Use of Radiomic Features combined with Hybrid Machine Learning to Robustly Identify Parkinson's Disease Subtypes

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➢ INTRODUCTION

- ✓ Parkinson's disease (PD) is a chronic, heterogenous and progressive neurodegenerative disease, and the 2nd most common neurodegenerative disorder after Alzheimer's disease, affecting 2–3% of the population over 65 years of age [1,2].
- ✓ PD is characterized by widespread neuronal loss, resulting in a range of motor and non-motor symptoms.
- ✓ It is important to subdivide Parkinson's disease (PD) into specific subtypes, since homogeneous groups of patients are more likely to share genetic and pathological features, enabling potentially earlier disease recognition and more tailored treatment strategies [3,4].

➢ AIM

- ✓ To identify reproducible PD subtypes using clinical and imaging information including radiomics features, via optimized hybrid machine learning (HML) methods that are robust to variations in the number of subjects and features.

➢ METHODS

- ✓ We developed advanced HML methods that were robust to variations in the number of subjects and features, for longitudinal datasets (years 0, 1, 2 & 4; Parkinson's Progressive Marker Initiative).
- ✓ The following steps were taken: 1) Segmentation of dorsal striatum on DaT SPECT images: (i) via MRI, and (ii) directly on SPECT; 2) Extraction of radiomic features (RFs) using our standardized SERA software; 3) generation of 15 datasets: 5 with only non-imaging clinical information (1 timeless data; 4 cross-sectional data), and also including SPECT segmented using MRI (5 sets) or SPECT itself (5 sets); 4) applying HMLs constructed using 16 feature reduction algorithms, 8 clustering algorithms and 19 classifiers; 5) cluster number optimization; 6) applying modified information criterion (MIC) for optimal subtypes selection; 7) Cross-linking subgroups; 8) Confirming the findings using High Dimensional Hotelling's T2 Test; and 9) Independent validation: t-SNE (T-distributed Stochastic Neighbor Embedding) plot.

➢ RESULTS

- ✓ Our modified information criteria enabled selection of consistent clusters across different hybrid methods.
- ✓ When using no radiomics features, the clusters were not robust to variations in features, whereas utilizing radiomics information enabled consistent generation of clusters (rest of this work).
- ✓ We arrived at 3 distinct subtypes in years 0, 1, 2, and 4, and on timeless datasets, which were also confirmed to be consistent with one another, using training and testing process of k-means, as well as Hotelling's T2 test.
- ✓ Relative to MRI-based segmentation of SPECT images, subtypes generated using SPECT-based segmentation or solely using conventional SPECT features remained less consistent when the number of subjects changed.

Fig 1. Fusion of MRI segmentations on SPECT images for radiomics analysis

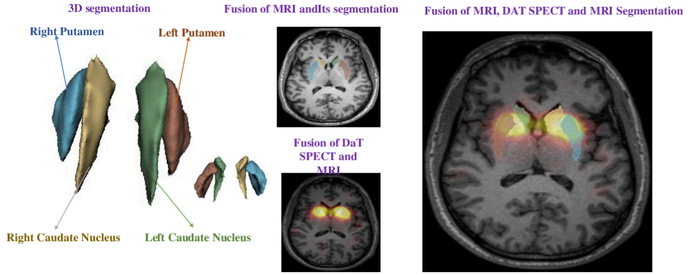


Fig 2. Reproducibility test: X axis represents how many parts the dataset was divided into, and Y axis represents correlation factor between sub-types resulting from each data subset (division) and the original sub-types from the entire timeless dataset.

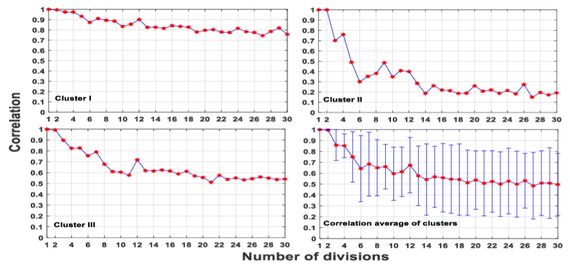


Fig 3. Spider plot of three kinds of features, non-motor (N), motor (M) and imaging (I), for our 3 identified PD sub-clusters.

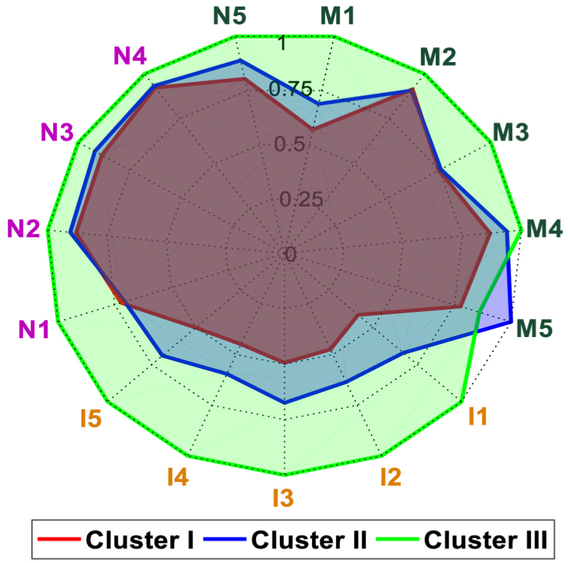
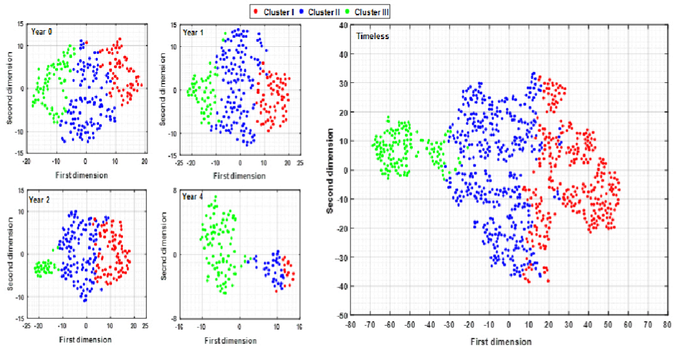


Fig 4. Independent validation of our ML methods using t-SNE Dimensionality Reduction Plot.



➢ INNOVATION & IMPACT

- Analysis of previously published data-driven PD subtype classification systems suggests lack of reproducibility [5,6], suggesting need for establishment of standards for validation and use of clustering systems.
- Clinical measurements based on visual examination in different clinical centers have several sources of error, and can be a major challenge.
- Systematic analysis of images may provide help to this end.
- In this work, radiomics features were extracted from SPECT images systematically segmented via MRI, with features generated through our standardized program based on guidelines from IBSI (Image Biomarker Standardization Initiative).

➢ CONCLUSIONS

- ✓ Appropriate hybrid ML and independent statistical tests enabled robust identification of 3 subtypes in PD. This was achieved by combining clinical information with radiomic features extracted from SPECT images segmented using MRI, also demonstrating robustness to the number of subjects and features.

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