IEEE Journal of Translational Engineering in Health and Medicine

Received 13 October 2018; revised 31 March 2019; accepted 30 April 2019. Date of publication 24 July 2019; date of current version 9 August 2019.

Digital Object Identifier 10.1109/JTEHM.2019.2919029

Defining the Relationship Between Compressive Stress and Tissue Trauma During Laparoscopic Surgery Using Human Large Intestine

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This work was supported in part by the Hospital for Sick Children's Perioperative Services Grant for Research.

ABSTRACT Excessive magnitudes of compressive stress exerted on gastrointestinal tissues can lead to pathological scar tissue or adhesion formation, bleeding, inflammation or even death from bowel perforation and sepsis. It is currently unknown however, at exactly what magnitude of compressive stress that these pathologies occur. A novel simple compressive device was engineered to provide an objective means of producing discrete compressive stresses on human tissues. Samples of human large intestine (colon) were removed from consenting patients as a part of their standard surgical procedure. These samples were compressed with a range of loads normally produced by standard laparoscopic graspers in representative abdominal surgeries. After compression, specimens were processed for histological analysis and assessed. The two independent pathologists who were blinded to stress magnitudes were both able to quantify increasing tissue damage that corresponded to increasing amounts of compressive force. A threshold between 350-450 kPa was discovered that corresponded to both significant serosal thickness change and a positive histological trauma score rating. Whether the tissue injury quantified is pathologic is subject for future *in-vivo* longitudinal investigation but certainly based on literature, can be the basis of pathological adhesion formation or an area for hemorrhage and scar formation.

INDEX TERMS Laparoscopic surgery, tissue trauma, stress, intestine, compression.

I. INTRODUCTION

Laparoscopic minimally invasive surgery (MIS) approaches have been adopted for a wide range of procedure types in general surgery, urology and gynecology [1]. This is because the use of thin laparoscopic tools inserted through small keyhole incisions in the abdominal wall can reduce overall trauma and blood loss and subsequently decrease patient pain scores when compared to an open surgical approach. Post-operative complications such as infection, tissue herniation and wound dehiscence are also decreased as the surgeon can avoid creating large open incisions [2]. However, the switch from open surgery to MIS has introduced new challenges for surgeons and can increase certain types of surgical errors and complications [3]. The largest difference between the two surgical approaches is the relative loss of direct sensory feedback to a surgeon's hand. In open surgery, a surgeon can directly touch and manipulate delicate gastrointestinal tissues with their fingers. Intuitively they can sense and modulate how much pressure they are exerting in exquisite detail. With the adoption of laparoscopic surgery however, there is: a) an estimated decrease between 8- and 20-fold in palmar sensory stimuli when using a laparoscopic tool and b) a loss of operative workspace as the tight working constraints of the trocar and closed abdominal cavity equals to a significant loss in degrees of freedom [4], [5]. Adjusting to these constraints takes time and surgical residents have a steep learning curve to surmount. In fact, a patient's risk of an adverse surgical event occurring is significantly associated with a surgeon's experience and number of previous surgeries performed, with the risk being highest in the first 50 cases they perform than in their next 30 [6], [7].

Learning laparoscopic skills requires many hours of specialized practice and simulation by residents to address the steep learning curve associated with this change in workflow. The Society of Gastrointestinal and Endoscopic Surgeons (SAGES) is currently recommending that all residents demonstrate competency by successfully finishing the Fundamentals of Laparoscopic Surgery (FLS) course [8]. The FLS course uses laparoscopic tools for specific tasks in a box trainer. The FLS exam combines a written component with a timed and scored laparoscopic skills evaluation in the box trainer. Surgical educators often use FLS scores to grade and assess trainee surgical ability [9]. While speed and precision are taken into account, not a single task has its force measurements assessed or graded [10]. Current surgical training programs also do not evaluate objective measures of force for trainees in regards to the physical forces they exert intraoperatively on tissues [11]. This is remarkable because it misses a critical component of the recreation of the surgical environment: safe tissue handling.

A. INJURY AND ADHESION FORMATION DUE TO INAPPROPRIATE MECHANICAL STRESS

It is estimated that surgery contributes to almost 50% of all patient adverse events and 13% of all hospital-related deaths. However, studies show that most of these adverse events are preventable [12]. The two most commonly injured tissues in laparoscopic surgery are the small bowel (55.8%) followed by the large bowel (38.6%) with an overall incidence of laparoscopy-induced GI tissue injury of 0.13% but a high mortality rate of 3.6% [13]. Injury due to inappropriate mechanical stress occurs when force magnitudes on tissues exceed a safe threshold. For example, when grasping tissue for elevation, exposure or movement, excess force exertion at the grasper's jaw can cause inadvertent compression and necrosis of that tissue. Grasper design also plays a large role in how stress concentrations are generated. de Visser et al., notes that grasper jaws with unsuitable rounded-off edges and sharp grip profiles can lead to very high pressure peaks in colon tissues. This can lead to colon perforations either intraoperatively or 2-5 days after a procedure and can cause potentially fatal peritonitis and sepsis [14]. Laparoscopic grasper use accounts for a 2-4% risk of injury to structures such as the bile duct and bowel, which is significantly higher than that in open abdominal surgical approaches [15]. In fact, Tang et al., showed that the majority of human errors found during laparoscopic cholecystectomy were related to graspers and 11.3% of these errors were of significant consequence and was directly from excessive force exertion [12]. To design safer laparoscopic instruments, knowledge of the maximum local amount of pressure a tissue can endure is necessary. Pressure by a tool jaw is determined by the size of the contact area and the distribution of the pinch force over this area.

Excessive magnitudes of force exerted on gastrointestinal tissues can lead to: pathological scar tissue formation, bleeding, inflammation, coagulation and loss of function [3]. Long-term unintended consequences such as infection and sepsis can occur as well due to a local breach of the bowel's protective barrier. This results from the interruption of the blood supply to the tissue and crushing of intracellular structures [16]. One of the most studied side effects of inappropriate surgical forces is the formation of intestinal adhesions. Peritoneal adhesions are found in up to 93% of patients post intra-abdominal surgery [17]. Adhesions can cause a number of significant clinical problems including bowel obstruction, chronic abdominal pain, infertility and organ tissue injury, leading to higher rates of morbidity and mortality post-surgery. They occur from trauma to serosal surfaces and the subsequent altered complex healing cascade that occurs 7-10 days after surgery [18]. Once a serosal surface is disrupted, during the wound healing inflammatory process, mesothelial cells recruit cells that express fibrin. If there is an imbalance between the degradation of fibrin and procoagulatory factors, then a fibrin clot is formed, leading to permanent fibrous band formation [17]. These fibrin bands can form the basis of attachment of neighbouring structures such as intestinal loops or the abdominal wall. Kalff et al. also looked at surgical compression of the bowel in a rat model and found that inappropriate compression decreased electromechanical activity of the gut and caused mucosal sloughing, loss of architecture and inflammatory changes. They found that the degree of gut paralysis was proportional to the degree of trauma and cellular infiltration which supports the hypothesis that postsurgical ileus is a result of an inflammatory response to grasper trauma from leukocytes and macrophage populations [19].

B. ESTABLISHING THE RELATIONSHIP BETWEEN COMPRESSIVE FORCE AND GASTROINTESTINAL TISSUE TRAUMA

A relevant literature search demonstrates that determining the mechanical properties of soft tissue is not a trivial task [20]–[25]. Soft tissues have very low resistance to deformation in their physiological rest state and even careful handling can cause them to deform and change their perceived initial length. Therefore, tissue deformation is a complex matter and still the subject of much research. Tissue modeling via numerical methods such as finite element analysis (FEA) which predicts how objects react to real-world forces, is considered complex because of the non-homogeneous, anisotropic, non-linear, and elastic viscous behavior of the biological tissue [20]. There are also discrepancies between material properties obtained from different approaches or test geometries. Standard procedures need to be adopted in the field of soft tissue analysis to achieve and maintain accuracy [26].

There are numerous papers that characterize the mechanical properties of various gastrointestinal organs. However, most papers or textbooks focus on the properties of animal (especially porcine or rabbit) tissues, because of the legal, ethical and logistical issues surrounding the use of human organs. For example, examining Rosen et al.'s and De et al.'s foundational papers, this University of Washington group designed a customized grasper to quantify stress magnitudes and developed a database of the average elastic and relaxation parameters of a variety of porcine gastrointestinal organs [16], [22]. Kalff et al. looked at surgical compression of the bowel in a rat model and found that inappropriate compression decreased electromechanical activity of the gut and caused mucosal sloughing, loss of architecture and inflammatory changes. They found that the degree of gut paralysis was proportional to the degree of trauma and cellular infiltration which supports the hypothesis that postsurgical ileus is a result of an inflammatory response to grasper trauma from leukocytes and macrophage populations [19]. Chandler et al. designed a novel compressive device to produce objective grasp forces on porcine colon with six different loads (50, 100, 150, 200, 250 and 300 kPa) and three different load rates. They analyzed the colon tissue post-grasp via histology for significant tissue compression. They found that significant tissue thickness change occurred at pressures above 150 kPa [27].

There is currently a severe dearth of human data that specifically correlates laparoscopic grasper compression force and gastrointestinal injury via cellular examination under a microscope (histology). A histological analysis where a pathologist directly visualizes cellular change and can objectively quantify tissue damage is the gold standard for truly understanding the effects of compressive stress on organs. There is only one study that was found to date that specifically looked at compressive forces on human bowel but this study did not feature a histology component. Heijndijk et al. compressed both porcine and human small and large bowels with a pinching lever device. A pertinent outcome that this group found in humans, was that there were large inter-individual variation and that bowel strength *could differ by a factor of two between patients*. This means that the highest perforation force in the study was twice as large as the lowest. Due to this large variation in bowel strength, forces that could be safely applied to one patient may cause an inadvertent perforation in another. This is extremely important to reflect upon, as it seems that human tissues may have a very large range of acceptable forces; lower thresholds of this range must be incorporated into the practice of surgical tissue handling [28].

C. STUDY DESIGN

A novel compression device was engineered to provide an objective means of applying discrete pressures on human tissues to induce compressive mechanical stress. A study to test the device was approved by the Research Ethics Office of St. Michael's Hospital (SMH REB #15-299) in Toronto, Ontario. Samples of large intestine (colon) were removed from five consenting patients as a part of their standard surgical procedure. No extraneous tissue was removed for the express purpose of this study. Two pathologists (CS, CR) were responsible for examining all tissue removed, preparing all histological sections and analyzing all slides under the microscope.

The purpose of this study is twofold: a) to test a prototype device that is capable of producing compressive stress on human gastrointestinal tissues in a range of forces used intraoperatively and b) to establish preliminary data on the relationship between compressive stress and tissue trauma in these tissues. To our knowledge, we will be the first group to correlate different levels of pressure and its effect on tissue trauma in human large intestine.

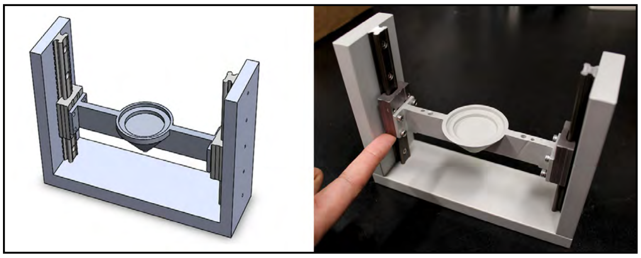

FIGURE 1. Left: Computer design of the SimpleCAT. Right: the final, machined SimpleCAT, made out of anodized aluminum.

II. METHODS

A. COMPRESSION DEVICE DESIGN AND FABRICATION

The simple crush apparatus for tissue (SimpleCAT, Fig. 1) is a straightforward novel device that produces an even pressure in compression on tissues. It consists of an upper platform where standardized weights are loaded, a U-shaped frame with linear rails and guide carriages that are Frelon-lined and self-lubricating to allow the platform to translate up and down with low friction (McMaster-Carr, Aurora, Ohio, USA). A horizontal flat pin plat, rather than an actual grasper jaw was used to induce stress because actual grasper jaws have numerous different geometries and hinge mechanisms, all with different local stress concentration patterns with the highest area of stress closest to the hinge mechanism. A flat pin plate would allow a pure analysis between the relationship between compressive stress and tissue damage without any confounding factors.

The frame and upper platform were both machined out of 6061 aluminum and then anodized for easy sterilization and durability. The upper platform consists of a cylindrical weight loading area that ends in a circular end pin tip and two support braces. The weight of the upper loading platform (107.4 g) was made as light as possible to produce a minimum pressure well below the reported average amount of force exerted on tissues by surgeons during a standard abdominal laparoscopic procedure which is 8.52 ± 2.77 N as reported by De et al. [29]. This minimal weight was purposely chosen so that the experimental focus would be on loading the upper platform with standardized weights to produce controlled pressures. All pressures reported in this paper include the pressure generated by the weight of the upper platform.

To compress a tissue sample, a small square piece of extra low-lint cellulose fiber paper was laid on the base and a sectioned specimen (10 mm × 10 mm) placed on top. This paper was used to prevent the specimen from moving or slipping when compressed.

The specimen was positioned visually under the location where the upper loading platform's end pin tip would

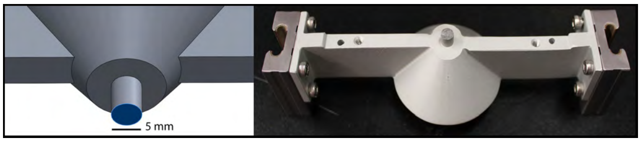

FIGURE 2. **The surface area of the pin tip of the upper platform of the SimpleCAT was precision engineered to produce an even pressure distribution on the tissue with minimal areas of stress concentration.**

FIGURE 3. **Weights are first loaded on to the platform and then the platform lowered onto the tissue to induce compressive stress.**

compress it. The platform's end tip pin was precision milled to a diameter of 5.0 mm and surface area of 19.64 mm^2 so that precise stress calculations could be performed (Fig. 2). The pin tip was painted before every compression with a thin layer of blue tissue marking dye (#1003-5 Blue, Davidson Marking System, Minnesota, USA) so that when the pin tip made contact with the tissue, it would be easy to identify the area of compression for slide creation and subsequent microscopic analysis. Standardized weights were loaded onto the platform (Fig. 3). The more weight loaded (force) corresponded to a greater amount of pressure generated at the pin tip and therefore mechanical tissue stress (Equation 1).

$$\sigma = F/A \tag{1}$$

The weight platform was manually lowered until the tip was right above the specimen and then lightly released by the experimenter's finger until the pin made direct contact with the tissue. The platform was then allowed to fully compress the tissue. Contact with the tissue is confirmed by the use of a feeler gauge. The platform was allowed to make contact with the tissue for 10 s and then was raised. This time parameter was chosen because Brown et al. notes that 95% of grasps in three common laparoscopic bowel-handling tasks occurred for a duration of 8.86 s ± 7.06 s or less [30].

B. EXPERIMENTAL PROTOCOL

Specimens obtained for this study were taken as part of the normal surgical workflow for various gastrointestinal laparoscopic procedures. Tissues were procured minutes after extraction from the body and immediately transported to an adjacent histology suite for experimentation. Tissues were tested fresh, without being put into formalin or other preserving agents. Two trained pathologists, CS and CR separated healthy tissue for experimentation from inflamed, damaged or pathological tissue. Standardized precision weights of 200, 400, 600, 800, 1000 and 1200 g were used as load forces, for a total of six different experimental conditions. With the weight of the upper platform included, these gram weights equal to approximately 150, 250, 350, 450, 550 and 650 kPa or 3, 5, 6.9, 8.9, 10.9 and 12.8 N.

These weights were chosen to align with De et al.'s stresses of 0 to 300 kPa when translated from a gram weight into a surface pressure and Li et al's applied forces that found that hemorrhage and hematoma occurred between 7 - 11 N in liver tissues [15], [29].

After each tissue specimen was compressed with a load condition, the two pathologists would immediately process each sample for histological analysis. The order the samples were compressed in was randomized, and the order of tissue processing was also blinded. Local control measurements were taken from the areas of tissue that were not compressed.

C. HISTOLOGICAL AND STATISTICAL ANALYSIS

Tissue processing and staining was performed in the surgical histological suite of St. Michael's Hospital in Toronto, Ontario. Tissues were fixed in 10% buffered formalin and embedded in paraffin. A 4 micrometer thick section was cut and the tissues were mounted to glass slides. Sections were chosen that were parallel to the direction of the applied pressure induced by the SimpleCAT. Sections were stained with hematoxylin and eosin (H&E) for visualization of overall changes in morphology and cellular architecture.

Slides were scanned at 400× and analyzed using Aperio ImageScope (Leica Biosystems, Wetzlar, Germany). Two damage metrics were utilized: an intestinal layer thickness calculation where the serosal (outermost) layer was measured in the area of compression (C) and compared to a local control (LC) region that was not compressed as a percent deformation (Fig. 4) and a histological scoring scale for tissue trauma. Serosal thickness was specifically targeted for quantification because it is serosal disruption that is hypothesized as the basis of adhesion formation. Adhesions can cause a number of significant clinical problems including bowel obstruction, chronic abdominal pain, infertility and organ tissue injury, leading to higher rates of morbidity and mortality post-surgery. It is hypothesized that trauma to serosal surfaces and the subsequent altered complex healing cascade can lead to permanent fibrin bridges that can form the basis of intestinal adhesion attachment to neighboring structures such as other intestinal loops or the abdominal wall [17].

The histological scoring scale was created by the two pathologists in this study, as we were unable to find a suitable pathologist-validated scale endorsed in the literature. The criteria for the scale is outlined in Table 1.

The two pathologists, who were blinded to all experimental conditions, quantified serosal thicknesses and individually graded each slide and an average of the two grades served as the final tissue trauma score. Serosal thickness measurements

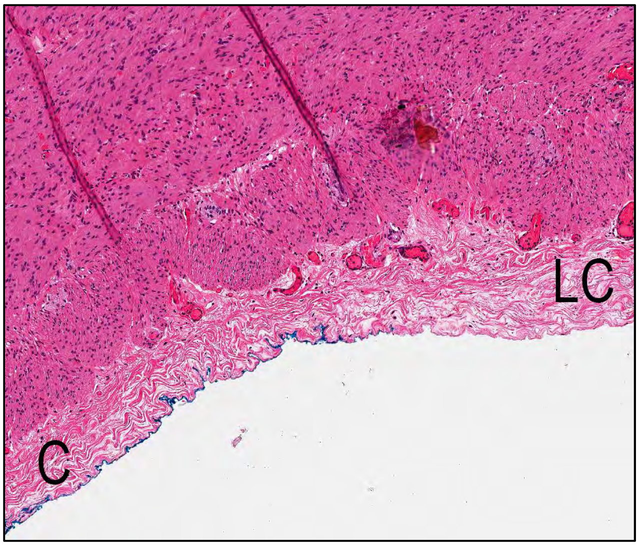

FIGURE 4. The area of compression (C) visualized here with blue tissue marking dye compared to a local control (LC) area which is unstained.

TABLE 1. Tissue trauma scoring criteria.

Trauma Score	*Cellular Architecture*
Grade 0	Nuclei of serosal and bounding muscularis externa cells are smooth, oval and uniformly shaped.
Grade 1	Elongation and mild hyperchromasia of nuclei in muscle/connective tissue in both the serosa and muscularis externa, but in less than 50% of cells in our region of interest (ROI), representing slight trauma to the cells.
Grade 2	Clear and significant damage to the serosa and muscularis externa layers, with more than 50% of nuclei in the cells in our ROI appearing significantly elongated and thinned and there is the presence of multiple hyperchromatic nuclei.
Grade 3	Tissue thinning and nuclear changes evident in the submucosa layer.

were performed at the center of the area of compression (as visualized on processed histological slides via the dye applied to the pin tip). This is because the center region is the most representative of the average stress of the weight platform pin.

One-sided t-tests were performed to determine statistical significance of tissue deformation at each compressive load condition in comparison to local control measurements. Standard deviations were calculated to determine data variance in the samples.

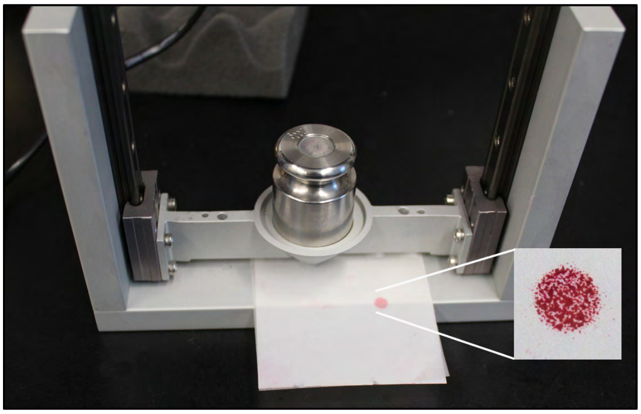

FIGURE 5. The SimpleCAT was validated using Fujifilm's Prescale Extreme Low Pressure two-sheet system. Note the uniformity of color distribution, correlating to an even pressure distribution.

III. RESULTS

A. CONSISTENCY OF PRESSURE FORCE PRODUCTION

The SimpleCAT's ability to produce a uniform compression via the platform tip on tissue samples was validated using Fujifilm Prescale film (Fujifilm, Tokyo, Japan). Prescale film can precisely measure pressure distribution and balance. The two-sheet system for Extreme Low Pressure was used (Prescale 4LW, R310 3M, 0.05 MPa).

The ability of the SimpleCAT's upper platform to linearly transmit force to the tissue via the pin tip was tested using a high precision scale at all loading conditions within the linear rail system. The maximum force transmission loss with the system was 2.5% at 200 g, which decreased to 0.4% at 1200 g.

B. DEMOGRAPHICS

Five patients undergoing elective laparoscopic surgery were included in this study (Table 2). All patients had large intestine (colon) tissue removed. There was a 3:2 split between females and males and the average patient age was 66.4 years.

C. SEROSAL THICKNESS MEASUREMENT

Five measurements were taken of tissue thickness of the serosal layer in the area of compression and five measurements were taken in an adjacent non-compressed local control area. Multiple data points were sampled for each patient to counteract histology artifacts due to slide processing that can shrink or warp tissue presentation on slides. Percent deformation (rather than an absolute delta in micrometers) was used to compensate for the natural variation that occurs in human colon thickness between patients as evidenced by previous ultrasonography experiments [31].

The relationship between stress and tissue deformation is displayed in both a bar graph and box plot. There is a clear step-change in the average percent deformation around the 450 kPa range. For the box plot, both the lower stresses of 150 and 250 kPa and the highest stress condition of 650 kPa, the interquartile range (IQR) which represents 50% of all data, is narrow, so there is the least amount of variation between patients at these stresses. The largest IQR

TABLE 2. Patient demographics.

Patient Code	*Gender*	*Age*	*Diagnosis*
1	F	55	Ulcerative colitis
2	F	65	Polyposis syndrome
3	M	59	Ulcerative colitis
4	M	74	Colorectal cancer
5	F	79	Colorectal cancer

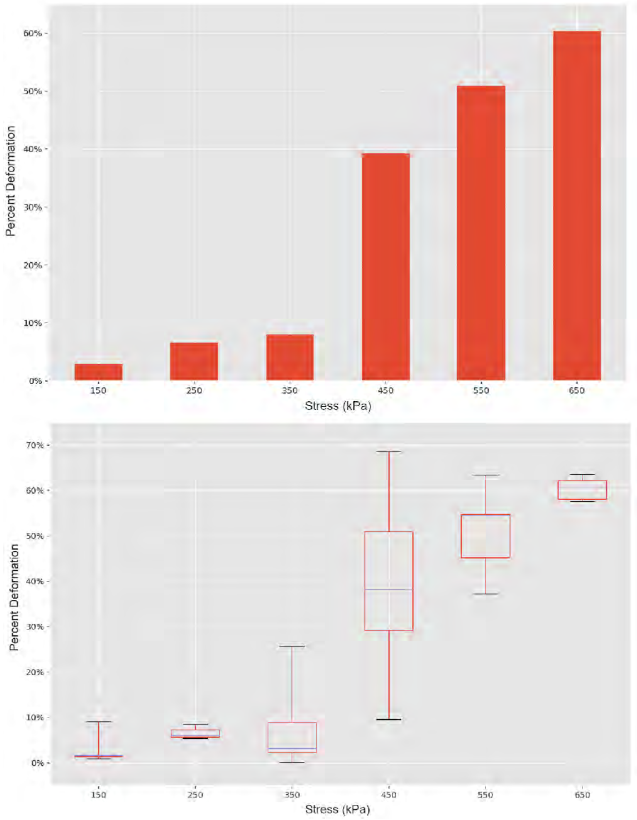

FIGURE 6. The average percent deformation plotted for all 5 patients at each stress condition in a bar graph (above) and box plot (below). There is a clear relationship between an increase in stress and a corresponding increase in tissue deformation.

occurs at 450 kPa which indicates a large spread in the data at this stress condition but also symmetry as the whiskers are fairly even and the median line is almost in the middle of the IQR. At other stress conditions such as 350 kPa, there is the presence of outliers that skew the top whisker upwards from the IQR range.

D. HISTOLOGICAL TISSUE TRAUMA SCORE

The two pathologists individually rated each slide and then an overall average score was assigned to each slide and loading condition. The two pathologists had a 100% trauma score agreeance rate on all rated slides.

There was a marked increase in trauma score rating between the 350 and 450 kPa stress conditions, similar to the serosal thickness percent deformation. There were no assigned trauma scores of 3 because at no stress condition was there tissue perforation to the muscularis layer.

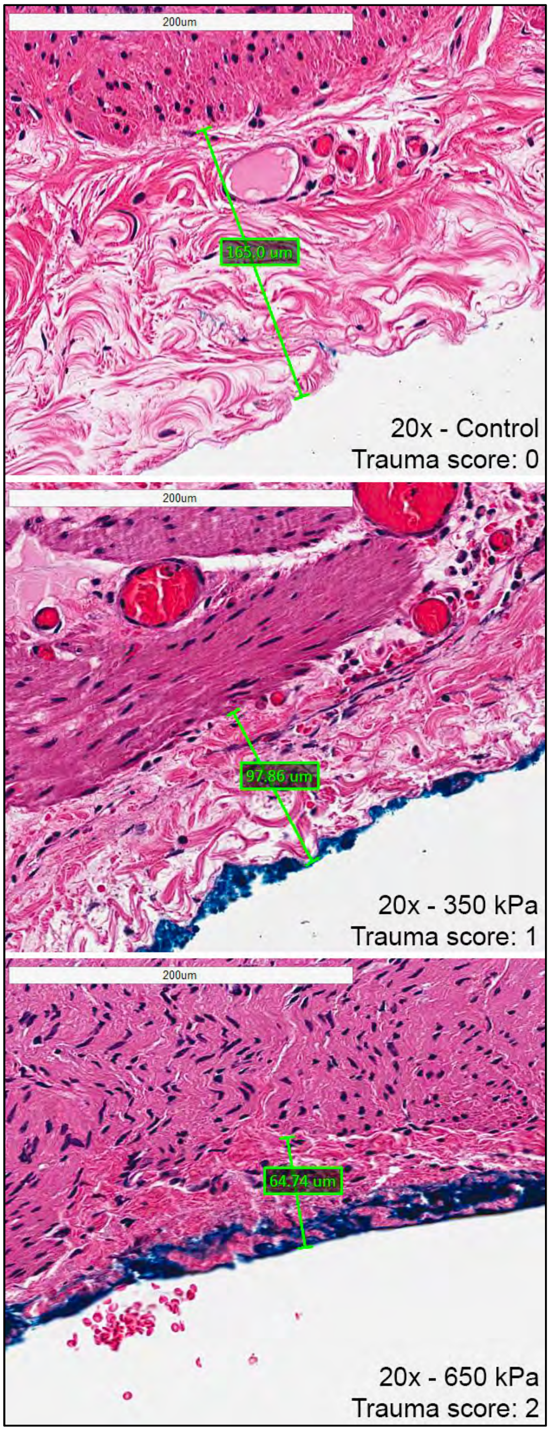

FIGURE 7. Representative histological sections for each tissue trauma score. There were no slides in this study that qualified for a grade of 3. Note the decrease in serosal thickness as indicated by the green measurement on each slide and increasing amount of cellular elongation and hyperchromasia of the nuclei as stress increases.

E. STATISTICAL ANALYSIS

A series of individual t-tests were conducted between the five serosal control measurements and the five compression site measurements at each stress condition to determine significance (Table 3), where p-values ≤ 0.05 are indicated by bold text and missing values indicate that the slide was unable to be analyzed due to poor orientation.

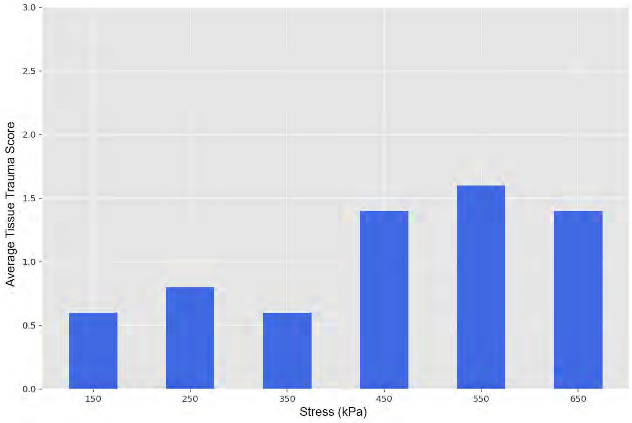

FIGURE 8. **The average tissue trauma score plotted for all 5 patients at each stress condition. There is a marked divide in scores between the 350 and 450 kPa stress conditions.**

TABLE 3. **T-test results between control and compression sites.**

P	*150 kPa*	*250 kPa*	*350 kPa*	*450 kPa*	*550 kPa*	*650 kPa*
1	0.164	0.281	-	**<0.001**	**<0.001**	**<0.001**
2	0.099	-	0.216	**<0.001**	**0.001**	**<0.001**
3	0.343	0.174	**<0.001**	**<0.001**	**<0.001**	**<0.001**
4	0.448	-	0.251	**<0.001**	**<0.001**	**<0.001**
5	0.238	0.167	0.495	**<0.001**	**<0.001**	**<0.001**

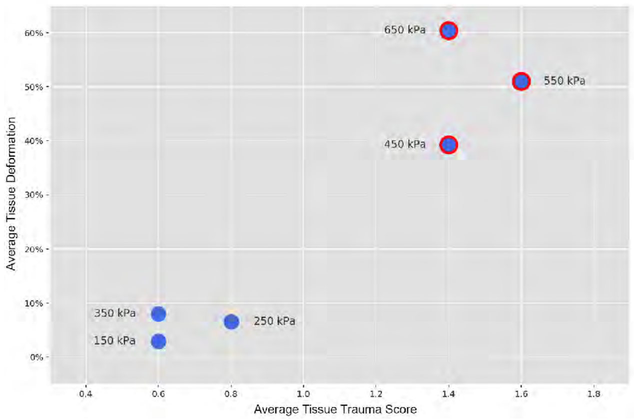

FIGURE 9. **The relationship between the two trauma metrics where average tissue trauma score is plotted against average tissue deformation at each stress condition. When all 5 patients had significant p-values of $\leq$0.05, this is indicated with a red circle.**

In our analysis, all 5 patients had a significant p-value starting at 450 kPa. This is higher than the minimum pressure of 150 kPa that Chandler et al.'s group found for damage to the porcine colon, but their measurements were for the mucosal and muscle layers of the colon and did not focus on serosal change as they had this layer of tissue stripped [27].

Comparing the two metrics (Fig. 9) we can see a clear correlation between high trauma score rating and large tissue deformation. Furthermore, there is a large separation between the two groups of significant and non-significant change.

Heijnsdijk et al., found that human small bowel tissue perforates at a force of 10.3 ± 2.9 N, which on our experimental setup would equal 528 kPa ± 150 kPa [28]. This is lower than our highest tested compressive stress. However, it is hard to draw meaningful conclusions in comparison to Heijnsdijk's work because we do not know the dimensions of their crush pin for their experimental set up; surface area of the crush pin largely influences its ability to damage or penetrate tissue. Colon tissue also tends to be thicker and stronger than small bowel tissue in humans [31]. One conclusion we can draw however is that full-thickness perforation of the colon occurs at compressive stresses greater than 650 kPa.

TABLE 4. **Build of materials for the SimpleCAT.**

Part	*Description*	*Product Code*
U-Shaped frame and weight platform	Machined out of 6061 aluminum via hospital machine shop, then anodized	N/A
Anodized aluminum guide rails x2	12 mm wide guide rail for high temperature sleeve bearing carriage; 120 mm rail length	McMaster-Carr 9880K12
Sleeve bearing carriage x2	High temperature sleeve bearing carriage for 12 mm wide rail	McMaster-Carr 9880K2
316 Stainless Steel Socket Head Screw	Thread Size: M3 Thread Pitch: 0.5 mm Length: 12mm	McMaster-Carr 92290A117
316 Stainless Steel Hex Nut	Size: M3 Pitch: 0.5 mm Width: 5.5 mm Height: 2.4 mm	McMaster-Carr 94150A325
316 Stainless Steel Pan Head Phillips Screws	Size: M3 Pitch: 0.5 mm Length: 50 mm	McMaster-Carr 90116A188

IV. DISCUSSION

This paper aimed to test a simple device that is capable of producing compressive stress in human tissues. As far as we know, we are one of the first groups to publish data based on the relationship between compressive stress and human gastrointestinal tissue trauma via a histological analysis.

In these preliminary results, it is clear that tissue damage correlates to how much force is exerted on that tissue in compression. The two pathologists who were blinded to all experimental conditions, were both able to quantify increasing tissue trauma amounts at increasing pressures. From our data there is a clear threshold between non-significant and significant serosal thickness change between 350 and 450 kPa. The histological trauma score rating also demonstrates a threshold within the same range. Thus, compressive tissue trauma occurs between these compressive stresses. The high variance between 350 to 550 kPa suggests that the exact threshold however is patient-dependent, thus a conservative cut-off would be 350 kPa.

Whether the tissue injury quantified is pathologic is subject for future *in-vivo* longitudinal investigation but certainly based on literature, can be the basis of pathological adhesion formation or an area for hemorrhage and scar formation. While more experimentation is needed to further explore inter-individual variation between humans and their tissue characteristics, these pilot data points can help inform the force limits of a new generation of smart sensorized laparoscopic graspers that can integrate intraoperative stress boundaries to ensure that surgeons are restricted to utilizing only safe amounts of force. Results need to be viewed in context of the limitations of an *ex-vivo* study however, as there was an inability to acquire useful *in-vivo* data such as neutrophil recruitment or long-term adhesion formation as visually verified in future abdominal procedures.

CONFLICTS OF INTEREST

The authors would like to disclose that they have no conflicts of interest in regard to the material in this paper.

APPENDIX

See Table 4.

ACKNOWLEDGMENT

The authors would like to thank all the patients involved in this study for allowing us to use their tissues. They would also like to thank Michael Pozzobon of the Advanced Machine Shop at Sunnybrook Hospital in Toronto for help with the machining of the SimpleCAT, Jeff Hollefriend from Holly's Anodizing for anodizing the crush apparatus, all of the general surgeons from St. Michael's Hospital who participated in this study and Granitus MKM for ongoing manuscript formatting and proofreading support.

REFERENCES

[1] M. A. Secretariat, "Robotic-assisted minimally invasive surgery for gynecologic and urologic oncology: An evidence-based analysis," *Ontario Health Technol. Assessment Ser.*, vol. 10, no. 27, pp. 1–118, 2010.

[2] R. Agha and G. Muir, "Does laparoscopic surgery spell the end of the open surgeon?" *J. Roy. Soc. Med.*, vol. 96, no. 11, pp. 544–546, Nov. 2003.

[3] E. P. Westebring-van der Putten, J. J. van den Dobbelsteen, R. H. Goossens, J. J. Jakimowicz, and J. Dankelman, "Force feedback requirements for efficient laparoscopic grasp control," *Ergonomics*, vol. 52, no. 9, pp. 1055–1066, Sep. 2009.

[4] T. P. Cundy *et al.*, "Force-sensing enhanced simulation environment (ForSense) for laparoscopic surgery training and assessment," *Surgery*, vol. 157, no. 4, pp. 723–731, Apr. 2015.

[5] O. A. J. van der Meijden and M. P. Schijven, "The value of haptic feedback in conventional and robot-assisted minimal invasive surgery and virtual reality training: A current review," *Surg. Endoscopy*, vol. 23, no. 6, pp. 1180–1190, Jun. 2009.

[6] V. N. Palter and T. P. Grantcharov, "Simulation in surgical education," *Can. Med. Assoc. J.*, vol. 182, no. 11, pp. 1191–1196, Aug. 2010.

[7] E. M. Wohaibi, R. W. Bush, D. B. Earle, and N. E. Seymour, "Surgical resident performance on a virtual reality simulator correlates with operating room performance," *J. Surg. Res.*, vol. 160, no. 1, pp. 67–72, May 2010.

[8] B. Zevin, R. Aggarwal, and T. P. Grantcharov, "Surgical simulation in 2013: Why is it still not the standard in surgical training?" *J. Amer. College Surg.*, vol. 218, no. 2, pp. 294–301, Feb. 2014.

[9] T. M. Kowalewski *et al.*, "Beyond task time: Automated measurement augments fundamentals of laparoscopic skills methodology," *J. Surg. Res.*, vol. 192, no. 2, pp. 329–338, Dec. 2014.

[10] E. M. Ritter and D. J. Scott, "Design of a proficiency-based skills training curriculum for the fundamentals of laparoscopic surgery," *Surg. Innov.*, vol. 14, no. 2, pp. 12–107, Jun. 2007.

[11] M. C. Vassiliou *et al.*, "The MISTELS program to measure technical skill in laparoscopic surgery : Evidence for reliability," *Surg. Endoscopy*, vol. 20, no. 5, pp. 744–747, May 2006.

[12] B. Tang, G. B. Hanna, P. Joice, and A. Cuschieri, "Identification and categorization of technical errors by observational clinical human reliability assessment (OCHRA) during laparoscopic cholecystectomy," *Arch. Surg.*, vol. 139, no. 11, pp. 1215–1220, Nov. 2004.

[13] M. Van Der Voort, E. A. Heijnsdijk, and D. J. Gouma, "Bowel injury as a complication of laparoscopy," *Brit. J. Surg.*, vol. 91, no. 10, pp. 1253–1258, Oct. 2004.

[14] H. de Visser, E. A. M. Heijnsdijk, J. L. Herder, and P. V. Pistecky, "Forces and displacements in colon surgery," *Surg. Endoscopy*, vol. 16, no. 10, pp. 1426–1430, Oct. 2002.

[15] W. Li, Z. G. Jia, J. Wang, L. Shi, and Z. R. Zhou, "Friction behavior at minimally invasive grasper/liver tissue interface," *Tribology Int.*, vol. 81, pp. 190–198, Jan. 2015.

[16] S. De, J. Rosen, A. Dagan, B. Hannaford, P. Swanson, and M. Sinanan, "Assessment of tissue damage due to mechanical stresses," *Int. J. Robot. Res.*, vol. 26, nos. 11–12, pp. 1159–1171, Nov. 2007.

[17] C. Brochhausen *et al.*, "Current strategies and future perspectives for intraperitoneal adhesion prevention," *J. Gastrointestinal Surg.*, vol. 16, no. 6, pp. 1256–1274, Jun. 2012.

[18] İ. Yıldız and Y. S. Koca, "To investigate the effect of colchicine in prevention of adhesions caused by serosal damage in rats," *Surg. Res. Pract.*, vol. 2015, p. 4, 2015, Art. no. 315325. [Online]. Available: https://www.hindawi.com/journals/srp/2015/315325/cta/. doi: 10.1155/2015/315325.

[19] J. C. Kalff, W. H. Schraut, R. L. Simmons, and A. J. Bauer, "Surgical manipulation of the gut elicits an intestinal muscularis inflammatory response resulting in postsurgical ileus," *Ann. Surg.*, vol. 228, no. 5, pp. 652–663, Nov. 1998.

[20] P. Ciarletta, P. Dario, F. Tendick, and S. Micera, "Hyperelastic model of anisotropic fiber reinforcements within intestinal walls for applications in medical robotics," *Int. J. Rob. Res.*, vol. 28, no. 10, pp. 1279–1288, Oct. 2009.

[21] N. Famaey, E. Verbeken, S. Vinckier, B. Willaert, P. Herijgers, and J. Van der Sloten, "*In vivo* soft tissue damage assessment for applications in surger," *Med. Eng. Phys.*, vol. 32, no. 5, pp. 43–437, Jun. 2010.

[22] J. Rosen, J. D. Brown, S. De, M. Sinanan, and B. Hannaford, "Biomechanical properties of abdominal organs *in vivo* and postmortem under compression load," *J. Biomech. Eng.*, vol. 130, no. 2, Apr. 2008, Art. no. 021020.

[23] V. I. Egorov, I. V. Schastlivtsev, E. V. Prut, A. O. Baranov, and R. A. Turusov, "Mechanical properties of the human gastrointestinal tract," *J. Biomech.*, vol. 35, no. 10, pp. 1417–1425, Oct. 2002.

[24] A. Nava, E. Mazza, M. Furrer, P. Villiger, and W. H. Reinhart, "*In vivo* mechanical characterization of human liver," *Med. Image Anal.*, vol. 12, no. 2, pp. 203–216, Apr. 2008.

[25] G. Dieter, "Mechanical behavior under tensile and compressive load," in *ASM Handbook*, H. Kuhn and D. Medlin, Eds. Materials Park, OH, USA: ASM International, 2000, pp. 99–108. [Online]. Available: https://www.asminternational.org/search/-/journal_content/56/10192/06772G/

[26] M. E. Kunkel, A. Moral, R. Westphal, D. Rode, M. Rilk, and F. M. Wahl, "Using robotic systems in order to determine biomechanical properties of soft tissues," *Stud. Health Technol. Inform.*, vol. 133, pp. 156–165, 2008. [Online]. Available: http://ebooks.iospress.nl/publication/11493

[27] J. H. Chandler, F. Mushtaq, B. Moxley-Wyles, N. P. West, G. W. Taylor, and P. R. Culmer, "Real-Time assessment of mechanical tissue trauma in surgery," *IEEE Trans. Biomed. Eng.*, vol. 64, no. 10, pp. 2384–2393, Oct. 2017.

[28] E. A. Heijnsdijk, M. van der Voort, H. de Visser, J. Dankelman, and D. J. Gouma, "Inter- and intraindividual variabilities of perforation forces of human and pig bowel tissue," *Surg. Endoscopy*, vol. 17, no. 12, pp. 1923–1926, Dec. 2003.

[29] S. De, J. Rosen, A. Dagan, B. Hannaford, P. Swanson, and M. Sinanan, "Assessment of tissue damage due to mechanical stresses," *Int. J. Rob. Res.*, vol. 2612, no. 11, pp. 1159–1171, Nov. 2007.

[30] J. D. Brown, J. Rosen, L. Chang, M. N. Sinanan, and B. Hannaford, "Quantifying surgeon grasping mechanics in laparoscopy using the blue DRAGON system," *Stud. Health Technol. Inform.*, vol. 98, pp. 6–34, 2004. [Online]. Available: http://ebooks.iospress.nl/publication/20647

[31] H. P. Haber and M. Stern, "Intestinal ultrasonography in children and young adults: Bowel wall thickness is age dependent," *J. Ultrasound Med.*, vol. 19, no. 5, pp. 315–321, May 2000.