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Education

Neuronavigation: How it continues to revolutionise neurosurgical practice

EDUCATION

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ABSTRACT

Summary
Neuronavigation is a surgical technology that gives real time image-guidance to neurosurgeons as they operate within the boundaries of the skull and spinal column. Prior to its development, the success of neurosurgery was highly variable as it was determined by the anatomical knowledge, experience and surgical aptitude of each neurosurgeon. However, operations were notoriously difficult, given lesions can be found deep within the brain or spinal cord. To accommodate for this, a large area of exposure was made, which increased the risk of damaging surrounding functional brain tissue. Neuronavigation revolutionised the neurosurgical practice of multiple subspecialites by providing intraoperative image guidance enabling neurosurgeons to precisely locate surgical targets and resect lesions with a minimally invasive technique.

Relevance
In neuro-oncology, neuronavigation has increased the proportion of a brain lesion that can resected safely, which has lengthened the duration of survival and reduced post-operative complication rates. In neurovascular surgery, neuronavigation has optimised surgical approaches to difficult to reach cerebral aneurysms and reduced the risk of losing surgical orientation intraoperatively if a haemorrhage is present. In epilepsy surgery, neuronavigation has increased the accurate localisation of epileptogenic zones, which once resected can dramatically reduce the frequency of seizures for epilepsy resistant to medical management. Ultimately, such improvements have transformed patient outcomes worldwide.

Take home messages
Neuronavigation has revolutionised the practice of neurosurgery by facilitating minimally invasive surgical technique in a range of neurosurgical subspecialties. It is not a static technology but continues to develop as new technologies continue to be integrated into it, and it presents further exciting prospects for the future of neurosurgery.

Keywords: Neuroimaging; brain shift; iMRI.

INTRODUCTION

The human brain has a complex structure, consisting of 86 billion neurons intricately connected together. (1) Injured neurons demonstrate limited capacity for regeneration and therefore neurosurgical procedures must be minimally invasive. This prevents surgical margins extending into surrounding brain tissue and causing neurological deficits. The ability for neurosurgery to innovate and overcome these inherent challenges has been inextricably linked to the creation and development of neuronavigation. This article discusses how neuronavigation has revolutionised neurosurgery and how it continues to pave the way for future neurosurgical innovations.

THE DEVELOPMENT OF NEURONAVIGATION

Neuronavigation or image-guided neurosurgery are computer-assisted technologies that allow neurosurgeons to navigate the confines of the skull and spinal column during an operation. (2) Prior to the development of neuronavigation, the success of neurosurgery relied heavily on neurosurgeons' visuospatial knowledge of neuroanatomy and manual dexterity. A neurosurgeon would have to orientate and identify surgical targets purely by utilising anatomical landmarks and clinical experience. This was notoriously difficult, given lesions can be found deep within the brain or spinal cord. To accommodate for these limitations, a large area of exposure was made, which increased the risk of damaging surrounding functional brain tissue. An early attempt to reduce surgical exposure was the introduction of a framed stereotactic tool by E. Spiegel et al. (1947), an Austrian-born neurologist and Professor at Temple School of Medicine, USA. (3) The frame attached to the patient's head and in conjunction with an anatomy atlas was used to identify internal brain anatomy. (4) Despite these measures, neurosurgery still lacked the precision that it required. Anatomical variation and space-occupying lesions would distort the anatomy leading to wildly inaccurate measurements on the location of deep brain structures. It was not until technological advances of medical imaging that neurosurgery was revolutionised with the subsequent development of neuronavigation.

HOW NEURONAVIGATION WORKS

Neuronavigation provides image guidance by rendering preoperative images into a three-dimensional computer model and calibrating them with the three-dimensional space of an operation. It can be split into four separate steps:

1. **Preoperative Imaging**: the patient is scanned as close to the time of surgery as possible. Scanning modalities include Computerised Tomography (CT), Magnetic Resonance Imaging (MRI), functional MRI (fMRI) and diffusion tensor imaging (DTI). (5)

2. **Surgical Planning:** the images are uploaded to a neuronavigation system and converted to a three-dimensional model where the neurosurgeon can identify the optimal approach to a lesion. If fMRI imaging was used in the previous step, 'surgical corridors' comprised of non-critical brain tissue can be dissected to reach a surgical target. (6) This reduces disruption of surrounding white matter tracts.

3. **Registration**: this is the accurate calibration of preoperative imaging with the intraoperative patient. To achieve this, anatomical landmarks such as the sagittal suture and/or fiducial markers are used. Fiducial markers are objects affixed to the head immediately prior to preoperative imaging that are visible on scans and provide a point of reference. (6) At the start of surgery, the surgeon individually touches these anatomical landmarks and/or fiducial markers with a tracked probe to pair the preoperative imaging with the points. (7)

4. **Intraoperative Navigation:** the navigation system allows the accurate visualisation of surgical targets during the operation. (5)

CLINICAL IMPORTANCE – NEURO-ONCOLOGY

In neuro-oncology, neuronavigation guidance has increased the percentage of tumour resected during surgery. (8) In a retrospective cohort study, 52 patients with primary glioblastomas who were operated on using neuronavigation were matched to patients who had resection of primary glioblastomas without use of neuronavigation. Gross Total Resection (GTR) defined as no visible tumour on post-operation MRI scans (9) was achieved in 31% using neuronavigation vs 18% without. (10) Due to low patient numbers in the study this result failed to reach statistical significance ($p = 0.167$). However, the rate of GTR had a downstream effect on patient survival – with a median survival of 18 months compared to 10 months without neuronavigation ($p < 0.0001$). (10) In another retrospective cohort study, 100 patients who received meningioma resections using neuronavigation were compared to 170 patients who received meningioma resections using without neuronavigation. The complication rate after meningioma surgery sharply decreased from 14% to 6% ($p = 0.019$) and hospital stay from 13.5 days to 8.5 days ($p = 0.017$). This resulted in a reduction of the overall cost of surgery, admission and follow-up by 20%. (11) Neuro-oncology has further benefitted from the integration of modern imaging modalities for functional mapping of eloquent brain tissue such as the cortical language area and corticospinal tract. (12,13) Among these imaging modalities include fMRI, repetitive Transcranial Magnetic Stimulation (rTMS) and DTI. rTMS is a non-invasive neurophysiologic technique that works by directing a strong magnetic field which causes neuronal activation in the brain. (14) This cortical reactivity can be assessed and used to map out functional brain tissue prior to an operation to plan the optimal surgical approach. (14,15) A meta-analysis comprising 1009 patients in 7 studies investigated the role of rTMS integrated into neuronavigation. It found that the integration rTMS into neuronavigation systems further reduced the risk of postoperative motor deficits (odds ratio = 0.54, $p = 0.001$) and increased the rate of Gross Total Resection (GTR) (odds ratio = 2.32, $p < 0.001$), when compared patients operated using neuronavigation without rTMS. (16)

CLINICAL IMPORTANCE – NEUROVASCULAR SURGERY

In neurovascular surgery, neuronavigation has optimised the surgical approach and intraoperative localisation of neurovascular pathologies. Dorsal anterior cerebral artery (DACA) aneurysms are particularly difficult to identify because, unlike other aneurysms, they lack an anatomical landmark. (17) Also, the surgical approach to clip a DACA aneurysm is via the interhemispheric fissure, which is difficult to dissect and has close relation to important arteries and brain structures. (17) Following subarachnoid haemorrhage even experienced surgeons could lose orientation within the surgical field. This resulted in increased length of procedure and even unexpected premature rupture of aneurysms intraoperatively. (17) Using neuronavigation, surgeons are able to precisely locate DACA aneurysms and increase operator confidence in clipping. This has resulted in a dramatic improvement in surgical success. A case series presented a single centre experience of consecutively clipping 12 DACA aneurysms under the direct guidance of neuronavigation. Patients had a mean age of 55 years and had CT proven DACA aneurysms ranging from 3-10mm. The clipping of DACA aneurysms with neuronavigation guidance had no technical or surgical complications, and all patients made a good recovery. (17) Arteriovenous malformations (AVMs) are abnormal connections between the venous and arterial system in the brain leading to large venous dilatations, which are prone to bleeding. Previously, the resection of small AVMs posed was problematic – they are difficult to locate intraoperatively by direct visualisation and can be located adjacent to eloquent brain tissue. However, with the assistance of neuronavigation, AVMs can be localised and resected with high precision. A cohort study of 25 patients with small AVMs found the accuracy of neuronavigation was 1.1mm and resulted in the complete removal of the AVM in 96% of cases. (18)

CLINICAL IMPORTANCE – EPILEPSY SURGERY

In epilepsy surgery, neuronavigation has a particularly important application because accurate localisation of epileptogenic zone, which once resected can dramatically reduce the frequency of seizures. (19) As previously mentioned, in cases where there is an obvious structure lesion such as a brain tumour, neuronavigation significantly increases GTR. (10) However, lesions may not be visible macroscopically as they may have only subtle subcortical dysplasia or may not be associated with an anatomical lesion at all. In these cases, neuronavigation can be invaluable because the epileptogenic zone may only be visible to specialised imaging modalities such as magnetoencephalography, single photon emission computed tomography and positron emission tomography. (20–22) These imaging modalities can then be fused with MRI images used for neuronavigation. This enables the accurate placement of subdural electrodes to diagnose epileptogenic brain tissue, and the resection of these areas to treat epilepsy resistant to medical management. (23) In a large, single-centre cohort study 415 patients underwent resection of epileptogenic zones using neuronavigation with integration of specialised imaging modalities. Despite the seizures being previously refractory to medical treatment, 72.7% of patients were completely seizure free at a mean follow-up of 36 months. (24) However, there have been no high-quality studies comparing neuronavigation with standard surgical resection. (25) This does not rule-out neuronavigation showing benefit in epilepsy surgery, but instead indicates an urgent need for well-designed studies.

CLINICAL IMPORTANCE – SPINAL SURGERY

In spine surgery, the precise placement of pedicle screws is paramount in the treatment of thoracic and lumbar degenerative disease. (26) Insertion of a pedicle screws poses a unique challenge to surgeons as imprecise screw placement not only increase the risk of neurological and neurovascular injury but also reduces the biomechanical strength of the screw. (26) Introduction of neuronavigation increased the accuracy of screw placement and reduced cases of misplacement. In a meta-analysis comparing pedicle screws inserted using a freehand technique compared to a technique utilising neuronavigation, insertion using neuronavigation was more accurate (odds ratio 2.46, 95% confidence interval, 1.92-3.16) $p = 0.021$ and operations had significantly less blood loss $p < 0.001$. (27) Inaccurate pedicle screw placement not only reduces the biomechanical strength of the screw, but also increases the risk of iatrogenic injury to the nearby spinal cord and spinal vasculature. (28)

CLINICAL IMPORTANCE – FUNCTIONAL NEUROSURGERY

Finally, in functional neurosurgery, neuronavigation has been used to improve the optimise the efficacy of deep brain stimulation in treatment of advanced Parkinson's disease. In this treatment, electrodes are inserted into the subthalamic nucleus, a deep brain structure. The electrodes act by applying high-frequency electrical stimulation to surrounding structures, causing a dissociation of input and output signals. (29) Cerebral vasculature is at risk of intersection during this procedure causing haemorrhagic complications. Using neuronavigation, a study made planned trajectories for the electrodes which intersected significantly finer vasculature than before, thus reducing post-operative bleeding. (30)

LIMITATIONS OF NEURONAVIGATION

Brain shift is a complex spatio-temporal phenomenon with a wide range of causes that neuronavigation systems using preoperative imaging do not account for. The removal of pathological brain tissue in tumour resection causes adjacent remaining brain tissue to sag into the space under gravity. Simultaneously, neurosurgery produces swelling of surrounding brain tissue and loss of cerebrospinal fluid. Over the course of an operation this can distort the position of the brain by up to 50mm relative to preoperative images. (31) Consequently, neurosurgeons depended on the neuronavigation guidance to identify a surgical target, but once it is reached rely on their own judgement. However, this has led to inaccurate assumptions over the extent of tumour resection resulting in residual tumour being left after surgery. In cases where there is residual high-grade tumour, patients are at over six-times higher risk of death in comparison to GTR. (32) To overcome this limitation, neuronavigation has seen the integration intraoperative MRI (iMRI) to accommodate for brain shift and aid the identification of residual tumour that would otherwise remain. iMRI continually updates the neuronavigation and image accuracy, resulting in precise tumour margins, high rates of GTR and improved monitoring capabilities for complications. (33) In a single-centre, randomised control trial of 58 patients with glioma cell tumours, rates of GTR were 96% when using iMRI compared to 68% when using standard neuronavigation (p = 0.023). Whilst this is only a surrogate marker of clinical benefit, previous studies have shown a considerable extended overall survival when GTR is achieved.(10) Unfortunately, iMRI has considerable installation costs of $3-8 million and prolongs surgery times by one hour on average. (34) Therefore, despite some compelling early data, currently there is limited evidence for its use because as it is restricted to a select group of well-funded neurosurgical centres.

THE FUTURE OF NEURONAVIGATION

Neuronavigation is not a static technology but continues to develop. Thus far, neuronavigation has required surgeons to continually refer to an external monitor. However, the emergence of augmented reality neuronavigation (ARN) would eliminate the need for this. In ARN a three-dimensional image would be overlayed intraoperatively onto the surgical field highlighting anatomy and disease. Currently, there is a lack of high-quality evidence for the use of ARN over existing neuronavigation but this may change. (35) Additionally, advancements in technology may entirely eliminate an operating surgeon completely with the integration of semi-independent robots into neuronavigation. For example, a neuronavigation system would provide intraoperative navigation to an operating robot, controlled remotely by an overseeing surgeon. The movements of the robotic arms would be controlled by voice commands or a handheld control device providing haptic feedback to the surgeon. (36) These predictions may seem speculative, but neuronavigation continues to be a rapidly evolving field and it is unclear what future directions it will take.

CONCLUSION

Previously, the outcomes of a neurosurgical procedure were entirely dependent of the skill and experience of the surgeon. Since then, neuronavigation has optimised surgical approaches and the intraoperative localisation of brain lesions. Subsequently, minimally invasive neurosurgery has developed – maximising the resection of brain lesions, whilst minimising damage to surrounding brain tissue. Neuronavigation has improved outcomes across multiple sectors of neurosurgery, including neuro-oncology, neurovascular surgery, epilepsy surgery, spinal surgery and functional neurosurgery. Neuronavigation will incrementally advance in years to come as new technologies continue to be integrated into it, and it presents further exciting prospects for the future of neurosurgery.

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