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MARIE SKŁODOWSKA-CURIE ACTIONS

Individual Fellowships (IF)
Call: H2020-MSCA-IF-2015

PART B

“ProDeepCAD”

This proposal is to be evaluated as:

Standard GF

TABLE OF CONTENTS

0 LIST OF PARTICIPANTS

Participants	Legal Entity Short Name	Academic	Non-academic	Country	Dept. / Division / Laboratory	Supervisor	Role of Partner Organisation
Beneficiary							
- NAME							
Partner Organisation							
- NAME							

Data for non-academic beneficiaries

Name	Location of research premises (city / country)	Type of R&D activities	No. of fulltime employees	No. of employees in R&D	Website	Annual turnover (approx. in Euro)	Enterprise status (Yes/No)	SME status (Yes/No)

Note that:

- Any inter-relationship between different participating institutions or individuals (e.g. family ties, shared premises or facilities, joint ownership, financial interest, overlapping staff or directors, etc.) must be declared and justified in this part of the proposal;
- The information in the table for non-academic beneficiaries must be based on current data, not projections;
- The data provided relating to the capacity of the participating institutions will be subject to verification during the Grant Agreement preparation phase.

1 EXCELLENCE

1.1 Quality, innovative aspects and credibility of the research

1.1.1 Introduction

In Europe, prostate cancer is reported to be the most frequently diagnosed cancer of men and thus one of the leading cause of death of cancer[1]. Currently, addressing this issue is a major public debate, in which the implementation of appropriate screening methods and subsequent treatments is key. In this regard, the European Randomised Study of Screening for Prostate Cancer (ERSPC) is conducted to investigate the potential benefits of a population-based screening[2]. The screening consists of a Prostate-Specific Antigen (PSA) test and depending of the PSA level measured, an additional "blind" biopsy is carried out. Despite that mortality significantly decreases, the employed screening strategy suffers of a high rate of over-diagnosis and over-treatment[3], due to the fact that prostate cancers grow either slowly or fast. The slow-growing tumours account for up to 85 % of all cancers and stay confined to the prostate gland, while the fast-growing tumours rapidly develop and metastasise to other organs, significantly affecting the morbidity and mortality rate. Furthermore, prostate cancer is more likely to develop in specific regions of the prostate: around 70-80 % of prostate cancers originate in the Peripheral Zone (PZ), whereas 10-20 % in the Central Gland (CG), but are more aggressive and more likely to invade other organs. **Thus, additionally to cancer detection, the screening methods need to estimate the cancer aggressiveness to allow clinicians to act accordingly.**

In addition, the investigators of the ERSPC have concluded that the use of *"multi-parametric Magnetic Resonance Imaging (MRI) and the development of new markers are the hope for the future"*. That is why, Computer-Aided Diagnosis (CAD) systems, revolved around mono- and multi-parametric MRI, are currently developed by the medical imaging community, and have been recently reviewed by Lemaître *et al.*[4]. The developed CAD systems are designed under the same architecture as depicted in Fig. 1. The available MRI modalities during prostate exam are T_2-Weighted (T_2-W)-MRI, Diffusion Weighted (DW)-MRI, Dynamic Contrast-Enhanced (DCE)-MRI, and Magnetic Resonance Spectroscopy Imaging (MRSI). Additionally, Apparent Diffusion Coefficient (ADC) map is based on the computation of a coefficient derived from multiple DW-MRI acquisition. **Currently, no CAD system has been developed using all the available modalities and thus discarding their potential discriminating power to diagnose prostate cancer.** The closest attempts have used three of these modalities (i.e., T_2-W-MRI, DW-MRI, DCE-MRI) and have discarded MRSI[5,6]. This latter, however, has been shown to be extremely helpful to grade cancer aggressiveness particularly in the CG[7], which is the most challenging zone in terms of cancer detection. **Furthermore, the current researches solely focus on the delineation of prostate cancers rather than on the cancer aggressiveness assessment.**

Therefore, the aim of this project is to design a CAD system able to both detect and assess prostate cancers using all currently available multi-parametric MRI modalities. To achieve this goal, we will revisit the different stages of the CAD framework. First, we will insure to work with the most consistent data, enhancing them using different types of pre-processing. Subsequently, we will segment the prostate zones using multi-parametric MRI images

These methodologies will be extensively presented and argued in Sect. 1.1.2.

1.1.2 Research methodologies

Data acquisition The unavailability of public dataset in medical imaging is a major drawback. Currently, no multi-parametric MRI prostate data are publicly available, implying that no fair comparisons can be drawn between the different developed CAD systems. Recently, Lemaître *et al.* launch a beta web-platform [8] intended

[1] J. Ferlay et al. "Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012". In: *Eur. J. of Cancer* 49.6 (2013).

[2] F. H. Schroder et al. "Screening and prostate cancer mortality: results of the European Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow-up". In: *The Lancet* 384.9959 (2015).

[3] C. Delpierre et al. "Life expectancy estimates as a key factor in over-treatment: the case of prostate cancer". In: *Cancer Epi.* 37.4 (2013).

[4] G. Lemaître et al. "Computer-Aided Detection and Diagnosis for Prostate Cancer based on mono and multi-parametric MRI: A review". In: *Comp. in Bio. and Med.* 60 (2015).

[5] G. Litjens et al. "Computer-aided detection of prostate cancer in MRI". in: *Med. Imag., IEEE Trans. on* 33.5 (2014).

[6] S. Viswanath et al. "Enhanced multi-protocol analysis via intelligent supervised embedding (EMPrAvISE): detecting prostate cancer on multi-parametric MRI". in: *Proc. SPIE 7963, Med. Imag. 2011: Computer-Aided Diagnosis*. 2011.

[7] E. K. Vos et al. "Multiparametric Magnetic Resonance Imaging for Discriminating Low-Grade From High-Grade Prostate Cancer." In: *Inves. Rad.* (2015).

[8] `http://visor.udg.edu/i2cvb/`

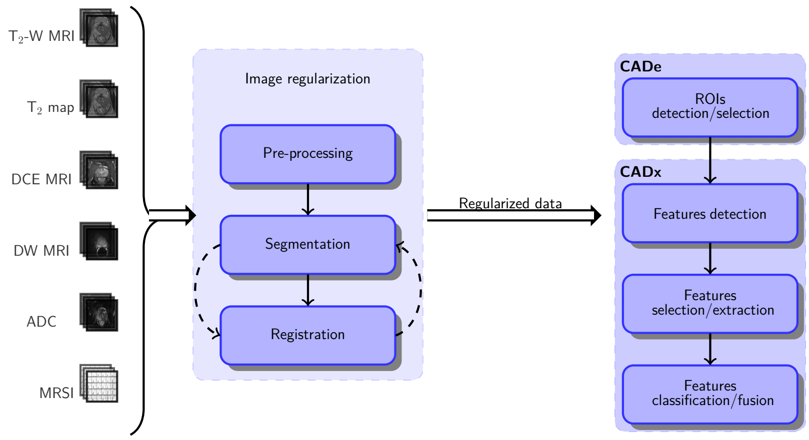

Figure 1: Common CAD framework based on MRI images used to detect prostate cancer.

for reporting the evaluation of CAD systems. A multi-parametric MRI dataset is made available, containing 60 patients and the following modalities: T_2-W-MRI, DW-MRI, DCE-MRI, and MRSI. Furthermore, the data are acquired from both 1.5 T and 3.0 T MRI scanner. Multiple ground-truths (i.e., prostate zones, cancer lesions) are compiled by experienced radiologists and additional biopsy tests. However, the web-platform need to be finalised before to be fully available. **Consequently, we will finalise the dataset and release it publicly through our web-platform.**

Pre-processing MRI images are corrupted by different phenomena: (i) bias field, (ii) noise, and (iii) inter-patient variations. In this regard, particular attention to correct each of these drawbacks will be addressed.

MRI images are affected by the inhomogeneity of the MRI field called bias field, resulting in a smooth variation of the intensities across each image. Although bias correction methods are commonly used to enhance brain MRI images[9], only one CAD system for prostate has reported to use such pre-processing[10]. The same authors have empirically evaluated the state-of-the-art methods[11] concluding that N3 algorithm[12] yields to better classification performance than other methods[13,14]. Recently, Lin *et al.*[15] have proposed a method combining the N3 algorithm with the FCM algorithm[16] which outperforms the original methods, in terms of breast segmentation. **Therefore, we will compare these state-of-the-art methods, by ensuring the benefit of the method of Lin *et al.* for our specific application.**

Apart of the bias field, MRI images are also degraded by a Rician noise. Similarly to bias correction, only two CAD systems have filtered the images using wavelet-based techniques[17,18], which offer a proper theoretical baseline for Rician corruption[19]. Non-Local Means-based denoising techniques have extensively and successively

[9] U. Vovk, F. Pernus, and B. Likar. "A review of methods for correction of intensity inhomogeneity in MRI". in: *Med. Imag., IEEE Trans. on* 26.3 (2007).

[10] S. Viswanath et al. "Integrating structural and functional imaging for computer assisted detection of prostate cancer on multi-protocol in vivo 3 Tesla MRI". in: *Proc. SPIE 7260, Med. Imag. 2009*. Vol. 7260. 2009.

[11] S. Viswanath et al. "Empirical evaluation of bias field correction algorithms for computer-aided detection of prostate cancer on T2w MRI". in: *Proc. SPIE 7963, Med. Imag. 2011*. 2011.

[12] J. G. Sled, A. P. Zijdenbos, and A. C. Evans. "A nonparametric method for automatic correction of intensity nonuniformity in MRI data". In: *Med. Imag., IEEE Trans on* 17.1 (1998).

[13] M. Styner et al. "Parametric estimate of intensity inhomogeneities applied to MRI". in: *Med. Imag., IEEE Trans. on* 19.3 (2000).

[14] M. S Cohen, R. M DuBois, and M. M Zeineh. "Rapid and effective correction of RF inhomogeneity for high field magnetic resonance imaging". In: *Human brain mapping* 10.4 (2000).

[15] M. Lin et al. "A new bias field correction method combining N3 and FCM for improved segmentation of breast density on MRI". in: *Med. Phy.* 38.1 (2011).

[16] M. N. Ahmed et al. "A modified fuzzy c-means algorithm for bias field estimation and segmentation of MRI data". In: *Med. Imag., IEEE Trans. on* 21.3 (2002).

[17] S. Mallat. *A wavelet tour of signal processing, Third Edition: The sparse way*. 3rd. Academic Press, 2008.

[18] A. Pizurica et al. "A versatile wavelet domain noise filtration technique for medical imaging". In: *Med. Imag., IEEE Trans in* 22.3 (2003).

[19] R.D. Nowak. "Wavelet-based Rician noise removal for magnetic resonance imaging". In: *Image Proc., IEEE Trans. on* 8.10 (1999).

been used for other MRI applications, but never for MRI prostate images[20]. **Thus, we will evaluate the Non-Local Means-based techniques[21,22] and wavelet-based technique to select the appropriate method to our application.**

CAD systems are based on machine learning classifiers which are trained to differentiate cancerous from healthy tissue. The classification performance of these classifiers highly relies on the consistency of the dataset. Subsequently, one can emphasize the desire to reduce the inter-patient variability of the MRI dataset. In this regard, each patient dataset needs to be standardised/normalised to a common basis, modality by modality. Only two methods have been used in CAD for prostate: the first method consists in normalising the images via the z-score, while the second technique is based on a linear normalisation by parts[23]. Lemaître *et al.* have developed a normalisation technique using the Rician properties of the MRI signal [24], which outperforms the previous methods for T_2-W-MRI images. **Thus, we will extend this work to the other DCE-MRI and DW-MRI modalities**.

MRSI is a modality related to one dimensional signal, and the enhancing techniques differ from the one used in MRI. The MRSI spectra have to be corrected for several phenomena: phase correction, water and lipid residuals filtering, baseline correction, frequency alignment, and normalisation. This set of enhancement techniques has already been investigated by Lemaître *et al.* in a study focusing solely on the MRSI modality for prostate cancer detection[25]; **this knowledge will be the basis of MRSI enhancement.**

Segmentation To achieve robust cancer detection, the classification has to be carried out only on the prostate area, motivating the need to perform a segmentation of the organ in the MRI images. Furthermore, as mentioned in Sect. 1.1.1, the membership *a-priori* of a voxel to belong to a zone (i.e., PZ or CG) has a high potential to increase the performance to assess the aggressiveness of prostate cancer. Therefore, the prostate zones need to be segmented instead of solely the prostate organ. In this regard, only the work of Litjens *et al.* have segmented the prostate zones using a probabilistic multi-atlas approach[26]. However, the segmentation was performed using only the T_2-W-MRI modality and the ADC map. Although atlas-based methods are robust to intensity variations, they lack of accuracy in the boundary delineations[27]. The potential of machine learning methods to carry out such task is currently underestimated, but has been shown to be suitable in combination with the other approaches (i.e., deformable models or atlas-based)[28]. **Thus, we will design a hybrid system to segment the prostate zones, based on Convolutional Neural Networks (CNN) and Active Shape Models using all multi-parametric images.** The choice of CNN is motivated by the recent breakthrough of deep-learning in multiple fields of computer vision. Deep-learning, however, has still not be extensively used in the field of medical imaging as attested by the organisation of the first workshop specifically dedicated to this topic at MICCAI 2015. Deep-learning relies on a data-driven training stage in which large amount of data are required, which is a serious drawback in medical imaging. However, this problem is addressed by transfer learning which allow to use deep-learning to medical imaging.

Registration In multi-parametric MRI, the data are collected in a sequential manner, involving a possible misalignment between the different modalities. During her PhD at the Universitat de Girona, Mitra *et al.* developed an automatic multi-modal non-rigid registration method[29], which has been shown to outperform the state-of-the-art methods. This method has initially been used for registration between T_2-W-MRI and

[20] J. V. Manjón et al. "MRI denoising using non-local means". In: *Med. Image Anal.* 12.4 (2008).

[21] J. V. Manjón et al. "New methods for MRI denoising based on sparseness and self-similarity." In: *Med. Image Anal.* 16.1 (2012).

[22] P. Coupé et al. "Adaptive Multiresolution Non-Local Means Filter for 3D MR Image Denoising". In: *IET Image Proc.* 11 (2011).

[23] A. Madabhushi and J. K. Udupa. "New methods of MR image intensity standardization via generalized scale". In: *Med. Phy.* 33.9 (2006).

[24] This work is submitted for publication.

[25] G. Lemaître. "Absolute quantification at 3 T". MA thesis. Université de Bourgogne, Heriot-Watt University, Universitat de Girona, 2011.

[26] G. Litjens et al. "Evaluation of prostate segmentation algorithms for MRI: the PROMISE12 challenge". In: *Med. Image Anal.* 18.2 (2014).

[27] S. Ghose et al. "A survey of prostate segmentation methodologies in ultrasound, magnetic resonance and computed tomography images". In: *Comp. Met. Prog. Biomed.* 108.1 (2012).

[28] S. Ghose et al. "Graph cut energy minimization in a probabilistic learning framework for 3D prostate segmentation in MRI". in: *Pat. Rec. (ICPR), 21st Int. Conf. on.* IEEE. 2012.

[29] J. Mitra et al. "A spline-based non-linear diffeomorphism for multimodal prostate registration". In: *Med. Image Anal.* 16.6 (2012).

Ultra-Sound prostate images; **therefore, we will extend this method to align our multi-parametric MRI dataset.**

Detection and assessment Up to now, CAD developed systems solely focus on the detection of prostate cancers, omitting a real assessment of the lesion aggressiveness. The detection of cancers is commonly performed using machine leaning classifiers, designing frameworks as depicted in Fig. 1. These frameworks rely on two compulsory stages and an intermediate optional one: (i) features detection, (ii) features selection/extraction and (iii) features classification. Lemaître *et al.* have extensively reviewed researches carried out in each of this stage for the development of CAD for prostate cancer[30]. These stages are organised in a sequential manner and thus stages upstream part of the features classification have a tremendous importance on the classification performance. Consequently, the use of discriminative features is certainly key and most probably the bottleneck of CAD systems, justifying the attention given by researchers to evaluate multitude of low- and high-level visual features, inspired by computer vision or biology. As aforementioned, deep-learning has been recently shown to be one of the most successful machine learning technique in broad types of classification tasks. CNN has the ability to generate automatically low- and high-level visual features in the network itself[31] by only supplying the raw data as inputs. Furthermore, CNN can be trained using the Gleason grade obtained through biopsy in order to get an assessment of the aggressiveness of the cancer. **Thus, we will detect and assess prostate cancers with CNN. In addition, we will investigate the low- and high-level features to find potential new markers which can be used by clinicians or other machine learning methods.**

Evaluation using PI-RADS The European Society of Urogenital Radiology together with the American College of Radiology have recently published the Prostate Imaging and Reporting and Data System (PI-RADS), which is the standard way to assess and report prostate lesions using multi-parametric MRI. This standard allows to assign a score depending of multiple criteria such as signal intensity, texture, size of lesion, modality, prostate zones, etc. None of the current CAD systems offer a PI-RADS score when detecting potential lesions in multi-parametric MRI. **Thus, we will report the output of our classification framework in terms of PI-RADS score, applying the provided criterion.**

1.2 Clarity and quality of transfer of knowledge/training for the development of the researcher in light of the research objectives

The main objective of the present project is to establish a mutually beneficial partnership between the host institute, the Florida State University, the fellow and the beneficiary, the Universitat de Girona (UdG), with the goal to develop the first multi-parametric CAD system for prostate cancer detection and diagnosis. The proposed research will allow the fellow to continue gaining experience in his former research line, the design of multi-parametric CAD systems portable to many other cancers such as breast and brain. The fellow will gain expertise in developing intelligent CAD systems, novel pre-processing techniques to be applied to prostate images and integrated in the CAD system, and in cancer research in general. In addition he will acquire knowledge in the molecular basics of cancer. With the acquired skills he will continue the development of this very comprehensive CAD system for prostate cancer that will be the first prototype on the European market. Prof. Meyer-Baese has developed an intense and prolific research activity in breast cancer diagnosis through the last decades. She wrote the first research monograph in "Pattern recognition in Medical Imaging" (Elsevier) and "Biomedical Signal Processing: Contemporary Methods and Applications" (MIT Press). She has an extensive experience in research and training in this field making her the most appropriate person to supervise this research given also her extensive experience in post-graduate and graduate educations. In addition to the pure scientific knowledge transfer included in the aims of this project, her expertise in the field also include success in coordinating research projects that involve multidisciplinary agents. Specifically, she is trained in the following skills: patient management; understanding cutting-edge medical methods and techniques; collaborating with physicians; algorithm implementation; mathematical modelling; radiological sources and MR

[30] Lemaître et al., "Computer-Aided Detection and Diagnosis for Prostate Cancer based on mono and multi-parametric MRI: A review".
[31] M. D. Zeiler and R. Fergus. "Visualizing and Understanding Convolutional Networks". In: *CoRR* (2013).

images management; database management, storage and processing; ability to attract funding; expertise as editor of books and journal special issues; and student tutoring, curriculum development, and doctoral committee chair. The accomplishment of the aims of this project will serve as bridge to transfer the aforementioned skills under the supervision of Prof. A. Meyer-Baese. Also, the host institution in USA will benefit from the previous knowledge of the applicant in biomedical image processing in prostate cancer research, as the aims of this project converge into global policies of USA and also research objectives of the host team, creating synergies and guarantees of lasting collaborations. The applicant brings in an enormous expertise in prostate cancer research that will flow into the group of Prof. Meyer-Baese and will enhance the current cancer research work. It is also important to stress that a native English spoken host will serve to significantly improve the language skills of the researcher, which are of fundamental importance in communication of research results: writing papers, oral presentations in workshops/conferences and discussions between researchers.

The young and active research group computer vision and robotic (ViCOROB), to which the host institution in Europe belongs, will definitely benefit from this project in the incoming phase, capitalising on the works carried out for the last decade in the area of prostate cancer. The fellow will play an indispensable role in the group by: training new researchers, superivising PhD candidates and MSc students, attracting interest for funding, applying for new grants/projects, establishing collaborations with other groups, contacting industry related agents, strengthen hospitals and health services relations, participating in seminars, publishing papers, and attending to conferences.

Concerning the gender issues, it is worth to mention that there exists a perfect balance between the supervisor's gender of this project and him.

1.3 Quality of the supervision and the hosting arrangements

Qualifications and experience of the supervisor(s)

Prof. A. Meyer-Baese and Prof. Dr. Robert Martí have demonstrated their expertise in supervising researchers. They have also the endeavor, knowledge, experience and commitment to be able to offer the candidate appropriate support to continuously progress and to review his research plans, as well as providing the necessary feedback mechanisms. They will act as excellent mentors for this project. Guillaume Lemaître will establish a structured and regular communication with both scientists and all the members of theirs research groups and collaborators, to take full advantage of the arising research opportunities between the groups. Furthermore, he will keep records of all work progress and research findings, obtaining feedback by means of reports, monthly seminars, applying such feedback and working in accordance with agreed schedules, milestones, deliverables and research outputs which are described in Sect. 3. In the outgoing phase, he will also have access to datasets from his home institution and computational/institutional resources, computer clusters for intensive computation provided by the host institution, and excellent facilities and experience in scientific studies aiming at the evaluation of CAD methods for prostate cancer. For the re-integration of the researcher, the host will reincorporate the researcher into ViCOROB, where he has developed his main research activity. ViCOROB belongs to the UdG and is modern research centre speacialised in computer-vision and robotics

For the re-integration of the researcher, the host will reincorporate the researcher into the CITIC, where he has developed his main research activity. The CITIC belongs to the Campus of International Excellence in Biohealth, and is a modern research centre specialized in information and communication technologies, in which the University of Granada stands out as one of the 50 best Universities worldwide according to Shangai's index in computer science. The present project fits perfectly with the hosting priorities and guarantees a promising long term research career. (Please adapt for Girona)

Qualifications and experience of the supervisor(s): Prof. Meyer-Baese is an internationally and nationally recognized expert in her field and has won many scientific prizes and awards. Professor Meyer-BaeseâĂŹs core research is at the frontier of medical sciences and engineering. She has an outstanding publication record including 3 research monographs published by MIT Press and Elsevier, and more than 180 refereed journal and peer-reviewed conference papers in her field. She is also an outstanding citizen of the scientific community and very active in the organization of conferences and workshops as a Chair, serves on the Editorial Board of journals and as the Editor in Chief on many Special Issues in medical imaging. Prof. Meyer-Baese led over twenty funded research projects in her field with a total volume of six million dollars. Prof. Meyer-Baese worked interdisciplinary with the world- famous MD Anderson and Lee-Moffitt Cancer Center, and the National High Magnetic Field Laboratory in cancer research. Her research contributions demonstrate her capability to provide innovative concepts in the highly interdisciplinary area of biomedical engineering.

Career development

1.4 Capacity of the researcher to reach and re-enforce a position of professional maturity in research

2 IMPACT

2.1 Enhancing research- and innovation-related human resources, skills, and working conditions to realise the potential of individuals and to provide new career perspectives

There are many extremely important scientific, technological and socio-economical reasons for extensively pursuing both fundamental and applied research in this field. According to the document âĂŸ2020 Vision for the European Research AreaâĂŹ, European research policy should be deeply rooted in European society. This document establishes that European research should support knowledge advancement in fields of major public concern such as health, facilitating the free circulation of researchers, knowledge and technology. The proposed research aims at developing the first comprehensive CAD system for prostate cancer that can be easily adapted for breast cancer detection and diagnosis. It will constitute an unique tool for enhancing the radiologistâĂŹs interpretation with quantitative measurements using intelligent CAD systems. Based on these objective measurements, this novel CAD will have the potential to be easily integrated into the clinical work-flow, advancing CAD systems beyond the current âĂIJcomputer-aided displayâĂİ-stage and one-parametric imaging. This research will enable the translation of basic and applied data mining and computer vision algorithms to many cancer research areas besides prostate. These will include the main lethal cancers such as breast and brain. The system will enable the development of unique prostate cancer biomarkers unknown before that will pave the pathway to personalized management for future patients diagnosed with early-stage prostate t cancer.

In addition, it will improve early diagnosis and treatment of prostate cancer through improved quantitative evaluation methods and data mining methods including deep learning that will lead to reduced cost in prostate cancer screening by ultimately reducing the number of unnecessary biopsies. Furthermore, the developed algorithmic tools will be relevant for breast and brain cancer diagnosis as well, and will be also applicable in other disciplines such as neuroscience or study of neurodegenerative diseases since the engineering mechanisms are the same.

The methods and results included in this project present a wide range of multidisciplinary aspects which will maximise the impact on the researcher's activity on European society, impacting on: -Basic research: study of the registration, segmentation, and deep learning algorithms and their properties. Development of novel CAD methods to be used in large datasets and multiparametric images. -Strategic research: nowadays biomedical image processing is a relatively new discipline within signal processing with active challenging topics. -Applied research: applications to challenging problems with social relevance in Europe as aggressive and non-aggressive tumour detection for prostate cancer diagnosis. -Transfer of knowledge: development of a software with the results of the investigation to be used in real applications by companies, researchers and practitioners. Dissemination of results in international journals and conferences.

Additionally, the students who will work on associated aspects of this proposal will acquire skills that they can take with them to public and private sector jobs within the European Union. Thus, the applicant would serve in a multifaceted role as supervisor, mentor, career advisor and project coordinator, which would lead him into a position of professional maturity benefiting alumni, researchers, patients, physicians and industrial sector. Therefore, the present project has impact in three fundamental sectors for European society: academics/education, health and industry.

2.2 Effectiveness of the proposed measures for communication and results dissemination

Communication and public engagement strategy of the action: The topic and potential results of this project are important for the general public. Dr. Lemaitre has experience in public engagement with research projects. On several occasions he presented his work to a very broad scientific and non-scientific audience. He contacted consumer groups to advocate for his research and draw the attention to early detection and diagnosis to a very deadly cancer among men. Prostate cancer is extremely prevalent among African Americans in the US and talking to these under-represented and under-privileged groups will be extremely beneficial for the large-scale dissemination of the research results achieved in this project. This project is planned to take advantage of the worldwide spreading possibilities of both languages (Spanish and English) and have a similar communication procedure through FSU research news and FSU channel and Girona press channel, media, scientific-spreading blogs, digital media (the applicant is an active user of facebook and twitter with a science-lover network of contacts), press and TV (Communication 1 (C1), see Gantt chart). In addition, the applicant plans to participate in Open-Doors day activities to attract highschool students for interdisciplinary research and for the new direction scientific computing. Dissemination of the research results: Sharing of data generated by this project is an essential part of the proposed outreach activities and will be carried out in presenting the research at international scientific meetings in radiology and medical imaging, high impact journals and books. An additional goal of this project, which has been outlined throughout this document, is the dissemination of the results by developing the CAD as a software tool with independent modules that will find applicability in many cancer research areas. He will re-visit and refine existing components of this software tool. Dr. Leamitre will develop a versatile, modular, open-source toolbox of algorithms readily usable by radiologists which is platform independent, robust, fast and easy to use in routine clinical practice, test this toolbox and distribute it to the scientific community. He will create a project home page for the software (C2). This will allow future interested researchers to continue development of the toolbox and will preserve its utility to the community. He will be primarily responsible for software dissemination and support through direct training of experienced radiologists and residents, via conferences, radiological journals and online tutorials. In addition he will train radiologists how the proposed CAD system can be employed as a decision making mechanisms in breast cancer. The fellow has also active accounts for spreading results in scientific social-networks as: google-scholar, researchGate, scopus.

Exploitation of results and intellectual property: In about three years a direct knowledge utilization from the proposed research in form of a first prototype of a CAD for prostate cancer detection and diagnosis will emerge that could be tested in clinical routine. This project offers a high probability that intellectual property (IP) of significant commercial value due to its novelty (by being the first comprehensive CAD for prostate cancer) and its translational research applications for example in breast cancer research. The applicant will look for opportunities through patents and disclosures to transfer this IP to the private sector. All the necessary steps will be taken in order to protect, assess, transfer/license, any exploitable results arising from this project, in accordance with the rules of the 2020 Horizon Program for Research. The exploitation of results will be based on: the manifested interest of Quiron group on SIPBA research activities; the help of living-lab salud Andalucia, a living lab agency operating in the regional south of Spain (Andalusia); and CESEAND, the andalusian node of the Enterprise Europe Network, which are already known contacts to the applicant (C3). (Please adapt for Giirona)

Dissemination, exploitation of results All researchers should ensure, in compliance with their contractual arrangements, that the results of their research are disseminated and exploited, e.g. communicated, transferred into other research settings or, if appropriate, commercialised. Senior researchers, in particular, are expected to take a lead in ensuring that research is fruitful and that results are either exploited commercially or made accessible to the public (or both) whenever the opportunity arises.

3 IMPLEMENTATION

3.1 Overall coherence and effectiveness of the work plan

The proposal is split into 8 work packages (WPx) and subdivided into tasks (Tx):

WP1: Data acquisition and dissemination (duration of 5 months)

- **T1.1** Prepare the multi-parametric MRI dataset
- **T1.2** Finalise the web-platform
- **T1.3** Publicly publish the dataset
- **T1.4** Organise a *Grand-challenge*

WP2: Pre-processing (duration of 7 months)

T2.1 Evaluate the bias field correction methods on our public dataset (1.3)
T2.2 Evaluate the denoising methods on our public dataset (1.3)
T2.3 Extend the normalisation methods on our public dataset (1.3)
T2.4 Apply and evaluate MRSI pre-processing methods on our public dataset (1.3)

WP3: Segmentation (duration of 7 months)
T3.1 Design the hybrid segmentation method
T3.2 Develop the segmentation
T3.3 Validate the segmentation method on our public dataset (1.3)

WP4: Registration (duration of 7 months)
T4.1 Extend the current registration method
T4.2 Validate the registration method on our public dataset (1.3)

WP5: Detection and assessment (duration of 8 months)
T5.1 Design the classifier architecture
T5.2 Develop the classifier
T5.3 Validate the classifier on our public dataset (1.3)

WP6: PI-RADS evaluation (duration of 2 months)
T6.1 Transpose the PI-RADS markers to computer vision marker
T6.2 Develop the PI-RADS-based grading
T6.3 Validate this approach on our public dataset (1.3)

WP7: Communication to general public (duration of 36 months)
T7.1 Internal seminars in FSU and UdG
T7.2 Publish in general public press such as *Engega*
T7.3 Scientific blog with periodic entries
T7.4 Enrollment to educational workshop such as *Yong Research Campus* at UdG

WP8: Scientific dissemination (duration of 36 months)
T8.1 Maintenance of the web-platform by publishing code and results
T8.2 Publish the works in peer-review journals
T8.3 Publish the works in peer-review international conferences

The following deliverables (Dx) will be released during the project:

D1.1 Multi-parametric MRI database
D2.1 Software toolbox for multi-parametric MRI images pre-processing
D3.1 Software toolbox for multi-parametric MRI images registration
D4.1 Software toolbox for multi-parametric MRI images segmentation
D5.1 Software toolbox for multi-parametric MRI images classification
D6.1 Software toolbox for PI-RADS grading

To achieve the proposed goals, the following milestones (Mx) are defined:

M1.1 Deadline December 2016 — Grand-Challenge submission at the conference MICCAI 2017, "Prostate detection and grading using multi-parametric MRI"
M2.1 Deadline October 2016 — Paper submission at the conference ISBI 2017, "Empirical evaluation of bias field correction methods for multi-parametric MRI"
M2.2 Deadline October 2016 — Paper submission at the conference ISBI 2017, "Empirical evaluation of noise reduction methods for multi-parametric MRI"
M2.3 Deadline March 2017 — Paper submission at the conference MICCAI 2017, "Normalisation techniques for multi-parametric MRI"
M2.4 Deadline March 2017 — Paper submission to a peer-review journal, "Pre-processing tools for multi-parametric MRI"
M3.1 Deadline October 2017 — Submission to PROMISE12 challenge of results using only T_2-W-MRI

M3.2 Deadline October 2017 — Paper submission to peer-review journal *Medical Image Analysis*, "Zonal segmentation of the prostate using deep-learning and multi-parametric MRI"
M4.1 Deadline June 2018 — Paper submission at the conference ICIP 2018, "Prostate registration using multi-parametric MRI and spline-based non-linear diffeomorphism"
M5.1 Deadline January 2019 — Paper submission to peer-review journal *IEEE Transactions on Medical Imaging*, "Prostate cancer detection and assessment using deep-learning and multi-parametric MRI"
M6.1 Deadline March 2019 — Paper submission to peer-review journal *Journal of Magnetic Resonance Imaging*, "Evaluation of a prostate CAD systems using PI-RADS"

3.2 Appropriateness of the management structure and procedures, including quality management and risk management

Develop your proposal according to the following lines:

- Project organisation and management structure, including the financial management strategy, as well as the progress monitoring mechanisms put in place;
- Risks that might endanger reaching project objectives and the contingency plans to be put in place should risk occur.

The following could be also included in the Gantt Chart:

- Progress monitoring;
- Risk management;
- Intellectual Property Rights (IPR).

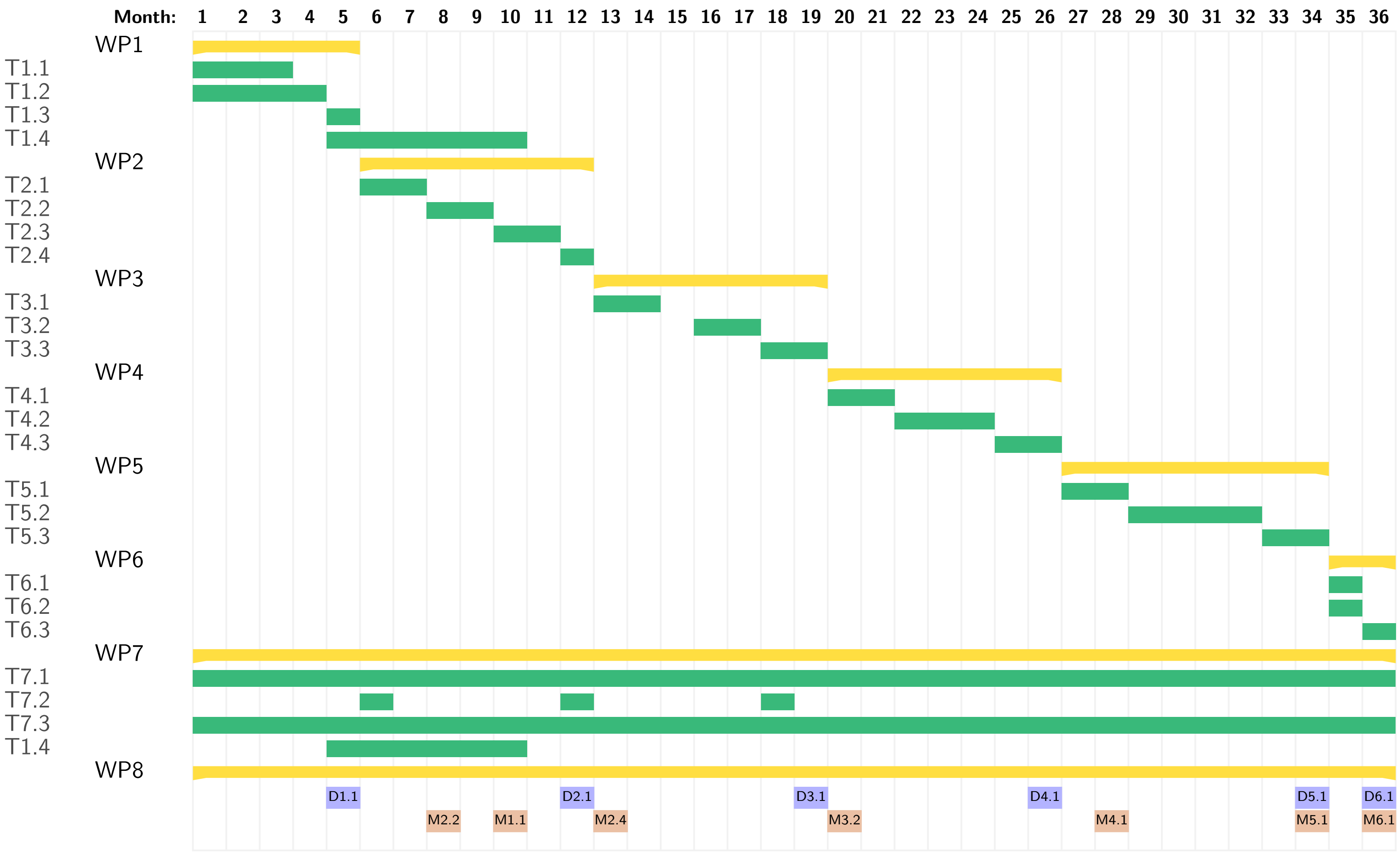

Figure 2: Example Gantt Chart

3.3 Appropriateness of the institutional environment (infrastructure)

Give a description of the legal entity/ies and its main tasks (per participant). Explain why the fellowship has the maximum chance of a successful outcome.

NB: Each participant is described in Section 6. This specific information should not be repeated here.

3.4 Competences, experience and complementarity of the participating organisations and institutional commitment

Here describe how the fellowship will be beneficial for both the Experienced Researcher and host organisation(s).

- Commitment of beneficiary and partner organisations to the programme (for partner organisations, please see also section 6)

Partner organisations: The role of Partner organisations in MS/AC for secondments and their active contribution to the research and training activities should be described.

4 CV OF THE EXPERIENCED RESEARCHER

4.1 PERSONAL INFORMATION

Name: Guillaume Lemaître
Date of birth: 27^{th} April 1988, 27 years old
Personal website: `https://sites.google.com/site/glemaitre58`

4.2 EDUCATION

07/2012 — 12/2015 **Co-joint PhD in Medical Imaging**
"Computer Aided Diagnosis system for prostatic biopsy guidance and follow-up fusing multi-modal imaging"
Supervised by Dr. R. Martí, Prof. F. Mériaudeau, Dr. J. Freixenet, and Dr. P. M. Walker
ViCOROB, Universitat de Girona — LE2I, Université de Bourgogne

09/2012 — 09/2014 **Master in Business Innovation and Technology Management**
"Valorisation of computerized technology in the health care sector"
Supervised by Dr. A. Bikfalvi and Dr. J. Llach
Universitat de Girona

09/2009 — 06/2011 **Master of Excellence Erasmus Mundus in Vision and Robotics**
"Absolute Quantification in 1H MRSI of the Prostate at 3.0 T"
Supervised by Dr. P. M. Walker
Université de Bourgogne, Universitat de Girona, Heriot-Watt University

09/2016 — 09/2009 **Bachelor Eng. Electronic, Signal, and Image**
Université de Bourgogne

4.3 WORKING EXPERIENCE

03/2015 — 01/2016 **Assistant professor (ATER)**
184 hours of lecturing in databases, pattern recognition and machine learning, programming, image processing
Université de Bourgogne

06/2011 — 06/2012 **R&D researcher**
Barcelona Digital — ViCOROB, Universitat de Girona

4.4 FELLOWSHIPS AND AWARDS

4.5 PARTICIPATION IN PUBLIC-FUNDED PROJECTS

- Temporal analysis and automatic detection of lesions in multi-modal images (IA-BioBreast)
- Identification of retinal deseases on OCT images (PHC MERLION)
- Erasmus+ educational project (Early Mastery)

2012	**OMJ Grant**, Minitère Français des Affaires Etrangères et Européennes, France
2012	**FI-DGR PhD Grant**, Generalitat de Catalunya - AGAUR, Spain
2011	**Research Master Scholarship**, Burgundy Region, France
2010	**Erasmus Spanish Scholarship**, Spanish Ministry, Spain
2010	**Merit-based Scholarship**, French Ministry, France
2010	**Merit-based Scholarship dedicated to Research Masters**, Burgundy Region, France
2009	**Spanish Ministry Mobility Scholarship**, Spanish Ministry, Spain
2009	**Merit-based Scholarship**, French Ministry, France
2009	**Erasmus French Scholarship**, French Ministry, France
2009	**Mobility Grant**, Burgundy Region, France
2009	**Region Mobility Scholarship**, Burgundy Region, France
2009	**Rotary Scholarship**, Rotary Club Le Creusot, France
2009 — 2011	**Erasmus Mundus Grant**, Heriot-Watt University, Universitat de Girona, Université de Bourgogne, Scotland, Spain, France
2008	**Erasmus French Scholarship**, French Ministry, France
2008	**Mobility Grant**, Burgundy Region, France

July, 2008	**Student Autonomous Underwater Competition - Europe**, Nessie III - Heriot-Watt University
July, 2008	**THALES Special Award for innovation**, Nessie III - Heriot-Watt University

4.6 TEACHING

24 h **Medical Imaging: Segmentation and registration methods**
Master Erasmus Mundus ViBOT
Universitat de Girona

24 h **Pattern Recognition and Machine Learning**
Master Erasmus Mundus ViBOT, https://github.com/ViBOT-Erasmus/B31XI-SI-Syllabus
Université de Bourgogne

48 h **Introduction to image processing**
Master Erasmus Mundus ViBOT
Université de Bourgogne

16 h **Software engineering**
Master Erasmus Mundus ViBOT
Université de Bourgogne

74 h **Introduction to databases**
Bachelor of Electrical Engineering
Université de Bourgogne

4.7 COMMUNICATION

- Chair and actor in regular internal seminars at the Université de Bourgogne (RE-COOP)
- Chair of regular scientific reading groups
- Chair for Doctoral Day at the Université de Bourgogne (http://le2i.github.io/doctoral-day-2015/)

4.8 SUPERVISION

- Supervision of 3 BSc. and MSc. students during their summer internships

4.9 PUBLICATIONS

Peer-Review Journals Papers:

1. **G. Lemaitre, R. Marti, J. Freixenet, J. C. Vilanova, P. M. Walker, and F. Meriaudeau**, "Computer-Aided Detection and Diagnosis for prostate cancer based on mono and multi-parametric MRI: A Review", *Computer in Biology and Medicine*, vol. 60, pp 8 - 31, 2015. **(Citations: 3)**

Peer-Review International Conferences Papers:

1. **A. Meyer-Baese, J. Massich, G. Lemaitre, and M. Rastgoo**, "Real-Time Optical Flow with Theoretically Justified Warping Applied to Medical Imaging", *Breast Image Analysis Workshop (BIA), Medical Image Computing and Computer Assisted Interventions (MICCAI) 2015*. Munich: Germany (Oct. 2015). **(Citations: 0)**

2. **J. Massich, G. Lemaitre, J. Marti and F. Meriaudeau**, "An Optimization Approach to Segment Breast Lesions in Ultra-Sound Images using Clinically Validated Visual Cues", *Breast Image Analysis Workshop (BIA), Medical Image Computing and Computer Assisted Interventions (MICCAI) 2015*. Munich: Germany (Oct. 2015). **(Citations: 0)**

3. **G. Lemaitre, M. Rastgoo, J. Massich, S. Sankar, F. Meriaudeau, and D. Sidibe**, "Classification of SD-OCT volumes with LBP: Application to DME detection", *Ophthalmic Medical Image Analysis Workshop (OMIA), Medical Image Computing and Computer Assisted Interventions (MICCAI) 2015*. Munich: Germany (Oct. 2015). **(Citations: 0)**

4. **J. Massich, G. Lemaitre, J. Marti, and F. Meriaudeau**, "Brest Ultra-Sound image Segmentation: an Optimization approach based on super-pixels and high-level descriptors", *International Conference on Quality Control and Artificial Vision (QCAV) 2015*. Le Creusot: France (Jun. 2015). **(Citations: 0)**

5. **G. Lemaitre, J. Massich, R. Marti, J. Freixenet, J. C. Vilanova, P. M. Walker, D. Sidibe, and F. Meriaudeau**, "A Boosting Approach for Prostate Cancer Detection using Multi-parametric MRI", *International Conference on Quality Control and Artificial Vision (QCAV) 2015*. Le Creusot: France (Jun. 2015). **(Citations: 0)**

6. **G. Lemaitre, A. Bikfalvi, J. Llach, J. Massich, and F. Julian**, "Business Model Design for University Technology Valorisation", *International Technology, Education and Development Conference (INTED) 2015*. Madrid: Spain (Mar. 2015). **(Citations: 0)**

7. **M. Rastgoo, G. Lemaitre, X. Rafael, F. Miralles, and P. Casale**, "Pruning AdaBoost for Continuous Sensors Mining Applications", *Ubiquitous Data Mining Workshop, 20th European Conference in Artificial Intelligence 2012*. Montpellier: France (Aug. 2012). **(Citations: 2)**

8. **G. Lemaitre, E. Vargiu, J.A. Lorenzo FernÃąndez, and F. Miralles**, "Real-Time 2D Face Detection and Features-based Tracking in Video", *IADIS Multi Conference in Computer Science in Computer Graphics, Visualization, Computer Vision and Image Processing 2012*. Lisbon: Portugal (Jul. 2012), 2012. **(Citations: 0)**

9. **J. Cartwright, N. Johnson, B. Davis, Z. Qiang, T.L. Bravo, A. Enoch, G. Lemaitre, H. Roth, and Y. Petillot**, "Nessie III Autonomous Underwater Vehicle for SAUC-E 2008", *The Unmanned Underwater Vehicle Showcase (UUVS)*, 2008. **(Citations: 5)**

5 CAPACITIES OF THE PARTICIPATING ORGANISATIONS

All organisations (whether beneficiary or partner organisation) must complete the appropriate table below. Complete one table of maximum one page for the beneficiary and half a page per partner organisation (min font size: 9). The experts will be instructed to disregard content above this limit.

Beneficiary X	
General Description	
Role and Commitment of key persons (supervisor)	(Including names, title, qualifications of the supervisor)
Key Research Facilities, Infrastructure and Equipment	(Demonstrate that the team has sufficient facilities and infrastructure to host and/or offer a suitable environment for training and transfer of knowledge to recruited Experienced Researcher)
Independent research premises?	
Previous Involvement in Research and Training Programmes	
Current involvement in Research and Training Programmes	(Detail the EU and/or national research and training actions in which the partner is currently participating)
Relevant Publications and/or research/innovation products	(Max 5)

Partner Organisation Y	
General Description	
Key Persons and Expertise (supervisor)	
Key Research facilities, infrastructure and equipment	
Previous and Current Involvement in Research and Training Programmes	
Relevant Publications and/or research/innovation product	(Max 3)

ENDPAGE

MARIE SKŁODOWSKA-CURIE ACTIONS

Individual Fellowships (IF)
Call: H2020-MSCA-IF-2015

PART B

"ProDeepCAD"

This proposal is to be evaluated as:

[Standard EF]