Advancements in Magnetic Resonance–Guided Robotic Interventions in the Prostate

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Abstract: Magnetic resonance imaging (MRI) provides more detailed anatomical images of the prostate compared with the transrectal ultrasound imaging. Therefore, for the purpose of intervention in the prostate gland, diagnostic or therapeutic, MRI guidance offers a possibility of more precise targeting that may be crucial to the success of prostate interventions. However, access within the scanner is limited for manual instrument handling and the MR environment is most demanding among all imaging equipment with respect to the instrumentation used. A solution to this problem is the use of MR-compatible robots purposely designed to operate in the space and environmental restrictions inside the MR scanner allowing real-time interventions. Building an MRI-compatible robot is a very challenging engineering task because, in addition to the material restrictions that MRI instruments have, the robot requires actuators and sensors that limit the type of energies that can be used. Several important design problems have to be overcome before a successful MR-compatible robot application can be built. A number of MR-compatible robots, ranging from a simple manipulator to a fully automated system, have been developed, proposing ingenious solutions to the design challenge. Several systems have been already tested clinically for prostate biopsy and brachytherapy. As technology matures, precise image guidance for prostate interventions performed or assisted by specialized MR-compatible robotic devices may provide a uniquely accurate solution for guiding the intervention directly based on MR findings and feedback. Such an instrument would become a valuable clinical tool for biopsies directly targeting imaged tumor foci and delivering tumor-centered focal therapy.

Key Words: interventional MR, image-guided intervention, MR robot, MR-compatible, MR motors

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The estimated number of prostate biopsies performed yearly[1] in the United States is 1,300,000. In 2007, these resulted in the detection of 186,320 new cases of prostate cancer (PC).[2] The large difference accounts not only for true-negative tests but also for those in which the biopsies missed sampling the cancer. The number of false-negative biopsies is estimated at approximately 30% for primary sextant prostate biopsies.[3–5]

The use of prostate-specific antigen (PSA) testing and screening programs in the last decade has shown outstanding results. In 2007, 91% of the true-positive biopsies were detected at local or regional stages, and whereas these represented 25% of all cancers in men, the death rate from PC was 10%, clearly showing the benefit of detection at a curable stage.[2] But the clinical diagnosis of PC still heavily relies on the biopsy because PSA levels can be elevated owing to benign pathologic lesions such as benign prostatic hyperplasia and prostatitis. The management of patients in whom a first set of biopsies was negative for cancer is a daily problem for urologists and creates uncertainty and emotional stress for the patients. This also starts a cascade of repeat biopsies,[4,6,7] with cancer detection rates of 34%, 25%, 24%, and 21% for the first, second, third, and fourth biopsies as shown in a recent comprehensive study of 10,429 biopsies.[4] Moreover, with the current stage migration,[8,9] the smaller tumors are becoming ever more difficult to sample, yet the staging of the disease becomes increasingly dependent on the results of the biopsy.

The primary cause of biopsy failure is missed sampling, and that happens because PC presents a multifocal heterogeneous distribution of variable cellular maturity throughout the gland[3,7] and the fact that tumor-directed image guidance is not yet clinically used for guiding the biopsy. The routine modality for imaging the prostate during biopsy is transrectal ultrasound (TRUS), which has known limitations in visualizing PC.

Although numerous PC imaging methods show promising results, these are not currently integrated clinically[10] to guide interventions, one of the reasons being that few image-guided technologies are available. The total volume of the cores extracted in a biopsy session is very small compared with the gland volume, less than 1%.[10] As such, the probability of intersecting a malignant tumor in the early stage of the disease is low, and lower for larger prostate volumes.[6] A study on 1875 men who underwent biopsies found the rate of PC detection to be 19.9% for the primary biopsies and 11% for the repeat.[11] Yet, the pathological characteristics of the samples in the 2 steps were similar, but only the sizes of the prostate diagnosed in the repeat biopsies were larger. As such, with current techniques, positive biopsy sampling is a probabilistic event.

Moreover, similar problems occur for therapies. Prostate gland– or pelvic region–distributed therapies are used for

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established methods, such as the external beam radiation and brachytherapy, and for novel methods, such as cryotherapy,[12] high-intensity focused ultrasound,[13] and photodynamic therapies.[14,15]

New image-guided instruments are needed to increase the accuracy and repeatability with which needles are placed in the gland.

Magnetic resonance imaging (MRI) provides more detailed anatomical images of the prostate compared with TRUS imaging. Therefore, for the purpose of intervention in the prostate gland, diagnostic or therapeutic, MRI guidance offers a possibility of more precise targeting that may be crucial to the success of prostate interventions. However, limited space inside the MRI scanner prevents physicians from making real-time intervention to the prostate under direct MRI guidance, which has been possible under ultrasound guidance. Instead, patients are moved in and out of the scanner, and intervention is done based on the previously acquired MRI data while patients were inside the scanner, without the benefit of real-time imaging guidance. The advantage of using the MRI guidance because of its detailed depiction of the prostate anatomy is undermined by this limitation. A solution to this problem would be the development of MR-compatible robots that can operate in the space and environmental restrictions inside the MR scanner, allowing real-time interventions. There are several important design issues, namely, the use of MR-compatible material, MR-compatible actuators and position sensors, and implementation of image-to-robot registration, which have to be overcome before a successful MR-compatible robot application can be built. A number of MR-compatible robots, ranging from a simple manipulator to a fully automated system, have been developed with different solutions to the design problems. Up to now, only few manual devices and MR robots providing a guide for manually inserting the needle have been tested clinically, and applications have been limited to biopsy and brachytherapy. Advanced image-guided instruments are needed, such as robot imager–embedded systems in which the robot is controlled under direct MRI guidance allowing for reimaging during the intervention, treatment planning updates, and quality control.

In this article, we describe advantages of the MR-guided robotic interventions in the prostate, review design and engineering requirements, and discuss several robotic systems developed to date.

DESIGN REQUIREMENTS OF MR-COMPATIBLE ROBOTS

Numerous forms can be found for the definition of a robot. Joseph Engelberger, who is considered the father of robotics, said, "I can't define a robot, but I know one when I see one." According to the Robot Industries Association, a robot is a reprogrammable multifunctional manipulator. This is a machine programmed to do a task, for which the program can be changed to accomplish different functions, and the task necessarily involves motion.

Is a robot what most people recognize as a robot? For image-guided applications, a robot is a mechanical system actuated under computer control based on the images. If a mechanism has motors but no computer, or uses computer but is manual, that is a device and not a robot.

Designing an MR-compatible robot for real-time guidance inside the MR scanner is recognized to be a complex task consisting of several steps and numerous demanding considerations: selecting MR-compatible materials, building MR-compatible actuators and position sensors, designing a robot-to-image registration system that would allow precise guidance of the robot based on MR image feedback, and, nevertheless, performing and tracking its development according to device regulations for clinical use and implementation of clinical trials.

Robots not only augment physician's manipulation capabilities but also establish a digital platform for integrating medical imaging data.[16] This gives robots abilities unattainable to humans because, unlike humans, robots and imagers are digital devices. Robots have stringent requirements for imager compatibility, precision, sterility, safety, size, and ergonomics. A robot's compatibility with a medical imager refers to the capability of the robot to safely operate within the confined space of the imager while performing its clinical function, without interfering with the functionality of the imager.[17] Among all types of imagers, the MRI is the most demanding, and the development of MR robots is a very challenging engineering task.[18,19] However, this also makes MR-compatible devices multi-imager–compatible; if radiolucent, artifact-free materials are used for the parts located in immediate proximity of the imaging site.[17]

MR-Compatible Materials

Magnetic resonance scanners use magnetic fields of very high density (3 T becomes common), with pulsed magnetic and radiofrequency fields. Within the imager, ferromagnetic materials are exposed to very high magnetic interaction forces, and heating may occur in conductive materials by electromagnetic induction. The use of electricity may cause interference leading to signal-to-noise attenuation, signal distortions, and image artifacts. As such, most of the components commonly used in robotics may not be used in close proximity of the MRI. For example, the ubiquitous electromagnetic motor is clearly MRI-incompatible because it functions based on magnetism.

Several nonferrous metals such as titanium and nitinol have been found to be acceptable for small size parts and are being used in commercial MRI instrumentation. However, for noninterference with electromagnetism, the ideal materials should be not only nonmagnetic but also dielectric. There are plastics, ceramics, rubbers, glasses, and so on. From the energetic point of view, electricity is not MRI-compatible because currents generate electromagnetic waves and require conductors for wirings. Hydraulics could be a good choice but raises contamination concerns because of leakage. Pneumatics and light, on the other hand, are ideal choices, because of being decoupled from electromagnetism.

Actuators

Previous research has commonly used piezoelectric motors,[18] also called ultrasonic motors. The piezoelectric effect is the ability of some crystals and certain ceramic materials to

generate a voltage in response to applied mechanical stress. The effect is reversible, so in motors, the crystals change shape and produce motion when subjected to an externally applied voltage. The problem is that the change in the shape of the piezo crystal is very small (~0.1%), and this is only achieved under high voltages. To create usable motion, the voltage needs to be pulsed at high frequencies. These violate the patient's safety and imager noninterference requirements.

Piezo motors have various characteristics, but regarding imaging, they commonly create distortions if operated closer than 0.5 m from the image isocenter.[20] Even without power, the wiring of the motors still takes a significant part of the MRI signal debasing the signal-to-noise ratio by as much as 50%.[21] Electric screening and filtering solutions were used to cope with these problems, but minimal gain was paid off with complicated solutions. A recent study[22] addressed the compatibility of a new piezoelectric motor made of ceramics (SQUIGGLE Motor; New Scale Technologies, Rochester, NY) in a 4.7-T animal research scanner. Unfortunately, image distortion tests were not performed, but they mentioned that the motor has to be kept distal and additional electronic filtering work is in progress. Turowski et al[22] and Wendt et al[21] also reported that specific MRI sequences (SE) had to be used to reduce artifacts. Moreover, piezo motors also have performance, controllability, and wear problems because of their inherent friction drives.[18]

The piezoelectric effect is magnetism-free; however, piezoelectric motors are not MRI-compatible. Piezo motors operate at voltages unsafe for patient and interfere with the functionality of the imager. Magnetic resonance imaging sequences may not be selected based on imaging requirements but are limited by compatibility. Their applicability is also limited to low magnetic field scanners. Piezoelectric actuation is a compromise with limited applicability, which has been used in the absence of a better solution.

Pneumatic actuation is a fundamentally flawless option for MRI compatibility.[17] The German research group from Institute for Medical Engineering and Biophysics, Karlsruhe, was the first group to realize this after multiple unsuccessful attempts with piezo actuation.[23,24] Their last version used a cylinder for driving an end-effector axis,[20] and their report gives a well-reasoned presentation of these advantages. It is sad that this outstanding German institute is no longer active, but fortunately, a spin-off company was created (Innomedic, Germany).

The major limitation of pneumatic actuators in general has been their reduced precision in controlled motion.[25] Pneumatics is traditionally used for free spinning motion such as drills (MRI-compatible[26]) or in industrial automation such as opening and closing gates. Pneumatic motors (turbine or cylinder based) are fast and powerful but notoriously hard to control for precise motion. In MRI, pneumatic servo control is even more intricate because long hoses are needed for the connection to the valves. The compressibility of the air in the hoses coupled with the friction of the actuator and valves makes the system highly nonlinear, hardly manageable, and susceptible to small disturbances and raises significant safety concerns for use in medical applications. A system currently under development considers the use of piezoelectric valves, which would allow for placing the valves closer to the scanner to shorten the hoses.[27]

In any case, the main safety concern for using cylinders in medical applications is that these are direct drive actuators. If malfunctioning, direct drive systems may swiftly spring off, fully and quickly unwinding and potentially hurting the patient or personnel. Direct drive robots are being used in industry for their fast response, but those are typically fenced. Direct drive robots are not recommended in medical applications.[16] Medical applications require small, slow, precise, and safe actuation. No classic pneumatic motor could collectively satisfy the reliability, precision, and safety required for a medical robot.

Few other actuators were used. A group from Switzerland has recently reported developments on using hydraulic actuation[28] and is advocating the advantages of hydraulic master-slave coupling.[18] Moreover, the group has also reported on optical force sensors developments. Fluid leakage is always a major concern with hydraulic actuators, but if reliably controlled, hydraulics is a very promising solution because it could be made nonmagnetic and dielectric as required for full MR compatibility.

Rather than coping with the incompatibilities of piezoelectric motors, trying to manage the existing types of pneumatics, and avoiding known engineering problems, the Johns Hopkins Urology Robotics Laboratory chose to create a new type of motor specifically for clinical applications, that is, the PneuStep Motor, which is a breakthrough technology for MR compatibility.[29] The off-the-shelf motors are not made of MRI-compatible materials, and none of their principles were adequate. The precision of motion, noninterference with the MRI, and medical safety requirements could not be met collectively.

The PneuStep motor is a pneumatic step motor (Fig. 1). Directional motion in incremental steps is controlled by a signed digital input. Stoianovici et al[29] shows the closed loop control of the PneuStep motor. Motion is controlled from a standard step motion control card (MCC). A special electronic driver was designed to cyclically actuate 3 binary pneumatic valves based on the pulse and direction signals of the MCC. Three air hoses drive the new motor. Directional step motion is achieved by sequentially pressurizing its 3 ports, with pneumatic commutation pressure waves. Internally, a new

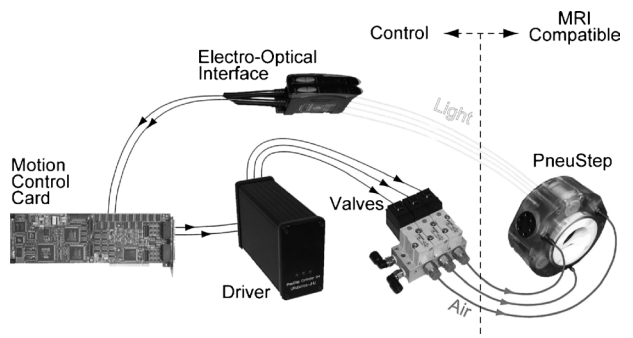

FIGURE 1. PneuStep motor schematic diagram: a pneumatic stepper motor with optic feedback. An easily controllable, precise, reliable, and safe actuator purposely developed for MR interventions.

mechanism is used to convert the pneumatic waves in a stepped, high-precision, rotary motion. The basic motor is rotary, but the built-in gear-head transmission can be configured for either rotary or linear output of various step sizes. As for electric steppers, the motor could be controlled open-loop. However, for medical safety, the motor was instrumented with sensors. These measure the motion of the motor and can be used either for control feedback or as a redundant sensor. The sensors are optical and are connected with fibers. An electro-optical interface connects the sensors back to the MCC transmitting quadrature encoded signals. This closes the feedback loop. The motor was also designed with fail-safe operation as a hardware characteristic. In case of malfunction, it may only stall but not unwind.

The PneuStep is entirely constructed of nonmagnetic and dielectric materials: plastics, ceramics, crystals, and rubbers. It operates on air and light and is electricity-free. The motor operates precisely and without interfering with the MRI, even if located at the image isocenter of virtually any magnetic field imager (shown later). Four long hoses connect the motor to its control in an adjacent room. Three of these carry air and the fourth carries optic fibers.

Unlike other pneumatic motors, the stepper achieves easily controllable precise motion independent of the supply pressure. Moreover, it satisfies the combined imager compatibility, medical safety, and reliability required for precision MRI instrumentation for clinical applications.

Image-to-Robot Registration

For any type of image guidance, a most important component affecting the precision with which the instrument is guided based on the images is the mapping of the image and instrument spaces, commonly referred to as the registration. Several registration methods have been proposed, generally grouped in 2 categories: methods that use the gradient field of the MR equipment to determine the location of a sensor mounted on the instrument typically called active marker methods and more common methods that use fiducial markers placed on the instrument for observing it in the image and calculating the position of the instrument in the image space. Generally, gadolinium-doped water markers, which create clear signal on the MR image, are used as passive fiducials. Passive fiducials with specific geometry are placed on the instrument/robot, and the MR image of the robot is taken. The image of the fiducial is recognized in a more or less automatic manner by an image processing algorithm. Several registration methods have been proposed for obtaining the registration mapping based on imaged fiducials. The most general perhaps is the image-to-model method, in which the known geometry of the fiducial (the model) is superimposed over the segmented geometry of the imaged fiducial (the image). The transformations (rotations and translations) applied to one of these geometries in the overlap process conduct to the mathematical estimation of the registration mapping, which is typically represented in the form of a 4×4 transformation matrix.

If a target is selected in the image, the registration gives its correspondent in robot coordinates, which, if passed through the inverse kinematics of the robot, gives the position of the robot required to aim the robot to the target. Vice versa, if the robot is reoriented, the registration could tell what image point it targets. Registration is a one of the most important factors in image-guided navigation.

In general, both the active marker and the fiducials are capable of providing good registration results. The main advantage of the active markers is that, in addition to the registration, these also provide continuous position measurements that are very instrumental in the navigation process. With fiducial markers, the registration is performed typically once at the beginning of the procedure and, after navigation, is robotic or tracked with other methods. Despite these advantages, the active marker has seen limited applications because its structure and calibration are highly dependent on the MR scanner hardware, creating a serious obstacle for the interscanner portability of the device.

MAGNETIC RESONANCE–GUIDED PROSTATE INTERVENTIONS WITH SPECIAL PASSIVE DEVICES

A few studies investigated direct MR-guided needle interventions despite the limited access within the scanner and the lack of remotely controlled instruments.

Dr Menard at the National Institutes of Health (Bethesda, Md) performed several high-dose brachytherapy cases using a needle template guide registered to the MRI.[30] The study not only demonstrated both the feasibility and advantages of MR guidance but also revealed the need for remote instrumentation because numerous table moves were required to access the patient.

Drs D'Amico and Tempany at Brigham and Women's Hospital performed numerous transperineal biopsy and brachytherapy in a 0.5-T open MR scanner.[31] They also reported a transperineal prostate biopsy in a patient with recurrent PC after brachytherapy[32] and showed that MR guidance was useful for targeting.

In Germany, 2 studies reported MR-guided biopsies in patients with elevated PSA levels and without previous TRUS-guided biopsies[33] and for repeat biopsies.[34]

Also, at the National Institutes of Health, transrectal MR-guided prostate biopsies and brachytherapy were performed in a closed-bore 1.5-T scanner.[35] A custom endorectal MR probe incorporating an imaging coil, special position tracking coils (active marker), and a needle guide was used.[36–38] Position tracking from the coils is used to calculate the desired orientation of a needle guide. On the basis of this information, the physician manually adjusts the device and inserts the needle. A recent report showed improved cancer detection in MR-guided biopsies but only for patients for whom the repeat biopsies were not immediately after the TRUS.[39,40] One of the limitations of passive devices is dependence on manual operation.

MR ROBOTS

The earliest work on the development of MRI-compatible robots has been performed at the Brigham and Women's Hospital, Boston, Mass, in collaboration with AIST-MITI,

Japan.[41] A robotic intervention assistant was constructed for open MRI to provide a guide for needles and probes.[42] To minimize image interference from the piezo motors, the robot had to be located distally, at the top of the imager between the vertical coils of the MRI. Long arms extended to reach the isocenter, which made them flexible and less precise. Work has continued[43,44] but with the same actuation. The system assists the physician by positioning a needle guide for manual needle intervention. Applications included prostate biopsy and brachytherapy.[45] The system works with open MRI that reduces imaging capabilities.

Another MRI-compatible needle insertion manipulator was built at the Medical Precision Engineering laboratory of the University of Tokyo.[46] The system was designed for neurosurgery applications and tested in vitro. The same group has also designed a neurosurgical microforceps manipulator.[47] Washington University in St Louis, Mo, is also working on a prototype for interventions in the abdominal and thoracic cavities.[48] All these use piezoelectric motors.

The Institute for Medical Engineering and Biophysics, Karlsruhe, Germany, reported several versions of a robotic system for breast lesion biopsy and therapy under MR guidance.[23,24] Piezoelectric motors were also used and were located in a driving unit distal from the high-intensity magnetic field.

In April 2007, the University of Calgary in collaboration with MacDonald, Dettwiler and Associates Ltd, Canada (who constructed the CanadArm for National Aeronautics and Space Administration and the International Space Station), has reported the development of an MRI-guided neurosurgical assistant with bilateral arms, NeuroArm. They reported that hydraulic actuation was excluded primarily because of potential fluid contamination at the operative site, and piezoelectric motors were chosen. In addition, the manipulator includes numerous metallic components, electric sensors, and apparent wirings. Unfortunately, neither imager compatibility data nor MRI images taken with the robot in the field were reported,[49] so its ability to work in the MRI remains unclear.

The German company Innomedic has developed a pneumatic robot for general computed tomography– or MRI-guided needle procedures.[50] Although this uses pneumatic cylinders that are notoriously difficult to control and unsafe for clinical applications, the company developed a very ingenious pneumatic cylinder to cope with these deficiencies based on the idea of exploiting a high sliding friction for a relatively low stiction. The robot attaches to the mobile table of the MR with an arch structure over the patient, presents 5 degrees of freedom (DOF), and uses optical encoders, and image registration is performed by using passive fiducial markers. The robot is made for abdominal access, so it can not be positioned in the scanner for prostate access. However, a group from Frankfurt, Germany, has recently used the system for targeting the prostate on the transgluteal path in a cadaver experiment.[51,52] This path of needle insertion is much deeper than transperineally (~14 cm reported in the cadaver experiment) and a 15-G needle was used to prevent deflections. Nevertheless, the Innomedic is fully MRI-compatible, it is the first commercial MRI-compatible robot, and it is cleared for clinical use in Europe.

Another system was developed in Switzerland. Gassert et al[28] used hydraulics directly connected in a back-to-back master-slave operation. A substantial advantage of the approach is that the hydraulic transfers forces reflecting the action of the manipulator to the user and vice versa, so enabling force feedback. Optical sensors are also used. The system is designed for functional MRI in neuroscience.

A light puncture robot has been developed in Grenoble, France.[53] This was designed for abdominal and thoracic percutaneous intervention under MRI or computed tomography image guidance. The robot has been designed to be placed on and supported by the patient's body. This design provides intrinsic compensation to the physiological motion of patient's body surface such as respiratory motion. Yet, this also makes image registration, guidance, and navigation difficult. The robot presents 3 DOF. Actuation is provided by an original design based on a clocklike mechanism that is perhaps just a few steps short of being a great candidate for MR compatibility. During the operation, the robot is placed on the patient and enters MRI scanner with the patient. The position and orientation of a needle guide is determined by imaging fiducial markers attached to the robot.

The invention of the PneuStep motor allowed us to develop a fully automated MRI Stealth robot, MrBot.[54] MrBot is designed for transperineal needle access, and its architecture is been optimized for prostate access (Fig. 2). The space in closed-bore MRI scanners alongside the patient is very limited. Previous clinical trials[30] revealed that perineal access legroom is gained if the patient is positioned in the MRI head first in the left lateral decubitus position.[30]

MrBot is also multi-imager–compatible,[17] compatible with all classes of imaging equipment (ultrasound, x-ray, and MR-based imagers). All robotic components are constructed of nonmagnetic and dielectric materials. The sensors are optic, so that the entire robot is electricity-free.

A needle driver was made to automatically place brachytherapy seeds. The robot presents 6 DOF: 5 DOF for positioning and orienting the injector and 1 DOF for setting the depth of needle insertion. In addition, the needle driver presents several other DOF for operating the needle, stylet, and loading the markers. The robot is constructed in the form

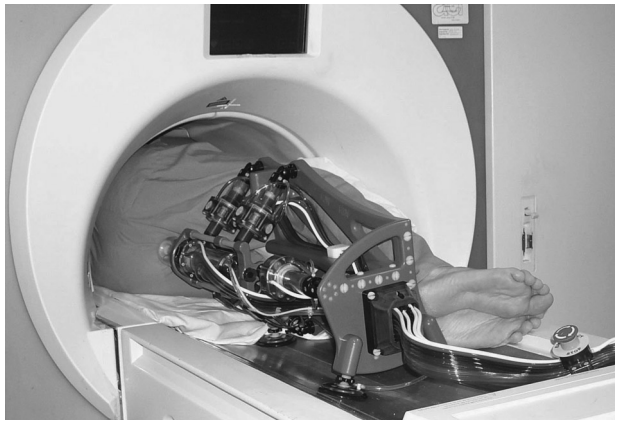

FIGURE 2. The Johns Hopkins MrBot.

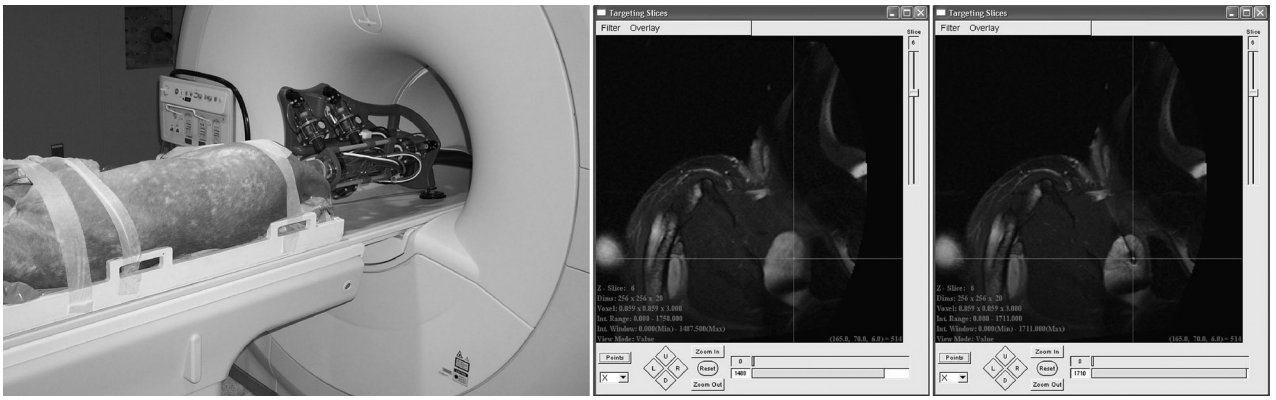

FIGURE 3. MrBot animal tests: setup (left), target definition (center), and needle at target (right).

of a platform supported by articulated linear actuators in a 5-DOF parallel link structure, which is known to have outstanding rigidity as needed for targeting precision.

The MrBot is invisible in MRI, but a high-contrast marker was built in the robot for registration purposes. The marker is located on the front part of the robot, in close reach of the imaging field and filled with MRI contrast (radiance imaging liquid, MR-SPOTS; Beekley, Bristol, Conn). The accuracy of registration using 3 different registration methods including the classic image-to-model method shows targeting errors due to registration to be as low as 0.3 mm.[55] Image-targeting experiments show mean vector norm errors of 1.145 mm with 0.41 mm SD.[55] These cumulate robot errors, image registration errors, needle bending, deflections of the mockup during needle insertion, errors of releasing the markers (commonly known as seed migration errors), imaging errors, and marker position estimation errors (Fig. 3).

The robot was tested on a canine model under the guidelines of the local Animal Care and Use Committee (ACUC).[56,57] Muntener et al[57] show the sedated animal in a 3-T scanner with the robot in place. Two SENSE Flex-S coils (Philips, Andover, Mass) are used on the lateral sides of the dog. Images were acquired for registration, organ visualization, and target specification. A target was selected by clicking an image point of the prostate. The robot automatically oriented and then inserted the needle remotely operated from the control room. The 2 MR images show the marked (target definition) and aimed target of the prostate. The void of the needle path and the artifact at the needle tip are visible. The needle targeting error was less than 1 mm. This is an impressive result because dog's prostate is highly mobile. Fast needle insertion was used for reducing soft tissue deflections.

The ultimate MR target of the robot for prostate biopsy purposes will most likely be provided by advanced multiparametric examinations such as MR spectroscopy, diffusion-weighted imaging, and dynamic contrast-enhanced MRI. Robotic targeting tests are being conducted for aiming simulated cancer lesions.

Mockups have been built with metabolites (citrate 26.5 g, choline 1.4 g, creatine 1.2 g, NaCl 3.5 g, and H_2O in a 100-mL solution), covered in wax and submersed in a gelatin base, and imaged with MR and spectroscopy. Figure 4 shows that the overlaid voxels and spectral signatures of the metabolites are distinctive from the gelatin base and can be directly used for robotic targeting tests. The homogeneity of the magnetic field is not affected by the presence of MrBot in the scanner's bore allowing acquisition of spectral data from tissues. On the basis of the promising preclinical data, the project continues with a pilot clinical feasibility study for MR-guided biopsy.

SUMMARY

The most challenging problem in PC care today is the inability to accurately assess cancer location, volume, and aggressiveness in individual patients. Imaging could play a significant role in achieving this goal, but all the current PC imaging techniques still require further validation. A precise image-guided biopsy approach would allow for a direct

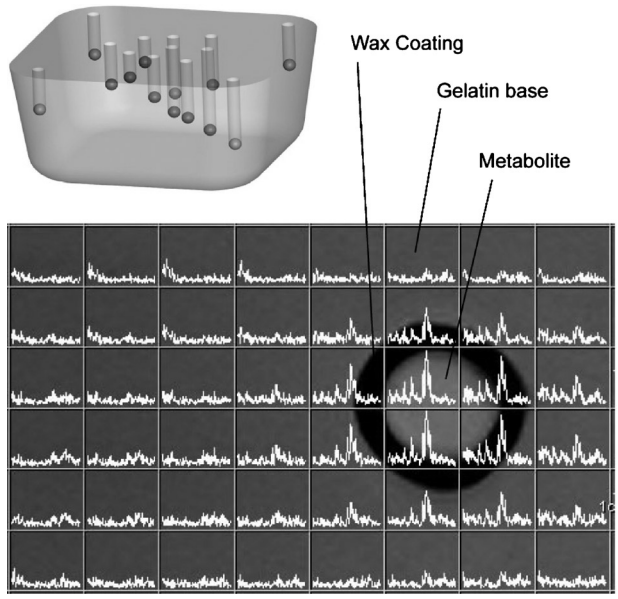

FIGURE 4. Metabolite solution in wax shell suspended in gelatin base. The image is an anatomic MRI with overlapped spectral voxels.

analytical correlation of the imaging abnormality and pathologic lesion. Currently, these correlations are typically performed only on radical prostatectomy patients who are imaged preoperatively and who experience difficulty in aligning the imaging data with the step-sectioned histopathology of the resected prostate. Having the exact in situ location of the tissue samples would also allow for repeat imaging of the sites and their matching to the pathologic lesion known from the robotic biopsy. New genomic and proteomic biomarkers could be combined with imaging biomarkers to better characterize the aggressiveness, distribution, and containment of PC within the gland. With very few exceptions, all MR robots use piezoelectric actuation. These were constantly confronted with image deterioration problems, various methods being derived to cope with image interferences, but these were never eliminated. Piezoelectric motors may not be operated close to the image isocenter and this typically translates to distally located robots which are less precise. As technology matures, a precise imaging guidance during prostate interventions with MR-compatible robot may provide the solution of the future; such an instrument would become a valuable clinical tool for biopsies directly targeting imaged tumor foci and delivering tumor-centered focal therapy.

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