

Computer-Aided Diagnosis for Prostate Cancer using mp-MRI

PhD Defence
28th November 2016

Guillaume Lemaître

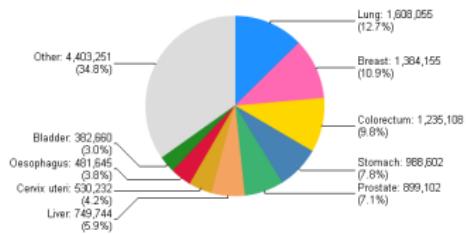
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Université de Bourgogne Franche-Comté - LE2I*

Supervised by:

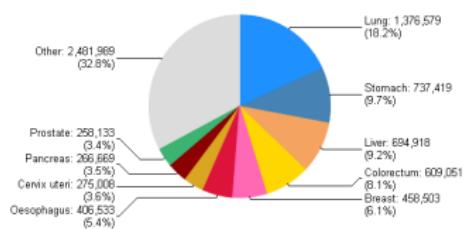
Robert Martí - Fabrice Mériauveau
Jordi Freixenet - Paul M. Walker



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

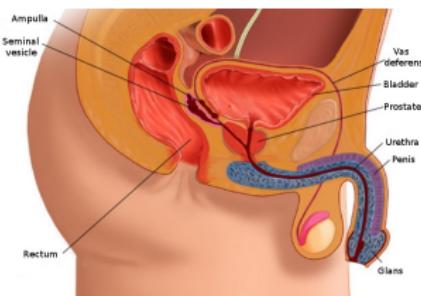
¹ J. Ferlay et al. "Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008". In: *Int. J. Cancer* 127.12 (Dec. 2010), pp. 2893–2917.



The prostate organ



Anatomy



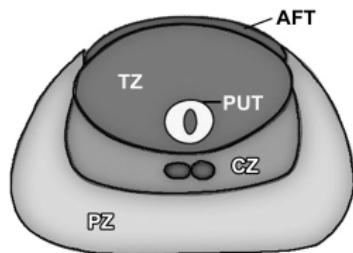
Localization of the prostate organ, image source²

Characteristics

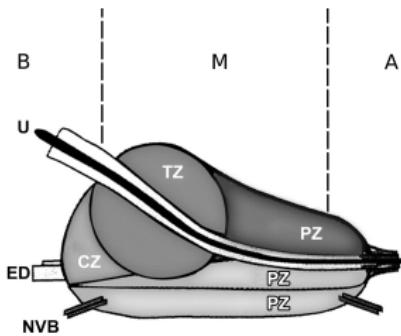
- ▶ Height: 3 cm
 - ▶ Depth: 2.5 cm
 - ▶ Weight: 7 g to 16 g

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

Anatomy



(a) Transverse plane



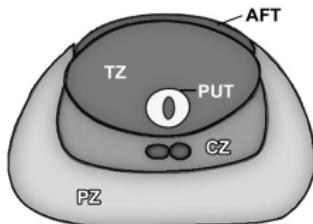
(b) Sagittal plane

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 %
 - ▶ CZ → 5 %

What clinicians need?

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

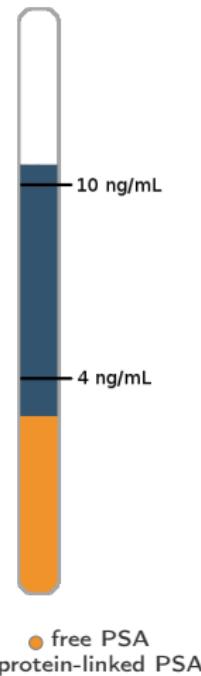


Screening



Prostate-specific antigen

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



"Blind" transrectal ultrasound biopsy

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

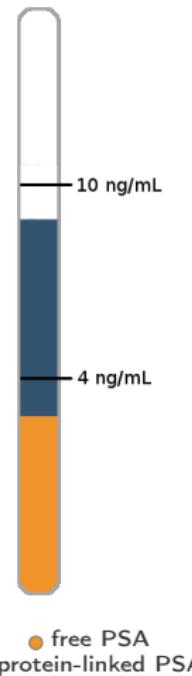


Screening



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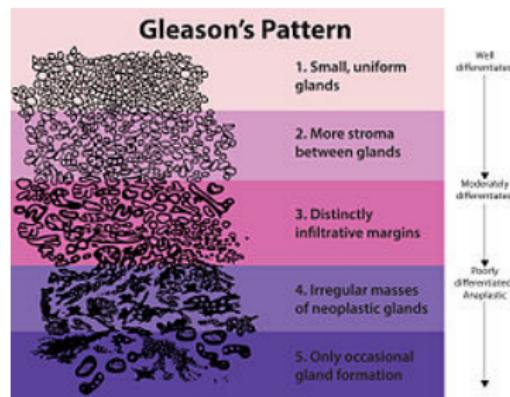


Image source: <https://goo.gl/fEVQXQ>



Screening



Pros

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

Cons

- ✗ Up to 30 % of over-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 mp-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

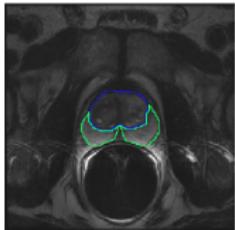
5 Conclusions



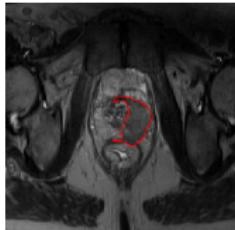
MRI modalities



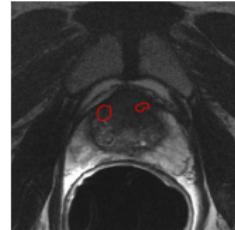
T₂W-MRI



(a) Healthy



(b) CaP PZ



(c) CaP CG

Healthy

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

CaP

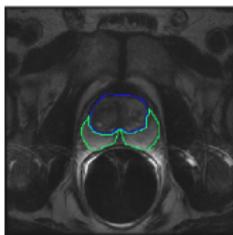
- ▶ Low-SI
- ▶ Round and ill-defined mass in PZ
- ▶ Homogeneous with ill-defined edges in CG



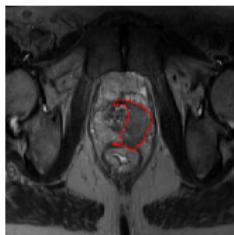
MRI modalities



T₂W-MRI



(a) Healthy



(b) CaP PZ



(c) CaP CG

Pros

- ▶ Highest spatial resolution
- ▶ Anatomy nicely depicted

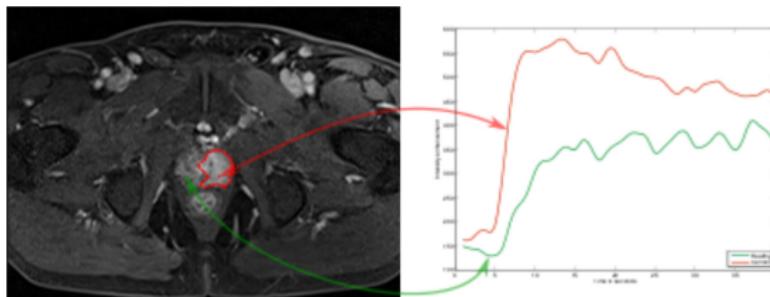
Cons

- ▶ 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

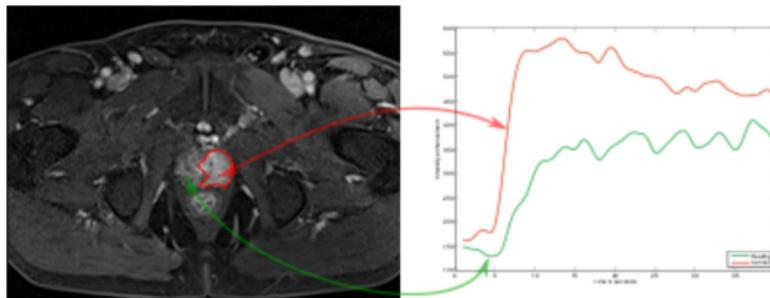
- ▶ Faster wash-in, wash-out, time-to-peak enhancement
- ▶ Higher integral under the curve, max SI



MRI modalities



DCE-MRI



Green: healthy - Red: CaP

Pros

- ▶ Information about vascularity

Cons

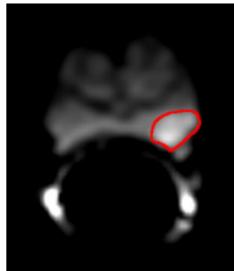
- ▶ Spatial mis-registration
- ▶ Lower spatial resolution than T₂W-MRI
- ▶ Difficult detection in CG



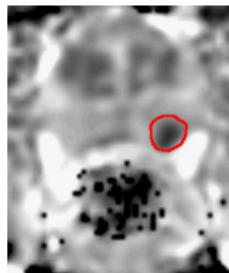
MRI modalities



DW-MRI - ADC



(a) DW MRI



(b) ADC

Healthy

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

CaP

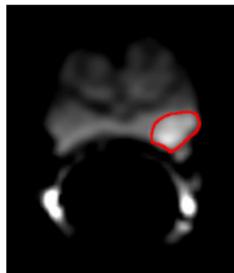
- ▶ DW-MRI: higher SI
- ▶ ADC: lower-SI



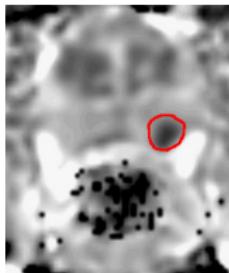
MRI modalities



DW-MRI - ADC



(a) DW MRI



(b) ADC

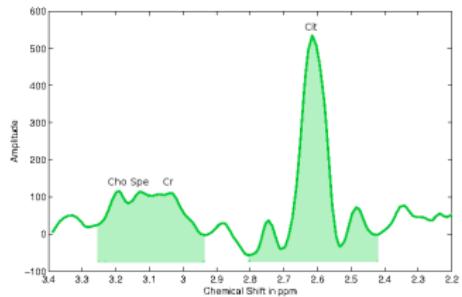
Pros

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

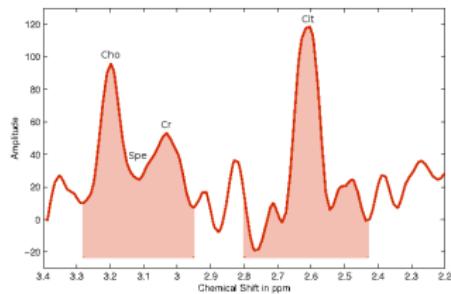
Cons

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

MRSI



(a) Healthy



(b) CaP

Healthy

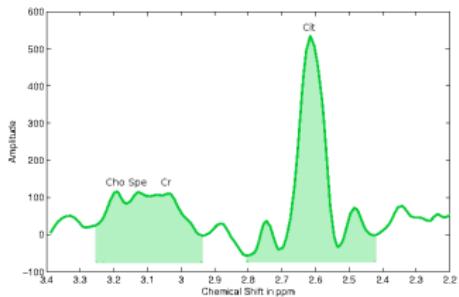
- ▶ High citrate concentration
- ▶ Moderate choline and spermine concentrations

CaP

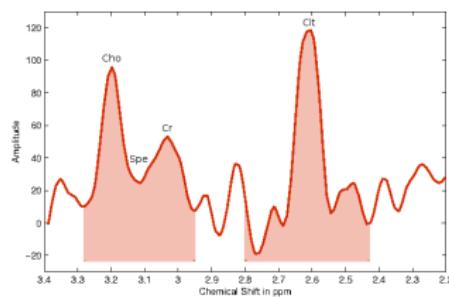
- ▶ Decrease of citrate and spermine concentrations
- ▶ Increase of choline concentration

MRI modalities

MRSI



(a) Healthy



(b) CaP

Pros

- Citrate correlated with Gleason score

Cons

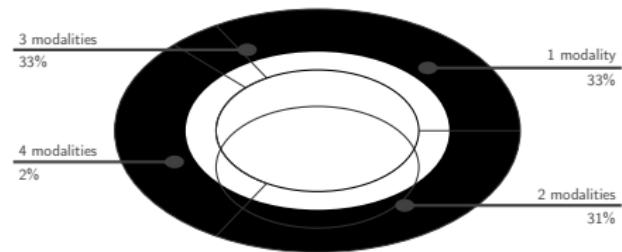
- Low spatial resolution
- Variation inter-patients



CAD for CaP



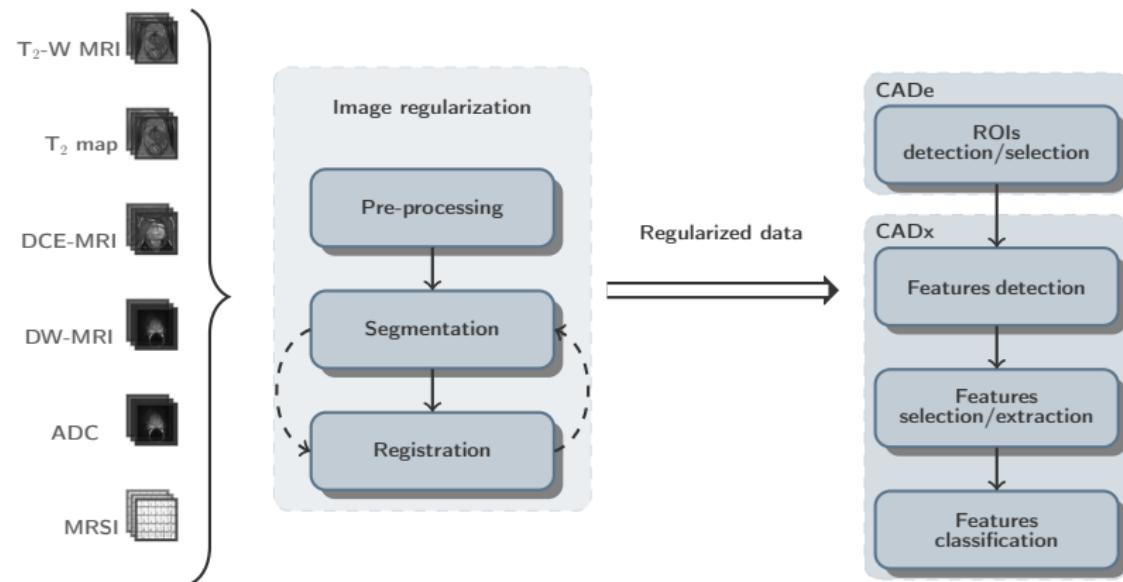
block





CAD for CaP

Full CAD for detection and diagnosis of CaP



Common CAD framework based on MRI images used to detect CaP

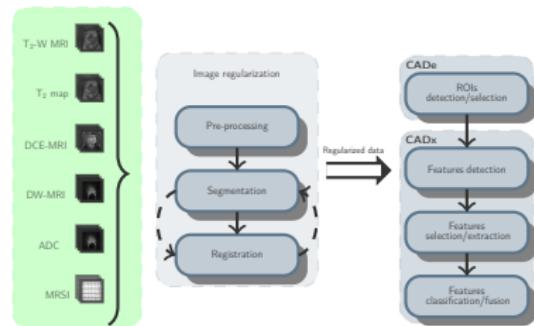


CAD for CaP



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.)



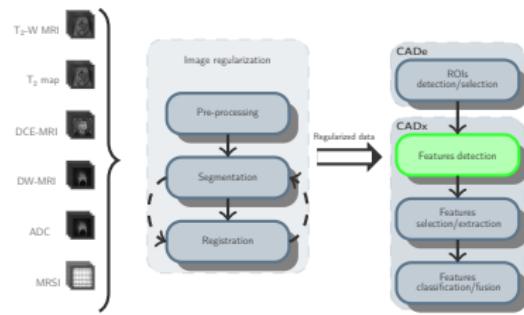


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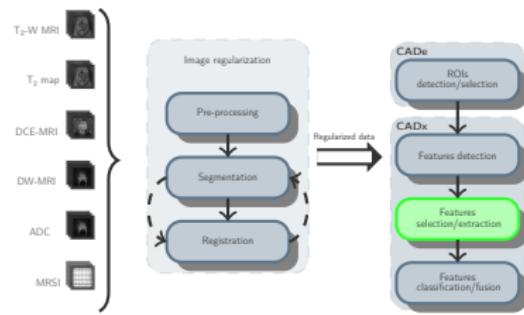


CAD for CaP



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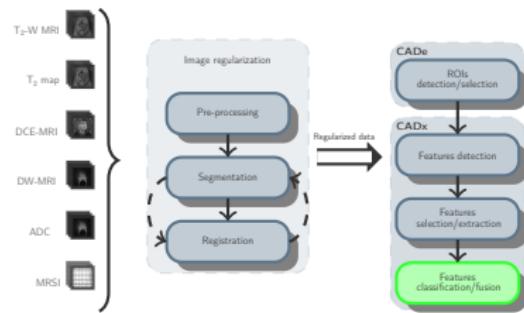


CAD for CaP



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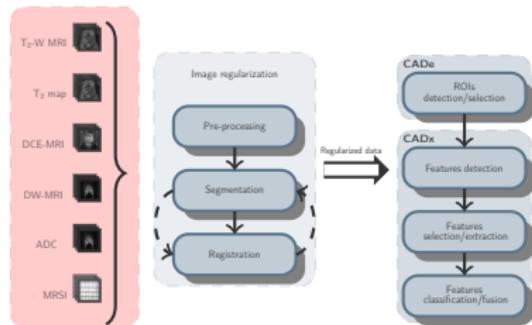
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Scientific and technical challenges

- ✗ 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

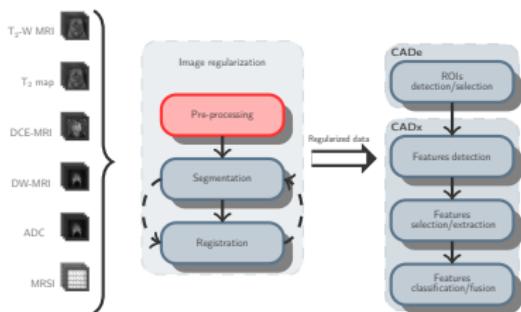


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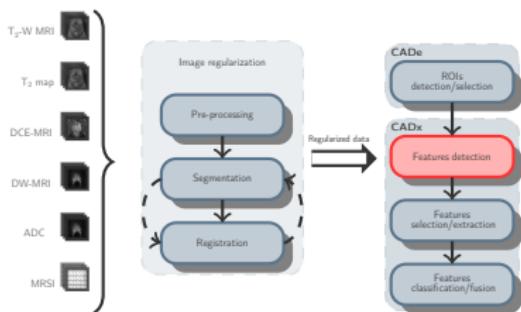


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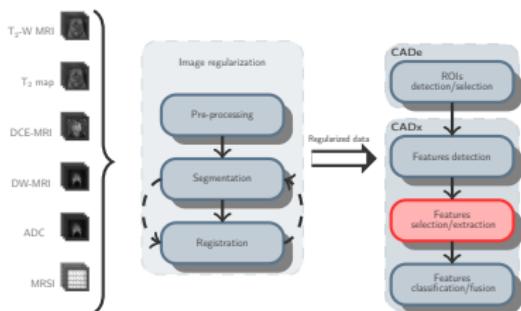


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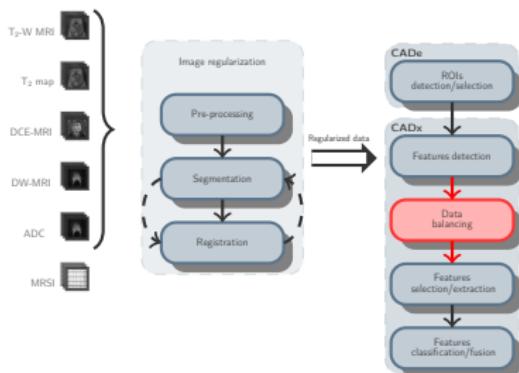


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CAD for CaP



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- ✗ No work regarding data balancing
- ✗ 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

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



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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



I₂C_VB platform

Initiative for Collaborative Computer Vision Benchmarking

Home Benchmarks Contact

ICCVB in a nutshell

I₂C_VB 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

- 1 Introduction
- 2 State-of-the-art
- 3 I2CVB
- 4 Toward a mp-MRI CAD for CaP
 - Image regularization
 - CADe-CADx
 - MRSI benefit
 - Fine-tuned combination
- 5 Conclusions

Toward a mp-MRI CAD for CaP

Mp-MRI CAD for CaP

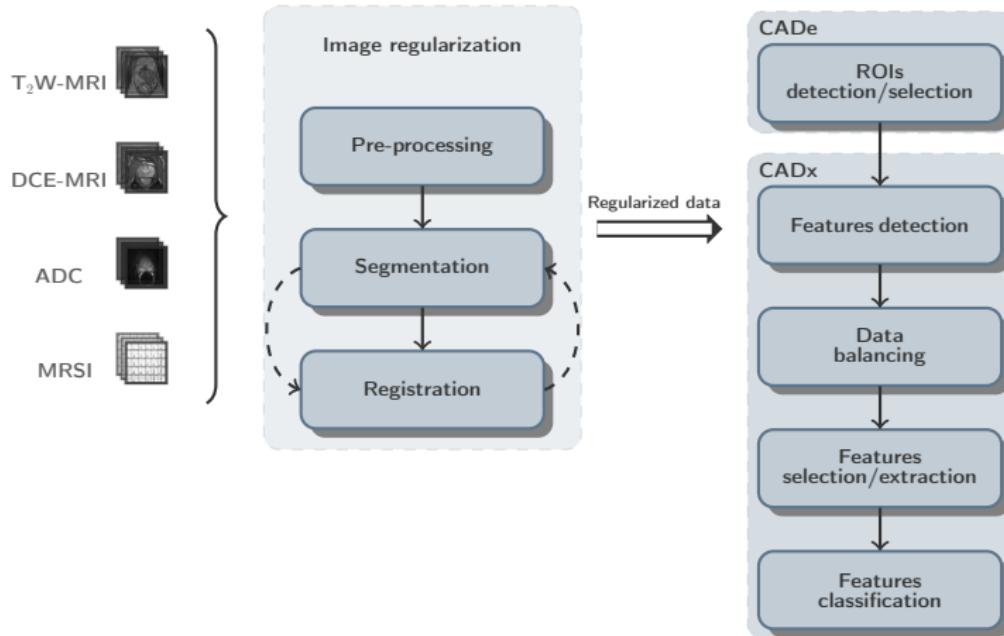
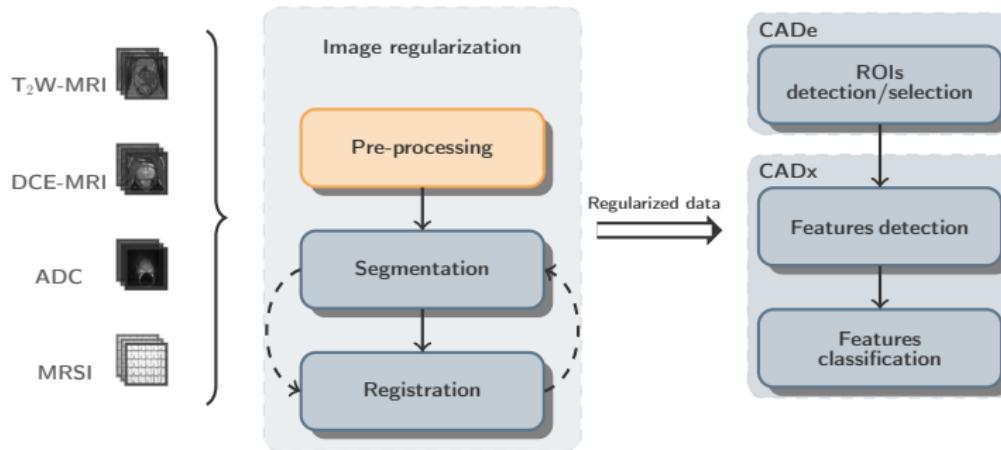




Image regularization



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.



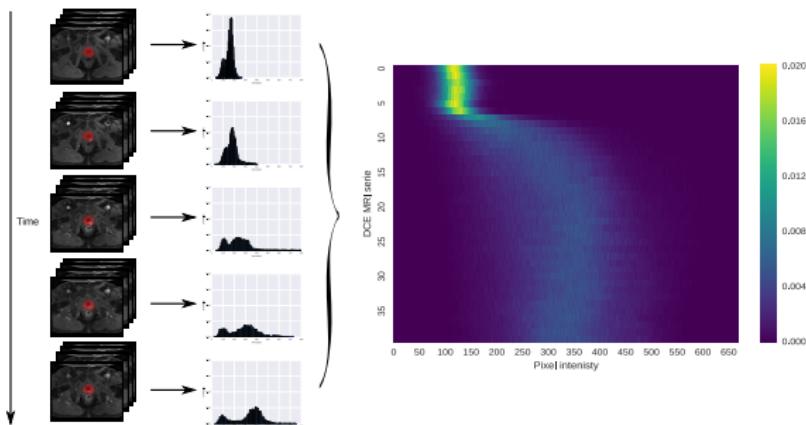
DCE-MRI normalization



Contribution¹³

- ▶ Propose a method to normalize DCE-MRI data

Heatmap representation



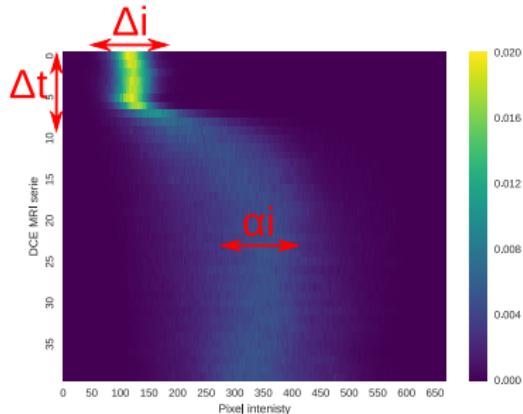
¹³Lemaitre et al., "Automatic prostate cancer detection through DCE-MRI images: all you need is a good normalization".



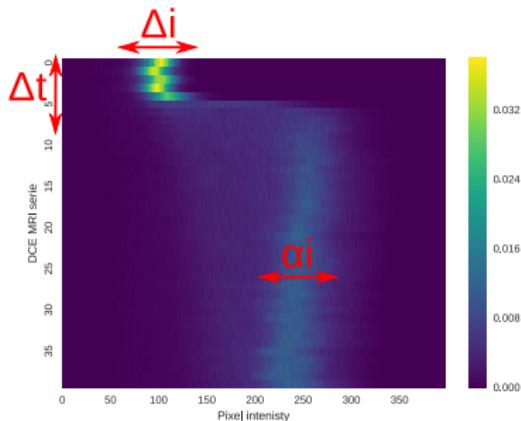
DCE-MRI normalization



Inter-patients variations



(a) Patient #1



(b) Patient #2

Variations driven by Δ_i , Δ_t , and α_i



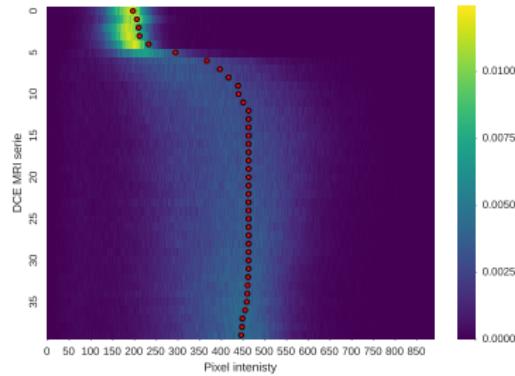
DCE-MRI normalization



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



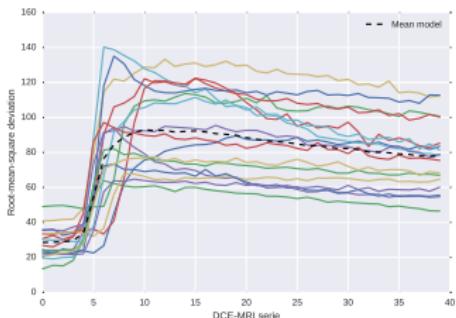
Correction of Δ_t and α_i

Register all RMSD to a mean model such that:

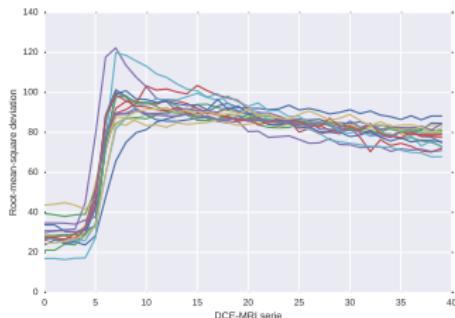
$$\arg \min_{\alpha, \tau} = \sum_{t=1}^N [T(\alpha, \tau, f(t)) - \mu(t)]^2, \quad (2)$$

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

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



(a) RMSD before correction



(b) Registered RMSD



DCE-MRI normalization



Evaluation through pharmacokinetic models

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

Other approaches

- ▶ Semi-quantitative model
- ▶ Entire enhanced signal

Classification

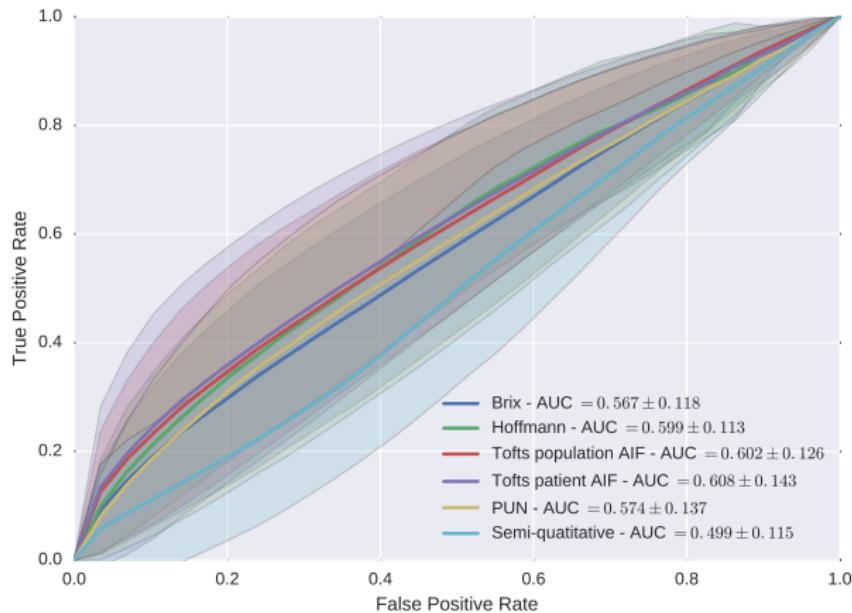
- ▶ Classification with random forest (RF)
- ▶ Leave-one-patient-out cross-validation (LOPO)
- ▶ Receiver operating characteristic (ROC) analysis
- ▶ Area under the ROC curve (AUC)



DCE-MRI normalization



Quantitative and semi-quantitative models



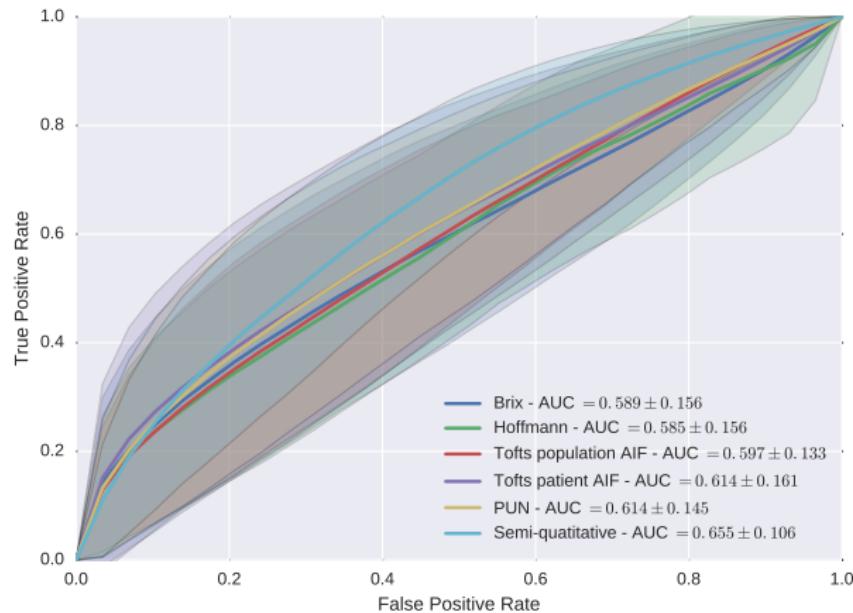
ROC analysis without normalization



DCE-MRI normalization



Quantitative and semi-quantitative models



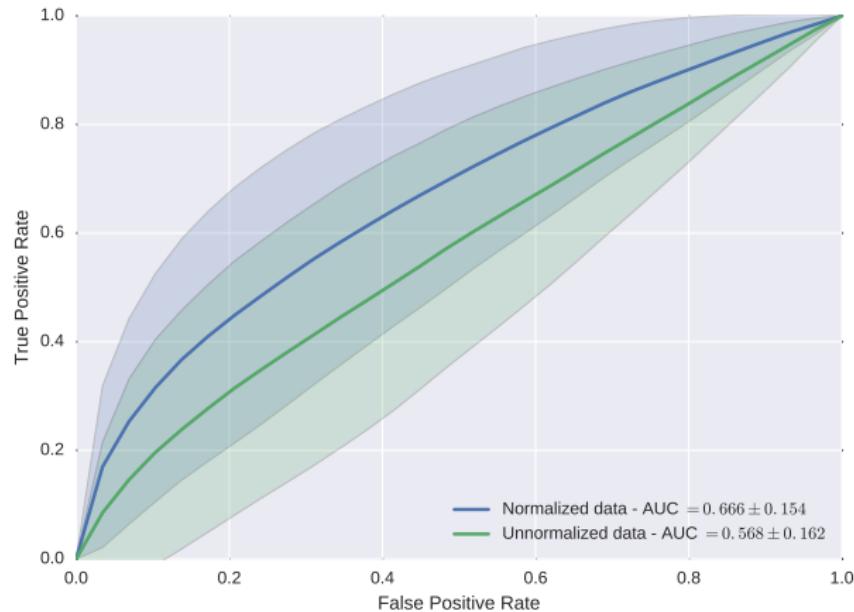
ROC analysis with normalization



DCE-MRI normalization



Entire signal

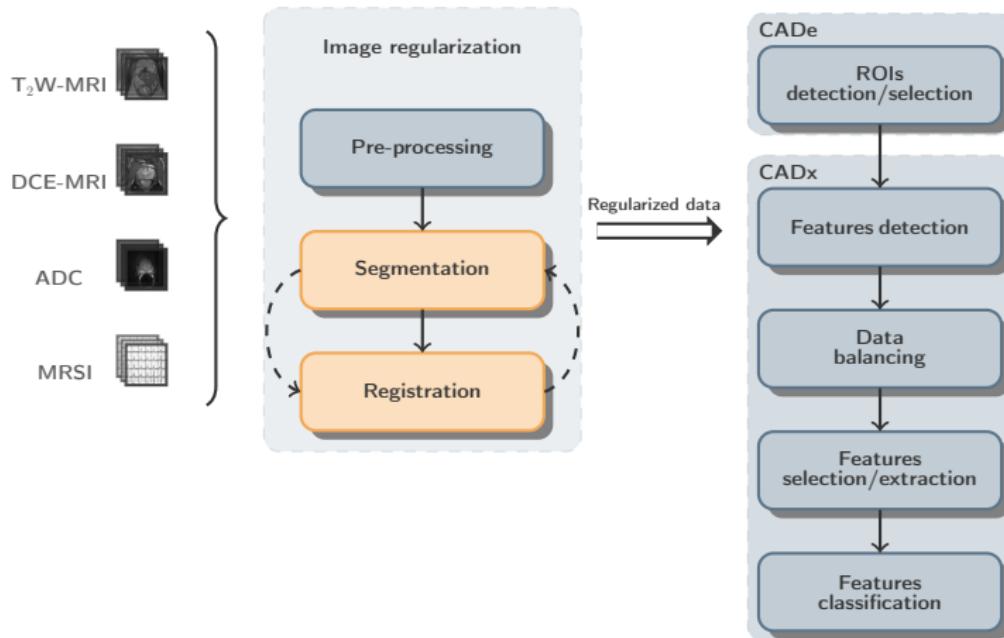


ROC analysis with entire enhanced signal



Image regularization

Segmentation & registration





Segmentation & registration



Resampling

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

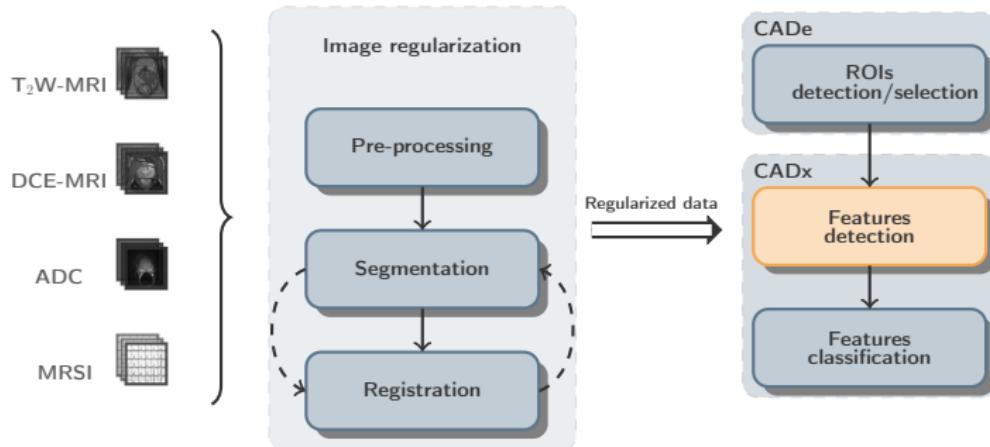
Segmentation

- ▶ 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

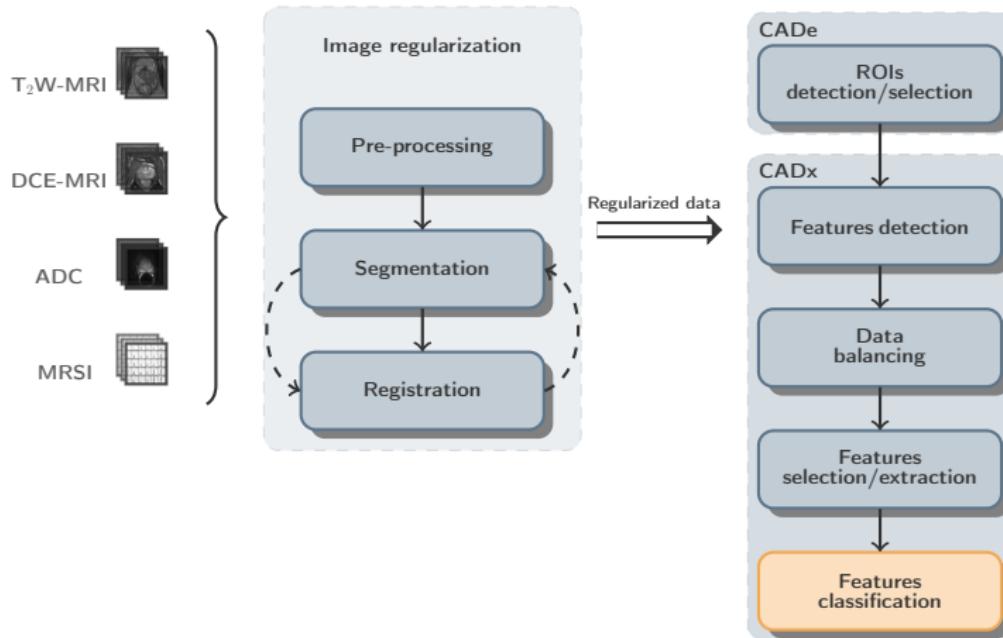
MRSI features

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

Spatial information

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

Features classification



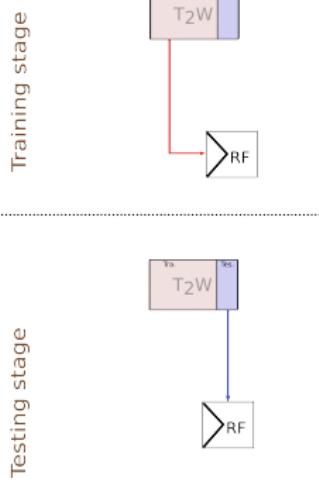


Features classification



Classification as fusion

- ▶ 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

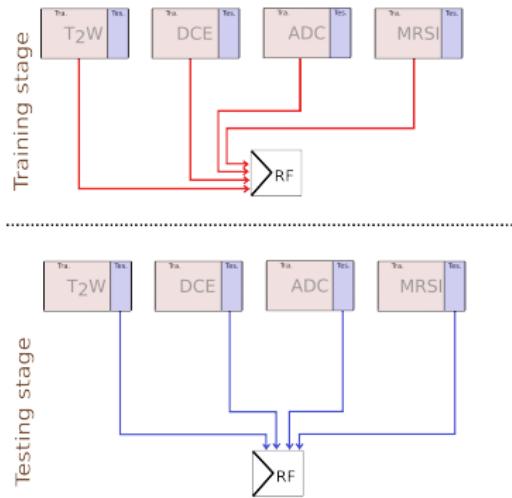


Features classification



Classification as fusion

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- ▶ Single RF → aggregated features of modalities
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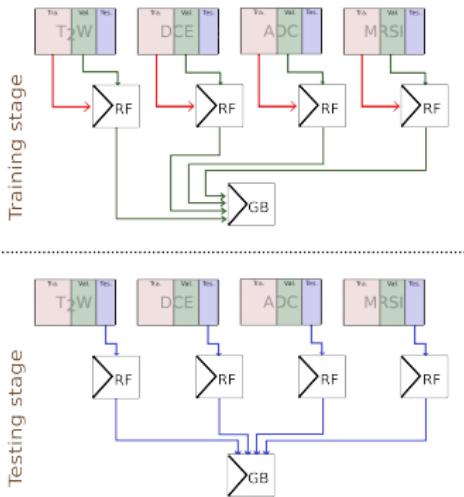


Features classification



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

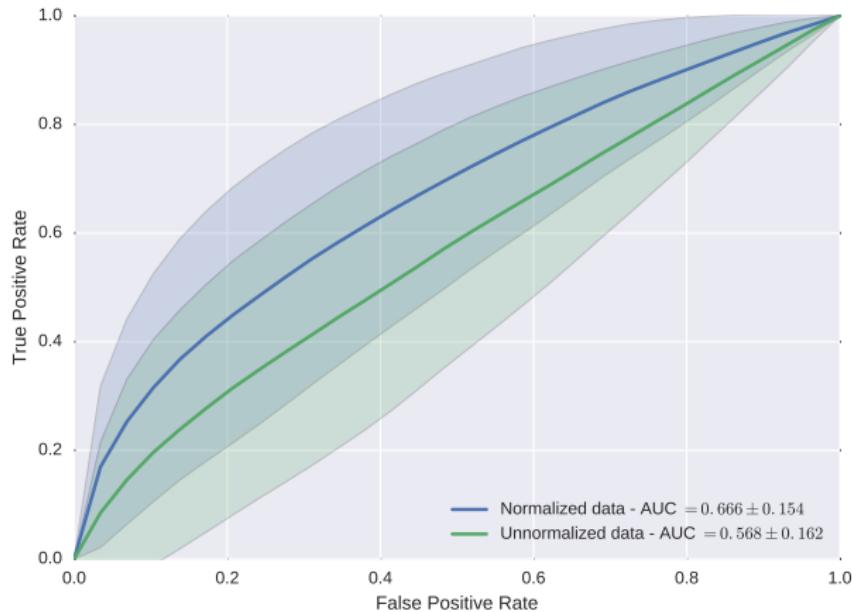
- ▶ LOPO CV
- ▶ ROC analysis
- ▶ AUC



DCE modality



Entire signal



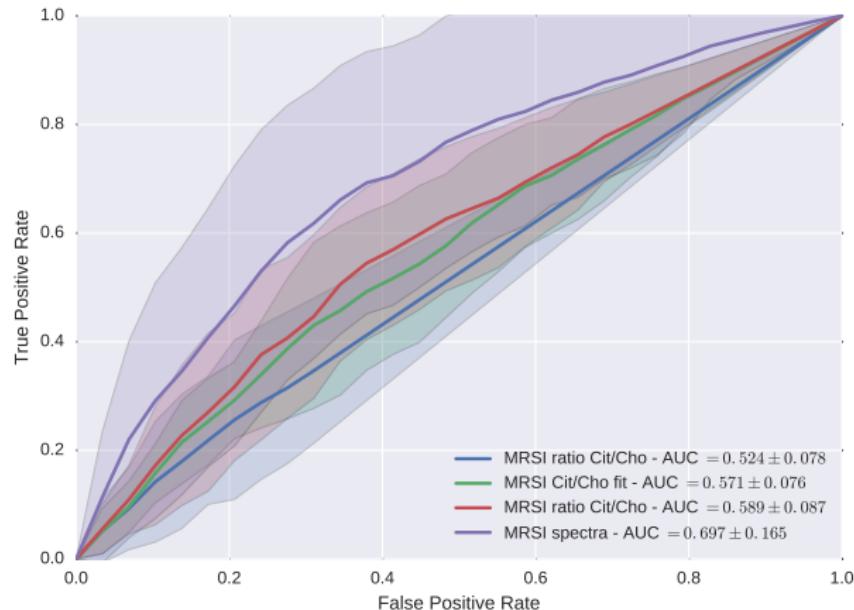
ROC analysis for the entire enhanced signal



MRSI modalities



ROC analysis



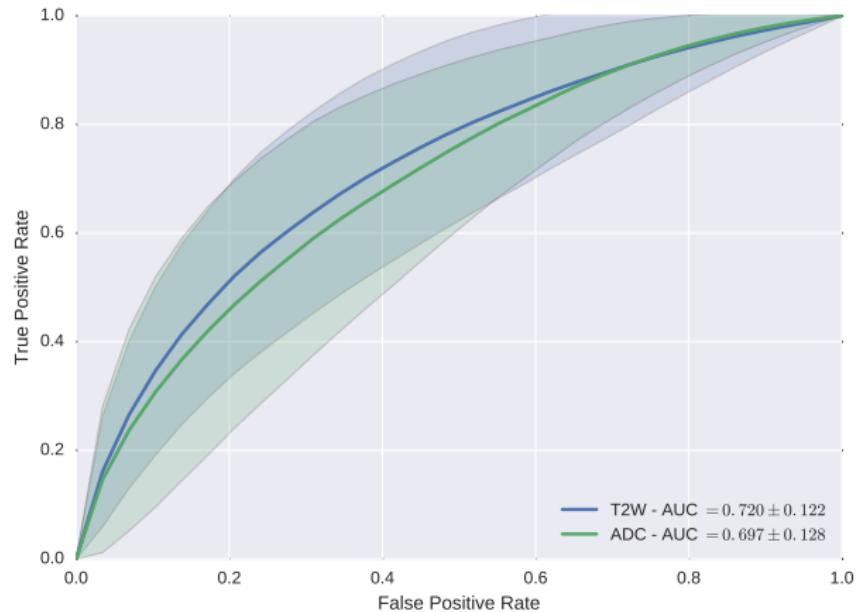
ROC analysis for the MRSI modality



T₂W-MRI, ADC, and MRSI modalities



ROC analysis



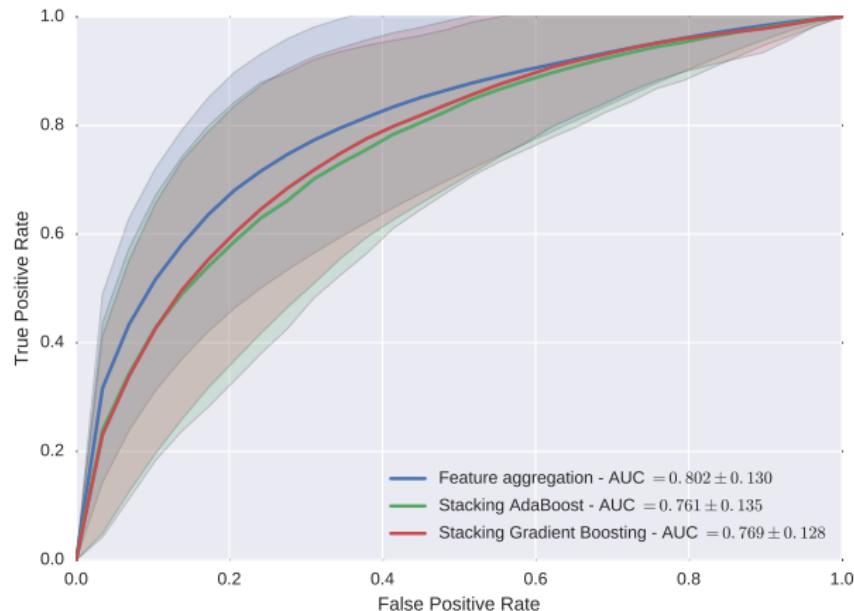
ROC analysis for T₂W-MRI and ADC modalities



Coarse combination



Aggregation vs. stacking



ROC analysis for the fusion strategies



T₂W-MRI, ADC, and MRSI modalities



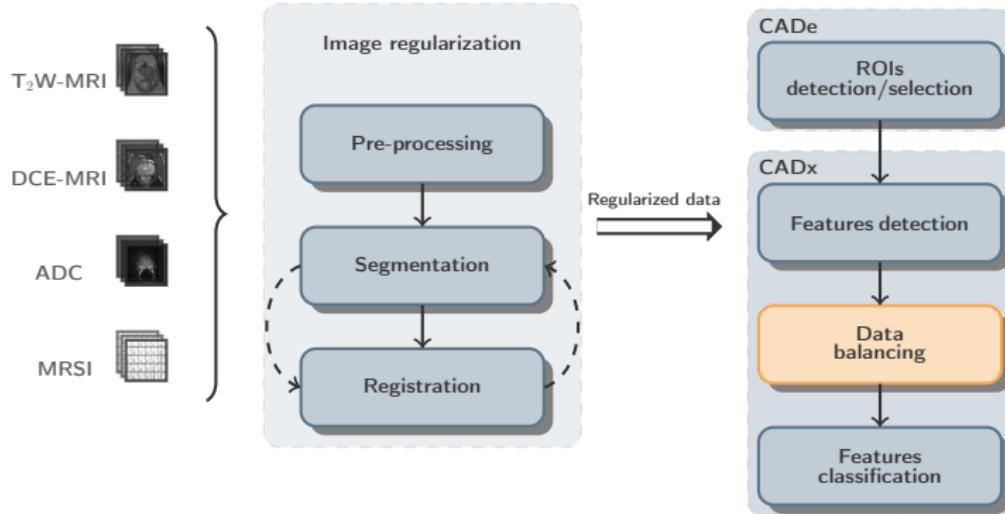
Overall best performance

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

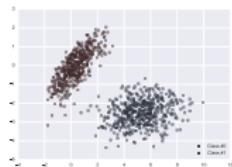




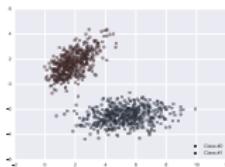
Data balancing



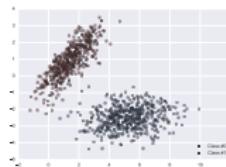
Under-sampling



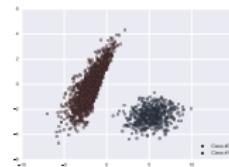
(a) NM1



(b) NM2

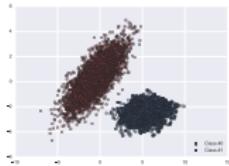


(c) NM3

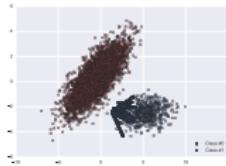


(d) IHT

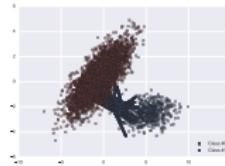
Over-sampling



(e) SMOTE

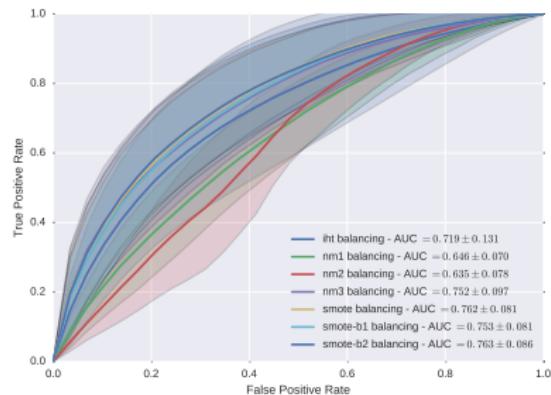
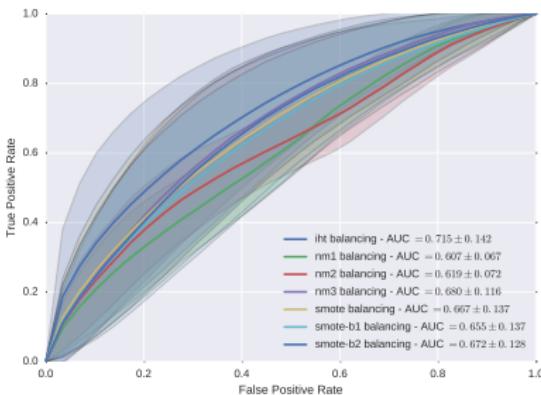


(f) SMOTE-b1



(g) SMOTE-b2

Data balancing

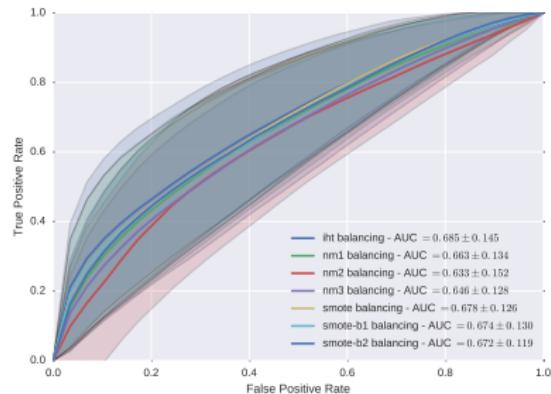
T₂W-MRI and ADC(a) T₂W-MRI

(b) ADC

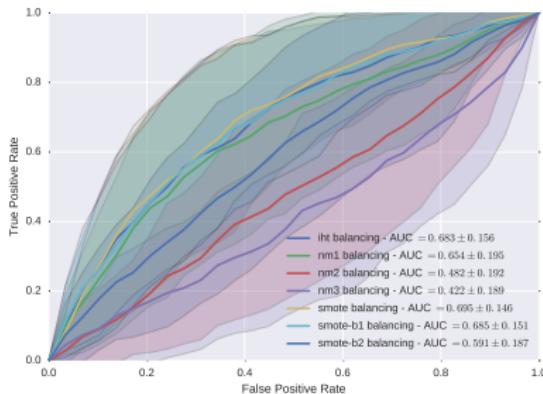
ROC analysis for T₂W-MRI and ADC

Data balancing

DCE-MRI and MRSI



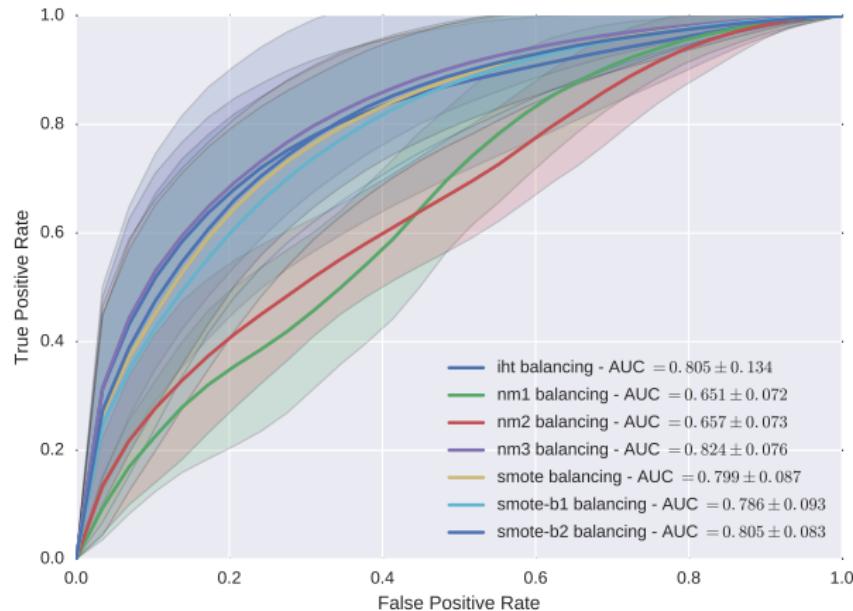
(a) DCE-MRI



(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

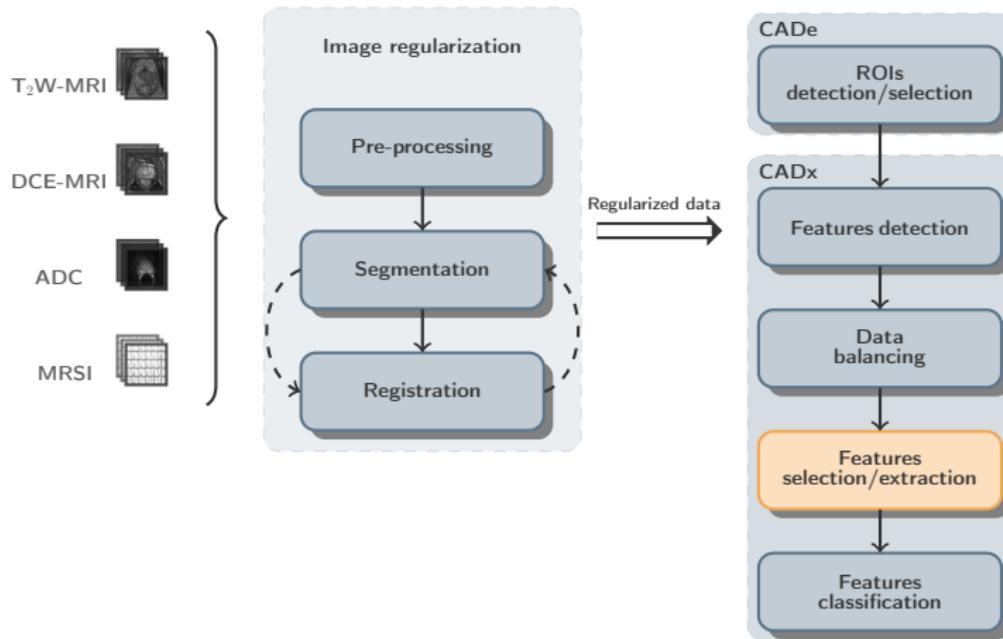
Before data balancing

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

Selected features with aggregation

T ₂ W-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			



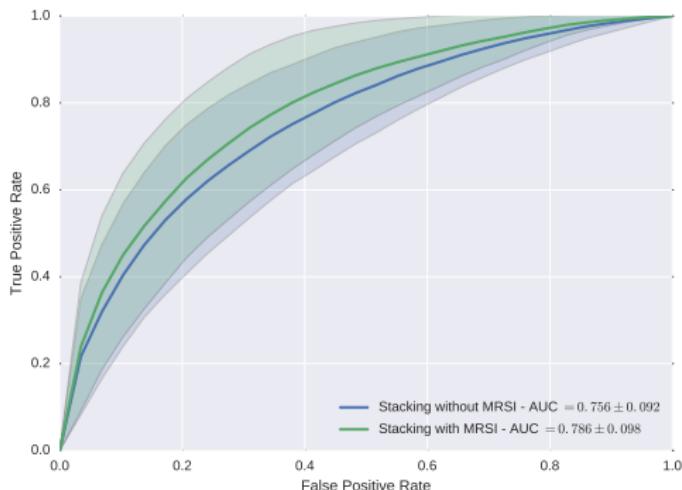
MRSI benefit



Importance of MRSI in aggregation

- Features from MRSI are the most selected features

Stacking with/without MRSI

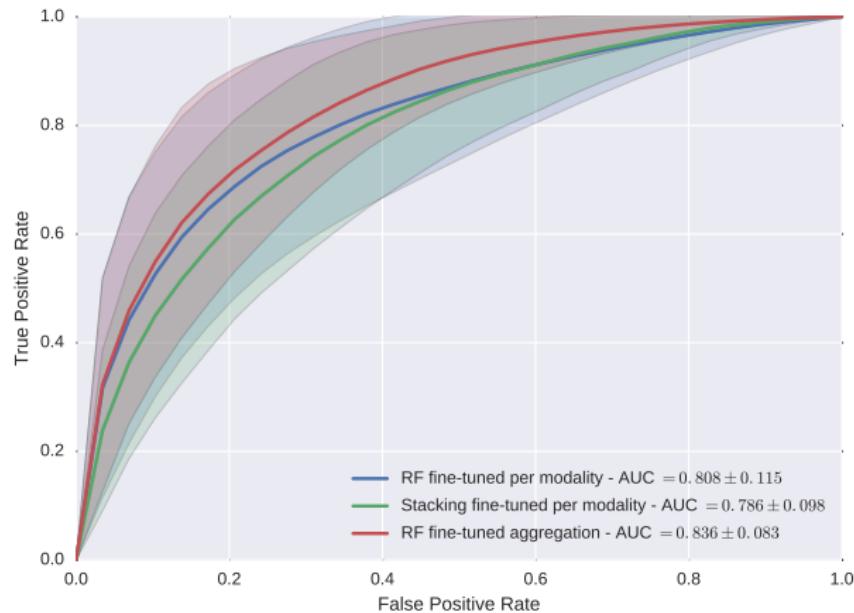


ROC analysis with/without MRSI



Fine-tuned combination

Aggregation vs. stacking

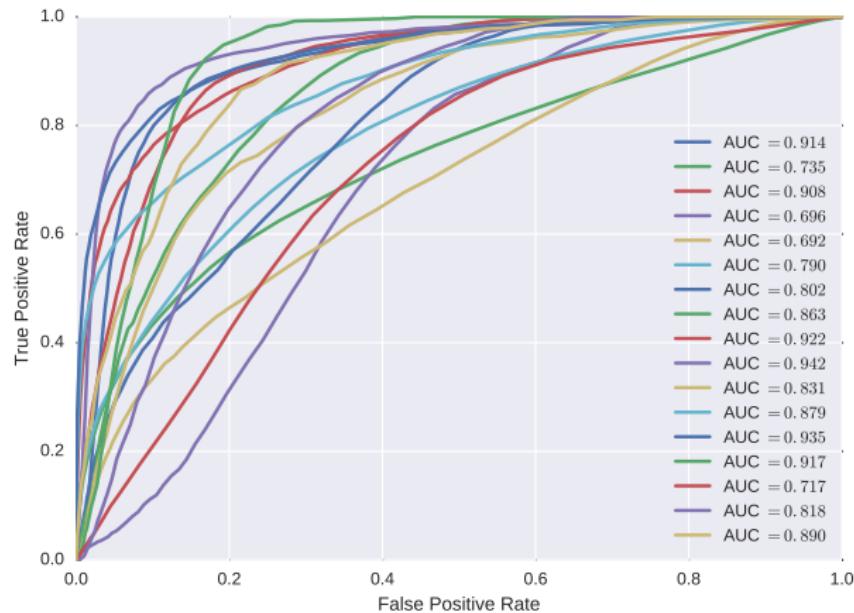


ROC analysis with the different fusion strategies



Fine-tuned combination

ROC for each patient



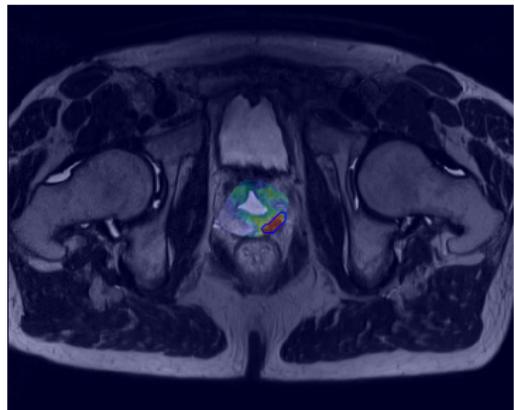
ROC analysis for each patient



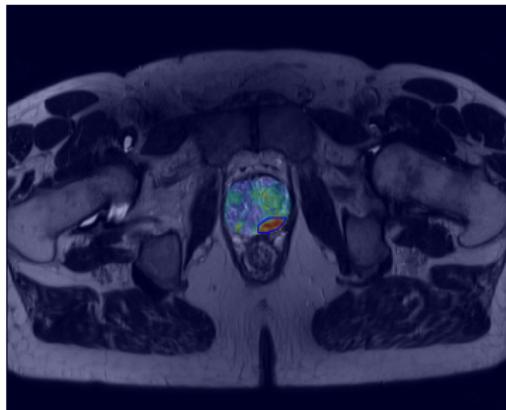
Fine-tuned combination



"Outstanding" discrimination level



(a) $AUC = 0.922$



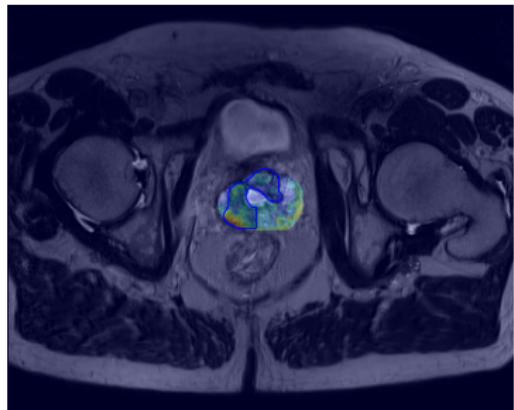
(b) $AUC = 0.914$



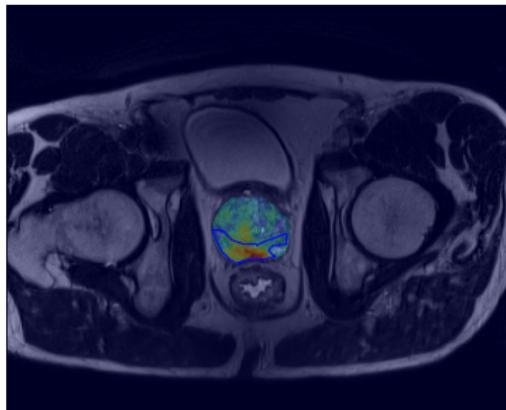
Fine-tuned combination



"Acceptable" discrimination level



(c) AUC = 0.692



(d) AUC = 0.735

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

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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

