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Highlights:

- Different analysis methods of diffusion data differ in performance in terms of sensitivity, reproducibility, and spatial specificity;
- ROI analysis is poorly reproducible, but extremely sensitive to changes in small well defined brain areas;
- Histogram analysis is indicated when dealing with a diffuse disease; however CSF removal can be critical;
- Tractography can be used to define ROIs with improved anatomical specificity.

**Diffusion goes mad: Single Subject Diffusion Analysis - ROI, Histogram, Tractography**

Target Audience: Physicists and clinicians who wish to learn about available strategies for post processing of diffusion data, but also about the potential pitfalls associated with them.

Outcome: After this lecture, participants should be able to choose the best strategy to extract quantitative information from diffusion imaging data for a specific application, being aware of the potential sources of bias.

Purpose: Most studies based on the use of diffusion MRI for clinical-research set out to compare diffusion parameters between a group of subjects affected by the disease of interest and a group of healthy individuals (the control group). In this talk we will review some of the available methods for extracting quantitative information from diffusion parametric maps, in a format suitable for a statistical comparison.

Methods: Relatively simple approaches are region of interest (ROI) analysis and histogram analysis. While relatively easy to implement, ROI analysis is time-consuming and poorly reproducible. It is highly operator-dependent and its accuracy relies on the minimization of both noise and partial volume effects. When studying conditions that affect large portions of the brain, histogram analysis can be used to reduce some of the problems of ROI analysis. The histogram is a frequency distribution showing the number of voxels with a particular range of values (defined by “bins”). Several features (e.g., peak height, peak location, etc) can be extracted from the histogram and analysed statistically. When comparing two populations with differing degrees of atrophy, poor segmentation of CSF might result in differering degrees of partial volume, with atrophy having an undefined contribution to any observed changes. The introduction of diffusion tractography, and the resulting capability to reconstruct white matter pathways in vivo, has also initiated a number of novel approaches to image analysis. Tractography offers the possibility of automatically segmenting a specific white matter tract or structure, from which it is possible to derive the average strength of connectivity, the tract-volume, as well as other tract-specific summary statistics such as the average fractional anisotropy. These quantitative parameters can be used for further statistical analysis. Far from being an established methodology, the limitations of tractography should always be taken into account when planning a study.

Conclusion

Different analysis methods differ in performance in terms of sensitivity, reproducibility, and spatial specificity. When planning a study based on the quantification of diffusion indices, the researcher

should formulate a clear hypothesis and then select the method of analysis most suitable to test that hypothesis.

### **References**

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