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## **Report on the PhD dissertation from Guillaume LEMAÎTRE**

**Title of the thesis: Computer-Aided Diagnosis for Prostate Cancer using  
Multi-Parametric Magnetic Resonance Imaging**

The prime goal of this thesis is to develop a Computer-Aided Diagnostic (CAD) system using Multi-Parametric Magnetic Resonance Imaging (mpMRI). Four types of MRI are used: T2-W-MRI, DCE-MRI, DW-MRI and MRSI spectrum. The proposed system is designed mainly for prostate cancer segmentation. Towards this end, this research makes a number of interesting contributions.

In the first two chapters, prostate anatomy and different MRI imaging techniques are introduced to understand the objectives of the thesis and advantages of combining mpMRI. An exhaustive analysis and a comparison of the state of the art regarding CAD methods are reviewed in Chapter 3. The author chooses to investigate classification based frameworks to delineate prostate cancer. As a CAD system includes a chain of processing, each step in the chain is important. The author focuses on dealing with the intensity normalization of T2-W-MRI and DCE-MRI and the problem of imbalanced data for training classifiers. To make the proposed system reproducible, all used materials are explained in Chapter 4. A website, namely I2Cvb, is developed to publish all related works to the thesis, such as image data and software. The last two chapters, Chapter 5 and Chapter 6, consist in the undertaken works.

The first contribution, provided in Chapter 5, focuses on developing intensity normalization methods that can overcome the inter-patient intensity variations, so that they make classifiers more robust. This normalization is studied for two types of MRI. The first one concerns the normalization of T2-W-MRI images. A parametric normalization based on Rician distribution and a non-parametric normalization based on SRSF (Square-root slope function) are proposed. An evaluation metric using PCA is also proposed and used to compare different methods, showing then the superiority of the normalization based on Rician distribution. Due to the complexity of DCE-MRI, the normalization for T2-W-MRI cannot be used. The author

developed a second normalization method using a graph-based approach for intensity offset correction and a root-mean-square deviation as criterion to register images sequences. From the corrected DCE-MRI images, pharmacokinetic parameters of different medical models are then estimated, which are considered as features for classification. Experimentations carried out on 17 patients with 3T images show that the proposed normalizations can generally improve the prostate cancer segmentation, and directly using normalized DEC-MRI images for classification can achieve better results than using estimated pharmacokinetic parameters as features for classification.

The second contribution described in Chapter 6 is to develop and study a CAD system using four types of MRI that provide different information about the cancer. The system consists of seven steps: preprocessing, segmentation, registration, feature detection, balancing, feature selection/extraction and classification. The author mainly investigated the last three steps. He tested different existing methods for each step in order to find the best ones measured by using AUC as criterion. As medical data are usually imbalanced, this issue is well taken into account in the system. The authors studied two techniques: under sampling and over-sampling. Regarding the fusion of mpMRI, two strategies are compared: a single learner using aggregated features and the stacking-based classifier. Experimentations are carried out with the same data as in Chapter 5, showing that it is important to use the feature selection step, the data balancing and the fusion of mpMRI in the CAD system.

Next, I provide a number of technical suggestions and clarifications that can be addressed to improve the manuscript.

#### Technical Comments:

1. In Chapter 3, the presentation of the state of the art classification methods are rich. However, it would be better to present in more details the used classification methods in the proposed system, such as RF and GB.
2. As one of the objectives of the thesis is to combine different types of images, the author should highlight this issue and analyze existing fusion strategies in the literature, not necessary in the prostate case only, then allowing to illustrate the challenges.
3. Why is a metric based on PCA in Chapter 5 the proposed to measure quantification results? Why is it better than others? What impact will there be for the normalization if other metrics are used?
4. As the system is designed to segment prostate cancer, why didn't the author use the Dice index or Hausdorff distance which are commonly applied to measure and compare segmentation results?
5. Although the author concludes by stating the good performance obtained by using the four MRI sequences, I wonder if it is really necessary to use them all at the clinical level? If one MRI sequence is missing, does the proposed system work?
6. As all four sequences provide different information concerning the cancer, is it judicious to put all features together to train classifiers with same level?
7. I guess that there are parameters to be regulated in the pipeline, what is their impact on the final results? How to choose the ROI region to carry out in the normalization step?

8. The proposed system gives encouraging results. However, it would be interesting to compare the proposed system with other segmentation methods to demonstrate its superiority.

In view of the above assessment, this dissertation clearly provides several novel contributions for designing a prostate cancer CAD system using mP-MRI. Guillaume LEMAÎTRE has positively investigated and evaluated the proposed pipeline throughout a lot of experimentations, and obtained good results, as acknowledged by the publications made in Computer in Biology and Medicine, Journal of Ophthalmology and several international conferences. As such, his thesis is worthy of being defended. Guillaume LEMAÎTRE deserves in my opinion, to obtain the degree of Doctor from the University of Bourgogne and the University of Girona.



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