JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS 27 (2013) 143–153

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A novel procedure for the mechanical characterization of the uterine cervix during pregnancy

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ARTICLE INFO

Article history:
Received 27 September 2012
Received in revised form
20 November 2012
Accepted 27 November 2012
Available online 11 December 2012

Keywords:
Uterine cervix
Aspiration experiment
In-vivo measurements
Inverse analysis

ABSTRACT

An in-vivo measurement procedure is presented to characterize the mechanical behavior of human uterine cervix during pregnancy. Based on the aspiration method, a new instrument was developed to provide an inherently safe and easy-to-use mechanical testing technique. Initial measurements were performed on non-pregnant women to develop an appropriate measurement protocol. An inverse analysis was carried out to determine representative model equations for cervical tissue. This model was used in a FE based parametric study focusing on the uncertainties related to the experiment. On this basis, a novel procedure was established which enabled for the first time to conduct mechanical measurements on 50 pregnant women in over 600 applications during gestation. An inverse analysis of the average tissue response at each trimester was performed to determine representative model equations for the cervix in the course of pregnancy.

1. Introduction

The cervix is the neck of the uterus and plays a crucial role in maintaining pregnancy despite an increasing pressure in the uterine cavity due to the growing fetus. The development of diagnostic tools to determine the risk of preterm delivery requires further understanding of the mechanical behavior of the uterine cervix and its changes during gestation (Parra-Saavedra et al., 2011; Lang et al., 2010; House et al., 2009, 2006). In finite element simulations of pregnancy and birth, constitutive models are needed to investigate the influences of cervical deformation, including the effects of surgical interventions on the cervix (cerclage) conducted in risk patients for preterm delivery (Paskaleva, 2007). Knowledge of the mechanical behavior of the cervix is required also to study the interaction between the fetal membrane and cervix in advanced gestation and for the investigation of vaginal delivery related damage of the pelvic floor (Cosson et al., 2012).

Tensile testswere performed ex-vivo on human cervical tissue to determine constitutive model equations (Myers et al., 2010), and to qualitatively assess the correlation of stiffness parameters and microstructural components (Oxlund et al., 2010). Ex-vivo experiments achieve, to some extent, tight control of kinematic and kinetic boundary conditions (see also Paccini et al., 2005), but they are performed on non-physiological tissue configurations. Very limited quantitative data are available to describe the mechanics of the cervical tissue in gestation because of the technical and ethical problems related to the experiments. Recently, non-invasive in-vivo measurement procedures such as Electrical Impedance Spectroscopy, Collascope and Elastography have been proposed to assess the changes of

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http://dx.doi.org/10.1016/j.jmbbm.2012.11.020

mechanical properties of the uterine cervix in pregnancy (Molina et al., 2012; Schlembach et al., 2009; Gandhi et al., 2006). These methods could not be validated for clinical applications so far. Feltovich et al. (2012) review technologies for assessing the pregnant cervix and describe methods that can determine quantitatively the microstructural properties of cervical stroma, such as Second Harmonic Generation (Akins et al., 2010), Raman Spectroscopy (Vargis et al., 2012) or Shear Wave Speed. All these techniques could only be applied ex-vivo or in animal studies so far.

The present work introduces an in-vivo measurement procedure based on the pipette aspiration technique (Aoki et al., 1997). The aspiration technique has been successfully applied in clinical studies on the liver, (Hollenstein et al., 2010; Nava et al., 2008; Mazza et al., 2007) and in preliminary investigations on the uterine cervix (Bauer et al., 2009; Mazza et al., 2008). The same measurement principle was used in the so called "light aspiration device" (Schiavone et al., 2009) which provided in-vivo mechanical data of the human brain. In the present work, a novel procedure for the realization of aspiration measurements on the cervix during gestation has been developed. To this end, the existing aspiration device was re-designed to simplify trans-vaginal application during regular pregnancy consultations. Quantitative local measurement of the mechanical properties of cervical tissue has the potential to provide a method for accurate tissue classification and early detection of a risk of preterm birth. Finite element calculations were performed to analyze the main sources of measurement uncertainties and to determine indicative model equations from an inverse analysis of the data from non-pregnant organs. Based on these results a measurement procedure was defined and applied in a clinical study with >600 measurements on 50 pregnant women, to characterize the evolution of the mechanical properties of human uterine cervices during pregnancy.

2. Experimental method

The instrument, illustrated in Fig. 1, consists of a circular tube connected to a peristaltic pump, used to generate a progressive vacuum inside the tube. The round opening (diameter of eight millimeters) at one extremity of the tube is placed orthogonally on the cervix protruding into the vaginal canal. With progressive vacuum increase, cervical tissue is sucked into the tube and forms a nearly spherical cup. Once the apex of the cup protrudes four millimeters into the tube it touches and closes the thin pipe used to evacuate the tube (Fig. 1b). The (negative) pressure required to deform the tissue up to four millimeters, called p_{cl} (closure pressure), is the outcome of the experiment. This provides an inherently safe, displacement controlled end-point of the experiment. In fact, the corresponding level of tissue deformation is low enough not to induce tissue damage or bleeding. The pressure required to achieve this prescribed level of deformation is proportional to the stiffness (or, more in general, resistance to deformation) of the tissue.

A digital camera and glass fibers (for illumination) are integrated in the tube, Fig. 1d. This arrangement allows the physician to use the instrument as an endoscope to facilitate the placement on the selected location of the cervix. During the aspiration phase, the camera provides a top-view of the cervical tissue being sucked up, but this information is not used to quantify tissue deformation. The following video sequence shows instrument insertion, placement and cervical tissue aspiration.

Supplementary material related to this article can be found online at http://dx.doi.org/10.1016/j.jmbbm.2012.11.020

The whole measurement procedure is controlled by the physician using two foot pedals, Fig. 1a: one serves as a vacuum releaser and the second pedal as the emergency stop. A digital display provides the investigator with the current value of the pressure inside the tube. An additional sensor measures the pressure in the thin pipe and compares it with the value in the aspiration cavity. Closure of the internal pipe is detected as a threshold difference of these two values. The procedure is then automatically stopped with an acoustic and light signal, and the pressure histories are recorded. The whole device is mounted on a trolley (Fig. 1a). A diagram representation of the measurement system is shown in Fig. 2.

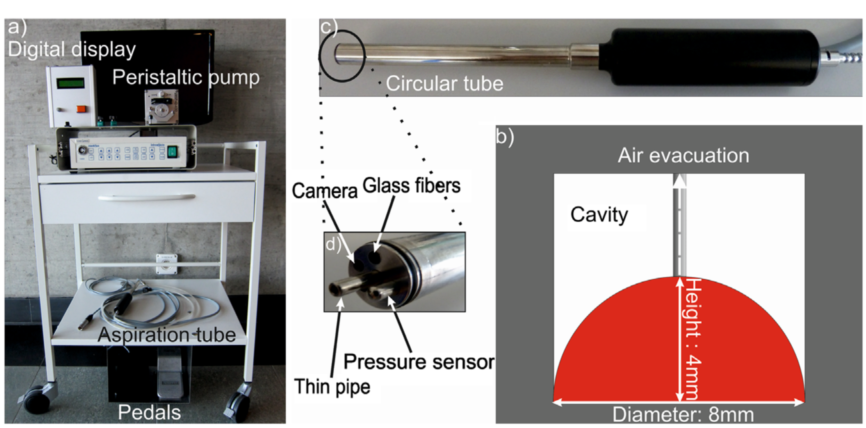

Fig. 1 – Aspiration device: (a) trolley with the peristaltic pump, monitor, aspiration tube, and pedals are visible, (b) measurement principle: cervical tissue is sucked into the tube and forms a nearly spherical cup until it touches and closes the thin pipe, (c) aspiration tube with circular opening at one extremity, (d) the integrated camera, glass fiber and pressure sensor are placed within the tube.