

Mixed reality for brain functional and structural navigation during neurosurgery - MRbrainS -

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ABSTRACT

We implemented the complex analysis of non-invasive functional and structural MRI presurgical mapping of brain tumors in a single software platform usable in a clinical setting. Moreover, the imaging results are transformed into holograms in the Microsoft HoloLens wearable mixed-reality device. This approach offers an increased ergonomics with respect to standard neuronavigation systems, allowing the surgeon to better explore critical brain structures that need to be preserved. We expect that our system will extend advanced presurgical mapping procedures to hospitals outside the research community, and foster a strong cooperation between fundamental research and industrial companies, with large economic/healthcare benefits.

Keywords: fMRI; Holography; Mixed Reality.

1. INTRODUCTION

Brain tumor surgery presents complex challenges due to a delicate tradeoff between removing as much neoplastic tissue as possible and minimizing the loss of brain function. This is usually obtained using intraoperative direct cortical stimulation (DCS) which is considered the gold standard for reliable functional mapping of the cortex. Nevertheless, DCS may trigger seizures and can only be performed intraoperatively, thus extending the duration of the procedure and preventing detailed pre-planning of the intervention. In the last two decades, functional magnetic resonance imaging (fMRI) has emerged as a valuable tool for non-invasive assessment of human brain activity and is now used to determine brain regions that should be spared to prevent functional impairment after surgery. In this regard, fMRI (complemented with other MRI modalities) offers a unique opportunity to optimize treatment planning with a significant reduction of surgical time. However, despite the scientific bases of fMRI are well established, a specialized software tool that calculates, integrates and promptly outputs the imaging results to surgical navigation systems is still lacking. Furthermore, current neuronavigation systems offer only a 2D representation of preoperative images and virtual surgical instruments, with a useful but limited advantage in terms of surgery

planning. In the present project we developed a dedicated software platform to analyze the complex data from multimodal presurgical imaging and send the results to both standard neuronavigation systems and a commercially available wearable mixed reality system (the Microsoft HoloLens).

The proposed implementation offers breakthrough features from a clinical perspective, integrating existing software packages mainly developed for research purposes in a single application specifically designed to release the clinical user from the complexities of research tools. Moreover, this platform automatically transforms the brain mapping results in 3D holograms that can be integrated in the HoloLens. This mixed reality approach offers a striking improvement in terms of ergonomics with respect to standard neuronavigation systems, allowing the surgeon to retain his natural oculo-manual coordination while virtually exploring critical brain structures that need to be preserved.

Currently, our prototype is able to start the analysis by simply connecting to the scanner and loading the patient data. The user is only requested to perform a visual check of the correct coregistration between the different image modalities. The holograms are then automatically anchored with the physical head of the patient in the HoloLens, allowing the surgeon to scroll through different image modalities and 2D sections.

2. STATE OF THE ART

Advanced neuroimaging techniques such as fMRI and white matter tractography obtained with Diffusion Tensor Imaging (DTI) offer relevant information on the anatomic-functional organization near brain tumours [1]. However, image analysis is currently performed using packages developed for research purposes. While these programs have reached a considerable level of complexity and performance, their use is not straightforward in a clinical setting. A complex cascade of operations is indeed required to import, analyze, reformat and output the data to a neuronavigator. Moreover, each software is generally optimized for a specific imaging modality, so that the mastery of different packages is required to accomplish the entire procedure, restricting MRI presurgical mapping to centres that can count on a multidisciplinary research team in addition to the clinical staff. A main challenge is then represented by the implementation of a dedicated neuroimaging tool with a user-friendly interface and a sufficient automation to be used in a clinical setting. Furthermore, we highlight the limitations of standard neuronavigation devices. In these systems a 2D virtual environment is created into a workstation screen showing virtual surgical instruments and patient-specific virtual anatomic/functional details obtained from preoperative CT or MRI scans. The surgeon places a pointer on a real anatomical target and observes its correspondence with the virtual one on the screen that contains also the additional information (e.g. eloquent cortical areas and white matter fibres that are obviously not visible on the exposed brain). Then, he has to “mentally” integrate this information to get a 3D spatial relationship between the tumour and surrounding critical structures in order to choose the best surgical strategy. Thus, the overall procedure is rather cumbersome requiring a significant effort, with prolonged intervention duration and increased error risk. These issues strongly motivated our project.

3. BREAKTHROUGH CHARACTER OF THE PROJECT

To release the clinical user from the typical complexities of research tools, we designed our platform to minimize manual procedures. Indeed, the analysis can be executed by a clinical operator that is only required to perform a final visual check (e.g. on the correct coregistration between images) before enabling the output to the neuronavigator and HoloLens.

Furthermore, our approach based on the emerging mixed reality techniques offers a much larger ergonomics with respect to both standard neuronavigation systems and augmented reality devices. Indeed, with mixed reality the virtual information is “anchored” to the real object and not simply shown together. This means that, once the anchorage has been performed correctly, the overlay

between the real head and 3D holograms from presurgical mapping is automatically updated as the surgeon change position and looks at the patient’s head from different directions, thus allowing a prompt and improved understanding of the spatial relationship between tumour, eloquent areas, white matter fibres, blood vessels and the external skull. In this regard, our application also allows the surgeon to scroll through volumetric data to estimate the exact location of the lesion with respect to critical brain structures that need to be spared. This feature greatly facilitates the planning of both craniotomy and surgical resection.

Moreover, the surgeon can choose different visualization options using simple mid-air “gesture” commands without physically touching any object, which is an important asset to keep everything sterile in the operating room.

So far, the application of a wearable mixed reality system to neurosurgery has only been tested as a proof of concept study using limited preoperative information (just the structural scans) and a manual real-to-virtual anchorage [2]. As a significant improvement we introduced in the mixed reality system based on the HoloLens the full potential of multimodal presurgical mapping and implemented an automatic real-to-virtual anchorage procedure. These features will result in both increased accuracy and reduced intervention time.

We also emphasize the potential of the system to create customized training sessions according particular lesion positions for neurosurgery residents.

4. PROJECT RESULTS

The platform is able to perform the complex cascade of operations needed to analyse presurgical mapping data with just a few commands, starting with the loading of the MRI exam from a Picture Archiving and Communication System (PACS). The prototype has been implemented in a 3-tier infrastructure (Fig. 1):

- Public Layer: Frontend Angular
- Application Layer: Backend Ruby on Rails
- Database Layer: MongoDB

The authentication between the frontend and the backend is done through JavaWebToken. The frontend can be published through HTTPS using a valid certificate. The 3-tier structure of the solution allows the implementation of a network segregation assuring that the data could be stored in a most secure environment not accessible by external networks. The implementation of the frontend/backend is done through the exchange of JavaScript Object Notation (JSON) Documents. This solution increases the scalability of the technology, optimizing the implementation of future features such as a Mobile app, because the backend can be shared with Mobile and Desktop client. Calculation modules have been developed in Python (<http://www.python.org>).

The platform requires the operator to perform just a few steps: i) start the analysis by connecting to a PACS and loading the patient data, ii) perform a visual check of the correct coregistration between the different image modalities, iii) send the results to the neuronavigator system and the Microsoft HoloLens, a commercially available, wearable, computer-integrated mixed reality device (<https://www.microsoft.com/en-us/hololens>). The visual check of the correct coregistration between the different MRI modalities is the only manual step required to the operator. Dedicated modules handle internally the different image formats, generally starting with the conversion from the DICOM standard (the scanner output) to the Neuroimaging Informatics Technology Initiative (NIFTI) format which is the most common input for various open-source software routines currently available for specific analyses. After image processing, the mapping results are again transformed in DICOM format which is the standard accepted by current neuronavigation systems, or they are left in NIFTI to be sent to the HoloLens (Fig. 1).

The mixed reality application has been implemented using the Unity graphical package (<https://unity.com>), allowing the HoloLens to receive the presurgical mapping results analysed by our platform. The whole setup has been developed working on a head phantom realized with a 3D printer from a high-resolution anatomical MRI scan acquired on a volunteer. Using this setting, an automated anchorage procedure between the head and the virtual information (the different presurgical mapping images) has been implemented. Moreover, our solution allows the surgeon to choose which virtual information (fMRI, DTI, structural) visualize as a 3D hologram on the head (Fig. 2). Furthermore, using simple mid-air handle gestures as commands, the surgeon can reslice the volumetric images according to a preferred angulation, thus scrolling through 2D slices to view internal sections highlighting deep critical brain structures (Fig. 2).

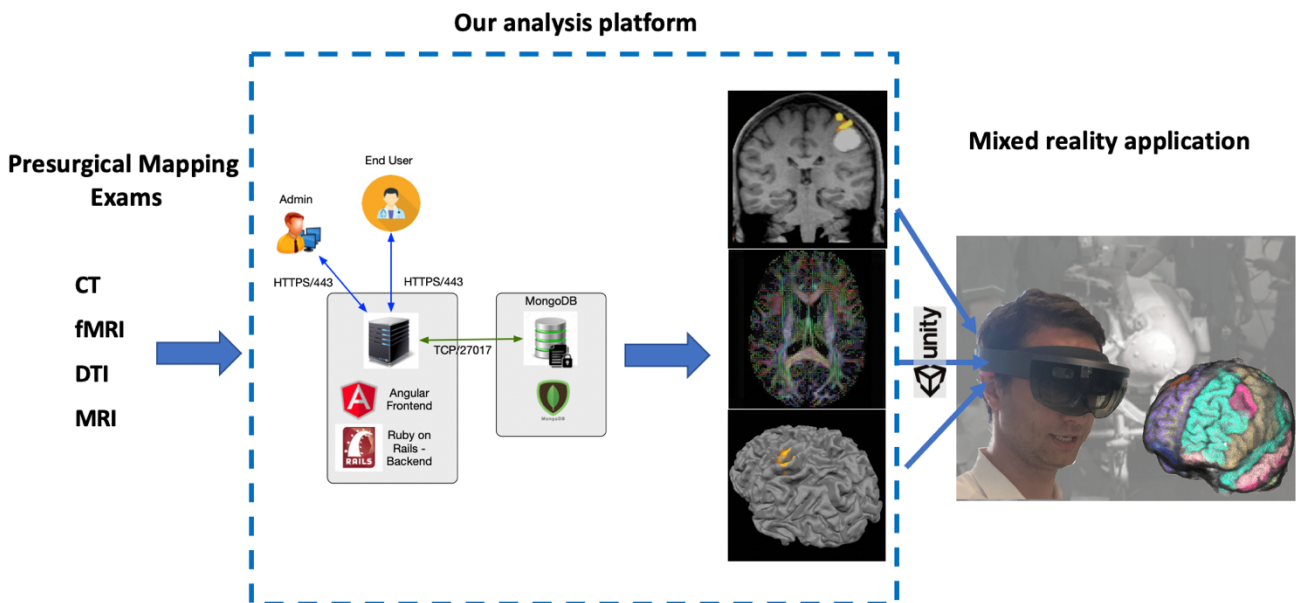


Fig. 1. Schematic representation of our 3-tier infrastructure platform prototype for the analysis of presurgical mapping data and the Unity application allowing the visualization of the results as 3D holograms in the Microsoft HoloLens.

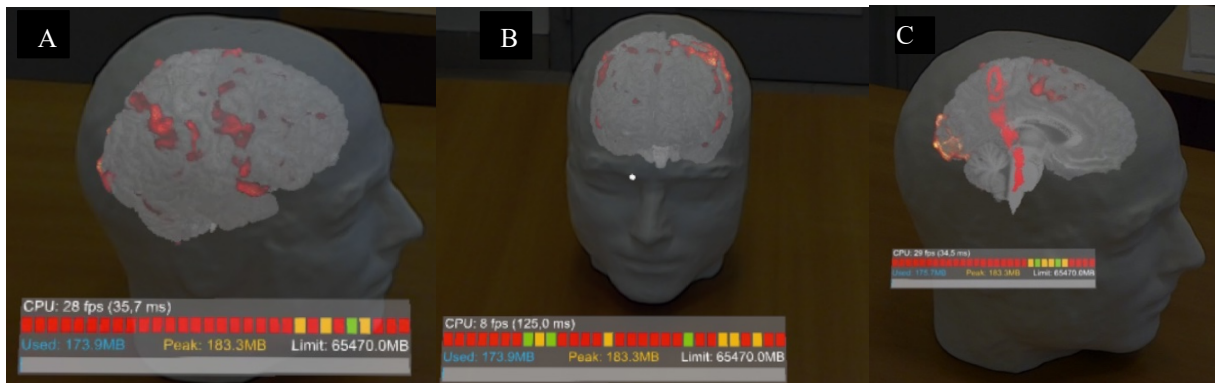


Fig. 2. Examples of the presurgical mapping results as seen in the HoloLens after the automatic coregistration with the head. For practical reasons the procedure has been developed working with a phantom obtained by 3D printing the structural scan of a volunteer. The functional imaging has been performed on the same subject. A and B: eloquent activated areas (fMRI). C: white matter fibres and other activated areas (DTI + fMRI) visible in a mid-sagittal slice obtained with the “scrolling” option.

5. FUTURE PROJECT VISION

In particular, we aim to extend the application of our system beyond brain tumour surgery, including e.g. fetal interventions, deep brain stimulation, epilepsy and mapping of tissue metabolic information. Moreover, we aim to extend the mixed-reality approach from surgery planning to the intervention phase by developing a dedicated wearable device able to provide some magnification factor, ideally integrating the neuronavigator and surgical microscope in a *single* instrument with the added potential of 3D visualization.

5.1. Technology Scaling

A first important technological scale up would be the addition of processing algorithms based on advanced Artificial Intelligence (AI) approaches. These methods would significantly enhance the performance of the current system, also allowing an important breakthrough towards an almost unsupervised procedure. In particular, we plan to apply AI not only to improve image processing but also for automatic preoperative trajectory planning to reach deep brain lesions, thus further reducing the burden on clinical personnel and risks of hemorrhagic complications or postoperative neurological deficits. Furthermore, as an example of additional calculation modules, we’ll include non-invasive mapping of metabolic information (e.g. oxygen consumption or hypoxic areas) obtained with emerging MRI methods to inform advanced radiotherapy treatments (e.g. hadron therapy) by selectively targeting radioresistant areas such as hypoxic ones [3].

Moreover, as a fundamental breakthrough, we aim at integrating both neuronavigator and surgical microscope/exoscope functionalities in a single holographic wearable device. This means that a

dedicated device should be developed, able to provide magnification of virtual and real objects as well.

These steps would allow to reach a Technology Readiness Level (TRL) of 6-7 and to markedly increase the general performance of the system.

5.2. Project Synergies and Outreach

We plan to liaise with both industrial and academic centres, including MRI vendors, a company involved with neuronavigation systems and/or surgical microscopes, centres with a strong background in AI and possibly European Research Infrastructures with HPC resources. We also envision the possibility to cluster with the ATTRACT project MIIFI that is developing a similar technology but applied to fetal surgery.

Regarding dissemination, in addition to the ATTRACT Phase 1 actions, we would consider specific initiatives to deepen the interfaces between science and society such as the European Researchers’ Night. In this regard, during the presentation of our project at the 2019 edition, we noticed that it is a valuable showcase for public dissemination and would suggest it for Phase 2 as well.

5.3. Technology application and demonstration cases

We’ll demonstrate the potential of our system for preoperative planning and its functioning during live neurosurgery. For example, we’ll highlight how the improved image processing based on AI approaches can address the currently unresolved misalignment issue between (undeformed) preoperative images and real brain images as seen after craniotomy (deformed due to intracranial pressure changes). Moreover, we’ll demonstrate the potential of the new AI based platform in further assisting the surgeon with e.g. automatic preoperative trajectory planning to reach deep brain lesions avoiding critical structures (vessels, white matter fibres and eloquent areas) that need to be spared.

With the magnification capability of the new holographic system, we'll also demonstrate its value as a stand-alone system that, by integrating different functionalities in a single powerful and wearable instrument, can greatly simplify the whole surgical procedure.

As a distinctly multidisciplinary proposal, we expect a strong feedback across the different disciplines involved, stimulating fundamental research with new and challenging issues (e.g. new fMRI/DTI techniques to increase spatial resolution and specificity or new AI algorithms). We also expect a strong interaction between academy and industry, as the increased demand of specific imaging modalities will spur larger investments in the development and commercialization of emerging MRI techniques and advanced versions of the proposed holographic device. Finally, we envision a strong reciprocal benefit by a partnership with European Research Infrastructures endowed with HPC resources (including CERN), that would be a real asset for the new, high computational demanding, image processing.

5.4. Technology commercialization

An important action in this direction would be the implementation of our platform using Cloud Computing approaches (eventually through the GÉANT pan-European network). This would significantly increase the market demand, meeting the needs of small hospitals that cannot invest in computational resources to process complex images.

5.5. Envisioned risks

The most challenging objective of our proposal for the Phase 2 is probably the realization of the new holographic device with magnification capability that should replace the HoloLens. While we are confident that we'll find a European company/centre interested in this effort, unexpected technical difficulties could arise. In this case, an alternative approach would be to integrate the images obtained from the surgical microscope/exoscope into the current device. Although this will require the development of dedicated coregistration algorithms it is an easier task. This solution will enable to merge the microscope vision of the surgical field of view with the holograms derived from presurgical mapping, ideally allowing the surgeon to operate with the HoloLens alone. This would remain a huge asset, avoiding the continuous switching between different instruments and allowing the surgeon to retain his natural oculo-manual coordination.

5.6. Liaison with Student Teams and Socio-Economic Study

We just started an MSc in biomedical engineering at University of Chieti-Pescara that will offer great opportunities for this action. Some of us (A.F and P.C.) have extensive teaching records in both applied physics and image processing and would be ideally suited for this task. Finally, we are certainly willing to contribute to socio-economic studies with interviews, technology impact references and other tools used in Science and Technology Studies (<https://ec.europa.eu/jrc/en/research-topic/science-and-technology-studies>).

6. ACKNOWLEDGEMENT

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7. REFERENCES

- [1] Castellano, A., Cirillo, S., Bello, L., Riva, M., Falini, A., 2017. Functional MRI for Surgery of Gliomas, *Current Treatment Options in Neurology*, 19(10):34-56.
- [2] Incekara, F., Smits, M., Dirven, C., & Vincent., A., 2018. Clinical Feasibility of a Wearable Mixed-Reality Device in Neurosurgery, *World Neurosurgery*, 118:e422-e427.
- [3] Gérard, M., Corroyer-Dulmont, A., Lesueur, P., Collet, S., Chérel, M., Bourgeois, M., Stefan, D., Limkin, E.J., Perrio, C., Guillamo, J.S., Dubray, B., Bernaudin, M., Thariat, J., Valable, S., 2019. Hypoxia Imaging and Adaptive Radiotherapy: A State-of-the-Art Approach in the Management of Glioma, *Frontiers in Medicine (Lausanne)*, 12(6):117.