Neuronavigation: geneology, reality, and prospects

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Currently, neuronavigation is an indivisible and indispensable part of the neurosurgical reality with a significant potential impact in each neurosurgical procedure. The history of neuronavigation is quite short (< 3 decades), but full of highly promising achievements. The advent of neuronavigation would be unimaginable without the development of imaging technology, electronics, robotics, and space technology. The history of neuroradiology is reviewed briefly parallel with the detailed evolution of frame-based stereotaxy and its successor—neuronavigation. The historic milestones and the state of the art of neuronavigation are discussed in a genealogical manner. The future trends of neuronavigation as integrated with intraoperative CT, MR, and ultrasonography, as well as with robotic systems are outlined. (DOI: 10.3171/2009.6.FOCUS09109)

KEY WORDS • neuroradiology • frame-based stereotaxy •
neuronavigation • robotics

NEURONAVIGATION simultaneously represents a complex, multimodal, information-based, widely adaptable technique, method, or device using frameless stereotaxy for precise intraoperative guidance, orientation, and localization, with consequently greater surgical precision and possibilities for preoperative virtual simulation and postoperative analysis of the surgical procedure.

Neuronavigation and Neurosurgery

Neurosurgery will never be the same after the introduction of neuronavigation. The possibilities for the application of neuronavigation to contemporary neurosurgery are practically unlimited, with the potential to supply better guidance, orientation, and localization, and hence a higher confidence level for the surgeon and an improved outcome for the patient.^{24–29,68}

Genealogy of Neuronavigation

Neuronavigation is an emanation of the development of neuroradiology. Neuronavigation is the ultimate achievement of the aspiration to transfer multimodal image information in the operative field. The genealogical relations of neuronavigation, as a successor of frame-based

stereotaxy with CT, MR imaging, SPECT, PET, and ultrasonography are indisputable. The aim of the present study was to review the fascinating past, the glorious present, and the exciting future of neuronavigation (Table 1).

History of Neuroradiology

Until the end of the 19th century, the only way to look into patients' bodies was through invasive procedures.

In 1895, Wilhelm Conrad Roentgen discovered x-rays, and the imaging of the CNS began with radiographs (plain roentgenograms) of the skull.⁵⁴

In 1918, Walter Dandy, a prominent neurosurgeon at Johns Hopkins Hospital, introduced ventriculography,²⁰ and 1 year later reported on the first use of pneumoencephalography.¹⁹

In 1927, Egas Moniz, a Portuguese neurologist, introduced opacification of the carotid artery with contrast medium, using a solution of sodium iodide.⁶²

However, planar radiographs were not satisfactory, and clinicians urged the radiologists to provide better images.

The methods of brain imaging were profoundly and irreversibly changed with the subsequent invention and introduction of the contemporary imaging techniques. The history of CT,^{4,16,42,70,77,78,82,91,97} MR imaging,^{5,8,13,18,21,30,31,33,37,40,43,49–53,59,60,63,66,67,69,85} SPECT,^{38,48} PET,^{1,8,12,48,86} and ultrasonography,^{10,17,22,23,45,56,58,81,89,92} representing a fundamental and integral part of the history of neuronavigation, has been thoroughly described and analyzed in the literature (Table 1).

Abbreviations used in this paper: DW = diffusion weighted; fMR = functional MR; iCT = intraoperative CT; iMR = intraoperative MR; LED = light-emitting diode; MEG = magnetoencephalography.

TABLE 1: Summary of historical milestones of CT, MRI, SPECT, PET, and ultrasonography in parallel with the evolution of the frame-based stereotaxy and neuronavigation*

Year	Technique	Protagonists & Milestones
1842	US	Austrian physicist Christian Doppler described the Doppler principle. ¹⁰
1880	US	Curie brothers discovered the reverse piezoelectric effect that produces US. ¹⁷
1882	MRI	Nikola Tesla discovered the rotating magnetic field. ⁸⁴
1890	FBS	Zernov described the encephalometer: a skull-fixed device for intracranial localization based on superficial landmarks. ⁹⁶
1891	FBS	Altuchow studied the basal ganglia w/ the encephalometer. ³
1895		Wilhelm Conrad Roentgen discovered x-rays. ⁵⁴
1897	MRI	Sir Joseph Larmor developed the Larmor relationship. ⁵⁰
1900s	US	The first ultrasonic devices were designed & used among other things for detection of submarines. ¹⁰
1908	FBS	Horsley & Clarke ⁴¹ defined stereotactic calculation based on a coordinate system. They created a frame fixed to the skull which would accurately locate any intracranial point in 3D & guided the introduction of an electrode into the dentate nucleus of monkeys.
1914	CT	Mayer suggested the idea of tomography. Bocage, Grossman, & Vallebona developed the idea further. ⁷⁷
1918	FBS	Walter Dandy introduced ventriculography. ¹⁹
1919		Dandy reported on the first use of pneumoencephalography. ²⁰
1927		Egas Moniz introduced angiography. ⁶²
1931	CT	Ziedses des Plantes published the most extensive & thorough study on tomography. ⁹⁷
1933	FBS	Kirschner ⁴⁶ was the first surgeon to apply frame-based stereotaxy in humans.
1936	US	Ultrasonic microscopy was first proposed by Sokolov. ⁸⁹
1940s	CT	Frank & Takahashi published the basic principles of axial tomography. ⁸²
	US	Ultrasonic energy was first applied to the human body for medical purposes by George Ludwig. He used A-mode presentation of reflected echoes exclusively. ⁵⁸
1942	US	Dussik ²² first tried to use US in medical diagnosis, but instead of an echo-reflecting technique, he attempted a through-transmission method in the case of the head.
1944	MRI	Nobel Prize in Physics to Isador Isaac Rabi for developing molecular beam MR as a technique for studying the magnetic properties & internal structure of molecules, atoms, & nuclei. ⁶⁹
1947	FBS	Spiegel & Wycis ⁸⁰ introduced the first framed stereotactic tool that targeted in 3D using internal brain anatomy. Performed the first stereotactic thalamotomy in humans.
1949	MRI	The phenomenon known as “spin echo” is discovered by Erwin Hahn. ³⁷
	FBS	Leksell ⁵⁵ developed arc-centered stereotactic apparatus for intracranial surgery. It was the first stereotactic device to use transcutaneous pin fixation to the skull.
	FBS	Jean Talairach ⁸³ described a grid-based stereotactic instrument & introduced the concept of “layering” of angiography on radiographs in the development of surgical stereotactic maps.
1950s	SPECT, PET	Kuhl & Edwards introduced the concept of emission & transmission tomography. ⁴⁸
1952	MRI	Nobel Prize in Physics to Bloch & Purcell for MRS. ⁵
	US	Wild & Reid published the first paper on US for medical diagnosis. ⁹²
	FBS	Riechert & Wolff ⁷⁴ described their own stereotactic device for functional procedures.
1954	US	Edler & Hertz 23 described M-mode imaging used to generate echoencephalograms.
1956	MRI	The “Tesla Unit”—introduced by the International Electro-technical Commission-Committee of Action.
1960s		The advent of computers
	US	Development of bistable 2D imaging & gray scale 2D imaging. ¹⁰
	FBS	Todd & Wells ⁷ invented the Todd-Wells Stereotactic Unit: the first widely produced stereotactic frame.
1962	US	Holmes, Wright, & Meyerdirk developed the first compound contact B-mode (brightness mode) scanner. ¹⁰
1971	CT	Hounsfield developed the CT, initially called “computerized axial tomography (CAT)”. ⁴²
	CT	CT was introduced clinically by Ambrose. ⁴
1973	MRI	Paul Lauterbur obtained the first NMR image. He described a new imaging technique termed Zeugmatography. ^{51,52} Peter Mansfield further developed the utilization of gradients in the magnetic field & the mathematical analysis of these signals for more useful imaging techniques. ⁸⁰

(continued)

Neuronavigation: past, present, and future

TABLE 1: Summary of historical milestones of CT, MRI, SPECT, PET, and ultrasonography in parallel with the evolution of the frame-based stereotaxy and neuronavigation* (*continued*)

Year	Technique	Protagonists & Milestones
1974	MRI	Raymond Damadian patented the design & use of NMR for detecting cancer. ¹⁸
	US	Kessler ⁴⁵ developed the scanning laser acoustic microscope.
1975	MRI	Richard Ernst introduced 2D NMR ("NMR Fourier Zeugmatography"). ³⁰
	US	Lemons & Quate ⁵⁶ described the biomedical application of the scanning acoustic microscope.
	PET	Ter-Pogossian et al. ⁸⁴ developed an apparatus for obtaining transaxial emission images of organ sections containing positron-emitting radiopharmaceuticals.
1976	PET	Alavi ¹ was the first to administer 18F-FDG, the most commonly used PET scanning isotope carrier, to humans.
1977	MRI	Raymond Damadian produced the first MR scanner (Indomitabile).
1979	CT	The Nobel Prize in Physiology or Medicine was awarded to Hounsfield ⁴² & Cormack ¹⁶ for the development of CT.
	CT	Shalit et al. ⁷⁸ described the first neurosurgical procedure guided by iCT.
	US	Geoff Stevenson first demonstrated color Doppler. ⁸¹
	FBS	Brown, Roberts, & Wells developed a stereotactic instrument w/ ability to translate CT imaging data to the operating room. ^{6,39,90} Subsequent developments led to introduction of flexible Cosman-Roberts-Wells stereotactic system.
1980s	CT	Single-slice helical CT scanners. ⁹¹
1986	MRI	The technique of rapid acquisition w/ relaxation enhancement (RARE) — Hennig, Nauerth, & Friedburg. ⁴⁰
	NN	David Roberts et al. developed concept of frameless stereotaxy or NN & described the first NN system. ⁷⁵ Roberts' device was composed of an operating microscope on a solenoid floating stand and tracked in 3D by a sonic digitizer.
1987	MRI	Dumoulin ²¹ patented MRA.
	FBS	Young ⁹³ reported a stereotactic system based on a robotics model. The robotic CT stereotactic system was mounted in a special operating suite, containing a CT scanner & adjacent computer room.
	NN	Watanabe ⁸⁸ developed multiaxis mechanical measuring arms equipped w/ potentiometric angular sensors & video equipment for digitizing of CT scans from conventional films.
	NN	Reinhardt ⁷² developed multiaxis mechanical measuring arms equipped w/ potentiometric angular sensors & video equipment for digitizing of the CT scans from conventional films.
1988	MRI	Magnevist (Gd-DTPA dimeglumine) — Schering
1990s	US	Most of the really major advances in ultrasonic imaging have resulted from technology push: real-time scanning, endoluminal & intravascular scanning, Doppler blood flow detection, pulsed Doppler & duplex scanning, color flow imaging, 3D display, contrast agents, & harmonic imaging. ¹⁰
	CT	Multislice CT Scanning ⁹¹
	MRI	Introduction of the modalities of DW-MRI (tractography) & PW-MRI.
1991	MRI	Nobel Prize in Chemistry — Richard Ernst — high-resolution NMR spectroscopy. ³¹
	MRI	fMRI — independently by the University of Minnesota's Center for MR Research & Massachusetts General Hospital's MR Center.
	NN	Kato et al. ⁴⁴ introduced a frameless, armless navigational system based on magnetic sources.
1992	MRI	The BOLD fMRI technique for mapping neuronal activation was first demonstrated in the human brain. ^{8,49,67}
	FBS	Benabid et al. ¹¹ described the development of a 6-axis stereotactic robot that had been linked to a stereotactic frame for routine stereotactic procedures.
1993	SPECT	Hasegawa et al. ³⁸ developed first combined clinical CT & SPECT prototype scanner.
	NN	Reinhardt et al. reported an armless navigation system which used a pointer emitting US signals. ⁷³
	NN	Barnet et al. ⁹ described a technique of "frameless" stereotaxy. The system was composed of a hand-held probe containing 2 ultrasonic emitters, a microphone array that is rigidly affixed to the operating table in proximity to the surgical field, hardware to control & detect timing of signal production & reception, & a computer workstation w/ software to calculate & present the location of the probe tip on reconstructed neuroimaging studies. Unlike previously reported mechanical or sonic navigational devices, this system was adaptable to a wide array of neurosurgical instruments, allowed free movement of the operating table & conventional patient draping, & had accuracy which rivaled that of frame stereotaxy.
	NN	Zamorano et al. ⁹⁵ reported a NN device based on optoelectronic measuring principles. The infrared LEDs were applied as emitting sources.
	NN	Koivukangas et al. ⁴⁷ reported a computer-assisted NN system consisting of a neuronavigator arm w/ 6 degrees of freedom & high-precision potentiometers to indicate joint movements. Intraop US verified the accuracy of the neuronavigator & checked the results of the procedures.

(continued)

TABLE 1: Summary of historical milestones of CT, MRI, SPECT, PET, and ultrasonography in parallel with the evolution of the frame-based stereotaxy and neuronavigation* (*continued*)

Year	Technique	Protagonists & Milestones
1995	NN	Performance of the first neuronavigated neurosurgical procedure in iMRI (the 0.5-T suite widely known as the “double doughnut” magnet), which was integrated w/ a LED-based flashpoint navigational system for tracking w/in the 3D space at the center of the magnet. ¹³
	MRI	The first iMRI setup—the Brigham & Women's Hospital in Boston, & General Electric Medical Systems. ^{13,33}
1997	NN	Tronnier et al. ⁸⁷ described 0.2-T iMRI, installed adjacent to the operating theater, for intraop update of the NN data sets.
1998	PET	First prototype PET-CT scanner is designed & built by CTI PET Systems. ¹²
	NN	Matula et al. ⁶¹ connected a fixed iCT to a LED-based navigation in one operating room. The patients were positioned on a specially developed scanner table, which permitted movement from a scanning position to the operating position at any time during surgery. The procedure was completed w/ updated navigational data.
	NN	Grunert et al. ³⁶ reported their concept: to adapt a mobile CT scanner to an NN system. Slices were obtained by gantry translation & not by CT table movement. Updated CT image data were matched onto the preop CT data set.
1999	NN	Ganslandt et al. ³² superimposed MEG-source localizations onto a 3D MR image, & the image data set was then implemented into an NN system.
	NN	Nimsky et al. ⁶⁶ described functional NN based on fusion of fMRI & MEG data w/ an anatomic 3D MR image set. The matched 3D image data set was transferred to the navigation microscope & displayed in it operating viewing field during surgery.
1999	NN	Samset & Hirschberg ⁷⁶ described adaptation of a standard NN system into a 0.5-T iMRI scanner. The scanner had a 60-cm-wide vertical gap where both imaging & surgery are conducted & in-bore infrared linear cameras & monitors for NN.
2000	NN	Gronningsaeter et al. ³⁴ described the integration of an optical NN system into a US scanner. Single-rack system was developed which enabled the neurosurgeon to perform frameless, armless neuronavigation using preop MR or CT images & intraop 3D US data.
2001	PET	The first commercially available PET-CT scanner was announced (Discovery LS, GE Healthcare). ⁸⁶
	NN	Braun et al. ¹⁴ reported the first case of direct integration of fMRI & PET data into cranial NN.
	NN	Nimsky et al. ⁶⁵ reported a new concept of anatomic & functional microscope-based NN combined w/ iMRI by positioning a new navigation microscope w/in the fringe field of the MRI scanner.
	NN	Zaaroer et al. ⁹⁴ reported novel electromagnetic NN system.
2002	NN	Zimmermann et al. ⁹⁸ described their preliminary experience w/ robot-assisted neuronavigated neuroendoscopy.
2003	MRI	Nobel Prize in Medicine or Physiology to Paul Lauterbur & Peter Mansfield for invention of MRI. ^{53,59}
	NN	Nakao et al. ⁶⁴ reported a technique for complete updating of the NN w/ the aid of a mobile CT scanner used to acquire intraop images for a subsequent new registration.
	NN	Lindseth et al. ⁵⁷ reported an image fusion between preop MRI & intraop 3D US in US-based NN for visualizing the brain shift & improving interpretation.
2005	NN	Coenen et al. ¹⁵ presented their technique for intraop display of brain shift & its effects on fiber tracts. Preop DWI data were fused w/ anatomic T1-weighted MRI data. Intraoperatively, a single-rack 3D US NN system, displaying simultaneously the MRI scan & the corresponding US image, was used for navigation, manual definition of fixed & potentially shifting US landmarks near the fiber tract, & sequential image updating at different steps of resection. The result was time-dependent brain shift data.
2006	PET	PET-only scanners were no longer obtainable & replaced world-wide by PET-CT. ⁸⁶
2007	NN	Rasmussen et al. ⁷¹ described functional NN combined w/ intraop 3D US. The authors developed protocol for integration of fMRI & DTI data in a US-based NN system. A coregistration method for automatic brain shift correction of preop MR data using intraop 3D US was demonstrated.

* BOLD = blood oxygenation level-dependent; DTI = diffusion tensor imaging; DW-MRI = DW MR image; FBS = frame-based stereotaxy; MRA = MR angiography; MRS = MR spectroscopy; MRV = MR venography; NN = neuronavigation; NMR = nuclear MR; PW-MRI = perfusion-weighted MR imaging; US = ultrasonography.

Attempts to construct mechanical devices for localization of intracranial structures began at the end of 19th century. In the absence of any imaging techniques at that time, this task was doomed to failure. The subsequent introduction of radiography, CT, MR imaging, SPECT, PET, ultrasonography, and other technological advancements led to the development of frame-based stereotaxy and its evolution into neuronavigation.

History of Frame-Based Stereotaxy

In 1890, Zernov,⁹⁶ a Russian anatomist, described the “encephalometer”—an arc-based skull-fixed device for intracranial localization based on superficial landmarks and polar coordinates—that was designed for anatomical operations on the human brain. This device was actually used on at least 3 occasions.

FIG. 1. Photographs showing components of the frameless stereotaxic system. *Upper Left:* The Plexiglas bracket with a non-linear array of 3 spark gaps. This component of the acoustic localization system attaches to the operating microscope. *Upper Right:* The adapted operating microscope with spark gap bracket and optical projection system attached. *Lower:* The optical projection system. A miniature cathode ray tube is attached to a beam-splitting assembly that can be inserted into the operating microscope between the magnification changer and the binocular. Reproduced with permission from Roberts et al: A frameless stereotaxic integration of computerized tomographic imaging and the operating microscope. **J Neurosurg** 65:545–549, 1986.

In 1891, Zernov's pupil Altuchow studied the basal ganglia with the encephalometer.³

In 1908, Sir Victor Alexander Haden Horsley⁴¹ (Horsley's first 2 names were given him by Queen Victoria), a neurophysiologist and neurosurgeon, and Robert Henry Clarke, a mathematician, engineer, and inventor, defined stereotactic calculation based on a coordinate system. They created a frame fixed to the skull, which could accurately locate any intracranial point in 3D and guide the introduction of an electrode into the dentate nucleus of monkeys. The stereotactic frame used skull landmarks for intracranial targeting, so an atlas of brain anatomy coordinated to those external landmarks was also created. The frame was used only for experimental studies. With the specially devised apparatus, Horsley and Clarke pro-

duced a minimal electrolytic lesion of a cerebellar nucleus without involving the cerebellar cortex. This was the first use of electrolysis in experimental physiology. Horsley and Clarke concluded that the cerebellar cortex is practically inexcitable, but this has been disproved by subsequent investigation with the use of a stronger electrical current. Clarke suggested to Horsley that the stereotactic method could be useful in neurosurgical procedures in human patients. However Horsley laughed at this idea, and it ended their fellowship. Nevertheless, Clarke submitted a patent application for a human stereotactic instrument in 1912. Extension of the technique for use in patients was restricted, however, because of the immense variability between cerebral structures and skull landmarks in humans. Sir Victor Horsley was knighted in 1902 for his

FIG. 2. Block diagram of the frameless, armless navigational system based on magnetic sources introduced by Kato et al. Computed tomography scans or MR images were entered into the system as digital data and displayed on the color monitor. The spatial information of the probe in the operative field was sampled with a magnetic field sensor and was translated by the computer to display a cursor on the corresponding location of the images. CRT = cathode ray tube. Reproduced with permission from Kato et al: A frameless, armless navigational system for computer-assisted neurosurgery. Technical note. *J Neurosurg* 74:845–849, 1991.

many contributions to medicine, several years before the introduction of his best known innovation, the Horsley-Clarke apparatus (developed in 1908). Besides being a pioneer of neurosurgery, Horsley was also a champion of many social causes, including the temperance movement, women's suffrage, medical reform, and free health care for the working class. He died of heatstroke at the age of 59 years during the First World War as a volunteer surgeon in Iraq.

In 1918, Walter Dandy¹⁹ accidentally invented ventriculography after performing radiography in a patient with an open, penetrating head injury, and observing the ventricles filled with air. Ventriculography became a fundamental technique for calculating stereotactic targets in the basal ganglia and thalamus because of their definite and stable relationship to the third ventricle topography.

In 1933, Kirschner⁴⁶ was the first surgeon to apply frame-based stereotaxy to human patients. He punctured the skull base's foramen ovale to treat idiopathic trigeminal neuralgia. The individual variations in the intracranial structures in humans as opposed to animals and the absence of imaging techniques to visualize these variations, however, limited the stereotactic calculation of deep brain targets.

In 1947, the doctors Ernest Spiegel (a conservative Austrian-trained experimental neurologist who escaped to the US from Nazi occupation during World War II) and his student Henry Wycis (a colorful but talented neurosurgeon)⁸⁰ introduced the first framed stereotactic tool with 3D targeting using internal brain anatomy. Their apparatus—called the “stereoencephalotome”—was similar to Horsley and Clarke's prototype. Its design included a plaster cap adaptable to each individual patient. A head ring was suspended from the adaptable cap, and an electrode carrier was fixed to the head ring. Spiegel and

FIG. 3. Schematic drawing of the surgical setup with the computer-assisted neurosurgical navigational system. Both the patient's head and the magnetic source (O) were fixed with a Mayfield skull clamp. The position and orientation angles of the sensor (P) were measured with the 3D digitizer with respect to the source reference frame (O: X, Y, Z) by the magnetic field modulation method. The position of the probe tip (Q) was then calculated, translated with respect to the CT reference frame (R: x, y, z), and displayed on the CT or MR images with a cursor. Reproduced with permission from Kato et al: A frameless, armless navigational system for computer-assisted neurosurgery. Technical note. *J Neurosurg* 74:845–849, 1991.

Wycis' unique contribution was the idea of relating anatomical targets to internal brain landmarks—hence the name “stereoencephalotomy.” The frame was attached to a patient's head, and orthogonal pneumoencephalograms were used to visualize the key internal brain landmarks. The therapeutic targets were identified using an accompanying atlas. Spiegel and Wycis performed the first stereotactic thalamotomy in humans using the pineal body or commissura posterior as an internal individual reference system. They also suggested the application of stereotaxy for the treatment of intractable pain, movement disorders, and cystic tumors. Since the advent of the Spiegel-Wycis technique, frames and atlases have evolved. Functional operations with similar frames and techniques have been introduced by various authors.

In 1949, the electrophysiologist Lars Leksell⁵⁵ in Stockholm developed his own arc-centered stereotactic apparatus for intracranial surgery. It was the first stereotactic device with transcutaneous pin fixation to the skull. This instrument used a new concept: the arc quadrant, and

FIG. 4. Diagram of a prototype armless localizing device for frameless stereotaxy using ultrasonic 3D digitization. This technique may be modified for use with other surgical instruments. Lettering refers only to the line segments shown. Reproduced with permission from Barnett et al: Intraoperative localization using an armless, frameless stereotactic wand. Technical note. *J Neurosurg* 78:510–514, 1993.

was different in principle from the work of Spiegel and Wycis: instead of using the Cartesian coordinate frame, it used polar coordinates. Leksell's apparatus consisted of a fixation device for the patient's skull and a movable arc quadrant attached to the fixation device. The arc quadrant was moved so that the arc center was positioned at the desired intracranial target point. The stereotactic localization system was also used by Leksell in his next invention, a device for radiosurgery of the brain.

The same year, Jean Talairach⁸³ in Paris described a grid-based stereotactic instrument and introduced the concept of layering angiography on radiographs in the development of surgical stereotactic maps. Radiographs obtained with the fixed grid demonstrated overlaying of the grid holes over a positive contrast ventriculogram. Talairach also introduced the concept of teleradiography, in which precise measurements could be made directly from intraoperatively obtained radiographs. The Talairach frame could be removed and fixed again at precisely the same position of the patient's head. Thus images obtained in one operation could be used to guide subsequent procedures.

In 1952, Riechert and Wolff⁷⁴ in Germany reported on their own stereotactic device for functional procedures, which was similar to that described by Kirschner. This apparatus included an aiming bow attached to a circular base ring for fixation to the patient's head. The aiming bow was transposed to a phantom base ring on which the surgeon set up his target coordinates on a simulator. The instrument was used in many tumor and functional stereotactic procedures.

In the mid-1960s, neurosurgeon Edwin Todd and biomedical engineer Trent Wells invented the Todd-Wells Stereotactic Unit, which was the first widely produced stereotactic frame, used at many clinics worldwide.⁷

In 1979, Russell Brown, a medical student, neurosurgeon Theodore Roberts, and the aforementioned Trent

Wells developed a stereotactic instrument with capabilities to translate CT data into an operational setting—the Brown-Roberts-Wells stereotactic system.^{6,39,90} Subsequent developments led to the introduction of the flexible Cosman-Roberts-Wells stereotactic system.

In 1987, Young⁹³ reported on a stereotactic system based on a robotics model. The robotic CT stereotactic system was mounted in a special operating suite, which contained a CT scanner and adjacent computer room. Stereotactic coordinates were derived from CT data obtained intraoperatively and transferred by computer link to the robotic stereotactic system. The robotic arm was driven into place to align it with predetermined coordinates.

During the 1980s, as stated by Apuzzo and Sabshin⁷ “the computer became a ‘neurosurgical tool,’ and elements of stereotaxy became part of the repertoire of the general neurosurgeon.”

In 1992, Benabid et al.¹¹ described the development of a 6-axis stereotactic robot that had been linked to a stereotactic frame for routine stereotactic procedures, including placement of electrodes for deep brain stimulation. Robot software allowed the positioning of a probe holder to reach a given target.

Frame-based stereotaxy, even with its high application accuracy, limits the range of surgical approaches, does not allow for integration of more than 1 type of structural or functional imaging data, and causes preoperative patient discomfort.

History and Present Status of Neuronavigation

In the 1980s, progress in the fields of imaging technology, electronics, computers, and robot technology was the background for the development of more sophisticated devices for stereotactic surgery.³⁵

In 1986, Roberts and colleagues⁷⁵ developed the con-

FIG. 5. Schema for determining the effects on system accuracy of the wand position with respect to the microphone array. A = azimuth; D = declination; R = rotation. Reproduced with permission from Barnett et al: Intraoperative localization using an armless, frameless stereotactic wand. Technical note. *J Neurosurg* 78:510–514, 1993.

cept of frameless stereotaxy or neuronavigation. Roberts' device was composed of an operating microscope on a solenoid floating stand, which was tracked in 3D by a sonic digitizer (Fig. 1). The microscope adapted for navigated surgery was equipped with ultrasound-emitting sources and microphones arranged outside the operating field. The microphone data were processed by a computer, which calculated the microscope's position in space. The predefined target point on CT or MR images could be projected into the microscope ocular and used for intraoperative navigation.

In 1987, Watanabe in Tokyo and Reinhardt in Basel each independently developed multiaxis mechanical measuring arms equipped with potentiometric angular sensors and video equipment for digitizing of the CT scans from conventional films.^{72,88} These arm-based navigation systems were used for neurosurgical procedures.

In 1991, Kato et al.⁴⁴ introduced a frameless, armless navigational system based on magnetic sources. The device included a 3D digitizer, a personal computer, and an image-processing unit (Fig. 2). Applying magnetic field modulation technology, the 3D digitizer determined the spatial position and orientation angles of the probe, triangle-shaped pointer, or suction tube with a small attached magnetic field sensor (Fig. 3). Four fiducial markers on the scalp were used to translate the spatial data of the

probe onto the preoperative CT scans or MR images of the patient.

In 1993, Reinhardt et al.⁷³ reported on an armless navigation system that used a pointer emitting ultrasound signals. Localization in space was made by measuring the traveling time of sonic waves in air. The applied free-hand targeting instruments were light and mechanically simple.

In the same year, Barnett et al.⁹ described a technique of frameless stereotaxy that allowed real-time intraoperative neurosurgical localization. The system was composed of a hand-held probe containing 2 ultrasonic emitters, a microphone array that is rigidly affixed to the operating table in proximity to the surgical field, hardware to control and detect timing of signal production and reception, and a computer workstation with software to calculate and present the location of the probe tip on reconstructed neuroimaging studies (Figs. 4 and 5). Unlike previously reported mechanical or sonic navigational devices, this system was adaptable to a wide array of neurosurgical instruments, allowed free movement of the operating table and conventional patient draping, and had accuracy rivaling that of frame stereotaxy.

In 1993, Zamorano et al.⁹⁵ reported on a neuronavigation device based on optoelectronic measuring principles. Infrared LEDs were applied as emitting sources. Additional intraoperative digitization of the surgical instruments can be achieved by affixing infrared-based digitizers to them.

In 1993, Koivukangas et al.⁴⁷ reported on a computer-assisted neuronavigation system that consisted of a neuronavigator arm with 6 degrees of freedom and high-precision potentiometers to indicate the movement of the joints. Intraoperative ultrasonography helped to verify the accuracy of the neuronavigator and check the results of the procedures.

Soon after these iMR imaging systems were implemented, there was the wish to combine them with neuronavigation.

In 1995 the first neurosurgical procedure was performed in the 0.5-T iMR imaging suite, widely known as the General Electric "double doughnut," with a 56-cm-wide vertical gap at the center of the magnet. This system permitted 2 neurosurgeons to stand on either side of the patient and perform procedures completely within the bore of the magnet.¹³ An LED-based neuronavigational system was integrated with the iMR imaging unit, which provided neuronavigation within the vertical gap at the center of the magnet. In iMR imaging, the neuronavigational image data set guiding the surgery could be continually assessed by visual inspection of MR imaging scans obtained throughout the course of the procedure at the request of the neurosurgeon. Imaging was performed without moving the patient in and out of the magnet. The "double doughnut" unit combined intraoperative scanning and neuronavigation with surgery within the same space of the operating theater. With the iMR imaging suite, the whole surgical procedure could be performed in 1 room; neither the patient nor the magnet needed to be moved intraoperatively, 2 neurosurgeons could have access to the patient simultaneously, and near real-time images were

FIG. 6. A: In this patient the motor evoked field (MEF) dipole representing the motor cortex is displayed on the same gyrus as the tumor, which indicates that a resection is not possible. The asterisk represents the sensory evoked field phase reversal and indicates the central sulcus. B: Screenshot of the MR imaging data set as displayed on the workstation, showing the tumor contour and MEF dipole (green triangle in the precentral gyrus). Reproduced with permission from Ganslandt et al: Functional neuronavigation with magnetoencephalography: outcome in 50 patients with lesions around the motor cortex. *Neurosurg Focus* 6:E5, 1999.

provided. The disadvantages to this system included: a lower image quality compared with the high-field 1.5-T in closed MR suites; the inability to undertake functional, diffusion-perfusion, and spectroscopic studies because of the relatively low magnetic field strength; a limited working space for the surgeons, especially in transsphenoidal surgery; and increased costs because of the use of MR-compatible nonferromagnetic surgical equipment.

In 1997, Tronnier et al.⁸⁷ described iMR imaging for intraoperative update of the neuronavigation data sets. A 0.2-T magnet (Magnetom Open, Siemens AG) inside a special cabin with a radiofrequency-shielded sliding door was installed adjacent to the operating theater. A specially designed patient transport system was used to carry the patient in a fixed position to the magnet and back to the operating room. The operations were performed as routine image-guided microsurgical procedures with different neuronavigational devices. Following the surgeon's judgment regarding the extent of tumor resection, 4–5 fiducial markers were charged with Gd and screwed into the skull around the craniotomy. These markers were registered as intraoperative reference markers with the neuronavigation. The patient was transferred to the scanner covered with a sterile drape, leaving the skin and dura mater open. After the imaging procedure, in case of residual tumor, the 3D data set was sent to the neuronavigation workstation via ethernet, and data processing was performed (in 20–40 minutes) while the patient was being transferred back to the operating theater. The procedure was continued with the new updated navigational data set, reflecting brain shift.

In 1998, Matula et al.⁶¹ connected a fixed iCT scanner (Philips Tomoscan M) to a LED-based navigation system (Philips EasyGuide system) to provide an integrated solution to the problem of brain shift. The gantry

was fixed and the patients were positioned on a specially developed scanner table that permitted movement from a scanning position to the operating position at any time during surgery. The procedure was completed with the updated navigational data. The authors' idea was to work in a closed system where everything was performed in the same room.

The same year, Grunert and colleagues³⁶ reported on their concept: to adapt a mobile CT scanner to a neuronavigation system. They integrated the intraoperative mobile Philips Tomoscan M, which has a portable lightweight gantry on 4 wheels and can be moved by a single person, with 1 of the following neuronavigation devices: the Radionics optical tracking system, the Philips EasyGuide system, the Radionics arm-based operating arm system, or the Zeiss microscope-based MKM system. In contrast to the other intraoperative CT devices, the slices were performed by gantry translation and not by CT table movement. The updated CT image data were matched onto the preoperative CT data set.

In their 1999 study in 50 patients with lesions around the motor cortex, Ganslandt et al.³² superimposed MEG-source localizations onto 3D MR images, and the image data set was then implemented into a neuronavigation system. The sensorimotor cortex was identified correctly in all patients with the use of MEG (Fig. 6). The authors concluded that this method of incorporating functional data into neuronavigational systems is a promising tool that can be used during more radical surgeries to reduce injury to eloquent brain areas.

In 1999, Nimsy et al.⁶⁶ described functional neuronavigation based on the fusion of fMR imaging and MEG data with an anatomical 3D MR imaging set by a contour fit. The matched 3D image data set was transferred to the navigation microscope and displayed on the operating

FIG. 7. Photograph of frameless, armless, image-guided neuronavigation system, based on passive reflection of infrared light (VectorVision2, BrainLab).

viewing field during surgery. Additionally, intraoperative recording of somatosensory evoked potentials was performed for verification of the central sulcus. In all 7 cases, the projection of fMR imaging and MEG data allowed easy identification of the central region, which was confirmed by somatosensory evoked potentials.

In 1999, Samset and Hirschberg⁷⁶ described an adaptation of a standard neuronavigation system (OTS Radionics) into a 0.5-T iMR imaging scanner (Signa SP, General Electric Medical Systems). The scanner has a 60-cm-wide vertical gap where both imaging and surgery are conducted and in-bore infrared linear cameras and monitors for neuronavigation. The incorporation of intraoperatively updated MR imaging data sets into neuronavigation helps to overcome the challenge of brain shift. Performing surgery within the imaging volume of the iMR scanner eliminates the problems associated with patient or scanner transport during the procedure, and patient immobilization during the procedure obviates the need for reregistration of the patient, because of the fixed camera system in the bore of the iMR system.

In 2000, Gronningsaeter et al.³⁴ described the integration of an optical neuronavigation system into an ultrasound scanner. In this way the authors developed a single-rack system (SonoWand, MISON A/S) that enabled the neurosurgeon to perform frameless/armless neuro-

navigation using preoperative MR or CT images as well as intraoperative 3D ultrasonography data.

In 2001, Braun et al.¹⁴ reported on the first case of direct integration of fMR imaging and PET data into cranial neuronavigation (Zeiss MKM system navigation microscope, Carl Zeiss Co.), which was performed in a patient with a left precentral oligodendroglioma. The correct fMR imaging localization of the precentral gyrus was intraoperatively verified by cortical somatosensory evoked potential monitoring. Although the tumor was not clearly defined on MR images, [¹¹C] methionine PET scans demonstrated a clear tumor border, enabling the authors to achieve gross-total tumor removal without post-operative functional deficits.

In 2001, Nimsy et al.⁶⁵ reported a new concept of anatomical and functional microscope-based neuronavigation combined with intraoperative MR imaging by positioning a navigation microscope within the fringe field of the MR imaging scanner. Each patient was laid directly on the table of the iMR scanner (0.2-T Magnetom Open), which was placed in a radiofrequency-shielded operating theater. The patient's head was fixed in an MR imaging-compatible ceramic head holder. The NC-4 navigation microscope (Zeiss) with a camera for tracking the microscope movements was positioned at a distance of ~ 1.5 m in the 5-G perimeter. The navigation and iMR imaging workstations were placed outside the radiofrequency-shielded operating room. The margins of the tumor, the predefined surgical approach, and the functional data were displayed in the surgeon's microscope viewing field. The neuronavigation update added approximately an additional 15 minutes to operating time, including the time for image transfer, segmentation of suspected remaining tumor, defining the surgical approach, and rereferencing. The advantages of the described iMR imaging system included: increased access to the patient (the surgery is performed in an ordinary operating room) in contrast to the ergonomic restrictions of the earlier "double-doughnut" system; elimination of needless cumbersome and time-consuming patient transport; ability to use MR imaging-incompatible surgical instruments, thus obviating the need for a full set of MR imaging-compatible instruments, which could be of inferior quality; expense; and restricted in available range. The disadvantages of this low-field 0.2-T imager included: less tissue resolution; inability to undertake functional, diffusion-perfusion, and spectroscopic studies because of its relatively low magnetic field strength; the requirement for intraoperative transport of the patient into and out of the magnet, thus increasing the time of surgery; and the potential risk of intraoperative infection.

In 2001, Zaaroor et al.⁹⁴ reported on a novel magnetic technology for intraoperative intracranial frameless neuronavigation. The Magellan electromagnetic neuronavigation system (Biosense Webster) was developed to provide real-time tracking of the distal tips of flexible catheters, steerable endoscopes, and other surgical instruments using ultralow electromagnetic fields and a novel miniature position sensor for image-correlated intraoperative navigation and mapping applications. The system provided precise lesion localization without limiting the

Fig. 8. Screenshot showing the intraoperative application of LED-based neuronavigation in a patient with right frontoparietal cerebral arteriovenous malformation. Preoperative fusion of MR imaging and MR angiography images was performed. Yellow lines represent the pointing instrument.

line of vision, the mobility of the surgeon, or the flexibility of instruments.

In 2002, Zimmermann et al.⁹⁸ described their preliminary experience with robot-assisted neuronavigated neuroendoscopy in 3 patients. The Evolution 1 precision robot (Universal Robot Systems), especially designed for neurosurgery, was used simultaneously with the VectorVision2 neuronavigation system (BrainLab). The time for the registration process and for the robot setup decreased from 1 hour in the first case to half an hour in the last case. The duration of the endoscopic part of the surgical procedure ranged from 17 to 65 minutes. No device- or surgery-related deaths or complications were reported in their series. Based on their limited experience, the authors concluded that the advantage of using the Evolution 1 robot as a holding and positioning device for the neuroendoscope was the possibility of performing precise, smooth, and slow motions in critical regions. Neuronavigation increased the accuracy and safety of robot-assisted endoscopic procedures, supplying visual feedback regarding the intracranial position of the endoscope. The main disadvantage of the described robot was that it could not be

used for endoscopic procedures requiring a larger range of motion.

In 2003, Nakao et al.⁶⁴ reported on their technique of updating neuronavigational data with a mobile CT scanner used to acquire intraoperative images at a 2-mm-slice thickness. Several skull-fixed titanium screws were used as reference points for the intraoperative registration of the neuronavigation updating. Following the processing of the intraoperatively obtained CT image data from the workstation of the neuronavigation system, the navigational data were updated by registering the mentioned reference points. Under the guidance of the fully updated neuronavigation, the residual lesions were defined and further resected. The authors concluded that this technique, compared with iMR imaging, could be performed in an ordinary operating room without requiring special surgical instruments.

In 2003, Lindseth et al.⁵⁷ reported an image fusion between preoperative MR imaging and intraoperative 3D ultrasonography in an ultrasonography-based neuronavigation system (SonoWand, MISON A/S) for visualizing brain shift and improving intraoperative interpretation.

Fig. 9. Screenshot showing the intraoperative application of LED-based neuronavigation in a patient with a chordoma engaging the clivus and C-1 and C-2 vertebrae. For better visualization of bone and soft tissues, MR images and CT data sets were fused preoperatively.

The authors evaluated the integration of pre- and intraoperative data for surgical planning, guidance, and resection control as a useful means of improving the quality of the surgical procedure and, hence, patient outcome.

In 2005, Coenen et al.¹⁵ presented their technique for intraoperative display of brain shift and its effects on fiber tracts. The technique was performed in 3 patients with intracranial lesions in contact with important fiber tracts. Preoperative DW imaging data were fused with anatomical T1-weighted MR imaging data. Intraoperatively, a single-rack 3D ultrasonography neuronavigation system, which displayed the MR image and corresponding sonogram simultaneously, was used for navigation, manual definition of fixed and potentially shifting ultrasound landmarks near the fiber tract, and sequential image updating during the different steps of resection. The result was time-dependent brain shift data. The lesions were removed without complications. Postoperative DW imaging confirmed the predicted fiber tract deformation.

In 2007, Rasmussen et al.⁷¹ described functional neuronavigation combined with intraoperative 3D ultrasonography. The authors developed a protocol for integration of fMR and DT imaging data in an ultrasonogra-

phy-based neuronavigation system (SonoWand, MISON A/S). A coregistration method for automatic brain shift correction of preoperative MR data using intraoperative 3D ultrasonography was demonstrated. Intraoperative ultrasonography volumes were acquired as needed during surgery, and the multimodal data were used for guidance and resection control. The surgeons reported that the integration of fMR and DT imaging data in the neuronavigation system represented valuable additional information presented in a more user-friendly and efficient way compared with the traditional display on a separated monitor. The automatic ultrasonography-based updates of the preoperative MR imaging data were valuable for surgical planning and guidance.

Because no frame is attached to the patient's head that could interfere with the surgical approach, neuronavigation techniques have broadened the range of possible surgical approaches and opened logistical advantages in terms of scheduling diagnostic studies, in that imaging studies need not necessarily be acquired the same day as surgery (Figs. 7–12). Neuronavigation allows the fusion of > 1 structural and/or functional imaging data sets for planning, virtual simulation, and optimization of surgi-

FIG. 10. Screenshot showing the intraoperative application of LED-based neuronavigation in a patient undergoing repeated operation for a pituitary adenoma. The tumor is outlined in yellow and the internal carotid arteries in pink. The red cross is the targeted anterior border of the tumor, most remote of the carotid arteries.

cal procedures. Neuronavigation supplies intraoperative orientation, localization, and guidance with a high level of accuracy and precision. Thus, neuronavigation elevates the neurosurgeon's confidence and reduces the risks for the patient. Neuronavigation acts as a high-tech intraoperative neurovascular protection. The main disadvantage of neuronavigation is the brain shift problem, which has several possible solutions (already discussed).

Neurosurgery currently relies on navigation more than any other specialty. The fact is obvious even from the use of the term neuronavigation, which is in common use in the literature, in contrast to terms like orthonavigation (for orthopedic surgery), which do not actually exist. Presumably, the particular features of the brain (complex anatomy and functional distribution together with vulnerability and lack of regenerative possibilities) impose the requirements for perfect orientation, extreme precision, and minimal invasiveness of neurosurgical procedures. Neuronavigation represents a crucial step forward in this direction and is therefore widely applied to neurosurgical procedures.

Neurosurgical procedures have been compared with

sailing;⁷ however, I believe that it is more correct to compare it with space flight: every neuron is a star, every fasciculus is the Milky Way, every brain lobe is a galaxy, and the brain itself is the universe with its specific dynamics. Neuronavigation functions as a space guide that can potentially supply multimodal structural, functional, and chemical information. In our everyday space missions as neurosurgeons, neuronavigation is not obligatory; however, there are not any meaningful arguments against its clinical application.

The term astronaut derives from the Greek words "ástron," meaning star, and "nautes," meaning sailor. Navigated neurosurgery is transforming to "neuronautics," and neurosurgeons to "neuronauts." The growing distribution and application of neuronavigation inevitably necessitates close cooperation between these neuronauts and engineers, software specialists, and other technology professionals connected with the development of the software and hardware.

The Future of Neuronavigation

Current intraoperative imaging modalities include

FIG. 11. Screenshot showing the intraoperative application of LED-based neuronavigation in a patient with a colloid cyst. The colloid cyst is outlined in pink, the entry point is marked with a green cross, and the foramen of Monro with a red cross. Parallel yellow lines represent the endoscope shaft. In this case the “auto pilot function” was applied.

radiography, x-ray fluoroscopy, ultrasonography, and CT and MR imaging. Radiography and x-ray fluoroscopy supply only 2D images, and thus have limited application in neuronavigation.⁷⁹ Of the other modalities, MR imaging is the only technique that can provide functional data in addition to structural and anatomical information. With the incorporation of multimodality data sets with structural and functional information, image-guided neurosurgery has evolved into information-guided surgery.

Neuronavigation and Intraoperative CT

In the future, integration of neuronavigation and iCT will not be the leading direction of development of image-guided technology because of the radiation burden to the patients. The advantage of the iCT-based technology compared with iMR imaging is the simplicity of the solution combined with sufficient image quality. If iMR imaging is used, then either the operating theater and all its instruments must be made MR imaging compatible or

the patient must be transferred intraoperatively inside a special cabin with a radiofrequency-shielded sliding door, installed adjacent to the operating room or to be rotated in the 5-G perimeter of iMR imaging. The combination of iCT and iMR imaging would be extremely useful in skull base neurosurgery.

Neuronavigation and Intraoperative MR Imaging

The overlay of functional, diffusion, and perfusion data would constitute a virtual reality view of the brain, and continuous updating of this image would guide the neurosurgeon perfectly with the least possible margin of error in localizing, targeting, and reevaluating the lesion and surrounding tissue intraoperatively. The usefulness and effectiveness of these supplementary modalities still need to be tested in larger series before their standardization. Imaging modalities that use parameters based on the metabolic, diffusion, and perfusion characteristics of neural tissue (fMR, DW, MR angiography, MR venography,

FIG. 12. Screenshot showing the intraoperative application of LED-based neuronavigation in a patient with 2 metastatic tumors (outlined in purple and pink), which were removed simultaneously in a single procedure.

diffusion tensor imaging, and MR imaging spectroscopy) necessitate higher field systems. In the future high-field iMR imaging systems will probably prevail over low-field systems because they provide functional data, more refined anatomical data, increased signal-to-noise ratio, and higher spatial and contrast resolution.² Most likely, advancements in neuronavigator and MR scanner computer system software would make real-time, intraoperative MR imaging scans available.

Neuronavigation and Intraoperative SPECT and PET

Both SPECT and PET imaging techniques require radionuclides with their subsequent concerns, expenditures, and radiation hazards. At present, their introduction into the operating room is actually impossible and not cost-effective. Future technological decisions will probably prevail over these obstacles and will allow their real intraoperative integration with neuronavigation.

Neuronavigation and Intraoperative Ultrasonography

Ultrasonography provides real-time imaging with-

out a radiation burden to the patient. Intraoperative ultrasonography does not entail any special requirements on the neurosurgical armamentarium or the environment of the operating theater. Ultrasonographic devices are significantly cheaper than iCT and especially iMR imaging. Intraoperative ultrasonography has been successfully integrated into neuronavigation systems, providing the potential for brain shift evaluation and correction. It is therefore easy to suppose that intraoperative ultrasonography has its place in the neuronavigation of the future.

Microscanning is an exciting and quite promising aspect of ultrasonography. It is essentially the same process as traditional ultrasonographic body scanning, but at higher ultrasonic frequencies.⁸⁹ The ability of microscanning to image thick histological specimens rapidly in 3D, without the need for staining or sectioning, will provide previously inaccessible information about the structure of normal and pathological tissues in the 10–100 mm resolution range. This may have practical application in the operating theater for *in vivo* investigations. Another potentially important application, as described by Wells,⁸⁹ is in image-guided trackless microintervention; for example,

it may be possible for gene transfection of individually targeted cells to be achieved by delivering localized, high intensity ultrasound at the beam focus.

Neuronavigation and Robotics

Robots are devices invented to complete actions automatically with the ultimate degree of mechanical precision. Robots are extremely useful for the performance of repetitive, monotonous, or tiring tasks.⁸⁹ The use of robots perfectly complements the idea of the neuronavigation.^{2,98} In the near future, robots probably will become integral to neurosurgical treatment. Robots integrated with neuronavigation and equipped with a specially designed artificial intellect will be the neurosurgeons of the future, and telerobotics may enable the remote performance of neurosurgical procedures at distant locations.

Conclusions

The neuronavigation of the future will be cost-effective, intuitive, ergonomic, user friendly, accurate, and precise, with possibilities for structural, physiological, functional, and biochemical multimodal image fusion and intraoperative real-time update of image data, integrated with robots and indispensable to neurosurgical training, virtual simulation, surgical planning, intraoperative reality, and postoperative analysis of every neurosurgical procedure.

Disclaimer

The author reports no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Neuronavigation: past, present, and future

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