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Robotic Manipulator for Positioning a Magnetic Actuator Dedicated to Drug Delivery in the Cochlea

Manel Abbes^{1,2}, Karim Belharet³, Mouna Souissi³, Hassen Mekki¹ and Gérard Poisson²

Abstract—The actuators dedicated to micrometric applications are known for their precision but also for their restricted workspace. The use of a robotic manipulator as a carrier makes it possible to considerably increase this workspace. In this paper, we present a novel robotic system specially designed for positioning a magnetic actuator based on permanent magnets, used as an end-effector of the robot for steering magnetic microrobot throughout the cochlea. Using the classical mathematical tools of serial robotics, we determined the direct and inverse kinematic models of the manipulator, thus defining a reference trajectory to move the microrobot on a space as small as possible and take account of the geometrical specifications based on medical needs. A prototype has been realized with a 3D printer to experimentally validate the numerical results. In addition, the mechanical considerations for the construction of the prototype are presented.

Index Terms—Inner ear drug delivery, Cochlea, Medical robotics, Robotic manipulator, RCM Mechanisms, Magnetic actuator, Microrobot.

I. INTRODUCTION

The conventional routes of administration to the inner ear, such as oral or parenteral routes are largely ineffective principally because the blood-perilymph barrier isolates this organ from the blood [1]–[3]. Indeed, the extreme inaccessibility of the cochlea and its very small volume, makes the inner ear one of the most challenging target organs for local drug delivery [4]–[7].

In fact, the ear is composed of three parts: external, middle and inner ear. The inner ear, which contains both the organ of hearing (cochlea) and the organ of balance (vestibular system).

The cochlea is the organ where acoustic signals are transformed into neural pulses which are then signaled to the brain. The two human cochleae are mirror-shaped, fluid filled, coiled, fairly symmetrical bony tubes situated in the petrous pyramids of the temporal bones. Perilymph; the fluid inside the scalae vestibuli and tympani communicates with the cerebrospinal fluid (CSF) via the cochlear aqueduct. This route of fluid communication can allow spread of infections between these fluid compartments such as Vestibular neuritis, Labyrinthitis, Meniere’s disease, Vestibular migraine and Conductive hearing loss. Accessing the inner ear has always been a tough mission as it is well protected by the presence

of the blood-cochlear barrier. Therefore, researches have continuously evolved in order to find out new strategies for treating and restoring hearing loss. There are two main techniques for delivering a therapeutic agent to the inner ear. The first method is Intracochlear administration that consists on depositing drugs in the perilymphatic spaces of the cochlea. This method offers a great potential for the control with no dependence on the permeability of the round window membrane. It permits drugs to directly reach the inner ear’s cells by passing through the middle ear. But, there are risks of a total hearing loss caused by high hydrostatic pressure. The second method is Intratympanic administration that is an old one but commonly used technique for treating inner ear diseases. It consists on placing drugs in the middle ear, then this therapeutic agent accesses the inner ear through the round window membrane which is permeable to many drugs. But there are concerns about the health of the patient as there is a risk of toxicity, also a poor diffusion in the cochlea or a massive leakage through the eustachian tube are possible. The Hydrogel-based intratympanic delivery consists on loading drugs into the hydrogel matrix thanks to the extremely porous structure of the hydrogel. Then, once instilled into the middle ear, hydrogel releases drug in a controlled way. However, it is a long-lasting technique, it is not easy to remove the gel’s agents and there are risks of poor diffusion in the superior areas of the cochlea. The administration via magnetic nanoparticles represents a promising and challenging new avenue for controlled drug delivery to the inner ear. Nanoparticles have a considerable capacity to easily cross the round window membrane offering an intended delivery of drugs to targeted cells in the cochlea. This technique lasts for a short period of time and allows the diffusion of drugs in all regions of the cochlea without causing any damage to the round window membrane when a specific magnetic system for inner ear drug delivery is used. We have proposed a magnetic prototyping platform for drug delivery in the inner ear using magnetic particles. This platform is composed of a magnetic actuator based on permanent magnets [8], a tracking vision system and a robotic manipulator.

In this paper we propose a novel robotic system for positioning a magnetic actuator based on permanent magnets. Section (II) presents the anatomy of the cochlea and the operating principle of the magnetic actuator. This represents the constraints to be considered in the design of the robotic manipulator. Section (III) describes the direct and inverse kinematic models of the proposed robot. Section (IV) shows the simulation results to validate the robotic structure. Fi-

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nally, section (V) depicts the realized prototype with a 3D printer. The paper is concluded in section (VI).

II. SYSTEM REQUIREMENTS

A. Clinical procedure of targeted drug delivery in the inner ear

Targeted drug delivery in inner ear is a non-invasive method which allows to steer magnetic particles to targeted cells in the ear. This operation is performed in several steps and lasts for around 30 minutes. Before all, the patient lies on the operating table with a specific position of the head, using a fixing tool. Several markers are fixed on the patient's head and used to correct the robot's motion. Then a Magnetic Resonance Imaging (MRI) scan is realized to locate the cochlea and extract its position, in the 3D space, relative to the markers' frame. After that, the patient is moved to the operating room where the drug delivery procedure will be performed. A tracking vision system is developed and used to compensate any possible motions of the patient's head. Indeed, it uses the markers frame in order to define the cochlea's position relative to the cameras frame. Once the head moves, the vision system calculates the new position of the cochlea and sends it to the robot controller in order to redefine the trajectory. In addition, a magnetic actuator is used to steer the magnetic particles inside the cochlea. The later is developed, in our laboratory, specifically for targeted drug delivery and has a specific operating mode. The actuator's axis has to be aligned with the direction of the particle displacement in order to be able to push or pull particles in this direction. Therefore, to perform the different directions, we need to move the actuator around the head in the 3D space. This requires the use of a robotic manipulator, adapted to the sphericity of the workspace and the constraints related to the cochleas anatomy and the magnetic actuator.

B. Anatomical constraints

The cochlea as it can be viewed in Fig.1 is a set of membranous tubes, 31–33mm in human. This tube is coiled much like a snail shell to form 2 and a half turns around its axis [9]. There are two orifices in the surface of the cochlear bone, both of which are located at the base of the cochlea. The *round window* is a membranous opening in the bone within the *scala tympani* and the *oval window*, in the *scala vestibuli*. Perilymph is the primary fluid of the cochlea and its volume in the human cochlea is about $70\mu\text{L}$. The height of the bony cochlea is approximately 4mm and the width of its basal coil, which is the largest, is about 7mm (see Fig.1). We note also the presence of a slight inclination between turns, approximately 9 degrees between the basal and the middle turn and about 2.4 degrees between the middle and the spacial turn [10]. Moreover, the spatial cochlea's orientation in the skull is defined in [11]. The modiolar axis of the cochlea makes an average angle (A) of about 40 degrees with the Midsagittal plane. Also, the cochlea axis is almost horizontal since that the lateral semicircular canal (LSC) forms 30 degrees forward and upward to the skull's horizontal plane [12].

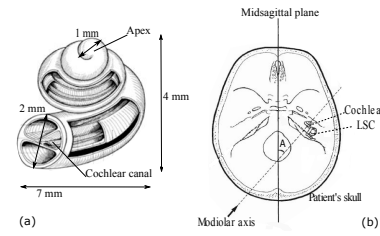


Fig. 1. Geometrical characteristics of the cochlea: (a) Cochlear channel (b) Cochlea's position

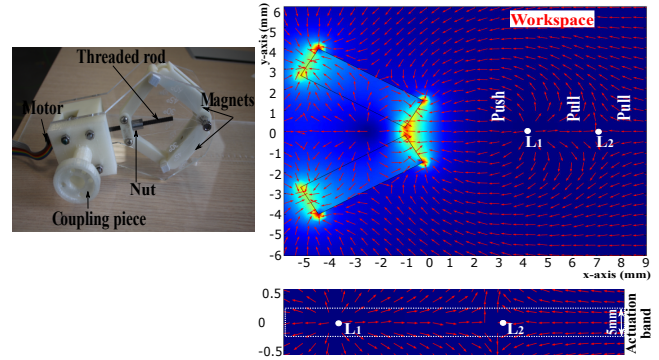


Fig. 2. Magnetic actuator and the magnetic gradient generated

C. Actuator constraints

The location of the inner ear and the anatomical obstacles such as the head, make pulling the particles by an external magnet not optimal and neither possible. Indeed to pull a particle into the inner ear, the pulling magnet must be placed on the opposite side of the head at a long working distance. Unlike the systems that use a single permanent magnet, a motorized device that combines two permanent magnets has been developed for this application (see Fig.2) and has demonstrated its ability to create both push and pull forces [8]. The area between the pushing and the attractive forces has canceled forces that are called Lagrangian points. The actuator creates five Lagrangian points but only one of them is stable and allows to fix the microrobot in a targeted position, which is the Lagrangian point L_2 . Once we change inclination between the two permanent magnets, the magnetic fields' configuration and so the position of the Lagrangian points are modified. As shown in Fig.2 the push and pull forces are created over an interval of about 5mm called actuating band. Any particle positioned in this band can be either pushed or pulled according to its position relative to the Lagrangian point L_2 . To guide a magnetic particle on the helical path of the cochlea, the actuator must rotate with respect to the revolution axis of the cochlea (see Fig.1). The strategy adopted, to drive the nanoparticles to the cochlea's apex, is to firstly divide the cochlea into linear segments. Then, a robotic manipulator moves the actuator until the superposition of the actuator's x-axis and the desired segment to push or pull microrobot inside the cochlea.

D. Safety constraints

Alike new collaborative robots in industry, medical ones are designed to act in proximity of patients. Therefore, there are many concerns about safety, sterilization and accuracy. Since the application is not invasive we do not have to deal with sterilization issues. Safety is a critical concern because the manipulator is designed to act in a fully automatic mode. The patient's head must be fixed in a definite position in order to define the robot's workspace and guarantee that no interference with the patient is possible in any case while keeping a minimal safety distance of 2cm between the magnetic actuator and the patient's head. Moreover, it is necessary to privilege a system with mechanical stops in addition to the software ones (software programmable workspace limitations). Finally, since the patient will not be anesthetized during the process of targeted drugs administration, potential movements of the head have to be considered. For this reason, the robot uses informations received from the vision system to compensate those movements.

The characterization and specification of the medical needs and different constraints allow us to choose functional and technological specifications of the robotic system. The first step consists of choosing the kinematic architecture. In the next section, we propose the kinematics modeling of the novel manipulator that fulfills the previous constraints.

III. MODELING AND MECHANICAL DESIGN OF THE MANIPULATOR

A. Medical robots state of art

To validate drug delivery strategy, preliminary experiences had been realized using a 6 degree of freedom (DOF) serial manipulator, the FANUC LR Mate 200iD robot. However, some positions are not reachable because of the limitations of its workspace [13]. Moreover, there are several concerns about the safety of the patient with this type of robots, as there is a potential risk of collision between the robotic manipulator and the patient. The desired kinematic architecture must allow 3D guidance of the magnetic actuator around the patient's head, by realizing a spherical movement whose center of rotation is the center of the cochlea (away from the structure). This need of kinematic structure with a fixed point is common for several medical robots, and is called Remote Center of Motion (RCM) mechanism. The latter can be achieved mechanically or virtually. However for clinical applications, mechanical RCM systems are more favorable due to their reliability, rigidity and easy control systems which make them more safe. These mechanisms are well classified and systemized in [14].

A parallel system was implemented in a vitreoretinal surgery robot [15]. With 6-DOF this robot is capable of performing high positioning accuracy within the eye. A double parallelogram structure was also used for minimally invasive surgery, it is a 7-DOF mechanism that fulfills the incision point constraints and provides a high degree of dexterity [16]. Although the simplicity of these parallel structures and the large movement range that they can offer,

they present many singularities and lack rigidity because of their numerous revolute joints.

Another commonly used mechanism is the spherical one which is suggested for several clinical applications. A needle guidance system for MRI-guided liver interventions was presented in [17]. It is a compact device with 2-DOF that allows angling the needle at the skin entry using a double ring RCM mechanism. Also a spherical serial mechanism (IRISS), able to perform many intraocular surgical steps with high accuracy, was introduced in [18]. A serial robotic device with 7-DOF, was developed and commercialized by Axilum Robotics for Transcranial Magnetic Stimulation (TMS) [19]. The latter used two spherical mechanisms to adapt the workspace's shape which is almost a sphere centered on the patient's head.

Despite the fact that spherical mechanisms supply exact spherical motion at the fixed point, a defined number of DOF as well as a specific alignment of the joints are needed to perform the drug delivery to the inner ear procedure. Moreover, there is a need of a specific workspace adapted to the actuator dimensions; an architecture dedicated to this task that minimizes the ratio between accessible and useful workspace by taking advantage of the geometry of the work area. In view of all the above, the development of a novel robotic manipulator dedicated to inner ear drug delivery is clearly necessary.

The challenge in the conception of medical robots is to design more precise, lighter, less energy-consuming and more compact structures. To achieve this goal, it is important to optimize the robot structure, the links shape and the position of the actuators.

B. Description of the manipulator

In this subsection we present a new mechanism to position a magnetic actuator around the patient's head. A RCM mechanism is adopted to guarantee safety and avoid any risks of collision between the robot and the patient. We used an arc guide mechanism to restrict the motion and make sure that no interference with the patient is possible in any case [20]. The architecture conceivable for the choice of the serial bearer is consisting of two segments of circular shape each having an arc length of 90° as shown in Fig.3. The first arc connects J_1 and J_2 and the second arc carries the magnetic actuator (Fig.4).

This mechanism is equivalent to a serial spherical system. It can be represented by three revolute joints with concurrent axes (Fig.4) J_1, J_2 and J_3 . The three joints are intersected in the center of cochlea. 3 DOF are sufficient to realize all the needed displacements, around the patient's head, while respecting the constraints mentioned previously. Moreover, the spherical architecture offers a light weight and a high precision.

C. Kinematic and inverse kinematic models

The mechanism motion is computed using the Euler angles. The rotated system is specified as follows: first rotation about Z-axis by an angle ψ (precession), then about X-axis

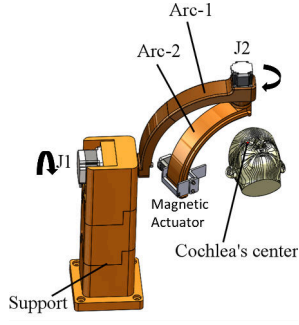


Fig. 3. The mechanism designed with Solidworks software

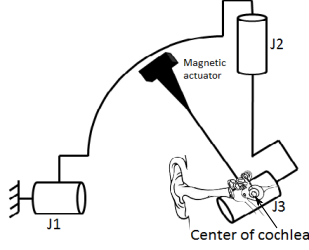


Fig. 4. Mechanism's Kinematics

by an angle θ (nutation) and finally about Z-axis by an angle ϕ (own rotation). Thus, a Z-X-Z scheme. For the mechanism, ψ corresponds to the joint J_1 , θ corresponds to the joint J_2 and ϕ corresponds to the joint J_3 (see Fig.5).

The transformation matrix R_T is defined as a sequence of three rotations:

$$R_T = R(Z, \psi)R(X, \theta)R(Z, \phi) \quad (1)$$

The result of multiplication gives:

$$R_T = \begin{pmatrix} X_x & Y_x & Z_x \\ X_y & Y_y & Z_y \\ X_z & Y_z & Z_z \end{pmatrix}$$

On another hand, Euler angles can be identified from the terms of the transformation matrix, which is well known in Euler formalism.

$$\psi = \text{atan2}(-Z_y, Z_x) \quad (2)$$

$$\theta = \arcsin(\sqrt{X_z^2 + Y_z^2}) \quad (3)$$

$$\phi = \text{atan2}(Y_z, X_z) \quad (4)$$

The angle axis representation defines the orientation of two coordinate frames as a rotation of an angle α around an axis k . The angle axis α is given by:

$$\alpha = \arccos\left(\frac{X_x + Y_y + Z_z - 1}{2}\right) \quad (5)$$

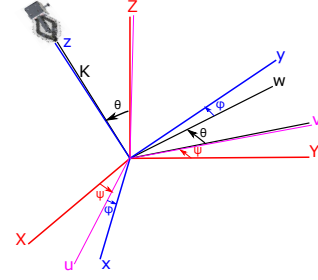


Fig. 5. Euler Angles with 'Z-X-Z' formalism

And the axis k is given by:

$$k = \frac{1}{2 \sin \alpha} \begin{pmatrix} X_x - Y_x \\ X_y - Y_y \\ X_z - Y_z \end{pmatrix} \quad (6)$$

This presentation of the angle axis encounters a singular configuration for $\alpha = 0^\circ$ and $\alpha = \pi$. For $\alpha = 0^\circ$ it can have any direction, for $\alpha = \pi$ it can point in two opposite directions. The singular configurations of such mechanism are obtained when it is completely folded, or completely stretched.

The angular velocity in body coordinates can be expressed as the time derivative of the Euler angles.

IV. SIMULATION AND RESULTS

A. Planning trajectory of the manipulator

The objective is to determine the magnetic actuator coordinates (x,y,z) that allows it to reach the given orientation. The complete simulation chain, starting from the calculation of the command angles in Matlab-Simulink until the execution of the motion in Adams.

The process consists in injecting a series of effector orientations in the inverse kinematic model and studying the actuator coordinates. The three orientations correspond to the precession, nutation and own rotation joints. For our application the orientation of the magnetic actuator is given. Using the inverse kinematic model, the position of the actuator is calculated by the angle axis. The coordinates of the actuator are given in the Tab.I.

Case	Orientation (J_1, J_2, J_3)	Position (x,y,z)
1	(0, 12, -50)	(241.86, 205.77, -46.67)
2	(0, -12, -50)	(242.62, 207.82, 53.2)
3	(90, -24, -80)	(292.62, 130.17, 56.43)
4	(90, -57, -80)	(147.3, 268.17, 56.8)
5	(90, -50, -68)	(193.8, 231.2, 121.7)

TABLE I

POSITIONS AND ORIENTATIONS OF THE MAGNETIC ACTUATOR.

The work area is determined by the positions of the magnetic actuator relative to the cochlea. There are five positions to reach with the manipulator in order to steer drugs

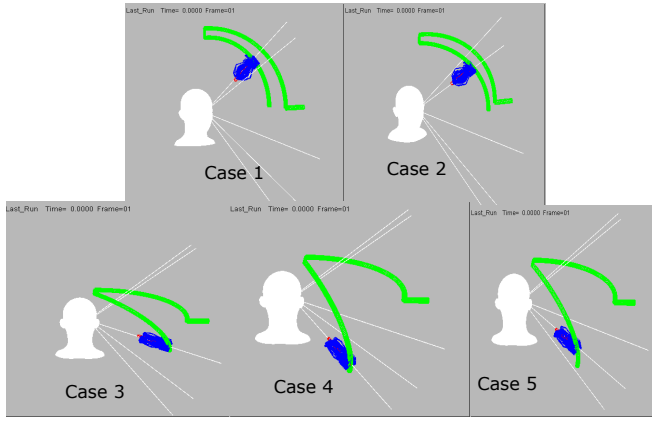


Fig. 6. The five positions of the magnetic actuator.

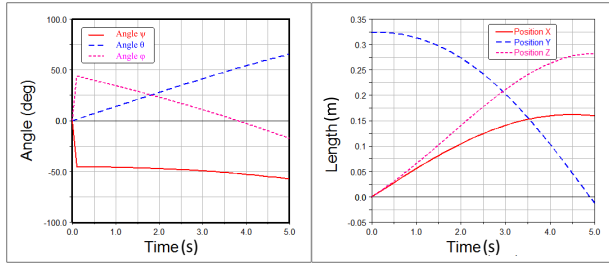


Fig. 7. Motions and displacement of magnetic actuator

throughout the cochlea. The five cases are presented in the Tab.I.

To reach the different cases, we control the three joints and determine the position of the magnetic actuator. These simulations permit to fix the application's work area and limit the angle of orientation of the three joints.

The joints' stops are deliberately limited to $\pm 90^\circ$, in order to take into account collisions with the patient and to reach all points of the work area. The first joint J_1 is limited to $\pm 90^\circ$. Second joint J_2 is comprised between 12° and -57° . Third joint, the displacement of the magnetic actuator can take three values -50° , -80° and -68° . The five cases of magnetic actuator are simulated with Adams in Fig.6. Respecting the different constraints, the manipulator can reach all the desired positions.

Angular velocities applied to the motors are the inputs of the system in order to check the dynamic behavior of the manipulator and calculate the magnitude of torques and forces of translator and rotational motors. Fig.7 shows the trajectories of the three joints and the displacement of the magnetic actuator.

In the case where all the joints are bent from an angle varying from 0° to $\pm 50^\circ$, the magnetic actuator moves of a length of 0.325m in the three planes while remaining in the same positive side. It can be concluded that with small engine rotations we can reach a large workspace.

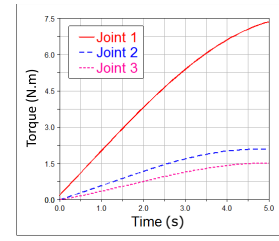


Fig. 8. Torque of the three joints

V. PROTOTYPING

Before designing the real system, a physical prototype has been realized in order to identify the major characteristics and the potential pitfalls of the proposed architecture.

A. Motors sizing

The material used for 3D printing prototype is an industrial thermoplastic PC-ABS. Setting this material to the model of the robot, designed in Solidworks software, permits to get the exact characteristics of components. The characteristics of the manipulator's bodies are presented in Tab.II.

Body	Mass (kg)	Characteristics
Arc 1	1.55	Angle extent = 90° , Major radius = 0.45m
Arc 2	1.25	Angle extent = 90° , Major radius = 0.40m
Actuator	0.3	Length = 0.012m
Support	4.8	Length = 0.51m

TABLE II
PARAMETERS OF THE MANIPULATOR

After a preliminary study our choice was fixed on electric actuators. To size the motors, we used ADAMS software (Automatic Dynamic Analysis of Mechanical System) in order to define the different torques. The torque of the three joints during the considered time and trajectories is illustrated in Fig.8. The most important torque is in the first joint J_1 , it has a magnitude of 7.5N.m. For J_2 and J_3 , the torque's magnitude is less than 2N.m. These values are so interesting in the design since the manipulator will be lighter and less energy-consuming.

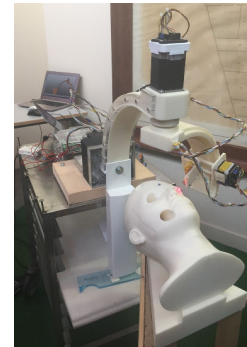


Fig. 9. 3D printed prototype

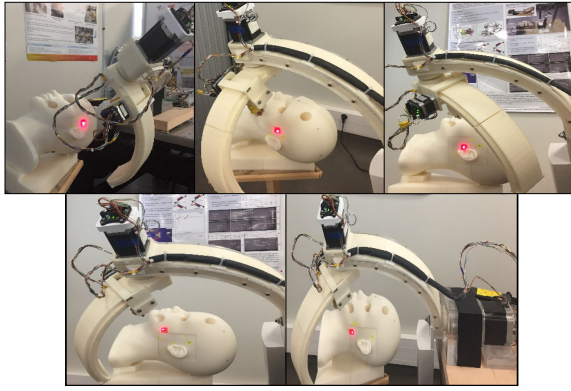


Fig. 10. The five positions of actuation

Characteristic	Motor J1	Motor J2	Motor J3
Rated Current (A)	10	3	2
Holding Torque (N.m)	9.8	2.4	2.3
Step Angle (deg)	1.8	0.9	0.9
Length (mm)	126	77	77
Weight (kg)	3.8	1	1

TABLE III

PARAMETERS OF THE MOTORS

Based on these values obtained from dynamic simulations using ADAMS software, we have chosen the adequate electric motors for our system. Since the positioning process is discontinuous, the motors must start and stop frequently. Stepper motors are well-suited for our application since they combine high torque and compact design, which in turn gives them excellent response and acceleration. Furthermore, stepper motors are easy to use in a position control. Therefore, our choice was fixed on stepper motors of MOONS company. A Nema 34 Standard Hybrid Stepper Motor (ML34HD2L4X00) for the first joint J_1 . A NEMA 23 High Precision Hybrid Stepper Motor (MS23HAAP4300-E) is chosen for the second joint J_2 and for the third joint J_3 we have chosen another NEMA 23 High Precision Hybrid Stepper Motor (MS23HAAP4200). The different parameters of the three motors are detailed in Tab.III.

B. Experimental validation

To validate the process of magnetic actuator positioning. The prototype has been realized in ABS-PC using a 3D printer (see Fig.9). We also realized a head in a human scale in ABS-PC (in which we planned in advance the locations of the microscopes and markers) in order to simulate the effective operating workspace while respecting the different constraints to guarantee the non collision with the patient. A laser has been attached to the latter to verify that all the desired positions (see Tab.I) are attainable. We used an Arduino Mega for controlling the motions of the manipulator. For test, we injected the different positions in the system and we tracked if we are able to pass through all the regions of the cochlea. Fig.10 shows the different orientations

of the actuator to perform these positions. The results of the experiments using this manipulator correspond to the simulation results (with Matlab/SimMechanics) and show its ability to perform all the needed orientations in order to reach accurately the different positions. However, our results suggest that a closed-loop control could enhance the degree of accuracy and repeatability. Therefore, the prototype needs further optimization.

VI. CONCLUSION

In this paper we propose a robotic manipulator for the positioning of a magnetic actuator around the patient's head. This actuator is used to guide magnetic particles inside the cochlea. For this reason and in order to propose an adapted kinematics, we first studied the anatomical constraints and the operation of the magnetic actuator. A compact robotic manipulator is developed to guide a magnetic actuator to reach all positions required to steer the magnetic particles inside the cochlea. The next steps consist of optimizing the realized prototype and controlling the robot using a closed-loop control system. Accuracy and repeatability of the robotic arm will then be identified thanks to a Vicon capture motion.

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