

ADMAIORA

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Project title: ADvanced nanocomposite MAterIals fOr in situ treatment and
ultrASound-mediated management of osteoarthritis

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Report on 1st ADMAIORA workshop

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Deliverable author: [Irene Bernardeschi (SSSA), Leonardo Ricotti (SSSA), Denise
Amram (SSSA)]

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PU	Public	X
PP	Restricted to other programme participants (including the Commission Service)	
RE	Restricted to a group specified by the consortium (including the Commission Service)	
CO	Confidential, only for members of the consortium (including the Commission Service)	

Document History

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1	07/01/2020	Irene Bernardeschi, SSSA	First version of the template for project Deliverables
2	24/01/2020	Leonardo Ricotti, Denise Amram, SSSA	Contribution to the Deliverable from SSSA
3	31/01/2020	Irene Bernardeschi, Leonardo Ricotti, SSSA	Final revisions and Deliverable submission

Table of Contents

1	Executive summary	4
2	Introduction	5
2.1	Mini-Symposium: Physical triggers and nano-biomaterials for tissue regeneration	5
2.2	Workshop with end-users (OA patients): “ <i>Understand, know and cure – the joint at present and in the future</i> ”	11
2.2.1	Questionnaire results	15
3	Conclusions	20

1 Executive summary

This deliverable describes the key events organized in the first year of the ADMAIORA project, as devised in the preliminary dissemination, communication and exploitation plan. In particular, the first project-related scientific workshop has been organized during the IEEE/EMBS Engineering in Medicine and Biology Conference (EMBC) in Berlin by the Project Coordinator, Prof. Leonardo Ricotti. During this event, the project strategy and preliminary results were disseminated to a broad audience of potential users, stakeholders, and scientists.

A second non-technical workshop has also been organized by the Project Coordinator in collaboration with Dr. Gina Lisignoli from IOR and with the involvement of AMRER, an Italian association of rheumatic patients. Such a second event aimed at describing the project approach and preliminary results to patients affected by osteoarthritis and, in general, to elderly people affected by rheumatic problems, thus to make them aware of the technologies under development in ADMAIORA and to get a useful feedback from them. End-users concrete needs and their opinion of the different project aspects were collected and will be taken into serious consideration by the Consortium, to properly shape technical efforts towards impactful and user needs-compliant results.

The deliverable describes the objectives and the details of both events, including an analysis of the patients' feedbacks.

2 Introduction

The dissemination plan, described in the Deliverable D7.2 - Preliminary report of the preliminary dissemination, communication and exploitation plan, includes presentations at scientific and technological events. In particular, one workshop per year dedicated to the ADMAIORA themes is foreseen, to present the project results to a broad audience of potential users, stakeholders, and scientists. To this purpose, a mini-symposium focused on a scientific topic closely adherent to the ADMAIORA scope has been organized by the Project Coordinator, Leonardo Ricotti, during the IEEE/EMBS Engineering in Medicine and Biology Conference (EMBC). The title of the event was "*Physical triggers and nano-biomaterials for tissue regeneration*" (see section 2.1).

According to the Deliverable D7.2, within special communication activities, four non-technical workshops are expected to be organized during all the project duration to communicate results to healthcare system actors and stakeholders, and to train osteoarthritis (OA) patients and in general elderly people to the technologies that are under development in the project, thus to prevent possible barriers to a future adoption of the project results. In particular, two events are expected for healthcare system actors and stakeholders and two for OA patients and elderly people. In this context, a seminar (see section 2.2) has been organized by SSSA in collaboration with IOR and in strong synergy with Dr. Daniele Conti, member of the ADMAIORA End-users Board and counsellor of the *Associazione Malati Reumatici Emilia Romagna* (AMRER), which is an association of patients involving OA ones. AMRER has been a supporter of the ADMAIORA project during the proposal submission phase, through a supporting letter. During this workshop, entitled "*Capire, Conoscere e Curare - L'articolazione tra presente e futuro*" (Understand, know and cure – the joint at present and in the future), Professor Ricotti's talk was entitled "*The ADMAIORA project: Mesenchymal cells together with new technologies to regenerate cartilage*". In this talk, he described the ADMAIORA project to the end-users. Other talks given by healthcare professionals highlighted important aspects of the OA pathology (i.e., pain, diet, lifestyle, etc.). During the event, a survey was distributed to the patients, in order to receive their feedbacks on the project approach and preliminary (non-confidential) results (see section 2.2.1).

2.1 Mini-Symposium: Physical triggers and nano-biomaterials for tissue regeneration

This Mini-Symposium has been organized by Prof. Leonardo Ricotti, in collaboration with Dr. Lino Silva Ferreira, Full Professor at the Faculty of Medicine, University of Coimbra (Portugal) and head of the Biomaterials and Stem cell-based therapeutics Lab at the Center of Neurosciences and Cell Biology, and Dr. Salvador Pané i Vidal, IEEE Member and Senior Research Scientist at the Institute of Robotics and Intelligent Systems at ETH Zürich (Switzerland), where he leads the Electrochemistry Laboratory. Prof. Ricotti was the chair of the symposium, Dr. Ferreira and Dr. Pané i Vidal were the co-chairs.

The Mini-Symposium was entitled "*Physical triggers and nano-biomaterials for tissue regeneration*" and it touched themes related to Micro/Nano-bioengineering, Cellular/Tissue Engineering and Biomaterials, and Bio-Robotics and Biomechanics, with the following specific keywords, highlighted in the flyer of the event:

- Regenerative medicine;
- Nano-biomaterials;
- Physical stimulation;
- Triggerable materials;
- Cell fate modulation.

The abstract of the Mini-Symposium is reported below:

"Smart nano-biomaterials with tuneable properties can be used as versatile transducers able to transform a physical stimulus into another physical response. For example, magnetic nanoparticles convert magnetic fields into mechanical force and heat. Noble metal nanoparticles, quantum dots, and upconversion nanoparticles can transform light into heat, piezoelectric nanoparticles turn mechanical stimuli into electric fields. These features can be exploited to convert an external (out-of-the-body) stimulus into a nanomaterial-mediated one (in-body), able to trigger beneficial effects in cells and tissues.

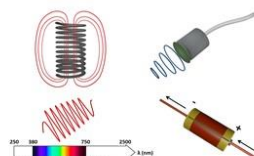
This Mini-Symposium focuses on this paradigm, grounded on a synergy between physical triggers and nano-biomaterials for tissue regeneration. The key features of these systems are: (i) remote spatiotemporal controllability, (ii) ability to modulate cell functions by mediating physical inputs, and (iii) high biocompatibility/low cytotoxicity, enabling their future clinical application. Besides nanomaterial features, another crucial aspect concerns the ability of input source signals such as magnetic fields, light, ultrasound waves, etc. to non-invasively penetrate biological tissues and activate the implanted nano-biomaterials.

The above-mentioned opportunities and issues will be discussed within the Mini-Symposium, with five talks touching different aspects and covering different possible approaches to be pursued in this field. Finally, a round table will allow to wrap-up the key messages emerged in the Mini-Symposium and will foster a direct interaction between the speakers and the audience, to further discuss the most intriguing aspects of this research field."

The overall duration of the Mini-Symposium was 90 minutes. Five speakers were involved and gave their presentation on themes related to the Symposium, with a final round table in which the speakers interacted with the audience, wrapping up the key messages emerged during the mini-symposium and highlighting the research issues and bottlenecks still open in this field, also trying to identify the most promising routes for pushing ahead the presented research paradigm in the next years. The list of speakers is reported below:

- Yu Cheng, Tongji University (Shanghai, China)
Presentation title: *Magnetic nanomaterials for mechanotransduction and cell fate regulation*
- Salvador Pané i Vidal, ETH Zurich (Zurich, Switzerland)
Presentation title: *Magnetic locomotion and magnetoelectric effect for targeted drug delivery and regenerative medicine*
- Jiaojiao Wu, Tongji University (Shanghai, China)
Presentation title: *Iron oxide nanoparticles as the magneto-mechanical and hyperthermia responders on eradication of cancer cells*
- Lino Silva Ferreira, University of Coimbra (Coimbra, Portugal)
Presentation title: *Light-triggered nanomaterials to modulate cell/tissue functions*
- Leonardo Ricotti, The BioRobotics Institute, SSSA (Pisa, Italy)
Presentation title: *Piezoelectric nanomaterials and ultrasound for tissue regeneration*

The Introductory slides of the Mini-Symposium, which were used to introduce the scientific themes to the audience, are shown in Figure 1.



July 26, 2019 - Hall A4, Level 1 Mini-Symposium: Physical Triggers and Nano-Biomaterials for Tissue Regeneration



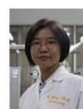
Leonardo Ricotti
Scuola Superiore
San'Anna
(Pisa, Italy)



Lino Ferreira
University of
Coimbra
(Coimbra, Portugal)



**Salvador Pané
i Vidal**
ETH Zurich
(Zurich,
Switzerland)



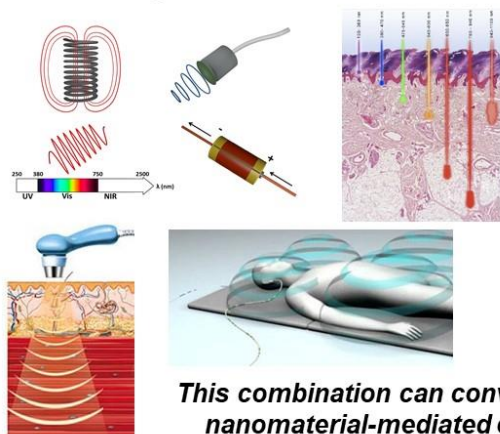
Yu Cheng
Tongji University
(Shanghai, China)



Jiaojiao Wu
Tongji University
(Shanghai, China)

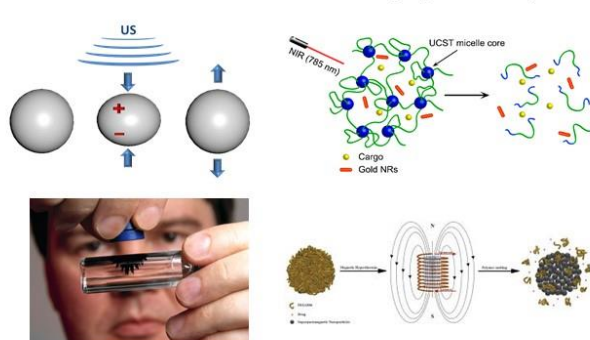
Remote physical triggers...

Input source signals such as magnetic fields, light, ultrasound waves, etc. can non-invasively penetrate biological tissues



...and smart nano-biomaterials

Smart nano-biomaterials can be used as versatile transducers able to transform a physical stimulus into another physical response

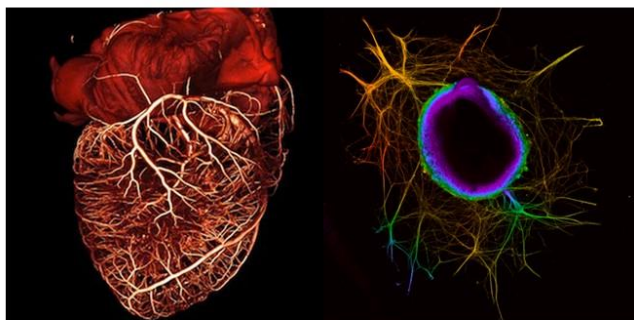


This combination can convert an external (out-of-the-body) stimulus into a nanomaterial-mediated one (in-body), able to trigger beneficial effects

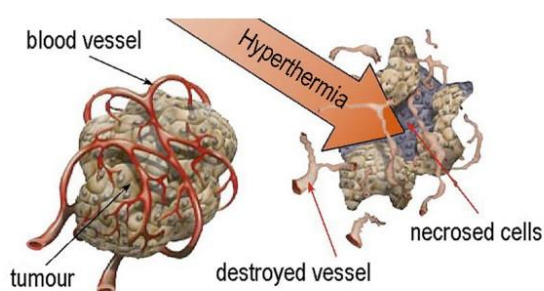
Remote physical triggers...

...and smart nano-biomaterials

REGENERATION OF HEALTHY TISSUES (acting on intra/extra-cellular pathways)



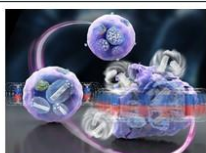
DEATH OF ABNORMAL TISSUES (through hyperthermia or targeted drug delivery)



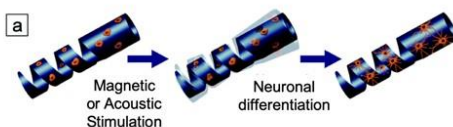
This combination can convert an external (out-of-the-body) stimulus into a nanomaterial-mediated one (in-body), able to trigger beneficial effects

Mini-Symposium program

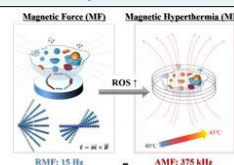
Talk 1: Magnetic Nanomaterials for Mechanotransduction and Cell Fate Regulation
Yu Cheng (15 min)



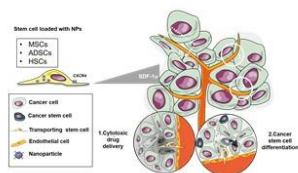
Talk 2: Magnetically Driven Ferroelectric Micromachines for Delivery and Remote Electrical Stimulation of Neuronal Cells
Salvador Pané i Vidal (15 min)



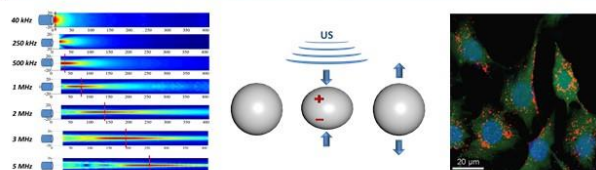
Talk 3: Iron Oxide Nanoparticles As the Magneto-Mechanical and Hyperthermia Responders on Eradication of Cancer Cells
Jiaojiao Wu (15 min)



Talk 4: Light-Triggered Nanomaterials to Modulate Cell/tissue Functions
Lino Ferreira (15 min)



Talk 5: Piezoelectric Nanomaterials and Ultrasound for Tissue Regeneration
Leonardo Ricotti (15 min)



Round Table (15 min)

Figure 1: Introductory slides of the Mini-Symposium, used to present the speakers and prepare the audience to their talks.

In Figure 2 some pictures of Prof. Ricotti during his presentation are shown.

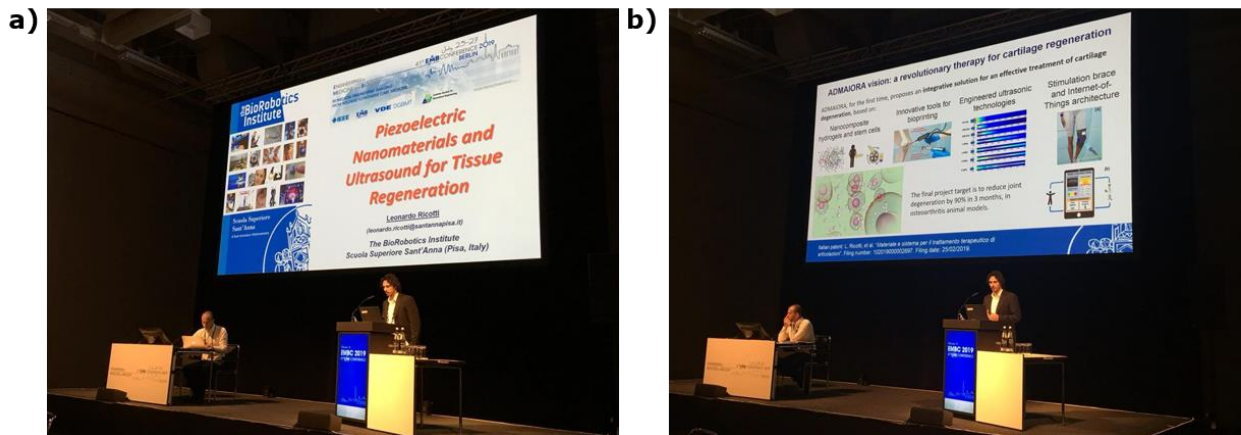


Figure 2 - Professor Ricotti during his talk at the EMBC Mini-Symposium on "Physical triggers and nano-biomaterials for tissue regeneration", during which he described the ADMAIORA project approach and preliminary (non-confidential) results.

During the Mini-Symposium about 70 ADMAIORA brochures were distributed to the attendants. Overall, ~ 70 people participated in the event, but the event flyer (with the acknowledgments to the ADMAIORA project) and the project brochures were disseminated during the whole Conference duration and thus surely reached a higher number of people (EMBC welcomes over 3000 attendees from over 73 countries each year).

The event was properly promoted on the project social networks (see Figure 3 and Figure 4). The total number of interactions with the related posts on the social networks pages was 257. In particular, the number of people reached with the post on Facebook was 1485, while the post was viewed 1645 times on Twitter.



Figure 3 - Post on the Facebook page of the ADMAIORA project advertising the Symposium.



Figure 4 - Post on the twitter page of the ADMAIORA project advertising the Symposium.

2.2 Workshop with end-users (OA patients):

"Understand, know and cure – the joint at present and in the future"

As previously mentioned, this Workshop has been organized in collaboration with Dr. Gina Lisignoli from IOR and Dr. Daniele Conti, member of the End-users board and counsellor of the AMRER association. Figure 5 shows the program of the workshop that took place at IOR on October 19, 2019.

The all-day Workshop was divided into two sessions. It started with some greetings by public authorities:

- Dr. Giuliano Barigazzi – Health Councillor, Municipality of Bologna
- Prof. Mario Cavalli – Director of the IRCCS Istituto Ortopedico Rizzoli
- Guerrina Filippi – President of the AMRER Onlus

In the first part of the Workshop, Prof. Riccardo Meliconi from IOR described the general characteristics of osteoarthritis (OA), also providing an overview of traditional (non-surgical) treatments used at present in the clinics and giving recommendations in terms of lifestyle and dietary habits. Then, Dr. Mariada Perrone from IOR faced one of the major problems associated with OA, namely the joint pain, which is the main cause of immobilization for OA patients. She described this issue by also highlighting the general biological mechanisms that are responsible for pain and by describing the pharmacological and non-pharmacological treatments currently available, as well as their side effects. Then, different therapies for the treatment of OA were described in more detail. Dr. Giovanni Ciano from the hospital of Ferrara talked about pharmacologic therapy, while Prof. Stefano Zaffagnini and Dr. Alessandro Russo from IOR described the surgery scenarios in OA treatment. Then, Prof. Maria Grazia Benedetti approached the issues related to the rehabilitation process, which is needed after the surgery treatment, as well as after substitution of the joint with a prosthesis. Finally, Dr. Marieta Terrafino from IOR presented the pros and cons of different possible lifestyles and diets to be adopted and their possible impact in delaying OA effects.

The second part of the Workshop was dedicated to the role of research efforts for OA treatment, and the possibility to regenerate the joint tissues, especially the cartilage. Dr. Gina Lisignoli from IOR described the role of researchers in the society and how to perform research in tissue regeneration field, especially for cartilage repair/healing. Then, Prof. Leonardo Ricotti illustrated the ADMAIORA project, explaining the objectives of the project and how people with OA may benefit from the project results. He outlined the innovative therapeutic paradigm proposed in ADMAIORA, which associates stem cells, directly obtained from the patient, smart materials containing micro- and nanoparticles for cell stimulation, and new technologies based on low intensity ultrasound, wearable braces, printing instruments and Internet-Of-Things architectures to target the regeneration of cartilage and, overall, the healing of the joint affected by OA.

**Capire, conoscere e curare
L'ARTICOLAZIONE
TRA PRESENTE E FUTURO**

SABATO 19 OTTOBRE 2019 - ore 9,30

**Aula Anfiteatro
Istituto Ortopedico Rizzoli
c/o Centro di ricerca
Codivilla-Putti
Via di Barbiano, 1/10
40136 BOLOGNA**

Incontro medici pazienti

**Incontro gratuito
è richiesta iscrizione sul sito www.amrer.it**

PROGRAMMA

PRIMA PARTE

CAPIRE, CONOSCERE E CURARE L'ARTICOLAZIONE

9.30 **Apertura lavori: salute autorità - sono invitati:**
Giuliano Barigazzi - Assessore Salute - Comune di Bologna
Mario Cavalli - Direttore Generale IRCCS Istituto Ortopedico Rizzoli (IOR)
Guerrina Filippi - Presidente AMRER Onlus
Moderatore:
Nazzarena Malavolta

10.00 **Osteoartrite e Osteoartrite**
Riccardo Meliconi - Bologna (IOR)

10.20 **Il Dolore articolare**
Mariada Perrone - Bologna (IOR)

10.40 **Dibattito**
Moderatore:
Massimo Reta

ASPETTI DI CURA E PREVENZIONE PER L'ARTICOLAZIONE:

11.10 **Terapia farmacologica**
Giovanni Ciancio - Ferrara (Aosp)

11.30 **Chirurgia**
Stefano Zaffagnini / Alessandro Russo - Bologna (IOR)

SECONDA PARTE

RICERCA E CELLULE MESENCHIMALI: È POSSIBILE RIGENERARE L'ARTICOLAZIONE?
Moderatore:
Milena Fini

11.50 **Riabilitazione**
Mariagrazia Benedetti - Bologna (IOR)

12.10 **Stili di vita**
Mariela Terrafino - Bologna (IOR)

12.30 **Dibattito**

12.50 **Pausa Pranzo**

14.00 **La ricerca: che cos'è e cosa si fa?**
Gina Lisignoli - Bologna (IOR)

14.20 **Progetto Europeo ADMAIORA: Cellule mesenchimali insieme a nuove tecnologie per rigenerare il tessuto cartilagineo**
Leonardo Ricotti - Pisa (Scuola Superiore Sant'Anna)

15.00 **Rilevazione dei bisogni dei pazienti**
Questionario

16.00 **Termine lavori**

Medici ed esperti del Servizio Sanitario Nazionale incontrano i pazienti per affrontare i principali aspetti legati alla cura dell'articolazione danneggiata da osteoartrite. Sarà favorito dibattito e confronto con il pubblico.

Per informazioni AMRER Onlus Ass. Malati Reumatici Emilia Romagna
Via Ca' Selvatica, 10/B - 40123 Bologna
ass.amrer@alice.it - www.amrer.it
Tel. 051.249045 - Fax. 051.0420251 - Cell 335.6223895 - 349.5800852

Amreri il 5x1000
A favore dei Malati Reumatici a AMRER onlus
Cod. Fiscale 09099410379

Figure 5 Program of the first workshop with end-users

All the technical aspects of the project were explained in a simplified language, suitable for end-users, by also exploiting the ADMAIORA concept video and other animations prepared ad hoc for the Workshop.

Some pictures from the event are shown in Figure 6. The end-users attending the Workshop were ~ 150.



Figure 6 - a), b) Prof. Ricotti introducing the ADMAIORA project during his presentation. c) Picture of the audience attending the Workshop.

At the end of the talk, an anonymous questionnaire has been delivered to the attendants who were asked to reply to the following questions:

- Gender (M/F) _____ Age _____
- After today's meeting, is it clearer what is osteoarthritis, how it progresses over time and which treatments are available? (1 – not clear / 10 – perfectly clear)
- Did you find the ADMAIORA project interesting? (1 – not interesting / 10 – very interesting)
- Does the new solution proposed by the ADMAIORA project seem promising? (1 – not promising/ 10 – very promising)
- Do you think that the development of these technologies could prevent the patient from undergoing knee replacement surgery? (1 – it cannot prevent / 10 – it can surely prevent)
- Do you think this new approach could be actually useful for patients affected by osteoarthritis? (1 – not useful / 10 – very useful)

- Do you know which is your class of pathology?
- Would you be in favour of undergoing this treatment when this technology will be available? (1 – not in favour / 10 – totally in favour)
- What is the maximum time that you consider acceptable for daily therapy at home, during which you would remain seated wearing the knee brace? (express in minutes / hours)
- Do you think that using the App developed by the project on your mobile phone can be a simple tool? (1 – not simple / 10 – very simple) Please, indicate the reason of the answer
- Do you think that using the bracelet developed within the project could interfere with your daily activities? (1 – no interference / 10 – much interference). Indicate the reason of the answer
- Is there something that does not convince you or is not clear to you? If yes, indicate what
- What would you change to make the ADMAIORA treatment more acceptable?
- Do you have any other suggestions?

The answers have been elaborated and the results are shown in the next section.

During the seminar, project brochures in Italian language have been disseminated among the attendants. Furthermore, the event has been advertised by AMRER with a radio message and through internet news on AMRER, IOR, and ADMAIORA websites, as shown in Figure 7.



Figure 7 - Internet news advertising the workshop on a) IOR, b) AMRER association, and c) ADMAIORA webpages.

Finally, the first ADMAIORA newsletter has been released in Italian language on October 15th, 2019 for promoting the workshop (Figure 8). The newsletter was sent to 80 recipients.

ADMAIORA

[View in browser >](#)

Newsletter del progetto di ricerca ADMAIORA, coordinato dall'Istituto di BioRobotica della Scuola Superiore Sant'Anna e finanziato dall'Unione Europea



CHI SIAMO

ADMAIORA (ADvanced nanocomposite MAterials fOr in situ treatment and ultrAsound-mediated management of osteoarthritis) è un progetto di ricerca coordinato dall'Istituto di BioRobotica della Scuola Superiore Sant'Anna (Pisa) e finanziato dalla Commissione Europea all'interno di Horizon 2020, il programma europeo per la Ricerca e l'Innovazione (Call: H2020-NMBP-TR-IND-2018, Research and Innovation action).

L'obiettivo del progetto è **esplorare trattamenti alternativi per l'osteoartrosi**, al fine di migliorare la qualità della vita dei pazienti e di ridurre i costi a carico del sistema sanitario.

Figure 8 - First ADMAIORA newsletter in Italian language.

2.2.1 Questionnaire results

The Workshop attendants were completely free to fill or not to fill the questionnaires. The answers obtained from the questionnaire have been anonymously collected and elaborated as aggregate data considering the current legislation on data protection (EU Reg. 2016/679 and Italian Legislative Decree 196/2003, as modified by the Legislative Decree 101/2018, and the Ethics rules on data processing for statistics and scientific research purposes issued by the Italian Data Protection Authority). To avoid possible re-identification of participants, in particular, an aggregation threshold for personal data has been identified in 3 units. In addition, results concerning personal data have not been elaborated together with the expressed opinions.

The total number of filled questionnaires was 65. The amount of women was higher (65%) with respect to men (35%), as shown in Figure 9. About age distribution, only the 5% of the attendees that filled the questionnaire was 30 years old or less, the 6% had an age between 30 and 55 years old, the 14% was 55 or more but less than 75 years old and the 75% was 75 years old or more (Figure 10).

Gender distribution

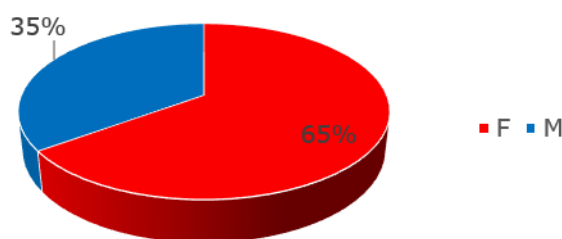


Figure 9 - Gender distribution of the attendants that filled the questionnaire.

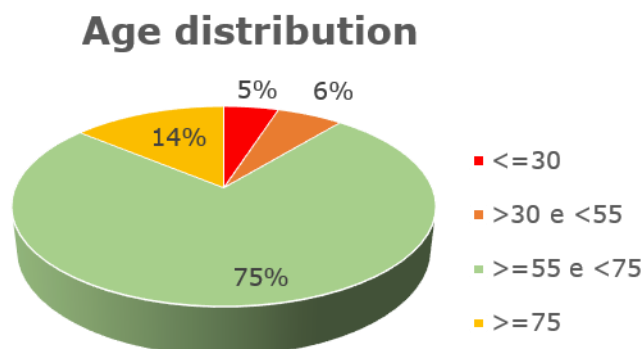


Figure 10 - Age distribution of the attendants that filled the questionnaire.

At the end of the meeting, almost all the participants declared to be more aware about the OA pathology, its progress over time and the available treatments (Figure 11), and they also found the ADMAIORA project very interesting (Figure 12). Most of them replied that the new solution proposed by the ADMAIORA project is promising (Figure 13), that they found the new approach useful for the patients with OA (Figure 14) and they thought the development of ADMAIORA technologies could prevent patients from undergoing knee replacement surgery (Figure 15). Also, it seems that many of them would be in favour of undergoing this kind of treatment, once available (Figure 16) even if the use of the App (Figure 17) and of the bracelet (Figure 18) left people more skeptical, probably because most of them were elderlies, not so confident with digital technologies. This is an important indication for the Consortium, who has to pursue technologies as simple as possible (especially software ones). Similarly, the possible interference of the bracelet with the daily activities should be carefully considered by the partners.

Finally, the survey outlined many useful comments on which aspects of the project resulted less clear and provided possible suggestions to make them more acceptable. Most of the comments were related to the role of cells and how cells can become cartilage, along with some concerns related to having materials/cells inside the body or on the age of the patients to whom the therapy is addressed.

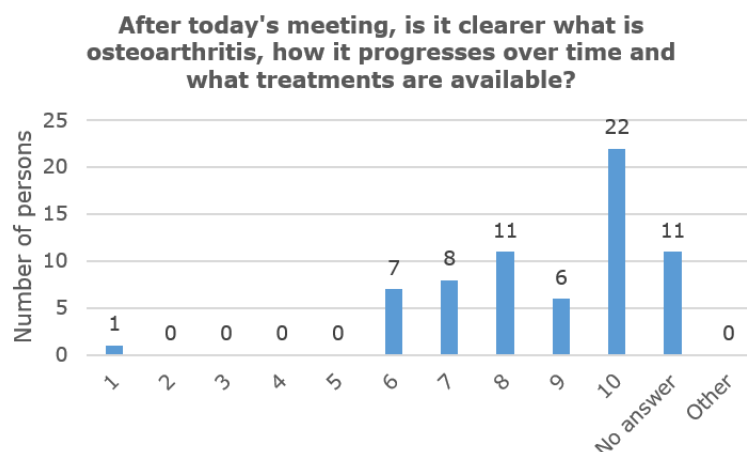


Figure 11 – Audience feedback on the awareness of what is osteoarthritis, how it progresses over time and what treatments are available.

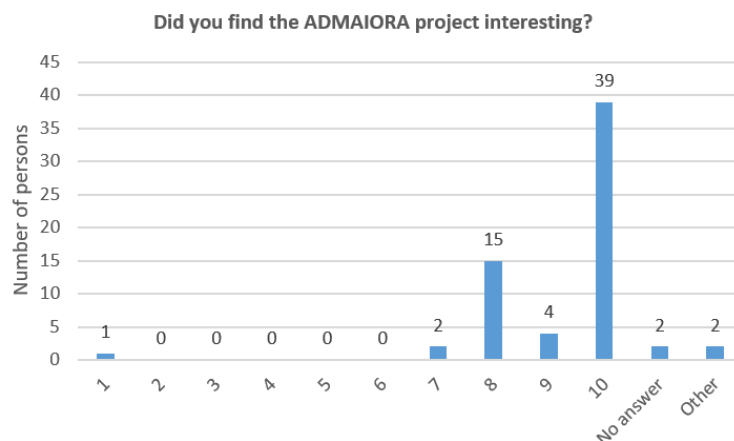


Figure 12 – Audience interest in the ADMAIORA project.

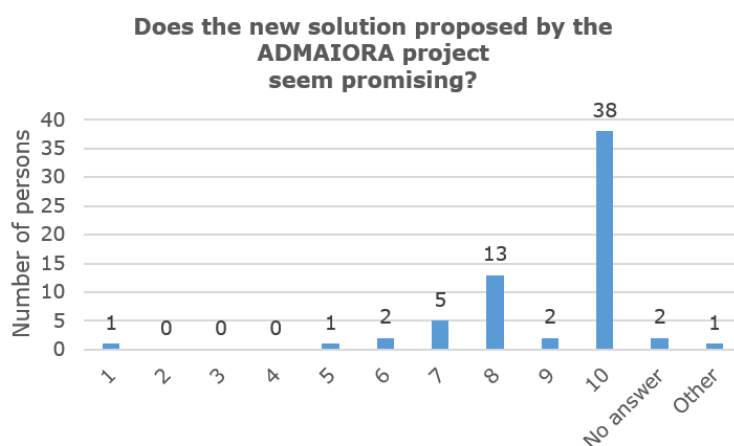


Figure 13 - Audience feedback on how much the new solution proposed by the ADMAIORA project seems promising.

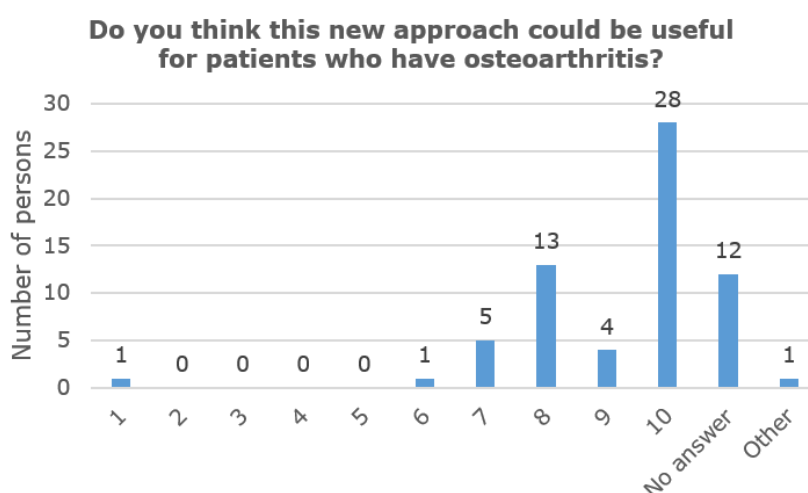


Figure 14 - Audience opinion on the usefulness of the new ADMAIORA approach for patients with osteoarthritis.

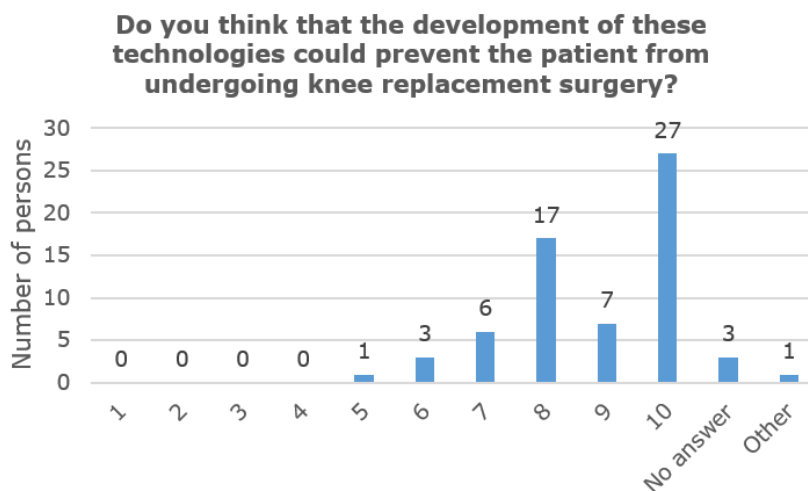


Figure 15 - Audience feedback on the possibility to prevent the patient from undergoing knee replacement surgery, thanks to the ADMAIORA paradigm.

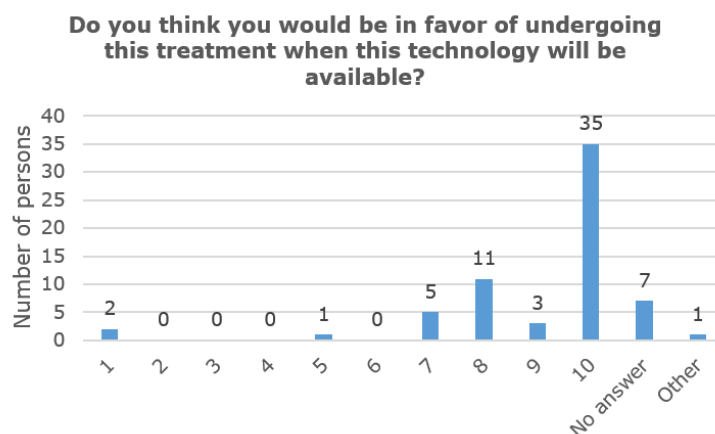


Figure 16 - Audience feedback on their availability to undergo the ADMAIORA treatment once this technology would be available.

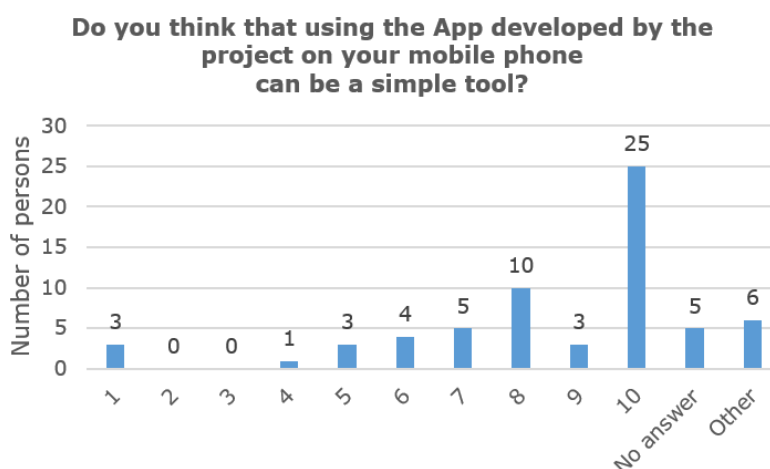


Figure 17 - Audience opinion on the ease of use of the App.

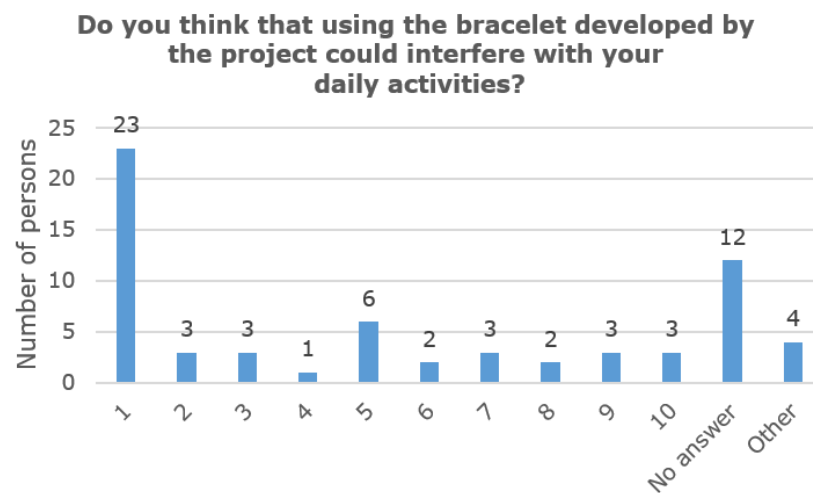


Figure 18 - Audience opinion on the possible interference of the bracelet with the daily activities.

3 Conclusions

This deliverable describes in detail the two key dissemination and communication events organized during the first year of the ADMAIORA project, as planned in the deliverable D7.2 - Preliminary report of the preliminary dissemination, communication and exploitation plan. In particular:

- The Mini-Symposium organized by Prof. Leonardo Ricotti, in collaboration with Dr. Lino Silva Ferreira, and Dr. Salvador Pané i Vidal, during the IEEE/EMBS Engineering in Medicine and Biology Conference (EMBC), in which the project approach and results were disseminated to a broad audience of potential users, stakeholders, and scientists.
- The non-technical Workshop organized in collaboration with Dr. Gina Lisignoli from Istituto Ortopedico Rizzoli and Dr. Daniele Conti from AMRER association and partner of the end-users board, in which patients affected by osteoarthritis and in general elderly people were informed about the ADMAIORA project approach, advancements and possible future applications.

In particular, during the Workshop with the end-users, very useful feedbacks from patients have been collected. Such a direct interaction with the real needs of the patients will surely help to properly shape the project activities towards the development of user-friendly usable technologies and bottom-up oriented strategies for treating the osteoarthritis, in addition to training patients and possible end-users to the technologies under development for decreasing the barriers for adoption of the project results.