Abstract — Robotic manipulators have emerged and are continuously evolving as a valuable tool in medical applications. This work introduces a new biomedical application for robotics: multimodality imaging by facilitating scanning of spatially localized bio-sensing and co-registration. Established or currently emerging molecular and near cellular modalities, such as optical and magnetic resonance spectroscopy, offer new opportunities for assessing tissue pathophysiology in situ. The limited tissue penetration of those modalities can be addressed by locally placing the sensor, i.e. with a minimally invasive trans-needle or trans-catheter approach. Herein, we describe the use of a robotic manipulator to scan the area of interest by carrying such a sensor for generating 1-D scans while registering them to a guiding modality. The approach is demonstrated by using a miniature RF coil for collecting proton MR spectra (MRS) and scanning an area of interest on phantoms with the manipulator. MRI is used to guide this procedure as well as co-register MR imaging and spectroscopy. LineScans on two compartment phantoms demonstrated a clear spatial distribution of the resonances originating from those compartments in agreement with the scout guiding MR images. The system described herein, is a generalized platform for performing MR-guided multimodality and multilevel sensing.

I. INTRODUCTION

Recent advances in the assessment of the molecular and cellular features of lesions in vivo and the concurrent emergence of molecular and near-cellular imaging as well as the spectroscopy modalities offer new opportunities in basic research and clinical diagnosis, such as the possibility for assessing the malignancy of a tumor in situ (e.g. [1, 2]). In addition, it is well recognized that, in several clinical paradigms, multimodality approaches are more appropriate for the collection of complementary diagnostic information (e.g. in the case of breast cancer [3-5]). However, molecular and cellular level modalities, such as optical coherence tomography (OCT) and light induced fluorescence (LIF) [6], have limited tissue penetration (~2 mm). Likewise, spectroscopic methods such as magnetic resonance spectroscopy (MRS) may have low signal sensitivity, especially if it is localized in a small volume of tissue. In particular, to address the low penetration or sensitivity of those “Limited field-of-view (FOV)” modalities, trans-catheter and trans-needle approaches are used. As an example, in the field of MR to address the limited inherent sensitivity of the modality, miniature radiofrequency (RF) coils, have been used for intra-vascular [7], intra-rectal [8] and intra-urethral [9] access. Besides, to guide the placement of the Limited-FOV sensor, the area is imaged with a conventional imaging technique that offers far higher tissue penetration; such “Wide-FOV” modalities can be magnetic resonance imaging (MRI) or ultrasound [2].

The possibility to combine modalities that interrogate tissue at different levels, from the molecular to the macroscopic level, is a unique opportunity which however faces three challenges for in situ applications:
(a) Localization of a Limited-FOV sensor,
(b) Scanning one or more large area of tissue with the Limited-FOV sensor(s) to assess different types of tissue and inhomogeneities, and
(c) Ways for multimodality co-registration and co-visualization.

It is conceivable that, robotic methodology may address those challenges. A robotic manipulator can carry the Limited-FOV sensors and spatially scan by mechanically relocating those sensors. In addition, traditional methods that are used in surgical robotics can be adopted to facilitate co-registration of the different modalities.

To harness the potential power of multimodality imaging, in this work, we present a new application of robotics in multimodality imaging or bio-sensing in general based on the following aspects:
—Use a robotic manipulator to carry and mechanically scan an area of interest with one or multiple Limited-FOV sensor(s).
—Incorporate imaging with a conventional macroscopic level Wide-FOV modality to scan and identify the area where the robotic manipulator mechanically scans with the Limited-FOV sensor.
—Spatially registration of the robotic manipulator relative to the Wide-FOV modality and the use of forward
kinematics to spatially register the areas where the Limited-FOV collected.

- Based on the above registration of the robotic manipulator and the Limited-FOV, co-register the Limited-FOV scan with the Wide FOV images. Thus, generate inherently co-registered multimodality data.

In particular, in this proof-of-concept work we selected conventional MRI as the Wide-FOV and proton MRS for the Limited-FOV modality, performed with a 1.1 mm wide miniature RF coil (i.e. the antenna for collecting localized MR spectra). An MR-compatible manipulator was designed and constructed to carry this RF coil, localize spectra along the axis of the manipulator phantoms, thereby generating one-dimensional (1D) MR spectra (herein referred to as LineScans).

II. METHODS

A. Overview of the System:

The system is composed of several interconnected hardware components and software modules. Fig. 1 illustrates the architecture of the LineScan system, which is composed of four primary elements: the computational core, its hardware, its manipulator and the MR scanner. The computational core is composed of the LineScan Human Machine Interface (HMI) and the software modules. The HMI has a graphic user interface (GUI) that provides the operator with the graphical tools and appropriate routines for co-registration and acquisition planning. The hardware module performs closed-loop control of the actuator of the manipulator using feedback signals from optical encoders, and communicates with the MRI scanner for synchronizing motion and scanning via triggering signals.

The MR scanner is the data acquisition component for both the Limited-FOV and the Wide-FOV modalities. The MR scanner, as the guiding modality, provides a global view and the position of the area that is scanned, and provides the needed global coordinate system for co-registration of modalities as well as the manipulator. The latter function is an essential part of the LineScan system, since the global coordinate system of the MR scanner is used for (1) registering the initial position of the sensor, (2) calculating the transient position of the sensor, (3) consequently, registering and knowing the positions where data is collected with the Limited-FOV sensor. As an outcome, the modalities are inherently co-registered and thus, methods for co-visualization can be implemented. All studies were performed on a Varian DirectDrive 4.7 Tesla MR scanner (Varian NMR Systems, Palo Alto, CA, USA).

The computational core of the system performs all data management and communicates with the MR scanner by means of the dual-triggering mentioned above via a Data Acquisition Unit (DAU). This triggering mechanism facilitates unsupervised scanning protocols. A log file is also created during the scan to save date, time and coordinate of each data collection instance.

In our experiments, for mobility, the host PC was a Laptop that is running the planning GUI and control software. The host PC is connected to the MC-1000 motor controller (MC-1000, New Scale Technologies Inc., Victor, NY) via a serial port and to a DAU (DI-148U, DATAQ Instruments Inc, Akron, OH) via a USB port. As illustrated in Fig. 1, this data acquisition unit is used for performing a dual triggering scheme: (1) a TTL pulse is sent to the MR scanner to initiate the acquisition of an MR spectrum, (2) a TTL pulse is acquired from the MR scanner after collection of the spectral data, consequently the Limited-FOV sensor (i.e. the miniature RF coil) is translated to its next position.

Registration and control of the core software are developed on Matlab (Mathworks, Inc., Natick, MA), using the ActiveX library for the motor controller (NstSquiggleCTRL ActiveX by New Scale Technologies) and the ActiveX control interface for communication with the DAU (UltimaSerial by DATAQ Instruments Inc.). The dual triggering scheme is implemented by running two coaxial cables from the DAU to the MR scanner controller.

B. Design, Prototyping and Control

An MR-compatible manipulator was designed and constructed to carry the miniature RF coil, localize spectra...
along the axis of the manipulator phantoms, thereby generating one-dimensional (1D) MR spectra (herein referred to as LineScans). In its current form the method was tested with a trans-needle approach. Therefore, the system was implemented with only 1 DOF for linear translation along the axis of the needle. It should be noted that oblique orientations of scanning can be achieved by carrying and aligning the needle by means of a robotic manipulator to access a targeted tissue at any desired trajectory.

The manipulator was first designed with a 3D modeling software (Autodesk Inventor, Autodesk Inc. San Rafael, CA). On the 3D model, we included all components and optimized its design. The device was then physically prototyped using a rapid prototyping machine (model: Prodigy Plus, Stratasys, Eden Prairie, MN). The construction material is acrylonitrile butadiene styrene (ABS, a non-magnetic and non-conductive MR compatible material). Parts were individually built and then assembled to the final form as shown in the photograph in Fig. 2.

For actuation, piezoelectric Squiggle motors (SQ-100 NM, New Scale Technologies, Victor, NY) customized for MR compatibly were used. Specifically, its shaft (i.e. a screw) is made of titanium, and its power wiring is shielded and 6 meters long, thus its controller (MC-1000, New Scale Technologies Inc., Victor, NY) and power driver could remain away from the magnet of the MR scanner. Although this motor was proved to be MR compatible as it is reported in the Results section, it possesses a critical limitation: it is not capable of pulling or pushing to backward, as it designed “push forward” only. Thus, for reverse motion, we used a rather simple implement: a stretched elastic band (since we couldn’t locate suitable MR compatible spring)

In the preliminary prototype as Limited-FOV sensor we used the miniature RF coil shown in Fig. 3. This was a four turn solenoid RF coil, with a diameter of 1.1 mm and a length of 1.2 mm that was attached onto the end-effector (i.e. the distal end of the manipulator). This coil was made of 32 AWG shielded magnet wire, and was connected to a tuning and matching circuit via a 15 cm long and 1.2 mm thick semi-rigid coaxial cable (Micro-Coax, Pottstown, PA). The balanced tuning and matching circuit was made with variable non-magnetic capacitors (Johanson Manufacturing Co, NJ) for fine tuning and matching at proton Larmor frequency of 201.5 MHz, operating at a 4.7 Tesla scanner.

C. Closed Loop Control

For the closed loop control of the manipulator two types of MR compatible optical sensors are developed to provide the needed feedback signals: (1) a quadrature linear optical encoder for location feedback (Fig. 4(a)), and (2) stop-switches (Fig. 4(c)) at the ends of motor stroke to prevent over extending the motor shaft. Both sensors are made MR-compatible by placing the electronics (Fig. 4(b)) at a distance of 7 m from the magnet of the MR scanner and using 7 m long optical fibers (OF) to connect the circuitry to the sites of sensing (remote sensing). The in-house developed quadrature encoder circuit, shown in Fig. 4(b), is constructed using two light emitting diodes (LED) and two Photo-activated Schmitt Triggers (PAST). The LEDs are model IF E97 and the PASTs model Photologic Detector IF D95T (both from Industrial Fiber Optics, Inc., Tempe, AZ); the optical fibers are ESKA SH 3001 (Mitsubishi Rayon Co., Japan). The encoder strip has 0.25 mm wide alternating transparent and non-transparent slits and is attached onto the moving component of the manipulator (Fig. 4(a)).

With the circuit shown in Fig. 4(b), light emitted from the LEDs is transferred via the OF to the encoder interface that is fixed on the static base of the manipulator. The light passes through the slits on the encoder strip and reaches the PASTs via the return OF. When the moving component is actuated, the two PASTs generate two lagging square wave signals due to the modulated light which is used to determine the extent and direction of the motion. Those PAST-generated square waves are directly fed to the quadrature decoder of the MC-1000 motor controller, stored into its register and then used by the closed loop control. The incremental digital quadrature encoder provides relative location information with respect to time, by incrementing or decrementing the corresponding register during the motion.

The same principle of operations applies to the optical stop-switches (Fig. 4(c)). Its circuit has one LED that provides light to a transmit-OF and two OF that return light to two PAST. The transmit-OF is attached onto the moving component of the manipulator. Each return-OF is attached onto one of the motion extremes on the static component of the manipulator. When the moving component reaches either
one of the extreme positions, active low signal is generated and the motor is blocked.

D. Co-Registration

To co-register MR images and MR spectra using the mechanical coupling provided by the robotic manipulator we used the inherent coordinate system of the MR scanner. Using this approach makes the system versatile and robust for using other types of Limited-FOV for co-registered scanning. To achieve this co-registration, we registered the initial position of the device to the MR coordinate system, and then the transient position of the Limited-FOV probe is calculated from the relative motion that is acquired from the signals of the quadrature linear optical encoder (Fig. 4).

The implemented registration is straightforward. Locating the initial position \( (Z_0) \) of the manipulator was performed by using the miniature RF probe as a fiducial marker (i.e. the Limited-FOV modality sensor) and collecting a sagittal image to view the Z-axis (i.e. along which the manipulator was scanning). Fig. 5(a) shows a representative example of such a registration image. Note that the signal is shown only from the sensitive area of the miniature RF coil that is far smaller than this collected with a volume RF coil (Fig. 5(b)). The projection of the image was then calculated to determine the center of the miniature RF coil that was assigned as \( Z_0 \).

Subsequently, the transient position \( (Z_N) \) of the sensor was calculated based on the relative motion \( (DZ) \) known from the encoder reading. (i.e. \( Z_N = Z_0 + DZ \)).

E. Experimental Studies

The system was tested with experimental studies on a UNITYINOVA (Varian, Palo Alto, CA) spectrometer imager system. Studies were performed using two-compartment rectangular phantoms (39.6 mm x 44.6 mm x 89 mm), one filled with gelatin and the other with commercially available vegetable oil. The device, with its distal-end that carries the miniature RF coil into the phantom, was placed inside a volume RF coil for collecting scout images. Initially, scout images were collected and the device was registered to the MR scanner. Subsequently, the operator used the GUI (Fig. 5 shows example output of its windows) to plan the exact scanning protocol (region, steps and speed of motion). LineScan MRS were then collected by translating the miniature RF coil in steps of 0.5 mm; after each translation the control software triggered the MR

![Fig. 4. (a) The in-house developed optical encoder, its optical fibers (OF) and the encoder strip attached onto the base of the manipulator...](image)

![Fig. 5. Snapshots from the GUI of the HMI. (a) The registration window showing an MR image collected with the miniature RF coil. Such images, that clearly demonstrate the limited FOV with this coil, were used for registering the initial position of the probe to the MR coordinate system (b) The planning window, showing an MR image of the phantom collected with the volume RF coil (note that depicts a larger portion of the phantom). The window shows the initial and the last position of scanning with the manipulator.](image)

![Fig. 6. Stack plot of MR spectra collected with the LineScan from the phantom shown in fig. 5. The manipulator scanned the selected area every 0.5 mm along the Z direction. The boundary between the two compartments is at Z = 0.5 mm (identified by the vertical grid). The spectral axis shows frequency in parts per million (ppm). The different proton resonances of the gelatin and the oil compartments are clearly differentiated. The plot shows 29 out of 89 MR spectra.](image)
spectrometer to collect the free induction decay (FID) after a single excitation pulse (with a flip angle = 45°; bandwidth = 5000 Hz and number of points = 2048). All data processing was performed with routines of the HMI. For each set of experimental data, the initial position of the miniature RF coil was determined from the MR images collected with it, like the one shown in Fig. 5(a). Subsequently, the acquisition strategy file that was stored during data collection was loaded; the positions where spectra were collected were extracted and then stored together with the corresponding spectra in an array. The raw data were Fourier transformed and the 4.79 ppm frequency was assigned at the water peak from the gelatin compartment. The HMI provided different outputs such as stacked plots of the spectra (Fig. 6) and grayscale maps of integrated intensities of the spectra at operator selected frequency bands (as example Fig. 7). Images collected with the volume coil were also loaded plotted together with the maps (Fig. 7(c)).

III. RESULTS

The device demonstrated MR compatibility with insignificant effect on the SNR of the images, as well as the SNR and linewidth of the spectra. The SNR was calculated as the ratio of the signal intensity of regions-of-interest (ROI) placed on the oil and gelatin compartments, to the standard deviation of the signal ROI placed on empty space (no signal area). The SNR was then extracted for a series of gradient recalled echo (GRE) images acquired while the motor was idling and operating at a set speed. Then the SNR is reported as value ± standard deviation. Specifically, with the motor idling, the GRE images manifested an SNR for the gelatin compartment of 7.08 ± 0.10 and vegetable oil compartment of 5.72 ± 0.07. When the motor was operating at its set speed, the SNR of the gelatin was 6.79 ± 0.11 and of the oil compartment was 5.62 ± 0.06.

Fig. 6 shows a stack plot of proton MR spectra collected every 0.5 mm along the Z axis of the scanner. The transition from the gelatin filled compartment to this with vegetable oil is apparent at Z = 0.5 mm. This is manifested with the reduction of the water signal and the emergence of the signals originating from the oil compartment.

To appreciate the operation of the manipulator for generating 1D LineScans, Fig. 7 shows the integrated intensity of two spectral areas vs. the position of the coil along the Z axis. Those LineScans illustrate the presence of the boundary between the two compartments, as well as a transition zone between them. The width of the transition zone measured from the 1D LineScans (Fig. 7(c)) is the same to the one extracted from the images (Fig. 7(b)). It is also noted that the assignment of the Z coordinates was based on the initial registration of the device and then using the recorded motion values, calculated from the linear encoder recordings, and saved into the log-file.

IV. DISCUSSION

This work describes a new biomedical application for robotic technology: the end-effector of a robotic manipulator carries a Limited-FOV sensor and scans an area of interest of a tissue to generate 1-D spatial distribution of the sensor data (i.e. a LineScan). The robotic manipulator is registered relative to the guiding Wide-FOV, as shown in Fig. 5, then the 1D LineScan is also co-registered to the images of the Wide-FOV modality, thus multimodal fusion is made possible (i.e. in Fig. 7).

This approach was demonstrated using MR methodology and based on four elements: (a) the use of MRI for tissue-level imaging to identify the areas for scanning, (b) an MR-compatible computer-controlled actuated manipulator for trans-needle positioning of the “Limited-FOV” modality sensor, (c) registration of this device and, thus, of the miniature RF coil sensor to the MR images, and (d) linear scanning of the area of interest with the “Limited-FOV” sensor for the generation of MRS LineScans. Although invasive in its nature, such approach is characterized as “minimally invasive”. Minimally invasive diagnostic approaches are commonly practiced, including biopsies and optical imaging. As far as clinical applications, the merit of such minimally invasive approaches should be evaluated within the context of the potential diagnostic information that maybe collected versus its invasive nature. As an example, it maybe justifiable to use this kind of minimally invasive approach in such cases, that the patient is a candidate for an invasive diagnostic procedure, i.e. tissue biopsy. The particular sensor presented herein, i.e. a miniature RF coil for MR spectroscopy, maybe beneficial for spectroscopy at lower magnetic field scanners where the proximity of the coil would improve the inherent low sensitivity of the modality especially for applications at
lower magnetic field scanners, as example in the case of combining MRI and MRS in breast cancer [10-12].

This proof-of-concept work, although it demonstrated the principals of operation of the proposed approach, has some certain limitations:

--First, studies were only performed on phantoms; in vitro and in vivo studies are planned to further investigate the method.

--Second, a simple miniature solenoid coil was used for both RF transmission and signal reception. We are investigating other shapes of RF coils as well as the option for using the miniature coil for reception-only with an external RF coil for transmission.

--Third, while the particular motors are MR-compatible, they are sub-optimal since requires special design provisions as it operates push-only, and its titanium screw might cause artifacts when it comes closer to the imaged area of the sample. Currently, an alternative commercial linear actuator integrated encoder is investigated to address the above listed limitations.

In these studies, the proposed approach was demonstrated using proton MR spectroscopy as the Limited-FOV modality. It should be emphasized that the system was designed as an enabling-technology platform that can be adopted to carry and perform scanning with other types of sensors, such as endoscopic optical-fiber sensors to perform OCT and LIF optical modalities. In addition, miniature RF coils tuned to the Larmor frequencies of other-than-proton nuclei, for example phosphorous (31P) and sodium (23Na), can be used to assay biochemical processes in situ. This work demonstrates a new possible use of robotic methodology in medical applications with potential impact to patient management.

V. CONCLUSION

This work describes a novel application for robotics to facilitate multimodality imaging by carrying, spatially scanning and co-registering localized bio-sensing. This specific application of robotics was pursued to address a critical limitation of emerging molecular and near-cellular modalities; the limited tissue penetration. Specifically, we describe a robotic manipulator and associated implements for registration and data processing to scan to generate 1-D scans with bio-sensors. In this proof-of-concept work, the approach is demonstrated with a miniature RF coil for collecting MRS on two compartment phantoms. The described system is under further development for the incorporation of a range of miniature biosensors.

REFERENCES