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Safe and rapid radial hemostasis achieved using a novel topical hemostatic patch: Results of a first-in-human pilot study using hydrophobically modified polysaccharide-chitosan

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Medcura, Inc. (formerly, gel-e, Inc.) Gel-E Human Radial Hemostasis Pilot Study

Abstract

Background: The transradial approach (TRA) for catheter interventions decreases vascular complications and bleeding versus transfemoral approach. Reducing time to hemostasis and preventing radial artery occlusion (RAO) following TRA are important and incompletely realized aspirations.

Objectives: This first-in-human study sought to evaluate the efficacy of a novel, topically applied compound (hydrophobically modified polysaccharide-chitosan, hm-P) plus minimal required pneumatic compression, to achieve rapid radial arterial hemostasis in post-TRA procedures compared with de facto standards.

Materials and Methods: About 50 adult patients undergoing 6 French diagnostic TRA procedures were prospectively enrolled. At procedure completion, a topical hm-P impregnated patch was placed over the dermotomy and TR Band (TRB) compression was applied to the access site. This patch was used as part of a novel rapid deflation protocol with a primary outcome of time to hemostasis. Photographic and vascular ultrasound evaluation of the radial artery was performed to evaluate the procedural site.

Results: Time to hemostasis was 40.5 min (IQR: 38–50 min) with the majority of patients (n = 39, 78%) not requiring reinflation. Patients with bleeding requiring TRB reinflation were more likely to have low body weight and liver dysfunction, with absence of hypertension and LV dysfunction. The rate of RAO was 0% with predischarge radial artery patency documented in all patients using vascular ultrasound. One superficial hematoma was noted. No late bleeding events or cutaneous reactions were reported in the study follow-up.

Conclusions: Topical application of hm-P in conjunction with pneumatic compression was safe and resulted in rapid and predictable hemostasis at the arterial puncture site.

KEYWORDS
chitosan, hemostasis, transradial, vascular access

Abbreviations: ACT, activated clotting time; BMI, body mass index; Fr, French; hm-P, hydrophobically modified polysaccharide-chitosan; IQR, interquartile range; LV, left ventricular; RAO, radial artery occlusion; TFA, transfemoral approach; TRA, transradial approach; TRB, TR Band (Terumo Interventional Systems, Somerset, NJ); TTH, time to hemostasis; UFH, unfractionated heparin.

1 | INTRODUCTION

The transradial approach (TRA) for catheter-based interventions as compared with transfemoral approach (TFA), is associated with cost savings and reductions in vascular complications, time to ambulation, and hospital length of stay.[1-9] Radial artery occlusion (RAO) is the most common vascular complication following TRA, with an incidence generally ranging 1–10%, precluding radial artery reuse and rarely, leading to patient discomfort and digital ischemia.[10,11] Reducing time to vascular hemostasis while improving rates of RAO, would further enhance the risk/benefit profile of TRA.

Strategies for RAO reduction have historically focused on minimizing sheath size and procedural anticoagulation.[12-14] It has also been shown that maintenance of antegrade radial flow during hemostasis ("patent hemostasis") further reduces RAO.[15-17] Greater duration and intensity of radial compression appear to increase RAO rates, however, there is no current standard for the length or technique of radial artery compression.[18,19] Informed, in part, by industry recommendations, compression time for diagnostic TRA procedures typically range from 90 to 120 min in the United States, but Asian centers routinely exceed 4–6 hr[18,19] Thus, further refinement of TRA hemostasis techniques remains a worthwhile endeavor.

To date, numerous topical hemostatic agents have been developed to stem surgical and traumatic hemorrhage, however early products meant primarily for cutaneous use were limited by efficacy, side-effects, cost, and production capability.[20,21] Chitosan, a linear polysaccharide composed of randomly distributed β-linked D-glucosamine and *N*-acetyl-D-glucosamine, is found abundantly in nature and unlike procoagulant products, chitosan works through tissue adhesion facilitating formation of a temporary hemostatic plug with shortened time to hemostasis (TTH) and reduced blood loss noted in preclinical models, albeit with inconsistencies across published data.[21-25] Human studies of topical chitosan in conjunction with pneumatic compression of TRA access sites, have yielded conflicting results. A plausible explanation for these disparate findings is molecular and functional variability in chitosan.[20]

Hydrophobically modified polysaccharide-chitosan (hm-P, Medcura, Inc., College Park, Maryland) is a more functionally consistent molecule with in vitro studies demonstrating greater tissue adhesion versus unmodified chitosan. Integration of hm-P hydrophobic moieties into exposed cellular membrane within the wound allows cross-linking of red blood cells with rapid organization of gel-forming networks and formation of a more reliable hemostatic plug.[25] In a porcine model of lethal, femoral arterial injury, hm-P demonstrated superiority to both unmodified polysaccharide-chitosan sponges as well as standard gauze compression.[20]

In this first-in-human clinical pilot study, we evaluated the effect of hm-P patch application in conjunction with pneumatic compression on (a) the achievement of hemostasis with reduced compression times and (b) the maintenance of vascular integrity and radial patency in patients undergoing elective angiographic procedures via TRA.

2 | MATERIALS AND METHODS

After approval by the Institutional Review Board, a total of 61 adult patients undergoing clinically indicated 6 Fr transradial arterial catheterization with diagnostic coronary or peripheral angiography were prospectively enrolled at a single academic medical center. Patients provided informed written consent for study participation. Ultimately, 50 patients met criteria (detailed below) for participation in the full study and comprised the final study cohort.

Patient exclusion criteria included patients under 18 years of age, pregnant patients, individuals unable or unwilling to provide written informed consent or participate in follow-up, and other vulnerable populations (developmentally delayed, incarcerated, and non-English speaking subjects). Patients who received oral anticoagulants (warfarin, dabigatran, rivaroxaban, apixaban, and edoxaban) or fibrinolytic therapy (t-PA) within 48 hr of the procedure and patients receiving uninterrupted parenteral anticoagulants (IV unfractionated heparin or IV/SC low-molecular weight heparin) or parenteral antiplatelet therapy (IV cangrelor or platelet glycoprotein IIb/IIIa receptor antagonists) were also excluded. This study focused on proximal transradial access and therefore patients with planned use of distal ("anatomical snuffbox") radial access were excluded. Finally, patients that required ad hoc conversion from a diagnostic procedure to a therapeutic vascular intervention were excluded as additional anticoagulation and antiplatelet therapies would potentially confound the TTH in a feasibility and safety pilot study.

Patients underwent careful physical examination of the radial puncture site and forearm and the plethysmography based Barbeau test to confirm dual arterial supply to the hand prior to the procedure. All relevant demographic and clinical information were ascertained from patient interview and review of electronic medical records. Procedural notes, medication data, and laboratory values were abstracted from medical records available immediately following the procedure. All data were entered into a secure, de-identified database.

2.1 | Photograph and vascular imaging preprocedure and postprocedure

Prior to the procedure, the volar aspect of the forearm at the radial artery puncture site was photographed for comparison with postprocedure images. Figure 1 shows the segments of the radial artery evaluated using two-dimensional (2D) vascular ultrasound and color Doppler flow (Site–Rite Vision, Bard Access Systems, Salt Lake City, Utah). After achieving postprocedure hemostasis and removing the TR Band (TRB, Terumo Interventional Systems, Somerset, NJ)/hm-P patch, repeat photographic and ultrasound images were taken. All images were collected and archived on a HIPAA-secure encrypted drive. Patients were contacted more than 30 days postprocedure to discuss any changes noted at the site of vascular access. Patients also provided pictures of the access site to study investigators via email or text messages (Figure 2). Patients with postprocedure vascular ultrasound findings concerning for radial artery occlusion or damage

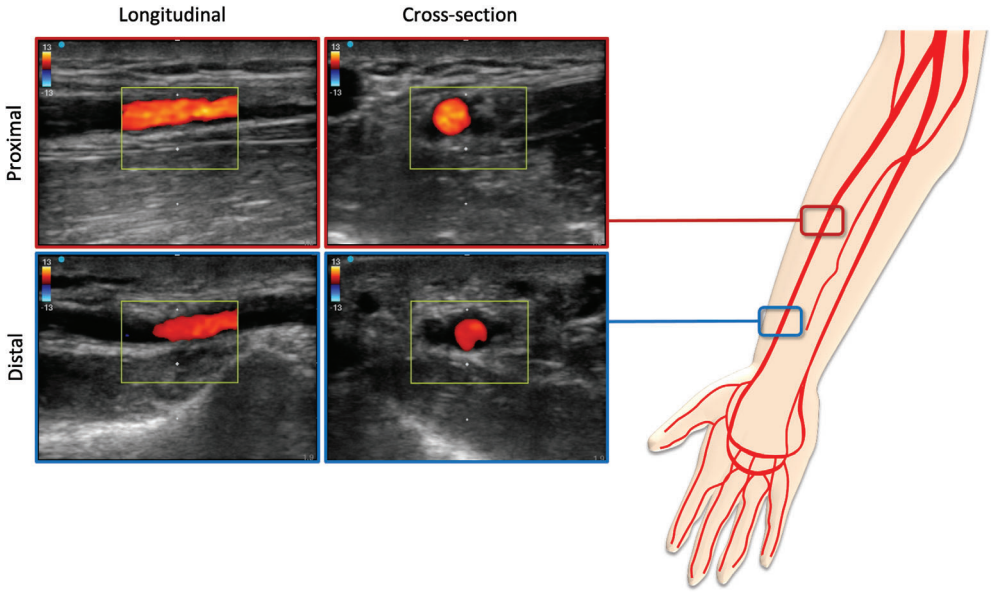

FIGURE 1 Represents typical arterial anatomy of the upper extremity with the distal and proximal radial arterial sites identified and examples of vessel patency as assessed with 2D vascular ultrasound color Doppler in cross-section and longitudinal planes [Color figure can be viewed at wileyonlinelibrary.com]

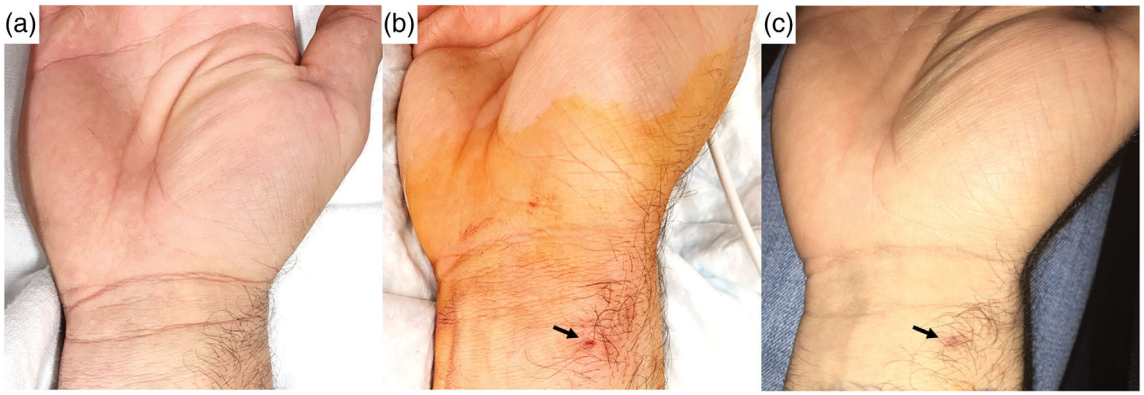

FIGURE 2 (a–c), Photograph of distal wrist pre-procedure (a), post hemostasis (b), and at 30-day follow-up (c). Arrow in panels b and c marks the site of arterial puncture. Patient consent obtained prior to publication [Color figure can be viewed at wileyonlinelibrary.com]

underwent a formal repeat vascular ultrasound at their clinically indicated 30-day clinic follow-ups.

2.2 | Arterial access and sheath removal

Percutaneous radial artery access was obtained using standard vascular access techniques (micropuncture-based anterior wall puncture or 20 G angiocath-based counter-puncture/"double-wall" techniques). Once a 6 Fr × 10 cm standard Terumo Glidesheath (Terumo Interventional Systems, Somerset, New Jersey) had been successfully placed, an anticoagulant and spasmolytic "cocktail" was administered through the radial artery sheath per local standard of care. The cocktail included a combination of verapamil 2.5 mg and/or nitroglycerin 100–200 μg plus mandatory use of unfractionated heparin 50 units/kg bodyweight (to a maximum dose of 5,000 units). The number, French (Fr) size, and types of catheters used during the procedure were chosen at the operator's discretion and practice standards. Additional anticoagulation beyond the initial 50 u/kg UFH bolus was not permitted. Routine radial artery angiograms were performed after placement of the arterial sheath. An activated clotting time was measured immediately prior to sheath removal, per standard of care.

2.3 | Hemostatsis protocol

At the completion of the procedure, the vascular sheath was withdrawn 2–3 cm, an hm-P patch was placed over the puncture site with the TRB positioned over the hemostatic patch. The TRB was inflated per device-specific instructions (15 ml of air) and the arterial sheath was removed from the body. Next, the TRB was rapidly deflated until a flash of blood was noted under the hm-P patch or to a minimum air level of 5 ml in the TRB. The band was then reinflated by 2–3 ml or until cessation of oozing (typically 8–10 ml of air). Finally, ipsilateral ulnar compression was performed while evaluating plethysmography to identify a pulsatile waveform, confirming patent hemostasis of the radial artery.

2.4 | Deflation protocol

Time of sheath removal was recorded, and the patient was monitored in the recovery area. If there was any bleeding noted, 2–4 ml of air was injected into the TRB. After 30 min of compression, the TRB was deflated by 5 ml of air and evaluated for 1–2 min for signs of bleeding. This process was repeated until the TRB was fully deflated. If bleeding occurred at any point, an additional 5 ml of air was injected into the compression device for an additional 15 min prior to repeating the aforementioned deflation sequence. Time to hemostasis was defined as the time from inflation of the TRB with vascular sheath removal to full deflation of the TRB with surface hemostasis. The deflation protocol was undertaken and overseen exclusively by the study investigators to maintain consistency and decrease confusion with nonenrolled patients. Once hemostasis was reliably achieved, the TRB was removed and a transparent film dressing was placed over the hm-P patch for 30 min of clinically mandated observation. If no bleeding occurred, the film dressing and hm-P patch were removed and repeat photograph and ultrasound images were taken of the wrist, after which a final sterile film dressing was applied to the skin (without the hm-P patch). Patients were instructed to not manipulate or bear weight with the wrist for 24 hr after which the transparent bandage could be removed. The remainder of postprocedure care and precautions were per local standards of care.

2.5 | Study endpoints

The study design sought to assess the feasibility of reducing TTH following diagnostic TRA procedures to near 30 min as compared with the current de facto US standard of 90–120 min. The mechanism for this reduction was the addition of an hm-P patch in concert with standard TRB pneumatic compression applied at the minimum pressure necessary to provide patent hemostasis at the site of radial artery access. The primary outcome was TTH and secondary outcomes were the number of TRB reinflation cycles, changes in vessel caliber or patency on vascular ultrasound, and presence of access-site complications (hematoma, persistent access site bleeding, pseudoaneurysm, and early or late cutaneous hypersensitivity reactions). Access site hematomas were graded using the Early Discharge After Transradial Stenting of Coronary Arteries Study (EASY) hematoma scale: Grade I, <5 cm in diameter (nonsignificant); Grade II, 5- to 10-cm diameter

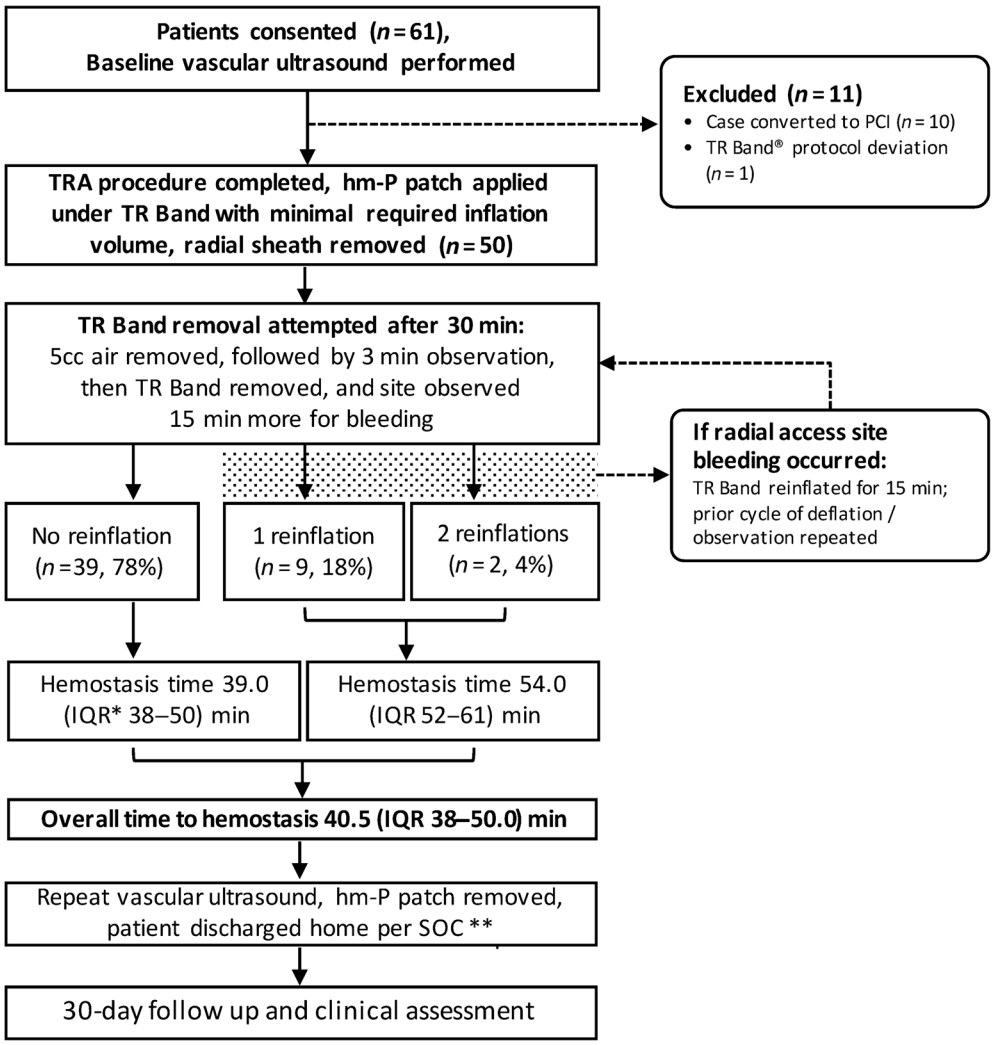

FIGURE 3 Flow diagram of study enrollment, execution, clinical assessment, and follow-up. IQR: Inter-quartile range; values are expressed as median (IQR), or *n* (%) due to non-Gaussian distribution of data. **SOC: Standard of care

TABLE 1 Baseline patient clinical characteristics

Characteristic	All patients (*n* = 50)
Age, years	59.9 ± 13.0
Race	
African American	20 (40%)
Asian	1 (2%)
Caucasian	29 (58%)
Male	35 (70%)
BMI	31.0 (25.9-38.9)
Hypertension	46 (92%)
Hyperlipidemia	40 (80%)
Diabetes mellitus	17 (34%)
Chronic kidney disease	17 (34%)
Dialysis	3 (6%)
Cirrhosis	4 (8%)
Obstructive CAD	19 (38%)
NYHA II-IV symptoms	16 (32%)
Ejection fraction <40%	14 (28%)
Medications	
Aspirin	29 (58%)
$P2Y_{12}$ inhibitor/cilostazol	6 (12%)
DVT prophylaxis	3 (6%)
Allergies	
Iodinated contrast	3 (6%)
Shellfish	1 (2%)
None	29 (58%)
Other	22 (44%)
Preprocedure labs	
Serum creatinine, mg/dl	1 (0.9-1.4)
Platelet count, $\times 10^3$/ml	220 ± 83

Notes: Values are mean ± *SD*, Median (IQR), or *n* (%).

TABLE 2 Procedural characteristics

Characteristic	All Patients (n = 50)
Diagnostic procedure	50 (100%)
6 Fr arterial sheath	50 (100%)
First radial procedure	42 (84%)
Arterial access attempts	1.6 ± 0.9
1 attempt	28 (56%)
2 attempts	14 (28%)
3 attempts	8 (16%)
Right radial access	36 (72%)
Procedure duration, min	31.5 (20.0–39.0)
Final ACT, seconds (*n* = 13)	232 (213–254)
TR band size, regular	43 (86%)
Time to first deflation, min	34 ± 4

Notes: Values are mean ± *SD*, Median (IQR), or *n* (%).

(mild); Grade III, >10 cm but distal to the elbow (moderate); Grade IV, extending above the elbow (severe); and Grade V, anywhere with ischemic threat to the hand (compartment syndrome).[22]

2.6 | Statistical analysis

In this pilot study, there was no control group, and therefore, the primary outcome of TTH was described as the median (interquartile range, IQR). In the case of vascular changes, patients served as their own control comparing preprocedure versus postprocedure measurements using either paired *t*-tests or Wilcoxon signed-rank tests. For secondary outcomes and baseline characteristics, categorical data were presented as frequencies with their corresponding percentages and analyzed using Chi-square tests of association or Fisher exact tests. Likewise, for secondary outcomes and baseline characteristics, continuous variables were reported as mean (±*SD*) or median (IQR) and compared with Student *t*-tests or Mann–Whitney *U* (Wilcoxon) tests. Tests were two-tailed and considered statistically significant with a *p*-value <.05. Statistical analyses were performed using STATA MP 15 (College Station, Texas).

3 | RESULTS

From July 2018 to December 2018, 61 patients were enrolled (Figure 3). Ten patients were excluded due to an unplanned (ad hoc) conversion from a diagnostic to therapeutic procedure and one patient was excluded for tampering with the TRB prior to protocol completion. In total, 50 patients successfully completed the protocol and were included in the analysis. Table 1 demonstrates the baseline patient characteristics and Table 2 shows the procedure characteristics. Patients were predominantly male (70%) with a mean age of 59.9 ± 13.0 years and a typical distribution of cardiovascular risk factors. The majority of patients were on some form of oral antiplatelet therapy, with the majority on aspirin monotherapy. However, by protocol, no patients were re-loaded with oral antiplatelet or anticoagulant agents in the periprocedural period. Final median activated clotting time (ACT, Hemochron Jr., Instrumentation Laboratory, Bedford, Massachusett) was 232 s (213–254), which is in range with therapeutic heparin anticoagulation.

The primary outcome variable of median TTH was achieved in 40.5 min (IQR: 38–50), well under the de facto standard of 90–120 min (Figure 4; Table 3). The majority (*n* = 39, 78%) of patients did not require TRB reinflation and hemostasis was achieved in 39.0 min (IQR: 38–42) in this sub-group. In those patients who required at least one reinflation cycle (*n* = 11, 22%), hemostasis was achieved in 54 min (IQR: 52–61). The time from first TRB deflation to complete deflation of the device was a median of 6 min (IQR: 4–13) with only two patients (4%) requiring two reinflation cycles. One patient sustained a forearm hematoma, classified as EASY Grade I or mild. This patient did not suffer any clinical sequela and was discharged per usual with no additional medical diagnostics or therapeutics required and no deviation from standard of care treatment.

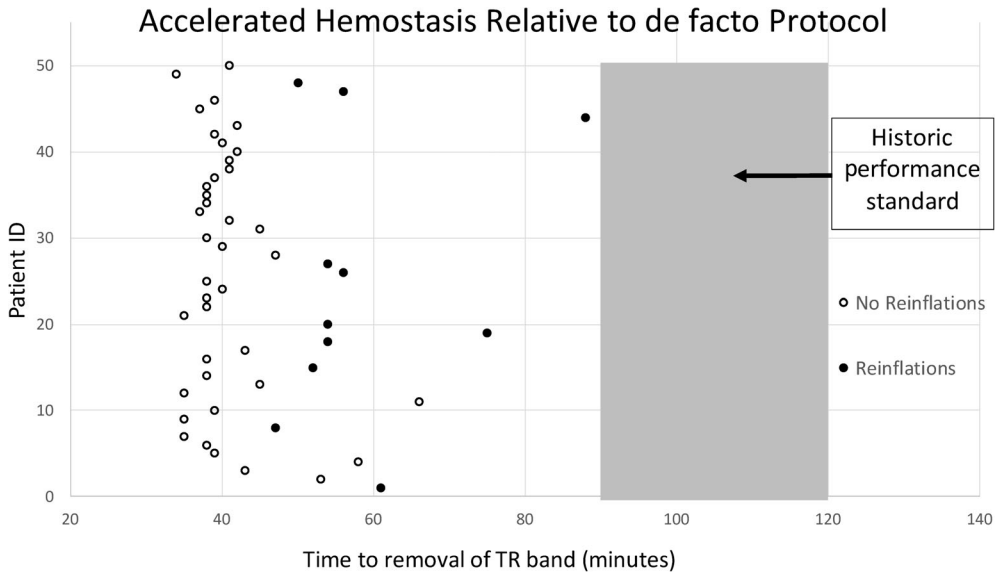

FIGURE 4 Patient-level data of the TTH when combining hm-P with a protocol of reduced surface compression. The primary outcome, median TTH, was 40.5 min (38–50). Open markers represent patients that did not require TRB reinflation while closed markers represent patients requiring at least 1 TR-band reinflation. The shaded region denotes the de facto US standard duration of post-TRA compression, 90–120 min. Abbreviations: time to hemostasis (TTH), hydrophobically modified polysaccharide-chitosan (hm-P), IQR (interquartile range), terumo radial band (TRB), transradial approach (TRA)

TABLE 3 Clinical outcomes

Time to hemostasis	Median (IQR)
All patients (n = 50)[a]	40.5 min (38–50 min)
Patients without TRB reinflation (n = 39)	39.0 min (38–42 min)
Patients with ≥1 TRB reinflation (n = 11)	54.0 min (52–61 min)
Incidence of complications	**n, (%)**
Any hematoma	1 (2%)
Grade I (<5cm) EASY hematoma	1 (2%)
Grade II-V EASY hematoma	0 (0%)
Radial artery occlusion	0 (0%)
Uncontrolled access site bleeding	0 (0%)
Pseudoaneurysm	0 (0%)
Cutaneous reactions (early/late)	0/0 (0%/0%)

[a]Denotes primary outcome.

TABLE 4 Patient subgroups who did versus did not require TR band reinflations

Characteristic	Reinflation (n = 11)	No reinflation (n = 39)	p-value
BMI	24.9 (24.2–29.3)	32.0 (27.4–40.2)	.007
Hypertension	8 (73%)	38 (97%)	.03
NYHA II-IV	0 (0%)	16 (41%)	.01
LVEF <40%	0 (0%)	14 (36%)	.02
Cirrhosis	3 (27%)	1 (3%)	.03

Notes: Values are median (Q1–Q3), n (%).

TABLE 5 Preprocedural and postprocedural vascular ultrasound data

	Pre	Post	p-value
Procedure site (distal), mm			
Horizontal diameter	2.7 ± 0.6	2.7 ± 0.5	.28
Vertical diameter	2.3 ± 0.5	2.4 ± 0.4	.48
Circumference	8.1 ± 1.7	8.4 ± 1.4	.07
Proximal site, mm			
Horizontal diameter	2.5 ± 0.5	2.6 ± 0.5	.006
Vertical diameter	2.3 ± 0.5	2.5 ± 0.5	<.001
Circumference	7.8 ± 1.4	8.5 ± 1.5	<.001

Notes: Values are mean ± *SD*.

Characteristics of patients who did versus did not require reinflation are summarized in Table 4. Patients with bleeding requiring TRB reinflation had lower body weight [BMI 24.9 (24.2–29.3) vs. 32.0 (27.4–40.2), p = .007], liver dysfunction [3 (27%) vs. 1 (3%), p = .03], and lower likelihoods of hypertension [8 (73%) vs. 38 (97%), p = .03] and left ventricular dysfunction [0 (0%) vs. 14 (36%), p = .02].

Predischarge radial artery patency at proximal and distal surveillance points on the forearm was documented in 100% of patients by vascular ultrasound. There was no evidence of vessel dissection or wall thickening. However, in one patient, there was the suggestion of a small amount of clot overlying the radial artery on longitudinal imaging, which was consistent with the aforementioned finding of an EASY grade I hematoma. Table 5 demonstrates dimensions of the radial artery pre-TRA and post-TRA with larger proximal RA dimensions

following the procedure. No late bleeding or neurologic, motor, or cutaneous reactions were reported in follow-up of the study cohort conducted a minimum of 30 days postprocedure.

4 | DISCUSSION

This single-arm, pilot study of 50 patients evaluated the safety and feasibility of a shortened duration of radial artery compression facilitated by a novel hydrophobically modified polysaccharide chitosan (hm-P) patch after diagnostic transradial procedures. Utilization of a topical hm-P patch achieved a time to hemostasis (TTH) of approximately 40 min, which is substantially shorter than our identified de facto US standard of 90–120 min radial artery compression (Figure 4). The 90- to 120-min comparator for duration of compression was chosen predominately based on institutional and regional trends; however, worldwide published TRA hemostasis literature suggests that this may underestimate the true duration in clinical practice. Aminian et al recently published an international multicenter randomized trial, RAP and BEAT, including 1,838 patients undergoing either 5 or 6 Fr vascular access TRA catheterization. Despite low overall rates of RAO near 2–3%, a substudy from this trial demonstrated that only 15% of patients achieved radial artery hemostasis in less than 120 min and nearly 65% of patients received more than 240 min of radial artery compression.[19,26] This further amplifies the divergence of hm-P facilitated hemostasis compared with current global practices and if validated in a larger dataset, may define a new TTH benchmark.

Previous studies focused on vascular preservation and RAO prevention through smaller hydrophilic sheaths, adequate periprocedural anticoagulation, and patent hemostasis with or without ulnar compression. For example, in the PHARAOH study by Pancholy et al., patent hemostasis was repeatedly monitored with subsequent compression device titration.[23] This type of protocol requires close monitoring and may be a resource intensive task that is difficult to standardize across institutions. Conversely, the use of the novel hm-P patch in our study was easily applied to the access-site without impediment of a standard pneumatic compression device. Furthermore, the time from first TRB deflation to complete deflation of the device was only 6 min, demonstrating a protocol that can be completed in a relatively short period of time without frequent adjustment or staff monitoring.

Current prospective and retrospective trial data has demonstrated a feasible reduction in TTH when a potassium ferrate hemostatic patch (PFHP, StatSeal Advanced disc) is combined with standard radial artery compression post-TRA procedures.[27-29] The 2017 STAT trial by Seto et al demonstrated a TTH of 43 ± 14 min which was similar to that achieved in our study; however, this trial also conferred a 17.2% rate of hematoma formation that was not statistically different from the control group but raised clinical concerns. The experience of Ayyaz Ul Haq et al. with PFHP similarly reduced TTH, but the rate of hematoma formation was higher compared with the control group, 12.1 versus 4.7% ($p < .009$). This study is the first reported clinical experience with hm-P for vascular access demonstrating feasible TTH reduction, while also withstanding a significant increase in vascular complications, such as late bleeding, hematoma, or RAO. Specifically, this is the only study protocol to our knowledge in which pre and post vascular ultrasound was performed and evaluation of RAO was assessed with color Doppler. In Tables 3 and 5, we showed that there were no complications of RAO and the vessel caliber was unchanged on postprocedure vascular ultrasound.

Additional hemostatic products have been evaluated as well, the results of which have been less promising. In 2019, a study by Pawel et al. involving a kaolin-based patch showed that kaolin-facilitated TRA hemostasis increased the TTH and had 5% incidence of EASY Grade IV hematomas.[30] Multiple studies have explored the efficacy of various hemostatic devices to reduce TTH and thereby facilitate discharge[28,31-34]; however, our study demonstrates a clinically meaningful reduction in TTH with all 50 patients undergoing same-day radial artery ultrasound imaging with vessel patency, preserved to greater radial artery dimensions, and the lowest rates of access site bleeding and hematoma among the literature surveyed.

In our study, patients with lower BMI were more likely to have initial bleeding and subsequent TRB reinflation. Garg et al. similarly demonstrated that low BMI was an independent predictor of postprocedure bleeding complications in a prospective analysis of more than 500 patients who underwent TRA PCI.[35] It seems plausible that the novel hm-P patch functions via accelerating superficial hemostasis from the skin surface along the tract of the sheath while the pneumatic compression device works by stabilizing the vessel and compressing the deeper soft tissue around the vessel, above the boney structure of the distal forearm. Our study suggests that hm-P can lead to more reliable hemostasis and obviate compression device retightening which has also been independently associated with subsequent RAO.[36] The exact duration of compression before device deflation will still need to be explored with the hope of identifying the point at which compression device reinflation is minimized while safely reducing the overall TTH.

Finally, the cost savings and operational efficiencies gained by rapid radial hemostasis pathways can potentially be offset or even eclipsed if not appropriately scrutinized in the context of downstream complications, specifically RAO, bleeding, and hematoma formation. In a meta-analysis by Mitchell et al. demonstrating the overall cost savings of TRA compared with TFA, the authors highlight the potential for further cost reduction through improved TRA hemostasis practices.[9] This 2012 study predicts the role for a novel adjunctive topical hm-P patch that safely shortens procedure recovery, decreases skilled staff monitoring, and facilitates higher throughput in catheterization and recovery areas. In the context of the aforementioned published investigations, utilization of the hm-P patch in this first-in-human pilot study appears to offer the desired, elusive balance of more rapid TTH with a simple-to-follow protocol and no demonstrable compromise of patient safety.

4.1 | Limitations

The main limitations of this study are its small sample size ($n = 50$), the single-center experience, the lack of a control group, and the use of a

single hemostasis device (TRB). Furthermore, it was not possible to attend each patient at exactly 30 min as specified in the protocol, due to logistical constraints. After the device had been inflated and sheath removed, the first observation and device deflation occurred at a median of 33 min (IQR: 31–35). Three patients received the first device deflation after more than 40 min of compression versus the protocol goal of 30 min which may have affected the TTH. Future planned studies will enroll a control group and focus on the potential resource savings from shorter postprocedure monitoring. Further device innovation is expected and a multicenter, prospective registry study is actively being designed.

5 | CONCLUSIONS

The adjunctive use of topical hm-P in conjunction with minimal required pneumatic compression resulted in rapid and predictable hemostasis of the radial artery puncture site following 6 Fr diagnostic angiography procedures. The achieved median time of 40.5 min represents a greater than 50% decrease of the de facto time to hemostasis in the United States. Hemostasis was achieved without reinflation of pneumatic compression devices in the majority of patients enrolled, despite therapeutic levels of parenteral anticoagulation at the time of sheath removal. Importantly, the minority of patients who manifested bleeding after initial TR Band deflation did so immediately and were, therefore, handled with rapid reinflation and no clinical sequelae or bleeding. Equally important, the rate of vascular ultrasound identified radial artery occlusion in this pilot study was 0%, which is a remarkable finding. The nonoccurrence of RAO was undoubtedly influenced by the short duration and light intensity of pneumatic compression afforded by the topical application of the novel hemostatic agent, hm-P. While this compound is biologically sourced as detailed, it was reassuring to note that there was no evidence of early or late cutaneous sensitivity reactions by examination and no impact whatsoever on the radial artery by ultrasound. If larger studies using hm-P facilitated hemostasis yield similar results, this approach may represent an important step forward for safely reducing both radial artery time to hemostasis and the incidence of radial artery occlusion.

CONFLICT OF INTEREST

Dr. Sandeep Nathan has served as a consultant and proctor for Terumo Interventional Systems, Medtronic, Inc. and Merit Medical. The other authors have reported no disclosures.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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