Usefulness of histogram analysis for the investigation of tumour heterogeneity

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Purpose: The purpose of this educational poster is to review the advantages and pitfalls of histogram analysis in cancer MR imaging. Some of the most used techniques for the assessment of tumour features and tumour response to treatment such as Dynamic Contrast Enhanced MRI (DCE-MRI), Diffusion-weighted MRI (DWI) as well as Susceptibility-weighted MRI (SWI) are reviewed in conjunction with histogram methods to investigate parameter heterogeneity over tumours.

Outline of Content:

I. Tumour heterogeneity : methods are needed to investigate it

We will briefly review what is meant by tumour heterogeneity and explain why it is of paramount importance to find accurate methods to investigate it in oncologic MR imaging.

II. Principles of histogram analysis and Description of parameters of interest

Most histogram analyses use descriptive parameters to characterize and compare distributions of tumour biomarkers in a quantitative manner. A descriptive analysis reports the following quantitative factors: Mean, standard deviation, kurtosis, skewness and percentiles. The meaning of these metrics in cancer studies is often ambiguous. We will give the definitions of these parameters and explain their value as "surrogate markers" of tumour heterogeneity in the assessment of response to treatment or tumour progression.

III. Review of the current techniques investigating tumour heterogenity with histograms

We will review the current literature regarding the clinical and experimental utility of histogram analyses in DCE-MRI, DWI and SWI.

- **a. DCE-MRI**
- **b. DWI**
- **c. SWI**

IV. Pittfalls of histogram analyses and introduction to other techniques for evaluating tumour heterogeneity

We will review some of the pittfalls of histogram analyses such as scaling issues, choice of number of bins and variability across patients or animals. We will introduce other techniques derived from histogram analyses: texture analysis, indexed distribution analyses…

Summary: In most tumours, heterogeneity is everywhere. Tumours are defined by marked differences in cells, microenvironmental factors (oxygenation levels, pH, VEGF, VPF, TGF-α...) metabolism, vasculature, structure and function that in turn translate into heterogeneous drug delivery and therapeutic outcome. Ways to estimate quantitatively tumour heterogeneity can improve drug discovery, treatment planning and therapeutic responses. It is therefore of paramount importance to have reliable and reproducible biomarkers of cancerous lesions' heterogeneity. During the past decade, the number of studies using histogram approaches increased drastically with various MRI techniques (DCE-MRI, DWI, SWI...) although information on tumour heterogeneity remains poorly exploited. We attribute this fact to a poor knowledge of the available metrics and of their specific meaning as well as to the lack of literature references to standardized histogram methods to which surrogate markers of heterogeneity can be compared.

References: 1. Airley RE, Mobasheri A. Hypoxic regulation of glucose transport, anaerobic metabolism and angiogenesis in cancer: novel pathways and targets for anticancer therapeutics.Chemotherapy. 2007;53(4):233-56. 2. Alic L, van Vliet M, van Dijke CF et al. Heterogeneity in DCE-MRI parametric maps: a biomarker for treatment response?Phys Med Biol. 2011;56(6):1601-16. **3.** Rosenkrantz AB. Histogram-based apparent diffusion coefficient analysis: an emerging tool for cervical cancer characterization?AJR Am J Roentgenol. 2013;200(2):311-3. **4.** Baek HJ, Kim HS, Kim N et al. Percent change of perfusion skewness and kurtosis: a potential imaging biomarker for early treatment response in patients with newly diagnosed glioblastomas.Radiology. 2012;264(3):834-43.