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PREOPERATIVE PLANNING OF APPROACH AND EXTENT OF RESECTION IN THE TREATMENT OF BRAIN TUMORS IN THE CONTEXT OF CURRENT CONCEPTS OF THE FUNCTIONAL ORGANIZATION OF THE HUMAN BRAIN: A NEUROSURGEON'S PERSPECTIVE

**Paweł Daszkiewicz^{1(A,B,E)}, Agnieszka Maryniak^{2(C,D,F)},
Hanna Cygan^{2(C,D)}, Katarzyna Nowak^{3(C)}**

¹Department of Neurosurgery, Children's Memorial Health Institute,
Warsaw, Poland

²Developmental Neuropsychology Unit, Department of
Neurosurgery, Children's Memorial Health Institute, Warsaw,
Poland

³Department of Radiology, Children's Memorial Health Institute,
Warsaw, Poland

SUMMARY

This article addresses the issue of preoperative planning in the surgical treatment of brain pathologies in the light of current concepts of the functional organization of the human brain. The primary issues discussed here include general neurosurgical strategy, modern diagnostic techniques (including functional magnetic resonance, tractography, and cortical stimulation), image guided surgery, basic issues in neurosurgical preoperative planning, the concept of eloquent brain areas, current views on the functional organization of human brain and its modification under the influence of pathological processes, surgery, and rehabilitation. To sum up, the neuroimaging techniques now available enable the increasingly effective and safe surgical treatment of neurological diseases. Clinical neurosurgery not only benefits from the achievements of basic sciences, but also contributes considerably to the understanding of brain functions. Brain plasticity and functional reorganization in response to a growing tumor may be basic premises for the concept of functional neurooncology, a novel approach to the diagnosis and treatment of brain tumors.

Key words: neuronavigation, tractography, cortical stimulation, fMRI

INTRODUCTION

Medical statistics consistently report an increasing incidence of neoplasms, including those located within the central nervous system (Berger 2007). The annual rate of increase in the incidence of brain tumors is estimated at 0.8%, and the risk of a brain tumor in children and adolescents under 15 is estimated at 1 per 625 persons. In the US alone, there are about 18,000 new cases each year. Over half of these are high-grade gliomas (WHO grades III and IV), where median survival ranges from 1 to 3 years (McGirt 2009). In low-grade gliomas (WHO grades I and II), 50-75% of patients will survive 5-10 years (McGirt 2008). In spite of improving diagnostic modalities, surgical techniques and oncological therapies, since the large-scale introduction of modern CT-based imaging in the mid-1980s, no significant progress has been made in cure rate, survival time or quality of life in patients with CNS malignancies (Keles 2001).

Extensive infiltration of neuropil by glial tumors greatly hinders the effectiveness of surgical treatment. With the exception of the most benign types of low-grade gliomas, many patients experience a recurrence or progression of their tumor in spite of an apparently radical excision (McGirt 2008, Shaw 2008). Nevertheless, before really effective methods of elimination of neoplastic cells are developed, surgical cytoreduction will remain the cornerstone of treatment. At present, it enables tumor debulking, decompression of adjacent brain tissue, relief of intracranial pressure and acquisition of tissue samples for histological verification. In this setting, the realistic goals of neurosurgical intervention are:

- curative excision (in the case of circumscribed tumors);
- reduction of tumor burden (in the case of diffuse or high-grade tumors);
- palliative procedures to relieve symptoms and prolong survival;
- diagnostic biopsy providing histological verification and enabling optimal planning of further therapy (Sanai 2008, Hentschel 2003).

Another important issue in pediatric neurosurgery is the patient's size and circulating blood volume. These factors determine the child's tolerance for intra-operative blood loss, ability to maintain homeostasis and feasibility of surgery. These issues concern both the surgeon and the anesthetist, but, being purely somatic, they exceed the scope of this article.

TREATMENT STRATEGY

From the clinical neurosurgeon's perspective, indications for the surgical treatment of diseases of the central nervous system may be classified as those which involve:

- saving the patient's life;
- saving a function;
- improving the quality of life.

The first require immediate action, while the second and the third allow time for planning, in order to obtain the best possible results.

Progress in neurosurgical technique has induced major changes in the approach to the planning and execution of surgical procedures. Initially, preoperative planning was limited to a rough determination of lesion location, mainly based on clinical signs and very crude indirect imaging (X-ray, ventriculography, angiography). In short, the preoperative work-up was short, surgery was long and traumatic (both for the patient and the surgeon) and its outcome was uncertain. A breakthrough occurred with the introduction of non-invasive *in vivo* imaging techniques and neuro-physiological studies, enabling the precise preoperative determination of lesion location and its relation to adjacent functionally important centers and pathways (Mikuni 2007). Preoperative planning of approach and the extent of resection ensures maximal therapeutic efficacy with minimal disruption of neural function. Treatment outcomes are better, hospitalization time is shorter, patients' quality of life is greatly improved, and treatment costs can be reduced, even considering the significant cost of modern neurosurgical equipment. Currently, we are able to access brain areas previously considered out of the surgeon's reach, and successfully excise tumors previously considered inoperable. In short, preoperative work-up takes much longer, but the surgery itself is much more straightforward and shorter.

Recent advances in structural imaging (CT, MR, MR tractography), functional imaging (fMRI) and metabolic imaging (MR spectroscopy, PET) aid in the location of pathological tissue, functional centers and neural pathways prior to planned surgery. Integrated neuronavigation technology enables real-time integration of these data with the surgical field (Roux 2001). This paved the way for the development of "image-guided surgery," currently considered standard technique worldwide.

TREATMENT PLANNING

When planning tumor resection, we must consider two vital but opposed priorities and a therapeutic dilemma: completeness of resection vs. the functional risk involved. The extent of resection is a basic prognostic factor affecting treatment outcome, the natural course of low-grade glial tumors, reducing the risk of malignant transformation and improving the patients' survival rates. In high-grade tumors, radical excision delays disease progression and improves patients' survival. We aim at the most radical excision possible, including also directly adjacent brain tissue at risk of being infiltrated by frankly neoplastic cells or apparently normal cells affected by molecular alteration favoring malignant transformation in the future (Standlbauer 2007).

On the other hand, our basic task is to preserve neurological function. The tumor resection limit should not exceed the line beyond which there is a risk of permanent loss of neurological and cognitive functions. Preservation of neural function requires preservation of the structural and functional integrity of cortical centers, as well as the afferent and efferent pathways responsible for the execution of a particular function (Fontaine 2002). The concept of "eloquent brain

areas" will be discussed below. We must keep in mind that functional integrity depends on the structural integrity not only of the brain, but of the organism as a whole. Last but not least, other issues to be considered include the cosmetic aspect of skin incision and craniotomy (the former should be kept concealed under hair and the latter – as small as possible, yet enabling anatomical orientation and efficient performance of surgery).

ELOQUENT BRAIN AREAS

The first attempts at the correlation of particular brain functions and personality traits with particular anatomical structures date back to the turn of the 18th century. Franz Josef Gall (1758-1828) and Johann Spurzheim (1776-1832) developed a theory called "phrenology," assuming the subdivision of cerebral cortex into definite centers, each constituting a structural-physical substrate for mental and neural phenomena. Inter-individual differences in aptitudes and penchants would be a result of differences in the level of development and sheer size of corresponding brain centers, which would in turn result in different skull shapes. Attempts to determine the character traits, talents, and limitations of a person based on their skull shape became very popular at that time, but in the light of current knowledge the theory has been entirely disproved. Nevertheless, this theory paved the way for attempts at evidence-based location of particular brain functions. Gall himself claimed that the "speech organ" is located in the anterior part of brain, behind the ocular globe. The idea was supported by the French physician Jean Baptiste Bouillaud, but met with severe criticism from outstanding representatives of the 19th-century scientific community. Therefore, in 1857 Bouillaud funded a prize of 500 francs for scientific elucidation of this issue. In 1861, French surgeon Paul Broca (1824-1880) presented the case of a patient who had lost speech 20 years before his death. While maintaining his intellectual abilities and comprehension for heard words intact, he was able to pronounce only "tan-tan." Today, we would probably call this motor aphasia. At autopsy, Broca found a circumscribed lesion in the posterior-basal part of the left frontal lobe. Some time later, he was faced with a similar case and found a cortical lesion at exactly the same place. Based on these observations, he concluded that here resides the center responsible for the ability to speak, and particularly to articulate (Broca 1863). When the issue of the location of speech center appeared to be elucidated, German psychiatrist and neurologist Carl Wernicke (1848-1905) demonstrated that persons with lesions in the temporo-parietal area of the left hemisphere did not understand simple commands. They were essentially able to speak, but their words could not be made into sensible statements. Based on these findings, Wernicke located here the center responsible for comprehension of speech and defined two basic "speech centers" – one responsible for production of speech (originally described by Broca) and the second – responsible for reception of speech (described by himself) (Wernicke 1882). Now we know that even as apparently simple a function of speech as calling a hammer a "hammer"

is an extraordinarily complex process, involving several brain areas (attention, vision, memory, association and speech) (FitzGerald 1997, Friederici 2003, Dufau 2008, Brown 2008). Much more complex are such processes as monologues or jokes with subtexts. All these mechanisms may be disrupted in varying configurations, resulting in the various types of aphasia known to modern neuropsychology. An in depth discussion of this issue is beyond the scope of the present study.

The complexity of the subject and the obvious methodological limitations (direct extrapolation of conclusions based on animal studies onto humans is impossible, while isolated lesions affecting a single brain center or pathway are very rare in clinical practice) result in problems with interpretation and mutually exclusive hypotheses. To simplify the issue, the essence of the dispute comes down to two basic approaches: **localization** and **anti-localization**. The former assumes the functional differentiation of particular brain structures and the strict correlation of particular mental processes with particular brain structures. The latter, in its extreme form, negates the existence of any functional differentiation within the brain. According to this theory, particularly concerning cognitive and mental functions, the brain would be an “equipotential” structure, where efficient functioning requires the preserved integrity of the entire brain. A variant of localization theory is the **connectionism**, which emphasizes the role of connections between particular brain centers in the effective performance of particular tasks. It encompasses the acquisition of information, its processing and synthesis, and the development of a coherent plan of action. In the case of speech, only humans possess the neural pathways that constitute a neuro-anatomical substrate for this ability. According to currently prevailing views, brain functioning is best explained by **dynamic localization or functional systems** theory (Bulinski et al. 2009). This assumes that the brain functions as a system of cooperating components, creating new connections and recruiting new elements in order to acquire new skills or to effectively execute a particular function. According to this concept, any more complex function will be a function of the entire brain. The contribution (share) of particular structures in the execution of particular processes will vary, and damage to the former will result in varying degrees of disturbance of the latter. One function depends on the effective cooperation of several centers, and one center may participate in the execution of several functions.

Eloquent brain areas playing a role in neurosurgical clinical practice include:

- the precentral gyrus (cortical motor center for contra-lateral body half);
- the post-central gyrus (cortical sensory center for contra-lateral body half);
- the frontal operculum in the dominant hemisphere (cortical speech motor center – Broca’s area);
- the posterior part of the superior temporal gyrus (cortical speech sensory center – Wernicke’s area);
- the insular cortex (vicinity of sub-cortical nuclei and internal capsule);
- the central region of the brain (pyramidal tract);
- the temporal-parietal-occipital trigone;
- the medial aspect of the occipital pole (Meyer’s loop and vision center);

- the brainstem (location of the reticular formation responsible for consciousness).

It is useful to distinguish the so-called “true” (or “key”) eloquent areas, whose integrity is a precondition for the preservation of a particular function, the “presumed” eloquent areas, and “non-eloquent” areas, damage to which does not result in a permanent loss of function. From the cyto-architectonical point of view, functionally critical areas feature tightly packed functional neurons or fibers and constitute the only substrate for a given function. Non-functionally critical areas either have loosely packed neural elements or there is a certain redundancy of neurons and their connections. Therefore, a lesion of similar size will result at most in a transient loss of function (Bertani 2009, Skirboll 1996, Mikuni 2007).

Nevertheless, in view of the results of recent neuropsychological studies and functional magnetic resonance imaging, there is a shift away from a stiff and static conceptualization of such systems. The cortical representation model, prevalent until now, has turned out to be oversimplified. Motor representation is located in the pre-central gyrus in about 80% of cases, but in the post-central gyrus in the remaining 20%. Similarly, sensory representation is located in the post-central gyrus in about 75%, of cases and in the precentral gyrus – in 25% (Berman 2004). A particular cortical region most probably integrates a specific pattern of movement, and not movement of a particular part of the body or particular muscles. Furthermore, a particular part of the body and a particular muscle may be controlled by several cortical centers. One center may be involved in both the preparatory and execution phase of a particular action. And all this concerns relatively simple motor tasks. In the case of higher motor functions, the organizational complexity is much higher. For example, in primates the analysis of visual stimuli involves 32 cortical centers connected by 305 neural pathways (Hubel 1962, Felleman 1991).

In pathological conditions, the brain may use preserved neuronal networks to maintain or restore lost function. Its cortical representation may be relocated to an adjacent or contra-lateral locus (“peri-lesional” or “contra-lesional” shift), enabling the return of that function after several weeks or months (Lazar 2000, Holodny 2002). Recent studies have demonstrated a redistribution of functional neuronal networks and neosynaptogenesis secondary to various brain lesions, explaining in part the transient nature of many postoperative neurological deficits. This phenomenon is known as “functional remodeling,” and involves the mobilization or unmasking of secondary or tertiary cortical centers, taking place after destruction or dysfunction of the primary center by the pathological process. Slowly progressive or chronic conditions (e.g. a slow-growing tumor) provide ample time for functional reorganization of the brain, resulting in inconsistency, scarcity, and late development of symptoms, particularly in the case of children, given the plasticity of their brains. In acute and sub-acute neurological conditions (injury, stroke or rapidly progressing malignant tumor), there is no time for reorganization, so symptoms develop earlier and are much more explicit. This may justify multi-staged procedures with a progressively enlarged extent of resection,

enabling functional adaptation of the brain to an altered anatomical and functional situation (Desmurget 2007, Duffau 2002). The phenomenon of the functional adaptation of the brain to a growing tumor and to neurosurgical interventions constitutes the basis for the concept of functional neurooncology, a novel approach to the diagnosis and treatment of brain tumors.

MAGNETIC RESONANCE IMAGING (MRI) AND MR TRACTOGRAPHY

Magnetic resonance imaging enables non-invasive visualization of the brain and lesions located within it. An MRI is in fact a graphic representation of electromagnetic signal. The object studied is subjected to a strong magnetic field (0.5-3.0 tesla), whose energy creates an electronic spin (vector of rotation) of all atoms making up the organism. The field is then switched off and the atoms return to their resting state, emitting excess energy in the form of photons at a definite wave amplitude and frequency. Based on analysis of the data acquired within a particular plane, a cross-sectional image of the organism is built. By modifying the applied energy, relaxation time and parameters of signal analysis, different aspects of tissues may be visualized, e.g. water and fat content, or the motion of liquid medium ("flow void") within a given area. The study also enables the analysis of the content of particular substances in the tissue studied (MR spectroscopy), providing a rough insight into the histology of the lesion (normal vs. inflammation vs. ischemia vs. necrosis). Further information concerning the intensity of blood flow through the tissue studied may be provided by the addition of paramagnetic contrast material (gadolinium pentatechinate). Anisotropy (differences in concentration and direction) of water diffusion enables the determination of the predominating direction of myelinated nerve fibers in a particular segment of the brain ("eigenvector"). The result is the visualization of the main fiber tracts within the white matter and their relation to the tumor. This depends largely on the adopted threshold of fractional anisotropy, the histological type and location of the tumor, and the edema associated with it (Beaulieu 2002, Clark 2003). Due to the technical complexity of the procedure and inter-individual variations, the determination of the predominating direction of fibers may be largely subjective and operator-dependent. Further problems arise with intraoperative shift caused by the excision of the tumor, the relief of hydrocephalus, and edema in manipulated tissues.

According to the Savay classification, a tumor-related lesion may be far from an eloquent area (category I), close to an eloquent area (category II), and within an eloquent area (category III). A similar classification applies to the relation of tumors to nerve fiber pathways, which may be far from the tumor, or may be displaced, infiltrated or transected by the tumor (or surgeon) (Nimsky 2005).

FUNCTIONAL MAPPING (FMRI) AND ELECTROCORTICAL STIMULATION

In the clinical setting, the mapping of particular functions and centers is performed as part of the preparation for planned surgery in or near the above-mentioned eloquent areas and/or their afferent or efferent pathways, particularly those affecting speech, vision and motor functions. Other skills, e.g. reading, calculating, writing, spatial orientation and operational memory are rarely tested, as they are not as vulnerable as speech and movement. The functions analyzed include the movement of limbs, touch, speech, memory and vision. A clinical neuropsychologist participates in the study, and good cooperation from the patient is paramount, making this method completely impractical in the case of infants or persons with compromised contact.

The imaging of cortex brain activity is possible thanks to functional magnetic resonance imaging (fMRI). Scanning of the brain at high frequency (every 2-3 seconds) but at low resolution enables to determine areas activated during the performance of specific tasks. The registered images are obtained secondary to changes of signal emitted by brain tissue as a consequence of a changed neuronal activity level, inducing altered regional blood flow and oxygen consumption, resulting in an elevated level of deoxyhemoglobin in venous blood. This, the so-called BOLD (blood oxygen level-dependent) effect in active areas of the brain, is visualized as an enhanced signal in T2-weighted scans (Holodny 2000, Stadlbauer 2007). During the study, the patient executes several tasks, alternating them with resting periods or another well-defined task. Brain scans obtained during activation and during rest undergo statistical processing, correlations are calculated, and areas of significant differences are color-coded and overlaid on the baseline image. Repetition of the task and image acquisition is necessary in order to differentiate activity-related signal alteration from background noise (Bizzi 2008, Duffau 2005).

fMRI provides information concerning the spatial and temporal organization of neuronal activity when executing a particular task. Significantly, the BOLD-marked area and the actual location of active tissue may differ by even 3-6 mm. Furthermore, there is always a few seconds' delay between the start of an event at the neuronal level and the BOLD effect visualized by MRI, while chronological relations between activity and hemodynamic response are constant in particular brain areas. This may be used to study the chronological order of activation in particular networks and centers, to monitor and study their features and to differentiate normal and pathological behaviors. Coupled high-frequency oscillators will be visualized by fMRI as parallel areas of activation.

fMRI maps are integrated with neuronavigation systems and used during surgery, showing the location of functional structures in the operating field, but they are not entirely reliable. Their interpretation and use requires considerable expertise and experience. Contrary to many authors' suggestions and manufacturers' claims, there are no standardized and objective (operator-independent) fMRI

protocols, which might easily and reliably localize even the simplest functions, e.g. primary motor activity. It is difficult, if not impossible, to create a task protocol, involving only one particular function and differentiating brain areas primarily involved in its execution from those secondarily involved. An example of this is the activation of primary motor areas, secondary motor areas and association fields in response to the command "move your hand." fMRI-derived location of a given function incompatible with what was expected may be due to artifacts-related bias or a too low statistical threshold. It may also show the actual location of that function, resulting from atypical primary location or secondary displacement (see below).

An equally important issue is lack of activation, also dependent on several factors, some of which may be difficult, if not impossible to control. A tumor or vascular malformation may cause a brain shift or disturb local blood flow, attenuating or eliminating the BOLD effect, providing a false-negative result. On the other hand, activity visualized within the tumor-infiltrated tissue may not necessarily be false-positive and may reflect actual functional status, which has been confirmed several times by electro-cortical-stimulation studies (Holodny 2000).

The inconsistency of fMRI results is an important clinical problem. fMRI findings largely depend on the changing neurophysiological status of the particular patient at the time of the study. Their interpretation is biased by subjectivism, particularly concerning the selection of tasks, the selection of a biomathematical model, and the assessment of the degree of vascular-nervous coupling. Therefore, repeated examination of the same person using the same protocol may yield different results. Some factors responsible for this phenomenon are known (e.g. the technical parameters of MRI hardware, fluctuating intensity of the magnetic field, respiration- and pulse-related artifacts). To a certain extent they may be controlled, but some discrepancies between consecutive studies in the same person may be due to factors so far unknown.

In this setting, the "golden standard" in locating functional cortex is electrophysiological stimulation, enabling individual tracking of neural function centers, precise determination of the extent of resection and optimal treatment outcomes. Unfortunately, its use necessitates the patient's cooperation. In the case of children with cognitive or emotional disturbances or neurological deficits, this is often impossible. Electrophysiological techniques consist in direct intra-operative stimulation of brain tissue. A few seconds' depolarization of a limited cortical area causes local excitatory or inhibitory potential, resulting in altered function. Problems with the execution of a particular task after stimulation of a particular area imply correlation between that particular area and that particular function. Such a correlation may be "positive", i.e. stimulation of a particular area affects particular functions, or "negative", i.e. stimulation does not affect the function studied. Initially, cortical mapping relied more on positive findings, while at present investigators focus rather on negative findings. This enables smaller craniotomy and probing over a smaller cortical area, reducing the time spent on mapping and the duration of surgery. Unfortunately, in the case of speech centers, negative mapping does not imply the lack of functionally critical tissue. Permanent neuro-

logical deficits have been reported in spite of negative mapping, seriously undermining the rationale for using this relatively burdensome technique.

Studies comparing fMRI, electrostimulation mapping and amobarbital (Wada) test revealed an incomplete concordance between these modalities (Binder 1996, Kho 2005). Therefore, fMRI may not replace the other techniques, and further studies and improvements are warranted. Entirely concordant results will probably never be obtained, due to fundamental methodological differences. All these methods provide an insight as to immediate postoperative results, but not as to delayed or ultimate functional status, i.e. if and to what extent preserved local and distant neuronal networks will be able to compensate for the loss of a given function. Concordance between fMRI and ESM is estimated at 92% and their sensitivity at 88%. The sensitivity of PET and fMRI is estimated at 75% and 81%, respectively. The specificity of PET and fMRI is estimated at 81% and 53%, respectively (Hunter 1999). All phases of fMRI study (data acquisition, processing and interpretation) are inter-dependent, and even small changes in any component of the procedure may considerably affect maps of activation obtained. Therefore, contrary to investigators', clinicians' and patients' expectations, there is not a 100 % guarantee of success.

CONDITIONING

Prior to the fMRI session proper, patients may need a training session, in order to familiarize themselves with the study procedure and the type of stimuli provided. However, persons with neurological deficits or cognitive disorders may have problems with attention span and fatigue. On the other hand, having learned expected behaviors prior to the fMRI session, the patient may mobilize memory and associative areas in addition to first- or second-order areas responsible for execution of a given function. Recently introduced MR imaging techniques (e.g. resting state functional connectivity mapping) should address these issues and eliminate the impact of disturbances in the execution of commands on the activation maps obtained, but protocols of these studies are still not entirely reliable and consistent on the individual level, as postulated in the microgenetic model of symptom formation proposed by Brown and Pachalska (2003).

CONCLUSIONS

Current views on the functional organization of the human brain and modern neuroimaging techniques enable increasingly effective and safe surgical treatment of neurological diseases, including brain tumors. The data provided by fMRI may contribute to the development of individualized rehabilitation techniques, supporting the reorganization of brain function and providing an optimal functional outcome. Clinical neurosurgery not only benefits from the achievements of basic sciences, but contributes considerably to the progress of brain function studies. Still, the currently available techniques used for objective assessment of brain activity are imperfect, enabling an at most approximate localization of

functionally critical areas. Consequently, neurosurgical procedures at or near eloquent areas are still associated with a considerable risk of transient or permanent postoperative dysfunction. Hopefully, this is a rapidly expanding domain of research and further progress is to be expected.

REFERENCES

- Beaulieu, C. (2002). The basis of anisotropic water diffusion in the nervous system—a technical review. *NMR Biomedicine*, 15, 435-455.
- Berger, M.S. & Hadjipanayis C.G. (2007). Surgery of intrinsic cerebral tumors. *Neurosurgery*, 61 (1 Suppl), 279-305.
- Binder, J.R., Swanson, S.J., Hammeke, T.A., Morris, G.L., Mueller, W.M., Fischer, M. et al. (1996). Determination of language dominance using functional MRI: a comparison with the Wada test. *Neurology*, 46, 978-984.
- Bizzi, A., Blasi, V., Falini, A., Ferroli, P., Cadioli, M., Danesi, U. et al. (2008). Presurgical functional MR imaging of language and motor functions: validation with intraoperative electrocortical mapping. *Radiology*, 248, 579-589.
- Broca, P. (1863). Localisation des fonction cérébrales. Siege de la faculte de language articule. *Bulletin de la Faculte d'Anthropologie*, 4, 200-208.
- Brown, J. (2008). Time and process in neuropsychology. *Acta Neuropsychologica*, 6(3), 215-236.
- Brown, J.W. & Pachalska, M. (2003). The symptom and its significance in neuropsychology. *Acta Neuropsychologica*, 1(1), 1-11.
- Bulinski, L., Pachalska, M. & Brown, J. (2009). Language processing : a neuropsychological perspective. *Acta Neuropsychologica*, 7(2), 93-112.
- Clark, C.A., Barrick, T.R., Murphy, M.M. & Bell, B.A. (2003). White matter fiber tracking in patients with space-occupying lesions of the brain: a new technique for neurosurgical planning? *NeuroImage*, 20, 1601-1608.
- Coenen, V.A., Krings, T., Mayfrank, L., Polin, R.S., Reinges, M.H., Thron, A. et al. (2001). Three-dimensional visualization of the pyramidal tract in a neuronavigation system during brain tumor surgery: first experiences and technical note. *Neurosurgery*, 49, 86-93.
- Desmурget, M., Bonnetblanc, F. & Duffau, H. (2007). Contrasting acute and slow-growing lesions: a new door to brain plasticity. *Brain*, 130, 898-914.
- Duffau, H. (2005). Lessons from brain mapping in surgery for lowgrade glioma: insights into associations between tumour and brain plasticity. *Lancet Neurology*, 4, 476-486.
- Duffau, H., Lopes, M., Arthuis, F., Bitar, A., Sicchez, J.P., Van Effenterre, R. et al. (2005). Contribution of intraoperative electrical stimulations in surgery of low grade gliomas: a comparative study between two series without (1985-96) and with (1996-2003) functional mapping in the same institution. *Journal of Neurology, Neurosurgery & Psychiatry*, 76, 845-851.
- Felleman, D.J., Van Essen, D.C. (1991). Distributed hierarchical processing in the primate cerebral cortex. *Cerebral Cortex*, 1, 1-47.
- FitzGerald, D.B., Cosgrove, G.R., Ronner, S., Jiang, H., Buchbinder, B.R., Belliveau, J.W. et al. (1997). Location of language in the cortex: a comparison between functional MR imaging and electrocortical stimulation. *AJNR American Journal of Neuroradiology*, 18, 1529-1539.
- Holodny, A.I., Schulder, M., Liu, W.C., Wolko, J., Maldjian, J.A. & Kalnin, A.J. (2000). The effect of brain tumors on BOLD functional MR imaging activation in the adjacent motor cortex: implications for image-guided neurosurgery. *AJNR American Journal of Neuroradiology*, 21, 1415-1422.
- Holodny, A.I., Schulder, M., Ybasco, A. & Liu, W.C. (2002). Translocation of Broca's area to the contralateral hemisphere as the result of the growth of a left inferior frontal glioma. *Journal of Computer Assisted Tomography*, 26, 941-943.
- Hubel, D.H. & Wiesel, T.N. (1962). Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *Journal of Physiology*, 160, 106-154.
- Hunter, K.E., Blaxton, T.A., Bookheimer, S.Y., Figlozzi, C., Gaillard, W.D., Grandin, C. et al. (1999). ^{(15)O} water positron emission tomography in language localization: a study comparing positron

- emission tomography visual and computerized region of interest analysis with the Wada test. *Annals of Neurology*, 45, 662-665.
- Inoue, T., Ogasawara, K., Beppu, T., Ogawa, A. & Kabasawa, H. (2005). Diffusion tensor imaging for preoperative evaluation of tumor grade in gliomas. *Clinical Neurology & Neurosurgery*, 107, 174-180.
- Keles, G.E., Lamborn, K.R. & Berger, M.S. (2001). Low-grade hemispheric gliomas in adults: a critical review of extent of resection as a factor influencing outcome. *Journal of Neurosurgery*, 95, 735-745.
- Kho, K.H., Leijten, F.S., Rutten, G.J., Vermeulen, J., Van Rijen, P. & Ramsey, N.F. (2005). Discrepant findings for Wada test and functional magnetic resonance imaging with regard to language function: use of electrocortical stimulation to confirm results. *Journal of Neurosurgery*, 102, 169-173.
- Lazar, R.M., Marshall, R.S., Pile-Spellman, J., Duong, H.C., Mohr, J.P., Young, W.L. et al. (2000). Interhemispheric transfer of language in patients with left frontal cerebral arteriovenous malformation. *Neuropsychologia*, 38, 1325-1332.
- McGirt, M.J., Chaichana, K.L., Attenello, F.J., Weingart, J.D., Than, K., Burger, P.C. et al. (2008). Extent of surgical resection is independently associated with survival in patients with hemispheric infiltrating low-grade gliomas. *Neurosurgery*, 63, 700-708.
- McGirt, M.J., Chaichana, K.L., Gathinji, M., Attenello, F.J., Than, K., Olivi, A. et al. (2009). Independent association of extent of resection with survival in patients with malignant brain astrocytoma. *Journal of Neurosurgery*, 110, 156-162.
- Mikuni, N., Okada, T., Enatsu, R., Miki, Y., Hanakawa, T., Urayama, S. et al. (2007). Clinical impact of integrated functional neuronavigation and subcortical electrical stimulation to preserve motor function during resection of brain tumors. *Journal of Neurosurgery*, 106, 593-598.
- Nimsky, C., Ganslandt, O., Hastreiter, P., Wang, R., Benner, T., Sorensen, A.G. et al. (2005). Intraoperative diffusion-tensor MR imaging: shifting of white matter tracts during neurosurgical procedures-initial experience. *Radiology*, 234, 218-225.
- Schiffbauer, H., Ferrari, P., Rowley, H.A., Berger, M.S. & Roberts, T.P. (2001). Functional activity within brain tumors: a magnetic source imaging study. *Neurosurgery*, 49, 1313-1321.
- Shaw, E.G., Berkey, B., Coons, S.W., Bullard, D., Brachman, D., Buckner, J.C. et al. (2008). Recurrence following neurosurgeon-determined gross-total resection of adult supratentorial low-grade glioma: results of a prospective clinical trial. *Journal of Neurosurgery*, 109, 835-841.
- Skirboll, S.S., Ojemann, G.A., Berger, M.S., Lettich, E. & Winn, H.R. (1996). Functional cortex and subcortical white matter located within gliomas. *Neurosurgery*, 38, 678-685.
- Stadlbauer, A., Nimsky, C., Buslei, R., Salomonowitz, E., Hammen, T., Buchfelder, M. et al. (2007). Diffusion tensor imaging and optimized fiber tracking in glioma patients: histopathologic evaluation of tumor-invaded white matter structures. *Neuroimage*, 34, 949-956.
- Wernicke, C. (1882). Über Aphasie und Anarthrie. *Deutsche Medizinische Wochenschrift*, 8, 163.

Address for correspondence:

Paweł Daszkiewicz
Klinika Neurochirurgii
Instytut Pomnik Centrum Zdrowia Dziecka
Al. Dzieci Polskich 20
04-730 Warszawa
Phone : 22 815 75 60
Fax : 22 815 75 57
e-mail: pmdaszewicz@o2.pl