Image Registration and Subtraction in the Detection of Marginal Changes in Tumour Volume

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Introduction

The major cause of mortality in patients with low grade gliomas is transformation to higher grade tumours. Although low grade gliomas are generally slow growing there is some evidence that an increased growth rate is predictive of subsequent transformation to a higher grade.[1] Imaging techniques capable of detecting marginal changes in tumour volume in the clinical setting would provide insight into the biological behaviour of the tumour and aid therapeutic decisions. The purpose of this study was to compare image registration and subtraction techniques in their ability to detect marginal changes in low grade glioma volume when applied to standard clinical imaging protocols, and to assess the interrater variability of observers using these techniques.

Methods

Since low-grade gliomas generally do not undergo gadolinium enhancement tumour size was assessed on the basis of increased signal on T2-weighted images. 13 patients (10 male, 3 female) were selected on the basis of minimal or no change in tumour size reported after serial imaging. Where multiple scans were available, only pairs of images demonstrating no obvious change in tumour size were chosen for comparison. In total 42 comparisons were drawn between pairs of serial images (27 T2/15 FLAIR), acquired with standard clinical protocols. (T2: TR = 3.2s, TE = 72ms, FOV = 22cm, matrix = 256^2, slice thickness = 5mm, spacing = 2mm; FLAIR: TR = 9s, TE = 160ms, TI = 2.2s, matrix = 256^2, slice thickness = 5mm, spacing = 2mm.) Imaging was performed with 1.5T GE Signa Horizon and LX scanners (GE Medical Systems, Milwaukee, WI, USA). For each patient, the earliest T2 and FLAIR imaging studies available were used as baseline scans, and all subsequent studies were registered to the appropriate baseline scan using a maximisation of correlation technique.[2,3] Subtraction images were generated for each comparison and the anonymised images were assessed by three independent raters using a non-parametric rating scale ranging from -2 to 2, (-2: definite decrease in tumour size, -1: possible decrease, 0: no change, 1: possible increase, 2: definite increase). The ratings from the three raters were then combined into an average rating for each comparison and the inter-rater variability was evaluated. The statistical analysis was performed in SPSS (SPSS Inc, Chicago, IL, USA).

Results

For the T2-weighted images, the mean tumour ratings were 0.7 (unregistered), 1.1 (registered) and 1.0 (registered/subtracted) whilst for FLAIR images the mean tumour ratings were 0.9 (unregistered), 1.2 (registered) and 1.4 (registered/subtracted). Statistically significant differences were demonstrated in the mean ratings between all registered versus unregistered images ($p= 0.001$, Wilcoxon signed ranks test), and all registered/subtracted versus unregistered images ($p<0.001$, Wilcoxon signed ranks test). In 22 of the 42 comparisons the average tumour rating was upgraded after registration; in one case it was downgraded, and in the remaining 19 cases the rating remained unchanged. For the matched comparisons where both T2 and FLAIR images were available, the mean tumour rating for was consistently higher for the FLAIR comparisons relative to the T2 comparisons for registered (1.2 vs. 1.0), unregistered (1.1 vs. 0.7), and subtracted images (1.4 vs. 1.1). However, this difference in tumour rating only reached significance for the registered images ($p=0.02$, Wilcoxon signed ranks test). The results for the inter-rater variability for the FLAIR and T2 images are shown in table 1. An example subtraction image shown in figure 1 demonstrates a medial rim of increased signal intensity indicating minor tumour growth.

Discussion

Registration and subtraction techniques can be applied successfully to images acquired with standard clinical protocols. Registration significantly increases the detection of small changes in tumour volume however this detection rate is not significantly improved by subtraction of the registered images. These techniques are most sensitive and reproducible when FLAIR sequences are used.

Figure 1

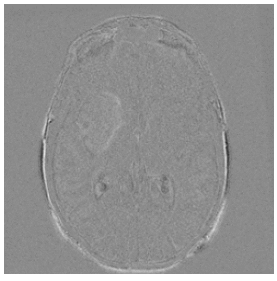

Table 1: Inter-rater variability

	Average κ	σ
T2 unregistered	0.64	10%
T2 registered	0.54	18%
T2 subtracted	0.34	25%
FLAIR unregistered	0.43	21%
FLAIR registered	0.65	14%
FLAIR subtracted	0.63	13%

References

1. Rees et al. Proc. Association British Neurologists 2002
2. Jenkinson et al. Medical Image Analysis 5 (2001) 143-256
3. Jenkinson et al. Neuroimage 17 (2002) 825-841