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MARIE SKŁODOWSKA-CURIE ACTIONS

**Individual Fellowships (IF)**
**Call: H2020-MSCA-IF-2016**

PART B

"PREDICATE"

"comPuteR-aidEd diagnosis using Deep learning and radIomiCs for prostATE cancer"

**This proposal is to be evaluated as:**

**Standard GF**

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# 0 LIST OF PARTICIPANTS

| Participants | Legal Entity Short Name | Academic | Non-academic | Country | Dept. / Division / Laboratory | Supervisor | Role of Partner Organisation |
|---|---|---|---|---|---|---|---|
| Beneficiary | | | | | | | |
| Universitat de Girona | UdG | ✓ | | Spain | Computer Vision and Robotics Institute (ViCOROB) | Dr. Robert Martí | |
| Partner Organisation | | | | | | | |
| Florida State University | FSU | ✓ | | USA | Scientific Computing | Prof. A. Meyer-Baese | Host outgoing phase |

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 and credibility of the research/innovation action

### 1.1.1 Introduction

In Europe, prostate cancer is reported to be the most frequently diagnosed cancer among men and thus one of the leading causes of death of cancer[1]. Currently, addressing this issue is a major public debate, where 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 has been decreasing, the employed screening strategy suffers of a high rate of over-diagnosis and over-treatment[3], and misses the more aggressive cancers in the Central Gland (CG). **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 currently multi-parametric MRI are developed by the medical imaging community, and have given rise to the field of **radiomics** consisting in automatically extracting large a number of quantitative features[4]. Recently, Lemaître *et al.* extensively reviewed the developed CAD systems for prostate cancer detection[5]. The developed CAD systems are designed under the same architecture composed of: (i) pre-processing, (ii) registration-segmentation, (iii) feature detection, (iv) feature extraction/selection, and (v) feature classification. 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 imaging modalities and taking into account the radiomics signature but they discarded their potential for 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[6,7]. This latter, however, has been shown to be extremely helpful to grade cancer aggressiveness particularly in the CG[8], which is the most challenging zone in terms of cancer detection. **Furthermore, the current research mainly 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 and the radiomics paradigm, by analyzing different automated and traditional imaging features.

### 1.1.2 Research methodologies

**Data acquisition** The unavailability of a 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.* have launch a beta web-platform [9] intended 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,

[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] Philippe Lambin et al. "Radiomics: extracting more information from medical images using advanced feature analysis". In: *European journal of cancer* 48.4 (2012), pp. 441–446.

[5] 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).

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

[7] 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.

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

[9] `http://i2cvb.github.io/`

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 needs to be completed before being made 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 given.

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[10], only one CAD system for prostate has reported to use such pre-processing[11]. The same authors have empirically evaluated the state-of-the-art methods[12] concluding that N3 algorithm[13] yields to better classification performance than other methods. Recently, Lin *et al.*[14] have proposed a method combining the N3 algorithm with the Fuzzy C-Means algorithm 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 from 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[15,16], which offer a proper theoretical baseline for Rician corruption[17]. Non-Local Means-based denoising techniques have extensively and successively been used for other MRI applications, but never for MRI prostate images. **Thus, we will evaluate the Non-Local Means-based techniques[18] and wavelet-based technique to select the appropriate method for our application.**

Only two methods have been used in CAD for prostate to reduce the inter-patient variability in the MRI dataset: the first method consists in normalising the images via the $z$-score, while the second technique is based on a linear normalisation by parts[19]. Lemaître *et al.* have developed a normalisation technique using the Rician properties of the MRI signal[20], which outperforms the previous methods for $T_2$-W-MRI images. Furthermore, Lemaître *et al.* have developed a method to standardized DCE-MRI data, showing the benefit when detecting prostate cancer in comparison with un-normalized data and quantitative methods. **Thus, we will extend this work to DW-MRI modalities and on larger cohort of patient to test the reliability of these methods.**

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[21]; **this knowledge will be the basis of MRSI enhancement.**

**Segmentation** To achieve robust cancer detection, the classification has to be carried out only in 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 *a-priori* membership of a voxel to belong to a zone (i.e., Peripheral Zone or CG) has a high

[10] U. Vovk et al. "A review of methods for correction of intensity inhomogeneity in MRI". in: *Med. Imag., IEEE Trans. on* 26.3 (2007).

[11] 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.

[12] 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.

[13] J. G. Sled et al. "A nonparametric method for automatic correction of intensity nonuniformity in MRI data". In: *Med. Imag., IEEE Trans on* 17.1 (1998).

[14] 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).

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

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

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

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

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

[20] G. Lemaitre et al. "Normalization of T2W-MRI Prostate Images using Rician a priori". In: *SPIE Medical Imaging*. 2016, pp. 978529–978529.

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

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. Previous segmentation methods only used $T_2$-W-MRI modality and sometimes ADC map. **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 been extensively used in the field of medical imaging.

**Registration** In multi-parametric MRI, the data are collected in a sequential manner, involving a possible misalignment between the different modalities. Mitra *et al.* developed an automatic multi-modal non-rigid registration method[22], 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 Ultra-Sound (US) prostate images; **therefore, we will extend this method to align our multi-parametric MRI dataset.**

**Detection and assessment** Up to now, CAD developed systems have solely focused on the detection of prostate cancers, omitting a real assessment of the lesion aggressiveness. The detection of cancers is commonly performed using machine learning classifiers, designing frameworks relying 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 research carried out in each of this stage for the development of CAD for prostate cancer[23]. 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 a multitude of low- and high-level visual features, inspired by computer vision or human perception. Deep-learning has been recently shown to be one of the most successful machine learning techniques in broad types of classification tasks. CNN has the ability to generate automatically low- and high-level visual features in the network itself[24] by only supplying the raw data as inputs. Additionally, CNN might be considered as a good candidate to automatically generate large number of features, which can be later analyzed. 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 and validate the classifier using Receiver Operating Characteristic analysis. 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 as the basis for radiomics applied to prostate cancer.**

**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 on 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.**

### 1.1.3 Originality and innovative aspects of the research programs

In response to the urgent needs that the medical community is facing, the principal investigators seek to address the grand challenge in the **early detection and accurate assessment** of prostate cancer by (i) developing an advanced CAD system based on novel image analysis and data mining techniques and **PI-RADS** scores, and (ii) evaluating and validating it in the clinical practise. Mining imaging features in a non-invasive and cost-effective way is known as **radiomics**. The central premise this study is that these imaging features quantify phenotypic characteristics of the entire tumour and reflect the underlying gene and protein expression patterns. **Correct decoding of the radiomics signature of prostate cancer in multi-parametric MRI may allow**

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

[23] Lemaître et al., "Computer-Aided Detection and Diagnosis for Prostate Cancer based on mono and multi-parametric MRI: A review".

[24] M. D. Zeiler and R. Fergus. "Visualizing and Understanding Convolutional Networks". In: *CoRR* (2013).

**differentiation between lethal and non lethal prostate cancers in a non invasive manner at the time of detection.** This project will revolutionize prostate cancer screening by increasing its efficacy and decreasing negative side effects. PREDICATE will serve as a blueprint for screening and diagnosis of other cancers.

### 1.2 Quality and appropriateness of the training and of the two way transfer of knowledge between the researcher and the host

The main objective of the present project is to establish a mutually beneficial partnership between the host institute, the Florida State University (FSU), 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.

At the start of his training in FSU, G. Lemaître will be required to attend an **orientation session hosted by the Office of Postdoctoral Affairs (OPDA)**, which will provide information on postdoctoral policies, campus resources (e.g., libraries, computing facilities, grants office), and coursework, teaching, and funding opportunities. FSU currently offers a **postdoctoral seminar series** at which postdocs can present and receive feedback on their research, as well as courses in pedagogy, grants management, organizational behavior, and the structure of colleges and universities. FSU also has several certificate programs aimed at providing additional training to postdocs. For example, the **Postdoctoral Certificate Program in Research** offers coursework in research ethics, mentoring, and becoming an independent investigator, as well as traditional journal club and research training experiences. FSU has an **biannual Industry Day** where medical companies present their research and PhD students and postdocs as well and new research lines can be exchanged and established. The host's department has two visiting professors in radiology, Prof. K. Pinker-Domenig and M. Lobbes, specialized in prostate research who have strong connections to **General Electric, Philips, and Siemens**, which will help the fellow in the development of adequate CAD solution for clinicians. The close proximity of the **Lee-Moffitt-Cancer Center**, the biggest in the Southeast of US, and the strong ties to **MD Anderson** ensure an additional link to the cutting edge clinical research in prostate cancer. OPDA also regularly hosts career development seminars, to which the fellow will participate, on topics such as grant writing, lab management, research ethics, networking and interviewing, and teaching, and it has staff experienced at providing career advising suited to biomedical science researchers.

At both FSU and UdG, G. Lemaiître will participate actively in weekly group meetings discussing current literature, grant applications, manuscripts, and programming/algorithmic problems. Additionally, G. Lemaître will mentor PhD students together with Prof. A. Meyer-Baese and Dr. R. Martí. Furthermore, they will transfer to the fellow additional skills which they gain during their research years such as: algorithm implementation; mathematical modelling; ability to attract funding; expertise as editor of books and journal special issues; and student tutoring, curriculum development, and doctoral committee chair. Prof. A. Meyer-Baese will also share her expertise in clinical domain: patient management; understanding cutting-edge medical methods and techniques; collaborating with physicians; radiological sources and MR images management; database management, storage and processing.

In the outgoing phase, it should be emphasize that 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 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.

Finally, G. Lemaître is the perfect candidate for the propose challenge related to the transfer of knowledge between two international institutions as UdG and FSU: although G. lemaître is a junior scientist, he successfully tackled the challenge of working interdisciplinary with two research groups located in two different countries during his joint PhD at UdG and Université de Bourgogne, to which he successfully met as his research records show. Furthermore, he already proved is competence to perform delocalized research has shown by his enrolment in the open-source software community, by collaborating with researchers from different institutions[25]. Additionally to the knowledge gain during his PhD, he will be able to apply his knowledge in technology transfer in medical care acquired during MSc in Business Innovation and Technology Management.

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 integration in the team/institution

**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. Prof. Meyer-Baese's 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.

Dr. R. Martí obtained his PhD in 2002 in mammographic image analysis from the University of East Anglia, UK. He is currently an assistant professor of ViCOROB. His main research interests are in the field of medical image analysis, specially focusing on feature extraction, pattern-recognition and image registration and its application to mammographic and prostate image analysis and CAD system. He has co-authored more than 70 international peer-reviewed papers including journals, conferences and book chapters. From 1999, he has participated as a researcher or principal investigator in various research projects funded by the Spanish and Catalan Governments and EPSRC (UK) with a total funding over 700,000 €. He directed an EU FP7 project as a partner (ASSURE project, 355,290 € for UdG) and have also directed R&D contracts with companies (over 50,000 €). He is currently directing the national Spanish project (SMARTER, 114,440 €) which is related to the development of smart image analysis tool for the detection of breast cancer. Furthermore, he has been successively involved in the supervision of 8 PhD students in the last 5 years showing his outstanding ability in research mentoring, publishing around 30 high-impact peer-reviewed journals and 80 international recognized conferences. He will be involved in supervising the research on medical imaging aspects with special emphasis on cancer lesion detection tasks and software development. He will establish during the whole project a strong collaboration with A. Meyer-Baese ensuring that research synergies between the host and beneficiary are properly carried out. His expertise complements A. Meyer-Baese's and the fellow can profit from this constellation.

**Hosting arrangements**

Prof. A. Meyer-Baese and Dr. R. 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. At the start of the project, the fellow, the scientist in charge and the host institutions — UdG and FSU represented by the Research & Technology Transfer Office (OITT) and the OPDA — will sign an *Agreement* (as annex to the employment contract), ensuring that the terms of the Grant Agreement will be complied as regards to rights and obligations of the intellectual property resulting from the project, the payments, reports, and deliverables and corresponding deadlines, publications, and communications. Additionally, a personal *Career Development* plan will be agreed with the scientist in charge, the fellow, and the host institutions through OPDA and will be revised annually. G. 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,

[25] `https://github.com/scikit-learn-contrib/imbalanced-learn`

he will keep records at both institutions FSU and UdG, 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 is part of the *Technological Innovation Network Centre* (TECNIO) recognised by the Catalan Government which allows their researchers to advance their career in an entrepreneurial environment and to be more effective with their managerial skills. Indeed, they will gain new skills: (i) teamwork, (ii) personal development, (iii) project management, and (iv) entrepreneurship. Additionally, the European R&D Programs Unit at the OITT at the host institution UdG will offer assistance and support with all the administrative, legal and financial aspects related to the management and execution of the project, including the financial reporting, according to the terms established in the Grant Agreement.

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

G. Lemaître has demonstrated to be a young and very talented researcher of a highly promising career in biomedical research. He demonstrated a highly independent research profile at the early PhD level stage. He acquired a very in-depth knowledge in the new and challenging area of prostate cancer research and wrote the first state-of-the-art journal paper in CAD systems in multi-parametric MRI. He became aware of the lacking accurate diagnostic tools in the clinical practise and developed the desire to advance current CAD systems and especially develop in prostate cancer research a reliable diagnostic tool. During his PhD, he has developed general pattern recognition and machine learning approaches which have been deployed to a large field of application in medical imaging: (i) detection of prostate cancer in multi-parametric MRI, (ii) detection of retinal diseases in Optical Coherence Tomography images, (iii) detection of melanoma in dermoscopic images, and (iv) breast cancer detection in MRI images and US images. Furthermore, he has gained knowledge in the business-related aspects of CAD system for prostate system and technology valorization, as shown by his recently published Master thesis. His knowledge about the scientific- and business-related aspects of prostate CAD system, together with the career development plan as part of the fellowship, will allow him to become an attractive candidate for fund and grant rising within his working institution. **The current proposal could lead to the development of the first commercial CAD system in Europe.** This excellent and unique opportunity will allow the fellow to re-enforce his entrepreneurial skill with the help of OITT.

## 2 IMPACT

### 2.1 Enhancing the potential and future career prospects of the researcher

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 “2020 Vision for the European Research Area”, 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 radiologist’s 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 “computer-aided display”-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 and will be also applicable in other disciplines such as neuroscience or study of neurodegenerative diseases since the engineering mechanisms are the same. The system will enable the development of unique prostate cancer biomarkers unknown before through improved quantitative evaluation methods and data mining methods including deep-learning, that will pave the pathway to personalized management for future patients diagnosed with early-stage prostate cancer, leading to reduced cost in prostate cancer screening by ultimately reducing the number of unnecessary biopsies.

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 multi-parametric MRI 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 Quality of the proposed measures to communicate the action activities to different target audiences

**Communication and public engagement strategy of the action** The topic and potential results of this project are important for the general public. G. Lemaître 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 high-school students for interdisciplinary research and for the new direction scientific computing as well as publishing blog post to popularize the pattern recognition and medical aspects of his research.

**Dissemination of the research results:** The scientific community will clearly benefit from the PREDICATE project through the publication of results and methods in high impact and open access journals to accelerate dissemination, uptake of results and enable possible exploitation. The project findings will be carefully analyzed, with the support of the host institution. Those not considered to be patented, exploited commercially and transferred, will be made available to the scientific community by participating in high-impact peer-reviewed journal articles and conference. Research results will be shared to the research and clinician communities by reporting results in adequate support: pattern recognition, machine learning, and computer science aspects will be: (i) reported in high-impact journals such as Medical Image Analysis, IEEE Transactions on Medical Imaging, Pattern Recognition, Computer Vision and Image Understanding, or Pattern Recognition Letters and (ii) disseminated in recognized conference such as MICCAI, IEEE ISBI, SPIE Medical Imaging, IEEE EMBC, IEEE ICIP, or ICPR. However, clinical findings linked to the use of the proposed CAD system, with the partnership of clinicians will be reported in journals such as Clinical Oncology, Radiology, European Radiology, Investigative Radiology, or Medical Physics, and in conferences such as the ECR, RSNA, or ISMRM. For the publication of scientific papers it will be followed the institutional policy of UdG on "Open Access to scientific information and communication" approved on December 2011 and implemented starting with 2012. Therefore, the scientific publications will be either included in a institutional repository DUGi (http://dugi.udg.edu) which is compliant with OpenAIRE (https://www.openaire.eu/) or published in scientific journals with supporting "Open Access". Furthermore, pre-print version will be made available on arXiv and Zenodo platform[26]. Additionally, G. Lemaître will create a project home page for the software (C2) and report findings, publications, and access to research data by using the Zenodo platform, as previously done for his scientific research[27]. Before publication, research data will be anonymized and deidentified. Furthermore, coverage of essential results will be pursued on community internet sites for medical imaging professionals, such as MedicalPhysicsWeb and AuntMinnie.

**Exploitation of results and intellectual property:** Host institutions, hereby FSU and UdG, and the beneficiary will be required to bring in existing background knowledge and provide transparent access to other partners for the successful execution of the project. Prior to the start of the project and signing the *Grant Agreement*, the different parties will draw up a *Partnership Agreement*. *Partnership Agreement* will specify the background brought into the project per partner and lay down rules for collaboration and matters regarding the usage of back- and foreground. All project participants are expected to enter the *Partnership Agreement* in order to ensure confidentiality and facilitate knowledge transfer.

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 in conjunction with the OITT and the technology transfer office at FSU 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. Protecting intellectual property generated within PREDICATE will be essential for securing the technological leadership of the participating institutions. In order to ensure that valuable IP is identified and appropriately protected at an early stage, all partners will review all scientific output from their respective WPs and seek IP protection for the corresponding results if deemed appropriate. To allow the proper exploitation of Foreground knowledge that will require the involvement of larger industrial parties, the partners will contact third-party companies. If considered appropriate, additional collaborators will be approached by the project members during the course of the project. The expertise of the participating academic partners, and the contacts that are already in place, it will be highly feasible to properly exploit the knowledge and the results generated within PREDICATE. The exploitation of results will be based on the interaction with the OITT at the UdG in order to define a strategy for a successful deployment of the developed CAD system (C3).

# 3 QUALITY AND EFFICIENCY OF THE IMPLEMENTATION

## 3.1 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).

[26] https://zenodo.org/ - funded by CERN/OpenAIRE/EU H2020
[27] http://i2cvb.github.io/

**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).

The following deliverables (Dx) will be released during the project: **D1.1** Multi-parametric MRI database and report with dataset presentation and online availability of the dataset; **D1.2** Deadline December 2017 — Grand-Challenge submission at the conference MICCAI 2018, "Prostate detection and grading using multi-parametric MRI"; **D2.1** Deadline October 2017 — Paper sbumission at the conference ISBI 2018, "Empirical evaluation of bias field correction methods for multi-parametric MRI" & "Empirical evaluation of noise reduction methods for multi-parametric MRI"; **D2.2** Deadline March 2018 — Paper submission at the conference MICCAI 2018, "Normalisation techniques for multi-parametric MRI"; **D2.3** Deadline April 2018 — Paper submission to a peer-review journal, "Pre-processing tools for multi-parametric MRI"; **D2.4** Software toolbox for multi-parametric MRI images pre-processing; **D3.1** Deadline September 2018 — Submission to PROMISE12 challenge of results using only $T_2$-W-MRI; **D3.2** Deadline October 2018 — Paper submission to peer-review journal *Medical Image Analysis*, "Zonal segmentation of the prostate using deep-learning and multi-parametric MRI"; **D3.3** Software toolbox for multi-parametric MRI images segmentation; **D4.1** Deadline August 2019 — Paper submission at the conference SPIE Medical Imaging 2019, "Prostate registration using multi-parametric MRI and spline-based non-linear diffeomorphism"; **D4.2** Software toolbox for multi-parametric MRI images registration; **D5.1** Deadline January 2020 — Paper submission to peer-review journal *IEEE Transactions on Medical Imaging*, "Prostate cancer detection and assessment using deep-learning and multi-parametric MRI"; **D5.2** Software toolbox for multi-parametric MRI images classification; **D6.1** Deadline March 2020 — Paper submission to peer-review journal *Journal of Magnetic Resonance Imaging*, "Evaluation of a prostate CAD systems using PI-RADS". **D6.2** Software toolbox for PI-RADS grading.

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

**M1.1** Check availability multi-parametric MRI dataset; **M1.2** Check availability of ground-truth and anonymization as well as deidentification of the multi-parametric MRI dataset; **M2.1** Implementation and results of pre-processing tools for multi-parametric MRI; **M3.1** Implementation of state-of-the-art segmentation methods; **M3.2** Implementation and results of segmentation for multi-parametric prostate MRI; **M4.1** Implementation of state-of-the-art registration methods; **M4.2** Implementation and results of registration for multi-parametric prostate MRI; **M5.1** Implementation of hand-crafted features for classification of prostate cancer; **M5.2** Implementation and results of deep-learning based classification for prostate cancer detection; **M6.1** Complete development of the framework.

### 3.2 Appropriateness of the allocation of tasks and resources

Describe how the work planning and the resources mobilised will ensure that the research and training objectives will be reached.

Explain why the amount of person-months is appropriate in relation to the activities proposed.

### 3.3 Appropriateness of the management structure and procedures, including quality management and risk management

This fellowship will provide the applicant with the generous and unique financial opportunity to accomplish the realization of the first prototype of CAD for prostate cancer detection. He is fully aware of the goal of this ambitious and interdisciplinary project. It is very important for him to determine more accurately whether or not the project is on schedule. He will pay special attention to the most important conferences and special issues deadlines in the field (see Sect. 3 for further information). They will be used as milestones to monitor progress and also as an opportunity to disseminate and share the results of the work with other cancer experts. A special budget will be allocated for them. Increased attention will also be paid to the submission of international journal papers in journals with a high reputation in the field.

The previous experience of the applicant in applying his developed machine learning approaches to research lines ranging from prostate, brain and skin cancer to retinal diseases, and the collective endeavor of all involved scientists and their research groups along with the intensive experience of the hosts institutions in managing projects, are indicative of the feasibility of this project. Nevertheless, G. Lemaître is well aware of the importance of developing a contingency plan to minimize the risks and present a mitigation strategy to surmount the possible issues: **Risk 1(R1)** Potential problems: Insufficient number of cases. Probability: low. Alternative strategies: Consult with major cancer centers in US and Spain. Contingency plan: Meeting and consulting with prostate cancer specialists at the Lee-Moffitt Center in Tampa, Florida; **Risk 2 (R2)** Potential problems: Insufficient pre-processing results. Probability: medium. Alternative strategies: Joint segmentation and registration implementation based on optical flow and active contour model. Contingency plan: Meeting and consulting with researcher and image registration expert Joachim Weickert, Saarland University (Germany); **Risk 3 (R3)** Potential problems: Non-representative feature extraction and poor classification results. Probability: Very low. Alternative strategies and contingency plan: apply dynamic texture techniques for spatio-temporal feature extraction and employ gray-level run-length matrix (GRRL) and gray level intensity size zone matrix (GLISZ). This methodology has been a successful approach in different applications, and the applicant has the associated theoretical knowledge. Consider selecting Random Forest Trees as alternative classifiers. Meeting and consulting with data mining expert, Claudia Plant, head of the scientific computing research group in the Helmholtz Zentrum in Munich; **Risk 4 (R4)** Description: Insufficient number of companies interested in the software. Probability: Low. Contingency plan: (i) Seek and arrange meetings with companies and the industry sector to show beta-version of the software at early stage. (ii) Schedule the meetings efficiently by not waiting until the last stage of the fellowship. (iii) Invite companies to monitor the development of the software. Thus, they could make recommendations in terms of interface and practical operation under an end user perspective. (iv) Request for support from OITT at the UdG, a service devoted to give advice on knowledge and technology transfer between university and industry.

### 3.4 Appropriateness of the institutional environment (infrastructure)

**Florida State University** According to Shaingai's ARWUA, FSU is between the 200 best universities worldwide. Its research infrastructure includes one of the largest high magnetic field laboratory worldwide, closely related to this project. (1) Institutional resources: One 7T, two 3 T and two high-end 1.5 T MR scanners for image acquisition, (2) Clinical resources: Excellent facilities and experience in scientific studies aiming at the evaluation of CAD methods for MR mammography, counting on the collaboration of Prof. Adrian Barbu, a computer scientist with expertise in CAD design. This aspect can be essential for documenting the real-world impact of research progress in the project w.r.t. practical health care. (3) Workstation facilities: office space equipped with a desktop computer and network connections. In addition, designated visitor offices are available. The DSC also manages approximately 30 servers for core network services using primarily generic Intel-compatible servers running CENTOS. Special staff support is offered for publications and graphics.

**ViCOROB** ViCOROB is a research institute specialized in computer vision and robotics at UdG. The laboratories of ViCOROB are well-equipped with computers, servers, and specific software required for processing clinically data acquired. The Image Analysis Lab has recently been equipped with 2 high-performance servers (featuring 4 quad-core processors and 128 GB of RAM), a Totoku MS31i2 Diagnostic Displays system, and access to the use of CESCA facilities (the Supercomputing research center in Barcelona) which offers supercomputing shared-memory and distributed-memory machines suitable when dealing with such huge amount of data. Furthermore, the fellow will have access to a wide range of scientific journals and books via institution authentification.

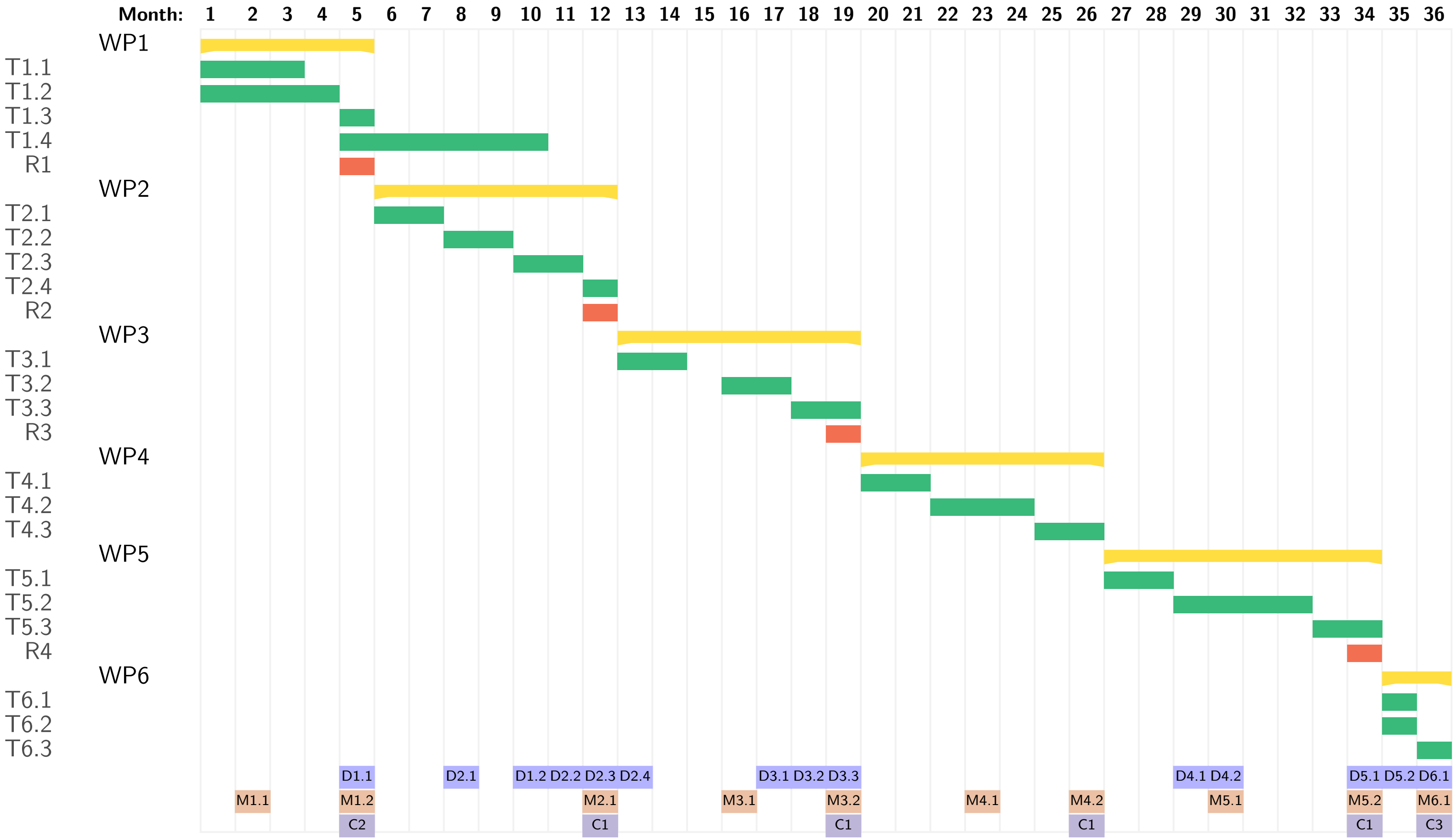


Figure 1: Gantt Chart of the proposal.

# 4 CV OF THE EXPERIENCED RESEARCHER

## 4.1 PERSONAL INFORMATION

*Name*: Guillaume Lemaître
*Date of birth*: 27$^{th}$ April 1988, 28 years old
*Personal website*: `https://sites.google.com/site/glemaitre58`

## 4.2 EDUCATION

| | |
|---|---|
| **07/2012 — 12/2016** | **Co-joint PhD in Medical Imaging**<br>*"Computer Aided Diagnosis system for prostatic biopsy guidance and follow-up fusing multi-modal imaging"*<br>Supervised by Dr. R. Martí, Prof. F. Mériaudeau, Dr. J. Freixenet, and Dr. P. M. Walker<br>ViCOROB, Universitat de Girona — LE2I, Université de Bourgogne |
| **09/2012 — 09/2014** | **Master in Business Innovation and Technology Management**<br>*"Valorisation of computerized technology in the health care sector"*<br>Supervised by Dr. A. Bikfalvi and Dr. J. Llach<br>Universitat de Girona |
| **09/2009 — 06/2011** | **Master of Excellence Erasmus Mundus in Vision and Robotics**<br>*"Absolute Quantification in 1H MRSI of the Prostate at 3.0 T"*<br>Supervised by Dr. P. M. Walker<br>Université de Bourgogne, Universitat de Girona, Heriot-Watt University |
| **09/2016 — 09/2009** | **Bachelor Eng. Electronic, Signal, and Image**<br>Université de Bourgogne |

## 4.3 WORKING EXPERIENCE

| | |
|---|---|
| **03/2015 — 03/2016** | **Assistant professor (ATER)**<br>184 hours of lecturing in databases, pattern recognition and machine learning, programming, image processing<br>Université de Bourgogne |
| **06/2011 — 06/2012** | **R&D researcher**<br>Barcelona Digital — ViCOROB, Universitat de Girona |

### 4.4 FELLOWSHIPS

| | |
|---|---|
| 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 |

### 4.5 AWARDS

| | |
|---|---|
| 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 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)

### 4.7 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

### 4.8 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/`)

### 4.9 SUPERVISION

- Supervision of 1 MSc. student during is master thesis in computer vision
- Supervision of 3 BSc. and MSc. students during their summer internships

### 4.10 PUBLICATIONS

*Peer-Review Journals Papers:* (8)

1. **K. Alsaih, G. Lemaitre, J. Massich, M. Rastgoo, D. Sidibe, and F. Meriaudeau**, "Machine Learning Techniques for DME Classification on SD-OCT images", *BioMedical Engineering OnLine*, Submitted.
2. **G. Lemaitre, R. Marti, M. Rastgoo, J. Massich, F. Freixenet, J. C. Vilanova, and F. Meriaudeau**, "Automatic prostate cancer detection through DCE-MRI images: all you need is a good normalization", *Medical Image Analysis*, Submitted.
3. **I. P. Houben, P. Van de Voorde, C. R. Jeukens, J. E. Wildberger, G. Lemaitre, I. A. Illan, A. Meyer-Baese, L. F. Kooreman, M. L. Smidt, and M. B. Lobbes**, "Contrast-enhanced spectral mammography as work-up tool in patients recalled from breast cancer screening: risks versus benefits", *European Radiology*, Submitted.
4. **G. Lemaitre, F. Nogueira, and C. Aridas**, "Imbalanced-learn: A Python Toolbox to Tackle the Curse of Imbalanced Datasets in Machine Learning", *Journal of Machine Learning Research*, Submitted.
5. **D. Sidibe, S. Sankar, G. Lemaitre, M. Rastgoo, J. Massich, C. Y. Cheung, G. S. Tan, D. Milea, E. Lamoureux, T. Y. Wong, and F. Meriaudeau**, "An anomaly detection approach for the identification of DME patients using spectral domain optical coherence tomography images", *Computer Methods and Programs in Biomedicine*, Submitted.
6. **G. Lemaitre, M. Rastgoo, J. Massich, C. Y. Cheung, T. Y. Wong, E. Lamoureux, D. Milea, F. Meriaudeau, and D. Sidibe**, "Classification of SD-OCT Volumes using Local Binary Patterns: Experimental Validation for DME detection", *Journal of Ophthalmology*, vol. 2016, Mai 2016.
7. **M. Belkacemi, C. Stolz, A. Mathieu, G. Lemaitre, J. Massich, and O. Aubreton**, "Non Destructive Testing based on a Scanning-From-Heating approach: Application to non-through Defect Detection and Fiber Orientation Assessment", *Journal of Electronic Imaging*, vol. 24(6), pp 1-8, Nov/Dec 2015.
8. **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.

*Peer-Review International Conferences Papers:* (18)

1. **J. Massich, M. Rastgoo, G. Lemaitre, C. Cheung, T. Y. Wong, D. Sidibe, and F. Meriaudeau**, "Classifying DME vs normal SD-OCT volumes: A review", *23$^{rd}$ International Conference on Pattern Recognition (ICPR) 2016*. Cancun: Mexico (December 2016).
2. **K. Alsaih, G. Lemaitre, J. Massich, M. Rastgoo, D. Sidibe, T. Y. Wong, E. Lamoureux, D. Milea, C. Leung, and F. Meriaudeau**, "Classification of SD-OCT volumes with multi-pyramids, LBP and HoG descriptors: Application to DME detection", *38$^{th}$ International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2016*. Orlando: USA (August 2016).

3. **A. Pampouchidou, K. Marias, M. Tsiknakis, P. Simos, F. Yang, G. Lemaitre, and F. Meriaudeau**, "Video-based depression detection using local curvelet binary patterns in pairwise orthogonal planes", *38th International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2016*. Orlando: USA (August 2016).

4. **S. Hoffmann, M. Lobbes, I. Houben, K. Pinker-Domenig, G. Wengert, B. Burgeth, U. Meyer-Baese, G. Lemaitre, and A. Meyer-Baese**, "Computer-aided diagnosis of diagnostically challenging lesions in breast MRI: a comparison between a radiomics and a feature-selective approach", *SPIE Commercial+ Scientific Sensing and Imaging*. Baltimore: USA (July 2016).

5. **M. Belkacemi, C. Stolz, A. Mathieu, G. Lemaitre, and O. Aubreton**, "A combined three-dimensional digitisation and subsurface defect detection data using active infrared thermography", *13th Quantitative Infrared Thermography Conference (QIRT)*. Gdansk: Poland (July 2016).

6. **M. Belkacemi, J. Massich, G. Lemaitre, C. Stolz, V. Daval, G. Pot, O. Aubreton, R. Collet, and F. Meriaudeau**, "Wood fiber orientation assessment based on punctual laser beam excitation: A preliminary study", *13th Quantitative Infrared Thermography Conference (QIRT)*. Gdansk: Poland (July 2016).

7. **M. Rastgoo, G. Lemaitre, J. Massich, O. Morel, F. Marzani, R. Garcia, and F. Meriaudeau**, "Study of Data Imbalancing for Melanoma Classification", *3rd International Conference on BIOIMAGING*. Rome: Italy (February 2016).

8. **G. Lemaitre, M. Rastgoo, J. Massich, J. C. Vilanova, P. M. Walker, J. Freixenet, A. Meyer-Baese, F. Meriaudeau, and R. Marti**, "Normalization of T2W-MRI prostate images using Rician a priori", *SPIE Medical Imaging 2016*. San Diego: USA (February 2016).

9. **M. Rastgoo, G. Lemaitre, O. Morel, J. Massich, F. Marzani, R. Garcia, and D. Sidibe**, "Classification of melanoma lesions using sparse coded features and random forests", *SPIE Medical Imaging 2016*. San Diego: USA (February 2016).

10. **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).

11. **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).

12. **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).

13. **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).

14. **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).

15. **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).

16. **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).

17. **G. Lemaitre, E. Vargiu, J.A. Lorenzo Fernandez, 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.

18. **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.

*Thesis:* (2)

1. **G. Lemaitre and P.M. Walker**, "Absolute Quantification in 1H MRSI of the Prostate at 3T", *Thesis for Master in Science Vision and roBOTic (ViBOT)*, 2011.

2. **G. Lemaitre, A. Bikfalvi, and J. Llach**, "Valorisation of Computerized Technology in the Health Care Sector", *Thesis for Master in Science Business Innovation and Technology Management (BITM)*, 2014.

# 5 CAPACITIES OF THE PARTICIPATING ORGANISATIONS

**Beneficiary ViCOROB research institute (Universitat de Girona)**

| | |
|---|---|
| **General Description** | ViCOROB research institute belongs to the Department d'Aquitectura i Technologia de Computadors at the Universitat de Girona, a public university in Girona since 1992. ViCOROB is a research institute specialized in computer vision and robotics at UdG. In 2013, the UdG has rewarded ViCOROB by promoting the group into a Research Institute funded by the university itself. VICOROB has been always highly motivated to solve different and challenging societal problems and succeeded to obtain outside funding for solving them. The scientific results have been disseminated not only in form of peer-reviewed articles but also to the broad public audience by participating in several media events, speeches and published material. Three spin-off companies emerged: Coronis Computing SL, AQSENSE and BonesNotes. |
| **Role and Commitment of key persons (supervisor)** | Dr. Robert Martí, PhD, is associate professor in the Image Analysis Lab within ViCOROB. His main research interests are in the field of medical image analysis, specially focusing on feature extraction, pattern-recognition and image registration and its application to mammographic and prostate image analysis and CAD system. |
| **Key Research Facilities, Infrastructure and Equipment** | The laboratories of ViCOROB are well-equipped with computers, servers, and specific software required for processing clinically data acquired. The Image Analysis Lab has recently been equipped with 2 high-performance servers (featuring 4 quad-core processors and 128 GB of RAM), a Totoku MS31i2 Diagnostic Displays system, and access to the use of CESCA facilities (the Supercomputing research center in Barcelona) which offers supercomputing shared-memory and distributed-memory machines suitable when dealing with such huge amount of data. |
| **Independent research premises?** | Yes — 2 clusters with 32 nuclei for massive and parallel computing |
| **Previous Involvement in Research and Training Programmes** | During the last 3 years, UdG has coordinated 6 individual MCA and 2 Research Networks (RESKITCHLAB and CHEMEVE). In the last decade, the UdG has participated in more than 160 European projects. The following most noticeable research projects related to medical imaging have been developed at ViCOROB: Proscan (Help with location of prostate cancer) and M3CAD (Multi-modality and Multi-view Mammographic Computer Aided Diagnosis System) |
| **Current involvement in Research and Training Programmes** | UdG is currently coordinating an ITN action, SANITAS, and is participating as a full partner in ENDURE and ROBOACADEMY. Also, UdG is coordinating 3 IRSES actions (CANIOC, CLIMSEAS, and IREBD) and participating in one IAPP (PEP2BRAIN). Moreover, it is the main beneficiary of 8 individual Marie Curie actions. UdG is coordinating two Starting Grant projects (ERC) one Proof of Concept (ERC) and one COST action, among other participation, both as a partner and coordinator, in R&D European and national funded projects. Current projects under development in ViCOROB include: ASSURE (Adapting Breast Cancer Screening Strategy Using Personalised Risk Estimation), IA-BioBreast (temporal analysis and automatic detection of lesions in multimodal images). Furthermore, ViCOROB organises the Erasmus Mundus Master in Computer Vision and Robotics (Vibot) and the Erasmus+ Joint Master in Medical Imaging and Applications (MaIA). |
| **Relevant Publications and/or research/innovation products** | • **R. Martí et al.**, "Computer-Aided Detection and Diagnosis for prostate cancer based on mono and multi-parametric MRI: A review", *Computers in Biology and Medicine*, vol. 60, pp 8 - 31, 2015). [IF 1.475, Q2(41/85) B]<br>• **R. Martí et al.**, "A supervised learning framework of statistical shape and probability priors for automatic prostate segmentation in ultrasound images", *Medical Image Analyis*, 7(6), pp 587-600, 2013. [IF 4.087, Q1(7/115) CSAI]<br>• **R. Martí et al.**, "A spline-based diffeomorphism for prostate multimodal registration", *Medical Image Analyis*, 16(6), pp 1259-1279. 2012. [IF 4.087, Q1(7/115) CSAI]<br>• **R. Martí et al.**, "A survey of prostate segmentation methodologies in ultrasound, magnetic resonance, and computed tomography images", *Computer Methods and Programs in Biomedicine*, 108(1), pp 262-287. 2012. [IF 1.555, Q1(21/100) CSTM]<br>• **R. Martí et al.**, "Statistical shape and texture model of quadrature phase information for prostate segmentation", *International Journal of Computer Assisted Radiology and Surgery*, 7(1), pp 43-55, 2012. [IF 1.364, Q3(76/120) RNMMI] |

**Partner Organisation Florida State University**

| | |
|---|---|
| **General Description** | Florida State University (FSU) |
| **Key Persons and Expertise (supervisor)** | Anke Meyer-Baese, PhD, Professor at the Department of Scientific Computing in the FSU |
| **Key Research facilities, infrastructure and equipment** | National high magnetic field laboratory. FSU research foundation, multi-parametric MRI, MR scanners. Clinical resources, clusters for intensive computing. |
| **Previous and Current Involvement in Research and Training Programmes** | Prof. Anke Meyer-Baese led over twenty funded research projects (NSF, NIH) in her field with a total volume of six million dollars. Currently, she directs among others, a research project on CAD for breast cancer with NIH funding. Her interaction with students is exemplary: she directed two research professors, six post-docs, over 21 PhD students graduated and 6 current PhD students, achieving teaching evaluations among the best at FSU, and attaining one of the highest students' retentions. Many of her former doctoral and postdoctoral students have obtained positions in academia. |
| **Relevant Publications and/or research/innovation product** | • **A. Meyer-Baese, V. J. Schmid**, "Pattern Recognition and Signal Analysis in Medical Imaging", *Elsevier*<br>• **A. Meyer-Baese et al.**, "Global exponential stability of competitive neural networks with different time scales", *Neural Networks, IEEE Transactions on*, 14(3), pp 716-719<br>• **A. Meyer-Baese et al.**, "Comparison of two exploratory data analysis methods for fMRI: unsupervised clustering versus independent component analysis", *Information Technology in Biomedicine, IEEE Transactions on*, 9(3), pp 387-398 |

# 6 ETHICS ASPECTS

According to the article 8 of the Charter of Fundamental Rights of the European Union: “Everyone has the right to the protection of personal data concerning him or her”. Concerning this fact, the present project has a potentially sensitive issue, as the collected data comes from real patients suffering prostate cancer. It is important to stress that the participants of the database are fully informed of the aims and uses of the MRI images, and a signature is required for consent. But more importantly, *no personal data is used or available* in this project, as every image is thoroughly anonymized before the data is transferred to processing for research.

# 7 LETTER OF COMMITMENT OF PARTNER ORGANISATION

FLORIDA STATE UNIVERSITY | *The* FSU RESEARCH FOUNDATION
2000 Levy Avenue, Suite 351
Tallahassee, Florida 32310
850.644.8650 • Fax 850.644.3658

September 9, 2015

The Marie Sklodowska-Curie Actions
in Horizon 2020

RE: H2020-MSCA-IF-2015
Project: "Deep-learning based multi-parametric MRI computer-aided diagnosis for prostate cancer (ProDeepCAD)"
Principal Investigator: Guillaume Lemaitre

This letter is to advise that the above-referenced project will be administered by the Florida State University Research Foundation, Inc., a direct support organization of Florida State University. The Research Foundation is a non-profit, educational corporation with an IRS 501(c) (3) designation.

Checks should be made payable to the FSU Research Foundation Inc. and sent to the following address:

The Florida State University Research Foundation, Inc.
2000 Levy Avenue, Suite 351
Tallahassee, FL 32310

Questions concerning administrative matters should be directed to Cathy Flynn, Grants Compliance Analyst, at (850) 644-2130 or via email at cflynn@fsu.edu.

Sincerely,

Cathy Flynn

Cathy Flynn
Grant Compliance Analyst
FSU Research Foundation, Inc.
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2000 Levy Avenue
Tallahassee, Florida 32310
850/644-2130
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# ENDPAGE

MARIE SKŁODOWSKA-CURIE ACTIONS

**Individual Fellowships (IF)**
**Call: H2020-MSCA-IF-2016**

PART B

"PREDICATE"

"comPuteR-aidEd diagnosis using Deep learning and radIomiCs for prostATE cancer"

**This proposal is to be evaluated as:**

**[Standard GF]**