# Computer-Aided Diagnosis for Prostate Cancer using mp-MRI

PhD Defence
28th November 2016


Guillaume Lemaître

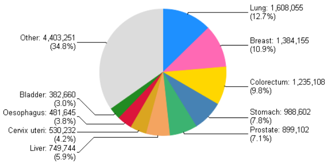
*Universitat de Girona - ViCOROB*
*Université de Bourgogne Franche-Comté - LE2I*


Supervised by:

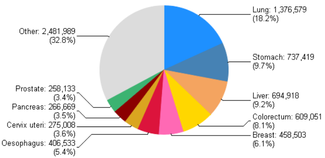
Robert Martí - Fabrice Mériaudeau
Jordi Freixenet - Paul M. Walker

# Motivations

## Statistics




(a) # of cancer cases




(b) # of cancer deaths

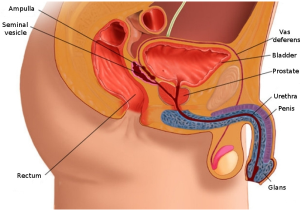
## Implications, image source[1]

- 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]

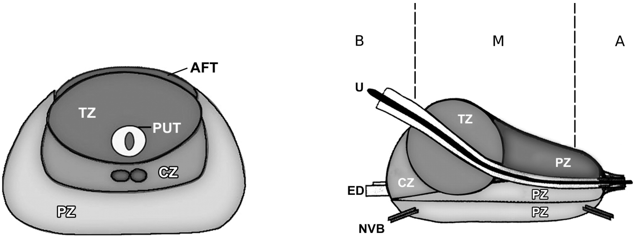
## Characteristics

- 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

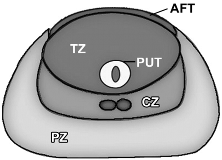



(a) Transverse plane (b) Sagittal plane

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

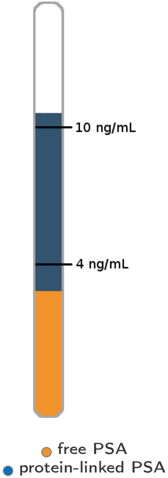
# Screening

## Prostate-specific antigen

- $> 10\,\text{ng}\,\text{mL}^{-1} \rightarrow$ biopsy
- From $4\,\text{ng}\,\text{mL}^{-1}$ to $10\,\text{ng}\,\text{mL}^{-1}$
  $\rightarrow \frac{\bullet}{\bullet + \bullet} > 15\% \rightarrow$ biopsy
- ✗ Not reliable

## "Blind" transrectal ultrasound biopsy

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



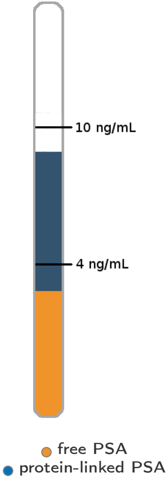
# Screening

## 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

## 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

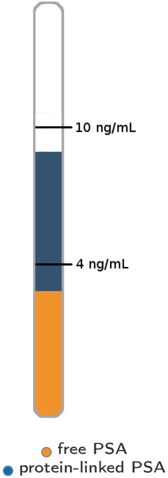
✗ Not reliable

## “Blind” transrectal ultrasound biopsy

- Take samples from different locations
- Grade using Gleason score

✗ Invasive procedure

✗ Lead to false positives & negatives



# Screening

## 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

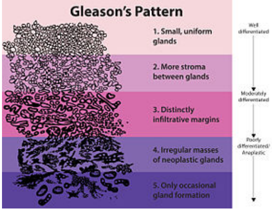



Image source: `https://goo.gl/fEVQXQ`

# Screening

## Prostate-specific antigen

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

  $\rightarrow \frac{\bullet}{\bullet + \bullet} > 15\% \rightarrow$ biopsy
- ✗ Not reliable

## "Blind" transrectal ultrasound biopsy

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

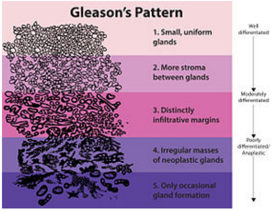



Image source: `https://goo.gl/fEVQXQ`

# Screening

## Prostate-specific antigen

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

✗ Not reliable

## "Blind" transrectal ultrasound biopsy

- Take samples from different locations
- Grade using Gleason score

✗ Invasive procedure

✗ Lead to false positives & negatives

## 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

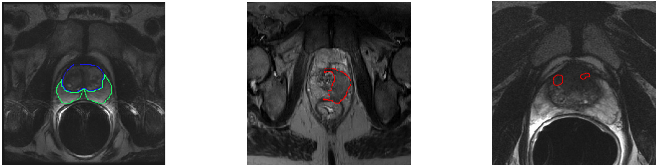
# Research objectives

## 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

# MRI modalities

## $T_2$W-MRI



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

## Healthy

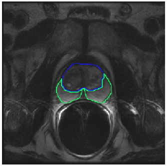
- Intermediate to high-signal intensity (SI) in PZ
- Low-SI in CG

## CaP

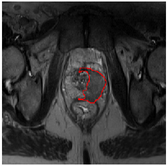
- Low-SI
- Round and ill-defined mass in PZ
- Homogeneous with ill-defined edges in CG

# MRI modalities

## $T_2$W-MRI



(d) Healthy



(e) CaP PZ

(f) CaP CG

### Pros

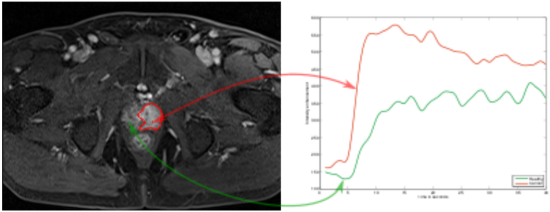
- Highest spatial resolution
- Anatomy nicely depicted

### Cons

- Low sensitivity in CG
- Lower specificity due to outliers

# MRI modalities

## DCE-MRI



Green: healthy - Red: CaP

### Healthy

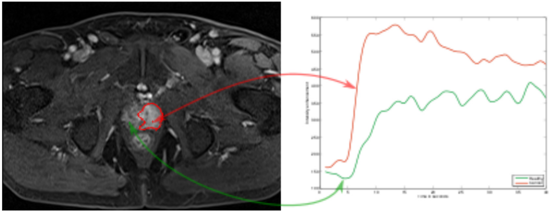
- Slower wash-in, wash-out, time-to-peak enhancement
- Lower integral under the curve, max SI

### 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

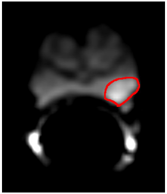
- Information about vascularity

### Cons

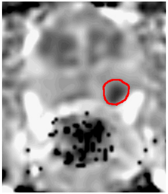
- Spatial mis-registration
- Lower spatial resolution than $T_2$W-MRI
- Difficult detection in CG

# MRI modalities

## DW-MRI - ADC



(a) DW MRI



(b) ADC

### Healthy

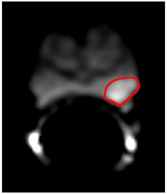
- DW-MRI: lower SI
- ADC: higher-SI

### CaP

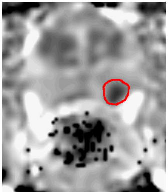
- DW-MRI: higher SI
- ADC: lower-SI

# MRI modalities

## DW-MRI - ADC



(c) DW MRI



(d) ADC

### Pros

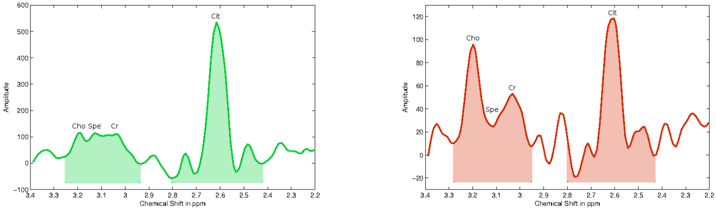
- Information about tissue structure
- ADC correlated with Gleason score

### Cons

- Poor spatial resolution
- Variability of the ADC coefficient

# MRI modalities

## MRSI




(a) Healthy (b) CaP

### Healthy

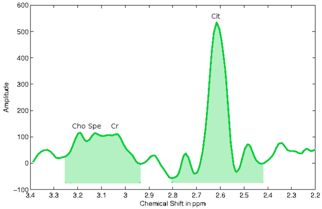
- High citrate
- Moderate choline and spermine

### CaP

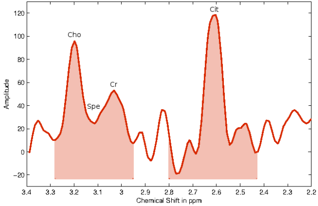
- Decrease of citrate and spermine
- Increase of choline

# MRI modalities

## MRSI




(c) Healthy




(d) CaP

### Pros

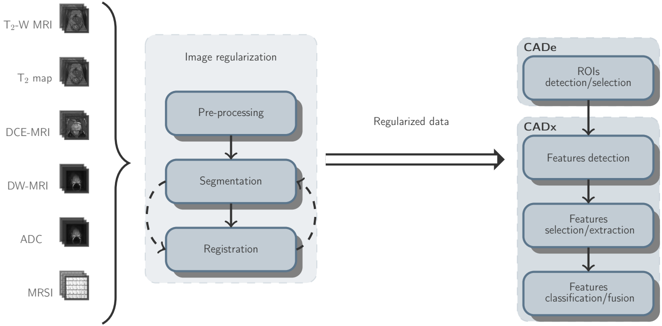
- Citrate correlated with Gleason score

### Cons

- Low spatial resolution
- Variation inter-patients

# CAD for CaP

## Full CAD for detection and diagnosis of CaP

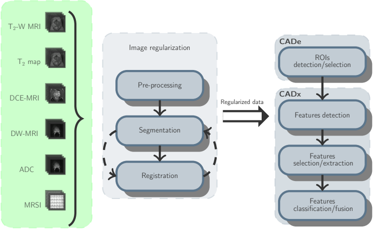



Common CAD framework based on MRI images used to detect CaP

# CAD for CaP

## Conclusions

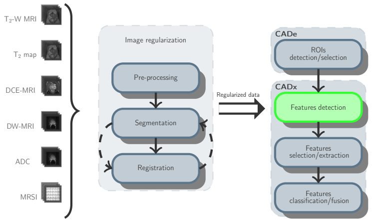
- ✓ 3 modalities better than 2
- ✓ Texture and edge features are predominant
- ✓ Feature selection/extraction tends to improve performance
- ✓ Pre-eminence of SVM and ensemble classifier (i.e., AdaBoost, RF, etc.)



# CAD for CaP

## Conclusions

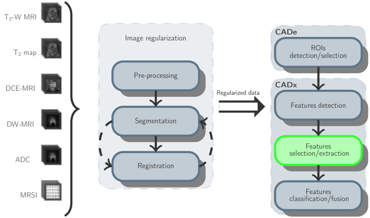
- ✓ 3 modalities better than 2
- ✓ Texture and edge features are predominant
- ✓ Feature selection/extraction tends to improve performance
- ✓ Pre-eminence of SVM and ensemble classifier (i.e., AdaBoost, RF, etc.)



# CAD for CaP

## Conclusions

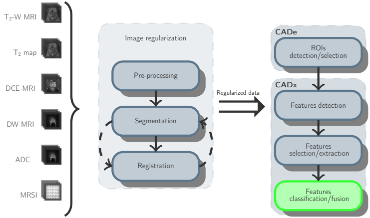
- ✓ 3 modalities better than 2
- ✓ Texture and edge features are predominant
- ✓ Feature selection/extraction tends to improve performance
- ✓ Pre-eminence of SVM and ensemble classifier (i.e., AdaBoost, RF, etc.)



# CAD for CaP

## Conclusions

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



# CAD for CaP

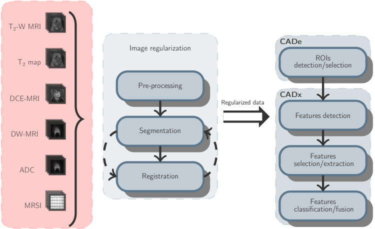
## Conclusions

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

## Scientific and technical challenges

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

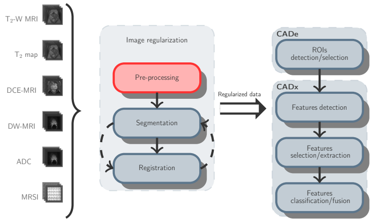
# CAD for CaP




## Scientific and technical challenges

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

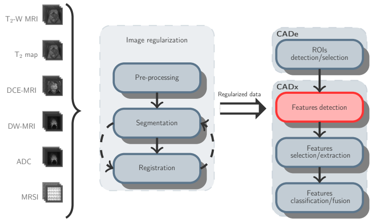
# CAD for CaP




## Scientific and technical challenges

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

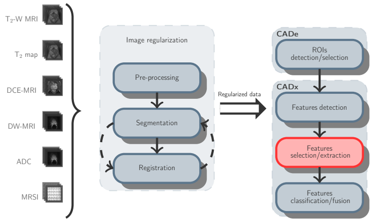
# CAD for CaP




## Scientific and technical challenges

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

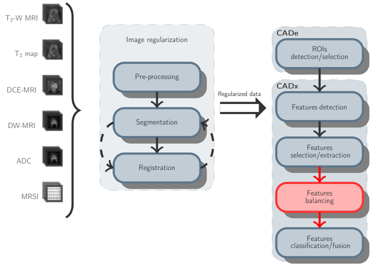
# CAD for CaP




## Scientific and technical challenges

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

# CAD for CaP




## Scientific and technical challenges

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

# CAD for CaP

## Conclusions

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

## Scientific and technical challenges

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

# CAD for CaP

## Conclusions

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

## 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

## 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

# Mp-MRI prostate datasets

## 1.5 T General Electric scanner

- $T_2$W-MRI, DW-MRI, DCE-MRI, and MRSI
- Ground-truth (GT) for CaP, PZ, and CG associated to $T_2$W-MRI modality
- Healthy: $4$ *vs.* CaP: { PZ: $14 + 3$, CG: $0 + 3$ }

## 3 T Siemens scanner

- $T_2$W-MRI, ADC, DCE-MRI, and MRSI
- GT for CaP, PZ, and CG associated to $T_2$W-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

- $T_2$W-MRI, DW-MRI, DCE-MRI, and MRSI
- Ground-truth (GT) for CaP, PZ, and CG associated to $T_2$W-MRI modality
- Healthy: $4$ *vs.* CaP: { PZ: $14 + 3$, CG: $0 + 3$ }

## 3 T Siemens scanner

- $T_2$W-MRI, ADC, DCE-MRI, and MRSI
- GT for CaP, PZ, and CG associated to $T_2$W-MRI modality
- Additional GT of the prostate for DCE-MRI and ADC
- Healthy: $2$ *vs.* CaP: { PZ: $12 + 2$, CG: $3 + 2$ }

# Open source initiative

## protoclass toolbox

- Data management
- Feature detection

## imbalanced-learn toolbox[7]

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

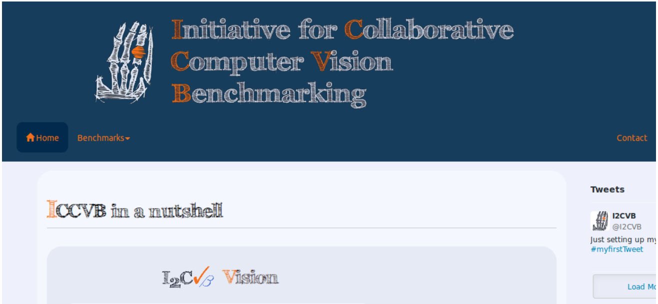
## Third-party toolboxes

NumPy
SciPy
matplotlib
IP[y]: IPython Interactive Computing
SimpleITK
scikit-image image processing in python
scikit learn

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

# A web platform

## $I_2CVB$ platform

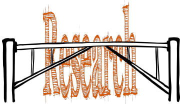



## Hub for our different resources

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

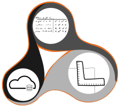
# Manifesto

## Vision



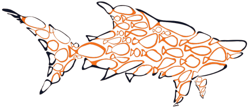

- Ease the access to make research

## Mission



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

## Protagonists



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

## Strategy

- Use successful practises from Free Software and Quality Management