, the efficacy of TenaTac in human surgery has not been reported in the literature. The data presented are the first reports of TenaTac in an uncontrolled, human setting and as such represent valuable real-world experience of this new haemostat.

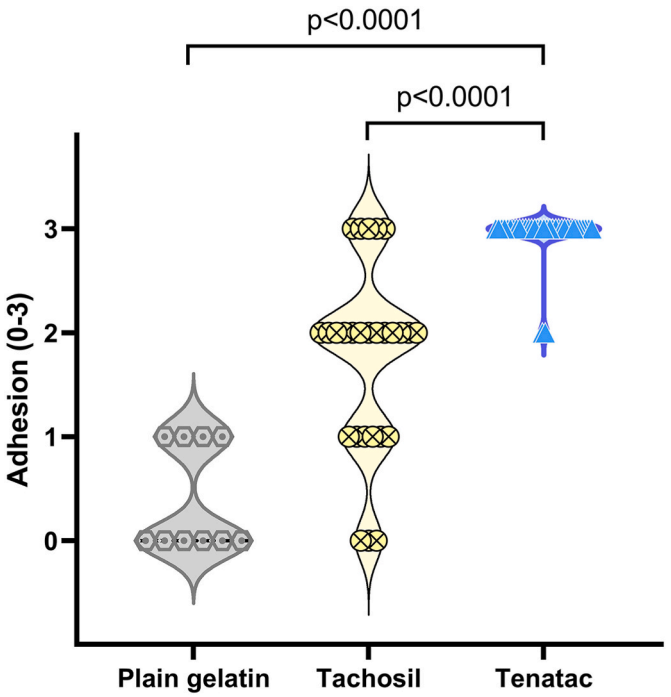

Fig. 2. TenaTac patches (n = 35, blue) exhibited significantly stronger adhesion to bleeding liver sites than either Tachosil (n = 27, yellow) or plain gelatin sponges (n = 10, grey). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

2. Methods

As this first-in-human, prospective case series aimed to capture real-world usage relating to TenaTac, there were no inclusion or exclusion criteria stipulated. The device under investigation was fully approved (CE-marked) and patients were treated within the device's Indications for Use. No patient level data at all were collected. As such, ethical approval and informed consent were not required to collect data on the device performance, and the study was not submitted to the Ethics Committee. The trial was registered with ISRCTN https://www.isrctn.com/ISRCTN54521345.

Any type of operation that the surgeon felt might benefit from the use

Fig. 1. TenaTac has a uniquely modified surface that consists of over 1000 columns (each 3–4 mm high and 1.5 mm wide) which increase surface area. In addition, the columns can also each interdigitate with the irregular surface of bleeding tissues, thereby greatly increasing surface contact. In addition, because the patch is made of gelatin, each column acts as an elastic attachment to the surface helping to resist any applied shear force.

of a haemostat was eligible for inclusion. The procedures were undertaken in both University and general hospitals. For most surgeons, the reports were created early in their learning curve (all less than 5 previous cases) and so represent a real-world setting. The surgeons were directed to the Instructions for Use for the product but were free to follow their own clinical judgement as to how and when to best use the haemostat. If the bleeding area was larger than a single sponge, or the bleeding more severe, then additional TenaTac sponges could be applied. Each time the surgeon used a TenaTac, a structured evaluation from was completed (see Appendix A) which captured procedural data along with data on the performance of the TenaTac. This was completed as soon as possible after surgery. The device, a TenaTac haemostatic patch was supplied by CuraMedrix Ltd (Netherlands) under licence from Selentus Science (UK).

The data were analysed using GraphPad Prism V9.5.0. The individual operations were grouped into procedural types by an experienced General Surgeon (PDH). The individual haemostats were also grouped in bundles of products with the same or very similar modes of action. Not all data fields on every form were completed and the proportions are reported as percentage (event/completed fields). A significant proportion of the data were not normally distributed and as such are presented as median plus inter-quartile ranges (IQR). Continuous data was compared using a Mann-Whitney *U* test, and categorical data compared using the Fisher's exact test. A p-value of <0.05 was labelled significant.

This case series has been reported in line with the PROCESS Guideline.

3. Results

3.1. Overview

TenaTac was evaluated by 40 surgeons in 13 countries. In total, 63 completed evaluation forms have been analysed, covering 29 different surgical procedures. Open surgery accounted for the majority of the evaluations (54/63), with TenaTac being studied in 9 laparoscopic operations. In 48.3 % of the evaluations (28/58), it was the first time the surgeon has used TenaTac in surgery.

TenaTac was evaluated in a range of major surgical interventions. The most common procedure was partial liver resection (14/63), followed by 12 patients undergoing craniotomy or spinal surgery. The evaluations also covered some particularly challenging cases including aortic surgery, redo carotid endarterectomy, kidney transplant, anterior resection and 3 cases of pelvic wall tumour excision. The procedures are detailed in Table 1.

3.2. Grading for the whole cohort

Surgeons graded the bleeding to be treated on a scale of 0–4 (negligible to severe). The median bleed was 2/4 (IQR 1–2), with 52 % of cases in this grade. In 21 % of cases (12/58) the TenaTac was used to treat moderate to severe bleeding. In 70.5 % of cases (43/61), the bleeding site was large enough to need the largest TenaTac sponge (80 × 50mm), with 18 % (11/61) requiring the medium size (50 × 40mm). In 18.5 % of cases (10/54), two sponges were required to cover the bleeding area.

At the end of surgery, the surgeons completed a structured form evaluating their experience of using TenaTac. The questionnaire graded performance from "unacceptable" to "excellent" (grades 1–5). For "ease of use", the median score for TenaTac was 5/5 (IQR 4–5), with 100 % of surgeons rating TenaTac as good, very good or excellent. When the "adherence" of the TenaTac was evaluated visually, the median score was 4/5 (IQR 4–5), with 83 % (48/58) of the surgeons assessing the adhesion as very good or excellent. Both "haemostatic effect" and "time to haemostasis" achieved median scores of 4/5, which equated to "very good" on the questionnaire. The "sealing ability" was scored as 4/5 as well (IQR 4–5), with 82.5 % (47/57) of surgeons recording this as very good or excellent, and this remained true when the different sub-types of surgery were evaluated. The surgeons were asked about their overall impression of TenaTac, and in this regard, 94 % scored TenaTac as good, very good or excellent. These data are present in detail in Fig. 3.

As part of the data collection, surgeons completed fields relating to which haemostat they would normally use in the procedure that they were undertaking. A total of 20 different haemostats, or techniques were recorded. Tachosil was the most common haemostat recorded, with 37.9 % (22/58) of surgeons indicating that it would be their usual haemostat for the level of bleeding encountered during that particular surgery. Cellulose and gelatin-based products were next most common, followed by flowable haemostats containing blood proteins, and then active patches. When Tachosil was the surgeon's usual product, they rated the efficacy of TenaTac as "very good" across all the evaluation categories. When compared to flowable products such as Floseal or Evicel, TenaTac was rated as "excellent" for ease of use and "very good" for all other comparators including haemostatic efficacy and sealing. The median scores against each product are detailed in Table 1.

When surgeons were asked to compare their experience with TenaTac against their usual haemostat, 91.7 % (55/60) rated it as good, very good or excellent. The median score for this was 4/5 (IQR 3–4). The final section of this part of the analysis was to ask surgeons if they would recommend the use of TenaTac to others. Overall, 96.5 % (55/57) of the surgeons responded positively to this question. When surgeons who had used the product more than a single time were considered, the

Table 1
The performance of TenaTac was graded 1–5 b y surgeons, across a number of categories and the median score is presented (grade 5: excellent; 4: very good; 3: good; 2: acceptable; 1: unacceptable). The upper half of the table relates to the type of surgery in which TenaTac was used and the lower half compares TenaTac performance against the surgeon's usual haemostat.

	N =	Ease of Use	Visual adhesion	Physical adhesion (if checked)	Haemostatic efficacy	Time to haemostasis	Sealing ability
Liver	19	4	4	4	4	4	4
Kidney	3	4	4	3	4	4	4
Abdominal & pelvis	10	5	4	4	4	4	4
Neuro & spinal surgery	15	5	4	4	4	4	4
Vascular	8	5	4	4	4	4	4
Thoracic	5	4	4	4	4	4	4
ENT	3	5	4	4	4	4	4
Scores for TenaTac when compared to other products							
Tachosil	22	5	4	4	4	4	4
Active patches	6	5	4.5	3.5	4.5	4.5	4.5
Flowable	11	5	4	4	4	4	4
Cellulose based	9	4	4	4	4	3	4
Gelatin based	11	5	4	4	4	5	5
Collagen	3	5	5	4	4	4	4

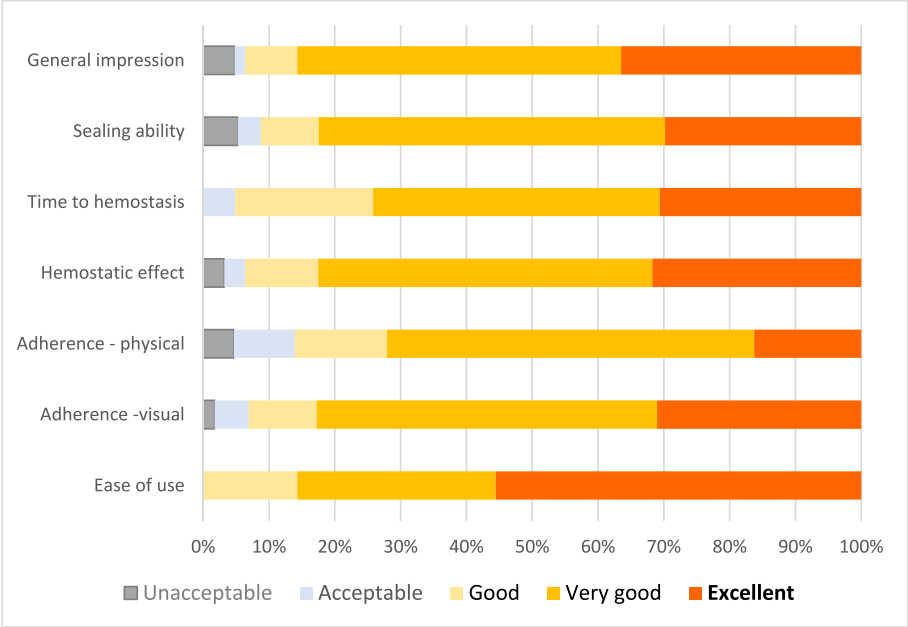

Fig. 3. Surgeons' ratings for seven parameters relating to TenaTac's clinical performance as a proportion of all responses.

"recommend" rate increased to 100 % (30/30). See Table 2 for details.

3.3. Procedure type

Examining surgeon's satisfaction with TenaTac further showed that 100 % of neuro, vascular, thoracic and ENT surgeons would recommend the product. Only a single liver surgeon (5.5 %) said they would not recommend TenaTac. When grouped by the surgeon's usual haemostat, 90.5 % of Tachosil users said they would recommend TenaTac. All 11 users of flowable products said they would recommend TenaTac, as did 100 % of Veriset or Hemopatch users. With regards to the surgeon's "overall impression" of TenaTac, this was rated as very good for all surgical procedures, apart from abdominal/pelvis where it was rated very good to excellent. The "overall Impression" of TenaTac scored a rating of at least "very good" against other haemostat groups and was rated as "excellent" against active patches and gelatin haemostats. See Table 2 for further details.

Procedural and surgical parameters were then examined with regards to their effect on the efficacy scores previously reported. The scores between those with mild bleeding and those with moderate-severe bleeding were not statistically different, although for stronger bleeding TenaTac scored higher than "very good" in 6 out of 8 categories, as opposed to more mild bleeding which scored "very good" in 7 out of 8 categories (see Table 3 for details). The surgeons' usual haemostats were grouped into either standard or advanced categories (advanced being defined as those with added chemicals for haemostasis; those containing blood derived components; or those with physical modifications of standard products). TenaTac scored equally across all the attributes studied. When the bleeding severity was higher, the surgeons compressed for longer, as would be expected ($P = 0.001$), however the satisfaction scores did not vary, with TenaTac being equally efficacious. Finally, when TenaTac was assessed in either open or laparoscopic surgery there were no significant differences.

Table 2
The median score for TenaTac for overall impression and when compared to surgeons' other haemostats (grade 5: much better; 4: very good; 3: good; 2: acceptable; 1: unacceptable), and the answer to whether they would recommend TenaTac for future use.

	Overall impression (grade 1–5)	Compared to current haemostats (grade 1–5)	Would recommend TenaTac	Would not recommend
Liver	4	3	18	1
Kidney	4	4	2	1
Abdominal & pelvis	4.5	5	9	1
Neuro & spinal surgery	4	4	12	0
Vascular	4	4	6	0
Thoracic	4	3	5	0
ENT	4	4	3	0
Scores for TenaTac when compared to other products				
Tachosil	4	4	19	2
Active patches	5	3	6	0
Flowable	4	4	11	0
Cellulose based	4	3	9	1
Gelatin based	5	4	7	0
Collagen	4	5	3	0

4. Discussion

The value of real-world data is increasingly being recognised by Regulatory agencies [15,16]. This is because randomised controlled trials have a number of limitations. They usually report on a single organ intervention, have limits on the severity of the disease treated and very often do not cover the whole range of patients with which the medical device is intended for use in [17]. Medical devices can function well in the tight constraints of an RCT, but once exposed to real-world practice they often fail to deliver their promise shown in the trial.

The data collected in this study represent a real-world view of a novel haemostat, with inputs from 40 surgeons across 13 countries. The device was tested on nearly all of the major organs including the brain, lungs, liver, kidneys, intestines, vascular tree and soft tissues, with only heart surgery absent. During most trials of medical devices, company clinical specialists will be present in theatre to guide surgeons about best practices to get the most out of the device. In this case, most of the data were collected during the period when hospitals faced COVID-related

Table 3
Comparison of efficacy scores between strengths of bleeding, type of usual haemostat, compression time and surgical type.

	N =	Ease of Use	Visual adhesion	Physical adhesion	Haemostatic efficacy	Time to haemostasis	Sealing ability	Overall impression	Compared to current haemostats
<moderate bleeding	46	5	4	4	4	4	4	4	4
moderate - severe bleeding	12	5	5	4.5	5	4	4.5	4.5	4
P =		0.837	0.131	0.326	0.381	0.132	0.756	0.437	0.469
Standard haemostat	20	5	4	4	4	4	4	4	4
Advanced haemostat	38	5	4	4	4	4	4	4	4
		0.880	0.903	0.467	0.813	0.551	0.419	0.991	0.143
<3 min compression	30	5	4	4	4	4	4	4	4
3+ mins compression	28	4	4	4	4	4	4	4	4
P =		0.361	0.674	0.438	0.329	0.370	0.699	0.373	0.251
Open surgery	54	5	4	4	4	4	4	4	4
Laparoscopic	9	4	4	4	4	4	4	4	3
P =		0.468	0.520	0.464	0.762	0.075	0.666	0.558	0.962

restrictions, and as such represent the surgeon simply opening the box and using the device for haemostasis without any external guidance.

TenaTac achieved a very high level of satisfaction amongst all types of surgery, with the scores in Tables 1 and 2 being remarkably consistent across different specialities. Part of this may well relate to the product's ease of use, where 100 % of the surgeons graded it as good, very good or excellent. In addition, the product adapts to the environments in which it is placed. When first removed from the packaging, the TenaTac is a fairly rigid sponge but some light compression between the surgeon's fingertips greatly increases its flexibility. As it is a patch, it can be very rapidly applied across a fairly wide area to cover larger bleeding sites. Unlike the flowable products, such as Floseal or Evicel, it doesn't run off when applied to sloping or vertical surfaces. As the TenaTac sponge moistens with the presence of blood, it becomes increasingly flexible and as such can be used to fill cavities in the way that oxidised or regenerated cellulose products are used.

Plain gelatin sponges have an excellent safety record, having been used in human surgery for over 75 years ([13,18]. However, they are poorly adhesive, and this has limited their use in recent years as surgeons across all specialities have come to understand the great increase in post-operative safety offered by haemostats that actively adhere to the bleeding site in the post-operative period and prevent post-operative haemorrhage. TenaTac is manufactured from a plain gelatin sponge through a process of physical modification, without the addition of human blood proteins or other active chemicals. This physical modification has been shown to greatly increase adhesion to bleeding sites in rabbit models (Fig. 4). This human study has confirmed that adhesive nature of TenaTac with surgeons rating both the "visual appearance of adhesion" and the "adhesion when physically tested" as very good. In total, 93 % (54/58) of surgeons carefully looking at adhesion to the bleeding site, scored the adhesion as good, very good or excellent.

Most controlled trials simply compare one haemostat against another. However, in reality, surgeons utilise a variety of haemostats depending on the site of the bleeding or the severity of such bleeding. The real-world data collected in this study mirrors patterns of haemostat usage seen in the operating theatre. As opposed to stipulating which haemostat a surgeon had to compare against in this study, the evaluation sheet collected data on which haemostat the surgeon would normally use in this setting. This is arguably a fairer way to test a new haemostat's performance. Tachosil, Veriset and Hemopatch are probably the most closely related to TenaTac in terms of physical structure, and surgeons who would normally use these three advanced haemostats scored TenaTac as "very good" for adhesion and haemostasis, and "excellent" for ease of use. TenaTac scored equally well when compared to the more expensive agents, such as the flowable product, Floseal®, and the liquid sealant, Evicel®.

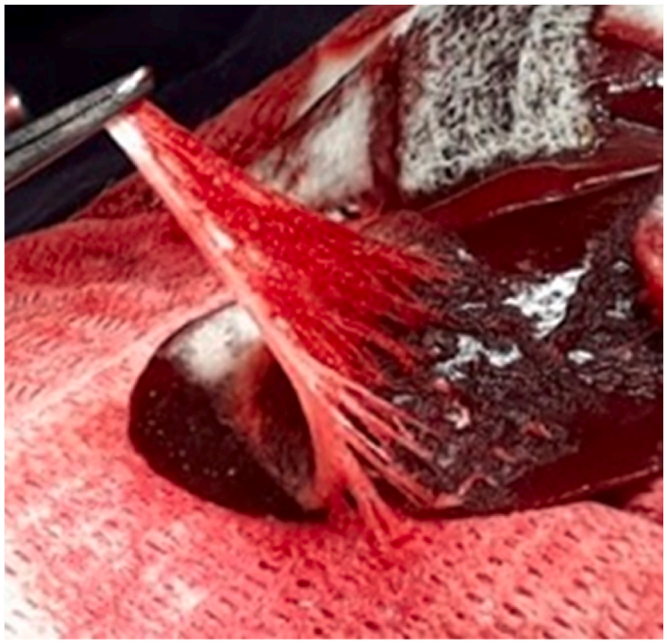

Fig. 4. The individual columns on the surface of the TenaTac patch can be seen actively stretching and resisting removal from the bleeding liver surface.

The final question that surgeons were asked was "Would you recommend TenaTac for future surgical procedures?". Overall, 96.5 % (55/57) of the surgeons responded positively to this question. When surgeons who had used the product more than a single time were considered, the "recommend" rate increased to 100 % (30/30). A ≥90 % recommendation rate was recorded for all types of surgery and across all types of alternate haemostat choices (Fig. 5).

The prospective, real-world nature of the study is a strength, reflecting the use of the haemostat in an all-comer population without artificial inclusion and exclusion criteria. It is the first time that clinical data has been reported for this device. Another positive point about the study is that it covered a very wide range of surgical types from aortic surgery to pelvic tumour surgery to delicate cranial procedures. A potential weakness is that it does not represent a consecutive series, although very few surgeons ever stick to the use of a single haemostat

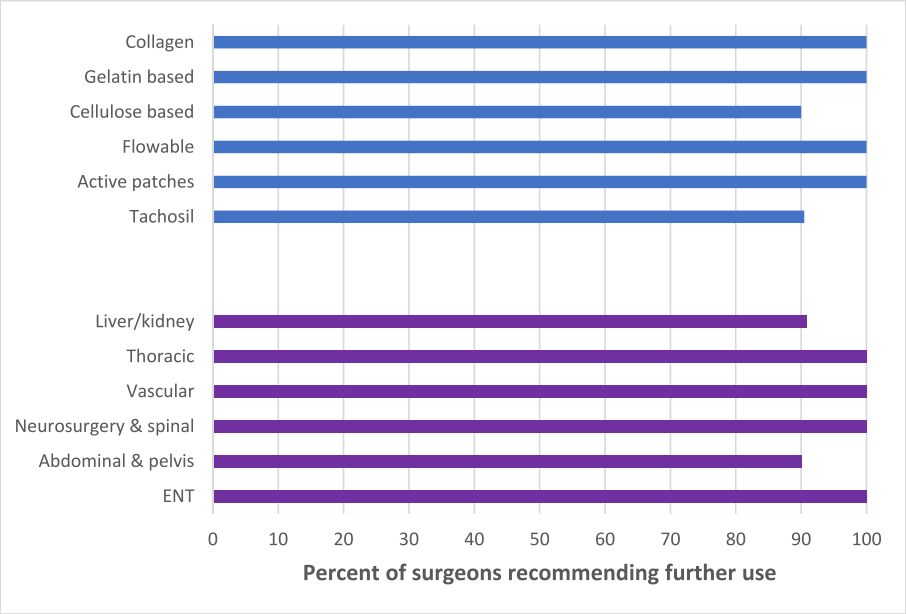

Fig. 5. The percentage of surgeons who would recommend using TenaTac based on either the type of haemostat they normally use (blue) or by the type of surgery in which the TenaTac was evaluated (purple). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

through a number of surgical procedures, rather choosing the one that suits the current situation. A future study may look to capture how often TenaTac could be used in a consecutive surgical series. This case series has been reported in line with the PROCESS Guideline [18].

5. Conclusion

The physical modification of a gelatin sponge has created an advanced haemostatic patch that has been rated as very good in terms of adhesion, haemostasis and sealing abilities across a wide range of surgical specialities. Furthermore, when compared to the surgeon's usual choice of haemostat, TenaTac was rated as good, very good or excellent 92 % of the time. TenaTac therefore represents a very promising new alternative to the current haemostats used by surgeons and benefits patients as blood derived ingredients are not used.

Sources of funding

No funding for the sites was provided apart from free clinical samples.

Ethical approval/Declaration of Helsinki

As a post-market clinical follow up study of real-world use, which did not collect any patient information, no ethics approval was required.

Patient consent

See above.

Trial registration

Completed with ISRCTN.

Data availability

The data may be available after discussion with the corresponding author.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Study funding

Product samples were supplied free of charge by CuraMedrix BV.

Ethical approval

The study was an ad hoc evaluation of a CE-marked medical device being used within its Instructions for Use. No structured protocol was followed and the surgeons were free to choose when to use the device. No patient related data were collected only the performance of the device. As such Ethical Approval was not required.

Please state any sources of funding for your research

The study sponsors provided free haemostatic patches for the study. They were also involved in collecting and analysing the data, plus helping in preparing the manuscript for publication.

Author contribution

Grosheva M: surgical procedure, data collection, critical manuscript appraisal, final approval.

Liese M: surgical procedure, data collection, critical manuscript appraisal, final approval.

Menovsky T: surgical procedure, data collection, critical manuscript appraisal, final approval.

Rasschaert R: surgical procedure, data collection, critical manuscript appraisal, final approval.

Galun D: surgical procedure, data collection, critical manuscript appraisal, final approval.

Maric N: surgical procedure, data collection, critical manuscript appraisal, final approval.

Hayes PD: data collection and analysis, writing manuscript, final approval

Van Herzeele I: surgical procedure, data collection, critical

manuscript appraisal, final approval.

Registration of research studies

Trial registration: https://www.isrctn.com/ISRCTN54521345.

Guarantor

Paul Hayes BSc MB ChB MD FRCS had full access to the data, the conduct of the study and the decision to publish and accepts full responsibility for the work.

Consent

The study was an ad hoc evaluation of a CE-marked medical device being used within its Instructions for Use. No structured protocol was followed and the surgeons were free to choose when to use the device. No patient related data were collected at all, only the performance of the device. As such patient consent was not required.

No patient images are used. The one image of the device in place on a liver is taken from our rabbit study (this is noted in the paper).

Declaration of competing interest

PH is an equity holder and consultant to Selentus Science, the IP holders of the technology. No other authors have a conflict of interest or personal relationship which would be considered as a potential competing interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijso.2023.100690.

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