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Non-rigid alignment of pre-operative MRI, fMRI, and DT-MRI with intra-operative MRI for enhanced visualization and navigation in image-guided neurosurgery

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Objective: **The usefulness of neurosurgical navigation with current visualizations is seriously compromised by brain shift, which inevitably occurs during the course of the operation, significantly degrading the precise alignment between the pre-operative MR data and the intra-operative shape of the brain. Our objectives were (i) to evaluate the feasibility of non-rigid registration that compensates for the brain deformations within the time constraints imposed by neurosurgery, and (ii) to create augmented reality visualizations of critical structural and functional brain regions during neurosurgery using pre-operatively acquired fMRI and DT-MRI.**

Materials and methods: **Eleven consecutive patients with supratentorial gliomas were included in our study. All underwent surgery at our intra-operative MR imaging-guided therapy facility and have tumors in eloquent brain areas (e.g. precentral gyrus and cortico-spinal tract). Functional MRI and DT-MRI, together with MPRAGE and T2w structural MRI were acquired at 3 T prior to surgery. SPGR and T2w images were acquired with a 0.5 T magnet during each procedure. Quantitative assessment of the alignment accuracy was carried out and compared with current state-of-the-art systems based only on rigid registration.**

Results: **Alignment between pre-operative and intra-operative datasets was successfully carried out during surgery for all patients. Overall, the mean residual displacement remaining after non-rigid registration was 1.82 mm. There is a statistically significant improvement in alignment accuracy utilizing our non-rigid registration in comparison to the currently used technology ($p < 0.001$).**

Conclusions: **We were able to achieve intra-operative rigid and non-rigid registration of (1) pre-operative structural MRI with intra-operative T1w MRI; (2) pre-operative fMRI with intra-operative T1w MRI, and (3) pre-operative DT-MRI with intra-operative T1w MRI. The registration algorithms as implemented were sufficiently robust and rapid to meet the hard real-time constraints of intra-operative surgical decision making. The validation experiments demonstrate that we can accurately compensate for the deformation of the brain and thus can construct an augmented reality visualization to aid the surgeon.**

Keywords: MRI; DT-MRI; fMRI; Brain; Image-guided neurosurgery; Navigation systems; Non-rigid registration

Introduction

The American Cancer Society estimates that 18,820 new brain tumors will be diagnosed in 2006 in the United States, with an estimated 12,820 deaths. Low-grade gliomas account for 25% of all primary brain tumors.

One of the principal causes of death among patients with low-grade glioma (LGG) is progression of the tumor to a malignant form (i.e., anaplastic degeneration). Surgical resection of low-grade gliomas may decrease the rate of recurrence and increase the time to tumor progression (Piepmeier et al., 1996; Berger et al., 1994). Additionally, a maximal resection and a smaller volume of postoperative residual tumor are associated with an improved prognosis for the patient (Philippon et al., 1993; Piepmeier et al., 1996; Janny et al., 1994; Healy et al., 1991). But increased resection margins can increase the risk for postoperative neurologic deficits, due to possible damage of eloquent brain areas, such as the precentral gyrus and cortico-spinal tract, which concern motor function. Therefore, the principal challenge and objective of surgical intervention is to maximize the resection of tumor, while also minimizing the potential for neurological deficit by preserving critical tissue.

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One of the challenges for neurosurgeons is to preserve the function during surgery for lesions in the central region. Cortical stimulation is commonly used to localize motor function and has become the “gold standard” when performing surgery in and adjacent to the motor cortex (Atlas et al., 1996). However, it does not allow for ascertaining the risk of a new postoperative motor deficit before surgery. Moreover, cortical stimulation is a demanding, time-consuming, and costly procedure and as such is often not possible during surgery. Therefore, because fMRI of motor and language tasks is feasible in patients with cerebral tumors (Mueller et al., 1996), several groups have proposed the integration of functional data into the neuronavigation system in recent years (Krishnan et al., 2004; Nimsky et al., 1999; Ganslandt et al., 1999; Gralla et al., 2003; Jannin et al., 2002; Roessler et al., 2005; Reithmeier et al., 2003; Talos et al., 2003; O’Shea et al., 2006; Lehericy et al., 2000; Maldjian et al., 1997; Ogawa et al., 1990). And strong evidence that a more radical tumor resection may be achieved by using fMRI information during neurosurgery has been demonstrated by Krishnan et al. (2004) and Haberg et al. (2004).

Diffusion tensor imaging (DTI) has recently emerged as a potentially valuable tool for pre-operative planning (Tummala et al., 2003; Field et al., 2004; Mori et al., 2002; Clark et al., 2003; Wieshmann et al., 2000; Holodny et al., 2001a,b; Witwer et al., 2002a,b; Moller-Hartmann et al., 2002; Coenen et al., 2003) and postoperative follow-up (Alexander et al., 2003) of surgically treated brain tumors and vascular malformations. DTI provides information about the normal course, displacement, or interruption of white matter tracts in and around a tumor, as well as detecting the widening of fiber bundles due to edema or tumor infiltration (Beppu et al., 2003; Clark et al., 2003; Hendler et al., 2003; Lu et al., 2003; Price et al., 2003; Tummala et al., 2003; Wieshmann et al., 1999; Witwer et al., 2002a,b; Yamada et al., 2003). Consequently, efforts have been made in recent years to integrate DTI data with neurosurgical navigation systems (Nimsky et al., 2005a,b, 2006; Coenen et al., 2003; Talos et al., 2003; Berman et al., 2004; Shinoura et al., 2005; Kamada et al., 2003). Such a study on the role of diffusion tensor imaging of the corticospinal tract (CST) before and after mass resection, and the correlations with clinical motor findings, was recently published by Laundre et al. (2005).

Interventional MRI (iMRI) has proven to be an effective tool for improving the completeness of low-grade glioma resection (Claus et al., 2005; Bradley, 2002; Schwartz et al., 1999; Schneider et al., 2001, 2005; Knauth et al., 1999; Wirtz et al., 2000; Black et al., 1997; Black et al., 1999; Hall et al., 2003; Jolesz et al., 2001; Keles et al., 2004; Kucharczyk and Bernstein, 1997; Schmidt et al., 1998; Schulder and Carmel, 2003). However, brain deformations typically occur during the neurosurgical procedure, which results in a misalignment between the pre-operatively acquired datasets and the intra-operative brain position. Commonly, commercial systems (such as those developed by Medtronic or BrainLab) only use rigid registration algorithms to project the pre-operatively acquired fMRI and DTI into the navigational system. Intra-operative re-acquisition of fMRI and DTI with iMRI is impractical at present due to long image acquisition and processing times. Non-rigid registration algorithms are therefore necessary to preserve the accuracy of the pre-operative fMRI and DTI data.

Intra-operative changes in the shape of the target anatomy impose a stringent requirement upon navigation systems. In order to capture such shape changes it is often necessary to make use of non-rigid registration techniques, which are characterized by a capacity to estimate transformations that model not only affine parameters (global translation, rotation, scale and shear), but also local deformations. This typically requires higher order transformation models, with increased numbers of parameters, and is usually more computationally expensive.

Modeling the behavior of the brain remains a key issue in providing navigation in image-guided neurosurgery. The biomechanical property experiments of Miller (2002) have contributed significantly in the understanding of the physics of brain tissue. He and his colleagues have explored and evaluated several constitutive models (Miller and Chinzei, 1997, 2000, 2002; Chinzei and Miller, 2001; Miller et al., 2000), which have shown very good concordance of the hyper-viscoelastic constitutive equation with in vivo and in vitro experiments (Miller et al., 2000). Additionally, Miga, Paulsen and their collaborators (Miga et al., 1999a,b, 2000a,b,c, 2001; Paulsen et al., 1999; Roberts et al., 1998, 1999, 2001) have developed a sophisticated model of brain tissue while undergoing surgery, incorporating simulation of retraction, resection and local stress associated with tumor tissue. Careful validation experiments indicate their model is capable of closely matching observed deformations (Platenik et al., 2002). Their experiments also indicate further improvements in accuracy will be possible by incorporating sparse data from inexpensive intra-operative imaging devices. This work has demonstrated that computer-aided updating of pre-operative brain images can restore close correspondence between the pre-operative data and the intra-operative configuration of the subject. But a practical difficulty of these models is the extensive time necessary to mesh the brain and solve the problem, which is takes too much time for intra-operative purposes. Davatzikos et al. (2001) proposed a statistical framework consisting of pre-computing the main mode of deformation of the brain using a biomechanical model. And recent extensions of this framework show promising results for intra-operative surgical guidance based on manually extracted data (Lunn et al., 2003).

Simple biomechanical models have been used to interpolate the full brain deformation based on sparse measured displacements. Audette et al. (2003; Audette 2003) and Miga et al. (2003) measured the visible intra-operative cortex shift using a laser range scanner. The displacement of deep brain structures was then obtained by applying these displacements as boundary conditions to the brain mesh. A similar surface based approach was proposed by Skrinjar et al. (2002) and Roberts et al. (2003), whereby they imaged the brain surface with a stereo vision system.

Previously, we created a full, three-dimensional non-rigid registration implementation using the mean square intensity difference in local regions as the similarity metric, constrained by a linear elastic material (Ferrant et al., 1999). In practice, the method was successful in clinical applications where an assumption of constant image intensities for corresponding structures held true (Navabi et al., 2001). Our most recent work has built upon our earlier efforts and explorations in non-rigid registration for segmentation, pre-operative planning, and enhanced visualization in support of image-guided surgery, and has been described previously (Warfield et al., 1998, 2000a,b, 2002; Ferrant et al., 2000; Rexilius, 2001; Ferrant et al., 2001; Guimond et al., 2002; Rexilius et al., 2001).

A robust volumetric non-rigid registration scheme for brain deformations has been introduced by our group (Clatz et al., 2005). These studies, using intra-operative brain non-rigid registration, were demonstrated using only retrospective data. To our knowledge, there is no published prospective study on non-rigid registration of pre-operative imaging (T1, fMRI, DTI) with intra-operative images (T1).

Five major contributions are presented in our manuscript: (i) our study is prospective, with 11 patients enrolled over 1 year; (ii)