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Performance analysis of bone scaffolds with carbon nanotubes, barium titanate particles, hydroxyapatite and polycaprolactone

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Abstract. This paper presents a novel structural composition for artificial bone scaffolds with an appropriate biocompatibility and biodegradability capability. To achieve this aim, carbon nanotubes, due to their prominent mechanical properties, high biocompatibility with the body and its structural similarities with the natural bone structure are selected in component of the artificial bone structure. Also, according to the piezoelectric properties of natural bone tissue, the barium titanate, which is one of the biocompatible material with body and has piezoelectric property, is used to create self-healing ability. Furthermore, due to the fact that, most of the bone tissue is consists of hydroxyapatite, this material is also added to the artificial bone structure. Finally, polycaprolactone is used in synthetic bone composition as a proper substrate for bone growth and repair. To demonstrate, performance of the presented composition, the mechanical behaviour of the bone scaffold is simulated using ANSYS Workbench software and three dimensional finite element modelling. The obtained results are compared with mechanical behaviour of the natural bone and the previous bone scaffold compositions. The results indicated that, the modulus of elasticity, strength and toughness of the proposed composition of bone scaffold is very close to the natural bone behaviour with respect to the previous bone scaffold compositions and this composition can be employed as an appropriate replacement for bone implants.

Keywords: artificial bone scaffold; carbon nanotube; hydroxyapatite; polycaprolactone; barium titanate; finite element analysis

1. Introduction

Bone is an extraordinary bio composite that, in addition of having low inertia to minimize the amount of energy needed to move the body, it must also have enough strength to withstand the body weight and the common forces involved in daily activities. Bones are continually restoring tissue, and are usually self-repaired and welded by itself due to non-acute fractures or damages. Therefore, bone is one of the tissue with the self-healing ability. But after 25 years, the amount of bone resorption is slightly increased, which leads to a gradual decrease in bone density.

In severe injuries that result in large amounts of bone loss or localized infection, the bone will no longer be able to fully restored, and the defects will remain intact. Also due to diseases such as osteoporosis, the bone regeneration cycle is slowed down and its density decreases significantly. It

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followed considerable reduction in the elasticity modulus and bone strength. In these situations, the problem of choosing an appropriate replacement for bone is mentioned. So that it can performed the duties of the natural bone as much as possible and have minimal side effects for the patient simultaneously.

Significant statistics of osteoporosis patients as well as severe injuries from incidents in which the amount of bone loss is so high that self-repair is not feasible. Therefore, many researchers have been carried out to achieve an appropriate replacement of damaged bones.

The early researches in the field of modern tissue engineering are as follows: Langer and Vacanti (1993) discussed the foundations and challenges of tissue engineering as an interdisciplinary field to provide solutions to tissue creation and repair. Nerem and Sambanis (1995) reviewed the history of tissue engineering, as well as the current status and future possibilities in the development of different bio-artificial constructs.

The first attempt to employed nano composites in the bone scaffolds is performed by Hao *et al*. (2003), they used experimental tests and analytical modelling to prove that; the composition of poly ($\mathcal{E}$-caprolactone) with hydroxyapatite nanocrystals are biodegradable and bio-compatible nano composites. Williams *et al*. (2005), designed porous Polycaprolactone scaffolds, using finite element method (FEM) and then fabricated it via selective laser sintering.

Fang *et al*. (2005) presented a computer aided characterization approach to evaluate the effective mechanical properties of porous tissue scaffold. Zhao *et al*. (2005), used chemically functionalized single-walled carbon nanotubes (SWNTs) as a scaffold for the growth of artificial bone material. Zanello *et al*. (2006) explored the use of carbon nanotubes (CNTs) as suitable scaffold materials with the aim of controlling cell growth for osteoblast proliferation and bone formation.

Shi *et al*. (2007) investigated the fabrication of highly porous scaffolds made of poly propylene fumarate (PPF) polymer, an ultra-short single-walled carbon nanotube nanocomposite, and a dodecylated US-tube nanocomposite. They also evaluated the effects of material composition and porosity on the scaffold pore structure, mechanical properties, and marrow stromal cell culture. Clendenin *et al*. (2007) suggested to design and fabrication of a bio-sensor based on aligned single wall carbon nanotubes for the aim of DNA detection.

Hilder and Hill (2008), proposed to employed carbon nanotubes as drug delivery nanocapsules. They determined the suction behaviour of cisplatin and a platinum-based anticancer drugs, containing carbon nanocapsules. PourAkbar Saffar *et al*. (2008) presented finite element method for modelling chemical bonding between functionalized carbon nanotubes and matrix in carbon nanotube reinforced composites. They also presented a simplified model for estimating the axial Young's modulus of artificial bone scaffold with the composition of carbon nanotubes and hydroxyapatite (Hilder and Hill 2010).

Li (2010) in his PhD dissertation, developed methods and models to represent the dispensing-based solid free form scaffold fabrication process with and without the presence of living cells. Jamilpour *et al*. (2011) used finite element modelling and studied the cracks behaviour in both natural and artificial bones. Hirata *et al*. (2011), applied surface coating treatment with multi-walled carbon nanotubes to the 3-dimensional collagen scaffold for bone tissue engineering.

Mattioli-Belmonte *et al*. (2012), suggested to utilize the microfabricated carbon nanotube-polycaprolactone composite for bone tissue engineering scaffolds. They analyzed the creep and stress relaxation behaviour of the composite material to identify an optimal composition for bone tissue engineering. Rodrigues *et al*. (2012), investigated the potential use of polyvinyl alcohol hydrogel, alone and reinforced with two types of carbon nanoparticles, in treating osteochondral defects.

Doty *et al*. (2015) investigated single and dual-delivery of two antibiotics, vancomycin and amikacin, targeting different classes of microorganism from a biodegradable calcium sulfate-chitosan-nHA microsphere composite bone scaffold. Xing *et al*. (2016) developed the integration design approach for the artificial bone scaffolds based on the computer aided design, finite element analysis and computational fluid dynamics. Recently, Gutiérrez-Hernández *et al*. (2017) explored the use of native bacterial cellulose in combination with functionalized multi-walled carbon nanotubes as an original biomaterial, suitable three-dimensional scaffold for osteoblastic cell culture.

According to the above-mentioned research, bone scaffold with a combination of all four materials of carbon nanotubes, barium titanate particles, hydroxyapatite and polycaprolactone has not yet been studied. Therefore, this paper presents a novel structural composition for application in artificial bone scaffolds with an appropriate biocompatibility and biodegradability capability.

2. Materials and methods

2.1 Materials

This section presented, the characteristics and properties of the proposed four materials used in the artificial bone scaffolds. Firstly, in this study, carbon nanotubes due to the prominent properties and high biocompatibility with the body and its structural similarities with the natural bone tissue, as well as the very good mechanical properties exhibited under stress and strain, is considered in the component of the artificial bone scaffold. Carbon nanotubes have many important characteristics such as: high mechanical strength and elastic properties, excellent heat conduction, variety in the electronic properties in the range of semiconducting to metal, electronic sensitivity to chemical absorbers and mechanical strains, high ratio of length to diameter and high ratio of surface to volume as well as high biocompatibility with the human body.

The bone is living and dynamic tissue and is frequently exposed to stress and damage from the outside and internal environment. So that having a self-healing ability for bone (whether natural or artificial) is very important. The bone is also a piezoelectric material that is produced electric current by applying stresses and strains. It has a great role in sending messages and forming an electromagnetic field, which is one of the factors in the initiation of the bone reconstruction process. Therefore, in the proposed bone scaffold to achieve this property, the barium titanate, which is one of the biocompatible material with body (Ball *et al*. 2014, Genchi *et al*. 2016) and has piezoelectric properties, is used to create self-healing ability.

Hydroxyapatite is the most important mineral component of bone tissue and has a good biocompatibility and bioactivity properties. Unfortunately, this substance is very brittle in normal condition and does not have the ability to replace bone tissue. The structure of hydroxyapatite is very similar to bone structure. Calcium phosphate as well as hydroxyapatite has similar chemical composition to bone tissue. It has many advantages such as: biocompatibility, no inflammation and no inflammatory reaction, and having the ability to produce bone cells. The combination of these features makes this material particularly suitable for implantation in the bone.

Polycaprolactone is a biocompatible polymer that is used to absorb and release drugs effectively, to enhance growth and regeneration rate in the bone defect process. One of the advantages of this polymer is the biodegradability of this material in comparison with other bio-

Table 1 Modulus of elasticity and Poisson's ratio of the carbon nanotubes, barium titanate particles, hydroxyapatite and polycaprolactone (Williams *et al*. 2005, PourAkbar Saffar *et al*. 2009, 2010, Jamilpour *et al*. 2011a, b and Meyers *et al*. 2008)

Item No.	Material	Modulus of elasticity (Gpa)	Poisson's ratio
1	Carbon nanotube	1010	0.28
2	Hydroxyapatite	130	0.3
3	Barium titanate	67	0.23
4	Poly-caprolactone	1.2	0.3

polymers. The other advantages of this material are: good mechanical properties and easy formability to create a porous structure with suitable dimensions for cell growth. Therefore, polycaprolactone is used in synthetic bone composition as a proper substrate for bone growth and repair. Table 1, presented the modulus of elasticity and Poisson’s ratio of the carbon nanotubes, barium titanate particles, hydroxyapatite and polycaprolactone.

Based on this, and taking into account the characteristics of natural bone, the materials proposed in this design are selected in the best way possible and in harmony with each other, provided the restore and repair of the bone. For example, the substance of barium titanate, by simulating the piezoelectric properties of the natural bone in the field of sending nerve signals, together with a carbon nanotube that is an electrical conductor, can created the electrical potential generated by stress or strain induced fields in the natural bones.

2.2 Methods

In this section, to demonstrate the performance of presented bone scaffold composition, the finite element modelling method of the proposed bone scaffold is introduced. It can be assumed that the mechanical stimulus system of bone growth and restoration is sensitive to the maximum amount of strain energy in a loading period (Huiskes *et al*. 2000). In this study and in accordance with the presented results by (Huiskes *et al*. 2000, Ruimerman *et al*. 2005), the maximum amount of strain energy generated by the quasi-static load applied to the bone scaffold is simulated using the ANSYS Workbench finite element software.

The research is based on the hypothesis that bone marrow osteocyte cells act as sensors and measure stresses and strains under different conditions in the bone, and then proportional signals sent for osteoclasts and osteoblasts which is responsible for bone resorption and bone repair. Accordingly, due to any changes in the magnitude of bone stress and strain, the bone renewal rate and subsequently the magnitudes of bone density and mechanical strength are also affected.

Conventional analytical mathematical tools available for stress analysis are not widely used to simulate body organs, which have very complex geometry and behaviour. Among the numerical methods, the finite element method, which is a high-performance methodology in complex modelling and analysis, is recognized as the most widely used method in biomechanical simulations. The FEM is widely used to analyze the stress and strain in the bone, the fracture condition and the design and optimization of joints.

Here according to Fig. 1, modelling of the bone scaffold element is considered as a four-layer elastic solid nano-cylinder. So that each layer represented one of the four materials with the stacking sequences of carbon nanotubes, hydroxyapatite, barium titanate particles and polycaprolactone respectively from the inner to outer surface of nono-cylinder. The carbon

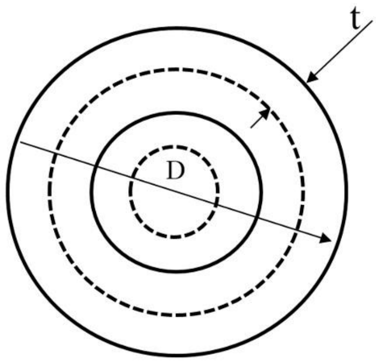

Fig. 1 Cross section of bone scaffold model

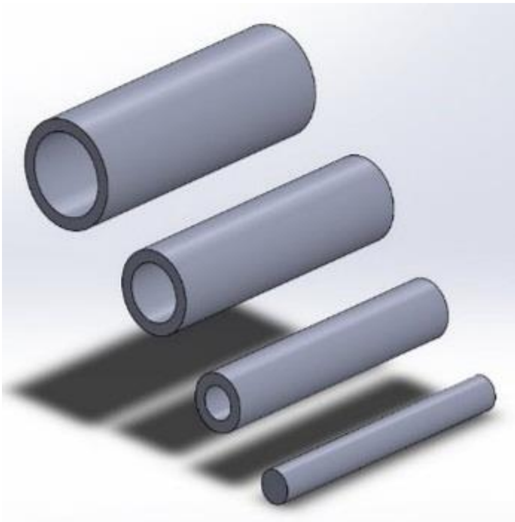

Fig. 2 Solid and hollow cylindrical components represented the four materials in the FEM modelling

nanotube cylinder's thickness in many researches such as (Tserpes and Papanikos 2005) is assumed to be equal to the diameter of a carbon atom and the Van der Waals equilibrium distance between two adjacent graphite atoms is 0.34 nm. With an appropriate approximation, the carbon nanotubes can be considered as solid cylindrical shells. Therefore, the model used for carbon nanotubes is a solid cylinder with a diameter of 1.08 nm, which has similar dimensions with the nanotubes. It has shown that the presence or absence of a cap on a carbon nanotube has no significant effect on the results of modelling (Gao and Li 2005).

The bone is a non-homogeneous, anisotropic, and viscoelastic substance, but in the physiological load range, bone can be considered as a linear elastic material with negligible viscoelastic effects. Here solid cylinder beam elements with diameter of 1.08 nm is used for finite element modelling of carbon nanotubes and the beam elements that represented other materials are in the form of hollow cylinders whose thickness and diameter are determined by the volume fractions of that layer in the bone scaffold. Knowing the modulus of elasticity and volume fraction of each material, the total modulus of elasticity of the bone scaffold can be calculated using the rule of mixture.

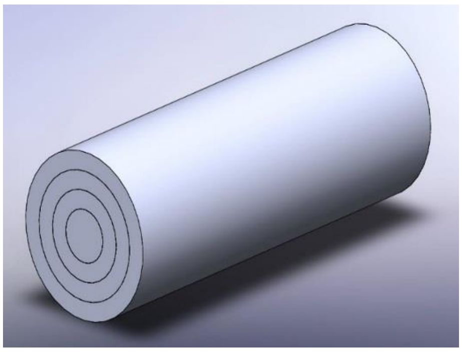

Fig. 3 The artificial bone scaffold model used for finite element analysis

Table 2 Comparison of the modulus of elasticity of nano bone scaffold calculated in the presented solution method with the cross-linking model

Carbon nanotubes volume fractions (%)	Modulus of Elasticity (GPa)	
	Presented method	Cross-linking model presented by (PourAkbar Saffar *et al.* 2008, 2009)
1	138.4	134.7
2	147.1	144.9
3	155.7	150.9
4	164.4	156.0
5	173.1	164.6
8	181.9	173.4
10	189.7	185.3

In Fig. 2, an illustration of each of the solid and hollow cylindrical components used in this modelling is shown. Each cylinder represented one of the four materials. Then, according to Fig. 3, by combining of these four cylinders, the artificial bone scaffold model used for finite element analysis is created. This bone scaffold is considered to be fixed at one end and the free end is subjected to tensile axial force.

3. Results and discussions

3.1 Validation

To demonstrate the validity and precision of the presented modelling method, the properties of the bone scaffolds obtained by the presented modelling method is compared with the results available in the literatures. It is noteworthy that, due to lack of artificial bone scaffolds with the presented composition, the solution method is validated by two-phase nano bone scaffold composed of carbon nanotubes and hydroxyapatite investigated by (PourAkbar Saffar *et al*. 2008, 2009).

In Table 2, the modulus of elasticity of nano bone scaffold calculated in the proposed solution method with the carbon nanotubes volume fractions of 1, 2, 3, 4, 5, 8 and 10 percentages is

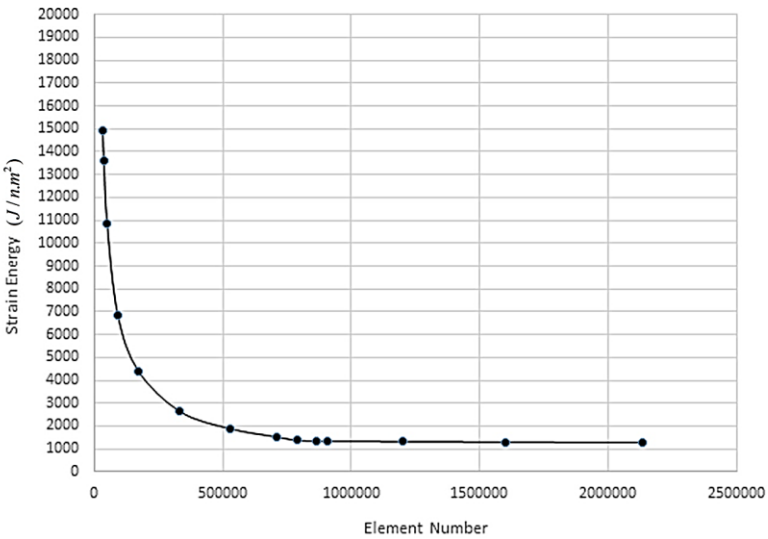

Fig. 4 Diagram of strain energy in terms of element numbers

compared with the results calculated by the cross linking model, presented by (PourAkbar Saffar *et al*. 2008, 2009).

It can be seen that the modulus of elasticity obtained from the simulation are considerably close to those obtained by (PourAkbar Saffar *et al*. 2008, 2009).

3.2 Convergence study

At first, the convergence study for selecting the optimized element numbers is carried out. For this aim by decreasing the element size and followed by an increase in the number of elements, the sensitivity of the bone scaffold model with 1% volume fraction of carbon nanotubes on the strain energy magnitude is investigated. Fig. 4, presented the diagram of strain energy in terms of element numbers.

It can be seen that in the cases with low number of elements, the amount of strain energy decreases rapidly with increasing element numbers. However, with an increase in the number of elements from 864200, the reduction in the amount of strain energy is negligible. Therefore, 864200 elements are selected as optimized element numbers for this bone scaffold problem.

3.3 Numerical results and discussions

It is obvious that, the natural bone exhibits less resistance to tensile stress than compressive stress. The ultimate strength of compact bone in a compression state is about 170-140 MPa and in tensile mode varied from 72 to 77 MPa. Also, in the case of alternating loads with a stress amplitude of more than 29 MPa, a compact bone can sustain sever damages caused by the fatigue phenomenon. The modulus of elasticity in the compact bone is also about 32 GPa.

Fig. 5, presented the diagram of elastic modulus of the bone scaffold introduced in this study in terms of the volume fraction of carbon nanotubes. The obtained results are compared with elasticity modulus of bone scaffolds with combination of carbon nanotubes and hydroxyapatite,

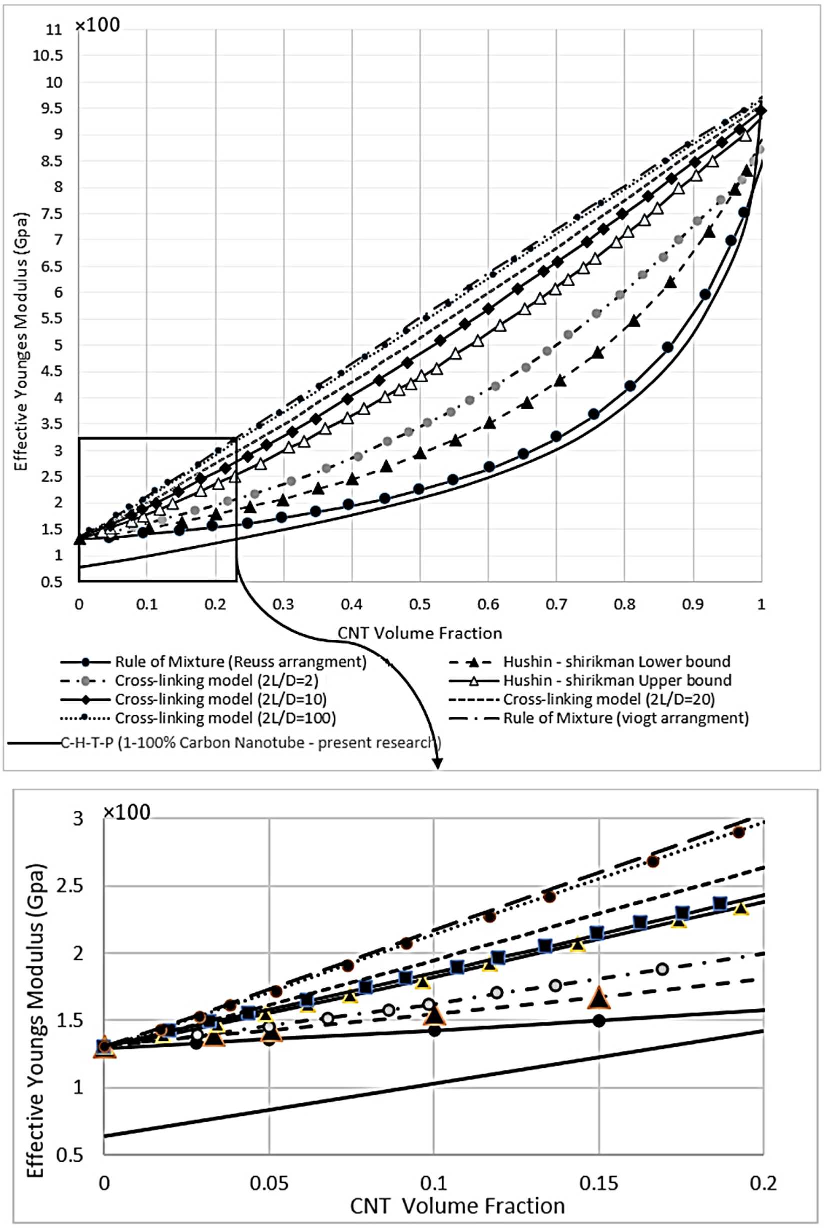

Fig. 5 Compression of elasticity modulus in the introduced bone scaffold with the bone scaffolds presented by (PourAkbar Saffar *et al*. 2010), in terms of volume fraction of carbon nanotubes

calculated with different modelling methods that study by (PourAkbar Saffar *et al*. 2010).

It is observed that the modulus of elasticity predicted by the presented model at the same volume fraction of carbon nanotube is always less than the modulus of elasticity obtained in the previous research and is always closer to the natural bone elasticity modulus.

As can be seen that in Fig. 5, the applied modelling method predicts the value of the modulus of elasticity less than the other models. The reason of this difference is the existence of complete

Table 3 Comparison of the modulus of elasticity of nano bone scaffold calculated in the presented solution method with the cross-linking model

Carbon nanotube volume fraction	Tensile strength (MPa)	Strain energy (J/nm^2)
1%	166.35	1634.08
2%	153.58	1348.76
3%	138.1	1146.97
4%	132.64	983.62
5%	128.27	713.20
10%	116.15	367.14

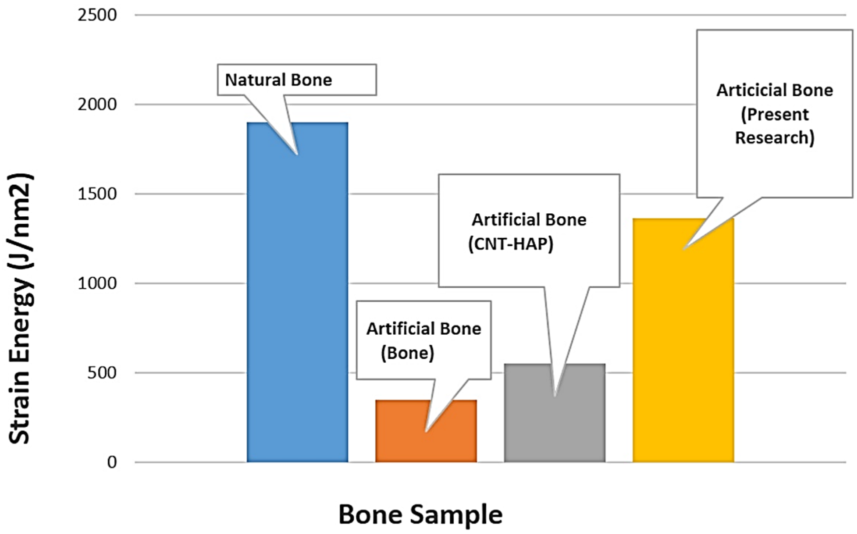

Fig. 6 Compression of strain energies between the introduced bone scaffold with a 1% carbon nanotube volume fraction with two phase bone scaffolds, common metallic artificial bone and with the natural bone (PourAkbar Saffar *et al.* 2010, Jamilpour *et al.* 2011)

contact between each components. The assumption of considering the interaction between the matrix and the reinforcement phase in the elastic cross-link model, predicted Youngs modulus more than its real magnitude. However, the present model, looked more realistic to the two-phase contact region, which is physically closer to reality.

Strain energy is a very important criterion for indicating bone resisting to fracture and bone resorption. Table 3, listed the average tensile strength and maximum magnitudes of strain energy in the introduced bone scaffolds in terms of carbon nanotube volume fraction.

The results of Table 3 showed that, the highest magnitude of maximum strain energy and also the closest tensile strength and strain energy to the natural bone, belong to the bone scaffold with a 1% carbon nanotube volume fraction. Finally, column diagrams of Fig. 6, illustrated the, strain energy magnitude calculated for the introduced bone scaffold with a 1% carbon nanotube volume fraction and compared with the strain energies in the two phase bone scaffolds presented by (PourAkbar Saffar *et al.* 2010), common artificial metal bone and also with the natural bone (Jamilpour *et al.* 2011).

It is demonstrated that, the strain energy of the presented bone scaffolds is very close to the strain energy of the natural bone with respect to the two phase and common artificial bone scaffolds. So that the amount of strain energy in the proposed bone scaffold is only 15% less than that the natural bone.

4. Conclusions

In the presented research, the design of artificial bone scaffolds, in the dry condition outside the human body, was considered from two points of view. At first, this scaffold was study from a biological point of view, so that biocompatible and biodegradable materials are used to provide similar and close properties with the natural bone properties. An appropriate bone scaffolds should have the capabilities of bone resorption and repair in the post-treatment and bone formation stages, due to the forces applied on the artificial bones and also provided the self-healing capability and synchronizing the process of artificial bone repair with natural bone.

To achieve the desired biological vision, carbon nanotubes, due to their prominent mechanical properties, high biocompatibility with the body and its structural similarities with the natural bone structure are selected. According to the piezoelectric properties of natural bone tissue, the barium titanate, which is one of the biocompatible material with body and has piezoelectric properties, is used to create self-healing ability. Furthermore, due to the fact that the most of the bone tissue is consists of hydroxyapatite, this material is also added to the artificial bone structure. Finally, polycaprolactone is used in synthetic bone composition as a proper substrate for bone growth and repair.

The second characteristic is the bone repair process from a mechanical point of view. As stated in this paper, the important mechanical issues are the modulus of elasticity, ultimate strain energy and the strength of the bone scaffold. So that the values of these properties are sought to be closer to the corresponding properties in the natural bone. In such a way that; these mechanical properties in the artificial bone scaffolds, should be as close as possible to the corresponding mechanical properties in the natural bone.

The validity of the presented simulations is demonstrated by comparing the obtained results by the experimental results in the available literatures. The numerical results reveal that the best and the nearest properties of the bone scaffold is achieved with 1% carbon nanotubes volume fractions. It was observed that the proposed composition for bone scaffold, in addition to the biological properties described above, has closer mechanical properties to the natural bone, than the previous bone scaffolds. The proposed composition is a novel design with very close properties to the natural bone and can be used as benchmark solutions for upcoming researches of artificial bone scaffolds.

It is noticeable that, the introduced bone scaffold is simulated only on dry condition, and the effect of the internal moisture of the human body is not considered in this simulation. Also the interaction of environmental wet condition from blood and other internal body organs on the bone scaffold are not considered too. Therefore, although the presented bone scaffold is made from an appropriate biocompatible materials, but experimental evaluations should be carried-out to validate the effectiveness of the proposed bone scaffolds under environmental wet conditions. Before implantation of them in the internal body, that can be a topic for future researches.

References

Ball, J.P., Mound, B.A., Nino, J.C. and Allen, J.B. (2014), "Biocompatible evaluation of barium titanate foamed ceramic structures for orthopedic applications", *J. Biomed. Mater. Res.*, **102**(7), 2089-2095.

Clendenin, J., Kim, J.W. and Tung, S. (2007), "An aligned carbon nanotube biosensor for DNA detection", *Proceedings of the 2nd IEEE Conference on Nanotechnology*, Bangkok, Thailand, April.

Doty, H.A., Courtney, H.S., Jennings, J.A., Haggard, W.O. and Bumgardner, J.D. (2015), "Elution of amikacin and vancomycin from a calcium sulfate/chitosan bone scaffold", *Biomater. Biomech. Bioeng.*, **2**(3), 159-172.

Fang, Z., Starly, B. and Sun, H. (2005), "Computer-aided characterization for effective mechanical properties of porous tissue scaffolds", *Comput. Aid. Des.*, **37**(1), 65-72.

Gao, X.L. and Li, K. (2005), "A shear lag model for carbon nanotube-reinforced polymer composite", *Int. J. Sol. Struct.*, **42**(5-6), 1649-1667.

Genchi, G.G., Marino, A., Rocca, A., Mattoli, V. and Ciofani, G. (2016), "Barium titanate nanoparticles: Promising multitasking vectors in nanomedicine", *Nanotechnol.*, **27**(23), 232001.

Gutiérrez-Hernández, J.M., Escobar-García, D.M., Escalante, A., Flores, H., González. F.J., Gatenholm, P. and Toriz, G. (2017), "In vitro evaluation of osteoblastic cells on bacterial cellulose modified with multi-walled carbon nanotubes as scaffold for bone regeneration", *Mater. Sci. Eng. C*, **75**, 445-453.

Hao, J., Yuan, M. and Deng, X. (2003), "Biodegradable and biocompatiable nano composite of poly ($\mathcal{E}$-caprolactone) with hydroxyapatite nanocrystals: Thermal and mechanical properties", *J. Appl. Polym. Sci.*, **86**, 676-683.

Hilder, T.A. and Hill, J.M. (2008), "Carbon nanotubes as drug delivery nanocapsules", *Curr. Appl. Phys.*, **8**(3-4), 258-261.

Hirata, E., Uo, M., Takita, H., Akasaka T., Watari, F. and Yokoyama, A. (2011), "Multiwalled carbon nanotube-coating of 3D collagen scaffolds for bone tissue engineering", *Carb.*, **49**(10), 3284-3291.

Huiskes, R., Ruimerman, R., Van Lenthe, G.H. and Janssen, J.D. (2000), "Effects of mechanical forces on maintenance and adaptation of form in trabecular bone", *Nat.*, **405**(6787), 704-706.

Jamilpour, N., Fereidon, A. and Rouhi, G. (2011a), "The effects of replacing collagen fibers with carbon nanotubes on the rate of bone remodeling process", *J. Biomed. Nanotechnol.*, **7**(4), 1-7.

Jamilpour, N., Fereidon, A. and Rouhi, G. (2011b), "Cracks behavior in artificial and natural bone samples; a comparison from bone remodeling point-of-view", *Proceedings of the 2nd International Conference on Nanotechnology: Fundamental and Applications*, Ottawa, Canada, July.

Langer, R. and Vacanti, J.P. (1993), "Tissue engineering", *Sci.*, **260**(5110), 920-926.

Li, M. (2010), "Modeling of the dispensing-based tissue scaffold fabrication processes", Ph.D. Dissertation, University of Saskatchewan, Canada.

Mattioli-Belmonte, M., Vozzi, G., Whulanza, Y., Seggiani, M., Fantauzzi, V., Orsini, G. and Ahluwalia, A. (2012), "Tuning polycaprolactone-carbon nanotube composites for bone tissue engineering scaffolds", *Mater. Sci. Eng. C*, **32**(2), 152-159.

Meyers, M.A., Chen, P.Y., Lin, A. and Seki, Y. (2008), "Biological materials: Structure and mechanical properties", *Prog. Mater. Sci.*, **53**(1), 1-206.

Mullender, M.G., Van der Meer, D.D., Huiskes, R. and Lips, P. (1996), "Osteocyte density change in aging and osteoporosis", *Bone*, **18**(2), 109-113.

Nerem, R.M. and Sambanis, A. (1995) "Tissue engineering: From biology to biological substitutes", *Tissue Eng.*, **1**(1), 3-13.

PourAkbar Saffar, K., Arshi, A.R., Jamilpour, N., Najafi, A.R., Rouhi, G. and Sudak, L. (2010), "A cross-linking model for estimating Young's modulus of artificial bone tissue grown on carbon nanotube scaffold", *J. Bomed. Mater. Res.*, **94A**(2), 594-602.

PourAkbar Saffar, K., Jamilpor, N. and Rouhi, G. (2009), "Carbon nanotube in bone tissue engineering, in biomedical engineering", *InTECH*.

PourAkbar Saffar, K., Reaisi Najafi, A., Rouhi, G., Arshi, A. and Fereidon, A. (2008), "A finite element model for estimating Young's modulus of carbon nanotube reinforced composites incorporating elastic cross-links", *Int. J. Mech. Syst. Sci. Eng.*, **2**, 11-25.

Rodrigues, A.A., Batista, N.A., Bavaresco, V.P., Baranauskas, V., Ceragioli, H.J., Peterlevitz, A.C., Santos, J.A.R. and Belangero, W.D. (2012), "Polyvinyl alcohol associated with carbon nanotube scaffolds for osteogenic differentiation of rat bone mesenchymal stem cells", *Carb.*, **50**(2), 450-459.

Ruimerman, R., Hilbers, P., Van Rietbergen, B. and Huiskes, R. (2005), "A theoretical framework for strain-related trabecular bone maintenance and adaptation", *J. Biomech.*, **38**(4), 931-941.

Shi, X., Sitharaman, B., Pham, Q.P., Liang, F., Wu, K., Billups, W.E., Wilson, L.J. and Mikos, A.G. (2007), "Fabrication of porous ultra-short single-walled carbon nanotube nanocomposite scaffolds for bone tissue engineering", *Biomater.*, **28**(28), 4078-4090.

Tserpes, K.I. and Papanikos, P. (2005), "Finite element modeling of single-walled carbon nanotubes", *Compos. Part B*, **36**(5), 468-477.

Williams, J.M., Adewunmi, A., Schek, R.M., Flanagan, C.L., Krebsbach, P.H., Feinbergd, S.E., Hollister, S.J. and Das, S. (2005), "Bone tissue engineering using polycaprolactone scaffolds fabricated via selective laser sintering", *Biomater.*, **26**(23), 4817-4827.

Xing, X., Chen, Y., Yan, X.T. and Zhang, G.Y. (2016), "Design of the artificial bone scaffolds based on the multi-field coupling model", *Proc. CIRP*, **56**, 95-99.

Zanello, L.P., Zhao, B., Hu, H. and Haddon, R.C. (2006), "Bone cell proliferation on carbon nanotubes", *Nano Lett.*, **6**(3), 562-567.

Zhao, B., Hu, H., Mandal, S.K. and Haddon, R.C. (2005), "A bone mimic based on the self-assembly of hydroxyapatite on chemistry functionalized single-walled carbon nanotubes", *Chem. Mater.*, **17**(12), 3235-3241.

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