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RESEARCH ARTICLE

A new head-mounted display-based augmented reality system in neurosurgical oncology: a study on phantom

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ABSTRACT

Purpose: Benefits of minimally invasive neurosurgery mandate the development of ergonomic paradigms for neuronavigation. Augmented Reality (AR) systems can overcome the shortcomings of commercial neuronavigators. The aim of this work is to apply a novel AR system, based on a head-mounted stereoscopic video see-through display, as an aid in complex neurological lesion targeting. Effectiveness was investigated on a newly designed patient-specific head mannequin featuring an anatomically realistic brain phantom with embedded synthetically created tumors and eloquent areas.

Materials and methods: A two-phase evaluation process was adopted in a simulated small tumor resection adjacent to Broca's area. Phase I involved nine subjects without neurosurgical training in performing spatial judgment tasks. In Phase II, three surgeons were involved in assessing the effectiveness of the AR-neuronavigator in performing brain tumor targeting on a patient-specific head phantom.

Results: Phase I revealed the ability of the AR scene to evoke depth perception under different visualization modalities. Phase II confirmed the potentialities of the AR-neuronavigator in aiding the determination of the optimal surgical access to the surgical target.

Conclusions: The AR-neuronavigator is intuitive, easy-to-use, and provides three-dimensional augmented information in a perceptually-correct way. The system proved to be effective in guiding skin incision, craniotomy, and lesion targeting. The preliminary results encourage a structured study to prove clinical effectiveness. Moreover, our testing platform might be used to facilitate training in brain tumour resection procedures.

Introduction

In the last decades, neuronavigation quickly became an essential neurosurgical tool, when pursuing minimal invasiveness along with maximal safety [1]. Unfortunately, ergonomics is still sub-optimal.

In neurosurgery, the surgical access is often small and the neurosurgeon, for avoiding unnecessary manipulations or inadvertent injuries to vascular or nervous structures, is forced to develop a sort of "X-ray" view through the anatomical borders of the surgical approach itself [2].

This characteristic has been emphasized by the increasing demand for minimally invasive neurosurgery, mandating the smallest possible accesses for a given intracranial pathology [1]. Minimizing patient

trauma whilst achieving maximal neurosurgical efficiency constitute the cornerstones of minimally invasive neurosurgery.

Accordingly, minimally invasive neurosurgery represents the appropriate balance between minimally traumatizing cranial opening, and optimal lesion control [3,4]. These two surgical goals are complex, challenging, and often conflicting in the daily practice and this fact has encouraged the research for new image-guided surgery systems. Consequently, augmented reality (AR) technology appears as the optimal solution, since it can integrate complex 3 D visualizations of the anatomy contextually to the surgical scene [5].

In a recent work [6], a literature review on AR-based surgical neuronavigators was presented; main goal of

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that study was to provide insight into advantages and shortcomings of different systems tested in vivo in humans. Eighteen state-of-the-art research papers in the field of AR neuronavigation, were classified by using a group of key factors: the real data source (e.g. microscope, external camera, etc.), the tracking modality (e.g. optical, electromagnetic, etc.) the registration technique (e.g. marker-based, surface-based, etc.), the visualization processing technique (surface mesh, color maps, etc.), the display type (e.g. external monitor, microscope eyepieces, etc.), and the perception location (patient, stand up monitor, etc.).

Based on that systematic review, it appears that great effort is nowadays still required for improving the efficacy and the ergonomics of such devices throughout all the different phases of the surgery and across different surgeries. In fact, many proposed solutions have revealed limitations in terms of ergonomics, visualization modality, and general reliability [7–21].

Up-to-date, different AR systems were applied in vivo in neuro-oncological surgery, as well as in neurovascular surgery. In neuro-oncological surgery, AR was mostly applied to the open resection of gliomas and meningiomas. The study comprising the largest tumor series reported a unique advantage in minimizing skin incisions and craniotomies [9,11]. When opening the dura, the AR guide provides a clear visualization of the venous sinuses underneath, as in the case of falcine meningiomas [11,19]. Additionally, when tumors are hidden in depth of a cerebral sulcus, the visualization of the tumor shape under the brain surface can help in the selection of the sulcus to dissect [10]. When the surgeon performs the corticectomy and the tumor resection, the relevant surrounding vascular and nervous structures can be visualized, including eloquent areas and white matter tracts [12]. In an old, yet wide, series of mixed oncological and epilepsy cases, AR allowed reducing the size of the craniotomy needed to position subdural electrodes for monitoring cortical activity [20].

In neuro-vascular surgery, the AR was mainly applied to the open treatment of aneurysms [15,16] and arteriovenous malformations (AVMs) [14]. As proven in all these studies, AR can build up a useful asset in neurovascular surgery for its ability to improve the craniotomy placement and dural opening.

Furthermore, presenting AR through the surgical microscope can facilitate aneurysm treatment, since it allows the minimization of the subarachnoid dissection, and the selection of the proper clip placement site by a thorough visualization of the vascular anatomy near the aneurysm [16]. Besides that, when by-pass surgery is the designated treatment option for multiple

aneurysms, the donor vessel and of the recipient intra-cranial vessel can be easily identified [15].

In case of intraoperative AVM rupture, AR proved also to yield a reliable visualization of the main arterious feeders of an AVM, indicating precisely where proximal control should be performed. Finally, AR injection into the surgical microscope proved to be useful in aiding the resection of deeply-seated or close to eloquent areas cavernomas [21].

In any AR-based system, the visualization processing technique implemented heavily affect depth perception, and therefore the actual efficacy of the surgical navigation system.

Several visualization modalities in literature were proposed in order to improve depth perception [22,23]. One of the simplest and more intuitive tools is to adjust color coding depending on object depth (e.g. superficial objects can be rendered as clear and bright, while deeper structures foggy and opaque).

Among the aforementioned parameters characterizing a specific AR neuronavigators, the real data source and the perception location are those that critically affect objects localization along the three dimensions and depth perception. Furthermore, if not properly evaluated, their management can raise issues of hand-eye coordination and parallax [24,25].

For instance, problems in hand-eye coordination affect those AR systems that rely on handheld video probes (Dex-Ray) [11], since the line-of-sight of the camera probe is not aligned with the one of the surgeon's eye. Unwanted parallax is introduced in those systems that feature a video projector for the presentation of virtual information deep into the anatomy [24], because the misalignment between the projector and the user's line of sight causes a wrong perception of the AR view.

In non-endoscopic neurosurgical procedures, a parallax-free condition can be achieved through devices that offer the AR scene in the line of sight between the surgeon and the surgical field, as in the case of microscope-based neuronavigators [14–16,21] or through solutions based on light-field displays [17].

Following this line of research, the present work, is aimed at investigating the effectiveness of a novel and quasi-orthoscopic wearable AR system as an aid in complex neurological lesion targeting for which an egocentric approach is preferable. The system, based on a head mounted stereoscopic video see-through display (HMD), has already been tested in a variety of surgical specialties including, vascular surgery [26], maxillofacial surgery [27,28], and orthopaedic surgery [29,30].

The ergonomics and usefulness of the HMD have been preliminary tested on a newly designed patient-

specific head phantom for neurosurgery by twelve different operators, nine of whom without any neurosurgical training.

Materials and methods

In this section, we provide a detailed description of the experimental set-up including the HMD and the patient-specific head phantom that was designed as testing platform for our AR-based neuronavigation system. Further, we briefly outline the video marker-based method implemented for tackling the image-to-patient registration problem.

System overview

Our stereoscopic video see-through HMD for AR-based neuronavigation comprises the following two major components (Figure 1): a commercial 3 D visor (Sony HMZ-T2) provided with dual 720p OLED panels and a horizontal field of view of 45°; 2 external USB cameras (IDS uEye XS) equipped with a 5 Megapixel CMOS sensor (pixel size of 1.4 μm) that achieve a frame rate of 15 fps at 1280x720 resolution. As described in more details in [31–34], the two external cameras were mounted at an anthropometric interaxial distance of ~7 cm, as done by [35] and [36]. By doing so, and by matching the field of view of the displays to that of the cameras, a quasi-orthoscopic view of the augmented scene mediated by the visor was provided. The AR application was implemented using a custom-made software library built in C++ easily configurable and extensible thanks to the employment of two text configuration files [37]. The management of the virtual 3 D scene was carried out through the open-source software framework OpenSG 1.8 (www.opensg.org), while regarding the machine vision routines, needed for implementing the video-based tracking method, we employed the Halcon 7.1 software library by MVTec®. The whole system runs on a gaming laptop Alienware® M14 provided with an Intel Core i7-4700 @ 2.4 GHz quad core processor and 8 GB RAM. The graphics card is a 1GB nVidia® GeForce GTX 765 M.

Video see-through paradigm

Here is a functional and logical overview of the video see-through paradigm that underpins our AR mechanism: the two external cameras grab video frames of the real scene; the video frames are screened as backgrounds onto the corresponding display of the visor; the software application elaborates the same grabbed video frames to perform the real-time registration of

Figure 1. Wearable video see-through display. The head mounted stereoscopic video see-through display.

the virtual content, dictated during the surgical planning, to the underlying real scene (Figure 2).

The accurate patient-to-image registration is the fundamental prerequisite for yielding geometric coherence in the AR view of the surgical scene. This condition is satisfied if the virtual content of the scene is observed by a couple of virtual viewpoints (virtual cameras) whose processes of image formation mimic those of the real cameras in terms of intrinsic and extrinsic parameters. To accomplish this goal a stereo rig calibration, which encompasses the estimation of the projective parameters of both cameras (i.e. intrinsic parameters) as well as the estimation of the relative pose (position and orientation) between the two cameras (i.e. extrinsic parameters), is performed offline by implementing a standard calibration routine [38].

The online estimation of the transformation matrix [R|T], which encapsulates the pose of the stereo rig reference system (CRS) in relation to the reference system of the surgical planning (SRS), is the result of a marker-based video registration method [29,31,34]. This video-based tracking modality relies on the localization of at least three spherical markers rigidly constrained to the head phantom and whose position in the virtual scene (SRS) is recorded during planning.

The key characteristic of the implemented method for registering the preoperative planning to the live views of the surgical scene (i.e. the patient phantom) is that it is not based on the adoption of a cumbersome external tracker. Standard surgical navigation systems, featuring the use of external infrared trackers, may in fact introduce unwanted line-of-sight constraints into the operating room as well as add error-prone technical complexity to the surgical workflow [39]. Our video-based algorithm provides sub-pixel fiducial registration accuracy on the image plane [34].
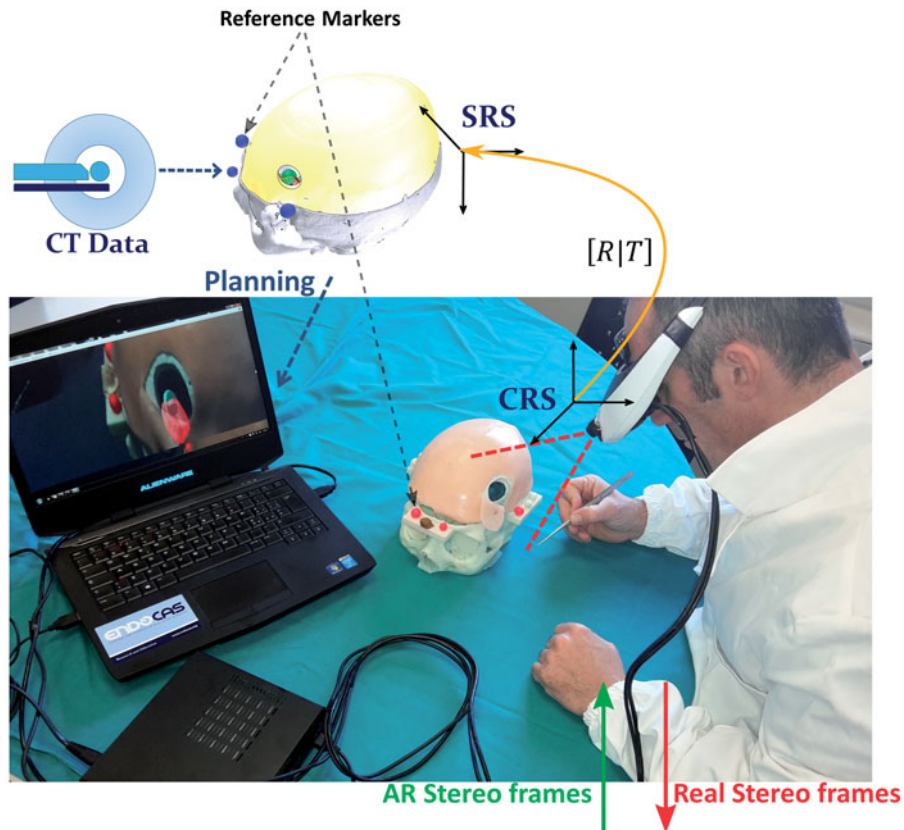
Figure 2. Video see-through paradigm of the augmented reality neuronavigator. The software application merges the virtual three-dimensional surgical planning with the stereoscopic views of the surgical scene grabbed by the stereo rig. Thereafter, the augmented reality stereo frames are sent to the two internal monitors of the visor. Alignment between real and virtual information is obtained by a tracking modality that relies on the localization of at least three reference markers rigidly constrained to the head phantom and whose position in the virtual scene (SRS) is recorded during surgical planning.

Surgical planning and AR visualization modalities

To assess our AR-based surgical navigation system we conducted preliminary tests on an acrylonitrile butadiene styrene (ABS) replica of a patient-specific head phantom. From a surgical standpoint, we tested our system in a simulated high-risk neurosurgical scenario: the resection of a small tumor (or tumor portion) medially adjacent to the posterior part of the inferior frontal gyrus, where the Broca's area is generally located.

The patient-specific phantom has been designed from the segmentation of an anonymized preoperative computed tomography (CT) dataset: the DICOM files were segmented using a semi-automatic segmentation tool integrated into the open-source platform Insight Segmentation and Registration Toolkit [40]. The resulting 3 D virtual anatomic details of the head, in the form of an STL file, were exported to a CAD software to layout the rigid parts of the 3 D patient phantom as described in details in the following paragraph.

The rendering of the anatomical details consisted of: skull base, skull cap before craniotomy, skull cap

after planned craniotomy, lesions, and eloquent areas. Lesions and eloquent areas were synthetically added in the 3 D reconstruction of the head by mimicking small tumour(s) adjacent to Broca's area. Furthermore, geometrical structures were also designed as key elements for the AR visualization modalities.

The 3 D rendering of all the anatomically relevant structures of the head, together with the synthetically created anatomical structures and purely geometrical elements, were exported to a 3 D graphics-modelling tool (Deep Exploration by Right Hemisphere) to elaborate the visualization modalities.

We considered six possible visualization processing modalities to be offered to the end user through the visor.

In AR-based surgical navigation systems, according to the DVV taxonomy [23,41], the output of the visualization processing modality (i.e. the visually processed data) represents the type of virtual content introduced to aid the surgeon throughout the surgical task. Depending on the specific surgical scenario considered, the semantic of the visually processed data may
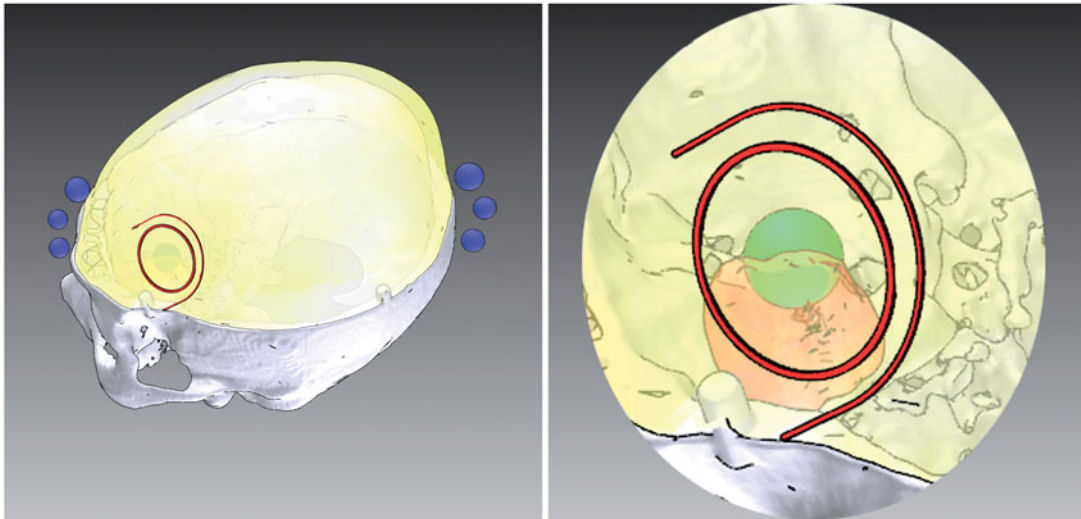
Figure 3. Surgical planning for skin incision and craniotomy. Elaboration of the surgical planning on the three-dimensional rendering of the segmented anatomy, obtained by means of a semi-automatic segmentation software. Left: visualization modalities exploited to depict the planned skin incision and the planned craniotomy. Right: a zoomed detail with enhanced transparency of the surgical planning scene. The size, shape, and location of the craniotomy and of the skin incision were deducted on the basis of the optimal dissection corridor planned for accessing the surgical target whilst avoiding the eloquent area.

be anatomical, that is dealing with the anatomy or pathology of the patient, operational, that is in relation to the surgical act itself, or strategic, that is dealing with data primitives associated to the surgical planning (e.g. lines, points, contours, geometric shapes).

The six visualization processing modalities which were considered in our surgical scenario, exploited different visual cues to help the user in understanding the spatial relationships between real scene and visually processed data. Nonetheless, depth perception was not a major issue in performing the craniotomy procedure: the two subtasks herein involved, which are the skin incision and the craniotomy, are fundamentally bi-dimensional tasks because they both involve a bi-dimensional movement of the surgical instrument on a surface. For this reason, the first two visualization modalities were very simple and intuitive:

Virtual Line of Skin Incision: we contemplated that the most ergonomic AR-modality for guiding the incision of the skin were a planned/virtual contour of the incision, represented as a virtual U-shaped line, superimposed to the real skull vault (Figure 3).

Virtual Contour of Craniotomy: the exact size, shape and location of the craniotomy can be deducted by superimposing to the real skull vault a virtual quasi-circular shape representing the contour of the planned craniotomy (Figure 3).

The remaining four visualization modalities were all conceived to aid the surgeon in planning the optimal dissection corridor for accessing the surgical target as well as for avoiding the eloquent area (Figure 4):

1. *3D grid effect*: The first modality was inspired by the work of Abhari et al. [42], whose primal goal was to develop and evaluate an AR environment to facilitate training in planning brain tumour resection. One of the visualization techniques tested to promoting depth perception was the Grid Lines technique (Figure 4(A)). The peculiarity of this strategic technique is to evoking a strong and unambiguous sense of depth by promoting the motion parallax cue caused by the relative motion between observer and scene. This is achieved by emphasizing the apparent motional displacement between the tumour and background by means of a 3D grid behind the tumour.

2. *Occluding virtual viewfinders*: In this *strategic* modality, two virtual viewfinders were added to the scene as coaxially aligned to the optimal dissection corridor: the surgeon is aided at orienting the dissecting instrument toward the lesion by aligning the back of the surgical forceps to the two viewfinders. The first viewfinder indicates the ideal entry point for the surgical tool onto the external surface of the brain, whereas the second viewfinder defines the optimal trajectory of dissection (Figure 4(B)). The position of both the viewfinders is preoperatively defined during surgical planning. A small sphere anchored to the back of the forceps, is intended to allow a more immediate detection of the optimal alignment. This strategic modality was already positively tested as aid in the percutaneous reaching of lumbar pedicles in a study on a patient-specific spine phantom [29].
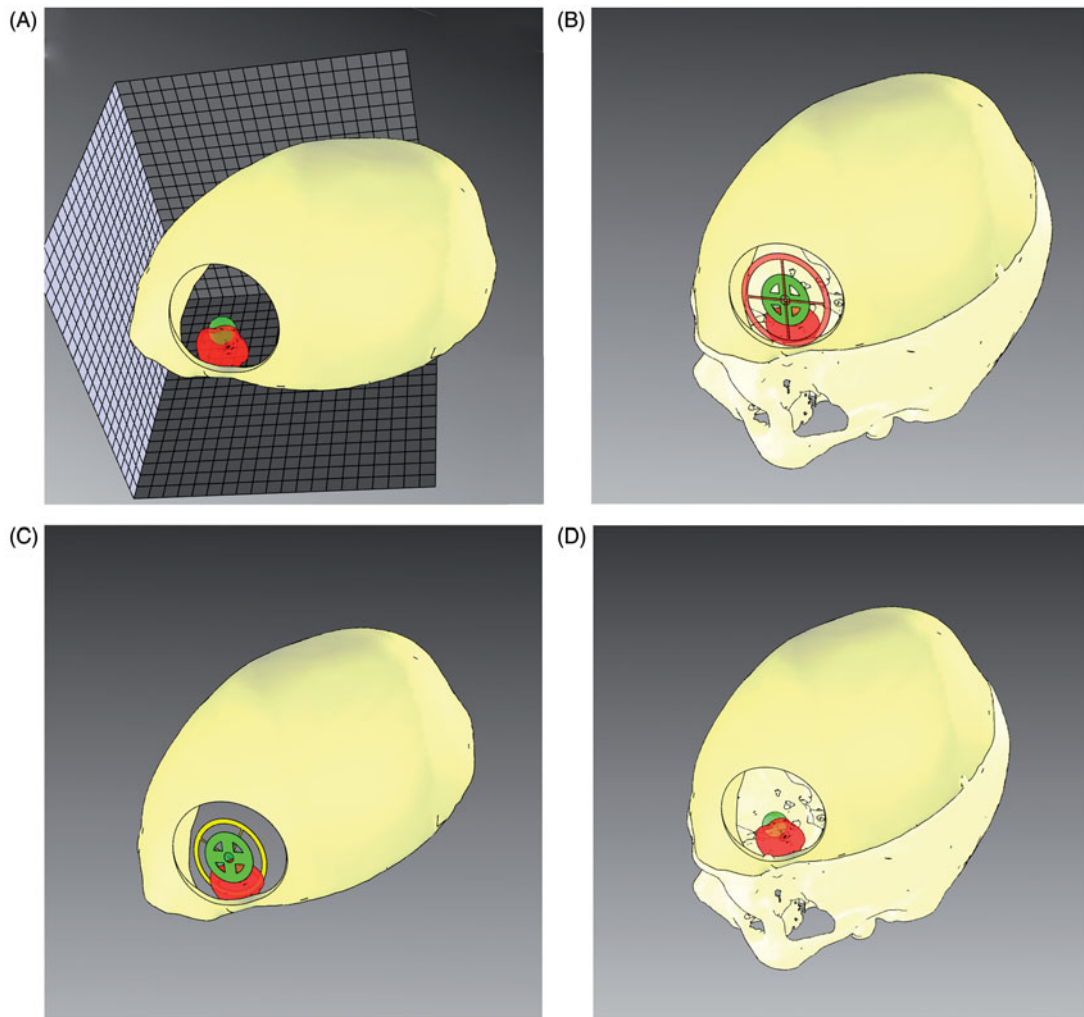
Figure 4. Surgical planning for lesion targeting. Visualization modalities conceived to aid the surgeon in planning the optimal dissection corridor for accessing the surgical target as well as for avoiding the eloquent area: A) *3D grid effect* – The sense of depth is obtained by promoting motion parallax cue through the apparent motional displacement between tumour and background by means of a 3D grid behind the tumour. (b, c) *Occluding and Non-occluding virtual viewfinders* – Efficient handling of the occlusion cue between two viewfinders to aid the surgeon in aligning the surgical tool with a predefined trajectory. The first viewfinder indicates the ideal entry point for the surgical tool, whereas the second viewfinder defines the optimal trajectory of dissection. To avoid the occlusion of the real surgical field the second viewfinder, in the *Non-occluding modality* is moved out of the line of sight of the surgeon, behind the lesion.

3. *Non-occluding virtual viewfinders*: Just as in the previous modality, the key idea of this one relies on the efficient handling of the occlusion cue between the two viewfinders to aid the surgeon in aligning the surgical tool with a predefined trajectory. The main shortcoming of this approach lies in the fact that the two viewfinders might too heavily occlude the surgical field. To cope with this problem, we moved the second viewfinder, which defines the ideal trajectory, out of the line of sight of the surgeon, behind the lesion (Figure 4(C)).
4. *Anatomical Occlusions and transparencies*: This anatomical modality is the most intuitive for strengthening the understanding of the spatial relationships between objects [22]. By means of the mutual integration between occlusions, motion parallax, and stereopsis the surgeon can perceive the relative proximities between tumour and eloquent area, and therefore he can be smoothly guided in accessing the surgical target (Figure 4(D)).

The patient-specific phantom

An experimental set-up was appositely developed to test the whole system and to evaluate the ergonomics of the different visualization modalities. The set-up is depicted in Figure 5. The whole anatomical structure except for the skin, lesions and eloquent areas was
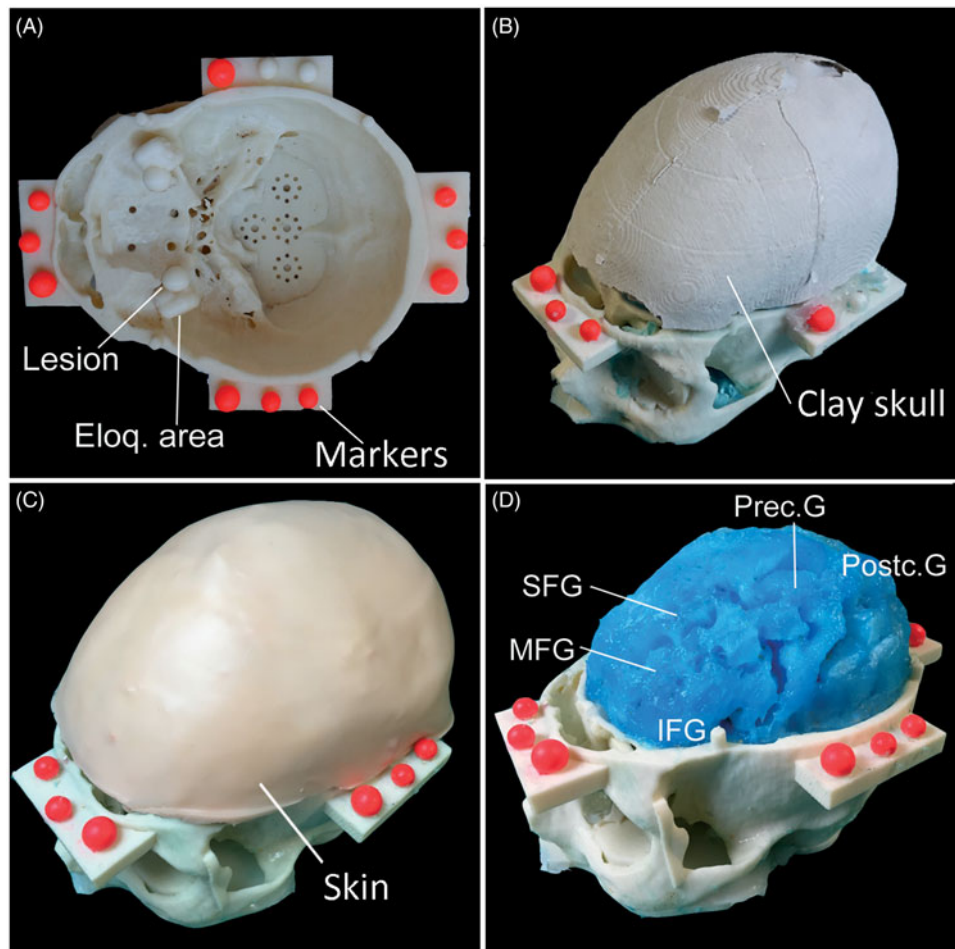
Figure 5. Patient-specific head phantom. A) The skull base is embedded with bilateral frontal lesions both medial to the adjacent eloquent areas (Eloq. area). The inner surface of the skull base presents several housing designed to insert further lesions or eloquent areas. Four lateral shelves served as support for optical reference markers (fluorescent dyed spheres). B) The skull clay vault. C) The liquid polymer used to reproduce the brain was spilled in a complete skull model. After removing the vault, brain perfectly reproduced the details of gross superficial cerebral parenchyma, including: inferior frontal gyrus (IFG), middle frontal gyrus (MFG), superior frontal gyrus (SFG), precentral gyrus (Prec. G), postcentral gyrus (Postc. G.). D) The complete phantom with the vault covered with a skin-like silicon layer.

obtained, as aforementioned, from the segmentation of an anonymized CT dataset (1.25 slice thickness) [40,43].

Motivation for the use of the CT dataset for modelling the bony structures as well as the brain parenchyma was twofold. First, the greater level of detail offered by CT-scan for modelling the bony structures. Second, the need for a 3 D model of the brain that could be easily replicated with our mould-based approach still ensuring a realistic brain consistency and elasticity. This last point set a limit to the level of details permitted in the brain parenchyma: a trade-off was found between the level of detail in the representation of the bivalve-mould and the possibility to extruding the synthetic brain from the mould, given its consistency and elasticity.

The skull base and brain container, after segmentation and surface generation, were exported to a CAD software (PTC® CREO) where the model was modified. In a real set-up, the reference markers needed for the registration, should be put along the Mayfeld® U-shaped skull clamp. Therefore, we added four shelves around the skull as housing structures for the spherical markers, as they would be if anchored on a Mayfeld® U-shaped skull clamp.

We added an array of housing holes along the skull basal surface for holding the supports of the lesions and of the eloquent areas (synthetically added in verisimilar and predetermined positions). The obtained models (skull base, lesions and eloquent areas with their supports) were printed with a 3 D rapid prototyping machine (Stratasys® Elite Dimension). The fluorescent dyed spherical markers and the skull base are shown in Figure 5(A). The synthetically created lesions and eloquent areas were anchored to the skull base
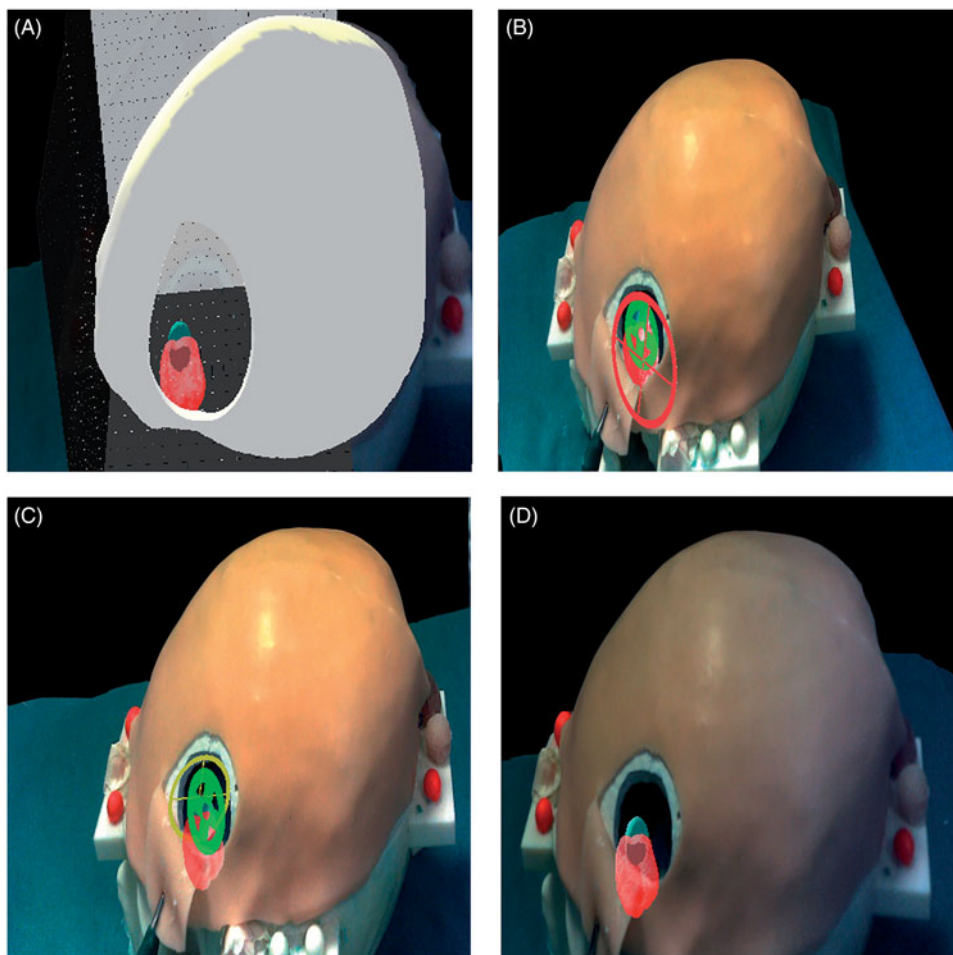
Figure 6. Phase I of the experimental evaluation. Phase I: The four augmented reality visualization modalities as they appear to the user during the evaluation test. A) *3 D grid effect,* B) *Occluding virtual viewfinders,* C) *Non-occluding virtual viewfinders,* D) *Anatomical Occlusions and transparencies.*

through their supports, so that their planned positions could be retrieved.

We inserted four lesions and four eloquent areas. Lesions and eloquent areas shared the same material and the same colour.

The skull cap, still obtained through segmentation from the same dataset, was 3 D printed and used as reference to create a mould with the Mold Max® Performance Silicone Rubber (Smooth-On Inc.). The mould was used to reproduce the skull cap by ceramic clay. Such a choice allows the consistent reproduction of all the skull caps needed for intensive testing. We carefully selected a type of ceramic dental clay that ensures good detail reproduction and provides a correct mechanical feedback during craniotomy (Figure 5(B)). As for the brain parenchyma the needs were threefold: (1) to reproduce brain sulci and gyri in order to provide realistic anatomical landmarks, (2) to reproduce brain consistency and elasticity for the lesion excision task, and (3) to determine a procedure that allows for relatively quick fabrication of several

brains for repeated tests. As for the first requirement, a mould was generated starting from the brain segmentation of the dataset; the negative of the segmented 3 D model of the brain was elaborated in the aforementioned CAD software; thereafter a bivalve mould was designed and 3 D printed. As regards the second and third requirements, we selected a non-toxic durable material easy to handle in order to be able to reproduce brain phantoms for intensive testing. The selected material was a PVA-C -based hydrogel [44,45]. A variety of PVA samples were produced with different PVA concentration and different numbers of freezing thawing cycles before reaching a consistency and elasticity that could meet clinical needs. Clinicians qualitatively assessed the different samples and chose a composition of a 4% PVA-H2O solution concentration with 4 Freezing/ Thawing cycles to obtain the desired consistency and elasticity. In Figure 5(D) the resulting brain parenchyma comprising the main sulci and gyri is depicted.

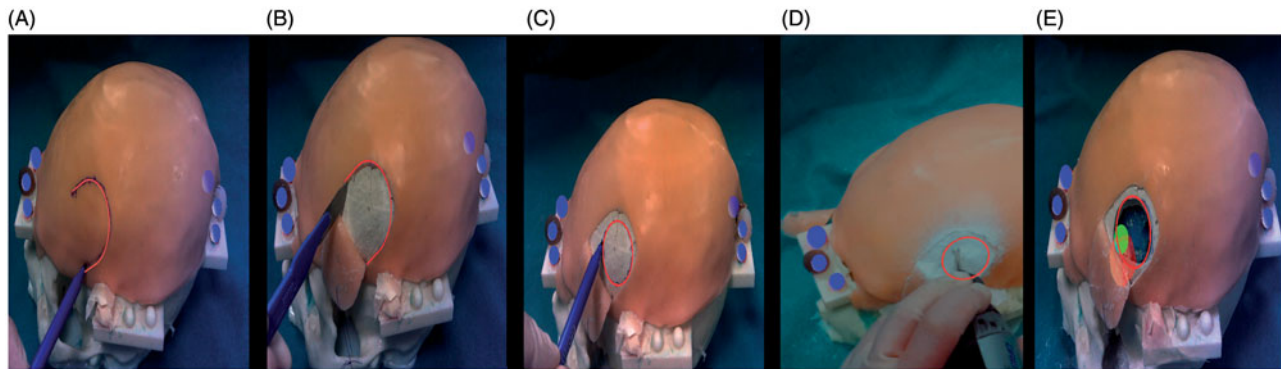The skin was obtained using Ecoflex® Silicone Rubber (Smooth-On Inc.). The clay skullcap was hand

Figure 7. Phase I of the experimental evaluation. Phase II: Augmented reality guided incision of the skin and craniotomy. A) The surgeon marks with a pen the path of the skin incision on the skin following on the augmented reality path (red). B) Scalpel incision. C) After removing the skin incision path, the craniotomy perimeter is displayed and marked with a pen. D) Osteotomy drilling. E) Osteotomy completed: behind the exposed surface of the brain, the surgeon can perceive the position of the target lesion and of the surrounding eloquent area.

coated with three layers of approximately 0.5 mms/ each. Figure 5(C) shows the complete "closed" phantom.

Experiments

Details on the preliminary laboratory testing conducted at the EndoCAS center of the University of Pisa are presented in the following paragraphs.

Phase I: Ergonomics of the AR environment

Phase I involved nine subjects without neurosurgical training in performing spatial judgment tasks while using our AR system for conducting small-lesions targeting and eloquent areas avoidance during the planning of an imaginary brain tumor resection. The goal of this first series of 36 experiments ($= 4$ trials $\times 9$ subjects) was to assess the ergonomics of the four visualization modalities above described. For each one of the four visualization modalities randomly presented to him/her, each participant was asked to navigate the augmented scene and estimate the ergonomics and the effectiveness of the AR guide in planning the optimal surgical access to the tumor (Figure 6). After each trial, the subject was asked to fill out a structured questionnaire on the ergonomics and on the level of depth perception of the specific AR modality tested. The questionnaire included 4 questions with a five point scale ($0 =$ strongly disagree to 4 strongly agree) [46]. Each item was explained to the participant in advance, in particular the first two assumptions were relative to the actual ergonomics of the AR modality, whereas the last two assumptions were related to the depth perception provided.

Statistical analysis of data was performed using the SPSS® Statistics Base 23 software (IBM). The central

tendencies of responses to a single Likert item were summarized by using median, with dispersion measured by interquartile range.

The Wilcoxon signed-ranks test was used to determine the significance of the responses to each item and globally evaluating if the operators were significantly more likely to agree or disagree with each of the statements. A p-value <0.05 was considered statistically significant.

Phase II: Preliminary tests.
The goal of these trials was to provide a preliminary evaluation of the effectiveness of our AR-based neuronavigation approach as an aid into the definition of the skin incision and craniotomy and of the optimal surgical corridor to reach the target and avoid the eloquent area (Figure 7). Thus, three surgeons were required to perform the same neurosurgical procedure on the left and right side of the patient-specific head phantom, respectively without and with the AR guidance.

When the experiment was conducted without AR, the surgeon was asked to reach the tumor, by properly tailoring the skin incision, osteotomy and cortical dissection, just relying on the preoperative images and on the anatomical landmarks replicated in the phantom, as in a traditional intervention without neuronavigation.

Otherwise, when the experiment was conducted under AR guidance, the determination of the optimal skin incision, of the craniotomy perimeter, and of the surgical access to the target was aided by providing AR visualization.

Prior to the surgical session, the three surgeons were also asked to select the visualization modality that, in their view and amongst the four modalities proposed, was deemed by them as the most effective

Table 1. Questionnaire results.The central tendency of responses is summarized by using median with dispersion measured by Interquartile range (25°;75°). Statistically significant p-values (<0.05) are highlighted. The last row gives evidence of the modality which resulted more effective and of the significativeness of the evaluation for each modality (bold).

		OCCLUDING VIRTUAL VIEWFINDERS		3D GRID EFFECT		NON-OCCLUDING VIRTUAL VIEWFINDERS		ANATOMICAL OCCLUSIONS AND TRANSPARENCIES	
		Median (IQR)	P	Median (IQR)	P	Median (IQR)	P	Median (IQR)	P
Ergonomics	The viewing modality is effective to target the lesion	3.00 (1.00;4.00)	0.317	0.00 (0.00;1.00)	**0.003**	3.00 (3.00;3.00)	**0.02**	4.00 (3.00;4.00)	0.058
	The virtual information can compromise task execution because of scene occlusion	1.00 (1.00;3.00)	0.317	0.00 (0.00;1.00)	**0.003**	3.00 (1.00;3.00)	0.317	4.00 (3.00;4.00)	**0.003**
Depth perception	The viewing modality allows for a complete perception of the spatial relationships between real scene and visually processed data	3.00 (2.00;3.00)	0.317	4.00 (3.00;4.00)	**0.003**	3.00 (3.00;4.00)	**0.035**	3.00 (3.00;4.00)	0.058
	The motion parallax cue does not affect the depth perception	3.00 (3.00;4.00)	**0.003**	3.00 (3.00;3.00)	**0.003**	3.00 (3.00;4.00)	**0.003**	3.00 (3.00;4.00)	**0.003**
	Whole results: MEDIAN (IQR)	**3.00 (1.50; 3.50)**	**0.083**	**2.00 (1.50; 2.00)**	**0.046**	**3.00 (3.00;3.50)**	**0.010**	**3.50 (3.00;4.00)**	**0.008**

in navigating to the target lesion. At first, all the virtual content was presented to the surgeon so as to provide an overall understanding of the surgical planning merged with the real surgical field. Thereafter, the AR modalities dedicated to the execution of the specific surgical subtasks, were stepwise provided to the surgeon, following the workflow of a traditional procedure of brain tumor resection. Thus, as a first step, the perimeter of the skin incision was shown. After skin incision, the virtual line of incision was replaced in the AR scene by the contour of the craniotomy. Finally, the optimal dissection corridor for accessing the lesion, as well as for avoiding the eloquent area, was determined using the selected visualization/s modality/s.

The surgeons performed the same task on the contralateral side of the brain without the aid of the AR view. As soon as the surgeon perceived to have hit a solid area with the tip of the surgical forceps (lesions and eloquent areas are made in ABS), he/she was asked to remove the surgical instrument and mark the area with a red pen. At the end of the experiments on both sides, the results were visually evaluated after the removal of the simulated brain tissue.

Results

Phase I results

Results are summarized in Table 1. According to the responses given by the non-clinicians, among the four proposed modalities, the "*Anatomical Occlusions and Transparencies*" appeared as the preferred one in terms of ergonomics and depth perception. The "*3 D Grid Effect*" was effective in terms of depth perception, but extremely poor in terms of ergonomics for the augmented reality task, being more suitable for surgical planning. The two "*Virtual Viewfinders*" modalities were deemed effective in terms of definition of the surgical access, but not as good in terms of ergonomics and depth perception due to the tendency of the virtual content to occlude too heavily the underlying anatomy.

Phase II results – system evaluation

In apparent contradiction with the results of Phase I, yet in accordance to the results of the ergonomic evaluation carried out in the in vitro study in orthopaedic surgery [29], all the surgeons opted for the "*Occluding virtual viewfinders*" visualization modality. Nonetheless, the traditional AR visualization modality, featuring the superimposition of the semi-transparent virtual replica of the lesion and of the surrounding eloquent area, was not totally ruled out for its ability of strongly aiding spatial judgment and depth perception. For this reason, the determination of the optimal dissection corridor for accessing the lesion as well as for avoiding the eloquent area was aided by means of a virtual content obtained by merging the "*Occluding virtual viewfinders*" and "*Anatomical Occlusions and Transparencies*" visualization modalities (Figure 8).

The surgeons oriented the dissecting instrument (resembling bipolar forceps) and navigate to the surgical target relying on the task-oriented AR guide and
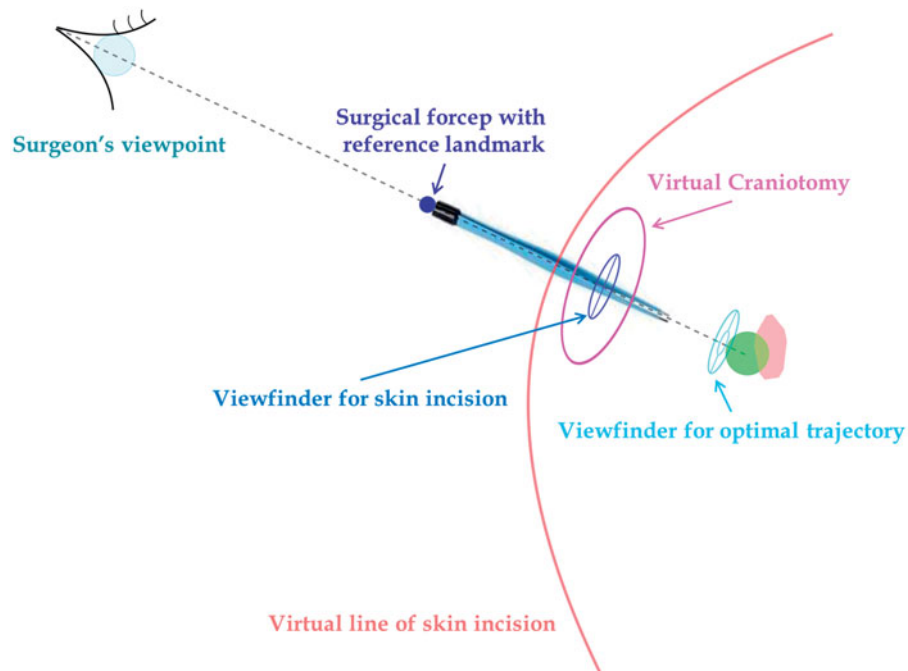
Figure 8. Schematic drawing of the AR visualization modality chosen by the surgeons. The AR visualization modality selected by the surgeons for aiding the targeting of the lesion was obtained by merging the traditional anatomy-based visualization modality that resulted the most effective in evoking depth perception (i.e. *Anatomical Occlusions and transparencies*) with the one allowing a more accurate definition of the ideal trajectory for targeting the hidden lesion (i.e. *Occluding virtual viewfinders*).
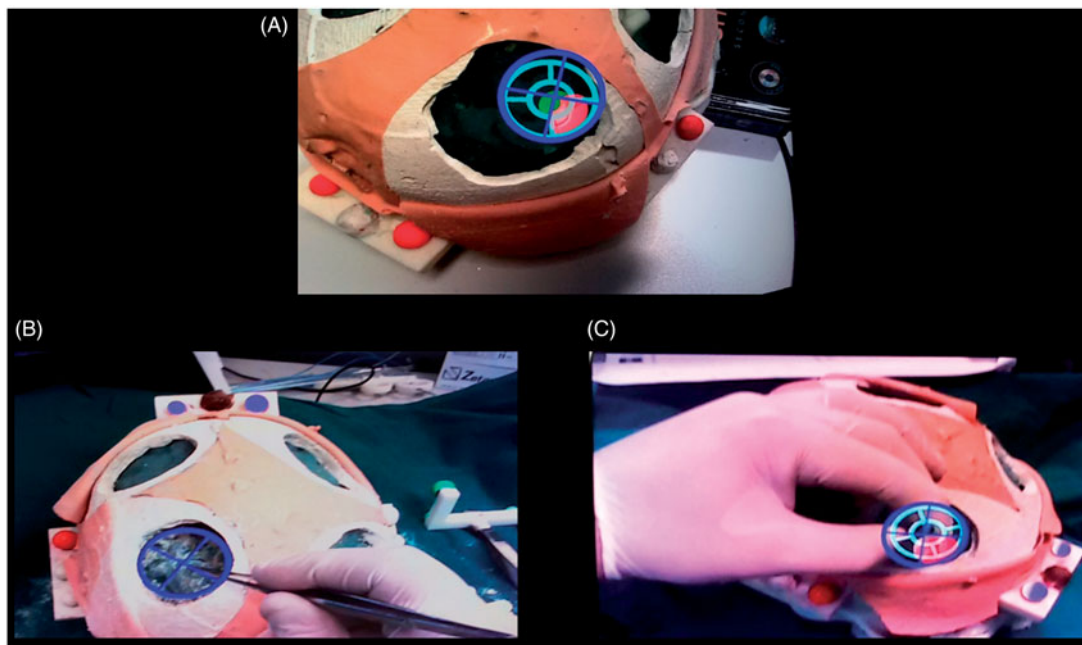

Figure 9. The AR-aided surgical tasks. A: The surgeon first aligns the tip of the dissecting instrument to the center of the dark blue viewfinder he/she sees in the AR scene; B: the surgeon coaxially aligns the back of the surgical forceps to the two viewfinders (dark blue and light blue). The two viewfinders define the optimal trajectory of dissection.

on their augmented perception of the surgical field (Figure 9(A)).

In more details, the surgeons aligned the tip of the dissecting instrument to the center of the first viewfinder projected over the brain parenchyma (hence managing 2 positional degrees of freedom) (Figure 9(B)). The second viewfinder was used by the surgeon to pivoting the surgical tool around the entry
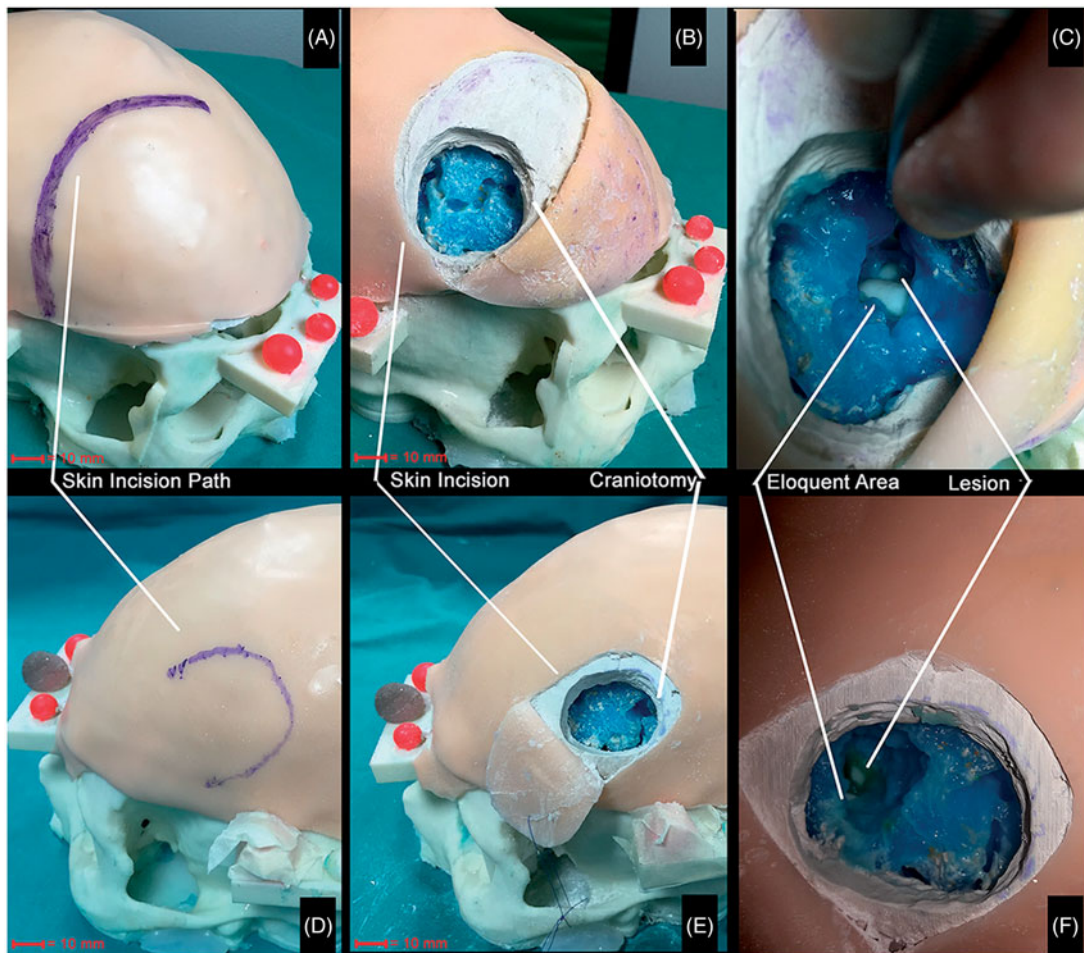
Figure 10. Qualitative comparison between AR and traditional surgical approaches to accessing the artificial lesions. Qualitative comparison between the two approaches to accessing the lesion: augmented reality-based approach (bottom row) vs standard approach (top row). A vs D: by using the augmented reality guidance the size of the skin incision results significantly smaller since the surgeon does not need to expose a large part of the skull vault to targeting the lesion. B vs E: the same concept supports the fact that the osteotomy results wider with the standard approach since the surgeon needs to expose parenchyma sulci and gyri as reference landmarks to navigate towards the lesion. C vs F: the target lesion was reached with both the approaches. However, with the standard approach (C) the eloquent area was considerably exposed (thus implying its possible damaging) and the lesion was not targeted at the center, whereas with the augmented reality approach (F) the lesion was centered and the eloquent area was only slightly exposed.

point so as to be aligned to the planned insertion direction into the pedicle (managing 2 rotational degrees of freedom) (Figure 9(C)).

As for the skin incision subtask, the AR guidance allowed an evident reduction on the size of the incision (Figure 10(A,D)). A similar result was obtained on the craniotomy subtask: the use of the AR visualization proved to be an effective aid in tailoring the craniotomy that, otherwise, would be defined on the sole basis of the skull bony landmarks (Figure 10(B,E)). Finally, the optimal trajectory for accessing the lesion was improved by means of the AR guidance (Figure 10(C,F)). Such approach seems to complement the surgeon's anatomical knowledge of the brain surface with additional and intuitive real-time information. As reported in the results in Table 2, with AR

guidance all surgeons were able to reach the lesion avoiding the close eloquent area, while, without AR guidance an eloquent area was touched.

It is important to outline that the reported results do not intend to have any statistical significance yet they strongly encourage to conducting a more thorough and quantitative study. Nonetheless, the testing platform was judged as very realistic and worthy of

Table 2. Trials results.

	LESION TARGETING	
	With AR-guidance	Without AR-guidance
Surgeon 1	2/2	1/2
Surgeon 2	2/2	2/2
Surgeon 3	2/2	2/2
All Surgeons	6/6	5/6

being utilized also for training purposes in combination or separately to the AR neuronavigator.

Discussion

The neurosurgeon is often required to work in deep and narrow corridors, surrounded by critical nervous and vascular structures and with a limited perception of the surgical field. Therefore, neurosurgery constitutes a unique opportunity for the development of new AR systems since the concept of minimally invasive neurosurgery mandates the smallest possible approaches for a given pathology.

As general rule, the ideal AR-based navigator should show several anatomical and/or operational details in a very limited space, it must not hide the real anatomy underneath, it should mimic the depth perception of the human visual system, and yield highly accurate virtual to real registration.

One of the main difficulties that significantly affect the smooth introduction of AR-based neuronavigators into the clinical practice is the lack of a focus on the clinical assessment of the ergonomics and effectiveness of the visualization modality employed for each specific surgical task [6,47].

The proposed AR neuronavigator was tested on a newly designed patient-specific head mannequin featuring an anatomically realistic brain phantom with included synthetically created tumors and eloquent areas. Our experimental set-up was designed to simulate a high-risk neurosurgical scenario: the resection of a small tumor (or tumor portion) medially adjacent to the posterior part of the inferior frontal gyrus, where the Broca's area is generally located.

As a general rule, when designing a new surgical navigation system, a key factor is represented by the perception location, that is where the surgeon is normally focused throughout the entire procedure or during a single surgical task; in non-endoscopic neurosurgical procedures like ours, it is highly desirable to use an AR neuronavigator with the perception location directly on the patient. This condition can be achieved through devices that present the AR scene in the line of sight between the surgeon and the surgical field, as in the case of microscope-based neuronavigators [14–16,21] or through solutions based on light-field displays [17], that provide a parallax-free view. Following this line of research, the present work, was therefore primarily devoted to investigating the effectiveness of a novel quasi-orthoscopic binocular AR system as an aid in a complex neurological lesion targeting for which an egocentric and unconstrained approach is preferable.

As for the assessment of the ergonomics of the visualization modality, in the surgical planning, we considered six possible AR modalities to aid the surgeon in the correct performance of all the tasks involved in defining a dissection corridor towards the lesion. The visualization modality that subjects without neurosurgical training considered as the most effective in terms of depth perception was the "*Anatomical Occlusions and Transparencies*" which relies on anatomical occlusions and motion parallax, whereas the one that was preferred by neurosurgeons was the one based on two viewfinders (i.e. the "*Occluding virtual viewfinders*"). The reason for this is owing to the different attitude that non-surgeons and surgeons have towards AR visualization modalities. As the AR visualization modality is to be focused on the specific surgical task and knowing the requirements of the entire intervention, namely not only committed to stimulate depth perception, neurosurgeons opted for a modality that could be more of aid in the definition of the ideal trajectory for targeting the hidden lesion.

Our study could not provide any statistically significant result because of tests shortage. Nonetheless, it suggests 4 major conclusions: first, our AR system is intuitive, easy-to-use, and it provides 3D augmented information in a good fashioned way: it provides a precise definition of the spatial relationships between real scene and visually processed data along the three dimensions. Second, our AR system proved to be an effective tool in the "macroscopic" part of the intervention, including skin incision, craniotomy, and dural opening. Third the preliminary results herein presented strongly encourages to conducting a more structured study to prove the clinical effectiveness of our AR-based neuronavigator in aiding the surgical access to small lesions adjacent to eloquent areas. By using the AR guidance, the surgeons were able to orient the dissecting instrument (resembling bipolar forceps) and navigate to the surgical target relying on their augmented 3D perception of the surgical field and on a task-oriented visualization modality featuring a pair of virtual viewfinders. The mutual integration between occlusions, motion parallax, and stereopsis allow the surgeon to perceive the relative proximities between tumour, eloquent area and surrounding brain parenchyma.

Finally, our testing platform might as well be used for training purposes, in combination or separately to our AR neuronavigator.

System ergonomics could be improved, by both changing the semantics of the virtual content as well as by tracking the surgical instrument. The use of intraoperative imaging is likely to be appropriate for

compensating brain shift. Finally, a more structured validation study is needed, that would involve virtual information derived from MRI, fMRI, magnetoencephalography, transcranial magnetic stimulation and tractography.

Conclusions

When compared to similar systems [10,11,18,19,24,48], the HMD-based AR neuronavigation system herein presented proved: to provide an unpreceded 3 D visualization both of the surgical field and of the virtual objects, to provide an improved depth-perception of the augmented scene, to be ergonomic and unaffected by the parallax problem, and to be a useful tool for the macroscopic part of neuro-oncological procedures. Further, our testing platform might be used for training purposes, in combination or separately to the AR neuronavigator. Finally, the preliminary results herein presented strongly encourages to conducting a more structured study to prove its clinical effectiveness.

Disclosure statement

No potential conflict of interest was reported by the authors.

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References

[1]   Perneczky A, Reisch R, Tschabitscher M. Keyhole approaches in neurosurgery. Wien, New York: Springer; 2008.

[2]   Rhoton AL, Rhoton AL. Congress of Neurological Surgeons. Rhoton cranial anatomy and surgical approaches. Philadelphia (PA): Lippincott Williams & Wilkins; 2003.

[3]   Reisch R, Stadie A, Kockro RA, et al. The keyhole concept in neurosurgery. World Neurosurg. 2013;79:S17 e9–S13.

[4]   Kockro RA, Stadie A, Schwandt E, et al. A collaborative virtual reality environment for neurosurgical planning and training. Neurosurgery. 2007;61:379–391.

[5]   Kersten-Oertel M, Jannin P, Collins DL. The state of the art of visualization in mixed reality image guided surgery. Comput Med Imag Graphics. 2013;37:98–112.

[6]   Meola A, Cutolo F, Carbone M, et al. Augmented reality in neurosurgery: a systematic review. Neurosurg Rev. 2016;1–12.

[7]   Kawamata T, Iseki H, Shibasaki T, et al. Endoscopic augmented reality navigation system for endonasal transsphenoidal surgery to treat pituitary tumors: technical note. Neurosurgery. 2002;50:1393–1397.

[8]   King AP, Edwards PJ, Maurer CR, Jr., et al. A system for microscope-assisted guided interventions. Stereotact Funct Neurosurg. 1999;72:107–111.

[9]   Edwards PJ, Johnson LG, Hawkes DJ, et al. Clinical experience and perception in stereo augmented reality surgical navigation. In: Jiang ZG, Jiang T, editors. MIAR. Berlin (Germany): Springer-Verlag; 2004. p. 369–376.

[10] Lovo EE, Quintana JC, Puebla MC, et al. A novel, inexpensive method of image coregistration for applications in image-guided surgery using augmented reality. Neurosurgery. 2007;60:366–371.

[11] Kockro RA, Tsai YT, Ng I, et al. Dex-ray: augmented reality neurosurgical navigation with a handheld video probe. Neurosurgery. 2009;65:795–807.

[12] Inoue D, Cho B, Mori M, et al. Preliminary study on the clinical application of augmented reality neuronavigation. J Neurol Surg A Cent Eur Neurosurg. 2013;74:71–76.

[13] Masutani Y, Dohi T, Yamane F, et al. Augmented reality visualization system for intravascular neurosurgery. Comput Aided Surg. 1998;3:239–247.

[14] Cabrilo I, Bijlenga P, Schaller K. Augmented reality in the surgery of cerebral arteriovenous malformations: technique assessment and considerations. Acta Neurochir. 2014;156:1769–1774.

[15] Cabrilo I, Schaller K, Bijlenga P. Augmented reality-assisted bypass surgery: embracing minimal invasiveness. World Neurosurg. 2015;83:596–602.

[16] Cabrilo I, Bijlenga P, Schaller K. Augmented reality in the surgery of cerebral aneurysms: a technical report. Neurosurgery. 2014;10(Suppl 2):252–260.

[17] Iseki H, Masutani Y, Iwahara M, et al. Volumegraph (overlaid three-dimensional image-guided navigation). Clinical application of augmented reality in neurosurgery. Stereotact Funct Neurosurg. 1997;68:18–24.

[18] Deng W, Li F, Wang M, et al. Easy-to-use augmented reality neuronavigation using a wireless tablet PC. Stereotact Funct Neurosurg. 2014;92:17–24.

[19] Low D, Lee CK, Dip LL, et al. Augmented reality neurosurgical planning and navigation for surgical excision of parasagittal, falcine and convexity meningiomas. Br J Neurosurg. 2010;24:69–74.

[20] Doyle WK. Low end interactive image-directed neurosurgery - Update on rudimentary augmented reality used in epilepsy surgery. St Heal T. 1996;29:1–11.

[21] Stadie AT, Reisch R, Kockro RA, et al. Minimally invasive cerebral cavernoma surgery using keyhole approaches - solutions for technique-related limitations. Minim Invasive Neurosurg. 2009;52:9–16.

[22] Kersten-Oertel M, Chen SJS, Collins DL. An evaluation of depth enhancing perceptual cues for vascular volume visualization in neurosurgery. IEEE Trans Visual Comput Graphics. 2014;20:391–403.

[23] Kersten-Oertel M, Jannin P, Collins DL. DVV: a taxonomy for mixed reality visualization in image guided surgery. IEEE Trans Vis Comput Graph. 2012;18: 332–352.

[24] Mahvash M, Besharati Tabrizi L. A novel augmented reality system of image projection for image-guided neurosurgery. Acta Neurochir. 2013;155:943–947.

[25] Ferrari V, Cutolo F. Letter to the Editor: augmented reality-guided neurosurgery. J Neurosurg. 2016;125: 235–237.

[26] Parrini S, Cutolo F, Freschi C, et al. Augmented reality system for freehand guide of magnetic endovascular devices. Conf Proc IEEE Eng Med Biol Soc. 2014;2014: 490–493.

[27] Badiali G, Ferrari V, Cutolo F, et al. Augmented reality as an aid in maxillofacial surgery: validation of a wearable system allowing maxillary repositioning. J Cranio-Maxillofac Surg. 2014;42:1970–1976.

[28] Cutolo F, Badiali G, Ferrari V. Human-PnP: ergonomic AR interaction paradigm for manual placement of rigid bodies. augmented environments for computer-assisted interventions. AE-CAI. 2015;9365:50–60.

[29] Cutolo F, Carbone M, Parchi PD, Ferrari V, Lisanti M, Ferrari M. Application of a new wearable augmented reality video see-through display to aid percutaneous procedures in spine surgery. In: De Paolis TL, Mongelli A, editors. Augmented reality, virtual reality, and computer graphics: third international conference. Lecce, Italy: AVR, 2016, June 15-18, Proceedings, Part II. Cham: Springer International Publishing; 2016. p. 43–54.

[30] Cutolo F, Carli S, Parchi PD, Canalini L, Ferrari M, Lisanti M, Ferrari V. AR interaction paradigm for closed reduction of long-bone fractures via external fixation. Proceedings of the 22nd ACM Conference on Virtual Reality Software and Technology; 2016; 2996317.

[31] Cutolo F, Parchi PD, Ferrari V. Video see through ar head-mounted display for medical procedures. Paper presented at IEEE International Symposium on ISMAR, Munich, Germany; 2014. p. 393–396.

[32] Ferrari V, Cutolo F, Calabro EM, et al. HMD video see though ar with unfixed cameras vergence. Paper presented at IEEE International Symposium on ISMAR, Munich, Germany; 2014. p. 265–266.

[33] Ferrari V, Megali G, Troia E, et al. A 3-D mixed-reality system for stereoscopic visualization of medical dataset. IEEE Trans Biomed Eng. 2009;56:2627–2633.

[34] Cutolo F, Freschi C, Mascioli S, et al. Robust and accurate algorithm for wearable stereoscopic augmented reality with three indistinguishable markers. Electronics. 2016;5:59.

[35] Kanbara M, Okuma T, Takemura H, Yokoya N. A stereoscopic video see-through augmented reality system based on real-time vision-based registration. Proceedings of the IEEE Virtual Reality, New Brunswick, NJ; 2000.

[36] State A, Keller KP, Fuchs H. Simulation-based design and rapid prototyping of a parallax-free, orthoscopic video see-through head-mounted display. Proceedings of the International Symposium on Mixed and Augmented Reality. 2005. p. 28–31.

[37] Cutolo F, Siesto M, Mascioli S, Freschi C, Ferrari M, Ferrari V. Configurable software framework for 2D/3D video see-through displays in medical applications. In: De Paolis TL, Mongelli A, editors. Augmented reality, virtual reality, and computer graphics: Third International Conference, AVR 2016, Lecce, Italy, June 15-18, 2016 Proceedings, Part II. Cham: Springer International Publishing; 2016. p. 30–42.

[38] Zhang ZY. A flexible new technique for camera calibration. IEEE Trans Pattern Anal Machine Intell. 2000;22:1330–1334.

[39] Navab N, Heining SM, Traub J. Camera Augmented Mobile C-Arm (CAMC): calibration, accuracy study, and clinical applications. IEEE Trans Med Imaging. 2010;29:1412–1423.

[40] Ferrari V, Carbone M, Cappelli C, et al. Value of multi-detector computed tomography image segmentation for preoperative planning in general surgery. Surg Endosc. 2012;26:616–626.

[41] Kersten-Oertel M, Jannin P, Collins DL. DVV: towards a taxonomy for mixed reality visualization in image guided surgery. Med Imag Augment Reality. 2010; 6326:334–343.

[42] Abhari K, Baxter JSH, Chen ECS, et al. Training for planning tumour resection: augmented reality and human factors. IEEE Trans Biomed Eng. 2015;62: 1466–1477.

[43] Condino S, Carbone M, Ferrari V, et al. How to build patient-specific synthetic abdominal anatomies. An innovative approach from physical toward hybrid surgical simulators. Int J Med Robotics Comput Assist Surg. 2011;7:202–213.

[44] Chen SJ, Hellier P, Marchal M, et al. An anthropomorphic polyvinyl alcohol brain phantom based on Colin27 for use in multimodal imaging. Med Phys. 2012;39:554–561.

[45] Chiarelli P, Lanata A, Carbone M. Acoustic waves in hydrogels: a bi-phasic model for ultrasound tissue-mimicking phantom. Mater Sci Eng C-Biomimetic Supramol Syst. 2009;29:899–907.

[46] Jamieson S. Likert scales: how to (ab)use them. Med Educ. 2004;38:1217–1218.

[47] Drouin S, Kersten-Oertel M, Collins DL. Interaction-based registration correction for improved augmented reality overlay in neurosurgery. Lect Notes Comput Sci. 2015;9365:21–29.

[48] Kantelhardt SR, Gutenberg A, Neulen A, Keric N, Renovanz M, Giese A. Video-assisted navigation for adjustment of image-guidance accuracy to slight brain shift. Oper Neurosurg. 2015;11:504-511.