DETECTION OF TISSUE REACTION TO FOREIGN BODIES

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Abstract

Human body normally reacts to the presence of foreign bodies by inflammation, fibrosis, and infection. Such reactions may negatively affect the function of implant or may harm the host. Body reactions lead to alterations in the mechanical properties, such as increase in the stiffness of the tissue. Here we develop a noninvasive method for studying changes in the mechanical properties of tissue near a foreign body. For this purpose, we use modulated focused ultrasound to generate a harmonic radiation force on the object and we use an ultrasound Doppler system or an accelerometer to detect object motion. The frequency response of the object is determined by recording object motion at a range of vibration frequencies and is used to determine changes in the mechanical properties of the tissue at the site of the foreign body. Potential applications of this method include non-invasive monitoring of tissue reaction to foreign bodies.

Introduction

Foreign bodies are non-biological objects, such as sensors or implants, or other materials, which are placed in body for various reasons. Medical implants are devices planted inside the human body for monitoring or controlling biological functions. All foreign bodies interact to some extent with host tissues. Some foreign bodies produce adverse patient-device interactions that harm the host tissue [1]. Important body reactions to most foreign bodies include injury, inflammation, and wound healing with or without fibrosis, immunological reaction, toxicity, infection, and tumorigenesis. Foreign body reactions consist mainly of macrophage cells and foreign body giant cells (FBGC) at the object surface. In severe foreign body reaction, many macrophages and FBGC are present and may persist for years. This coating may persist, but generally, there is granulation tissue and then fibrosis leading to a fibrous encapsulation. Most body reactions described here result in changes in the viscoelastic properties of the tissue adjacent to the foreign body. For instance, inflammation normally causes tissue hardening. The vision of this study is that by detecting such changes in tissue properties, one can obtain useful information about body reaction to the foreign body. The ultimate goal of this research is to develop a method for evaluating tissue reaction to a foreign body by assessing physical changes produced in the tissue adjacent to the foreign body. For this purpose, we use modulated focused ultrasound to generate a harmonic radiation force on the object, and use an ultrasound Doppler system or an accelerometer to detect object motion. The frequency response of the object is determined by recording object motion at a range of vibration frequencies. We use this frequency response to characterize changes in the mechanical properties of the tissue. Our method is based on a technique called vibro-acoustic spectrography (VAS) [2], in which we use the radiation force of ultrasound to measure the dynamic behavior of an object. This technique is both remote and noninvasive. In previous studies, we have used the radiation force of ultrasound to measure the shear viscosity of liquids [2], measure the shear elasticity and viscosity of gel blocks [3], and to measure the Young's modulus of a metal object [4]. Our main objective here is to evaluate changes in the mechanical parameters of the tissue at the site of the foreign body by VAS technique.

Method

Principles of Vibro-acoustic Spectrography (VAS) are well discussed before [2, 5]. The general approach in VAS is to measure tissue motion caused by a force and use it to evaluate the viscoelastic parameters of the tissue. Specifically in this method, the radiation force of ultrasound is used to vibrate the tissue. Acoustic radiation force is the time average force exerted by an acoustic field on an object. Several benefits may result from using ultrasound radiation force for evaluating tissue properties, including: (a) acoustic (ultrasound) energy is a noninvasive means of exerting force; (b) radiation force can be generated remotely inside tissue without disturbing its superficial layers; (c) radiation force of ultrasound can be focused to a small region, thus allowing the force to be exerted to a small region or object; (d) radiation force can be produced in a wide range of frequencies or temporal shapes. We use a

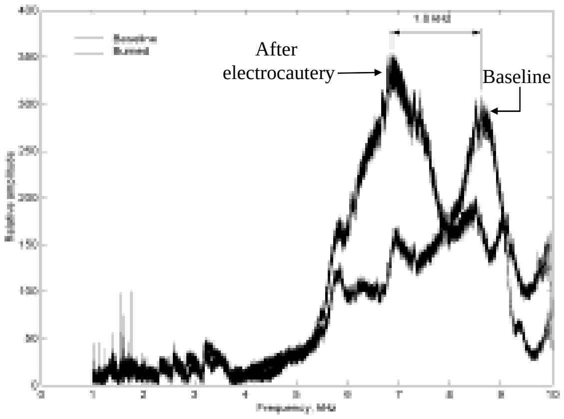

Figure 1. VAS spectrum of implanted wire in pig's leg, before (baseline) and after electrocautery. The resonance peak shifts down after electrocautery. (Reproduced with permission from the International Institute of Acoustics and Vibration.)

dynamic (oscillating) radiation force to remotely vibrate the foreign body in the tissue and measure its motion. The collected acoustic emission information is used to evaluate the frequency response of the foreign body.

To test our method we conducted experiments on pig muscle specimens, and *in vivo* pig muscle. We implanted small (~20x1x1 mm) of aluminum or steel pieces in the tissue. To increase tissue stiffness around the implants we connected an electrocautery device to the implants and produced a small burn around each implant. We recorded the frequency response of the implant before and after electrocautery. Using an accelerometer, we detected displacements as small as 16 nm of the vibrating implant. Also, we observed the shift of the peak of the frequency response after electrocautery of the implants in pig's muscle. This shift is correlated to the increase in tissue stiffness.

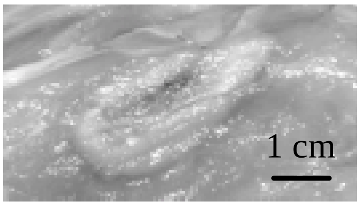

Figure 2.Tissue burn at the site of implanted wire. (Reproduced with permission from the International Institute of Acoustics and Vibration.)

The anesthetized pig is placed on the air table. A small (25 cm in diameter) water bath is created using a plastic sheet. The water bath is shaped as a bottomless cylinder, with the bottom edge completely glued and water-sealed to animal's groin. This water bath provides an acoustic path for direct coupling of the ultra-sound beam to the groin area. The confocal ultrasound transducer is immersed in the water bath and positioned such that the ultrasound beam is focused on a spot on the implanted wire under the skin. To measure wire motion an accelerometer (Bruel&Kjaer, Naerum, Denmark, Model 4378) is screw-clamped to the exposed end of the wire. For each VAS scan, the vibration frequency is slowly swept from zero to 10 kHz. The VAS scans are performed on the steel wires before electrocautery (baseline spectrum) and after electrocautery.

Results

Figure 1 shows a pair of spectra for the wire. Both spectra show resonance peaks. These peaks occur at 8.7 kHz before and 6.9 kHz after electrocautery. It is seen that electrocautery has introduced a downshift of about 1.8 kHz (or a change of 20%) in the resonance frequency. In our experiment, the burned region tissue felt to the fingers like a lump around the wire. In addition, we noticed that the tissue adjacent to the wire stuck more firmly to the wire after electrocautery. Figure 2 shows the burned region in the tissue.

The VAS results indicate that the resonance frequency of the implanted wires shifts down as a result of tissue cauterization. The interpretation for this shift is as follows. Burning hardens the tissue around the wire, which in turn increases the loading effect of the tissue on the wire. That is, the effective mass of the wire increases after electrocautery. We may model the wire as a beam with one end clamped (to the accelerometer) and one end free, but loaded by the tissue. Referring to the well-known theory of beam vibrations [6] it can be shown that loading (increased effective mass) lowers the resonance frequency of fundamental mode. This experiment demonstrates that changes in tissue stiffness can be detected from the frequency response of the implant as measured by VAS.

Discussion

There are a number of issues that need to be addressed when developing a VAS system for in-vivo tissue evaluation. In a practical situation, we cannot use a contact accelerometer for motion detection; instead, we need to use alternative approaches such as Doppler methods. Employing a continuous wave ultrasound Doppler method can be an effective non-contact method to detect motion. In particular, because the frequency of vibration is known a priori, one can custom design a Doppler system to receive the known frequency with high sensitivity.

The proposed method is not limited to a particular type of foreign bodies. That is because VAS treats the implant as a "vibrating object" irrespective of its function. Hence, the proposed method can be adaptable to a wide variety of applications. Further development of VAS will open the way for a novel class of noninvasive tools for characterization of tissue reaction at the site of foreign bodies.

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