Quantitative neuroimaging in multiple sclerosis

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Overview

- **Background**
  Relevance, ‘MRI quantification’ approaches, overview of Radiomics approach
- **Objectives**
  Hypothesis and objectives
- **Materials and methods**
  Data description, MRI processing pipeline, analysis pipeline
- **Results**
  Models internal and external validation
- **Conclusion**
  Current results + future study

Background

Multiple sclerosis

- **'Disease assessment'**
  Important for personalized medicine
- **Multiple sclerosis**
  Heterogeneity and lack of pathognomonic signs
- **Pathological changes**
  Brain tissues demyelination and inflammation
- **MRI**
  Non-invasive, 3D, repeatable, with corresponding contrast

Background

What is MRI signal?

MRI 'measurements'
Properties of H atoms

H nucleus
- spinning charged particle
- produces magnetic field = magnetic moment

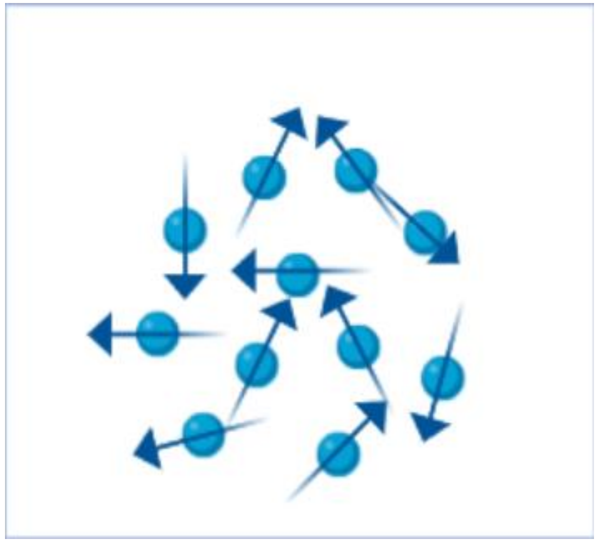
In external magnetic field
Magnetic moment precession (Larmor precession)

$$\omega = -\gamma B$$

Background

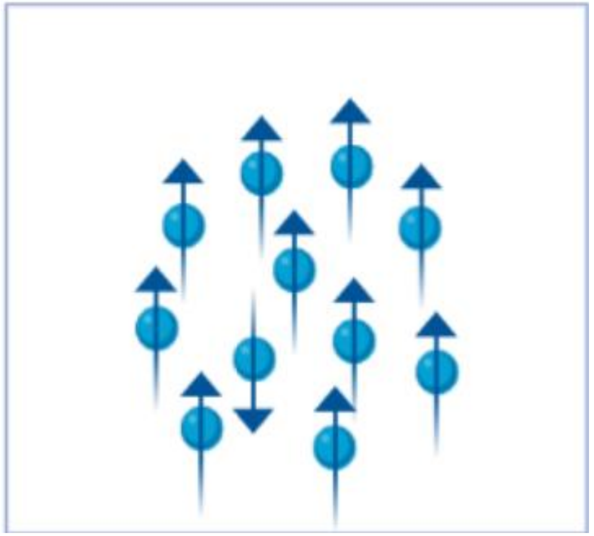
What is MRI signal?

z



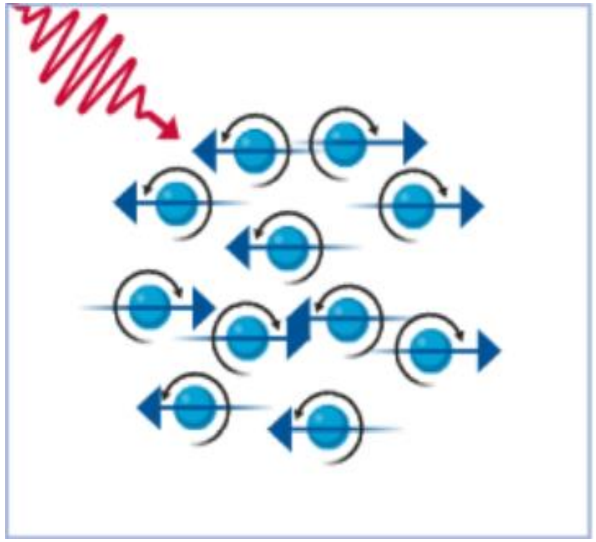
No magnetic field

Spins randomly positioned



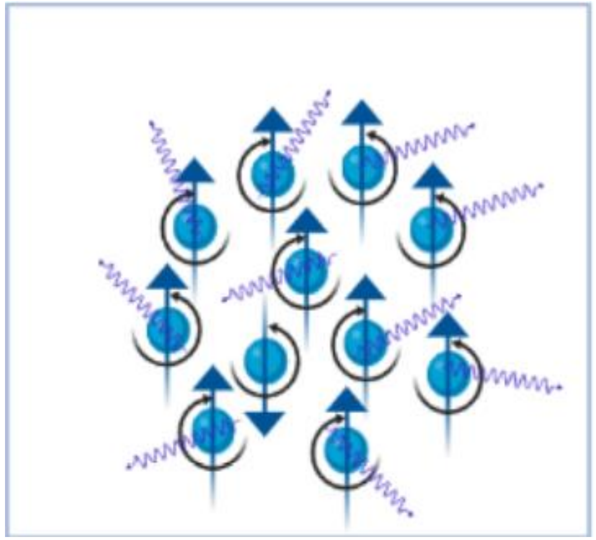
Constant magnetic field

Spins mostly aligned



Radio pulse

- Longitudinal magnetization ↓
- Transversal magnetization ↑



Protons relax

Radiosignal released

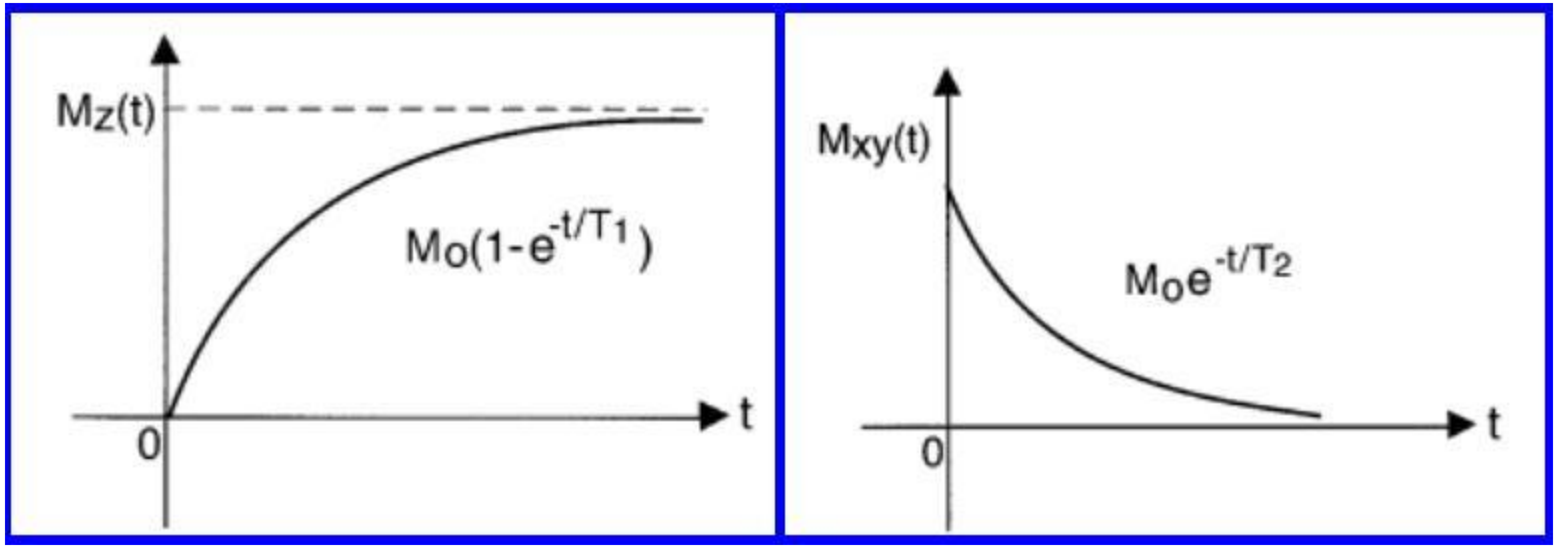
Relaxation measured in longitudinal and transversal directions

y

x

Background

What is MRI signal?



Longitudinal relaxation

Spin-lattice

Towards thermal equilibrium

Characterized by T1

Transversal relaxation

Spin-spin

Out of phase

Characterized by T2

(in reality)

T2 = real value

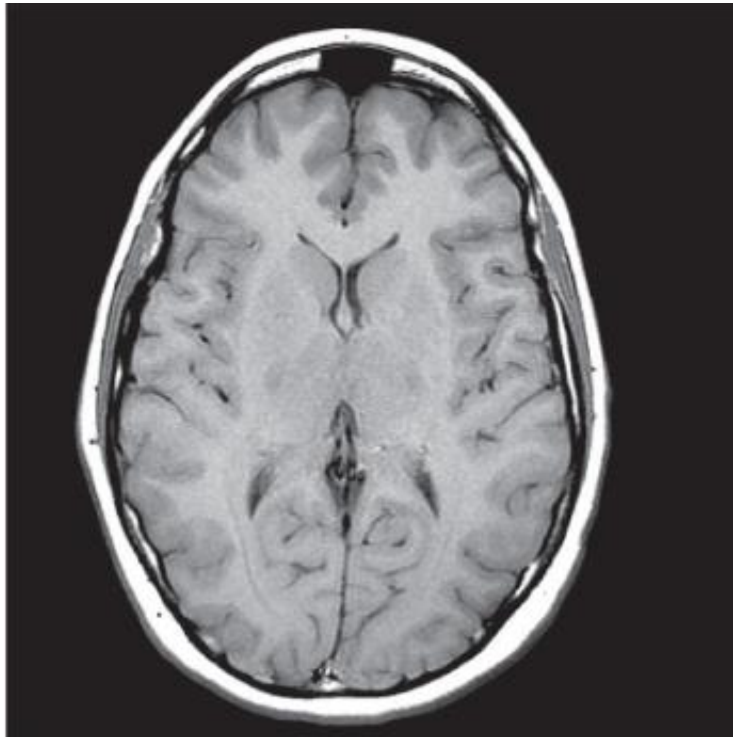
T2* = observer value

T2* < T2

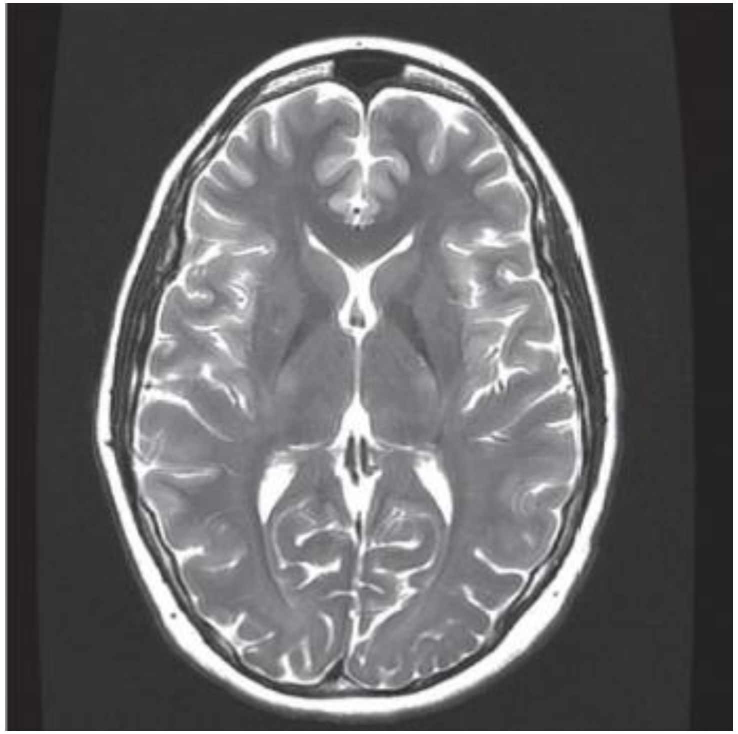
$$\frac{1}{T2^*} = \frac{1}{T2} + \frac{1}{T2_{inhom}}$$

Background

What is MRI signal?



T1w



T2w

Background

What is MRI signal?

No ionizing radiation

Can visualize 'any' structure, playing with sequences

Expressed in arbitrary units → good for visual analysis only

Low reproducibility across centers, vendors, scanners, protocols, etc

Objective reproducible MRI-based analysis is required!

Background

‘MRI quantification’ approaches

NeuroImage: Clinical 23 (2019) 101879

ELSEVIER

Contents lists available at ScienceDirect

NeuroImage: Clinical

journal homepage: www.elsevier.com/locate/ynicl

Multiparameter MRI quantification of microstructural tissue alterations in multiple sclerosis

Emilie Lommers[a,b,*], Jessica Simon[c], Gilles Reuter[a,d], Gaël Delrue[b], Dominique Dive[b], Christian Degueldre[a], Evelyne Balteau[a], Christophe Phillips[a,e], Pierre Maquet[a,b]

[a] GIGA – CRC in vivo Imaging, University of Liège, Liège, Belgium
[b] Clinical Neuroimmunology Unit, Neurology Department, CHU Liège, Belgium
[c] Psychology and Neurosciences of Cognition Research Unit, University of Liège, Belgium
[d] Neurosurgery Department, CHU Liège, Belgium
[e] GIGA – in silico Medicine, University of Liège, Liège, Belgium

nature reviews clinical oncology

Review Article | Published: 04 October 2017

Radiomics: the bridge between medical imaging and personalized medicine

Philippe Lambin, Ralph T.H. Leijenaar, Timo M. Deist, Jurgen Peerlings, Evelyn E.C. de Jong, Janita van Timmeren, Sebastian Sanduleanu, Ruben T.H.M. Larue, Aniek J.G. Even, Arthur Jochems, Yvonka van Wijk, Henry Woodruff, Johan van Soest, Tim Lustberg, Erik Roelofs, Wouter van Elmpt, Andre Dekker, Felix M. Mottaghy, Joachim E. Wildberger & Sean Walsh

Nature Reviews Clinical Oncology **14**, 749–762 (2017) | Download Citation

MRI quantitative multi-parameter mapping (qMRI)

Liege University

Radiomics

Maastricht University

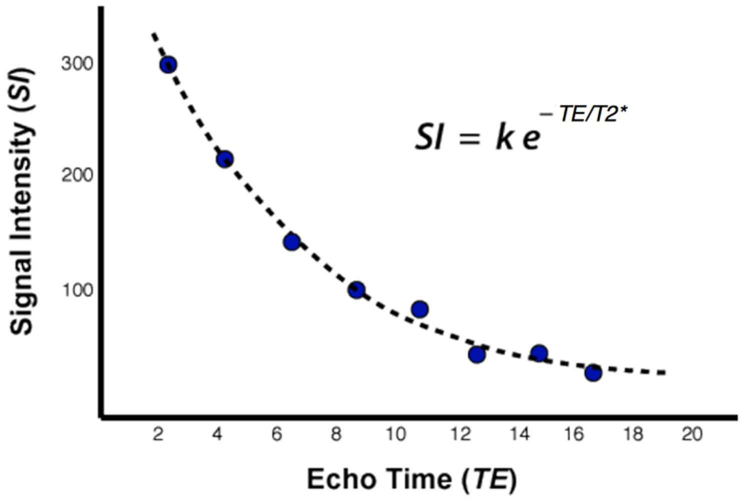
Maastricht University

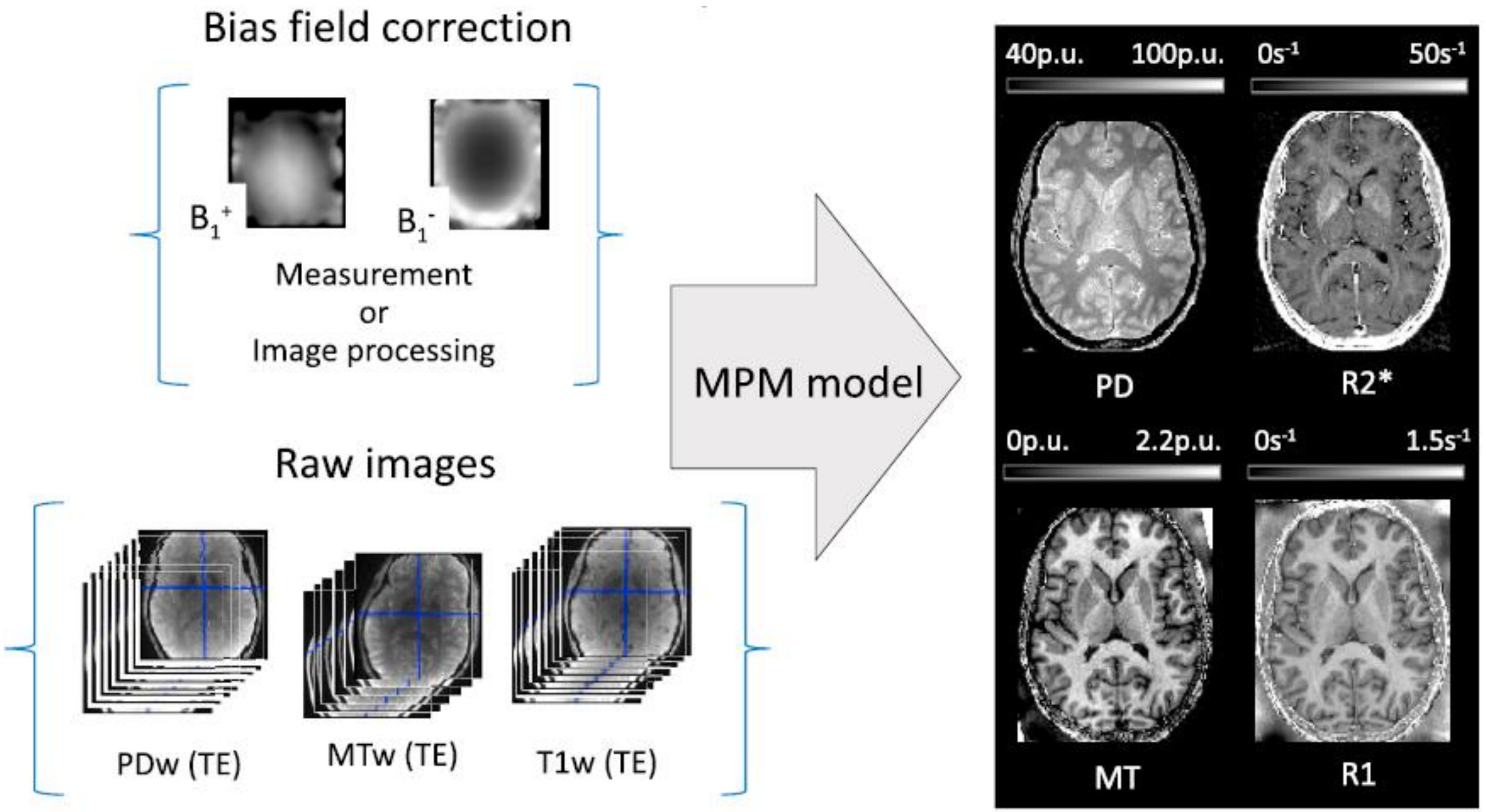
LIÈGE université GIGA CRC In vivo Imaging

THE D-LAB Decision Support For Precision Medicine

Background

What is qMRI?





NIfTI images and JSON metadata (acquisition parameters: flip angle, TE, TR, MT on/off, ...)

NIfTI images and JSON metadata (processing parameters & description)

Tabelow K., Balteau E., Ashburner J., Callaghan M., Draganski B., Helms G., Kherif F., Leutritz T., Lutti A., Phillips C., Reimer E., Ruthotto L., Seif M., Weiskopf N., Ziegler G., Mohammadi S. (2019). hMRI – A toolbox for quantitative MRI in neuroscience and clinical research. Neuroimage, 194(2019), 191-210.

Backgroung

What is qMRI?

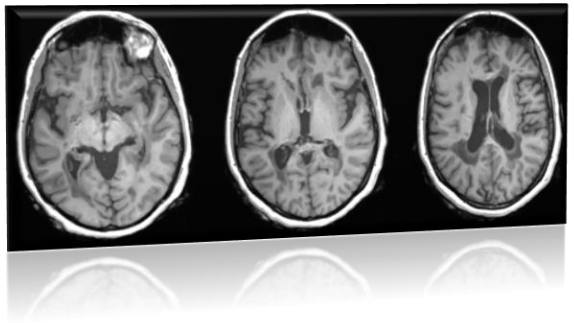
Map	Name	Possible biological interpretation	Units
PD	Proton density	Free water	%
MT	Magnetization transfer saturation	Axonal myelination	%
R1	Longitudinal relaxation time	Axonal myelination	Hz
R2*	Transverse relaxation time	Iron accumulation	Hz

quantitative, in physical units

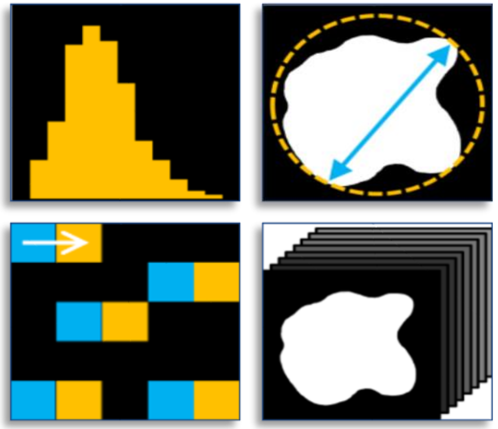
Background

Radiomics pipeline

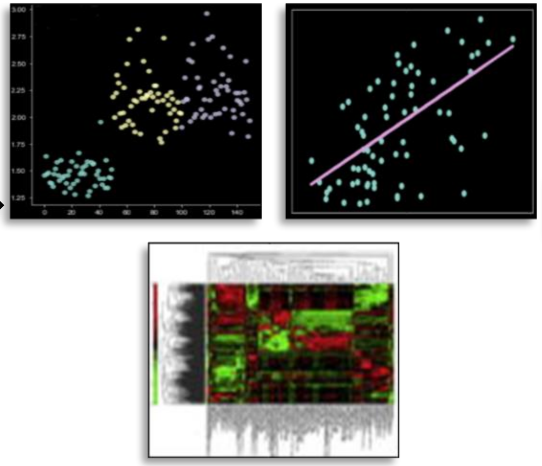
Medical Imaging



ROI Features Extraction



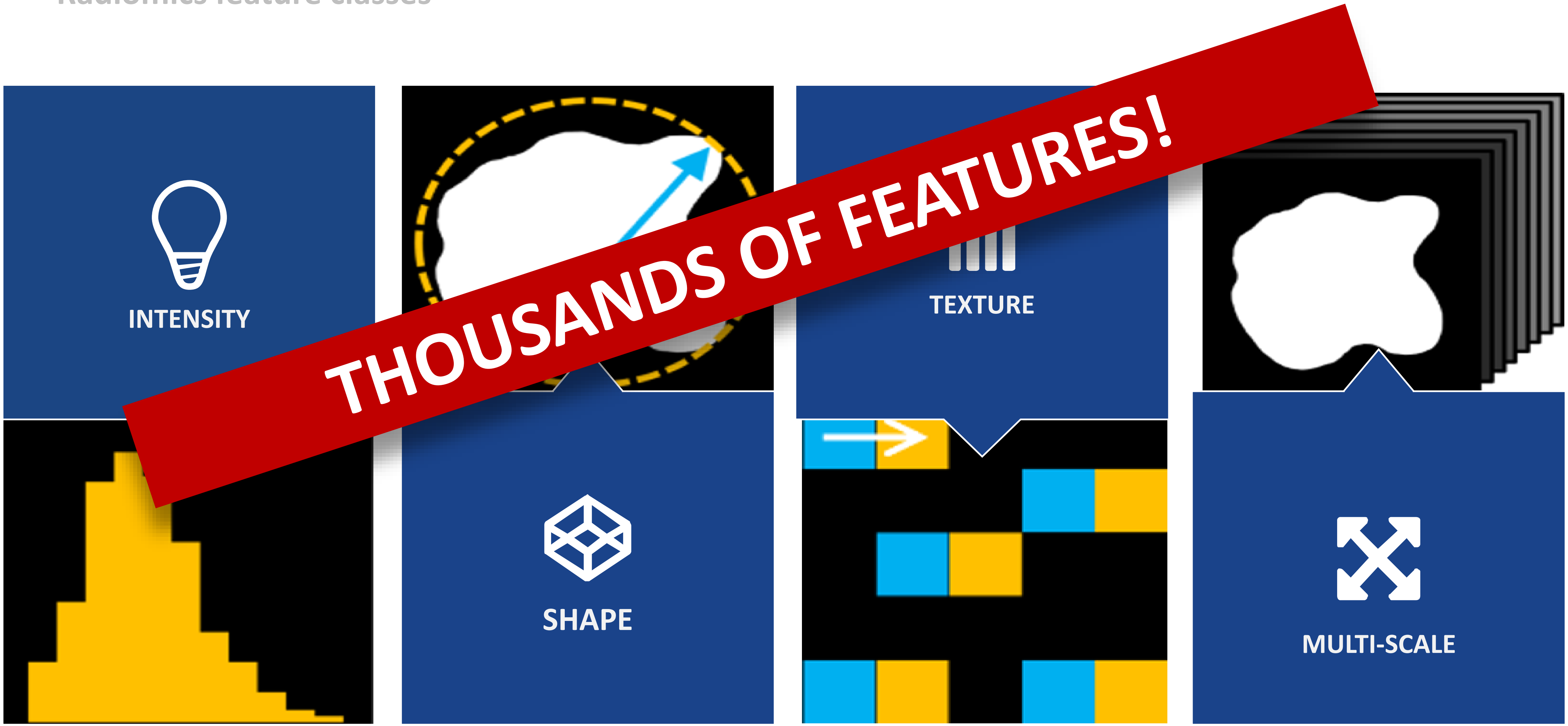
Radiomic Analysis



Actionable insight

Background

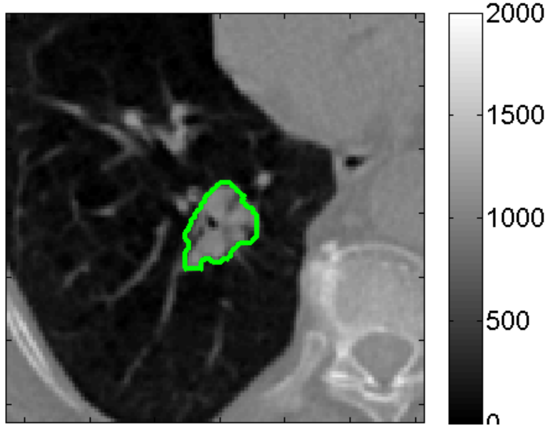
Radiomics feature classes

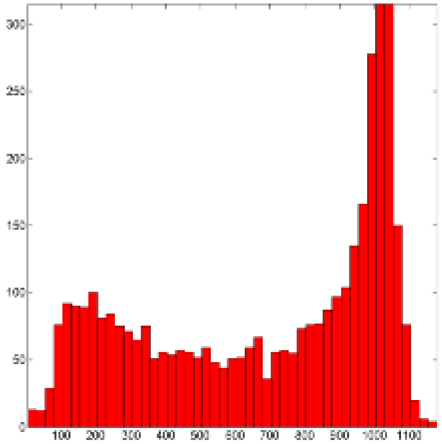


Lambin et al. EJC, 2012;; Lambin et al. Nat Rev Clin Oncol 2017

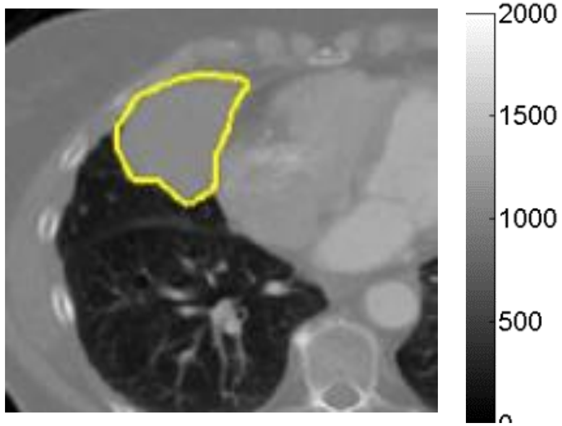
Background

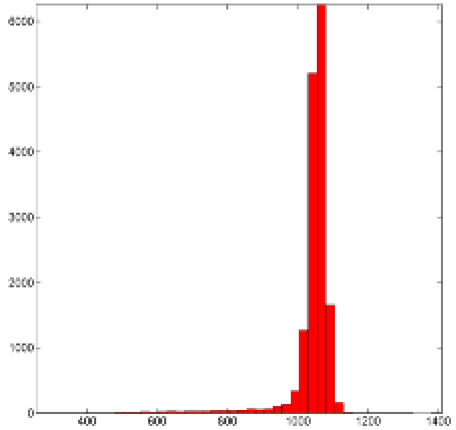
Radiomics feature example: Tumour intensity





Minimum	4
Maximum	1180
Mean	687,13
Range	1176
Standard deviation	336,51
Variance	113237,17
Median	799
Skewness	-0,46
Kurtosis	1,70
Entropy	6,49
RMS	765,08
Total energy	6432571,20
Mean deviation	302,00



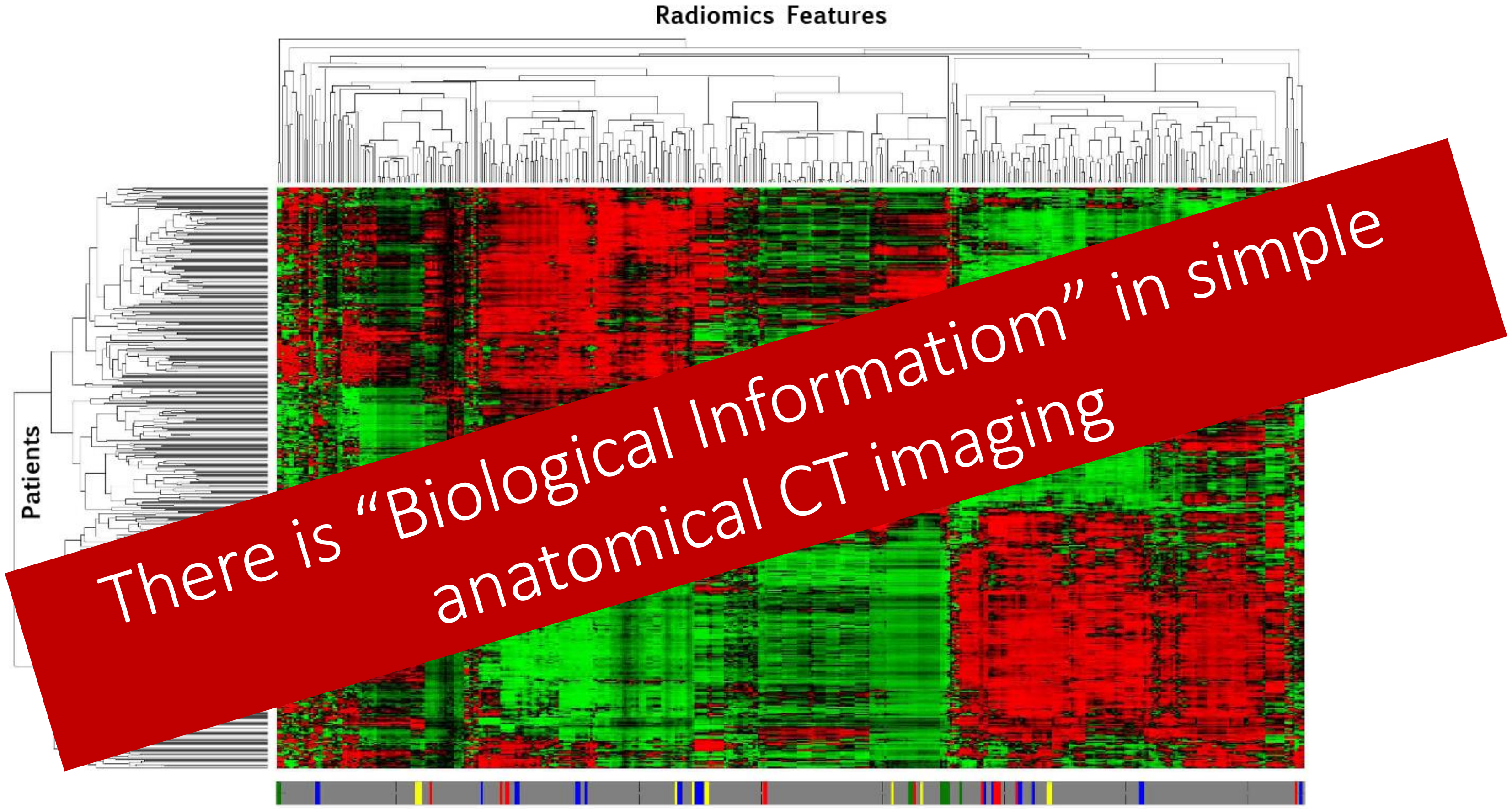


Minimum	254
Maximum	1411
Mean	1043,75
Range	1157
Standard deviation	65,78
Variance	4327,46
Median	1055
Skewness	-5,18
Kurtosis	37,88
Entropy	3,58
RMS	1045,82
Total energy	49141473,18
Mean deviation	30,63

Lambin et al. EJC, 2012;; Lambin et al. Nat Rev Clin Oncol 2017

Background

Rationale



Significant association with histology (p-value = 0.003): *squamous cell carcinoma, as opposed to adenocarcinomas,* showed a higher presence in cluster II.

Aerts, Lambin et al. Nat Commun 2014; Lambin et al. Nat Rev Clin Oncol 2017

Objectives

Hypothesis and objectives

Hypothesis

Radiomics features, extracted from MS PA and HS MRI, show significant differences in distributions

qMRI improves Radiomics analysis

Radiomics could be used to rapidly diagnose MS on routine MR

Radiomics features contain information about pathological biological processes

Objectives

To create Radiomics signatures of pathological and healthy brain tissue

To compare conventional MRI- and qMRI-based Radiomics analysis results

To investigate ability of Radiomics models to differenciate between MS PA and HS

To perform early diagnostics of MS, based on qMRI and Radiomics approaches

Materials and methods

Data

	DATASET 1	DATASET 2	DATASET 3
	T1w + qMRI (PD, MT, R1, R2*)	T1w	T1w
Dataset	Private CHU, Liege, dataset	CC-359	MICCAI 2016 MSSEG challenge dataset
Subjects	MS patients (36), HCS (37)	HCS (359)	MS patients (15)
Sites	CHU, Liege, Belgium; GIGA-CRC in vivo imaging, University of Liege, Liege, Belgium	from Campinas, Sao Paulo, Brazil; Calgary, Alberta, Canada	CHU Rennes, Rennes, France; CHU Lyon, Lyon, France
Equipment	3 T Siemens Magnetom Allegra; 3 T Siemens Magnetom Prisma	1.5 T and 3 T Siemens, Philips, GE Healthcare MRI scanners	3 T Siemens Magnetom Verio; 1.5 T Siemens Magnetom Aera; 3 T Philips Ingenia
Age, $\mu \pm \sigma$, years	45.7 ± 11.9	53.5 ± 7.8	41.6 ± 9.8
Gender balance, M/F	0.73	0.96	0.88

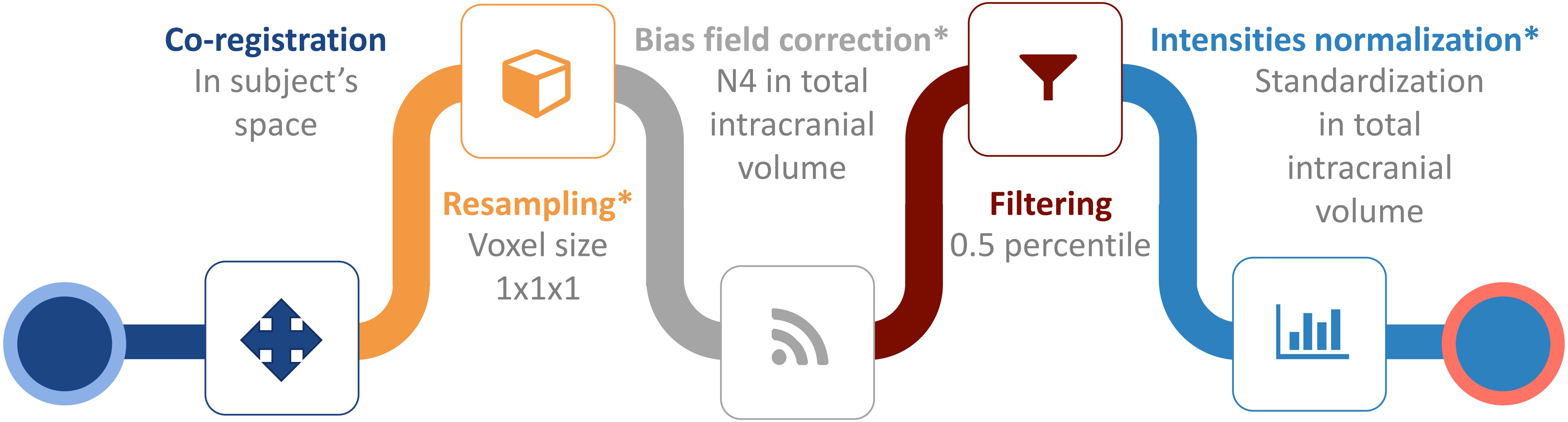
Lommers, et al. (2019). Multiparameter MRI quantification of microstructural tissue alterations in multiple sclerosis. NeuroImage: Clinical, 101879.

Souza, et al. (2018). An open, multi-vendor, multi-field-strength brain MR dataset and analysis of publicly available skull stripping methods agreement. NeuroImage, 170, 482-494

Commowick, et al. (2018). Objective evaluation of multiple sclerosis lesion segmentation using a data management and processing infrastructure. Scientific reports, 8(1), 13650.

Materials and methods

MRI preprocessing



** For conventional MRI only*

DS1
Segmentation provided
Performed with qMRI toolbox

DS2
Segmentation provided
Consensus of methods

DS3
Segmentation of only lesions maps provided
Performed with SPM

Materials and Methods

Radiomics features extraction

- From total WM
- PyRadiomics toolbox
- 107 features/ROI: intensity, shape, texture (GLCM, GLRLM, GLSZM, GLDM, NGTDM)
- Fixed number (50) of greyscale levels in texture analysis

Materials and methods

Features selection

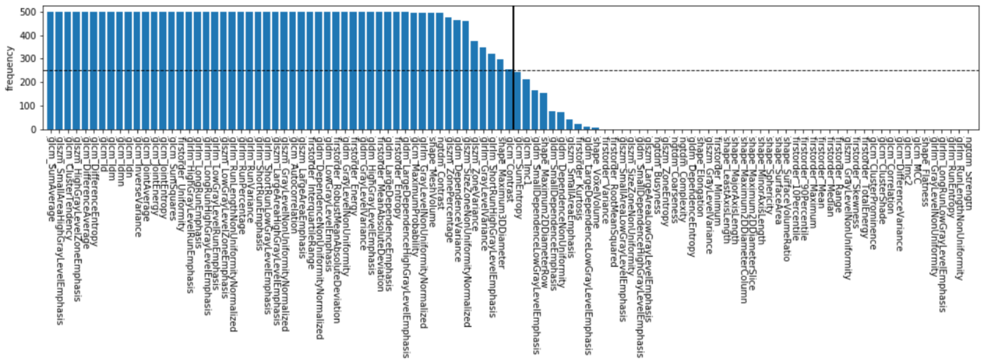
Redundancy	'Informativeness'	'Predictiveness'	Robustness
Removing intercorrelated features	Mann-Whitney test ANOVA F-test Model filling (RFC)	Recursive features elimination	Bootstrapping

For each image type (T1w, PD, MT, R1, R2* + for mixed qMRI), 5 best features are selected

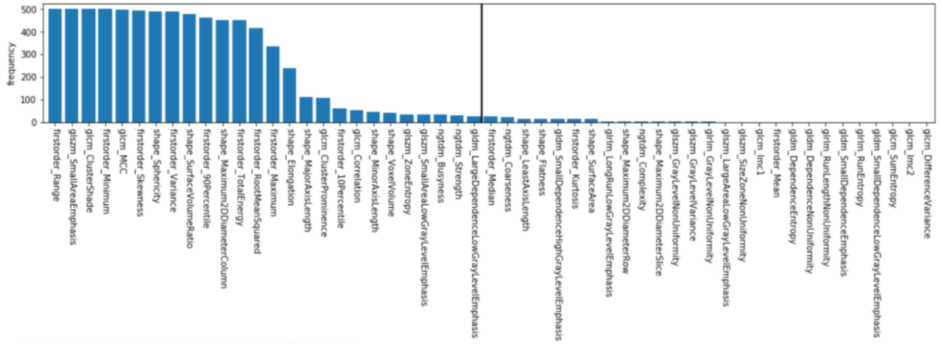
Materials and methods

Features selection

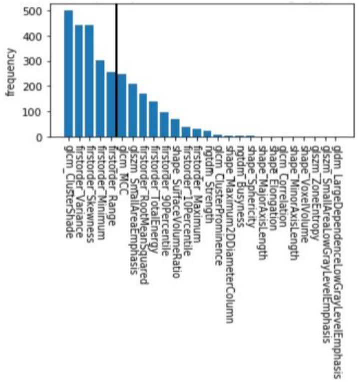
Removing intercorrelated features



Selecting ‘important’ features
(Mann-Whitney test, RFC model fitting, F-test)



Selecting the best performing features with RFE



Materials and methods

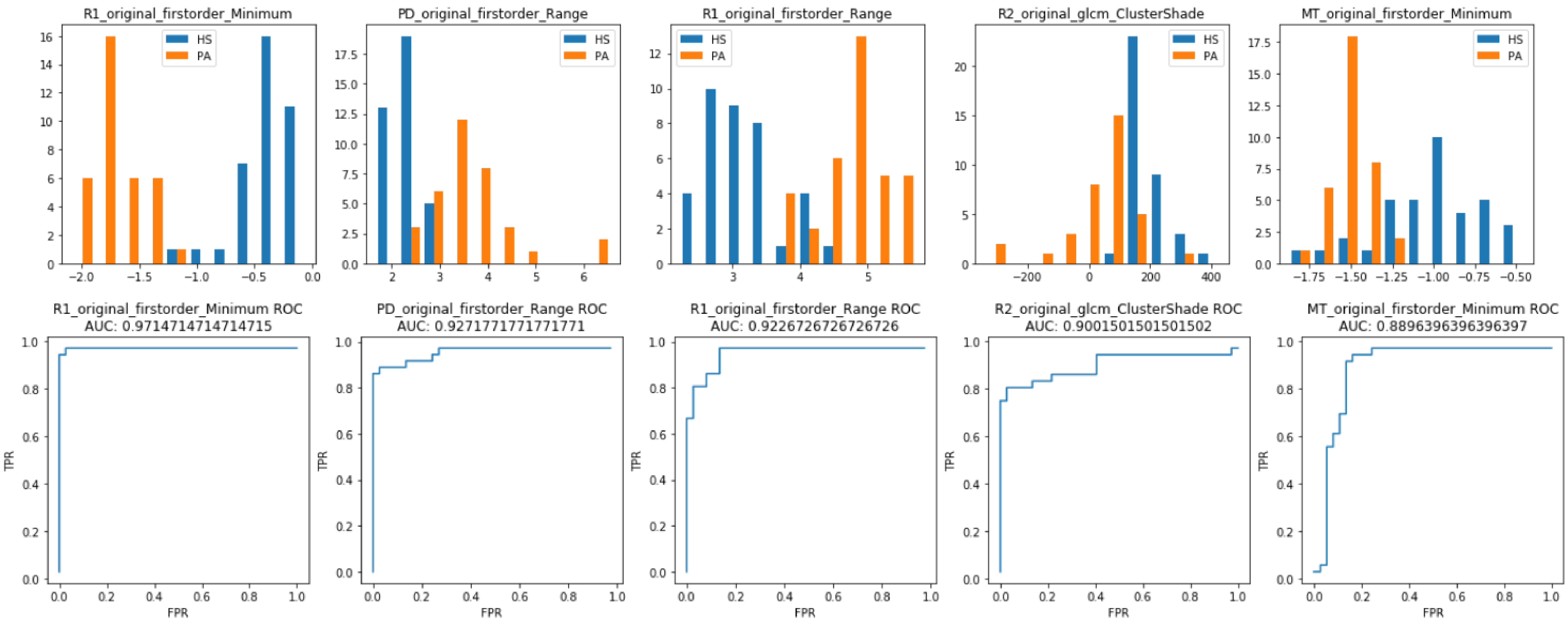
Features to model

T1	'glcm_ClusterShade', 'firstorder_Variance', 'firstorder_Skewness', 'firstorder_Minimum', 'firstorder_Range'
MT	'firstorder_Minimum', 'firstorder_10Percentile', 'firstorder_Range', 'firstorder_Kurtosis', 'firstorder_RobustMeanAbsoluteDeviation'
PD	'firstorder_Range', 'firstorder_Skewness', 'firstorder_Variance', ‘gldm_SmallDependenceHighGrayLevelEmphasis', 'glcm_MCC'
R1	'firstorder_Range', 'firstorder_Minimum', 'firstorder_Skewness', 'firstorder_Kurtosis', 'gldm_LargeDependenceHighGrayLevelEmphasis'
R2*	'gldm_SmallDependenceLowGrayLevelEmphasis', 'firstorder_Skewness', 'glcm_ClusterShade', 'ngtdm_Busyness', 'shape_SurfaceVolumeRatio'
qMRI	'R1_firstorder_Minimum', 'PD_firstorder_Range', 'R1_firstorder_Range', 'R2_glcm_ClusterShade', 'MT_firstorder_Minimum'

Not correlared to volume!

Materials and methods

Features to model



Maastricht University

THE D-LAB
Decision Support For Precision Medicine

Materials and methods

Classification MS vs non-MS

Training – with DS1

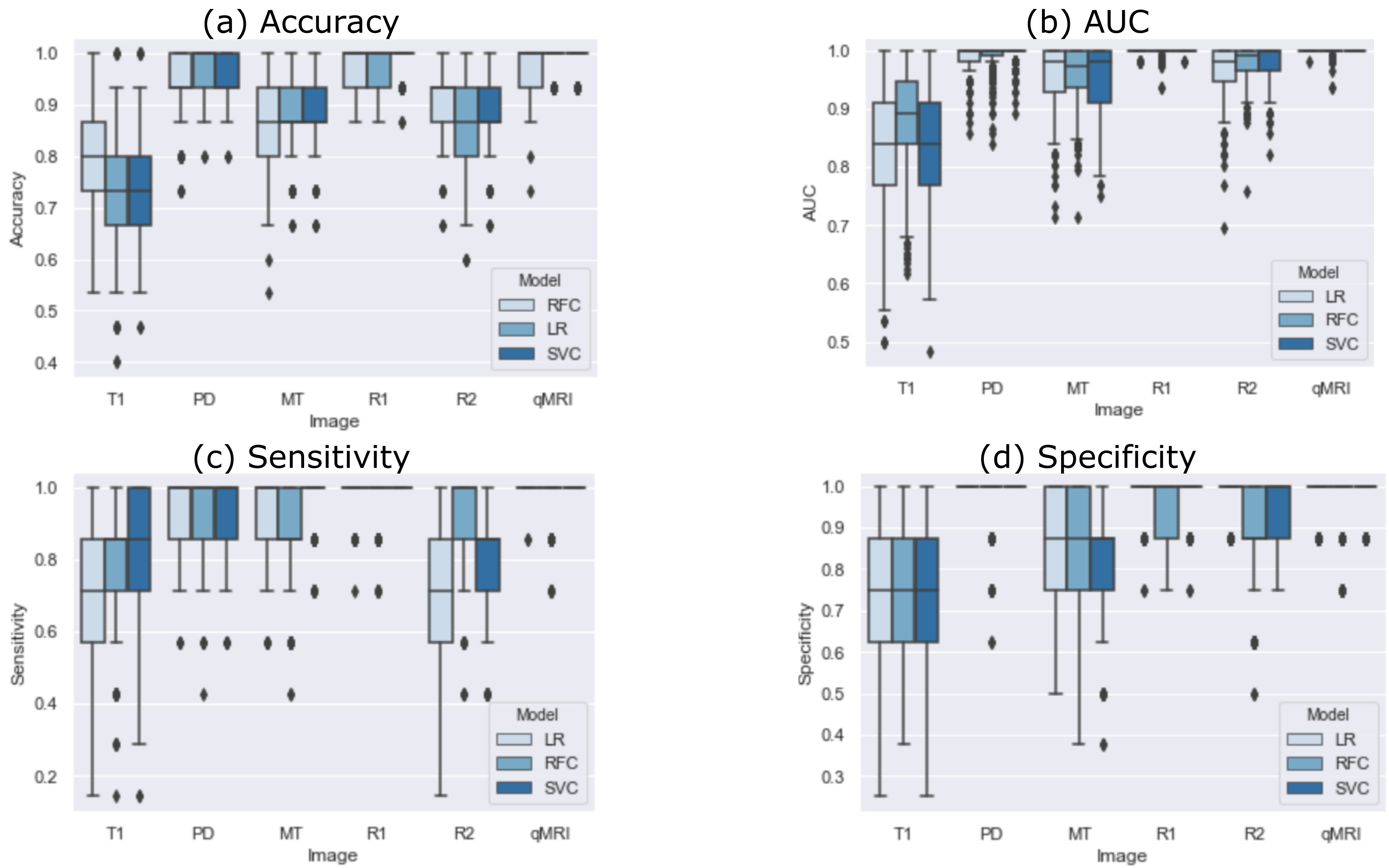
	T1w	PD	MT	R1	R2*	mixed qMRI
RFC	CV/EV	CV	CV	CV	CV	CV
SVC	CV/EV	CV	CV	CV	CV	CV
LRC	CV/EV	CV	CV	CV	CV	CV

CV – internal cross-validation with DS1
EV – external validation with DS2 and DS3

**RFC – Random Forest Classifier, SVC – Support Vector Classifier, LRC – Logistic Regression Classifier*

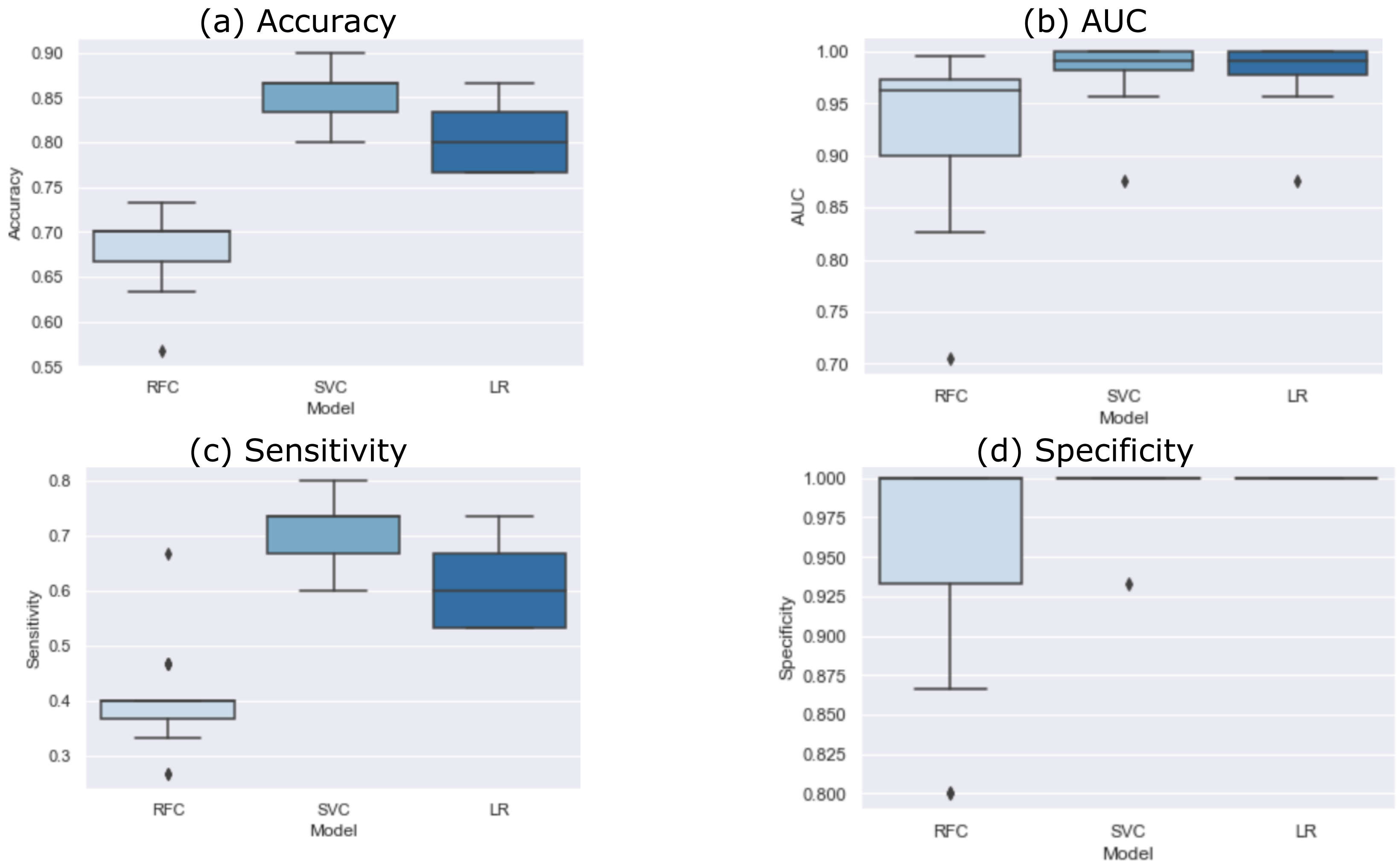
Results

Models testing



Results

Models validation on external data



DS2 is splitted for classification data balance

Results

(further work: NAWM AUCs)

	T1w	PD	MT	R1	R2*	qMRI
RFC	0.81 (+/-0.21)	0.92 (+/-0.13)	0.89 (+/-0.16)	0.90 (+/-0.15)	0.82 (+/-0.19)	0.94 (+/-0.12)
SVC	0.79 (+/-0.22)	0.88 (+/-0.19)	0.90 (+/-0.16)	0.87 (+/-0.15)	0.79 (+/-0.20)	0.94 (+/-0.11)
LRC	0.77 (+/-0.22)	0.90 (+/-0.16)	0.91 (+/-0.15)	0.87 (+/-0.18)	0.80 (+/-0.21)	0.95 (+/-0.11)

Feature groups to model

T1w	Glcm, firstorder, glszm, gldm, firstorder,
PD	Gldm, glcm, glcm, firstorder, glrlm
MT	Glcm, glcm, glcm, glcm, gldm
R1	Firstorder, firstorder, firstorder, gldm, glcm
R2*	Ngtdm, glszm, glszm, glszm, gldm

Conclusion

MS RADIOMICS FEATURES VECTORS

The best 5 features are selected for each image type (T1, PD, MT, R1, R2*):

- not correlated to volume,
- not shape features,
- are understandable and interpretable

PRELIMINARY CLASSIFICATION MODELS

- Fully automated pipeline
- qMRI perform better on teaching data,
- External validation for qMRI is needed

EXTERNAL VALIDATION

T1w-based models are validated on external data, performance is comparable to shown on teaching data

FURTHER STUDY

- Another tissues study
- Another diagnosis study
- Aging study

‘TECHNICAL TASKS’

- Brain tissues segmentation
- Image quality assessment and preprocessing

LIÈGE université
GIGA
CRC In vivo Imaging

Maastricht University

GROW School for Oncology & Developmental Biology

THE D-LAB Decision Support For Precision Medicine

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