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Intestinal Staple Line Reinforcement Using MatriStem

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Abstract

Background: Staple line reinforcement material has been demonstrated to raise the burst pressure threshold after linear intestinal stapling. Numerous bioprosthetic materials have been utilized in surgical practice. Porcine urinary bladder matrix (ACell, Inc.) is an extracellular matrix material derived from porcine bladder used to reinforce surgically repaired soft tissue, and facilitate the body's regenerative capacity. Objective: This study represents the first evaluation of urinary bladder matrix in gastrointestinal staple line reinforcement. Methods: Pathogen-free pigs underwent midline laparotomy under general anesthesia. Small intestinal division was performed with an endoscopic linear stapler. Nineteen intestinal divisions were performed with urinary bladder matrix staple line reinforcement, and twenty divisions were unreinforced. Staple lines were then subjected to burst pressure analysis by intraluminal infusion of dyed Krebs solution at an infusion rate of 20 ml·min^{-1} under manometric monitoring. Upon visible staple line extravasation, intraluminal pressure was recorded. Results: Intestinal staple lines reinforced with urinary bladder matrix exhibited significantly higher burst pressure threshold ($p < 0.05$). Reinforced staple lines had an average burst pressure of 99 ± 33 mmHg, compared to 61 ± 37 mmHg for unreinforced staple lines. Conclusion: Staple line reinforcement using urinary bladder matrix acutely improves burst pressures of intestinal staple lines when compared with unreinforced staple lines. Its regenerative properties may confer a long-term advantage to staple line reinforcement. These findings, along with previous findings of constructive remodeling in the presence of urinary bladder matrix in treatment of the gastrointestinal system, suggest that UBM may serve a role in gastrointestinal staple line reinforcement.

Keywords

Surgical Staples, Extracellular Matrix, Porcine Urinary Bladder Matrix, Surgical Anastomosis, Small Intestine

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1. Introduction

Gastrointestinal surgical technique has relied increasingly on mechanical stapling devices, which have proven reliable with low rate of leak or staple line disruption. Anastomotic leak is associated with a high rate of mortality and other complications, including abscess, fistula, and reoperation [1] [2]. Efforts to reduce the likelihood of staple line leakage have led to the development of several bioprosthetic materials for use as staple line reinforcement [3]. Numerous studies have supported the use of staple line reinforcement material, and several of these materials are available for clinical use [4]-[11].

MatriStem is a unique biological material, which consists of the epithelial basement membrane and lamina propria of the porcine urinary bladder, referred to as urinary bladder matrix (UBM). After decellularization, it retains a rich biochemical diversity, an architecture that is similar to the normal tissue, and robust mechanical behavior [12]-[15]. UBM has shown effectiveness for management of complex wounds and reinforcement of surgically repaired soft tissue with constructive tissue remodeling in anatomic settings as diverse as esophageal, urinary bladder, and body wall repair [16]-[18]. It has not been studied to date as a staple line reinforcement material, but its properties and handling characteristics suggest it may improve the staple line burst pressure threshold and potentially facilitate favorable tissue remodeling responses.

2. Methods

A 150lb pathogen-free pig was induced with tiletamine/zolazepam 500 mg intramuscularly and 6 mg atropine subcutaneously. The animal was then intubated with a 9 mm endotracheal tube, an 18 gauge intravenous catheter was inserted into the lateral ear vein, and lactated ringers solution was infused. Anesthesia was maintained with 3% gas isofluorane and ketamine 100 mg as needed. Pulse oximetry and body temperature were monitored, ventilation was maintained with a mechanical ventilator, and body temperature was maintained with a Bair Hugger warming device. A midline laparotomy was performed and small intestinal division was carried out utilizing an endoscopic linear stapling device (Echelon 60 mm linear stapler using 3.5 mm staple loads, Ethicon Corporation). Thirty-nine staple line burst pressure tests were performed. Nineteen of the intestinal divisions were performed with staple line reinforcement material utilizing MatriStem RS devices (ACell, Inc.), and twenty of the staple lines had no reinforcement. Each of the MatriStem RS devices was trimmed to 1.11 cm by 6.5 cm for use as a staple line reinforcement device then hydrated in saline for a minimum of 15 minutes. One device was placed onto the cartridge and anvil of each endoscopic stapler (**Figure 1**). The tests were conducted using 10 cm segments of ileum in the live pig, alternating between reinforced and unreinforced staple lines after each test. The staple lines were then subjected to a burst pressure analysis by intraluminal infusion of dyed Krebs solution under constant manometric monitoring rate of 20 $ml \cdot min^{-1}$ and simultaneous manometric monitoring (**Figure 2**). Burst pressure was defined as the pressure at which visible blue dye extravasated and dripped from the tissue, or when an overt rupture occurred (**Figure 3**). The location of burst was recorded as occurring at the staple line, at the infusion catheter entry site, or due to a ruptured intestinal wall. The animal was then euthanized with pentobarbital sodium 4000 mg intravenously. The animal received humane care throughout the pre-experimental and experimental processes.

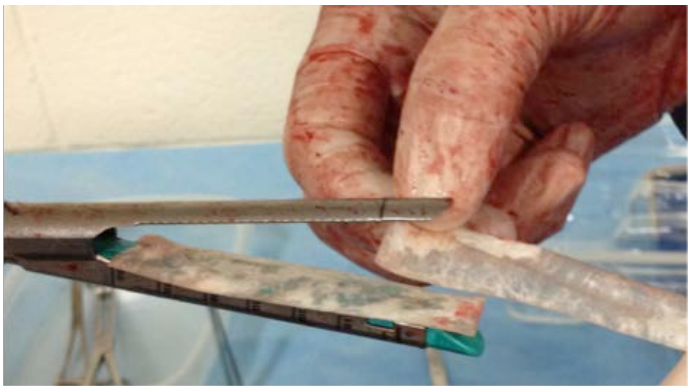

Figure 1. Hydrated MatriStem Surgical Matrix (RS) was placed onto the cartridge and anvil of each endoscopic stapler to serve as staple line reinforcement.

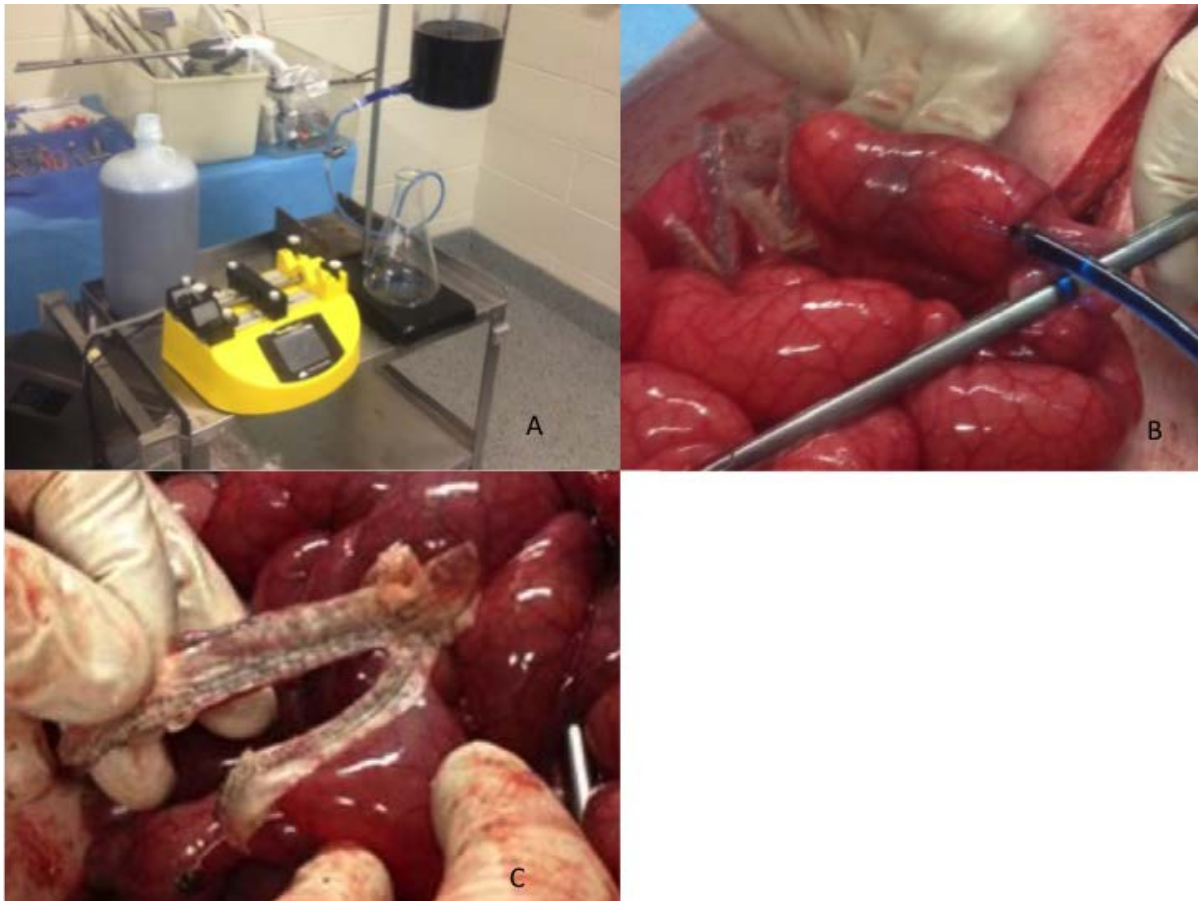

Figure 2. (A) Custom apparatus for continuous infusion of dyed Krebs solution; (B) Fixturing for infusion of fluid into the intestinal segment; (C) Completed staple firing with MatriStem reinforcement.

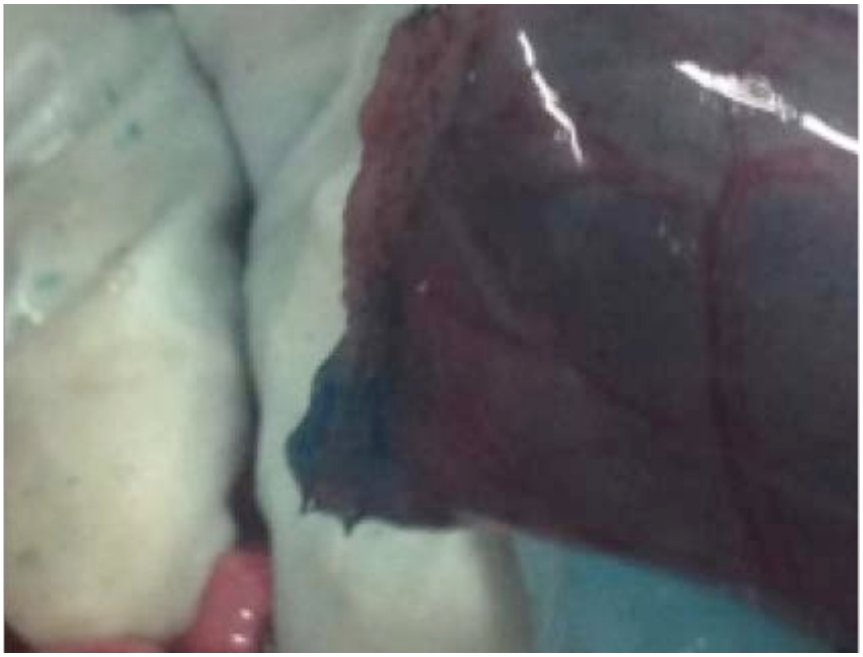

Figure 3. Extravasation of dyed Krebs solution from the staple line.

3. Results

Intestinal staple lines reinforced with MatriStem showed significantly higher burst pressure threshold as compared with non-reinforced controls (**Table 1**) ($p < 0.05$). MatriStem-reinforced staple lines had an average burst pressure of 99 ± 33 mmHg, compared to 61 ± 37 mmHg for unreinforced staple lines. The location of the burst occurred at the staple line in all the unreinforced staple line tests. In the tests involving staple line reinforcement with MatriStem, the location of the burst was staple line 68%; infusion catheter entry site 5% and intestinal wall rupture 32%. Kaplan-Meier curve of intactness of MatriStem reinforced vs. unreinforced staple lines further illustrates the advantage of MatriStem reinforcement (**Figure 4**).

4. Discussion

Staple line reinforcement using MatriStem material improved the burst pressure of intestinal staple lines. The burst occurred at sites other than the staple line in 35% of the tests when using MatriStem as a reinforcement material, so the actual burst pressure for the reinforcement site are greater than the values measured.

Table 1. Comparison of small intestinal burst pressure with MatriStem reinforced stapling versus unreinforced stapling.

With MatriStem Reinforcement			Without Reinforcement		
Trial	Location of Failure	Burst Pressure (mmHg)	Trial	Location of Failure	Burst Pressure (mmHg)
1	Intestinal Wall	100	1	Staple Line	107
2	Intestinal Wall	130	2	Staple Line	43
3	Intestinal Wall	145	3	Staple Line	60
4	Staple Line & Serosa	140	4	Staple Line	25
5	Intestinal Wall	125	5	Staple Line	125
6	Entry Point for Cath	140	6	Staple Line	60
7	Intestinal Wall	130	7	Staple Line	50
8	Staple Line	125	8	Staple Line	95
9	Staple Line	70	9	Staple Line	150
10	Staple Line	100	10	Staple Line	80
11	Staple Line	125	11	Staple Line	20
12	Staple Line	75	12	Staple Line	40
13	Staple Line	88	13	Staple Line	55
14	Staple Line	100	14	Staple Line	56
15	Staple Line	48	15	Staple Line	88
16	Staple Line	45	16	Staple Line	57
17	Staple Line	78	17	Staple Line	35
18	Staple Line	46	18	Staple Line	40
19	Staple Line	71	19	Staple Line	22
			20	Staple Line	10
	Mean	99		Mean	60.9
	Standard Deviation	33.8		Standard Deviation	36.7
	p-value ($p < 0.05$): 0.000885				
	T-value: 3.370001				

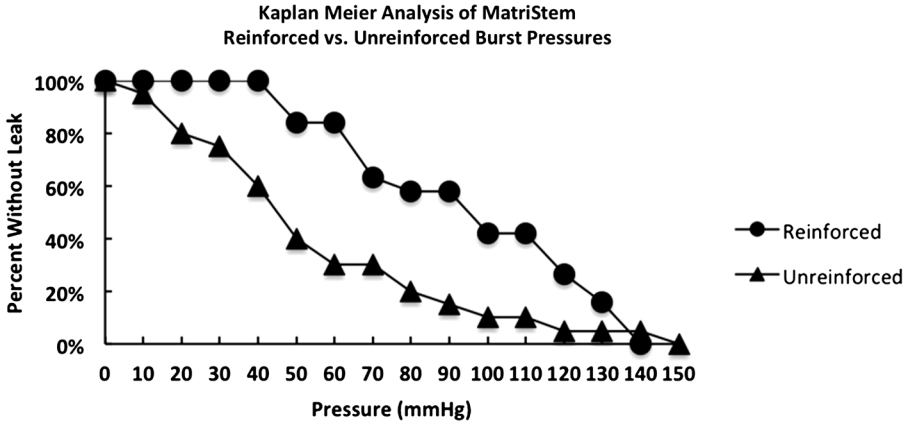

Figure 4. Kaplan-Meier analysis of MatriStem reinforced vs. unreinforced burst pressure. The curve shows progressive increase in percentage of ruptured intestinal staple lines with increasing pressure, and an increased resistance to rupture with reinforcement.

Previous testing has been performed on similar devices for staple line reinforcement of the gastrointestinal tract. Earlier work involved the use of bovine pericardial strips to buttress the staple line, which demonstrated increased burst pressure from an average of 58 mmHg to 125 mmHg, as well as an 8% rate of failure at the reinforced staple line versus 100% rate of failure at the unreinforced staple line [4]. In a similar model, small intestinal submucosa was shown to increase the average burst strength from an average of 53 mm Hg to 83 mmHg, which is comparable to the results observed in the present study [3].

The primary weakness of the present study is that it only evaluated the burst pressure in the acute setting. However, the increased burst pressures observed provide some confidence that the results will be no worse than without reinforcement. Furthermore, UBM has previously been investigated for anastomotic reinforcement of the esophagus in a canine model. None of thwe animals treated with UBM showed signs of leaks at the anastomosis, and there were fewer strictures at the anastomotic site as compare to non-treated controls. Additionally, UBM reinforcement facilitated the formation of skeletal muscle that bridged the transection, while the control simply showed the presence of dense collagenous tissue [15].

5. Conclusion

Currently available materials for staple line reinforcement increase the stapled intestinal burst pressure threshold. MatriStem utilized for staple line reinforcement increased the burst pressure threshold significantly as well, while offering the potential to facilitate constructive remodeling. In summary, these findings encourage additional evaluation of MatriStem for clinical use in staple line reinforcement.

Acknowledgements

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Conflicts of Interest

Dr. Sasse serves as a consultant to ACell, Inc., Columbia, MD. All other authors have nothing to disclose.

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