



# Self-expanding intestinal expansion sleeves (IES) for short gut syndrome

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## Abstract

**Purpose** Many disease processes (*necrotizing enterocolitis, caustic esophageal injury, malrotation with volvulus*), can result in short-gut syndrome (SGS), where remnant intestinal segments may dilate axially, but rarely elongate longitudinally. Here we mechanically characterize a novel model of a self-expanding mesh prototype intestinal expanding sleeve (IES) for use in SGS.

**Methods** Gut lengthening was achieved using a proprietary cylindrical layered polyethylene terephthalate IES device with helicoid trusses with isometric ends. The IES is pre-contracted by diametric expansion, deployed into the gut and anchored with bioabsorbable sutures. IES expansion to its equilibrium dimension maintained longitudinal gut tension, which may permit remodeling, increased absorptive surface area while preserving vascular and nervous supplies. We performed mechanical testing to obtain the effective force–displacement characterization achieved on these prototypes and evaluated minimal numbers of sutures needed for its anchoring. Furthermore, we deployed these devices in small and large intestines of New Zealand White rabbits, measured IES length–tension relationships and measured post-implant gut expansion *ex vivo*. Histology of the gut before and after implantation was also evaluated.

**Results** Longitudinal tension using IES did not result in suture failure. Maximum IES suture mechanical loading was tested using 4–6 sutures; we found similar failure loads of  $2.95 \pm 0.64$ ,  $4 \pm 1.9$  and  $3.16 \pm 0.24$  Newtons for 4, 6 and 8 sutures, respectively ( $n = 3$ , n.s). Pre-contracted IES tubes were deployed at  $67 \pm 4\%$  of initial length (i.l.); in the large bowel these expanded significantly to  $81.5 \pm 3.7\%$  of i.l. ( $p = 0.014$ ,  $n = 4$ ). In the small bowel, pre-contracted IES were  $61 \pm 3.8\%$  of i.l.; these expanded significantly to  $82.7 \pm 7.4\%$  of i.l. ( $p = 0.0009$ ,  $n = 6$ ). This resulted in an immediate  $24 \pm 7.8\%$  and  $36.2 \pm 11\%$  increase in gut length when deployed in large and small bowels, respectively, with maintained longitudinal tension. Maintained IES induced tension produced gut wall thinning; gut histopathological evaluation is currently under evaluation.

**Conclusion** IES is a versatile platform for gaining length in SGS, which may be simply deployed via feeding tubes. Our results need further validation for biocompatibility and mechanical characterization to optimize use in gut expansion.

**Keywords** Short gut · Intestinal expansion device · Necrotizing enterocolitis · Intestinal lengthening

## Background

Pediatric surgeons often encounter patients with intestinal failure due to inadequate intestinal length. These patients are challenging, because the adaptive process for reaching enteral goals is slow. Patients with short gut compensate with gastroparesis and slow dilation of the intestinal diameter [1]. This process may take weeks, months or years requiring supplemental parenteral nutrition for adequate growth [2]. Native elongation of the short intestine usually is frequently limited. Two surgical elongation procedures have been developed—the Bianchi [3] and serial transverse

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enteroplasty (STEP) procedure [4]. Both procedures require that the patient has developed sufficient dilation of bowel diameter [5]. The medical care of these patients is encumbered by daily needs for total parenteral nutrition (TPN), central line access, and metabolic derangements [6].

One possible solution to managing this clinical dilemma is to initiate an intestinal elongation strategy early. Distraction enterogenesis (DE) with various devices has been shown in animal models to enable elongation of the intestine [7]. These devices cause longitudinal tension on a segment of intestine resulting in elongation of the segment by 50% or more [8]. Some of these devices include springs, [9] and balloon devices, [10]. Initial studies have these devices placed out of continuity of the gastrointestinal tract, such as in a Roux limb [11]. The spring device has so far been successfully placed in continuity in a rat model [12]. The potential improvement in the clinical course of these patients is tremendous with decreased days on TPN, decreased need for central access and decreased line infections.

There are several potential benefits/advantages of the expanding intestinal sleeves over other prototypes. The device is porous making successful placement in continuity likely. The contracted device expands radially in proportion to the amount of shortening in length of the IES. The radial expansion should make the device easier to secure to the intestine in a future noninvasive model. Finally, the fully expanded sleeve has a decreased diameter making eventual passage of the IES in the stool more likely.

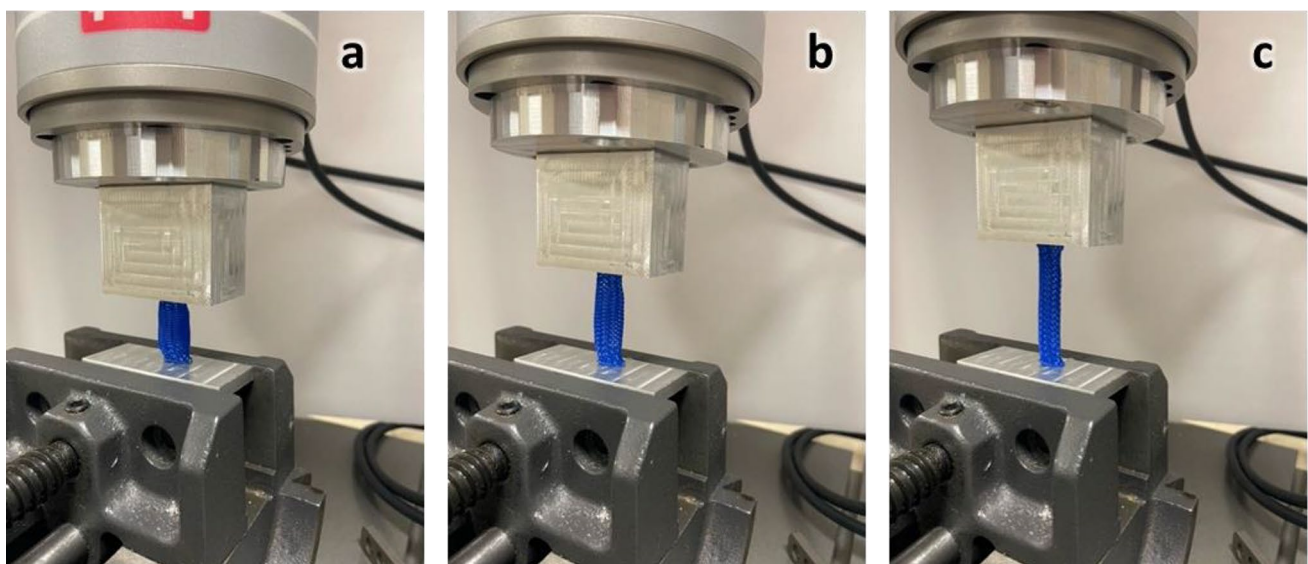
Our DE device is an implantable porous mesh sleeve intended to be attached at each end to the intestine with absorbable sutures. The device is designed to exert a linear force curve as it expands lengthening the intestine.

The segment would eventually be passed in stool once the absorbable sutures have dissolved. Ultimately, to save the patient operations and potential intestinal length, the device would be fixed to the end of a long transpyloric feeding tube and deployed without surgery. Multiple deployments of these sleeves should be possible. In this study, we sought to evaluate the achieved force–strain relationship in the built prototypes, evaluate the achievable tensioning force in relation to the number of sutures used for its anchoring, and present an initial feasibility of placing the novel sleeve in rabbit intestine. We hypothesize that an expansion greater than 40% of the initial device length is achievable with no more than six sutures.

## Methods

### Sleeve preparation and characterization

Intestinal expansion sleeves (IES) were produced as cylindrical layered polyethylene tubes with helical trusses. The ends of the sleeves were heat-treated to smooth the edges. These sleeves are demonstrated in Fig. 2. Edges of sleeves were inspected and milled smooth as needed. The sleeve lengths were measured individually in their native form (initial length, i.l.). Mechanical characterization was performed using an Instron 8874 Biaxial Servo Hydraulic Fatigue Testing System and applying a cycle of compression followed by expansion at a rate of 50 mm/min (see Fig. 1). With reference to the nominal length of the DE



**Fig. 1** Mechanical Characterization of the DE device during the expansion phase at strains of 50% (a), 25% (b), and at its nominal length (c)



**Fig. 2** Representative sleeve and introduction into intestine (left). Intestine after expansion of the sleeve (right)

devices, force values were recorded during the expansion phase at strain values 10, 20, 30, 40 and 50%.

### Implantation of the sleeves

Using small and large intestines from New Zealand White rabbits, several test sleeves were implanted. Bowel was harvested from the recently sacrificed rabbits and lumen washed with isotonic saline. Measurements of the bowel in native form were obtained and sleeves were then placed over a 0.8 cm plastic tube with an end tapered to 3 mm (Fig. 2). The placement of the sleeve over the tubing resulted in shortening of the sleeve to its pre-contracted form which was recorded. An enterotomy was made in intestinal segment and the tube containing the pre-contracted sleeve placed into the intestinal segment. Four sutures (4–0 polydioxanone, Ethicon) were placed at both ends to secure the sleeve inside the intestinal wall in the pre-contracted state. Removal of the pipette resulted in immediate partial expansion of the sleeve within the intestinal segment; the extent of bowel length extension was measured using calipers.

### Mechanical testing of the bowel/device connection

Intestinal segments instrumented with the DE device were tested to determine maximum force prior to failure in relation to the number of sutures used for the anchoring of the DE device. The testing was performed on the same Instron machine used for the characterization (Fig. 3). The specimens, composed by a DE device connected to a bowel segment were held in place by two pneumatic grips at 25



**Fig. 3** Mechanical testing of IES bowel connection

psi of pressure, as shown in Fig. 2 (pics). For comparison, specimens of the bowel alone were also tested Fig. 4. Sleeve placement in the rabbit small intestine vs length of IES ( $n=3$  for each group).

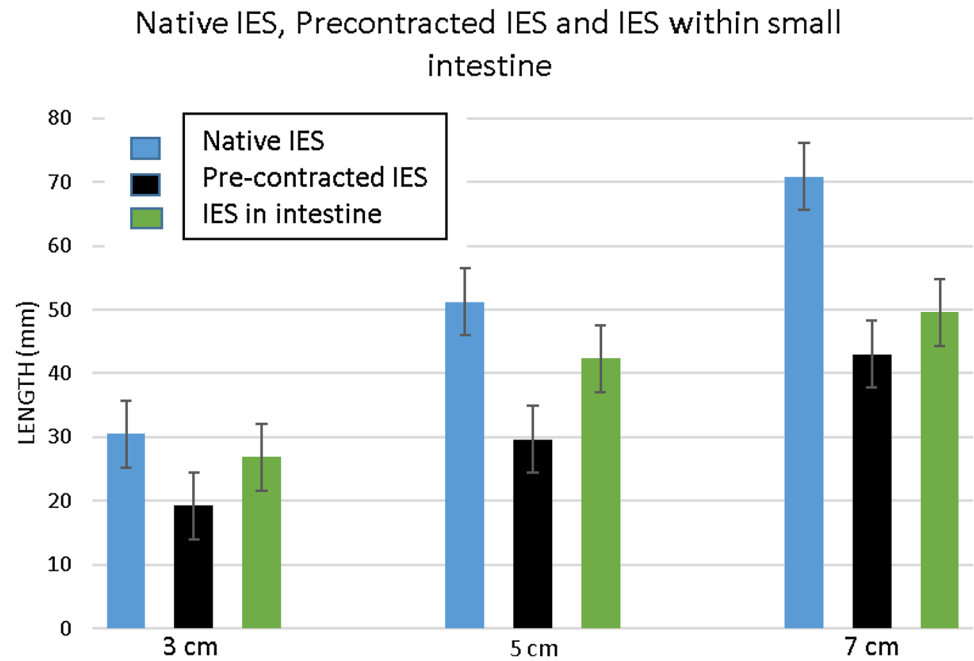
as controls. Testing to failure was performed tensioning the specimens at a rate of 50 mm/min until failure. The three configurations tested, included DE devices connected with 4, 6 or 8 sutures. Load displacement data was recorded at a frequency of 100 Hz and for every 0.1 N increments. The peak load measured during testing was considered as the failure load for the specimen.

## Results

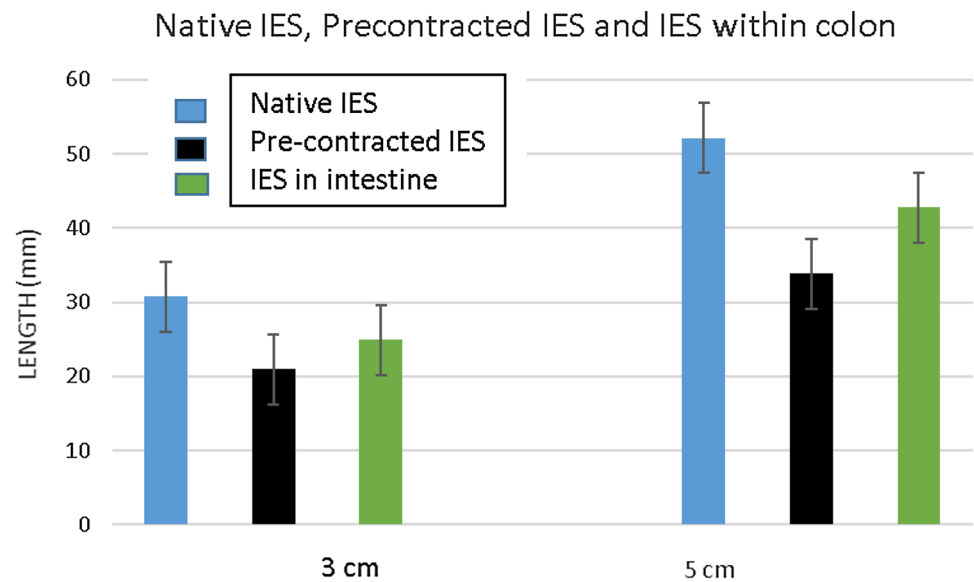
### Animal model

Six (6) sleeves were placed in colons and 9 sleeves were placed in small bowels. Measurements were taken by a caliper and lengths recorded in mm. The sleeves used in the colon showed a pre-deployment decrease in length of  $67 \pm 3.6\%$  of i.l. The sleeves expanded in the colon to  $81.6 \pm 3\%$  of i.l. of the sleeve ( $p=0.014$ ,  $n=6$ ). In the small bowel pre-contracted IES were  $60.6 \pm 3.7\%$  of i.l.; these expanded significantly to  $80.2 \pm 8.4\%$  of i.l. ( $p=0.0009$ ,  $n=9$ ). This resulted in an immediate  $24 \pm 7.8\%$  and  $36.2 \pm 11\%$  increase in gut length of the colon and small bowel, respectively.

**Fig. 4** Sleeve placement in the rabbit small intestine vs length of IES ( $n=3$  for each group)



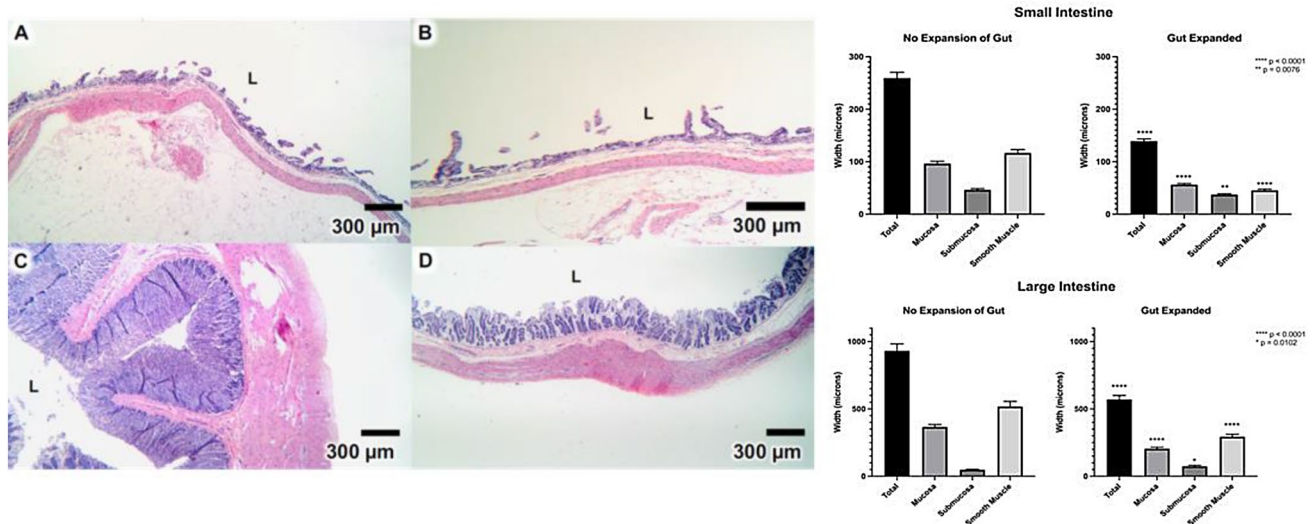
**Fig. 5** Sleeve placement in the rabbit colon vs length of IES ( $n=three$  for each group)



Average increase of intestinal length for 3 cm and 5 cm sleeves in the small intestine was  $39 \pm 3\%$  and  $44 \pm 13\%$ , respectively. Interestingly, the percent increase in length for 7 cm was only  $16 \pm 8\%$  (Fig. 4). The colon data were similar (Fig. 5,  $n=3$  in each group). The IES colon percent increase in i.l. was  $19 \pm 8.5\%$  for 3 cm sleeve and  $26.7 \pm 3.5\%$  for 5 cm (Fig. 5).

Load testing was done on IES sutures to small bowel with 4, 6 or 8 sutures. Failure under load as defined by a sudden drop in tension was seen at  $2.95 \pm 0.64$ ,  $4 \pm 1.9$  and  $3.16 \pm 0.24$  Newtons for each respective number of

sutures. There was no significant difference between these groups regarding failure load. Failure load of small intestine alone was  $4 \pm 1.5$  Newtons. The expansion force was measured for each length of sleeve 3, 5, and 7 cm. Representative histology sections from small and large intestine show significant wall thinning (Fig. 6).



**Fig. 6** Histology of the small intestine (left) with IES showed significant wall thinning in all layers of the small and large intestines in response to dilation of the lumens with IES. **A** Small intestine undilated and **B** dilated. **C** Large intestine undilated and **D** dilated. Bar = 300  $\mu$ m

## Discussion

Short bowel syndrome (SBS) is considered the most common cause of intestinal failure in pediatric patients. Loss of small bowel length results in inadequate nutrient absorption due to a lack of functional surface area, leading to increased morbidity and mortality [6]. The most common etiologies of short bowel syndrome in infant and pediatric patients include necrotizing enterocolitis, abdominal wall defects, jejunal ileal atresia, and mid gut volvulus [1]. Bowel lengthening surgical procedures have been developed; however, they carry substantial risks for morbidity due to their invasive nature and exclude patients with undesirable anatomy [13–15]. Other methods of treatment include medications to slow intestinal transit and parenteral nutrition. Most patients are dependent on the parenteral nutrition route, which leads to risks, such as sepsis, metabolic derangements and hepatic dysfunction. Remaining bowel length has been shown to positively correlate with the ability to wean from parenteral nutrition [2, 16, 17]. Distraction enterogenesis (DE) is a recently developed method, whereby small intestine elongation is accomplished by the use of longitudinal mechanical force, which has been hypothesized to provide a therapeutic option for those with SBS [7, 8, 18]. The main challenge with DE has been developing a method which minimizes axial expansion while maximizing longitudinal lengthening. Previous successful methods of attaining longitudinal bowel lengthening include hydraulic pistons, spring loaded devices, and osmotic distension. Unfortunately, all of these methods have been limited by their transmission of axial force against the bowel wall, which leads to risks such

as perforation and necrosis secondary to compression of the blood supply of the bowel wall [10]. The excessive axial force component of these previous methods has led to significant challenges in translating these basic science experiments to clinically applicable technology.

Despite its challenges, DE has shown promise in obtaining sustained intestinal lengthening with concomitant functionality. Previous studies have characterized this preserved functionality by the presence of mesenteric neovascularization, muscular hypertrophy, increased epithelial cell proliferation, and increased villus height and crypt depth [19, 20]. Early studies testing DE in pigs required creation of blind-ending segments of intestine [8, 18] or the use of vessels loops or full thickness sutures to facilitate mechanical force transmission to the bowel wall [19]. These methods required multiple separate open operations to both place and remove the devices or restore intestinal continuity, which adds substantial surgical complexity and potentially results in the loss of gained intestinal length after anastomosis creation [21]. Further advancements led to the creation of devices which could provide longitudinal force via reversible endoluminal attachments. This improved delivery system obviated the need for additional procedures to remove the device. Challenges with this new approach included an efficient delivery system and atraumatic distraction attachments [10].

Mechanical data (Table 1) show that average failure load for native rabbit intestine is  $2.48 \pm 0.19$ . Failure load with four fixation sutures was similar and 2/3 of failures occurred in bowel and not the connection of device to intestine ( $n=9$ ). Increasing the number of sutures to the IES device did not significantly affect the failure load. These data support four fixation sutures for the IES device.

**Table 1** Bowel/device connection

Number of sutures	Failure load [N]	Localization of the failure formation
0	2.75	Proximity of the grip
0	2.31	Bowel
0	2.38	Bowel
0	2.49	Bowel
4	2.85	Bowel
4	3.64	Bowel
4	2.37	Stitches
6	2.46	Bowel
6	3.33	Bowel
6	6.25	Stitches
8	3.42	Stitches
8	2.94	Bowel
8	3.12	Bowel

**Table 2** Mechanical characterization of the created prototypes

DE nominal length [mm]	Strain				
	10%	20%	30%	40%	50%
30	0.46	1.61	2.32	2.82	6.08
30	0.62	2.07	2.84	3.31	7.29
30	0.85	2.37	2.99	3.54	7.59
40	0.10	1.10	1.82	2.26	3.99
40	0.70	1.76	2.14	2.83	7.63
40	1.01	1.83	2.18	2.78	6.57
50	0.98	1.91	2.23	2.78	6.41
50	0.94	1.77	2.15	2.55	5.78
50	0.91	1.80	2.10	2.67	6.64

Load values [N] recorded at various strain values for each tested nominal length of the DE device

Our strain data on prototypes of varying lengths show that the sleeves exceed the failure load of rabbit intestine when compressed more than 30% (Table 2). This will require some widening of helical trusses and dampening of the load values of IES prior to placing in vivo in New Zealand white rabbits.

Our data demonstrate a significant immediate expansion of the intestine (small bowel or colon) and the resilience of the suture fixation of the IES. Mechanical testing also demonstrated the load properties of the intestine before elongation by the IES. This information is vital to the design of IES devices. Optimally, the force (N) of expansion of the IES should be less than the failure load of the intestine. Histology shows the stretching of the intestinal wall and flattening of villi. Designing IES devices with sub intestine failure load force dynamics will decrease the potential for intestinal perforation.

When we compare different lengths of IES, the initial expansion benefit appears to diminish at the 7 cm ( $16 \pm 8\%$ ) vs 5 cm ( $44 \pm 13\%$ ) length. This seems to indicate an optimal length for the IES and longer lengths are not always better. Key to gaining maximum length may be deployment of multiple IES devices or serial deployments over time. Future studies will focus on optimal length of IES and potential for multiple deployments.

Distraction enterogenesis has the potential to treat short bowel syndrome. Our IES offers multiple improvements compared to prior devices. The sleeve is porous and should be deployable in continuity with GI tract. In addition, the IES will not require removal as it will be held in place with absorbable sutures. The device has limited axial expansion and excellent linear expansion as shown by this study. Finally, the future use of IES may enable device to be deployed over a feeding catheter as well as coated with drugs to promote healing or decrease inflammation.

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