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Yan Yu Thomas Jefferson University

Tarun Podder Thomas Jefferson University

Y D. Zhang University of Rochester

W S. Ng Nanyang Technological University

V Misic Thomas Jefferson University

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Authors

Yan Yu, Tarun Podder, Y D. Zhang, W S. Ng, V Misic, J Sherman, L Fu, D Fuller, D J. Rubens, J D. Strang, R A. Brasacchio, and E M. Messing

Robot-Assisted Prostate Brachytherapy

Y. Yu¹, T.K. Podder¹, Y.D. Zhang², W.S. Ng⁵, V. Misic¹, J. Sherman², L. Fu², D. Fuller², D.J. Rubens³, J.G. Strang³, R. A. Brasacchio², E.M. Messing⁴

¹Department of Radiation Oncology, Thomas Jefferson University, Philadelphia, PA 19107, USA. Departments of ²Radiation Oncology, ³Radiology and ⁴Urology, University of Rochester, Rochester, NY 14642, USA. ⁵Department of Mechanical and Aerospace Engineering, Nanyang Technological University, Singapore 639798.

Abstract: In contemporary brachytherapy procedures, needle placement at the desired target is challenging due to a variety of reasons. A robot-assisted brachytherapy system can potentially improve needle placement and seed delivery, resulting in enhanced therapeutic delivery. In this paper we present a 16 DOF (degrees-of-freedom) robotic system (9DOF positioning module and 7DOF surgery module) developed and fabricated for prostate brachytherapy. Strategies to reduce needle deflection and target movement were incorporated after extensive experimental validation. Provisions for needle motion and force feedback were included into the system for improving robot control and seed delivery. Preliminary experimental results reveal that the prototype system is sufficiently accurate in placing brachytherapy needles.

1 Introduction

In modern brachytherapy procedures, the needles are inserted transperineally under the guidance of transrectal ultrasound (TRUS) images (Figure 1). Both the needle and the TRUS are operated manually; the seeds are deposited using a manual applicator. The needles are inserted through fixed holes of a physical template. Therefore, flexibility and maneuverability of needle insertion is severely limited. Sometimes it is difficult to avoid pubic arch (especially for patients with large prostates) because the needles can only be inserted straight through the template's holes. The consistency and efficiency of the treatment procedure are highly dependent on the clinicians. In order to assist clinicians, it was proposed to develop a motorized semi-automated robotic system for prostate brachytherapy. Robotic system will not only place the needle and deliver seeds with accuracy, but also can assist less skilled or inexperienced surgeons to perform the procedures with higher consistency and efficiency.

Several researchers have been developing robotic systems for prostate brachytherapy procedures [1]-[8]. The needle placement robot system developed by Fichtinger et al. [1] and Stoianovici et al. [2] comprised a 3 degree-of-freedom (DOF) Cartesian bridge over the patient, a 2DOF remote center of motion (RCM), and a 1DOF needle insertion with a motorized driver using an axially loaded friction transmission. A 7DOF passive arm was employed between the Cartesian stage and the other two modules (RCM and needle inserter) to position and orient the needle in imaging instruments. Although the stages had sufficient encoders, the needle driver lacked precise encoding of the depth of needle insertion which was performed by a friction drive. In this system, seeds can only be deposited manually. Wei et al. [3],[4] and Wan [5] et al. developed a robotic system for prostate brachytherapy where they used an industrial robot to position and orient a single hole template through which a needle can be inserted manually. A separate motorized device was developed to rotate the needle and another module used for operating the US probe. The needle placement robot system designed by Kronreif et al. [6], [7] consisted of two offset x-y stages which allow positioning and orienting the needle over the perineum in 4DOF (two translational and two rotational). The needle can be inserted through the needle guide manually by the clinician. Needle insertion depth is monitored in US images.

The available workspace for the robot is quite limited while the patient is in the lithotomy position for transperineal prostate brachytherapy (Figure 2). Thus most of the industrial robots may lose dexterity (or lose DOF / encounter singularity) working in severely constrained workspace in the operating room (OR). Currently, hardly any robotic/mechanized system is available for the full functionalities that are required during actual brachytherapy in the OR. Recently, a group of researchers [8] reported a robotic system for brachytherapy that is more equipped to perform most of the required procedures automatically (or semi-automatically). This paper extends the research and development efforts that have been presented in [8]. In this paper, we present a detailed design and development of a prototype robotic system (called *Euclidean*), sequence of operations using Euclidean in clinical procedures, and experimental results to evaluate Euclidean's accuracy and repeatability. In this paper we focused mainly on engineering development of preliminary experimental results of a complex robotic system for surgical procedure required in prostate seed implant.

2 Materials and Methods

2.1 System Design and Development

At this time, there is no complete mechanized/motorized system available for performing prostate brachytherapy semi-automatically (motorized system working under the supervision of the surgeon). Euclidean was designed and fabricated as a more complete robotic system for assisting clinicians during prostate brachytherapy procedures. Measurements of the available workspace were made in the OR during actual brachytherapy procedures for a robot (Figure 2). The knowledge gleaned form these measurements was useful in designing a compact robotic system that would work efficiently in the severely constrained workspace in the OR.



Figure 1: Conventional brachytherapy procedure (Seattle method).



Figure 2: Workspace for robotic insertion of brachytherapy needle (i) front view, (ii) top view.

2.1.1 Objectives

The main objects of this robotic system are to

- improve accuracy of needle placement and seed delivery;
- improve avoidance of critical structures (urethra, pubic arch, bladder, etc.);
- update dosimetry after each needle is implanted (automatic seed localization);
- detect tissue heterogeneities and deformation via force sensing and imaging feedback;
- reduce trauma and edema;
- reduce radiation exposure;
- reduce learning curve;
- reduce OR time.

2.1.2 Functional Requirements

The functional requirements of the system are as follows:

- Quick and easy disengagement in case of emergency
- Provision for reverting to conventional manual brachytherapy method at any time
- Improvement of prostate immobilization techniques
- Provision for periodic quality assurance checking
- Updating implant plan after implanting the periphery of the prostate, or after most of the needles have been placed and seeds implanted, or at any time
- A method for the clinician to review and approve the motion plan before needle placement
- Ability to modulate velocity and needle rotation by automatic feedback control
- Visual confirmation by the chosen imaging technique of each seed deposition or the needle tip at the resting position
- Steering of the needle by automatic feedback control
- Visual/haptic force feedback during needle insertion
- A teach mode to simulate force/velocity patterns of expert practitioners

- Ease of operation and safety for the patient and OR environment
- Ease of cleaning and decontamination
- Compatible for sterilization

2.1.3 Prototype Robotic System

The prototype robotic system comprised of a 9DOF Positioning Module and a 7DOF Surgery Module.

Positioning Module

- (a) 3DOF Cart the cart can move in x-y horizontal plane and rotate about a vertical axis. It consists of a base having four wheels capable of rotating about two of its own axes (a horizontal axis and a vertical axis) and a floor locking mechanism; when being locked, four legs drop to the floor and lift the whole system off the wheels. This ensures rigid locking on any floor and provides greater rigidity to the system. Above the base, all the electronic and electrical components including an industrial computer are housed in an enclosure. The cart is brought near the patient's bed to a relatively close operating position and locked on the floor by pressing a lever, after which the positioning platform is suitably adjusted.
- (b) *6DOF Platform* it connects the surgery module to the cart. The platform has 3DOF translational motions and 3DOF rotational motions. Thus it can position and orient the surgery module at any location in the 3D space so that the ultrasound (US) probe can be positioned and oriented in the patient's rectum easily and comfortably, and at the same time the needling mechanism should be suitably aligned with the patient's perineum. The vertical lift (y-motion) of the platform is motorized for ease of operation and avoiding gravitational effects on the braking system. The translational motions in the horizontal plane (x- & z- motions) are manual, however these joints are unlocked using two solenoids; for safety and stability they are locked by default. The 3DOF rotational motions (roll-pitch-yaw) are achieved by using a spherical joint, which can be mechanically locked at a desired orientation.

Surgery Module

(a) 2DOF Ultrasound Probe Driver – the US probe (typically having two transducers for axial and longitudinal planes) can be translated and rotated separately by two DC servo motors fitted with encoders and gear boxes. This enables imaging in transverse as well as in fan-beam (sagittal) directions, providing the capability for improved 3D prostate modeling for dosimetric planning as well as for image-guide dose verification on the fly. Working ranges of motion for the US probe are 0-185mm and -91° to +91° in translation and rotation, respectively. The clinician can also drive the US probe manually using the knobs; during this mode the motors will be automatically disengaged by the electrical clutches (Figure 3). Provision for an optional template holder at the end of the US probe driver will permit manual takeover, if required. The prostate stabilization needle guide can orient the needle at any desired angle in both horizontal and vertical planes resulting in improved stabilization of the prostate and thereby enhanced accuracy of seed placement.



Figure 3: Ultrasound probe driver.

- (b) *3DOF Gantry* it connects the needle driving module to the positioning platform. The gantry has two translational motions (x- & y- direction) and one rotational motion (pitch). The motions are achieved by DC servo motors and optical encoders fitted with the motors (Figure 4). The working range of motion is 0-62mm in the x-direction and 0-67mm in y-direction, which are sufficient to cover the projected treatment area of a conventional template grid ($60\text{mm} \times 60\text{mm}$). The rotational range for angulating the needle to avoid pubic arch is -5° to +5°. The 3DOF motions of the gantry position can orient the needle at any desired location on the patient's perineum with greater freedom due to the absence of a physical template used in conventional brachytherapy. Once the needle is positioned at the desired location close to the perineum, the needle driver inserts the needle into the patient. The motions of the US probe driver and the rest of the surgery module (gantry and needle driver) are decoupled by making two separate open kinematic chains attached to the same positioning platform.
- (c) 2DOF Needle Driver the needle components consisting of a hollow cannula and a solid stylet are driven separately by two DC servo motors. Since the stylet and cannula motions are concentric, they essentially provide a single DOF. However, the cannula can be rotated continuously or partially using another tiny DC motor. Thus, with 3 motorized motions the needle driver actually has 2DOF. Both the stylet and the cannula are driven from the back (they are pushed); therefore there is no chance of slipping. During actual brachytherapy procedures, the needle traverses different types of tissues to reach the target point in the prostate, and these tissues have different types of boundary conditions that cannot be assessed from experimental data obtained from ex-vivo tissue/organ samples. Therefore, in-vivo measurement of needle insertion force (Figure 5) [9] is very useful in designing and controlling any robotic system that will work in such a constrained space. In our design process, collection and detailed analysis of this *in-vivo* information were found to be very useful. It was demonstrated that continuous rotation improved targeting accuracy and reduced insertion force [10], whereas partial rotation increased needle placement accuracy [5]. Therefore, we incorporated the provision for needle rotation in the Euclidean system for improving accuracy and seed delivery. To measure and monitor force profiles during the operational procedures, the design incorporated two single-axis force sensors (Model 13, Honeywell Sensotech, Columbus, OH) each at the proximal ends of the stylet and cannula, and one six-axis force-torque sensor (Nano17, ATI Industrial Automation, Apex, NC) at the distal end of the cannula (Figure 6). Monitoring of these forces is useful in detecting pubic arch interference (PAI) and will help in assessing needle bending. The travel range of both the cannula and the stylet is 0-312mm. The cannula does not need to move so far for normal operation except in initial installation; however, the stylet needs to move further than the cannula for removing seeds from the cartridge and depositing them. Unlike commercially available seed cartridges (hold 15 seeds), this cartridge can accommodate 35 seeds at a time, resulting in less frequent replacement of the cartridge, thereby reducing potential radiation exposure as well as reducing OR time.



(d) Seed Pusher – a flat ended stylet (for beveled-tip brachytherapy needle) is used to push the seed out of the cartridge and to deposit it at the planned locations in the prostate; the stylet's motor is deployed to push the stylet from the proximal end (Figure 6). All the sequence of motions during the seed delivery is fully automatic; however, at any time the clinician can interrupt the motion. The force sensor at the proximal end of

the stylet monitors the force profile on the stylet and thereby confirms seed removal from the cartridge to the cannula. Experiments showed that on average about 2.5N force is required to push the seed out of the cartridge. This is also checked by monitoring the stylet's motor current.

(e) *Teach-Pendant* – the teach-pendant with 10 buttons provides the surgeon the freedom to take over the control of the surgery module at any desired time. From the teach-pendant the surgeon can control the needle insertion, needle rotation, seed deposition, x-y movement of the gantry and system abort.

At the distal end of the US probe driver there is a provision for holding a conventional template, which will be useful for manual takeover (if requested by the clinician). Thus the patient treatment will not be affected if the clinicians wish to switch to manual/conventional mode. In manual mode the needle driving mechanism will be taken off the gantry to make room for the clinician, the US probe will be operated by handwheels (knob 1 and 2, see Figures 5 & 7). An emergency button on the top of the cart can be used to stop the whole system in case of emergency (Figure 8).

The surgery module is quite compact to work in the constrained workspace available during prostate brachytherapy procedures (Figures 7 & 8). The system's rigidity (stress-strain), deformation and factor safety characteristics have been analyzed using COSMOS, a commercial finite element analysis software. The maximum dimensions (length × width × height) of the surgery module are: $510\text{mm} \times 290\text{mm} \times 185\text{mm}$ for US Probe Driver, $500\text{mm} \times 140\text{mm} \times 70\text{mm}$ for Needle Driver and overall $510\text{mm} \times 290\text{mm} \times 235\text{mm}$; width at patient's end (distal end) of US Probe Diver is 100mm, and that of Needle driver is 60mm. The gross weight of the surgery module is about 9kg, which can be reduced significantly by using plastic/nylon instead of presently used surgical grade stainless steel and aluminum.



Figure 7: Assembled surgery module: (a) drawing, and (b)fabricated prototype.

Figure 8: Prototype robotic system.

2.2 System Software and Control

System architecture is shown in Figure 9. The surgery module is fully motorized. An industrial computer having Pentium4 processor, 2.8GHz, 1GB RAM, and 8 PCI slots (Chassis Plans, San Diego, CA) is used for controlling the system. We used two Galil control cards (Model DMC-1842; Galil Motion Control, Inc., Rocklin, CA): one card to control the US probe driver and gantry motions and the other card to control needle driver and seed pusher. A robust PID (proportional, integral and derivative) controller has been developed for the system control. We have tuned the PID gains in such a manner so that the system's stability is maintained when the needle changes its states from mere position control in air to both position and force control mode in the patient's body. The needle can achieve up to about 100mm/s velocity which is sufficient for brachytherapy procedure.



Figure 9: Schematic diagram of the system architecture.

We used one frame grabber (FlashBus, Integrated Technologies, Indianapolis, IN) for US image capture, three force-torque sensors (ATI's Nano17, Honeywell's M13) for needle insertion force monitoring and robot control feedback. All the motors are fitted with optical encoders (MicroMo Electronics, Inc., Faulhaber Group, Clearwater, FL) which provide final motion resolutions (considering gear ratios and screw leads) of 0.0007mm for gantry x-y translations, 0.004mm for stylet and cannula motions; 0.005mm and 0.06⁰ for US probe translation and rotation, respectively.

We have developed software in C++ that is capable of dosimetric planning, 3D visualization, needle tracking and seed detection for dynamic planning. The optimized dosimetric plan is achieved using a genetic algorithm modified to permit both non-parallel and conical needle coverage of the target volume [11]-[12]. Intraoperative isodose delineations are displayed on transverse, sagittal and coronal views of the prostate model built from US images.

2.3 Clinical Procedures

In setup state, the EUCLIDIAN is initialized and patient information is entered into the computer by the user. Then the TRUS is moved to scan the prostate in transversal plane and the images at a desired interval are saved. In the next step, modeling state, the TRUS images are used in delineating the prostate boundary, urethra, pubic bone, rectum, and seminal vesicle. Then a 3D model of the prostate is generated automatically. This 3D model of the prostate is used for dosimetric planning to obtain the desired coordinates of the radioactive seed distribution. The software can display the planned isodose contours, needle position and seed locations in 3D. This provides the clinicians useful visualization of the whole treatment plan, and if required, the clinicians can edit the plan.

Once the plan is approved by the clinician, a single needle is inserted into the patient according to the plan. At this stage the TRUS is employed in sagittal plane to track the needle location. To ensure patient's safety, this needle insertion is performed in a sequential order, i.e. first, the gantry moves in the x-y direction to bring the tip of the needle close to the perineum of the patient; second, the gantry is stopped and then the needling mechanism pushes the needle (stylet & cannula together) into the patient to a predefined depth; third, the clinician uses the user's pendant to insert the needle to the final depth. The last stage of user's takeover is to ensure patient's safety as well as to accommodate any change in planned depth that may be required due to tissue/organ deformation or needle deflection. After the needle insertion, the system is in the implanting state. Seeds are loaded from the cartridge and implanted according to the plan, and then the needle is withdrawn automatically.

As seeds are being delivered, the user may request the system to go to validation state to determine the latest dose delivery, or to skip the validation and return to the needling state. In the validation state, the prostate is scanned and seeds are located by image processing in order to update the dosimetry based on where the seeds are actually deposited. If the clinician finds that the dosimetry is not satisfactory, the system can return to the planning state to make adjustment for the remaining seeds to be inserted.

3 Results and Discussions

Experiments were performed to evaluate the system's accuracy and repeatability. The system was run in a pattern (as shown in Figure 12) for 2 hours at a time. An 18 gauge beveled-tip brachytherapy needle was inserted into a graph paper pasted in front of foam block, which provided adequate and uniform support to the graph paper. There were 16 total penetration locations in a $60\text{mm} \times 60\text{mm}$ area. The gantry moved the needle driver in a sequence (1-2-3-...-16), as shown in Figure 12 (a), so that the mechanical systems go through back and forth motion to experience backlash/slack errors in the motion transfer trains/linkages. After a single penetration at each location the needle was moved to the next location, and this was repeated for 100 times. The x and y speed of the gantry was 10mm/s, and the needle speed was 50mm/s. To assess the error and deviation, we also performed the same for a single insertion at each location (Figure 12(b)). It was very difficult to distinguish the deviation of the penetration holes after 100 runs. Optical image of the holes were magnified by 5 times to measure the errors. The average errors in x and y motions that the system (needle tip) encountered after 100 insertions was $\pm 0.2\text{mm}$ with a standard deviation of 0.045mm.





Figure 12: Position and size of holes (a) after one hundred penetrations at each location by moving the needle from one location to the next location after each penetration, and (b) after single penetration at each location.

Preliminary seed implant experiments were carried out to assess the performance characteristics of the system in realistic conditions. We used tissue equivalent soft material phantom prepared from polyvinylchloride (PVC) by mixing supersoft plastic and softener in the ratio of 70% and 30%, respectively (MF Manufacturing, TX). As seen in Figure 13, the brachytherapy seeds are deposited in the PVC phantom at 1cm distance (in x, y and z directions). Assessment of the deposited seeds revealed that the accuracy (rms error) of seed placement is 0.67mm in x direction (SD=0.58mm), 0.13mm (SD=0.12mm) in y direction, and 0.11mm (SD=0.11mm) in z direction. The 3D (Euclidean) rms error is 0.69mm, which is quite small as compared to the typical 2.0mm that is generally considered acceptable (or desirable) clinically. It has been observed that the seed placement inaccuracy in x direction is much greater than in y or z direction; we are investigating this issue and performing rigorous experimentations.



Figure 13: seed delivery in soft material (polyvinylchloride) phantom.

4 Conclusions

This paper presents the design and development of a compact robotic system for prostate brachytherapy treatment with radioactive permanent seed deposition. Numerous techniques and sensors were incorporated into the prototype to improve the needle insertion accuracy, and thereby reduce the seed delivery errors. The system can be operated in both automated and semi-automated modes. In case of any emergency, the system can be stopped immediately and the clinicians can switch to conventional manual mode. To achieve patient's safety, a variety of hardware (sensors and stops) and software checks are incorporated into the system design and development. Needle and seed placement accuracy and repeatability of the prototype system were tested and found sufficient for clinical needs. Additional more rigorous experiments are being conducted in phantoms to evaluate the overall performance of the system. A clinical study will be carried out after full characterization of this prototype robotic system in phantoms. The clinical protocol is under IRB review. In addition to US guidance, we are considering the use of CT (computed tomography) as an alternative imaging modality.

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References

- [1] Fichtinger, G., DeWeese, T. L., Patriciu, A., et al. System for robotically assisted prostate biopsy and therapy with intraoperative ct guidance. Academic Radiology, Vol. 9, (2002) 60–74.
- [2] Stoianovici, D., Cleary, K., Patriciu, A., et al. AcuBot: A Robot for Radiological Percutaneous Interventions. IEEE Transactions on Robotics and Automation, Vol. 19(5), (2003) 927-930.

- [3] Wei, Z., Wan, G., Gardi, L., et al. Robot-assisted 3D-TRUS guided prostate brachytherapy: System integration and validation. Medical Physics, Vol. 31(3), (2004) 539–548.
- [4] Wei, Z., Wan, G., Gardi, L., Downey, D.B., and Fenster, A.: Robotic Aided 3D TRUS Guided Intraoperative Prostate Brachytherapy. SPIE, Vol. 5367, (2004) 361-370.
- [5] Wan, G., Wei, Z., Wan, G., Gardi, L., Downey, D.B., and Fenster, A.: Brachytherapy Needle Deflection Evaluation and Correction. American Association of Medical Physics, Vol. 32(4), (2005) 902-909.
- [6] Kettenbach, J., Kronreif, G., Figl, M., et al. Robot-assisted biopsy using computed tomography-guidance: initial results from in vitro tests. Investigative Radiology, Vol. 40, (2005) 219-228.
- [7] Kettenbach, J., Kronreif, G., Figl, M., et al. Robot-assisted biopsy using ultrasound guidance: initial results from in vitro tests. European Radiology, Vol. 15, (2005) 765-71.
- [8] Yu, Y., Podder, T.K., Zhang, Y., Ng, W.S., Misic, V., Messing, E.M., Rubens, D.J. Strang, J.G., and Brasacchio, R.A. "Robot-Assisted Platform for Intratumoral Delivery (Euclidean)," in the World Congress on Medical Physics and Biomedical Engineering (WC-BME), Seoul, Korea, (submitted) Aug. 27 – Sept.1, 2006.
- [9] Podder, T.K., Messing, E.M., Rubens, D.J., Strang J.G., Brasacchio, R.A., Clark, D.P., Fuller, D., Liao, L., Ng, W.S., and Yu, Y.: Evaluation of Robotic Needle Insertion in Conjunction with in Vivo Manual Insertion in the Operating Room. Proceedings of the 14th IEEE International Workshop on Robot and Human Interactive Communication (RO-MAN). Nashville, TN, (2005) 356-362.
- [10] Podder, T.K., Liao, L., Sherman, J., Misic, V., Zhang, Y.D., Fuller, D., Rubens, D.J., Messing, E.M., Strang, J.G., Ng, W.S., and Yu, Y.: Assessment of Prostate Brachytherapy and Breast Biopsy Needle Insertions and Methods to Improve Targeting Accuracy. In: The IFMBE Proceedings of the 12th International Conference on Biomedical Engineering (ICBME), Vol. 12, Singapore (2005).
- [11] Fu, L., Liu, H., Ng, W.S., Rubens, D., Strang, J., Messing, E., Yu, Y., Hybrid dosimetry: Feasibility of mixing angulated and parallel needles in planning prostate brachytherapy. *Med. Phys.* 33 1192-1198, 2006.
- [12] Fu, L., Ng, W.S., Liu, H., O'Dell, W., Rubens, D., Strang, J., Schell, M.C., Brasacchio, R., Liao, L., Messing, E., Yu, Y., Bouquet brachytherapy: Feasibility and optimization of conically spaced implants. *Brachytherapy* 4 59-63, 2004.