At the beginning of the 1950s, the meeting of Jean Bancaud and Jean Talairach represented a turning point in epilepsy surgery. Their idea was to accurately record the electrical activity of different brain structures during the course of a seizure. Soon, the term of stereoelectroencephalography was adopted for this new method. New concepts arose, followed by new concepts of surgery, techniques, neuroimaging tools and stereotactic procedures.

Stereotaxy and Epilepsy surgery, written by Jean-Marie Scarabin and a number of recognized experts in the field, presents its most recent advances, always respecting Sainte-Anne school’s spirit, and especially the value of clinical semiology and its integration through anatomo-electroclinical correlations. Its extremely precise descriptions of the methodologies and its rich contents of figures and plates, including a particularly interesting DVD with videos and 51 clinical cases, certainly make this book a reference in the domain of epilepsy surgery.
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10. Talairach methodology in the multimodal imaging and robotics era

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Introduction and original methodology

The original Talairach methodology was based on three main features. Neuroimaging techniques to collect patient-specific brain anatomical data, a probabilistic morpho-functional atlas and surgical tools developed to implant intracerebral electrodes in accurate and safe conditions. Brain anatomy was obtained indirectly by means of cerebral angiography and ventriculography. Both techniques were performed in stereotactic (coordinate system), telemetric (reduced magnification and distortion) and stereoscopic (pseudo-3D effect) conditions (Figure 1). The following step was to normalize patient’s specific data to the atlas space using the bicommissural coordinate system. The normalization to the atlas was fundamental in order to integrate the images with structural (gyri and sulci), cytoarchitectural (Brodmann areas) and functional (electrical stimulations) data. Then, in order to position the guiding screws along the pre-planned trajectory, a double grid was attached onto the frame, allowing drilling in the orthogonal direction (Figure 2).

Nowadays modern technological tools facilitate the workflow, but the main concepts of this methodology are still valid. We use algorithms completely automated with software applications to expand the multimodal integration of data so that MRI, rotational angiography, fMRI and DTI-FT data can all be coregistered together. It is now possible to obtain real 3D viewing by multi-planar reconstructions (MPR), volume and surface rendering. The tool holder for the surgical implantation is now fixed onto the passive robotic arm of the stereotactic image-guided system Renishaw neuromate®, so that the number of possible trajectories is no more discrete (as using the double grid), but virtually infinite with any desired obliquity.

The aim of this chapter is to describe our present workflow. We will underline the methodological continuity with basic Talairach and Bancaud principles, highlighting how modern tools can help in saving time and improve safety, accuracy and the amount of information. Moreover, we report our quantitative results regarding geometrical accuracy at the cortical entry point with this new methodology.
Figure 2
The Talairach frame
(A) The Talairach frame and the mounted double grid. The grid is a simple tool holder that allows aligning the surgical devices (drill, monopolar coagulator, guiding screws and screw driver) along the pre-planned path. The same grid can be used for trajectories orthogonal to the sagittal (as in the picture) or coronal plane. A similar grid can be mounted with a special support for trajectories with single obliquity in the sagittal or coronal plane (or both when mounted on a Scerrati arc). (B) Detailed view of the double grid.

Procedures and methods

● Workflow
The main steps of our workflow are:
● pre-implantation:
  – imaging acquisition;
  – loading of the images into the planning software;
  – trajectory planning;
● implantation:
  – registration to the stereotactic space;
  – implantation of the guiding screws;
  – implantation of the electrodes
  – verification of the positioning and electrical testing of the electrodes;
● post-implantation:
  – building of 3D scenario with contacts position and multimodal data;
  – video-SEEG monitoring;
  – electrodes removal;
  – data analysis and surgical resection planning.

● Planning principles
Entry point (EP) and target point (TP) commonly define each stereotactic trajectory. In this chapter we adopt this conventional terminology; by the way we would like to point out a main difference between SEEG and other stereotactic procedures. In Deep Brain Stimulation (DBS) and biopsy procedures the interest is focused on the deep target, and the EP can be "freely" changed pivoting around it. This is not the case for SEEG, where the target is not just the TP itself but the whole trajectory. In fact the multi-lead electrodes record brain activity of white and gray matter in the whole trajectory that lies between EP and TP (Figure 3). Therefore, in our case the TP does not represent a real target but just the deepest point of our stereotactic trajectory.

To plan the trajectories we need anatomical information regarding brain tissue, lesions, cerebral vessels and skull. When necessary, fMRI and DTI-FT must be considered too.

In order to define the trajectories in the planning software, MPR views are mandatory. Reformatting images all along the trajectories and orthogonal to them, and 3D views of pial surface and vascular tree, are very useful tools for a more advanced planning.

● Hardware tools
The eight channel coil and Sense® technology of the Philips Achieva 1.5 T MRI scanner, allow a reduction in acquisition time with only minimal image deterioration (Figure 4). In order to
Figure 3
Entry Point (EP) and Target Point (TP)
In the case of trajectories for biopsies or DBS (A), the proper target is at the level of the TP, and the EP can be planned pivoting around it (the dotted line represents the trajectory projection; only the lower continuous segment really lies on this slice). In SEEG trajectories (B, C and D) the whole trajectory is the real target. This electrode (represented as a yellow line in the 3D views) records electrical activity from the middle occipital gyrus, the optic radiation (DTI-FT reconstructed) and the baso-mesial occipital cortex.

Figure 4
Structural MRI
MPR views of structural MR acquired in the sagittal plane and reformatted in the axial one directly at the console of the scanner. High-resolution imaging provides high quality reconstructions. The sagittal plane acquisition and the SENSE technology help to save time, maintaining optimal geometrical accuracy. The high contrast between gray and white matter is important for the automatic segmentation processes performed by FSL and FreeSurfer packages.

guarantee the geometrical accuracy of the images, frequent and careful maintenance of the scanner is strongly recommended.

The O-arm™ 1000 System by Medtronic is a mobile radiographic device for intraoperative imaging. It was principally developed for orthopedic and spine surgery (Figure 5). It is a cone-beam CT, with an X-ray tube and a flat panel detector isocentrically rotating inside the gantry. The O-arm provides 2D and 3D images. The reconstructed 3D volume is a 200 × 150 mm cylinder (192 slices, 512 × 512 matrix, 0.4 × 0.4 × 0.8 mm anisotropic voxels).

We still use the Talairach frame, originally designed with orthogonal headrest supports, transcranial pins for optimal repositioning and double grid mounting system. Currently we use it mainly to fix the head and to provide a coordinate system for the stereotactic robot neuromate. We can register the frame’s geometry to the robotic stereotactic space mounting 2D localizers on it.

The neuromate (Renishaw) is a mobile robotic device developed specifically for neurosurgical procedures, in use in our center since 2001 (Figure 7). This passive robot has an arm with five degrees of freedom (DOF) that allows aligning the tool holder along a trajectory previously planned with the Voxim® (IVS Technology GmbH) software. In this package, running on Microsoft Windows®, we plan the trajectories defining EP and TP in a DICOM dataset. There are two main available workspaces. The first one combines MPR views and 3D rendering of segmented regions of interest (ROI) (Figure 8). In the second one there are two “trajectory cut” slices, reformatted along the path of the planned electrode, and seven slices of the “surgeons eye view”, orthogonal to that (Figure 9). In all views it is possible to visualize up to two coregistered datasets, fading between them. Moreover it is possible to visualize a coregistered pair of 2D
The O-arm

The O-arm 1000 System by Medtronic is a mobile radiographic device for intraoperative imaging, originally developed mainly for orthopedic and spine surgery. It is a cone-beam CT, with an X-ray tube (Varian B100) and a flat panel detector (Varian Paxscan 4030 CB) isocentrically rotating inside the gantry. The detector is 400 × 300 mm large, with a 2000 × 1500 pixel matrix and 0.192 mm dot pitch. The O-arm provides 2D and 3D images. 2D images are obtained in pulsed fluoroscopy modality, with a maximum frequency of 30 Hz. It is possible to store images 1, 2, 3 or 5 frames per second. 3D modality acquisition is based on 394 exposures during a 360 degrees rotation of the tube-detector complex. The acquisition takes about 12 seconds for the "standard" modality, 24 for "HD" and "Enhanced" acquisitions. The reconstructed 3D volume is a 200 × 150 mm cylinder (192 slices, 512 × 512 matrix, 0.4 × 0.4 × 0.8 mm anisotropic voxels). The picture shows the O-arm in operative conditions.

Voxim provides, as complementary features, registration and segmentation tools. Manual segmentation of simple ROIs is relatively easy, while the cortical surface segmentation is time-consuming and complex, like in other similar packages. Sometimes the automatic coregistration tool is not satisfactory, especially in inter-modal cases (MRI-CT), while manual point-to-point matching is easy and effective, as in the case of 2D-3D coregistrations. NMControl is an auxiliary software provided with the neuromate, able to do the main checks and to reproduce the 3D configuration of the robotic arm (Figure 10).

The Cranial Marker System® (Leibinger) is a set of fiducial markers constituted by cranial screws supporting the proper localizers for CT or MRI (Figure 11). The CT fiducials, containing a radiopaque metallic sphere, are compatible with the O-arm. Positioning the fiducials on the skull takes about ten minutes. We prefer the Cranial Marker System compared to the skin adhesive fiducial markers because they do not move and hence they improve the accuracy of the registration.

We currently use intracerebral electrodes manufactured by Dixi Medical (Microdeep Intracerebral Electrodes D08®) (Figure 12) or Alcis (Depth Electrodes Range 2069®). These multi-lead electrodes are semirigid, with 0.8 mm external diameter and have no stylet inside. Every contact is 2 mm long, with 1.5 mm inter-leads gap. These electrodes are available with 5, 8, 10, 12, 15, 18 contacts, and must be implanted through the 2.45 mm guiding screws. The length of the screws ranges between 15 and 35 mm, in increments of 5 mm. The skull hole must be performed with a 2.1 mm drill. A special cap locks the electrodes to the screws, avoiding movements and CSF leakage.

The Medtronic StealthStation Treon Plus® is the neuronavigation system in use in our center for resective surgery. In the SEEG workflow its use is limited to immediate postoperative coregistrations between pre-implant MRI and post-implant 3D O-arm datasets. The Stealth-Merge fusion package is fast; so that coregistration is available right after surgery during electrical testing of the electrodes.

Our video-EEG system (Nihon-Kohden) has 192 channels for high rate sampling (1,000 Hz) recording, and permits to store a large amount of electrical data.
Figure 6

2D registration

(A) The 2D localizers fixed to the frame. The yellow arrows indicate the four plastic plates (anterior, posterior, left, right) that incorporate the metallic spheres, that serve as fiducials. Blue arrows indicate the localizers in the left plate. (B) The geometry of the localizers is described in Voxim, the planning software. Once the AP and LL projective images are loaded, and the localizers are pointed with the mouse by the user (green crosses), the frame is registered. It means that clicking on both images allows defining X, Y and Z for every point in the frame coordinates system. It is important to underline that telemetry is not necessary for this, and 2D O-arm images are perfectly usable.

Figure 7

The neuromate

Neuromate (Renishaw) is a mobile robotic device developed specifically for neurosurgical procedures. Its frame adaptor has been redesigned to interface with the O-arm.

General-purpose computers are Apple Mac Pro®, with 30" Apple Cinema Display® monitors. We chose these computers for the high computational power, and to run simultaneously Apple Mac OS X® and Microsoft Windows operative systems, so that Voxim and other medical packages can be utilized. Moreover, the planning of the trajectories is more straightforward on wide monitors (Figure 13).

● Software tools

Neuroimaging post-processing is completed with Open Source or Freeware software’s, freely downloadable from the Internet.

The first software is Osirix (<http://www.osirix-viewer.com>), which must be used on the Apple Mac OS X. This sophisticated DICOM viewer, provides many tools for 2D and 3D MPR views (Figure 4), curved reconstructions, volume and surface rendering. In our workflow, we use it mainly for querying and retrieving images from a PACS system.
this Voxim screen capture shows a trajectory planned to explore mainly the insular lobe. The dotted yellow line represents the projection of the trajectory on each anatomical reconstructed plane. Only the continuous tract of the line really lies on the slice. In the axial view the visualization fading is tuned 50% for MR and 50% for 3D angiography. In the coronal view the fading is 100% MR; in the sagittal one it is 100% angiography. It is possible to read the distance between EP and TP in the magnified frame.

The second application is MRicron (<http://www.sph.sc.edu/comd/rorden/MRicron>), and its specific module for the conversion from DICOM to NIfTI format. This software is available for Apple MAC OS X, Linux and Microsoft Windows.

The third one is FSL (<http://www.fmrib.ox.ac.uk/fsl>), a software library compiled for Apple Mac OS X and Linux. It provides several tools, some of which constitute the core of our IT workflow: BET for brain extraction, FLIRT for linear registrations, fslmaths for mathematics, FEAT for fMRI post-processing, FDT and BEDPOSTX for DTI-FT post-processing. Most of these
tools are available with graphic interface and a command-line. This last feature is important to develop Script files for automatic running of complex workflows.

The fourth package is FreeSurfer (<http://surfer.nmr.mgh.harvard.edu>), available for Apple Mac OS X and Linux. This command-line package provides tools for high quality brain segmentation, hemispheres splitting, cortex parcellation and labeling, calculation of cortical thickness (Figure 14).

The fifth application is NIfTI2DICOM, developed in collaboration with the Biolab laboratory in Genoa (<http://www.bio.dist.unige.it>). This package, available for Apple Mac OS X and Linux with command-line and graphic interface, is able to reconvert from NIfTI to DICOM format, the only format accepted by Voxim and neuronavigator. It is still not available on the Web, but the specific module included in 3D Slicer can be used instead.

3D Slicer (<http://www.slicer.org>), the sixth application, provides an integrated multimodal environment with multi-planar and 3D views (Figure 15), used in our workflow mainly to collect data in the post-implant phase.

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**Figure 10**

NMControl

The NMControl software provides a preview of the available configurations for the robotic arm. In (A) and (B) the software shows two alternatives for the same trajectory. In (C) it shows a different trajectory, similar to (A). In this example, moving from the first to the second trajectory will only take seconds between (A) and (C), compared to moving from trajectory (B) to (C). This helps to optimize procedure time.

**Figure 11**

Cranial Marker System

(A) The components of Leibinger Cranial Marker System, from the left to the right: the bone screws (short and long type), the localizer holder, the CT marker (with the metallic ball inside), the verification marker, and two assembled sets. The verification markers allow reaching a point corresponding to the centre of the localizer, for a visual check. (B) CT markers positioned to the head.
Intracerebral electrodes

Picture of an electrode (Microdeep Intracerebral Electrodes D-08 15 AM) manufactured by Dixi Medical. The yellow arrows indicate two out of fifteen platinum-iridium electrodes, 2 mm long, with 1.5 mm interval. On the opposite end the green connector is visible. An important feature is that the tip is constituted by a recording lead: it is not necessary to pass over a deep structure for recording from it.

Presurgical Planning Lab

Two Apple Mac Pro computers are visible in our Presurgical Planning Lab. SEEG planning is more comfortable on such large monitors as the 30" Apple Cinema Display. Despite their top-level computational power, some tasks are heavily time consuming. This is the reason why we are setting up a grid computing system for parallel computation. The Bayesian estimate of probability families for DTI-FT post-processing takes about 12-24 hours on this computer. In a preliminary test we ran this task in about 20 minutes, recruiting three 8-multithread-core computers.

All post-processing steps are almost fully automated via PHANTOMS (PHysiology and ANaTOmy Management for Surgery), a Bash script developed by the first author that provides an easy to use interface. It is available for Apple Mac OS X or Linux.

Preoperative imaging

The acquisition of preoperative images does not need the positioning of a stereotactic frame or fiducial markers. The anatomo-functional data are acquired with the patient awake (except for children) and well in advance of surgery, outside the operating room.

MRI is the gold standard investigation; CT is performed only when a pathological calcification is suspected.

Structural MRI

The morphological sequence we use is T1-FFE 3D. Images are acquired on the sagittal plane with 284 × 232 matrix (0.90 × 1.07 × 0.90 mm voxel), then reconstructed and reformatted on the axial plane with 560 × 560 matrix (0.46 × 0.46 × 0.90 mm voxel), without any inter-slice gap. The acquisition takes 6'55" (Figure 4). It is important to enlarge the field of view (FOV) in order to include facial anatomy. In fact, its unambiguous geometry is essential for pre-SEEG and neuronavigation registrations (Figure 16). Other complementary MRI sequences (FLAIR, T1 plus gadolinium, etc.) are sometimes performed as needed, even in separate sessions. We
recommend to avoid gadolinium administration during T1-FFE 3D sequence not to compromise automatic segmentation processes.

**fMRI and DTI-FT**

Morphologic pre-operative imaging is increasingly integrated with non-invasive functional imaging. fMRI and DTI-FT can provide useful functional information. fMRI maps changes in the gray matter metabolism that correspond to a given brain activity pattern (*Figure 17*). The DTI-FT studies the three-dimensional architecture of white matter tracts, by detecting the anisotropy of Brownian movements of water molecules (*Figure 18*). It is important to underline
Facial anatomy must be included in the FOV of structural 3D MR. In fact, its unambiguous geometry is essential for pre-SEEG and neuronavigation registrations. In this screen capture, taken from the Cranial Package of the Medtronic StealthStation Treon Plus navigator, the green dots were traced on the skin of the head with the manual pointer, and the facial points constitute the most important information for the registration algorithm.

how SEEG and these recent imaging techniques can be mutually validated (Figure 19). The imaging acquisition must be followed by a post-processing step (Figures 20 and 21). The statistical computation originates probabilistic maps, useful for pre-surgical planning.

3D angiography

3D reconstruction of the vascular tree is per se the most comfortable imaging technique to plan complex procedures such as SEEG. This technique is based on the acquisition of several 2D images obtained by selective intra-arterial injection of contrast medium during the rotation of X-ray tube and detector around the patient’s head. A specific software algorithm reconstructs a CT-like 3D dataset from these multi-angled 2D images. This technology is already available on the vast majority of modern angiographic imaging systems. However, the X-ray image-intensifier-based Philips Allura System, available in our hospital, does not optimize the reconstruction of cortical vessels. This task can be achieved with the O-arm. Unfortunately this system still does not support the common features of angiographic equipment, such as bone mask subtraction and vascular segmentation. Therefore we need to post-process O-arm datasets with other software (Figure 22).

Post-processing

Several features provided by Voxim such as MPR views, Trajectory Cut and Surgeons Eye View, make the stereotactic planning easy. However, for a more advanced planning other specific features are needed. 3D reconstruction of the vascular tree and pial surface, brain splitting and automatic coregistrations can make this process faster, safer and multimodal.

Since the implantation is not an open surgical technique, the visualization of vessels at the cortical EP is not possible. Therefore we consider the angiography essential for surgical
planning. We acquire O-arm 3D angiography. This dataset, obtained for instance from injection of the right carotid artery, is used as the reference space for all the other imaging modalities. It means that MRI series, CT scans and other O-arm datasets will be coregistered to it. Once the coregistration is done it is also possible to add different angiographic datasets and to subtract the 3D bone mask (Figure 23). The post-implantation O-arm dataset is post-processed in the same way. The bone subtraction and a simple gray scale thresholding allow easy segmentation of the electrodes.

MRI provides detailed information about brain anatomy, however in some regions can be difficult to recognize specific gyri and sulci. For example, while temporal and frontal gyri are usually easily distinguished on standard MPR views, occasionally this is not the case for more complex regions such as temporo-parieto-occipital junction. In addition it does happen that gyral patterns can be profoundly altered by developmental abnormalities. In these situations, FreeSurfer 3D reconstructions of the pial surface and brain splitting can facilitate the planning (Figure 24). Structural and functional MRI sequences are coregistered to the vascular reference space, using FLIRT (Figure 25).

All these post-processing steps are performed with the tools provided by FSL and FreeSurfer. These packages do not support DICOM, which is why at the beginning and the end of the multistep automatic process it is necessary to convert between different file formats (Figure 26).
Imaging acquisition for DTI-FT

(A) Repeated acquisition of PGSE (Pulsed Gradient Spin Echo) sequence is the basis for DTI-FT investigation. It is also known as “Stejskal and Tanner sequence” (B), and is repeated 66 times for acquiring the whole brain with 50 slices (2 × 2 × 2.6 mm). The first series is T2 weighted, because it is acquired without any diffusion gradient. Subsequent series are acquired with diffusion gradients on 65 different directions. Information about water Fractional Anisotropy and Fiber Tracking are computed in the post-processing step.

SEEG and DTI-FT (crossed viewing)

(A) Two small white matter regions, involved by bipolar stimulations on two pairs of contacts along the same electrode. (B and C) Stereoscopic pair of images, with a 3D reconstruction of amygdala (yellow), hippocampus (light blue), lateral ventricle (violet). The model of the electrodes (green) was obtained with the Gray Scale Model Maker module of 3D Slicer, using the information of post-implant 3D O-arm dataset. FreeSurfer automatically segmented all the anatomical structures. Electrical stimulation of the lateral point (yellow on 2D and 3D images) caused clonic movements of the contralateral orbicular muscle of eye. Stimulation of the mesial point (red) caused clonic movements of the contralateral hand. DTI-FT probabilistic analysis was performed, with the seeding mask in the cerebral peduncle. The coordinates of the stimulated points were used as waypoint masks. Note the two different components inside the cortico-spinal (and cortico-pontine) tract, with the “hand” fibers that move laterally going down, reaching their correct mesencephalic position.

The planning

To start the planning we load the 3D angiography (our reference space) and the segmented hemisphere dataset. We define EP and TP looking simultaneously at vessels and brain targets, in MPR views, 3D view (Figure 27), Trajectory Cut and Surgeons Eye View (Figure 28). The following step is loading the non-segmented MRI, in order to refine EP and TP on high magnification images. For each trajectory it is then possible to read the useful length. In other words the useful length represents the distance between EP and TP along which brain activity will be recorded. On the base of the useful length we can then choose the most appropriate electrode (Figure 29).

Once the bone dataset is loaded, it is possible to check the skull thickness for the positioning of the hollow screw, taking care of bony defects and paranasal sinuses. Moreover, we can
fMRI data analysis

We perform fMRI data analysis with FEAT, the specific FSL package for the application of Generalized Linear Models. Pre-analysis features like motion correction, smoothing, intensity normalization and high-pass filtering are available. The picture illustrates the first case of fMRI and SEEG based surgical planning in our Centre (2004). The hemispheric dominance for language functions was studied with fMRI, and high definition relationship between Broca’s area and lesion was cleared by intracerebral stimulations (gray and white matter). In (A) preoperative images are visible. In (B) the preoperative fMRI is coregistered to the preoperative fMRI. fMRI analysis and coregistration were performed with SPM2, multimodal visualization with MRicro.

Figure 21

DTI-FT data analysis (crossed viewing)

BEDPOSTX (for Bayesian probabilistic approach) and FDT (for Fiber Tracking) are the two FSL packages for DTI-FT pre-processing and analysis. Once the Principal Diffusion Direction and the Probability Density Function are computed, Fiber Tracking is performing defining seeding, waypoint, inclusion and exclusion masks. (A) The color map: the red color indicates that water molecules preferentially move along the X axis (LL direction), suggesting the morphology of myelinated fibers, but not their functional way. Green color is for AP direction, blue for cranio-caudal. (B and C) Stereoscopic pair of images of a 3D Slicer view: the electrodes named Z', H', K' and Q' pass through the reconstructed arcuate tract.

measure the distance between EP and inner skull surface, which will be useful during drilling (Figure 30).

When necessary other structural and functional datasets can be loaded at any moment during planning.

• Implantation of the electrodes

The procedure is performed under general anesthesia. The different steps for surgical implantation are briefly described below.
Figure 22

3D O-arm angiography (crossed viewing)

First we acquire a 3D dataset without any contrast medium. Subsequently we acquire a 3D dataset during the selective injection of iopamidole (300 mg/mL) into the artery of interest. Infusion rate is 2 mL/s, and the duration of infusion is 15 seconds, with a total volume of 30 mL (1.5 mL/s × 15 seconds in children). In the case of anterior unilateral SEEG investigation, one vascular dataset with selective injection of the corresponding internal carotid artery is enough. For investigation of the posterior regions one more acquisition with injection in one vertebral artery will be needed. In case of bilateral anterior investigation, both internal carotid arteries will be injected, and the maximum number of vascular acquisitions will be three in case of posterior bilateral electrodes implantation. So, the total number of 3D acquisition ranges from two to four. In (A) and (B) two corresponding axial slices are extracted from two datasets without and with contrast medium injection into the left ICA. In (C) the result of the algebraic subtraction (B – A) of the two datasets is reported. (D) and (E) are a stereoscopic pair of images of 3D volume rendering of the subtracted dataset. In this case the movement between the two acquisitions (A and B) is minimal, so that subtraction can be performed efficiently without any preliminary coregistration. On the contrary, in the vast majority of cases motion correction is necessary. This is the reason why this step is automatically performed in our workflow.

Coregistration to the frame space

Four percutaneous bone fiducial markers (Figure 31) are positioned and a new 3D dataset is acquired with the O-arm. The just acquired dataset is coregistered to the vascular reference space and then loaded into the Voxim. The transfer of all pre-planned trajectories is now possible. Subsequently the Talairach frame is positioned, the localizers are mounted, and AP and LL 2D projective images are acquired with the O-arm. The frame can now be registered in Voxim (Figure 6). The last step is the manual coregistration between 2D and 3D datasets (Figure 32).

Before proceeding with the implantation, we execute a test trajectory targeting one of the fiducial markers. This way we can visually check the correct relationship between the robotic arm and the head of the patient (Figure 33).
3D angiography post-processing

The main vascular volume (for example, the selective angiography of right ICA for an investigation centered mainly on right posterior regions) is the coordinates reference space for all pre-, intra- and post-operative datasets. It means that all other datasets (O-arm, structural and functional MRI, CT) will be coregistered to it. The coregistration between O-arm datasets is intramodal, which is why it is performed it with a 6 DOF modality, adopting a Correlation Ratio algorithm. Once the coregistration is done, it is possible to subtract the bone mask, in order to obtain a new dataset with only contrast enhanced objects. Moreover, vascular datasets can be added in a unique one with information about all vessels of interest. Other O-arm datasets, subsequently acquired in the workflow (for example, the final post-operative dataset with the implanted electrodes), will be coregistered to this reference space, and, again, the bone mask will be subtracted. After a thresholding process, these images will be ready for the segmentation of the electrodes with the Gray Scale Model Maker module in 3D Slicer.

In (A) and (B) two analogous slices extracted from 3D angiography during contrast medium injection in the right ICA and left VA are visible. The sum of these two datasets is visible in (C), and the corresponding slice from the dataset without contrast medium in (D). In (E) there is the result of the bone mask subtraction (C-D), and the 3D MIP is visible in (F).

Implantation of the guiding screws and electrodes

The robot, guided by the software, moves from one trajectory to another, aligning the tool holder along the desired path.

The tool holder guides percutaneously the 2.1 mm drill. The dura mater is opened with a monopolar coagulator and then the hollow screw is positioned. The length of all the instruments (drill, monopolar coagulator, screw-driver) is set with a stop device, according to the pre-planned depth (Figure 34).

Once all the screws are in place, the O-arm is repositioned allowing the fluoroscopic control of the electrodes’ implantation. Since the recording electrode is semi-rigid it is necessary to prepare a track before its insertion. We use a 0.8 mm blunt tip stylet. Once the stylet is removed, the electrode is implanted and locked with the screw cap (Figure 35).
Automatic 3D reconstruction of pial surface is computed by FreeSurfer, and is very useful for anatomical recognizing in a case like the one depicted in this Figure. The gyral and sulcal pattern of this patient is deeply altered by the presence of a large focal cortical dysplasia (IIa type at histological examination), so that it is impossible to assess with certainty the morphology of sensorimotor cortex. The 3D surface reconstruction helps the surgeon in understanding the spatial configuration of a malformation like this.

All MR datasets are coregistered to the T1-FFE 3D sequence, using a 12 DOF modality with a Mutual Information algorithm. This 3D MR is registered to the vascular reference space with the same modalities, and the coregistration matrices can be concatenated. It means that the matrix computed for the coregistration of a coronal FLAIR series to the T1 3D series can be concatenated with the matrix computed for the coregistration from T1 3D to 3D angiography. The resulting matrix allows reslicing the coronal FLAIR series in the space of 3D angiography. In this way every dataset can be coregistered to the vascular reference space. In the picture are visible: the volume rendering of a segmented brain (A), the 3D MIP of O-arm angiography (B), an axial slice from the fused datasets (C), a pair of stereoscopic images of fusion volume rendering (D and E).
Testing of positioning and functioning of the electrodes

At the end of the surgical procedure both placement and functioning of the electrodes is checked radiologically and electrically.

A 3D dataset is acquired with the O-arm, and coregistered with the pre-implantation MR. This process is done by means of the neuronavigator. We can check in operating room the relationship between the implanted electrodes and the explored structures. The patient can then be awakened.

The last O-arm dataset containing the implanted electrodes is coregistered using FSL and imported into Voxim. We can compare the real position of the electrodes with the planned trajectory and measure the error (Figure 36).
Planning: step 1
In order to start planning, the reference vascular and the segmented brain hemisphere are loaded. In this way it is possible to define trajectories looking simultaneously at vessels and brain structures. EP and TP are defined on MPR and 3D views. In this screen capture the projection of the trajectory (dotted yellow line) is visible on MPRs, where visualization fading is 50% for angiography and 50% for MR. The vector of the trajectory is visible on the 3D view too. This workspace allows planning trajectories taking care of fundamental information. In all subsequent steps trajectories will be refined.

Planning: step 2
In this workspace the surgeon checks for vessels at the cortical EP. The visualization fading is set to 100% for vascular images. The seven slices of the Surgeons Eye View are focused on the first millimeters of the subdural path, where the risk of bleeding is higher (mainly due to the monopolar coagulator).
Planning: step 3

Once the original MR (coregistered but not segmented) is loaded, EP and TP must be refined on high magnification images of the Trajectory Cut view. The model of the electrode is chosen in this step, in order to have the correct number of leads recording from the brain tissue included between EP and TP. Moreover, on the 3D view it is possible to check for possible conflicts between the surgical devices just outside the skin. When the diameter of trajectory vectors is set to 5 mm, the surgeon can visually check if the screws or the caps collide.

Planning: step 4

Once the O-arm dataset without contrast medium injection is loaded, it is possible to measure on the Trajectory Cut view the distance between the cortical EP and the inner skull surface. This distance will be useful to calculate the depth for drilling coagulating and screw positioning, in order to avoid brain damage. It is also possible to check for bone thickness, paranasal sinuses and skull defects.
The 3D O-arm dataset (A) acquired after the positioning of four bone fiducial markers, is coregistered (B) to the vascular reference space (6 DOF modality and Correlation Ratio algorithm). The segmented vessels are added to allow eventual last minute planning of new trajectories (C). Once this dataset is loaded into Voxim, it is possible to transfer all the pre-planned trajectories with the specific module (D).

2D-3D coregistration

Once the AP and LL projective images are loaded, it is possible to register the frame (Figure 6). Because the localizers and frame geometry are known, this step enables the software to calculate where the X-ray source is. This is the reason why, once the frame is registered, it is possible to define the 3D coordinates of a point clicking on 2D images. Because the position of the frame on the neuromate support is fixed, the last step is to coregister 2D and 3D datasets. The calculated rotation-translation matrix can be applied to the trajectories coordinates in order to transfer them into the frame space. This registration is very accurate (0.2 mm is the mean value of quadratic mean error in our series) and fast (about 5 minutes). Moreover, it is very simple: it is performed pointing with the mouse on the bone markers in both 2D and 3D images.

Video-SEEG monitoring and anatomical information

During the Video-SEEG monitoring it is essential to know the exact position of the electrodes. For this purpose, we use the 3D Slicer software to gather all the morpho-functional images acquired so far. In this environment, it is possible to load the 3D datasets and the surface model for white and gray matter extracted by FreeSurfer, parcellated and labeled. Simply setting threshold for the gray scale we can obtain 3D models, for instance the geometry of the electrodes and the vascular tree (Figures 37 and 38).

Electrodes removal

The removal of the electrodes takes about 30 minutes. The procedure is well tolerated by patients under local anesthesia; occasionally sedation is required especially for children. The small skin defect left by the screw is sutured.

Planning of the surgical operation

The 3D multimodal reconstructions represent the basis for planning the surgical strategy appropriately for both resections and disconnections. The most relevant data such as cortical surface, vascular tree and silhouette of the electrodes can be transferred on the StealthStation via DICOM files elaborated at the end of the process (Figure 39). Moreover, even without the
Before implanting the electrodes, we execute a test trajectory with the TP on the centre of a bone marker. This step allows us to perform a visual check for the positioning of the robotic arm related to the head. The yellow arrow indicates the verification marker mounted onto the bone screw. The orange arrow indicates the drill correctly pointing the marker. The light-blue arrow indicates the tool holder, with the adapter (green arrow) for the drill. Once this test is performed, the surgeon is confident about the accuracy of registration between planning and surgical spaces.

Guiding screws implantation

The depth for drilling, coagulation and screw positioning is pre-planned (B). It is possible to set the Tool Length (TL) on the planning software, and the tool holder will be positioned, along the trajectory, as far from the TP as the TL is. The subtraction of the Useful Distance (the segment between EP and TP) and the EP-Bone distance from TL gives the precise drilling depth. The surgeon can mount a stop device at the calculated distance to avoid brain damage. When the drilling is finished, the rigidity of the robotic arm reduces the undesired flexion towards the head, minimizing the risk of excursion into the subdural space (A). The software for aligning the tool-holder with the planned directions drives trajectory by trajectory the robotic arm. These movements take just a few seconds when the 3D configuration of the robotic arm is accurately chosen looking at the NMControl preview (Figure 10).
Electrodes implantation

The electrodes are very thin, in order to minimize cerebral trauma. For this reason they are semirigid, and can be bent by arachnoidal membranes or other brain structures during their insertion (Figure 36). In order to reduce this risk, the path is first traced with a rigid 0.8 mm blunt tip stylet. Once the planned depth has been reached, the stylet is removed and the electrode is implanted instead. The cap locking prevents electrode’s movements and CSF leakage.

Verification of the positioning

The post-implant O-arm dataset, after the FSL coregistration to the vascular reference space, is imported into Voxim, in order to compare the plan and the real position. This quality control step serves to the implantation error, mainly at the cortical EP, where the bleeding risk is higher. In (A) the correct positioning of an electrode, with the yellow planned trajectory well superimposed on it, as clearly visible on the Trajectory Cut. In (B) an electrode correctly aligned at the EP, but bent in its deepest part, is visible. In (C) the method for measuring geometrical accuracy is illustrated. The dotted green line is the projection on MPR views, and the green arrow indicates its EP. The continuous red line highlights the major axis of the implanted electrode. The red arrow indicates the TP of a short trajectory starting from the planned EP. The length of this trajectory is the Euclidean distance, measured at highly magnified viewing, between the planned EP and the major axis of the electrode (in this case 0.53 mm).
During long-term Video–SEEG monitoring, for several days following implantation, it is important to have intuitive and accurate mapping tools for localizing the sources of the signal. In order to reach this aim, we integrate all the information in 3D Slicer, a package able to load all data. It is in fact possible to import all datasets and surface models computed by FreeSurfer (white and gray matter, with parcellations and labels). Moreover, it is possible to create other models such as the vascular tree and the electrodes leads. This is done very simply with the Gray Scale Model Maker tool. 3D Slicer is installed on all team members’ computers, so that epileptologists are able to look at these scenes when interpreting the SEEG traces. (A and B) constitute a pair of stereoscopic images with the reconstruction of pial surface, vessels and labeled electrodes. (C, D and E) are the MPR views, with the visualization fading 50% for MRI and 50% for post-implant O-arm dataset. The crosshair indicates the second lead of an electrode exploring first temporal gyrus, temporal transverse gyri and insular long gyri.

**Figure 37**
3D Slicer scene with MPR and 3D views (crossed viewing)

**Figure 38**
Electrodes 3D reconstruction (crossed viewing)

Two pairs of stereoscopic images for the same patient as Figure 37. In these LL and AP views the electrodes are green, EPs and labels are yellow, the lateral ventricle is violet, the amygdala is light blue, the hippocampus is yellow, the ascending frontal gyrus is blue, the ascending parietal gyrus is red. FreeSurfer automatically parcellated all the anatomical structures. The electrodes were rapidly segmented with the Gray Scale Model Maker of 3D Slicer.
Figure 39

Neuronavigation for resective surgery

DICOM files produced at the end of automatic workflow can also be used with the neuronavigator. In the picture two screens captured from the navigator Medtronic S7 are visible. In (A) a benign tumor of the frontal ascending gyrus, with the segmented main veins (from a phase-contrast angio-MR) and a navigated intraoperative bipolar cortical stimulator, are visible. In (B) a case of posterior focal cortical dysplasia explored with SEEG electrodes, represented as colored trajectories, with the 3D reconstruction of 3D angiography. In both case FreeSurfer segmented the cortex.

support of the navigation or when the accuracy of it is impaired by important brain shift it is extremely easy to recognize vascular and gyral-sulcal pattern comparing the cerebral cortex visible in the surgical field with the model prepared with the software (Figure 40).

- Fully frameless planning technique

To better understand the results mentioned below, it should be noted that the change between the traditional technique and the current one has been gradual and smooth. New techniques and technologies have been utilized parallel to the old methodology so that they could be clinically validated by the experience of the neurosurgical team. We consider September 2009 as a milestone, when stereoscopic 2D angiography and the positioning of the Talairach frame during the acquisition of the vascular images have been abandoned. As stated before, preoperative images are acquired without any attachment of frames or fiducial markers. Therefore at the moment of implantation the Talairach frame can be freely positioned on the patient's head, while earlier it was necessary to reposition it exactly as it was placed at the moment of acquisition of the vascular images.
Results

● Clinical data

In the period between May 1996 and July 2010 we performed 451 SEEG procedures in 438 patients (260 males, 178 females). We implanted 5,838 electrodes (mean 12.94 ± SD 2.49, range 3-20). Mean age of the patients was 25.78 ± 12.11 years.

412 SEEG procedures (5,514 electrodes) were planned with the traditional methodology progressively supported by new technologies (neuromate and O-arm were respectively introduced in 2001 and 2008). Since September 2009, 26 SEEG procedures (324 electrodes) were planned and carried out entirely with the current technique: 3D cerebral angiography and positioning of trajectories exclusively with neuromate.

● Qualitative results

Every time the entire volume of the head was completely included in the 3D reconstructed O-arm FOV, allowing the segmentation of skull and intracranial vascular tree.

3D digital angiography has abolished the cost for purchasing and developing traditional radiographic films.

While the classical stereotactic localization (Talairach’s “repérage”) used to be done under general anesthesia in the operating theatre, nowadays it is feasible in the angiographic room as standard DSA procedures, without any frame or localizing tool mounted on patient’s head. The trajectories can then be planned comfortably before the day of surgery integrating other imaging modalities requiring a long post processing time.

Multiplanar reconstructions of 3D angiography and MR are sufficient to plan the stereotactic trajectories. However, the 3D rendering of the vascular tree and brain surface, which are more realistic, speed up the planning procedure.

Since all the preoperative imaging does not require the positioning of the frame, the day of surgery it can be fixed with transcutaneous pins, with no need for drilling the skull. This was necessary with the traditional technique to secure sufficiently accurate repositioning.

The duration of surgery, unfortunately, has not been systematically annotated; therefore it is difficult to assess the difference between the two techniques. However, we can say that the implantation with the new method does not take longer than the previous one even if we are now planning more difficult trajectories with double obliquity. Moreover, a careful choice of the spatial configuration of the robotic arm significantly reduces the time it takes to move from one trajectory to another.

With the information on the skull morphology integrated within the robot software we can precisely calculate how deep we need to drill to position the guiding screws, hence avoiding drilling in the subdural space by accident.
The automatic coregistration of the post implantation 3D dataset (O-arm or CT) was successful in all cases. The more expensive and time consuming post implantation MR is no longer needed.

- **Quantitative results**

To check the geometric accuracy we measured the Euclidean distance between the cortical planned EP and the major axis of the implanted electrode. The median value is 0.73 mm, with interquartile range of 0.48–1.02. The highest value of this distance has been 3.27 mm, and in 13 out of 324 (4%) electrodes was more than 2 mm.

- **Complications**

The main complications we had using the traditional methodology were vascular, infective, obstructive hydrocephalus, retained electrode.

Directly attributable to SEEG procedure we had five intracerebral hemorrhages (1 extradural post repérage, 1 subdural, 3 intraparenchymal). Two out of three intraparenchymal hemorrhages had a permanent motor deficit (hemiplegia). We also assessed on images 9 bleedings without any clinical consequences. Two patients developed intracranial infections requiring antibiotic systemic treatment. One obstructive hydrocephalus was treated by a temporary external ventricular drain. The cause of it was a small clot in the aqueduct of Sylvius. One broken retained electrode was observed in a pediatric patient, which required a minor surgical procedure for extraction.

We report one death of a 3-year-old child. The autopsy showed massive cerebral edema in absence of intracranial hemorrhages. The most probable cause of the death was an impairment of the hydro-electrolytic balance, unlikely directly related to SEEG procedure itself.

With the current methodology we did not have any permanent deficit or major complication requiring a surgical procedure. We only report one transitory brachial hemiparesis due to a minor bleeding.

**Discussion**

For many years the traditional Talairach methodology, developed in Paris at the Sainte Anne Hospital starting from 1950, has been the only satisfactory way to implant a sufficient number of intracerebral electrodes to analyze seizures and identify the epileptogenic zone. Originally based on stereotactic and stereoscopic acquisition of ventriculographic and angiographic images, this technique allowed (and still allows in specialized centers) collecting epileptologic data essential for patient treatment with a very low rate of complications. However, we would like to remind how demanding this methodology was both for patients, who had to undergo two procedures under general anesthesia, and surgeons for whom the planning of trajectories was extremely time consuming. The extremely low rate of complications represented the main reason that kept our and other centers growing on the shoulders of the Parisian school faithful to its technique for such a long time. However, we had to face the problem that the whole technique with its diagnostic procedures and medical tools despite being fascinating and ingenious was becoming obsolete. During the course of the years we combined the traditional methodology with some newer technologies. However, they were essentially minor changes.

The decision to face drastic technological renewal became necessary when it was no longer possible to guarantee the proper maintenance of the intraoperative radiological and stereotactic equipment. Since no other solution was ready and directly available on the market, guided by and strongly based on the previous experience we started to build a more advanced methodology combining modern tools and software.

The O-arm has been extremely useful for several reasons: the high geometric accuracy of the 3D datasets, the high grade of conformity to the standard DICOM format that allows exporting and using the images with other software, the mobility that allows to comfortably place either in the angiographic room at the moment of repérage or in the operating theatre at time of
surgery. Moreover it is an easy to use device that can be used by the neurosurgeon without the requirement of a radiologist in continuous attendance.

The free availability of sophisticated medical software together with good ability of programming and use (so called power user level), allowed us to prepare an almost completely automatic IT workflow that can post-process the images. The post-processed images are imported into the stereotactic software allowing a faster, multimodal and effective planning.

The high accuracy of our implantations is certainly ascribable, above all, to the high geometric accuracy of the neuromate and O-arm systems that make them perfectly suited for stereotactic procedures.

We have to underline that between data on the geometric accuracy there are some outliers. Despite the very low value of the median error, in 4% of the cases this error was more than 2 mm. The most likely reason is that those were the electrodes with a trajectory tangent to the skull that made the drilling more fiddling for the surgeon. This data need to be carefully taken into account for potential implications in terms of safety and represent a stimulus that encourages the improvement of the mechanical tools so far available.

Classically, in the traditional methodology, the trajectories were distinguished as orthogonal and oblique. Typical example of orthogonal trajectory is the electrode passing through the middle temporal gyrus and exploring mesial structures, while electrodes positioned to explore the orbital cortex or the insular lobe were oblique. With the neuromate we can obviously position both orthogonal and oblique electrodes but we would like to underline how even the classically so-called “orthogonal” electrodes should be considered nowadays as “oblique”. The movements of the robotic arm of the neuromate give us a range of freedom in choosing the EP that was not achievable by means of the Talairach grids. Therefore during the planning we can make minimal adjustments in order to avoid vessels, to enlarge avascular corridors, to optimize the angle between the drill and the skull. Therefore, the neuromate system provides image-guided, accurate, and stiff but highly flexible tool guidance unlike other stereotactic targeting systems.

One of the limitations of our data is that we recently started to check the electrodes positioning via CT scanner or O-arm without performing post implantation MR. Therefore the incidence of minor and subclinical bleedings might be underestimated because of huge metal-induced artifacts.

Another limitation is the method we used to check the geometric accuracy. The Euclidean distance between the cortical planned EP and the major axis of the implanted electrode was only measured indirectly, loading the pre and post implant imaging on the planning software. The error incorporates the possible interference of the coregistration processes, the distortions of the images and the variability in the manual measurement, which are all believed to be small. In fact the value 0.73 mm of the median accuracy is similar to the accuracy reported by Li et al. in 2002 in studies performed with neuromate on phantoms. Moreover, to our knowledge, our study is the only one reporting results obtained in a surgical procedure in vivo.

**Conclusion**

The advent of new technologies and the arrangement of an optimized and original workflow allowed realizing a more advanced planning of SEEG with a low incidence of complications still maintaining valid and unaltered the core of the traditional methodology proposed by Talairach and Bancaud.

The main advantages during the pre-implant phase lie in the possibility of multimodal integration of morphological and functional images extremely useful for the planning, in the acquisition of those images without any frame or fiducials, in the almost complete computation of the repetitive software processes, in the entirely 3D planning of the trajectories, and in the extensive use of open source software.

Regarding the surgical procedure the main improvement is that it does not require a specifically dedicated operating theatre since all the tools are transportable. Moreover the accuracy and
precision of the implantations performed is very high, and last but not least the cost of X-ray films was nullified.

Finally, after the implantation, we can build a high-resolution virtual 3D scenario. In these scenes it is possible to integrate multimodal imaging and reconstructed electrodes, and these tools aid the interpretation of Video-SEEG monitoring. Moreover, these virtual images are useful for planning and execution of resective surgery.

● Disclosure

The first author is a consultant to Renishaw mayfield, the manufacturer of neuromate, and a former consultant to Medtronic, the manufacturer of O-arm and navigators mentioned in this paper.

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References


At the beginning of the 1950s, the meeting of Jean Bancaud and Jean Talairach represented a turning point in epilepsy surgery. Their idea was to accurately record the electrical activity of different brain structures during the course of a seizure. Soon, the term of stereoelectroencephalography was adopted for this new method. New concepts arose, followed by new types of surgery, techniques, neuroimaging tools and stereotactic procedures.

Stereotaxy and Epilepsy surgery, written by Jean-Marie Scarabin and a number of recognized experts in the field, presents its most recent advances, always respecting Sainte-Anne school’s spirit, and especially the value of clinical semiology and its integration through anatomoelectroclinical correlations. Its extremely precise descriptions of the methodologies and its rich contents of figures and plates, including a particularly interesting DVD with videos and 51 clinical cases, certainly make this book a reference in the domain of epilepsy surgery.