

Computer-Aided Diagnosis for Prostate Cancer using mp-MRI

PhD Defence
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- 1 Introduction
- 2 State-of-the-art
- 3 I2CVB
- 4 Toward a mp-MRI CAD for CaP
- 5 Conclusions

1 Introduction

Motivations

The prostate organ

Prostate carcinoma

Screening

CAD and mp-MRI

Research objectives

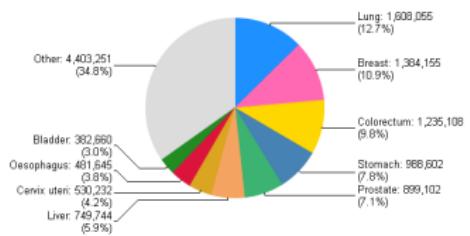
2 State-of-the-art

3 I2CVB

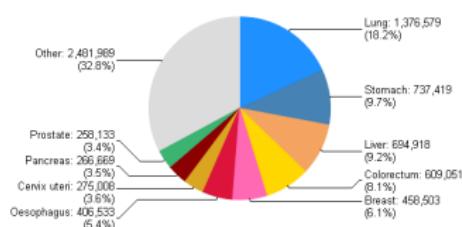
4 Toward a mp-MRI CAD for CaP

5 Conclusions

Statistics



(a) # of cancer cases



(b) # of cancer deaths

Implications¹

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

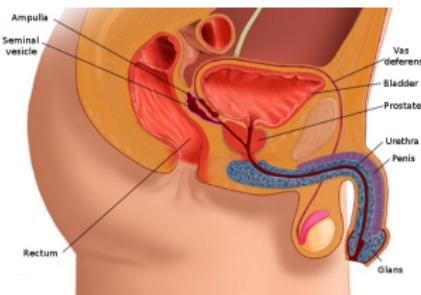
¹J. Ferlay et al. "Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008". In: *Int. J. Cancer* 127.12 (Dec. 2010), pp. 2893–2917.



The prostate organ



Anatomy



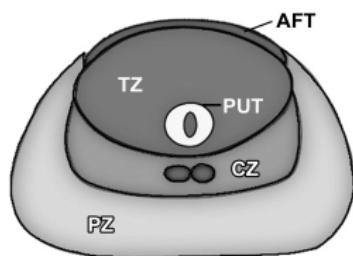
Localization of the prostate organ, image source²

Characteristics

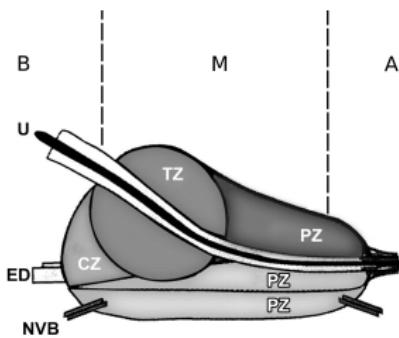
- ▶ Height: 3 cm
 - ▶ Depth: 2.5 cm
 - ▶ Weight: 7 g to 16 g

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

Anatomy



(a) Transverse plane



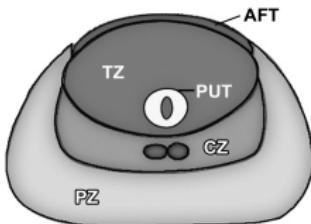
(b) Sagittal plane

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 source³

³Y. 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 %
 - ▶ CG → 5 %

What clinicians need?

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

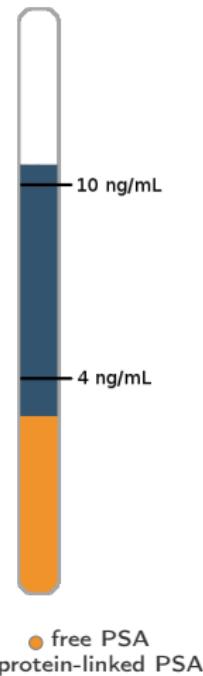


Screening



Prostate-specific antigen

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



"Blind" transrectal ultrasound biopsy

- ▶ Take samples from different locations
- ▶ Grade using Gleason score

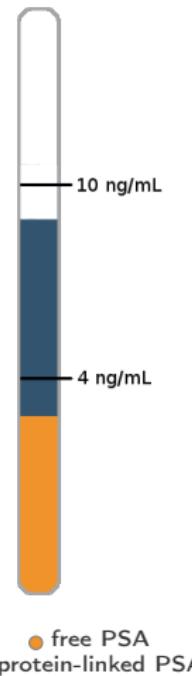


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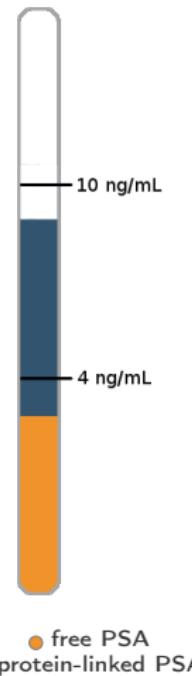


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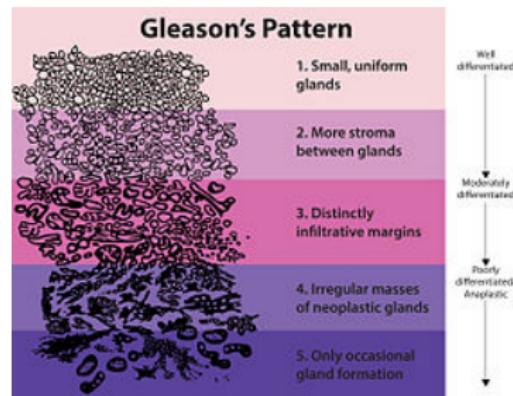


Image source: <https://goo.gl/fEVQXQ>

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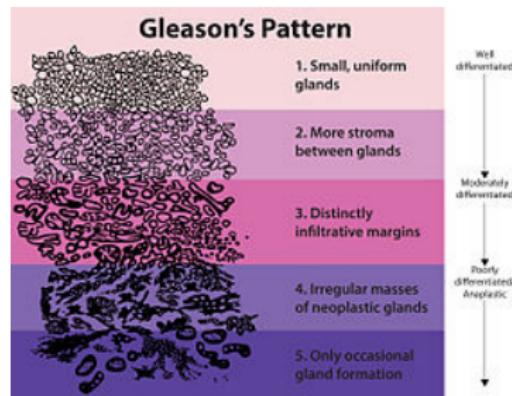


Image source: <https://goo.gl/fEVQXQ>



Screening



Pros

- ✓ Reduce CaP-related mortality between 21 % to 44 %⁴

Cons

- ✗ Up to 30 % of over-diagnosis⁵
- ✗ Up to 35 % of undiagnosed CaP⁶
- ✗ Biopsies are invasive

⁴Fritz 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.

⁵G. 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.

⁶A. 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 MRI CAD for CaP
- ▶ Identify the scientific barriers
- ▶ Design a mp-MRI CAD addressing these issues
- ▶ Investigate and analyze the proposed CAD

1 Introduction

2 State-of-the-art

MRI modalities
CAD for CaP

3 I2CVB

4 Toward a mp-MRI CAD for CaP

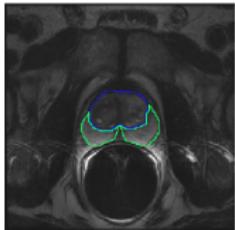
5 Conclusions



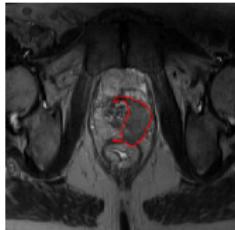
MRI modalities



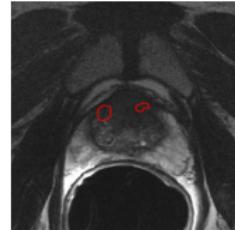
T₂W-MRI



(a) Healthy



(b) CaP PZ



(c) CaP CG

Healthy

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

CaP

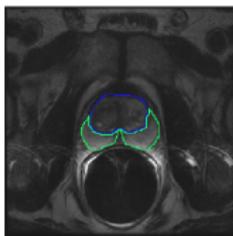
- ▶ Low-SI
- ▶ Round and ill-defined mass in PZ
- ▶ Homogeneous with ill-defined edges in CG



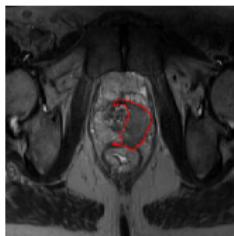
MRI modalities



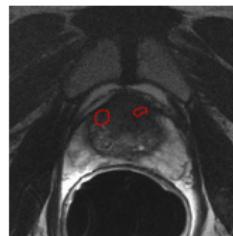
T₂W-MRI



(a) Healthy



(b) CaP PZ



(c) CaP CG

Pros

- ▶ Highest spatial resolution
- ▶ Anatomy nicely depicted

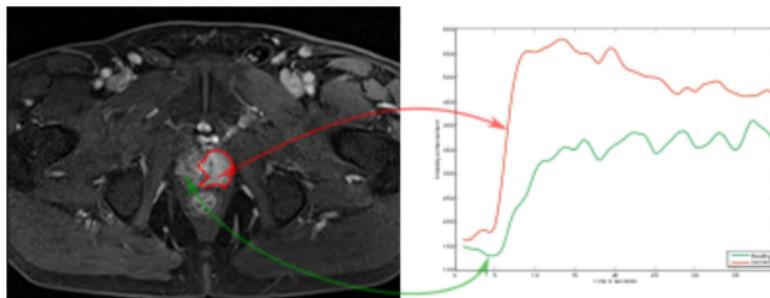
Cons

- ▶ 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

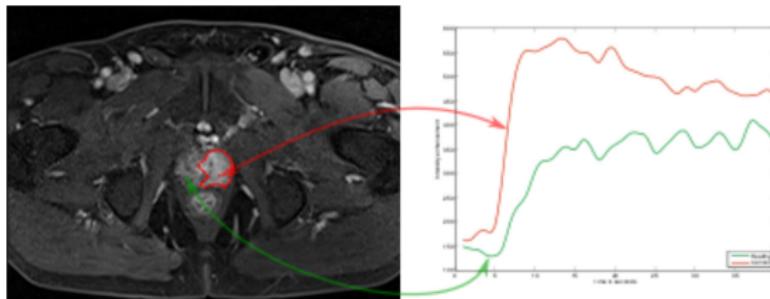
- ▶ Faster wash-in, wash-out, time-to-peak enhancement
- ▶ Higher integral under the curve, max SI



MRI modalities



DCE-MRI



Green: healthy - Red: CaP

Pros

- ▶ Information about vascularity

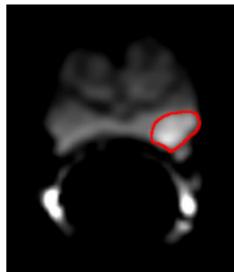
Cons

- ▶ Spatial mis-registration
- ▶ Lower spatial resolution than T₂W-MRI
- ▶ Difficult detection in CG

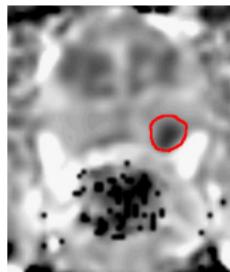


MRI modalities

DW-MRI - ADC



(a) DW MRI



(b) ADC

Healthy

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

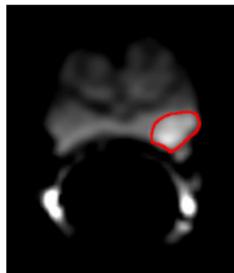
CaP

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

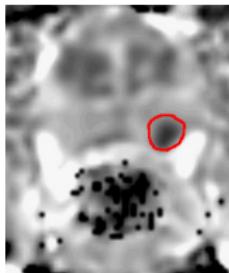


MRI modalities

DW-MRI - ADC



(c) DW MRI



(d) ADC

Pros

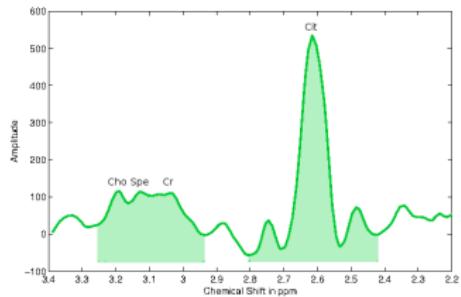
- ▶ Information about tissue structure
- ▶ ADC correlated with Gleason score

Cons

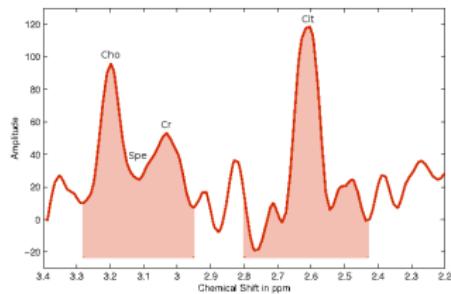
- ▶ Poor spatial resolution
- ▶ Variability of the ADC coefficient

MRI modalities

MRSI



(a) Healthy



(b) CaP

Healthy

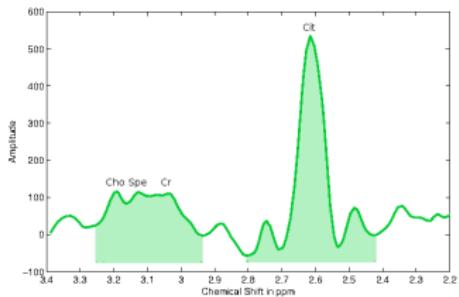
- ▶ High citrate concentration
- ▶ Moderate choline and spermine concentrations

CaP

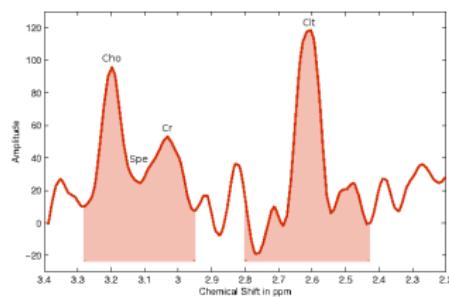
- ▶ Decrease of citrate and spermine concentrations
- ▶ Increase of choline concentration

MRI modalities

MRSI



(c) Healthy



(d) CaP

Pros

- Citrate correlated with Gleason score

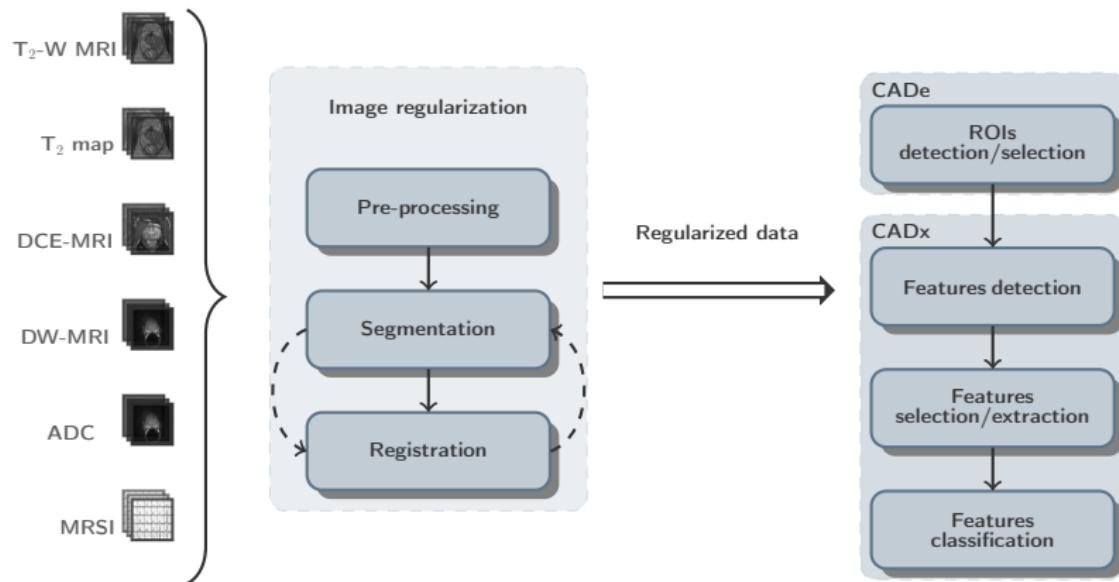
Cons

- Low spatial resolution
- Variation inter-patients



CAD for CaP

Full CAD for detection and diagnosis of CaP



Common CAD framework based on MRI images used to detect CaP

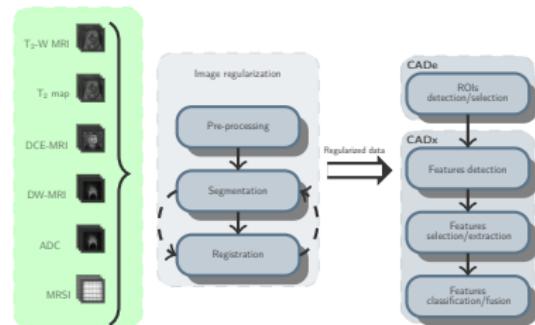


CAD for CaP



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.)



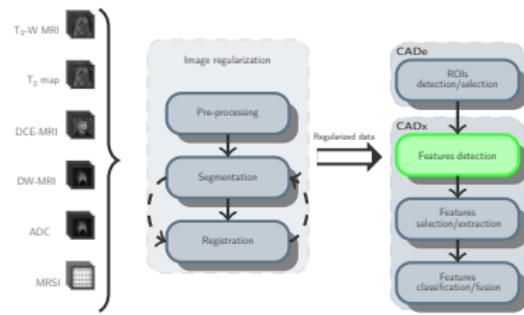


CAD for CaP



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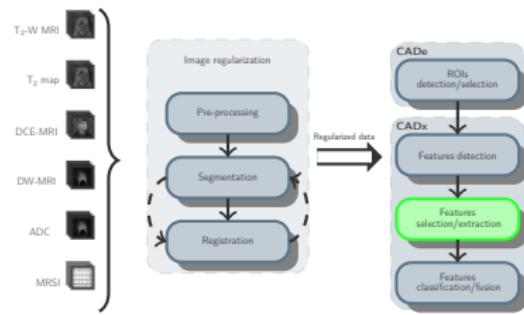


CAD for CaP



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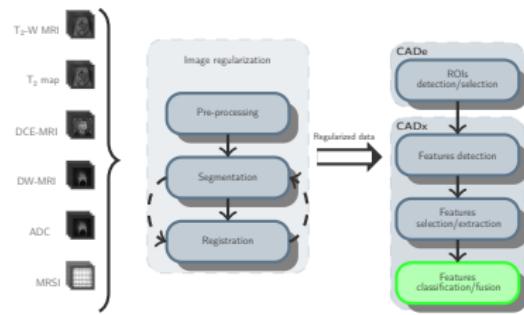


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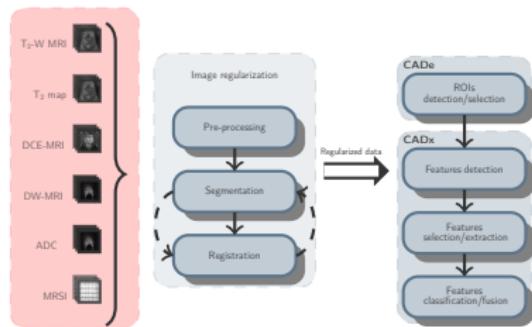
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Scientific and technical challenges

- ✗ 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

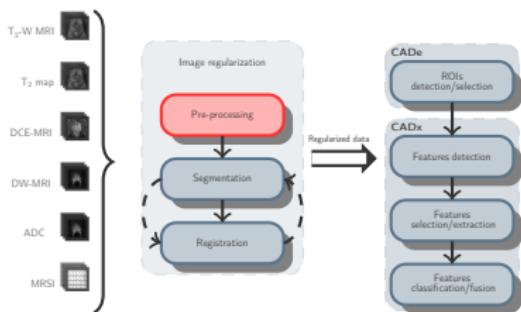


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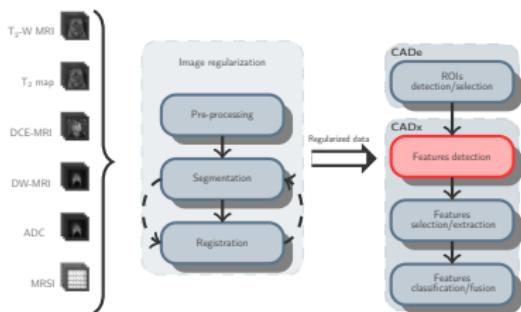


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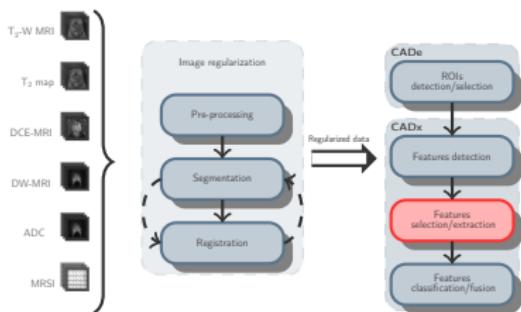


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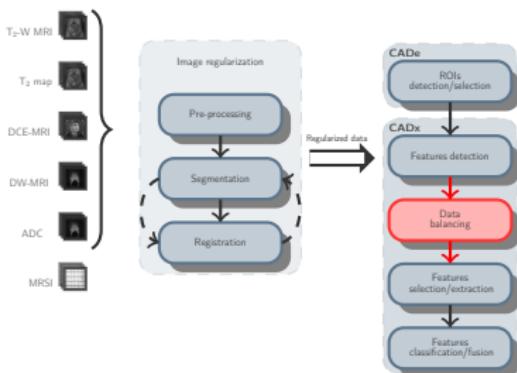


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Research objectives

- ▶ 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

1 Introduction

2 State-of-the-art

3 I2CVB

- Mp-MRI prostate datasets
- Open source initiative
- I2CVB

4 Toward a mp-MRI CAD for CaP

5 Conclusions



Mp-MRI prostate datasets



1.5 T General Electric scanner

- ▶ T₂W-MRI, DW-MRI, DCE-MRI, and MRSI
- ▶ Ground-truth (GT) for CaP, PZ, and CG associated to T₂W-MRI modality
- ▶ Healthy: 4 vs. CaP: { PZ: 14 + 3, CG: 0 + 3 }

3 T Siemens scanner

- ▶ T₂W-MRI, ADC, DCE-MRI, and MRSI
- ▶ GT for CaP, PZ, and CG associated to T₂W-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



1.5 T General Electric scanner

- ▶ T₂W-MRI, DW-MRI, DCE-MRI, and MRSI
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Open source initiative



protoclass toolbox

- ▶ Data management
- ▶ Features detection

imbalanced-learn toolbox⁷

- ▶ Part of the scikit-learn-contrib projects

Third-party toolboxes



⁷Guillaume Lemaître 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

Initiative for Collaborative Computer Vision Benchmarking

Home Benchmarks Contact

ICCVB in a nutshell

I₂CVB Vision

Tweets

 I2CVB
@I2CVB
Just setting up my
#myfirstTweet

Load More

Hub for our different resources

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

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4 Toward a mp-MRI CAD for CaP

Image regularization

CADe-CADx

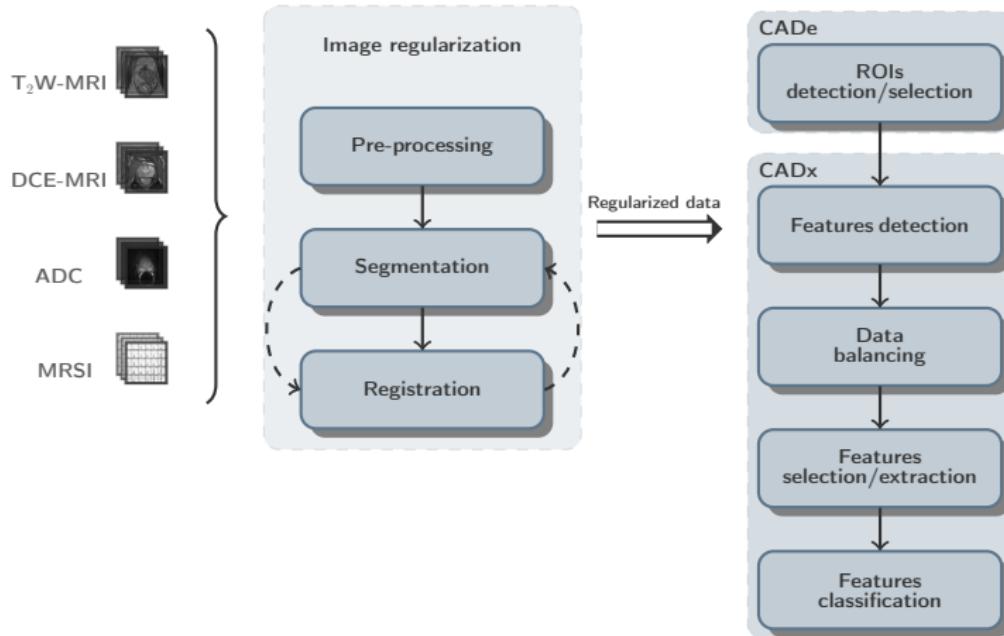
Fine-tuned combination

MRSI benefit

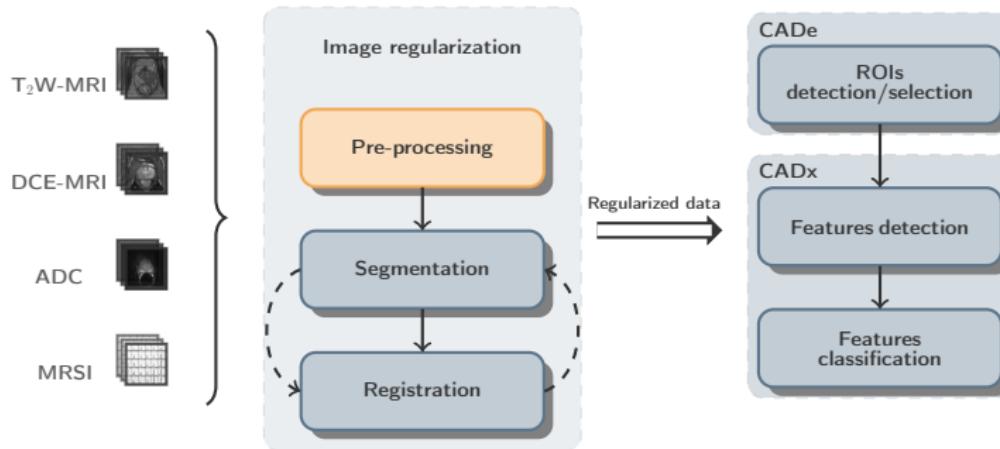
5 Conclusions

Toward a mp-MRI CAD for CaP

Mp-MRI CAD for CaP



Pre-processing





Pre-processing



T₂W-MRI normalization

- ▶ Rician normalization⁸

DCE-MRI normalization

- ▶ Graph and deviation based normalization⁹

ADC normalization

- ▶ Piecewise-linear normalization

MRSI normalization

- ▶ Phase correction¹⁰
- ▶ Frequency alignment
- ▶ Baseline correction¹¹

⁸Guillaume Lemaître et al. "Automatic prostate cancer detection through DCE-MRI images: all you need is a good normalization". In: *Medical Image Analysis - Submitted* (2017).

¹⁰Guillaume Lemaître 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.

¹¹Li 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.

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



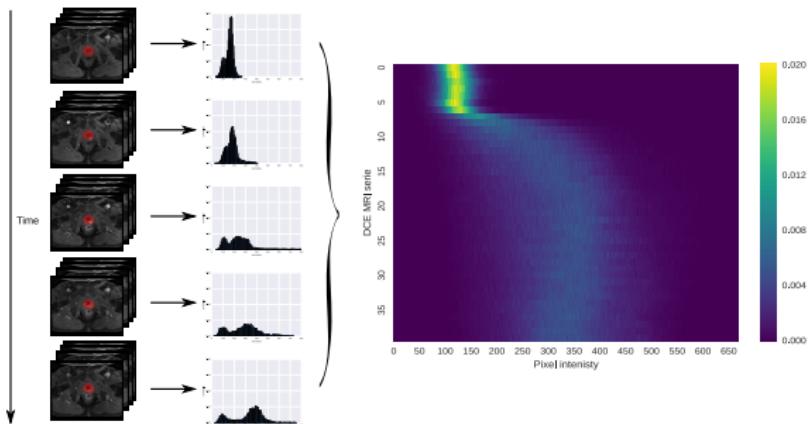
DCE-MRI normalization



Contribution¹³

- ▶ Propose a method to normalize DCE-MRI data

Heatmap representation



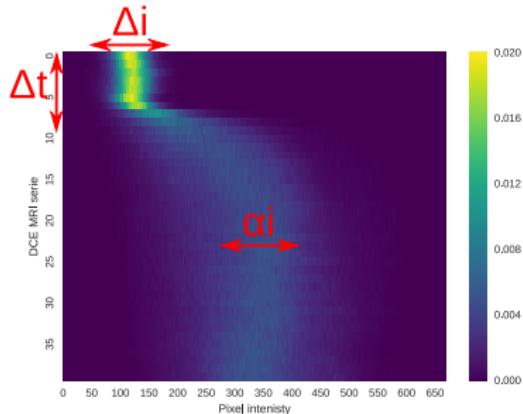
¹³Lemaitre et al., "Automatic prostate cancer detection through DCE-MRI images: all you need is a good normalization".



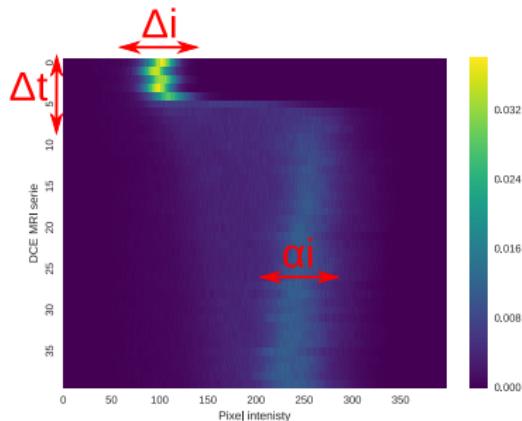
DCE-MRI normalization



Inter-patients variations



(a) Patient #1



(b) Patient #2

Variations driven by Δ_i , Δ_t , and α_i



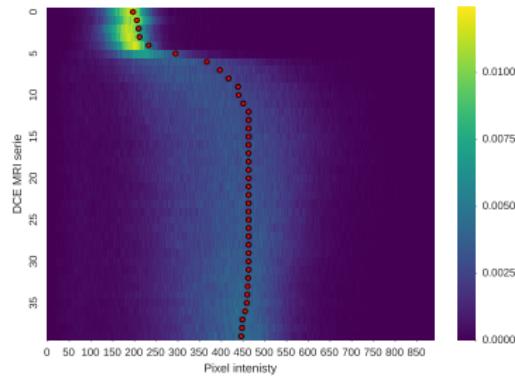
DCE-MRI normalization



Correction of Δ_i

Find the shortest path in a directed weighted graph $\mathcal{G} = (\mathcal{V}, \mathcal{E})$ with the edge weight w_{ij} between 2 nodes i and j corresponding to 2 pixels at position (x_i, y_i) and (x_j, y_j) , respectively defined as:

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





DCE-MRI normalization



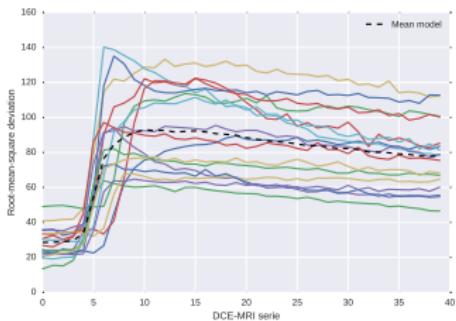
Correction of Δ_t and α_i

Register all RMSD to a mean model such that:

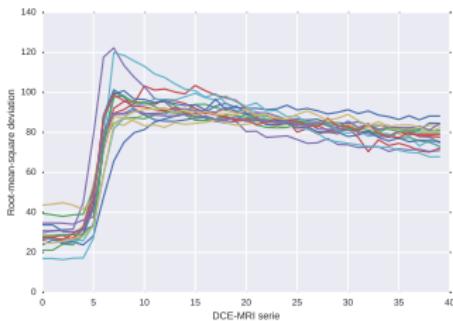
$$\arg \min_{\alpha, \tau} = \sum_{t=1}^N [T(\alpha, \tau, f(t)) - \mu(t)]^2, \quad (2)$$

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

$$T(\alpha, \tau, f(t)) = \alpha f(t - \tau). \quad (4)$$



(a) RMSD before correction



(b) Registered RMSD



DCE-MRI normalization



Evaluation through pharmacokinetic models

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

Classification

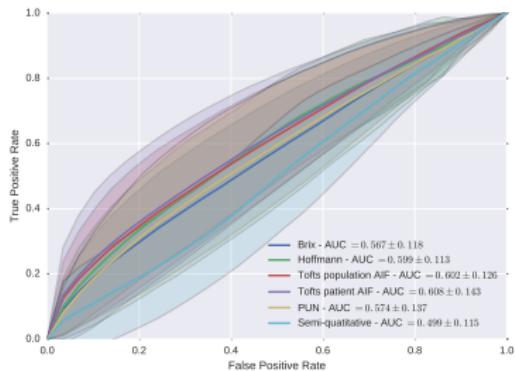
- ▶ Semi-quantitative model
- ▶ Entire enhanced signal

Classification

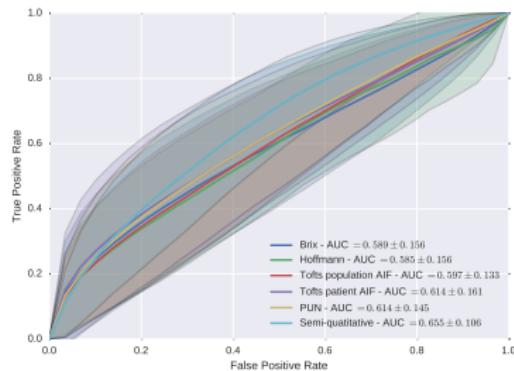
- ▶ Classification with random forest (RF)
- ▶ Leave-one-patient-out cross-validation (LOPO)
- ▶ Receiver operating characteristic (ROC) analysis
- ▶ Area under the ROC curve (AUC)

DCE-MRI normalization

Quantitative and semi-quantitative models



(a) Without normalization



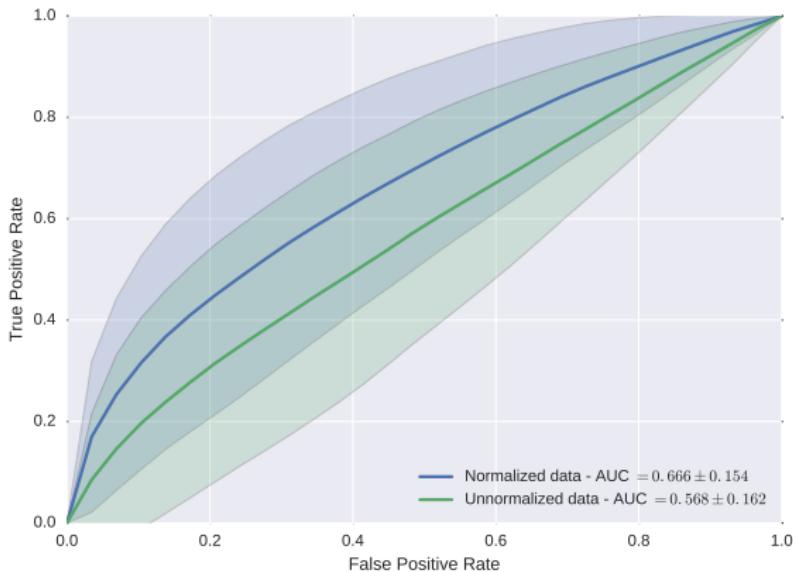
(b) With normalization

ROC analysis for pharmacokinetic model



DCE-MRI normalization

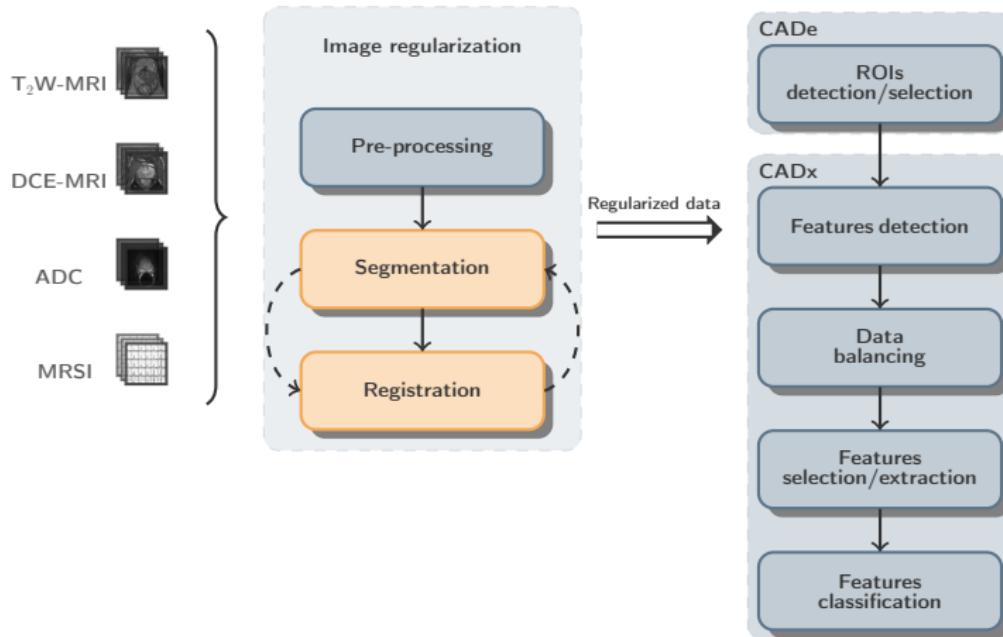
Entire signal



ROC analysis with entire enhanced signal

Image regularization

Segmentation & registration





Segmentation & registration



Interpolation

- ▶ ADC and DCE-MRI are interpolated to the T₂W-MRI resolution

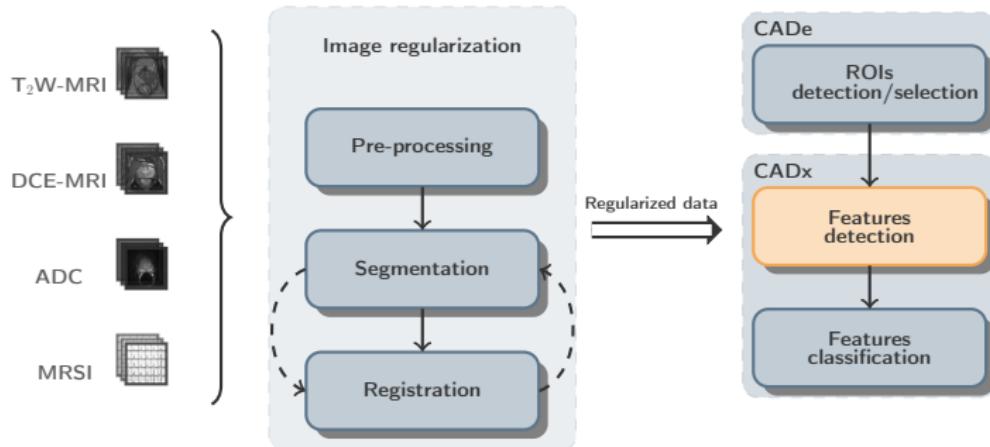
Segmentation

- ▶ Manual prostate segmentation available for T₂W-MRI, DCE-MRI, and ADC
- ▶ Cap, PZ, and CG manual segmentation available for T₂W-MRI

Registration

- ▶ Intra-patient motions correction in DCE-MRI: rigid registration using mutual information
- ▶ DCE-MRI is registered to T₂W-MRI using the prostate segmentation
- ▶ ADC is registered to T₂W-MRI using the prostate segmentation

Features detection





Feature detection



T₂W-MRI and ADC features

- ▶ Intensity
- ▶ Kirsch filter
- ▶ Laplacian filter
- ▶ Prewitt filter
- ▶ Scharf 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

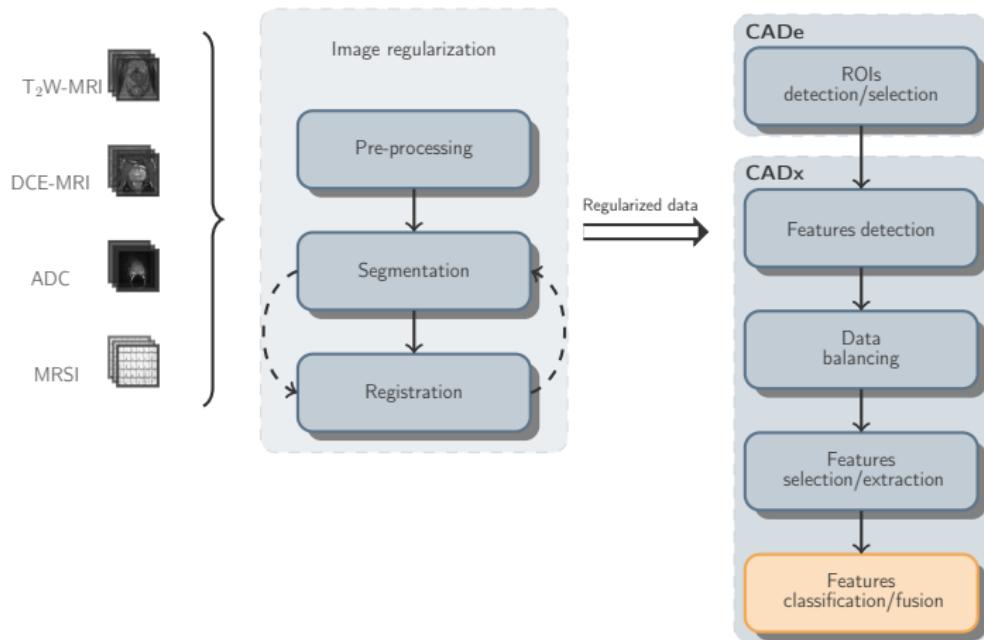
MRSI features

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

Spatial information

- ▶ Relative distance
- ▶ Relative position
- ▶ Prostate zone

Features classification

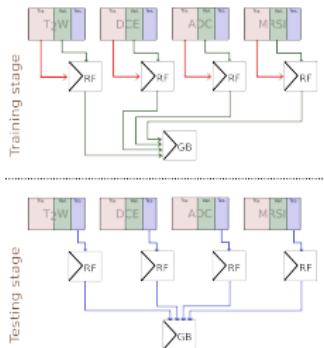




Features classification

Classification as fusion

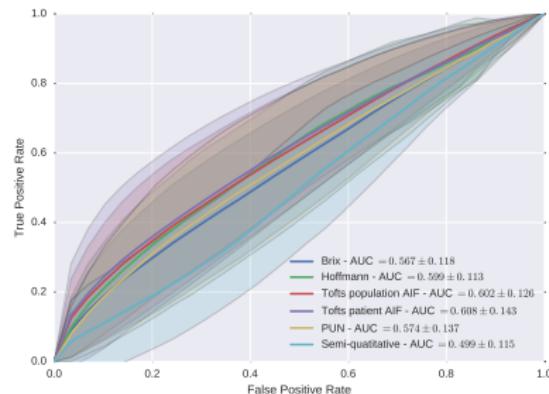
- ▶ RF used as classifier for each modality and aggregation of features
- ▶ Stacking of RF with an adaboost and gradient-boosting meta-classifier



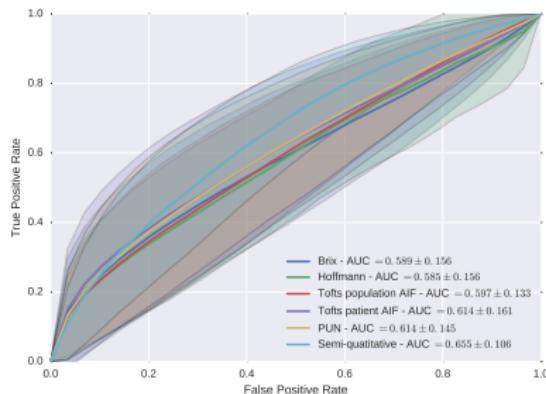
Validation

- ▶ LOPO CV
- ▶ ROC analysis
- ▶ AUC

Quantitative and semi-quantitative models



(a) Without normalization



(b) With normalization

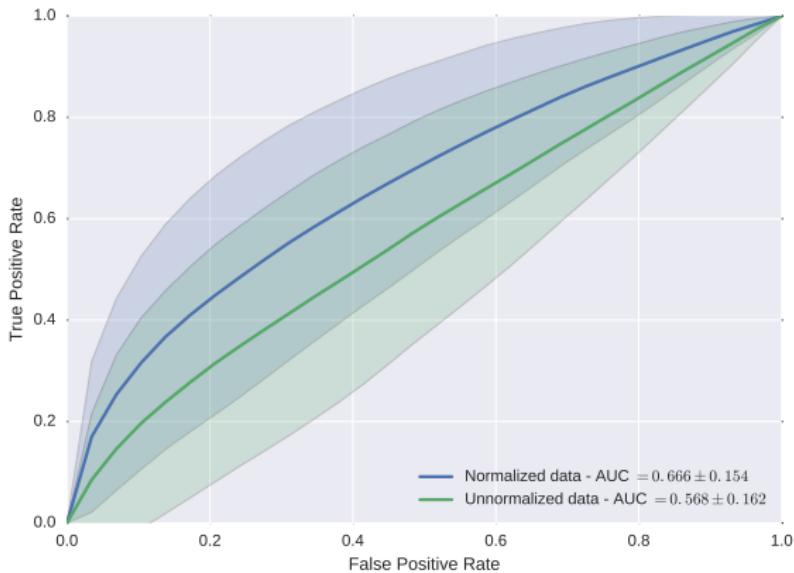
ROC analysis for pharmacokinetic model



DCE modality

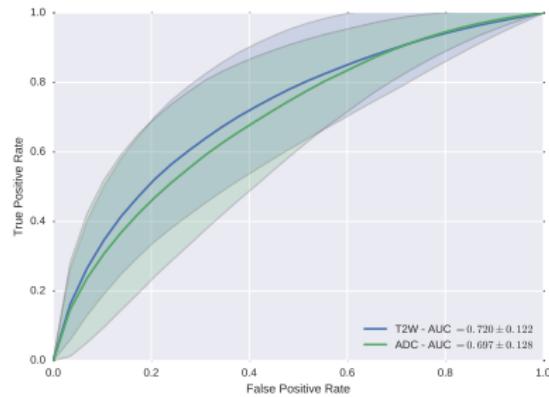
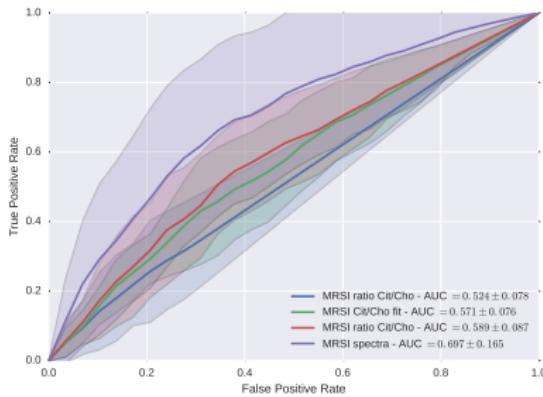


Entire signal



ROC analysis for the entire enhanced signal

ROC analysis

(a) T₂W-MRI and ADC

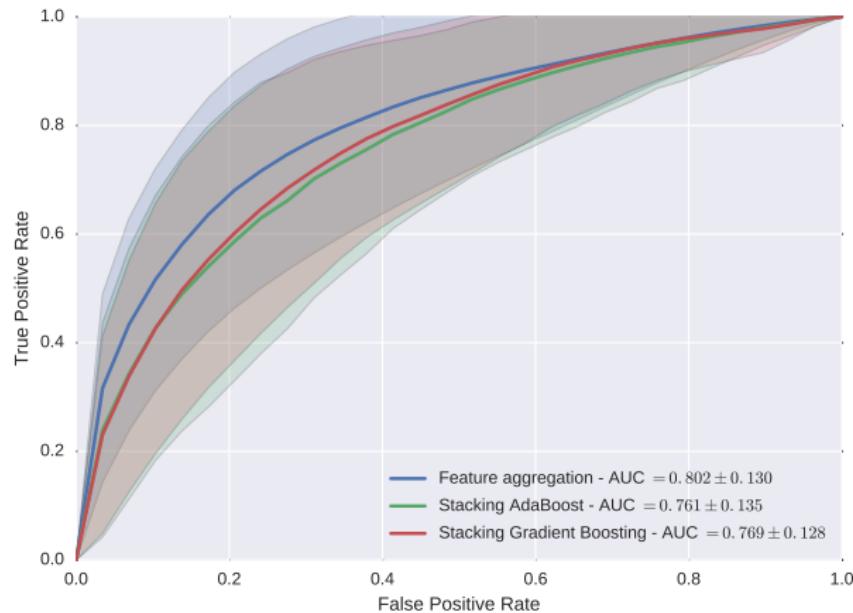
(b) MRSI

ROC analysis for T₂W-MRI, ADC, and MRSI modalities



Coarse combination

Aggregation vs. stacking



ROC analysis for the fusion strategies



T₂W-MRI, ADC, and MRSI modalities



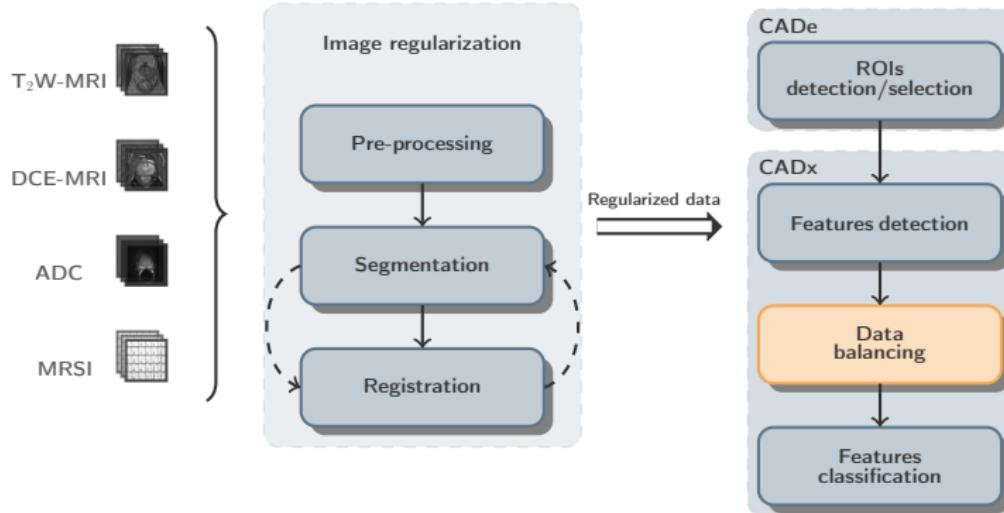
Overall best performance

AUC	T ₂ W-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 → best performance
- ▶ DCE-MRI: entire signal better than models
- ▶ MRSI: fitting better than bounds approach
- ▶ MRSI: entire spectra better than others
- ▶ T₂W-MRI > ADC = MRSI > DCE
- ▶ Performance at an “acceptable” level of discrimination - AUC ∈ [0.7, 0.8]
- ▶ Aggregation better than stacking

Data balancing

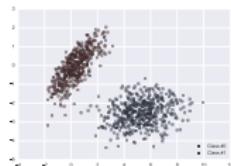




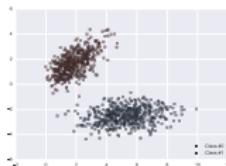
Data balancing



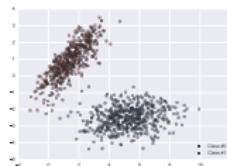
Under-sampling



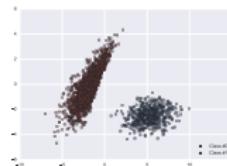
(a) NM1



(b) NM2

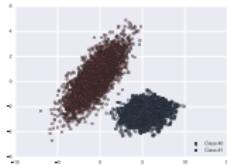


(c) NM3

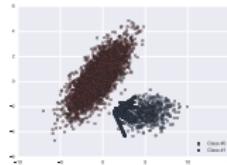


(d) IHT

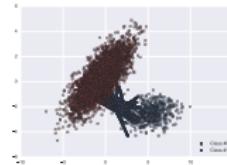
Over-sampling



(e) SMOTE

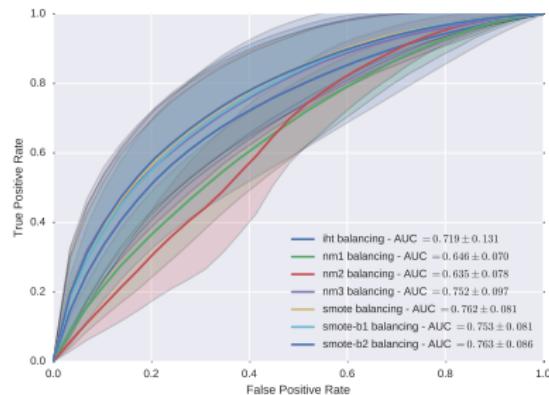
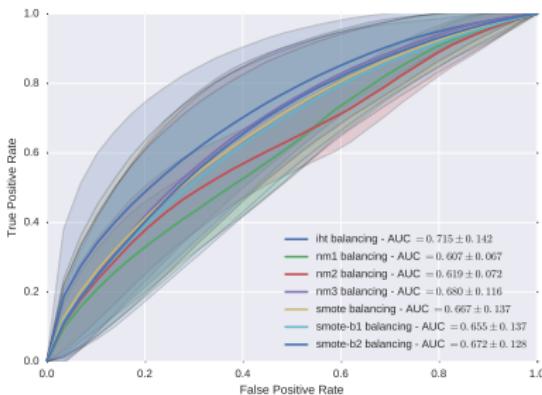


(f) SMOTE-b1



(g) SMOTE-b2

Data balancing

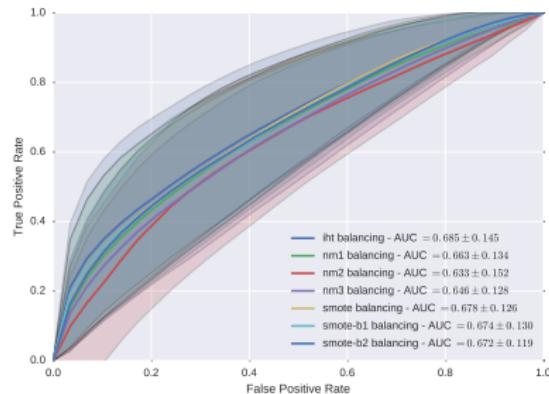
T₂W-MRI and ADC(a) T₂W-MRI

(b) ADC

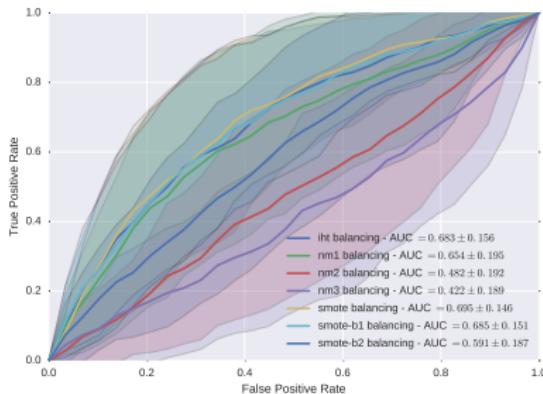
ROC analysis for T₂W-MRI and ADC

Data balancing

DCE-MRI and MRSI



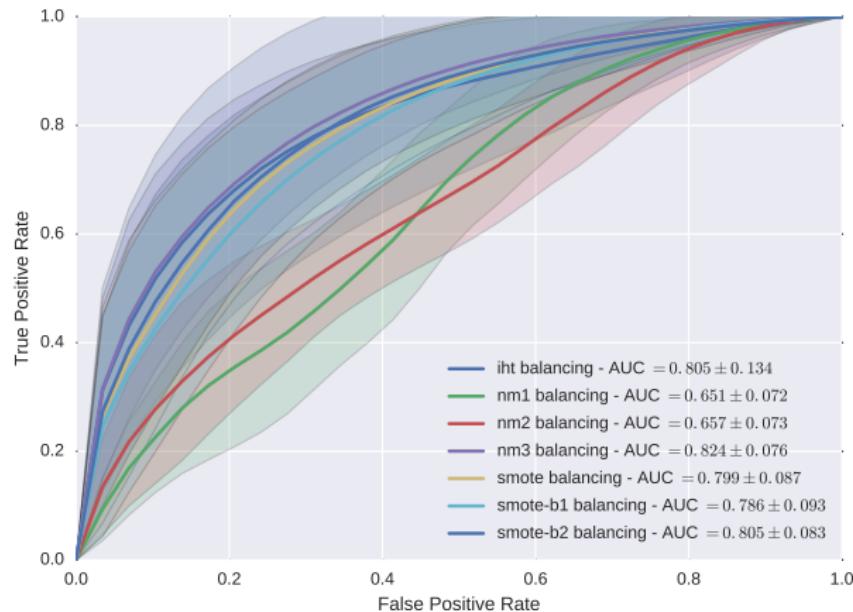
(a) DCE-MRI



(b) MRSI

Data balancing

Aggregation



ROC analysis while aggregating the features



Data balancing



Conclusions

- ✓ IHT → ADC and DCE-MRI
- ✓ SMOTE → T₂W-MRI and MRSI
- ✓ NM3 → aggregate feature

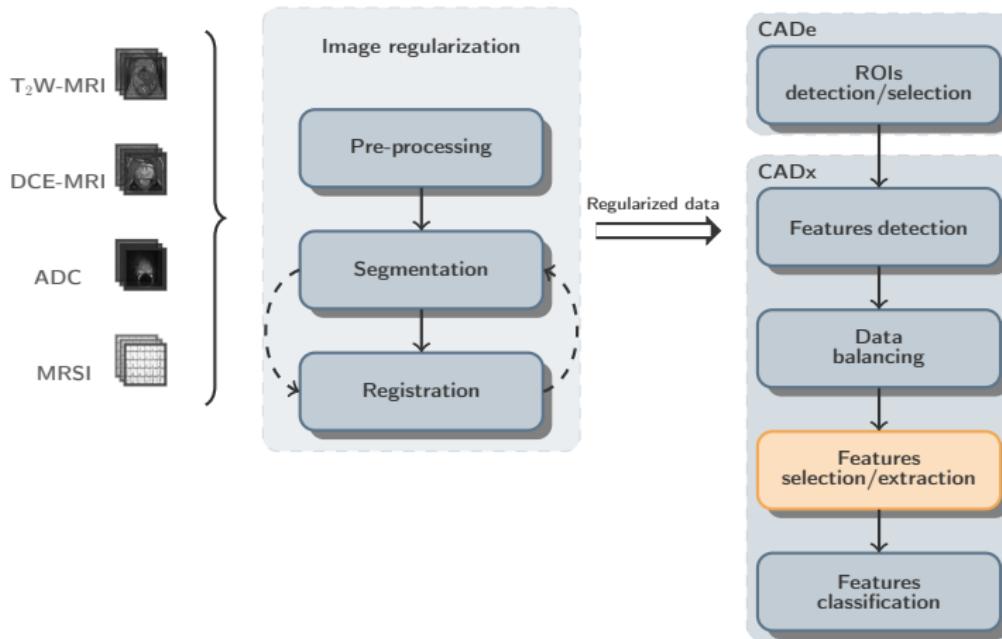
Before data balancing

AUC	T ₂ W-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 ₂ W-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
Tendency	✓	✓	✓	✓	✓

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

- ✓ T₂W-MRI: ANOVA-based selection with 25 % of the data
- ✓ ADC: Gini importance-based selection with 5 % of the data
- ✓ DCE-MRI: ICA with 24 components
- ✓ MRSI: ICA with 36 components
- ✓ Aggregation: Gini importance with 17.5 % of the data



Data balancing



Before features selection/extraction

AUC	T ₂ W-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 ₂ W-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 T₂W-MRI and ADC

T ₂ W-MRI	ADC
8 edges	1 DCT
155 Gabor filters	32 Gabor filters
2 Haralick features	1 phase congruency
1 intensity	
4 LBP	
2 phase congruency	
<hr/>	
172 features	34 features
<hr/>	

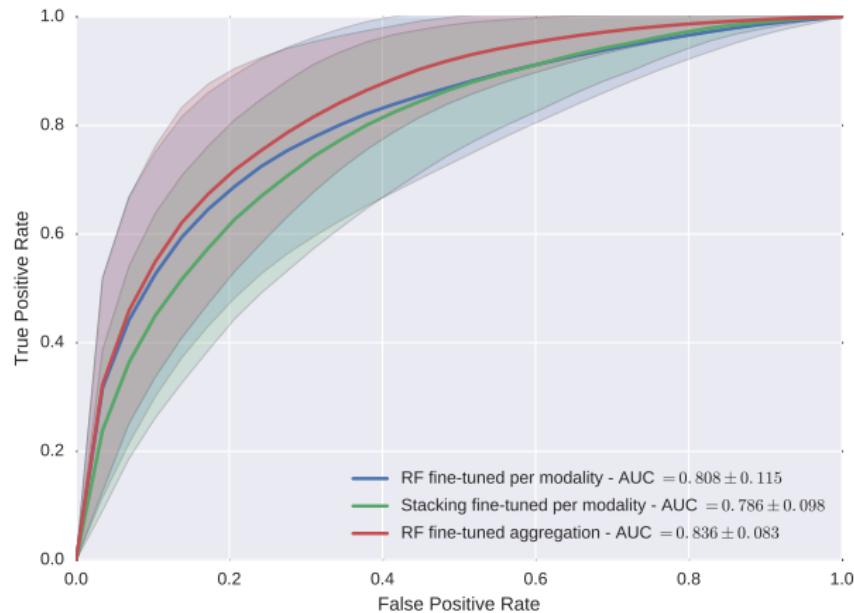
Selected features with aggregation

T ₂ W-MRI	ADC	DCE-MRI	MRSI		
113 Gabor filters	53 Gabor filters	14 samples	78 samples		
1 phase congruency	2 phase congruency				
4 edges					
1 intensity					
<hr/>		<hr/>			
267 features					
<hr/>					



Fine-tuned combination

Aggregation vs. stacking

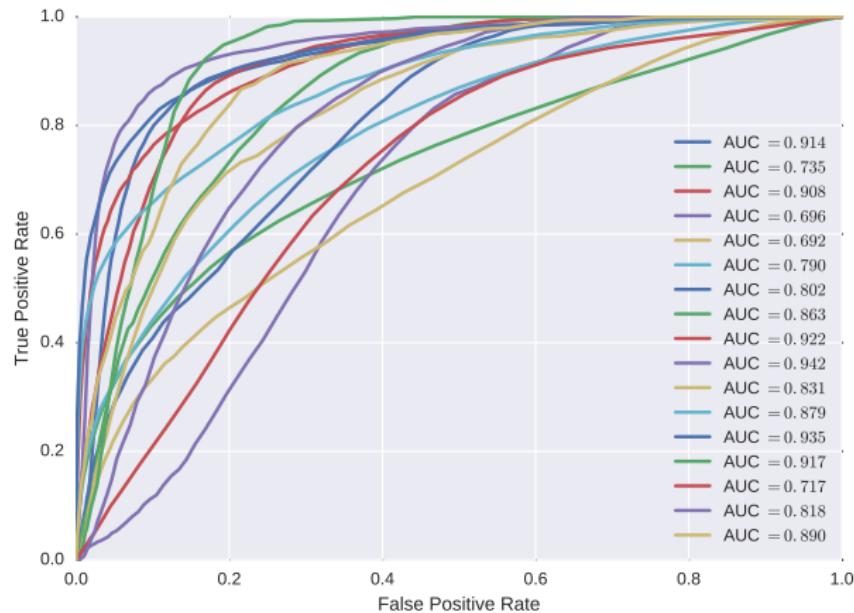


ROC analysis with the different fusion strategies



Fine-tuned combination

ROC for each patient



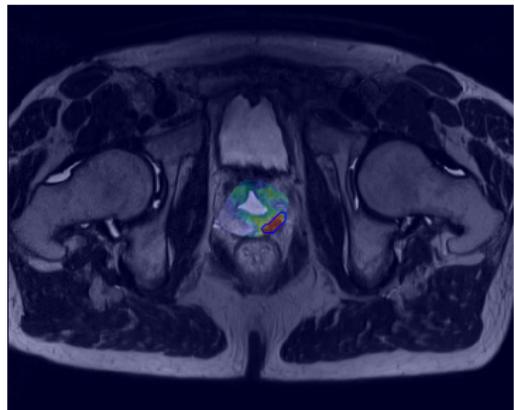
ROC analysis for each patient



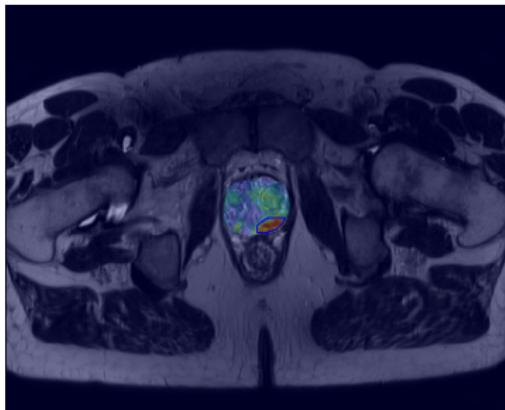
Fine-tuned combination



"Outstanding" discrimination level



(a) AUC = 0.922



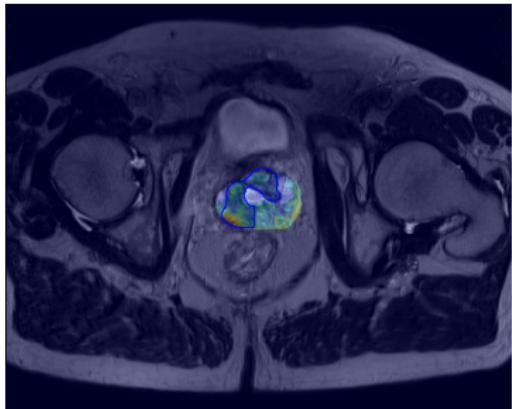
(b) AUC = 0.914



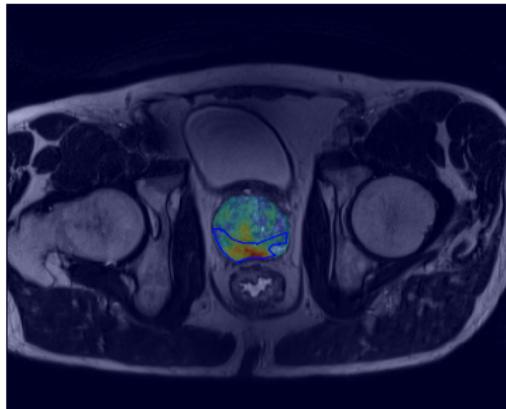
Fine-tuned combination



"Acceptable" discrimination level



(c) AUC = 0.692



(d) AUC = 0.735



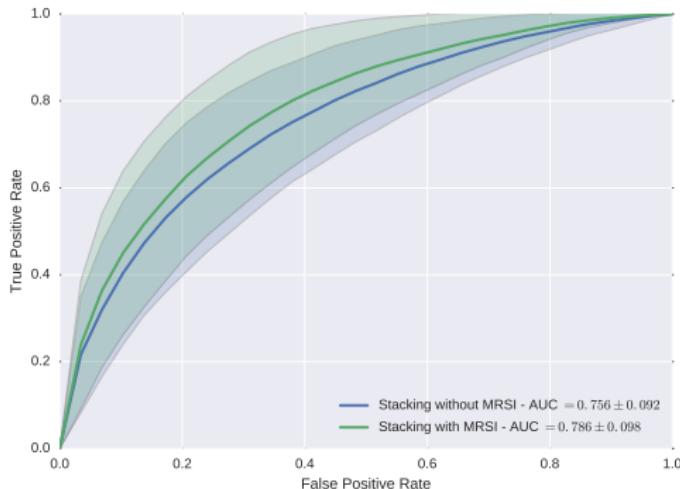
MRSI benefit



Importance of MRSI in aggregation

- Features from MRSI are the most selected features

Stacking with/without MRSI



ROC analysis with/without MRSI

1 Introduction

2 State-of-the-art

3 I2CVB

4 Toward a mp-MRI CAD for CaP

5 Conclusions

Contributions & future works

Timeline



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

- ✓ 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

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

