Interpretability of Uncertainty: Exploring Cortical Lesion Segmentation in Multiple Sclerosis

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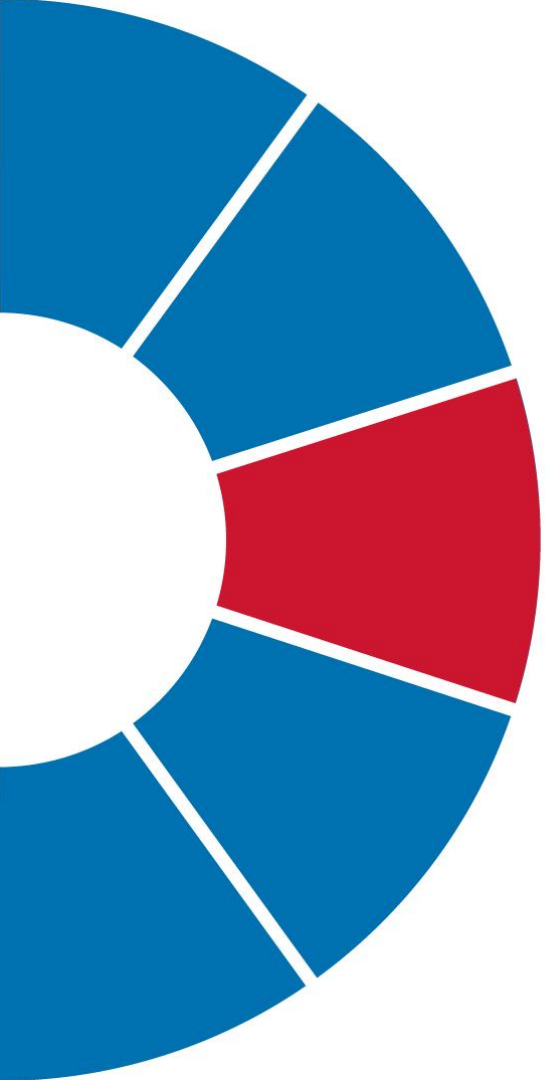
6th of October 2024

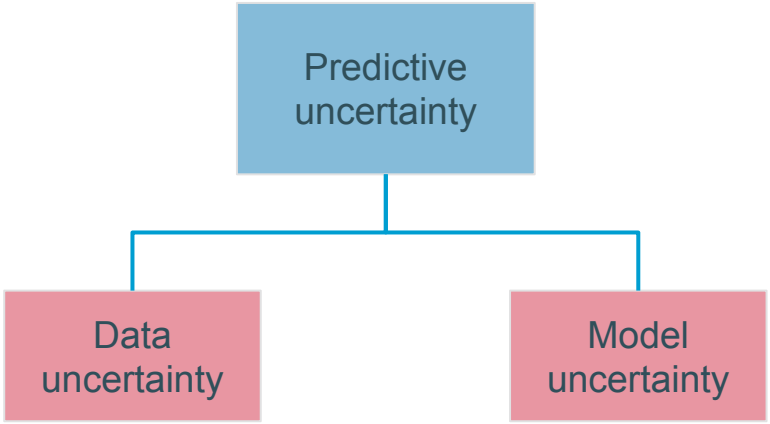
iMIMIC Workshop @ MICCAI 2024

This work was supported by the Hasler Foundation Responsible AI programme (MSxplain project)



Introduction

Uncertainty quantification



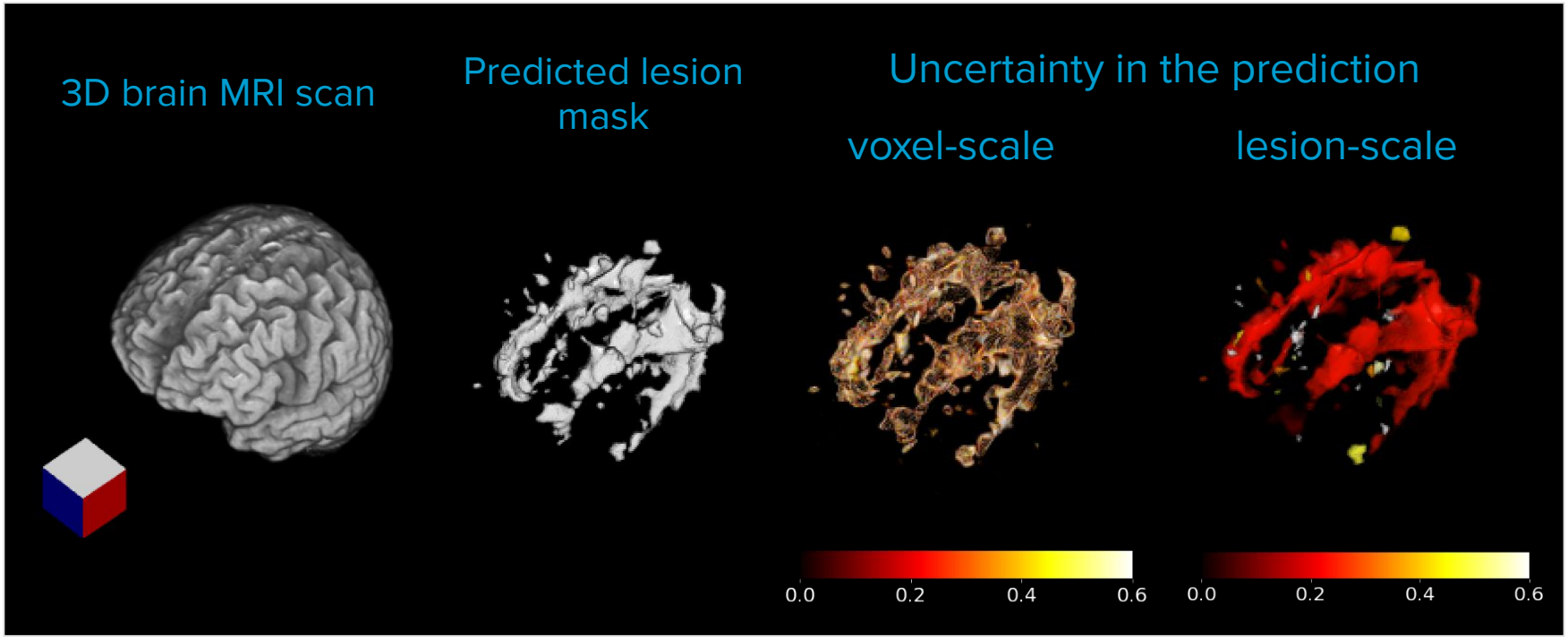
- Noise in the labels
- Noise in the input

- Sparsity of the data
- Domain shift
- Stochasticity of training

- **Uncertainty quantification (UQ)** helps to assess the **reliability of the DL** model predictions
- **Sources of predictive uncertainty** in DL
- Sources of uncertainty in **medical imaging**:
  - Limited resolutions
  - Errors in annotations
  - Low data regimes
  - Domain shifts
  - …

Gawlikowski et al., Artif. Intell. Rev., 2024

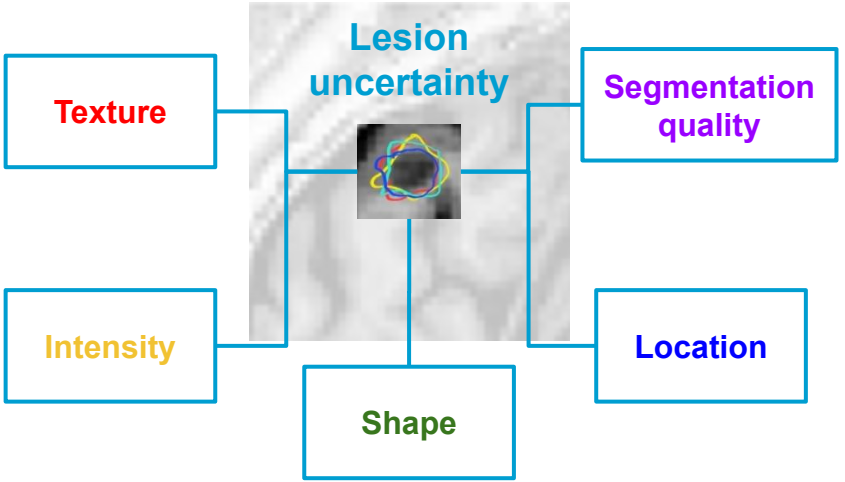
UQ for medical imaging segmentation

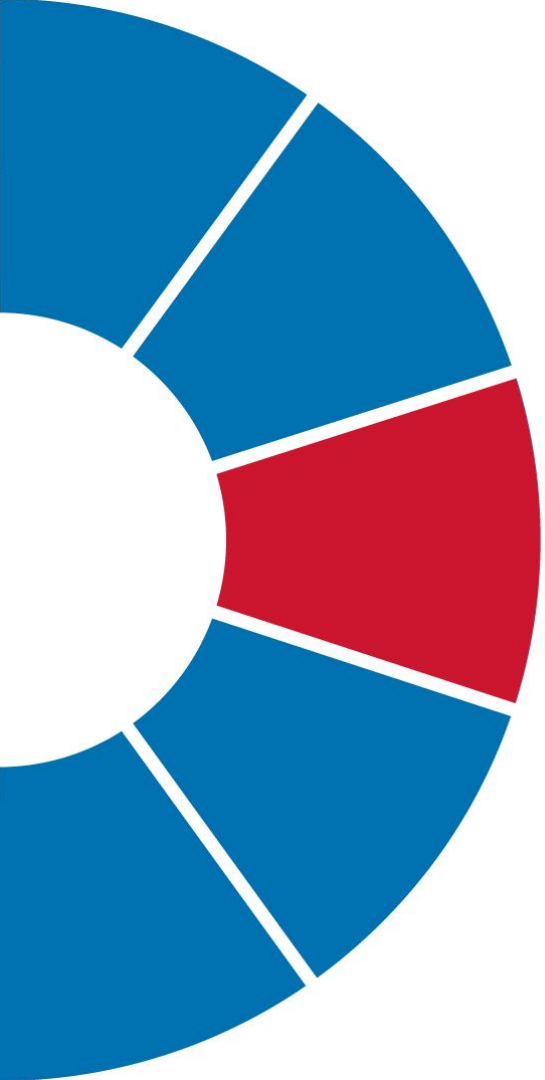


Nair et al., Med. Image Anal., 2020; Lambert et al., MICCAI UNSURE 2022; Molchanova et al., ISBI, 2023

Research objectives

- **Uncertainty has a strong relationship with model errors:** ↑ uncertainty ~ ↑ likelihood of errors
- Analysis **interpreting uncertainty values:**
  - Detecting biases in model behaviour
  - Assessing the sanity of uncertainty values
  - Extracting information beyond errors
- **Proposed analysis:** explaining the variability in the lesion-scale uncertainty in terms of relevant lesion features

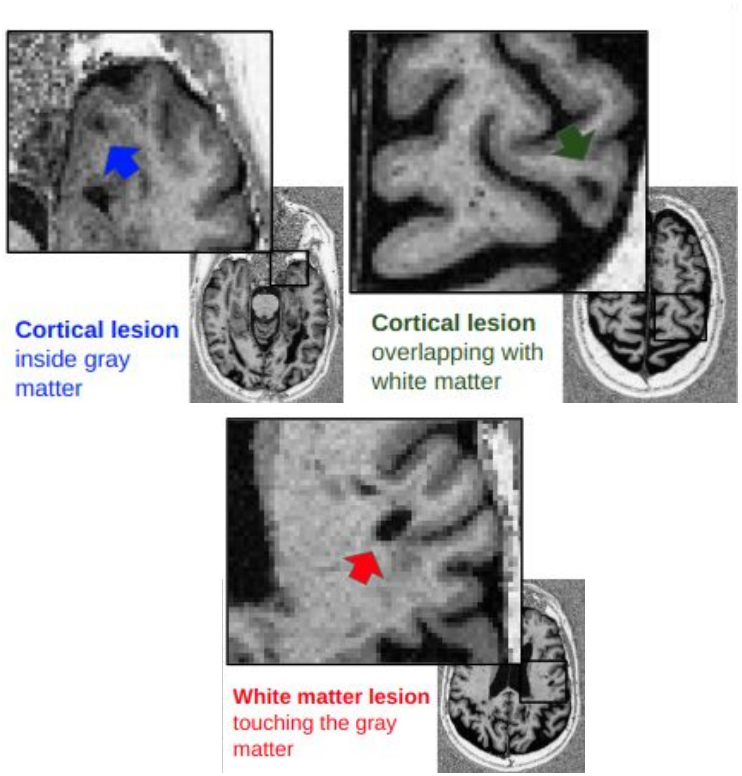




Materials and Methods

Data

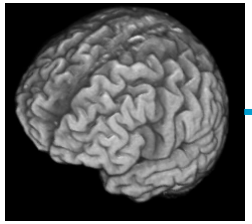
- Data provider: Basel University Hospital, Switzerland
- **Cortical lesions (CL)** are annotated on 3T MP2RAGE MRI scans (Magnetom Prisma, Siemens Healthineers) by a **consensus of two radiologists**
- Train:val:test = **79:8:30 patients**, corresponding to **859:69:302 CLs**



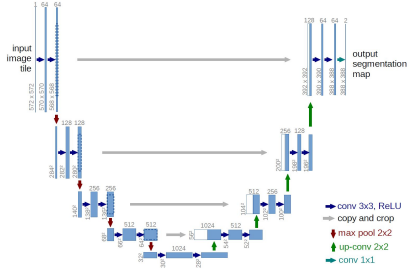
Granziera, https://clinicaltrials.gov/study/NCT05177523, 2019

I. Model training

Input MRI scan



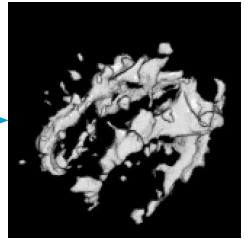
Model capable of UQ



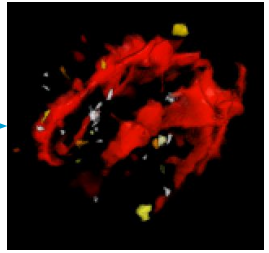
UQ methods:

1. Deep ensembles (DE)
2. Monte Carlo dropout (MCDP)

Predicted lesion mask



Lesion-scale uncertainty map

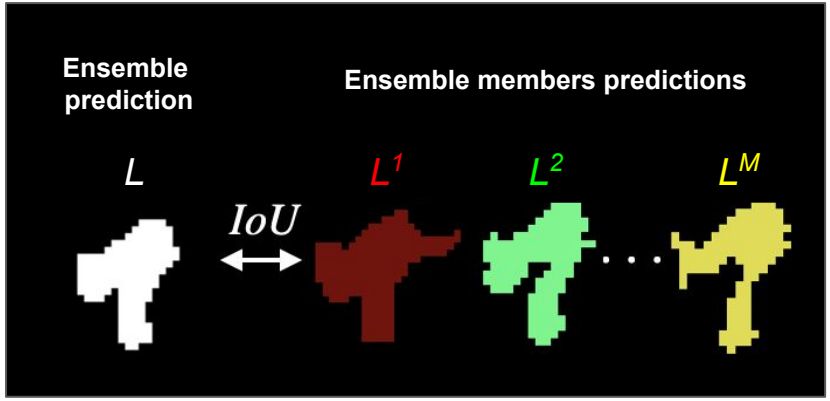


Çiçec et al., MICCAI, 2016; Lakshminarayanan et al, NIPS 2017; Gal and Ghahramani, ICML 2016.

II. Lesion uncertainty computation

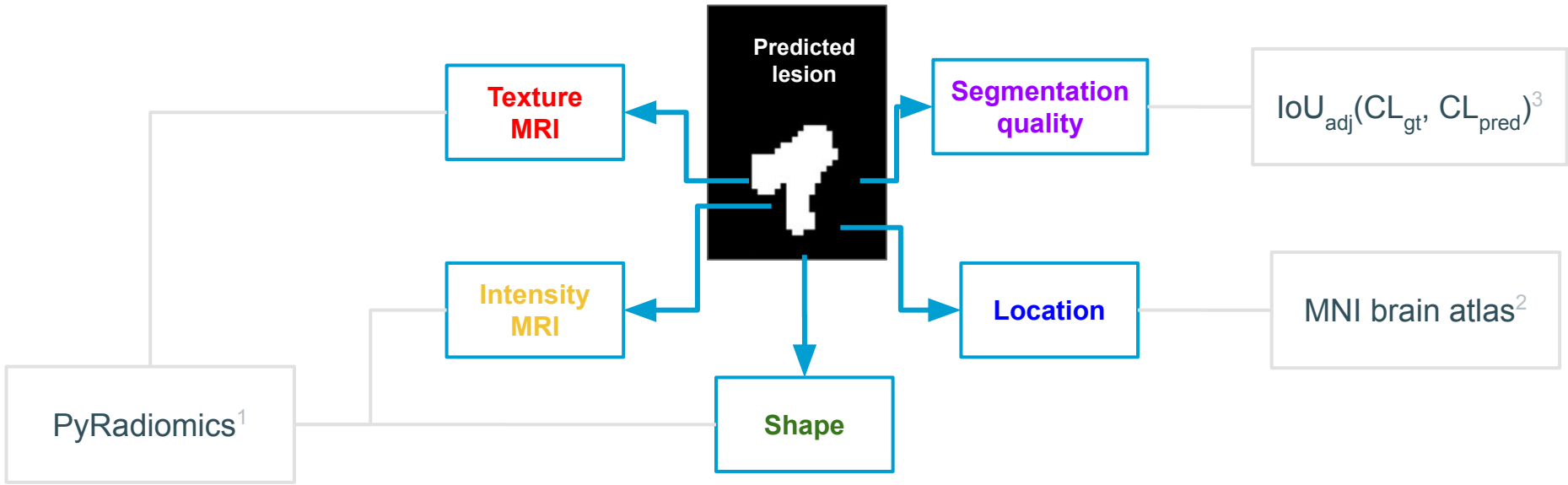
Lesion structural uncertainty (LSU) measure

$$LSU = 1 - \frac{1}{M} \sum_{m=0}^{M-1} IoU(L, L^m)$$



Molchanova et al., ISBI, 2023; Molchanova et al., Under revision Comput. Biol. Med., 2023.

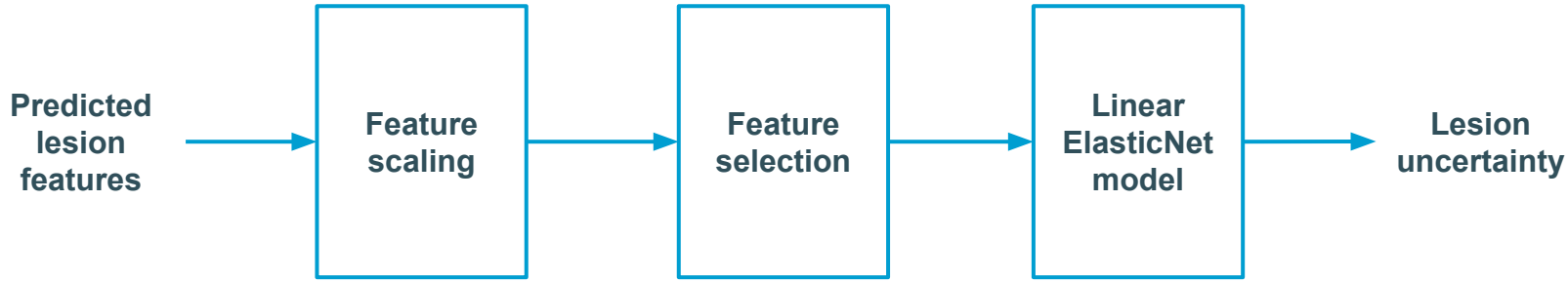
III. Lesion features computation



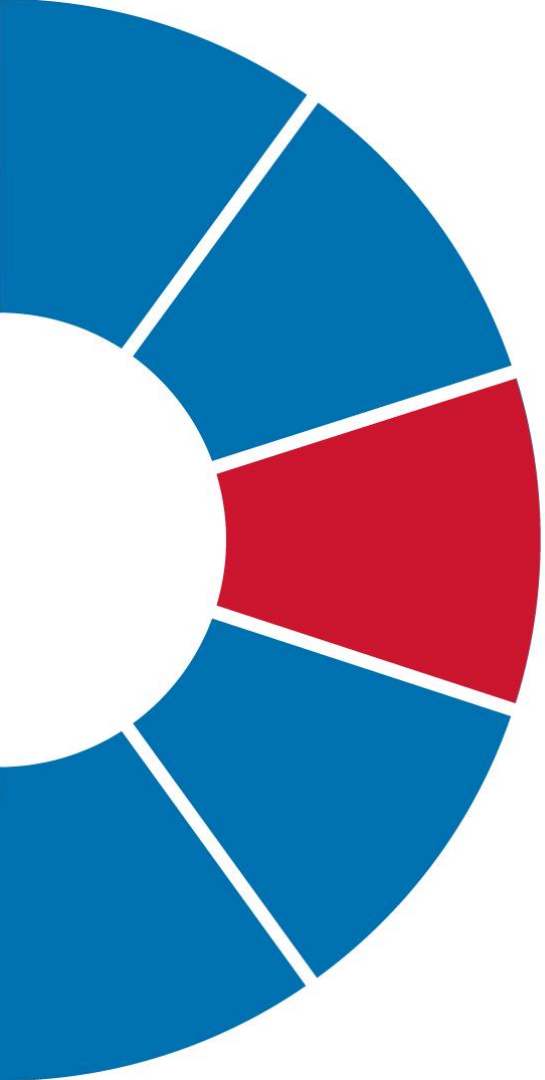
[1]Griethuysen et al., Cancer Res., 2017; [2]Grabner et al., MICCAI, 2016; [3]Rottmann et al, IJCNN, 2020.

IV. Uncertainty regression model

Lesion uncertainty regression pipeline



- Model selection: grid search cross-validation
- Feature importance analysis: repeated 10 times with different random seeds



Results

Regression quality

Coefficient of determination R2 (↑) of ElasticNet model explaining uncertainty

	Cross validation (train set)		
	Only IoU	No IoU	All
DE	**0.520±0.006**	**0.598±0.004**	**0.661±0.004**
MCDP	0.393±0.006	0.589±0.014	0.604±0.013

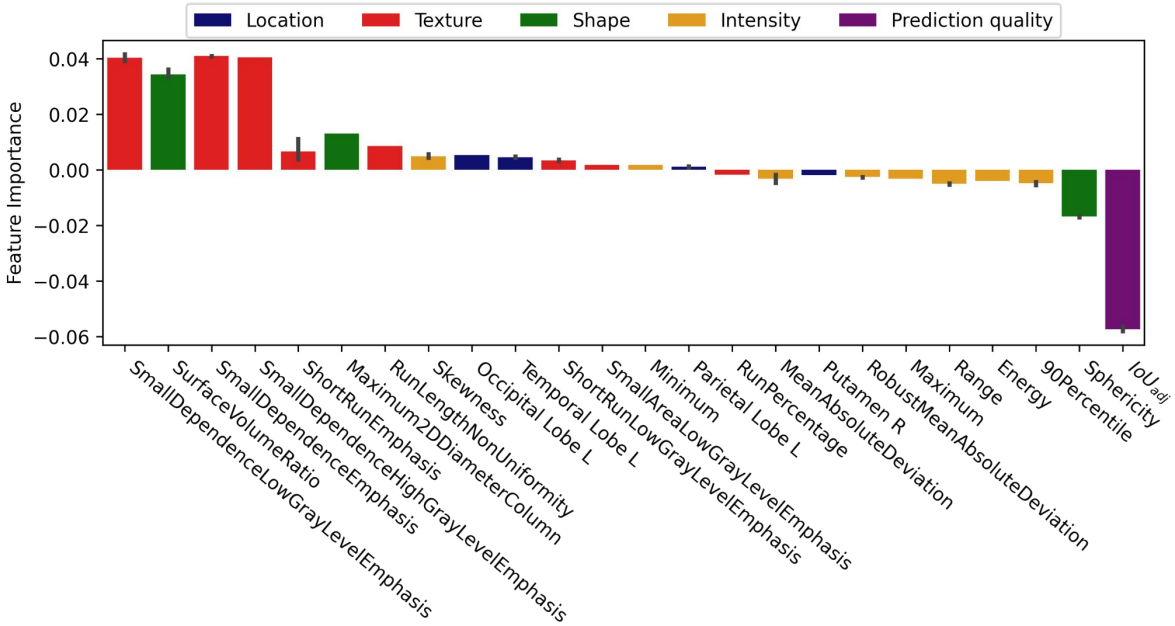
Regression quality

Coefficient of determination R2 (↑) of ElasticNet model explaining uncertainty

	Cross validation (train set)			Test set		
	Only IoU	No IoU	All	Only IoU	No IoU	All
DE	**0.520±0.006**	**0.598±0.004**	**0.661±0.004**	**0.431±0.001**	**0.512±0.002**	**0.632±0.004**
MCDP	0.393±0.006	0.589±0.014	0.604±0.013	0.261±0.003	0.425±0.013	0.494±0.004

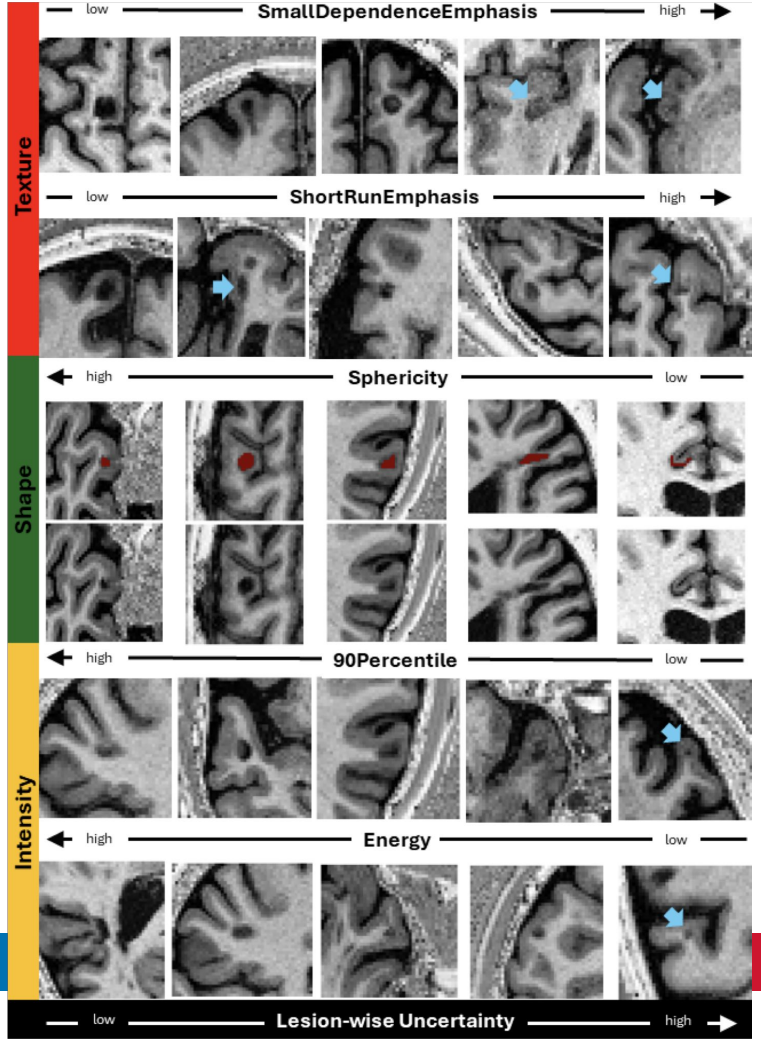
Feature importances

Deep ensemble



Sampled lesion examples

- **Clinical feedback**: these factors are likely to be associated with lower annotators confidence and higher inter-rater disagreement
- Location features lack interpretability from the clinical perspective, however might be related to lesion visibility



Conclusions

- **Proposed analysis** aims at **explaining instance-wise uncertainty** values
- Strong relationship with error additioned by other factors (texture, shape, etc.)
- **Clinical feedback** reveals that additional factors are associated with **low annotator confidence**

- **Unexplained uncertainty:**
  - non-linear relationships
  - lack of relevant features
  - UQ quality
- **Future work:**
  - unexplained uncertainty
  - structured clinical feedback
  - outliers analysis

THANK YOU FOR YOUR ATTENTION

Conclusions

Factors associated with high lesion uncertainty:

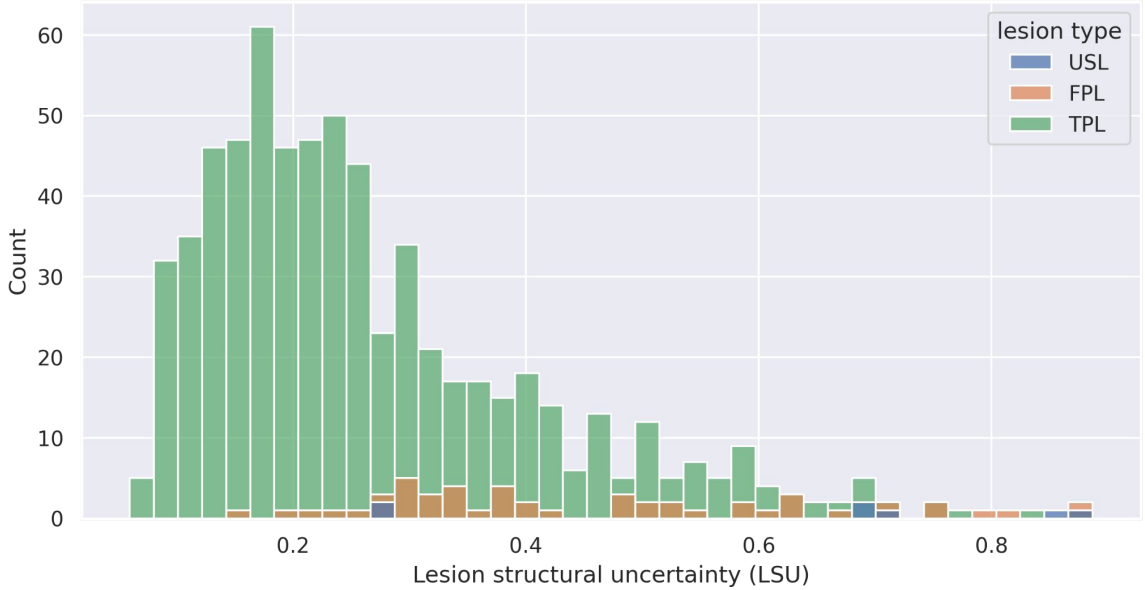
- Prediction quality
- Inhomogeneous textures
- Elongated and spiculated shapes
- Small lesions
- Location at the periphery of the occipital and temporal left lobes
- Absence of high intensity voxels within the lesion

Clinical perspective: these factors are likely to be associated with lower annotators confidence and higher inter-rater disagreement

Unexplained uncertainty: linear model for explanations, incomplete features, UQ quality

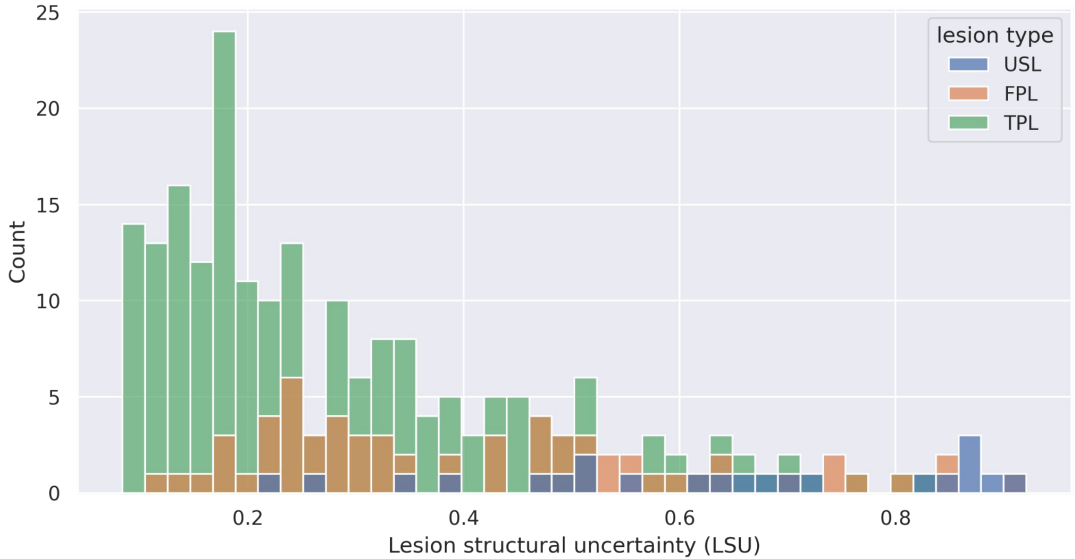
Distribution of lesion uncertainty

Train data



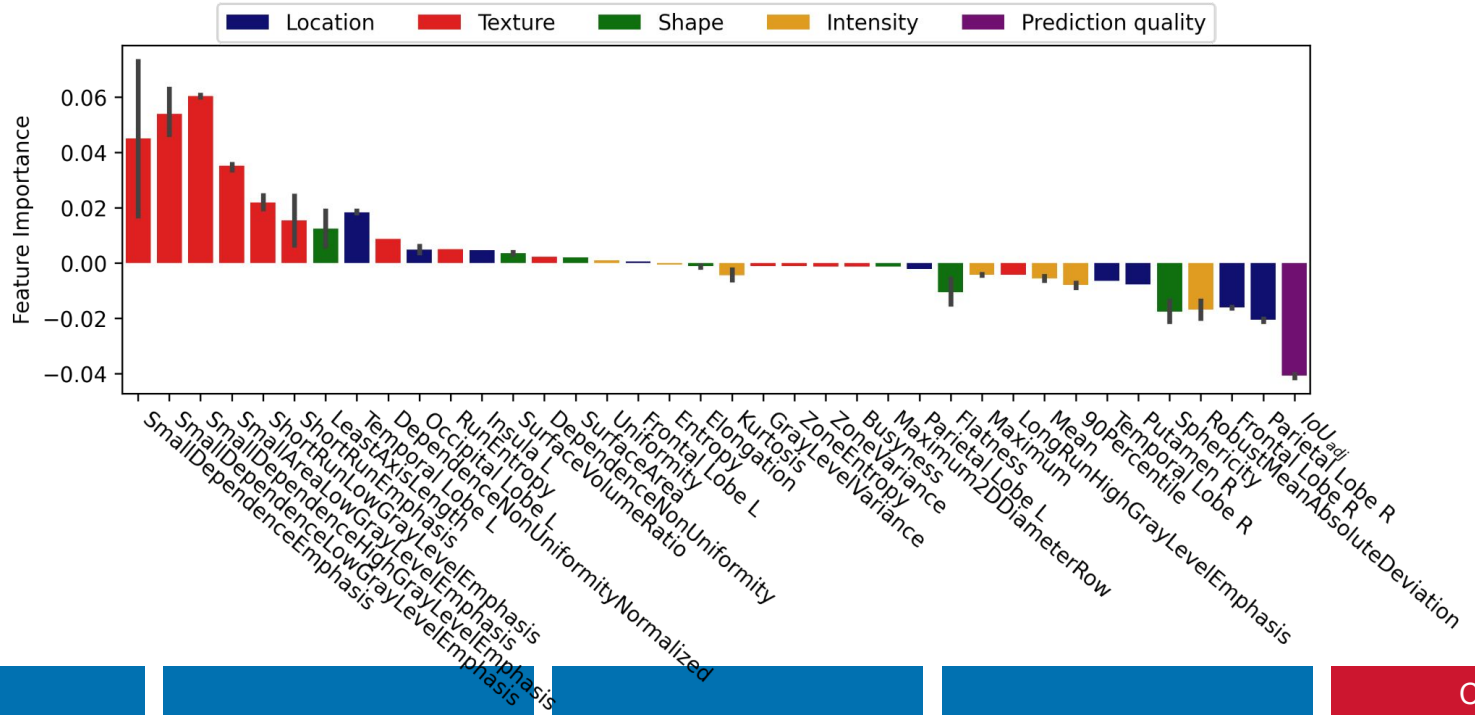
Distribution of lesion uncertainty

Test data

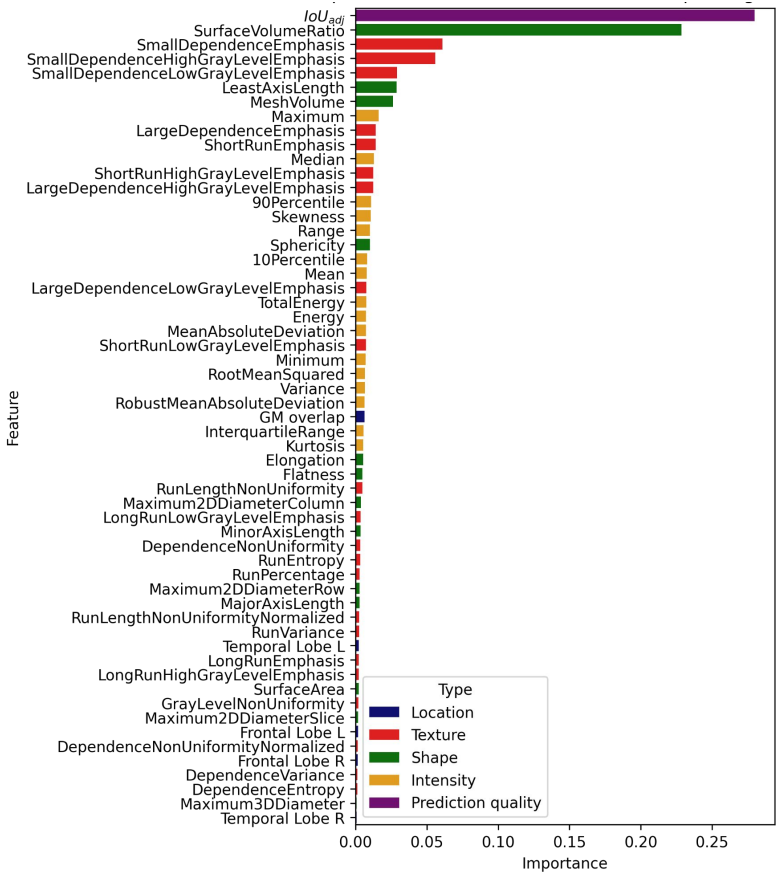


Feature importances

Monte Carlo dropout

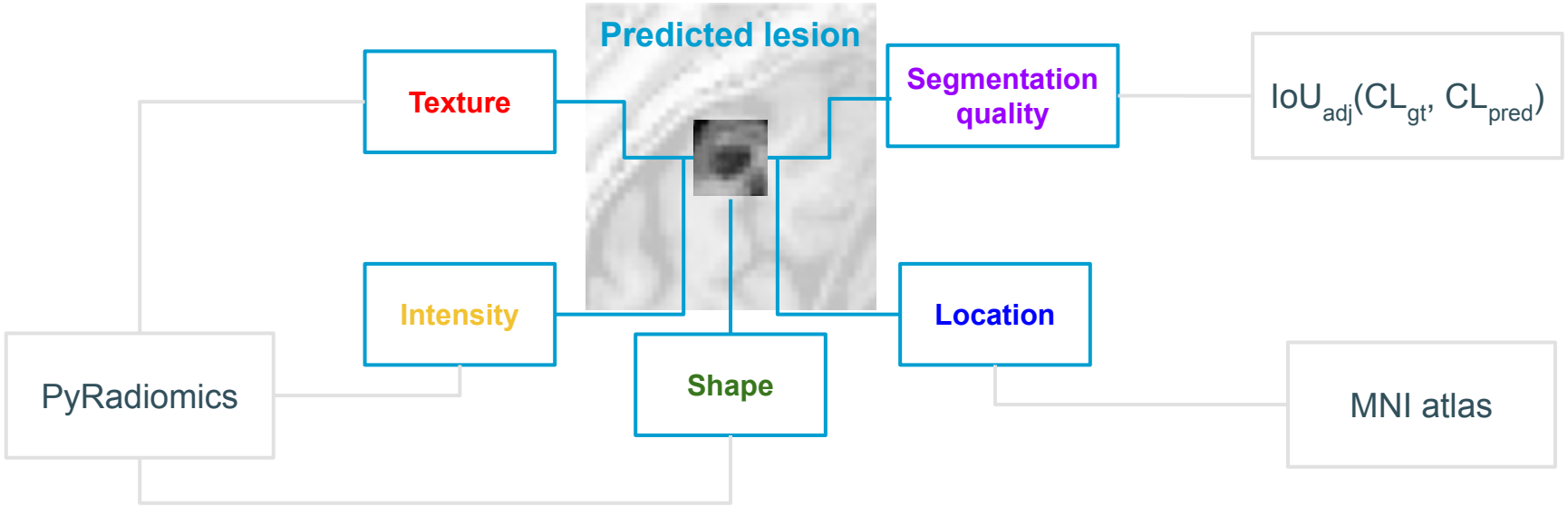


Results: Random forest explainer



Test MSE	Test MAE	Test Explained Var.	Test R2	CV R2
0.014307	0.08503	0.661889	0.652084	0.64692

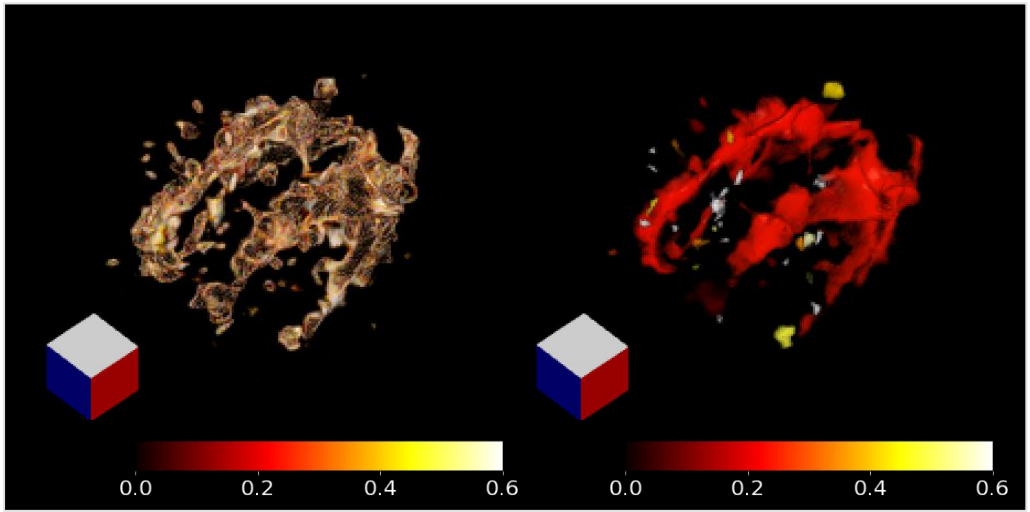
III. Lesion features computation



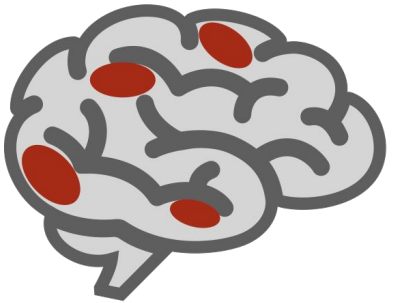
UQ in multiple sclerosis lesion segmentation

Voxel-scale uncertainty map

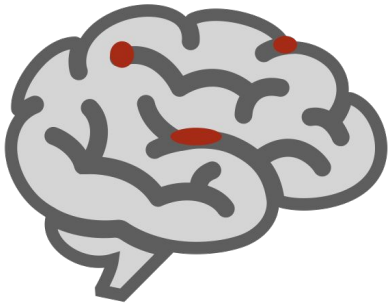
Lesion-scale uncertainty map



White matter lesions



Cortical lesions



Nair et al., Med. Image Anal., 2020; Lambert et al., MICCAI UNSURE 2022; Molchanova et al., ISBI, 2023

UQ for medical imaging segmentation

3D brain MRI sca

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