Real-time Software Platform Design for *In-Vivo* Navigation of a Small Ferromagnetic Device in a Swine Carotid Artery Using a Magnetic Resonance Imaging System

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***Abstract*—Using an 1.5T Siemens clinical Magnetic Resonance Imaging system (MRI), a 1.5 mm diameter ferromagnetic bead is moved across a pre-planned path in the carotid artery of a 25 kg living swine. The software architecture for the navigation and path planning is herein described. Using the real-time feedback capabilities of recent MRIs, the device is moved, controlled and tracked using the magnetic gradients coils already present for imaging puporses. Navigation of the ferromagnetic device has been achieved with a peak velocity of about 13 cm/s through a set of pre established 11 waypoints. The dedicated software architecture presented in this paper lies in a modified real-time MRI imaging sequence. The dedicated architecture permits the navigation of the ferromagnetic bead with an operating frequency of 24 Hz Real-time control of the magnetic core is achieved through the implementation of a simple 2D PID controller incorporated in the presented software plateform.**

Keywords—**Real-time navigation, *in-vivo* procedure, magnetic resonance, software architecture, interventional procedure**

I. Introduction

Magnetic resonance imaging system has been widely used for interventional procedures coupling the high resolution physiological imaging capabilities with standard medical procedures. As such, many catheter based interventions are now executed under MRI supervision [1, 2]. Since MRI systems offer an increased SNR and resolution in physiological imaging, a significant amount of research on new interventional magnetic resonance imaging procedures is being carried out

However, catheter based procedures are limited by the size and flexibility of the tool itself, complicating the reach of smaller vessels in the human body. New emerging technologies are now suggesting smaller devices or particles able to attain the micro circulation vasculature level [3] in order to target specific sites for either drug delivery or contrast agents. However, as small as micro or nano particles become, none, to our knowledge, are able to be controlled in order to reach their destination which makes such devices, passive in terms of *in-vivo* navigation. The presented work takes place in a wider research context known as the Magnetic Resonance Submarine (MR-Sub) project [4] which aims at resolving these constraints with the use of untethered controllable ferromagnetic devices designed for minimally invasive *in-vivo* interventions. Through the use of a ferromagnetic core propelled, tracked and guided inside an MRI system, we propose an alternative technology which could overcome actual medical tools limitations as well as providing a fully controllable aspect for current nanomedicine main issues. Precedent results [5, 6] introduced feasibility tests in diverse MRI phantoms. However, recent advances allowed the validation of such new technology in an *in-vivo* environment [7].for which a dedicated software platform has been adapted and included in the considered MRI software environment This dedicated software environment presented here was used for the *in-vivo* navigation of a 1.5 mm diameter in the swine carotid artery is presented in this paper.

II. Methodology

A. System Overview

The MRI system considered for the *in-vivo* procedure is a Siemens Avanto 1.5T (Siemens Magnetom Avanto 1.5T, Erlangen, Germany) with real-time feedback capabilities. Using the magnetic gradients coils, a magnetic force is induced in the ferromagnetic material as described in [8] which allows the device to be moved in the considered environment. The propulsion force is proportional to the magnetic gradient amplitude, the device's volume and to the device's magnetization as expressed in [9]. Current maximum unipolar magnetic gradients amplitude is limited to 45 mT/m on the z axis and 40 mT/m on the x and y axis. Figure 1 illustrates the MRI standard coordinate system used throughout this paper.

The Avanto system consists of four distinct computers for

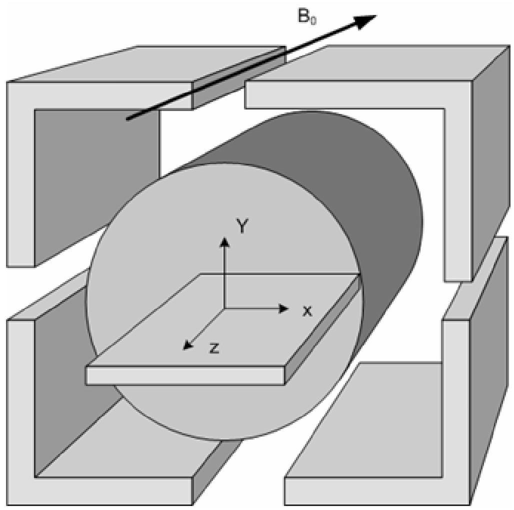

Fig. 1. Standard MRI system coordinate referential

the user interaction, sequence processing, sequence execution (the scanner itself) and data analysis. A standard MRI scan involves the execution of a set of instructions known as events in a micro second time frame precision which is repeated over time forming a sequence until the desired image is constructed. Common events found in a sequence are magnetic gradients, RF pulses and ADC events. On older MRI systems, image data are acquired by the scanner and then sent to a data processing computer for final image computation with possibility of a feedback interaction between the image computation process and the sequence execution. The MR-Sub project takes advantage of recent modern real-time MRI feedback capabilities which allows the image construction computer to react over the running sequence allowing the presence of a closed loop control infrastructure

B. . Software platform and navigation pulse sequence

The developed software architecture consists of a dedicated set of software modules integrated in a real-time sequence as described in [6, 10]. The pulse sequence is responsible for the application of propulsion magnetic gradients and the execution of the tracking sequence more thoroughly described in [8]. Since the tracking technique is based on a off resonance technique, no susceptibility artefacts are present on the acquired projections. Beside, the pulse sequence also contains a trigger event which remotely starts the execution of the control routine located on the data analysis computer. The elaborated software environment is responsible for the tracking, control, propulsion and path planning operations.

A path planning module is responsible for the placement of waypoints used as navigation beacons during the intervention. Once the animal is placed inside the MRI bore, a common angiography with gadoteridol (ProHance, Bracco Diagnostics, Mississauga, Canada) is executed in order to obtain a road map. Using an external visualization software (Volview 2.0, Kitware, New-York, USA) and a custom made plugins, waypoints are placed on the rendered volume obtain from the angiography. Once the path has been validated by the medical personnel, it is exported in a ASCII file for importation into the architecture prior to the intervention. Fig.3 illustrates the selected 11 waypoints used for the intervention. The path consists of a back and forth trajectory between the two positions. In fact, the 11 waypoints are scattered across 3 positions in space. After the first waypoint is reached, the subsequent 10 waypoints are distributed across a back and forth path formed by 2 waypoints. A total distance of about 15 cm has been traveled in the swine carotid artery.

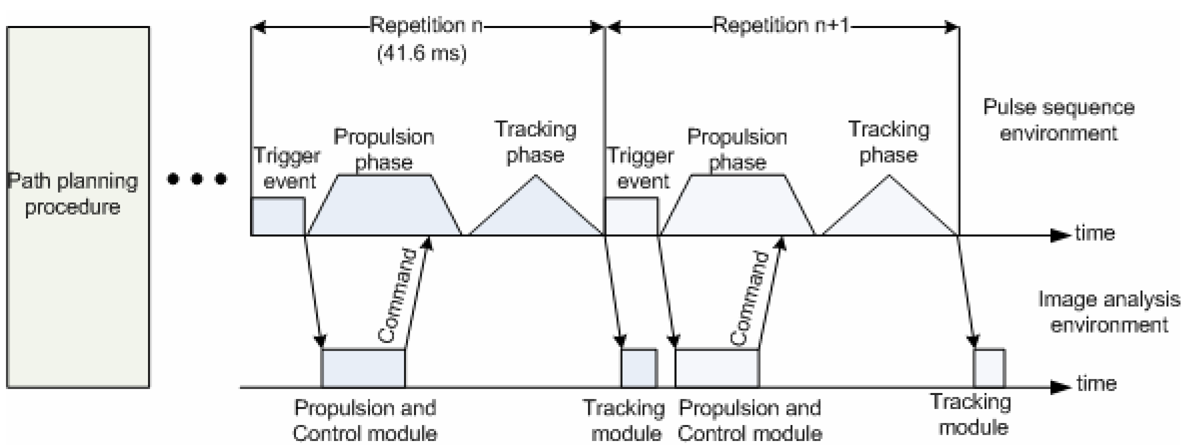

Fig. 2. Overview of the real-time pulse sequence for the in-vivo navigation procedure

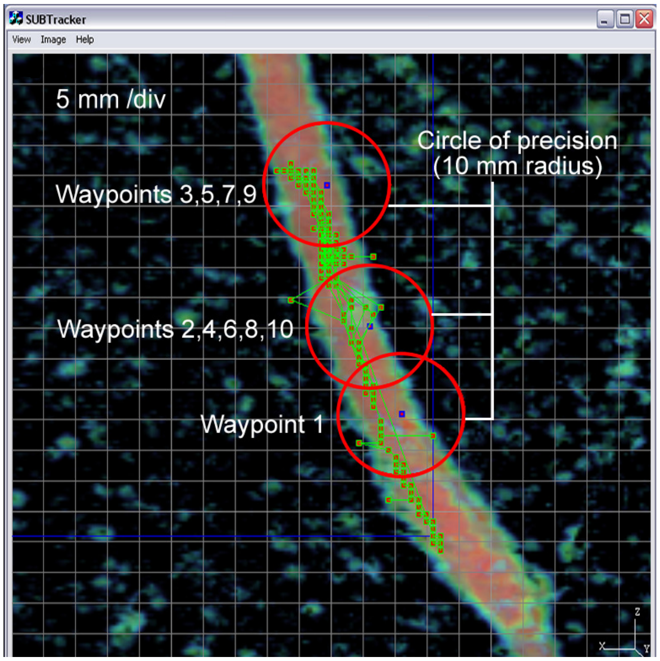

Fig. 3. Selected path for the *in-vivo* intervention

The propulsion and controller module contains the closed loop controller and is triggered during the beginning of each sequence repetition as illustrated in Fig. 2. The controller considered for the device navigation in the artery is a an adapted version of the previously presented 2D PID in [11]. The controller part of the module is responsible for the command computation based on the magnetic signature selective excitation tracking [8] technique data obtained during the tracking part in the pulse sequence as well as the chosen waypoints positions. Once the command is computed on the image analysis computer, it is sent back to the running sequence via the real-time feedback channel. The command which consists in magnetic gradient amplitude to be applied on each axis is executed during the next propulsion phase of the pulse sequence. In order to allow a certain tolerance in the achievement of the waypoints location, a concept of precision circle has been opted for. Around each waypoint position, a virtual circle with a user define radius is placed. During the intervention, if the device's position is inside the target waypoint precision circle, the waypoint is considered reached and the next waypoint is loaded in the propulsion and controller module.

The tracking module is responsible for the device position computation from the obtained projection tracking data. Once obtained, the device's actual position is sent to the propulsion and controller module for the next command to be computed during the next trigger located at the beginning of the real-time pulse sequence. Finally, a central agent is responsible for the synchronisation and real-time communication between the image analysis computer and the running pulse sequence

Figure 2 illustrates two repetitions of the real-time pulse sequence. The first event of the sequence is the trigger signal which remotely starts the controller command computation routine from the analysis computer. The duration of the trigger event is 0.6 ms. It is followed by a propulsion phase which lasts 19 ms. The applied magnetic gradients in this portion of the sequence is the last computed command from the controller and propulsion module located on the analysis computer. Finally, the tracking pulse sequence follows and terminates the pulse sequence kernel. This final phase lasts 22 ms and allows the 3D positioning of the device. During the tracking phase, each acquired projection data on each axis is sent to the tracking module on the image analysis computer via another set of trigger events. The whole process is repeated until the bead has moved across all selected waypoints.

III. Interventional Procedure and Results

The i*n vivo* procedure was performed on a 25 kg domestic pig under general anaesthesia (Pentobarbital). This assay study was pre-approved by the animal care and use committee. A short 5-F introducer is positioned in the left femoral artery and a 5 mm × 18 mm angioplasty balloon (AV100, Medtronic, Santa Rosa, CA) is advanced, prior to the intervention, under fluoroscopic guidance. Since this study was conducted to proove the faisability of such new automaticaly guided interventional procedure, standard fluoroscopic catheter placement was choosen in order to accelerate the intervention and prevent eventual complications with catheter positioning under MRI. The introducer is used as the release route for the magnetic sphere to be controlled whereas the balloon catheter is used to control the flow and eventually block the sphere in order to facilitate its retrieval at the completion of the control experiments. The angioplasty balloon was a supplementary safety measure which will be omitted once the navigation procedure will be refined and mature. The swine is then placed in the MRI scanner. A set of body array coils are used to collect the MRI signal. The device is brought into the MRI uniform region inside the catheter which safely constrains it before the release. A 6-F catheter is used to push the 1.5 mm diameter chrome steel sphere device in the carotid artery as soon as the procedure is started. The device is moved across the selected waypoints with a velocity ranging from 8.43 cm/s to 13 cm/s. A circle precision radius of 10 mm is set. Once the last waypoint is reached, the device stabilizes around its final position. The total repetition duration is 41.6 ms, leading to an operation frequency of 24 Hz. After the intervention, the bead is retrieved using a custom magnetic tipped catheter under a standard interventional pulse sequence (Trufi-irttt).

IV. Discussion

Since the bead can travel as fast as the peak flow velocity of 13 cm/s with an operation frequency of 24 Hz, a control cycle can thus be executed each 5.5 mm. In order for the device not to miss a bifurcation, path planning must be accordingly prepared to ensure that sufficient waypoints are present near steep turns or change in direction in order to allow a more precise control of the device. The pulsed aspect of the blood flow can be sustained with no major device position shift as long as the operational frequency of the controller is high enough and that the available magnetic force can keep the device steady during the peak blood flow velocity in the artery. Also, since the intervention was conducted in the swine carotid artery under general anaesthesia, the animal movement was not an issue. No major device position shift was observed due to the animal breathing movement since the procedure was conducted away from the animal lungs and thoracic cage.

For the presented *in-vivo* intervention and software environment, only a 2D control model is considered along the carotid artery. Indeed, the provided magnetic gradient coils are not strong enough to allow the levitation of the considered device. Although previous phantom experiments suggested that more complex in plane vessel configuration such as bifurcations could be navigated with no major complications under constant flow [10], such magnetic force limitation could be overcome by the use of stronger, custom made gradient coils allowing even more complex trajectories such as vertical displacement against the flow to be followed. However, the main goal of such technological breakthrough is to minimize the device's dimension in order to reach smaller vessel sizes such as capillaries (5-10 μm diameter) and due to scale effect, the gravitational forces are negligible compared to the drag force when considering nano or even micro devices.

V. Conclusion

A custom made software architecture allowing the automatic guidance of a 1.5 mm diameter ferromagnetic sphere in the carotid artery of 25 kg living swine was presented. The architecture allows the navigation of the device with an operational frequency of 24 Hz. The sphere is driven along a set of 11 waypoints, placed prior to the intervention. Through the use of a special feedback loop, a dedicated controller computes the required command in terms of magnetic gradient amplitude and direction based on the device's position and selected path to be achieved.

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