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MIRA V: An Integrated System for Minimally Invasive Robot-Assisted Lung Brachytherapy

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***Abstract*—An integrated system for minimally invasive robot-assisted image-guided lung brachytherapy has been developed. The system incorporates an experimental setup for accurate radioactive seed placement with commercially available dosimetry planning software. The end result is a complete system that allows planning and executing a brachytherapy procedure with increased accuracy. The results of the *in vitro* seed placement evaluation show that seed misplacement has a significant effect on the volume receiving more than 200% of the dose (V200), and the minimum dosage received by 90% of the volume (D90).**

I. Introduction

THIS paper describes the development and initial testing of an integrated system for minimally invasive robot-assisted (MIRA) lung brachytherapy.

A. Lung Cancer and Brachytherapy

Although great efforts are being made to reduce the incidence of lung cancer, it remains the most common cause of death from cancer [1]. Surgical removal of the tumour is the treatment of choice. However, patients who are weak or have poor pulmonary function are not eligible for this procedure. It has also been found that morbidity rates following resection range between 20% and 44% [2]. Brachytherapy is an alternative treatment to surgery that has minimal side effects to the patient. This procedure provides high doses of radiation localized within the diseased tissue.

Brachytherapy can be classified into different types depending on the dosage, the method of delivery and the amount of time the patient is exposed to the radiation source. This paper focuses on the application of interstitial low dose rate (LDR) brachytherapy, in which radioactive seeds are permanently implanted into a tumour using long needles. These seeds contain a radioactive isotope inside a titanium shell. To achieve adequate dose distribution, the seeds are separated inside the needle using inert spacers. Each needle must then be inserted into the tissue in a particular orientation and to a specified depth. Once the needle is accurately placed, a stylet inserted inside the needle is used to drop the seeds and spacers.

There is limited experience in the application of interstitial brachytherapy in the lung: via an open thoracotomy [3], through the bronchi [4] or percutaneously with CT guidance [5]. Results showed that the symptoms were controlled, but there were technical complications related to the inability to penetrate certain tumours and mediocre dose distributions. Careful planning and delivery is required to optimize the clinical outcome and minimize side effects [6]. Adequate dosage can only be achieved through an accurate seed placement, since small deviations in seed alignment can create significant areas of over and under dosage.

To address these issues, an experimental setup has been designed and tested by the authors that incorporates technological developments in image guidance, electromagnetic navigation and robotic assistance for surgical procedures.

B. State of the Art

Some surgical robots have been designed for minimally invasive surgery (MIS). In this type of procedure, the instruments and a camera (endoscope) are inserted into the patient's body cavity through small incisions. The AESOP® (Computer Motion Inc.) was the first surgical robotic arm approved for clinical use to hold and move a camera during MIS. Other systems were then developed for MIS, consisting of three or four remotely-controlled robotic arms. The ZEUS® (Computer Motion Inc.) was the first of these systems to be approved for MIS in North America, and has now been replaced by the da Vinci® (Intuitive Surgical, Inc.). A recent study evaluated the use of the da Vinci to suture seeds on the lung surface after surgically removing the tumour using sublobar resection [7]. This method may provide an alternative for some patients who are eligible for standard surgical resection by lobectomy.

Many researchers have developed robotic systems and software for accurate needle placement in prostate

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brachytherapy. However, these systems cannot be used in a lung brachytherapy procedure for two main reasons: i) the presence of the ribs makes accessing the lung considerably more difficult, and ii) accuracy requirements are more critical in the lung due to the proximity to vital structures.

A critical aspect in accurate needle placement is the ability to guide the needle inside the tissue. In general, real-time patient imaging (e.g., magnetic resonance, computed tomography or ultrasound imaging) provides better targeting of anatomical sites during surgical procedures. In particular, ultrasound (US) imaging is a well established, versatile, and widely used diagnostic tool in medicine and is the second most common imaging modality (after radiographs) [8]. It provides safe (non-ionizing) real-time images, and is affordable, portable and readily available.

Image guidance integrated with a tracking system provides the ideal combination for surgical navigation. The objective of tracking systems is to provide the position and orientation (pose) of an object. This usually involves attaching a sensor to the object of interest and using specialized hardware and software algorithms to determine the pose. Electromagnetic (EM) tracking systems are ideal for medical applications in which an unobstructed line-of-sight is not possible. The sensors can be easily attached to various instruments and their poses tracked inside and outside of the patient.

C. Previous Work

The proposed alternative to existing brachytherapy systems involves the use of MIS robotic systems to access the lung, allowing the position and orientation of the needle to be adjusted inside the patient's thorax prior to penetrating the target tissue. The main characteristics of the method are: (1) the procedure is performed through small openings in between the ribs on the patient's chest (2) commercially available robotic systems are used to hold and control the motion of a needle and deploy radioactive seeds; (3) visualization of vital structures on a video monitor provides a view of the lung surface to aid in needle guidance; and (4) navigational software provides three-dimensional (3D) guidance of the needle tip by incorporating real-time US images and EM tracking.

Table I shows a summary of the developmental stages of the project. The main limitations with the previous version were that the EM sensor used to track the needle tip position was mounted on the outside of the needle barrel, since it was too large to fit within the needle itself, and that the US transducer used was not an MIS transducer. This presented a significant limitation for clinical applications. Furthermore, the software did not allow a dosimetry plan to be transferred to the navigational software.

D. Surgical Planning of Radiation Therapy

For LDR brachytherapy there are many different guidelines on how to properly plan the procedure and calculate seed placement. Most interstitial brachytherapy procedures use ^{192}Ir, ^{125}I, or ^{103}Pd as the radiation source. Dosimetry planning involves determining the type of isotope to be used, the strength, number and location of the seeds that will ensure that the amount of radiation absorbed by the tissue is sufficient to kill the cancerous cells. To do this, the gross tumour volume (GTV) is defined as the volume that can be clinically identified as the location and extent of the malignant tumour [9], i.e., the extent of the tumour that can be identified in the US images. Based on this, the planning tumour volume (PTV) is defined by adding a margin around the GTV to compensate for identification uncertainties. The amount of this margin depends on the accuracy of the tumour localization procedure. A typical value of 3 mm for the margin has been selected for these experiments. There is also a wealth of information on how to determine the prescription doses depending on the tissue being treated, the type of isotope being used and the delivery method, e.g., [10].

TABLE I
PREVIOUS ITERATIONS OF THE MIRA SYSTEM.

Stage	Technology	Results
MIRA I	ZEUS system, ATL HDI 5000 US system with the ATL Lap L9-5 transducer, and a hydraulic seed injection system.	Initial feasibility of the approach was shown [11]. Zeus system performed well in *in vivo* animal testing and was able to remotely manipulate the US transducer and the needle to allow deployment of the seeds. US images of the lung were of good quality.
MIRA II	MIRA I with the addition of a customized seed injection instrument that holds the needle and deploys the seeds (the seed injector) [12].	*In vitro* evaluation using transparent agar cubes with visible steel spheres as targets [13]. Compared the manual technique, VATS*, and MIRA II. Accuracy: 0.6, 1.2 and 2.4 mm. Average number of attempts: 1, 4 and 3. Average task completion time: 3.0, 86.5, and 64.5 s. These experiments suffered from a complete lack of depth perception caused by the two-dimensional endoscopic image.
MIRA III	ZEUS system, the seed injector, the Phillips IU-22 US System with the C-9 transducer, and the MicroBIRD™ EM tracking system. Image guidance achieved via InterNAV™ [14] for "hidden" targets.	Same *in vitro* evaluation using opaque agar cubes. Manual, VATS*, and MIRA III were compared. Accuracy: 2.7, 2.5 and 2.8 mm. Average number of attempts: 2.3, 5.2 and 1.8. Average task completion time: 41, 163, and 98 s. Although significant improvements were possible, the system lacked intuitiveness and the accuracy with the robotic system was limited by the robot controls used [15].
MIRA IV	MIRA III with the redesigned InterNAV2.0™. AESOP arm was used for instrument manipulation so that the new software could better control robot motion and seed deployment. The user interface was made more intuitive and user-friendly.	Same *in vitro* evaluation as above. New system performance showed an accuracy of 0.9 mm, average number of attempts of 1, and average task completion time of 40.5 s. Excellent performance results [16], but the system still lacks the ability to be used in a clinical setting.

* Video Assisted Thoracoscopic Surgery is a minimally invasive approach in which handling of the thoracoscopic instruments is done manually through small incisions.

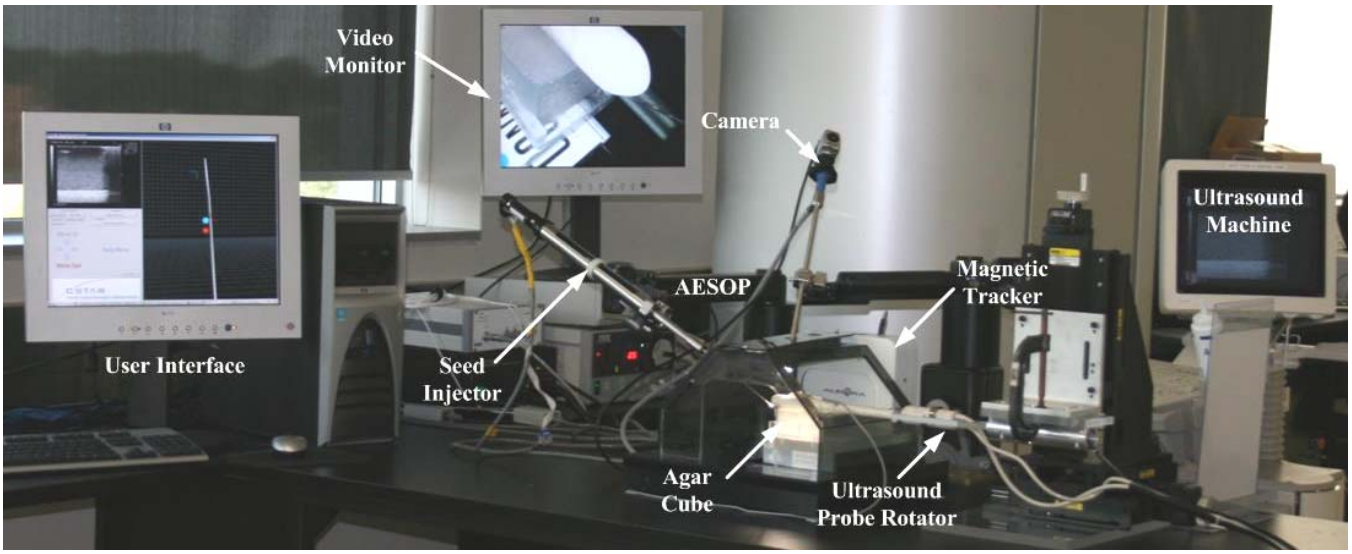

Figure 1. The MIRA V integrated system for lung brachytherapy.

II. Integrated System

Based on the limitations encountered with MIRA IV, a new system has been developed and shown in Fig. 1. MIRA V has incorporated significant hardware and software modifications to create a clinically feasible system for accurate dosimetry planning and seed implantation.

A. Hardware

Two major modifications were done to the hardware to address clinical applicability. First, the US system was replaced by the ALOKA SSD-1000 US Machine with the UST-672-5/7.5 bi-plane transrectal transducer. This new probe is small enough to enter a patient's body through 2 cm incisions. In order to reconstruct a 3D tumour volume from the 2D US images, the US probe was mounted on a custom designed rotator assembly that includes a zero backlash Faulhaber 2232U024 motor with an 879:1 gearhead and a 512 CPR encoder. Fig. 2 shows the CAD model of the rotator assembly. This assembly rotates the transducer about its longitudinal axis as a set of 100 2D B-mode US images of the target are acquired. The reconstructed 3D model is used pre-operatively for target selection and dose planning, intra-operatively for needle guidance and post-operatively for seed placement evaluation. The rotator is manually positioned using a precise 3D linear stage.

The second modification addressed the issue of the sensor being attached to the outside of the needle. Since the needle must accommodate the seeds and the spacers, the sensor could not be attached to the inside of the needle barrel. Instead, it was decided to attach the sensor to the stylet itself. The main difficulty in accomplishing this task was to find an EM sensor small enough to be encased within the stylet body, since the shaft of the stylet for an 18 gauge needle is less than 1 mm in diameter. Furthermore, it was found during previous experiments that if the tip of the stylet was close to the sensor (within 5 cm), it created enough magnetic distortion to significantly affect the position tracking signal.

A new 5 degree-of-freedom (DOF) "thin" sensor has been released by NDI, Inc. for the Aurora EM tracking system [17]. This sensor is only 0.55 mm in diameter and 8 mm long, making it an ideal candidate for this application. To minimize the effect of magnetic distortion, a custom stylet was designed with a plastic tip that completely encloses the sensor. A picture of the stylet and a close up of the EM sensor are shown in Fig. 3. The seed injector was modified to accommodate the new stylet.

In the configuration shown in Fig. 4, the Aurora system has a manufacturer supplied static root-mean-square error of 0.7 mm in position and 0.3° in orientation. A 6 DOF EM sensor was also attached to the US probe to track the position and orientation of the US plane. As the probe rotates, the 3D pose of each scan is recorded for accurate model reconstruction.

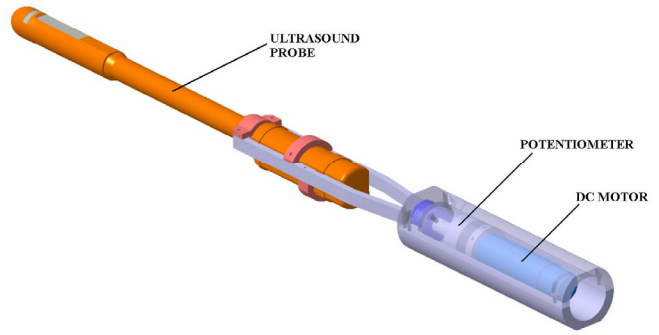

Figure 2. CAD model of rotator assembly for US probe.

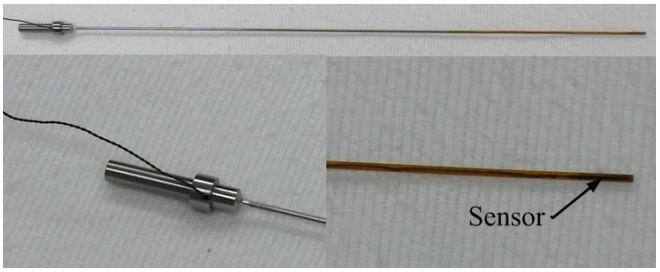

Figure 3. Sensorized stylet (*top*), close-up of the stylet head (*bottom left*) and close-up of the stylet tip (*bottom right*).

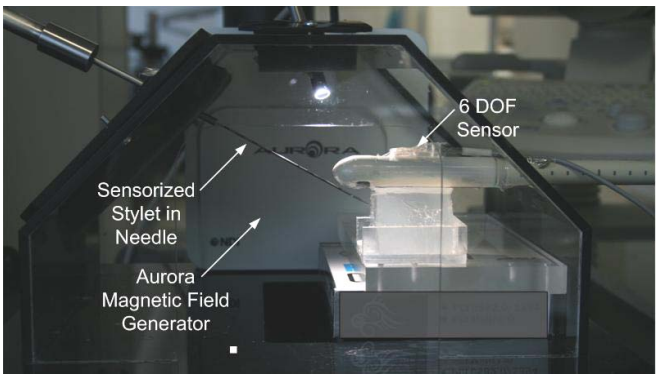

Figure 4. Magnetic tracker configuration.

Since the US probe is now mounted on the 3D stage, the ZEUS system is no longer needed. Two AESOP arms are used to control the video camera and the instrument via voice control and the InterNAV3.0^{TM} interface, respectively. These robotic arms are no longer commercially available. However, they have been chosen for the prototype evaluation and proof of concept as they are available for research purposes at CSTAR.

B. Software

The software used in the previous MIRA version, InterNAV2.0^{TM}, was limited in the sense that it only allowed the user to pick one target at a time and deposit seeds at that location. The MIRA V software allows the user to identify the margins of the tumour, select the proper radiation dosage, and implant as many seeds as needed in order to meet this plan. This has been accomplished by combining two well developed software packages: a dosimetry planning software and InterNAV3.0^{TM}.

1) Dosimetry Planning Software

The dosimetry planning software incorporated into MIRA V is a modified version of a previously developed software for needle guidance in prostate brachytherapy. The details of this software, developed at the Robarts Imaging Laboratories, can be found in [18,19]. The input to this system is the set of US images that are obtained by scanning the anatomical area of interest (i.e., rotating the US probe in 1º increments). The software creates a 3D reconstruction of the scans, which can then be used to manually identify the margins of the tumour. The medical physicist uses these margins to decide on the number, strength and location of the seeds. Prior to needle insertion, the pre-plan can be evaluated to ensure that the distribution of the seeds adequately radiates the tumour.

A critical difference between the dosimetry software for prostate brachytherapy, and the minimally invasive lung brachytherapy procedure, is with respect to the allowable needle paths. In a prostate brachytherapy procedure the needles enter the body percutaneously through parallel paths, while in MIS all the needle paths must intersect at the entry port location through which the instruments enter the body. The dosimetry planning software was modified to restrict the needle paths to intersect at the port location.

2) Navigation Software

InterNAV3.0^{TM} is the new version of the software used for navigation and seed deployment. This interface addresses the difficulty of guiding the user to deposit radioactive seeds inside a tumour by providing accurate information on the location of the needle tip with respect to the target. It incorporates the US image, information from the EM sensors, and calibration data. The Graphical User Interface (GUI), shown in Fig 5, consists of three views as well as the Systems Control dialog. Collectively these components allow the user to perform scans of the anatomical areas of interest, export the scans to the dosimetry software, import target information and provide all of the information required to guide the needle towards the target quickly and intuitively.

When targets are imported from the dosimetry planning software, their physical positions are shown in the World View as blue spheres. The view point in the image is in line with the axis of the needle, so that it becomes intuitive for the user to know in which direction to move its tip to properly orient it. This is accomplished by clicking on the arrows displayed on the GUI. The needle can then be moved along this trajectory (using the GUI) until the depth view indicates that the target has been reached. For details of the original InterNAV^{TM} and the calibration process, see [14].

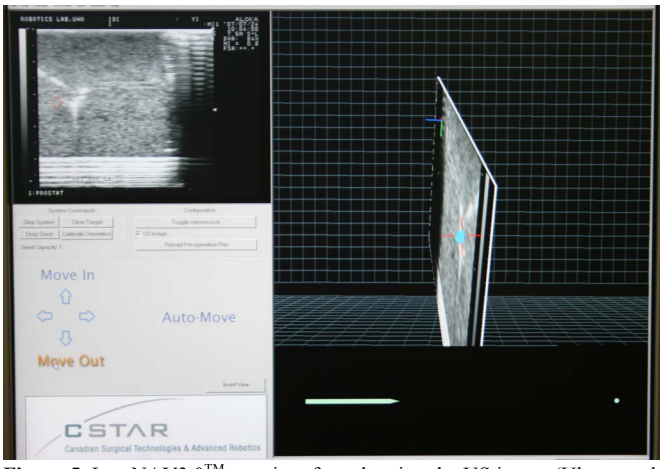

Figure 5. InterNAV3.0^{TM} user interface showing the US image (Ultrasound View — top left corner), the position of the target (blue sphere) with respect to the needle tip (World View — top right), and the depth of the needle tip with respect to the target (Depth View — bottom right).

III. Experimental Evaluation

To simulate lung tumours, spherical agar phantoms of different sizes were constructed and embedded in opaque agar cubes of a slightly different consistency. Moulds of three different diameters (1.59 cm, 2.22 cm, and 2.54 cm) were filled with a warm mixture of 2.5% gellan gum (Sigma-Aldrich), and then cooled. After they were formed, the phantom tumours were embedded into a mixture of 0.2% cellulose particles (Sigma-Aldrich) added to the agar slurry as scattering agent. This created different acoustic properties in the materials, which allowed the spheres to be observed in the US image [20]. The tumour phantoms that resulted had surface irregularities but remained roughly spherical.

In each test, after performing a scan of the agar using InterNAV3.0^{TM}, the dosimetry planning software was used

to determine appropriate brachytherapy seed placement. The gross tumour volume (GTV) was defined by manually tracing out the border of the tumour in 2D planes that were 1 mm apart. A 3 mm margin was added to mark the border of the planning target volume (PTV). A prescription dose of 144 Gy to the PTV was used [10] for an ^{125}I isotope.

The dosimetry software was used to develop a pre-plan for which ^{125}I seeds were placed approximately 1 cm apart from each other, on the periphery of the GTV. This kind of distribution was chosen by the medical physicist because it concentrates the majority of the energy within the volume of the tumour while ensuring adequate dosage to the margin. The radioactive levels of the seeds are chosen for each of the different sized tumours, such that the minimum level of radiation covers 99.9% of the PTV with the prescribed dose.

For this set of experiments, a total of 18 samples were performed. In each case, 2 seeds were deposited with each needle insertion using the seed injector. A single subject performed the entire planning and insertion process in all 18 cubes (7 with small 1.59 cm tumours, 6 with medium 2.2 cm tumours and 5 with large 2.54 cm tumours), and performed a total of 129 needle insertions. For plan verification, a post-implant US scan was taken. Two independent subjects repeated tumour segmentation and identified actual seed location. The dose distribution was calculated automatically by the software based on the actual seed locations. Dose volume histograms (DVHs) were then used to measure the radiation coverage.

IV. Results

The accuracy achieved by MIRA V was evaluated by comparing the dose coverage of the GTV and the PTV in the pre-plan versus that of the achieved seed placement. Four parameters were used to assess implantation accuracy: V100 (volume receiving at least 100% of the prescribed dose), V90 (volume receiving at least 90% of the prescribed dose), V200 (volume receiving more than 200% of the prescribed dose), and D90 (minimum dosage received by 90% of the volume). The results are summarized in Table II and Fig. 6.

In two cases (1.56%), when the needle was inserted, the user felt that the target had not been properly reached due to bending of the needle, and so decided to pull the needle out and try again. Furthermore, three seeds were undetectable in the post-implantation 3D US scan. As a result, slightly diminished radiation coverage was seen in those cases.

Fig. 7 shows a sample radiograph of one of the cubes with the seeds in place. Fig. 8 shows a representative post-implantation seed distribution map with isodose curves.

V. Discussion

Current practice in dose planning aims to ensure proper radiation coverage of the tumour. In order to compensate for inaccuracies in seed placement, the tendency is to select an overpowered plan that is less sensitive to deviations in seed placement. This is reflected in Fig. 6 by the planned V200 and D90 values, and effectively shows that the V100 and V90 measures remain at 100% despite seed misplacement.

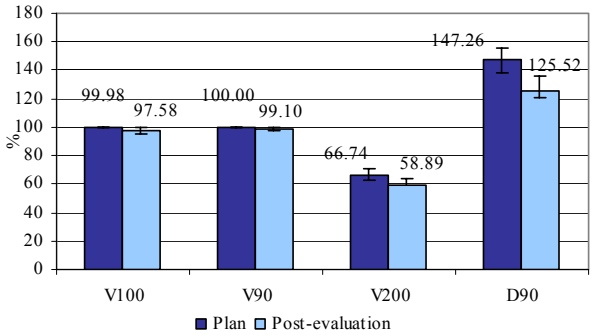

Figure 6. Dosimetry evaluation results: volume receiving at least 100% of the prescribed dose (V100), volume receiving at least 90% of the dose (V90), volume receiving more than 200% of the dose (V200), and minimum dosage received by 90% of the volume (D90). The error bars indicate ± one standard deviation.

TABLE II
Accuracy of the Dosimetry Evaluation

		Accuracy in the GTV	Accuracy in the PTV
V100	Average	98%	100%
	Range	94 – 100	100 – 100
V90	Average	99%	100%
	Range	97 – 100	100 – 100
V200	Average	88%	88%
	Range	75 – 98	77 – 94
D90	Average	85%	79%
	Range	76 – 91	65 – 91

Averages were calculated by comparing the dose coverage of the pre-plan versus that of the achieved seed placement.

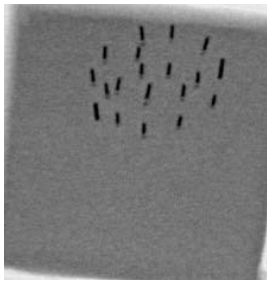

Figure 7. Radiograph of an agar cube after seed implantation.

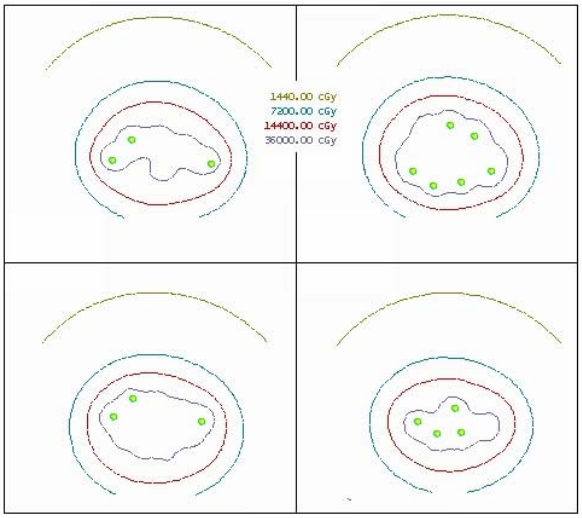

Figure 8. Representative post-implantation isodose curves on 4 transverse planes 5 mm apart, for a large tumour phantom.

Results show that the accuracy in the V200 and D90 parameters compared to the planned values was as low as 65%. These parameters show to be the most sensitive measures of the effect that seed misplacement has on dose distribution. Improving seed placement accuracy could allow the medical physicist and the radiation oncologist to select more adequate dose plans that are not trying to compensate for seed misplacement.

Seed placement accuracy was affected by several different sources of error including: artifacts and inaccuracies generated in the US image and the reconstruction of the 3D model, errors from the EM sensors, calibration errors between the needle sensor and its tip, calibration errors between the objects on the US image and their tracked positions, error in needle placement caused by the inability to properly compensate for its bending, errors when dropping the seeds, and errors when manually selecting tumour margins and final seed location. Since some of these errors cannot be measured independently, the accuracy measures used in these experiments provide an evaluation of the overall effect of seed misplacement in the achieved radiation dosage, which is the ultimate goal of the system.

It was noted that precise seed segmentation in the post-implantation 3D US scan was sometimes difficult, especially when a large number of seeds were deposited in a small volume. Acoustic shadows cast by the more proximal seeds occasionally lowered the image contrast for the more distal seeds. In the future, CT scans will be used for post-implantation assessment.

Although this integrated system has been successfully evaluated, there are still some limitations that remain to be addressed in the near future. First a smaller laparoscopic US probe should be employed instead of the current transrectal probe. Second, the problem of seed migration and possible embolization is expected to occur in a clinical setting, and needs to be addressed. Commercially available strands of seeds could be used to prevent embolization; however, a modification to the seed insertion instrument will be required to incorporate this change. Lastly, the effect of motion (due to respiration and other effects) on seed placement accuracy has not been addressed. Work is currently underway to develop algorithms to compensate for lung motion.

VI. Conclusion

MIRA V is an integrated system for minimally invasive robot-assisted lung brachytherapy that has evolved from the initial MIRA I prototype. Design modifications and real-time dosimetry planning capabilities were integrated into the current generation of the MIRA system. *In vitro* testing showed acceptable and encouraging results. *Ex vivo* and *in vivo* testing will follow.

Acknowledgment

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