Future surgery commission: Translating tomorrow's technologies into today's surgical practice.

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1) Introduction

It is often stated that future technologies are already present, but have not yet been evenly distributed. This is clearly evident with medical devices of the future which take many years to translate into clinical care. We are currently celebrating 30 years since the first robot-assisted brain biopsy was undertaken and this procedure is only now gaining widespread acceptance. The development and translation of novel technologies into surgical practice is enabled by an emerging collaboration between surgeons, engineers and computer scientists. The introduction of novel devices however is slow and acceptance is varied amongst surgeons and patients alike. Unlike drug trials, medical devices do not undergo a uniformly accepted process in which they are developed and through which clinical trials for safety and efficacy are undertaken. The IDEAL framework is a collaborative effort that aims to apply the same phases of trials that are traditionally performed for drug therapies to medical devices.[1–3] An observation by the co-founder of Intel, Gordon Moore, predicted the number of transistors in the central processing unit (CPU) of a computer would continue to double every 2 years. This later became known as Moore's law and the resulting improvement in computer processing power has been the driving force of the semiconductor industry since it was predicted in 1965. Over this period the number of transistors within a CPU has risen from $4x10^3$ with the 4004 chip in 1970 to over $1x10^8$ with the Intel Core i7 released in 2010. This explosion in computing power is now set to deliver a renaissance in surgical technology and how healthcare as a whole is delivered in the future.

Here we present a number of novel technologies that are likely to shape the future of surgical practice and use epilepsy neurosurgery as an exemplar to illustrate the impact of these technological advancements. We highlight how complementary technologies can be used to form a pipeline for clinical translation to guide surgical planning and be seamlessly integrated into the operating theatre. These advances are readily transferable to other surgical disciplines and will usher in a paradigm shift in surgical practice toward more focal interventions that utilise computer algorithms to improve safety and outcome metrics. As we embrace novel surgical devices it is incumbent upon all healthcare professionals and commissioners to ensure that these devices undergo rigorous clinical evaluation before they are adopted into wider clinical practice.

2) Epilepsy

Epilepsy is a condition in which abnormal paroxysmal electrical activity in the brain results in seizures, with risks of physical and cerebral injury and with devastating social, psychological, neurological and psychiatric sequelae for patients as well as broader economic impacts on society as a whole[4]. It is estimated that epilepsy effects 1% of the population and over 1/3 of these patients are not controlled with anti-seizure medications. Surgery offers a potential cure for drug resistant focal epilepsy (DRFE) if the seizure onset zone in the brain can be adequately defined and resected.[5] Other surgical interventions such as deep brain stimulation (DBS) and vagal nerve stimulation (VNS) have been used as palliative treatments in DRFE and generalised epilepsies. As few as 2% of patients who are eligible for curative epilepsy neurosurgery are referred for surgical evaluation and in many cases when surgery is performed it is delayed by up to two decades after the initial diagnosis.[6] Epilepsy patients undergo an in-depth evaluation which includes, but is not limited to, structural and functional MRI, video-telemetry, positron emission tomography, single photon emission CT (SPECT), magnetoencephalography (MEG), neuropsychological and psychiatric assessment. If there is concordance between imaging, video-EEG telemetry and neuropsychological assessments surgical resections can be performed with high chances of long-term remission of the epilepsy.[7,8] Alternatively, if the presurgical evaluation is discordant invasive EEG recordings are utilised. Stereoelectroencephlography (SEEG) is one such modality that involves the stereotactic insertion of multiple (8-16) electrodes within predefined brain regions. The electrophysiological recordings performed between and during seizures allows the seizure onset to be defined prior to definitive surgical resection. Tailored surgical resections can be then performed that spare eloquent cortical and subcortical structures to maximise seizure freedom rates and reduce neurological and psychological side-effects.

3) Computer assisted planning

a) Multimodal imaging

Given the multitude of imaging investigations performed in the presurgical evaluation of epilepsy, a method to accurately co-register the images into a common space is critical to interpreting the results and guiding further management.[9,10] The introduction of 3D multi-modal imaging to the presurgical evaluation of epilepsy has been shown to change clinical practice in 81% of all individuals and in 100% of patients specifically undergoing SEEG[11]. SEEG electrodes are inserted through bolts placed within the skull that dictates the electrode trajectory. Meticulous planning and accurate implementation of the plan is required as this is a diagnostic procedure that carries a significant risk of intracranial haemorrhage when the electrode is passed through the brain[12]. Accurate vascular imaging registration and segmentation is paramount to ensuring that intracranial vascular is visualised and avoided.

b) Trajectory planning

Figure 1:

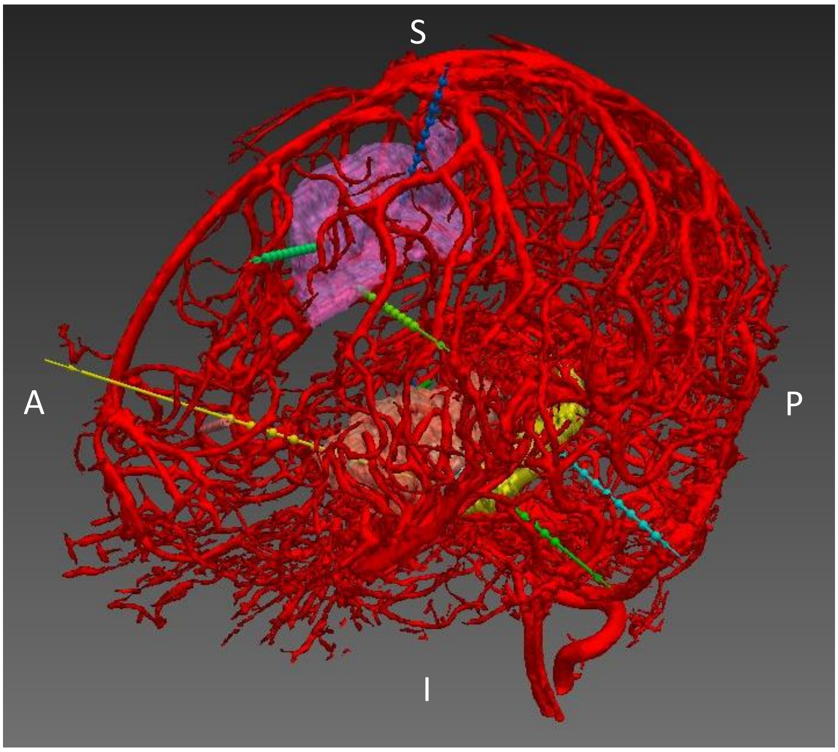

Figure 1 Legend: Image of a left hemispheric SEEG electrode implantation with vascular segmentation derived from injection of left internal carotid and vertebral arteries via catheter angiogram. Computer generated electrode trajectories shown targeting anatomical structures include the left hippocampus (yellow), anterior insula (orange) and supplementary motor cortex (pink). For simplicity only a proportion of the anatomical structures and planned electrodes are shown.

Multimodal imaging forms the basis upon which computer assisted planning (CAP) can be performed. The necessary requirements for SEEG electrode insertion include maximising distance from intracranial vasculature, increasing grey matter sampling, ensuring drilling angles orthogonal to the skull to maintain insertion accuracy, identifying anatomically labelled regions of interest, critical structure segmentation and cortical and skull model generation.[13] From a single T1 MRI sequence whole brain parcellations can be performed that accurately label >180 anatomical structures within the brain.[14] Cortical, grey matter and sulcal models can all be subsequently derived from this. PseudoCT algorithms generate a skull model from an MRI scan negating the need for radiation exposure. Vascular models can be generated from MRI based vascular sequences (MRA / MRV) or catheter digital subtraction angiography (see Figure 2).[15] CAP can be used to simultaneously place multiple electrodes within the brain that maximise distance from vasculature, reduce intracerebral length, optimise orthogonal drilling angles and improve grey matter sampling.[16] Trajectory risk is calculated as the cumulative distance from vasculature along the intracranial length of the electrode[13]. In comparison with manually (expert surgeon) planned electrode implantations we have shown that CAP significantly reduced drilling angles, intracerebral electrode length and overall implantation risk whilst improving grey matter sampling.[17] Furthermore, when the CAP and manually planned electrodes were evaluated by five blinded external expert surgeons there was no compromise of feasibility ratings. CAP was able to find clinically feasible electrode trajectories in 20% of cases in whom the manually planned trajectories were deemed infeasible by expert raters.[17] The conclusion is that CAP for stereotactic planning provides safer trajectories that are equally feasible to those planned by neurosurgeons, and in a fraction of the time.

Figure 2

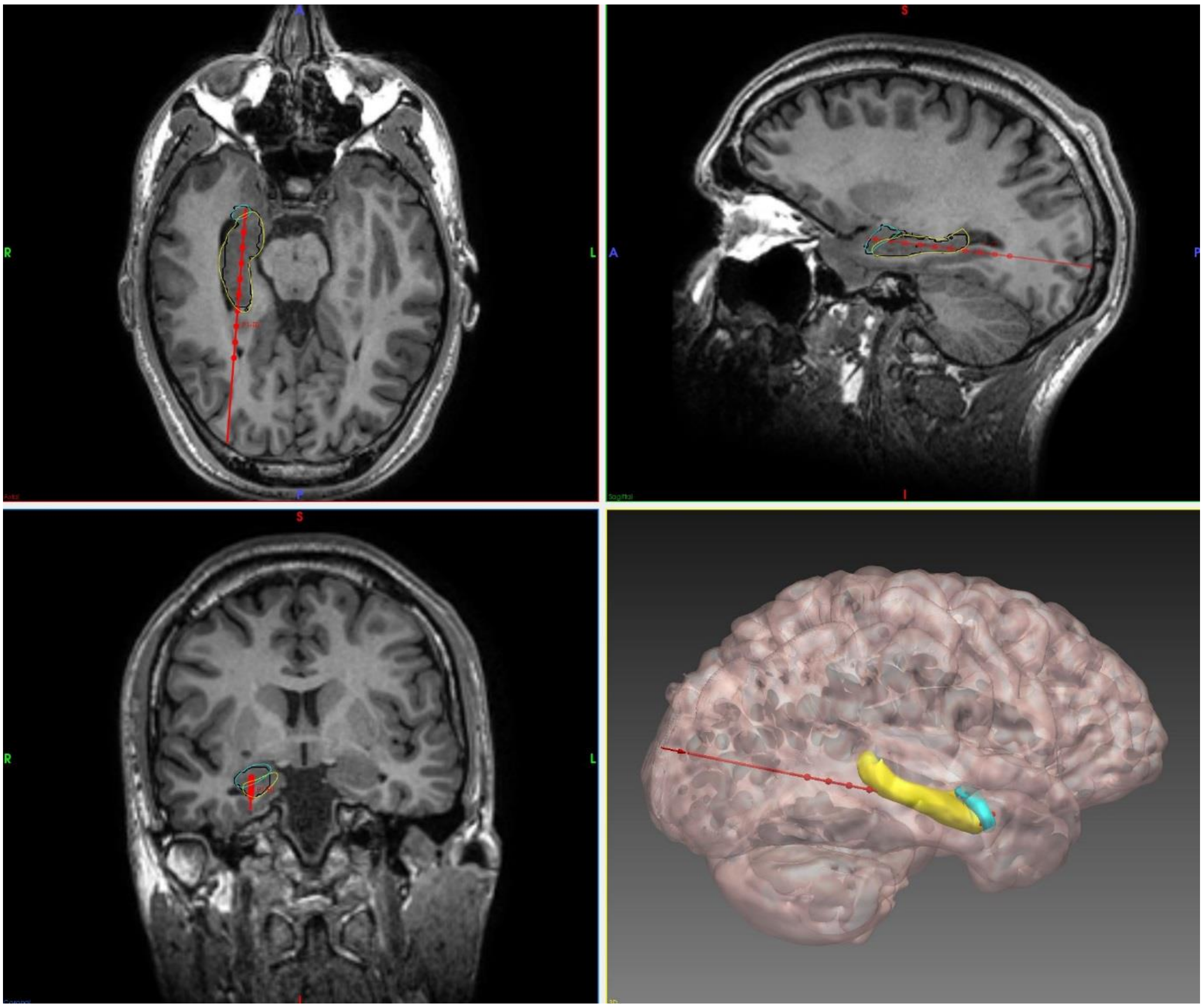

Figure 2 Legend: Right sided computer planned laser catheter trajectory for LiTT of the right amygdalohippocampal complex entering through the right lateral occipital gyrus, passing between the collateral sulcus and the occipital horn of the lateral ventricle and cannulating the right hippocampus at the level of the tectal plate. Hippocampus shown in yellow and amygdala shown in blue.

CAP trajectory planning has multiple other surgical applications including tumour biopsy, stereotactic catheter placement for drug or gene therapy delivery, neuroendoscopy and novel ablation techniques.[18–21] Laser interstitial thermal therapy (LiTT) is one such novel therapy that has been developed as a minimally invasive alternative to open surgery for mesial temporal lobe epilepsy and hypothalamic hamartomas.[22] The procedure involves the stereotactic placement of a laser catheter within a lesion or brain structure and an ablation diameter between 5-20 mm is produced under MR thermography guidance. The catheter is then withdrawn in 10 mm increments so that further ablations can be performed if required.[23] The amygdalohippocampal complex (AHC) is a longitudinal structure that is ideally shaped to allow ablation along its long axis. The volume and safety of the ablation are dependent on the entry, trajectory and target point along which the laser catheter is inserted.[24] Mesial trajectories carry a risk of heat transfer to the brainstem, whilst lateral targets are at risk of inadequate ablation of the mesial hippocampal head. Superior trajectories may transgress the optic radiation and occipital horn of the ventricle, whilst inferior trajectories may ablate the parahippocampal gyrus and increase risk of neuropsychological morbidity.[25] A safe 'posteroinferior corridor' has been described which utilises an occipital entry and targets the anterior border of the amygdala.[24] The trajectory runs between the collateral sulcus and the occipital horn of the ventricle allowing cannulation of the AHC at the level of the cerebral aqueduct (see Figure 3). We have applied CAP for LiTT and compared this to manually planned ablations performed using systematically planned trajectories along the posteroinferior corridor in 25 patients[26]. CAP was able to find a feasible trajectory in all cases and if these CAP trajectories were implemented instead of the manually planned trajectories overall calculated trajectory risk score would have been reduced by 50%, ablation of the AHC increased by 11% whilst reducing the ablation of the parahippocampal gyrus by 11%.[26] The implication therefore is that this could potentially improve the safety of this novel intervention whilst increasing seizure freedom rates and reducing neuropsychological morbidity.[25,27] A prospective multicentre study of LiTT trajectory planning currently being formulated.

As novel interventions are introduced to clinical practice each institution will undergo a learning curve which is related to surgeon experience and complexity of the intervention. CAP is one means of overcoming this learning curve by systematically providing optimal trajectories that implement evidence based algorithms. This *Baysian* form of learning minimises the number of patients that are exposed to the learning curve of novel interventions and lends itself towards machine learning and artificial intelligence.

c) Resection planning

Figure 3:

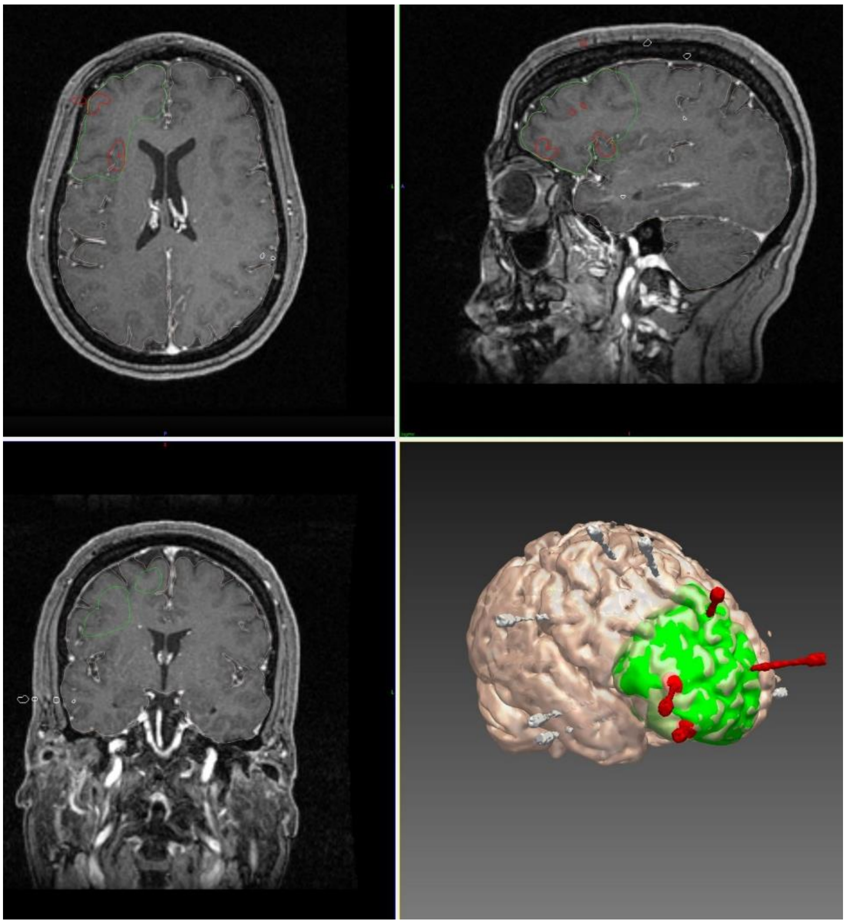

Figure 3 Legend: Example of tailored resection planning following computer assisted SEEG electrode implantation of the right hemisphere. Red bolts demarcate regions in which the electrode contacts are active at the time of seizure onset and therefore within the presumed epileptogenic zone. The suggested resection volume is represented in green to guide the surgeon intraoperatively.

Figure 4:

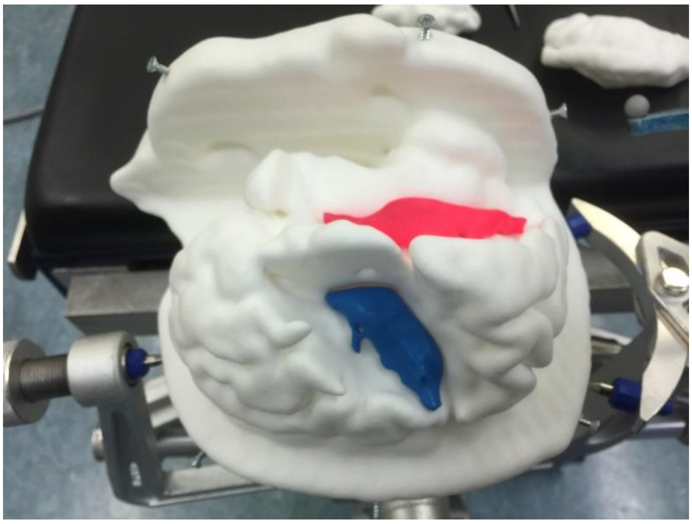

Figure 4 Legend: Full size 3D printed head in which the scalp, bone and dura have been removed over the right hemisphere to reveal the underlying cortex. Regions of cortex (see in the background) have been removed to demonstrate the optic radiation (pink) and corticospinal tract (blue). The phantom was placed in a Mayfield clamp and registered to the neuronavigation system via bone screw fiducials and the tracts were visualised through the operative microscope.

Patients with discrete cerebral lesion such as benign brain tumours and dysplasia, or in whom the epileptogenic focus has been defined using invasive EEG may be offered a neurosurgical resection. The risks associated with neurosurgical resections are dependent on the anatomical location and proximity to critical functional brain regions. Functional MRI (fMRI), MEG and diffusion tensor imaging (DTI) provide non-invasive methods of identifying critical cortical and subcortical structures. Novel methods utilising anatomically constrained probabilistic tractography identify clinically relevant tracts whilst removing those that are anatomically infeasible.[28] Combining these data with whole brain parcellations allows specific seed, inclusion and exclusion structures to be defined and provides a means of automating tractography for surgical relevant white matter fibre tracts. With this technology and the use of seed growing algorithms computer assisted resection plans can be proposed that model maximal safe resections whilst preserving functionally relevant cortex and subcortical structures (See Figure 3). The application of tractography to preserve critical subcortical structures has been shown to prevent clinically relevant visual field deficits in patients undergoing anterior temporal lobectomy[29,30]. It is estimated that the risk of a significant visual field deficit that precludes driving, even when seizures are cured following surgery, is up to 25-50% with modern open microsurgical approaches.[31,32] Performing tractography of the optic radiation preoperatively and overlaying this in the microscope display allows the surgeons to visualise the fibre tract intraoperatively and hence avoid damaging it (See Figure 4). This has been shown to prevent a significant visual field deficit that prevented driving in all study cases.[29,33]

4) 3D printing

Three-dimensional printing has a growing range of clinical applications in surgery from pre-surgical planning to intraoperative jigs and custom implantable devices. Patient specific tissues can be segmented from routine MRI and CT scans and printed in life size proportions. As hospitals invest in 3D printers it is likely that complex operative approaches will be practiced by surgeons in advance of the procedure to help detect any unforeseen complications and improve performance.

a) Simulation

Figure 5:

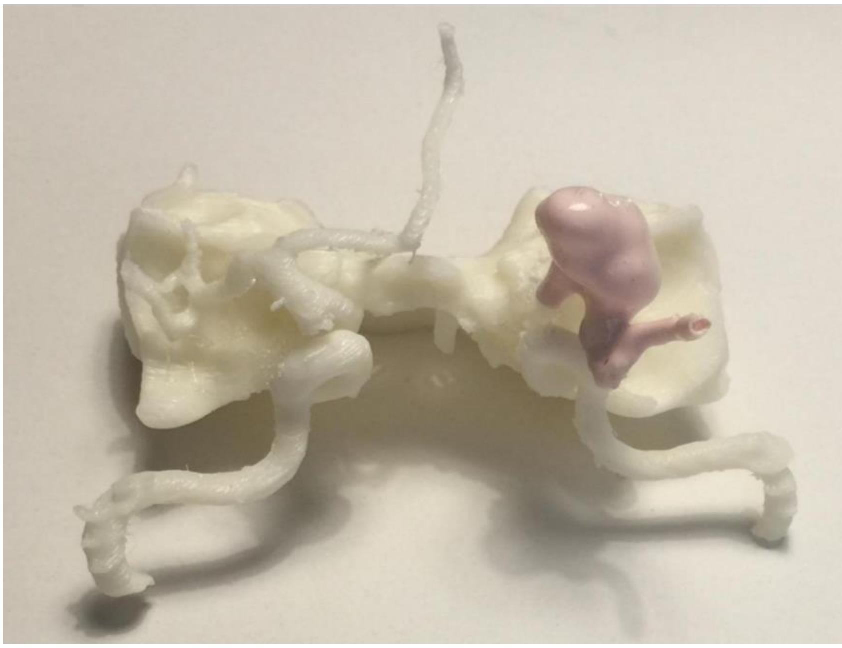

Figure 5 Legend: Full size multimodal 3D printed model of the anterior circulation and sphenoid bone viewed from posterior. The right sided multi-lobulated terminal internal carotid artery aneurysm has been printed in silicon. The aneurysm neck can be seen to extend into the proximal right middle cerebral artery. Various clipping strategies were simulated and practiced preoperatively prior to the operation. Note is made of a congenital absence of the right A1 segment of the anterior cerebral artery.

Vascular neurosurgery is an area that has seen a dramatic reduction in the number of operative cases over the last decade due to the emergence of interventional radiology coiling services.[34] The aneurysms that undergo surgery are therefore those that are complex and not amenable to coiling or where coiling has been attempted and failed due to residual or recurrent aneurysm. This prevents surgeons from performing the procedure regularly and makes training opportunities for future neurosurgeons scarce. From contrast enhanced CT scans (CT-angiogram) we have segmented and printed the circle of Willis and vascular arborisations along with the skull base to provide the neurosurgeon with a life size 3D model (see Figure 5). Multimodal 3D printers allow a variety of materials to be printed to simulate the mechanical properties of tissues such as brain, bone and vasculature.[35] A variety of operative approaches can then be practiced and potential complications avoided, such as perforator injury, by testing different aneurysm clips prior to surgery. The benefit of not trying multiple clips intraoperatively is a reduced risk of intraoperative haemorrhage and shorter operative time[36]. It also provides a safe environment in which surgical training can be performed on patient specific pathologies with the appropriate haptic feedback and use of operative instruments that is lacking with expensive augmented and virtual reality simulators. High fidelity 3D printed simulators are available for a wide variety of neurosurgical procedures including endoscopic transsphenoidal surgery and brain tumour resection.[37,35,38]

b) Preclinical device testing

Figure 6:

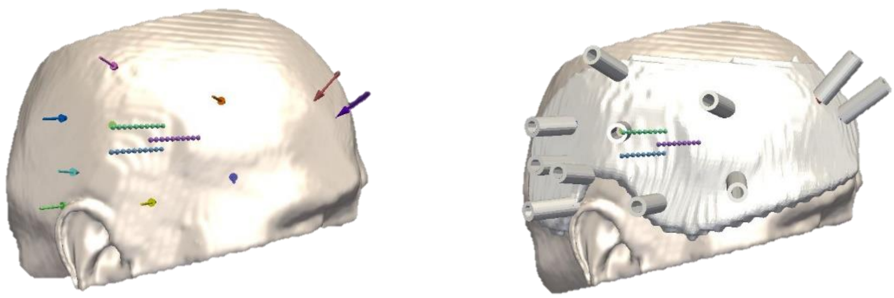

Figure 6 Legend: A right hemispheric SEEG implantation plan was generated through CAP and is shown on the scalp in the left image. A patient specific 3D printed custom jig can then be automatically generated to provide working channels through which the surgeon can drill and insert the electrodes intraoperatively.

The wide range of materials available for 3D printing allows a number of tissues to be simulated with realistic biomechanical properties. This allows novel medical devices to undergo preclinical testing in patient / pathology specific phantoms that closely simulate operative conditions. We have demonstrated an example of this with a novel robotic device for SEEG bolt insertion where anatomically accurate skull phantoms were printed for patients that had previously undergone SEEG implantations.[39] The electrode implantation schema performed in the patient was replicated using the novel robotic device and compared to the gold standard method used at the institution. The improvement in SEEG bolt insertion accuracy with the robotic device provided the ethical justification upon which a clinical randomised clinical trial was undertaken (see section 5). In addition to providing vital safety information the phantom implantation allowed the surgeon's learning curve to be quantified and overcome prior to performing implantations on patients.[39]

Patient specific 3D printed jigs are now commercially available for stereotactic electrode placement in DBS and SEEG procedures.[40] We have shown how these can be integrated with the previously mentioned computer assisted trajectory planning software to provide a seamless pipeline that can be directly translated to the operating theatre allowing surgeons to implement stereotactic procedures in an efficient manner that utilises presurgical planning safety algorithms (see Figure 6).

5) Robotic assisted surgery

Figure 7:

Figure 7 Legend: Simulation of a robot assisted SEEG implantation on a 3D printed phantom providing preclinical accuracy and safety metrics.

The introduction of robotic devices into operating theatres is still in its infancy but is becoming more widely accepted by surgeons and patients in developed countries. When coupled with neuronavigation systems robotics allows high precision stereotactic targeting throughout the entire neuroaxis. It is due to this that the first robot assisted neurosurgical procedure was for brain biopsy (30 years ago).[41] To date this remains the most common indication for robot assisted neurosurgery, although the introduction of intraoperative CT imaging and dedicated spinal robots such as the Renaissance device (Mazor Robotics) has seen an explosion in clinical trials being performed for spinal pedicle screw fixation.[42]

A systematic review and meta-analysis of SEEG implantations revealed that surgeons use a variety of implantation methods, including frame-based, frameless, custom-jig and robotic methods.[43] These methods are also applicable to other stereotactic neurosurgery procedures including brain biopsy and deep brain stimulation. In each of these indications there is little evidence to suggest that one method is superior to the other as there are no prospective comparison studies. Many units that invest in a robotic device have changed practice without any evidence that doing so will not have deleterious effects on patient outcomes. Thus the introduction of novel technologies in the future will need to overcome a number of potential hurdles, most critical of which is prospective evidence that the device is safe and poses no more risk than current techniques. This is confounded by the fact that novel medical devices maybe associated with an initial learning curve (surgeon and institution specific) and even if the device is safer in the long-term, this may lead to patients being exposed to undue risk in the short-term. Through the use of high fidelity patient specific 3D printed phantoms coupled with early warning detections systems we have shown this can be overcome[39]. Cumulative summation (CUSUM) analysis is one such system that allows changes in clinical performance or outcome to be flagged before these become statistically significant. Another consideration is the cost associated with clinical trials and the availability of funding. Focused methodologically sound clinical trials provide the highest quality of evidence when comparing surgical interventions. Clinical trials are not only expensive but take a significant period of time to set up and analyse. Furthermore, surgeon and institution specific factors introduce bias and the results may not be applicable to other institutions. Tele-robotics is a potential future technology that would allow a surgeon in another institution or part of the world to remotely control a robotic surgical device to undertake a specific procedure. In the first instance this would still need a local team to be at hand to ensure the correct set up and smooth running of the device. As robotic devices become more self-sufficient the need for local human input will gradually diminish. Lessons from autonomous driving vehicles will be pivotal in translating robotics to surgery. Nevertheless, in the future pipelines will be required to facilitate translation of novel device trials focusing on high volume centres with robust safety monitoring methods to ensure testing is rigorous and efficient. This will not only provide a cost saving but also dramatically reduce the time required.

We are currently undertaking the first prospective single blinded randomised control trial comparing a robotic trajectory guidance device to a human operator for SEEG.[44] The device links seamlessly to the previously mentioned computer assisted planning software. SEEG electrode plans are then transferred to a neuronavigation system which connects directly to the robotic device. When a specific trajectory is chosen the device aligns to this with a precision of <0.1 mm and provides a working channel through which the surgeon undertakes the drilling and electrode insertion. The device was initially developed and intended for use in percutaneous interventional radiological procedures, such as injections and biopsies, to reduce radiation exposure to the operator. By extending the CE mark of a previously developed device to a new indication we have substantially reduced the clinical translation cost and timeline.

6) Conclusion

Here we demonstrate a number of novel technologies that integrate to form a seamless pipeline delivering pre-operative planning directly into the operating theatre. The utilisation of 3D printing for preclinical testing, patient specific intra-operative jigs and custom implants is likely to become more widespread as more hospitals adopt this technology locally. The integration of computer algorithms not only provides safer and more efficient surgical plans it can be also be coupled with a robotic trajectory guidance system to aid the surgeon in achieving this. We have shown that computer assisted planning software has a number of different surgical applications and can be coupled with novel technologies, such as LiTT, to provide safer and more efficacious minimally invasive alternatives to conventional surgery. The principles underlying these technologies however are broadly applicable and not limited to neurosurgery. Future technologies that are likely to revolutionise surgery may make use of this for gene therapy distribution, computer-brain interface devices, closed-loop deep brain stimulation and targeted drug delivery.

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