OActive

NEWSLETTER

Advanced Personalised, Multi-Scale Computer Models Preventing Osteoarthritis

Issue 2: April 2019

Welcome to the M18 issue of the OActive Newsletter!

Join us at:

OActiveProject

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Grant Agreement No. 777159.

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OActive at a Glance

The OActive project focuses on the development of advanced, personalised, multi-scale computer models for combating OsteoArthritis. The VISION of the OActive consortium is to improve radically the healthcare of people with osteoarthritis of the knee.

Osteoarthritis is a degenerative disease of the cartilage and the other tissues in the joints and is the most common form of arthritis that causes pain, limits mobility and reduces independence and quality of life in millions of people in Europe and around the world. Increasingly, it is not only older people in their 60s or 70s that are affected, but younger individuals, including athletes, in many cases years after a knee injury or after the end of their competitive career.

Osteoarthritis is a complex disease in which various biological, social and even environmental factors are involved, in addition to genetics and family history of disease. Although we understand the roles of the main modifiable or nonmodifiable risk factors in the development and progression of osteoarthritis, there is no exploration of the interaction and integration of the many different influences from different domains such as environmental, social, economic, and lifestyle factors, and their links to medical, physiological, and biological indicators for the different tissues affected in the joint and throughout the body, in a patient-specific manner.

The OActive project intents to make a significant leap forward by adopting a multi-scale holistic approach where patient-specific information from various levels, including cell, tissue, organ and whole body will be integrated and combined with information from other sources such as biochemical/ inflammatory biomarkers, behaviour and social/ environmental risk factors to generate robust predictors for new personalised interventions for delaying the onset and slowing down the progression of OA.

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Clinical Trials

Data collection in three countries (Spain, Greece and Cyprus)

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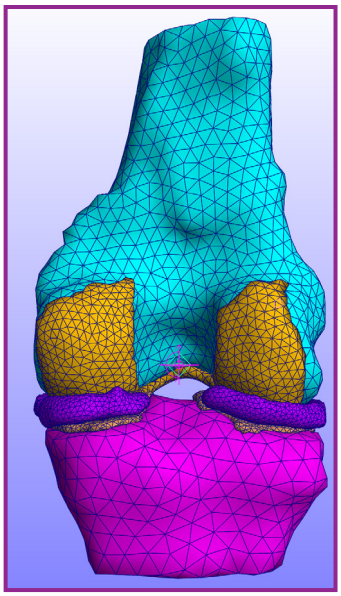
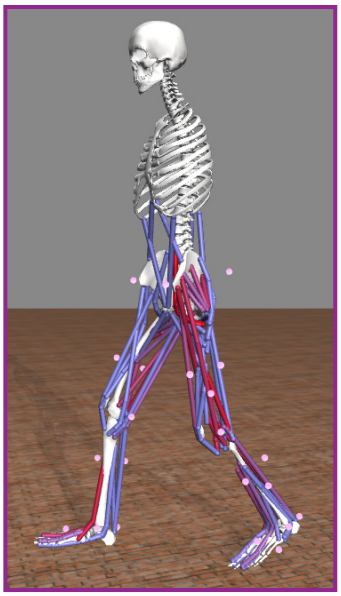
	HULAFE	ANIMUS	UNIC
TARGETED PATIENTS	Healthy ones in high risk of developing OA	Post-traumatic evaluation of athletes	Elderly people
POPULATION SIZE	More than 100 patients	More than 90 patients	More than 130 patients
INFORMATION SETS	Behaviour, imaging, Biochemical, Socio-economic. Target: data collection, examination of the relationship between various collected biomarkers for OA and clinical diagnosis (physical examination of clinicians).		
DURATION	27 months. Starting from month 10 of the project and will last until the end of the project		
OUTCOMES	These results will be used for the development of advanced computer modelling and simulation tools in order to be used in early diagnosis or prognosis of OA.	These results will be used for the development of advanced computer modelling and simulation tools in order to be used in post-traumatic OA prediction	These results will be used for the development of advanced computer modelling/simulation tools in order to be used in OA prediction in elderly people
INTERVENTION	-	Testing the efficiency of gait re-training and exercise intervention using AR.	

OActive Project Progress

During the first 18 M of the OActive project the progress of the project was recorded per work package. WP2 was finalized, where the modelling requirements needed were acquired and the computational processing power requirements were determined. The Data Collection Protocol was designed in order to define the timing, content, screening, assessment, and evaluation tests and other rules related to the ascertainment and collection of data over the life cycle of OActive. Standardized ways of measure in physical examination for all clinical partners was established, based on reviewed literature.





LJMU partner in WP3 analysed data from the osteoarthritis initiative (OAI) using statistical and machine learning algorithms to identify the main risk factors for diagnosis of osteoarthritis at first presentation. The emphasis of this work is on interpretable models, complementary to the use of deep learning neural networks by CERTH to build a predictive model for the same research question. The initial analysis is now being extended using a richer set of biomarkers with the aim of providing an interpretable predictive analytics tool with practical clinical value. Work has been undertaken to build the neuro-musculoskeletal (NMS) pipeline in order to allow for easy processing of data collected by other partners. The work will provide insight into the role of joint loading in the development of OA and develop methods which will be of use to the wider community involved in biomechanics research.

Under WP4, once the Ethical Committees from all hospitals involved in clinical studies have approved the proposed study protocol, UNIC, HULAFE and ANIMUS have started the recruitment of patients and healthy donors. Then, the samples required for the biochemical and analytical studies, as well as, for the discovery of new biomarkers using the exosome content and faecal microbiome analysis are being collected, so it is expected to be processed between the next 6 months. Concerning WP4, where LEITAT is leading activities, more than one third of the target population (OA patients >50 yrs.) have been recruited and blood samples have been collected in order to determine the levels of serum biomarkers related to the development and progress of the disease. In order to aid the initial slow recruitment, a leaflet has been prepared in plain language in Greek, English and Spanish which outlines the benefits for the participation to the study. In addition, a workshop was organized during which the aims of the OActive project were presented to the public. The seminar was held at the Apollonion hospital, in Nicosia, Cyprus.

WP4 results are crucial for the successful progression of the project. The results of this WP will be used for the development of a computational hyper-model for the early prognosis and the monitoring of the process of Osteoarthritis. The hyper-model will be utilized in the combat against OA, improving the quality of life of patients.

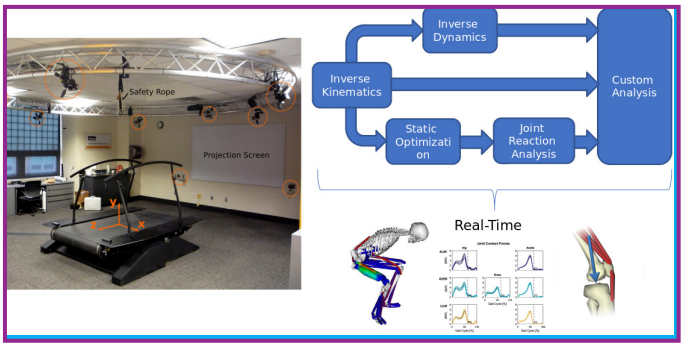
Under WP5 a solid and operationally defined framework to study socioeconomic and environmental factors in knee osteoarthritis is available for use by the consortium, under the lead of KU Leuven. A

OActive Project Progress

pilot questionnaire on socioeconomic and environmental factors can be implemented in the OActive studies, which will be updated after the systematic literature review and hand-on experience in the observational pilot cohort.

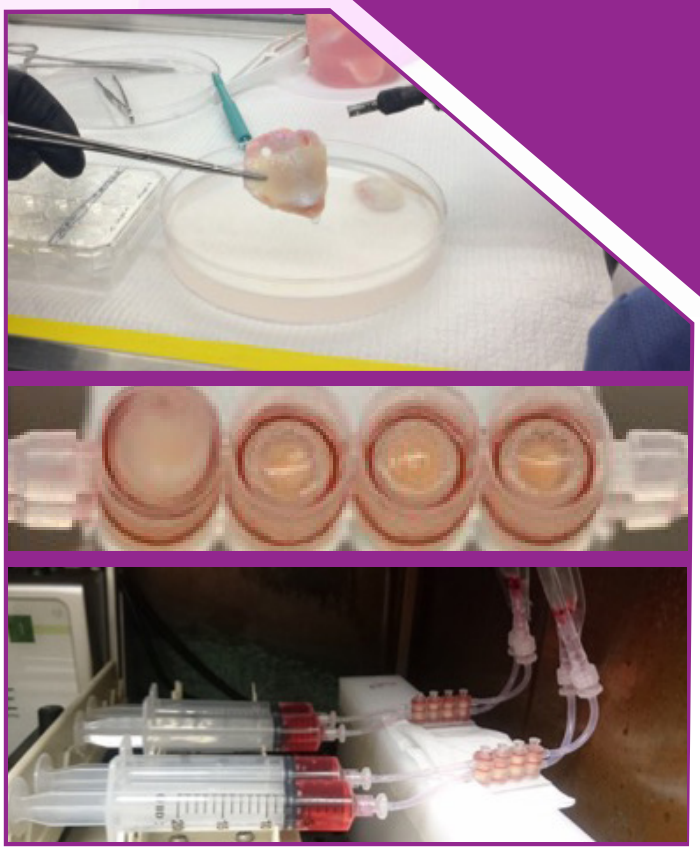
In WP6 the modeling process is still ongoing, and the results up to now belong in the data preprocessing and data representation stages. Big data analytics and computational intelligence tools will generate personalised 'hyper-models' under the operational conditions imposed by clinical usage. In contrast to currently used predictive modes in the health care sector, a number of computational efficient 'local' predictive/diagnostic models will be developed addressing specific OA stages in the disease continuum of a patient (early stages, mild/ moderate OA and post-treatment) serving as a time-varying measure of health status.

UPatras in WP7 has already worked extensively on the development of a real time gait retraining module within the OActive system. The data collected is analyzed in the gait retraining module and feedback to the subject/patient through augmented reality assets to guide the correction and retraining of gait.



In WP8 RIMED collected sample from donors of different age, gender and OA degree to produce a dataset useful for the Hypermodel. The data will contribute to better understand the role of soluble markers in the develop of the OA, and the response to osteochondral tissue to the rehabilitative movements. The experiments for the baseline screening of in vitro OA osteochondral units and evaluation of hormone-related, gender specific cellular responses are completed and the data are being analyzed. Experiments regarding the development of in vitro induced OA models are ongoing.

Under the activities of WP9 57 subjects have already been recruited by HULAFE, 36 from UNIC and 30 from ANIMUS. During WP9 clinical evaluation, physical examination, collection of samples, laboratory tests, imaging tests, and distributed questionnaires regarding social participation, pain and quality of living scales, and psychological factors is performed.



Collaboration with visual analysis and interactive knowledge discovery (WP3) by providing imaging and biomechanical tests from the selected population is ongoing, as well as the study of some blood parameters and sharing of biological samples (blood, urine, faeces) with LEITAT for the study of biomarkers (WP4) is performed. In the recruited subjects, social determinants, such as social position, social context and personal risk factors are asked (WP5).

In WP10 the OActive Website is functioning and the Social media platforms (facebook, twitter and Linkedin) are regularly updated. The project dissemination material include a Brochure, a Poster, a Roll-up, a Flyer, a teaser video and dedicated brochures targeting to specific audiences (recruitment, workshop announcement etc.). Currently, the project resulted in two (2) accepted and two (2) submitted publications in international journals and partners have participated in more than 20 conferences/ events/ workshops. Contact with medical associations, aging people associations and commercial associations is addressed. The process of identifying relevant EU and/or National projects has begun, in order to reinforce clustering activities that could increase the public visibility of the project. Regarding the exploitation strategy, a clear consensus is built on the market gap that the project aspires to fill, which in turn leads to the identification of potential customers and competitors.

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OActive Publications

Journals:

D. Stanev and Konstantinos Moustakas, Modeling musculoskeletal kinematic and dynamic redundancy using null space projection, PLoS ONE, 14(1): e0209171, Jan. 2019, DOI.

S. Moustakidis, E. Christodoulou, E. Papageorgiou, C. Kokkotis, D. Tsaopoulos, N.Papandrianos. Application of deep learning for osteoarthritis classification using self-reported clinical data from the osteoarthritis initiative study. Submitted.

T. Iseki, B.B. Rothrauff, S. Kihara, H. Sasaki, S. Yoshiya, F.H. Fu, R.S. Tuan, R. Gottardi. Early Weight-Bearing Improves Cartilage Repair in an in vitro Model of Microfracture: Comparison of Two Mechanical Loading Regimens on Simulated Microfracture Based on Fibrin Gel Scaffolds Encapsulating Bone Marrow Mesenchymal Stem Cells. In revision.

D. Stanev and K. Moustakas, Stiffness Modulation of Redundant Musculoskeletal Systems, Journal of Biomechanics, vol. 85, pp. 101-107, Mar. 2019, DOI.

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Attendance to events

European Symposium on Artificial Neural Networks, Computational Intelligence and Machine Learning 2019, 24-26 April 2019, Belgium

LJMU participated at the ESANN 2019, at the Special Session on 'Societal Issues in Machine Learning: When Learning from Data is Not Enough' on 24-26 April 2019, in Bruges (Belgium). This event builds upon a very successful series of conference organized each year since 1993. ESANN has become a major scientific event in the machine learning, computational intelligence and artificial neural networks fields over the years. The two main tracks are "Theory and methods", and "Information processing and applications".

Biomechanics section meeting of BASES, 10th April 2019, UK

National Biomechanics Day April 10, 2019

Prof. V. Baltzopoulos delivered the keynote presentation at the Biomechanics section meeting of BASES taking place on10th April 2019, at University of Huddersfield, UK. During the meeting he presented the recent work in the OActive project based on the exciting breakthroughs in real-time musculoskeletal modelling and simulation in OA. The British Association of Sport and Exercise Sciences (BASES) is the professional body for sport and exercise sciences in the UK. Its mission is to drive excellence in sport and exercise sciences through the promotion of evidence-based practice and the development and enhancement of professional and ethical standards.

Attendance to events

Society For Biomaterials 2019 Annual Meeting and Exposition, April 3-6, 2019, Washington

RiMED presented their work during the Annual Meeting and Exposition of the Society for Biomaterials that took place on 3-6 Aril 2019, in Seattle, Washington. The presented work was titled "An in vitro Chondro-Osteo-Vascular Triphasic Model Of The Osteochondral Complex" co-written by R. Gottardi, A. Pirosa, P. Alexander, P. Manner, D. Puppi, F. Chiellini, and R.S. Tuan. In this work, a chondro-osteo-vascular (COV) triphasic model of the OC complex was developed within a recently developed 3D printed microphysiological tissue system (MPS) bioreactor (2) that allows the separate flow of specific media to the chondral and osseous components while maintain them in contact and allowing tissue-tissue communication.

The XXVIII Congress of SVMEFR, 1 & 2 March 2019, Spain

HULAFE attended the XXVIII Congress of SVMEFR held on 1 and 2 March 2019 in Benidorm, Valencia. The conference's agenda includes a scientific program that combines both the interventionist advances, with a list of first level experts, in the presentation of "Therapeutic nerve blocks", as well as the plans of attention to disabled patients in the paper "Brain damage". HULAFE gave a brief description of the project and its main objectives, and a summary of their work, including inclusion criteria, number of subjects recruited and a table reflecting a tendency to a difference among groups (healthy and initial OA) in functional tests and pain and quality of life scales.

Poster presentation of HULAFE at the SVMEFR, Spain

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Attendance to events

ORS 2019 Annual Meeting, February 2 – 5, 2019, Texas

RIMED attended the 2019 annual meeting of the Orthopedic Research Society, taking palce in Austin Texas, on the 2nd-5th of February 2019. The work of R. Gottardi, E. Capuana, D. Marino, V. La Carrubba, V. Brucato, and R.S. Tuan. was focucing on: "HiT-MACE: A High-Throughput Mechanical Activator for Cartilage Engineering to Study the Early Cartilage Response to Physiological and Supra-Physiological Loads". In this work a novel device for the high throughput compressive loading of native and engineered cartilage called HiT-MACE (High Throughput Mechanical Activator for Cartilage Engineering) was developed, to allow for the screening of a high number of samples under different conditions.

OpenSim Workshop at KU Leuven, Nov 6-8, 2018

UPatras and KU Leuven have attended the OpenSim Workshop, on November 6-8 2018, Which was held in Belgium, at the premices of KU Leuven. The workshop focused on getting started with OpenSim for new research projects, including data import and using OpenSim's workflow tools. This workshop targeted OpenSim users who are familiar with the tutorials but wanted to gain more insight in the data processing workflow in OpenSim and seek fot support from experienced OpenSim users to import their own motion capture data.

OpenSim

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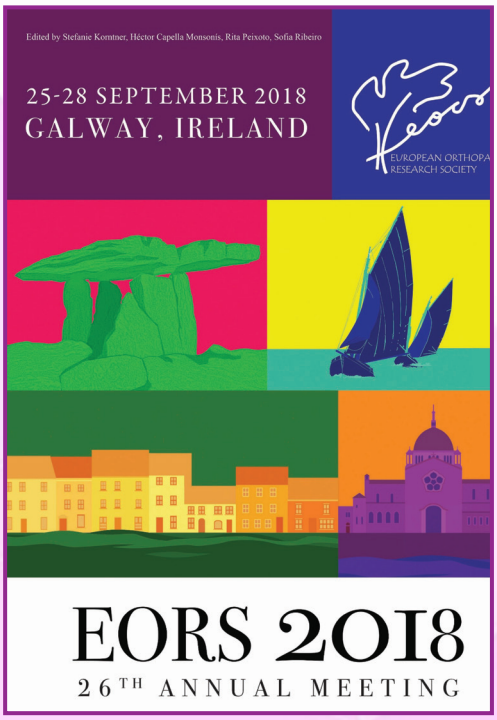
Attendance to events



26th EORS Annual Meeting, 25th – 28th September 2018, Ireland

RIMED participated at the 26th EORS Annual Meeting, as an invited speaker, during 25th – 28th September 2018, in Galway, Ireland. The European Orthopaedic Research Society (EORS) meetings provides a forum to discuss achievements, challenges and opportunities in orthopaedic, musculoskeletal and trauma education, research, development and clinical translation. During the meeting they presented their work on 3D osteochondral microphysiological systems: "From cartilage-bone crosstalk, to screening regenerative approaches, to space research." under different conditions.

Workshop

APOLLONION PRIVATE HOSPITAL

Workshop on Osteoarthritis and a description of the European Research Program OActive, 16 March, 2019, Apollonion Hospital, Cyprus

The UNIC panel during the OActive workshop

A Workshop entitled "Osteoarthritis and description of the research project OActive" has been organized on Mar 16th, 2019, at Apollonion Hospital (Nicosia, Cyprus) aiming to increase the awareness of OA patients about OActive and to inform them about the benefits they will have by participating in this study. The topics discussed can be summarized as: 1. "Osteoarthritis: What is it and how it is treated", 2. "OActive Research Program: Benefits of Participation in the Project", and 3. "Gait Analysis - How Can it Help You".

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Upcoming Events

PatrasIQ, 12-14 April, 2019, Patras, Greece
https://www.patrasiq.gr

3rd International Meeting of Osteoarthritis Patients, 3-5 October, OAFI Foundation, Barcelona, Spain
https://oafifoundation.com/en/home

XXVII Congress of the International Society of Biomechanics (ISB2019), 31 July- 4 Aug. 2019, Calgary, Canada
https://isb2019.com/en

27th EORS Annual Meeting, 2 - 5 October 2019, Maastricht, The Netherlands
https://eors2019.org

2019 Osteoarthritis Research Society International (OARSI) World Congress, 2-5 May 2019, Toronto, Canada
https://2019.oarsi.org/general-information

25th annoual congress of the sport science in the heart of arts, ECSS 2020, 01-04 July 2020, Seville, Spain
http://ecss-congress.eu/2020

Termis EU, 27-31 May 2019, Rhodes, Greece
https://www.termis.org/eu2019

Movement and Cognition Tel-Aviv International Conference, 22-24 July 2019, Tel-Aviv, Israel
https://10times.com/international-movement-conference

15th Annual International Conference on Sport & Exercise Science, 29-31 July & 1 August 2019, Athens, Greece
https://www.atiner.gr/fitness

BOA Annual Congress 2019, 10-13 September. Liverpool, UK
https://www.boa.ac.uk/events/boa-annual-congress-2019.html

Special Session on "Explainable Machine Learning" at IJCNN 2019, 14-19 July 2019, Budapest, Hungary
https://www.ijcnn.org

World Congress on Osteoporosis, osteoarthritis and musculoskeletal diseases, 2-5 April 2020, Barcelona, Spain
https://www.wco-iof-esceo.org

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Deliverables & Milestones

Deliverables

WP1

D1.1: Project Management, Quality Assessment and Financial (M3)

D1.2 First version of Ethics and Safety Manual (M6)

D1.3: Data management plan Strategy (M6)

WP2

D2.1: User requirements analysis report (M4)

D2.2: Data Collection protocol (M6)

D2.3: System specification report (M6)

WP7

D7.1: Analysis of hardware devices and software tools. Game hardware and software design (M13)

WP10

D10.1: OActive Web Site and media presence (M1)

WP11

D11.1: HCT - Requirement No. 1 (M6)

D11.2: HCT – Requirement No. 2 (M6)

D11.3: H – Requirement No. 3 (M6)

D11.4: HCT – Requirement No. 4 (M6)

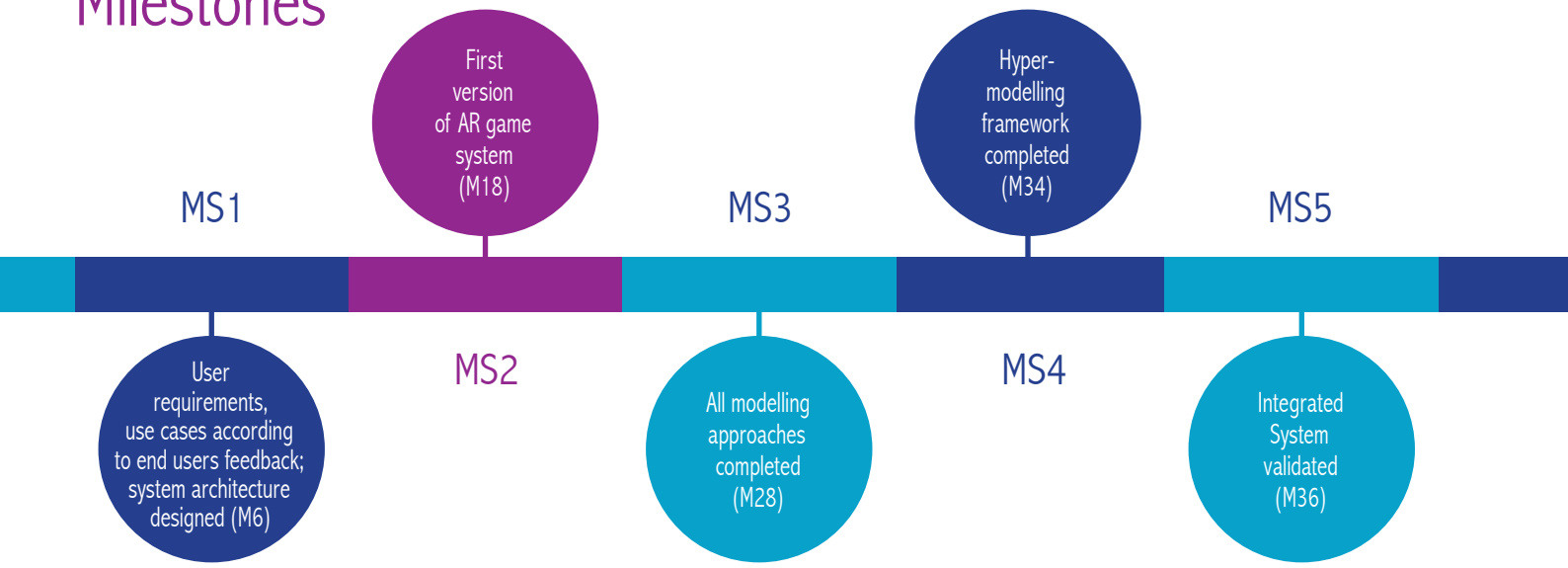
D11.5: NEC – Requirement No. 5 (M6)

D11.6: H – Requirement No. 6 (M6)

D11.7: HCT – Requirement No. 7 (M6)

D11.8: POPD – Requirement No. 8 (M6)

Milestones



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The Consortium

Join us at:

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13 PARTNERS

7 COUNTRIES

3 YEARS

5M. FUNDING

Project Title:
Advanced personalised, multi-scale computer models preventing osteoarthritis
SC1-PM-17-2017 – Personalised computer models and in-silico systems for well-being
Type of action: Research and Innovation action (RIA)

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Instituto de Investigación Sanitaria La Fe

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