Numerical optimization of open-porous bone scaffold structures to match the elastic properties of human cortical bone

Jan Wieding*, Andreas Wolf, Rainer Bader

Biomechanics and Implant Technology Research Laboratory, Department of Orthopaedics, University Medicine Rostock, Doberaner Strasse 142, 1895718057 Rostock, Germany

Article history:
Received 9 December 2013
Received in revised form 29 April 2014
Accepted 3 May 2014
Available online 14 May 2014

Keywords:
Optimization
Open-porous scaffolds
Biomechanical loading
Femoral bone
Design variations
Strut thickness
Pore size

Abstract
Treatment of large segmental bone defects, especially in load bearing areas, is a complex procedure in orthopedic surgery. The usage of additive manufacturing processes enables the creation of customized bone implants with arbitrary open-porous structure satisfying both the mechanical and the biological requirements for a sufficient bone ingrowth. Aim of the present numerical study was to optimize the geometrical parameters of open-porous titanium scaffolds to match the elastic properties of human cortical bone with respect to an adequate pore size. Three different scaffold designs (cubic, diagonal and pyramidal) were numerically investigated by using an optimization approach. Beam elements were used to create the lattice structures of the scaffolds. The design parameters strut diameter and pore size ranged from 0.2 to 1.5 mm and from 0 to 3.0 mm, respectively. In a first optimization step, the geometrical parameters were varied under uniaxial compression to obtain a structural modulus of 15 GPa (Young's modulus of cortical bone) and a pore size of 800 μm was aimed to enable cell ingrowth. Furthermore, the mechanical behavior of the optimized structures under bending and torsion was investigated. Results for bending modulus were between 9.0 and 14.5 GPa. In contrast, shear modulus was lowest for cubic and pyramidal design of approximately 1 GPa. Here, the diagonal design revealed a modulus of nearly 20 GPa. In a second step, large-sized bone scaffolds were created and placed in a biomechanical loading situation within a 30 mm segmental femoral defect, stabilized with an osteosynthesis plate and loaded with physiological muscle forces. Strut diameter for the 17 sections of each scaffold was optimized independently in order to match the biomechanical stability of intact bone. For each design, highest strut diameter was found at the dorsal/medial site of the defect and smallest strut diameter in the center.

In conclusion, we demonstrated the possibility of providing optimized open-porous scaffolds for bone regeneration by considering both mechanical and biological aspects. Furthermore, the results revealed the need of the investigation and comparison of different load scenarios (compression, bending and torsion) as well as complex biomechanical loading for a profound characterization of different scaffold designs. The usage of a numerical optimization process was proven to be a feasible tool to reduce the amount of the required titanium material without influencing the biomechanical performance of the scaffolds.
scaffold negatively. By using fully parameterized models, the optimization approach is adaptable to other scaffold designs and bone defect situations.

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1. Introduction

By the use of additive manufacturing (AM) processes, both standard and custom-made implants as well as open-porous scaffolds can be fabricated in a wide range of design possibilities (Murr et al., 2009, 2010; Parthasarathy et al., 2010; Schwerdtfeger et al., 2010; Harrysson et al., 2008; Bandyopadhyay et al., 2009). Furthermore, AM offers the possibility to gain control about the geometrical shape and about the mechanical properties in order to cope with various requirements, e.g. in the field of scaffolds for bone regeneration (Wieding et al., 2012). This opens up an entirely new field of unique implants with specific characteristics.

For scaffolds being designated to replace large segmental bone defects, caused by tumors, severe fractures, infections or implant loosening (Attias and Lindsey, 2006; Mavrogenis et al., 2009; Desai et al., 2012) various requirements have to be satisfied. Especially for load-bearing areas of the lower extremity (pelvis, femur, and tibia), these scaffolds are under high mechanical stress. Therefore, in order to act as a bone scaffold, mechanical as well as biological aspects have to be considered for sufficient bone regeneration and long-term stability within large segmental bone defects.

There is a general consensus about the necessity of an open-porous scaffold structure with an interconnecting pore system (Karageorgiou and Kaplan, 2005; Kienapfel et al., 1999; Salgado et al., 2004; Yang et al., 2001). But the specifications vary in a wide range of preferred values for the pore size. Although most studies investigated the pore size between 200 and 500 μm (Ryan et al., 2008; van der Stok et al., 2013; Ponader et al., 2010), there are also studies with much smaller pores (<200 μm) (Itala et al., 2001; Murphy et al., 2010) and larger pores (>500 μm) (Wieding et al., 2012; Lopez-Heredia et al., 2008; Hollandier et al., 2006) and even with pores up to 2200 μm (Holy et al., 2000) with promising results. Findings obtained from in vitro or in vivo studies provide different specifications for sufficient bone cell ingrowth.

Besides the biological aspects scaffolds must exhibit sufficient mechanical stability for load-bearing areas. Titanium and its alloys are successfully used in clinical application as an implant material due to high biocompatibility and good mechanical properties (Donachie, 1998; Down, 1973; Niinomi, 2008; Mueller et al., 2006). Nevertheless, to be suitable as a bone scaffold, the elastic properties shall be adapted to those of the surrounding bone tissue in order to avoid shielding of mechanical stimuli, which can lead to insufficient bone ingrowth and stress-shielding of the adjacent bone stock (Niinomi and Nakai, 2011; Engh et al., 1992; Merle et al., 2011). As the mechanical properties of titanium (e.g. Young’s modulus of 114 GPa) are lower than other metals like cobalt-chrome (224 GPa) or stainless steel (210 GPa) (Long and Rack, 1998) but still higher than cortical bone (Ohman et al., 2011), open-porous structures are implemented to reduce the stiffness of the scaffolds and to offer an suitable environment for bone ingrowth.

Therefore, the mechanical behavior of open-porous scaffolds has to be adapted for the application area in order to reduce the risk of implant loosening by stress shielding (Bandyopadhyay et al., 2009; Huiskes et al., 1992; Kuiper and Huiskes 1997). Hence, the investigations of bone scaffolds with defined biomechanical properties, suitable for carrying the load within the application field are of great importance.

To cope with all those requirements AM techniques like electron beam melting (EBM) or selective laser melting (SLM) offer a wide range of structural design variations. Thus, scaffolds can be fabricated with specific geometrical shape and sub-sequentially adjustable mechanical properties (Murr et al., 2010; Parthasarathy et al., 2010; Wieding et al., 2012). Moreover, the mechanical properties of AM fabricated dense scaffolds are comparable to those, fabricated with classical fabrication processes like casting and forging (Koike et al., 2011; Wieding et al., 2013). As there are nearly no limits for the fabrication, the question for the mechanical properties becomes more and more important.

Experimental studies for the characterization of the mechanical properties are often time-consuming and cost-intensive and were, therefore, mostly performed under uniaxial loading conditions and for only few design variations. In contrast, by the means of finite element analysis (FEA) the mechanical properties for different structural designs and porosities can be calculated prior to the cost-intensive and time-consuming fabrication (Olivares et al., 2009; Luxner et al., 2005; Chesh et al., 2004; Chua et al., 2003a, 2003b; Boccaccio et al., 2011; Sanz-Herrera et al., 2010; Wettergreen et al., 2005). In addition with optimization tools the mechanical and biomechanical properties can be directly controlled to match the necessary requirements (Hollister et al., 2002; Chan et al., 2010; Almeida, 2010; Adachi et al., 2006; Challis et al., 2010; Kapfer et al., 2011; Lin et al., 2004). This will lead to optimized scaffolds with desired and suitable mechanical properties.

However, considering the physiological environment, where the scaffolds are designated to be placed in, is essential to judge their ability as bone regeneration scaffold because their biomechanical behavior is different from those determined under uniaxial mechanical testing (Wieding et al., 2013).

Therefore, the aim of this numerical study was to utilize an optimization approach to match the mechanical properties of cortical bone under both mechanical and biomechanical loading with respect to the biological aspects in order to offer an open-porous scaffold structure for sufficient bone ingrowth.

2. Materials and methods

The general investigations of the scaffolds are illustrated in Fig. 1. In a first step the mechanical properties of the open-porous scaffolds have been investigated under uniaxial compression testing in order to determine the influence of the variation of the geometrical parameters (Fig. 1a), (Design
Fig. 1 – (a) D.O.E. procedure was used to determine the mechanical response of the open-porous scaffolds under uniaxial compression testing due to the variation of the geometrical parameters as well as the characterization of the sensitivity of the mechanical response due to variations of the input values. (b) Optimization procedure was performed first under mechanical (uniaxial compression) loading condition to match the desired target values. Furthermore, the optimized structures were analyzed under compression, bending and torsion as well as under biomechanical loading. Second, the optimization procedure was performed directly under biomechanical (physiological) loading conditions within a segmental defect of the distal femoral bone.

Fig. 2 – Upper row: parameterized models of the cubic structure (left), diagonally orientated struts (middle) and modified truncated pyramid (right) with the strut diameter (d), size of the basic cell (c) and pore size (a). Bottom row: mechanically tested scaffolds, consisting of 3 x 3 x 3 basic cells (cubic and diagonal design) and 2 x 2 x 2 basic cells for the modified truncated pyramid design (with additional connection elements). Struts are shown as cylindrical beams with their analytical cross-section.

Of Experiments, D.O.E). In a second step (Fig. 1b) the mechanical properties of the open-porous scaffolds have been optimized to match the biomechanical requirements of cortical bone under both mechanical (uniaxial compression) and biomechanical (physiological situation within the femoral bone) loading conditions. Structures derived from mechanical optimization approach have been, furthermore, investigated under bending and torsion as well as within the physiological loading environment.

2.1. Generating the open-porous scaffolds

For this numerical study, three different structural designs of open-porous titanium scaffolds have been investigated. A cubic design with the struts orientated perpendicular in all three spatial directions, a design with diagonally orientated struts, where the strut crossings are normal to all three spatial directions and a modified truncated pyramid design with additional connection elements (Fig. 2). The latter one
provides a combination of diagonally orientated struts in a moderate manner for load directions under bending and torsion as well as rectangular orientated struts for reducing the transverse deformation. Thus, the pyramidal design offers advantages for a combination of different loading situations as well as an adequate mechanical response for each of the investigated loading scenarios.

Generation of the numerical models was performed by using the finite element software package Abaqus (version 6.12-EF, Dassault Systèmes, Velizy-Villacoublay, France). Scaffolds for the mechanical analysis were generated as linear pattern of one structure, having three basic cells in a row in each spatial direction (for cubic and diagonal design), thus consisting of 27 basic cells. Due to the non-symmetric structure of the pyramidal design, this scaffold consisted only of 9 basic cells, four on the upper layer, four on the lower layer and one in the center. Using basic cells was found to offer adequate mechanical properties with similar results compared to experimental testing (Ryan et al., 2009).

The pore size \( a \) was calculated based on the geometrical parameters, i.e. cell size \( c \) and strut diameter \( d \) for the cubic design by:

\[
a = c - d
\]  

for the diagonal design by:

\[
a = \sqrt{2} \cdot \left( \frac{c}{2} - d \right)
\]  

and for the pyramidal design by:

\[
a_1 = \frac{\sqrt{17}}{4} \cdot c - d
\]
\[
a_2 = \frac{c}{2} - d
\]

### 2.2. Element type and material properties

All designs have been generated as fully parameterized models (i.e. strut diameter, size of the basic cell and subsequently the outer dimensions of the scaffold could be controlled by parameter variation) by use of the Finite Element software package Abaqus. Struts have been implemented as structural beams featuring a circular cross-section. Each segment (beam section between two adjacent beam intersections) was meshed with at least three elements (five elements for the diagonal design), using Timoshenko’s theorem with linear interpolation function in order to provide sufficient mechanical behavior. Accuracy of the mesh density was verified by convergence analysis under different loading conditions (compression, bending and torsion) for mesh densities of 1, 2, 3, 5, 10 and 30 elements per strut. Furthermore, influence of the utilized element types (beam elements) for the lattice structures on the structural modulus was investigated and compared to models generated with continuum elements (hexahedral) for the cubic design. Height and diameter of the scaffold as well as pore size and strut thickness was identical for both models.

All scaffolds are meant to be made of titanium alloy (Ti6Al4V) being fabricated via selective laser melting (SLM). Therefore, material properties were modeled as linear elastic and homogeneous with Young's modulus of 114 GPa (Wieding et al., 2013) and Poisson's ratio of 0.3 (Suansuwan and Swain, 2001).

### 2.3. Loads and boundary conditions

The edges on the lower surface of the scaffolds were constrained in the vertical \( z \)-direction. Furthermore, one edge was constrained in horizontal \( x \)-direction; the other edge was constrained in \( y \)-direction in order to prevent rigid body motions but allow transverse deformation. Displacement of 10% of the scaffolds height (depending on the size of the basic cell) was applied to the edges on the upper surface in vertical direction without inhibiting the transverse deformation.

Geometric parameters were chosen according to match the requirements for fabrication as well as for the cell ingrowth. For the EBM and the SLM fabrication process the thickness of each layer is approximately 100 \( \mu \text{m} \) (Koike et al., 2011). Hence, in order to guarantee mechanical integrity of the fabricated scaffolds, a minimum strut diameter of 200 \( \mu \text{m} \) was defined as a lower limit. An upper limit of 1500 \( \mu \text{m} \) was set in order to limit the size of the scaffolds in combination with the required pore size for cell ingrowth. Geometric data for all three designs are listed in Table 1.

### 2.4. Characterizing the mechanical properties of the open-porous scaffolds

As the following optimization approach would only offer a local optimum for the parameter variation, the entire range of the parameter field was investigated by using a D.O.E. algorithm. Hence, a region of interest (R.O.I.) for the optimization approach could be indicated. Parameters, controlling the size and the structural architecture, were implemented into the automatization software Isight (version 5.7, Dassault Systems). The pore size \( p \) was calculated based on the geometrical parameters, i.e. cell size \( c \), strut diameter \( d \) and cell size \( f \):
where $p$ is the enclosed surface area of the scaffolds (neglecting the edges). The reaction force, which is necessary for the deflection $w$ of the beam, is given by:

$$\Delta = \frac{F_R \cdot l_0}{A}$$

and

$$E_s = \frac{F_R \cdot l_0}{A \cdot \Delta}$$

(5)

where $F_R$ is the reaction force for given displacement of $\Delta l$ (compression length, i.e. 10% of the initial scaffold height), $A$ is the initial length of the scaffolds (three times the size of the basic cell), and $l_0$ is the initial length of the scaffolds (three times the size of the basic cell).

Finally, a further set of parameters was created by Isight and the next loop was started. A total amount of 100 calculations with different parameter sets was calculated for each of the three scaffold designs. The results for the structural moduli were analyzed as against the geometrical parameters.

2.5 Optimizing the mechanical properties under mechanical load

For the first approach of the optimization, the scaffolds were loaded under uniaxial compression. The workflow for the optimization was similar to that used for the characterization of the mechanical properties. Instead of the DOE, a Sequential Quadratic Programming (SQP) procedure was used as optimization algorithm. The SQP is well situated for non-linear and continuous design spaces and for long running simulations. It exploits the local area around an initial design point and, therefore, finds rapidly a local optimum design.

As the open-porous scaffolds are designated to be placed within a biological environment, both mechanical and biological aspects have to be considered for stabilization and sufficient incorporation with bone. Therefore, limits for the geometrical parameters for the scaffolds are based on the tolerances of the fabrication process as well as on the findings in the literature for cell ingrowth into open-porous structures. The limits for the optimization are the same as listed in Table 1.

Under uniaxial compression the parameters have been optimized to exhibit a structural modulus of 15.0 GPa as a target value to be in the range of human cortical bone (Ohman et al., 2011). In order to induce a mechanical stimulus on the bone and to avoid stress shielding this value was kept at the lower range. Size of the basic cell and the pores were set to match the findings in the literature for sufficient bone ingrowth into open-porous structures with a pore size of approximately 800 μm (Ponader et al., 2010; Lopez-Heredia et al., 2008; Li et al., 2007).

2.6 Mechanical behavior of the optimized structures under bending and torsion

Besides the determination of the mechanical behavior under axial compression, the structures were further analyzed under bending and torsion. Therefore, beam-like structures were generated from each of the three optimized scaffold designs as derived from compression testing. These beams again consisted of a linear pattern of the basic cells of the optimized design. Hence, length of the models was 29.2, 96.6 and 37.8 mm and width (equal to height) was 7.7, 25.6 and 6.9 mm for the cubic, the diagonal and the pyramidal design, respectively.

Bending of the beam was performed with the edges on one end fully constrained and a deflection applied on the opposite side. Bending modulus for the structures was calculated as follows:

$$E_b = \frac{F_R \cdot 4 \cdot l_0}{w \cdot b^3}$$

where $F_R$ is the reaction force, which is necessary for the deflection $w$ of the beam. Torsional loading was performed also with the edges on one end fully constrained and a rotational boundary condition on the edges on the opposite side. Shear modulus for the torsional loading was calculated as follows:

$$G_T = \frac{M_T \cdot l_0}{I_p \cdot \phi}$$

where $M_T$ is the torsional moment and $I_p$ is the polar moment of inertia, i.e. $1/6 b^4$, $(b=h)$. 

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2.7. Biomechanical behavior under physiological load

In the second step, the mechanically optimized structures were used for creating large scaffolds for bone regeneration in order to determine their behavior in a biomechanical environment. These scaffolds were tested under physiological loading conditions within a segmental bone defect, as described in detail in Wieding et al. (2013). Geometry of the bone was based on a composite femur (4th generation, large left, Sawbones AB, Malmö, Sweden). A segmental defect of 30 mm was created within the distal diaphysis of the femoral bone, stabilized with an osteosynthesis plate and seven titanium screws. The shape of the scaffolds was adapted to the bone within the defect being replaced by the scaffolds and exhibited a height of 30 mm. The values for the geometrical parameters were obtained from mechanical optimization and applied on the entire scaffold.

The femur has been meshed with linear hexahedral elements with an edge length of approximately 2 mm. Material properties for the composite femur were modelled as isotropic and linear elastic with an inhomogeneous material distribution as derived from CT-data, following the convenient approach of Klouess et al. (2009). Hence, a smooth material distribution was implemented, exhibiting Young’s moduli of 16.7 and 0.137 GPa, respectively (Wieding et al., 2012). Young’s modulus for the medullary cavity was set to 0 MPa in order to avoid numerical problems.

The distal end of the femur was fully constrained. Physiological hip reaction force and five additional muscle forces (M. gluteus maximum, M. gluteus minimum and M. gluteus medius, M. iliopsoas, M. piriformis and M. vastus lateralis) according to Heller et al. (2005) and Bitsakos et al. (2005) were applied to the bone, simulating the loading situation during normal walk. The scaffolds were placed into the defect and relative displacement between bone and scaffold was inhibited in order to avoid slipping within the bone-implant interface during loading.

In order to compare the different designs with each other, the alteration of the gap distance was considered for determination of the biomechanical behavior. Therefore, displacement of two nodes on each end of the gap was used for the calculation of the gap alteration (Wieding et al., 2013).

2.8. Optimization the biomechanical properties under physiological load

For the second optimization approach, the scaffolds were directly optimized under physiological loading conditions within the femoral bone defect as described earlier. Large scaffolds were generated for each of the three designs in order to optimize their structure, depending on the biomechanical loading. The scaffold’s height was set to 30 mm but the outer shape of the scaffolds was adapted to the shape of the bone defect (Fig. 4). For the structural composition, the geometrical parameters of the mechanically optimized structures, i.e. cell size and strut diameter, were used as initial adjuvant start values for the subsequently biomechanical optimization. Due to the specific height of 30 mm for the defect area, size of the basic cell was not varied. Thus, only the strut diameter was used for the optimization in order to fit the biomechanical criterion for the gap stabilization. Lower and upper limits for the strut diameter were the same as for the mechanical optimization as listed in Table 1.

Moreover, for the optimization of the structures, the scaffolds exhibited 17 independent sections (Fig. 4c). For each section the strut diameter could be varied separately according to the requirements for gap stabilization. As a criterion for the optimization, the range for the gap alteration was set to 0.03 mm with a range between 0.02 and 0.04 mm in order to match the displacement of a healthy bone as calculated for an intact bone with additional osteosynthesis plate (Wieding et al., 2013). Furthermore, in order to reduce the weight of the scaffold and the amount of artificial material the strut diameter was minimized.

3. Results

3.1. Influence of the mesh density and utilized element type

Results for the highest mesh density, i.e. 30 elements per strut, were assumed to be the converged solution for calculated compression, bending and shear modulus. Deviations for each model design and loading case were calculated with respect to the converged solution. Under compression deviations for a mesh density of three elements per strut were less than 0.3% for all designs. Under bending deviations for three
elements per strut were 0.9%, 0.34% and 0.45% for the cubic, the pyramidal and the diagonal design, respectively. High deviations were found under torsion for the cubic and the pyramidal design for coarsest mesh densities and quickly decreased with increasing number of elements. For a mesh density of three elements per strut deviations were 2.1%, 1.5% and 0.02% for the cubic, the pyramidal and the diagonal design, respectively.

The structural modulus for an entire cubic scaffold generated with beam elements for the lattice structures was approximately 15% less compared to a scaffold modelled with hexahedral elements.

3.2. Sensitivity analysis

The results of the sensitivity analysis under axial compression loading for all three designs are shown in Fig. 5. They represent the distribution of the influence on the structural modulus for the four investigated input parameters compared to each other for each design. Exemplarily, for the cubic design the initial values revealed a structural modulus of 13.3 GPa that differed between 8.9 and 19.8 GPa due to the variation of the input parameters.

For all designs fluctuations of Poisson’s Ratio revealed only minor influence of less than 1% on the structural modulus. Altogether, for the different designs, variations in the Young’s modulus revealed an influence on the mechanical properties, between 17% and 23% for the cubic and the pyramidal design, respectively. In contrast, variation of the two geometric parameters, i.e. strut diameter and size of the unit cell showed the highest influence on the mechanical properties. Strut diameter had an influence of approximately 40% for all designs. Variations in the cell size revealed an influence between 36% and 42%. Similar influences on the mechanical properties for the four parameters have been found under bending and torsional testing.

3.3. Mechanical response under axial compression

The results for the characterization of the mechanical properties for the entire range of the geometrical parameters under axial compression testing by using the D.O.E. are shown in Fig. 6.

In general, variation of the geometrical parameters cell size and strut diameter revealed similar influence on the mechanical properties for all three investigated structural designs (Fig. 6a, c and e). Structural modulus increased by decreasing size of the unit-cell and by increasing strut diameter. Furthermore, results showed a steady but nonlinear correlation between mechanical properties and geometrical parameters. For most of the parameter combinations results for the structural modulus are situated below 50 GPa. Furthermore, range of the optimum structural modulus, i.e. between 10 and 20 GPa is indicated by the white marked corridor in the 3D plots (Fig. 6). It has to be recognized that for decreasing cell size and increasing strut diameter, overlapping of the analytical cross sections occur when the values for the strut diameter exceed the size of the unit cell (pore size ≤ 0 μm because both parameters have been varied independently from each other). Hence, results for the structural modulus partly exceeded values for dense Ti6Al4V of 114 GPa (Wieding et al., 2013).

Taking into account the pore size of the different designs (variation of cell size and strut diameter depend on each other in order to lead to the desired pore size), distribution of the structural modulus was different for the three designs. Results for the structural modulus also showed a steady but nonlinear correlation (Fig. 6b, d, and f). For the cubic design (Fig. 6b) a maximum modulus of approximately 90 GPa could be achieved but only few parameter combinations revealed a modulus of more than 50 GPa. For the entire range of the pore size a structural modulus between 10 and 20 GPa can be enabled. In contrast, for the diagonal design (Fig. 6d) the maximum result was approximately 30 GPa, only one third of the cubic design. Furthermore, due to the structural composition for this design only for a pore size of up to 1500 μm a structural modulus of more than 10 GPa could be achieved and most of the values were situated below 10 GPa. Results for the pyramidal design (Fig. 6f) were similar but slightly lower than the cubic design. Values of approximately 80 GPa were found for a small number of design variations and with a less even distribution. Again, for the entire range of the pore size a structural modulus between 10 and 20 GPa could be achieved and also only a small number of variation were below 10 GPa. Hence, the range of results of the parameter variation for the subsequent optimization approach can be already estimated from these plots. Moreover, concerning the pore size, none of the designs revealed a structural modulus of dense Ti6Al4V even for a pore size of 0 μm because the circular shape of the struts will always reveal a residual porosity within the scaffolds.

3.4. Mechanical and biomechanical properties for the optimized structures under mechanical load

The results of the mechanical optimization approach for the three designs are listed in Table 2. For all investigated designs the desired structural modulus of 15.0 GPa and a pore size of approximately 800 μm were achieved due to the optimization procedure. Moreover, for the pyramidal design pore size of the smaller pores was approximately 200 μm.
Fig. 6 – 3D distribution of the mechanical structural modulus for the cubic (first row: a, and b), the diagonal (second row: c, and d) and the pyramidal design (third row: e and f) with respect to cell size and strut diameter (left side: a, c, and e) and with respect to pore size and strut diameter (right side: b, d, and f).
Under uniaxial compression testing the cubic and the pyramidal design revealed similar geometrical results with the smallest strut diameter of approximately 400 μm. Cell size of both designs varied due to the different geometrical structure. Smallest size of the unit cell was found for the pyramidal design. In contrast, diameter for the diagonal orientated strut design was more than three times thicker than for the other designs due to the diagonal orientation of the struts with regard to the load direction. Thus, due to the geometrical composition of the diagonal design, size of the basic cell has to be increased in order to ensure the desired pore size of 800 μm. Hence, largest cell size was required for the diagonal design.

Although all three designs had the same mechanical response under compression their behavior under bending and torsion was different. Under bending all three designs revealed comparable mechanical results between 9.0 and 14.5 GPa. But under torsional loading the cubic and the pyramidal designs exhibited a clearly lower shear modulus of approximately 1 GPa. In contrast, the diagonal design revealed a shear modulus of nearly 20 GPa.

Furthermore, results under physiological loading of the large-size scaffolds, made of the mechanically optimized geometrical structures for all three designs have been calculated. Highest alteration of the gap displacement within the femoral defect was found for the cubic design. Although the mechanical properties for the diagonal design were highest for all investigated loading conditions, the biomechanical stability was twice as large as that for the cubic design (i.e. lower gap alteration). Highest stability and subsequently lowest gap alteration were found for the pyramidal design, being only a quarter of the cubic design.

### 3.5. Optimization results for the biomechanical approach

Under biomechanical loading the gap alteration for all investigated models was 0.030 mm. Results for the distribution of strut diameter and pore size for the 17 sections after

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Design</th>
<th>cubic</th>
<th>diagonal</th>
<th>pyramidal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geometrical</td>
<td>Strut diameter (μm)</td>
<td>416</td>
<td>1448</td>
<td>392</td>
</tr>
<tr>
<td>Size of basic cell (μm)</td>
<td>1215</td>
<td>4024</td>
<td>1182</td>
<td></td>
</tr>
<tr>
<td>Pore size (μm)</td>
<td>799</td>
<td>797</td>
<td>789b</td>
<td></td>
</tr>
<tr>
<td>Mechanical</td>
<td>Structural modulus (GPa)</td>
<td>15.0</td>
<td>15.0</td>
<td>15.0</td>
</tr>
<tr>
<td>Bending modulus (GPa)</td>
<td>9.0</td>
<td>14.5</td>
<td>12.6</td>
<td></td>
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<tr>
<td>Shear modulus (GPa)</td>
<td>0.96</td>
<td>19.96</td>
<td>1.74</td>
<td></td>
</tr>
<tr>
<td>Biomechanical</td>
<td>Gap alteration (mm)</td>
<td>0.115</td>
<td>0.055</td>
<td>0.032</td>
</tr>
</tbody>
</table>


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*a* Pore size \( a_1 \),  
*b* Pore size \( a_2 \).

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*Fig. 7 – Distribution of the strut diameter of the 17 sections for the biomechanically optimized scaffold with diagonal design (a). Results for the strut diameter (b) and the pore size (c) of each section for all three investigated designs.*
optimization under physiological loading are shown in Fig. 7. For the cubic design load-bearing struts were only necessary in sections 2–5 (posterior-medial area) for sufficient mechanical stabilization of the gap with a diameter of equal or less than 800 μm. All other sections exhibited only the minimum specified strut diameter of 200 μm. Subsequently, the pore size for the scaffold was approximately 1000 μm for most sections, except the load-bearing ones with approximately 500 μm.

Similar results were found for the pyramidal design. Sections 1–5 and 10–12 revealed a strut diameter of nearly 600 μm. Again, these sections are generally located in the posterior and medial area of the scaffold. Pore size of the larger pores (a1) exhibited values between 650 and 1000 μm, pore size for the smaller pores (a2) exhibited values between 50 and 400 μm. Larger pore size was subsequently situated in section areas with small strut diameter.

In contrast, largest strut diameter was found for the diagonal design with values between 950 and 1400 μm for the sections of the entire outer circle 1–8 and additional for section 11. For the sections within the inner circle (9–16, except 11) strut diameter was approximately 250 μm. Only for the inner section (17) the strut diameter was 200 μm. Due to the size of the basic cell pore size of the scaffold was between 900 and 1500 μm for the sections with larger strut diameter and 2500 μm for sections with smaller strut diameter.

In general, for all scaffolds the inner core (section 17) exhibited only the minimum specified strut diameter of 200 μm. Furthermore, sections for the inner circle in the entire anterior region (sections 13–16) revealed a small strut diameter of less than 300 μm or also the minimum specified diameter of 200 μm.

Furthermore, none of the scaffolds showed any risk of failure due to plastic deformation (yield strength for titanium approximately 820 MPa (Wieding et al., 2013)). Maximum von Mises stress under biomechanical loading within the struts was 265, 181 and 322 MPa for the cubic, the diagonal and the pyramidal design, respectively.

4. Discussion

The integration of an optimization algorithm has proved to be a useful approach to design open-porous scaffolds with adapted mechanical properties in order to provide advanced implants for bone regeneration. Three different geometrical designs have been examined, evaluated and compared with each other. Both mechanical properties and biological requirements for cell ingrowth have been considered. Furthermore, the results demonstrated that in addition to the investigation of the mechanical behavior under uniaxial compression bending and torsion, considering of biomechanical loading situations is needed for a reliable evaluation of bone scaffolds.

To ensure that the results are not adversely affected by neither the mesh density nor by the element types used, convergence analysis as well as comparison between structural and continuum elements has been performed prior to the optimization process. All three scaffold designs converged very fast for all three investigated loading situations due to the excellent mechanical behavior of the beam elements. Therefore, mesh density of three elements per strut was considered to be sufficient to describe mechanical response adequately.

In general, numerical models generated with hexahedral elements show good mechanical response compared to experimental testing (Wieding et al., 2013, 2012). Apparent softening for the beam model occurs due to the unrestricted transverse deformation in the area of the intersection points in contrast to the continuum model, where interference of transverse deformation occur. Thus, the strut thickness of the open-porous structures has to be slightly larger compared to the hexahedral element model to achieve the same structural modulus and can be interpreted as some kind of safety factor for the structures.

For the present numerical study we utilized open-porous scaffolds and explicitly modelled the geometrical structure instead of using an apparent material model (Harrysson et al., 2008; Yan et al., 2011), that will have several disadvantages. The entire elastic tensor of the apparent material has to be determined for each parameter composition in order to gather the anisotropic behavior due to the orientation and thickness of the struts and the size of the pores. Furthermore, the real stresses within the struts cannot be determined and will be much lower within the bulk implant model with only a lesser stiff material behavior due to increasing porosity. Moreover, cutting a regular lattice structure with an arbitrary cut will lead either to free strut ends with connectivity to only one end to the scaffold or, if the free strut ends shall be removed, a step-like structure (Emmelmann et al., 2011).

In both cases assigning an apparent material behavior to these regions lead to material invalidity as there are either no struts where a material can be implemented or the behavior of the free struts is completely different from the assumed one. In our case, the free ends remained within the models for the investigation of the biomechanical behavior within the femoral bone. Furthermore, via modelling the real lattice structure of the scaffold both anisotropic material behavior of the scaffold and reduced stiffness within the areas of the free strut ends have been considered.

The results for the parameter variation of the cubic structure are similar to our previously published work. Here the different strut geometry, i.e. circular and rectangular was taken into account for numerical investigations of open-porous titanium scaffolds that have been compared to results from experimental testing (Wieding et al., 2013). Furthermore, the influence of the variation of the input parameters, due to fabrication or material uncertainties, showed that variation of the structural parameters had the highest influence. Therefore, although results from the literature for Poisson’s ratio of titanium may vary between 0.30 and 0.34 (Suansuw and Swain, 2001; Senkov et al., 1996), the sensitivity analysis revealed only minor or neglectable influence on the mechanical properties of open-porous scaffolds. In contrast, fluctuations of the geometrical parameters had the highest influence on the mechanical properties. Thus, the mechanical response of fabricated scaffolds may slightly differ from the numerical predictions due to geometry deviations caused by fabrication tolerances and uncertainties (Parthasarathy et al., 2010; Ryan et al., 2009).

Using fully parameterized numerical models, the entire parameter field was obtained and showed a complete overview
about the mechanical properties of the investigated scaffold designs. This is especially important, when scaffolds with specific mechanical properties are to be determined. In contrast, using non-parameterized models is time-consuming and only few parameter combinations can be investigated at once.

Cubic titanium scaffolds were experimentally tested by Parthasarathy et al. (2010). Four different scaffold types with varying pore size and strut diameter have been fabricated via a EBm process. One of the models exhibited a pore size and a strut size of approximately 760 and 460 μm, respectively, which is comparable to our mechanically optimized cubic design although shape of the struts was different (rectangular vs. cylindrical). In contrast to our results of 15.0 GPa Parthasarathy et al. (2010) determined a compressive modulus of only 0.6 GPa. In contrast to the experimentally determined material properties, calculated results obtained using the formula given would lead to values about 14 GPa which again are similar to our numerical results.

Furthermore, Ryan et al. (2009) investigated the influence of open-porous scaffolds, made of titanium and compared the results to experimental testing. As they performed experimental testing as well as numerical analysis with models generated from μ-CT of the fabricated scaffolds and from CAD-data with idealized geometry, only three types of scaffolds with varying porosity have been analyzed. Moreover, they found that unit-cell models (consisting of only one basic cell) showed similar results compared to experimental testing.

In contrast to experimental testing in which the mechanical properties of the scaffolds are determined after fabrication, we were able to quickly obtain the mechanical properties prior to manufacturing by the use of numerical methods. Especially for bone scaffolds their fabrication with defined mechanical properties is required (Hollister et al., 2002; Almeida, 2010; Adachi et al., 2006).

Hollister et al. (2002) optimized scaffolds numerically that match the elastic properties of mandibular condyle using a homogenization optimization approach. In order to provide sufficient scaffolds for tissue regeneration, they defined constraints for the optimization, i.e. porosity, material modulus and pore size of the scaffold with three individual pore diameters. Although these investigated scaffold designs matched the elastic properties of mandibular condyle using a homogenization optimization approach. In order to provide sufficient scaffolds for tissue regeneration, they defined constraints for the optimization, i.e. porosity, material modulus and pore size of the scaffold with three individual pore diameters. Although all investigated scaffold designs matched the optimization criteria only a range and not specific target values were established.

Almeida (2010) used a topological optimization for the scaffold design in order to find the best distribution of material under various loading conditions. They clearly could show the influence of different loadings, i.e. tensile, shear and combination of both on the resulting scaffold topology. Furthermore, they presented an optimized scaffold with constant elastic properties for different values of porosity in contrast to other scaffolds, for which the elastic properties decreased with increasing porosity.

Although several studies investigated the mechanical properties of open-porous scaffolds, testing is almost solely performed under compression testing giving only a brief overview of the mechanical behavior. Therefore, by using mechanical (compression, bending and torsion) loading conditions, the mechanical response of the investigated scaffolds has been determined in detail in our present study.

Our data clearly demonstrate that not only uniaxial testing but also bending and torsion should be investigated in order to characterize the mechanical properties. Under axial compression testing, the cubic and the pyramidal design revealed higher mechanical stability due to the strut orientation parallel to the loading direction. Here, the diagonal design must provide much thicker struts in order to carry the load and to reveal a structural modulus of 15.0 GPa. With respect to the pore size of 800 μm the cell size of the diagonal design has to be several times larger than for the cubic or pyramidal design. In contrast, the diagonal design offers higher rigidity against bending and especially against torsion compared to the cubic and the pyramidal design. It has to be mentioned that differences under bending and torsion cannot be directly associated with the geometrical design. All designs have been initially modified to reach a specific structural modulus under compression condition with desired pore size. Therefore, the geometrical structure was different for all models tested under bending and torsion. Nevertheless, dimensions of the models have been taken into account for calculating the structural behavior.

Furthermore, we demonstrated the use of an optimization procedure for the modification of the mechanical properties of open-porous scaffolds under biomechanical loading conditions in order to fit a target value, e.g. the mechanical properties of human cortical bone. Our results show the accurate adaptation of the mechanical properties for titanium open-porous scaffolds to cortical bone by using a parametric optimization approach. For providing large-size scaffolds for bone ingrowth the scaffolds have to be analyzed within a physiological loading situation, as the mechanical response is different to that determined under uniaxial loading conditions (Wieding et al., 2013). Although the three scaffold designs has been initially optimized to match the elastic modulus of cortical bone, scaffolds based on that optimized design revealed different stability within the femoral defect model. In contrast, the biomechanically optimized scaffolds exhibited the same biomechanical stability for the magnitude of the gap alteration. Furthermore, for all scaffold designs, the inner core only revealed the minimum strut diameter. Therefore, the inner core does not contribute to the mechanical stability and can be left empty as already implied in our previous work (Wieding et al., 2013).

For all scaffolds, biological requirements for sufficient cell ingrowth have been considered within the optimization procedures in order to guarantee a biomechanically long-term stable implant. Solid arguments for an optimum pore size for open-porous scaffolds are rare in the literature. Findings differ between in vitro and in vivo experiments as well as for different scaffold materials. Nevertheless, for our optimization process we referred to an optimum pore size for cell ingrowth of approximately 800 μm (Ponader et al., 2010; Lopez-Heredia et al., 2008; Hollander et al., 2006; Li et al., 2007). For this range the geometrical parameters were optimized to match the mechanical properties of the target value (i.e. 15.0 GPa). Although most studies investigated the pore size between 200 and 800 μm with promising results, we assume that bone will also grow into pores larger than that due to the attraction of bone as long as the mechanical stimulus and the transport of nutrients are guaranteed. This
hypothesis has to be proved by in vivo testing. Nevertheless, as our numerical models are fully parameterized, the geometrical values can be modified in case of different findings about the optimum pore size.

In general, optimization tools should always be used to ensure the best possible adaptation especially since the manufacturing process will be able to produce even components with complex geometry. For further application the validation of the numerical data by experimental testing has to be performed. Furthermore, in vitro and in vivo testing should be conducted to show the ability of bone growth into the investigated open-porous structure.

Acknowledgments

The authors gratefully thank the Ministry of Economic Affairs, Employment and Tourism of Mecklenburg-Vorpommern, Germany and the European Union for financial support within the project “TiFоBone”. Furthermore, we would like to thank the colleagues from the Institute for Polymer Technologies e.V. for the cooperation on the development of the open-porous structures.

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