IN VIVO TESTING OF HYSTERESIS OF THE UTERINE SUSPENSORY TISSUE IN CHINESE WOMEN WITH PELVIC ORGAN PROLAPSE

Hui Wang (1), Zhuowei Xue (2), Chenxin Zhang (1), Fei Feng (3), Chengsheng Huang (2), Da He (3), Xinyi Wang (3), Qingkai Wu (2), Jiajia Luo (1)

(1) Biomedical Engineering Department, Peking University, Beijing, China
(2) Department of Obstetrics and Gynecology, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China
(3) University of Michigan-Shanghai Jiao Tong University Joint Institute, Shanghai Jiao Tong University, Shanghai, China

INTRODUCTION

Pelvic organ prolapse (POP) refers to downward displacement and deformation of the female pelvic organs [1]. In the United States, more than 200,000 surgeries are performed each year [2], with a 25% recurrence rate 10 years after surgery [3]. In China, the prevalence of symptomatic pelvic organ prolapse was 9.6% [4].

Pelvic organ prolapse usually occurs about 20-30 years after vaginal delivery, which is most likely closely related to prolonged and repeated loading and unloading of the uterine suspensory tissue (UST) over many years. The UST, consisting of the cardinal ligament (CL) and the uterosacral ligament (USL), is thought to play an important role in resisting pelvic organ prolapse [5]. However, the underlying mechanisms of tissue damage of the UST and prolapse caused by long-term repetitive loading remains unclear. Therefore, the aim of this study was to develop an MRI-based preoperative measurement technique to quantify the *in vivo* hysteresis of the UST in women with pelvic organ prolapse and to help understand the temporal mechanisms of the occurrence of pelvic organ prolapse.

METHODS

Six Chinese women with POP scheduled for surgery were selected from an ongoing POP research at the Shanghai Jiao Tong University Affiliated Sixth People's Hospital (Shanghai, China) with the approval of the Institutional Review Board.

Prior to surgery, the mechanical behavior of the CL and USL was tested using a newly designed computer-controlled linear servo system (Figure 1), similar to our previous work [6]. First, the patient's information and the max force used were entered through the computer. To obtain the initial position, a force of 1 N was preloaded to remove the slack of the UST. Then the linear actuator pulls the uterine cervix until the force reaches its maximum. Finally, the linear actuator was reversed to gradually release the UST. Force and displacement were recorded in real time during the test. A total of three trials were performed for each patient, with a two minutes interval for tissue recovery.

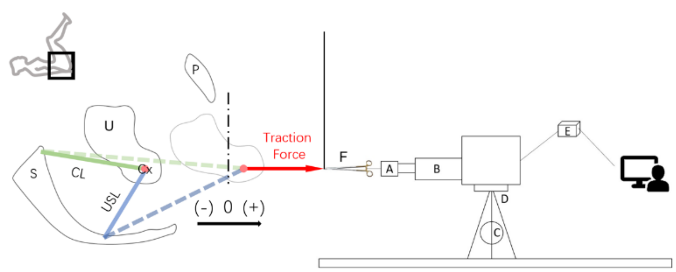

Figure 1: Schematic of the test setup. Zero indicates the location of the hymen, with −/+ meaning above or below the hymen. Cx, cervix; P, pubic bone; S, sacrum; U, uterus; A, B, and D denote the force sensor, linear actuator, and shell; C, the tripod; E, the motor controller; and F, the cervical forceps. The vertical dashed-dotted line represents the initial location of the hymenal ring. The green and blue dashed lines indicate CL and USL under load, respectively. Modified from [6].

Similar to our previous study [7], we used MRI scans of the CL and USL to create a specific 3D model for each individual, measuring the length, angle, and cross-sectional area of the CL and USL for each individual. A four-wire model was used to calculate the forces on the ligaments.

A typical loading and unloading of the UST is shown in Figure 2. The UST stiffness is defined by $\frac{f_2-f_1}{d_2-d_1}$, where f_2 and f_1 denote the maximum force and minimum force, and d_2 and d_1 denote the maximum displacement and minimum displacement. The hysteresis is defined by $\theta_1-\theta_2$, where θ_1 is the area under the loading curve and θ_2

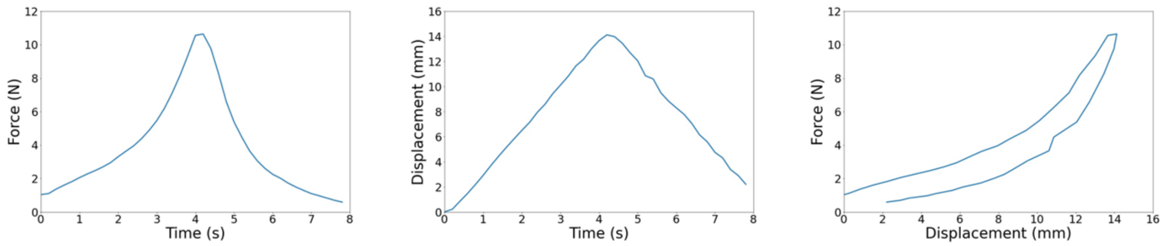

Figure 2: A typical loading and unloading test result (trial 1) for the UST (Patient #003).

is the area under the unloading curve of each trial. Python (v 3.7.2) and the corresponding NumPy (v 1.20.2) library were used to process the data and calculate the hysteresis and stiffness per person per trial.

For simplicity, CL and USL were assumed as incompressible isotropic hyperelastic materials, and the strain energy density was assumed to be a function of the first and second invariants of the strain tensor. A three-parameter hyperelastic Moony-Rivlin material model was thus selected to fit the CL and USL loading behavior, and the model was defined as follows:

$$W(0) = C_{10}(I_1 - 3) + C_{01}(I_2 - 3) + C_{11}(I_1 - 3)(I_2 - 3) \quad (1)$$

Where C_{01}, C_{10}, and C_{11} are material constants; I_1 and I_2 are the first and second invariants of rights Cauchy deformation tensor. A customized MATLAB (v.2019a) program was used to solve the strain and stress and fit the strain-stress curve.

Descriptive statistical analysis and two-sided T-test were used to compare the differences between the three trials.

RESULTS

The six Chinese women with POP had an age of 68 ± 12 years old ($mean \pm SD$), and parity of 1.8 ± 0.8. They all had anterior vaginal prolapse. The stiffness and hysteresis of the UST for those Chinese women are shown in Figure 3.

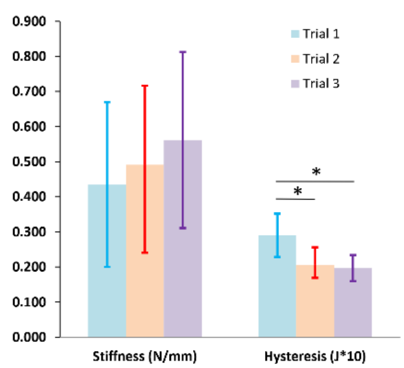

Figure 3: Uterine suspensory tissue stiffness and hysteresis in Chinese women with prolapse from trial 1 to trial 3 ($*, p < 0.05$). For demonstration purposes, we change the unit of hysteresis from J to $10J$.

For the UST, the stiffness was $0.434 \pm 0.235\ N/mm$ for trial 1, $0.492 \pm 0.227\ N/mm$ for trial 2, and $0.560 \pm 0.250\ N/mm$ for trial 3. The hysteresis was $0.029 \pm 0.006\ J$ for trial 1, $0.021 \pm 0.005\ J$ for trial 2, and $0.019 \pm 0.004\ J$ for trial 3. As can be seen from the results, the UST continues to harden with repeated loading. The hysteresis of the UST was significantly reduced from trial 1 to trial 2, not significantly from trial 2 to trial 3.

The stress-strain behavior in each trial and the fitted curves of CL and USL are shown in Figure 4. The three-parameter hyperelastic Moony-Rivlin material constants were fitted according to Eq. (1). For CL, C_{10} was $-0.04 \pm 0.05\ MPa$, C_{01} was $0.04 \pm 0.06\ MPa$, and C_{11} was $0.04 \pm 0.05\ MPa$. For USL, C_{10} was $-0.02 \pm 0.02\ MPa$, C_{01} was $-0.02 \pm 0.02\ MPa$, and C_{11} was $-0.02 \pm 0.02\ MPa$.

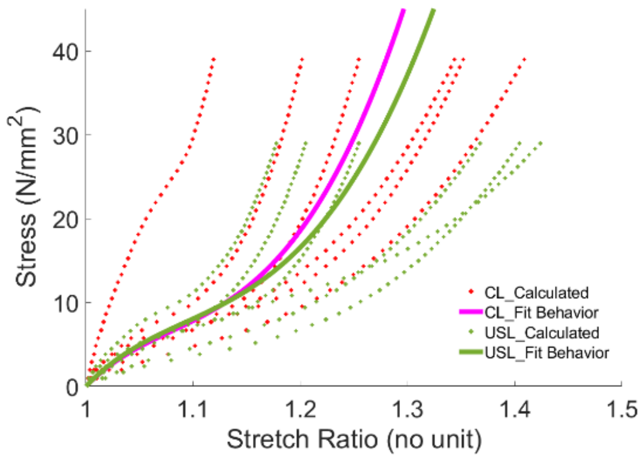

Figure 4: Stress-strain behaviors of the CL and USL. The calculated stress-strain data for each subject are shown as dotted lines, and the fitted stress-strain curves are shown as solid lines. The R^2 value for the CL is 0.6311 and for the USL is 0.6674.

DISCUSSION

This study is the first to examine *in vivo* hysteresis of the uterine suspensory tissue in Chinese women with pelvic organ prolapse. This helps us to understand the changes in uterine suspensory tissue and the temporal mechanism of pelvic organ prolapse under long-term repeated loading. This will allow us to better understand why vaginal delivery leads to pelvic organ prolapse after 20 to 30 years. So far, we have only provided partial results. In future work, a larger sample size might help us to find statistical differences between different categories of patients.

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