Computer-Aided Diagnosis for Prostate Cancer using mp-MRI

PhD Defence
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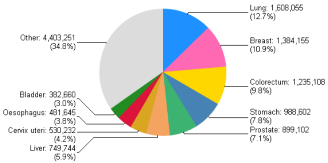
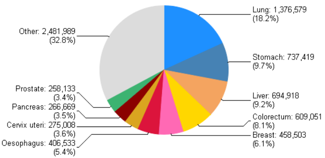
Statistics



(a) # of cancer cases



(b) # of cancer deaths

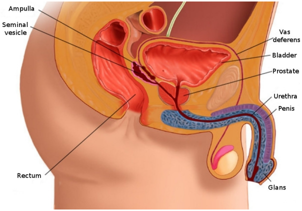
Implications[1]

- 2nd most frequently diagnosed men cancer
- Accounting for 7.1% of overall cancers diagnosed
- Accounting for 3.4% of overall cancers death

[1] J. Ferlay et al. "Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008". In: *Int. J. Cancer* 127.12 (Dec. 2010), pp. 2893–2917.

The prostate organ

Anatomy



Localization of the prostate organ, image source[2]

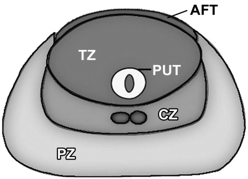
Characteristics

- Height: 3 cm
- Depth: 2.5 cm
- Weight: 7 g to 16 g

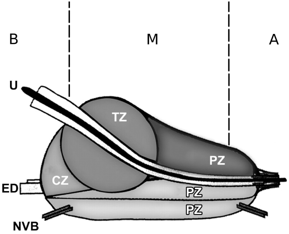
[2] Geckomedia. *Natom Anatomy*. French. June 2011. url: http://www.natomshop.com/.

The prostate organ

Anatomy



(a) Transverse plane

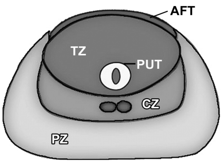


(b) Sagittal plane

Prostate zones - AFT: anterior fibromuscular tissue, CZ: central zone, ED: ejaculatory duct, NVB: neurovascular bundle, PUT: periurethral tissue, PZ: peripheral zone, U: urethra, TZ: transitional zone, B: base, M: median, A: apex; image source[3]

[3] Y. J. Choi et al. "Functional MR imaging of prostate cancer". In: *Radiographics* 27 (2007), pp. 63–75.

Prostate carcinoma (CaP)



CaP development

- Slow-growing → 85 %
- Fast-growing → 15 %
- CaPs in CG are more aggressive

Zonal predisposition

- PZ → 70 % to 80 %
- TZ → 10 % to 20 %
- CZ → 5 %

What clinicians need?

- Detect CaP
- Distinguish slow- from fast-growing CaP
- Active surveillance *vs.* prostatectomy/other treatments

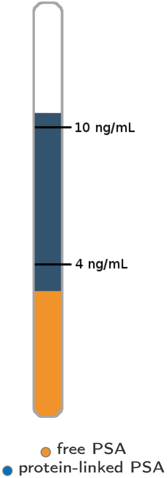
Screening

Prostate-specific antigen

- $> 10\,\mathrm{ng\,mL^{-1}} \rightarrow$ biopsy
- From $4\,\mathrm{ng\,mL^{-1}}$ to $10\,\mathrm{ng\,mL^{-1}}$
  $\rightarrow \frac{\bullet}{\bullet + \bullet} > 15\% \rightarrow$ biopsy

"Blind" transrectal ultrasound biopsy

- Take samples from different locations
- Grade using Gleason score



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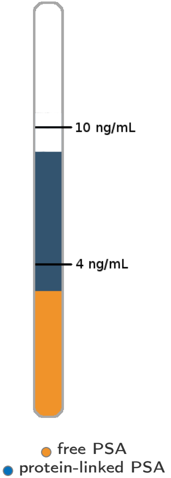

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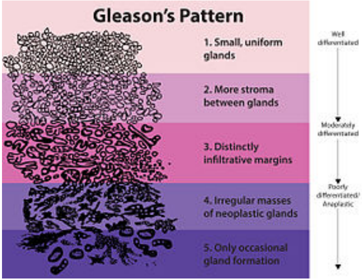


Image source: `https://goo.gl/fEVQXQ`

Screening

Pros

- ✓ Reduce CaP-related mortality between 21 % and 44 %[4]

Cons

- ✗ Up to 30 % of over-diagnosis[5]
- ✗ Up to 35 % of undiagnosed CaP[6]
- ✗ Biopsies are invasive

[4] Fritz H. Schröder et al. "Prostate-cancer mortality at 11 years of follow-up". In: *New England Journal of Medicine* 366.11 (2012), pp. 981–990.

[5] G. P. Haas et al. "Needle biopsies on autopsy prostates: sensitivity of cancer detection based on true prevalence". In: *J. Natl. Cancer Inst.* 99.19 (Oct. 2007), pp. 1484–1489.

[6] A. V. Taira et al. "Performance of transperineal template-guided mapping biopsy in detecting prostate cancer in the initial and repeat biopsy setting". In: *Prostate Cancer Prostatic Dis.* 13.1 (Mar. 2010), pp. 71–77.

CAD and mp-MRI

Current trendy techniques: mp-MRI

✓ Less invasive technique

Human diagnosis using mp-MRI

✗ Need further investigation of the mp-MRI modalities

✗ Low repeatability

- Observer limitations
- Complexity of clinical cases

Emergence of CAD

- CADe → detection of potential lesions
- CADx → diagnosis regarding those lesions

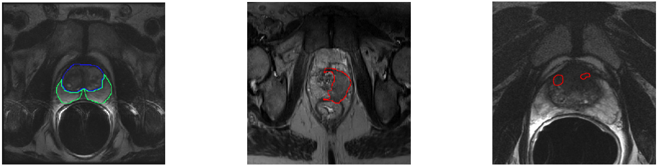
Research objectives

Propose a mp-MRI CAD for CaP

- Study and investigate the state-of-the-art on mp-MRI CAD for CaP
- Identify the scientific barriers
- Design a mp-MRI CAD addressing these issues
- Investigate and analyze the proposed CAD

MRI modalities

T_2W-MRI



(a) Healthy (b) CaP PZ (c) CaP CG

Healthy

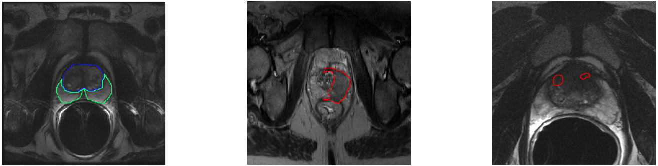
- Intermediate to high-signal intensity (SI) in PZ
- Low-SI in CG

CaP

- Low-SI
- Round and ill-defined mass in PZ
- Homogeneous with ill-defined edges in CG

MRI modalities

T_2W-MRI



(a) Healthy (b) CaP PZ (c) CaP CG

Pros

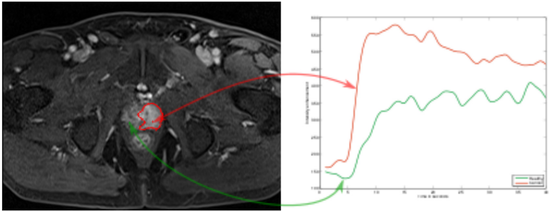
- Highest spatial resolution
- Anatomy nicely depicted

Cons

- Low sensitivity in CG
- Lower specificity due to outliers

MRI modalities

DCE-MRI



Green: healthy - Red: CaP

Healthy

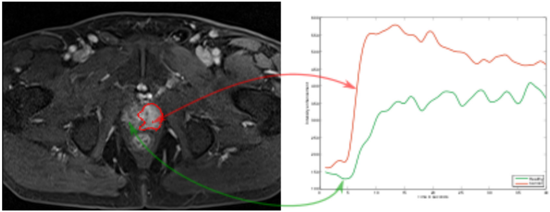
- Slower wash-in, wash-out, time-to-peak enhancement
- Lower integral under the curve, max SI

CaP

- Faster wash-in, wash-out, time-to-peak enhancement
- Higher integral under the curve, max SI

MRI modalities

DCE-MRI



Green: healthy - Red: CaP

Pros

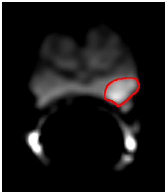
- Information about vascularity

Cons

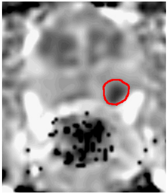
- Spatial mis-registration
- Lower spatial resolution than T_2W-MRI
- Difficult detection in CG

MRI modalities

DW-MRI - ADC



(a) DW MRI



(b) ADC

Healthy

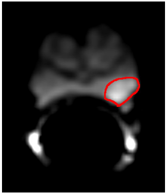
- DW-MRI: lower SI
- ADC: higher-SI

CaP

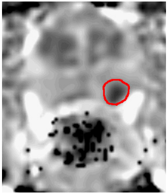
- DW-MRI: higher SI
- ADC: lower-SI

MRI modalities

DW-MRI - ADC



(a) DW MRI



(b) ADC

Pros

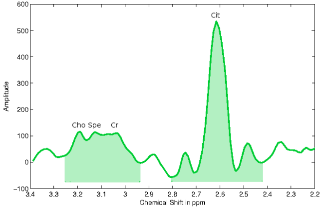
- Information about tissue structure
- ADC correlated with Gleason score

Cons

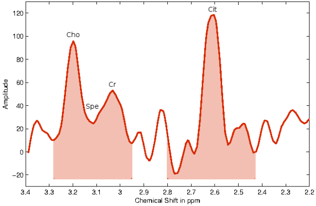
- Poor spatial resolution
- Variability of the ADC coefficient

MRI modalities

MRSI



(a) Healthy



(b) CaP

Healthy

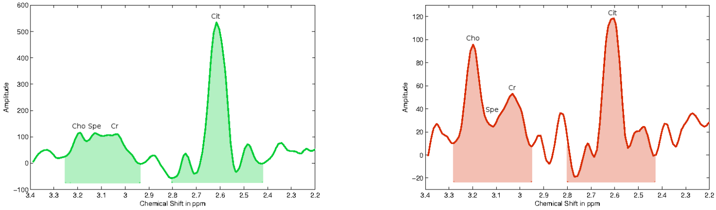
- High citrate concentration
- Moderate choline and spermine concentrations

CaP

- Decrease of citrate and spermine concentrations
- Increase of choline concentration

MRI modalities

MRSI



(a) Healthy (b) CaP

Pros

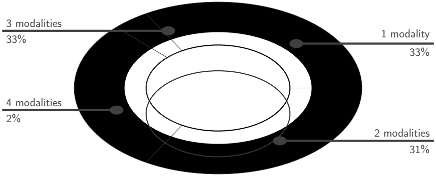
- Citrate correlated with Gleason score

Cons

- Low spatial resolution
- Variation inter-patients

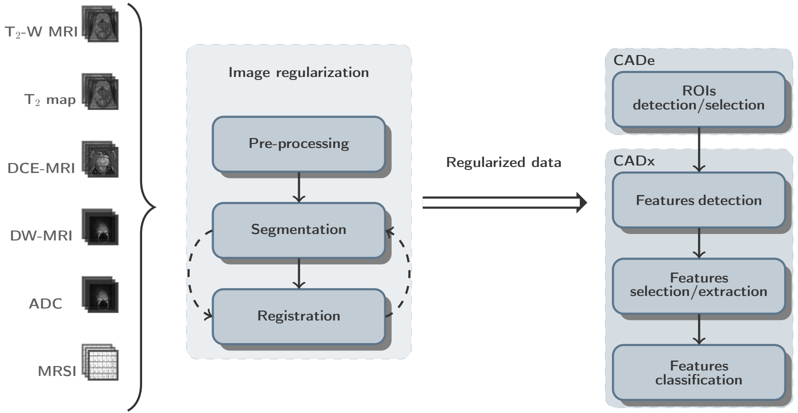
CAD for CaP

block



CAD for CaP

Full CAD for detection and diagnosis of CaP



Common CAD framework based on MRI images used to detect CaP

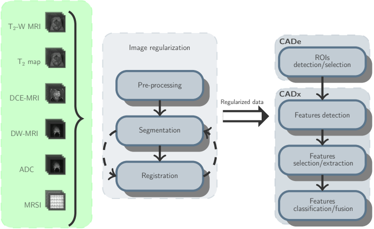
UdG

CAD for CaP

UBFC

Conclusions

- ✓ 3 modalities better than 2
- ✓ Texture and edge features are predominant
- ✓ Features selection/extraction tends to improve performance
- ✓ Pre-eminence of SVM and ensemble classifier (i.e., AdaBoost, RF, etc.)



CAD for CaP

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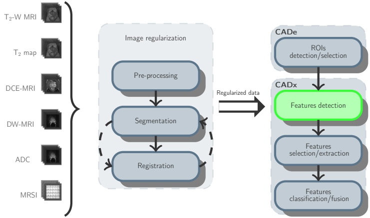

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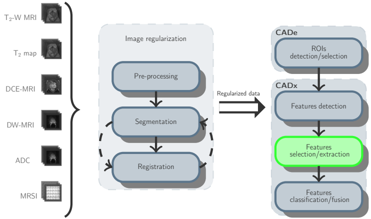

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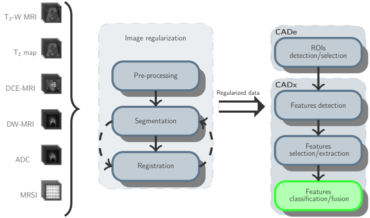

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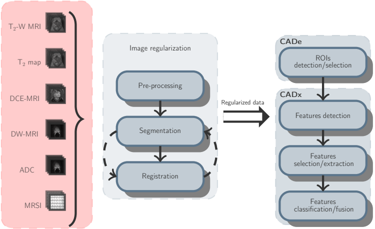
Scientific and technical challenges

- ✗ No publicly available mp-MRI dataset
- ✗ Only 1 study used 4 MRI modalities
- ✗ Limited work on data normalization
- ✗ A lot of features are extracted in 2D
- ✗ Limited work regarding selection/extraction
- ✗ No work regarding data balancing
- ✗ No source code available of any CAD

CAD for CaP



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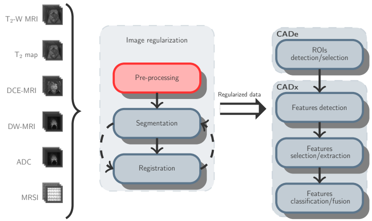

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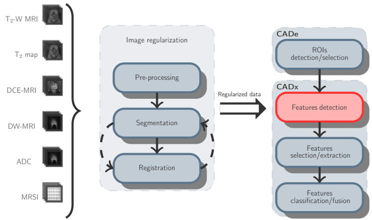

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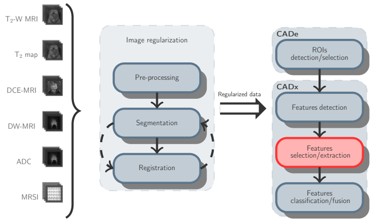

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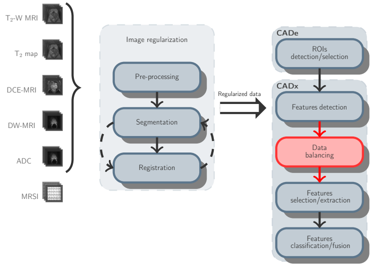

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CAD for CaP

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- ✗ No source code available of any CAD

Research objectives

- Collect a mp-MRI dataset
- Design a CAD for CaP using all mp-MRI modalities
- Investigate normalization, feature selection/extraction, data balancing
- Implement 3D features
- Release source code and dataset

Mp-MRI prostate datasets

1.5 T General Electric scanner

- T_2W-MRI, DW-MRI, DCE-MRI, and MRSI
- Ground-truth (GT) for CaP, PZ, and CG associated to T_2W-MRI modality
- Healthy: 4 *vs.* CaP: { PZ: $14 + 3$, CG: $0 + 3$ }

3 T Siemens scanner

- T_2W-MRI, ADC, DCE-MRI, and MRSI
- GT for CaP, PZ, and CG associated to T_2W-MRI modality
- Additional GT of the prostate for DCE-MRI and ADC
- Healthy: 2 *vs.* CaP: { PZ: $12 + 2$, CG: $3 + 2$ }

Mp-MRI prostate datasets

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UdG

Open source initiative

UBFC

protoclass toolbox

- Data management
- Features detection

imbalanced-learn toolbox[7]

- Part of the `scikit-learn-contrib` projects

Third-party toolboxes

NumPy SciPy matplotlib

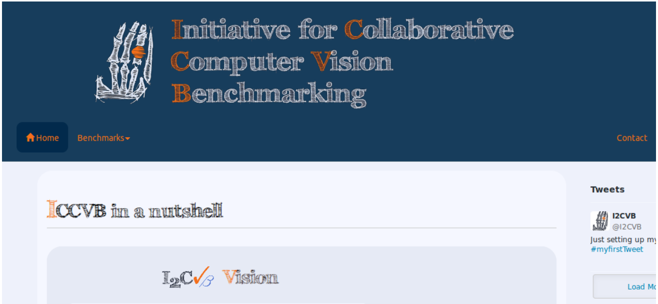
IP[y]: IPython Interactive Computing

SimpleITK scikit-image image processing in python scikit learn

[7] Guillaume Lemaitre et al. "Imbalanced-learn: A Python Toolbox to Tackle the Curse of Imbalanced Datasets in Machine Learning". In: *Journal of Machine Learning Research* (2017).

A web platform

I2CVB platform



Hub for our different resources

- GitHub for our source codes
- Zenodo for our datasets
- HAL, arXiv, ResearchGate for our publications

Toward a mp-MRI CAD for CaP

Mp-MRI CAD for CaP

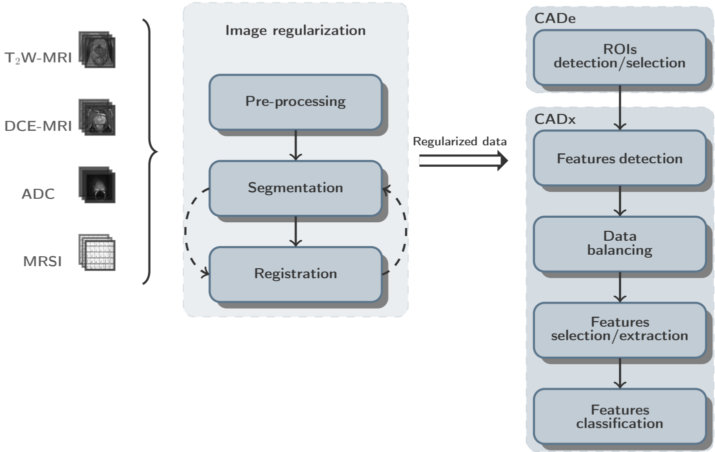
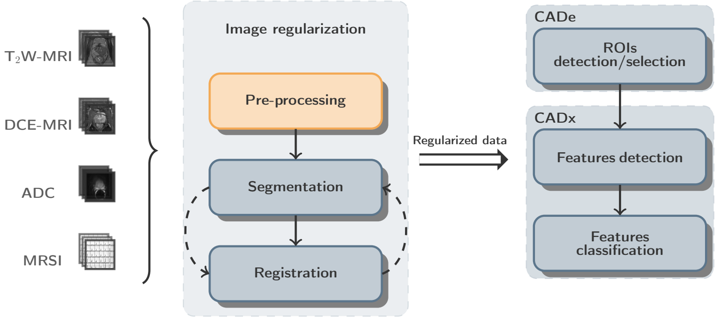


Image regularization

Pre-processing



Pre-processing

T_2W-MRI normalization

- Rician normalization[8]

DCE-MRI normalization

- Graph and deviation based normalization[9]

ADC normalization

- Piecewise-linear normalization

MRSI normalization

- Phase correction[10]
- Frequency alignment
- Baseline correction[11]

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[9] Guillaume Lemaitre et al. "Automatic prostate cancer detection through DCE-MRI images: all you need is a good normalization". In: *Medical Image Analysis - Submitted* (2017).

[10] Guillaume Lemaitre et al. "Normalization of T2W-MRI Prostate Images using Rician a priori". In: *SPIE Medical Imaging*. International Society for Optics and Photonics. 2016, pp. 978529–978529.

[11] Li Chen et al. "An efficient algorithm for automatic phase correction of {NMR} spectra based on entropy minimization ". In: *Journal of Magnetic Resonance* 158.1–2 (2002), pp. 164–168.

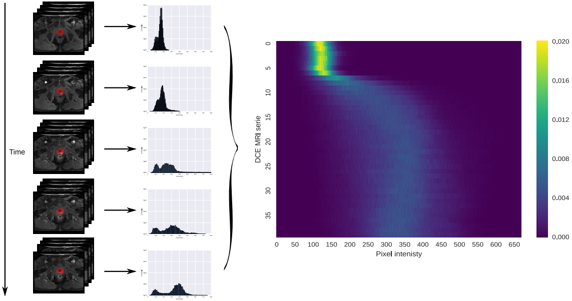
[12] Yuanxin Xi and David M Rocke. "Baseline correction for NMR spectroscopic metabolomics data analysis". In: *BMC bioinformatics* 9.1 (2008), p. 1.

DCE-MRI normalization

Contribution[13]

- Propose a method to normalize DCE-MRI data

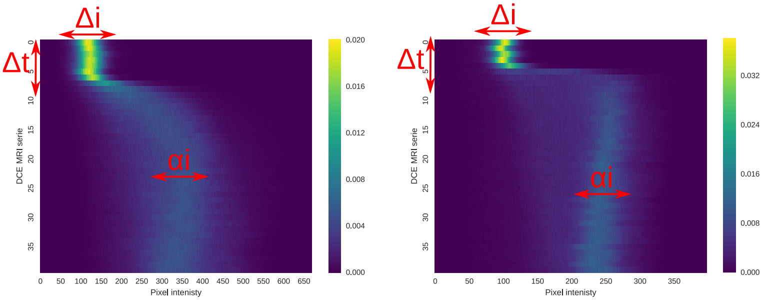
Heatmap representation



[13] Lemaitre et al., "Automatic prostate cancer detection through DCE-MRI images: all you need is a good normalization".

DCE-MRI normalization

Inter-patients variations



(a) Patient #1

(b) Patient #2

Variations driven by Δ_i, Δ_t, and α_i

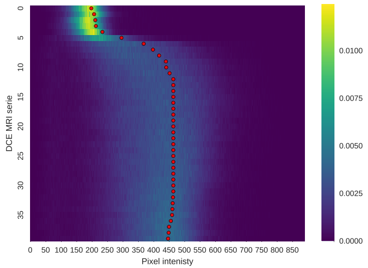
DCE-MRI normalization

Correction of Δ_i

- Estimate with smooth transitions
- Estimate the closest of the PDF peak

→ Find the shortest path in a directed weighted graph, with the edge weight w_{ij}:

$$w_{ij} = \begin{cases} \alpha \exp(1 - \frac{H(i)}{\max(H)}) & \text{if } x_j = x_i + 1 \text{ and } y_j = y_i , \\ (1 - \alpha) \exp(1 - \frac{H(i)}{\max(H)}) & \text{if } x_j = x_i \text{ and } y_j = y_i + 1 , \\ 0 & \text{otherwise,} \end{cases} \quad (1)$$



DCE-MRI normalization

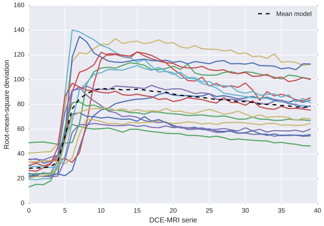
Correction of Δ_t and α_i

Register all RMSD to a mean model such that:

$$\underset{\alpha,\tau}{\arg\min} = \sum_{t=1}^{N} \left[T\left(\alpha, \tau, f(t)\right) - \mu(t)\right]^2 , \tag{2}$$

$$f(t) = \sqrt{\left(\frac{\sum_{n=1}^{N} x(t)_n^2}{N}\right)}, \tag{3}$$

$$T(\alpha, \tau, f(t)) = \alpha f(t - \tau). \tag{4}$$



(a) RMSD before correction

(b) Registered RMSD

DCE-MRI normalization

Evaluation through pharmacokinetic models

- Brix's model
- Hoffmann's model
- Tofts' model
- PUN model

Other approaches

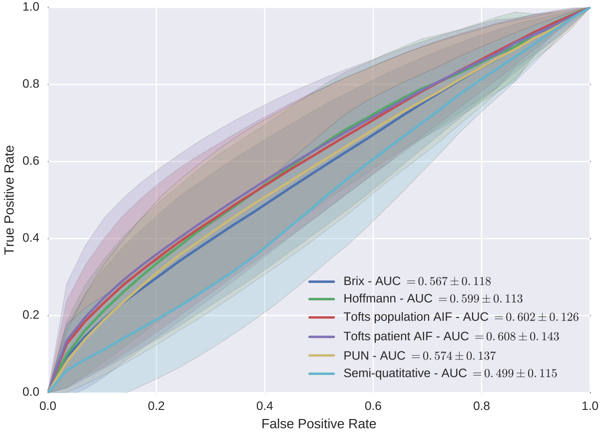
- Semi-quantitative model
- Entire enhanced signal

Classification

- Classification with random forest (RF)
- Leave-one-patient-out cross-validation (LOPO)
- Receiver operating characteristic (ROC) analysis
- Area under the ROC curve (AUC)

DCE-MRI normalization

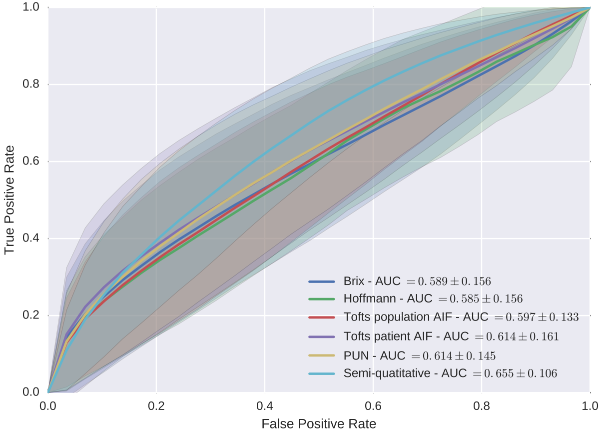
Quantitative and semi-quantitative models



ROC analysis without normalization

DCE-MRI normalization

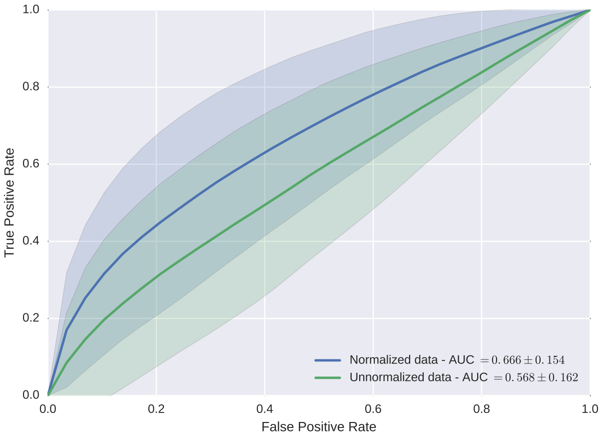
Quantitative and semi-quantitative models



ROC analysis with normalization

DCE-MRI normalization

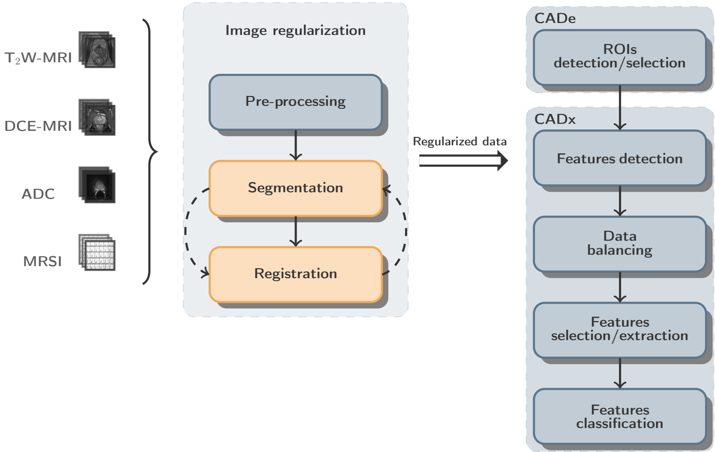
Entire signal



ROC analysis with entire enhanced signal

Image regularization

Segmentation & registration



Segmentation & registration

Resampling

- ADC and DCE-MRI are resampled to the T_2W-MRI resolution

Segmentation

- Manual prostate segmentation available for T_2W-MRI, DCE-MRI, and ADC
- CaP, PZ, and CG manual segmentation available for T_2W-MRI

Registration

- Intra-patient motions correction in DCE-MRI: rigid registration using mutual information
- DCE-MRI is registered to T_2W-MRI using the prostate segmentation
- ADC is registered to T_2W-MRI using the prostate segmentation

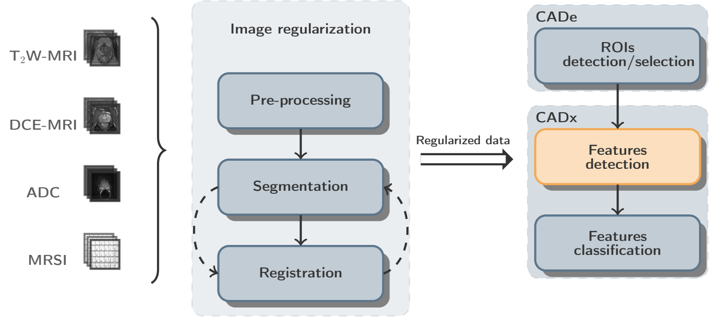
CADe-CADx

Summary of experiments

- Investigate the performance of features from each standalone modality
- Investigate the performance of the combination of features: *coarse combination*
- Investigate the effect of data balancing
- Investigate the effect of selection/extraction
- Investigate the performance of the combination of features: *fine-tuned combination*

CADe-CADx

Features detection



Feature detection

T_2W-MRI and ADC features

- Intensity
- Kirsch filter
- Laplacian filter*
- Prewitt filter*
- Scharr filter*
- Sobel filter*
- DCT decomposition*
- Gabor filters*
- Phase congruency filter
- Haralick filter*
- LBP filter*

DCE-MRI features

- Brix's model
- Hoffmann's model
- Tofts' model
- PUN model
- Semi-quantitative model
- Entire enhanced signal

MRSI features

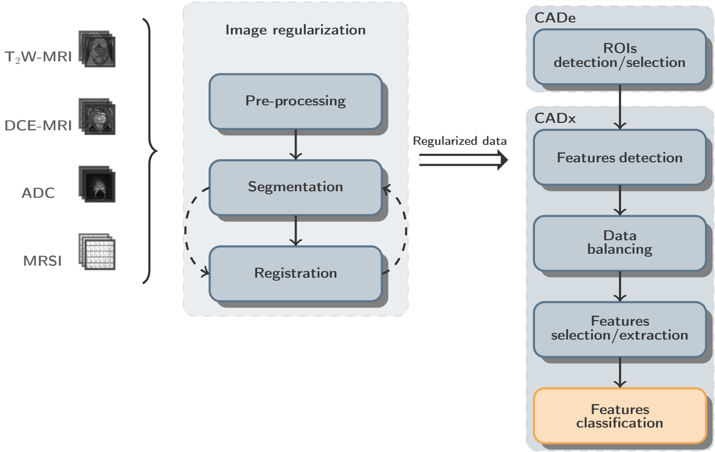
- Quantification with fixed bounds
- Quantification by fitting some modeled signal
- Entire spectra

Spatial information

- Relative distance
- Relative position
- Prostate zone

CADe-CADx

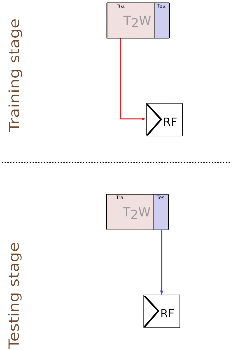
Features classification



Features classification

Classification as fusion

- Single RF → features of one modality
- Single RF → aggregated features of modalities
- Stack of RF with an adaboost and gradient-boosting meta-classifier



Validation

- LOPO CV
- ROC analysis
- AUC

Features classification

Classification as fusion

- Single RF → features of one modality
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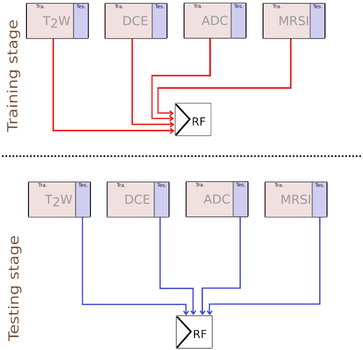
- Stack of RF with an adaboost and gradient-boosting meta-classifier



Validation

- LOPO CV
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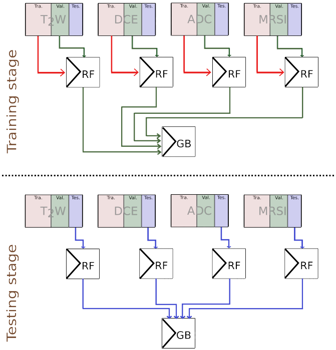
- AUC

Features classification



Classification as fusion

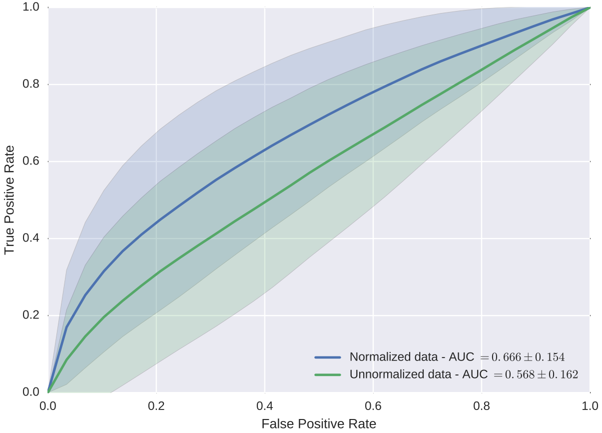
- Single RF → features of one modality
- Single RF → aggregated features of modalities
- Stack of RF with an adaboost and gradient-boosting meta-classifier

Validation

- LOPO CV
- ROC analysis
- AUC

DCE modality

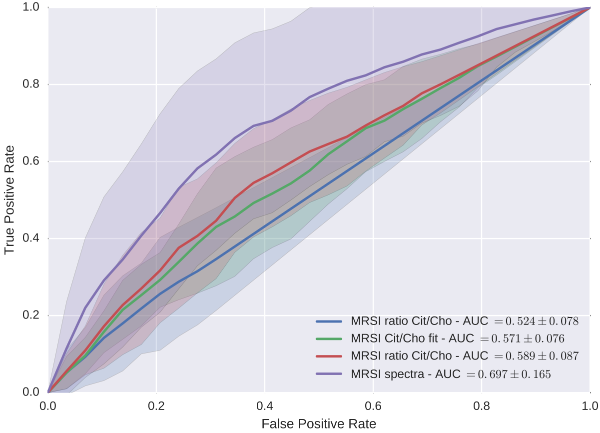
Entire signal



ROC analysis for the entire enhanced signal

MRSI modalities

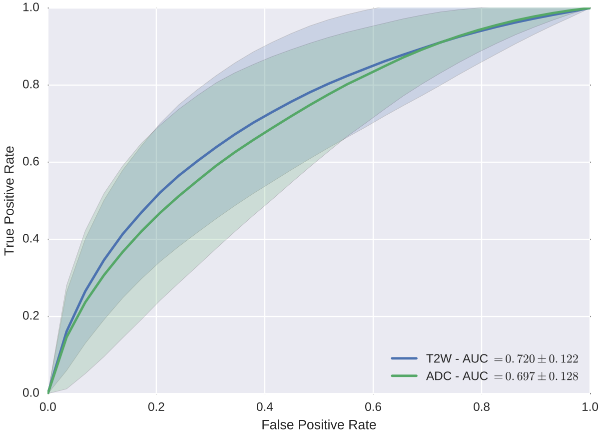
ROC analysis



ROC analysis for the MRSI modality

T_2W-MRI, ADC, and MRSI modalities

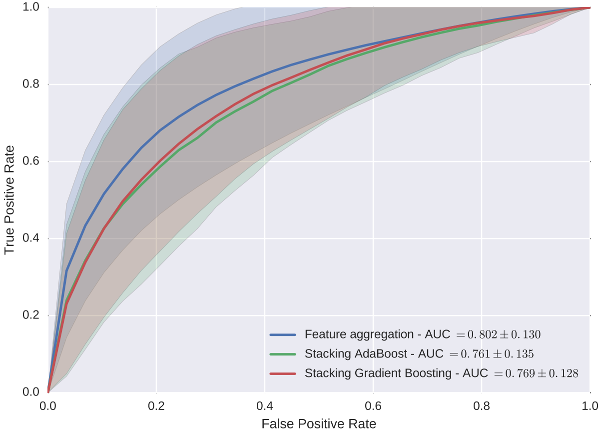
ROC analysis



ROC analysis for T_2W-MRI and ADC modalities

Coarse combination

Aggregation *vs.* stacking



ROC analysis for the fusion strategies

T_2W-MRI, ADC, and MRSI modalities

Overall best performance

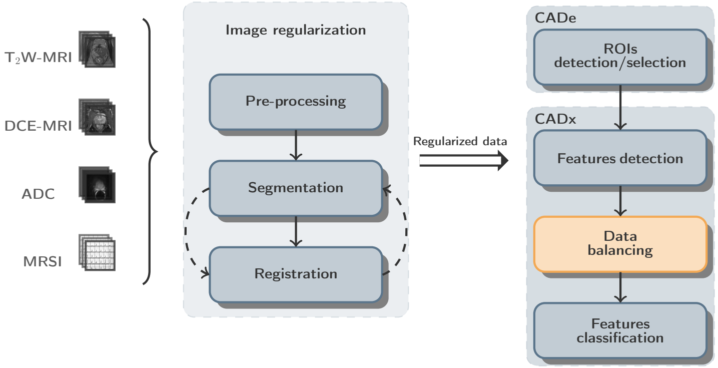
AUC	T_2W-MRI	DCE-MRI	ADC	MRSI	Aggregation
Mean	0.720	0.666	0.697	0.697	0.802
Std	0.122	0.154	0.128	0.165	0.130

Conclusions

- DCE-MRI: normalized data $\rightarrow$ best performance
- DCE-MRI: entire signal better than models
- MRSI: fitting better than bounds approach
- MRSI: entire spectra better than others
- T_2W-MRI $>$ ADC $=$ MRSI $>$ DCE
- Performance at an "acceptable" level of discrimination - AUC $\in [0.7, 0.8]$
- Aggregation better than stacking

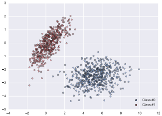
CADe-CADx

Data balancing

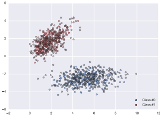


Data balancing

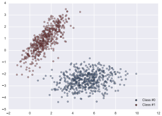
Under-sampling



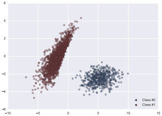
(a) NM1



(b) NM2

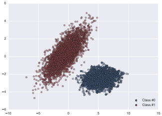


(c) NM3

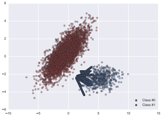


(d) IHT

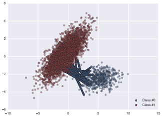
Over-sampling



(e) SMOTE



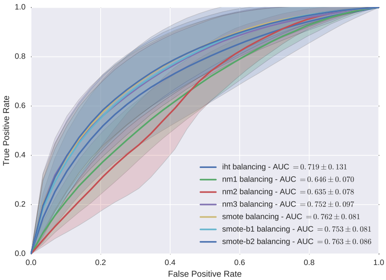
(f) SMOTE-b1



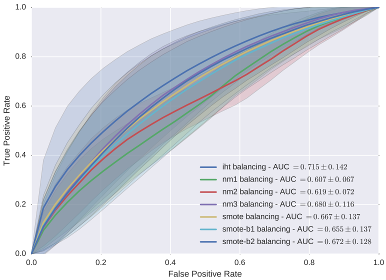
(g) SMOTE-b2

Data balancing

T_2W-MRI and ADC



(a) T_2W-MRI

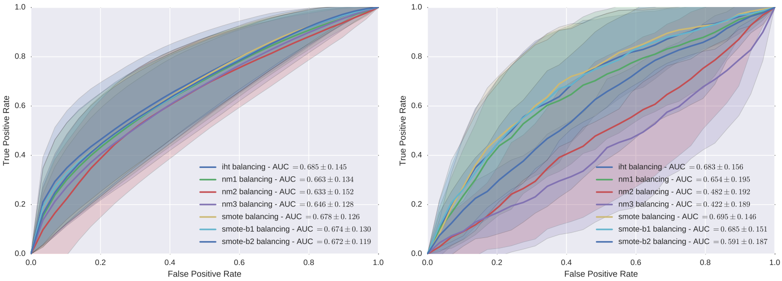


(b) ADC

ROC analysis for T_2W-MRI and ADC

Data balancing

DCE-MRI and MRSI

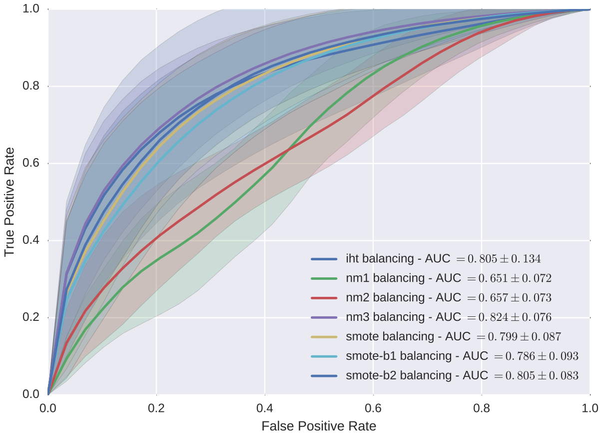


(a) DCE-MRI (b) MRSI

ROC analysis for DCE-MRI and MRSI modalities

Data balancing

Aggregation



ROC analysis while aggregating the features

Data balancing

Conclusions

- ✓ IHT → ADC and DCE-MRI
- ✓ SMOTE → T_2W-MRI and MRSI
- ✓ NM3 → aggregate feature

Before data balancing

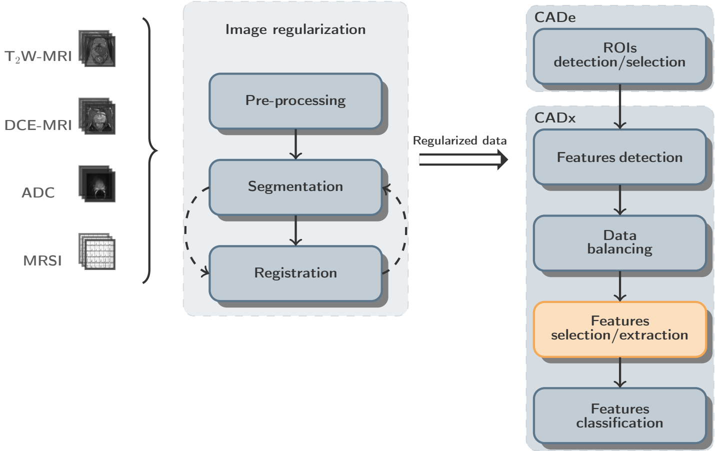
AUC	T_2W-MRI	DCE-MRI	ADC	MRSI	Aggregation
Mean	0.720	0.666	0.697	0.697	0.802
Std	0.122	0.154	0.128	0.165	0.130

After data balancing

AUC	T_2W-MRI	DCE-MRI	ADC	MRSI	Aggregation
Mean	0.762	0.685	0.715	0.695	0.824
Std	0.081	0.145	0.142	0.156	0.076
Tendency	✓	✓	✓	=	✓

CADe-CADx

Features selection/extraction



Features selection/extraction

Features extraction

- Independent components analysis (ICA)
- Principal components analysis (PCA)
- Sparse-PCA

Features selection

- One-way analysis of variance (ANOVA)
- Gini importance

Conclusions

- ✓ T_2W-MRI: ANOVA-based selection with 25 % of features
- ✓ ADC: Gini importance-based selection with 5 % of features
- ✓ DCE-MRI: ICA with 24 components
- ✓ MRSI: ICA with 36 components
- ✓ Aggregation: Gini importance with 17.5 % of features

Data balancing

Before features selection/extraction

AUC	T_2W-MRI	DCE-MRI	ADC	MRSI	Aggregation
Mean	0.762	0.685	0.715	0.685	0.824
Std	0.081	0.145	0.142	0.156	0.076

After features selection/extraction

AUC	T_2W-MRI	DCE-MRI	ADC	MRSI	Aggregation
Mean	0.784	0.691	0.743	0.677	0.836
Std	0.067	0.158	0.139	0.171	0.083
Tendency	✓	✓	✓	✗	✓

Features selection

Selected features in T_2W-MRI and ADC

T_2W-MRI	ADC
8/12 edges 155/256 Gabor filters 2/169 Haralick features 1/1 intensity 4/6 LBP 2/3 phase congruency	1/243 DCT 32/256 Gabor filters 1/3 phase congruency
172 features	34 features

Selected features with aggregation

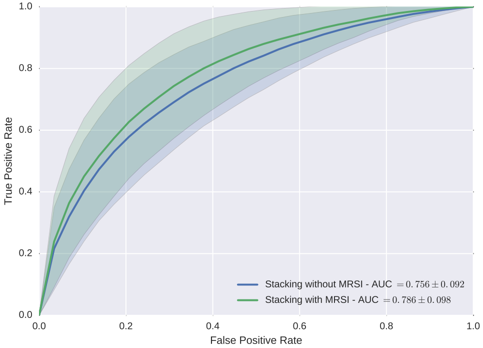
T_2W-MRI	ADC	DCE-MRI	MRSI
113/256 Gabor filters 1/3 phase congruency 4/12 edges 1/1 intensity	53/256 Gabor filters 2/3 phase congruency	14/40 samples	78/101 samples
267 features			

MRSI benefit

Importance of MRSI in aggregation

- Features from MRSI are the most selected features

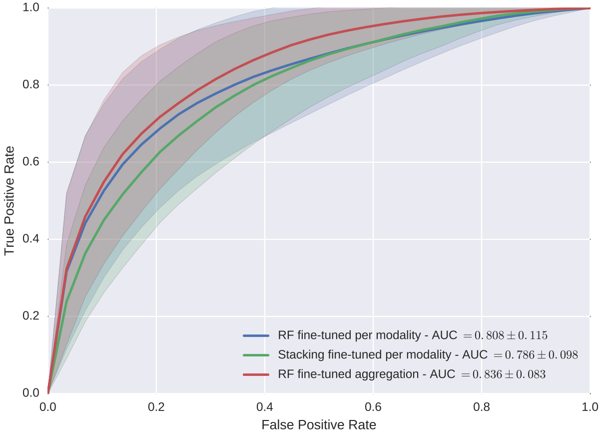
Stacking with/without MRSI



ROC analysis with/without MRSI

Fine-tuned combination

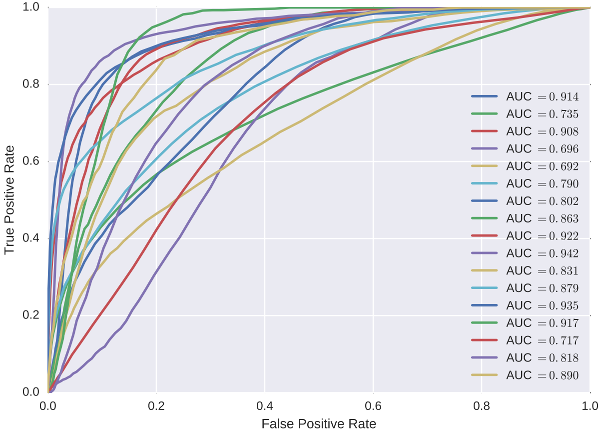
Aggregation *vs.* stacking



ROC analysis with the different fusion strategies

Fine-tuned combination

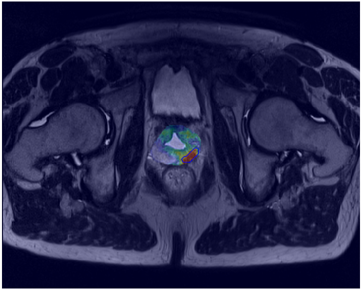
ROC for each patient



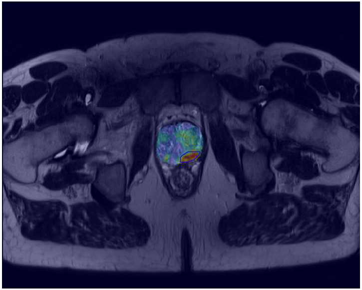
ROC analysis for each patient

Fine-tuned combination

"Outstanding" discrimination level



(a) AUC $= 0.922$



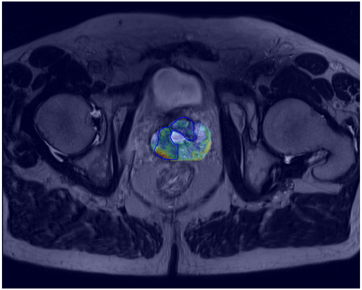
(b) AUC $= 0.914$

UdG

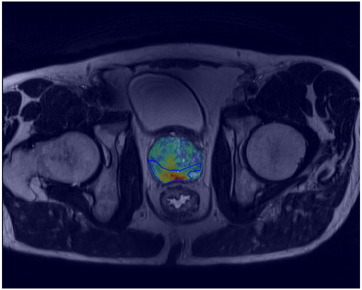
Fine-tuned combination

UBFC

"Acceptable" discrimination level



(c) AUC $= 0.692$



(d) AUC $= 0.735$

Contributions & future works

Research objectives

- Collect a mp-MRI dataset
- Design a CAD for CaP using all mp-MRI modalities
- Investigate normalization, feature selection/extraction, data balancing
- Implement 3D features
- Release source code and dataset

Contributions & future works

Contributions

- ✓ Collect a mp-MRI dataset
- ✓ Design a CAD for CaP using all mp-MRI modalities
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Contributions & future works

Contributions

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Avenue for future research

- ✗ Incorporate spatial connectivity in classification using super-voxels
- ✗ Dissociate classifiers for the PZ and CG regions
- ✗ Explore the features from PI-RADS v.2
- ✗ Investigate the benefit of deep-learning

Timeline