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● *Original Contribution*

NEAR REAL-TIME ROBUST NON-RIGID REGISTRATION OF VOLUMETRIC ULTRASOUND IMAGES FOR NEUROSURGERY

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Abstract—Ultrasound images are acquired before and after the resection of brain tumors to help the surgeon to localize the tumor and its extent and to minimize the amount of residual tumor after the resection. Because the brain undergoes large deformation between these two acquisitions, deformable image-based registration of these data sets is of substantial clinical importance. In this work, we present an algorithm for non-rigid registration of ultrasound images (RESOUND) that models the deformation with free-form cubic B-splines. We formulate a regularized cost function that uses normalized cross-correlation as the similarity metric. To optimize the cost function, we calculate its analytic derivative and use the stochastic gradient descent technique to achieve near real-time performance. We further propose a robust technique to minimize the effect of non-corresponding regions such as the resected tumor and possible hemorrhage in the post-resection image. Using manually labeled corresponding landmarks in the pre- and post-resection ultrasound volumes, we illustrate that our registration algorithm reduces the mean target registration error from an initial value of 3.7 to 1.5 mm. We also compare RESOUND with the previous work of Mercier et al. (2013) and illustrate that it has three important advantages: (i) it is fully automatic and does not require a manual segmentation of the tumor, (ii) it produces smaller registration errors and (iii) it is about 30 times faster. The clinical data set is available online on the BITE database website. (E-mail: hrivaz@ece.concordia.ca) © 2015 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Ultrasound registration, Non-rigid registration, Robust estimation, Normalized cross-correlation, Brain surgery, Image guided neurosurgery.**

INTRODUCTION

Not all pathologic tissue is removed during surgery. In some cases, residual tumor is left behind when it involves eloquent cortex and its removal will result in a functional or cognitive deficit in the patient. In other cases, the extent of brain tumors is difficult to define during neurosurgery. As a result, different studies report that the surgeons leave residual tumor in 64% (Stummer et al. 2006) and 54% (Knauth et al. 1999) of patients. Therefore, most neurosurgical systems are based on neuronavigation and pre-operative images. In these systems, the pre-operative images, usually magnetic resonance (MR) images, act as "GPS road maps," and an optical or electromagnetic tracking device, which tracks the tools, acts as the GPS location signal. This provides the surgeon with the guidance to locate the tumor and its extent in the operating room. Unfortunately, these neuronavigation systems do not usually provide the required accuracy for three main reasons. First the brain deforms after craniotomy and opening of the dura, and therefore, the maps are no longer accurate. This deformation is referred to as *brain shift* in the literature (Hill et al. 1998; Roberts et al. 1998). Second, image-to-patient registration is performed by selecting homologous landmarks on the skin and in the MR image, which is subject to error. And third, the tracking devices have errors, which further reduce the navigation accuracy. As a result, guidance with intra-operative imaging is becoming more widespread.

Magnetic resonance imaging (MRI) has been used during or after the operation (Claus et al. 2005; Hartkens et al. 2003; Hatiboglu et al. 2009; Nabavi et al. 2001; Nimsky et al. 2004). However, intra-operative MRI is expensive and is available at only a very limited number of centers. Tracked intra-operative ultrasound, on the other hand, is affordable and not cumbersome and has been successfully used in

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neurosurgery (Bucholz et al. 1997; Keles et al. 2003; Letteboer et al. 2005; Lunn et al. 2003; Rygh et al. 2008; Tirakotai et al. 2006; Unsgaard et al. 2002a, 2002b). In terms of accuracy, intra-operative ultrasound has been found to be as good as intra-operative MRI (Gerganov et al. 2009; Unsgaard et al. 2005). Our group has also focused on integrating ultrasound with neurosurgery, either using B-mode ultrasound (Arbel et al. 2004; De Nigris et al. 2012; Mercier et al. 2012, 2013; Rivaz and Collins 2012) or power Doppler (Reinertsen et al. 2007). In our institute, surgeons acquire ultrasound images before the resection, and after performing the resection, they perform a second ultrasound mainly to look for residual tumor by comparing the pre- and post-resection images. As the surgery goes on, the brain shift increases (Nabavi et al. 2001), and therefore, the two sets of images will be misaligned. In Figure 1 is an example of rigid alignment of the two ultrasound images using the tracking data. In the superimposed image, some areas have more than 7 mm of misalignment.

The registration of the two ultrasound volumes, one acquired before and another at the end of a tumor resection, is challenging for three main reasons. First, the tissue deforms during the resection, which requires the registration to be non-rigid. Second, the intensity and contrast of two ultrasound images of the same tissue target can change depending on the imaging angle, time gain control (TGC) settings, resection of some tissue in the path of the ultrasound wave and depth of the tissue in the ultrasound image. And third, there are some regions, such as the tumor and resection site, that do not have correspondence in the other image.

Previous works registered ultrasound images. Rohling et al. (1997, 1998) and Gee et al. (2003) performed rigid registration of two volumes using cross-correlation. Krucher et al. (2000) performed 3-D non-rigid registration using mutual information. Poon and Rohling (2006) divided the image volumes into subvolumes and performed rigid registration over these subvolumes using cross-correlation. Grau et al. (2007) and Rajpoot et al. (2009) used local orientation and phase differences as the similarity measure to perform rigid registration between volumetric echocardiograms. Foroughi et al. (2006) used attribute vectors (Shen and Davatzikos 2002) to automatically select a set of leading points in the first volume. The correspondences of these points are found in the second volume, and the volumes are warped accordingly. This algorithm was adapted in Leung et al. (2009) to perform non-rigid registration of 2-D ultrasound images in real time, and was also extensively validated in Khallaghi et al. (2012).

To the best of our knowledge, the recent work by Mercier et al. (2013) was the first attempt to register ultrasound images acquired before and at the end of the neurosurgery. To reduce the effect of missing data, they manually segmented the tumor and masked it out of the data. They then used the cross-correlation-based non-rigid registration algorithm of ANIMAL + INSECT (Collins et al. 1999). Manual segmentation in three dimensions is challenging and time consuming and can hinder widespread clinical application of such methods.

In this work, we describe a tool for non-rigid registration of ultrasound volumes (RESOUND) using a regularized cost function. Our cost function has an image similarity term based on the normalized-cross correlation (NCC) and a smoothness constraint. We use free-form cubic B-splines to model the deformation field. To optimize the cost function, we use the analytic derivative of NCC and exploit the computationally efficient stochastic gradient descent algorithm (Klein et al. 2007). We also perform hierarchical registration in three levels to speed the computations and prevent the algorithm from getting trapped in local minima. At the coarse levels, an approximate transformation is found, which is used as a starting point for the finer levels. Three features of RESOUND make it computationally efficient: stochastic gradient descent optimization, analytic estimation of the gradient of the cost function and hierarchical search. As a result, our basic implementation takes 5 s to perform non-rigid registration of volumetric data on a single core of a 3.6-

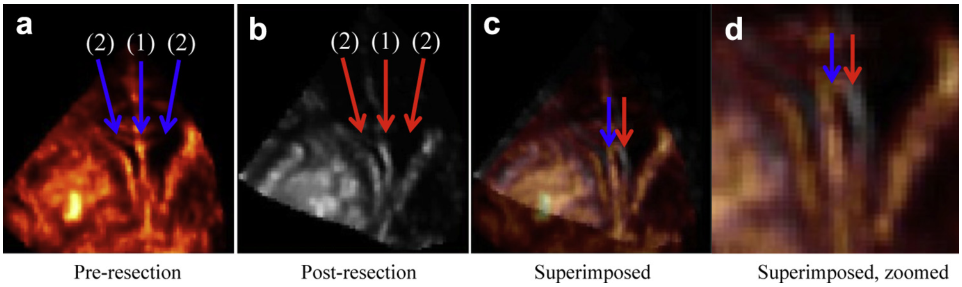

Fig. 1. Pre- and post-resection ultrasound images. The misalignment in the superimposed images in (c) and (d) is caused mainly by the brain shift. Structures (1) and (2) are respectively the septum and ventricles. The tumor and resection cavity are not present in these ultrasound slices.