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Mechanical analysis and additive manufacturing of 3D-printed lattice materials for bone scaffolds

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ABSTRACT

In this study, we have explored the potential application of three-dimensional (3D) lattice-structured materials in the bone scaffold implants by investigating the mechanical strength and porosity of various strut-based lattice designs. The aim is to propose a scaffold design that is strong enough to support the surrounding bone structure. Furthermore, the design should be porous enough to provide effective permeability that allows the integration of bone cells. Therefore, four different lattice-structured material samples with equal dimension of 50 mm in length, width, and height comprising of twenty-five lattice unit cells are designed and fabricated by Fused Filament Fabrication (FFF) 3D printing technique using polylactic acid (PLA) material. The samples have been investigated under compression loads by means of the universal test machine and then the strength of each lattice is measured. Furthermore, the porosity of each design is calculated to complete the investigation on the balance between the mechanical strength and porosity. Finally, the chosen lattice structured material from the investigation steps is prototyped into the imaginary damaged femur bone and fabricated with additive manufacturing to demonstrate the closed loop of design and implementation process.

1. Introduction

Bone transplantation is the second most common form of implant after blood transfusion [1]. The increase in bone related defects or disorders is predominantly due to the increasing life span of the population which makes bone transplants and bone implants in much demand [2]. A common existing technique for bone implants is the process of autogenous bone grafting [3]. This involves harvesting bone from a healthy region of the patient's body and transferring it into the site of the defect. A major benefit of this method is to use live bone cells instead of artificial material meaning the body can repair itself more effectively. Live bone also becomes vascularized meaning it provides the bone with blood vessels for blood supply. This can minimize the risk of infection as well as degradation from conditions such as avascular necrosis. Moreover, the bone graft is taken from the patient's own body therefore the risk of the immune response rejecting the implant is much lower [4].

There are many circumstances where a person might require a bone implant. Diseases such as osteoporosis and osteogenesis imperfecta (OI) can impact people's health in different ways. For example, osteoporosis, a common metabolic bone disorder, could increase the risk of fractures [5]. Other bone disorders can be genetic or could be caused by wear due to aging which would affect a wide range of people. Furthermore, a lack of bone around the defect can lead to health issues including pain, loss of function, and loss of mobility, therefore, it is essential to support the regrowth of bone and cells in these regions.

In tissue engineering, there are three main components for effective repair and growth of the tissue using artificial material. These components are (i) a scaffold to act as a support template at the site of the defect, (ii) the corresponding cells for the type of tissue being repaired, and (iii) a growth factor [2]. The process for in vivo tissue engineering follows four main steps using these components for effective growth and repair of the tissue. Firstly, a three-dimensional cylinder for the use of a bone implant is used as the biomaterial scaffold. The scaffold structure is then bioactivated with primary osteoblast cells or stem cells to seed the cells within the implant. The implant is then cultured in a bioreactor to simulate one or more features of the in vivo environment,

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including chemical aspects, mechanical stress and strain and temperature. Lastly, the scaffold is implanted into the patient's body where it can begin to repair the bone and tissue [6]. Nevertheless, some disadvantages of autogenous bone grafting include a prolonged operation to harvest the bone, donor site morbidity meaning pain or discomfort, and a reduction/loss of mobility and function at the site of harvested bone [7]. These common problems have led to alternative methods being researched recently such as 3D printing bone and tissue to be implanted into the live body [8–10].

With the recent advances in the field of additive manufacturing (AM) and novel materials design, an increasing number of engineering solutions are finding their way into the modern healthcare including tissue engineering, prosthetics, and other biomedical applications. This is mainly due to functionality of the additive manufacturing in fabricating complex geometries with various biocompatible materials and tailoring the mechanical properties of the structure [11–16]. One unique application of AM in healthcare is the use of artificial implants, fabricated from lattice-structured materials, to aid the repairment of damaged bone by growth of cells in the bone. Bone scaffolds are predominantly used to support the patients' health in terms of reducing pain and increasing functionality and mobility of the organ as well as providing appropriate domain for regrowth of bone and cells. Therefore, the bone scaffolds must be designed and manufactured in a way to tolerate mechanical loads as well as to provide a certain level of porosity to allow the effective cell growth. These two parameters usually contradict each other and thus, it is crucial to investigate both criteria and determine an optimum design for the purpose of creating an effective bone scaffold. It is also worth mentioning the strength of bone scaffolds is not directly affecting the cell growth in comparison to the other parameters such as stiffness of scaffold structures [17]. However, the strength would be an crucial parameter for structural integrity of the scaffold in live body specially when the organ is holding mechanical loads and need to be investigated in the early stages of scaffold design [18,19].

Lattice-structured materials are a group of materials with artificial engineered structures that exhibits customized properties which are not naturally available in other materials. These outstanding customized behaviors in lattice materials are mainly derived from their synthetic microstructures. The structure of lattice materials is made from a repetition of unit cells with small size in three orientations to generate specific mechanical properties. Therefore, these materials can be an excellent solution for bone scaffolding as they are able to provide a variety of mechanical strength, porosity and surface area through different lattice designs which are perfect for promoting osseointegration, bone ingrowth, and implant fixation. As a result, the transport of nutrients and metabolic waste is more efficient under these conditions [20,21]. High porosity also facilitates cell and bone ingrowth [22,23] which allows the implant to be incorporated into the bone that could either remain in vivo or degrade over time when the site of the defect no longer requires support. Strut-based lattice-structured materials can be defined as either bending-dominated or stretching-dominated. Bending-dominated lattice structures experience bending moments and therefore they are more compliant under the applied forces. On the other hand, stretching-dominated lattices experience axial loads. This makes them more

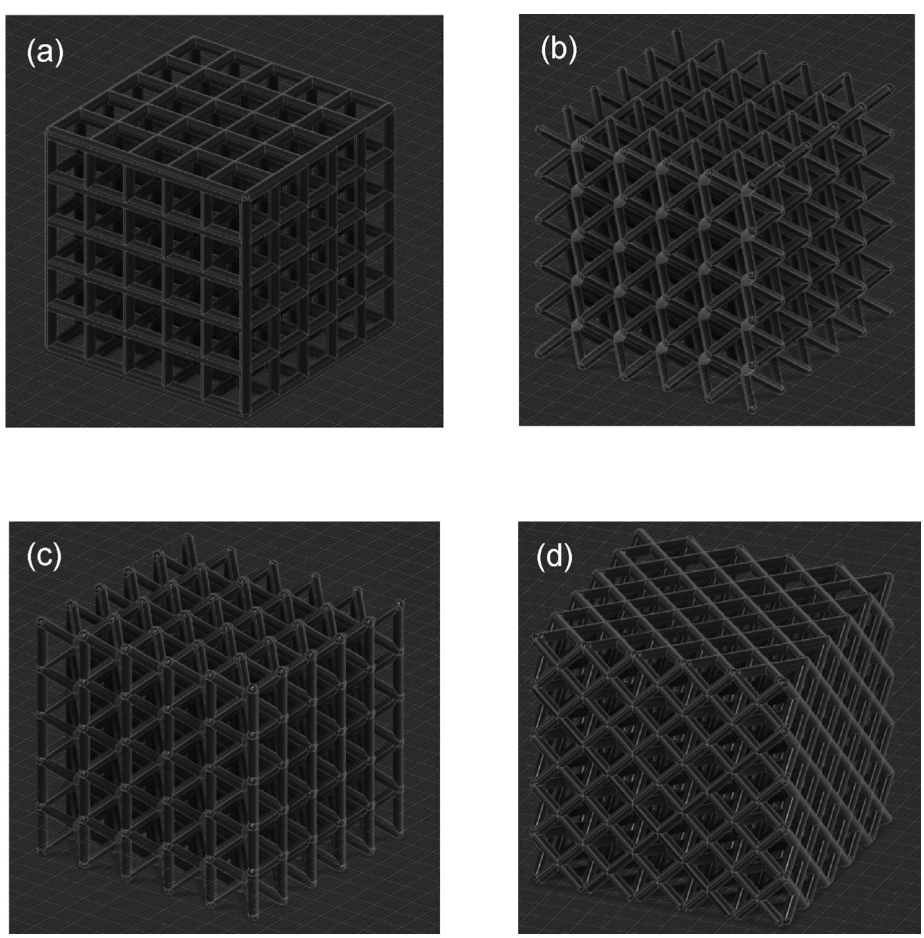

Fig. 1. Four lattice-structured material designs (a) simple cubic; (b) body-centred cubic (BCC); (c) body-centred cubic with z-struts (BCCZ); and (d) face-centred cubic (FCC).

rigid and strong compared to bending-dominated lattices under uniaxial loadings [23].

Furthermore, choosing the material that will be used as the base of the lattice-structured material in the scaffold is a crucial step in design process of a biomedical bone scaffold. Typically bone scaffolds are made from natural or synthetic polymers and this is the way we have investigated in this study. However, metals or metal alloys could be used for fabrication of bone scaffolds without affecting the general outputs of the investigations in this paper. Specifically, the metallic scaffolds could be an option for applications that require higher load bearing [24]. Commonly used metals include stainless steel, cobalt-chromium, and titanium alloys. These options are used for their mechanical characteristics as well relying on the effect of passivation. This process defines as the situation where the metal is surrounded by a thin oxide layer which increases the corrosion resistance of the implant [25,26].

In this study we will explore the use of three-dimensional lattice-structured materials for bone scaffolding. This exploration includes the investigation of mechanical behavior of the different lattice designs under compressive loads as well as consideration of porosity in lattice-structured material. The structure of the current paper is as follow: in Section 2, the methodology of the investigations including design and manufacturing of lattice-structured specimens is presented. In Section 3, the results of the compression tests and porosity calculations as well as step-by-step bone scaffold design procedure are discussed and finally, concluding remarks are given in Section 4.

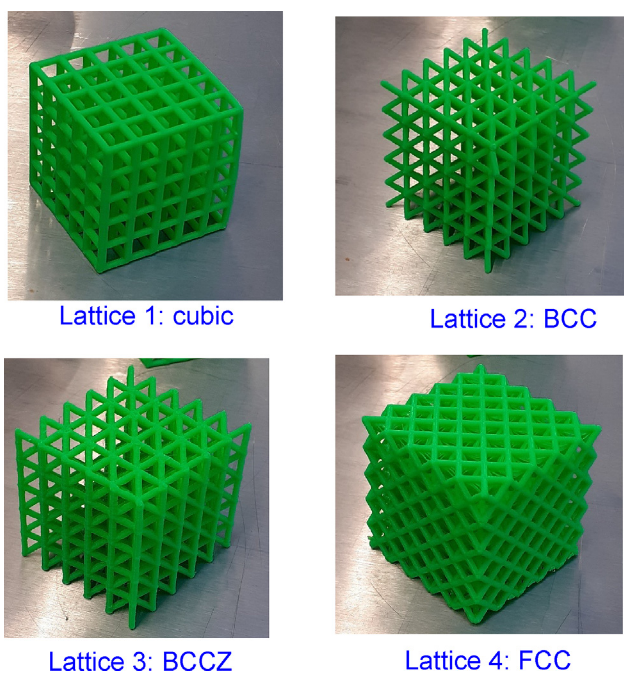

Fig. 2. Fabricated lattice-structured specimens including four different designs of cubic, BCC, BCCZ, and FCC using Fused Filament Fabrication.

2. Methodology

The purpose of this study is to investigate the mechanical performance of lattice material bone scaffolds under compression and observe the relationship of this behavior with respect to different lattice types and porosity. Therefore, it is required firstly to design and manufacture various types of lattice-structured material samples for experimental study.

2.1. Design and manufacturing of lattice-structured material

Among the various lattice-structured materials, four popular strut-based lattice designs are chosen. These include (i) simple cubic (ii), Body-Centred Cubic (BCC), (iii) Body-Centred Cubic with Z-struts (BCCZ), and (iv) Face-Centred Cubic (FCC). The lattice-structured material specimens are designed using Fusion 360 software with total size 50 mm in length, width, and height comprising of twenty-five lattice cells strut radius of 1 mm. Fig. 1 illustrates the four designed specimens. It is also worth mentioning that without losing any generality about the methodology of the analysis and experiments, the dimensions of the lattice structure design in this research are chosen according to our current available manufacturing and testing facilities.

As discussed earlier, AM technique is the most convenient approach to manufacture lattice-structured materials due to their complex geometries and slender internal struts. In this study the experimental specimens are fabricated by Fused Filament Fabrication 3D printing technique and integrating polylactic acid (PLA)

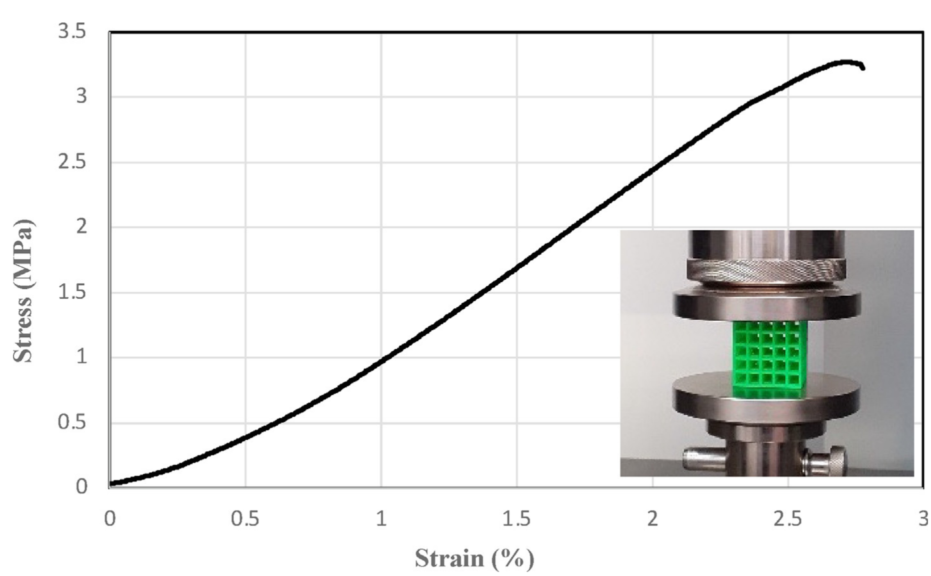

Fig. 3. Stress–strain curve of simple cubic lattice-structure sample under compression.

polymer. The 3D Printer used for fabrication of all samples is Prusa i3 Mk2.5 with layer height resolution of 0.2 mm and extruder temperature of 210 °C and bed temperature of 60 °C for PLA material. Although PLA material which is used in this research is a biodegradable and biocompatible polymer [27], this is not the main aim of this study as we have focused on investigating the effect of different lattice designs on mechanical strength and porosity of scaffolds. The fabricated specimens using FFF technology is presented in Fig. 2. The chosen parent material is also non-toxic, easy to print, and cost effective which make it a suitable option for the investigations. Furthermore, it is important to mention that the investigated mechanical properties of the lattice-structure materials such as strength in this study would depend on the mechanical behavior of the parent material which is chosen to be PLA here. This means that changing the parent material the experimental measurements need to be recalculated using the same approach and methodology.

2.2. Mechanical compression experiments

The mechanical behavior of each lattice-structured sample is characterized by simple compression tests using 50kN Zwick Roell (Z050) universal testing machine and testXpert III software to measure maximum strength of the scaffold under compression. All the samples are loaded similarly by displacement control method and strain rate of $0.00171/s$. The generated stress–strain curve and maximum strength of each sample will then be analyzed alongside the porosity of the structures. There should be a good balance between mechanical behavior and porosity of the structure to allow the scaffold to support the bone as well as providing space

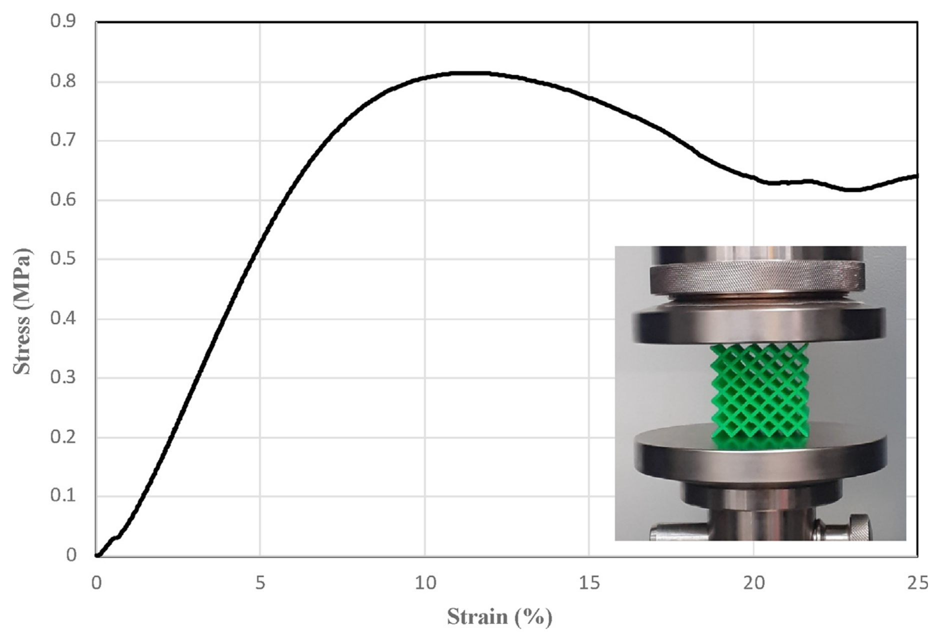

Fig. 4. Stress–strain curve of body-centred cubic (BCC) lattice-structure sample under compression.

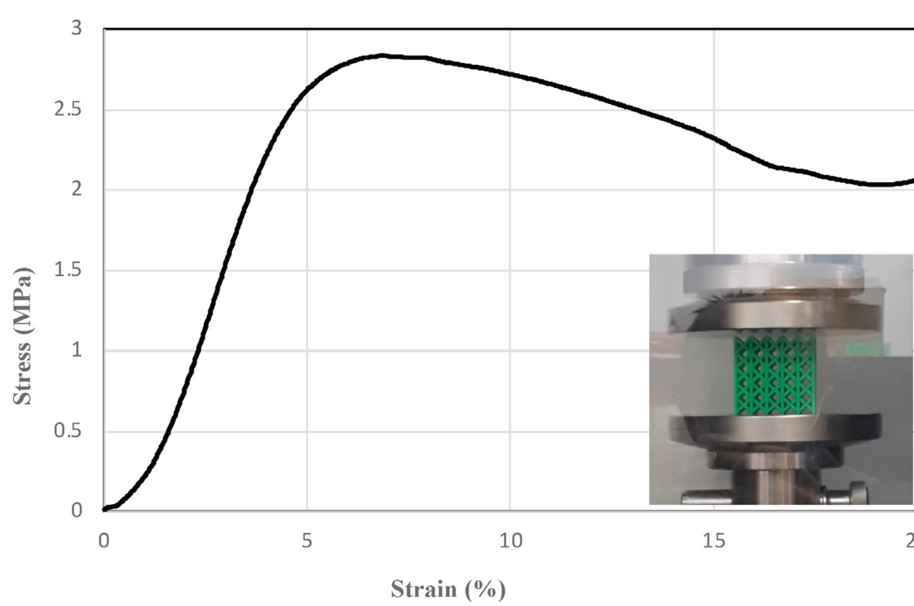

Fig. 5. Stress–strain curve of body-centred cubic with Z struts (BCCZ) lattice-structure sample under compression.

for cell growth. Furthermore, to ensure about the repeatability of the experiments and considering the experimental error in our analysis, the testing on each lattice-structured design has been repeated three times with three identical samples.

2.3. Porosity of Lattice-Structured materials

The size of the pores in the scaffold must be large enough to allow the movement and diffusion of cells through the structure, but small enough to allow the binding of organelles to the scaffold as well as provide strong support for the bone [28]. If the material used in the implantation were biodegradable, the degradation of the scaffold should be slower than the generation of the new cells at the site of the defect [29]. This would allow the body to form new bone tissues around the implant before it degrades.

In this study, we measure the porosity as the ratio of pore volume to the total volume, according to the Equation (1), as one of the parameters in our investigations.

$$Porosity(\%) = \frac{V_p}{V_t} \times 100 \quad (1)$$

where V_p is the pore volume and V_t is the total volume of the lattice-structured samples. The pore volume in Equation (1) has been calculated by deducting the material volume, which is measured in the CAD software, from the volume of a bulk cube with base dimension of 5 in length, width, and height.

3. Results and discussions

In this section, the results from mechanical behavior investigations of four different lattice-structured materials as well as porosity have been presented. As discussed, the performance of various bone scaffolds made from four different lattice-structured materials have been studied under compressive stresses. The compression test has been continued until the first strut in the structure is failed which indicates the failure of the whole scaffold structure.

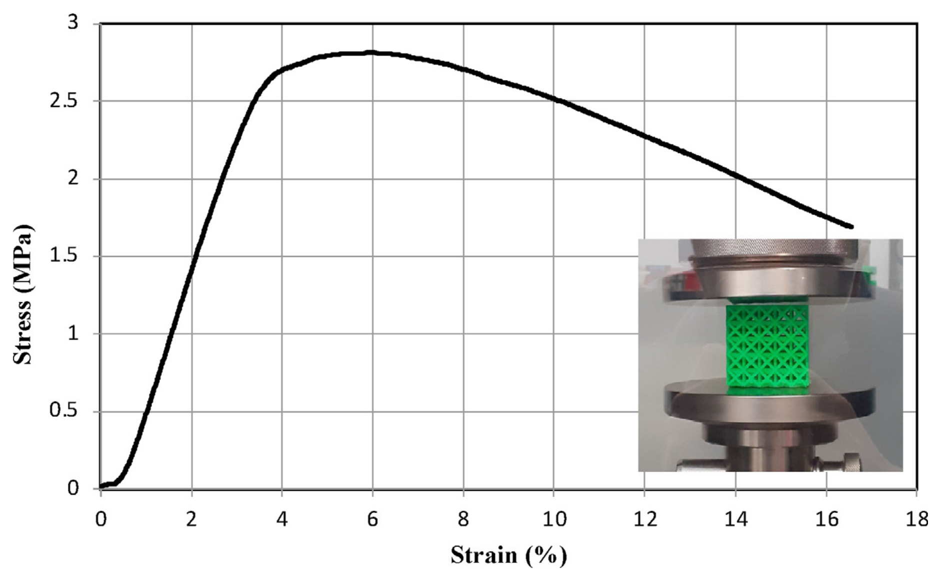

Fig. 6. Stress–strain curve of face-centred cubic (FCC) lattice-structure sample under compression.

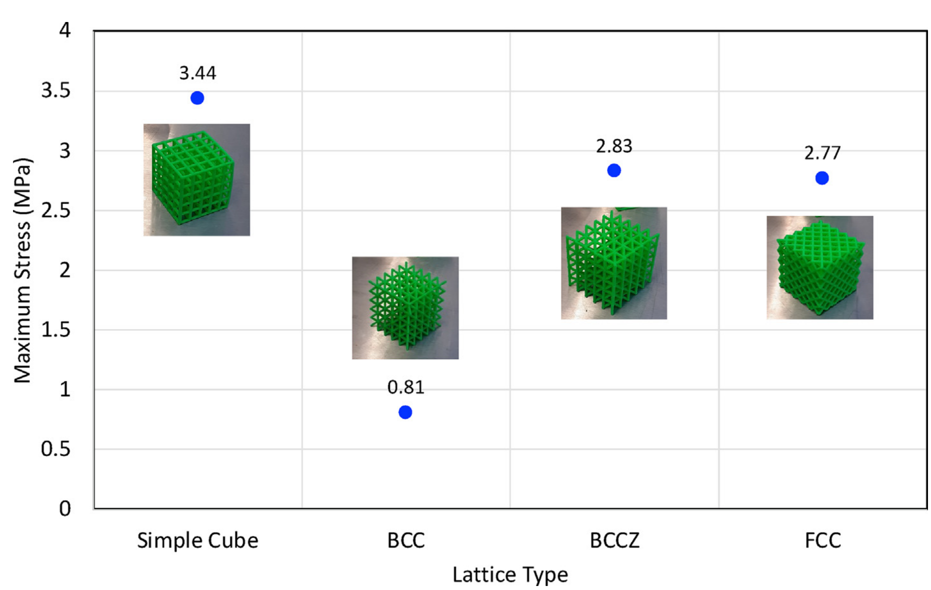

Fig. 7. Comparison of maximum compressive strength for Simple Cubic, BCC, BCCZ, and FCC lattice-structure materials.

The stress–strain curve of the cubic, BCC, BCCZ, and FCC lattice-structure specimens as well as compression test set-up are illustrated in Figs. 3-6, respectively. It is worth mentioning that, the stress–strain curves in these figures are the average of three identical repeated tests for each occasion.

The maximum compression stress for each lattice-structured sample is then measured from the stress–strain curves in Figs. 3-6 which indicates the strength of scaffolds under compressive loads. The maximum tolerated stresses of the four samples are then compared together in Fig. 7. As shown in Fig. 7, the simple cubic lattice has highest strength to the compression (3.44 MPa) while the BCC structure shows the weakest behavior among the four samples with strength of 0.81 MPa to the compressive load. This would be due to the highest number of vertical struts in the simple cubic design in comparison to the other designs and the effect of vertical struts in resistance against uniaxial loads.

As explained earlier, the porosity is another crucial parameter in bone scaffold design and fabrication. The porosity factor of bone scaffold must be large enough to allow the growth and diffusions of bone cells inside the lattice-structured scaffold whilst it should be small enough to enable the binding of organelles to the structure. In this study, the porosity of each lattice-structured material is calculated using equation (1) and then is illustrated in Fig. 8 for various designs.

By combining the compressive strength and porosity data of each lattice-structure material we then produced Fig. 9 which illustrates the change of mechanical strength against porosity for different designs. The graph in Fig. 9 would be a simple tool for initial bone scaffold design which allow the evaluation of various lattice designs to find and choose the suitable design for bone scaffold which provide the balance between two crucial parameters of strength and porosity. For example, FCC lattice would provide around 2.7 MPa strength against compression, where it has the lowest porosity among the four designs in this study. However, the simple cubic structure would provide highest strength and porosity among the four investigated designs in this study. As stated earlier, the mechanical strength and porosity are the two key qualities that are vital to create a bone scaffold implant. It should

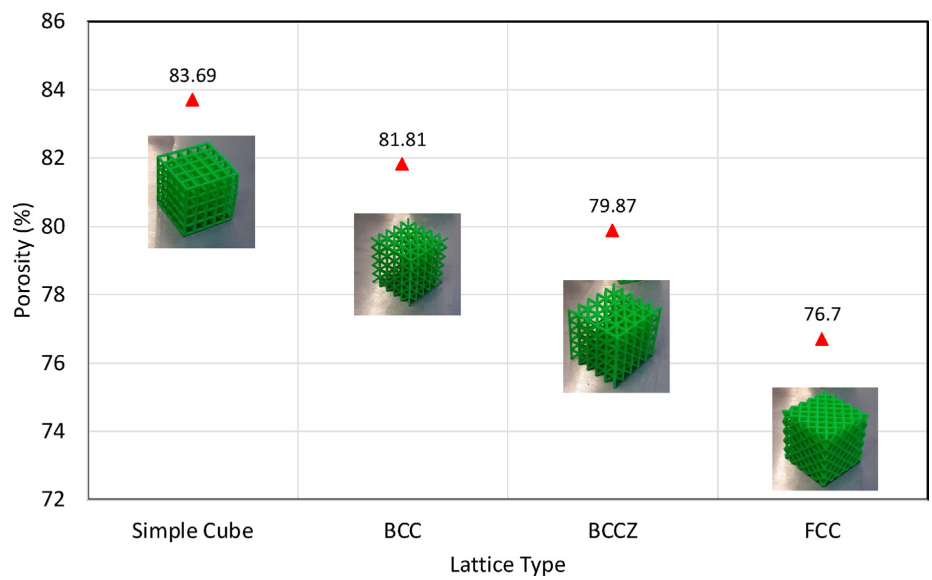

Fig. 8. Porosity of various lattice designs including simple Cubic, BCC, BCCZ, and FCC lattice-structure materials with strut radius of 1 mm.

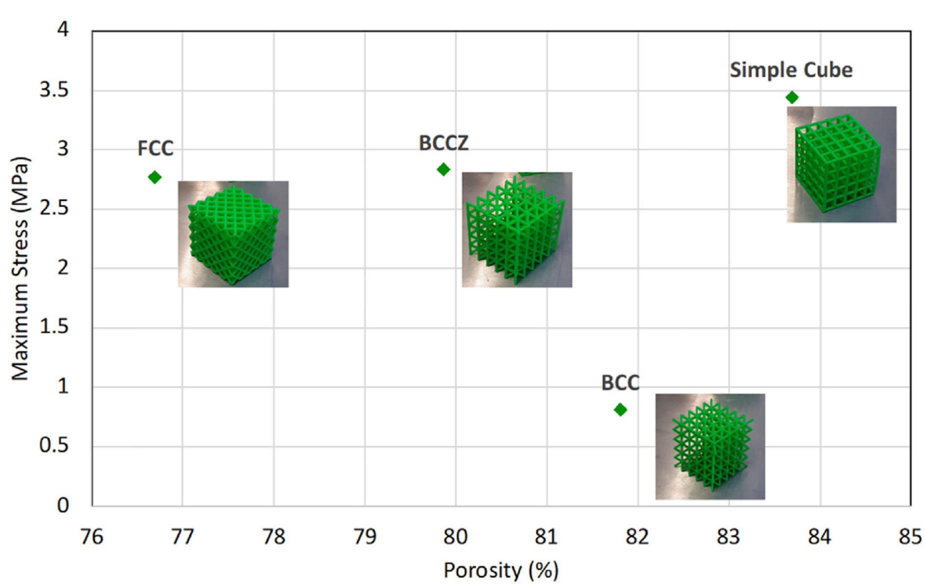

Fig. 9. Mechanical Strength against porosity for four lattice-structured material designs (simple Cubic, BCC, BCCZ, and FCC).

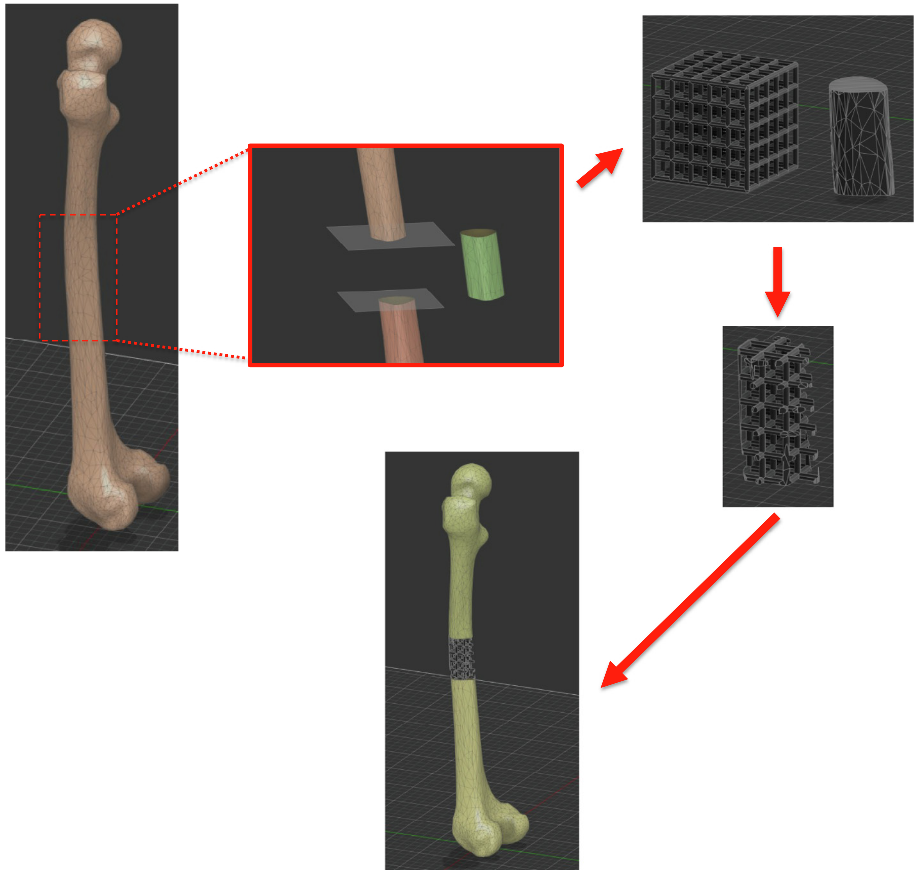

Fig. 10. Step-by-step procedure of integrating a lattice-structured bone scaffold into a sample femur bone.

have a high porosity to accommodate for cell movement and diffusion of nutrients and waste as well as having high strength and stability to support the bone during the healing and cell growth process. It is also worth mentioning that it is essential to expand the current study to higher number of lattice designs to have a more complete design tool for lattice-structured bone scaffolds in the future. This should then be expanded to various material options for different cases.

Finally, the simple cubic lattice-structured material design, which has the highest porosity and the highest mechanical strength among the four studied designs in this paper, is implemented into a new bone scaffold model of an imaginary defected femur bone using Fusion 360. This was done by importing the final design choice and merging it with a model of a bone to illustrate the typical process of integrating the lattice-structure scaffold to the bone model for future prototyping. Fig. 10 illustrates the step-by-step procedure of the removal of 50 mm length of a personalized femur bone and integrating the cubic lattice model as bone scaffold in it. This design was then prototyped using FFF 3D printing and PLA material for further visual and mechanical investigations as well as future lab-based cell growth experiments in biomedical labs.

4. Conclusions

In this study we have investigated the mechanical performance and porosity of four popular strut-based lattice-structured materials to accelerate the design and manufacturing of bone scaffolds. The studied lattice designs included simple cubic, body-centred cubic, body-centred cubic with z struts, and face-centred cubic. All the experiment specimens designed with 50 mm × 50 mm × 50 mm size comprising of twenty-five lattice cells of 10 mm × 10 mm × 10 mm and then were fabricated by FFF 3D printing technique using polylactic acid (PLA) polymer.

Thus, the compressive strength of each lattice design, as an important bone scaffold design parameter, was investigated experimentally through uniaxial compression test using Zwick Roell Z50 universal testing machine. The maximum stress of each sample was measured at the failure of the first strut in the lattice-structure specimens. It was observed that among the four studied lattice designs, the simple cubic design develops the highest strength whilst the BCC structure provides the weakest performance under compression load. This is due to the importance of the Z-direction struts in the lattice design for uniaxial loads. It is also worth mentioning that the behavior of lattices are considered only under compression here and other loading scenarios including shear, biaxial, and volumetric loadings which might be important in some specific cases are not considered in this study.

Furthermore, measuring the porosity of each lattice designs, it was found out that the simple cubic structure develops the highest porosity among the four investigated designs. The porosity is an important parameter for bone scaffolds as they should have enough internal spaces to accommodate for cell movement and diffusion of nutrients and waste as well as having high strength and stability to support the bone during the healing and cell growth process.

Finally, the step-by-step process of how to design personalized bone scaffold for a random bone using the appropriate lattice-structure material is demonstrated. This is through removing parts of a random femur bone and replacing the scaffolds design from simple cubic lattice material, which shows the highest compressive strength as well as highest porosity, instead of removed region. The design of femur bone with integrated lattice-structure scaffold was then available for prototyping and performing further test including lab-based cell growth test and visualizations. This is worth noting that although the process studied here is an investigation study, it was shown that similar approach could be implemented in a real personalized bone scaffold design.

CRediT authorship contribution statement

James Hulme: Data curation, Software, Visualization. **Amir Hosein Sakhaei:** Conceptualization, Methodology, Visualization, Writing – original draft, Investigation, Supervision. **Mahmood Shafiee:** Writing – review & editing, Investigation.

Data availability

Data will be made available on request.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] W. Wang, K.W. Yeung, Bone grafts and biomaterials substitutes for bone defect repair: a review, Bioactive Mater. 2(4) (2017) 224–47. (https://doi.org/10.1016/j.bioactmat.2017.05.007)
[2] P. Chocholata, V. Kulda, V. Babuska, Fabrication of scaffolds for bone-tissue regeneration, Materials 12 (2019). 10.3390/ma12040568.
[3] D.P. Emlyn Forsung, J.A. Cameron, Current concepts with autogenous bone grafting, Podiatry Today. 33 (7) (2020).
[4] G.F. Rogers, A.K. Greene, Autogenous bone graft: basic science and clinical implications, J. Craniofacial Surg. 23(1) (2012) 323-7. (https://doi.org/10.1097/SCS.0b013e318241dcba).
[5] C. Christodoulou, C. Cooper, What is osteoporosis? Postgraduate Med. J. 79 (929) (2003) 133–8. (http://dx.doi.org/10.1136/pmj.79.929.133).
[6] A. Rupani, R. Balint, S.H. Cartmell, Osteoblasts and their applications in bone tissue engineering, Cell Health Cytoskelet. 4 (2012) 49–61. http://dx.doi.org/10.2147/CHC.S21845.
[7] R.F. LaPrade, J.C. Botker, Donor-site morbidity after osteochondral autograft transfer procedures. Arthroscopy: J. Arthroscopic Related Surg. 20(7) (2004) e69-73. (https://doi.org/10.1016/j.arthro.2004.06.022).
[8] V.V. Popov, G. Muller-Kamskii, A. Kovalevsky, G. Dzhenzhera, E. Strokin, A. Kolomiets, J. Ramon, Design and 3D-printing of titanium bone implants: brief review of approach and clinical cases, Biomed. Eng. Lett. 8(4) (2018) 337–44. (https://doi.org/10.1007/s13534-018-0080-5).
[9] Z. Li, Q. Wang, G. Liu, A Review of 3D Printed Bone Implants, Micromachines 13 (2022). 10.3390/mi13040528.
[10] T. Poltue, C. Karuna, S. Khrueaduangkham, S. Seehanam, P. Promoppatum, Design exploration of 3D-printed triply periodic minimal surface scaffolds for bone implants, Int. J. Mech. Sci. 211 (2021). 10.1016/j.ijmecsci.2021.106762.
[11] Z.U. Arif, M.Y. Khalid, A. Zolfagharian, M. Bodaghi, 4D bioprinting of smart polymers for biomedical applications: recent progress, challenges, and future perspectives. React. Funct. Polym. (2022) 105374. (https://doi.org/10.1016/j.reactfunctpolym.2022.105374).
[12] S. Akbari, A.H. Sakhaei, S. Panjwani, K. Kowsari, Q. Ge, Shape-reversible 4D printing aided by shape memory alloys. Smart Materials in Additive Manufacturing, Volume 2: 4D Printing Mechanics, Modeling, and Advanced Engineering Applications, 2022; (pp. 387-406). Elsevier. (https://doi.org/10.1016/B978-0-323-95430-3.00014-2).
[13] A.H. Sakhaei, S. Kaijima, T.L. Lee, Y.Y. Tan, M.L. Dunn, Design and investigation of a multi-material compliant ratchet-like mechanism, Mechanism Mach. Theory. 121 (2018) 184–97. (https://doi.org/10.1016/j.mechmachtheory.2017.10.017).
[14] L. Podshivalov, C.M. Gomes, A. Zocca, J. Guenster, P. Bar-Yoseph, A. Fischer, Design, analysis and additive manufacturing of porous structures for biocompatible micro-scale scaffolds, Procedia Cirp. 5 (2013) 247–52. (https://doi.org/10.1016/j.procir.2013.01.049).
[15] P. Szymczyk-Ziółkowska, M.B. Łabowska, J. Detyna, I. Michalak, P. Gruber, A review of fabrication polymer scaffolds for biomedical applications using additive manufacturing techniques, Biocybernet. Biomed. Eng. 40(2) (2020) 624–38. (https://doi.org/10.1016/j.bbe.2020.01.015).
[16] P. Ahangar, M.E. Cooke, M.H. Weber, D.H. Rosenzweig, Current biomedical applications of 3D printing and additive manufacturing, Appl. Sci. 9 (2019). 10.3390/app9081713.
[17] A.J. Engler, S. Sen, H.L. Sweeney, D.E. Discher, Matrix elasticity directs stem cell lineage specification. Cell. 126(4) (2006) 677–89. https://doi.org/10.1016/j.cell.2006.06.044.
[18] S.H. Lee, K.G. Lee, J.H. Hwang, Y.S. Cho, K.S. Lee, H.J. Jeong, S.H. Park, Y. Park, Y.S. Cho, B.K. Lee, Evaluation of mechanical strength and bone regeneration ability of 3D printed kagome-structure scaffold using rabbit calvarial defect model, Mater. Sci. Eng.: C. 98: (2019) 949-59. https://doi.org/10.1016/j.msec.2019.01.050.
[19] E. Ryan, S. Yin, Compressive strength of β-TCP scaffolds fabricated via lithography-based manufacturing for bone tissue engineering, Ceram. Int. 48 (11) (2022) 15516-24. https://doi.org/10.1016/j.ceramint.2022.02.085.
[20] J.J. Bara, F. Guilak, Engineering functional tissues: in vitro culture parameters, Princ. Tissue Eng. (2020) 157-177. Academic Press. https://doi.org/10.1016/B978-0-12-818422-6.00011-3.
[21] S. Bose, M. Roy, A. Bandyopadhyay, Recent advances in bone tissue engineering scaffolds. Trends Biotechnol. 30(10) (2012) 546-54. https://doi.org/10.1016/j.tibtech.2012.07.005.
[22] V. Karageorgiou, D. Kaplan, Porosity of 3D biomaterial scaffolds and osteogenesis, Biomaterials 26(27) (2005) 5474–91. https://doi.org/10.1016/j.biomaterials.2005.02.002.
[23] T. Maconachie, M. Leary, B. Lozanovski, X. Zhang, M. Qian, O. Faruque, M. Brandt, SLM lattice structures: properties, performance, applications and challenges, Mater. Des. 183 (2019). 10.1016/j.matdes.2019.108137.
[24] K. Alvarez, H. Nakajima, Metallic scaffolds for bone regeneration, Materials. 2 (3) (2009) 790–832. 10.3390/ma2030790.
[25] L. Malladi, A. Mahapatro, A.S. Gomes, Fabrication of magnesium-based metallic scaffolds for bone tissue engineering, Mater. Technol. 33(2) (2018) 173-82. https://doi.org/10.1080/10667857.2017.1404278.
[26] D. Zhao, H. Liang, C. Han, J. Li, J. Liu, K. Zhou, C. Yang, Q. Wei, 3D printing of a titanium-tantalum Gyroid scaffold with superb elastic admissible strain, bioactivity and in-situ bone regeneration capability, Addit. Manuf. 47 (2021). 10.1016/j.addma.2021.102223.
[27] E.M. Elmowafy, M. Tiboni, M.E. Soliman, Biocompatibility, biodegradation and biomedical applications of poly (lactic acid)/poly (lactic-co-glycolic acid) micro and nanoparticles, J. Pharm. Invest. 49 (2019) 347-80. https://doi.org/10.1007/s40005-019-00439-x.
[28] J. Yu, H. Xia, Q.Q. Ni, A three-dimensional porous hydroxyapatite nanocomposite scaffold with shape memory effect for bone tissue engineering, J. Mater. Sci. 53(7) (2018) 734–44. https://doi.org/10.1007/s10853-017-1807-x.
[29] Y. Wen, S. Xun, M. Haoye, S. Baichuan, C. Peng, L. Xuejian, Z. Kaihong, Y. Xuan, P. Jiang, L. Shibi, 3D printed porous ceramic scaffolds for bone tissue engineering: a review, Biomater. Sci. 5 (9) (2017) 1690–1698. 10.1039/C7BM00315C.