The Detection and Significance of Subtle Changes in Mixed-signal Brain Lesions by Serial MRI Scan Matching and Spatial Normalisation

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Introduction:

The identification, localisation and classification of tumours in patients with medically intractable epilepsy is of crucial importance for patient management and in particular surgical decisions. In T1-weighted MR images indolent malignant lesions return low mixed signal with ill-defined boundaries. T1-weighted volume data are ideally suited for precise serial matching for the detection of subtle changes [1]. However, artefacts in these images due to pulsation susceptibility differences and flow effects give rise to signal variations that may mask or mimic changes in lesions. Artefacts may also arise from imperfect registration. The threshold of detectability of mis-registration artefacts can be estimated as the inverse of the maximum contrast-to-noise ratio (CNR) [2].

We have developed a method for the automated detection and quantification of signal changes in tumours. The method is based on the automatic segmentation of structure in the difference images from matched scan pairs. Genuine changes were identified based on the comparison of the structured differences in individual patients with a map of the artefacts obtained by spatial normalisation of the structured differences ('structured noise') in the group of normal controls.

Methods:

Seven patients and 20 normal subjects were scanned at least twice using a 1.5T GE Signa Echo-Speed imager (GE Medical Systems, Milwaukee). A 3D IR-prepared fast spoiled gradient echo "IRSPGR" sequence with the following parameters was used: TR/TE/TI=17.4/4.2/450ms, 124 1.5mm thick slices, FOV=24cm×18cm, acq. matrix: 256×192. The mean inter-scan interval was 10.4 months for the controls and 11.4 months for the patients. The maximum CNR is of the order of 20 (white matter *vs.* CSF or white matter *vs.* lesion) corresponding to a mis-registration threshold of 0.05voxels.

Scan matching: After automatic brain segmentation [3] pairs of datasets were coregistered using successive multi-scalar Simplex searches to determine the translation, rotation and scaling parameters (total: 9 parameters) which define the optimal rigid-body transformation matrix by maximizing the cross-correlation coefficient. Based on experiments with phantoms the accuracy of the registration is of the order of 0.02mm [2]. A difference volume was obtained by subtraction of the inital scan from the registered & sinc-interpolated follow-up scan, after intensity matching by linear regression of the voxel intensities. Non-uniformity correction of the difference volume was then performed using a Butterworth filter.

For the three patients who had three or more scans (6 scan triplets in total) registration consistency was assessed by calculating the root-mean square distance between brain voxels as mapped using the two transformation matrices obtained when interchanging the order of registration: (first->second & second->third) *vs* (third->first)$^{-1}$.

Segmentation of structured signal changes: The structured part of the difference volume was segmented for the controls and patients using the following automatic two-stage approach: first, the Gaussian noise level in the difference image (within the brain mask), σ_G, was estimated based on an automatic structured difference filtering (SDF) process [4]. The SDF is based on intensity and volume (8 voxels in this case) thresholds on signal change clusters. Second, the structured part of the difference image was segmented using the SDF again with a threshold value of $t=3\times\sigma_G$. As a result, brain voxels were assigned one of the following values: 0=no signal change; +1=signal increase; -1=signal decrease.

Noise in controls and genuine changes in patients: A structured noise map (SNM) was obtained as follows: First, the structured difference volumes from the 20 controls were transformed into Talairach space using the "Spatial normalisation" tool in SPM96 [5]. Second, the resulting normalised structured difference volumes were combined by summing the absolute voxel values (Σ) for voxels within the intersection of all the brains; the probability of structured noise, p_s, is Σ/N; all other voxels were labelled as 'non-brain' and excluded from analysis. We tested the effect of sinc-based (radius=2) vs linear interpolation, and non-uniformity correction, on the amount of structured noise.

The significance of structured changes in patients was assessed by comparison with the SNM after spatial normalisation of the segmented structured signal changes on a voxel-by-voxel basis: Changes were classified as genuine if $p_s < 5\%$ (ie noise was present in none of the 20 controls).

Results:

Registration consistency: The mean of the RMS distance over all scan triplets was 0.06mm (range: 0.03-0.06mm).

Noise in controls: The mean amount of structured noise was 1.57% of brain voxels for linear interpolation-based registration and with non-uniformity correction; the value was 1.55% for sinc-based registration (maximum relative difference in amount of structured noise between sinc- and linear interpolation based registration: -3%) and 2.68% without uniformity correction. Figure 1 shows the SNM.

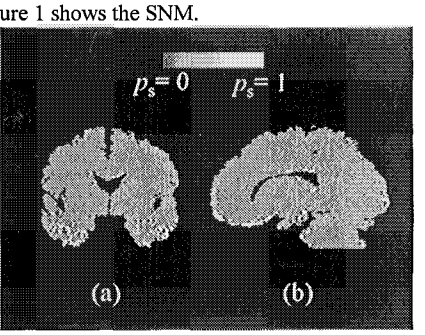

Figure 1. Two representative sections through the SNM. (a): coronal; (b): sagital. It shows the concentration of artefacts due to pulsation, flow, susceptibility differences and rf non-uniformity.

Changes in patients: In all patients, changes were detected which had eluded detection on routine inspection by an expert neuro-radiologist. Figure 2 shows the results for a patient (male, 37y) who was scanned five times within two years. Lesion volume measurements in the unmatched scans had revealed a degree of change between the first and last scans. Our analysis shows a gradual change throughout the scanning period. Histological findings were in keeping with a slowly growing tumour.

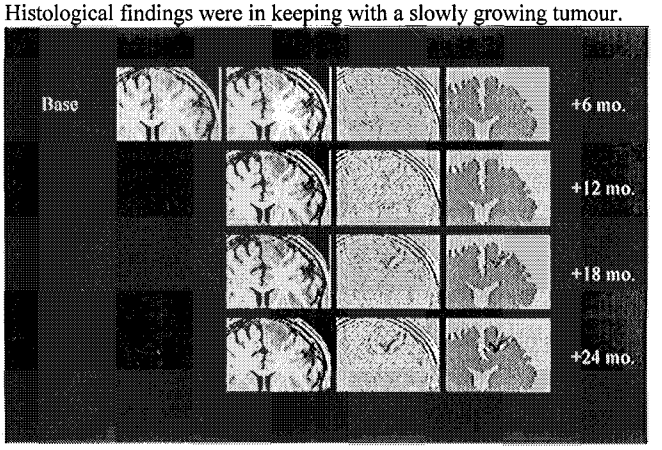

Figure 2. Results for a patient who had 5 scans at six month intervals. The top left image is the initial (base) scan; columns from left to right: repeat scans, difference, genuine changes (signal increase in white and signal loss in black).

Discussion and Conclusions:

We have demonstrated a new method for the identification and quantification of signal changes from matched scan pairs. Registration consistency errors in patients were near or below the level of mis-registration detectability. Sinc-based interpolation for registration did not significantly alter the results but uniformity correction did. Previously undetected changes in tumours were revealed. Their biological significance remains to be investigated.

References:

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