A Fully-Automatic Framework for Parkinson's Disease Diagnosis by Multi-Modality Images

CS 732 Advanced Machine Learning

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Introduction

- Parkinson’s Disease (PD) is the second-to-most prevalent long-term neurodegenerative disease, Causing about 340,600 deaths per year, PD is one of the major concerns in neurology.
- The gold standard of PD diagnostic criteria is the Movement Disorder Society Clinical Diagnostic Criteria for Parkinson’s disease (MDS-PD Criteria).
- The functional neuroimaging of the presynaptic dopaminergic system is underlined in the MDS-PD criteria.

Introduction: T1-MRI & CFT-PET

- Several PET tracers like 11C-CFT are developed to observe the activity of dopamine transporter (DAT), a biomarker of presynaptic dopaminergic system which has high sensitivity in detecting early stage of PD.
- **The information that CFT-PET alone can give is limited.**
- The structural neuroimaging methods like T1-weighted MRI are introduced to the multi-modality diagnosis of PD.

Introduction: SVM

- The support volume machines (SVM) have been widely used to improve the accuracies and reduce the time consumed in diagnostic methods.
- SVM has been used to to distinguish early PD patients form normal controls exploiting resting-state functional MRI, and obtained an accuracy of 86.96% ~ 97%.

This paper proposed an automatic, end-to-end, multi-modality diagnosis framework for PD, taking T1-MRI and CFT-PET images as input with the usage of U-Net for image segmentation.

Dataset

- PET images were performed by a Siemens Biograph 64 PET/CT scanner (Siemens, Munich, Germany) in three-dimensional (3D) mode.

Table 1. Summary for the studied dataset.

Subject	HY	Count	Gender (M/F)	Age	UPDRS
NL	0	18	4 / 14	64.1 ± 6.7	--
PD	1	15	10 / 5	61.2 ± 7.6	14.3 ± 5.1
	2	26	16 / 10	62.0 ± 7.9	21.6 ± 7.5
	3	8	4 / 4	58.8 ± 5.9	34.6 ± 7.4

Note: for age and UPDRS, the number means mean ± standard deviation

Methodology

- Segmentation using U-Net
- Combining Two Modalities by Registration
- Feature Extraction and Prediction

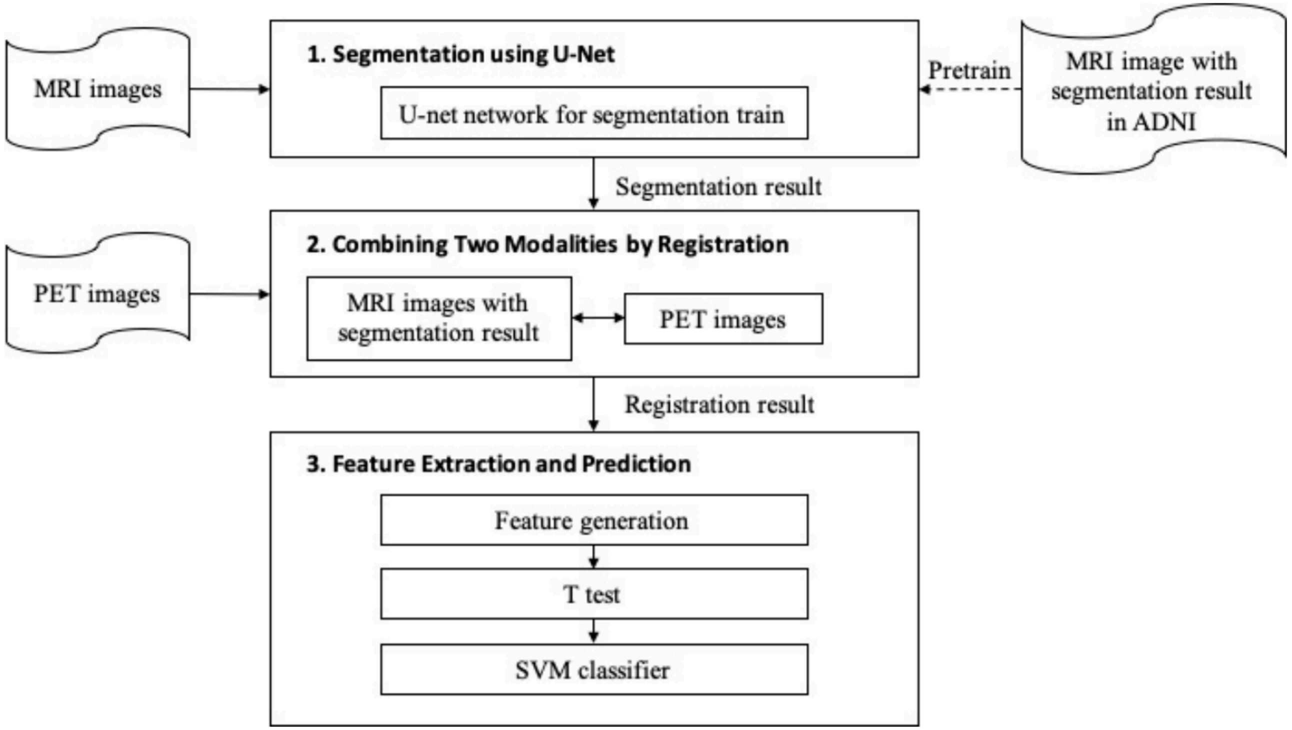


Figure 1 The architecture of our proposed framework.

Automatic Segmentation for PD Diagnosis

- Based on the U-Net
- Deep supervision for fast training convergence
- a well-designed loss function for accurate segmentation
- The network comprises encoding and decoding paths

Automatic Segmentation for PD Diagnosis

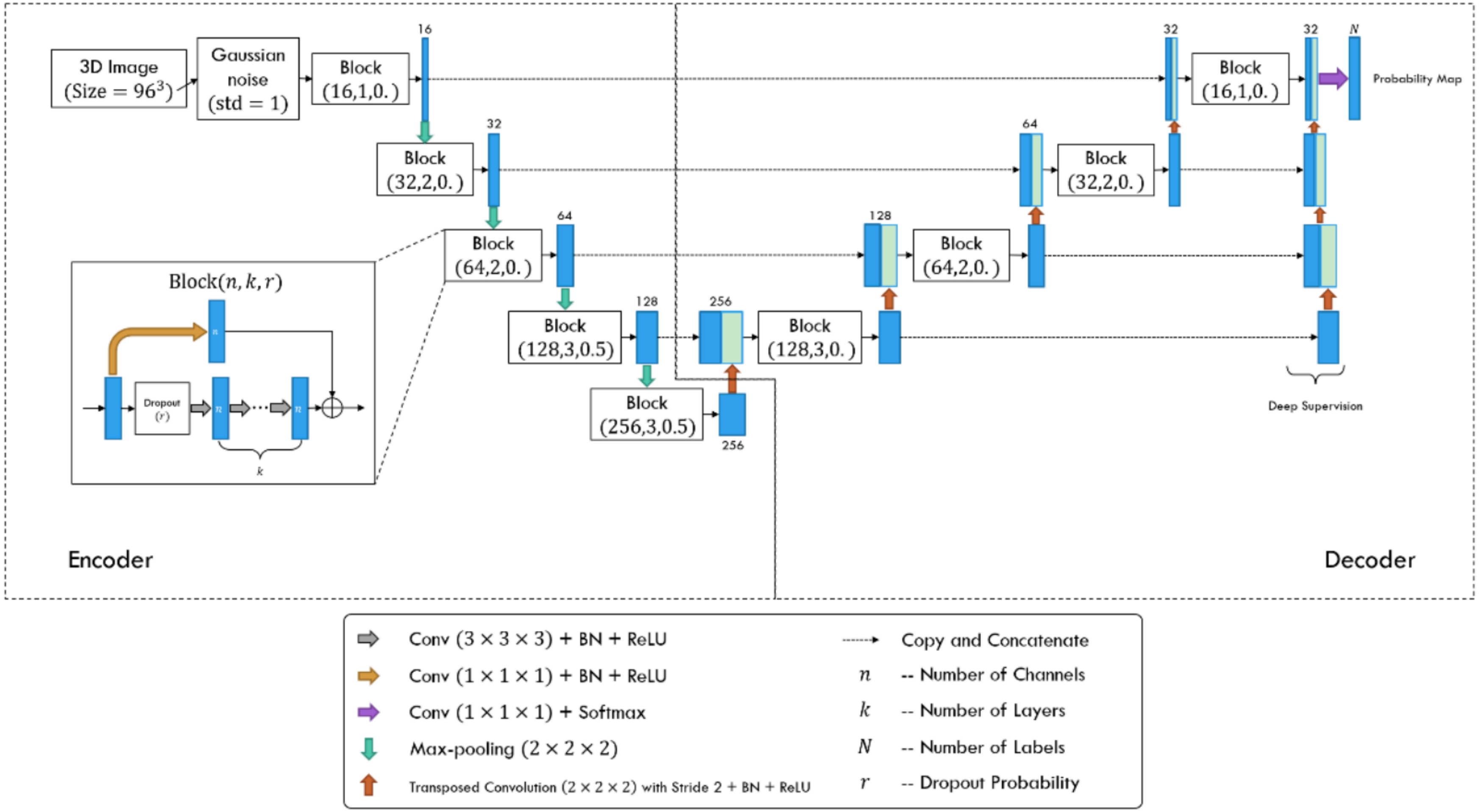


Figure 2 The proposed segmentation network architecture.

Loss Function

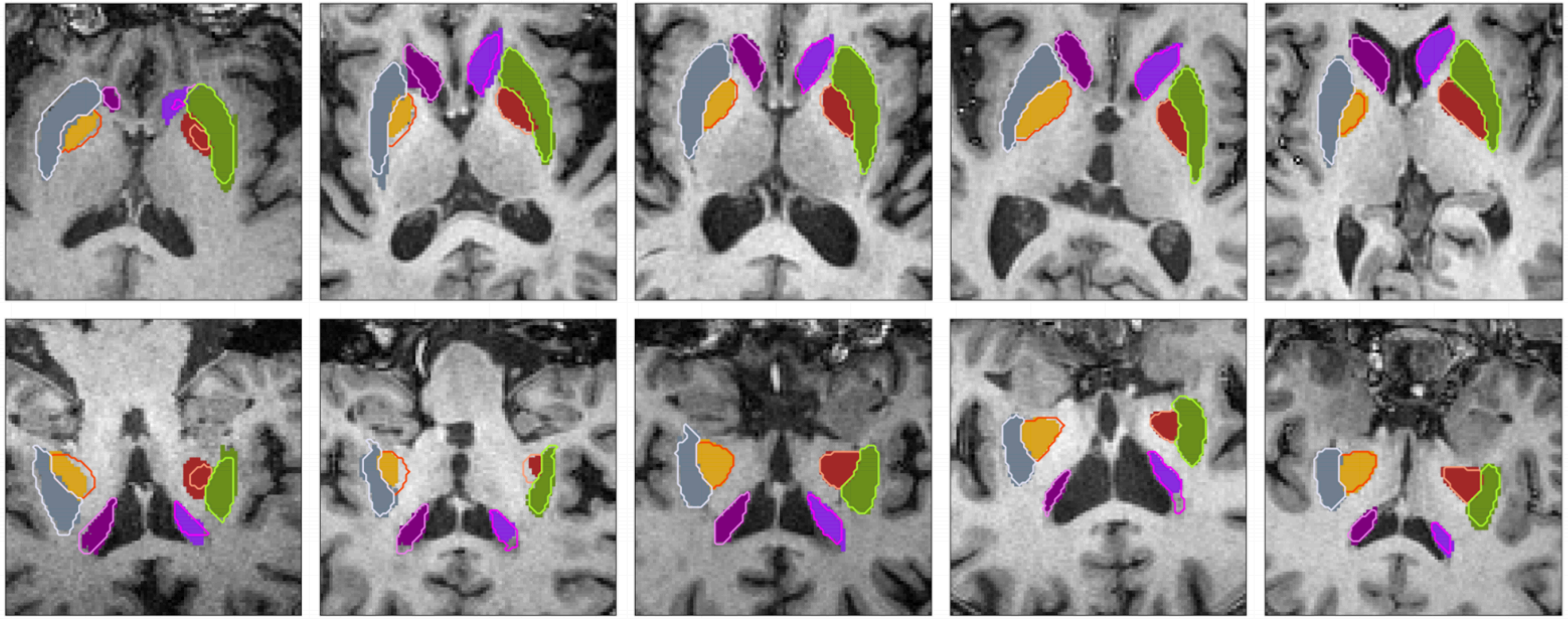
- $L = w_D L_{Dice} + w_C L_{Cross}$ where L_{Dice} denotes the exponential logarithmic Dice loss given by
- $L_{Dice} = \mathbb{E}_i[(-\ln Dice_i)^{\gamma}]$ with
- $Dice_i = \frac{2\left(\sum x \delta_{il}(x) \cdot p_i(x)\right)+\epsilon}{\sum x\left(\delta_{il}(x)+p_i(x)\right)+\epsilon'}$ and L_{Cross} denotes the cross-entropy given by
- $L_{Cross} = \mathbb{E}_x[-\ln p_l(x)]$

Here i is the segmentation label and l is the ground-truth label, both at the voxel position x. $\delta_{il}(x)$ is the Kronecker delta, which equals 1 if $i = 1$ and 0 otherwise. $p_i(x)$ is the probability of voxel x being labelled as i.

Training

- The segmentation U-Net were pre-trained using the Alzheimer’s Disease Neuroimaging Initiative (ADNI) data with segmentation labels from the Multi-Atlas Label Propagation with ExpectationMaximization (MALPEM) platform.
- ADNI database collects data including magnetic resonance imaging (MRI) images as predictors of the disease, to measure and track the progression of early Alzheimer’s disease (AD). http://adni.loni.usc.edu
- MALPEM is a software package to perform whole-brain segmentation of T1-weighted MRI images. https://biomedia.doc.ic.ac.uk/software/malp-em/

Result



Case 1 (0.804) Case 2 (0.835) Case 3 (0.909) Case 4 (0.908) Case 5 (0.910)

Figure 3 Visualization of the segmentation results, slices of the axial view (top row) and the coronal view (bottom row). The colored blocks and contours represent the ground truths masks and the automatic segmentation boundaries, respectively. Case 1 and case 2 are two worst segmentations, and case 3, case 4 and case 5 are three median results. Values in the parentheses refer to the corresponding DSCs.

Result

Table 2 Average DSCs of the segmentation of each anatomy with their corresponding inter-subject variations.

	Right Caudate	Left Caudate	Right Pallidum	Left Pallidum	Right Putamen	Left Putamen
Dice ± inter-subject variation (%) (95% confidence interval)	88.5 ± 6.3	90.1 ± 7.2	89.3 ± 11.4	86.9 ± 13.0	92.2 ± 5.0	91.4 ± 5.5

Feature Selection

Table 3 Feature importance of method with/without volume feature.

feature name	Importance With Volume Feature	Importance Without Volume Feature
mean	0.20295131	0.20060408
med	0.20240259	0.19645433
3^{rd} quantile	0.19605019	0.19460838
1^{st} quantile	0.18249546	0.18346047
max	0.14429148	0.14974968
min	0.0715383	0.07512307
volume	0.00027068	--

Discussion and Conclusion

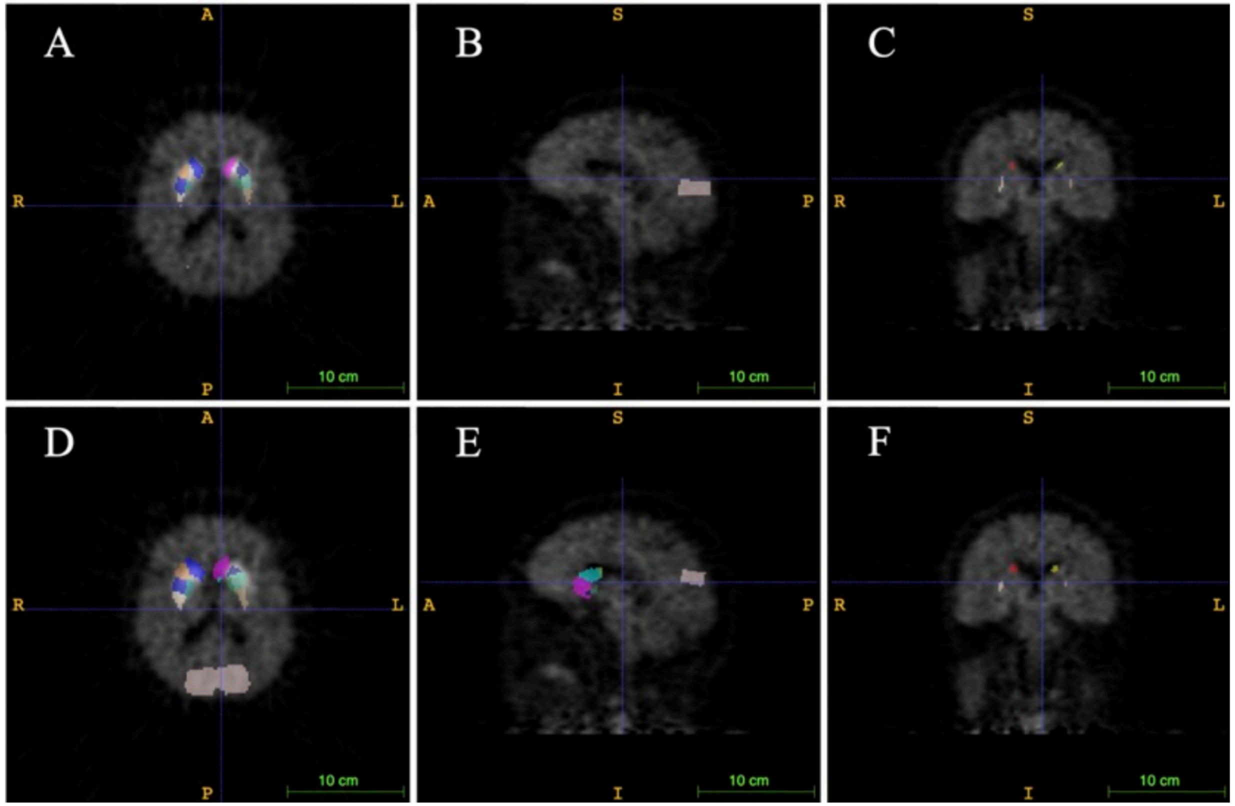
- Total of 90 features were selected, including the statistics of the radioactive uptake ratios and the volume information for each region. A t-test was performed to evaluate the significance of every feature:

Table 4 P values of t-test results from the selected features.

ROI		SOR						volme
		mean	max	min	1st quantile	median	3rd quantile	
Right Caudate	front	6.52E-10	2.55E-09	4.65E-06	2.87E-09	1.84E-09	3.41E-10	0.0544
	middle	7.02E-10	4.76E-10	0.001585	6.32E-09	7.02E-10	2.46E-10	
	rear	1.04E-07	1.78E-09	2.21E-07	3.94E-06	6.00E-07	3.06E-08	
Left Caudate	front	1.11E-08	2.70E-08	3.20E-07	2.75E-08	2.11E-08	8.46E-09	0.0321
	middle	5.52E-08	4.72E-08	2.51E-05	1.65E-07	6.76E-08	4.74E-08	
	rear	1.41E-06	2.03E-07	0.000103	3.78E-06	3.45E-06	1.82E-06	
Right Putamen	front	7.37E-18	2.80E-16	3.16E-07	2.03E-17	1.64E-17	1.19E-17	0.0469
	middle	1.18E-30	7.62E-26	1.13E-09	5.21E-14	6.58E-31	1.79E-30	
	rear	1.03E-13	1.57E-13	1.02E-07	1.20E-12	1.50E-13	6.86E-14	
Left Putamen	front	9.50E-15	5.80E-15	2.11E-06	5.24E-14	3.66E-14	8.96E-15	0.02
	middle	1.01E-27	3.03E-22	2.17E-10	1.80E-28	2.36E-28	5.97E-27	
	rear	3.26E-31	8.34E-14	9.98E-11	3.18E-29	1.02E-30	9.95E-32	
Right Pallidum		8.84E-23	4.07E-21	7.53E-07	4.72E-16	1.27E-21	1.60E-12	0.002
Left Pallidum		6.06E-19	1.50E-17	4.87E-07	1.75E-07	2.90E-08	2.13E-09	0.309

Discussion and Conclusion

- A, B and C show the segmentation result in gold standard; D, E and F show the segmentation in the wrongly predicted subject



Discussion and Conclusion

- This figure shows the importance of different categories of variables in the gold standard experiment using manual segmentation results, our automated segmentation results experiments, and experiments without volume feature.

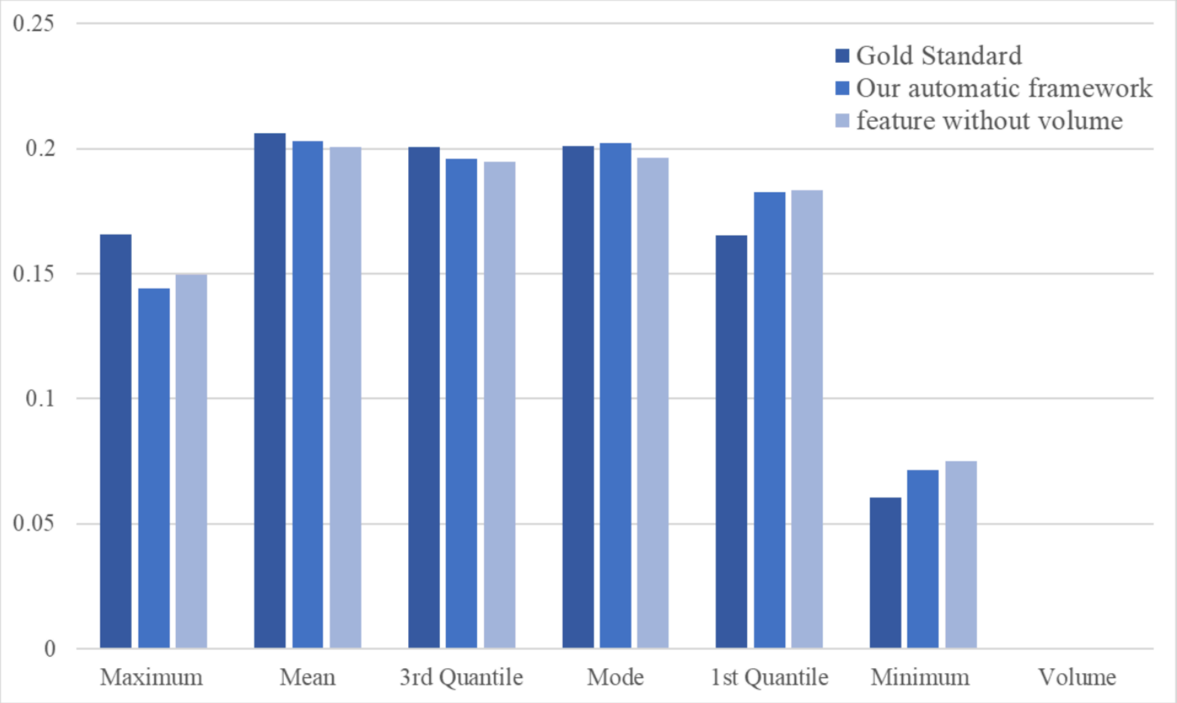


Figure 5 The importance of different categories in different methods

Discussion and Conclusion

- The most relevant region influencing the separation of PD/NL are localized in the middle and rear of putamen, then pallidum, and the caudate reveal the least significance on this task.

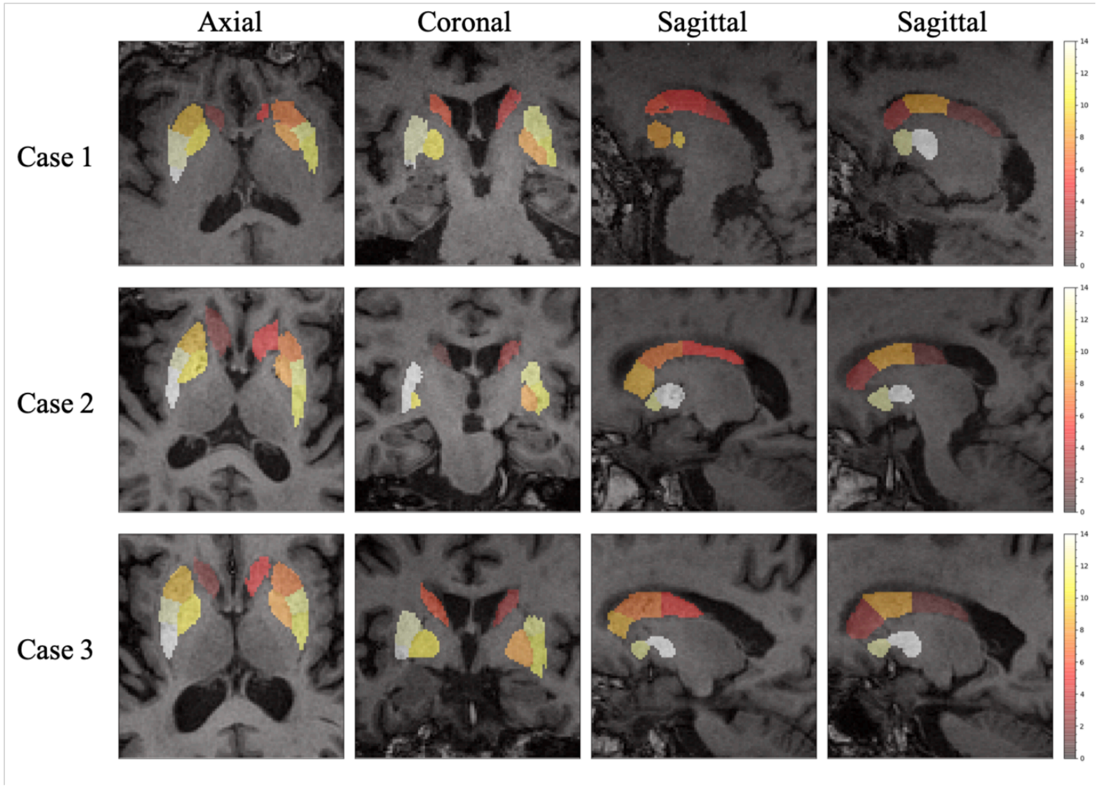


Figure 6 The importance of ROIs in the proposed framework. One axial slice, one coronal slice and two sagittal slices of three subjects are chosen to show the importance heatmap of the ROIs.

Discussion and Conclusion

- This paper proposed a fully automatic framework, combining two modalities, T1-MRI and CFT-PET, for PD diagnosis.
- This framework has been trained and tested by the dataset and reached 100% accuracy on the PD/NL task.
- This paper used multimodality method, and trained a U-Net to segment T1-MRI images to ensure the performance of the framework.
- This paper also emphasizes the high reference value the CFT-PET holds in the PD diagnosis.