Design of an Image-Guided Robot System for Measurement, Biopsy and Injection in Rodents

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***Abstract*— We are developing an image-guided robot system to achieve highly accurate placement of thin needles to in-vivo rodent tumor tissue in a predefined pattern of about 1 mm granularity. The multiple uses of needles are (1) oxygen tension measurement, (2) biopsy, and (3) injection of adenoviral sequences in form of a liquid agent. This paper focuses on the design of the base robot system to achieve the initial objective of inserting pO_2 probes in a three-dimensional (3D) grid pattern defined with respect to a Positron Emission Tomography (PET) scan of the tumor. The design is also compatible with other imaging modalities, including Single Photon Emission Computed Tomography (SPECT), Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), which will be used for future applications.**

I. Introduction

Oxygen-deficient or hypoxic cells in tumors are resistant to radiation treatment. By measuring the tissue oxygen tension (pO_2) level of the cells (using an Oxylite probe) [1] and correlating the readings with the microPET scan [2], the physician can tailor the radiation dosage directed at the hypoxic cells. This customized radiation technique should be more effective in controlling tumor growth.

Currently, the researcher places the rodent inside the rodent bed and performs two PET scans – one scan with fiducials and a second scan without (the second scan is needed to see the tumor without imaging artifacts due to the fiducials). Following the scan, the entire rodent and bed assembly are placed beneath a passive fixture that holds the Oxylite probe. The researcher puts an insertion template on top of the tumor on the rat. After puncturing the skin and tumor with a cannula and a needle, the Oxylite probe is inserted into the tumor manually, according to the predefined pattern of guide holes on the template, to measure tissue oxygen tension. The measured data are recorded by hand. Because these measuring procedures are highly repetitive, labor intensive, and performed on a large number of rodents, an image-guided robot system was suggested to perform this task with high accuracy and automated data collection.

This development is part of a collaborative project between Johns Hopkins University (JHU) and Memorial Sloan-Kettering Cancer Center (MSKCC). JHU is developing a multi-purpose robot system that will subsequently be used as a research tool at MSKCC for pO_2 measurement, biopsy, and injection of adenoviral sequences for gene therapy. This paper focuses on the engineering design of the robot system for pO_2 measurement.

II. System Design

Our initial plan was to physically attach the robot system to the scanner platform and perform the procedure in the scanner. This would have provided simple and efficient solutions for registering the scanner coordinate system to the robot coordinate system (for example, the robot can hold a stereotactic fiducials in the scanner's field of view). We could not, however, pursue this strategy because the rodent micro-scanners [3, 4] are too small to accommodate both the rodent and the robot. Building a mini-robot with these specifications would result in an unreasonably expensive device. We therefore had to consider a design where the robot is physically detached from the scanner. The procedure will be performed as follows: a) place an anesthetized tumor-bearing rodent in a specially-constructed fixture (rodent bed) that contains multimodal fiducial markers; b) place rodent bed in scanner and obtain image data; c) move rodent bed to robot system; d) load image data into computer workstation and identify target regions; e) register image data to robot by locating fiducials in both the image and robot frame coordinate systems; f) command the robot to move to the target positions.

The robot system is composed of a 2 degree-of-freedom X-Y horizontal platform and a vertical (Z) slide for the cannula insertion motion (see Figure 1). It has an approximate working volume of 10"×10" horizontally and 5" vertically. The horizontal platform contains a mounting mechanism for the rodent bed. The rodent bed is filled with foam that hardens to fixate the animal positioned in the bed. Several fiducials are mounted on the top surface of the rodent bed. The bed with the rodent in it is placed inside the microPET scanner (and later, scanners of other modalities) for scanning the tumor location. The rodent bed fiducials are compatible with the scanner and thus appear in the scans. A sufficiently large volume is scanned to contain all fiducials.

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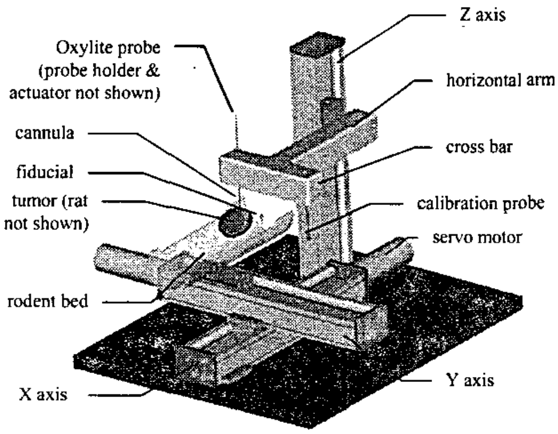

Figure 1: Conceptual Diagram of System

A horizontal aluminum arm is mounted on the vertical slide (Z-axis). This arm contains a cross bar that is oriented perpendicular to both the horizontal aluminum arm and the vertical slide. The probe holder system is at one end of the cross bar. It consists of a bevel-edged hollow cannula, an Oxylite pO_2 probe and a micro-linear actuator (20 mm range of motion) that moves the probe with respect to the cannula.

At the other end of the cross bar is a calibration probe mounted vertically at approximately 5 inches (fixed distance) from the cannula. The tip of the calibration probe is mounted on the same horizontal level as that of the cannula. The calibration probe is used for the registration procedure described below.

Inside the rodent bed, the rodent is placed in a prone position with a tumor on one of its hind legs facing upwards. The rodent bed fiducials are filled with a radioactive material that appears clearly in the PET image. With the rodent bed inside the scanner, two scans are performed (as before, one with the radioactive fiducials and one without). After the scans are completed, the rodent and bed are transported to the mounting bracket of the horizontal platform.

We are developing visualization software based on the 3D Slicer visualization software package [5] to provide a 3D model of the target volume with respect to the coordinate frame defined by the fiducials. The robot is registered to the image space by locating the fiducials in both (robot and image) coordinate systems and then using these positions to compute the required frame transformation. The fiducials are located in the image by a semi-automatic procedure in which the user clicks in the vicinity of each fiducial. The robot locates each fiducial using the calibration probe. The robot system will contain force sensors (not shown in Figure 1) to enable it to automatically move until the calibration probe is properly positioned with respect to each fiducial.

Once the frame transformation is computed, the software transforms the tumor position from image coordinates to robot coordinates. The software then drives the robot so that it positions the cannula at the initial entrance point on the top surface of the tumor.

The robot drives the cannula so that it punctures the tumor to a depth that is approximately 1 mm below the tumor surface. With the cannula inside the tumor, the computer drives the micro linear actuator, which in turn drives the Oxylite probe down, further penetrating the tumor. The Oxylite probe moves vertically inside the tumor in 1-mm increments. At each vertical stop, the Oxylite probe measures the tissue oxygen tension of the tumor and sends the result to the computer that stores all measurements in an array. When the Oxylite probe reaches the lower boundary of the tumor, the computer drives the micro linear actuator upward, retracting the probe back inside the cannula. Next the computer drives the cannula and Oxylite probe upward, pulling them out of the tumor. The computer then moves the cannula to the next entry point and repeats the cannula insertion and probe measurement sequence described above until the entire grid pattern has been traversed.

III. Conclusions

We presented a work in progress toward developing an image-guided robot system to assist with cancer research. The system is expected to improve the efficiency and accuracy of needle-based procedures for in-vivo measurement, biopsy, and injection in rodents. One notable feature is the support for a variety of imaging modalities, including CT, PET, SPECT, and MRI. A prototype system is currently being assembled. Preliminary experimental results will be presented at the conference.

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