Insular tumor surgery

- Hybrid Therapy for Newly Diagnosed and Recurrent Glioblastoma: Staged Procedure Integrating Open Surgical Resection With Laser Interstitial Thermal Therapy
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The development and implementation of cortical and subcortical motor mapping techniques under awake and sleep conditions have improved the safety of this operation. Although a number of review articles are available regarding the surgical management of insular gliomas, a discussion of technical nuances for handling these challenging tumors may be helpful to novice neurosurgeons who plan to evolve their technique [1].

Due to its challenging technical access [2] [3] [4] [5] [6] [7] [8] [9] [10] and until the publication of Yaşargil et al. [11] , the insula has been considered surgically inaccessible for a long time. Thanks to a better understanding of the insular functional anatomy, several experiences of insular surgery have been reported [12] [13] [14] [15] [16] [17] [18] [19].

The surgical treatment should aim to achieve the total (or more than total) resection while avoiding neurological deficits. To achieve these goals, a combination of functional neuroimaging, intraoperative neurophysiology and awake craniotomies have been introduced into the clinical practice of neurosurgical centers dealing with those lesions. Nevertheless, these instruments are insufficient without a deep understanding of regional functional and microvascular anatomy.

They have traditionally been approached through variations of a large frontotemporal craniotomy exposing much of the Sylvian fissure. Due to the importance of many structures exposed by such an approach, a less-invasive approach to these lesions is a viable alternative for resection.

The question of potential vascular injuries during resection of insular gliomas is well known, in particular with reference to the potential damage to the lenticulostriate arteries.

Since the first report by Yasargil, few authors have dealt with the surgical treatment of tumours infiltrating the insula.

A number of authors have emphasized the importance of functional mapping because of the eloquent nature of both insular and periinsular structures.

The use of sensory and/or motor evoked potentials or ESM provide additional intraoperative landmarks by which to safely resect insular masses. Dominant hemisphere cortical language localization is advisable although language interference from direct stimulation of the insular cortex has seldom been reported.

Rey-Dios and Cohen-Gadol prefer to resect both dominant and nondominant insular tumors under awake conditions. Nondominant insular tumors may be managed under anesthesia using sleep mapping techniques to maximize the patient's comfort.

They have found mapping more efficient under awake conditions, and they can continuously monitor the patient's neurological status during removal of the medial and posterior aspect of the tumor in close association with critical motor fibers. In ther experience, the patient's continuous feedback has allowed us to perform more aggressive resections without increasing neurological morbidity or causing any significant patient discomfort. During preoperative planning, the patient is carefully consulted regarding the process of an awake craniotomy to make him/her comfortable during the procedure. [20].

Outcome

see also Insular tumor surgery outcome.

PART 1: Insular Anatomy and Preoperative Planning

Introduction

The surgical resection of an insular tumor is one of the most delicate neurosurgical procedures, and has long fascinated neurosurgeons since the first attempts due to its high surgical skills requirement and challenging start up. Exposing the insular surface involves the Sylvian fissure splitting, entailing a careful dissection of the Sylvian superficial veins and deeply located arteries and veins, while the highly functional opercular lips must be delicately preserved. Once the insular cortex is exposed, its resection is limited deeply due to its close relationship with structures as the lenticulostriate artery LSAs, basal ganglia and internal capsule. Thus, brain tumors related to the insula and adjacent areas represent a great challenge for Neurosurgeons due to its surgical resection complexity. An optimal surgical treatment of these lesions involves various aspects, which could be resumed in a strong neuroanatomical knowledge, a careful and complete perioperative work-up, diagnostic and preoperative functional techniques, intraoperative neuromonitoring, modern intraoperative technologies, and finally microsurgical skills. All these elements contribute to fed the surgeon's experience, which will finally represent the only constant tool. A complete surgical resection minimizing the postoperative neurological deficits has been shown to be the best treatment for low-grade glial tumors. The cytoreduction provided by surgery will maintain its value, as it offers material for diagnosis and research, alleviates both the neurological and irritative impairments, as well as intracranial hypertension symptoms, and contributes to increase the interval to malignant progression. Following this line of reasoning, there is a large number of modern series supporting the idea of resecting the largest possible volume of tumor. The price to pay for radical resection may be an increase in morbidity, fact that reaches its peak in the case of insular tumors. In this sense, a great number of imaging, neurophysiological, neurochemical, and surgical techniques have recently been developed and incorporated into the general management of these tumors, with the ultimate objective being to optimize the resection limits, extending them to the maximum, while minimizing the eventual associated morbidity. Nevertheless, this diagnostic and therapeutic armamentarium should never obscure nor replace a strong neuroanatomical knowledge. In the human brain, pathology follows the anatomy, and this is the reason why neurosurgeons should accurately study the different cerebral functional compartments. After treating and observing the behavior of thousands of gliomas, Yasargil introduced the concept of functional units. He argued that gliomas tend to initially develop confined in a single functional unit, pushing away the surrounding compartments in different directions according to the location where they are growing, and invading adjacent areas in the intermediate and advanced stages through the subcortical white matter pathways.

Insular Anatomy

The definition of eloquent areas, generally misleads the surgical conception. In this sense, many not-considered eloquent territories may require surgical corridors related with highly functional compartments, as well as neighbor vascular structures feeding distant eloquent regions. In short, with respect to function, neighboring anatomy and surgical approach, most of the central nervous system lesions can be considered related with eloquent locations. The insular lobe perfectly illustrates the latter concept. The insula remains shielded by many neurovascular highly eloquent areas. The Sylvian fissure lips covering the insular cortex are, among others, conformed by the sensorymotor cortex, as well as the socalled Broca´s and Wernicke´s areas in the dominant hemisphere. The primary auditory area is also intimately related with the posterior aspect of the insular lobe. Moreover, relevant vascular structures as the MCA branches and Superficial (SSV) and Deep Sylvian Veins (DSV) lie all along the Sylvian corridor and insular surface. The Lenticulostriate Arteries (LSAs) branch off the proximal segments of the MCA, penetrating the anterior perforated substance just beside the anteroinferior aspect of the insular pole. These thin branches feed the substantia innominata, putamen, globus pallidus, caudate nucleus, internal capsule, and even the adjacent corona radiata. The latter subcortical compartments are also intimately related with the subcortical insular unit. Thus, it is understandable how, despite the functional theories and speculations about the role of the insular lobe, its hidden position in the depth of the Sylvian fissure makes resection of intrinsic insular tumors challenging, due to the attendant risk of postoperative neurological deficit. The key point to successfully resect insular tumors remains on a strong knowledge of the regional and internal insular anatomy, vascularization and topography. The anatomy gives the surgeon a great chance to remove these tumors, so, as already mentioned, the pathology follows the anatomical corridors. Sylvian fissure and opercula The insular lobe rests in the depth of the Sylvian cistern, and approaching it, requires passing through some natural corridors. This Sylvian cistern comprises three distinct parts the surgeon should be familiarized with, namely the Sylvian fissure, the interopercular sulci, and the Sylvian fossa. The Sylvian fissure is the most lateral gateway, and remains a constant surface landmark that should be initially identified. Usually, this goal is easily achieved due to the presence of the SSV delineating its lateral course. However, in a few cases this venous anatomy can be absent or deeply located, or even the outer arachnoid membrane can be as thick that obscures its course. In these cases, a recommended concept remains on identifying the prefrontal and middle temporal M4 branches, which usually curve superiorly and inferiorly respectively around the pars triangularis. The Sylvian fissure can be divided in two compartments. The anterior or Sylvian stem runs from the ICA bifurcation just inferior to the Sylvian vallecula, and following the path of the sphenoid wing reaches the pars triangularis of the frontoparietal operculum. Its course is covered between the orbital gyri and the planum polare of the superior surface of the temporal lobe. The point where the anterior stem becomes the posterior or insuloopercular compartment at the level of the pars triangularis is named the Sylvian point, and represents an important landmark when the Sylvian fissure splitting is necessary. The insuloopercular section is divided into three main rami with a common origin at the level of the Sylvian point. The horizontal ramus runs forward between the pars orbitalis and pars triangularis, while the ascending ramus runs upward separating the pars triangularis and pars opercularis. The posterior ramus runs backward in a moderate undulating path towards the supramarginal gyrus, where it opens in ascendant and descendant terminal limbs. The posterior ramus is the longest of the fissure, and represents the cortical translation of the anteroposterior extension of the insular lobe. It runs from the region of the pterion to its termination in the inferior parietal lobe separating the frontoparietal and temporal opercula forming the Sylvian line. Its course seems partially broken by some subsulci that enter the frontoparietal and temporal opercula. The most constant are represented by the diagonal sulcus in the pars opercularis, the anterior and posterior subcentral sulci delimiting the subcentral gyrus, as well as the side branch of the transverse temporal. Two lips join at the level of the Sylvian line, closing the direct visualization of the Sylvian fossa contents, the insular lobe. These both lips are generally termed as the opercula. The superior lip is divided in a frontoorbital and a frontoparietal sector. The frontoorbital is formed by the posterolateral aspect of the orbital gyri, but mainly by the pars orbitalis of the inferior frontal gyrus. It is delineated between the posterolateral part of the transverse orbital sulcus and the horizontal ramus of the insuloopercular compartment of the Sylvian fissure. This breach represents the edge between the frontoorbital (forward) and the frontoparietal (backward) opercula. From anterior to posterior the latter is divided in pars triangularis, ascending ramus, pars opercularis (diagonal sulcus not always present), anterior subcentral sulcus, subcentral gyrus, posterior subcentral sulcus, and finally superior aspect of the supramarginal gyrus. On the other hand, the temporal operculum follows a more clearly delineated forward course from the inferior part of the supramarginal gyrus towards the temporal pole, all along the superior temporal gyrus. The only constant indentation of this path is created by the connection of the transverse gyri of Heschl with the superior temporal gyrus. The opercula continue inside the Sylvian fissure with their medial aspect covering the insular surface. The 3D understanding of the medial sulcal and gyral architecture remains imperative, so their relations with the insular surface remain quite constant, and may help us to understand the field in which we will be working on. Two suborbital gyri (superior and inferior), located at the medial aspect of the frontoorbital operculum, cover the anterior surface of the insula. The inner expression of the pars triangularis (subtriangular gyrus), pars opercularis (subopercular gyrus), precentral (subprecentral and subcentral gyri) and postcentral gyri (subcentral and anterior transverse parietal gyri), as well as the superior aspect of the supramarginal gyrus (anterior, middle and posterior transverse parietal gyri), covers the superior surface of the insula. The planum polare (with the sulci and gyri of Schwalbe), anterior and posterior transverse gyri of Heschl, and the planum temporale represent the inner aspect of the temporal operculum, and cover the inferior surface of the insula and the anterior perforated substance. Some of these opercular segments are highly functional, representing the so-called eloquent areas. Pars opercularis and the posterior segment of pars triangularis are frequently known as Broca's speech area in the dominant hemisphere. The subcentral gyrus represents the junction of the precentral and postcentral gyri of the paracentral lobe, and so it belongs to the primary motor and sensitive areas. The inferior aspect of the supramarginal gyrus and the posterior lateral superior temporal area are commonly termed Wernicke's area in the dominant hemisphere, also related with speech functions. Finally, the transverse gyri of Heschl in the superior aspect of the temporal lobe, and its connection to the superior temporal gyrus represent the primary auditory areas. Protecting these areas during an insular tumor removal represents one of the challenges of these procedures, due to the high functionality they contain. In this sense, direct cortical stimulation in awake and non-awake procedures when dealing with the dominant and non-dominant hemispheres respectively, will allow us to directly check the functionality of the alleged cortical regions. This procedure will help us selecting relatively safe entry areas to perform a transopercular corridor in those insular tumor cases in which the opercula are also involved.

Cortical anatomy: sulci and gyri The insular lobe reminds a pyramidal structure on its surface, whose three sides (anterior, posterior and limen insula) meet at the insular apex. Peripherally it is clearly delineated by the anterior, superior and inferior peri-insular sulci. On its depth, it shows a continuum with the basal ganglia, also resembling a pyramidal structure, with the globus pallidus internus as the apex. The internal pyramid formed together by the extreme and external capsules, the claustrum and the basal ganglia is surrounded by important white matter systems as the internal capsule, whose anterior limb is related with the anterior peri-insular sulcus, the posterior limb with the superior peri-insular sulcus, and the sublenticular portion with the posterior part of the inferior peri-insular sulcus. The so-called temporal stem is closely related with the anterior two-thirds of the inferior peri-insular sulcus. The anterobasal face of the external pyramid is represented by the limen insulae, which consists of a narrow strip of olfactory cortex acting as the junction of the Sylvian vallecula, the insula and the frontoorbital and temporal pole. The anterior insula represents the anterodorsal face, and is limited anteriorly by the anterior peri-insular sulcus, posteriorly by the central insular sulcus, and superiorly by the anterior aspect of the superior peri-insular sulcus. It is composed by the transverse, accessory, anterior, middle and posterior short gyri. The transverse gyrus runs in a frontomedial direction towards the posteromedial orbital lobe, while the accessory gyrus joins the anterior portion of the anterior short gyrus with the suborbital gyri. Together these gyri represent the insular pole. The anterior and posterior short gyri are constant and join inferiorly at the level of the insular apex, while the middle short gyrus is frequently found underdeveloped. The anterior and middle gyri are separated by the anterior short sulcus of the insula, while the precentral sulcus separates the middle and posterior gyri. The confluence of the anterior and superior peri-insular sulci coincides with the connection of the anterior short gyrus and the subtriangular gyrus, in the so-called anterior insular point. The posterior insula is separated from the anterior insula by the central insular sulcus, which represents the anterior edge of the posterodorsal aspect of the pyramid. This posterior face is limited superiorly by the superior peri-insular sulcus, and inferiorly by the inferior peri-insular sulcus, which join at the posterior insular point. Its surface contains two long anterior and posterior gyri separated by the postcentral sulcus. Subopercular and insular relationships The insular apex is encountered just deep into the fissure at the level of the pars triangularis. Following its inner extension (subtriangular gyrus) allows carrying out the surgical exploration to the anterior insular point and the upper part of the anterior short insular gyrus. The horizontal and ascending rami of the Sylvian fissure represent the continuation of the superior and anterior peri-insular sulci respectively. The suborbital and subopercular gyri cover the anterior short gyrus anteriorly and posteriorly respectively. Moreover, the subopercular is posteriorly extended, covering the anterior short sulcus and the anterior aspect of the middle short insular gyrus. The subprecentral gyrus lies over the precentral insular sulcus, partially covering the posterior aspect of the middle short insular gyrus. The central sulcus is covered by the inner extension of the subcentral gyrus, which also covers the posterior short insular gyrus. The anterior, middle and posterior transverse parietal gyri represent the inner expression of the inferior postcentral and superior aspect of the supramarginal gyrus. The anterior transverse is the bigger and better developed gyrus, and arises posteriorly from the posterior insular point covering the postcentral insular sulcus and the superior aspect of the anterior and posterior long insular gyri. The posterior insular point is defined by the confluence of the posteromedial aspect of the anterior transverse parietal and anterior transverse gyrus of Heschl, with the superior and posterior peri-insular sulci. Thus, the middle transverse parietal gyrus covers the sulcus that separates the transverse gyri of the temporal operculum, while the posterior transverse parietal gyrus overlaps with planum temporale. In the anterior third of the temporal operculum, the planum polare covers the limen insula and the inferior surface of the insula adjacent to the anterior two-thirds of the length of the inferior peri-insular sulcus. Vascularization A vascular net displayed from all the branches of the MCA surrounds the insular lobe. The M1 segment of the MCA courses laterally within the Sylvian vallecula all along the Sylvian stem. Most of the LSAs arise at this level, however, it is possible to find branches coming from the main bifurcation, or even from the superior and/or inferior M2 trunks. Achieving enough visualization of the most lateral LSAs may represent a valuable landmark during tumor resection in the anteroinferior aspect of the insular thickness. Around the limen insulae the M1 turns 90º forming the genu, and the main bifurcation takes place. This main bifurcation has been highlighted as one of the main deep anatomical landmarks, and it is important to remind that in most of the cases it takes place at the level of the genu, however it is also possible to find it distally or proximally to the genu. Early small branches arise from the bifurcation, or even proximal to feed the limen insulae. Along its cortical course in the anterior insula, the inferior but mainly the superior M2 trunks showed several branches (8-12) before becoming M3 segment. The orbitofrontal artery supplies the anterior peri-insular sulcus and the accessory and transverse gyri. One of the most constant branches is supposed to be the prefrontal artery, which has been found to be in the anterior insular point, reaching the lateral hemispheric surface at the level of the Sylvian point. The prefrontal, precentral and central arteries usually extend small perforators to supply the anterior insula. The central artery runs along the central insular sulcus, which represents the most vascularized region of the insula. The anterior and posterior parietal arteries usually supply the anterior long gyrus, and some direct branches to the posterior short gyrus, while small perforators coming from the temporooccipital, angular and posterior temporal arteries, supplied the posterior long gyrus. In the anteroinferior aspect of the insula, the main blood supply comes from the anterior and middle temporal arteries. In 25% of cases, small perforators coming from M3 segments may also supply the insular lobe. In previous publications 96 insular arteries (range 77-112) were described by Türe at al. Special attention must be paid to a special pattern of long perforators arising from the same M2 branches. These arteries present larger calibers, showing the special features that extend as far as the corona radiata. These long perforators are mostly located in the posterior half of the central insular sulcus and on the long gyri, and special attention must be taken when tumor removal is carried out at this level, because damage of these thin vessels may provoke severe corona radiata infarctions and consequent hemiparesis44,47,53. The insular veins follow a parallel course to the insular sulci, draining into collecting veins along the superior and inferior peri-insular sulci. These collecting veins usually join at the level of the anterior third of the inferior peri-insular sulcus, and travel deep through the stem of the Sylvian fissure to join the DSV just beneath the MCA. The latter frequently drains into the basilar vein, but in some cases into the spheno-parietal sinus. Sometimes a connection between the most rostral insular veins and the superficial system through the frontosylvian veins is present. Subcortical anatomy The subcortical core of the insular lobe delimited by the peri-insular sulci is composed by a sequence of layers of white and gray matter. Just underlying the insular cortex, the short association fiber system covering the claustrum is termed the extreme capsule. The claustrum is a thin layer of gray matter mainly located deep into the core of the anterior insular region, and continues ventrally between different thin layers of white matter, which are represented by the occipitofrontal and uncinate fascicles. The claustrum is separating the extreme and the external capsule. The latter represents the theoretical edge of the subcortical insular tissue, and differentiates it from the next deep layer, which is composed by the lateral aspect of the putamen. Insular tumors generally grow pushing medially these structures, and respecting the putamen, which represents a wonderful deep anatomical landmark, especially in the central region. The average length and height of the putamen has been measured, reaching values of 44 mm and 41 mm respectively, according to Türe’s findings. The deep location of the putamen matches with the central aspect of the insular lobe, and the peri-insular sulci represent appropriate landmarks for centering this structure. However, some tumors expand the insular lobe beyond the normal limits of the peri-insular sulci, and that is the reason to study the anatomical structures underlying these peripheral areas. The cortex of the limen insulae lies over the uncinate fascicle, and further medially the most lateral lenticulostriate arteries can be visualized entering the anterior perforated substance. The intraaxial path followed by these arteries represents the best medial landmark during the anteroinferior tumor removal. Tanriover et al. demonstrated that most of the lateral LSAs were arising from the M1 segment, followed by the M2 inferior and superior trunks. Moreover, estimated in 15.3 mm the distance between the entrance of the most lateral LSA into the anterior perforated substance and the medial border of the limen insulae. Otherwise, the deep structures underlying the inferior peri-insular sulcus are represented by the so-called temporal stem, the amygdala, and the sublenticular and retrolenticular aspects of the internal capsule in a more posterior plane. The anterior peri-insular sulcus is related in the depth with the anterior limb of the internal capsule, while probably the most challenging area is in the posterior half of the superior peri-insular sulcus, due to its close relation with the fibers of the corona radiata entering the posterior limb of the internal capsule. The best tool the surgeon owns to distinguish the tumor and the normal tissue edges is the anatomical knowledge acquired after training with brain dissections in the laboratory, and the experience gained during many other procedures. However, some modern technological and surgical tools are being developed and recently introduced to the clinical work. Preoperative planning The preoperative work-up after the decision to operate represents one the most important therapeutic steps. During this stage, the surgeon should carefully study all the available information about a single case, and combine these data with his/her previous experiences and neuroanatomical knowledge, to try to elaborate a virtual three-dimensional image of the tumor location, as well as to be aware of potential pitfalls and drawbacks that could appear during the surgical procedure. In this sense, the most helpful available information might be inferred from the clinical records, but especially from the imaging studies. The management of insular tumors has dramatically changed since the improvement of diagnostic imaging techniques. Neuroimaging with magnetic resonance imaging improves the accuracy of diagnosis and remains indispensable for surgical planning. Nowadays, modern imaging techniques are necessary to detect or confirm a structural abnormality, localize, assess and characterize the abnormality, plan the surgical approach and extension, predict the possible postoperative neurological deficits, orient to the metabolism and metabolites composition of the tumor and surroundings, understand the 3D anatomical relation with brain eloquent areas (cortical and subcortical) through functional and anatomical sequences, as well as to rate the surgical extent of resection intra and postoperatively. A careful examination of the coronal, axial and sagittal views of the cerebrum in MRI, as well as the nowadays available 3D Multi-planar Reconstructions, is enough to understand and visualize the shape, dimensions, intrinsic features and volume of the tumor, and its relationships with the different aspects of the Sylvian fissure and the Superficial Sylvian vein and frontoparietal and temporal feeders, the frontoorbital, fronto-parietal and temporal opercula lateral and medial aspects, the peri-insular sulci, the central insular sulcus, and highly functional deep structures as the basal ganglia, internal capsule, or the anterior perforated substance and the Lenticulostriate arteries. Theoretically, all these structures belong to different functional and neurovascular units, and should be displaced by the tumor main volume. However, some of them, especially the opercula, and sometimes the anterior perforated substance, might be invaded by tumors growing mainly in the middle and posterior, or anteroinferior regions of the insula respectively. Patient’s presentation: clinical study, lateralization Insular tumors are often discovered as medium and big size lesions. It is quite uncommon to discover small ones, probably because of their indolent course until they reach a significant volume. Thus, significant mass effect, compression and shifting of the ipsilateral central core and ventricular system may be present in a patient clinically intact. However, in the recent period the improvement of the diagnostic methods has allowed earlier diagnosis. The most common clinical spectrum for insular tumors includes the presence of seizures (33-98%). These seizures are mostly complex partial (34-60%), generalized (27.5- 30%), and simple partial (8-13%). These seizures appear as medically refractory epilepsy in a relatively high number of cases (12-60%), fact that by itself should be considered as only indication for surgery. Other not so common but also presenting symptoms are those derived from the surrounding structures compression, which may cause certain degrees of neurological impairments (hemiparesis, hemianesthesia, dysphasia, aphasia, hemianopia, apraxia), and less commonly intracranial hypertension, as well as psychological alterations (organic psychosis, anxiety). The neurological impairments, as well as the psychoemotional disturbances and symptoms derived from intracranial hypertension, are generally related with high-grade tumors, while the low-grade gliomas generally course more indolently with a history of atypical seizures. The largest mass effect, as well as the possible extension beyond the insular functional unit, may explain easily the different behavior of the higher grades. Nevertheless, the big rates of seizures present in cases of low-grade tumors remains still unexplained. Neuropsychological assessment The insular cortex has been proved to have connections with the primary and secondary somatosensory areas, anterior cingulate cortex, amygdaloid body, prefrontal cortex, superior temporal gyrus, temporal pole, orbitofrontal cortex, frontal operculum, parietal operculum, primary auditory cortex, auditory association cortex, visual association cortex, olfactory bulb, hippocampus, entorhinal cortex and motor cortex. Thus, several higher functions have been attributed to this hidden lobe, such as processing of pain, temperature, touch, fear, conscious desires, olfactory and gustatory inputs, subjective emotional experiences, perception of effort during exercise, regulation of higher cognitive functioning, as well as somatic functions, autonomic regulation, verbal working memory, and secondary motor and language control. Most insular tumors are diagnosed due to presence of seizures. Nevertheless, some of them may show some psychological alterations, although most of these alterations are generally difficult to perceive. As most of low-grade insular tumors show an indolent course, these patients seem to be generally asymptomatic at diagnosis. Due to this fact, a carefully designed preoperative neuropsychological assessment has been proved to be useful to uncover some mental processing alterations. These tests consist of a battery of neuropsychological tasks that study cognitive, perception, motor, and psychological functions. It complements the neurologic examination and imaging studies and helps localizing cortical functions, and the assessment of personal and social consequences of the tumor or surgery. Imaging studies: CT/MRI Anatomic sequences: T1, T2 and flair Brain tumors precise localization and relations with their surroundings, reaches the highest challenge in cases of insular gliomas due to its central and hidden location. Once the tumor is diagnosed, the next point on its evaluation remains in the fact of its accurate anatomic location. Some MRI techniques are recommended for this purpose: T1- and T2-weighted sequences, including FLAIR, and after gadolinium T1-weighted sequences with at least one spin-echo sequence. With the aim of achieving a precise delineation of tumors in the different insular regions, we use to perform at least the T1- and T2-weighted sequences in the axial, coronal and sagittal planes of the space. After having grossly analyzed the main morphological and topographical features in the latter sequences, 3D Multi-planar Reconstructions performed with 1mm slice thickness remains extremely helpful in order to accurately study the detailed relationships and the tumor edges. Identifying the central insular sulcus is not an easy duty, especially in cases in which the tumor involves the whole insular lobe (anteroinferior, middle and posterior aspect). However, when the tumor mainly involves one of these insular regions, it is possible to identify the central insular sulcus in sagittal slices, representing in these cases a greatly useful intraoperative landmark. One of the most relevant details during this careful inspection remains on understanding the relation of the tumor within the peri-insular sulci and the adjacent opercula. For this target, the coronal and sagittal are the most appropriate views, in which we can discern if the opercula are invaded or just displaced at the level of the anterior, superior and inferior peri-insular sulci. The modern anatomic sequences allow visualizing with extreme accuracy the relation between insular tumors and some underlying and highly functional deep structures as the basal ganglia and the internal capsule. When contrast enhanced images are used, the anatomical landmarks provided by the M2 and M3 arteries may be of great interest. The latter sequence is also the most appropriate to discern the anterior perforated substance relative location, and the LSAs crossing its thickness. The extended use of carotid angiography is reserved nowadays for special cases. With the same goal, some authors have proposed other sequences as a 3D 3T time-of-flight (TOF), which provide a nice three-dimensional display of the LSAs and their relationship with the mediobasal aspect of the tumor. Any of these latter contrast and non-contrast based imaging modalities provides useful information about the MCA main branches distribution and relation with the insular surface. This data may help to distinguish between tumors mimicking the normal cortical architecture and vascular pattern, and tumors completely involving and hiding the M2 branches. Moreover, these contrast-enhanced images have resulted useful in our clinical practice to understand the venous cortical pattern at the superficial level of the Sylvian fissure. Functional MRI Its main goal is the preoperative localization of eloquent areas prior to tumor resection to minimize intraoperative damage to these brain areas and thereby to reduce postoperative morbidity. Functional MRI (fMRI) looks at changes in cerebral blood flow, and more specifically, in the balance of oxy and deoxyhemoglobin in the capillary circulation, and it can be viewed dynamically because of stimulation and performing tasks that are marked. Neuronal activation is measured indirectly through changes in blood oxygenation – dependent signal (BOLD). There is wide evidence that the location of motor and language areas by this technique is helpful for preoperative planning in addition to being a noninvasive technique. A concept we should not forget is that it remains a technique that without the ability to distinguish between the various components of any specific functional response, and therefore may overlap different functional areas of brain processes, magnifying certain eloquent regions. In surgical routine, the cortical regions mainly mapped through fMRI are speech, comprehension, motor, sensitive, visual and memory areas. To detect changes in blood oxygenation in speech areas, the patient is asked to pronounce different words or phrases. The chosen task in case of comprehension mapping consists on asking the patient to listen to and think about different phrases. If the chosen task is for motor mapping, patients are asked to move different parts of their bodies repeating the movements at least during 50 or 60 seconds to try to become these movements in a routine with the aim of avoiding blood oxygenation changes in prefrontal areas, cerebellum and basal ganglia. When the desired mapping is for sensory areas, the task will consist on pressing different parts of the body of the patient through a mechanic system. Memory mapping is performed through the task called "walking in my city", asking the patient to mentally remember all the details in a walk between two chosen points in his city. These fMRI findings may be of great help when deciding how to proceed in cases of insular gliomas. The philosophy of the transylvian approach consists on keeping intact the opercula as it goes through a natural corridor, but the fMRI is helpful to decide where and how to start the Sylvian fissure splitting and where to place the electrodes grid to check the motor pathways. On the other hand in cases of dominant hemisphere lesions, it may guide us through the non-functional invaded opercula to reach the insular component. DTI-tractography This imaging modality has been incorporated to the neurosurgical diagnostic armamentarium, being extremely useful during surgical planning. Diffusion tensor imaging (DTI) can detect the characteristics of water diffusion in tissue distribution and display particular dimensional Brownian motion. The diffusion of water particles is facilitated by the ordered distribution of neural fibers through the membranes covering the axons. This imaging modality allows displaying the white matter fiber tracts by selecting a place where they can be easily visualized and then performing a three-dimensional reconstruction of them. DTI allows the visualization of bundles of axons in the human brain, by selecting regions with the same values of Fractional Anisotropy as "seed" for the start of production of tracts in the three – dimensional space. Tractography provides information about the normal course, the displacement or disruption of white matter tracts around the tumor, as well as damage to these tracts due to vasogenic edema or tumor infiltration. In Neurosurgery tractography is started being used mainly to understand the subcortical relation between the tumor and clinically relevant white matter fiber tracts. It is important to have in mind that tractography is limited in areas where tracts cross tumors or peritumoral vasogenic edema, so this fact should be noticed when deciding the place for the seed. A great number of fascicles can be visualized through DTI-based tractography, but in the neurosurgical practice the main studied fiber bundles are the corticospinal tract that contain motor and somatosensory fibers from the central lobe, passing through the corona radiata to join the internal capsule where the sensory part incorporates from the thalamic nuclei, and the motor fibers will lead to the cerebral peduncle; the superior longitudinal fascicle contains the arcuate fasciculus, which joins Broca´s and Wernicke´s area, resulting of great interest in cases of tumors located in the surroundings of the inferior frontal, angular and superior temporal gyri; and the optic radiations are also of great interest dealing with tumors not only in the occipital lobe, but also deep in temporal and parietal lobes11. In the case of an insular tumor, surrounding white matter fiber tracts as the internal capsule or the superior longitudinal fascicle belong to different anatomic and functional compartments, and so they are generally free of tumoral invasion. However, in some cases the posterior deep limit of the tumor might be closely related especially with the posterior limb of the internal capsule. In this sense, the preoperative tractographic analysis of this bundle may provide very useful information to the neurosurgeon, to improve his/her three-dimensional understanding of the tumor and surrounding structures. These imaging modalities provide the chance to link all these data in the surgeon's mind with his/her anatomic knowledge, and his/her gained experience during previous procedures and follow-up, resulting in a perfect display of preoperative information which remains crucial to elaborate a 3D visualization of the tumor and surrounding neurovascular structures, thus facilitating the choice of the most adequate surgical strategy. Three-dimensional anatomic reconstructions Before approaching the insula, some surface landmarks must be comprehensively studied. This is the case of the opercular lateral surface, as well as the Sylvian fissure anatomical variations and the related SSV and feeders. This goal is better achieved through a Three dimensional cortical surface reconstruction, which allows visualizing all these data in a direct and easily integrated fashion. The best sequence to perform this step is the one known as Three-Dimensional Magnetization Prepared Rapid Acquisition Gradient Echo (3D MPRAGE). A 3D T2 –weighted image may be helpful in some cases, because it also offers a great accuracy of sulci and gyri anatomical disposition. These sequences offer the chance of performing a 3D reconstruction of the brain, being very helpful to plan the surgical approach and transsylvian or transopercular microsurgical technique.

PART 2: Intraoperative Technology and Tumor Growing Patterns

Introduction Since the first insulectomies reported by Penfield and Faulk, some controversies have surrounded this area as a clearly defined functional entity. Surgery on this region may induce postoperative hemiparesis. Moreover, different degrees of speech impairments after dominant insula infarctions, as well as mutism and apraxias after non-dominant insula damage have been reported. However, it should be noted, that in most of these cases the posterior pathological examination revealed damage on the surrounding opercular cortex and corona radiata, probably due to opercular and subcortical involvement of the lesion, or direct surgical manipulation of these neural structures and ischemic injury due to Middle Cerebral Artery (MCA) branches manipulation. The aforementioned pioneer surgical explorations of the insular lobe were reported by Penfield in the 1950’s, who performed direct stimulations on the insular cortex in awake patients, followed by various degrees of insular resection in certain epilepsy cases, reporting no immediate neurological deficits. The surgical technique he employed consisted on performing an anterior temporal lobectomy to safely expose the insular surface. Following the same philosophy, Guillaume et al. promoted the transopercular approaches (frontal or temporal depending on the electrocorticographic activity) to reach the insula. Yasargil’s first long series of limbic and paralimbic tumors included 57 insular and parainsular tumors, in which 93 more cases were lately added. The 93% of the benign reported cases (91% among the malignant tumors) showed good postoperative conditions, and acceptable rates of seizure-free patients. The clinical results were substantially improved after 3-6 months postoperatively. These first encouraging results reported by Yasargil after the advent of microsurgical techniques aimed many neurosurgeons to take a renewed interest in dealing with insular tumors surgery. However still nowadays, many controversies surround the optimal treatment for these lesions, and different options as observation, stereotactic biopsy, radiosurgery, and direct surgery have been proposed. Thus, the management of patients with insular tumors is dramatically changing during the last two decades, mainly due to the technological developments in neuroimaging and surgical armamentarium. The benefits provided by these technical upgrades have generally improved the decision-making process (diagnosis, treatment, prognosis) of intrinsic brain tumors. However, this evolution must be clearly understood and managed, because this leap in quality may also carry more complex decisions. The decision to operate should be based on each individual case, attending to the symptomatology, tumor topography and operability. Insular tumors generally appear as producing intermittent but recurrent symptoms, or sometimes asymptomatically. This ‘indolent’ clinical presentation, added to their deep location in the floor of the Sylvian fissure, covered by highly eloquent neurovascular structures, have encouraged many surgeons to recommend biopsies for large dominant-hemisphere insular tumors to avoid postoperative deficits. Nevertheless, it has been proven that this form of treatment does not provide any benefit when compared with large resections of these lesions. Another option is represented by the wait-and-see strategy. It is fair to highlight that most of these low-grade gliomas experience a prolonged and slowly progressive growing course not so aggressive as tumors in other locations. This fact allows the surgeon, but specially the patient to consider a future decision. These patients can be followed up closely for a period, and the decision to operate can be taken calmly in case of imaging progression or not response to the antiepileptic drugs in cases of seizures. However, in our opinion, the unpredictable natural history of these lesions must also be taken into consideration when deciding the optimal treatment, and surgery represents the safest therapeutic option. Some exceptions to this strategy are the presence of big and hemorrhagic tumors, as well as lesions causing an important mass effect and presenting as contrast enhancing tumors. Generally, these features correspond well with highgrade tumors, and the patients are generally more like to be operated without giving time to their worsening. According to the seizures, low-grade insular gliomas have achieved rates of 60% refractory epilepsy. In these cases, the microsurgical excision has been promoted as the only solution, achieving results in recent series of 73% seizure-free, 12% occasional, 11% reduced, and 3.6% unchanged seizures. Thus, when pharmacologically refractory seizures are present, the decision to operate seems clear. Attending to other features, Simon et al. demonstrated the importance of patient selection as an important factor determining functional outcomes. In this sense, most of the young patients free of neurological deficit and WHO grade I-III gliomas represent the ideal candidates for surgical resection, achieving a 3-months postoperative KPS score of 80-100. This good prognostic group excludes patients with GBM, which despite its general poor survival outcome, would benefit of a decompressive surgery. It has been reported the poor overall survival and high complication rates patients older than 60 years, with preoperative neurological impairment and a KPS score < 80. Recent groups have analyzed the extent of resection and other important factors as the overall survival and the progression free survival, showing better results in cases of insular low-grade gliomas when compared with gliomas with the same histologic features in different locations. Thus, it seems that young patients in a good clinical condition and low-grade neuroimaging characteristics, and patients in good general conditions with important mass effect and intracranial hypertension symptoms will benefit from a careful and gross total removal, providing strong benefits in terms of survival and symptoms alleviation. Consequently, the microsurgical removal appears in our opinion as the most adequate first option when a symptomatic insular glioma is diagnosed. To achieve this goal, the surgeon´s experience and anatomical knowledge and training, aided by the recently improved preand intraoperative tools represent the key points. Intraoperative techniques Intraoperative neuromonitoring Different intraoperative mapping techniques have improved the results when resecting brain tumors near eloquent areas. Some of these techniques require the patient´s collaboration to detect for example a speech arrest during Broca´s Area stimulation.

Asleep craniotomy for brain tumors surgery is a useful technique in selected cases. When the tumor invades the frontoparietal operculum near the area of language, the surgical procedure is performed under conscious sedation, in which the patient actively participates (object naming, counting and reading numbers) in much of the procedure. Therefore, they must understand exactly the technique, the objectives, limitations and complications of the method. In these cases, the aim consists on achieving conscious sedation, which means that the patient is asleep but responds to verbal commands. This sedation is objectified through an anesthetic depth monitor (Bispectral Index whose values should be between 70-80). With this level of sedation achieved good cooperation of the patient. If the patient's cooperation is not needed, there will be a total intravenous anesthesia preferably with appropriate depth level (BIS 40-50). Using propofol with remifentanil both in continuous intravenous infusion. The use of drugs that reduce or alter the potential such as neuromuscular relaxants, volatile anesthetics and benzodiazepines should be avoided. However, neuromuscular relaxants can be used to obtain a partial blockage, in such a way as to reduce an important part of the movement and to facilitate the surgical procedure, being able to obtain adequate monitoring (with an appropriate lock), except during the mapping. One of the possible complications of this method is the appearance of post-discharges associated with stimulation, such as to trigger a seizure. If a post-discharge appears over 30 secs, it suggests the use of midazolam 2 mg or lorazepam 2 mg, or low intravenous dose of barbiturates. It is also recommended the use of serum ringer at a lower temperature than ambient directly over the exposed cortex. Other factors that influence the monitoring are: an adequate blood flow, intracranial pressure, optimal hematocrit, adequate ventilation and oxygenation and temperature of the patient. Cortical mapping: awake and non-awake This neurophysiological technique allows the surgeon localizing the functional areas with awake (language areas) or non-relaxed (motor areas) patients, through direct brain stimulation. The technique of mapping by direct cortical electrical stimulation allows the creation of a functional map of the cerebral cortex exposed, both to identify areas that are functionally significant as areas that are not. The neurosurgeon places the electrode at a small region of cortical area of the brain, and the stimulator from the computer applies a train of stimuli, which can result in neurological changes as patient movement or numbness or inhibit neurological function as speech arrest. When stimulation of a focal brain region produces any of the aforementioned symptoms not accompanied by a crisis or post-discharge, it is confirmed that the stimulated cortex region is important for brain function. The criteria for considering an area as eloquent, involves that a functional response occurs for at least three separate stimuli into a single cortical region. The most employed technique for direct cortical stimulation is the repetitive bipolar cortical stimulation or Penfield technique. Bipolar stimulation technique of Penfield is based on the activation of the cortical circuit applying electrical pulses repeatedly. For the stimulation is commonly used a bipolar electrode with carbon tips 5 mm apart, with a cable connected to an external stimulator that acts as a generator of continuous electrical power trains of biphasic pulse. To assess motor or sensory function, applying a train of 2-3 seconds long is enough, while assessing language function requires longer durations of 5-7 seconds. Stimuli should not be encouraged two consecutive times to prevent post – discharges and seizures. Three positive tests in the same location are enough to ensure that it is essential for language. Occasionally it is necessary to extend the duration of the train to 7-10 seconds to map the language, due to the complexity of questions and answers to the questions. It is recommended to begin with a current of 1mA from 2 mA to increase to the minimum intensity that produces a sensorimotor response (not higher than 8-10 mA). The procedure finishes by marking with sterile labels the cortex with positive response using the legend chosen by each surgeon, to avoid damaging these eloquent areas. Motor areas. Theses test are mainly performed to identify the precentral, subcentral and ventral premotor areas above the Sylvian fissure. Registration can be done with the patient awake, determining the evoked movement by direct visualization or with the patient asleep using as control a continuous electromyographic recording. Recording electrodes should be placed when the patient is anesthetized. The needle electrodes are subcutaneous monopolar and disposable (12 mm or 20 mm in length, placed 2 separate needles 5-10 mm between them) and are placed in the muscle groups that correspond to the stimulated brain area (right / left, contralateral to the lesion; or bilateral), for example, it is possible to monitor facial muscles (orbicularis oris) upper limb muscles (deltoid, biceps, extensor digitorum and short Abductor) and lower limb (femoral adductor, quadriceps, tibialis anterior and abductor). Best when it is possible to monitor the entire side of the body, with impedances below 5 K Ω. The stimulus causes muscle jerking or tonic contractions that can start immediately to stimulation or after several seconds. In other regions, the stimulation can cause inhibition of movement (when an awake patient is told to move his fingers, stimulation can slow or halt the movement), as supplementary motor cortex stimulation and other regions that can assume an integrative role in motor function. Sensitive areas. The lower postecentral gyrus is mainly checked to look for sensitive responses during insular tumors surgery in case of awake patients. The presence of sensory impairment is assessed by the patient, paresthesias in the contralateral regions of the body and occasionally on both sides of tongue or face, or both sides of the neck. Language areas. It is performed with the patients awake and requires their collaboration. The administration of drugs must be stopped at least 15 minutes before beginning the cortical stimulation. It is desirable the involvement of a neuropsychologist for interpretation of different language errors caused by the stimulation. There should be a preoperative training about the tasks to be performed intraoperatively, and stop the monitoring in case the patient in a basal situation fails more than 25% of the tasks presented. In a first step the sensorimotor response should be mapped to confirm a positive response. After confirming the response, next steps are: a. Mapping cortical areas b. Language sites whose answers after stimuli are known are mapped and produce the same inhibition (speech arrest, dysarthria or anomia). A good beginning is naming and counting tasks (expressive language): asking the patient to count (1 to 10, again and again) or name objects presented visually (different test can be used, selected according to different variables such as frequency, familiarity, age of acquisition, and education). It helps to choose pictures of items that the patient can name quickly and easily in the test. Phonetic Association: asking the patient to tell as many names beginning with the letters F, P and L (one minute for each letter). Semantic association: the patient is asked to read the largest number of cars, fruits or animals. Nomination of famous faces: showing the patient 50 pictures from famous people and 50 non – famous. Object Naming. Simple calculations: multiplication or subtraction. c. Failures are coded and responsible areas are registered again with sterile labels: Aphasia (loss of the ability to produce and / or comprehend language). Phonemic paraphasias (changes in the articulation of one or more phonemes). Semantic paraphasias (changes in the phonology of the word, weakness with the onset of the alterations). Anomia (difficulty in retrieving words when speaking) Perseverance (repeat previous items as the following items were submitted) Speech arrest. Phase reversal of somatosensory evoked potentials technique: N20/P30 wave The N20 wave technique has been developed to identify the central sulcus and consequently the pre- and postcentral gyri. This fact will result of great help to place a flat electrodes grid in the precentral region during the whole procedure to have a continuous motor mapping. SEP can identify primary areas of sensory and motor control (precentral and postcentral grooves). The reverse phase of SEP is based on changes in the polarity of the dipole field generated by the cortical afferent pathway. The stimulus applied to a peripheral nerve generates an electric dipole on the postcentral gyrus. The polarity of this dipole changes on the adjacent precentral gyrus. Thus, a SEP (N20/P30) can register from the postcentral gyrus and a reverse image from the turn precentral (P'20 / N'30). Once performed the craniotomy and opened the dura, a strip of silicone that have set a variable number of electrodes (4 or 6) of platinum of 1-1.5 mm in diameter aligned in rows, with an interval of 0.5- 1 cm, will be placed over the cortex. The strip of electrodes should be placed across the alleged central sulcus, covering the area of the hand or foot at the sensorimotor gyri, with an angle of 15 ° to the sagittal direction. For the SEP of the median nerve, the electrode should be placed in a cortical area between 3 and 8 cm from the midline. An electrical stimulator current of constant voltage will be employed for this purpose. Intensity should be gradually increased until a motor response in the first finger (median nerve) appears. Once obtained the wave, it is easy to locate the central sulcus between the electrodes in which the phase reversal is given. Somatosensory evoked potentials The SEP consist on the distal stimulation of afferent pathways with the aim of identifying short latency responses evoked from specific cortical areas. When stimulating the sciatic nerve distally, the response is detected on its specific area of the contralateral postcentral gyrus devoted to the representation of the lower extremity, while stimulation of the upper extremity will elicit a similar response from a different portion of the contralateral postcentral gyrus. The evoked potential method has been subsequently developed as a practical noninvasive clinical method to study conduction in the visual, auditory, and somatosensory systems. In the clinical practice this technique is used to check the somatosensory pathway integrity before, during and after surgery. Its preoperative status is of great importance to have a control to fastly detect any changes during surgery. In cases of insular tumors, this is a good method to detect possible damages of the thalamocortical projections mainly located in the posterior limb of the internal capsule when dealing with the most posterosuperior aspect of these tumors around the posterior insular point. We combine this technique with the direct subcortical stimulation of the corticospinal fiber tract at this stage of the surgery. Motor evoked potentials Direct subcortical stimulation: classic bipolar and monopolar electrodes and continuous CUSAstim technique Subcortical stimulation is a technique that has reached as importance as cortical mapping in brain tumor surgery. Its main indication remains when dealing with tumors with a subcortical extension in the surroundings or inside important white matter fiber bundles. The technical details and the tools employed are the same explained in the section about direct cortical stimulation. Nowadays, insular tumors surgery cannot be understood without direct subcortical stimulation in our opinion. Once removed the main tumor volume, the oncologic surgical concept forces to resect as much surrounding tumor tissue as possible, to complete a total macroscopic resection respecting important white matter fiber tracts closely related with the deeper tumor components, as the inferior frontooccipital fascicle (IFOF), the superior longitudinal fascicle (SLF) and the corticospinal fiber tract. When the tumor resection is getting closer to some of these highly eloquent white matter fiber tracts, the prize to pay by a total resection may be too high. In this sense, the direct subcortical stimulation appears as a great tool. The most accepted approach consists on stimulating the walls of the resection cavity each 1 or 2 mm, using a bipolar stimulator during 2 – 4 secs, with intensities between 2 and 10 mA for the motor and sensitive pathways. In cases of language related fascicles as the IFOF and SLF, during tumor resection, the functional pathway mapping will follow outlining the eloquent cortical sites at depth. The patient should be nominating and counting in different phases until the end of tumor resection, especially when performing this deep resection. Recently, we have incorporated the suction pipe stimulator as well as the novel CUSA-stim, which both allow performing subpial and ultrasonic suction respectively, while continuously stimulating every single thin layer of tumor. This methodology has allowed us extending our resections in a safer, faster and more precise way, as the stimulation is being performed at the moment of the suction, letting the surgeon to discriminate how far the alleged functional fascicle remains from the resection edge. Intraoperative imaging modalities Class II data show that the extent of resection for malignant gliomas improves survival and in case of low – grade gliomas, improves survival and time to tumor recurrence. This is the main reason why until new treatments for glial tumors are developed, the cytoreductive treatment provided by surgery will maintain its value. In this sense, different intraoperative imaging modalities have been incorporated to the clinical practice with the ultimate objective being to optimize the resection limits; to extend them to the maximum while minimizing the eventual associated morbidity. Image-assisted surgery is continuously being developed to help neurosurgeons to practice surgery on brain tumors more safely and effectively. Neuronavigation allows surgeons to locate intra-axial brain tumors more accurately choosing the best path to the lesion. All intraoperative navigation systems are fed with imaging studies, either a CT or MRI. The choice of appropriate images is important, as for example, low-grade gliomas are best defined by T2-weighted sequences, whereas high-grade primary tumors are best seen on a T1 contrast. However, the main limitation of neuronavigation is its reliance on preoperative images. Upon opening the skull and dura mater, movements inevitably occur, making data derived from these images unreliable and then loosing accuracy. Only intraoperative imaging can offer the updated information needed to maintain accurate navigation during the surgical procedure. These images are useful to confirm that tumor resection has been completed, a fact often not verifiable under the surgical microscope vision. Intraoperative magnetic resonance Intraoperative magnetic resonance imaging (iMRI) is a technology not largely employed yet due to its high cost and its special needs in the operating room (OR). An OR must be previously designed to host an iMRI. The complexity of the OR setup is greater for the use of iMRI, and safety as well as equipment details increase proportionally to the field magnetic strength. How iMRI may influence quality of life and survival remains to be studied yet, but it seems that selected patients with low and high – grade gliomas will clearly benefit from the use of intraoperative imaging techniques as iMRI, due to the ability of them to offer in real-time a direct control of the extent of resection, the relative location of the cortical and subcortical eloquent regions with the tumor. Intraoperative ultrasound Intraoperative MRI technical pitfalls have let to the development of intraoperative ultrasonography in many centers. This is our preferred intraoperative imaging modality, when combined with other intraoperative vision techniques and the anatomical knowledge. The usefulness of this device in cases of insular tumors is focused in the first stages of the procedure, to confirm the surgeon’s view of the relation between the tumor with the opercula and the Sylvian fissure compartments. Its viability to check the tumor remnant compared with the intraoperative MRI is diminished, mainly due to the artifacts produced by the bleeding, and it loses its usefulness in cases of previously irradiated tumors. However, the comparison of the snapshot taken before the resection, with the post-resection picture, can result enough useful for experienced surgeons. Ideally all brain tumors are at least partially hyper echogenic. Diffuse calcifications inside lesions produces stronger echo patterns, while cysts or areas of necrosis are hypo echogenic. The local invasion of gliomas tends to appear as intermediate echogenicity. The edema can also be distinguished from the surrounding healthy parenchyma. The main limitation of ultrasound is image resolution and the correlation of preoperative MRI scans and intraoperative ultrasonography images. This problem has been partially solved with the aim of modern neuronavigation systems, which allow overlapping of real – time ultrasound images with preoperative MRI data. Indocyanine green technique (ICG) Intaoperative fluorescence videoangiography under indocyanine green has been a major practical advance in the practice of cerebrovascular microsurgery. ICG was first used and found wide acceptance. Numerous applications have been defined as an adjunct to surgical procedures as diverse as aneurysm clipping, bypass, arteriovenous malformation resection, and dural arteriovenous fistulae obliteration, among others. Due to the advent, safety and availability in most of the OR, numerous applications in tumor surgery have been recently reported. In our experience, ICG has been useful to understand the venous flow at the opercular and superficial Sylvian veins system, and to identify the safest way to perform the Sylvian fissure splitting. In some cases, this technology has been of great help to identify MCA branches vasospasm during the insular component resection. Ultrasonic aspirator (CUSA) This technology was first introduced in the neurosurgical procedures 25 years ago, and has become an indispensable tool in the neurosurgical armamentarium for the resection of intracranial tumors. The ultrasonic aspirator presents two effects over the tissue interface. The first effect supposes a suction that brings the surrounding tissue to the tip of the aspirator and forces it to vibrate, accelerate, and decelerate with the tip, fragmenting it away from harder tissues as vessels. The second important effect consists on a rapidly oscillating tip that produces localized pressure waves, which cause vapor pockets around cells in tissues with high water contents; the collapse of these pockets causes the tissue cells to rupture. The speed of fragmentation depends on the amplitude setting of the system. The use of this technology remains of great interest when dealing with intrinsic brain tumors, especially when these tumors are close to eloquent areas. Classical resection of intrinsic brain tumors is performed through an electric coagulating bipolar system to destroy tissue and a conventional suction system to aspirate it. This procedure can result as effective as ultrasonic aspiration, but there is a great difference. Bipolar coagulation systems increase the local temperature of the surrounding tissue and it has been demonstrated to be responsible of damaging neighbor areas to the resected tissue. On the contrary, the ultrasonic aspirator is at least as effective removing infiltrated tissue, but shows the advantage of not damaging the healthy surrounding healthy and sometimes functional tissue. The use of ultrasonic aspirators can increase the extent of resection, respecting vessels and healthy surrounding tissue, and then improving the functional result. Fluorescence guided resection with 5 – Aminolevulinic Acid (5-ALA) This technique allows the visualization of malignant tissue during surgery for malignant glioma (grades III and IV WHO). Tumor resection guided by fluorescence involves giving the patient a natural precursor, 5-aminolevulinic acid (5-ALA HCl), which is taken up by cells of malignant gliomas and, when summed, becomes a fluorescent substance. Thus, by applying a special light during surgery, the malignant cells are stained red offering the surgeon a clear distinction between the healthy and which are not, letting increasing the extent of tumor resection, minimizing brain damage. This technique still presents many pitfalls, and our recommendation is not to strictly follow the information it provides. However, it seems a promising tool, and in this sense, we must support and study it in real conditions with the aim of improving it. Surgical approaches attending to the relative location and growing patterns The insula has not been deeply studied, and its surgical interest has been classically carried out by a few surgeons, particularly due to its deep location and intrinsic difficulty to be explored. Recent advances on its study and understanding have been possible thanks to the development of functional mapping methods, supporting the fact that this region represents an anatomical, cytoarchitectonical and functional interface between the limbic system and the neocortex. This fact has been the key to understand the different behaviors and growing patterns among the insular tumors and tumors in other regions as the neocortex and the limbic areas, and among the insular tumors themselves. Thus, analyzing and understanding the phylogenetic and embryologic evolution of the insula, as well as the cytoarchitectonic features on its different cortical areas will provide a better understanding of the insular tumors invasion patterns, which will lead to a safer and optimal surgical treatment of the insular tumors themselves. Insular Tumors Understanding. Cytoarchitectural Anatomy of the Insula The cortical shield covering the basal ganglia and the internal capsule outline, form the insula near the 5th month of the embryological development. Later, this primitive insula begins enfolding in a central position due to the disproportionate growing of the adjacent neocortical areas, being finally covered by the frontal, parietal and temporal operculum. The insula of Reil belongs to the paralimbic system representing a transitional element between the allocortex and the neocortex of the human cerebrum. The paralimbic areas are commonly termed as mesocortical, due to its intermediate cortical architectonic features, and are represented by the orbitofrontal cortex, insula, temporal pole, parahippocampal and cingulate gyri. The gradual cortical differentiation between the old and centrally positioned limbic brain, and the new neocortical areas, uses the insula as an anatomical and cytoarchitectural link (paralimbic regions). Thus, the insular cortex presents three major patterns of progressive cortical differentiation. The anteroinferior part of the insular gyri shows a peripaleocortical architecture (agranular sector). A transition to the isocortex takes place in the pericentral part, which shows a proisocortical architecture (dysgranular sector), while the most posterior gyri show an isocortical architecture (granular sector). This cortical differentiation involves an increasing in complexity, while the piriform olfactory allocortex located covering the inner aspect of the limen insulae acts as the pivotal point during this process. From this central point, the development of the cortical layers follows a radiating centrifugal vector. Thus, the limen insulae is concentrically surrounded by those three mesocortical (paralimbic) layers, connecting the mesiobasal allocortical (limbic), with highly developed neocortical regions, mainly the opercula. Insular tumors seem to respect in the initial stages these cytoarchitectonic barriers, however after surgery, radiotherapy or even spontaneously in cases of advance high-grade gliomas, these edges may be crossed. After dealing with, removing, changing their natural history, and observing the behavior of hundreds of insular tumors, Yasargil described their propensity to spread within the confines of the allocortical/mesocortical zones, sparing the neocortical and medial structures such as the basal ganglia and internal capsule, stressing the idea that these tumors have a greater appetence for the phylogenetically primitive zones instead of the neocortical structures in most of the cases. Following this line of reasoning, he proposed a detailed insular tumors classification. So, the tumors mainly confined to the insula (3A) or slightly expanding to the inner border with the adjacent opercula (3B) seem to grow mainly in more complex insular regions (middle and posterior). On the other hand, those insular tumors involving one or both paralimbic areas, orbitofrontal and temporopolar, without (5A) or with (5B) limbic extension, seem to mainly develop in the anterior part of the insular, where the uncinate fascicle and the close relation with the piriform cortex may act as paths for transgression. Thus, four subcategories of insular tumor growth are differentiated: pure insular or insuloopercular growth in type 3 lesions and combined paralimbic or combined paralimbic– limbic involvement in type 5 tumors. In our opinion, understanding this anatomical and developmental understanding will result of gret interest to design a more accurate surgical strategy, and to gain a better comprehension of the spreading mechanisms along the adjacent eloquent areas. As pathology follows the anatomy, the point to completely remove these tumors following an anatomical concept, remains on attacking first the central core of the tumor, sometimes centered in the insula, and sometimes centered on the adjacent frontoorbital, frontoparietal or temporal opercula, and then to follow the tumor from its inner aspect, to remove the possible limbic and paralimbic extensions, causing the minimum damage to the surrounding healthy tissues. Depending on these general invasion and growing patterns, the surgical strategies will consist on a purely transylvian transinsular approach or a combined transopercular subinsular resection.

Lessons on ‘INSULAR BRAIN TUMOR SURGERY’ PART 2: Intraoperative Technology and Tumor Growing Patterns Introduction Since the first insulectomies reported by Penfield and Faulk, some controversies have surrounded this area as a clearly defined functional entity. Surgery on this region may induce postoperative hemiparesis. Moreover, different degrees of speech impairments after dominant insula infarctions, as well as mutism and apraxias after non-dominant insula damage have been reported. However, it should be noted, that in most of these cases the posterior pathological examination revealed damage on the surrounding opercular cortex and corona radiata, probably due to opercular and subcortical involvement of the lesion, or direct surgical manipulation of these neural structures and ischemic injury due to Middle Cerebral Artery (MCA) branches manipulation. 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The decision to operate should be based on each individual case, attending to the symptomatology, tumor topography and operability. Insular tumors generally appear as producing intermittent but recurrent symptoms, or sometimes asymptomatically. This ‘indolent’ clinical presentation, added to their deep location in the floor of the Sylvian fissure, covered by highly eloquent neurovascular structures, have encouraged many surgeons to recommend biopsies for large dominant-hemisphere insular tumors to avoid postoperative deficits. Nevertheless, it has been proven that this form of treatment does not provide any benefit when compared with large resections of these lesions. Another option is represented by the wait-and-see strategy. It is fair to highlight that most of these low-grade gliomas experience a prolonged and slowly progressive growing course not so aggressive as tumors in other locations. This fact allows the surgeon, but specially the patient to consider a future decision. These patients can be followed up closely for a period, and the decision to operate can be taken calmly in case of imaging progression or not response to the antiepileptic drugs in cases of seizures. However, in our opinion, the unpredictable natural history of these lesions must also be taken into consideration when deciding the optimal treatment, and surgery represents the safest therapeutic option. Some exceptions to this strategy are the presence of big and hemorrhagic tumors, as well as lesions causing an important mass effect and presenting as contrast enhancing tumors. Generally, these features correspond well with highgrade tumors, and the patients are generally more like to be operated without giving time to their worsening. According to the seizures, low-grade insular gliomas have achieved rates of 60% refractory epilepsy. In these cases, the microsurgical excision has been promoted as the only solution, achieving results in recent series of 73% seizure-free, 12% occasional, 11% reduced, and 3.6% unchanged seizures. Thus, when pharmacologically refractory seizures are present, the decision to operate seems clear. Attending to other features, Simon et al. demonstrated the importance of patient selection as an important factor determining functional outcomes. In this sense, most of the young patients free of neurological deficit and WHO grade I-III gliomas represent the ideal candidates for surgical resection, achieving a 3-months postoperative KPS score of 80-100. This good prognostic group excludes patients with GBM, which despite its general poor survival outcome, would benefit of a decompressive surgery. It has been reported the poor overall survival and high complication rates patients older than 60 years, with preoperative neurological impairment and a KPS score < 80. Recent groups have analyzed the extent of resection and other important factors as the overall survival and the progression free survival, showing better results in cases of insular low-grade gliomas when compared with gliomas with the same histologic features in different locations. Thus, it seems that young patients in a good clinical condition and low-grade neuroimaging characteristics, and patients in good general conditions with important mass effect and intracranial hypertension symptoms will benefit from a careful and gross total removal, providing strong benefits in terms of survival and symptoms alleviation. Consequently, the microsurgical removal appears in our opinion as the most adequate first option when a symptomatic insular glioma is diagnosed. To achieve this goal, the surgeon´s experience and anatomical knowledge and training, aided by the recently improved preand intraoperative tools represent the key points. Intraoperative techniques Intraoperative neuromonitoring Different intraoperative mapping techniques have improved the results when resecting brain tumors near eloquent areas. Some of these techniques require the patient´s collaboration to detect for example a speech arrest during Broca´s Area stimulation. Asleep craniotomy for brain tumors surgery is a useful technique in selected cases. When the tumor invades the frontoparietal operculum near the area of language, the surgical procedure is performed under conscious sedation, in which the patient actively participates (object naming, counting and reading numbers) in much of the procedure. Therefore, they must understand exactly the technique, the objectives, limitations and complications of the method. In these cases, the aim consists on achieving conscious sedation, which means that the patient is asleep but responds to verbal commands. This sedation is objectified through an anesthetic depth monitor (Bispectral Index whose values should be between 70-80). With this level of sedation achieved good cooperation of the patient. If the patient's cooperation is not needed, there will be a total intravenous anesthesia preferably with appropriate depth level (BIS 40-50). Using propofol with remifentanil both in continuous intravenous infusion. The use of drugs that reduce or alter the potential such as neuromuscular relaxants, volatile anesthetics and benzodiazepines should be avoided. However, neuromuscular relaxants can be used to obtain a partial blockage, in such a way as to reduce an important part of the movement and to facilitate the surgical procedure, being able to obtain adequate monitoring (with an appropriate lock), except during the mapping. One of the possible complications of this method is the appearance of post-discharges associated with stimulation, such as to trigger a seizure. If a post-discharge appears over 30 secs, it suggests the use of midazolam 2 mg or lorazepam 2 mg, or low intravenous dose of barbiturates. It is also recommended the use of serum ringer at a lower temperature than ambient directly over the exposed cortex. Other factors that influence the monitoring are: an adequate blood flow, intracranial pressure, optimal hematocrit, adequate ventilation and oxygenation and temperature of the patient. Cortical mapping: awake and non-awake This neurophysiological technique allows the surgeon localizing the functional areas with awake (language areas) or non-relaxed (motor areas) patients, through direct brain stimulation. The technique of mapping by direct cortical electrical stimulation allows the creation of a functional map of the cerebral cortex exposed, both to identify areas that are functionally significant as areas that are not. The neurosurgeon places the electrode at a small region of cortical area of the brain, and the stimulator from the computer applies a train of stimuli, which can result in neurological changes as patient movement or numbness or inhibit neurological function as speech arrest. When stimulation of a focal brain region produces any of the aforementioned symptoms not accompanied by a crisis or post-discharge, it is confirmed that the stimulated cortex region is important for brain function. The criteria for considering an area as eloquent, involves that a functional response occurs for at least three separate stimuli into a single cortical region. The most employed technique for direct cortical stimulation is the repetitive bipolar cortical stimulation or Penfield technique. Bipolar stimulation technique of Penfield is based on the activation of the cortical circuit applying electrical pulses repeatedly. For the stimulation is commonly used a bipolar electrode with carbon tips 5 mm apart, with a cable connected to an external stimulator that acts as a generator of continuous electrical power trains of biphasic pulse. To assess motor or sensory function, applying a train of 2-3 seconds long is enough, while assessing language function requires longer durations of 5-7 seconds. Stimuli should not be encouraged two consecutive times to prevent post – discharges and seizures. Three positive tests in the same location are enough to ensure that it is essential for language. Occasionally it is necessary to extend the duration of the train to 7-10 seconds to map the language, due to the complexity of questions and answers to the questions. It is recommended to begin with a current of 1mA from 2 mA to increase to the minimum intensity that produces a sensorimotor response (not higher than 8-10 mA). The procedure finishes by marking with sterile labels the cortex with positive response using the legend chosen by each surgeon, to avoid damaging these eloquent areas. Motor areas. Theses test are mainly performed to identify the precentral, subcentral and ventral premotor areas above the Sylvian fissure. Registration can be done with the patient awake, determining the evoked movement by direct visualization or with the patient asleep using as control a continuous electromyographic recording. Recording electrodes should be placed when the patient is anesthetized. The needle electrodes are subcutaneous monopolar and disposable (12 mm or 20 mm in length, placed 2 separate needles 5-10 mm between them) and are placed in the muscle groups that correspond to the stimulated brain area (right / left, contralateral to the lesion; or bilateral), for example, it is possible to monitor facial muscles (orbicularis oris) upper limb muscles (deltoid, biceps, extensor digitorum and short Abductor) and lower limb (femoral adductor, quadriceps, tibialis anterior and abductor). Best when it is possible to monitor the entire side of the body, with impedances below 5 K Ω. The stimulus causes muscle jerking or tonic contractions that can start immediately to stimulation or after several seconds. In other regions, the stimulation can cause inhibition of movement (when an awake patient is told to move his fingers, stimulation can slow or halt the movement), as supplementary motor cortex stimulation and other regions that can assume an integrative role in motor function. Sensitive areas. The lower postecentral gyrus is mainly checked to look for sensitive responses during insular tumors surgery in case of awake patients. The presence of sensory impairment is assessed by the patient, paresthesias in the contralateral regions of the body and occasionally on both sides of tongue or face, or both sides of the neck. Language areas. It is performed with the patients awake and requires their collaboration. The administration of drugs must be stopped at least 15 minutes before beginning the cortical stimulation. It is desirable the involvement of a neuropsychologist for interpretation of different language errors caused by the stimulation. There should be a preoperative training about the tasks to be performed intraoperatively, and stop the monitoring in case the patient in a basal situation fails more than 25% of the tasks presented. In a first step the sensorimotor response should be mapped to confirm a positive response. After confirming the response, next steps are: a. Mapping cortical areas b. Language sites whose answers after stimuli are known are mapped and produce the same inhibition (speech arrest, dysarthria or anomia). A good beginning is naming and counting tasks (expressive language): asking the patient to count (1 to 10, again and again) or name objects presented visually (different test can be used, selected according to different variables such as frequency, familiarity, age of acquisition, and education). It helps to choose pictures of items that the patient can name quickly and easily in the test. Phonetic Association: asking the patient to tell as many names beginning with the letters F, P and L (one minute for each letter). Semantic association: the patient is asked to read the largest number of cars, fruits or animals. Nomination of famous faces: showing the patient 50 pictures from famous people and 50 non – famous. Object Naming. Simple calculations: multiplication or subtraction. c. Failures are coded and responsible areas are registered again with sterile labels: Aphasia (loss of the ability to produce and / or comprehend language). Phonemic paraphasias (changes in the articulation of one or more phonemes). Semantic paraphasias (changes in the phonology of the word, weakness with the onset of the alterations). Anomia (difficulty in retrieving words when speaking) Perseverance (repeat previous items as the following items were submitted) Speech arrest. Phase reversal of somatosensory evoked potentials technique: N20/P30 wave The N20 wave technique has been developed to identify the central sulcus and consequently the pre- and postcentral gyri. This fact will result of great help to place a flat electrodes grid in the precentral region during the whole procedure to have a continuous motor mapping. SEP can identify primary areas of sensory and motor control (precentral and postcentral grooves). The reverse phase of SEP is based on changes in the polarity of the dipole field generated by the cortical afferent pathway. The stimulus applied to a peripheral nerve generates an electric dipole on the postcentral gyrus. The polarity of this dipole changes on the adjacent precentral gyrus. Thus, a SEP (N20/P30) can register from the postcentral gyrus and a reverse image from the turn precentral (P'20 / N'30). Once performed the craniotomy and opened the dura, a strip of silicone that have set a variable number of electrodes (4 or 6) of platinum of 1-1.5 mm in diameter aligned in rows, with an interval of 0.5- 1 cm, will be placed over the cortex. The strip of electrodes should be placed across the alleged central sulcus, covering the area of the hand or foot at the sensorimotor gyri, with an angle of 15 ° to the sagittal direction. For the SEP of the median nerve, the electrode should be placed in a cortical area between 3 and 8 cm from the midline. An electrical stimulator current of constant voltage will be employed for this purpose. Intensity should be gradually increased until a motor response in the first finger (median nerve) appears. Once obtained the wave, it is easy to locate the central sulcus between the electrodes in which the phase reversal is given. Somatosensory evoked potentials The SEP consist on the distal stimulation of afferent pathways with the aim of identifying short latency responses evoked from specific cortical areas. When stimulating the sciatic nerve distally, the response is detected on its specific area of the contralateral postcentral gyrus devoted to the representation of the lower extremity, while stimulation of the upper extremity will elicit a similar response from a different portion of the contralateral postcentral gyrus. The evoked potential method has been subsequently developed as a practical noninvasive clinical method to study conduction in the visual, auditory, and somatosensory systems. In the clinical practice this technique is used to check the somatosensory pathway integrity before, during and after surgery. Its preoperative status is of great importance to have a control to fastly detect any changes during surgery. In cases of insular tumors, this is a good method to detect possible damages of the thalamocortical projections mainly located in the posterior limb of the internal capsule when dealing with the most posterosuperior aspect of these tumors around the posterior insular point. We combine this technique with the direct subcortical stimulation of the corticospinal fiber tract at this stage of the surgery. Motor evoked potentials Direct subcortical stimulation: classic bipolar and monopolar electrodes and continuous CUSAstim technique Subcortical stimulation is a technique that has reached as importance as cortical mapping in brain tumor surgery. Its main indication remains when dealing with tumors with a subcortical extension in the surroundings or inside important white matter fiber bundles. The technical details and the tools employed are the same explained in the section about direct cortical stimulation. Nowadays, insular tumors surgery cannot be understood without direct subcortical stimulation in our opinion. Once removed the main tumor volume, the oncologic surgical concept forces to resect as much surrounding tumor tissue as possible, to complete a total macroscopic resection respecting important white matter fiber tracts closely related with the deeper tumor components, as the inferior frontooccipital fascicle (IFOF), the superior longitudinal fascicle (SLF) and the corticospinal fiber tract. When the tumor resection is getting closer to some of these highly eloquent white matter fiber tracts, the prize to pay by a total resection may be too high. In this sense, the direct subcortical stimulation appears as a great tool. The most accepted approach consists on stimulating the walls of the resection cavity each 1 or 2 mm, using a bipolar stimulator during 2 – 4 secs, with intensities between 2 and 10 mA for the motor and sensitive pathways. In cases of language related fascicles as the IFOF and SLF, during tumor resection, the functional pathway mapping will follow outlining the eloquent cortical sites at depth. The patient should be nominating and counting in different phases until the end of tumor resection, especially when performing this deep resection. Recently, we have incorporated the suction pipe stimulator as well as the novel CUSA-stim, which both allow performing subpial and ultrasonic suction respectively, while continuously stimulating every single thin layer of tumor. This methodology has allowed us extending our resections in a safer, faster and more precise way, as the stimulation is being performed at the moment of the suction, letting the surgeon to discriminate how far the alleged functional fascicle remains from the resection edge. Intraoperative imaging modalities Class II data show that the extent of resection for malignant gliomas improves survival and in case of low – grade gliomas, improves survival and time to tumor recurrence. This is the main reason why until new treatments for glial tumors are developed, the cytoreductive treatment provided by surgery will maintain its value. In this sense, different intraoperative imaging modalities have been incorporated to the clinical practice with the ultimate objective being to optimize the resection limits; to extend them to the maximum while minimizing the eventual associated morbidity. Image-assisted surgery is continuously being developed to help neurosurgeons to practice surgery on brain tumors more safely and effectively. Neuronavigation allows surgeons to locate intra-axial brain tumors more accurately choosing the best path to the lesion. All intraoperative navigation systems are fed with imaging studies, either a CT or MRI. The choice of appropriate images is important, as for example, low-grade gliomas are best defined by T2-weighted sequences, whereas high-grade primary tumors are best seen on a T1 contrast. However, the main limitation of neuronavigation is its reliance on preoperative images. Upon opening the skull and dura mater, movements inevitably occur, making data derived from these images unreliable and then loosing accuracy. Only intraoperative imaging can offer the updated information needed to maintain accurate navigation during the surgical procedure. These images are useful to confirm that tumor resection has been completed, a fact often not verifiable under the surgical microscope vision. Intraoperative magnetic resonance Intraoperative magnetic resonance imaging (iMRI) is a technology not largely employed yet due to its high cost and its special needs in the operating room (OR). An OR must be previously designed to host an iMRI. The complexity of the OR setup is greater for the use of iMRI, and safety as well as equipment details increase proportionally to the field magnetic strength. How iMRI may influence quality of life and survival remains to be studied yet, but it seems that selected patients with low and high – grade gliomas will clearly benefit from the use of intraoperative imaging techniques as iMRI, due to the ability of them to offer in real-time a direct control of the extent of resection, the relative location of the cortical and subcortical eloquent regions with the tumor. Intraoperative ultrasound Intraoperative MRI technical pitfalls have let to the development of intraoperative ultrasonography in many centers. This is our preferred intraoperative imaging modality, when combined with other intraoperative vision techniques and the anatomical knowledge. The usefulness of this device in cases of insular tumors is focused in the first stages of the procedure, to confirm the surgeon's view of the relation between the tumor with the opercula and the Sylvian fissure compartments. Its viability to check the tumor remnant compared with the intraoperative MRI is diminished, mainly due to the artifacts produced by the bleeding, and it loses its usefulness in cases of previously irradiated tumors. However, the comparison of the snapshot taken before the resection, with the post-resection picture, can result enough useful for experienced surgeons. Ideally all brain tumors are at least partially hyper echogenic. Diffuse calcifications inside lesions produces stronger echo patterns, while cysts or areas of necrosis are hypo echogenic. The local invasion of gliomas tends to appear as intermediate echogenicity. The edema can also be distinguished from the surrounding healthy parenchyma. The main limitation of ultrasound is image resolution and the correlation of preoperative MRI scans and intraoperative ultrasonography images. This problem has been partially solved with the aim of modern neuronavigation systems, which allow overlapping of real – time ultrasound images with preoperative MRI data. Indocyanine green technique (ICG) Intaoperative fluorescence videoangiography under indocyanine green has been a major practical advance in the practice of cerebrovascular microsurgery. ICG was first used and found wide acceptance. Numerous applications have been defined as an adjunct to surgical procedures as diverse as aneurysm clipping, bypass, arteriovenous malformation resection, and dural arteriovenous fistulae obliteration, among others. Due to the advent, safety and availability in most of the OR, numerous applications in tumor surgery have been recently reported. In our experience, ICG has been useful to understand the venous flow at the opercular and superficial Sylvian veins system, and to identify the safest way to perform the

Sylvian fissure splitting. In some cases, this technology has been of great help to identify MCA branches vasospasm during the insular component resection. Ultrasonic aspirator (CUSA) This technology was first introduced in the neurosurgical procedures 25 years ago, and has become an indispensable tool in the neurosurgical armamentarium for the resection of intracranial tumors. The ultrasonic aspirator presents two effects over the tissue interface. The first effect supposes a suction that brings the surrounding tissue to the tip of the aspirator and forces it to vibrate, accelerate, and decelerate with the tip, fragmenting it away from harder tissues as vessels. The second important effect consists on a rapidly oscillating tip that produces localized pressure waves, which cause vapor pockets around cells in tissues with high water contents; the collapse of these pockets causes the tissue cells to rupture. The speed of fragmentation depends on the amplitude setting of the system. The use of this technology remains of great interest when dealing with intrinsic brain tumors, especially when these tumors are close to eloquent areas. Classical resection of intrinsic brain tumors is performed through an electric coagulating bipolar system to destroy tissue and a conventional suction system to aspirate it. This procedure can result as effective as ultrasonic aspiration, but there is a great difference. Bipolar coagulation systems increase the local temperature of the surrounding tissue and it has been demonstrated to be responsible of damaging neighbor areas to the resected tissue. On the contrary, the ultrasonic aspirator is at least as effective removing infiltrated tissue, but shows the advantage of not damaging the healthy surrounding healthy and sometimes functional tissue. The use of ultrasonic aspirators can increase the extent of resection, respecting vessels and healthy surrounding tissue, and then improving the functional result. Fluorescence guided resection with 5 – Aminolevulinic Acid (5-ALA) This technique allows the visualization of malignant tissue during surgery for malignant glioma (grades III and IV WHO). Tumor resection guided by fluorescence involves giving the patient a natural precursor, 5-aminolevulinic acid (5-ALA HCl), which is taken up by cells of malignant gliomas and, when summed, becomes a fluorescent substance. Thus, by applying a special light during surgery, the malignant cells are stained red offering the surgeon a clear distinction between the healthy and which are not, letting increasing the extent of tumor resection, minimizing brain damage. This technique still presents many pitfalls, and our recommendation is not to strictly follow the information it provides. However, it seems a promising tool, and in this sense, we must support and study it in real conditions with the aim of improving it. Surgical approaches attending to the relative location and growing patterns The insula has not been deeply studied, and its surgical interest has been classically carried out by a few surgeons, particularly due to its deep location and intrinsic difficulty to be explored. Recent advances on its study and understanding have been possible thanks to the development of functional mapping methods, supporting the fact that this region represents an anatomical, cytoarchitectonical and functional interface between the limbic system and the neocortex. This fact has been the key to understand the different behaviors and growing patterns among the insular tumors and tumors in other regions as the neocortex and the limbic areas, and among the insular tumors themselves. Thus, analyzing and understanding the phylogenetic and embryologic evolution of the insula, as well as the cytoarchitectonic features on its different cortical areas will provide a better understanding of the insular tumors invasion patterns, which will lead to a safer and optimal surgical treatment of the insular tumors themselves. Insular Tumors Understanding. Cytoarchitectural Anatomy of the Insula The cortical shield covering the basal ganglia and the internal capsule outline, form the insula near the 5th month of the embryological development. Later, this primitive insula begins enfolding in a central position due to the disproportionate growing of the adjacent neocortical areas, being finally covered by the frontal, parietal and temporal operculum. The insula of Reil belongs to the paralimbic system representing a transitional element between the allocortex and the neocortex of the human cerebrum. The paralimbic areas are commonly termed as mesocortical, due to its intermediate cortical architectonic features, and are represented by the orbitofrontal cortex, insula, temporal pole, parahippocampal and cingulate gyri. The gradual cortical differentiation between the old and centrally positioned limbic brain, and the new neocortical areas, uses the insula as an anatomical and cytoarchitectural link (paralimbic regions). Thus, the insular cortex presents three major patterns of progressive cortical differentiation. The anteroinferior part of the insular gyri shows a peripaleocortical architecture (agranular sector). A transition to the isocortex takes place in the pericentral part, which shows a proisocortical architecture (dysgranular sector), while the most posterior gyri show an isocortical architecture (granular sector). This cortical differentiation involves an increasing in complexity, while the piriform olfactory allocortex located covering the inner aspect of the limen insulae acts as the pivotal point during this process. From this central point, the development of the cortical layers follows a radiating centrifugal vector. Thus, the limen insulae is concentrically surrounded by those three mesocortical (paralimbic) layers, connecting the mesiobasal allocortical (limbic), with highly developed neocortical regions, mainly the opercula. Insular tumors seem to respect in the initial stages these cytoarchitectonic barriers, however after surgery, radiotherapy or even spontaneously in cases of advance high-grade gliomas, these edges may be crossed. After dealing with, removing, changing their natural history, and observing the behavior of hundreds of insular tumors, Yasargil described their propensity to spread within the confines of the allocortical/mesocortical zones, sparing the neocortical and medial structures such as the basal ganglia and internal capsule, stressing the idea that these tumors have a greater appetence for the phylogenetically primitive zones instead of the neocortical structures in most of the cases. Following this line of reasoning, he proposed a detailed insular tumors classification. So, the tumors mainly confined to the insula (3A) or slightly expanding to the inner border with the adjacent opercula (3B) seem to grow mainly in more complex insular regions (middle and posterior). On the other hand, those insular tumors involving one or both paralimbic areas, orbitofrontal and temporopolar, without (5A) or with (5B) limbic extension, seem to mainly develop in the anterior part of the insular, where the uncinate fascicle and the close relation with the piriform cortex may act as paths for transgression. Thus, four subcategories of insular tumor growth are differentiated: pure insular or insuloopercular growth in type 3 lesions and combined paralimbic or combined paralimbic– limbic involvement in type 5 tumors. In our opinion, understanding this anatomical and developmental understanding will result of gret interest to design a more accurate surgical strategy, and to gain a better comprehension of the spreading mechanisms along the adjacent eloquent areas. As pathology follows the anatomy, the point to completely remove these tumors following an anatomical concept, remains on attacking first the central core of the tumor, sometimes centered in the insula, and sometimes centered on the adjacent frontoorbital, frontoparietal or temporal opercula, and then to follow the tumor from its inner aspect, to remove the possible limbic and paralimbic extensions, causing the minimum damage to the surrounding healthy tissues. Depending on these general invasion and growing patterns, the surgical strategies will consist on a purely transylvian transinsular approach or a combined transopercular subinsular resection.

Lessons on ‘INSULAR BRAIN TUMOR SURGERY’

Insular glioma surgery

see Insular glioma surgery.

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