Group 6 - EDEN2020

EDEN2020 (Enhanced Delivery Ecosystem for Neurosurgery) is a project subsidized by the EU program Horizon 2020. It focuses on one-stop diagnosis and minimally invasive treatment in neurosurgery. This is done by the engineering of a robotic, steerable catheter which is used for drug employment nearer to the actual tumor than with today’s technology. The steerable catheter does not have to be removed immediately, but can stay in the patient for longer periods. Furthermore, EDEN2020 aims at creating an intraoperative imaging application which can perceive the changes to the brain’s anatomy during surgery because of brain shift (cp. Imaging, Research on intraoperative MRI).

The project elements of EDEN2020 can be seen in figure 1 with TUM’s CAMPAR related projects being marked by the rectangle: human and sheep brain imaging, the image fusion of preoperative MRI and intraoperative US images as well as the catheter localization using the fused images. Other main aspects are the catheter planning, catheter navigation and catheter steering as well as the robotic positioning of the catheter with the Neuromate robot. Moreover, a brain diffusivity model to simulate the drug delivery in the tissue is also part of EDEN2020. The different research aspects then have to be verified in multiple steps. [3] Clinical trials (cp. Clinical trials and new methods undergoing clinical trials) are planned to start in 2020. [2]

Functional principle

Preoperative MRI (cp. Brain Tumor Diagnosis, Brain Scans) is taken and then analysed by a computer. The computer program creates the least invasive operation plan while maintaining the patient’s safety. This plan then has to be accepted by the surgeon. After the acceptance, a second program is given control over the Neuromate and the additional sensors which update the navigation data with intraoperative US. The robotic, steerable catheter is mounted on the Neuromate for the general positioning. Then the surgeon guides the catheter to the tumor tissue, using a haptic device.

During the procedure, the catheter perceives its changes of shape. These changes are matched with the preoperative MRI and the intraoperative US, enabling the localization of the catheter. This addresses the problem of brain shift in the localization process and allows the surgeon to optimally access the tumor tissue with the catheter, eventually inserting the drugs. Furthermore, the drug diffusion within the tissue is imaged and calculated by a brain diffusivity model.

The entire process can be seen on figure 2, showing the robotic system consisting of the Neuromate, the 3-D ultrasound device and the geometric sensing device, as well as the surgeon using the intraoperative imaging to guide the catheter and the in vivo diagnostics using the brain diffusivity model.

In the future, the techniques of EDEN2020 might also be used for brachytherapy (radioactive material that is inserted directly into the tumor tissue), laser ablation (an optical fibre in the catheter directs a laser beam to burn away tumor tissue) and deep brain stimulation (an electrode mounted at the top of the catheter stimulates certain brain regions). [2]
Engineering and research

Robotic, steerable catheter STING

In today’s mainly used methods for minimally invasive neurosurgery, rigid catheters are deployed to insert drugs into the tumor tissue. The steerable catheter of EDEN2020 is a bionic design, being an adaption of the wood-boring wasp. [2]

The steerable catheter – called Soft Tissue Intervention and Neurosurgical Guide (STING) – combines the advantages of rigid probes and thin flexible needles: a planable path with the ability to adapt to the tissue consistency, but without exerting as much pressure on tissue as the rigid probe and without buckling as easily as the flexible needles. Furthermore, the usage of a robotic catheter decreases the risks of hurting blood vessels and safety-critical structures because of better planning and ideally adjusted progressive velocity. Also, because of the curved trajectories it can follow, it can access deep anatomical structures which were very difficult to access with conventional catheters. [12]

The movement of soft tissue during catheter insertion can cause inaccuracies and path deviations. Instead of fixing the tissue, STING focuses on a different approach of insertion and steering. STING consists of four axially interlocked parts, which were 3D-printed and possess a 4mm diameter (later the diameter is going to be reduced). The interlocked parts are controlled independently and slide relative to each other (cp. fig. 6) [8]

STING has a programmable bevel tip, which controls the steering direction by changing the offset between its segments. Each segment can steer the catheter into its direction: by pushing the leading segment forwards, forces are exerted and bend it (cp. fig. 6). When the other segment is pushed forwards, it follows the curved outline of the leading segment. A linear relation was observed between the curvature of the trajectory and the offset between catheter segments.

Figure 5 shows a sectional view of the catheter and the interlocking mechanism. In one segment the drug delivery channel is located, in the adverse segment the channel for the EM sensor to sense the position is located.

It could be shown that the steering error increases if STINGs diameter decreases, but a causality for steering errors between different bevel-tip angles can not be found that easily. [12]

With this setup, two main types of straight movement possibilities exist. One is the direct push, for which all segments are aligned and moved forwards with the same speed. The second is the biologically inspired pullback, for which the segments are moved reciprocally: one segment is moved forwards for 4 mm, while the others are pulled backwards. Then the adverse segment is moved, then the third segment and finally the adverse of the third segment, resulting in all four elements being aligned again. This movement leads to higher tissue friction and results in less soft tissue movement.

The movement was validated with numerical models. For validating the straight movement concept, internal displacements and strains were measured and compared between the usage of direct push movement and pullback movement, the direct push movement being the same as a regular rigid needle insertion movement. The experiments yielded the possibility to reduce displacements by 30% and strains by 41% when using the pullback movement. Therefore, the bionic catheter concept is even superior to a conventional catheter for a straight movement. [8]
Catheter path planning with preoperative MRI and catheter navigation with image fusion of preoperative MRI images and intraoperative US

Preoperative imaging (especially MRI, but possibly also DTI and CT) is used for the preoperative planning. It is used to plan the entry point and the catheter trajectory, taking into consideration patient specific factors to lower the risks as well as the shortest path to the targets. After the acceptance of the plan by the surgeon, the operation takes place using the haptic device Neuroinspire to guide the robotic setup. Preoperative MRI and introoperative US images are fused to create a composition of the patient’s anatomy, the trajectory and the current position of the catheter. [4]

The implementation of the preoperative planning is currently done at the example of sheep. As sheep brains feature many similarities to human brains, they are more and more taken for neurosurgical clinical trials. Researchers from the Politecnico di Milano together with veterinary surgeons from the University of Milan developed a trajectory planner using automatic segmentation of certain brain areas for the insertion of a straight catheter.

At first, the preoperative MRI is registered to an open-source sheep brain atlas. Then white matter, gray matter and the CSF-system are segmented. The segmentation of white matter and gray matter already works quite well, but the ventricles/CSF-system are currently not equally good segmented. Therefore, an additional manual segmentation was used in the published paper for the ventricles (as well as for the cerebellum and the midbrain, cp. fig. 3 and 4).

The veterinary surgeon has to select a target point and an entry point region center. The trajectory planner then calculates within the radius of the entry point region center the entry point and the angle of insertion. For this, the segmented data is used. Multiple trajectories are calculated, taking into consideration the euclidean distance to safety-critical structures (sulci, white matter and ventricles). The sulci are not considered for the entry point, because blood vessels are mainly located in them.

In figure 4, the result is shown. The entry point region is seen consisting of gyri (green) and sulci (red), the trajectory being a straight path between entry point and target. The ventricles (cyan) and the additionally manually segmented midbrain (violet) and cerebellum (yellow) are also shown.

The developed trajectory planner was validated against the software FreeSurfer – currently the gold standard for computing the cortex curvature – and shows a good matching capability regarding different levels of gyri curvature thresholds. The validation used human MR cortical data. [7]

CAMPAR published two papers featuring current research of the chair on EDEN2020. In the first paper, a fully automatic three-dimensional preoperative trajectory planning program for US transducers is investigated. Planning is done with regard to the optimization of image quality when focusing on a specific amount of target points of a structure. The planning takes into consideration the transducer’s position, the transducer’s orientation and patient anatomy specific constraints. It was validated against a naive planning technique on virtual planning scenarios as well as on a tissue-mimicking phantom. [5]

CAMPAR's second paper features research on three-dimensional intraoperative US image registration specific for brain imaging. It uses and compares rigid and non-rigid registration techniques. The developed rigid and non-rigid techniques were validated against a non-brainshift-compensating system in a clinic, yielding an improvement before and after the opening of the dura mater, but not after resection. All in all, the investigated system improves the detection of brainshift and significantly increases the accuracy of neurosurgical navigation. [6]
Robotic positioning with Neuromate

Neuromate (cp. fig. 7) is a robot for neurosurgery, already successfully deployed in applications concerning for example stereotactic applications in neuroendoscopy and biopsy. In EDEN2020 it uses a stereotactic frame, but it can also be used frameless (cp. Robotics, State-of-the-art).

Brain diffusivity model

Another part of EDEN2020 is an in situ Raman imaging diagnostics system, used via optical fibres in the catheter. It enables the identification of transitions between benign and malignant tissue, the characterization of tissue morphology at specific points during the catheter insertion and the yet-to-be researched ability to monitor the chronological sequence of drug diffusion. [4]

Raman spectroscopy – which is based on the inelastic scattering of photons – can give detailed information on the chemical composition of cells and tissues and is therefore well-suited for biomedical applications. [9] It allows real-time, detailed biomolecule analysis without destroying the examined tissue and it was already possible to image and detect the in vitro diffusion of the neurotransmitters serotonin, adenosine and dopamine. [10]

Bibliography


