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Title: A semi-automatic pipeline for extracting static and dynamic parameters from 18F-DOPA PET in high- and low-grade pediatric gliomas

Introduction: Brain gliomas are one of the most common solid tumors among children. Positron emission tomography with 18-fluoro-dihydroxyphenylalanine ([18F]F-DOPA PET) allows the extraction of prognostic factors, including static and dynamic parameters, i.e., indices extracted from a single time point and from a continuous acquisition over 30', respectively. In clinical practice, manual segmentation on Fluid Attenuated Inversion Recovery (FLAIR) MRI is required to identify the tumor. Manual delineation is time-consuming and operator-specific. To overcome these issues, we conceived a pipeline to automate the extraction of static/dynamic parameters to improve the accuracy and reproducibility of [<sup>18</sup>F]F-DOPA PET imaging analysis. Methods: We retrospectively analyzed [18F]F-DOPA PET and FLAIR MRI data from 10 children diagnosed with diffuse high- and low-grade gliomas. The tumor was automatically segmented from PET scans using a thresholding algorithm. Volumes of interest (VOIs) delineated on FLAIR MRI were also considered. Static and dynamic parameters were extracted directly from [<sup>18</sup>F]F-DOPA PET within the defined VOIs. **Results**: Static and dynamic parameters obtained from subjects with high-grade tumors were compared with respect to the two segmentation methods. Tumor/Striatum and Tumor/Background ratios showed no significant differences between the two approaches (p > 0.05). Conversely, a significant difference was observed in the time-activity curve slope between the semi-automated and the automated methods (p = 0.031). Therefore, it was decided to resort to the automatic segmentation method for high-grade neoplasms, while the semi-automatic method is reserved for tumors with low-[<sup>18</sup>F]F-DOPA-affinity tumors. Conclusion: To sum up, the hybrid approach eliminated false positives in tumor identification due to elevated uptake in healthy brain tissue among patients affected by low-grade tumors. Furthermore, adopting a volumetric approach for identifying tumor lesions enhances parameter extraction accuracy, overcoming the inherent limitations of manual segmentation. Future investigations will focus on exploring the clinical significance of the extracted parameters.