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Constitutive modeling of the passive inflation-extension behavior of the swine colon

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ABSTRACT

In the present work, we propose the first structural constitutive model of the passive mechanical behavior of the swine colon that is validated against physiological inflation-extension tests, and accounts for residual strains. Sections from the spiral colon and the descending colon were considered to investigate potential regional variability. We found that the proposed constitutive model accurately captures the passive inflation-extension behavior of both regions of the swine colon (coefficient of determination $R^2 = 0.94 \pm 0.02$). The model revealed that the circumferential muscle layer does not provide significant mechanical support under passive conditions and the circumferential load is actually carried by the submucosa layer. The stress analysis permitted by the model showed that the colon tissue can distend up to 30% radially without significant increase in the wall stresses suggesting a highly compliant behavior of the tissue. This is in-line with the requirement for the tissue to easily accommodate variable quantities of fecal matter. The analysis also showed that the descending colon is significantly more compliant than the spiral colon, which is relevant to the storage function of the descending colon. Histological analysis showed that the swine colon possesses a four-layer structure similar to the human colon, where the longitudinal muscle layer is organized into bands called taeniae, a typical feature of the human colon. The model and the estimated parameters can be used in a Finite Element framework to conduct simulations with realistic geometry of the swine colon. The resulting computational model will provide a foundation for virtual assessment of safe and effective devices for the treatment of colonic diseases.

1. Introduction

The functions of the colon are essentially twofold (Shields and Miles, 1965; Beck et al., 2011). Firstly, it absorbs water and electrolytes from the incoming liquid chyme, and transfers them into the blood stream. This function is mainly ensured by the proximal part of the colon. Secondly, it stores the resulting semi-solid waste in its distal part until there is a voluntary discharge. The colon is a potential target for a large number of diseases such as diverticulosis, inflammatory bowel syndrome, and cancer (Sandler et al., 2002; Siegel et al., 2014). In addition to disturbing the colon functions, these colonic diseases disrupt the quality of life greatly. Unfortunately, no long-term minimally-invasive solutions are currently available for most of these diseases. The development of computational models that capture the biomechanics of the colon is thus crucial in guiding the design of safe and effective therapeutic devices to control progression, relieve symptoms, and ultimately cure these colonic diseases. A key requirement for such a computational model is the development of a suitable constitutive model that characterizes the mechanical behavior of the tissue by providing a mathematical formulation for the stress-strain relation. Reports on the constitutive modeling of the colon tissue are available in literature, but limited work has been achieved. Higa et al. (2007) have proposed a constitutive model for the goat colon. The model was validated via in-vivo compression tests that, however, do not present a significant physiological relevance. Moreover, an isotropic Mooney-Rivlin model was suggested whereas observations of the colon tissue microstructure revealed clearly an anisotropic nature. Sokolis et al. (2011) proposed a phenomenological constitutive model and later a structure-based constitutive model (Sokolis and Sassani, 2013) for the passive behavior of the rat colon. Two studies (Ciarletta et al., 2009; Carniel et al., 2014) proposed a structure-based constitutive model for the swine colon tissue, which has been shown to have greater similarities with humans (Kararli, 1995). No experimental validation or adequate references were, however, given for the assumed

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microstructure and fiber arrangement. Moreover, material parameters were estimated based on multiple uniaxial tensile tests only, whereas both extension and inflation simultaneously play an important role in the in-vivo colon mechanics. Additionally, no specifications were given regarding the region of the swine colon that was considered for the testing and modeling.

Hence, a constitutive model of the colon tissue validated against physiologically relevant inflation-extension data from a large animal model is currently unavailable. In the present study, we proposed to fill this gap by developing and validating a constitutive model for the passive mechanical behavior of the swine colon. Swine was chosen as animal model based on the structural similarities we found with humans. We proposed a structural material constitutive model that is an extension of the model proposed by Gasser et al. (2006) for blood vessels. The model is similar to that used in the previously mentioned rat colon (Sokolis and Sassani, 2013) and swine colon (Ciarletta et al., 2009) studies, but with additional consideration of fiber distribution since dispersion was seen in the submucosa layer of the colon. Material parameters from the model were estimated from physiologically relevant inflation-extension tests on swine colon specimens and the validity of the model was verified. The common approach for the constitutive modeling of tubular tissues was followed here to achieve that (Holzapfel et al., 2000; Sommer and Holzapfel, 2012). The swine colon is organized into two regions: a spiral portion (proximal) and a descending portion (distal). Specimens from both regions were tested to investigate the potential regional variability the mechanical behavior. The presence of residual strains in the tissue was also accounted to ensure accurate estimation of the parameters from the model. The passive behavior is of interest in this work, while the active tone of the smooth muscle cells is not considered. The active response will be studied in a subsequent work once the passive foundation is established here.

2. Material and methods

2.1. Materials

For this work, colon tissues from 12 swine were used. Tissues from two swine were used to observe the overall anatomy of the colon and to conduct histology analysis, while the remaining tissues were used for mechanical testing. These tissues were collected from in-house swine that weighted around 55 kg, and were being used for other studies unrelated to the gastrointestinal tract. After sacrifice of the swine, the colon was accessed by incision of the abdominal cavity. A descending colon portion was marked by attaching one 4-0 suture above the rectum and a second suture 15 cm proximal to the first suture. The spiral colon was similarly marked with one suture at the overlap with the small intestine, and a second suture 15 cm above going toward the proximal end. The colon specimens were sectioned at the sutures. Their luminal content was removed by gently flushing with a 0.9% NaCl physiological saline solution. The colon specimens required for histology were then fixed in 10% formalin for subsequent staining. The specimens required for mechanical testing were stored in saline at 4 °C, and mechanical testing was carried out within 6 h.

2.2. Histology

Since the macroscopic mechanical response of a tissue is determined by its microstructure, understanding the microstructural organization of a tissue is essential to select a relevant constitutive formulation. To that end, fixed specimens of spiral colons and descending colons were stained with Movat's pentachrome and subsequently imaged. Cross sectional and longitudinal areas were targeted.

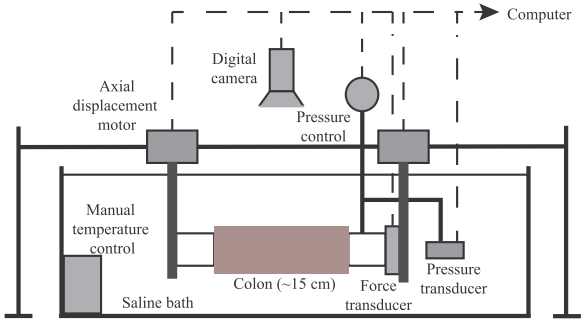

Fig. 1. Schematic representation of the experimental system used to conduct inflation-extension tests on colon specimens.

2.3. Mechanical testing

To estimate material parameters and validate the constitutive model proposed in this work, extension-inflation tests were performed using a biaxial testing system designed specifically to accommodate large tubular tissues. A schematic of the experimental setup is provided in Fig. 1. Several combinations of axial stretch and luminal pressure were applied on the colon specimens while the axial force and the outer diameter were being recorded. During testing, the specimens were immersed in a 0.9% NaCl physiological saline solution maintained at 37 °C. Sodium nitroprusside ($10^{-4}\mu mol/L$ Espín et al., 2014) was added to suppress the active response of the smooth muscle cells. The axial force was measured using a miniature load cell (Honeywell model 31, 3 lb range, ± 0.25% full scale accuracy). The diameter of the sample was measured using a digital camera (Basler ace acA3800-10gc, 10 MP, 10 fps) used in conjuncture with an automated edge detection program (Cyth systems). The diameter was measured toward the center of the specimen, away from the edges (to avoid errors due to end-effects), at three specified locations chosen arbitrarily where the largest variation of in diameter were visually noticed. The average value of the three measurements was then considered in the analysis. A sampling rate of 10 Hz was used for data recording .

No mention of physiological ranges for axial stretch and luminal pressure were found in the literature for the swine colon. To determine a suitable range for the axial stretch, the length of the colon specimens was measured in-situ before being sectioned. Because the amount of pressure in-situ varies between swine due to variable amounts of colonic gases, the in-situ length was measured after puncturing the cecum and the rectum in order to collect all the in-situ measurements at atmospheric pressure. We found that the ratio between in-situ and ex-vivo lengths was 1.12 ± 0.011 for the spiral samples and 1.10 ± 0.012 for the descending samples. Thus, axial stretch ratios between 1 and 1.20 were considered. Below a stretch ratio of 1, the specimens displayed warping, which is excluded from this study. Preliminary tests were conducted using 5 spiral colon specimens and 5 descending colon specimens to determine a suitable pressure range. We found that, for the prescribed axial stretch range, luminal pressure up to 1.5 kPa (12 mmHg) was suitable for both spiral and descending colon specimens. Above this value, tears were visible on the muscularis. An initial pressure of 0.05 kPa (0.38 mmHg) was applied to ensure proper opening of the tissue that would otherwise collapse. During these preliminary tests, we also determined that 5 pre-conditioning pressure cycles were sufficient to guarantee reproducible mechanical data at each stretch step. Testing was carried out with axial stretch ratios ranging from 1 to 1.20 in increment of 0.05, and luminal pressures ranging from 0.05 to 1.5 kPa in increment of 0.05 kPa. This resulted in a total of 150 data points per specimen. A dwell of about 30 s was maintained between each step before gathering the required data to allow the tissue to settle into a static state. If a variation in the pressure was observed during that dwell time, the pressure was adjusted again to the desired value. The value of the parameters at the end of a stable