Low invasive therapy under robotic guidance in the vascular district: a case study

A computer-assisted robotic platform for soft-wired therapy of vascular obstructions

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***Abstract*—Integration between surgery and robotics leads to new paradigms in clinical field. Innovative robotic solutions represent the enabling technology for highly targeted therapeutic actions, such as operating in the cardiovascular system. In this framework, the authors present a robotic platform for the treatment of vascular obstructions. It integrates a system for locomotion and navigation based on magnetic dragging and ultrasound tracking and a therapeutic module which involves mechanical attack to the obstruction by means of high intensity focused ultrasound. The system overview and the technical and theoretical instruments for developing the overall platform were illustrated; preliminary results, together with future planned works, are reported in order to demonstrate the feasibility of the proposed approach.**

***Keywords*—robotic magnetic guidance, cardiovascular therapy, robotic-assisted surgery, ultrasound-based tracking.**

I. INTRODUCTION

In the last decade, surgery and robotics have reached a maturity which has allowed them to be safely translated in a new kind of operating room [1]. However, medical robotics is a young and relatively unexplored research field where the enabling technologies continue to evolve, leading to even new interventional scenarios. For instance, there has been a recent trend away from autonomous or semiautonomous surgical robots, toward synergistic manipulation and virtual fixtures [2]. Thus, the robot acts as a guidance tool, providing information to keep the surgeon on target, yet guaranteeing accurate tissue localization thanks to advanced imaging solutions.

Cardiovascular system offers a perfect room for such innovations. Different platforms and strategies are under development worldwide (e.g. [3]): robotic wireless or softly tethered approaches could answer the quest for miniaturization, and interesting devices have been already developed by exploiting the knowledge gained in different setting [4]. However, due to challenging environmental conditions (physiological flows and reduced length scales), transferring the same technologies into the vascular system is not straightforward. Moreover, locomotion and tracking into the vascular system are still ongoing research issues [5-7]. Finally, as regards therapeutic strategies, removing vascular obstructions is a dynamic field of research and different approaches have been proposed in the latest years [8]. Keeping in mind potentials, challenges and limitations of robotic approaches, we present here the system design and initial investigations of an innovative computer-assisted robotic platform for the treatment of vascular occlusions. The proposed platform integrates safe navigation solutions with advanced therapeutic strategies. More in details, the platform (Fig. 1) consists of two robotic arms, respectively holding an external permanent magnet (EPM) and an ultrasound (US) probe. The EPM drags an internal softly-tethered magnetic unit, while US provides the tracking of the device with the help of pre-operative imaging. A low level control ensures that the endovascular device is constantly in the US field of view and that the movement of the device is consistent with the desired path. Once the occlusion is reached, the device will be able to release micro-bubbles to facilitate lysis through an external high intensity focused US high intensity focused ultrasound (HIFU) transducer, which is expected to be integrated with the diagnostic/tracking probe. Micro-agents can be released from the magnetic device via the micro-tether, which will also act as a retrieval system for safety. It is worth remarking that the micro-tether will not have any structural function, thus preventing damage to the internal walls of the vessel and increasing system flexibility and steerability. Debris resulting from the action of US lysis should be smaller than red blood cells in order to be absorbed by the reticuloendothelial system; however, some large fragments can detach, thus causing risk of embolization. In our platform the fragments of blood clots, properly functionalized, will be collected and dragged to a safe area for further removal.

Based on the target pathologies and the actual capabilities of driving a softly-tethered magnetic device, the current platform will mainly address carotid arteries and vessels of the lower limbs.

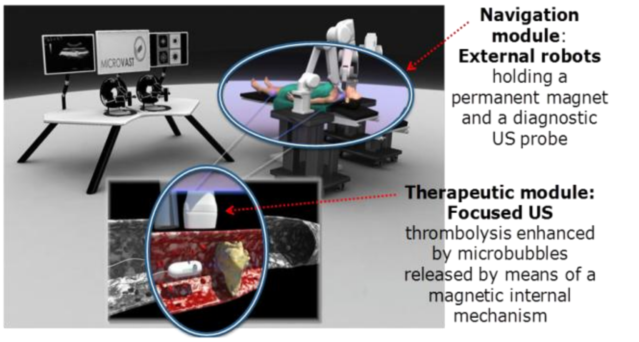

Fig. 1. Schematic representation of the computer-assisted robotic platform for softly-tethered therapy of vascular obstructions and operative modules.

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II. System Overview and Preliminary Results

In this section we discuss in details both the navigation and therapeutic modules of the proposed platform by highlighting the main features of the system and giving some preliminary results aiming to demonstrate the feasibility of the entire system.

A. Navigation module: locomotion and tracking

Combining the benefits of robot-aided magnetic navigation and US imaging, a methodology based on traditional Computer-Assisted Surgery (CAS) adapted to intravascular medical procedures has been developed for locomotion and tracking purposes. US-based intra-operative data, together with pre-operative lumen centerline reconstruction for optimal path definition, represent the navigation workflow for assisted or completely autonomous safe propulsion of an endoluminal device in cardiovascular procedures.

As schematically illustrated in Fig. 2, the robotic module for vascular navigation is composed by an EPM attached to the end-effector of a 6 Degrees of Freedom (DoFs) anthropomorphic robotic arm (RV-3SB, Mitsubishi Electric, Japan); a second anthropomorphic robotic arm with 6 DoFs (RV-6SL; Mitsubishi Electric) for holding and moving a US probe (CA430E; Esaote, Italy) for autonomous US-based servoing control; a human–machine interface (HMI) including an intuitive control peripheral; a softly-tethered endoluminal device with an internal permanent magnet (IPM). The interaction between the EPM and the IPM of the endovascular device is employed for propelling the softly-tethered endoluminal robot along the cardiovascular system while locomotion is supervised by the US-based methodology. In particular, an axially magnetized NdFeB N52 (remanence 1.48T) permanent magnet (KJ Magnetics, Jamison, USA) was selected as the EPM. It is 51mm in diameter, 25mm in thickness, and 0.4kg in weight. A rapid prototype miniaturized capsule (5mm in diameter, 10.6mm in length, and 0.75g in weight) equipped with a NdFeB N52 IPM, made up of 6 tablets, was developed as a first prototype for the vascular platform evaluation phase. Each tablet is axially magnetized; it has a diameter of 3.2mm and a thickness of 1.6mm [9]. The second robotic arm holds a US probe for a US-based control. The US probe is a convex array transducer with a working frequency between 3.5 and 5MHz and a radius of curvature of 40mm. With the aforementioned US system, an accuracy of about 0.2mm is derived by the entire acquisition and processing pipeline [10]. In case of assisted propulsion navigation modality, the operator can drive the system through a haptic input device (Phantom-Omni, Sensable Technologies, Wilmington, MA, USA) imposing motion commands to the robotic arm used for holding, moving, and orienting the EPM, while the second robot (holding the US probe) follows the motion of the endoluminal device for tracking purposes. In both the navigation modalities, the US-based tracking algorithm represents the navigation closed-loop control core for maintaining a reliable and effective magnetic link along the procedure. It consists of the tracking of the internal device by using a combination of features detection, optical flow and segmentation techniques. In particular, the algorithm segments the endoluminal device. On the segmented region of interest, the extraction of the object features and the knowledge of the

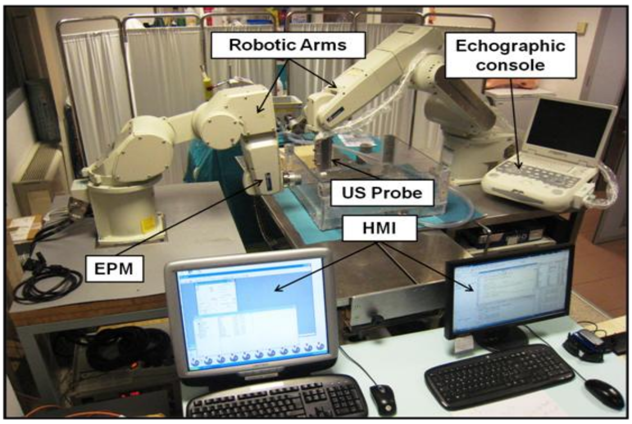

Fig. 2. Representation of the navigation module components.

intrinsic features dynamic state allow for the tracking of the object position and definition of the propulsion behavior. The US-based control loop is iterated until the end of the medical procedure in combination with the locomotion module for the cooperative control of the two robots. The two manipulators are moved together along the calculated pre-operative vascular path while a high-level algorithm calculates the endoluminal robot displacement and compares the device position with respect to an imposed action region centered in the US frame. If the endovascular device exceeds the imposed safe area, the procedure is retrieved in the previous state in order to maintain or to re-establish a reliable magnetic link.

Several preliminary trials were performed by dragging the magnetic capsule along an *in-vitro* vascular 3D mock-up by the dedicated software implementation, and tracking the endoluminal device by means of the US images mode control. The effectiveness of the magnetic dragging in well-defined operative conditions and the validation of the tracking of the device by the US-based algorithm have been assessed. The magnetic device was dragged by the EPM, in no-flow condition, with a velocity of 5mm/s and an average control loop time of 40ms, due to the US image acquisition frame rate. The tracking mode control algorithm enables a reliable trace of the endoscopic device and the accomplishment of the vascular task in the *in-vitro* conditions (Fig. 3).

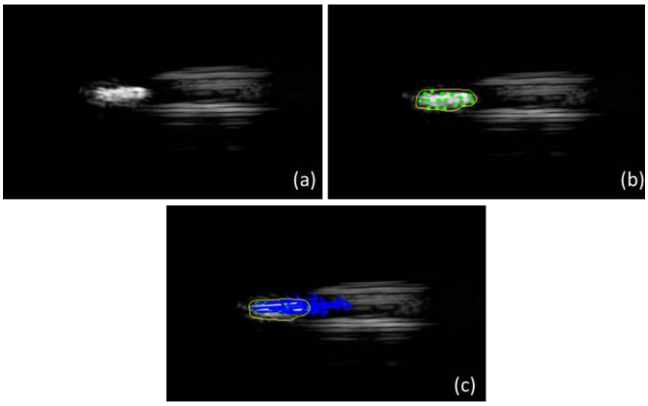

Fig. 3. US images of the tracking algorithm; the device at (a) $t=t_0$ and at (b) $t=t_0+\delta t$ is shown, where the detected features are represented in green while the segmented shape with the yellow line. The derived displacement of the selected features is visualized in (c) with blue arrows.

B. Therapeutic module

The aim of the therapeutic module is to remove vascular obstructions in order to restore physiological blood flow. Physical constraints of the environment and the required dimensions for magnetic locomotion make all those therapeutic strategies which demand bulky tools not suitable candidates. Considering the non-invasive, precise and fast dynamics of their action, external US are deemed to be an appropriate solution. The effectiveness of US in destroying thrombi has been demonstrated in several works (e.g. [11]) and important results have been achieved, mainly as an enhancement of chemical attack (by the addiction of thrombolytic drugs), both *in-vitro* and within some sound clinical trials [12]. However, limitations are related to the use of thrombolytic drugs, mainly due to their systemic effects. US thrombolysis without thrombolytic drugs has been proposed to overcome this limitation [13]. An in-house system has been developed to validate the therapeutic action of US in thrombolysis and to correlate the exposition dose to the generated effect. The system is able to map the US field generated by a commercial acoustic transducer. The acoustic field is generated by a HIFU transducer (Precision Acoustics, UK) with 1MHz center frequency, whose acoustic power can reach 85W in the focus; it is in series connected with a power amplifier (240L, Electronics & Innovation, USA) and a wave generator (33220A, Agilent Technologies, USA). A 0.2mm PVDF needle hydrophone (Precision Acoustics) is used to detect the pressure signal, transferred to an oscilloscope (InfiniiVision 7014A, Agilent Technologies, USA). The needle hydrophone is mounted on a 3 axis step-by-step motorized positioning frame (XXYZ BiSlide, Velmex) with a full range of approximately 500x1000x500mm^3 and a precision of 6µm. Wave generation, hydrophone position and signal acquisition are controlled and synchronized remotely by a home-made LabView (National Instruments, USA) interface. A 2D scan has been carried out by positioning the hydrophone parallel to the beam axis and measuring the pressure on an half-plane (axial-symmetry has been previously demonstrated by a 3D scan). This scan allows mapping the acoustic field around the focus in a y-x plane of 70x5mm with pitches of 0.5mm and 0.1mm respectively on beam axis and on its perpendicular direction. Data acquired are post-processed in MatLab (MathWorks, USA) environment. Electric signal is converted to pressure taking into account the hydrophone sensitivity at the center frequency. Results (Fig. 4) show the cigar-shape of the HIFU beam, with a focal length (-6dB) of 24.36mm and a focal diameter of 2.94mm. The scans are performed using low intensities (up to approx. 4W) in order to avoid to damage the hydrophone. For input power of 1W I_{SPTP} (Spatial Peak Time Peak Intensity) and I_{SATP} (Spatial Averaged Time Peak Intensity) are respectively 57.2W/cm^2 and 31.3W/cm^2.

Preliminary tests on porcine, human and fibrin clots have been carried out exploiting the presented setup. Human clots are obtained by collecting them into citrate vacutainers and then treating the blood with $CaCl_2$ and thrombin, while fibrin clots are obtained by simply mixing *in-vitro* fibrin and clotting factors. Porcine clots are obtained from spontaneous coagulation of fresh blood taken from local slaughterhouse; porcine clots have similar acoustic properties of human clots [14].

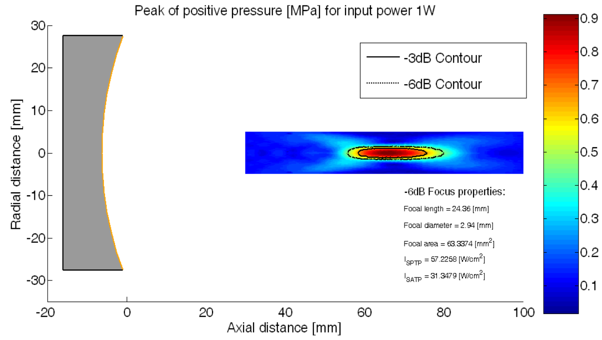

Fig. 4. Cigar-shape of the HIFU beam.

The different blood clots were placed in a low-density Polyethylene (LDPE) tube, with inner diameter of 7mm and thickness of 0.5mm. LDPE has been chosen because of its similar acoustic impedance with respect to water. A flow system has been included and all the experiments were carried out under a flow of water of 2ml/min. Acoustic parameters are reported in Table 1. They have been chosen basing on previous literature experiments [13] and on the specifications of the transducer. These parameters showed their efficacy in considerably reduce clot size in the proposed time. Fig. 5 shows the results in form of screenshots taken at 0s, 30s, 60s, 90s and 120s for human and porcine blood clots.

TABLE I. ACOUSTIC PARAMETERS FOR US THROMBOLYSIS TESTS

Frequency	Acoustic Power	Pulse Length	Duty Cycle	Treatment duration
1MHz	65W	450µs	10%	120s

Furthermore, physical mechanism on the basis of thrombus dissolution must be investigated in order to optimize the therapy, in particular for augmenting thrombolytic efficiency while avoiding damage to healthy tissues. Bioeffects of US include a plethora of phenomena, which usually contribute to the final result. Among these, thermal and cavitational effects are credited to play a major role. In US thrombolysis thermal damage is considered a drawback. However traditional methodologies for thermal measurement (i.e. thermocouples [15] or pulse-echo ultrasound [16]) are not applicable for the proposed experiments, so that qualitative assessment is commonly considered [13, 17].

In order to evaluate thermal effects, experiments have been carried out on porcine blood clots, shaped in order to fill the entire sample holder. Tests have been carried out keeping constant the quantity of energy delivered to the target, while varying the duty cycle from 0% (control) to 100% (continuous wave), and subsequently varying the duration of the treatment. Visual analysis and optical microscope (HiroxKH7700) zoom

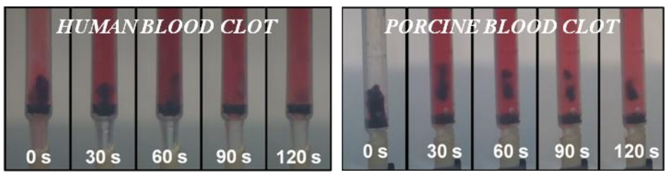

Fig. 5. Screenschoot of human and porcine thombi during US exposure.

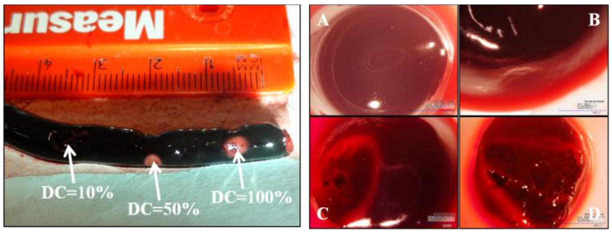

Fig. 6. Qualitative assessment of thermal damage, (left) treated porcine clot; (right) 0%(A), 10%(B), 50%(C), 100%(D) duty cycle treated section.

20x, (Fig. 6) show evidence of thermal damage for continuous and 50% duty cycle (DC) waves, while for the exploited parameters only evidence of surface erosion can be identified. Basing on these considerations, a passive cavitation detection (PCD) system has been implemented, in order to determine whether cavitational effects are present. As a matter of fact, by measuring the acoustic emission from oscillating/collapsing microbubbles, it is possible to determine and quantify the presence of cavitational effects.

III. Conclusions and Discussions

Frontier research in the management of vascular obstructions poses very challenging medical and technological problems and the quest for innovative strategies/platforms is continuously increasing. The here proposed platform includes some innovative solutions for navigation and therapy. Preliminary results show the feasibility of the proposed solution: the traditional CAS architecture was adapted to intravascular medical procedures and the feasibility of magnetic navigation and US tracking was assessed. Future works are planned for employing a 3D US system (in replacement to the 2D probe) for preoperative vascular tract reconstruction and intraoperative vessels registration and endoluminal probe tracking. The US thrombolysis setup demonstrates the ability to accurately map the acoustic field on the transducer axis and US thrombolysis efficacy was established. Future works aim at correlating the cavitational dose to thrombolytic efficiency: if this correlation exists, therapy could be optimized for enhancing cavitational effects.

New platforms such as the one proposed in this paper, which cannot exist without the fully exploitation of robotic strategies, will be developed over the next 10 years. The scenario including a multi-robotic platform paves the way for the reduction of invasiveness of surgical interventions and personalized medicine. The ideal and paradigmatic example of minimally invasive surgery (MIS) leads to the concept of therapy completely non-invasive, such as, for example, in focused ultrasound surgery (FUS), which involves the transmission of acoustic energy through the body from an external source. FUS is already used in several clinical applications, but it suffers from some drawbacks and limitations which narrow the applicability to non-moving and non-essential organs, mainly under guidance of magnetic resonance (MR). Developing an autonomous and human-supervised robotic platform to perform a completely non-invasive therapy by means of FUS will allow to overcome the current drawback of this technology. The robustness, safety, and accuracy of FUS procedures will be enhanced by exploiting robotic assistance, by using real-time therapy monitoring and self-learning procedures as closed-loop control. It is worthy to mention that this innovative application could be considered a step towards the real implementation of multifunctional and versatile robotic platforms for healthcare applications.

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