Medical Engineering and Physics 000 (2017) 1–6

Contents lists available at ScienceDirect

Medical Engineering and Physics

journal homepage: www.elsevier.com/locate/medengphy

Technical note

Ex vivo study of prostate cancer localization using rolling mechanical imaging towards minimally invasive surgery

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ARTICLE INFO

Article history:
Received 27 April 2016
Revised 11 January 2017
Accepted 31 January 2017
Available online xxx

Keywords:
Rolling mechanical imaging
Robotic minimally invasive surgery
Wheeled probe

ABSTRACT

Rolling mechanical imaging (RMI) is a novel technique towards the detection and quantification of malignant tissue in locations that are inaccessible to palpation during robotic minimally invasive surgery (MIS); the approach is shown to achieve results of higher precision than is possible using the human hand. Using a passive robotic manipulator, a lightweight and force sensitive wheeled probe is driven across the surface of tissue samples to collect continuous measurements of wheel-tissue dynamics. A color-coded map is then generated to visualize the stiffness distribution within the internal tissue structure. Having developed the RMI device in-house, we aim to compare the accuracy of this technique to commonly used methods of localizing prostate cancer in current practice: digital rectal exam (DRE), magnetic resonance imaging (MRI) and transrectal ultrasound (TRUS) biopsy. Final histology is the gold standard used for comparison. A total of 126 sites from 21 robotic-assisted radical prostatectomy specimens were examined. Analysis was performed for sensitivity, specificity, accuracy, and predictive value across all patient risk profiles (defined by PSA, Gleason score and pathological score). Of all techniques, pre-operative biopsy had the highest sensitivity (76.2%) and accuracy (64.3%) in the localization of tumor in the final specimen. However, RMI had a higher sensitivity (44.4%) and accuracy (57.9%) than both DRE (38.1% and 52.4%, respectively) and MRI (33.3% and 57.9%, respectively). These findings suggest a role for RMI towards MIS, where haptic feedback is lacking. While our approach has focused on urological tumors, RMI has potential applicability to other extirpative oncological procedures and to diagnostics (e.g., breast cancer screening).

1. Introduction

Prostate cancer [1] is the most common male malignancy and an average of 1 in 8 men will be diagnosed with prostate cancer during their lifetime. Treatment of prostate cancer by surgical extirpation (radical prostatectomy) or by tissue destruction in situ (e.g., radiotherapy or brachytherapy) frequently compromise potency and urinary control. The key tenet of preserving functional outcomes in prostate surgery is to effectively treat the prostate tumor, but spare adjacent tissues involved in urinary control (e.g., bladder neck and urethral length) as well as erectile function (cavernous nerves). This principle means that prostate surgeons walk a continual tightrope between removing adequate tissue to treat the cancer (the tumor plus a margin) and avoiding unnecessary resection of tissue important to functional outcomes.

For centuries, surgeons have used texture and firmness to discriminate between benign and malignant tissue when dissecting at operation. In the modern era of prostate cancer surgery, a surgeon subtly modifies dissection planes in real time during an operation,

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http://dx.doi.org/10.1016/j.medengphy.2017.01.021

combining subjective haptic data with visual cues and knowledge of pre-operative assessments (including imaging and statistical models). The advent of robotic surgery (such as the da Vinci Surgical System has provided a high definition stereoscopic vision, tremor free scalable manipulation with high degrees of freedom at the operating fulcrum, and an ergonomic operating position [2,3]. This significantly improves the ease at which prostate cancer surgery (radical prostatectomy) can be performed. However, robotic surgery throws down a new challenge, because it deprives surgeons of haptic feedback and therefore tissue stiffness assessment afforded by their fingers or dissection instruments. Therefore, dissection planes and in particular, bladder neck sparing or nerve sparing increments can be decided only by pre-operative assessments about tumor stage and visual cues [4].

It is possible that the loss of haptic feedback is one reason why robotic surgery has failed to deliver convincingly (at least to date) significant improvements in functional outcomes relative to open or conventional laparoscopic surgery. Furthermore, given tumor localization is critical to surgical precision and ultimately patient outcomes, new techniques to replace the loss of haptic feedback are paramount. Integration of MRI tumor localization into operative planning has been a recent advancement, but real time MRI remains impractical due to the physical size of the scanner and the expense involved. Early reports showed that only 60% of prostate cancer lesions which are greater than 5 mm could be detected [5]. MRI is useful for predicting tumor size of cancer foci greater than 10 mm in diameter [6]. But several studies also indicated that the external coil was not reliable enough for the detection of tumor volume [7,8]. In recent years, endorectal MRI (erMRI) has obtained improved results, reportedly achieving an accuracy of up to 82% in the prospective evaluation of patients previously diagnosed of prostate cancers [9]. Despite these technological advances, the use of MRI for the localization of prostate cancer is still controversial. Furthermore, it is difficult to register pre-operative imaging to intraoperative tumor locations in real time, due to the deformability and movement of the prostate during surgery.

Transrectal ultrasound (TRUS) was the first imaging technique to be used for prostate tumor localization [10] in the planning stage of prostate cancer surgery, and in real-time during radical prostatectomy. Prostate cancers typically appear as hypoechoic lesions on TRUS, but unfortunately, 80% of hypoechoic lesions found on TRUS are not cancer [11]. Furthermore, 30% of prostate cancers are iso-echoic on TRUS and will not be detected [12]. Thus, the utility of TRUS in localization of prostate cancer is limited. A newer development in ultrasound technology is elastography. The principle of ultrasonic elastography is similar to RMI, in that soft tissues exhibit greater deformation than stiff tissue. In the case of ultrasound, this difference in deformation can be detected by a speckle map of backscatter, which is converted to an elastogram as a qualitative readout of tissue stiffness [13]. Although some efforts of adapting elastography into laparoscopic surgery has been reported [14], however, numerous limitations still remain for its adoption: the required ultrasound transducers are difficult to miniaturize, the readout requires a deformation force to be applied by the operator (which can be variable from clinician to clinician) and the more distant tissue from the probe is less reliably assessed [15]. Thus elastography for large prostates and the prostatic base can be difficult to interpret and unfortunately, when it comes the preservation of functional tissue, it is exactly these positions wherein knowledge of tumor location can be extremely important. Additionally, TRUS-elastography has not been applied in real time during surgery, and continues to be marketed only as a diagnostic adjunct.

Here we report a new modality in development: rolling mechanical imaging (RMI) using a passive robotic manipulator. RMI is a novel approach using a force sensitive wheeled probe [16,17], which overcomes some of the limitations of the competing elastography technology. In particular, RMI provides a uniform deforming force (not operator dependent) and a readout of tissue elasticity or stiffness that is objective, quantitative, and can be acquired in real-time. Moreover, instead of performing a series of discrete uniaxial measurements [18], the probe allows for the continuous measurement of the tool–tissue interaction dynamics as it rolls over the surface of the tissue. Rapid surface coverage and enhanced sensitivity to tissue irregularities can hence be achieved. By fusing the tissue reaction forces measured along trajectories, the variations in mechanical tissue properties can be mapped to demonstrate the geometrical stiffness distribution of the examined tissue. The goal of this study is to assess the accuracy of RMI on freshly excised and extracted prostates under ex vivo situation for localization of cancer and compare it with the accuracy of MRI, DRE and TRUS biopsy.

2. Materials and methods

2.1. Human specimen preparation

The study was given full ethical approval by NHS Research Ethics Committee to be conducted at the Departments of Urology, Radiology and Histopathology, Guy's and St. Thomas' Hospital and the patients provided written informed consent allowing the post-operative examination. All patients had undergone radical prostatectomy to treat prostate cancer. The mean age of patients was 64.2 ± 5.2 years. Patients with clinically insignificant small cancers (< 0.5 mL) were excluded in the sample. In total, 21 prostate specimens were tested for analysis. The mean PSA level was 8.5 ± 3.4 ng/mL. The prostate cancer specimens were classified according to final pathologic findings. The stage of the prostate cancer obtained with this system was T2b in 5 patients; T2c in 6 patients; T3a in 10 patients. The specimen obtained contains various sizes of cancer tumors ranging from 5 mm to 20 mm in diameter.

2.2. Rolling mechanical imaging device

A device for performing rolling mechanical imaging (RMI) was developed as shown in Fig. 1. This device contains a haptic console (Phantom OmniTM) which providing six degrees of freedom position sensing. The haptic console is attached to a specially designed wheeled probe head integrated with a 6-DOF ATI Nano17 Force/Torque sensor (calibration SI-25-0.25, resolution 0.003 N with 16-bit DAQ), which can roll over a soft tissue while measuring the tissue stiffness, Fig. 1. The Phantom Omni is a passive robotic device which is moved into different configurations (positions and orientations) by hand wrist movements, with a nominal positional resolution of 0.055 mm. Three potentiometers and three encoders were used to read the outputs of the device – six variable angles – three joint angles for translation and three gimbal angles for rotation. The necessary probe trajectories can be set by programming based on dynamic link libraries provided. The protocol for measuring stiffness of a prostate specimen is described as follows: firstly, the three-dimensional (3D) surface registration was carried out by scanning the prostate specimen using the proposed apparatus. The 3D surface model representing dimensions of the measured specimen was created using MATLAB software package. The scanning trajectories then were defined and programed with a scanning resolution of ± 0.5 mm, Fig. 2. Secondly, the probe rolled again over the specimen for the second scanning with an indentation depth of 3 mm following the programmed scanning trajectories. The average scanning speed is set to 10 mm/s. The mechanical properties were acquired from the

Please cite this article as: J. Li et al., Ex vivo study of prostate cancer localization using rolling mechanical imaging towards minimally invasive surgery, Medical Engineering and Physics (2017), http://dx.doi.org/10.1016/j.medengphy.2017.01.021