

Using diffusion microstructure distributions for prediction of motor outcomes in stroke recovery

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Synopsis

We investigate the potential advantages of using distribution-valued variables to capture image information instead of the conventional techniques which use mean values to represent entire regions-of-interest. Using distribution-based distances in comparison with a mean-based approach, we explore various models to predict motor performance recovery in stroke patients. Our experiments indicate that for predictor variables Orientation Dispersion index and the Restricted Diffusion Index (diffusion scalars derived from the NODDI model), the distribution representations can lead to significantly improved regression models, over the respective mean values. Additionally, using the baseline Fugl-Meyer scores to predict follow-up Fugl-Meyer scores further enhances the model statistics.

Introduction

Regions-of-interest (ROIs) in medical images are often summarized using the ‘mean’ value of the parameter of interest within these regions. This oversimplification early in the pipeline can lead to a loss of variability information which can hold critical differentiating power later in the analysis. In this work, we propose using distribution-valued variables for representing information from image neighborhoods. This allows us to retain the nuances of the underlying image information in a structured manner and can be used to build more powerful regression models.

Regression modeling requires the concept of ‘distance’ between observations to estimate statistics like the mean and variance. To extend this to the current context, we use probabilistic distances between probability density functions (PDFs) captured from ROIs. Our driving application is the prediction of motor performance recovery in stroke patients. Baseline measurements of microstructure derived from diffusion-weighted images are known to be predictive even when using ROI mean-based analysis. Here we quantify the improvements provided by the inclusion of distribution-based distances. We also test the ability of PDFs of diffusion parameters combined with baseline measurements of a clinical motor score, the Fugl-Meyer Upper Extremity (FMUE) to predict follow-up FMUE scores.

Method

Previous work has highlighted the importance of the PLIC region for analysis involving motor functions.¹ Much of this work involves Fractional Anisotropy (FA) values expressed as a ratio or differences acquired from inter-hemispheric information.^{2,3} Recent work has also highlighted that NODDI parameters like the Orientation Dispersion Index (ODI) and neurite density (or RDI- Restricted Diffusion Index) correlates with motor recovery. Most of these studies use the mean differences of FA or ODI values from ROIs in the ipsilesional and contralesional sides. Instead, we find the inter-hemispheric differences as the Wasserstein distance between the respective PDFs. The Wasserstein distance (also known as the Earth Mover’s distance) is a distance metric, unlike other probabilistic distances like the Kullback Leibler divergence.^{4,5} It intuitively quantifies the distance as the transformation of one PDF into another while respecting the underlying geometry of the domain of the measurement variable. Using this metric, we explore different regression models using baseline measurements as the predictor variables and the follow-up FMUE scores (FMUE-TP2) as the response variable. Our predictor variables include: FMUE scores at time point 1 (FMUE-TP1), and diffusion parameters derived from the NODDI model- ODI and RDI.⁶ 8 stroke patients were imaged on a 3T scanner with diffusion spectrum imaging (203 directions, max b=4000).⁷ The MRI scans were acquired in the subacute phase (at 9±6 days post-stroke), and baseline FMUE measurements were performed within 1-2 days of the MRI scans. Follow-up FMUE assessment was performed at 53±21 days after stroke.

Results and discussion

Table 1 shows results for the analyses using the ipsi- and contralateral PLIC regions. We first estimate a linear model: FMUE-TP2 as the response variable, and interhemispheric difference in the mean-values of the individual diffusion parameters (Δ Mean ODI, Δ Mean RDI) as the predictor variable. Next, we replace the mean-based differences with the Wasserstein-distances between the ipsilesional and contralesional PLIC distributions (Δ Dist ODI, Δ Dist RDI). We report our results in terms of the model RMSE, coefficient of determination (R^2 adjusted for the number of variables), p-value (jointly for the model), t-statistic for the predictor variables and Pearson’s correlation coefficient r (when using a single predictor). Even with a single predictor variable, through reduced RMSE and p-values, increased R^2 and r , and significant t-statistics, distribution-based analysis shows improvement over the corresponding mean-based models.

Especially of interest are the results for RDI where a negative R^2 and very low r show that mean RDI values provide an ineffective model with no prediction power. However, RDI distributions remarkably improve the differentiating capacity of this variable. See the distribution plots for ODI and RDI in Fig. 1 and 2. For some subjects, the mean values almost coincide which can be misleading and can lead to a loss of statistical power in a data set that is already relatively small.

Next, we use FMUE-TP1 as the only predictor variable (Table 1) to show that it can independently predict FMUE-TP2 reasonably well. Joint use of FMUE-TP1 and either ODI or RDI improved predictive capability (Table 1, lower block of results). These results again show the potential gains from using distributions over mean values (specially for RDI) as well as adding FMUE-TP1 as a predictor variable. Overall, the best linear model for these datasets uses FMUE-TP1 and Δ Dist ODI as the two predictor variables. We have currently refrained from using three predictor variables jointly as our

sample size is limited and we risk overfitting when adding another variable.

Conclusion

Distribution-valued variables highlight and detect underlying differences which may be missed when using mean values to represent image regions. These probabilistic representations of the data exhibit the potential to improve distinguishing power in regression models. The 'information gain' achieved via retaining distributions can particularly help in offsetting the limitations posed by limited sample sizes. The combination of baseline clinical FMUE score and NODDI diffusion parameters (ODI and RDI) show promising results in their ability to quantify future recovery. If validated in larger datasets, this may allow for more efficient clinical management.

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References

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Figures

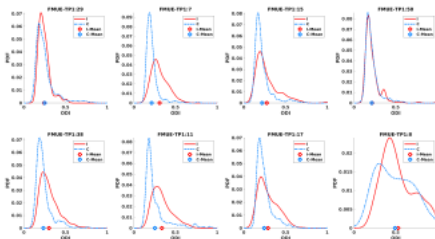


Figure 1: Probability density functions (PDFs) of Orientation Dispersion Index (ODI) values from the NODDI model⁶ for all stroke patients in the PLIC region of the brain. PDFs estimated for both, ipsilesional (I) and contralesional (C) sides of the brain. The corresponding mean ODI values for each PDF are also marked on the x-axis. The baseline Fugl-Meyer Upper Extremity score (FMUE-TP1) is also indicated on top of each subplot.

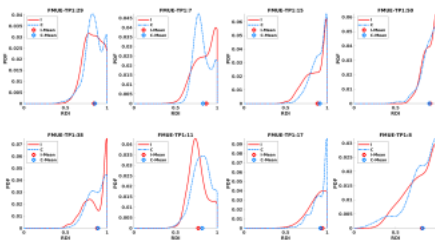


Figure 2: Probability density functions (PDFs) of Neurite Density or Restricted Diffusion Index (RDI) values from the NODDI model⁶ for all stroke patients in the PLIC region of the brain. PDFs estimated for both, ipsilesional (I) and contralesional (C) sides of the brain. The corresponding mean RDI values for each PDF are also marked on the x-axis. The baseline Fugl-Meyer Upper Extremity score (FMUE-TP1) is also indicated on top of each

subplot.

Response Variable: FMUE-TP2	Predictor Variable(s)				
	Δ Dist ODI	Δ Dist RDI	Δ Mean ODI	Δ Mean RDI	FMUE-TP1
RMSE	6.81	6.79	7.41	16.6	10.3
Adjusted R ²	0.811	0.812	0.777	-0.118	0.566
P-Value (Model)	0.0014**	0.0014**	0.0024**	0.628	0.019*
t-statistic	-5.575	-5.595	3.032	-0.510	3.182
Pearson's r	-0.91	-0.88	0.89	-0.20	0.79
	FMUE-TP1, Δ Dist ODI	FMUE-TP1, Δ Dist RDI	FMUE-TP1, Δ Mean ODI	FMUE-TP1, Δ Mean RDI	
RMSE	5.16	6.17	5.51	10.9	
Adjusted R ²	0.892	0.835	0.876	0.518	
P-Value (Model)	0.0016**	0.0048**	0.0023**	0.0695	
t-stat (FMUE-TP1)	2.472	1.349	2.409	2.987	
t-stat (Diffusion parameter)	-4.372	-3.283	3.998	-0.636	

Table 1: Linear regression statistics for various models for PLIC region. Followup FMUE-TP2: response variable. Predictor variables are chosen from baseline as follows: A) Upper-left block (blue highlight): distribution-valued ODI and RDI observations (Δ Dist). B) Upper-mid block: mean-based ODI and RDI observations (Δ Mean). C) Upper-last column: Only FMUE-TP1. D) Lower block (green highlight): combination of FMUE-TP1 with either ODI or RDI diffusion parameters.