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## **New approaches to reduce radiation dose in X-ray computed tomography perfusion imaging**

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Computed tomography perfusion (CTP) consists is a dynamic CT acquisition of the same body region of a patient during the injection of a compact bolus of iodinated contrast media. For each voxel, the so-called time-attenuation curves (TACs) are extracted, which are the plots of the CT value changes of that voxel versus the time. It is important to acquire a baseline value (i.e. before contrast media arrival) in order to have an initial value of the TACs, which will have to be subtracted for any post-processing, since the iodine concentration in CT is directly proportional to the changes of the CT values, not to the absolute CT values. The functional maps reflect different metabolic properties of the voxels, which can be correlated to tumor aggressiveness and therapy response, and to stroke damaged and savable tissue (to cite the most important clinical applications).

To keep radiation dose low, CTP scans are normally performed with low kV and mAs settings, which results in higher noise both in the spatial and in the temporal domain. A form of temporal smoothing is intrinsically performed during the modeling step, where the TACs are fitted to specific equations to extract the functional parameters. On the other hand, such models are very unstable and since each voxel is processed independently, the final functional maps are not smooth and present significant spatial noise which can mask the pathologies. Due to the big amount of data, iterative reconstruction can be too time consuming.

In this work two new approaches are proposed. First, an improvement of the multi-band frequency (MBF) filter is derived by adapting the width of the temporal average process independently for each voxel, instead of having a fixed value. Such filter was named as adaptive MBF or AMBF, and it was shown to outperform the conventional MBF on several clinical cases and one digital phantom.

Regarding the noise reduction in the spatial domain and the improvement of the maps quality, a novel 3D spatial filter (the KMGB) was developed, which efficiently uses the temporal information to detect a qualitative functional similarity between the voxels before calculating the maps. In this way it is possible to average the functionally similar voxels together, in each acquired phase, before running the modeling step. This has the same effect of averaging the similar TACs together before processing them in the modeling step. The key factor in this approach is to find a robust way to detect such functional similarity between the TACs. The singular value decomposition (SVD) was used to extract intrinsic features of the TACs and to be less dependent on the temporal noise. Successively a k-means clustering algorithm was employed to group together TACs that show similar features. The KMGB filter was compared with two

other methods that also use a TACs similarity measurement to guide a spatial smoothing (TIPS and PATEN filters). It was demonstrated how the TIPS and the PATEN methods are both limited by the presence of the baseline values and of the temporal noise in the TACs, while the KMGB approach overcomes both these issues. The final results have been shown to be consistently better both on a digital phantom in a quantitative study, and in a qualitative study on several clinical cases.

The higher radiation dose when compared to conventional CT is still the major limiting factor to the clinical spread and acceptance of CTP. On the other hand, no other CT technique has been capable to provide the same quantitative functional information, which have been proved to be very useful in more than one clinical application. Therefore, lots of effort is being made to formulate new filters, iterative reconstructions and dilution models, that can cope with the problem of higher noise.

The noise reduction together with the signal preservation suggest that the proposed algorithm might be successfully employed to reduce dose in CTP exams. Both from the phantom simulation and from the clinical cases investigated, it is possible to conclude that a dose reduction of 50-70% could be achieved, compared to the conventional standard protocols, and still obtaining high quality quantitative perfusion maps.

The new presented approaches are derived as a result of an extensive research on the state of the art in this field and have been inspired by more than one methods. The author hopes that this work might also serve as an inspiration for further improvements and new approaches in this delicate but very fascinating and promising topic.