Journal of Surgical Research **170,** 179–184 (2011)
doi:10.1016/j.jss.2011.03.058

ASSOCIATION FOR ACADEMIC SURGERY

Flow Through a Mechanical Distraction Enterogenesis Device: A Pilot Test[1]

Eiichi A. Miyasaka, M.D.,* Manabu Okawada, M.D.,* Richard Herman, M.D.,* Brent Utter, M.S.E.,† Jonathan Luntz, Ph.D.,† Diann Brei, Ph.D.,† and Daniel H. Teitelbaum, M.D.*,[2]

*Section of Pediatric Surgery, Department of Surgery and the C.S. Mott Children's Hospital, University of Michigan, Ann Arbor, Michigan; and †Department of Mechanical Engineering, University of Michigan, Ann Arbor, Michigan

Submitted for publication January 7, 2011

Background. **We tested the coupling portion of a prototype intraluminal distraction enterogenesis device to allow flow-through of simulated enteric contents (SEC) in both pig and human jejunum.**

Materials and Methods. **SEC was made using 80% corn syrup. Ten-cm pig and human intestinal segments had a spoke-shaped 2.2 cm coupling adaptor sutured in place, intraluminally. The adaptor had a flow-through area of 33.6 mm^2. SEC was pumped into the proximal part of the intestinal segment at 0.083 mL/s. The times to first passage of SEC through the coupler (first drop), 10 mL, and 20mL of SEC eluted from the distal end were recorded.**

Results. **Mean time to first drop elution was 155 ± 38 s with pig, and 149 ± 22 s with human bowel (P = 0.8). This corresponded to a hydrostatic pressure of 37.5 mmHg before the initial drop passed through. Mean flow rates were 0.094 mL/s in pig bowel and 0.084 mL/s in human bowel (P = 0.09). To account for occlusion from luminal debris, a 75% occlusion of coupler holes was studied in the smaller pig bowel to investigate if reductions in flow-through area could be tolerated. Mean time to first drop increased slightly to 171±15 s, but the elution rate stayed the same (P = 0.5).**

Conclusions. **After a physiologic level of initial pressure buildup allowing the first drop of SEC to pass the coupling adaptor, our prototype intestinal coupling adaptor did not obstruct flow-through of SEC, even after a 75% decrease in flow-through area. This type of attachment represents a viable approach to placing a device in-continuity without obstructing flow of enteric contents.**

Key Words: **distraction enterogenesis; short bowel syndrome; simulated enteric contents; viscosity; flow-through.**

INTRODUCTION

Short bowel syndrome (SBS) is a highly morbid condition in which patients have insufficient small bowel length for proper nutritional absorption. Patients with SBS require supplemental parenteral nutrition, and often suffer complications, including cholestatic liver disease, central line infections, and bacterial overgrowth [1]. Despite promising new advancements in the treatment of SBS, such as the advent of intestinal lengthening procedures (e.g., serial transverse enteroplasty) [2] and improved survival after intestinal transplantation [3], SBS remains a very difficult process to treat.

The prognosis of patients with SBS is known to be dependent on remaining bowel length. Patients with less than 10% of predicted small bowel length have little to no chance of weaning off of parenteral nutrition [1]. It therefore stands to reason that therapies that can increase small bowel length hold promise in improving the treatment of SBS patients. Previously, investigators have successfully achieved small bowel lengthening in a rat model, and showed that its histology was not compromised and enzymatic functions increased [4, 5]. Our group has successfully induced longitudinal growth in porcine small bowel [6]. Through the application of mechanical distractive forces, a 45% increase in longitudinal bowel length was achieved over a 10-d period. The lengthened intestine showed increased rates of epithelial cell proliferation, consistent with true growth due to mechanotransductive mechanisms.

[1] Presented at the 6th annual Academic Surgical Congress, February 2011, Huntington Beach, California.

[2] To whom correspondence and reprint requests should be addressed at Section of Pediatric Surgery, University of Michigan, Mott Children's Hospital, F3970, Ann Arbor, MI 48109-0245. E-mail: dttlbm@umich.edu.

0022-4804/$36.00

This bowel also demonstrated intact epithelial barrier function and transmucosal uptake of nutrient substrate. Such a rapid form of intestinal growth may offer a unique approach to treat SBS.

Previous strategies employed in our laboratory to apply distractive forces have used surgically isolated segments of bowel [6]. Two issues with this type of implantation are that the device will need to be implanted by open invasive surgery, and the stretched isolated segment will eventually require a re-anastomosis. To overcome these issues, we developed a prototype of an intestinal lengthening device that can be implanted in-continuity with the rest of the bowel. This novel approach has the advantages of requiring minimal bowel manipulation (including no need to re-anastomose intestine), and having the future potential to be placed endoscopically with improvements in bowel attachment techniques.

An obvious concern upon implementing this type of device is the risk of causing a small bowel obstruction. Both benign (e.g., intramural hematoma [7]) and malignant (e.g., metastatic disease [8]) natural space-occupying processes are known to cause bowel obstructions, but the extent to which such lesions must occupy luminal space before producing symptoms has not been fully evaluated. The larger the device can be, the more structural support it can have, and the easier it would be to engineer parts. However, a larger device is more likely to cause obstructive problems than a smaller device.

The purpose of this study is to test the ability of simulated small bowel enteric contents (SEC) to flow through the diminished area of the intestinal attachments of this new device in both pig and human jejunum. Tests were conducted to assess the initial resistance of the attachment to flow-through of SEC, and also to determine if the diminished flow-through area altered the speed of elution once SEC passed through the attachment. To further evaluate other factors that may impede flow-through ability, tests were repeated with 75% of the elution holes in the attachment plugged, and with SEC with particulate matter added. We performed these experiments to assess the feasibility of an in-continuity distraction enterogenesis device in future live animal models.

MATERIALS AND METHODS

Bowel Samples

Pig bowel was obtained from adult female Yorkshire swine immediately after their death. Bowel segments were cut into ~30 cm segments, and were immediately frozen in a −80°C freezer until they were used. Human jejunal segments were obtained from organ donors in coordination with the Gift of Life Michigan.

Approval for tissue usage was obtained from the University Committee on the Use and Care of Animals (protocol 09026), Gift of Life Michigan, and the Institutional Review Board (HUM00023670) at the University of Michigan.

Prototype of Intraluminal In-Continuity Intestinal Lengthening Device

Figure 1A shows a schematic of our prototype in-continuity intestinal lengthening device. The disks at both ends of the device are designed to act as attachments of the device to the bowel. The central tube contains a shape-memory alloy powered ratcheting system that allows for extension of the device and longitudinal intestinal growth. Details of the workings of this device can be found in Utter *et al.* [9]. The largest cross-sectional diameter (22 mm) is present at the attachment rings on both ends of the device. The total cross sectional flow-through area is 33.6 mm^2 divided in eight arced slots spaced equally (Fig. 1B). Therefore, to test the ability of enteric contents to flow through the device, we specifically tested the ability of simulated enteric contents to flow through the attachment (Fig. 1C).

Simulated Small Bowel Enteric Contents (SEC)

Pig cecal content viscosity has been described between 0.1 and 1.0 Pa-s over a range of shear rates [10]. Cecal contents will have a lower water content, hence a higher viscosity than small bowel contents, but we attempted to create a fluid with a similar coefficient of viscosity in order to be more rigorous with our testing. Varying dilutions of dark Karo corn syrup (ACH Food Companies, Cordova, TN) were measured using a falling sphere viscometer shown in Figure 2. A steel sphere was dropped from the top of the fluid column, and the terminal velocity of the sphere (of radius r in Fig. 2) was measured by calculating the time it took for the sphere to drop a pre-defined distance (d in Fig. 2). The coefficient of viscosity (μ) was calculated using the following formula:

$$\mu = 2 * r^2 * g * (\rho_p - \rho_f)/(9\ v)$$

where r is the radius of the steel sphere, g is the gravitational constant ($9.8 m/s^2$), ρ_p is the density of the steel sphere, ρ_f is the density of the tested fluid, and v is the measured terminal velocity of the sphere falling through the fluid [11].

Using this methodology, 80% corn syrup diluted in water (density 1.33g/mL) was found to have a viscosity coefficient between 0.29 and 0.61 Pa-s; therefore this solution was used as SEC. The density of this fluid was 1.33 g per mL.

Flow-Through Setup

For this part of the experiment, thawed bowel was cut into 10 cm segments, and its inner circumference was measured by splaying open a small segment of bowel radially and measuring the length of the mucosa. This circumference was used as a surrogate for inner bowel diameter because bowel is deformable. The spoke-shaped attachment (Fig. 1D and E) was sutured in place 3 cm from the distal end of the bowel segment. SEC was pumped into the proximal part of the intestinal segment at 300 mL/h (0.083 mL/s) using a Hospira Gemstar infusion pump (Lake Forest, IL) or a Harvard Apparatus syringe infusion pump (Holliston, MA). A goal for fluid passage was determined to be a rate of 300 mL/h (or 0.083 mL/s). This was derived from the known volume of 7 L of fluid s reted by the average adult human stomach and small bowel daily (7000 mL/24h = 291.6 mL/h)[12].

The times to first drop, 10 mL, and 20 mL of SEC elution from the distal end were recorded. First drop elution was defined as the time when the first drop of SEC to elute out of the distal end of the bowel segment landed into the measuring cylinder below the bowel (Fig.1E). Similarly, 10 mL SEC elution was defined as the time at which 10 mL of SEC accumulated in the measuring cylinder below the tested bowel segment. The time to first drop elution was measured as a surrogate for how much pressure (if any) needed to build up in