Published in final edited form as:

J Biomech. 2011 July 28; 44(11): 2077–2082. doi:10.1016/j.jbiomech.2011.05.017.

Stress and strain analysis of contractions during ramp distension in partially obstructed guinea pig jejunal segments

Jingbo Zhao^{1,2}, Donghua Liao^{1,2}, Jian Yang², and Hans Gregersen³

¹Institute of Clinical Medicine, Aarhus University, Aarhus, Denmark

²Mech-Sense, Aalborg Hospital, Aalborg, Denmark

³Sino-Danish Centre for Education and Research, and Aarhus Hospital, Aarhus, Denmark

Abstract

Previous studies have demonstrated morphological and biomechanical remodeling in the intestine proximal to an obstruction. The present study aimed to obtain stress and strain thresholds to initiate contraction and the maximal contraction stress and strain in partially obstructed guinea pig jejunal segments. Partial obstruction and sham operations were surgically created in mid-jejunum of male guinea pigs. The animals survived 2, 4, 7, and 14 days, respectively. Animals not being operated on served as normal controls. The segments were used for no-load state, zero-stress state and distension analyses. The segment was inflated to 10 cmH₂O pressure in an organ bath containing 37°C Krebs solution and the outer diameter change was monitored. The stress and strain at the contraction threshold and at maximum contraction were computed from the diameter, pressure and the zero-stress state data. Young's modulus was determined at the contraction threshold. The muscle layer thickness in obstructed intestinal segments increased up to 300%. Compared with sham-obstructed and normal groups, the contraction stress threshold, the maximum contraction stress and the Young's modulus at the contraction threshold increased whereas the strain threshold and maximum contraction strain decreased after 7 days obstruction ($P < 0.05$ and 0.01). In conclusion, in the partially obstructed intestinal segments, a larger distension force was needed to evoke contraction likely due to tissue remodeling. Higher contraction stresses were produced and the contraction deformation (strain) became smaller.

Keywords

Intestine; Partial obstruction; Contraction; Stress-strain; Guinea pig

1. Introduction

Small bowel obstruction is a common clinical problem that can result from congenital malformation (Hernanz-Schulman, 2003; Miyamoto et al., 2005; Park and Vaez, 2005) and from surgical-induced stenosis (Hsieh et al., 2005), neoplasm (Zollinger, 1986), Crohn's

© 2011 Elsevier Ltd. All rights reserved.

Address correspondences to: Jingbo Zhao, Mech-Sense, Aalborg Hospital, Sdr. Skovvej 15, DK-9000 Aalborg, Denmark. Telephone: +45 99326907, jz@rn.dk.

Conflict of interest statement We declare that we have no proprietary, financial, professional or other personal interest of any product, service and /or company that could be construed as influencing the position presented in, or the review of, the manuscript

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

disease (Froehlich et al., 2005) and in rare condition by intramural hemorrhage (Cheng et al, 2008). Longstanding partial obstruction causes changes in the intestinal segments proximal to the site of obstruction such as marked dilatation, increased collagen content, and hypertrophy of especially the muscle layer (Gabella, 1975, 1990), increased stiffness of the wall (Storkholm et al, 2007; Zhao et al., 2010) and motility disorders (Coelho et al, 1986; Bertoni et al, 2004; Storkholm et al, 2008).

Mechanical partial obstruction of the small intestine can be created experimentally in laboratory animals by a slowly-setting stenosis using rings of different materials (Bertoni and Gabella, 2001; Schulze-Delrieu et al, 1995; Stromberg et al., 1984, Storkholm et al, 2007; Zhao et al., 2010). Recently, several studies reported that partial intestinal obstruction caused pronounced changes of motility (Bertoni et al, 2004, 2008; Storkholm et al, 2008). Loss of interstitial cells has been reported in obstructed intestine (Ekblad et al, 1998) which may relate to the intestinal motility disorder. However, Schulze-Delrieu et al (1995) demonstrated that the peristaltic reflex in the obstructed guinea pig ileum was preserved. Despite these findings, studies on motility and biomechanical remodeling during chronic partial obstruction are sparse. An understanding of this relationship is important in deciphering how the gastrointestinal tract responds and adapts to changes in the physical environment. It seems likely that a relationship exists between the active and passive biomechanical properties during the intestinal contraction since these are determinants of force development in the muscle (Fung, 1993). The remodeled intestinal wall due to partial obstruction may change the mechano-sensory function, and then further affect the motility.

The hypotheses of the present study were that the threshold to evoke contractions was changed and the amplitude of distension-induced contraction increased due to the remodeling induced by chronic partial obstruction. The aim of this study was to test the hypotheses and thereby to compare the distension-induced contraction in the normal, sham-obstructed and obstructed guinea pig jejunum.

2. Materials and methods

2.1. Animals and groups

Male guinea pigs (600-800g) were allocated into 4 obstructed and 4 sham-obstructed groups living for 2, 4, 7 and 14 days. Ten age-matched guinea pigs not being operated on served as normal controls. We have long-term experience with the operative procedures which is likely the reason for the low mortality rate below 20%. The final number of animals was 6 in each obstructed group and 4 in each sham-obstructed group. The guinea pigs had access to water but were restricted from food intake from the night before the operations and experiments. The animals were weighted daily. The protocol was approved by the Danish Committee for Animal Experimentation.

2.2. Creation of partial small intestine obstruction in guinea pig

The surgical procedure for partially obstructing the small intestine is well-established (Storkholm et al., 2007, Zhao et al, 2010). Atropine (Atropin DAK, Denmark) 0.3 mg * kg⁻¹ s.c. was given 30 min prior to anesthesia with Hypnorm 0.5 mg and Dormicum 0.25 mg per 100 g body weight (Hypnorm: Dormicum: sterile water=1:1:2; subcutaneous injection). When surgical anesthesia was achieved, a small midline laparotomy was done. A loop of the mid-jejunum was selected. The mesentery was carefully incised close to the intestine to create a small window. Care was taken not to damage adjacent vessels or nerves.

A thick polyurethane 3.5 mm-wide band was passed through the mesenteric window and closed antimesenterically with a 6-0 silk suture at a circumference about one mm longer than the outer circumference of the small intestine. This secured a loose fit around the

intestine without any apparent compression of the tissue. In the sham-obstructed group a mesenteric incision was made and marked with a 6-0 silk suture but no band was placed. The abdominal wall including the skin was closed with 4-0 silk suture. Postoperatively, buprenorphine (Temgesic, Reckitt & Colman, UK) 0.05 mg * kg⁻¹ was given subcutaneously to counteract postoperative pain along with 10 ml saline to prevent dehydration. The animals were inspected and weighed daily after the operation. Animals in poor clinical condition were euthanized and excluded from the study.

2.3. In vitro intestinal preparation

When the scheduled time had arrived, the guinea pigs were anesthetized with Hypnorm 0.5 mg and Dormicum 0.25 mg per 100 g body weight. The abdominal cavity was opened. Ten centimeters small intestinal segments proximal to the band in the obstructed animals and segments at corresponding position from sham-obstructed and normal animals were removed. A short segment (0.5 cm long) from the proximal side was cut and used for histological analysis. Two short ring-shaped segments perpendicular to the longitudinal axis were cut and used for zero-stress state analysis. The remaining segment was immediately put into the organ bath containing Krebs solution of the following composition (mmol/L): NaCl, 118; KCl, 4.7; NaHCO₃, 25; NaH₂PO₄, 1.0; MgCl, 1.2; CaCl₂-H₂O, 2.5; Glucose, 11; ascorbic acid, 0.11. The Krebs solution was 37 °C aerated with a gas mixture (95% O₂ and 5% CO₂, pH 7.4). Thirty minutes equilibrating time was needed for motility to recover before the experiments started.

2.4. Ramp distension experimental set-up (Figure 1)

The *in vitro* length of the intestinal segment was measured. The proximal end of intestinal segment was tied on the cannula with silk threads. The cannula was via a tube connected to a syringe containing Krebs solution to apply luminal pressure using a pump (Genie Programmable Syringe Pump, World Precision Instrument, Stevenage, UK). The distal end of the intestinal segment was tied by a silk thread on the three-way stopcock connected to the micromanipulator. The segment was first stretched manually at a very low speed to stretch ratios of 0%, 10%, and 20%. At each stretch ratio, the segment was then inflated at an inflation rate of 0.8 ml/min up to distension pressure of 10.0 cmH₂O. The outlet was opened manually for deflation when the pressure reached 10.0 cmH₂O. The inflation test was repeated three times with three minutes interval between two tests. The first two tests were used for preconditioning and data from the last test were used for data analysis. The pressure probe was inserted into the intestinal lumen through the cannula. The luminal pressure was measured at three locations with 0.5 cm distance. The locations of the holes were marked on the intestinal surface. The intestinal diameters at the locations corresponding to the pressure recordings were videotaped by a CCD camera (Sony, Japan) through a stereomicroscope. The sampling rate for pressure and diameter data was 10 per second.

2.5. The zero-stress state of the intestinal segment

Methods for the determination of the gastrointestinal zero-stress state have been previously described (Gregersen, 2000, 2002). Rings about 1-2 mm wide obtained above were transferred to a calcium-free Krebs solution containing EGTA. This represented the no-load state and a photograph was taken. Then, each ring-shaped segment was cut radially under the microscope. The segments opened up into a sector and photographs were taken ~60 min after the radial cutting to allow viscoelastic creep to take place. This represented the zero-stress state.

2.6. Histological analysis of the small intestine

The segment was fixed in 10% buffered formalin over 24 hours. The specimen was dehydrated in a series of graded ethanol (70%, 96% and 99%) and embedded in paraffin. Five-micron sections were cut perpendicular to the mucosa surface and the paraffin was cleared from the slides with coconut oil (over 15 min. 60 °C). The sections were rehydrated in 99%, 96% and 70% ethanol followed by a 10 min wash in water and stained with hematoxylin and eosin. The layer thickness was measured at twelve points in the circumference of each specimen and averaged.

2.7. Stress and strain calculation

The following morphometric data were measured from digitized images of the segments in the zero-stress and no-load states by using image analysis software (Sigmascan Pro 4.0): the circumferential length (C), the wall thickness (h), and the wall area (A) at no-load and zero-stress state. Furthermore, the outer diameter (D) was measured from the images of the pressurized segments by using a self made software subroutine. The intestinal segment in the pressurized state is assumed cylindrical and the wall was regarded as a membrane.

Hence, the mean circumferential Cauchy stress $\sigma_\theta = \frac{\Delta Pr_{i-p}}{h_p}$ can be assumed uniformly distributed (Fung, 1993) and the circumferential Kirchhoff's stress was then derived as:

$$S_\theta = \frac{\sigma_\theta}{\lambda_\theta^2} = \frac{\partial(\rho_0 W)}{\partial E_\theta} = \frac{\Delta Pr_{i-p}}{h_p \lambda_\theta^2} \quad (1)$$

and the circumferential Green strain was computed from the circumferential stretch ratio λ_θ as:

$$E_\theta = \frac{1}{2} (\lambda_\theta^2 - 1) \quad (2)$$

r_{i-p} , h_p , λ_θ , ΔP , ρ_0 and W are the luminal radius, the wall thickness, the circumferential stretch ratio, the recorded pressure minus the baseline pressure, wall density and strain-energy function. Calculations of r_{i-p} , h_p and λ_θ have been described in detail by Gregersen and Zhao (Gregersen, 2002; Zhao et al., 2003). S_θ is the circumferential 2nd Piola-Kirchhoff's stress and E_θ is circumferential Green strain. Intestinal tissue undergoes large deformation during physiologic activity; therefore, the second Piola-Kirchhoff stress and Green strain were selected since those measures are directly related to the strain energy function.

The stress and strain at the onset of the contraction (stress and strain threshold) and at the maximum contractions point were determined manually.

2.8. Young's Modulus

The circumferential stress-strain curves showed a hyperelastic material pattern, consequently the exponential function (Fung, 1993):

$$S = (S^* + a) e^{b(E - E^*)} - a \quad (3)$$

was used for fitting.

Hence, the circumferential Young's modulus Y' can be denoted as:

$$Y' = dS/dE = bS + ab \quad (4)$$

where S and E are the circumferential stress and circumferential strain calculated from Eqs. (1) and (2), a and b are material constants obtained by non-linear curve fitting to stress-strain curves, and (S^*, E^*) represents one physiological point on the stress-strain curve. Young's modulus at the stress threshold point was calculated.

2.9. Statistical Analysis

The results are expressed as means $\pm$ SEM. The group differences in layer thickness, stress and strain thresholds to evoke contraction, maximal contraction stress and strain, and the Young's modulus were statistically analyzed using t-test and ANOVA. The results were regarded as significant when $P < 0.05$.

3. Results

3.1 General data

The peritoneal lining showed no signs of inflammation or adhesions that could influence the mechanical properties and intestinal contraction. The data obtained from different sham-obstructed subgroups did not differ. Consequently the data from the sham-obstructed groups were averaged.

The intestinal segments from the 2-days- and 4-days-obstruction animals were clearly dilated. After seven days, the intestinal wall was also thickened. No apparent changes were observed in the sham-obstructed and normal groups. Histological analysis showed that the thickness of both the submucosa layer and muscle layer increased post-obstruction (Table 1). Muscle layer thickening was observed after 4 days obstruction whereas submucosa layer thickening was observed after 7 days obstruction ($P < 0.05$, $P < 0.01$).

3.2. Pressure-diameter curves

The contraction pattern was not affected by longitudinal stretch from 0 to 20% (data not shown). The results were all obtained from segments stretched 10%. Furthermore, in the present study we did not analyze the contraction wave speed. The pressure and diameter data were obtained from the middle of the three pressure recording sites.

Waves of peristaltic contractions were clearly observed as pressure and diameter changes during ramp distension (Figure 2). The pressure increased and the diameter decreased at each contraction (Figure 2). The contraction pressure amplitude was bigger and the contraction diameter amplitude was smaller in the obstructed group (Figure 2, bottom) than in the sham obstructed (Figure 2, middle) and normal (Figure 2, top) groups. Furthermore, the pressure threshold to evoke contractions increased after partial obstruction. Quantitative analyses of the threshold to evoke contractions and contraction amplitude, in term of stress and strain, are presented below.

3.3. Stress-strain thresholds to evoke contractions

During the distension of the intestinal segment, the stress in the wall will gradually increase. Concomitantly the segment will deform and the strain will increase. When the stress and strain reach the threshold, intestinal contractions will be elicited. Figure 3 (top) illustrates the stress and strain at the contraction threshold in the different groups. The stress threshold increased whereas the strain threshold decreased in a time-dependent manner post-

obstruction. Significant differences were found after 4 days obstruction for the stress threshold (after 4 days: $P < 0.05$; after 7 and 14 days: $P < 0.01$) and after 7 days obstruction for the strain threshold (after 7 days: $P < 0.05$; after 14 days: $P < 0.01$) compared with sham-obstructed and normal control groups. The stress and strain threshold did not differ between sham-obstructed and normal control groups ($P > 0.05$). Plots of the stress and strain at the contraction threshold clearly showed an inverse relationship between the stress and strain post-obstruction (Figure 3, bottom). It demonstrates that the obstructed intestinal segment requires bigger stress but smaller strain to evoke contractions.

Non-linear curve fitting was made for the stress-strain curves before the contraction for the groups (Figure 4 top) to obtain the mechanical constants a and b . The average Young's modulus at the contraction threshold is presented in Figure 4 (bottom). After 7 days obstruction Young's modulus was significantly higher when compared with sham-obstructed and normal control groups ($P < 0.01$).

3.4. Maximum contraction stress and strain amplitude

Figure 5 shows the circumferential stress and strain (top) and stress-strain relation (bottom) at the maximum contraction amplitude for the groups. The maximum contraction stress increased whereas the maximum contraction strain decreased after 4 days obstruction (4 days: $P < 0.05$; 7 and 14 days: $P < 0.01$) compared with the sham-obstructed and the normal control groups. It demonstrates that the obstructed intestinal segment produced bigger contractile force but with a smaller wall deformation.

4. Discussion

Regardless of the initial cause of intestinal obstruction, a compensatory response in the intestinal wall itself eventually leads to structural and functional alterations. Intestinal smooth muscle proliferation is among the structural alterations frequently observed as a compensatory response. The present study confirmed that the thickness of the intestinal muscle layers increased in a time-dependent manner after obstruction. Furthermore, this study for the first time provides data on the stress and strain thresholds for distension-induced contraction. It demonstrated that the stress threshold to induce the contraction, the maximal contraction stress, and Young's modulus before the contraction increased post-obstruction. In these *in vitro* studies we were able to obtain measures of wall thickness for computation of stresses and strains however due to differences between *in vivo* and *in vitro* conditions and between guinea pigs and humans; the data should be interpreted with caution for clinical purposes. Since the longitudinal force during the distension and contraction was not recorded in this study, only the circumferential stress-strain relationship was investigated. For obtaining further 2D or 3D constitutive equation of the small intestine, biaxial testing with simultaneous distension and longitudinal stretch should be done.

Changes in contraction patterns after partial intestinal obstruction have been reported previously, such as clustered contractions with alternating quiescence (Cullen et al., 1989); increased spontaneous motility and contractile responses to exogenous agents in hypertrophic rat intestinal longitudinal segments (Bertoni et al., 2004), and increased amplitude and frequency of bolus-induced contractility in partial obstructed guinea pig intestine (Storkholm et al., 2008). In patients with chronic intestinal idiopathic pseudo-obstruction, smooth muscle cell contractility induced by acetylcholine was markedly decreased (Guarino et al., 2008). In contrary in the rat obstructed intestine the circumferential smooth muscle showed increased sensitivity to contractile agents and longitudinal smooth muscle had increased sensitivity to relaxing mediators (Bertoni et al., 2008). To the best of our knowledge, contraction thresholds in the partially obstructed intestine have not been reported before. It is well known that continued flow distention can

evoke intestinal contraction through neurogenic and/or myogenic pathways (Costa et al., 1998; Fiorenza et al., 1987; Donnelly et al., 2001). During distension, pressure and diameter increase until the contraction threshold is reached. The stress and strain can be computed knowing the wall thickness in vitro combined with the pressure and diameter changes. Knowledge on mechanical stress and strain is needed to describe the tissue mechanical properties such as the force production and tissue deformation. Furthermore, the mechano-sensory receptors located in the intestinal wall sense the stress and strain rather than the pressure and volume changes. Therefore, it is important to obtain the contraction thresholds in term of the stress and strain. The present study demonstrated that the stress threshold increased and strain threshold decreased post-obstruction. Furthermore, Young's modulus at the contraction threshold increased as function of the duration of the obstruction. Increased stress and Young's modulus indicated that a larger force was needed to induce contraction in the obstructed intestine. Thus, the sensitivity of mechano-sensory receptors to the stress post-obstruction decreased. Our previous studies have demonstrated that the intestinal wall became stiffer after obstruction (Storkholm et al., 2007, Zhao et al., 2010); therefore the stress level at the location of mechano-sensory receptors may be up-regulated. Furthermore, loss Cajal cells reported in the hypertrophic intestine (Ekblad et al, 1998) together with remodeled smooth muscle cells may also be associated with the increased stress threshold. It is interesting to notice that the strain at the contraction threshold decreased after obstruction. Though it may be related to wall stiffening, the mechanisms of stress and strain threshold changes in partial obstructed intestinal segments were not studied in detail. This important issue should be addressed in our future studies.

In the present study, we also demonstrated that the contraction amplitude increased after partial obstruction (Figure 2). Stress-strain analysis showed that the maximal contraction stress increased whereas the maximal contraction strain decreased (Figure 5). The higher contraction stresses post-obstruction is likely due to smooth muscle proliferation. Furthermore, the contraction deformation (strain) of obstructed intestine became smaller which likely is due to the stiffer wall (Storkholm et al., 2007; Zhao et al., 2010). Smooth muscle hyperplasia (increased cell number) and hypertrophy (increased cell size) post-obstruction were observed by others (Bertoni and Gabella, 2001; Bertoni et al., 2004; Chen et al., 2008; Gabella, 1990; Geuna et al., 1998; Storkholm et al., 2007, 2008). In accordance with the present study, increased contractility of the remodeled smooth muscle layer has been reported (Bertoni et al., 2008; Storkholm et al., 2008). However, when the motor response was normalized with respect to tissue wet weight, a remarkable reduction of contractile efficiency was observed post-obstruction (Bertoni et al., 2004). Earlier studies demonstrated that the hypertrophied muscle cells exhibit ultra-structural changes of sarcoplasmic reticulum, cytoplasmic content and increased ratio of myofilament to intermediate filament (Gabella, 1979a, 1979b). The relative decrease in myofilament content suggests a loss of contractile machinery in remodelled smooth muscle cells.

It is well known that biological tissue exhibits viscoelastic properties. The viscoelasticity of gastrointestinal tissue have been studied previously (Natali et al., 2009, Zhao et al., 2003). However, in this study, the stress-strain relationship on the small intestine was investigated using a low speed ramp distension test with and without obstruction. It has been pointed out that low speed ramp distension for most biological soft tissues is independent of the strain rate (Fung, 1993). For a more thorough study of visco-elastic effects on the small intestine, further relaxation or creep experiments are needed.

In conclusion, the stress threshold of distension-induced contractility was increased in the partially obstructed jejunal segment. Thus, a larger force is needed to induce contraction in the obstructed intestine which maybe due to changes in the mechano-sensory function caused by obstruction-induced intestinal wall remodeling. The obstructed intestine produced

higher contraction stresses than sham-obstructed and normal intestine which is likely due to the smooth muscle proliferation. Furthermore, the contraction deformation (strain) of obstructed intestine became smaller which likely is due to the stiffer wall as demonstrated in previous studies.

Acknowledgments

The studies were financially supported by NIH grant of 1R01DK072616-01A2. The technicians Ole Sørensen, Torben Madsen and Jens Sørensen are thanked for handling the animals.

References

- Bertoni S, Gabella G. Hypertrophy of mucosa and serosa in the obstructed intestine of rats. *Journal of Anatomy*. 2001; 199:725–734. [PubMed: 11787826]
- Bertoni S, Gabella G, Ghizzardi P, Ballabeni V, Impicciatore M, Lagrasta C, Arcari ML, Barocelli E. Motor responses of rat hypertrophic intestine following chronic obstruction. *Neurogastroenterology & Motility*. 2004; 16:365–374. [PubMed: 15198659]
- Bertoni S, Ballabeni V, Flammini L, Gobbetti T, Impicciatore M, Barocelli E. Intestinal chronic obstruction affects motor responsiveness of rat hypertrophic longitudinal and circular muscles. *Neurogastroenterology & Motility*. 2008; 20:1234–1242. [PubMed: 18684211]
- Chen J, Chen H, Sanders KM, Perrino BA. Regulation of SRF/CaRg-dependent gene transcription during chronic partial obstruction of murine small intestine. *Neurogastroenterology & Motility*. 2008; 20:829–842. [PubMed: 18557893]
- Cheng J, Vemula N, Gendler S. Small bowel obstruction caused by intramural hemorrhage secondary to anticoagulant therapy. *Acta Gastro-Enterologica Belgica*. 2008; 71:342–344. [PubMed: 19198584]
- Coelho JC, Gouma DJ, Moody FG, Li YF, Senninger N. Gastrointestinal motility following small bowel obstruction in the opossum. *Journal of Surgical Research*. 1986; 41:274–278. [PubMed: 3762133]
- Costa M, Hennig GW, Brookes SJ. Intestinal peristalsis: a mammalian motor pattern controlled by enteric neural circuits. *Annals of the New York Academy of Sciences*. 1998; 860:464–466. [PubMed: 9928340]
- Donnelly G, Jackson TD, Ambrous K, Ye J, Safdar A, Faraway L, Huizinga JD. The myogenic component in distention-induced peristalsis in the guinea pig small intestine. *American Journal of Physiology Gastrointestinal and Liver Physiology*. 2001; 280:G491–G500. [PubMed: 11171633]
- Cullen PT, Storey BE, Cuschieri A, Campbell FC. Detection of clustered gastrointestinal contractions in partial intestinal obstruction by surface vibration analysis. *Annals of Surgery*. 1989; 210:234–238. [PubMed: 2757425]
- Ekblad E, Sjuve R, Arner A, Sundler F. Enteric neuronal plasticity and a reduced number of interstitial cells of Cajal in hypertrophic rat ileum. *Gut*. 1998; 42:836–844. [PubMed: 9691923]
- Fiorenza V, Yee YS, Zfass AM. Small intestinal motility: normal and abnormal function. *American Journal of Gastroenterology*. 1987; 82:1111–1114. [PubMed: 3314483]
- Froehlich F, Juillerat P, Mottet C, Felley C, Vader JP, Burnand B, Gonvers JJ, Michetti P. Obstructive fibrostenotic Crohn's disease. *Digestion*. 2005; 71:29–30. [PubMed: 15711046]
- Fung, YC. Properties of living tissues. Berlin: Springer-Verlag; 1993. Biomechanics.
- Gabella G. Hypertrophy of intestinal smooth muscle. *Cell and Tissue Research*. 1975; 163:199–214. [PubMed: 1182787]
- Gabella G. Hypertrophic smooth muscle. II. Sarcoplasmic reticulum, caveolae and mitochondria. *Cell and Tissue Research*. 1979a; 201:79–92. [PubMed: 527017]
- Gabella G. Hypertrophic smooth muscle. IV. Myofilaments, intermediate filaments and some mechanical properties. *Cell and Tissue Research*. 1979b; 201:277–288. [PubMed: 574421]
- Gabella G. Hypertrophy of visceral smooth muscle. *Anatomy and embryology (Berl)*. 1990; 182:409–424.

- Geuna S, Cardillo S, Giacobini-Robecchi MG. Smooth muscle cell hypertrophy and hyperplasia in the partially obstructed gut of the rat: a quantitative evaluation. *Acta Anatomica (Basel)*. 1998; 163:69–74.
- Gregersen, H. *New perspectives in motility research and diagnostics*. London: Springer-Verlag; 2002. Biomechanics of the gastrointestinal tract.
- Guarino MP, Carotti S, Cogliandro R, Stanghellini V, De Giorgio R, Barbara G, Alloni R, Altomare A, Tarquini E, Coppola R, Corinaldesi R, Cicala M. Impaired contractility of colonic muscle cells in a patient with chronic intestinal pseudo-obstruction. *Digestive and Liver Disease*. 2008; 40:225–229. [PubMed: 17433796]
- Hernanz-Schulman M. Infantile hypertrophic pyloric stenosis. *Radiology*. 2003; 227:319–331. [PubMed: 12637675]
- Hsieh TK, Chen AC, Wu SF, Chen W. Postoperative intussusception in children with enterostomy. *Acta Paediatr Taiwan*. 2005; 46:166–169. [PubMed: 16231566]
- Miyamoto M, Egami K, Maeda S, Ohkawa K, Tanaka N, Uchida E, Tajiri T. Hirschsprung's disease in adults: report of a case and review of the literature. *Journal of Nippon Medical School*. 2005; 72:113–120.
- Natali AN, Carniel EL, Gregersen H. Biomechanical behavior of oesophageal tissues: material and structural configuration, experimental data and constitutive analysis. *Medical Engineering & Physics*. 2009; 31:1056–1062. [PubMed: 19651531]
- Park W, Vaezi MF. Etiology and pathogenesis of achalasia: the current understanding. *American Journal of Gastroenterology*. 2005; 100:1404–1414. [PubMed: 15929777]
- Schulze-Delrieu K, Brown B, Herman B, Brown CK, Lawrence D, Shirazi S, Palmieri T, Raab J. Preservation of peristaltic reflex in hypertrophied ileum of guinea pig. *American Journal of Physiology*. 1995; 269:G49–G59. [PubMed: 7631801]
- Storkholm JH, Zhao J, Villadsen GE, Hager H, Jensen SL, Gregersen H. Biomechanical remodeling of the chronically obstructed Guinea pig small intestine. *Digestive diseases and sciences*. 2007; 52:336–346. [PubMed: 17219069]
- Storkholm JH, Zhao J, Villadsen GE, Gregersen H. Spontaneous and bolus-induced motility in the chronically obstructed guinea-pig small intestine in vitro. *Digestive diseases and sciences*. 2008; 53:413–420. [PubMed: 17562174]
- Stromberg BV, Klein L. Collagen dynamics of partial small bowel obstruction. *American Journal of Surgery*. 1984; 148:257–261. [PubMed: 6465433]
- Zhao J, Yang J, Gregersen H. Biomechanical and morphometric intestinal remodelling during experimental diabetes in rats. *Diabetologia*. 2003; 46(12):1688–1697. [PubMed: 14593459]
- Zhao J, Liao D, Yang J, Gregersen H. Biomechanical remodeling of obstructed guinea pig jejunum. *Journal of Biomechanics*. 2010; 43:1322–1329. [PubMed: 20189575]
- Zollinger RM Jr. Primary neoplasms of the small intestine. *American Journal of Surgery*. 1986; 151:654–658. [PubMed: 2424326]

Figure 1.
Set-up of experiment.

The organ bath was composed of an inside small chamber and an outside larger chamber. The Krebs solution contained in the small chamber was maintained constant at 37 °C by circulating warm water in the big chamber using a heating machine. The intestinal segment was placed in the Krebs solution in the small organ bath. Distension was done using an infusion pump and the longitudinal length was set by a micromanipulator. A three-channel pressure probe was used to measure the pressures. The diameter changes of the intestinal segments were videotaped through a stereomicroscope.

Figure 2.

Examples of pressure and diameter curves obtained from a normal (top), sham obstructed (middle) and a 14 days obstructed intestine (bottom) during ramp distension. Contractions were clearly observed. The contraction produced higher pressure and smaller diameter in 14 days obstructed intestine compared with normal and sham-obstructed control. Furthermore the pressure threshold of contraction was higher in 14 days obstructed intestine (7.8 cmH₂O) than in normal (2.5 cmH₂O) and sham-obstructed (2.4 cmH₂O) controls.

Figure 3.

Illustration of circumferential stress and strain (top) and the stress-strain relation (bottom) at the contraction threshold during ramp distension. Compared with sham-obstructed and normal groups the stress at the contraction threshold was increased whereas the strain at the contraction threshold was decreased after 7 days obstruction (compared with normal and sham-obstructed groups stress threshold $P < 0.01$; strain threshold $P < 0.05$).

Figure 4. Example of non-linear fitting of stress-strain curves at onset of contraction in the groups (top). Young's modulus (bottom) increased as function of obstructed duration (** $P < 0.01$, compared with normal and sham-obstructed groups).

Figure 5.

The circumferential stress and strain (top) and the stress-strain relation (bottom) at maximum contraction during ramp distension. The maximum stresses of distension-induced contractions increased and maximal strains decreased post-obstruction (compared with normal and sham-obstructed groups, * $P < 0.05$; # $P < 0.01$).

Table 1Thickness (μm) in different layers

Groups	Submucosa	Circumferential muscle	Longitudinal muscle
Normal	42.9 $\pm$ 11.2	79.3 $\pm$ 24.1	36.2 $\pm$ 7.5
Sham obstructed	35.5 $\pm$ 12.6	90.4 $\pm$ 15.1	37.8 $\pm$ 8.8
Obstructed 2 days	45.3 $\pm$ 11.8	107.3 $\pm$ 31.4	37.4 $\pm$ 9.5
Obstructed 4 days	34.5 $\pm$ 8.5	116.5 $\pm$ 42.3 [*]	42.3 $\pm$ 15.3 [*]
Obstructed 7 days	55.7 $\pm$ 9.9 [*]	145.5 $\pm$ 57.9 [*]	57.9 $\pm$ 10.6 [*]
Obstructed 14 days	71.8 $\pm$ 18.7 ^{**}	240.2 $\pm$ 80.7 ^{**}	80.7 $\pm$ 28.9 ^{**}

^{*} P<0.05;^{**} P<0.01 (compared with normal and sham obstructed groups)