MR based longitudinal assessment of pituitary adenoma growth using fully automated coregistration and intensity normalization

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Purpose: To evaluate the clinical utility of a novel combined rigid body coregistration and intensity normalization method applied to 3D MR images in longitudinal monitoring of pituitary adenoma growth.

Background: Lifelong monitoring of residual tumor growth in patients diagnosed with pituitary adenomas is essential for their continued care and in the decision making of further therapy. MR imaging is currently the preferred imaging modality in these patients and adenoma growth is commonly assessed by visual comparison of 2D MR images acquired at different time points. Detection of small changes in tumor size is challenging using the current method based on visual inspection alone and is further complicated by lack of image registration of images acquired at different time-points which may make direct comparison difficult. It is our hypothesis that morphometric analysis of rigid-body coregistered, resampled MR images [1] from different time points may further aid the radiologist in making an accurate and objective assessment of structural changes than what can be achieved by visual inspection alone.

Methods: To date, 13 adult patients (8 females, 5 males, aged 29-76 yrs, mean age 53 yrs) previously diagnosed with a pituitary adenoma has been included in the study. Of these, 7 patients were imaged at two different time points, 4 at three time points and 2 at four time points. Mean (±std. errors) time between two consecutive MR exams was 444±32 days. The MR imaging protocol at 1.5 Tesla (Siemens Sonata) was as follows; axial 2D turbo spin-echo (TSE) T2-w images (TR=4000ms, TE=97ms, 0.6X0.4x5mm^3) and sagittal (pre- and post-contrast), coronal (pre- and post-contrast) and axial (post-contrast) 2D TSE T1-w images (516ms, 12ms, 0.7x0.4x3mm^3). In addition, a multi-echo post-contrast T1-w 3D image sequence (20ms, 1.8-15.8ms, 1.3x1.0x1.3mm^3) was acquired in all patients.

The 3D MR images were corrected for nonlinear gradient distortions, and then subsequent scans were aligned using affine registration, excluding points outside an individually defined brain mask. In a target image with N voxels, the problem is to find the 3N-dimensional displacement field that locates corresponding intensities in the other, deforming image. The displacement field is constrained to be smooth, local relative variation penalized and stretched or compressed at each point by the intensity difference between the images. It was found by minimizing a merit function for the whole system that describes locally the linear elastic environment. To facilitate minimization, the images were heavily smoothed so as to make them similar, i.e., so that the starting point was in the basin of the global minimum of the merit function. Registration (minimization) was then repeated with reduced smoothing, starting from the updated displacement field. The whole procedure was iterated for more precise registration.

In order to assess the diagnostic efficacy [2] of including the rigid-body coregistration routine, two board-certified neuroradiologists examined the patients in consensus with respect to tumor growth (yes/no) using the conventional method (visual inspection of non-coregistered 2D images; excluding the 3D image series) and the rigid-body coregistered 3D images. For the latter, the two 3D image sets from different time points were used as underlay-/overlay images and a transparency slider was used to assess any difference in adenoma size. . Image correction and registration was performed using custom-designed software written in C, and visualization was performed using nordicICE (NordicImagingLab, Norway).

Results: An example of the rigid-body coregistration is shown in Figure 1. For the visual comparison, the neuroradiologists observed a change in adenoma size in 4 of the 21 time points (in 4 patients). Using the coregistered 3D images, a change in adenoma size was observed in 11 of the 21 time points (in 7 patients). A summary of the results is shown in Table 1. Overall, when including the coregistered 3D images, the neuroradiologist changed their diagnosis in 5 of 13 patients (38%) at 7 of the 21 time points (33%). In addition, the use of coregistered 3D images was found helpful in making the diagnosis in 21 of the 21 time points (100%).

Discussion: Assessment of adenoma tumor growth from visual comparison of 2D MR images from different time points only, is both difficult and prone to errors due to variations in image projections. Our preliminary results suggest the use of a novel rigid-body coregistration and intensity normalization technique applied to 3D images may provide a more accurate and objective assessment of structural changes. A change in diagnosis was observed in 38% (5/13) of the patients included in the study when including the coregistered 3D images in the analysis compared to conventional visual inspection of 2D images alone. The discrepancy between the two methods investigated in this study mandate further investigations to validate the accuracy of the rigid-body coregistration routine. Although the potential gain due to a change in diagnosis is difficult to assess, our results suggest that the proposed method may aid in the decision making of further therapy. Also, the method is fully automated and can easily be implemented in the hospital PACS.

Conclusion: In this study, we have evaluated the use of a novel rigid-bogy coregistration and intensity normalization method applied to 3D MR images acquired at different time points in the longitudinal monitoring of pituitary adenoma growth. The method was found helpful in making the diagnosis and resulted in a change of diagnosis in 38% of the patients.

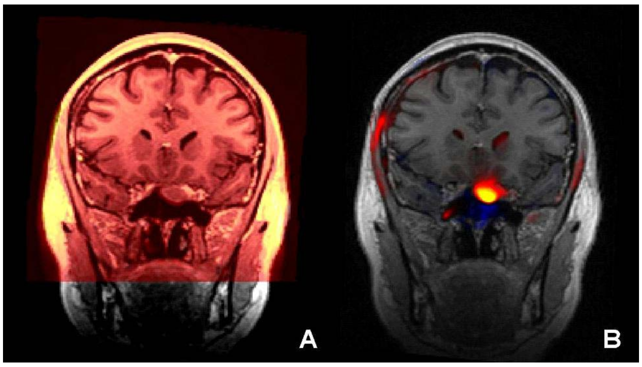

***Figure 1: (A)** Rigid-body coregistered 3D MR images from two time points (under-/overlay) of a patient with a pituitary adenoma. Presence or absence of tumor growth was assessed by using a transparency slider to toggle between the two image time points. **(B)** The net displacement field derived during the coregistering process allows visualization of volume change (in percent). Based on the Jacobian determinant of the displacement field, red values indicate areas of expansion whereas blue areas indicate compression.*

***Table 1:** Observed change in pituitary adenoma size between consecutive time points when using visual comparison of 2D MR images only **(A)** and including rigid-body coregistered 3D MR images in the analysis **(B)**. A line (-) indicate no observed difference in adenoma size.*

Pituitary Adenoma Growth				
Subject	**Time 1**	**Time 2**	**Time 3**	**Time 4**
1	-	B	B	A, B
2	-	B	-	
3	-	-		
4	-	-	-	
5	-	B		
6	-	-		
7	-	-		
8	-	-	A, B	
9	-	-	-	
10	-	A, B	B	B
11	-	B		
12	-	A, B		
13	-	-		

References:
[1] Holland et al. Proc ICAD 2008; p 249
[2] Fryback et al. Med Decis Making 1991; 11:88-94