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Investigation of manufacturing deviations of CPC scaffolds for improving the design process

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Abstract: In current implantology, calcium phosphate cement (CPC) is increasingly used. A special focus is given to CPC scaffolds, as they are suitable for cell settlement and growth due to their positive osteoconductive properties. The design of the scaffolds is of decisive importance for this. The value ranges of the geometric parameters of these scaffolds (e.g. path distance, path diameter), which are positive for both cell settlement and cell growth, are very small. Manufacturing deviations therefore have a significant impact on cell settlement and growth. The pasty manufacturing consistency can cause sagging at the path interstices of a layer immediately below, resulting in significant manufacturing deviations. A larger path distance and thus a larger path interstitial space promotes cell settlement, but at the same time increases the risk of CPC path shape inconsistency. This in turn can have a negative effect on cell settlement. Therefore, the aim of this paper is to investigate the discrepancies between the nominal and actual state at a path distance favourable to cell settlement on the basis of manufactured CPC scaffolds. In this context, geometric and manufacturing parameters of the shape deviation are to be identified and constructive design adaptations are to be derived on the basis of these. In addition, the effects of the shape and position deviations on the flow behaviour will be investigated.

Keywords: Bone Tissue Engineering, CPC, Numerical Simulation, CFD

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1 Introduction

For the treatment of defect sites in weakly loaded bone regions, scaffolds made of bioactive materials represent a new focus in research [1–3]. Due to their porous design, scaffolds are used as a tissue matrix for the settlement of cells in the defect area for better remodulation of the bone and to ensure the load-bearing capacity in this area until healing [1]. Especially bioactive materials such as magnesium, hydroxyapatite (HA) or calcium-phosphate cement (CPC) are suitable for manufacturing [1, 2, 4]. In this context, bioactive materials are characterised by the fact that they are degraded or transformed in vivo over a certain period of time. Thus, bioactive scaffolds are degraded by the body and, depending on the material, the resulting degradation products can be used by the body to build new tissue.

Regarding this, CPC in particular has proven to be very suitable for scaffolds in the treatment of low-load bone defects. Due to its easy processability, good osteoconductive properties can be achieved via the porosity, which makes the bioactive CPC particularly suitable as a material for scaffolds in bone tissue engineering (BTE). In addition, by adding further substances such as magnesium, even osteoinductive properties can be realized, as could be shown in a study with in vitro and in vivo tests. [5].

However, the constructive design and layout of scaffolds for optimal osteoconduction is very complex, because, in addition to the mechanical requirements for suitable strength and stiffness, the flow behaviour of the porous structures is also of decisive importance for cell settlement in the scaffold as well as subsequent cell growth [1, 6, 7]. The permeability of the scaffolds is a fundamental parameter for the initial cell settlement and the nutrient supply of the cells in the scaffold. An increase in permeability has a positive effect on cell settlement and nutrient distribution. Furthermore, the fluid-induced shear stress on the scaffold walls is a decisive parameter for cell settlement and cell differentiation of the stem cells [8–10]. However, positive properties in cell settlement, growth and differentiation are only shown in narrow value ranges. Thus, especially manufacturing deviations have a great impact on the osteoconductivity of the implants. As a result, the discrepancy between target and realised CPC implants is often very high. However, the effects of manufacturing deviations on the flow behaviour have not yet been sufficiently investigated. On the other hand, no suitable measures to reduce the manufacturing deviation of CPC implants are known so far. Therefore, this paper investigates to what extent the design of the layer alignment influences the manufacturing quality and consequently the flow behaviour.

2 Material and Methods

2.1 CPC und Scaffolds

The manufacturing of CPC is a patented and strictly regulated process. A company that produces CPC for medical use is INNOTERE GmbH (Radebeul, Germany). The CPC produced there consists of cement powder components (calcium hydrogen phosphate (α-$Ca_3(PO_4)_2$), calcium carbonate ($CaCO_3$), precipitated hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$)) and finely ground potassium hydrogen phosphate (K_2HPO_4). The components are mixed and acquire a paste-like consistency through the addition of a carrier liquid. [11]

Scaffolds made of CPC are usually manufactured additively in layers with orthogonally alternating orientation at 0° and 90° or at -45° and 45° [12]. The CPC is present in a pasty state and is printed onto a base or a shaping negative by air pressure from a vertically downward extruder [11]. Studies have shown that cell settlement is favoured by greater path distance and thus by greater porosity (approx. 60 % to 70 %) [12].

2.2 Additive Manufacturing

During slicing, the necessary processing parameters are set according to the requirements. The slicing tool used is an in-house software programme. In this work, it is to be investigated whether shape deviations can be manipulated by different alignments of layers lying on top of each other. With the help of the slicing software, the parameters are therefore selected in such a way that four- and six-layer CPC scaffolds are made, of which the lower three layers are unidirectional (all 0°) and the one or three following unidirectional layers are arranged orthogonally to this (all 90°). In order to achieve a porosity of approx. 70 % with a needle thickness of 0.33 mm, a path distance of 1.15 mm is used. The scaffolds are produced with a self-built 3D plotting device (based on a KOSY4 from Elektronik und Mechanik GmbH) and a feed rate of 250mm/min [12]. All parameters can be found in **Table 1** below.

Table 1: Slicing parameters of the CPC scaffolds

Parameter	Scaffolds B1-B3	Scaffolds B4-B6
Number of layers	4	6
Alignment of the layers	0°; 0°; 0°; 90°	0°; 0°; 0°; 90°; 90°; 90°
Track distance	1.15 mm	1.15 mm
Needle diameter	0.33 mm	0.33 mm
Feed rate	250 mm/s	250 mm/s

Curing of the specimens takes 10 days - 3 days in a water bath without contact with water, 3 days in a water bath with complete immersion in water, 4 days in air at room temperature. Both samples were made in triplicate and are shown in **Figure 1**.

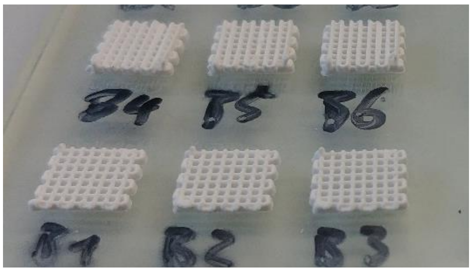


Figure 1: Fabricated CPC scaffolds (four layers: B1-B3; six layers: B4-B6)

2.3 3D scanning

To determine the manufacturing deviations of the scaffolds, the actual geometry was recorded using a fringe projection method. For this purpose, the 3D scanner ATOS Q from GOM GmbH was used, which measures the geometric shape of the scaffolds with a measuring volume of 100mm, starting from a specified measuring accuracy at evenly distributed measuring positions. All measurement views were taken with three different exposure times of 17 ms, 38 ms and 80 ms to handle shadowed pores of the scaffolds and reflective surface areas. The measurement deviation for the performed scans is 20 µm.

2.4 Numerical simulation model (CFD)

To estimate the influence of the manufacturing geometries on the flow behaviour of the scaffold, initial CFD analyses were carried out with Ansys Discovery. Ansys Discovery is characterised by fast calculations due to the voxel discretisation and the GPU-based calculation. In addition, geometric effects on the flow behaviour can be quickly evaluated initially using this approach. However, the underlying calculation algorithm shows inaccuracies in the calculation and the boundary layer resolution, which must always be counter-checked with conventional CFD methods for well-founded statements of considered flow variables. In this study, the flow velocities in the pores of the scaffolds for four-layer and six-layer scaffolds were investigated with Ansys Discovery and compared with the target geometries. The calculations were performed on an NVIDIA RTX 3090. The considered flow area was described by a cylinder with a diameter of 4 mm and a height of 2.5 mm. The considered flow volume was discretised with a homogeneous grid of 1e-2 mm voxels. A velocity of 1 $mm \cdot s^{-1}$ and an outlet pressure of 0 Pa were defined for the flow inlet. The boundary regions of the fluid volume with the CPC implant were assumed to be stationary hydraulically smooth no-slip walls.

3 Results & Discussion

3.1 Manufacturing deviation

The printed scaffolds deviate from the target geometry in all spatial directions. For quantification, the deviations between target and actual geometry are mapped onto the actual geometry (**Figure 2**). In addition, the porosity is determined by the volumes of the scaffolds. The porosity of the actual four-layered scaffold is 0.5 and deviates from the target porosity of 0.74 by 31.8 %. The porosity of the actual six-layered scaffold is 0.48 and thus deviates from the target porosity by as much as 36.0 %. The reduction in porosity can be attributed to the increase in volume of the CPC after leaving the pressure needle. Furthermore, the top path of the four-layer CPC sags significantly more (**Figure 2**a) than that of the six-layer CPC (**Figure 2**b). The average sagging in the Z-direction for the four-layer CPC scaffold is -0.0575 ± 0.02 mm and for the six-layer scaffold the sagging increases to a more homogeneous path with an average deviation of 0.0473 ± 0.02 mm. Thus, it can be seen that by adding more lanes, the stiffness of the upper lanes is increased and thus gravitational force induced deformation of the strong viscous fluids can be reduced. Thus, a more homogeneous path can be realised.

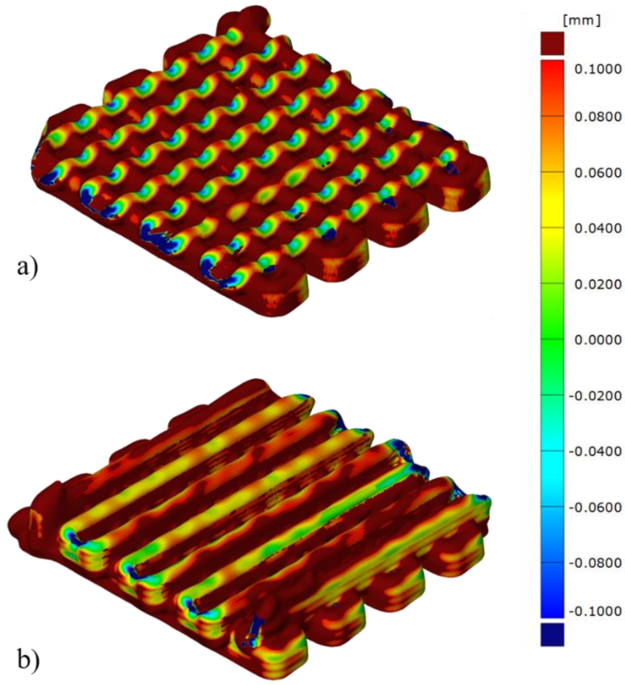
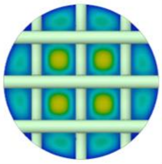
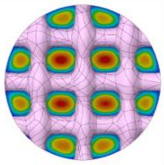
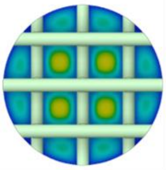
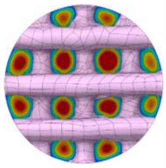


Figure 2: Absolut manufacturing deviation between target and actual geometry of a) four-layered scaffolds and b) six-layered scaffolds

3.2 Influence on flow characteristics

For the evaluation of the fluid properties of the CPC scaffolds, the flow patterns of the flow velocities in the pores are examined. It is shown that the manufacturing deviations have a considerable effect on the maximum occurring velocities and thus inevitably also on the wall-shear stresses. In the target geometries, homogeneous velocity fields with a maximum flow velocity of 3.8 $mm \cdot s^{-1}$ are formed. In contrast, the actual geometries have significantly higher velocities. In the four-layer CPC scaffold, maximum velocities of 6.8 $mm \cdot s^{-1}$ occur in the pores, and in the six-layer scaffold of 8.95 $mm \cdot s^{-1}$. Both scaffolds show inhomogeneous velocity distributions within the pores due to manufacturing (**Table 2**). The increased flow velocities can be attributed to the reduced porosity. Thus, it can be seen that the reduction of the porosity as well as the shape deviations between the target and the manufactured designs, result in a 78% increase in flow velocity for four-layered scaffolds and 135% for six-layered scaffolds.

Table 2: Magnitude velocity distribution

	Target geometry	Actual geometry	velocity magnitude [mm*s^{-1}]
4-layered CPC Scaffold			
6-layered CPC Scaffold			

4 Conclusion

In this study, a new approach was investigated to reduce the sagging of printed CPC scaffolds in order to improve the manufacturing deviation and its influence on the flow behaviour. It was shown that additional layers can reduce the overall stiffness of paths that are prone to sagging. However, the porosities of the printed scaffolds deviate up to 35% from the target porosities. Thus, on the one hand, the manufacturing process must be further optimised. Furthermore, it could be shown that the manufacturing-related deviations have considerable effects on the pore geometry and its flow behaviour. Therefore, on the basis of this publication, further CFD investigations should be carried out here in order to be able to quantify the flow behaviour at different flow velocities and the effects on the wall shear stress. Finally, it was shown that the design of CPC bone tissues using CFD analyses on target geometries alone is not sufficient and that an additional examination of the actual geometries is necessary.

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