# BIOMIMETIC TRIPHASIC CONSTRUCT FOR OSTEOCHONDRAL TISSUE ENGINEERING

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## Introduction

According to the last United Nation report, over 130 million people will suffer from Osteoarthritis (OA) worldwide by 2050, of whom 40 million will be severely disabled by the disease. OA is a long-term chronic disease that often develops in patients affected by non-treated traumatic osteochondral lesions [1].
The lack of effective treatments for osteochondral tissue (OTE) repair can be ascribed partially to the structural complexity of this region: this, in fact, is characterized by a multilayered architecture comprising of non-calcified – also referred to as hyaline – cartilage, calcified cartilage, and subchondral bone. In the last decade, various scaffold-based approaches for osteochondral repair have been investigated. Osteochondral tissue engineering strategies are generally categorized into monophasic, biphasic and triphasic models according to the number of biomaterials or cells present in the engineered structures [2–4].
From an engineering point of view, it is very challenging to fabricate structure with simultaneously concerted biological and mechanical characteristics between soft, viscoelastic hyaline cartilage and hard, stiff subchondral bone. The aim of the study was to combine the advances deposition systems based on (i) 3D Bioprinting combined with sprayed cross-linking system, (ii) innovative deposition system based on coaxial-needle extruder developed in-house, (iii) fused deposition modelling supplemented with post-printed treatment in order to fabricate the triphasic construct that could tailor structure and properties of native osteochondral tissue.

## Materials and Methods

Triphasic 3D construct is made of two bioinks (i) alginate (Alg) combined with short polylactide (PLA) fibers, (ii) alginate combined with gelatin methacrylate (GelMA) and ß-tricalcium phosphate particles that recapitulate cartilaginous parts of OTE. Corresponding to the subchondral bone we formulate the 3D scaffold with a potential to a stronger commitment toward early osteogenic differentiation of hMSC consisted of the 3D printed polycaprolacton scaffold subsequently modified with an innovative solvent treatment method based on acetone and ultrasounds impact.

## Results and Discussion

The multilayered TC structure was successfully fabricated by advanced fabrication techniques. Distinct zones were subsequently assembled into TC to recapitulate the osteochondral tissue.
Our results demonstrate the possibility of joining individually fabricated tissues into one integral triphasic model characterized by the proper biological and mechanical response. We successfully bioprinted the chondrocytes and the mesenchymal stem cells encapsulated in the hydrogel parts mimicking native non-calcified and calcified cartilage, respectively. Moreover, obtained surface topography increased osteogenic potential of the subchondral specific scaffold zone, making the proposed approach the best candidate to be bone substitute. Moreover, the conducted structure examination and mechanical testing of the constructs confirmed their potential use in osteochondral tissue engineering.

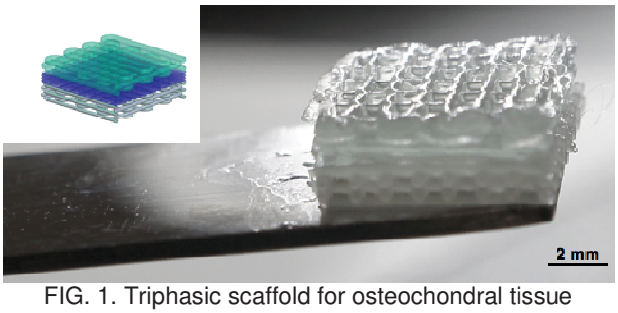


FIG. 1. Triphasic scaffold for osteochondral tissue engineering regeneration.

## Conclusions

The proposed triphasic construct provides an integral load-bearing structure and provides the individual functionality edifying the zonal structure of native osteochondral tissues.

## Acknowledgments

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