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False Sense of EPI-to-Structural Alignment with Common Cross-Modality Registration Methods

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Introduction: Accurate registration of FMRI T2*-weighted EPI volumes (E) to same-subject high-resolution T1-weighted structural volumes (S) is crucial for cortical surface-based analyses and pre-surgical planning. Such registration is commonly implemented by minimizing some cost-functional C[T(E),S] over affine transformations T(-). Joint-histogram-based cost-functionals are widely used (e.g., Mutual Information [**MI**], Correlation Ratio [**CR**]).

EPI-structural registrations using general-purpose functionals *appear* to yield decent alignments; however, inspection reveals that internal brain structures are often misaligned. What usually appears good is the match between brain surfaces, but this misleads because of the brain's smooth outline. The misregistration is most evident in ventricles, where CSF is concentrated and is bright in EPIs and dark in structurals. We present a method for examining registration quality and a new cost-functional that results in better alignment.

Methods: We used 27 EPI/structural pairs from several sources (at 1.5 and 3.0 Tesla) who had difficulty getting good alignments despite trying diverse tools. We didn't devise a quantitative metric to compare alignments: *our thesis is that no such automated ideal metric yet exists for comparing actual EPIs to structurals*. Three raters, blinded to registration methods, evaluated image alignments visually, using a four-point qualitative scale (0=awful..3=excellent); raters viewed melded images with edge enhancement, focusing on correspondences between ventricles and sulci (however, not all internal edges are expected to match well, since EPIs have lower resolution and contrast, with spatially varying quality). These cost-functionals were rated: MI, CR, Hellinger metric, and our new cost-functional **LPC**=Local Pearson Correlation: compute the inter-volume correlation coefficient over each of about 1000 local neighborhoods, preferentially weighting high-intensity EPI values (CSF); Fisher z-transform and sum this collection of values. LPC is most negative (optimal) when high-intensity EPI voxels overlay low-intensity structural voxels. Non-brain regions are filled with white noise to suppress spurious correlations.

Results: Figures 1-3 illustrates one effective display method for assessing alignment and typical results from different methods, with EPI overlaid in translucent and modulated color on the structural:

1: **Unaligned**: Blue and orange lines highlight edges from structural and EPI, respectively; dark-red lines are overlapping edges. Slight alignment errors are apparent. Dotted lines highlight 3 regions to compare across Figures.

2: **MI Alignment**: Clearly worse than Unaligned, despite overall brain contour alignment.

3: **LPC Alignment**: Best in all areas. By the MI criterion, this superior alignment is significantly worse than Figure 2's. Similar observations apply to CR and Hellinger cost-functionals.

Figure **4** shows rating statistics: raters all found LPC to be consistently superior to cost-functionals based on the joint histogram, which were indistinguishable in performance. Ratings were made after examining images in axial, sagittal, and coronal views. (All cost-functionals were implemented in AFNI, but similar problems were found with SPM and FSL implementations.)

Conclusions: Aligned images *must* be compared visually, since cost-functionals now widely used, which work in simulations, often fail in practice. AFNI tools can automatically produce such evaluation images. EPI-structural alignment *should* take into account the particular relationship between T2* and T1 contrasts and resolutions; the new LPC implementation registers real images well.

References: