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Integrated intervention program for prevention and treatment of cartilage lesions

This research is supported by the European Regional Development Fund (FEDER), through COMPETE2020 under the PT2020 program (POCI-01-0145-FEDER-023423), and by the Portuguese Foundation for Science and Technology (UID/Multi/04044/2013).

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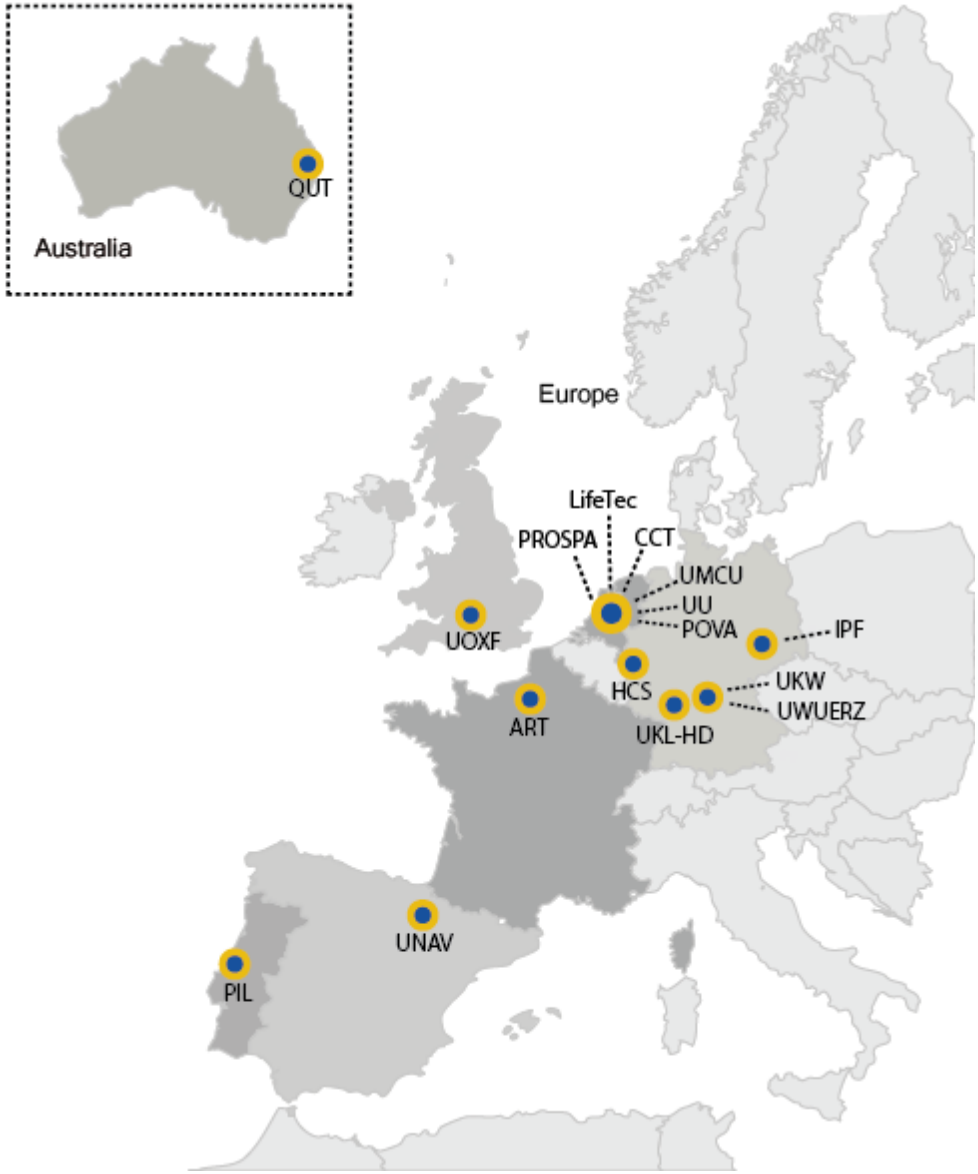
hydrozones

Bioactivated hierarchical hydrogels as zonal implants for articular cartilage regeneration

FP7 – NMP – 309962 ~10m€



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Osteoarthritis (OA) is a degenerative disease, promoted by abnormal chronic mechanical loading over the joint; for instance due to excessive body mass.

Thus, exercise should be a clear recommendation for OA prevention, but it is not. It will increase the load over the joints and if there is joint malalignment it will be worse than better.

On the other hand, recent improvements on tissue engineering have demonstrated the suitability of novel bilayer scaffolds.

But how will they respond to the normal mechanical loading over time?

And to the abnormal?

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So, should a patient treated with one of the mentioned scaffolds (e.g. MaioRegen®) enroll in exercise to decrease his/her body mass?

With which type of exercise?

Several questions demonstrating the stimulating triad that researchers should look up to for promising treatments of osteochondral defects.

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Integrated intervention program for prevention and treatment of cartilage lesions

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#Top facts related to OA#

(i) Disability due to musculoskeletal disorders increased by 45% from 1990 to 2010

(ii) OA is the fastest increasing health condition, affecting over 250 million people

(iii) It is not exclusive for the elderly: more than 50% adults with knee OA are <65

(iv) 2 out of 3 people with obesity are at risk developing knee OA in their lifetime

(v) Knee OA is the 11th leading cause of disability and shows a growing trend

(vi) People with OA have a 16% increased risk of developing cardiovascular disease compared to those without

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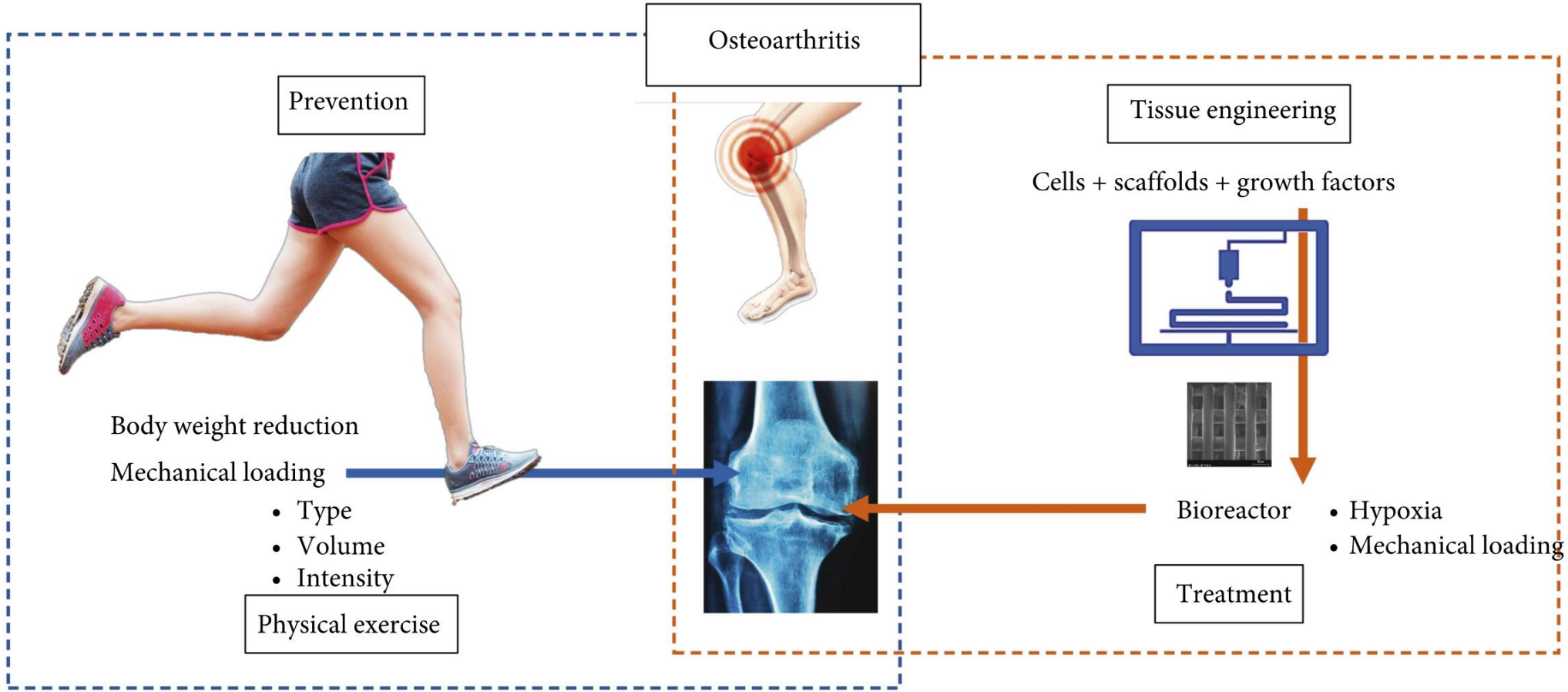

Morouço, Fernandes, Santos-Rocha (2019). J Aging Res

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#Where we at?#

- there are a significant number of repair strategies to treat an articular cartilage lesion; some already available, and others in an on-going research status.
- hyaline cartilage has remarkable mechanical properties (elastic modulus of ~123MPa; mechanical tensile strength of 17 MPa; compressive modulus varying between 0.53 and 1.82 MPa; and compressive stress between 14-59 MPa) and lasting durability, despite its few millimeters of thickness.
- many of the patients undergoing surgery are graded 4 – fissure extended until the subchondral bone (according to the International Cartilage Repair Society classification).

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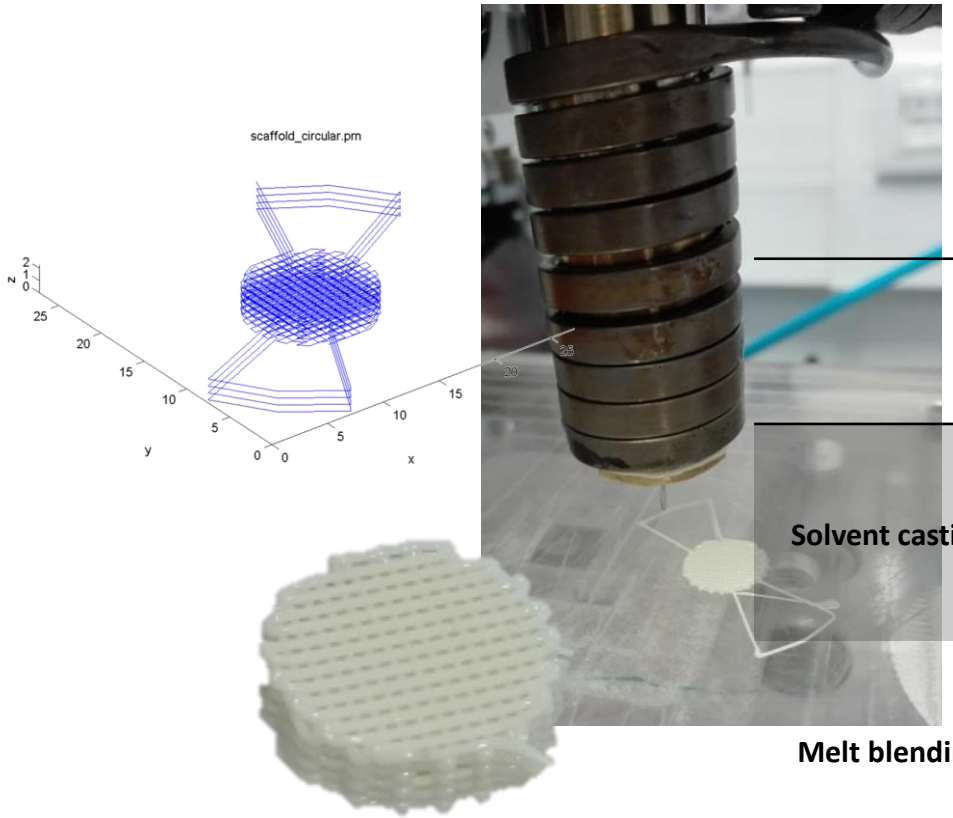

	PCL (%)	HA (%)	Compressive Modulus (MPa)	σ_{max}	ε %
Solvent casting	100	0	26,04 ± 1,86	58,81 ± 0,48	84,79 ± 0,51
	80	20	40,63 ± 1,96	58,24 ± 0,56	77,46 ± 0,99
	60	40	42,42 ± 2,05	58,40 ± 0,30	79,29 ± 3,88
Melt blending	100	0	57,28 ±2,06	58,41 ± 0,24	85,51 ± 1,99
	80	20	81,85 ±2,27	58,07 ± 0,42	69,58 ± 1,67
	20	40	85,39 ± 3,73	58,10 ± 0,29	79,34 ± 4,02

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Not only consideration should be given to the cartilage regeneration, but also to the subchondral bone, and their interface.

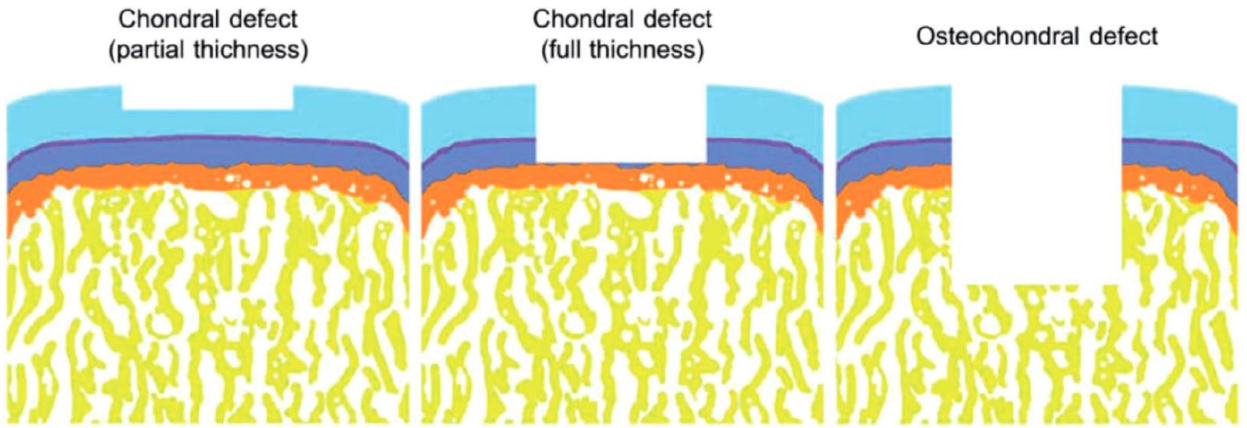

Fig. 5 Osteochondral defects extending deep into the subchondral bone. Reproduced from [77], with permission from Mary Ann Liebert, Inc

Abdulghani & Morouço (2019). J Mat Sci: Mat in Med

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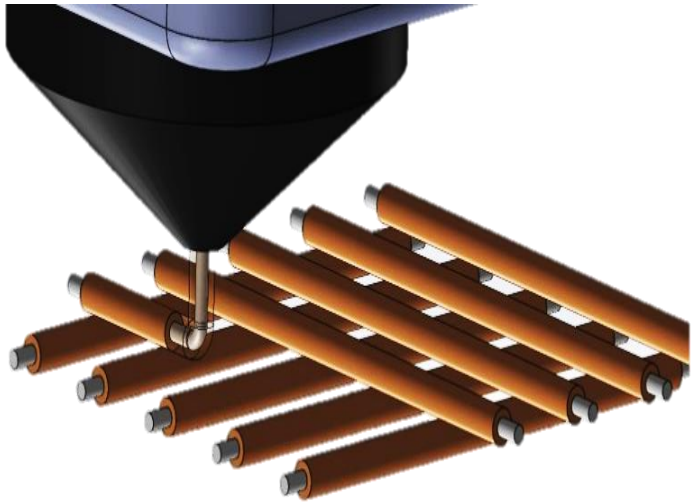

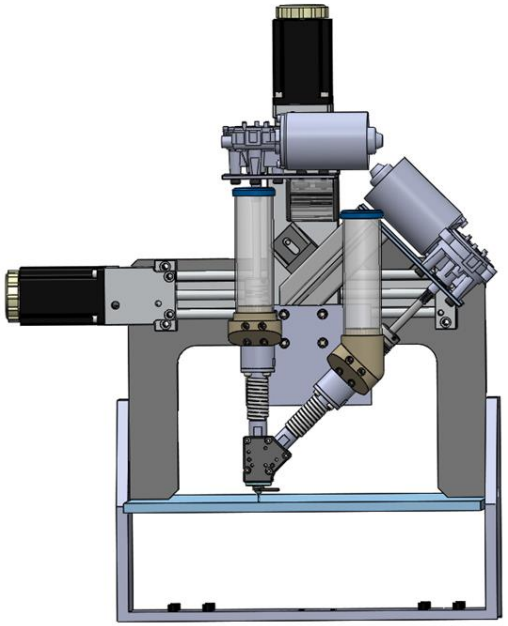

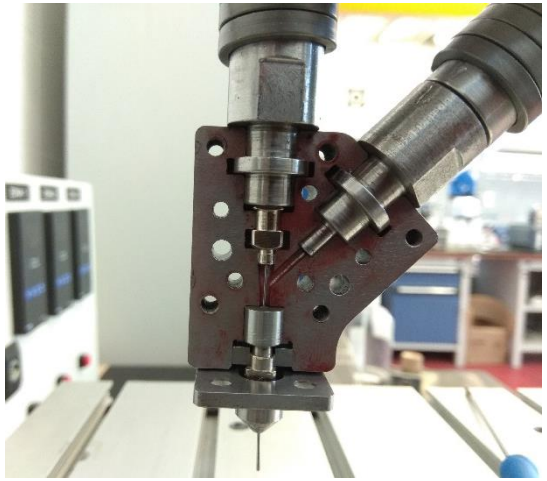

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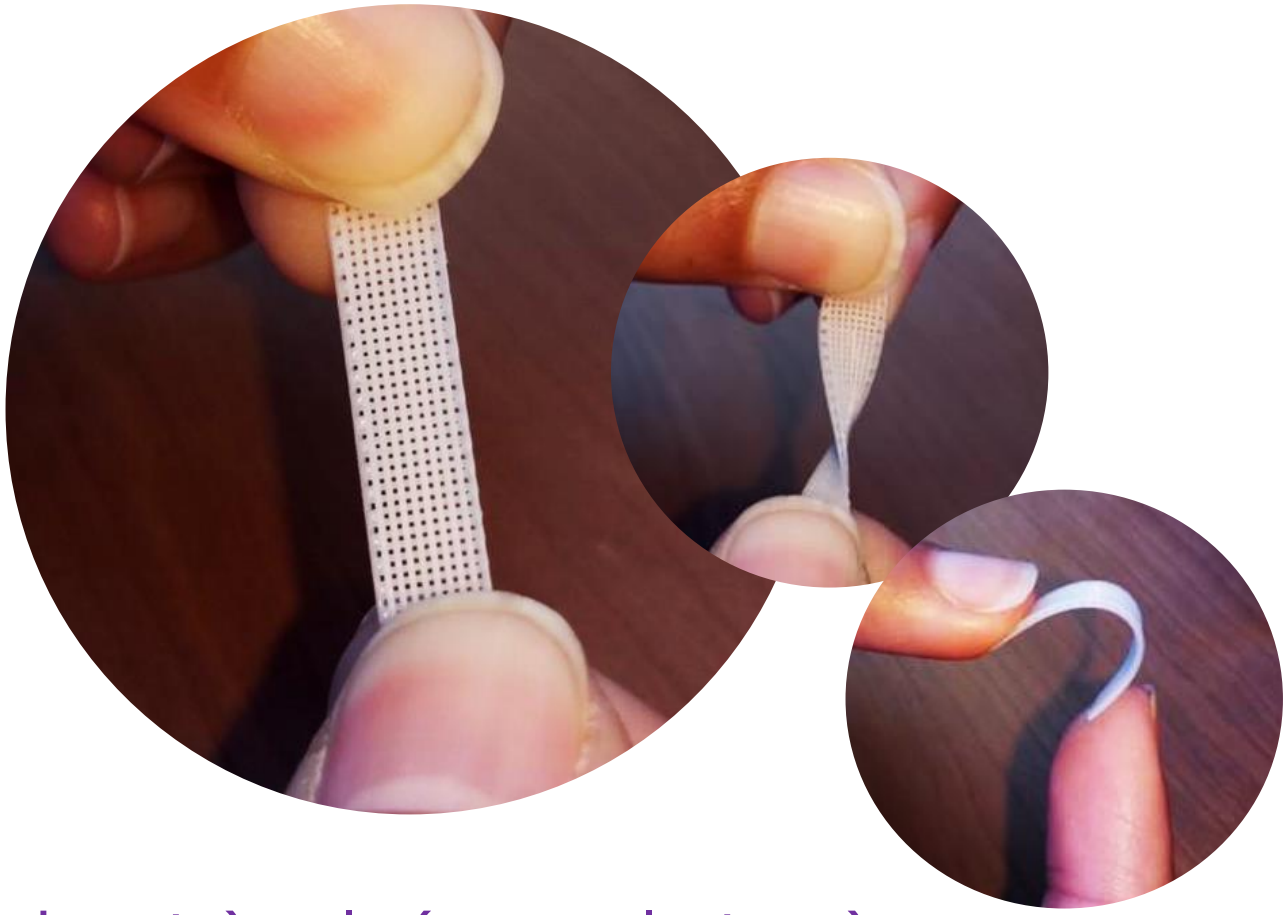

poly (glycerol sebacate)-poly (ε-caprolactone)

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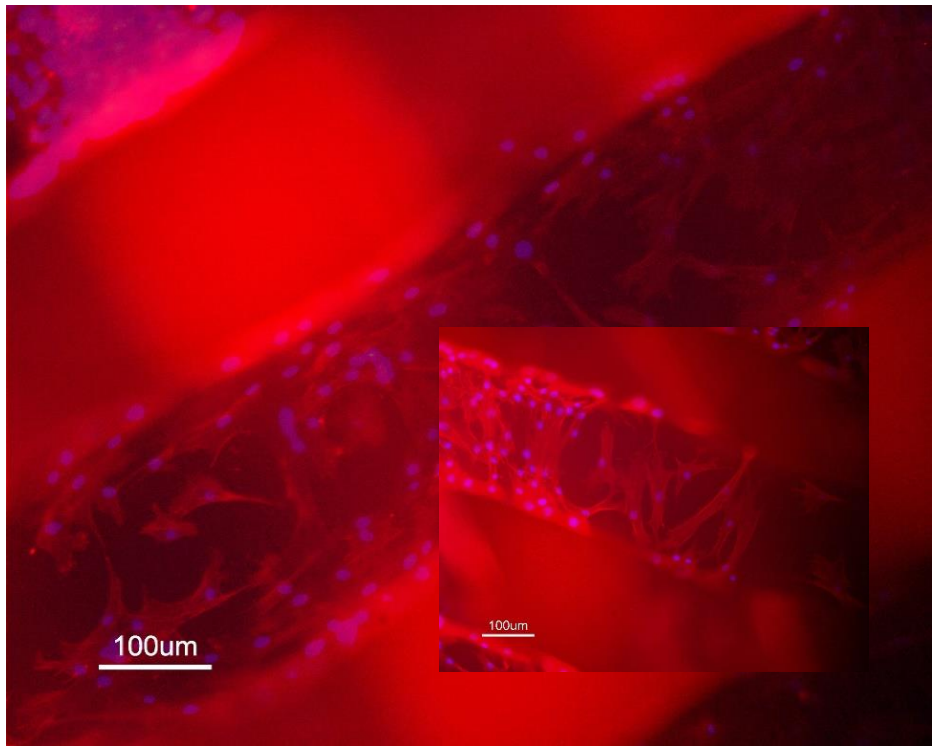
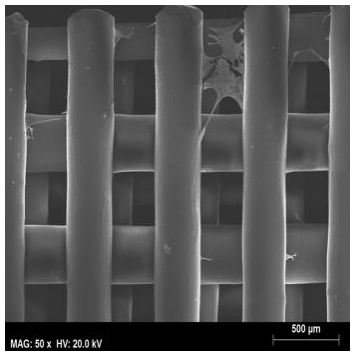
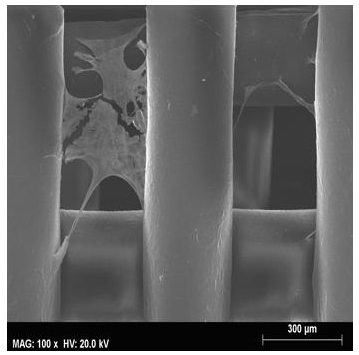
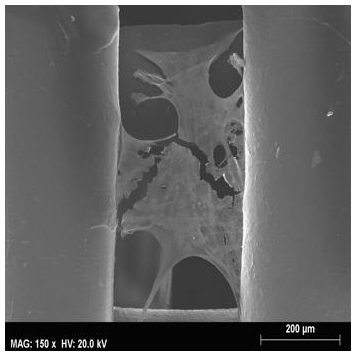
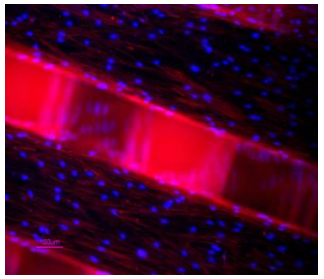
Polycaprolactone with graphene (0.25%; 0.50; 0.75%)

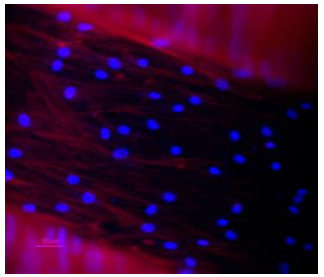


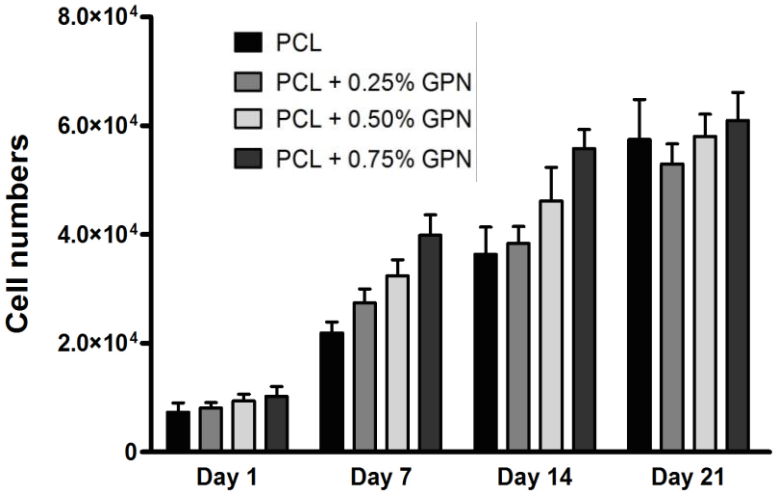












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What about the mechanical load over the joint?
EXERCISE

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Patients can be reassured that the exercise commonly prescribed to prevent or treat symptomatic knee OA seems to be safe for articular cartilage health.

PhD Academy Award

Exercise does not 'wear down my knee': systematic reviews and meta-analyses

Alessio Bricca

WHAT DID I DO?

I investigated the impact of exercise on knee joint articular cartilage. This aim was investigated in three different systematic reviews (SRs) of randomised controlled trials (RCTs) in healthy animals and in humans at risk of or with knee osteoarthritis (OA).

WHY DID I DO IT?

Exercise is the first-line treatment for knee OA.[1] Yet, many people still believe that exercise may '*wear down my knee*' creating a barrier to exercise.

Articular cartilage is the hallmark of OA and the structure I studied in my PhD. It is a connective tissue that covers bone ends in the joints and provides lubrication of the meeting surfaces, allowing the transmission of loads with a low frictional coefficient. Aggrecan, collagen and molecular biomarkers are the molecules responsible for maintaining cartilage integrity, function and metabolism, and the loss of some of these components, as occur when the OA disease progresses, jeopardises cartilage health.[2]

Mechanical loading is essential for articular cartilage thanks to the ability of articular cartilage to convert mechanical loading into cellular response that ultimately may lead to aggrecan and collagen synthesis. However, loading magnitudes and frequencies above (ie, overload) the loading range cartilage can tolerate or below it (ie, underloading) may be detrimental or insufficient to promote cartilage health.[3] Collectively, this knowledge suggests that theoretically the load generated by exercise to the knee joint, if not too high or too low, may actually be beneficial for cartilage.

HOW DID I DO IT?

I performed three SRs of RCTs spanning from healthy knees to knees with OA. The first SR included healthy animals where articular cartilage was assessed via histology, while the second and third SR included people at risk of, or with, knee OA with cartilage assessed via imaging biomarkers (ie, MRI) or molecular biomarkers from joint fluids (ie, blood, urine and synovial fluid), respectively.

I followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The literature searches were performed in at least five major databases, and the overall quality

- ✓ In the majority of patients, the evaluation protocols used for the adult population can be adopted, taking into account the specific functional limitations of each individual and the level of pain they present (ACSM, 2017);
- ✓ Avoidance of high intensity exercise when there is acute inflammation (ex: heat, swelling and joint pain), and all evaluation procedures should be postponed;
- ✓ Allow a warm-up period with moderate intensity before any progressive intensity test;
- ✓ Monitor the level of effort and pain during the test through the respective scales;
- ✓ The test should be discontinued when the patient reports severe pain.

#assessment

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- ✓ Start with short sessions and on alternate days;
- ✓ Reduce external resistance in the initial adaptation phase;
- ✓ Control the speed of execution and the amplitude of the movement;
- ✓ Avoid plyometric exercises;
- ✓ Avoid sudden movements;
- ✓ Work within the limit of pain;
- ✓ Confirm pain or discomfort 2 hours after training…

#proposal

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#land-based program

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#water-based program

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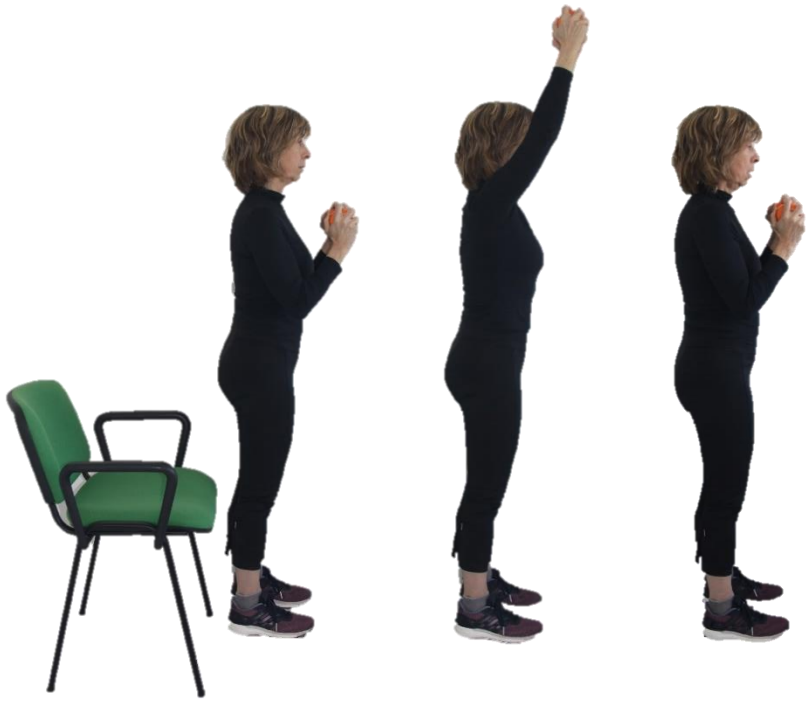

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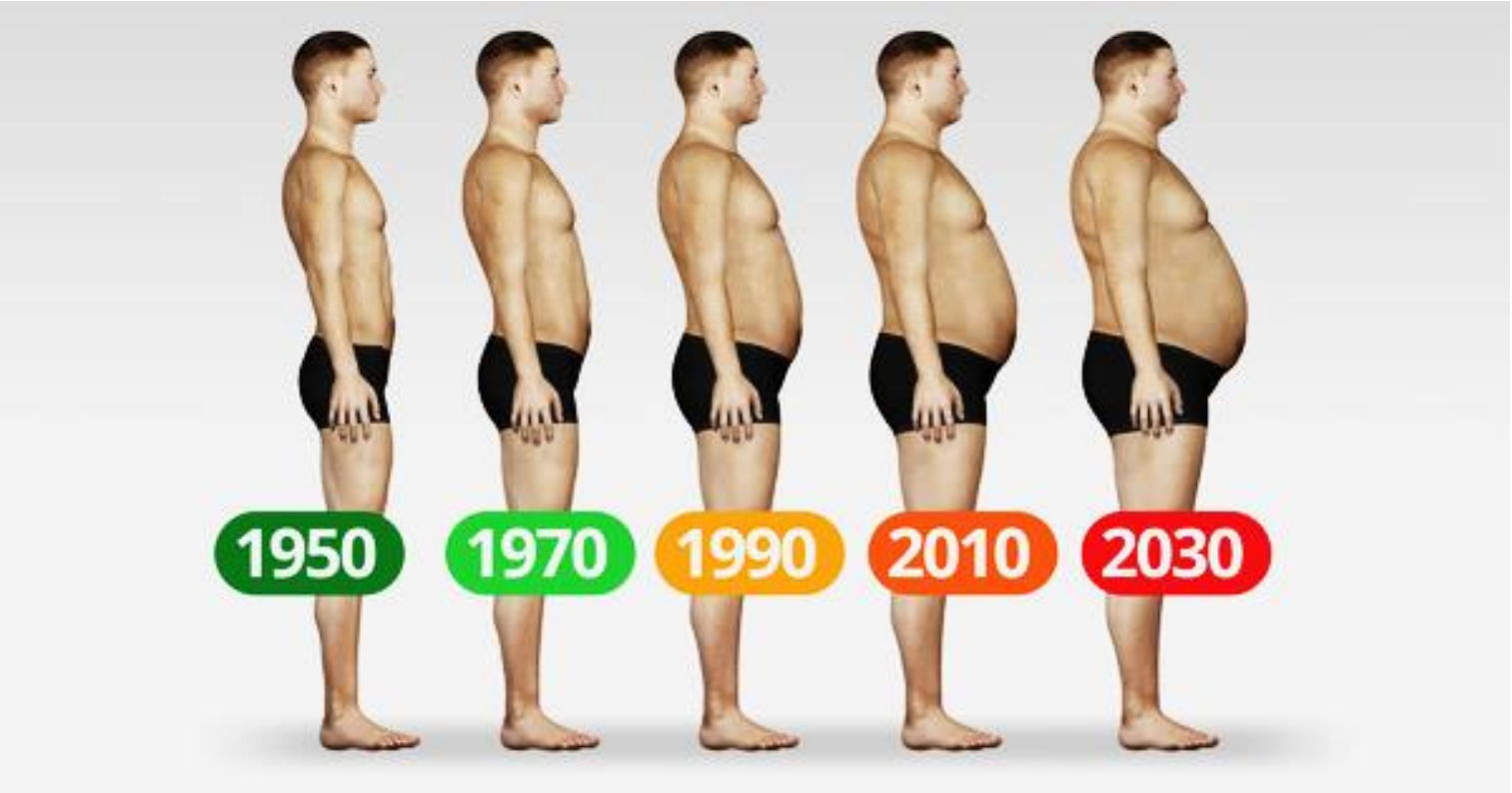

Yuri Teshler with image © iStock.com/angelhell

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What about further steps?

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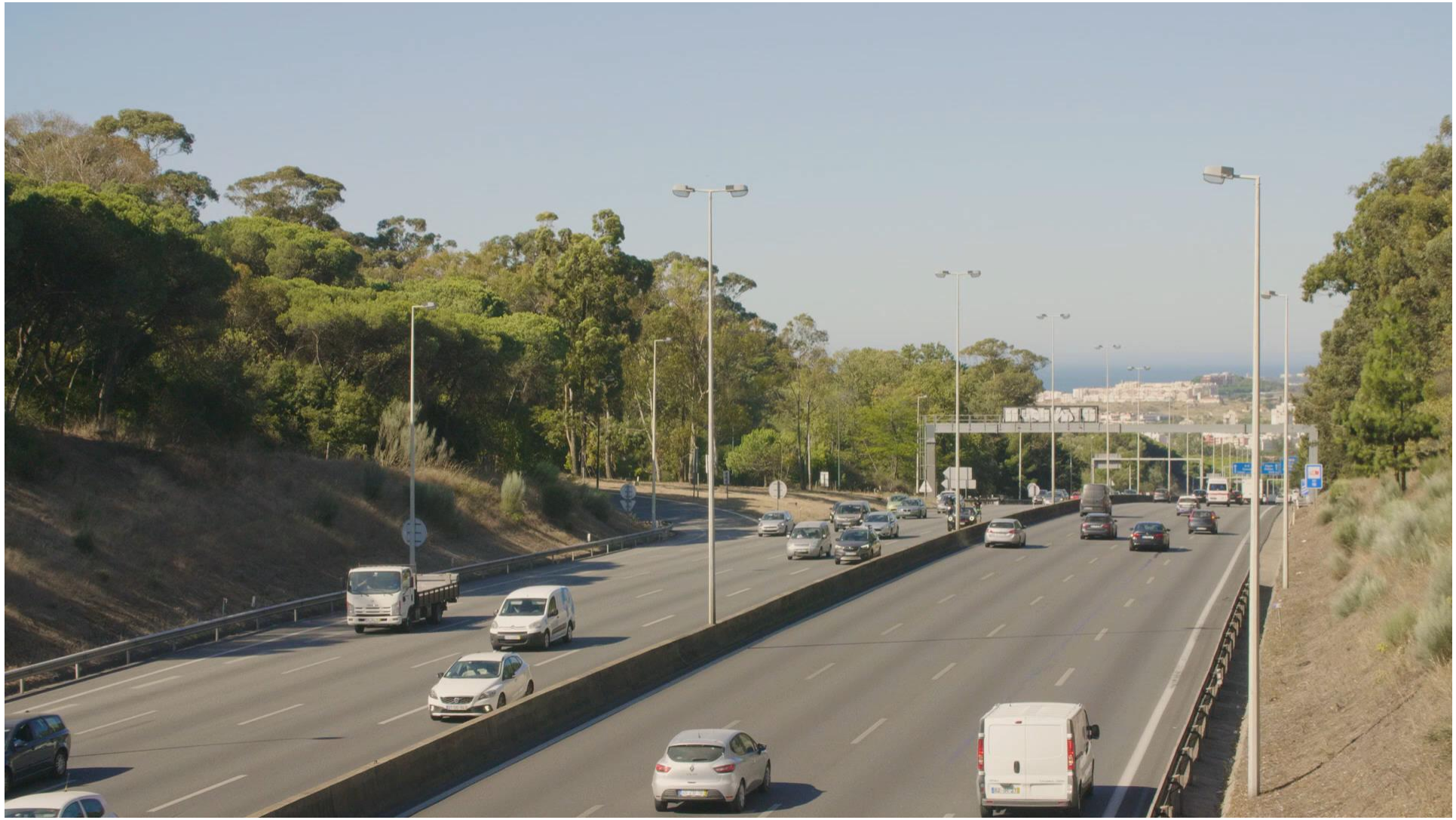

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Thank you for listening

Pedro Morouço, PhD, CSCS
pedro.morouco@ipleiria.pt
ORCID: 0000-0002-5956-9790
Researcher ID: K-9545-2013
Scopus Author ID: 24339135400
Twitter: pedromorouco

This research is supported by the European Regional Development Fund (FEDER), through COMPETE2020 under the PT2020 program (POCI-01-0145-FEDER-023423), and by the Portuguese Foundation for Science and Technology (UID/Multi/04044/2013).