The International Journal of **Medical Robotics** and **Computer Assisted Surgery**

THE INTERNATIONAL JOURNAL OF MEDICAL ROBOTICS AND COMPUTER ASSISTED SURGERY
Int J Med Robotics Comput Assist Surg (2013)
DOI: 10.1002/rcs.1508

ORIGINAL ARTICLE

A respiratory correlated image guided surgery method: quantitative accuracy results in swine and human cadaver environments

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Accepted: 25 March 2013

Abstract

Background Intervention on small targets in the lung is difficult, leading our team to develop a highly accurate respiratory correlated image guided surgery (RCIGS) system.

Methods Simulated point source targets were implanted into *ex vivo* porcine and human cadaver lungs attached to a ventilator. The RCIGS system was utilized to guide intervention in the presence of respiratory motion using a commercially available electromagnetic tracking solution. After intervention, the lungs were imaged to determine the target registration error between the target and needle.

Results The system tumor position modeling had sub-mm accuracy. The mean intervention error for 12 porcine targets was 3.8 mm. The mean target registration error on four targets in a human cadaver was 4.0 mm at a mean depth of 9 cm.

Conclusions The system provides an accuracy for intervention on targets of less than 1 cm in diameter at depths of up to 10 cm. A system of this accuracy outperforms current clinical standards. Copyright © 2013 John Wiley & Sons, Ltd.

Keywords respiratory gating; image guided surgery; lung; respiratory correlation; radio frequency ablation; biopsy

Introduction

Advancements in surgical intervention have dramatically improved outcomes and minimized complications associated with invasive procedures. Decreasing the invasiveness of surgery may potentially result in increased survival rates, fewer complications and reduced recovery times.

The advent of minimally invasive technologies has impacted medical practice from diagnostic to interventional procedures. Image guided surgery (IGS) offers the physician alternative imaging approaches during surgical intervention. Currently, commercial IGS products focus on neurosurgery (1), orthopedic (2) and otolaryngologic (3) applications. A surgical system capable of reducing trauma from procedures within the thorax and abdomen is a novel and useful advancement.

Procedures in the lung/abdomen that would benefit from IGS include radio frequency ablation (RFA), lung biopsies, and brachytherapy seed placement. In RFA, radio frequency energy is imparted through a catheter to ablate a tumor. RFA offers local heating from inside a tumor, assuming the guidance system aiding catheter placement is sufficiently accurate. As a result, this modality may potentially reduce trauma to adjacent healthy tissues when compared with conventional external beam stereotactic radiotherapy. While RFA is routinely performed for heart and liver lesions, it has not been clinically implemented for lung lesions on a routine basis.

The use of needle biopsy techniques is widespread in efforts to determine malignancy of lesions within the lung. In order to guide the physician, imaging techniques such as computed tomography (CT) and fluoroscopy are routinely employed. Even when using advanced imaging techniques, the diagnostic accuracies of needle biopsies are poor when the lesions are small (4,5). Li *et al*. report a drop in diagnostic accuracy from 96% to 74% when comparing nodules of diameter $>1.5\,\text{cm}$ and $\leq 1.5\,\text{cm}$, respectively. Tumors have been shown to move at amplitudes $>1\,\text{cm}$ due to respiration (6,7); failure to account for this motion will lower biopsy accuracy rates, especially for smaller lesions. As a result, many institutions currently will not attempt to biopsy lesions less than a centimeter in diameter. Creating a system capable of sufficient accuracy to biopsy small lesions could provide the potential for early detection. Early detection has shown to be a key factor in survival rates. Henschke *et al*. report early diagnosis of Stage I lesions resulted in a 5 year survival rate of 90%, compared with patients diagnosed with Stage III or IV lesions, who have 5 year survival rates of 15% (8).

Finally, brachytherapy seed placement could benefit from an accurate respiratory correlated guidance system. In brachytherapy, a radioactive source is placed inside the body in order to irradiate a tumor. This allows for more localized radiation and sparing of healthy tissue, however it is reliant on accurate placement of the seed source. As a result, the procedure has conventionally been limited to percutaneous use in the prostate, cervix, and breast. Brachytherapy has been used in the lung; however it has been limited to intraoperative use due to the imprecision of percutaneous or bronchoscopic seed placement in the presence of motion.

There are some current commercial minimally invasive lung guidance systems. The superDimension InReach system provides a minimally invasive means for bronchoscopic lung biopsies. The system relies on electromagnetic (EM) position monitoring of a catheter inserted through the working channel of a bronchoscope. Registration between *a prioi* acquired CT or magnetic resonance (MR) images and the room coordinate system is performed by advancing the bronchoscope down several pathways. The EM coordinates are then compared with the pathways on the autosegmented volumetric imageset. During a procedure, the bronchoscope is advanced until it cannot continue due to the width of the surrounding bronchiole. From here, the EM catheter and surrounding guide sheath are advanced without the use of real-time bronchoscopic imaging. The position of the catheter tip is shown on the previously acquired volumetric images. The catheter is mechanically steerable, and the position of the distal tip is updated in real-time on the computer console. Once in the correct location, the guide sheath surrounding the catheter is left in place, the catheter is removed and bronchoscopic tools are employed to gather tissue samples. The superDimension is novel in that it provides minimally invasive access to distal sites conventionally unreachable by a bronchoscope, however there are some limitations. The system does not attempt to account for tissue motion due to respiration. Most of the studies are performed on living patients and report the accuracy using diagnostic yield as a metric (9–11). Although the diagnostic yield is the end goal, it would be ideal to know the spatial interventional accuracy in terms of distance between the needle tip and the lesion centroid. This would allow for statistics to be performed in order to determine confidence intervals for a given lesion size. The studies reported above generally intervene on larger lesions (>2–$3\,\text{cm}$ diameter), decreasing the lesion size allows for earlier diagnosis and better outcomes.

Some studies have reported the spatial interventional accuracy; however this has not been verified by an independent metric such as volumetric imaging, largely due to the impracticality of imaging with the probe in place when performing biopsies on living patients. Eberhardt and Schwarz both report their spatial intervention errors (mean: 9 mm, 6 mm, respectively), however, these are not computed with respect to a following image, but with respect to the original planning image used for EM guidance (12,13).

The StealthStation Treon system from Medtronic Navigation is routinely used in minimally invasive craniospinal procedures. Similar to the previously mentioned systems, this system uses EM navigation in conjunction with volumetric images acquired *a priori*. The system is widely used in cranial applications, however, it is currently not used for the lungs or abdomen. The StealthStation offers two methods for registration. In point based registration a series of CT contrast markers are defined both on the CT image and in the room coordinate system by physically and systematically touching each marker with the EM tools. Alternatively, tracer based registration relies on tracing a known structure (such as the bridge of the nose and forehead) using an EM tool, and the acquired points are automatically matched to the autosegmented skull surface in the CT image. Once registration is performed, the system shows the position of the catheter in real time; however, there is currently no motion model for respiratory correlated IGS.

We incorporated previously published tissue modeling (14) based on respiratory correlated imaging (4DCT) in an effort to develop an IGS system that accounts for target motion and improves the accuracy of minimally invasive needle biopsy techniques in the lung. A temporal guidance and planning system was developed and the accuracy of the system is characterized in phantom, *ex vivo* porcine and human cadaver settings.

Methods

A commercially available IGS solution (StealthStation®) was employed in order to track the tips of interventional tools via electromagnetics. A field generator connected to the StealthStation creates a position-dependent magnetic field inside of the patient. The system uses tools with two copper wire coils near the tip that act as inductors. Based on the amount of current induced in the coils of the tool from the surrounding magnetic field, the positions of the AxiEM tools are determined to sub-mm accuracy in three dimensions. The RCIGS system consists of additional software that communicates with the StealthStation via application programming interfaces (APIs) to offer temporal guidance to the physician for intervention on moving targets. The RCIGS workflow is described in Figure 1.

System overview

4DCT acquisition

A respiratory correlated imaging technique (4DCT) using a commercial CT scanner (Philips Brilliance) was employed to obtain a series ($n = 4$) of volumetric images, each of which correlate with a specific phase of the breathing cycle as indicated by a respiratory surrogate. The respiratory surrogate used was a pneumotachograph, which provides an accurate, calibrated representation of tidal volume and airflow throughout the image acquisition. The scanner was operated in cine mode using a 0.5 s rotation, 360° reconstruction and standard filtered backprojection. The imaging mode was retrospective helical reconstruction, with a voltage of 120 kVp and current of 133 mAs (15).

Target position

After 4DCT imaging, the reconstructed DICOM images are network transferred to a research system containing Philips Pinnacle (version 8.1y). Pinnacle is a clinical radiation therapy treatment planning software package which offers a robust environment for manual image segmentation and contouring. Targets were defined on 4DCT images using a lung viewing window (W:1600, L:-600). Their position centroids were recorded on each of the volumetric phase imagesets from the 4DCT, providing target positions based on image data acquired using an external respiratory surrogate. At the completion of this stage, four target locations are available with corresponding tidal volume and airflow measurements from the respiratory surrogate.

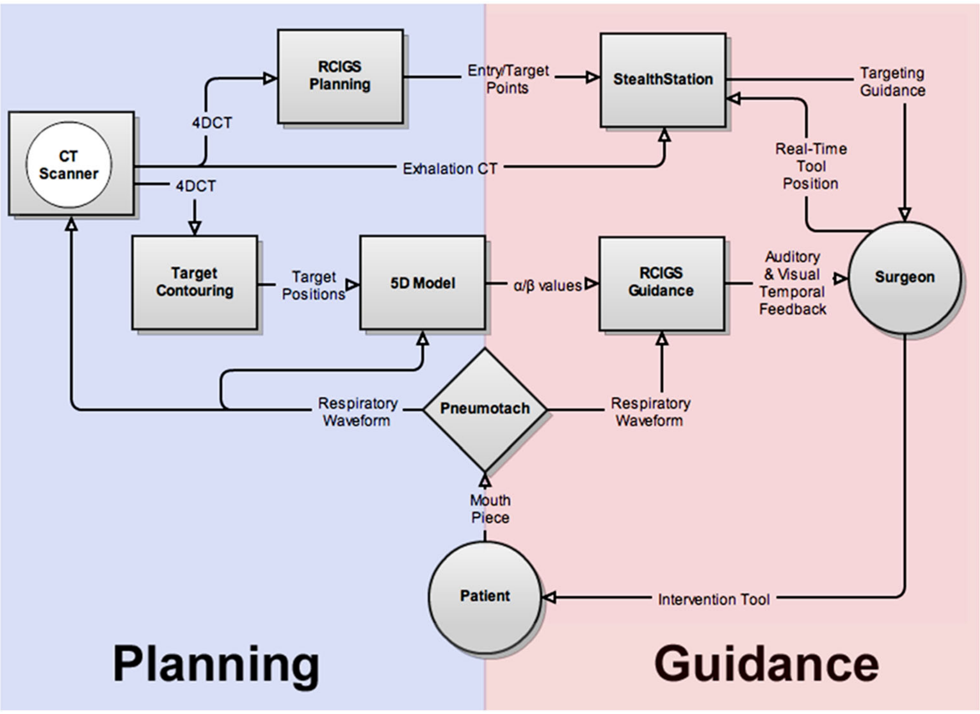

Figure 1. Lung IGS workflow. 4DCT images are acquired based on a respiratory waveform from a pneumotachograph connected to the patient's mouth piece. The 4DCT images are sent to the RCIGS planning software, as well as a contouring workstation for target definition with respect to respiratory phase. These four target points with respect to respiratory phase are sent from the Pinnacle workstation to the 5D model computer. The model parameters (α/β) are input to the RCIGS guidance software, along with the real-time respiratory waveform. From here, the RCIGS guidance software determines the position of the target in real time, and indicates the proper time for intervention to the physician via auditory and visual feedback. The StealthStation receives entry and target points from the RCIGS planning software, the exhalation CT, and the real-time tool position via EM position monitoring. The StealthStation offers real-time visual guidance to the physician on the location of the needle tip inside the patient

Model calibration

The four target positions along with tidal volume and airflow measurements are used to calibrate a previously described model for respiratory motion. In short, the model is parameterized via the four known target positions. At completion the model can accurately output the position of the target at any tidal volume and airflow rate in real time. The computation time is negligible compared with the overall planning process, on the order of seconds. The details of the model are not included here for the sake of brevity, but can be found in previously published work (14).

Surgical plan

Once the target position is known for any tidal volume and airflow, a location and time in the target's trajectory is selected for intervention. The location should attempt to maximize the time at which the target is relatively stationary and respiration is reproducible. This typically occurs at exhalation. The surgical entry and target points are virtually defined by the user on the volumetric image set loaded into the StealthStation. The planning software was written in C++ using the following open source libraries: the visualization toolkit (VTK) for image processing and visualization, the insight toolkit (ITK) for image segmentation and registration and the Fast Light Toolkit (FLTK) for graphical user interface (GUI) generation. The aforementioned toolkits provide a framework for reading and manipulating 3D medical image datasets without programming the low level functions for image interaction in C++.

The RCIGS planning software displays the trajectory of the needle tip with respect to the respiratory motion of the tissue. In order to achieve this, a 4DCT dataset consisting of a series (4–10) of 3D volumetric images is loaded from the hard drive into RAM. The memory required for this task is approximately 1.5 GB, which is currently available on affordable consumer computers. The CT images are displayed using three orthogonal views. Once the 4DCT datasets are loaded, the trajectory of the tooltip is overlaid with visual point indicators of the entry, target, and current slice intersection. The motion of the tissue due to respiration can be simulated, and the software loops through the various phases of the 4DCT while updating the displays in real time. This allows for evaluation of critical structure motion due to respiration, and the path to the target can be modified accordingly. The software also has basic window/level functionality available in most image display software in order to increase contrast depending on the region of interest within the body (Figure 2).

Once the surgical plan is established, the RCIGS guidance software instructs the physician on when to perform the intervention (Figure 3). The position of the target is known in real time based on the signal from the pneumotachograph and pre-calibrated 5D model parameters, and the target position is displayed to the physician. Additionally, visual and auditory feedback are given when the target is within a predefined volume. This allows the physician to advance the needle and/or perform the tissue resection when the target is in the appropriate location.

The StealthStation guides the physician using the approach trajectory defined in the planning phase. The position of the tip of the needle tool is monitored with high precision using electromagnetics. A position variant magnetic field is produced in the treatment room, and the induction in the coil at the tip of the needle allows the position to be calculated. The needle position is then displayed over the volumetric images acquired during the planning phase.

System accuracy: overview

In order to develop the RCIGS system and obtain quantitative measurements of the overall accuracy, a

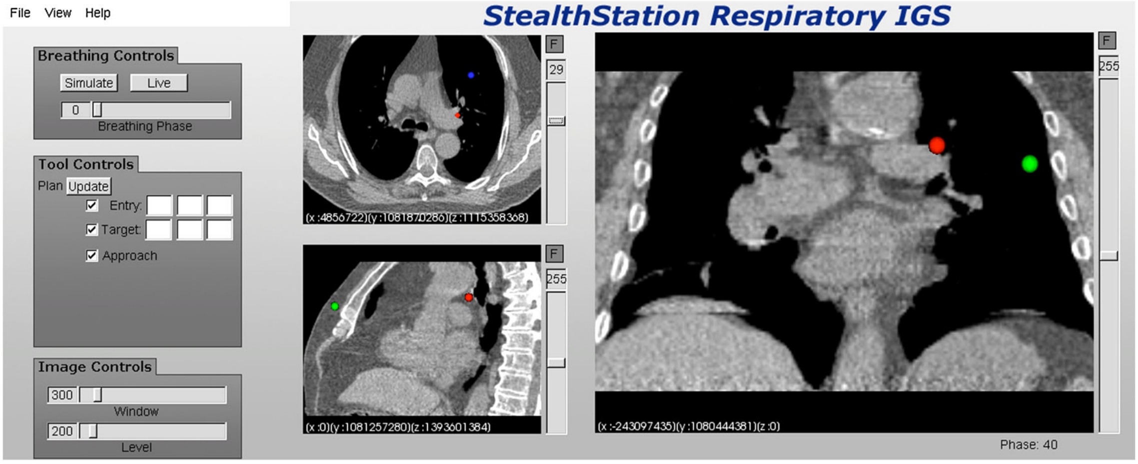

Figure 2. Lung IGS planning software. Target, entry and approach trajectories are visually displayed along with respiratory correlated imaging. This allows the physician to determine whether critical structures enter the approach path as a result of respiration prior to surgical intervention. (Target = red, Entry = green, Approach path through current slice = blue)

DOI: 10.1002/rcs

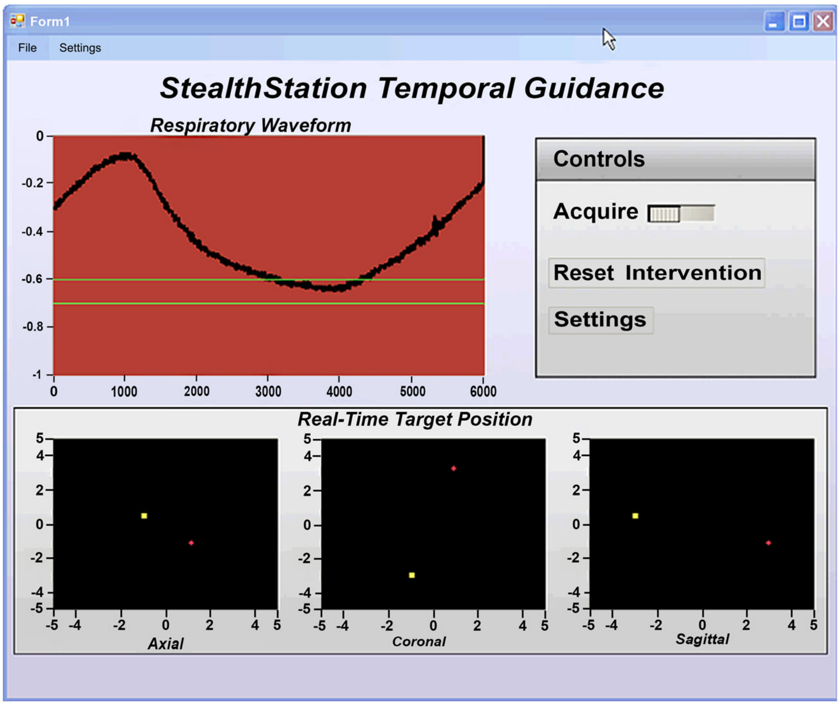

Figure 3. RCIGS guidance software. The respiratory waveform is displayed to the physician. Binary auditory and visual feedback is given to the physician when the target is within a predetermined range. The static intervention target is shown as a yellow dot with multi-plane views. The position of the red dot changes in real time based on the previously calibrated 5D model indicating the target position as a function of the respiratory surrogate

series of experiments were designed with increasing difficulty. Motion phantom, *ex vivo* porcine, and human cadaver models were successively employed and each stage had associated criteria for success. An overview of the success criteria and problems that each model attempted to address is included with details on each model found in Table 1.

System accuracy: phantom assessment

A robotic motion phantom was used to initially characterize the accuracy of the system. The goal of the motion phantom study was to characterize both the target motion modeling portion of the RCIGS package, as well as the intervention on a moving target by a surgeon. The phantom was programmed to reproduce the motion from a lung target recorded via an implanted position-monitoring device (Beacon, Calypso Medical®) in the lung of a human patient (16). A 4DCT imageset was acquired of the motion phantom as it moved, which was subsequently used for model calibration and intervention planning according to the RCIGS system.

Since the programmed trajectory is known, it is possible to compare the output from our model with the actual trajectory. This was performed both for the entire trajectory and the portion of the trajectory at exhalation, which is when the surgical intervention occurs. The mean discrepancy between measured and modeled data was reported as submillimeter during model validation by Low *et al.* (14). We set criteria for model calibration success as a mean error <1 mm at exhalation.

Point based registration between the CT image and surgical room coordinate system was performed by using an EM tool to touch several radiopaque markers (IZI Medical MM3005) affixed to the phantom arm, and virtually defining the corresponding positions on the CT images loaded into the StealthStation software. An EM ‘patient tracker’ sensor was affixed to the non-moving base of

Table 1. System accuracy models. The RCIGS system was tested in robotic phantom, porcine and human cadaver environments. The table outlines the problem each model attempted to address, as well as a quantitative success metric

Model	Purpose	Success criteria
Robotic phantom	- Software calibration - Motion intervention baseline	Mean errors Modeling: <1 mm Intervention: <3 mm
Ex vivo porcine lung	- Soft tissue effects: deformation, needle motion	Mean Error Intervention: <4 mm
Human cadaver	- Critical structures: ribs/vasculature - Realistic tissue characteristics - Registration on soft tissue - Increased depth	Mean target Registration error: <5 mm Stretch goal: all intervention <5 mm

the phantom. This sensor offers a coordinate transformation and ensures the registration is accurate even if the 'patient' moves with respect to the field generator. Since the target exhibits motion, it was necessary to know both the location of the surgeon's tool as well as the location of the phantom arm at the time of simulated intervention. Two electromagnetic tools (AxiEM) were used. One probe was handled by the surgeon performing the intervention [RS], while the other represented a surgical target and was affixed to the moving phantom arm, to measure real-time positional information. The phantom arm was hidden from the surgeon's view, leaving the StealthStation RCIGS software as the sole guidance for intervention.

After identifying the target on CT images, a static offset was added to the target position as defined virtually on the StealthStation. This was done to ensure that there was no physical contact between the motion arm and the intervention tool. Any physical contact would offer the surgeon extra guidance on the target position, confounding performance results of using the RCIGS guidance software alone. The motion phantom was programmed to run the same trajectory used during imaging. When the target and tool were in the correct location as indicated by the RCIGS software, the surgeon simulated intervention by depressing a footswitch. At this time the RCIGS software communicated via TCP/IP over an ethernet link with the StealthStation to obtain the position of both EM tools. The positions (n = 25) of the arm and intervention tool were simultaneously recorded for error analysis. Previous studies of the use of this system for intracranial surgeries have reported intervention accuracies <2 mm and <3 mm in phantom and clinical trials, respectively. We set criteria for success as 3D errors between the tool tip and the phantom arm <3 mm, indicating an accuracy of intervention sufficient for a 1 cm diameter spherical lesion while allowing for additional errors due to soft tissue registration and deformation in further studies. (Figure 4).

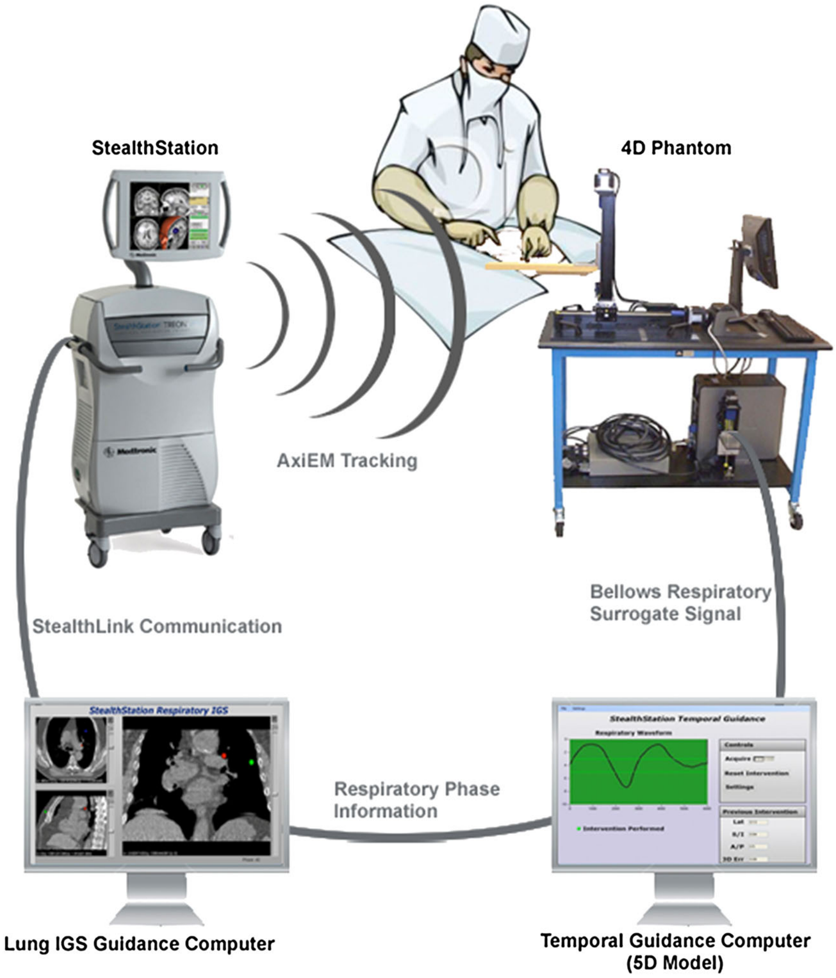

Figure 4. RCIGS phantom study schematic. A 4D motion phantom recreates realistic motion trajectories. A bellows device receives the respiratory signal via a surrogate axis and a computer calculates the target position using a pre-calibrated 5D model. This information is used to guide the physician on when to intervene. When an intervention is performed, the position of an AxiEM marker on the motion phantom arm and the position of the surgeon's tool tip are recorded. This allows for quantitative analysis of the accuracy of the temporal guidance system

DOI: 10.1002/rcs

System accuracy: *ex vivo* porcine assessment

Phantom characterization enables positional accuracy testing against a very exact reference; however, it ignores some of the problems associated with intervention in actual tissue. Most notably, the needle tip will move as a result of the motion imparted by surrounding tissue. Additionally, tissue will deform due to the forces imposed by an implantation needle. An *ex vivo* porcine model was employed to further analyze the system accuracy in the presence of the aforementioned difficulties.

The RCIGS system was used to guide intervention on simulated targets in porcine lungs (BioQuest®, eNasco). The lungs were preserved in propylene glycol, which prevents bacteria growth and acts as a desiccant to prevent the lungs from drying out and becoming rigid. The lungs were placed inside a plastic container supported with foam. Point based registration was performed on circular CT contrast markers affixed to the container holding the lungs. The trachea was held rigidly and the lateral and posterior walls of the lung were supported, allowing the superior and anterior walls to move freely. These efforts were made in order to maximize the amount of superior/inferior and anterior/posterior motion similar to that found *in vivo*. The lungs were permitted to slide with respect to the container. Twelve highly attenuating small pieces of 23 gauge copper wire were percutaneously implanted through a Teflon guide sheath into three sets of lungs to serve as targets.

The lungs were attached to a ventilator (Aequitron Medical, LP10) and inflated via positive pressure. The ventilation parameters were 30 bpm, 1.8 L volume, with 1.2 s inspiration time. The pressure exterior of the lung inside the housing was unregulated at atmospheric pressure. The expiratory pressure remained constant from breath to breath at 20 mm H_2O via a positive end expiratory pressure (PEEP) valve. The RCIGS system was used to image, plan, and intervene on each of the targets within the lungs.

During intervention, the EM tool was affixed inside of a piece of 16 gauge Teflon tubing (Small Parts, Inc.) in which the leading end was cut at an acute angle (Figure 5). The guide sheath was constructed with 0.4 mm thick walls in order to provide enough rigidity to pierce lung tissue. The EM tool is flexible, and deforms with the stresses imposed upon it due to moving tissue. There are two points of known position near the tip of the catheter. The deformation of the tool is minimal between these two points, which allows for accurate position measurement of the EM tool tip, even when the body is deformed. The EM tool and guide sheath combination was advanced manually by the physician during expiration when the target was in the static approach path defined during planning. Once in place, the EM tool was removed and a piece of copper wire was inserted into the guide sheath. The entire assembly was fixed in place with cyanoacrylate and after all interventions were performed the lungs were imaged again via 4DCT for interventional accuracy assessment.

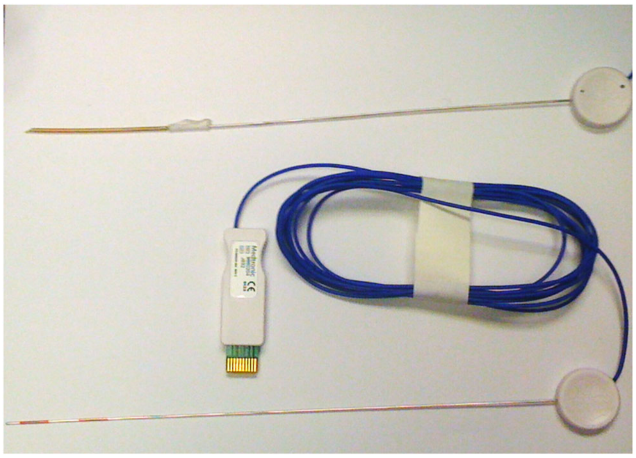

Figure 5. Surgical tools. An AxiEM stylette with PEEK guide sheath/needle (top) as well as a bare AxiEM stylette (bottom) are shown

After imaging, the exhalation 4DCT was loaded into clinical radiation therapy treatment planning software (Philips Pinnacle version 8.1y) in order to define the needle tip and target points in 3D. Error assessment was performed by measuring the three-dimensional distance between the needle tips and target points (Figure 6).

System accuracy: human cadaver assessment

Additional concerns arise when using the RCIGS system for intervention in the human lung. For instance, the approach plan must account for both rib and critical structure motion such as vasculature to ensure the needle does not interfere. Additionally, the registration technique used for the porcine trial is not applicable in a human subject. In order to determine the system accuracy in a clinically relevant scenario, a human cadaver was utilized.

The thorax of a human cadaver was prepared for respiratory correlated intervention. The carbon fiber couch on a Philips Brilliance CT Scanner was replaced with a wood plank in order to minimize interference with the magnetic fields required for 3D tool location. The torso was placed on the couch and bilateral chest tubes were implanted and affixed to a vacuum unit with a reservoir chamber to collect effusion fluid (Pleur-Evac). Once the pleural space was evacuated, a cuffed endotracheal tube was inserted and connected to a ventilator to inflate the lungs via positive pressure. The settings on the ventilator were as follows: volume = 1 L, breath per minute = 14, inspiratory time = 1 s, assist/control mode. The torso was imaged via CT to determine optimal locations for target implantation. Four small radiopaque markers constructed of single stranded copper wire were implanted percutaneously into the lungs to serve as targets. The targets were implanted laterally through a needle with a plunger to evacuate the targets. The targets

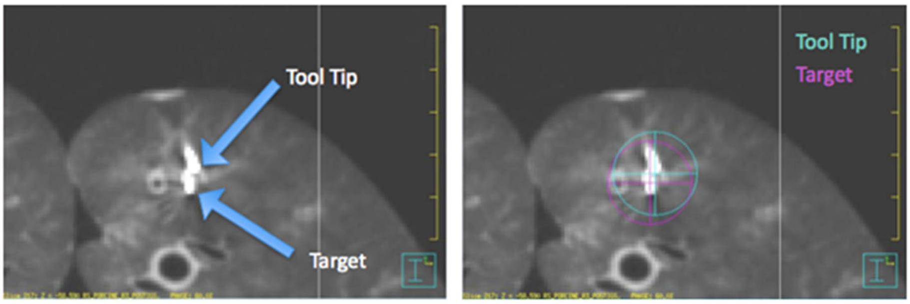

Figure 6. Target/intervention accuracy assessment. The needle tip and target are defined inside clinical treatment planning software. The 3D offset is recorded for each run. Yellow grid marks = 1 cm increments

were implanted with distances of approximately 10 cm from the anterior surface to ensure the system is accurate for intervention on deep lesions (Figure 7).

Once the targets were implanted, several circular radiopaque CT markers were affixed to the chest wall and the cadaver was imaged via 4DCT. Similarly to the previous porcine and phantom models, point based registration was performed using the CT markers. Unlike the previous models, the registration points were moving due to respiratory induced chest wall expansion and hence the registration must be gated at exhalation. Additionally, a patient tracker EM sensor was affixed to the torso. This sensor also moves/rotates due to chest wall motion. The position of the EM tool is constantly updated based on a coordinate system transformation obtained from the patient tracker. As a result, the position of any EM tracked tool is only accurate during the phase at which registration was performed (exhalation). This is acceptable since intervention and needle advancement will be gated at the same phase that registration was performed.

A guide sheath constructed of polyetheretherketone (PEEK) was placed around the EM tool to be used for intervention. PEEK was employed as opposed to the PTFE (Teflon) tubing used in the porcine model due to the need for a stronger polymer in order to penetrate the chest wall and tissue surrounding the lungs. A metal guide sheath would act as a Faraday cage, shielding the inner tool from the magnetic field and preventing 3D localization. PEEK offers rigidity comparable with steel in a non-ferromagnetic material. Prior to insertion of the tool/sheath, the estimate of the fiducial registration error provided by the EM navigational system was checked, and was always less than 1 mm prior to starting the procedure. The tool/sheath was advanced through a small incision on the anterior surface of the torso. This approach path was defined in a different direction from the lateral path used to implant the targets to ensure the intervention needle was not simply re-tracing the implantation pathway. Once the EM tool was guided to the appropriate position, it was removed from the guide sheath and a piece of copper wire was inserted and affixed with cyanoacrylate. The copper wire is readily visible via CT imaging and was used to determine the efficacy of intervention.

Results

Phantom assessment

The calibrated 5D model positions were compared with the actual positions delivered by the motion phantom during imaging to determine the 3D error at the end of modeling. A histogram of the errors is shown in Figure 8. Note that the modeling errors decrease when

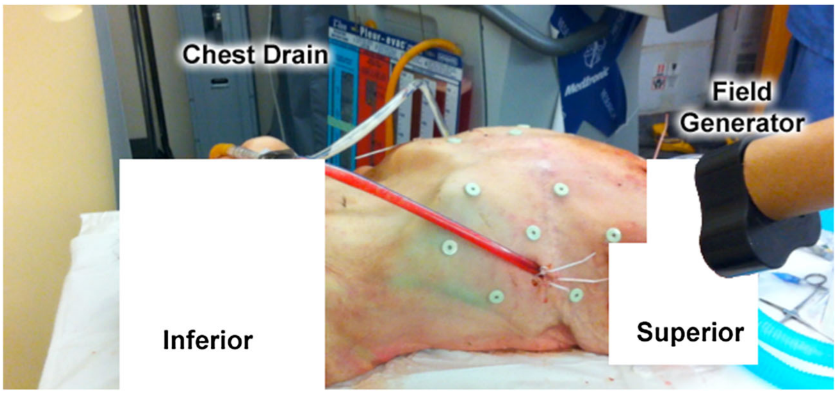

Figure 7. Cadaver registration. Several small radiopaque CT contrast markers were affixed to the chest wall for registration. The markers have a circular hole in the middle, which is the same size as the head of an EM tool. The tool is touched in each of the markers during exhalation, and the StealthStation matches these points in CT room coordinates (with respect to the black magnetic field generator) with the associated points defined on the CT image

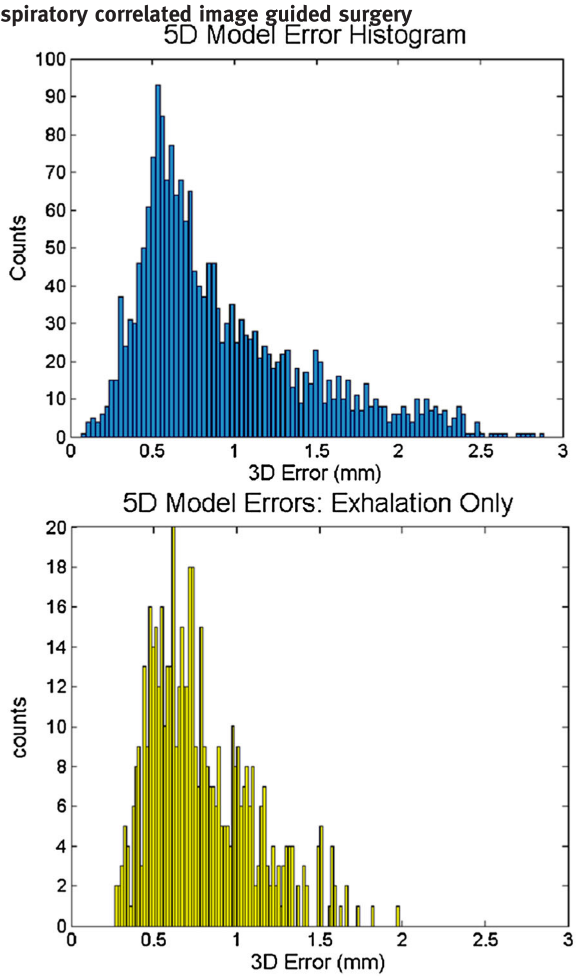

Figure 8. **Lung motion: modeling errors. The output from the 5D model used to determine the tumor position during treatment was compared with the actual tumor trajectory. Errors are reported for the entire waveform (blue) as well as only at exhalation (yellow)**

observing exhalation vs. the entire breathing waveform (mean: 0.8 vs. 0.9 mm; max: 2.0 vs. 2.9 mm, respectively).

Once the model was assessed for accuracy, 25 interventions on a moving target were performed. Errors from the interventions are reported (Figure 9). The intervention showed good agreement, with a mean error of 2.0 mm and a maximum error of 3.3 mm.

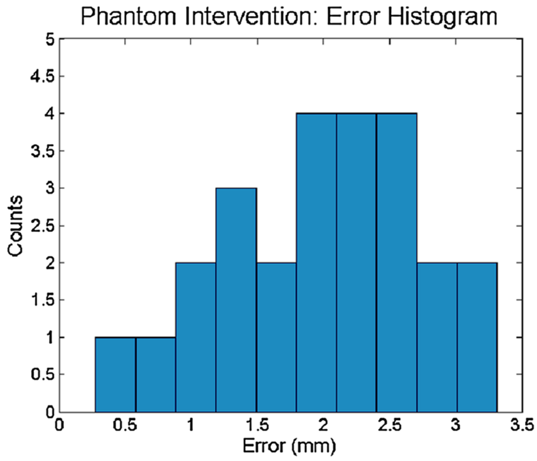

Figure 9. **Lung motion: phantom intervention errors. Intervention was performed on a moving target. A histogram of the errors from 25 interventions is shown**

Table 2. Porcine intervention accuracies. Target to needle tip errors are reported along with target motion and depth

3D error (mm)	Target motion (mm)	Target Depth (cm)
2.9	8	2.3
2.6	7	2.4
1.0	10	1.8
4.0	8	3.7
6.9	15	1.2
1.7	12	2.3
2.1	9	1.5
5.6	7	1.2
6.8	15	2.1
4.0	15	2.1
4.4	11	2.2
3.9	11	2.2
Mean Error:	3.8 mm	
RMS Error:	4.2 mm	

Table 3. Cadaver intervention accuracies. Target to needle tip errors are reported. Additionally, the target motion and depth are reported

Target	Target registration error (mm)	Motion (mm)	Target depth (cm)
1	4.5	2	7.8
2	4.8	2	10.1
3	3.2	4	8.9
4	3.4	5	9.3

Porcine assessment

Table 2 shows the 3D error between the target and tooltip for each run. Nine of 12 intervention attempts provided accuracy suitable for intervention on a 1 cm tumor. All attempts provided accuracies capable of intervening on a 1.5 cm diameter tumor. The mean error associated with intervention was 3.8 mm (SD = 0.8 mm).

Cadaver assessment

The RCIGS system displayed excellent accuracy in the human cadaver interventions. Table 3 contains target registration error, target depth and target motion for each run. The mean accuracy and RMS error of target registration were 4.0 mm, with a mean target depth of 9 cm. All target/tooltip errors were less than 5 mm, which indicates intervention is suitable for 1 cm tumors in four of four cases. Additionally, the target depths were large (8–10 cm). If a target was implanted at a depth larger than this, it is likely the intervention would have been performed from the posterior chest wall.

The motion, calculated via contouring on various phases of the 4DCT, for the first two targets was minimal (2 mm). These targets were both implanted in the right

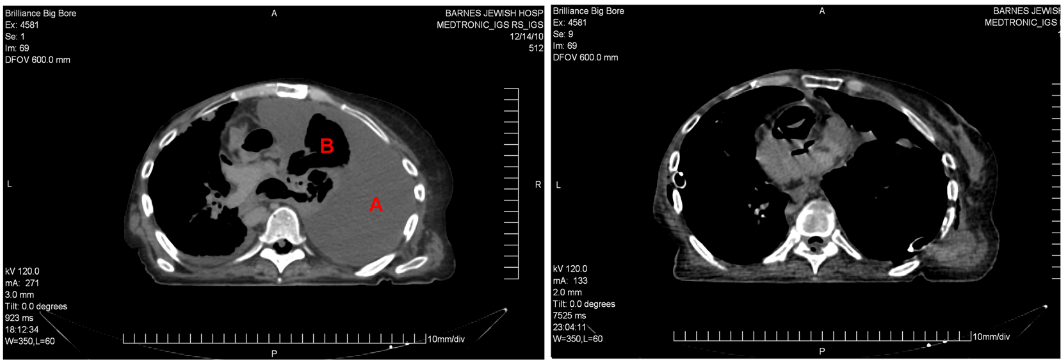

Figure 10. Pleural effusion. Substantial fluid buildup (A) was present in one lung prior to draining via a chest tube affixed to a vacuum source. The lung was collapsed (B) prior to draining and this might have reduced the amount of respiratory related target motion for the two targets implanted into this lung. The right is a CT of the same lung after draining the fluid

lung of the patient, which had to be drained of substantial fluid prior to implantation/intervention.

The 4DCT acquisition and planning encompasses the majority of the time for a given intervention. Once the plan was generated the registration and intervention were performed in approximately 15 minutes per target.

Discussion

The RCIGS system shows promise for minimally invasive intervention in the lung/abdomen. There are several commercial systems on the market to currently address the problem, but to date none have published results encompassing the spatial accuracy of the system for intervention on targets within the lung.

One group from Georgetown University has showcased their IGS software based on the open source Image Guided Surgery Toolkit (IGSTK) (17). In this study, three live swine were implanted with tumor analogues. The swine were sedated and intervention was performed to determine the accuracy of the guidance system in the presence of respiratory motion. The errors reported were higher than our system (9.4 ± 3.0 mm vs 4.0 ± 0.8 mm). The errors from our system are comparable with the spatial interventional errors reported for percutaneous EM guided intervention on the abdomen: mean: 5.4 mm ± 1.9 mm, max: 8.1 mm (18); 4+/−2 mm (19). This indicates that the system reported here is doing a reasonable job mitigating the effects of respiratory motion. With that said, it is unfortunate that half of the targets in the cadaver study were in a space previously filled with fluid. The fluid in the pleural space collapsed the lung substantially prior to draining via chest tubes, possibly causing the lung to exhibit less motion (Figure 10). Future work would incorporate intervention on highly mobile targets, potentially at less depth within the chest.

There are improvements to the RCIGS package that would need to be made prior to a clinical implementation. In practice, it is unlikely a pulmonologist would refer a patient to an imaging center at a remote location in order to obtain the 4DCT. Aside from workflow efficiency concerns, having the patient move between imaging and intervention has the potential to increase registration error. A mobile, compact system for performing CT acquisition has been developed (O-arm® Surgical Imaging, Medtronic Navigation). A CT system capable of imaging within a pulmonary intervention suite would allow for increased patient throughput. Additionally, the acquired images would be automatically registered to room coordinates, which alleviates the need for point based registration. This would allow for workflow improvements as well as decrease the errors associated with doing registration on moving soft tissue body surfaces, at the expense of increased cost and space. Bronchoscopic intervention (20) is typically favored over percutaneous intervention (21) due to the reduced rate of pneumothorax. Incorporation of flexible tools like those used in other studies (22,23) would make this improvement feasible.

In summary, a highly accurate system for intervention on moving tumors in the lung was quantified and the results were shown to be sufficient for intervention on 1 cm tumors. Additional studies are needed to increase the sample size to ensure the system is robust in a clinical environment.

Conflicts of interest

Work supported in part by Medtronic Image Guided Surgery Award.

Funding

No specific funding.

Ethical statement

Review and approval by an ethical board was not obtained for this research, as all subjects were non-living (either inanimate or deceased prior to study).

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