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The Effect of Bone Tissue Engineering Scaffold Architecture on Mechanical Modulation of Cell Layer Behavior

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ABSTRACT: Advances in additive manufacturing techniques have made the design, control and modification of bone scaffolds inner architectures and their mechanical properties possible. Combination of computer-aided design, with amplitude modulation techniques has developed production and application of innovative bone tissue engineering scaffolds. Of note, computer-aided design bone scaffolds based on triply periodic minimal surfaces have attracted attentions, due to their high surface area to volume ratio pore interconnectivity which enhances cell migration and attachment. The mechanical stimuli acting while fluid is flowing through scaffold pores can influence on proliferation, migration, differentiation, and the fate of mesenchymal stem cell. Furthermore, the inner architecture of scaffold can determine the distribution and magnitude of these mechanical stimuli. In the present study using a tool of computational fluid dynamics, the interaction between 2 triply periodic minimal surfaces-based bone scaffolds, termed G and I, with fluid in the presence 8.5 µm-cell layer (as mesenchymal stem cell accumulation) have been evaluated. The results demonstrated that the scaffold G can modulate the cells more adequate due to producing a homogenous distribution of mechanical stimuli comparing to scaffold I. The range of shear stress and von Mises stress for scaffold G are not wide which means the cells are sensing roughly the same mechanical stimuli. For both scaffolds in inlet velocities less than 50 µm/s, the magnitude of stresses is negligible. In addition, for scaffold I, there are dead zones which mechanical stimuli are approximately zero which prevents dynamic cell culture and homogenous signaling.

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1- Introduction

Bone is a dynamic tissue with high potential for repair and regeneration, mainly due to its continuous matrix remodeling. Injured bones with small sizes can be repaired spontaneously through natural healing and remodeling [1]. However, in large injuries accompanying with bone tissue integrity loss, the tissue cannot actively repair itself. The gold standard is autograft (a bone graft from the same patient). The limited bone graft sources in the body and multiple surgeries are demerits of this method [2]. The alternative method is allograft (a bone graft from the other donors) which is prone to transfer disease, infection, and rejection by the immune system [3]. Nevertheless, the bone tissue engineering provides a bone scaffold, a supportive structure recovering the integrity of tissue, to overcome the limitations associated with either autograft or allograft [4]. The Scaffolds designed using Computer-Aided Design (CAD) techniques offer a flexible approach to control over structural properties. Application of mathematical implicit surfaces, belong to a hyperbolic superfamily, is a novel approach to fabricate scaffolds with required properties [5]. Triply Periodic Minimal Surfaces (TPMSs), with zero mean curvatures and 3D periodicity, provide high available surface area per volume for cells to spread, migrate, proliferate and differentiate [1]. In the present study, the effect of inner architectures of two scaffolds designed based on TPMSs on the mechanical modulation of thin layers representing spread cells has been addressed using computational fluid mechanics.

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Methodology

1- 1- Scaffold and cell layer design

One of the challenges regarding bone tissue engineering is to design and fabricate biologically optimum porous scaffolds. Consolidation of CAD with advance additive manufacturing (3D printing) facilitates the production of the bone scaffolds with excellent structural properties [6]. Two surfaces, namely G and I, were drawn using K3DSurf software, Eqs. (1) and (2), respectively, and converted to the scaffolds by a CAD software with the size of 1.67mm×0.83mm×0.83mm, shown in Fig. 1.

$$G(r)=\mathrm{Cos}(X)\mathrm{Sin}(Y)+\mathrm{Cos}(Y)\mathrm{Sin}(Z)+\mathrm{Cos}(Z)\mathrm{Sin}(X) \quad (1)$$

$$I(r)=2\left[\mathrm{Cos}(X)\mathrm{Cos}(Y)+\mathrm{Cos}(Y)\mathrm{Cos}(Z)+\mathrm{Cos}(Z)\mathrm{Cos}(X)\right]-\left[\mathrm{Cos}(2X)+\mathrm{Cos}(2Y)+\mathrm{Cos}(2Z)\right] \quad (2)$$

The spread cell accumulation within the scaffolds was considered as a uniform layer with the thickness of 8.5µm (half of the mesenchymal stem cell diameter) and designed using CAD software, as illustrated in Fig. 1.

One of the most common biopolymers used for bone scaffold is polycaprolactone. Here, the mechanical properties this material have been considered for simulation of the scaffolds, Young's modulus of 0.3 GPa and Poisson's ratio of 0.3 [7]. The instantaneous Young's modulus of the human mesenchymal stem cells undergoing osteogenic differentiation has been measured 890±219 Pa and Poisson's ratio of 0.45 [8].

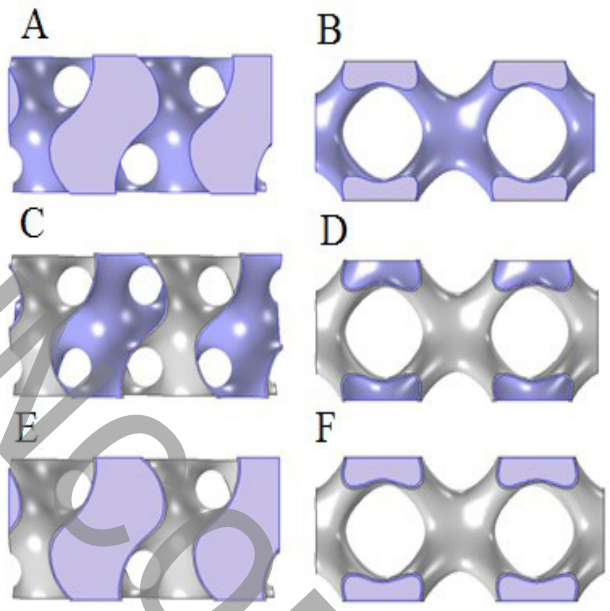

Figure 1. Designed structures: (A) Scaffold G; (B) Scaffold I; (C) Cell layer for scaffold G; (D) Cell layer for scaffold I; (E,F) Scaffold-Cell layer positioning.

1- 2- Fluid-structure interaction

The fluid has been considered as the cell culture medium, a Newtonian fluid with viscosity and density of 1.45 MPa.s and 1000 kg.m^{-3}, respectively [9]. The inlet velocities of 1, 10, 25, 50, and 100 µm.s-1 were applied and the outlet was a zero-pressure condition. COMSOL Multiphysics® software has been used to simulate the fluid flow through the scaffolds with the governing equations of Navier-Stokes.

2- Results and Discussion

The maximum velocities within the scaffold G are greater than scaffold I in different inlet velocities. It indicates that the available area for fluid is limited in this scaffold and the fluid flows with more difficulty through the pores. Of note, the difference in scaffold geometry definitely influences the velocity on the walls, where the cells are located and sense it. It should be considered that the high velocity within the scaffold may detach the cells. Even though the scaffold I facilitates the fluid flow through the pores, its geometry creates dead zones, the areas with near zero velocity. These dead zones induce static cell culture conditions and non-uniform velocity distribution.

Wall shear stress for the inlet velocities of 1, 10, 25, 50, and 100 µm/s for scaffold G resulted as 0.18-0.4, 1.8-4, 4.5-10, 9-20, and 18-40 MPa, and for scaffold I as 0.07-0.26, 0.7-2.6, 1.75-6.5, 3.5-13, and 7-26 MPa, respectively. Comparing these values with the effective shear stress range to induce the osteogenic differentiation in the mesenchymal stem cells, 0.4-2.2 Pa [10], indicates that neither of the scaffolds with inlet velocities less than 50 µm/s is not efficient for this goal. On the other hand, in biological conditions, human osteoblasts are sensing the shear stress of 0.8-3 Pa, which still higher than the results from these two scaffolds. Furthermore, shear stresses less than 10-4 Pa are negligible [11].

Von Mises stress for scaffold G in the inlet velocities of 1, 10, 25, 50, and 100 µm/s calculated as 0.65, 6.5, 16.2, 32.5, and 65 MPa, and scaffold I as 0.5, 5, 12.5, 25, and 50 MPa. The differences between the values are not significant, however, due to the scaffold I geometry, there are areas in this scaffold where both wall shear stress and von Mises stress are near zero. Even though this scaffold performs well in passing the fluid through the pores, these dead zones lead to unbalanced signaling to the cultured cells resulting in uneven differentiation. Fig. 2 demonstrates the scaffolds and cellular layers and the dead zones in scaffold I.

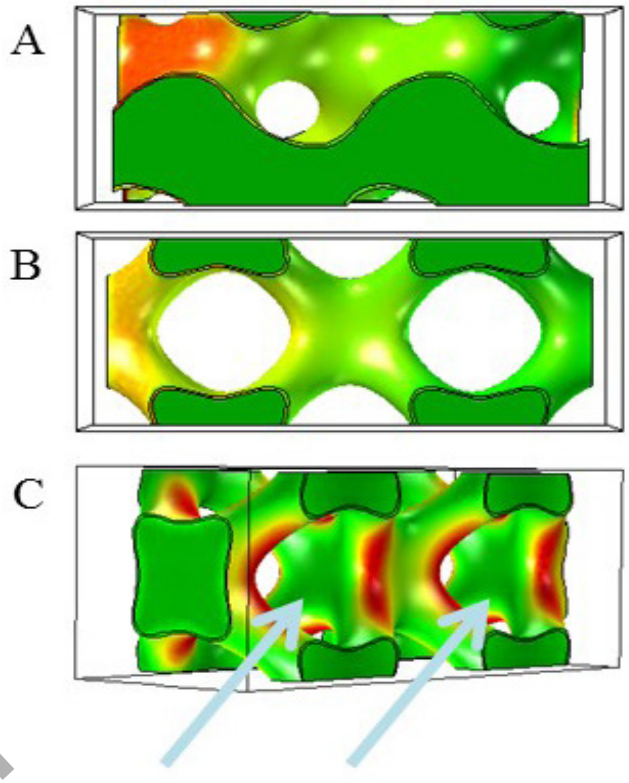

Figure 2. Von Mises stress distribution in: (A) Scaffold G; (B) Scaffold I; and (C) Dead zone in scaffold I.

3- Conclusions

In this paper, the interaction between the cellular layer, representing the cell accumulation, with mechanical properties of mesenchymal stem cells with two computer-aided design scaffolds based on triply periodic minimal surfaces, namely G and I, were evaluated. The results demonstrated scaffold G, due to its geometry, distributes wall shear stress and von Mises stress more evenly and has better performance in modulating the cultured cells. On the other hand, scaffold I creates zones with near zero stresses and fails to apply uniform mechanical forces. For both scaffold, in inlet velocity less than 50 µm/s, resulted stresses are negligible.

References

[1] A.B. Nik, B. Vahidi, The effect of bone scaffold gradient architecture design on stem cell mechanical modulation: a computational study, in Biomedical Engineering (ICBME), 2015 22nd Iranian Conference on biomedical engineering, IEEE, 2015, pp. 309-313.

[2] S. Wu, X. Liu, K.W. Yeung, C. Liu, X. Yang, Biomimetic porous scaffolds for bone tissue engineering, Materials Science and Engineering: R: Reports, 80 (2014) 1-36.

[3] R. Voronov, S. VanGordon, V.I. Sikavitsas, D.V. Papavassiliou, Computational modeling of flow-induced

shear stresses within 3D salt-leached porous scaffolds imaged via micro-CT, Journal of biomechanics, 43(7) (2010) 1279-1286.

[4] E. Baas, J.H. Kuiper, Y. Yang, M.A. Wood, A.J. El Haj, In vitro bone growth responds to local mechanical strain in three-dimensional polymer scaffolds, Journal of biomechanics, 43(4) (2010) 733-739.

[5] S. Giannitelli, D. Accoto, M. Trombetta, A. Rainer, Current trends in the design of scaffolds for computer-aided tissue engineering, Acta biomaterialia, 10(2) (2014) 580-594.

[6] D.-J. Yoo, Advanced porous scaffold design using multi-void triply periodic minimal surface models with high surface area to volume ratios, International journal of precision engineering and manufacturing, 15(8) (2014) 1657-1666.

[7] L. Elomaa, S. Teixeira, R. Hakala, H. Korhonen, D.W. Grijpma, J.V. Seppälä, Preparation of poly (ε-caprolactone)-based tissue engineering scaffolds by stereolithography, Acta biomaterialia, 7(11) (2011) 3850-3856.

[8] H. Yu, C.Y. Tay, W.S. Leong, S.C.W. Tan, K. Liao, L.P. Tan, Mechanical behavior of human mesenchymal stem cells during adipogenic and osteogenic differentiation, Biochemical and biophysical research communications, 393(1) (2010) 150-155.

[9] F. Zhao, T.J. Vaughan, L.M. Mcnamara, Multiscale fluid-structure interaction modelling to determine the mechanical stimulation of bone cells in a tissue engineered scaffold, Biomechanics and modeling in mechanobiology, 14(2) (2015) 231.

[10] G. Yourek, S.M. McCormick, J.J. Mao, G.C. Reilly, Shear stress induces osteogenic differentiation of human mesenchymal stem cells, Regenerative medicine, 5(5) (2010) 713-724.

[11] A.B. Yeatts, J.P. Fisher, Bone tissue engineering bioreactors: dynamic culture and the influence of shear stress, Bone, 48(2) (2011) 171-181.