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The role of energy dissipation of polymeric scaffolds in the mechanobiological modulation of chondrogenic expression

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ABSTRACT

Mechanical stimulation has been proposed to induce chondrogenesis in cell-seeded scaffolds. However, the effects of mechanical stimuli on engineered cartilage may vary substantially between different scaffolds. This advocates for the need to identify an overarching mechanobiological variable. We hypothesize that energy dissipation of scaffolds subjected to dynamic loading may be used as a mechanobiology variable. The energy dissipation would furnish a general criterion to adjust the mechanical stimulation favoring chondrogenesis in scaffold. Epiphyseal chondro-progenitor cells were then subject to unconfined compression 2 h per day during four days in different scaffolds, which differ only by the level of dissipation they generated while keeping the same loading conditions. Scaffolds with higher dissipation levels upregulated the mRNA of chondrogenic markers. In contrast lower dissipation of scaffolds was associated with downregulation of chondrogenic markers. These results showed that energy dissipation could be considered as a mechanobiology variable in cartilage. This study also indicated that scaffolds with energy dissipation level close to the one of cartilage favors chondrogenic expression when dynamical loading is present.

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1. Introduction

Mechanical stimulation has been demonstrated to be one of the strategies for enhancing chondrogenesis and improving the mechanical properties of cell-based constructs [1–4]. Li and coworkers have shown that frequency and amplitude of dynamic compression modulate chondrogenesis of human bone marrow mesenchymal stem cells seeded in polymeric scaffolds [5]. However, specific frequency and amplitude may induce an effect in a particular scaffold that would be different in another. Indeed, the effects of mechanical stimuli on engineered cartilage may vary substantially between different scaffold types [6], probably because of different cell–scaffold interaction [7]. Consequently, interplay between dynamic compression and cell–matrix interaction may inhibit [8] or induce [9] the formation of cartilage-like tissues by chondrocytes. The conflicting results regarding the beneficial effect on chondrogenesis of a dynamic compression advocate to identify an overarching mechanobiological variable. This variable could then be used as a general criterion to adjust the mechanical stimulation favoring chondrogenesis in scaffold under mechanical stimulation.

Energy dissipation is a typical characteristic of viscoelastic materials such as polymeric scaffolds or articular cartilage [10]. Dissipation in cartilage relies on two internal mechanisms during deformation [11]. These mechanisms arise from the biphasic nature of articular cartilage, composed of a solid phase and liquid phase as modeled by Mow et al. [12]. The first internal dissipative mechanism, called intrinsic viscoelasticity, is due to solid–solid interactions in the cartilage extracellular matrix [13–16]. Those interactions are characterized by mechanical friction, chemical and electrostatic interactions, as well as physical entanglements between solid components of articular cartilage [14]. The second internal dissipative mechanism, called frictional drag, results from fluid–solid interactions. When articular cartilage is compressed, fluid movement occurs inducing frictions relative to the solid phase [12]. The two dissipative mechanisms may influence the cells behavior, either mediated by the glycocalix in response to fluid shear stress, or initiated by the force-induced unfolding of ECM proteins [17].

The dissipative properties of cartilage are usually characterized by hysteresis stress–strain curve [18]. In this work, we propose to consider energy dissipation as an overarching mechanobiological variable measured through a hysteresis curve because: (i) it encompasses all dissipative mechanisms related to solid and fluid phases, which may affect cell behavior; (ii) it is correlated to the tissue or scaffold microstructure (e.g. crosslinking and

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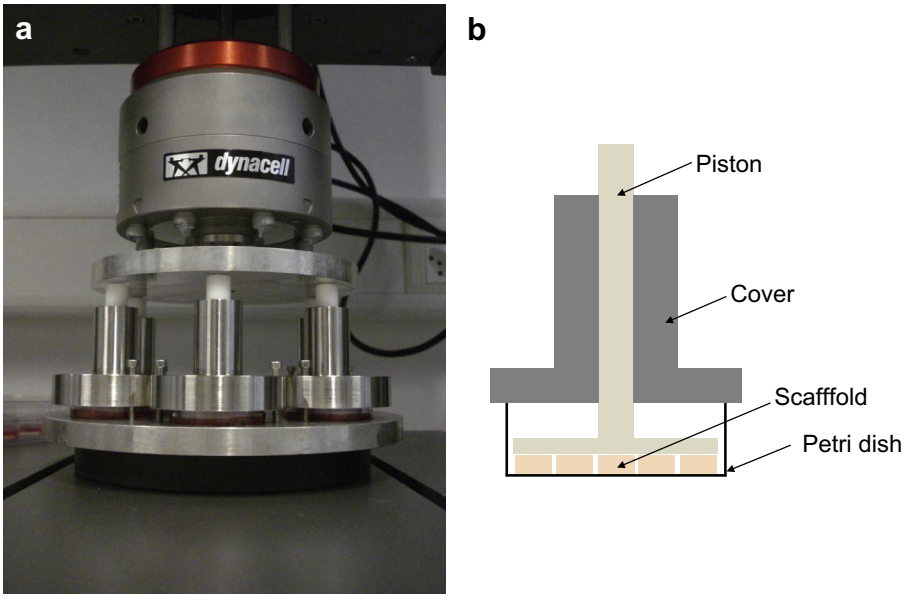

Fig. 1. (a). The custom-made bioreactor used to mechanically stimulate the cell–scaffold constructs. It consists of different testing chamber (up to six), each of which is composed of a petri dish containing a group of cell–scaffold constructs stimulated with a piston. All the testing chambers are loaded simultaneously with a plate, having a parallelism tolerance with pistons of 50 μm. The overall system is mounted on the Electropuls Dynamic Test System. (b) Scheme of a testing chamber, which loads a group of five cell–scaffold constructs.

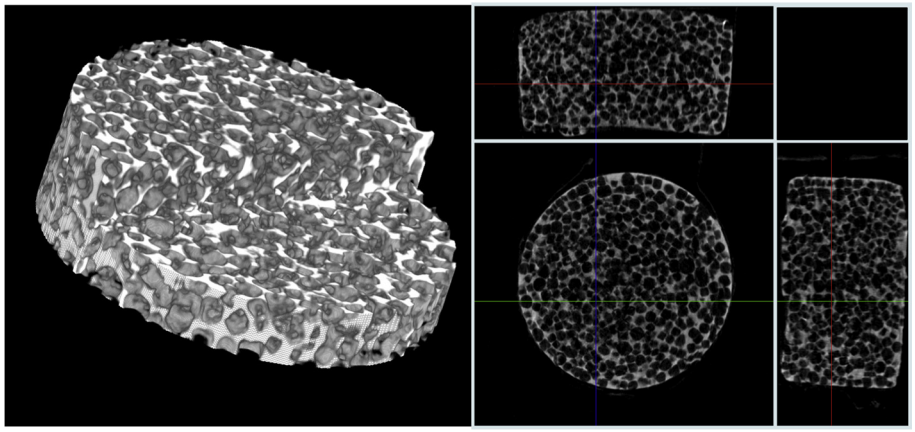

Fig. 2. Image of a reconstructed p(HEMA-co-EGDMA) scaffold from μCT scans, showing the pores interconnectivity.

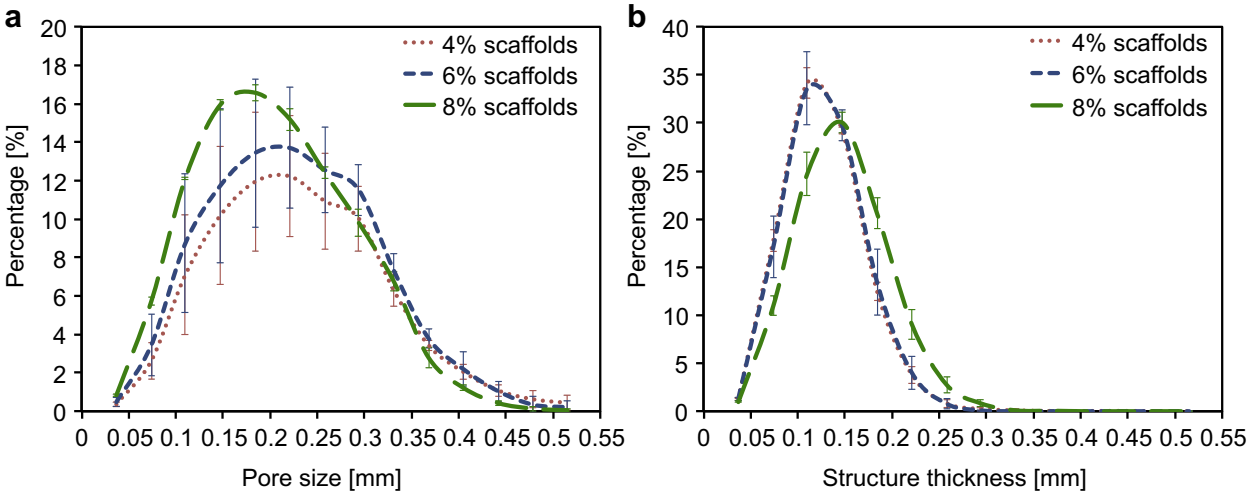

Fig. 3. Distribution of (a) pores size and (b) structure size in p(HEMA-co-EGDMA) scaffolds having 4%, 6% and 8% crosslinkers. For each group of scaffold $n = 3$.

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