Computer-Aided Diagnosis for Prostate Cancer using mp-MRI

PhD Defence
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Guillaume Lemaître

Universitat de Girona - ViCOROB
Université de Bourgogne Franche-Comté - LE2I

Supervised by:

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

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

1 Introduction
- Motivations
- The prostate organ
- Prostate carcinoma
- Screening
- CAD and mp-MRI
- Research objectives

2 State-of-the-art

3 I2CVB

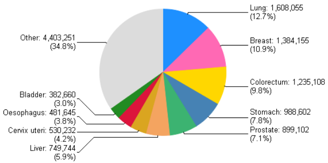
4 Toward a mp-MRI CAD for CaP

5 Experiments

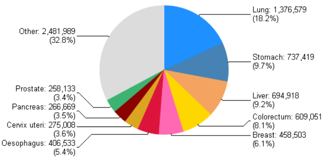
6 Conclusions

Motivations

Statistics



(a) # of cancer cases



(b) # of cancer deaths

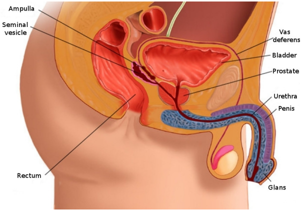
Implications, image source[1]

- 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]

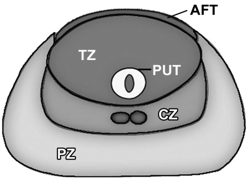
Characteristics

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

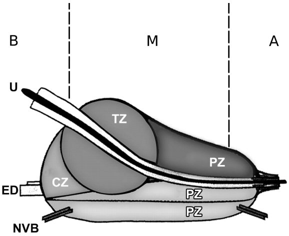
[2] Geckomedia. *Natom Anatomy*. French. June 2011. url: http://www.natomshop.com/.

The prostate organ

Anatomy



(a) Transverse plane

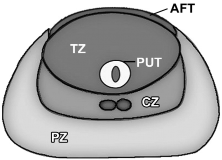


(b) Sagittal plane

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 %
- CG → 5 %

Goals

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

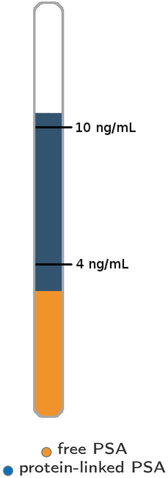
Screening

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
- ✗ Not reliable

"Blind" transrectal ultrasound biopsy

- Take samples from different locations
- Grade using Gleason score
- ✗ Invasive procedure
- ✗ Lead to false positives & negatives



Screening

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- $> 10\,\text{ng}\,\text{mL}^{-1} \rightarrow$ biopsy
- From $4\,\text{ng}\,\text{mL}^{-1}$ to $10\,\text{ng}\,\text{mL}^{-1}$

  $\rightarrow \frac{\text{free}}{\text{free} + \text{protein-linked}} > 15\% \rightarrow$ biopsy

✗ Not reliable

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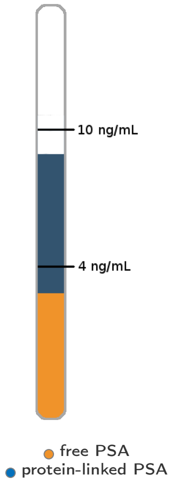

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Screening

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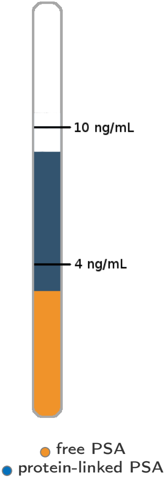

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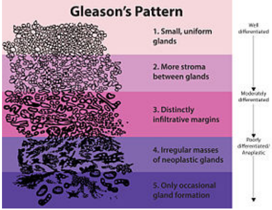

Image source: `https://goo.gl/fEVQXQ`

Screening

Prostate-specific antigen

- $> 10\,\mathrm{ng\,mL^{-1}} \rightarrow$ biopsy
- From $4\,\mathrm{ng\,mL^{-1}}$ to $10\,\mathrm{ng\,mL^{-1}}$

  $\rightarrow \frac{\textcolor{orange}{\bullet}}{\textcolor{orange}{\bullet} + \textcolor{blue}{\bullet}} > 15\% \rightarrow$ biopsy

✗ Not reliable

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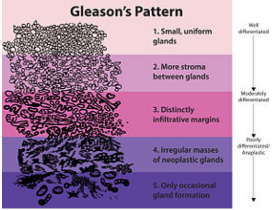

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Pros

✓ Reduce CaP-related mortality from 21 % to 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 $\rightarrow$ detection of potential lesions
- CADx $\rightarrow$ 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

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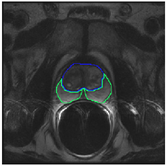
UdG

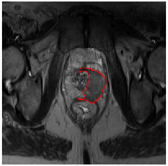
MRI modalities

UBFC

T_2W-MRI



(a) Healthy



(b) CaP PZ

(c) CaP CG

Healthy

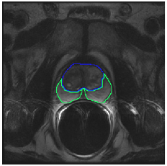
- Intermediate to high-signal intensity (SI) in PZ
- Low-SI in CG

CaP

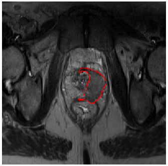
- Low-SI
- Round and ill-defined mass in PZ
- Homogeneous with ill-defined edges in CG

MRI modalities

T_2W-MRI



(d) Healthy



(e) CaP PZ

(f) CaP CG

Pros

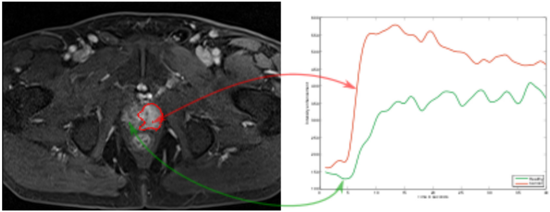
- Highest spatial resolution
- Anatomy nicely depicted

Cons

- Low sensitivity in CG
- Lower specificity due to outliers

MRI modalities

DCE-MRI



Green: healthy - Red: CaP

Healthy

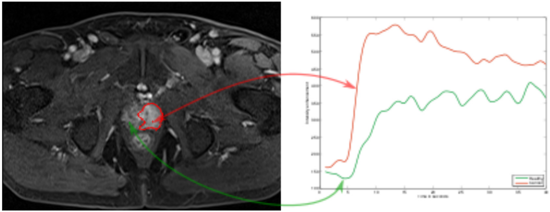
- Slower wash-in, wash-out, time-to-peak enhancement
- Lower integral under the curve, max SI

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

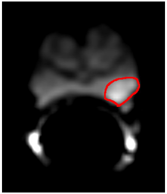
- Information about vascularity

Cons

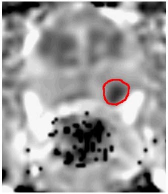
- Spatial mis-registration
- Lower spatial resolution than T_2W-MRI
- Difficult detection in CG

MRI modalities

DW-MRI - ADC



(a) DW MRI



(b) ADC

Healthy

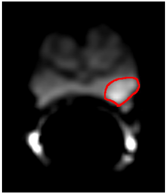
- DW-MRI: lower SI
- ADC: higher-SI

CaP

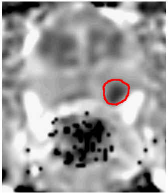
- DW-MRI: higher SI
- ADC: lower-SI

MRI modalities

DW-MRI - ADC



(c) DW MRI



(d) ADC

Pros

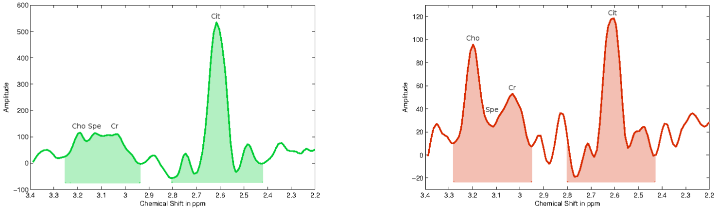
- Information about tissue structure
- ADC correlated with Gleason score

Cons

- Poor spatial resolution
- Variability of the ADC coefficient

MRI modalities

MRSI



(a) Healthy

(b) CaP

Healthy

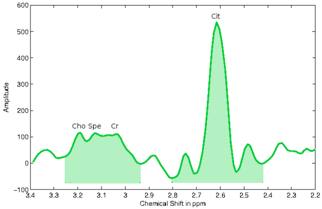
- High citrate
- Moderate choline and spermine

CaP

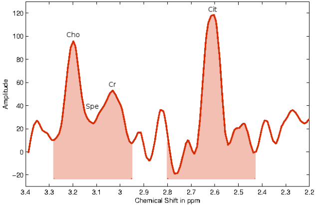
- Decrease of citrate and spermine
- Increase of choline

MRI modalities

MRSI



(c) Healthy



(d) CaP

Pros

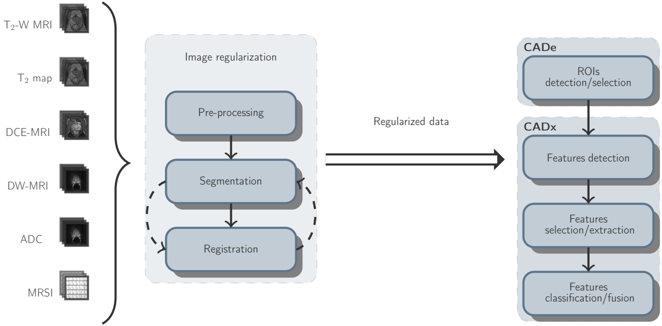
- Citrate correlated with Gleason score

Cons

- Low spatial resolution
- Variation inter-patients

CAD for CaP

Full CAD for detection and diagnosis of CaP

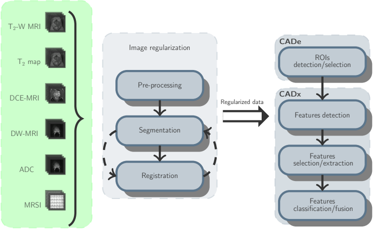


Common CAD framework based on MRI images used to detect CaP

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.)



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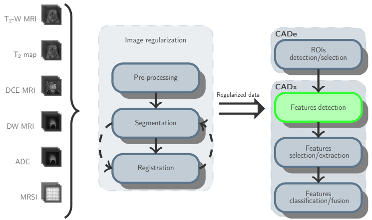

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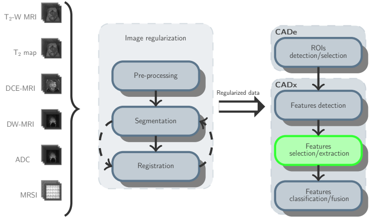

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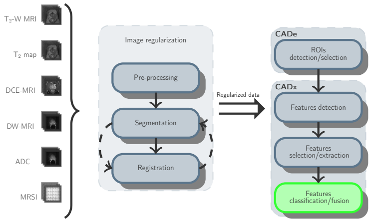

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Scientific and technical challenges

- ✗ 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

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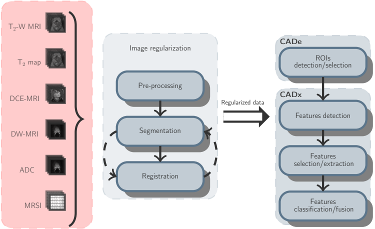

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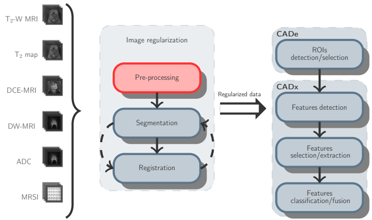

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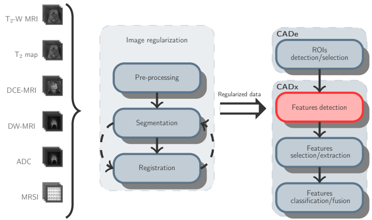

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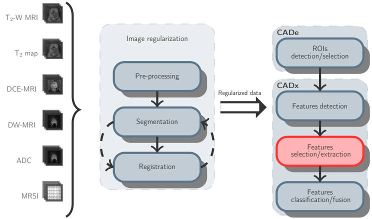

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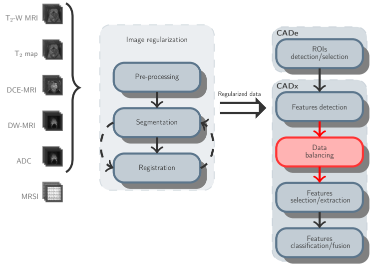

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- ✗ No source code available of any CAD

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

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 Experiments

6 Conclusions

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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Open source initiative

`protoclass` toolbox

- Data management
- Features detection

`imbalanced-learn` toolbox[7]

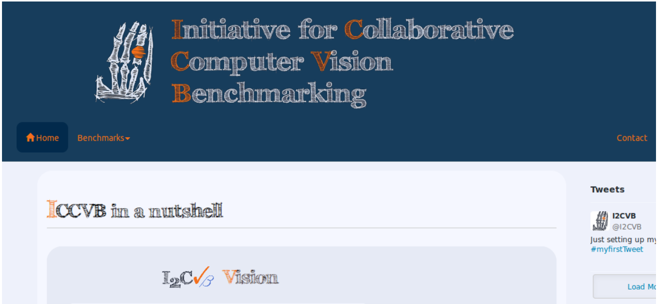
- Part of the `scikit-learn-contrib` projects

Third-party toolboxes

[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

I_2CV_B platform

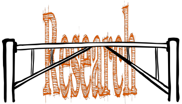


Hub for our different resources

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

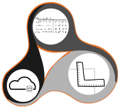
Manifesto

I2CVB Vision



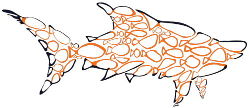
- Ease the access to make research

I2CVB Mission



- Open data; evaluation methods; comparison framework; reporting platform

I2CVB Protagonists



- Research groups and individuals from all walks of life to shape an open community

I2CVB Strategy

- Use successful practises from Free Software and Quality Management

1. Introduction
2. State-of-the-art
3. I2CVB
4. Toward a mp-MRI CAD for CaP
   - Image regularization
   - CADe-CADx
5. Experiments
6. Conclusions

Toward a mp-MRI CAD for CaP

Mp-MRI CAD for CaP

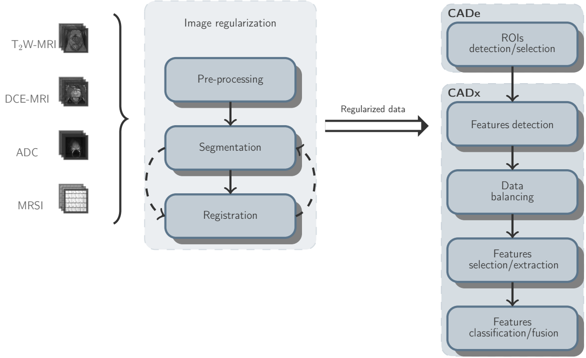
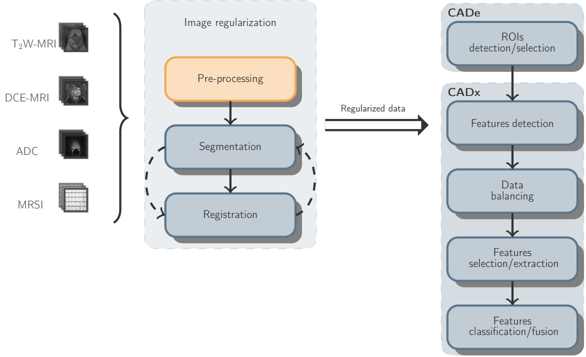


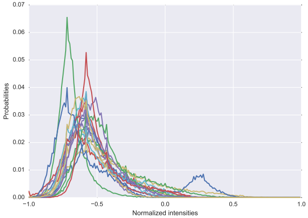
Image regularization

Pre-processing



T_2W-MRI normalization

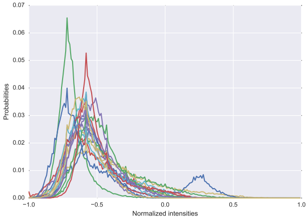
Inter-patients intensity variations



- Artan et al.[8] and Ozer et al.[9] normalized data based on the *z-score*.
- Lv et al.[10] and Viswanath et al.[11] used methods based on piecewise-linear normalization[12].

T_2W-MRI normalization

Inter-patients intensity variations



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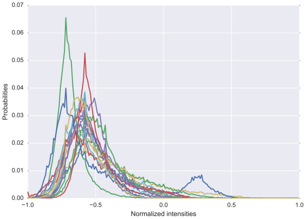
[8] Y. Artan et al. "Prostate cancer localization with multispectral MRI using cost-sensitive support vector machines and conditional random fields". In: *IEEE Trans Image Process* 19.9 (Sept. 2010), pp. 2444–2455.

[9] S. Ozer et al. "Supervised and unsupervised methods for prostate cancer segmentation with multispectral MRI". . In: *Med Phys* 37.4 (Apr. 2010), pp. 1873–1883.

T_2W-MRI normalization

Inter-patients intensity variations



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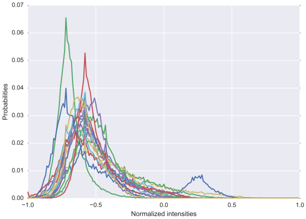
[10] D. Lv et al. "Computerized characterization of prostate cancer by fractal analysis in MR images". In: *J Magn Reson Imaging* 30.1 (July 2009), pp. 161–168.

[11] S. E. Viswanath et al. "Central gland and peripheral zone prostate tumors have significantly different quantitative imaging signatures on 3 Tesla endorectal, in vivo T2-weighted MR imagery". In: *J Magn Reson Imaging* 36.1 (July 2012), pp. 213–224.

[12] L. G. Nyul et al. "New variants of a method of MRI scale standardization". In: *IEEE Trans Med Imaging* 19.2 (Feb. 2000), pp. 143–150.

T_2W-MRI normalization

Inter-patients intensity variations



- Artan et al.[8] and Ozer et al.[9] normalized data based on the z-*score*.
- Lv et al.[10] and Viswanath et al.[11] used methods based on piecewise-linear normalization[12].

Contributions[13]

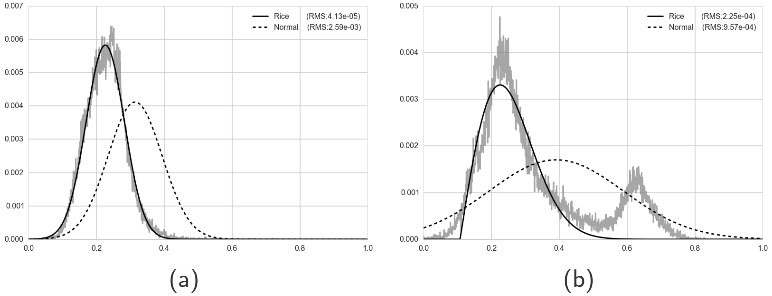
(i) a *model-based* approach using Rician *a priori*;

(ii) a *non-parametric based* approach based on the SRSF representation.

[13] 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.

T_2W-MRI normalization

Gaussian *vs.* Rician



Example of fitted functions

T_2W-MRI normalization

Gaussian normalization

$$I_s(x) = \frac{I_r(x) - \mu_G}{\sigma_G} \; . \qquad (1)$$

Rician normalization

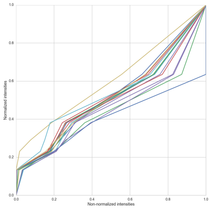
$$I_s(x) = \frac{I_r(x) - \mu_R}{\sigma_R} \; , \qquad (2)$$

$$\mu_R = \sigma \sqrt{\frac{\pi}{2}} \; L_{1/2}(-\frac{\nu^2}{2\sigma^2}) \; , \qquad (3)$$

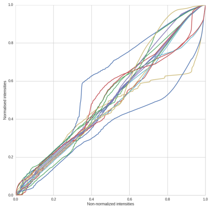
$$\sigma_R = 2\sigma^2 + \nu^2 - \frac{\pi\sigma^2}{2} L_{1/2}^2 \left(\frac{-\nu^2}{2\sigma^2} \right) \; . \qquad (4)$$

T_2W-MRI normalization

Comparison or warping function



(a) Piecewise-linear warping



(b) SRSF warping

Piecewise-linear normalization

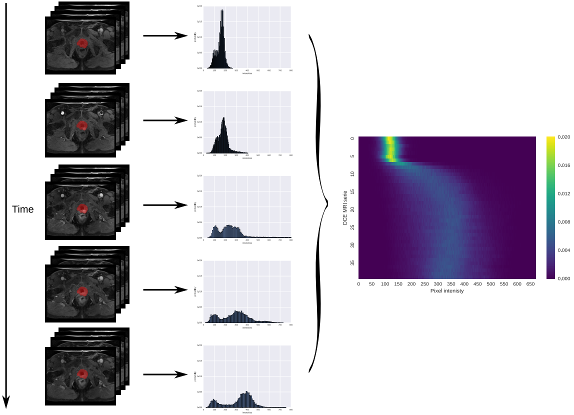
Minimize the distance between some standardized landmarks μ_i and some non-normalized landmarks λ_i

SRSF-based normalization

Minimize the distance between a mean PDF μ_f (i.e., the Karcher mean) and a given patient PDF f_i

DCE-MRI normalization

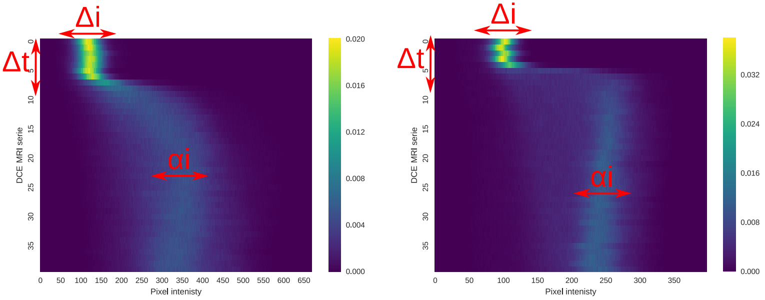
Heatmap representation[14]



[14] 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).

DCE-MRI normalization

Inter-patients variations



(a) (b)

Variations driven with Δ_i, Δ_t, and σ_i

ADC normalization

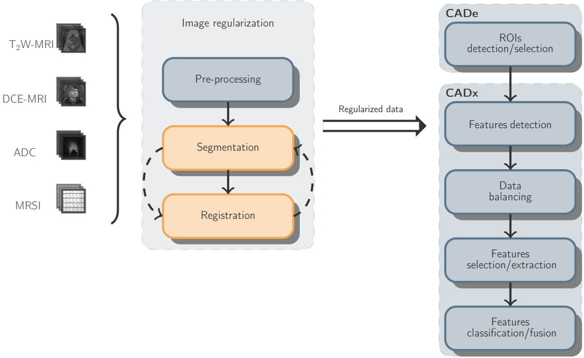
UdG

MRSI pre-processing

UBFC

Image regularization

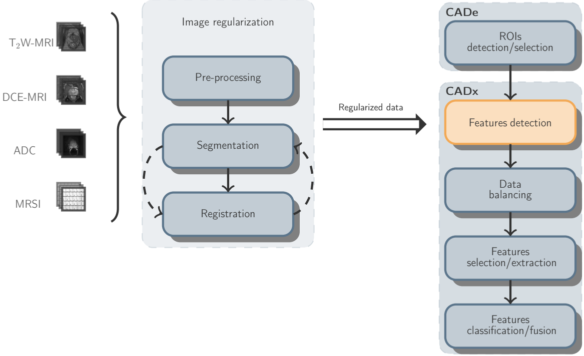
Segmentation & registration



Segmentation & registration

CADe-CADx

Features detection



T_2W-MRI and ADC map

UdG

DCE-MRI

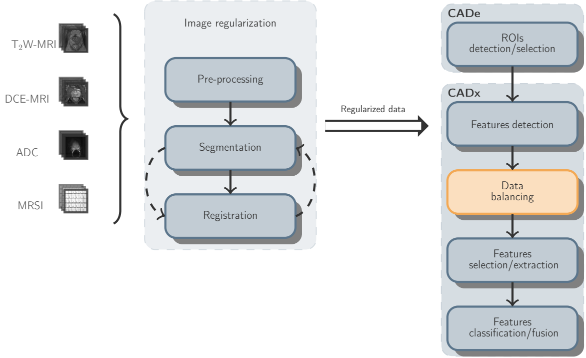
UBFC

MRSI

Anatomical features

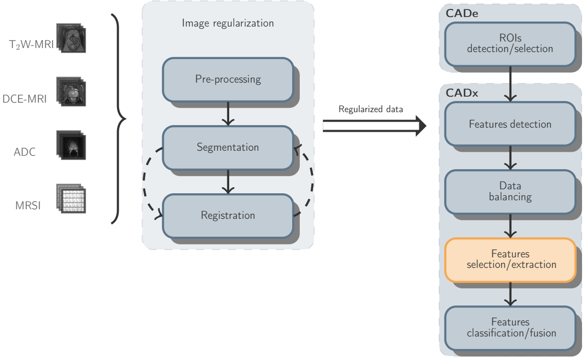
CADe-CADx

Data balancing



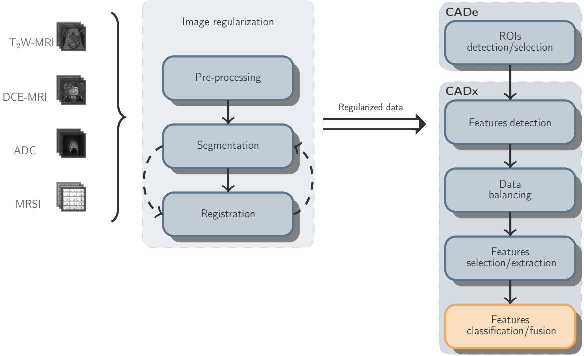
CADe-CADx

Features selection/extraction



CADe-CADx

Features classification



1 Introduction

2 State-of-the-art

3 I2CVB

4 Toward a mp-MRI CAD for CaP

5 Experiments
- T_2W-MRI normalization
- DCE-MRI normalization
- Standalone modalities
- Coarse combination
- Data balancing
- Features selection/extraction
- Fine-tuned combination
- MRSI benefit

6 Conclusions

T_2W-MRI normalization[15]

[14] Lemaitre et al., "Normalization of T2W-MRI Prostate Images using Rician a priori".

DCE-MRI normalization[16]

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

Standalone modalities

Coarse combination

Data balancing

Features selection/extraction

Fine-tuned combination

MRSI benefit

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   - Contributions
   - Future works
   - Timeline

Contributions

Future works

UdG

Timeline

UBFC