

Knowledge modeling in image-guided neurosurgery: application in understanding intraoperative brain shift

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ABSTRACT

During an image-guided neurosurgery procedure, the neuronavigation system is subject to inaccuracy because of anatomical deformations which induce a gap between the preoperative images and their anatomical reality. Thus, the objective of many research teams is to succeed in quantifying these deformations in order to update preoperative images. Anatomical intraoperative deformations correspond to a complex spatio-temporal phenomenon. Our objective is to identify the parameters implicated in these deformations and to use these parameters as constrains for systems dedicated to updating preoperative images. In order to identify these parameters of deformation, implementation and validation. A state of the art about cortical deformations has been established in order to identify relevant parameters probably involved in the deformations. As a first step, 30 parameters have been identified and described following an ontological approach. They were formalized into a Unified Modeling Language (UML) class diagram. We implemented that model into a web-based application in order to fill a database. Two surgical cases have been studied at this moment. After having entered enough surgical cases for data mining purposes, we expect to identify the most relevant and influential parameters and to gain a better ability to understand the deformations.

Keywords: Image-guided surgery, brain shift, knowledge modeling, formalization, data mining

1. INTRODUCTION

During an image-guided neurosurgery procedure, the first main deformation (also called brain shift) occurs while opening the dura matter and the arachnoid. Following deformations are related to the surgical event. These deformations are complex because they depend on many inter-dependent factors such as gravity, loss of cerebro-spinal fluid (CSF), lesion size, etc. Another aspect of this phenomenon's complexity is its spatio-temporal aspect. Deformations are different according to the timing of the surgical procedure and to the surgical action being performed. Deformations are also different according to the anatomical structures and their spatial location. As a consequence, the intraoperative cerebral anatomy diverges from the preoperative anatomy and therefore from its corresponding preoperative images. This can be problematic as surgeons partly base their action on functional and anatomical preoperative images. Thus, the objective of many research teams is to succeed in registering preoperative images regarding these deformations. This can be achieved by using intraoperative imaging¹ and/or biomechanical models². Nevertheless, current research cannot provide an image-only based complete working system for solving this complex problem because of several technical difficulties such as the limited intraoperative MRI spatial resolution and the poor temporal resolution of registration algorithms. For optimizing current systems we think that a better understanding of the deformation phenomenon would bring relevant constrains to the existing registration algorithms.

In this paper, we propose an approach based on numerical and symbolical information about the deformation phenomenon. This information can be either preoperative (e.g., patient positioning, lesion histology) or intraoperative (e.g., gravity direction, arterial partial pressure of CO_2 , loss of CSF). One objective is to identify such parameters in order to understand this deformation phenomenon more precisely. With our approach we want to isolate and to weight parameters involved in the anatomical deformations.

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2. MATERIAL AND METHODS

In order to identify causes related to the deformations we followed the iterative methodology used for cognitive system conception, i.e., identification, conceptualization, formalization, implementation and validation. Introduced by A. Gomez-Perez *et al.* for an industrial use, this iterative process tends to an optimal solution thanks to a progressive refinement^{3,4}. To apply this method to our context we studied the literature related to brain shift. Then, parameters probably involved in this phenomenon were considered. Software was developed to save into an SQL database parameters and cortical shift measurements for each surgical case. By now we have achieved the first four phases of the iterative schema which are described as follows.

The objective of the identification phase is to provide an exhaustive list of parameters probably involved in the deformations. We based our identification on the experts' consensus, which can be found in the literature. In this manuscript we only quote the most relevant articles that helped the identification phase. The iterative process will then confirm or infirm the relevance of each parameter. Some research groups have already partially started to identify parameters implicated in the deformations^{1,5,6,7}.

The conceptualization phase provides an ontology for organizing all parameters. Some logical concepts were extracted from the list of parameters in order to describe them more precisely (e.g., patient-linked parameters, physiological-linked parameters). To validate this phase, we presented our ontology to two neurosurgeons of the University Hospital Center in Rennes. They evaluated the relevance of our ontology by pointing out the redundancy of some parameters and by confirming the quasi-independence of each category of parameters. One main difficulty of this work was that each parameter may be related to one or more other parameters. Inter-dependences between parameters have been considered during this phase.

The formalization established an interface for all identified concepts to be understood. It provided a model of parameters based on a universal language. We chose the UML^{*} representation. This language has mostly been chosen in order to match an existing UML class diagram that models surgical procedure⁸.

During the implementation phase, we filled an SQL database with surgical cases. For each surgical case two kinds of data have been entered:

- Qualitative or quantitative measurements of parameters related to the deformations,
- Intraoperative cortical shift measurements.

Methods for measurement of parameters are described in table 1. Intraoperative cortical shift measurements were achieved with a surgical tool, which was localized by the infrared camera of the neuronavigation system. We measured the mean displacement of the cortical surface by taking some landmarks on the cortical surface and by comparing them with the preoperative MRI. This method has already been used for brain shift quantification¹.

3. RESULTS

As a first step, 30 parameters were identified as being involved in the anatomical deformations. All of them were described by a model following an ontological approach. They are listed on table 1. We also included inter-parameter dependences although these were not described at a numerical level. Indeed the difficulty was to stay at a general level of description for a better understanding of this notion of inter-dependence. We also specified on table 1 the manner of acquiring and representing some of the parameters. Subsection 3.1 presents the results of the identification and conceptualization phases and subsection 3.2 shows the UML model of parameters.

3.1. Identification process

Physical parameters. <u>Gravity</u> is the only parameter that was put under the physical category. Its influence on the main direction of matter displacement was often reported in the literature^{5,7,9,10,11,12,13,14,15}. While opening the arachnoid, the loss of CSF creates an unoccupied space within the intracranial cavity. As a consequence the brain collapses following

^{*} http://www.uml.org

the direction of gravity. Furthermore, during surgical resection the residual matter also tends to collapse. Gravity has no inter-dependence with other listed parameters.

Physiological parameters. Loss of CSF is also often quoted^{2,5,6,7,9,10,11,12,13,15,16,17,18}. As described previously the brain occupies CSF space during the intervention. This fluid flows through the cranial window but it can also be drained. In some cases, reduction of CSF production was noticed. Intracranial pressure is said to have direct influence on the deformations^{7,9,10}. Nevertheless one must be aware that the brain shift phenomenon is the direct consequence of an intracranial hyper- or hypo-tension while opening the arachnoid. We are here at the border between the cause and the description of the phenomenon. Anyway it may be of interest to consider this parameter as it can physically be quantified for our database. Edema presence and size influence the intracranial pressure and thus the brain shift^{6,7,11,12,13}. In the literature, tissue swelling was also mentioned as a parameter, but we chose not to distinguishing between tissue swelling and edema. Edema presence depends on steroid injection. The elasticity of the brain, including the arterial system, determines its potentiality of being deformed and thus its capability of replacing the CSF lost. It depends on patient age, on arteriosclerosis and on edema width. Although one can easily determine an average of the brain and arterial system's elasticity through extra-patient measurement, it is difficult to quantify these parameters for one patient. Cerebral blood volume has been reported as influencing the deformations^{7,13,14,18}. It depends on many factors such as CO_2 partial pressure, patient positioning, magnitude of bleeding and potential transfusion of colloid, crystalloid or blood. Arterial partial pressure of CO₂ is measured and controlled by anaesthetists. It determines vessel dilatation and thus the perfusion, which influences the deformations^{1,5,13}.

Surgical-related parameters. Type of surgical procedure may predict the magnitude of deformation^{5,7,9,11}. For instance, T. Hartkens et al. showed differences in amplitudes of deformation on 24 patients by comparing three kinds of intervention: resection, biopsy and functional interventions⁹. They underlined that in the case of a resection, deformations occurred at a higher degree. The notion of <u>surgical step</u> was considered as well^{7,10,12,13,15,16,17,18}. Indeed, we intuitively and obviously understand that hair shaving induces less deformation than dura matter opening and that the kind of deformation is different between the access to the lesional area (matter displacement) and the removal of the lesional area (matter removal). We can refer to a model of surgical procedures proposed by P. Jannin et al. that helps to clarify this notion of surgical step8. Step duration was also considered. For instance, D.L.G. Hill et al. underlined the implication of this parameter by quantifying cortical surface at a one-hour interval before resection¹. Furthermore, the type of surgical tool must be noticed as they do not all have the same influence on matter. The positioning of the patient may also have an influence on the brain shift phenomenon 1,6,7,12,15 . For instance, a ventral decubitus position induces an increase of the intracranial pressure; consequently when opening the dura matter the brain swells instead of collapsing. Patient positioning may depend on the gravity, the craniotomy localization and the age of patient because some positionings are too risky for elderly people (i.e., extreme angles between body's and head's axis). <u>Craniotomy size</u> and <u>craniotomy localization</u> are also involved in the deformations^{1,5,6,9,17,19}. These parameters naturally depend on the lesion localization and the positioning of the patient. Ventricular system opening may induce anatomical deformations that occur at a deeper level^{7,6,15}. <u>Hyperosmolar agent injection</u> has an influence on bleeding. This could have an impact on the deformations^{1,6,7,10,11,13,15,16,17,19}. To better understand these inter-dependences we can look at the Monroe-Kelly law, which correlates volumes of blood, CSF and tissue²⁰. As noted before, steroid injection has an influence on edema and thus on intracranial pressure, which is directly correlated to brain shift¹⁹

Patient-related parameters. These *a priori* known parameters include <u>age of patient</u>¹, <u>Arnold-Chiari malformation</u> (related to intracranial pressure and CSF flowing) and lesion-related information. We distinguished the <u>lesion</u> <u>size</u>^{6,7,15,16,19} (related to the loss of matter after resection), the <u>lesion localization</u>^{1,6,7,9,14,15,16,19} (related to the positioning of the patient), the <u>lesion shape</u> and the <u>lesion type</u> (related to edema). <u>Cerebral atrophy</u>, which is related to patient age, was sometimes quoted as being involved in the deformations^{14,19}. It determines the proportion of CSF within the intracranial cavity related to the brain volume. Its influences may be described as follows: when the neurosurgeon opens the dura matter, a higher quantity of CSF than normal flows out from the cranial window, the brain shift phenomenon may then be more substantial.

Biomechanical parameters. Biomechanical parameters are also related to the deformations, as they describe the brain's behaviour. We preferred to define a single biomechanical category rather than to include them in the physiological category, since their values are *a priori* known. These parameters are: the <u>Young modulus</u> (ratio of stress to strain on the loading plane along the loading direction), the <u>saturation coefficient</u> (describes the quantity of water within the brain),

the <u>Poisson ratio</u> (ratio of lateral strain to axial strain), the <u>hydraulic conductivity</u> (capacity of a soil to conduct water through it) and the <u>density</u> of tissues.

3.2. Working with the parameters

We proposed a UML model of parameters, which provides a convenient overview of all parameters implicated in the deformation (see figure 1). Each category of parameters was represented by a class. Each parameter of deformation was represented by a class attribute. We designated a 'Physical' class which contained the physical parameters, a class 'Physiological' which contained the physiological-related parameters, a 'Surgical' class which contained the parameters describing the surgical procedure, a 'Patient' class which contained the parameters, a 'Lesion' class which contained the lesion-related parameters and a 'Biomechanical' class which contained the parameters used in biomechanical brain modeling.

This model of parameters has been implemented into a web-based software in order to fill the database with surgical cases. Surgeons have also used this interface to plan surgical procedures, i.e., to enter information related to patient, pathology, positioning, and predictive surgical steps. The data of two surgical cases has already been entered. Both patients for whom the database has been filled underwent surgery for a tumor and a cavernous removal respectively.



Figure 1. UML class diagram showing parameters involved in brain deformations

	Dependences	Type	Representation	Environment	Acquisition methods
Physical parameters					*
Gravity	none	quantitative	vector	intraoperative	An horizontal plan was localized by the pointer of the neuronavigation system
Physiological parameters					
Loss of CSF	natural loss, decrease of CSF production, subarachnoid space drainage and aspiration	quantitative	volume (in L)	intraoperative	hard to quantify
Intracranial pressure	To be determined	quantitative	pressure (in Pa)	intraoperative	invasive pressure probe
Edema	lesion type, steroid injection	qualitative	arbitrary edema scale	preoperative	preoperative image analysis
Elasticity of the brain including cerebral arterial system	patient age, arteriosclerosis, edema	qualitative	elasticity (in Pa)	intraoperative	extra-patient measurement (see the biomechanical parameters part)
Cerebral blood volume	arterial partial pressure of CO ₂ , patient positioning, systemic blood pressure, hemorrhage, colloid, crystalloid or blood transfusion	quantitative	volume (in L)	intraoperative	hard to quantify
Arterial partial pressure of CO ₂	artificial ventilation	quantitative	pressure (in Pa)	intraoperative	measured and controlled by the anaesthetists
Surgical parameters					
Type of surgical procedure	lesion type	qualitative	resection, biopsy, electrodes placing, hippocampectomy, etc.	preoperative	surgical planning
Step type	none	qualitative	dura-matter opening, resection, etc.	intraoperative	surgical description
Step duration	none	quantitative	duration (in min)	intraoperative	measured with a chronometer
Step tool	surgical step	qualitative	scalpel, bipolar electrodes, etc.	intraoperative	surgical description
Positioning of patient (body)	lesion localization, patient age	qualitative	decubitus, etc.	preoperative	surgical planning
Positioning of patient (head)	lesion localization, patient age	qualitative, quantitative	angle deviation from known standard positions	preoperative	surgical planning
Craniotomy localization	lesion localization	quantitative	coordinates	intraoperative	craniotomy tracing with pointer
Craniotomy size	lesion size	quantitative	side length	intraoperative	craniotomy tracing with pointer
Ventricular system opening	lesion localization	qualitative	boolean	intraoperative	surgical description
Hyperosmolar agent injection	bleeding	qualitative, quantitative	molecule name, injected volume, time after injection, agent osmolarity	intraoperative	intraoperative data
Steroid type, quantity and time of injection	edema	qualitative	molecule name, volume and time	preoperative	preoperative data
Patient parameters					
Age of patient	none	quantitative	age (in years)	preoperative	patient data
Arnold-Chiari malformation	none	qualitative	Chiari I, II, III, IV	preoperative	preoperative image analysis
Lesion type	none	qualitative	cavernous, tumor, etc.	preoperative	preoperative image analysis
Lesion localization.lobe	none	qualitative	frontal, parietal, etc.	preoperative	preoperative image analysis
Lesion localization.zone	none	qualitative	gyrus, sulcus, etc.	preoperative	preoperative image analysis
Lesion shape	none	qualitative	oval, round	preoperative	preoperative image analysis
Lesion size	none	quantitative	volume, axis length	preoperative	preoperative image analysis and segmentation
Cerebral atrophy	age of patient	qualitative	atrophy scale	preoperative	preoperative image analysis
Biomechanical parameters					
Young modulus	none	quantitative	elasticity (in Pa)	preoperative	averaging of several physiological measurements, e.g., extrapoled values from pork.
Saturation coefficient	none	quantitative	in Pa-1	preoperative	id.
Poisson ratio	none	quantitative	no unit	preoperative	id.
Hydraulic conductivity	none	quantitative	in m ³ .s/kg	preoperative	id.
Density	none	quantitative	in kg.m ⁻³	preoperative	id.

Table 1. List of parameters involved in anatomical intraoperative brain deformations. L stands for Liter, Pa for Pascal, m for meter, s for second, kg for kilogram and min for minute.

4. DISCUSSION

Numerical and symbolical parameters involved in brain deformations were identified, organized under certain criteria and formalized into a UML class diagram. That model was implemented into a web-based software in order to fill a database. This database contains all parameters and cortical shift measurements related to each surgical case. After having entered enough surgical cases for data mining purposes, we expect to gain a better understanding of the deformation phenomenon and its most relevant parameters. Present literature only partially quotes probable parameters involved in the deformations. Our work enables a better understanding of these parameters by following an ontological approach. It also presents a new direction for finding constrains for algorithms dedicated to registering intraoperative with preoperative images.

4.1. Data acquisition

Intraoperative acquisition of some parameters is a difficult task. We proposed methods to acquire some parameters, e.g., measurement of the direction of gravity could be performed thanks to a neuronavigation system. Some other parameters are more difficult to quantify. For example, the volume of the intracranial cavity, which is often quoted in the literature, can be quantified by segmentation of the preoperative MRI, but the main difficulty would be to propose a standard edge for the region of interest. Furthermore, the shape of the intracranial cavity should also be considered because the brain does not behave the same way for different cranial shapes at equivalent intracranial volumes. We did however acquire some parameters that are not mentioned in the literature, such as the gender of the patient and its laterality.

4.2. Limits of the method

Although our aim was to reach an exhaustive identification, we are aware that this literature-based study is not fully objective. It was based primarily on the experts' consensus. Some questions remain concerning the comprehensiveness of our approach:

- How to estimate the relevance of each of the parameters quoted in the literature?
- Are there other parameters involved in the deformations that were not considered?

We chose an iterative method in order to validate the implication and weight of each parameter. Furthermore, this work is at the first step of that iterative process, which aims at identifying in a most relevant way all parameters involved in anatomical deformations. They will be of use either for understanding the deformation phenomenon or as complementary quantified data as input for preoperative images registration systems. The aim therefore is not to provide a methodology for modeling the brain behaviour like the ones used for biomechanical models. This is, rather, an approach of knowledge modeling applied to the problem of anatomical deformations.

The conceptualization phase was mainly based on intuition. Indeed, we could have chosen other criteria for the categorization and for the instancing of the parameters. This raises two other questions:

- Are the categories proposed to describe the parameters the most relevant?
- Are the dependences between parameters exhaustive?

Concerning the first point, the chosen categories were considered as help for future investigations rather than as a standard basis for categorization of parameters. The conceptualization phase had no influence on the parameters' intrinsic descriptions, but did have influence on their inter-dependences. These inter-dependences were designed with the help of a neurosurgeon, and were unequally hard to identify. On the one hand, some parameters have clearly identified dependences such as edema presence which is conditioned by the lesion type (e.g., a tumor will often generate edema and cavernous will not). On the other hand, parameters such as the cerebral blood volume or the intracranial pressure have poorly identified dependences. The difficulty is to set the granularity level we need for such an analysis. We have tried here to initiate a study of these inter-dependences that should be pursued through a collaboration between several expert groups such as physiologists, neurosurgeons, physicians and mathematicians. For instance, a more exhaustive description of the encountered inter-dependences could be achieved by integrating existing physical and physiological models for each of the parameters. The formalization provided in this paper brings a convenient overview of the parameters and could thus help such a collaboration.

4.3. Perspectives

The proposed UML class diagram does not show the weight of each parameter implicated in the deformations, e.g., we think that some parameters, such as gravity or loss of CSF, will have particular influences on the deformations. Thus, a graduation of each parameter towards their influence (amplitude of the deformations) and relevance (interest for the neurosurgeon) is conceivable. The notion of relevance corresponds to the interest for the neurosurgeon of being aware about certain deformations. For instance, if a deformation is detected far from the surgical region of interest, the neurosurgeon would be informed about both this deformation and its poor relevance.

The database of qualified and quantified parameters could provide several possibilities of investigation. Firstly, a data mining process could be of interest in order to extract the most relevant parameters related to anatomical deformations. This investigation could give us a new perspective on brain shift understanding. Secondly, a statistic-based algorithm could give for each surgical case a mean and a maximal deformation for *a priori* known parameters (e.g., patient positioning, lesion size, lesion location, gravity direction, etc.). These mean and maximum statistical values could then be used as input for registration processes based on intraoperative imaging or biomechanical models.

Moreover, one of the main difficulties of our work was the non-existence of standards for characterization of some physiological parameters. For instance, there is no consensus around edema qualification. An edema is said to be more or less prominent depending on the physician who qualifies it. We think therefore that the standardization of some parameters would increase the accuracy of some parameter qualifications.

This approach is the first step of an investigation for better understanding brain deformations during surgery. We believe that results from further studies will confirm some surgeons' intuition about brain behaviour and will provide additional information for the quantification of these deformations.

REFERENCES

- 1. D.L.G. Hill, C.R. Maurer, R.J Maciunas, J.A Barwise, J.M Fitzpatrick W.Y Wang, "Measurement of intraoperative brain surface deformation under a craniotomy", Neurosurgery, **43**(3), 514-526, 1998.
- 2. M.I. Miga, D.W. Roberts, F.E. Kennedy, L.A. Platenik, A. Hartov, K.E. Lunn and D.K. Paulsen, "Modeling of retraction and resection for intraoperative updating of images", Neurosurgery, **49**(1), 75-85, 2001.
- 3. A. Gomez-Perez, M. Fernandez and A.J. De Vicente, "Towards a Method to Conceptualize Domain Ontologies", ECAI-96 Workshop on Ontological Engineering, Budapest, 1996.
- 4. C. Warren and A.D. Whitefield, "The role of task characterisation in transferring models of users: the example of engineering design", Human-Computer Interaction Interact'87, 237-243, 1987.
- 5. D.W. Roberts, A. Hartov, F.E. Kennedy, M.I. Miga and K.D. Paulsen, "Intraoperative brain shift and deformation: a quantitative analysis of cortical displacement in 28 cases", Neurosurgery, **43**(4), 749-758, 1998.
- C. Nimsky, O. Ganslandt, S. Cerny, P. Hastreiter, G. Greiner and R. Fahlbusch, "Quantification of, visualization of, and compensation for brain shift using intraoperative magnetic resonance imaging", Neurosurgery, 47(5), 1070-1079, 2000.
- N.L. Dorward, O. Alberti, B. Velani, F.A. Gerritsen, W.F. Harkness, N.D. Kitchen and D.G. Thomas, "Postimaging brain distortion: magnitude, correlates, and impact on neuronavigation", Journal of Neurosurgery, 88(4), 656-662, 1998
- 8. P. Jannin, M. Raimbault, X. Morandi, L. Riffaud and B. Gibaud, "Model of surgical procedures for multimodal image-guided neurosurgery", Computer Aided Surgery, **8**(2), 98-106, 2003.
- T. Hartkens, D.L. Hill, A.D. Castellano-Smith, D.J. Hawkes, C.R. Maurer, A.J. Martin, W.A. Hall, H. Liu and C.L. Truwit, "Measurement and analysis of brain deformation during neurosurgery", IEEE Transaction on Medical Imaging, 22(1), 82-92, 2003.
- 10. O. Skrinjar, A. Nabavi and J. Duncan, "Model-driven brain shift compensation", Medical Image Analysis, **6**(4), 361-373, 2002.
- 11. R.D. Bucholz, D.D. Yeh, J. Trobaugh, L.L. McDurmont, C.D. Strum and C. Baumann, "The correction of stereotactic inaccuracy caused by brain shift using an intraoperative ultrasound device", Medicine and Medical Robotics and Computer-assisted Surgery, Springer-Verlag, Berlin, 459-466 1997.

- 12. P. Hastreiter, C. Rezk-Salama, G. Soza, M. Bauer, G. Greiner, R. Fahlbusch, O. Ganslandt and C. Nimsky, "Strategies for brain shift evaluation", Medical Image Analysis, **8**(4), 447-464, 2004.
- M.H. Reinges, H.H. Nguyen, T. Krings, B.O. Hutter, V. Rohde and J.M. Gilsbach, "Course of brain shift during microsurgical resection of supratentorial cerebral lesions: limits of conventional neuronavigation", Acta Neurochirurgica, 146(4), 369-377, 2004.
- M.I. Miga, J.M. Fitzpatrick, R.L. Galloway and K.D. Paulsen, "Incorporation of surface-based deformations for updating images intraoperatively", SPIE Medical Imaging 2001: Image Processing, 4319, 169-178, 2001.
- A. Nabavi, P.Mc.L. Black, D.T. Gering, C.-F. Westin, V. Metha, R.S. Pergolizzi, Jr.M. Ferrant, S.K. Warfield, N. Hata, R.B. Schwarts, W.M. Wells, R. Kikinis and F.A. Jolesz, "Serial intraoperative MR imaging of brain shift", Neurosurgery, 48, 787-798, 2001.
- 16. G.E. Keles, K.R. Lamborn and M.S. Berger, "Coregistration accuracy and detection of brain shift using intraoperative sononavigation during resection of hemispheric tumors", Neurosurgery, **53**(3), 556-62, 2003.
- X. Pennec, P. Cachier and N. Ayache, "Tracking brain deformations in time sequences of 3D US images", Pattern Recognition Letters - Special Issue on Ultrasonic Image Processing and Analysis, 24(4-5), 801-813, 2003.
- S.K. Warfield, S.J. Haker, I.-F. Talos, C.A. Kemper, N. Weisenfeld, A.U.J. Mewes, D. Goldberg-Zimring, K.H. Zou, C.-F. Westin, W.M. Wells, C.M.C. Tempany, A. Golby, P.M. Black, F.A. Jolesz and R. Kikinis, "Capturing intraoperative deformations: research experience at Brigham and Women's hospital", Medical Image Analysis, 9(2), 145-162, 2005.
- CR.Jr. Maurer, D.L.G. Hill, A.J. Martin, H. Liu, M. McCue, D. Rueckert, D. Lloret, W.A. Hall, R.E. Maxwell, D.J. Hawkes and C.L. Truwit, "Investigation of intraoperative brain deformation using a 1.5-T interventional MR system: preliminary results", IEEE Transaction on Medical Imaging, **17**(5), 817-825, 1998.
- 20. B. Mokri, "The Monro-Kellie hypothesis: applications in CSF depletion", Neurology, 56(12), 1746-1748, 2001.