論文の内容の要旨

Title: Towards a Paradigm Shift from Error to Uncertainty in Neuronavigation

(ニューロナビゲーションにおける誤差から不確実性へのパラダイムシフトに向けて)

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Surgical resection is the initial treatment for nearly all brain tumors. The achieved extent-of-resection is strongly correlated with prognosis and is the single most significant modifiable determinant of survival. Since brain tumors are intimately involved in surrounding functioning brain tissue, aggressive resection must be balanced against the risk of causing new neurological deficits.

Due to its potential for minimizing surgical trauma, neuronavigation (image-guided neurosurgery system) has been a ubiquitous tool for many neurosurgical procedures. In preoperative (p-) planning, neuronavigation offers surgeons the images, i.e., Magnetic Resonance (MR), necessary to understand patient-specific information and allow them to choose the most appropriate surgical strategy. During the surgery, neuronavigation provides a patient-to-image mapping so that surgeons can point to a specific location on the patient and see the corresponding anatomy in the p-MR image, helping them achieve a complete tumor resection while avoiding damage to surrounding functioning brain tissue. However, intraoperative (i-) deformation of the brain, also known as brain shift, invalidates the image-to-patient mapping, thus makes it unreliable to use p-MR for intraoperative surgical guidance.

The most successful way to compensate for the brain shift is using intraoperative images, i.e., i-MR or i-Ultrasound (US). By transforming the brain shift invalidated p-MR image to i-images via image registration, surgeons can get an updated view of the pre-surgical planning during surgery. The limitation of this strategy is that, even though the brain is experiencing non-rigid deformation due to tumor resection or retraction, standard neuronavigation in clinical practice only integrates sub-optimal rigid registration insufficient for accurate brain shift compensation. As a result, most surgeons use neuronavigation to approach a surgical target but justifiably do not trust it throughout the operation.

Incorporating non-rigid registration has long been a goal for neuronavigation, yet this goal is hampered because it is harder to predict, validate, and understand non-rigid registration errors. In practice, if surgeons see a discrepancy between two aligned image features, they may not be able to tell if it is caused by a registration error or an actual tissue deformation. In this case, providing surgeons with a spatial distribution of the expected registration error could help them make more informed decisions, e.g., ignoring the registration where the expected error is high. However, determining this spatial distribution of error is particularly tricky for neurosurgery because: 1) Many existing methods conduct multiple runs of the non-rigid registration algorithm and estimate the error based on the (in)consistency of registration results. These methods are too time-consuming to be practical in the operating room because feedback is required within a few minutes of i-image acquisition; 2) More importantly, most error estimation methods primarily look for discrepancies in aligned image features. They are inappropriate for neurosurgery because tumor resection and retraction significantly alter the surgical field's vicinity, particularly at the tumor margin. Thus inconsistency near the tumor margin, which is often expected, can be mistakenly reported as registration errors.

To address these challenges, we propose to use registration uncertainty as a surrogate to indicate registration error in neuronavigation. Registration uncertainty predicts the trustworthiness of registration results and can be helpful in clinical practice. For example, if surgeons observe a large discrepancy at location A and small discrepancy at location B, without knowledge of registration uncertainty, they would most likely assume a large error everywhere and thus ignore the registration. With accurate knowledge of uncertainty, once surgeons know that A lies in an area of high uncertainty while B lies in an area of low uncertainty, they would have greater confidence in the registration at B and other locations of low uncertainty.

In this dissertation, we attempt to establish an important foundation for utilizing registration uncertainty in neuronavigation. The main contributions of this dissertation are as follows:

1) Most registration approaches in neuronavigation have difficulties in registering image pairs with artifacts and missing correspondences, e.g., a part of the tumor volume in the p-image may be missing in the i-image. Another shortcoming of existing approaches is the lack of an uncertainty measure. Since brain shift is a complex spatiotemporal phenomenon, given the state of registration technology, it is reasonable to expect an indication of the estimated deformation's confidence level. We developed a fast probabilistic active image registration method that provides registration uncertainty and meanwhile is robust against image pairs with missing correspondence.

2) Registration uncertainty is a useful addition to the registration result. However, the majority of research takes registration uncertainty for granted and use it in ad hoc ways. We investigated the applicability of registration uncertainty and categorized it into transformation uncertainty and label uncertainty. We pointed out that using transformation uncertainty to quantify label uncertainty, which is widely adopted by the registration community, is inappropriate and can be misleading. We also shared a potentially critical finding that making use of the label uncertainty may not always be helpful.

3) A fundamental assumption for using uncertainty to indicate the error is that these two quantities are monotonically related. While this notion is intuitive and believed by some clinicians, it has never been examined in the image registration literature. We systematically investigated the putative monotonic association between Gaussian process registration uncertainty and error based on neuro-surgical data. We showed empirically that there is a weak-to-moderate positive monotonic correlation between point-wise GP registration uncertainty and error. This work also opens a new vista for the uncertainty/error relationship analysis.

4) During the course of the research, we also pursued two related projects. The first project is about using the variogram to screen outliers for vector fields. Since a critical step in the proposed active image registration is to interpolate a dense deformation field from a set of sparse vectors, adding an outlier screening step can improve the registration accuracy. In the second project, we used the variogram to perform a third-party screening on the annotation of two public datasets. We found that (1) a small number of annotations may have fiducial localization errors; (2) the landmark distribution, for some cases, is not ideal for offering fair comparisons. If unresolved, both findings could incur bias in registration evaluation.

In summary, this dissertation attempts to establish a foundation for using registration uncertainty to indicate errors in the context of neurosurgery. We developed methods that estimate, investigate, and understand registration uncertainty. We believe that our contributions can initiate a paradigm shift from error to uncertainty in neuronavigation.