Neuronavigation surgery in China: reality and prospects

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Objective  To review the history, development, and reality of neuronavigation surgery in China and to discuss the future of neuronavigation surgery.

Data sources  PubMed, the China Knowledge Resource Integrated Database, and the VIP Database for Chinese Technical Periodicals were searched for papers published from 1995 to the present with the key words “neuronavigation,” “functional navigation,” “image-guided,” and “stereotaxy.” Articles were reviewed for additional citations, and some information was gathered from Web searches.

Study selection  Articles related to neuronavigation surgery in China were selected, with special attention to application to brain tumors.

Results  Since the introduction of neurosurgical navigation to China in 1997, this core technique in minimally invasive neurosurgery has seen rapid development. This development has ranged from brain structural localization to functional brain mapping, from static digital models of the brain to dynamic brain-shift compensation models, and from preoperative image-guided surgery to intraoperative real-time image-guided surgery, and from application of imported equipment and technology to use of equipment and technology that possess Chinese independent intellectual property rights.

Conclusions  The development and application of neuronavigation techniques have made neurological surgeries in China more safe, precise and effective, and less invasive, and promoted the quality of Chinese neurosurgical practice to the rank of the most advanced and excellence in the world.

HISTORY AND DEVELOPMENT OF NEURONA VIGATION

The brain is the most complex and important part of the human body. The key challenge facing neurosurgeons is to accurately localize and resect lesions from intricate brain while minimizing injury to the normal tissues. Throughout its evolutionary history, operative neurosurgical technique has developed from primary to advanced levels, from single-function toward multi-function, and from localization of brain surface structures (early neurosurgery) to frame-based stereotaxy and microsurgery (modern neurosurgery), frameless stereotaxy and intraoperative imaging neuronavigation surgery (minimally invasive neurosurgery).

Localization of brain surface structures  Archaeologists have discovered unusual holes on some excavated human skulls of the Neolithic period (7000–3000 BC). Modern X-ray has proven that such holes were not caused by trauma or natural weathering, but by human tools, indicating that our early ancestors acquired the skill of cutting holes into the skull, the simplest craniotomy. This practice of trepanation was also described in the Chinese Inner Canon of the Yellow Emperor and in an ancient Egyptian document known as the Ebers Papyrus, written in 2600 BC. The great ancient Greek doctor, poet, and philosopher Hippocrates (460–370 BC) reported some brain and spinal cord surgical cases. Hua Tuo (145–208 AD), a Chinese physician highly skilled in surgery, also mastered the operation of opening the skull.

During the 14th to 17th centuries in Europe, surgeons from the missionary or the barber were in charge of both trauma and general surgeries. Some performed simple craniotomies for patients with brain trauma. Although early surgeons opened the skull only according to the site of force, they did manage to make some major brain...
discoveries. Broca (1824–1880) is famous for his discovery of the speech production center of the brain, which was typically referred to as the pars triangularis (Brodmann area 45) and pars opercularis (Brodmann area 44) of the inferior frontal gyrus (i.e., Broca’s area). Sir Victor Horsley (1857–1916) also demonstrated the relationship between the brain gyrus and the skull.

Because of localization inaccuracy, poor surgical lighting, simple surgical instruments, and other factors, a longer scalp incision and larger cortical exposure were necessary for early brain surgery. The inability to locate deep brain structures made operations of the brain parenchyma very difficult.

Frame-based stereotactic surgery: localization of deep brain structures
Frame-based stereotactic surgery was used to locate targets in the brain with the help of a three-dimensional (3D) coordinate system based on X-ray, computed tomography (CT), or magnetic resonance imaging (MRI) data and marked on a metal frame, which was fixed to the head. In 1908, Horsley and Clarke created a stereotactic frame for animal experiments. In 1947, the American doctors Spiegel and Wycis invented the first framed stereotactic instrument based on the data of ventriculography and performed the first stereotactic damage technique for mental disease. Thereafter, the Leksell, Reichert, and other frame-based stereotactic instruments emerged. In 1964, JIANG Da-jie, a Chinese pioneer in severe traumatic brain injury treatment and surgery for cranial-base tumors, developed China’s first stereotactic instrument, which was used on patients for two decades.

Early frame-based stereotactic surgery was performed with the help of ventriculography, pneumoencephalography, or X-ray; thus, it had shortcomings of both localization inaccuracy and invasion. In the 1960s and 1970s, the wide application of CT and MRI technologies rejuvenated frame-based stereotactic surgery by improving its accuracy and safety. However, its application was limited by the following shortcomings, which proved difficult to overcome: (1) it is cumbersome, uncomfortable, and inflexible; (2) its localization and orientation are not in real time and are not intuitive; (3) the calculation method is complex; (4) it is unsuitable for children or patients with thin skulls; and (5) because of its impact on endotracheal intubation, the frame must be worn after intubation in the case of general anesthesia, which increases the anesthesia and surgery time and prevents realization of a preoperative functional MRI. Therefore, frame-based stereotactic surgery is mainly used for the treatment of extrapyramidal disorders, such as Parkinson’s disease, intractable pain, mental illness, epilepsy, foreign body removal, biopsy, and deep electrode placement.

Frameless stereotactic surgery: localization of the whole brain and spine
Frameless stereotactic surgery is also known as image-guided surgery or neuronavigation surgery. In the late 1980s, frameless stereotaxy was developed based on the following technologies: (1) high-resolution, 3D neuroimaging technologies, such as CT and MRI; (2) 3D digital converters, which are able to accurately transmit the image information to computers; and (3) high-performance and high-capacity computers or workstations, which ensure the processing of large amounts of information effectively. In 1997, Chinese hospitals in Shanghai, Beijing, Guangzhou, and Tianjin have respectively introduced neuronavigation equipment to clinical practice and research. Recently, China-based neuronavigation equipment has been put into production in Shanghai and Shenzhen. For example, the Fudan dig-medical neuronavigation developed by the Digital Medical Research Center of Fudan University and Huashan Hospital has been approved for sale on the market.3

Compared with frame-based stereotaxy, frameless stereotaxy has the following advantages: (1) it can be used for preoperative planning; (2) the real-time 3D relationship between lesions and eloquent areas can be visualized intraoperatively; (3) structures in the surgical field are displayed on the navigation; (4) 3D spatial relationships between the current position and residual lesions are estimated; (5) intraoperative real-time adjustment of the surgical strategy is possible; (6) structures that may be encountered along the approach are shown; (7) crucial structures are shown; and (8) the extent of resection is shown. This frameless system has greatly expanded surgical indications, including those for various intracranial lesions such as brain tumors, cysts and abscesses, hematomas, vascular malformations, dural arteriovenous fistulas, skull-base tumors, epilepsy, congenital or acquired deformities, paranasal sinuses, and spine lesions.4-10

Frameless neuronavigation has now become a critical part of minimally invasive neurosurgery. Such technology contributes powerfully to microneurosurgery, keyhole surgery, endoscopic neurosurgery, and skull-base surgery. Frameless navigation is also used in other medical disciplines, such as maxillofacial surgery, otolaryngology, orthopedic surgery, radiosurgery, and conventional radiation therapy. The latter has been developed for use in conformal radiotherapy and 3D intensity-modulated radiation therapy by the application of navigation and localization technology.

**FUNCTIONAL NEURONA VIGATION**

Compared with conventional neuronavigation, functional neuronavigation allows the combination of anatomic imaging, which reveals the presence of tumors, and functional imaging, which shows the eloquent cortex and
subcortical fibers based on multi-image fusion technology. It therefore contributes favorably to achieving optimal surgical results; i.e., the maximal extent of resection and minimal injury of critical structures with the optimal functional outcome. The functional neuronavigation has been widely used in protecting neurological functions, such as motor, language, and vision.

Functional brain imaging
The cerebral cortex comprises many functional areas that control movement, sensation, language, vision, and so on. The functional areas were previously localized based on their approximate anatomical location, which is inaccurate and vulnerable to interference by various factors because their appearances are similar to other areas of the cortex in terms of appearance. Until 1990, Ogawa et al. first proposed the blood oxygen level-dependent (BOLD) technique, which could display the eloquent areas such as the motor cortex (the primary motor areas, premotor area, and supplementary motor area), somatosensory cortex, language cortex, and visual areas. This specialized technique is used to measure the hemodynamic response (change in blood flow) related to neural activity in human or animal brains.

Between the functional areas and dominant target organs or among brain areas, there are different connective pathways that send or receive a variety of important information to ensure the implementation of various brain functions. These dense, delicate fibers located within subcortical white matter are difficult to distinguish and are vulnerable to damage during surgery. Bassar et al. and Pierpaoli et al. first reported a fiber imaging technology (i.e., diffusion tensor imaging (DTI)) in 1996, opening the door to subcortical fiber tractography on MRI. During the past decade, a variety of subcortical pathways have been applied in functional navigation (such as pyramidal tract, arcuate fasciculus, and optic radiation).

Proposition of functional neuronavigation surgery
Resection of lesions within or adjacent to eloquent areas (such as tumors, arteriovenous malformations, and cavernoma) often damage functional cortex and/or subcortical tracts, resulting in postoperative complications such as paralysis, aphasia, alexia, or visual field defects. Therefore, the balance between maximizing lesion removal while minimizing functional damage has been a common challenge. Based on experimental and clinical studies, the new concept of functional neuronavigation surgery was proposed and verified in our center in 2003. The primary principles are as follows: (1) the datasets of multiple images (including structural MRI and functional images such as BOLD and DTI) are acquired, (2) accurate image fusion of structural and functional images is conducted through multi-modal medical image fusion technology based on rigid registration, and (3) the fused images are integrated with neuronavigation to guide the process of brain surgery, increasing the rate of lesion removal and avoiding neurological deficits.

Clinical application of functional neuronavigation
The most common central nervous system tumors are gliomas, accounting for approximately 28.9% of 55,889 cases of brain tumors and 76.4% of 18,151 cases of malignant brain tumors treated in Shanghai Huashan Hospital from 1951 to 2010. Less than 60% of these cases achieve image-verified complete resection despite the continuing progression of surgical technology. This is because there is no grossly distinguishable boundary between the tumor and normal brain tissue. It is particularly difficult to achieve “complete resection of the tumor with maximum preservation of brain function,” especially for tumors within eloquent areas. Considering individual differences and the reorganization and plasticity caused by disease, location of the distribution of cortical function using traditional anatomical landmarks has been unreliable. The BOLD technique, because of its advantages aforementioned, is widely used in preoperative brain function localization, intraoperative navigation, and postoperative assessment of brain function. Lehericy et al. and Wu et al. compared BOLD localization and the “gold standard” of intraoperative direct electrical stimulation of the motor cortex with highly consistent results. Studies by Rutten et al. and Lang et al. also showed substantial consistency between these two approaches in localization of the language cortex.

Similarly, the combination of DTI images with MRI structural images can clearly show the relationship between lesions and neurological pathways. It took 5 years for Huashan Hospital to complete large-scale prospective randomized controlled trials (n=238) of functional neuronavigation surgical treatment of glioma localization in the motor area and to show, using evidence-based medicine, that the new technologies can (1) increase the total gross resection rate of glioma in eloquent areas from 51.7% to 72.0% (nearly the cut rate of non-functional areas), (2) reduce postoperative morbidity from 32.8% to 15.3%, and (3) increase the long-term Karnofsky Performance Scale score of patients from 74 to 86. The study also confirmed significant independent survival advantages of functional neuronavigation. Compared with conventional neuronavigation surgery, this new technology reduces the risk of death after surgery by 43.0% in patients with malignant glioma (WHO grades III–IV) in functional areas.

BRAIN SHIFT IN NEURONAVIGATION SURGERY
One of the major technical challenges in conventional neuronavigation with preoperative imaging data is brain shift. Because brain tissue is non-rigid, brain deformation (i.e., brain shift or drift) inevitably appears during surgery because of tissue biomechanical properties, gravity,
changes in intracranial pressure, cerebrospinal fluid loss, operative manipulation, and anesthesia. A review of 1000 neuronavigation surgical cases at our department revealed that during surgeries, a dura shift of (2.80±2.48) mm, a cerebral cortex shift of (5.14±4.05) mm, and a tumor shift of (3.53±3.67) mm occurred. These values were especially high in surgeries involving the cerebral hemispheres. Brain shift reduces the localization accuracy of preoperative imaging navigation, resulting in reduced surgical accuracy and safety, an increased potential for residual tumor formation after surgery, and a higher risk of damage to normal neurovascular structures. Therefore, how to compensate for brain shift has become a popular issue.22,23 There are three general solutions to this issue: (1) micro-catheter localization technology, (2) computational model-updated imaging, and (3) intraoperative imaging.

**Micro-catheter localization technology**
In micro-catheter localization technology, the targets at the surface or periphery of the cerebrum show more shift than do the targets that are deep-seated or located in the center of the brain. For resection of multiple cavernomas, a 1.5-mm-diameter micro-catheter, guided by neuronavigation, is inserted into deep-seated lesions before dural opening. After resection of the superficial cavernoma, brain shift occurs, but the micro-catheter concomitantly shifts. Therefore, it is not difficult to reset the shifted cavernoma along the micro-catheter. We believe that this technique is useful, practical, and economical.6

**Computational model-updated imaging**
Computational model-updated imaging is based on non-rigid registration of brain images using a physical or mathematic model with compensation of 70% to 80%.24,25 Precision and reliability of the technique, however, are imperfect, and it is practically impossible to accurately model all complex phenomena that intraoperatively impact brain shift. One solution is to use additional intraoperative imaging (ultrasound, MRI, or CT) to drive the computational model, matching any preoperative data.26-29 The potential benefit of the technique is less interruption of the surgical technique for image acquisition.

**Intraoperative imaging**
Current intraoperative imaging models include radiography, X-ray fluoroscopy, ultrasonography, CT, and MRI. The first imaging techniques used in neurosurgery was CT and ultrasound, reported respectively by Shalit (1979) and Rubin (1980). Recent improvements permit CT of good resolution, especially for bones, but not yet for soft tissue. Nevertheless, intraoperative CT will not represent the leading direction for development of image-guided technology because of the radiation burden to patients. Recently, the rapid development of intraoperative ultrasound technology has allowed 2D and 3D imaging, but its resolution still cannot match that of CT or MRI; its penetration is inversely proportional to resolution. Therefore, the disadvantages of intraoperative CT and ultrasound have limited their application. Intraoperative MRI (iMRI) is currently the main technique with which to compensate for brain deformation.30-35

**INTRAOPERATIVE MRI AND NEURONAVIGATION**

**iMRI navigation**
iMRI navigation requires preoperative, intraoperative, and postoperative MRI scanning, image acquisition, and processing. The earliest report on its application came from Dr. E. Alexander III (1996).36 For more than 10 years, iMRI equipment and technology have been developed in three stages. The first two stages involved moving the operating room into the MRI room. The third stage employs design innovation of the scanning and magnets, enabling establishment of a true MRI system in the operating room. For example, the Medtronic PoleStar N20 0.15-T MRI, with vertical dual-plane magnets and low-field strength, is mobile and flexible enough to be placed in conventional neurological operating rooms. A digital integrated neurosurgical center devoted to iMRI has also been built. Now, 1.5- and 3.0-T iMRI have been installed and run in People’s Liberation Army General Hospital Beijing and Huashan Hospital Shanghai respectively. Since 2006, the Huashan Hospital has performed nearly 1000 surgeries with good results using both 0.15- and 3.0-T iMRI.

Intraoperative iMRI navigation has been widely used in neurosurgery, particularly for gliomas, pituitary tumors, functional neurosurgery, and needle biopsy.49 iMRI has the following advantages: it (1) provides real-time structural and functional images for neuronavigation to correct errors caused by brain tissue deformation and brain shift, (2) improves the extent of resection and avoids significant structural and functional damage, (3) provides real-time guidance and precise localization for stereotactic needle biopsy and surgical implants, and (4) allows for monitoring of early complications, such as cerebral ischemia and hemorrhage during surgery.

**Comparison between different MRI magnets’ fields in neurosurgery**
In terms of field strength, the MRI magnet’s field can be categorized as low-field (<0.5 T), middle-field (0.5–1.0 T), high-field (1.0–1.5 T), and ultra-high-field (>2.0 T).

**High-field iMRI**
As the signal-to-noise ratio (SNR) decreases with the low-field strength, the Maxwell term increases, and vice versa. Therefore, the overall image quality of high-field iMRI is better than that of low-field iMRI. The former also has the following advantages: (1) the acquisition time can be shortened by increasing the magnet field strength in the same SNR, (2) quantitative chemical
analysis of metabolites based on chemical-shift information can be performed by magnetic resonance spectroscopy (MRS), (3) enhanced susceptibility effects allow functional brain imaging (fMRI) of BOLD and DTI, and (4) a high gradient field and switching rate ensure the quality of angiography (magnetic resonance angiography (MRA) and magnetic resonance venography (MRV)), diffusion-weighted imaging, DTI, and perfusion imaging. Therefore, high-field iMRI has obvious advantages in the structural and functional imaging of the central nervous system despite its shortcomings, which include high cost, increased noise, accumulation of radio frequency pulse energy in the body, and metal artifacts.

Low-field iMRI
Compared with high-field iMRI, low-field iMRI has the following advantages: (1) less accumulation of radio frequency pulse energy in the body, (2) less ECG-gated signal distortion, and (3) increased comfort and safety. With the help of high-performance gradient systems, radio frequency (RF) systems, and computer systems, low-field iMRI is now capable of producing brain structural images comparable with those of high-field iMRI. Furthermore, it is relatively low-cost, small in size, and easy to operate and promote in a certain range.

However, low-field iMRI cannot acquire functional brain imaging, vascular imaging, or quantitative analysis of tissue metabolites. To address functional neuronavigation using PoleStar N20 (0.15-T), we successfully integrated the preoperative functional images, fMRI, BOLD, and DTI obtained from a 3.0-T MRI system and the intraoperative structural images obtained from the PoleStar N20 using a thin-plate spline model, thus realizing functional neuronavigation surgery in low-field iMRI. Further confirmation using 3.0-T iMRI is underway.

In summary, high-field iMRI not only opened up a new world for neuronavigation because of its efficient real-time imaging, high spatial and temporal resolution, and imaging of brain function and metabolism, but also inspired people to look for more technological advances.

FUTURE OF NEURONAVIGATION

Man and tool
During its 10 years of development, neuronavigation has made great strides in terms of equipment and techniques. Neuronavigation-related technologies have been broadly applied in China. Today, there are more than 150 neuronavigation systems and 7 iMRIs in China since their introduction in 1997.

Although the application of advanced neuronavigation systems will undoubtedly promote the development of minimally invasive neurosurgery and better patient service, we must be fully aware that such systems still require manual operation. Thus, the operator’s intelligence and three fundamental skills (basic theory, knowledge, and technique (especially microsurgical technique)) are critical for successful neuronavigation.

Future trends
Further development of hardware and software will make navigation systems more convenient, highly automated, and intelligent, with automatic registration and bias correction.

(1) A rapid processing system and high-performance personal computer can potentially replace the current workstation, making much smaller and cheaper portable navigation systems possible.

(2) A high-resolution 3D monitor screen will be conducive to the 3D display of complex, deep-brain structures.

(3) A touch control panel will enable neurosurgeons to directly manipulate the console, eliminating the need for a technician’s help.

(4) Multiple-image fusion (e.g., CT, MRI, Ultrasound, fMRI, DTI, MRA, MRV, MRS, PET, and CTA) will provide multimodal neuronavigation with those advantages already mentioned in this paper.

(5) Virtual Reality technology will allow neurosurgeons to preoperatively demonstrate each of the steps and possible surgical problems and treatment strategies, making navigation safer and more individualized and effective. Meanwhile, this technology benefits the training of young neurosurgeons as well as the preparation and review for complex surgery required for experienced neurosurgeons.

(6) Automatic compensation of brain shift is expected to increase the accuracy and safety of surgical navigation through the development of universal compensation software.

(7) iMRI hardware will be optimized. The modified equipment with higher resolution will obtain high-quality real-time images and make more space for surgical procedures which could acquire images during the operation without interruption. Special image anti-jamming technology will obtain images free from interference by external factors.

(8) Robots and mechanical arms have recently been applied to manipulate the surgical microscope, burr, traction control, electrode, and endoscope without being influenced by tremors, shaking, or the surgeon’s emotions. In the near future, robots will likely become widespread to neurosurgical treatment. Telesurgery, surgery performed by a robot under the control of a surgeon, will become a reality.
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