START PAGE

MARIE SKŁODOWSKA-CURIE ACTIONS

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

PART B

"proposal ACRONIM"

This proposal is to be evaluated as:

Standard EF

TABLE OF CONTENTS

0 LIST OF PARTICIPANTS 3

1 SUMMARY 4

2 EXCELLENCE 5

3 IMPACT 8

4 IMPLEMENTATION 9

5 CV OF THE EXPERIENCED RESEARCHER 11

6 CAPACITIES OF THE PARTICIPATING ORGANISATIONS 12

ipants

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 (Vi-COROB)	Dr. Joan Martí	
Partner Organisation							
Florida State University	FSU	✓		USA	Scientific Computing	Dr. Anke Meyer-Baese	Host Outgoing phase
UDIAT - Centre Diagnòstic - Institud Universitari Parc Taulí - UAB	UDIAT		✓	Spain	Dept. of breast and gynaecological radiology	Dr. Melcior Sentís	image acquisition, expert radiologist's feedback and clinical validation

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)
UDIAT - Centre Diagnòstic - Institud Universitari Parc Taulí - UAB	Sabadell, Spain	Medical research	350	2	www.tauli.cat/udiat/	15 millions	yes	no

ummary

1 SUMMARY

Breast cancer is the leading cause of cancer deaths among females worldwide.Nevertheless, death by breast cancer are highly reduced by early treatment. Thus, to run a chance of surviving breast cancer, it is uttermost important the early detection of malignant tumors. This has motivated the establishment of Breast Screening PolicyBreast Screening Policies (BSPs) to facilitate this breast cancer detection at an early stage. Despite X-ray Digital Mammography (DM) is considered the gold standard technique for BSP, other screening techniques like Ultra-Sound (US) and Magnetic Resonance Imaging (MRI) are being investigated to overcome DM limitations due to tissue superposition which can either mimic or obscure malignant pathology, and avoid X-ray radiation all together.

From the different DM alternatives, the most promising to overcome the aforementioned limitations is MRI. However, Non-mass-like enhancing (NMLE) lesions exhibit a heterogeneous appearance in breast MRI with high variations in kinetic characteristics and typical morphological parameters, and resulting in a lower reported specificity (69%) and sensitivity (75%) than mass-enhancing lesions. Combinations of morphological and temporal BI-RADS descriptors have proven to be insufficient to aid in the automated differential diagnosis of these lesions in Contrast-Enhanced MRI (CE-MRI). Newest clinical studies suggest that T2-weighted image sequences and Diffusion-Weighted Imaging (DWI) may provide additional specificity.

The aim of this fellowship is to translate these findings into a new Computer Aided Diagnosis (CAD) system. Our hypothesis is that a combination of novel descriptors extracted from multiparametric breast MRI has the potential to substantially improve the diagnostic value of the detection and classification of NMLEs.

This first and novel CAD system in multiparametric breast MRI will reduce false positive recalls and thus increase specificity. A reduction in recall of only 5% would already be clinically relevant, considering the costs and patient discomfort associated with second look ultrasound examinations and biopsies.

The experience of ViCOROB in Breast-CAD, the preliminary studies in multispectral MRI carried out in FSU at the scientific computing division, and the clinical support from UDIAT guarantee the success of this project as well as the correct transfer of knowledge from the laboratory to the clinical site. It is also planned to commercialise the output CAD tool to clinical sites through existing medical imaging companies or via a spin-off.

The specific aims of this proposed project are to:

Aim 1:

Develop an image regularization framework for multiparametric breast MRI that includes a novel simultaneous elastic registration and segmentation algorithm. ***Impact:*** *This methodology is fundamental for a correct image regularization and dramatically impacts the correct subsequent detection and diagnosis of NMLE lesions.*

Aim 2:

Develop and apply novel image descriptors for characterizing lesion heterogeneity in T2-weighted MRI and DWI. ***Impact:*** *A combination of these image descriptors may increase the diagnostic value of existing CAD systems in breast MRI.*

Aim 3:

Develop spatio-temporal feature extraction algorithms in CE-MRI. ***Impact:*** *These algorithms from Aim 2 and 3 will facilitate the categorization of NMLEs lesions.*

Aim 4:

Evaluation of the CAD system in terms of performance compared to trained readers and gold standard. ***Impact:*** *Radiologists can benefit from this system by reduced interobserver variation and improved interpretation of breast MRIs for the presence or absence of malignant non-mass-like enhancing lesions.*

llence
uality

2 EXCELLENCE

2.1 Quality, innovative aspects and credibility of the research

Introduction to breast cancer and multiparametric MRI Breast cancer is the leading cause of cancer deaths among females worldwide[1]. This has motivated the establishment of BSPs to facilitate breast cancer detection at an early stage. Despite X-ray DM is considered the gold standard technique for BSP, other screening techniques like US and MRI are being investigated to overcome DM limitations due to tissue superposition which can either mimic or obscure malignant pathology, and avoid X-ray radiation all together.

Though MRI is a promising alternative to DM, NMLE lesions exhibit a heterogeneous appearance in breast MRI with high variations in kinetic characteristics and typical morphological parameters.[2,3,4] Thus, diagnosis of NMLE lesions is thus far more challenging, resulting in a lower reported specificity (69%) and sensitivity (75%) than mass-enhancing lesions[5] in CE-MRI.

Malignant lesions such as Ductal Carcinoma in Situ and Inflating Lobular Carcinoma commonly exhibit a segmental or linear enhancement pattern and benign lesions such as fibrocystic changes present as well a NMLE[6]. However, a systematic classification of NMLE lesions is not in place. A classification of such lesions would be highly beneficial since they may reduce the biopsiesâĂŹ numbers. Recently, there have been new research initiatives to assess NMLE lesions using multiparametric MRI which combines T1-weighted contrast-enhanced MRI with DWI.[7,8]

It was shown that the combination of morphological, functional and molecular information offered by multiparametric MRI improves the diagnostic accuracy of breast cancer diagnosis. Another study showed that T2-weighted imaging can better represent the morphological features of small lesions[9] and combined with DWI it increased the diagnostic performance of MRI. CAD systems showed a much lower sensitivity (0.79 vs. 0.97) and specificity (0.56 vs. 0.8) for NMLE lesions compared with masses and suggested the need for more advanced algorithms for the diagnosis of NMLE.[10,11,12,13] Uniformity, and a clear set of imaging descriptors for the reporting of T2 and DWI features of NMLE is lacking. Furthermore, there is no quantitative technique for how to combine the morphological, functional and molecular information derived from multiparametric imaging.

The bottleneck that remains for providing an improved differential diagnosis of NMLE lesions and thus contribute to advancing CAD systems beyond the current level are determining descriptors that incorporate the diagnostic information from multiparametric MRI. **Our proposal to develop advanced image analysis**

[1] cancerStatistics2011
Ahmedin Jemal et al. "Global cancer statistics". In: *CA: A Cancer Journal for Clinicians* 61 (2011).

[2] rosen2007birads
Eric L Rosen et al. "BI-RADS MRI Enhancement Characteristics of Ductal Carcinoma In Situ". In: *The breast journal* 13.6 (2007), pp. 545–550.

[3] sakamoto2008categorization
Naomi Sakamoto et al. "Categorization of non-mass-like breast lesions detected by MRI". in: *Breast Cancer* 15.3 (2008), pp. 241–246.

[4] yabuuchi2010nmle
Hidetake Yabuuchi et al. "Non-mass-like enhancement on contrast-enhanced breast MR imaging: lesion characterization using combination of dynamic contrast-enhanced and diffusion-weighted MR images". In: *European journal of radiology* 75.1 (2010), e126–e132.

[5] liu2013intravoxel
Chunling Liu et al. "Intravoxel incoherent motion (IVIM) in evaluation of breast lesions: comparison with conventional DWI". in: *European journal of radiology* 82.12 (2013), e782–e789.

[6] liu2013intravoxel
Ibid.

[7] pinker2013combined
K Pinker et al. "Combined contrast-enhanced magnetic resonance and diffusion-weighted imaging reading adapted to the âĂIJBreast Imaging Reporting and Data SystemâĂİ for multiparametric 3-T imaging of breast lesions". In: *European radiology* 23.7 (2013), pp. 1791–1802.

[8] yabuuchi2010nmle
Yabuuchi et al., "Non-mass-like enhancement on contrast-enhanced breast MR imaging: lesion characterization using combination of dynamic contrast-enhanced and diffusion-weighted MR images".

[9] wu2014diffusion
Lian-Ming Wu et al. "Diffusion-weighted magnetic resonance imaging combined with T2-weighted images in the detection of small breast cancer: a single-center multi-observer study". In: *Acta Radiologica* 55.1 (2014), pp. 24–31.

[10] jansen2008dcemri
Sanaz A Jansen et al. "DCEMRI of breast lesions: Is kinetic analysis equally effective for both mass and nonmass-like enhancement?". In: *Medical physics* 35.7 (2008), pp. 3102–3109.

[11] jansen2011ductal
Sanaz A Jansen. "Ductal carcinoma in situ: detection, diagnosis, and characterization with magnetic resonance imaging". In: *Seminars in Ultrasound, CT and MRI*. vol. 32. 4. Elsevier. 2011, pp. 306–318.

[12] liu2013intravoxel
Liu et al., "Intravoxel incoherent motion (IVIM) in evaluation of breast lesions: comparison with conventional DWI".

[13] newell2010selection
Dustin Newell et al. "Selection of diagnostic features on breast MRI to differentiate between malignant and benign lesions using computer-aided diagnosis: differences in lesions presenting as mass and non-mass-like enhancement". In: *European radiology* 20.4 (2010), pp. 771–781.

algorithms to improve the differential diagnosis of the challenging NMLE lesions would provide the radiologist with a fast and accurate computational diagnosis support.

Here is missing a to state somewhere:
best career possibilities for the experiecned researcher and new collaboration opportunities for the host organization(s)

Research objectives With the aid of this fellowship, the experience in Breast-CAD of ViCOROB, the preliminary results in CE-MRI from FSU, and the clinical support from UDIAT, we aim to encode multiparametric MRI clinical findings into a new CAD with higher specificity that will reduce the costs and patient discomfort associated with second look examinations and biopsies. In order to successfully achieve this purpose, the following objectives will be pursued:

Aim 1: Develop a novel image regularization framework for NMLE lesions from multiparametric MRI.

The regularization step represents a crucial step for the subsequent feature extraction and classification since the images stem from heterogeneous sources. A standard preprocessing step is followed by a novel joint segmentation and registration algorithm. We propose a novel joint segmentation and registration algorithm based on a variational model and level set approach which incorporates spatial as well as temporal contrast-enhanced images. The multiparametric images are registered such that all segmented images will be in the same reference frame.

maybe make reference to ASURE project

Aim 2: Identifying novel descriptors such as structure tensors and texture from T2-MRI and Intravoxel Incohe

maybe MRF, to link with m thesis

The BI-RADS-based features from CE-MRI

proved to be insufficient to differentiate between malignant and benign for NMLE lesions and therefore additional descriptors from multiparametric images are needed[14]. Furthermore, the lesion heterogeneity is insufficiently described by a single ADC threshold and thus more detailed structural and functional image features have to be extracted from T2-MRI and DWI. The proposed novel descriptors include the additional information from multiparametric MRI and thus capture the structure of the breast tissue in a unique manner like no other method before.

describ BIRAD some-where?

Aim 3: Identifying novel spatio-temporal descriptors from CE-MRI as the most powerful discriminators of NM

ADC, stands for?

In the case of NMLE lesions, there is a high variance in morphological and kinetic characteristics and as a consequence a high proportion of false-positive diagnosis[15]. The automated extracted features that have been applied to lesion characterization capture either the variations in their temporal enhancement or in spatial (morphological) structures or they are global features unable to describe local information. To address this shortcoming we propose novel mathematical spatiotemporal feature descriptors such as local velocity moments, scaling index and dynamic texture derived from geometrical multiscale decomposition that are able to capture the segmental, focal, linear, regional, and diffuse, and internal enhancement patterns (homogeneous, heterogeneous, clumped, clustered ring enhancement, dendritic), and lesion heterogeneity and will compare their performance together with the features from Aim 2 regarding lesion classification.

Aim 4: Validation of the proposed system in terms of performance and direct comparison to that of the radiol

[14] pinker2013combined
Pinker et al., "Combined contrast-enhanced magnetic resonance and diffusion-weighted imaging reading adapted to the âĂIJBreast Imaging Reporting and Data SystemâĂİ for multiparametric 3-T imaging of breast lesions".

[15] liu2013intravoxel
Liu et al., "Intravoxel incoherent motion (IVIM) in evaluation of breast lesions: comparison with conventional DWI".

Statistical methods will evaluate its performance as a stand-alone system and in comparison with the radiologistâĂŹs competence. Adding novel algorithms to existing techniques will create a flexible toolbox that can be applied with minimal modifications to identifying other type of lesions or monitor response to chemotherapy.

Overview of the action The proposed 36 month fellowship will develop advanced image analysis algorithms to address the challenge of properly diagnose NMLE lesions in MRI. Multiparametric MRI information will be inserted for the first time in a new CAD system using previous experience of ViCOROB. Consequently the lesion detection in CAD systems will be improved, the false positive recalls reduced and thus a direct impact into society.

To ensure a sufficient volume of data to develop the CAD system, a database available at FSU with more than 400 patient cases of MRI-detected NMLE lesions will be used to start the project. While, the correct performance of the CAD, clinical validation and implantation, will be achieved with the support from expert radiologists from UDIAT, where 3 months secondments are planned.

The new research knowledge will be disseminated through open access journals. Finally, this feasible CAD system with potential to improve breast cancer detection will be promoted in technical exhibitions, such as European Congress of Radiology, in order to search for medical companies interested in distributing such tool in clinical sites. Alternative, the tool can be commercialised via a new spin-off created at ViCOROB, where three spin-off companies have already been created.

Research methodology and approach

Originality and innovative aspects of the research programme The proposed research aims at developing an innovative and robust CAD system for the evaluation of NMLE lesions, based on multiparametric MRI; thus increasing specificity without compromising the sensitivity of CE-MRI. Our believe is that conventional MRI acquisition protocols are unable to capture the physical properties of NMLE lesions. Therefore, rather than trying to implement a new CAD methodology to work in regular MRI as other researcher has shown, our proposal tries to stablish new MRI acquisitions protocol to build multiparametric MRI and improve the breast cancer detection through finding new bio-markers that are not identifiable when using conventional imaging and implementing them as a new CAD system.

Furthermore, the proposed CAD system not only will be developed in a research laboratory as observed in the literature, but it will go beyond and will be tested at the clinical facilities of UDIAT to create a commercialised product.

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

ansfer

How the Experienced Researcher will gain new knowledge The *Experienced Researcher, Dr. Joan Massich,* will be supervised principally by Dr. Anke Meyer-Baese and the *Dr. Massich*'s former PhD advisor, Dr. Joan Martí. However, they will have the support of the members in both teams: the Dept. of Scientific Computing at FSU, and ViCOROB institute at Universitat de Girona through regular meetings. This will open the possibility to open new collaboration between these teams in other medical fields like brain MRI or prostate cancer, which are medical areas currently being investigated by the two institutions with no collaboration.

Also, *Dr. Massich* will be involved in the supervision of research projects of the *Erasmus +* Master in MedicAl Imaging and Applications and new PhD student. *Dr. Massich*, with the supervision and guidance of Dr. Meyer-Baese and Dr. Martí will hone his research writing skills via writing grant proposals, which will also give a continuity to his research career.

http://
jointma

2.3 Quality of the supervision and the hosting arrangements

vision

to modify

Required sub-heading:

Qualifications and experience of the supervisor(s)

Information regarding the supervisor(s) must include the level of experience on the research topic proposed and document its track record of work, including the main international collaborations. Information provided should include participation in projects, publications, patents and any other relevant results. To avoid duplication, the role and profile of the supervisor(s) should only be listed in the "Capacity of the Participating Organisations" tables (see section 6 below). The text must show that the Experienced Researcher should be well integrated within the hosting organisation(s) in order that all parties gain the maximum knowledge and skills from the fellowship. The following section of the European Charter for Researchers refers specifically to career development:

Career development Employers and/or funders of researchers should draw up, preferably within the framework of their human resources management, a specific career development strategy for researchers at all stages of their career, regardless of their contractual situation, including for researchers on fixed-term contracts. It should include the availability of mentors involved in providing support and guidance for the personal and professional development of researchers, thus motivating them and contributing to reducing any insecurity in their professional future. All researchers should be made familiar with such provisions and arrangements.

turity

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

Please keep in mind that the fellowships will be awarded to the most talented researchers as shown by their ideas and their track record, where it is a fair indicator given their level of experience.

impact

3 IMPACT

cement

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

In this section, please explain the impact of the research and training on the Experienced Researcher's career. The fellowship, including any secondments in Europe should maximise the impact on the researcher's activity on European society, including the science base and/or the economy, in a manner appropriate to the research field.

3.2 Effectiveness of the proposed measures for communication and results dissemination

Required sub-headings:

Communication and public engagement strategy of the action
Dissemination of the research results
Exploitation of results and intellectual property

Concrete plans for the above must be included in the Gantt Chart. The new knowledge generated by the action should be used wherever possible to enhance the career of the researcher, to advance research, to foster innovation, and to promote the research profession to the public. The following sections of the European Charter for Researchers refer specifically to public engagement and dissemination:

Public engagement Researchers should ensure that their research activities are made known to society at large in such a way that they can be understood by non-specialists, thereby improving the public's understanding of science. Direct engagement with the public will help researchers to better understand public interest in priorities for science and technology and also the public's concerns.

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.

tation

4 IMPLEMENTATION

4.1 Overall coherence and effectiveness of the work plan

The proposal should be designed in the optimal way to achieve the desired impact. A Gantt Chart should be included in the text where the following should be listed:

- Work Packages description;
- List of major deliverables;
- List of major milestones;
- Secondments if applicable.

The schedule should be in terms of number of months elapsed from the start of the project.

4.2 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).

tution

4.3 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.

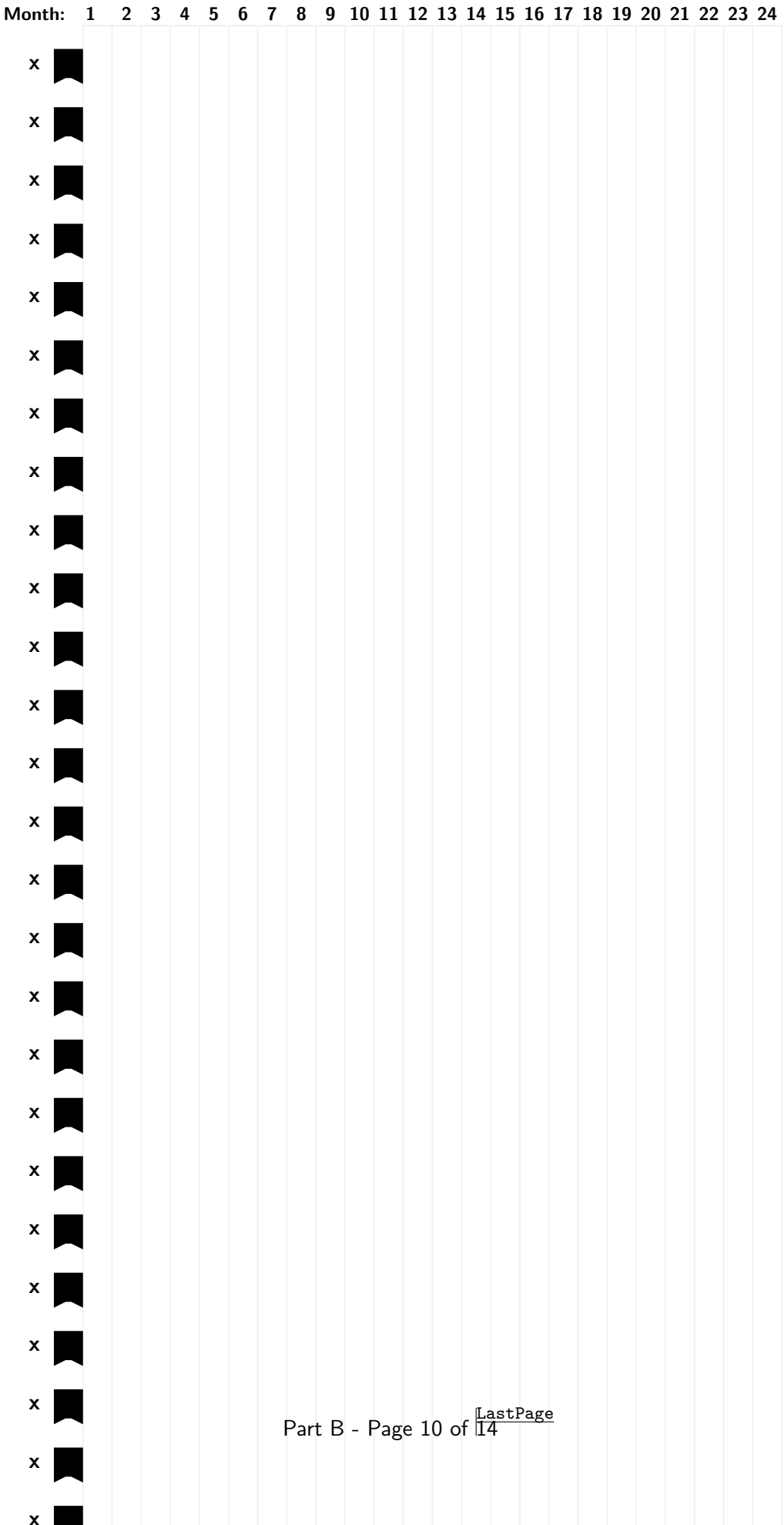
4.4 Competences, experience and complementarity of the participating organisations and institutional commitment

tences

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.


Month: 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x
x

sec:cv

5 CV OF THE EXPERIENCED RESEARCHER

This section should be limited to maximum 5 pages and should include the standard academic and research record. Any research career gaps and/or unconventional paths should be clearly explained so that this can be fairly assessed by the independent evaluators. The Experienced Researchers must provide a list of achievements reflecting their track, and this may include, if applicable:

1. Publications in major international peer-reviewed multi-disciplinary scientific journals and/or in the leading international peer-reviewed journals, peer-reviewed conference proceedings and/or monographs of their respective research fields, indicating also the number of citations (excluding self-citations) they have attracted.
2. Granted patent(s).
3. Research monographs, chapters in collective volumes and any translations thereof.
4. Invited presentations to peer-reviewed, internationally established conferences and/or international advanced schools.
5. Research expeditions that the Experienced Researcher has led.
6. Organisation of International conferences in the field of the applicant (membership in the steering and/or programme committee).
7. Examples of leadership in industrial innovation.
8. Prizes and Awards.

cities

6 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

"proposal ACRONIM"

This proposal is to be evaluated as:

[Standard EF]

Todo list

Here is missing a to state somewhere:
best career possibilities for the experiecned researcher and new collaboration opportunities for the host organization(s) . . . 6
maybe make reference to ASURE project . . . 6
maybe MRF, to link with my thesis . . . 6
describe BIRADS somewhere? . . . 6
ADC, stands for? . . . 6
http://maia-jointmaster.weebly.com/ . . . 7
to modify . . . 7