Novel bone fixation implants minimising stress shielding

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<td>Two-dimensional</td>
</tr>
<tr>
<td>3D</td>
<td>Three-dimensional</td>
</tr>
<tr>
<td>AM</td>
<td>Additive manufacturing</td>
</tr>
<tr>
<td>ANOVA</td>
<td>Analysis of variance</td>
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<tr>
<td>ASTM</td>
<td>American Society for Testing and Materials</td>
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<tr>
<td>ATOM</td>
<td>Abaqus topology optimisation module</td>
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<td>Body-centered cubic</td>
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</tr>
<tr>
<td>HCP</td>
<td>Hexagonal close-packed</td>
</tr>
<tr>
<td>HMDS</td>
<td>Hexamethyldisilazane</td>
</tr>
</tbody>
</table>
IM  Intramedullary nail
ISE  Isotropic solid or empty
ISO  International Organization for Standardization
LC-DCP  Limited contact-dynamic compression plate
LCP  Locking compression plate
LHS  Locking head screw
MMA  Method of moving asymptotes
MSCs  Mesenchymal stem cells
NPR  Negative poisson ration
OC  Optimality criteria
OP  Osteoporosis
ORIF  Open reduction and internal fixation
PBS  Phosphate-buffered saline
PC-Fix  Point-contactor fixator
PCL  Poly(e-Caprolactone)
PLA  poly-lactic acid
SEM  Scanning electron microscopy
SIMP  Solid isotropic microstructure with penalisation
SLP  Sequential linear programming
SLM  Selective laser melting
STL  Stereolithography format
TO  Topology optimisation
TPMS  Triply periodic minimal surfaces
TRIZ  Theory of inventive problem solving
UTS  Ultimate tensile strength
VC  Vertex cube
WHO  World health organisation
YS  Yield strength
XRD  X-ray diffraction
List of Notations

Chapter Two

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>z</td>
<td>Vector of the design parameters</td>
</tr>
<tr>
<td>f(z)</td>
<td>Cost function</td>
</tr>
<tr>
<td>g_j(x)</td>
<td>Equality constraint function</td>
</tr>
<tr>
<td>h_i(x)</td>
<td>Constraints of the problem</td>
</tr>
<tr>
<td>f_i</td>
<td>Objective function</td>
</tr>
<tr>
<td>u</td>
<td>Displacement vectors</td>
</tr>
<tr>
<td>f</td>
<td>Load vector</td>
</tr>
<tr>
<td>K</td>
<td>Global stiffness</td>
</tr>
<tr>
<td>K_e</td>
<td>Matrices of the element stiffness</td>
</tr>
<tr>
<td>ρ</td>
<td>Density</td>
</tr>
<tr>
<td>ρ_e</td>
<td>Relative element density</td>
</tr>
<tr>
<td>V*</td>
<td>Defined Volume</td>
</tr>
<tr>
<td>v_e</td>
<td>Volume of each element</td>
</tr>
<tr>
<td>V</td>
<td>Initial volume</td>
</tr>
<tr>
<td>r</td>
<td>Location vector in the Euclidean space</td>
</tr>
<tr>
<td>h_k</td>
<td>Lattice vector in reciprocal space</td>
</tr>
<tr>
<td>A_k</td>
<td>Magnitude factor</td>
</tr>
<tr>
<td>λ_k</td>
<td>Wavelength of periods</td>
</tr>
<tr>
<td>p_k</td>
<td>Phase shift</td>
</tr>
<tr>
<td>C</td>
<td>Constant</td>
</tr>
<tr>
<td>ω</td>
<td>Complex variable</td>
</tr>
<tr>
<td>θ</td>
<td>Bonnet angle</td>
</tr>
<tr>
<td>R(ω)</td>
<td>The function of different surfaces</td>
</tr>
</tbody>
</table>

Chapter Three

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ρ</td>
<td>Density</td>
</tr>
<tr>
<td>E</td>
<td>Young’s/Elastic Modulus</td>
</tr>
<tr>
<td>p</td>
<td>Penalisation factor</td>
</tr>
<tr>
<td>f</td>
<td>Volume fraction</td>
</tr>
<tr>
<td>V</td>
<td>Defined Volume</td>
</tr>
<tr>
<td>V_i</td>
<td>Initial Volume</td>
</tr>
<tr>
<td>F</td>
<td>Force vectors</td>
</tr>
<tr>
<td>U</td>
<td>Global displacement</td>
</tr>
<tr>
<td>K</td>
<td>Global stiffness</td>
</tr>
<tr>
<td>k_e</td>
<td>Element stiffness matrix</td>
</tr>
<tr>
<td>u_e</td>
<td>Displacement vector</td>
</tr>
<tr>
<td>ρ_e</td>
<td>Relative element density</td>
</tr>
<tr>
<td>ρ_min</td>
<td>Relative minimum density</td>
</tr>
<tr>
<td>C</td>
<td>Objective function</td>
</tr>
<tr>
<td>ε_xx</td>
<td>X-axis equivalent strain</td>
</tr>
<tr>
<td>ΔL</td>
<td>Change in length</td>
</tr>
</tbody>
</table>
$L_i$  Initial length
\(\sigma_{xx}\)  X-axis equivalent stress
$E_s$  Equivalent stiffness
$F_{xx}$  Average force reaction
$A$  Cross sectional area of the plate
$W_{xx}$  Work of the external loads
$U_{xx}$  Longitudinal displacement

**Chapter Four**
\(\rho_0\)  Non-zero minimum density
$E^i$  Initial Elastic modulus
$K_e$  Element stiffness matrix
$Z$  Objective function
$f$  Force vector
$u$  Displacement vector
$v_e$  Elemental volume
$K_{Ten}$  Equivalent tensile stiffness
$E_B$  Bending equivalent stiffness
$h$  Distance between the load and support points
$\xi$  Distance between the load points
$S$  Slope of the load-deflection curve
$K_{Tor}$  Equivalent torsional stiffness
$T_{xx}$  Torsion moment
$\Phi_{xx}$  Angle of twist

**Chapter Five**
\(\Theta\)  Orientation angle of the microstructure
$A$  Dimensions of the rectangular holes
$NC$  Number of applied load cases
$\alpha^p$  Load weight factor
$E^H$  Homogenised bone material properties
$M$  Bone density
$E$  Strain field
$A$  Weight factors of relative frequencies of arm movements
$\Delta bm$  Change in bone mass
$N$  Number of nodes

**Chapter Six**
$H$  Distance between the force points
$A$  Span between the force and support points
$K$  Stiffness
$RF$  Average reaction force
$D$  Maximum Displacement

**Chapter Seven**
$F$  Applied force
Δ         Displacement
K         Equivalent stiffness
Σ         Stress
E         Strain
E         Equivalent Young’s modulus
Hv        Vickers hardness
D         Arithmetic mean of the diagonals

Chapter Eight
W         Wear rate
V         Sliding speed
T         Duration of the wear experiment
V         Wear volumes
Abstract

In ageing countries, where the population is above the median age, the national health services are under enormous pressure to address problems related to bone fractures due to accidents or diseases. More effective and personalised medical treatments are critical, not only to improve the outcome of the clinical treatment but also to reduce costs.

Bone fractures require the use of fixation plates to stabilise the fracture and promote bone healing. These plates are produced using biocompatible metallic materials, presenting a significant stiffness mismatch in comparison to bone. This often results in lack of bone stimulation in the vicinity of the plate causing bone loss and plate instability. Moreover, commercial fixation plates are mass produced using conventional manufacturing methods and consequently not feasible for personalised medical strategies.

In order to solve these limitations, this research proposes a strategy based on the use of topology optimisation and bone remodeling together with powder bed fusion additive manufacturing. The aim is to design lightweight plates with reduced stress shielding and additive manufacturing (the ideal technology for mass personalisation) to produce optimised plates.

Bone fixation plates were successfully optimised considering different loading conditions and volume reductions. Electron Beam Melting and Selective Laser Melting were used to produce the optimised plates. Non-processed additive manufactured plates were mechanically, biologically and tribologically characterised. Results show that by increasing the volume reduction, the stress shielding problem is minimised, and it was also possible to obtain plate designs presenting mechanical properties in the range of cortical bone. Additive manufactured plates are also able to support cell attachment and to promote cell proliferation, showing significantly better biological performance than commercial plates.
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This section is dedicated to my beloved wife, Nawami, she is my pillar and my everlasting support, I sincerely thank you with all my heart for all your sincere love and support that you have given me and I cannot wait to face all the upcoming life challenges with you by my side, couldn’t wish for a more loving and kind person.

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I would like to express my deep sense of gratitude to my Thesis co-supervisor Mr Chris Peach, MD FRCS (Tr&Orth), Manchester NHS trust foundation, for his constant support, guidance and expert comments.

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إهداء إلى
والدي العزيزين
و
زوجتي الغالية

Dedicated to
my dearest parents
& my beloved wife
Chapter One

Introduction
Chapter One  Introduction

1.1 Background

Bone is a vascular and specialized tissue that plays a major biomechanical and metabolic role, being responsible for the shape of the skeleton, protecting soft tissues, transmitting forces of muscular contraction during movement and serving as a reservoir of important ions that contribute to the regulation of the extra-cellular matrix composition, blood production and blood pH (Liu et al. 2019). The mechanical properties of bone (e.g. Young’s modulus) strongly depend on the bone composition and bone structure (McNamara 2011, Jo et al. 2014, Liu et al. 2019). Two types of bones are identified, cortical or compact bone corresponding to a very dense region (porosity of 5-10%), surrounding the marrow space and representing 80% of the total bone mass with a Young’s modulus ranging from 11 to 25 GPa and a compressive strength between 107-146 MPa; and trabecular or cancellous bone which is a highly porous structure (porosity of 50-95%), composed of a honeycomb-like network of trabecular plates and rods interspersed in the bone marrow, representing 20% of the bone mass, with a Young’s modulus of 0.2-10 GPa and compressive strength of 5-10 MPa (Rho et al. 1997, McNamara 2011, Jo et al. 2014).

Bones are susceptible to fracture due to either traumatic forces or pathological diseases (Alsop 2013). Normally, bone is able to heal itself without developing a scar, through a complex physiological process consist of acute inflammatory responses, cartilage callus formation, endochondral ossification and bone remodelling (Bigham-Sadegh and Oryan 2015). However, in the case of bone fracture events such as high traumatic or pathological fractures, exceeding a critical size defect (which depends of the location, gender and age), bone fracture healing capabilities become limited causing delays or non-union problems, requiring further clinical interventions (May et al. 1989, Aho et al. 2013, Vorys et al. 2015). Currently, this represents a significant health problem. In 2050, it is expected that 6.3 million patients worldwide will suffer from hip fractures with estimated costs of around $13 billion (Johnell 1997). Trauma is also a leading cause of death (Miller and Goswami 2007).

Traditionally, fractured bones are clinically treated with metallic bone fixation implants (Ulhthoff et al. 2006). The most common bone fracture treatment approaches are either implementing the fixator internally (in situ) or externally (ex situ). Studies show that the internal fixation approach is the preferable one, as it shortens the healing time and improves the quality of the bone healing
process (Strømsøe 2004). These internal fixations (i.e. plate and screws) are usually referred in the literature as “bone fixation implant”, “bone plate”, “fixation plate”, “bone fixation plate”, “fracture plate” and “fracture fixation plate”.

The surgery strategy depends on the site of injury, fracture type and patient’s gender, age and clinical history. The bone fixation implant is selected based on the surgical strategy required by either applying absolute or relative stability which defines the healing process (Uhthoff et al. 2006, Szypryt and Forward 2009, Marsell and Einhorn 2011):

- **Absolute stability** - the surgical procedure of acquiring interfragmentary compression (e.g. Dynamic Compression Plate), to induce primary healing (i.e. no callus formation).
- **Relative stability** - the surgical procedure of acquiring interfragmentary motion (e.g. Locking Compression Plate), to induce secondary healing (i.e. callus formation).

Bone fixation implant can also be classified based on design parameters (number, type and position of screws, geometry, etc), place of injury, type of material and type of fracture. Their clinical and mechanical performance are also determined by the design, surgical procedure and the material used. Lane (1895) introduced for the first time metallic internal bone fixation implants, as plate and screws to internally stabilise the fractured bone (Uhthoff et al. 2006). Since then, several improvements have been made in terms of materials and manufacturing processes (Uhthoff et al. 2006). The first standard bone fixation implant was presented in 1969 under the name of Dynamic Compression Plate (DCP) (Parren et al. 1969). Afterwards, some designs were considered and commercialised such as Point-Contactor Fixator (PC-Fix), Less Invasive Stabilisation System (LISS) and Limited Contact-DCP (LC-DCP). These designs were proposed to improve the healing process and eliminate the disadvantages of the DCP, mainly devascularisation. This led to the current gold standard design of bone fixation implant called “Locking Compression Plate” (LCP), a hybrid screwing system, comprising the conventional screws found in the DCP and innovative locking head screws (LHS). This allows the LCP to have a greater mechanical performance and relative and absolute stability (Szypryt and Forward 2009).

Recent major developments in this field are related to the surface area design that is in contact to the underlying bony cortex “footprint” to allow blood supply, the hole/screw plating techniques to achieve optimal healing for different fracture types, complicated anatomy (i.e. reconstruction plates) and specific anatomical designs (i.e. Periarticular Locking Plate System) (Uhthoff et al.
Commercially available internal bone fixation implants are presented in Table 1.1.

**Table 1.1** Commercially available internal bone fixation implants (Wagner 2003, Uhthoff et al. 2006, Miller and Goswami 2007, Szypryt and Forward 2009).

<table>
<thead>
<tr>
<th>Type of Implant</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCP</td>
<td>- Bony union</td>
<td>- Only used for simple fractures</td>
</tr>
<tr>
<td></td>
<td>- Elimination of external immobilization</td>
<td>- Stabilisation depends on the friction between the plate and the bone</td>
</tr>
<tr>
<td>LC-DCP</td>
<td>- Less contact with bone</td>
<td>- No superiority over others</td>
</tr>
<tr>
<td></td>
<td>- Hybrid screw systems</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Allow callus formation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Good in comminuted and osteoporotic fractures.</td>
<td></td>
</tr>
<tr>
<td>LCP</td>
<td></td>
<td>- Limited in epiphyseal and metaphyseal fractures</td>
</tr>
<tr>
<td>Periarticular Locking</td>
<td>- Anatomically precontoured</td>
<td>- Only used for specific fractures</td>
</tr>
<tr>
<td>Plate System</td>
<td>- Hybrid screw systems</td>
<td></td>
</tr>
</tbody>
</table>

Currently, bone plates are made of Titanium alloys (particularly commercially pure Ti and Ti-6Al-4V) or 316L Stainless Steel (Miller and Goswami 2007). However, due to the far superior stiff material (e.g. Young’s modulus of Ti-6Al-4V is around 120 GPa) and according to Wolff’s law, current fixation plates present uneven stress distribution in the bone-plate interface which leads to poor bone healing causing the stress shielding effect (Elias et al. 2008, Prasad et al. 2017). Such effect will result in implant loosening and bone loss. Moreover, 30% of the surgeries comprising fixation plates are currently going under a second surgery procedure for plate removal (Hanson et
This procedure will increase the possibility of nerve damage and bone refracture due to the stress shielding effect. Alternatively, if plate removal is not considered and left in the body the persistence of implants behind the length of time needed for bone healing causes adverse reactions such as (Hofmann 1992, Inion 2015):

- Soft tissue irritation;
- Stress shielding effects;
- Growth disturbance;
- Toxic, allergic and potentially carcinogenic reactions.

This shows that there is a clear need to develop fixation plates with optimised properties and more customised for each patient. This is an important topic of research focusing on design, manufacturing processes and materials.

1.2 Research aims and objectives

The major aim of this research is to develop a combined methodology to produce optimised fixation plates, minimising stress shielding and bone loss. This methodology comprises a computational strategy based on topology optimisation, to redesign standard fixation plates considering different loading and volume reduction conditions, and a finite element analysis to investigate mechanical stability and bone remodeling. Digitally obtained designs are then produced using additive manufacturing, and the effect of the fabrication method on the physical and biological properties was investigated. Biological tests, including Live/dead and cell attachment and proliferation, using osteosarcoma cells were also used to investigate the need for time consuming and costly post-processing (surface finishing and polishing) steps. The proposed methodology can be in the future applied to produce personalised and optimised generic plates.

Specific objectives of this research are:

- **Objective 1**: evaluate the current state-of-the-art of using topology optimisation and additive manufacturing for the design and fabrication of medical devices;
- **Objective 2**: investigate the use of additive manufacturing to produce fixation plates;
- **Objective 3**: develop a topology optimisation methodology to design optimal fixation implants with an equivalent Young’s modulus similar to bone, assessing their mechanical stability and load transmission in order to promote bone remodeling thus reducing bone loss;
➢ **Objective 4:** use two different powder bed fusion techniques (electron beam melting and selective laser melting) to fabricate topology optimised fixation plates;

➢ **Objective 5:** Investigate the effect of the different fabrication methods in terms of the mechanical properties, wear resistance, coefficient of friction, surface hardness, surface roughness, cell attachment and proliferation. Fixation plates were mechanically tested considering tensile, bending and torsion;

➢ **Objective 6:** Investigate the need of post-processing fabricated fixation plates in terms of biological and tribological properties.

A summary of this research framework is presented in Figure 1.1.

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**Figure 1.1** Research Framework.
1.3 Thesis outline

This Thesis, comprising nine Chapters, is based on published and submitted articles and a book chapter following the specific objectives of this research. Chapter One describes the Thesis motivation and background, aims and key objectives. The contents of the remaining Chapters are summarised below. Figure 1.2 illustrates the Thesis structure.

Chapter Two introduces the state-of-the-art by covering the research objectives 1 and 2, by providing an insight of computational optimisation techniques with the combination of additive manufacturing for medical applications. This Chapter also introduces different metallic additive manufacturing techniques, providing examples of the use of these techniques to produce bone fixation plates.

Chapter Three investigates the use of topology optimisation to redesign two-dimensional (2D) bone plates. The same methodology is considered in Chapter Four but extended to a three-dimensional (3D) space. Different loading conditions (compression, bending, torsion and combination of these loads) and different volume reductions (25%, 45% and 75%) are considered. In both Chapters it is possible to observe the suitability of topology optimisation to minimise the stress shielding problem.

In Chapter Five stress shielding is evaluated, considering a bone remodeling model of the optimised bone plates (obtained in Chapter Four) when clinically applied to treat a fracture in a hemurs bone. Therefore, this Chapter investigates the impact of plate design on the bone mass. A load transfer analysis to assess the stress shielding effect of optimised plate designs when clinically used to treat a midshaft fracture of a cortical bone is presented in Chapter Six. The mechanical strength (stability) of the optimised designs is also assessed.

Chapter Seven investigates the combination of topology optimisation and additive manufacturing (Electron Beam Melting). Fixation plates optimised for compression were considered for additive manufacturing. Printed and commercially available plates were mechanically characterised, and the results compared against natural cortical bone. Non-post-processed plates were also biologically tested, and the results compared against polished commercial plates to investigate if costly post-processing procedures are required.
Chapter Eight considers both Electron Beam Melting and Selective Laser Melting systems to produce topology optimised designed fixation plates. Plates were tested considering tensile, bending and torsion tests and the results compared against native cortical bone properties. The non-post-processed additive manufactured plates were physically (surface finish and microstructure), biologically and tribologically assessed.

Chapter Nine provides an overall summary of the Thesis, main contributions and conclusions. Additionally, future directions for research based on the findings of this work are also presented.

1.4 List of publication

Chapter Two consist of two publications, a journal article and a book chapter:


Chapter Three is based on a journal article:


Chapter Four is based on a book chapter:


Chapter Five is based on a journal article:

**Chapter Six** is based on a journal article:


**Chapter Seven** is based on a journal article:


**Chapter Eight** is based on a journal article:

Figure 1.2 Thesis structure - Chapters and Sections.
Chapter Two

State-of-the-art
Chapter Two  **State-of-the-art**

This Chapter presents the current state-of-the-art of optimisation techniques particularly topology optimisation and additive manufacturing to produce medical devices. It consists of two main Sections.

The first Section is based on a review paper entitled “Topology Optimisation for Medical Implants through Additive Manufacturing” submitted to Progress in Additive Manufacturing. This Section introduces the concept of structural optimisation and topology optimisation in particular, and the use of optimisation techniques to produce tissue engineering scaffolds, metallic lattice structures and orthopaedic implants. Several examples are provided, and main research challenges discussed.

Bone fixation plates are currently made of metallic materials, mainly titanium alloys (e.g. Ti-6Al-4V). The second Section, based on a book chapter entitled “A review on powder bed fusion additive manufacturing for metallic fixation implants” included in the book “Virtual Prototyping & Bio Manufacturing in Medical Applications” published by Springer, introduces the most commonly used metallic materials to produce bone fixation plates. It discusses the two main powder bed fusion techniques (Electron Beam Melting and Selective Laser Melting) to process such materials with emphasis on Ti-6Al-4V. The effect of the two different techniques in terms of microstructure development is discussed and several examples provided. Future research challenges are also presented.

### 2.1 Topology Optimisation for Medical Implants through Additive Manufacturing*

Advanced manufacturing techniques are being explored to fabricate degradable and non-degradable, porous or non-porous implants for medical applications. These implants have been designed using standard computer-aided design (CAD) and computer aided engineering (CAE) tools and produced in a multitude of materials. The recent use of optimisation techniques, mainly topology optimisation, allows the development of additive manufactured medical devices with improved performance. This review discusses the combined use of optimisation techniques and

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additive manufacturing to produce biocompatible and biodegradable scaffolds for tissue engineering with improved mechanical and permeability properties, metallic lattice structures with reduced weight and minimal stress shielding effect and lightweight personalised orthopaedic implants. Major limitations and research challenges are highlighted and discussed.

2.1.1 Introduction

The design and fabrication of personalised lightweight and high-performance implants is a challenge in the medical field. Structural optimisation, in particularly topology optimisation, is being explored to create lightweight medical implants and, in the case of metallic structures, to improve the mechanical performance and fatigue behaviour minimising problems such as stress shielding or tissue bonding. However, the geometric complexity of some of the obtained designs are difficult to be converted into physical object due to the limitations of conventional manufacturing technologies. Emerging additive manufacturing technologies characterised by freedom of design, elimination of tooling, reducing assembly requirements by consolidating parts, elimination of production steps and allowing the fabrication of complex objects with marginal increase of costs, facilitates the implementation of design tools into the design and manufacturing process, allowing completely new approaches for designing novel medical implants. The combined use of optimisation schemes and additive manufacturing is recent (Zegard and Paulino 2016, Berrocal et al. 2019). Examples include the design of internal conformal cooling channels or part orientation in the fabrication chamber to reduce costs and the volume of support structures (Krol et al. 2012, Strano et al. 2013, Leary et al. 2014, Jahan et al. 2016, Langelaar 2016, Mass and Amir 2017, Li et al. 2018).

This Section describes the current state-of-art of using optimisation algorithms and additive manufacturing to produce medical implants (biodegradable scaffolds for tissue engineering, metallic lattices and orthopaedic implants) with reduced weight/volume and improved mechanical properties (increasing stiffness to values close to the stiffness of natural tissues but also minimising stress shielding and bone loss problems) and medical implant designs exploiting personalisation approaches enabled by additive manufacturing. Research challenges and areas for future research activities are also presented.

2.1.2 Structural optimisation

Structural optimisation is a numerical decision-making tool that defines the material distribution in a defined domain according to specific constraints and objective functions (Rozvany 2001,
Christensen and Klabring 2009, Haftka and Sobieszczanski-Sobieski 2009, Tsavdaridis et al. 2015). It is a problem focusing on minimizing cost functions subjected to a set of constrains (Spillers and MacBain 2009, Svanberg 2009, Haftka and Sobieszczanski-Sobieski 2009):

Minimise $f(z)$ where $z = \{z_1, z_2, \ldots, z_n\}$

subject to $\{h_i(x) \leq 0, i = 1, 2, \ldots, m \quad g_j(x) = 0, j = 1, 2, \ldots, n\}$

where $z$ is the vector of design parameters and $f(z)$ is the cost function. The inequality constraint function $g_j(x)$ and the equality constraint function $h_i(x)$ define the constraints of the problem. This formulation describes a constrained optimisation problem. However, in some cases, optimisation requires multiple objectives. This corresponds to a multi-criteria optimisation problem and can be described as follows (Spillers and MacBain 2009, Svanberg 2009):

$$\min \Sigma_{k=1}^{p} w_k f_k(x) \quad (2.3)$$

where $f_1, \ldots, f_k$ are the objective functions; or using one function and constraining the others:

$$\min_{x} f_i(x) \quad (2.4)$$

subject to $f_k(x) \leq \epsilon_k, k = 1, \ldots, p, k \neq j \quad (2.5)$

Structural optimisation comprises three main methods: sizing, shape and topology (Bendsøe and Sigmund 2004, Sigmund and Maute 2013). Sizing optimisation, in which the structure layout is prescribed and the only parameter that can be modified is the size of the object, it is commonly used to optimise truss-like structures (Al-Tamimi et al. 2017). The shape optimisation of a structure is obtained by changing the shape of a considered object with other objects of different shape (Al-Tamimi et al. 2017). Topology optimisation is the most common method (Hsu and Hsu 2005, Ansola et al. 2007, de Kruijf et al. 2007, Neches and Cisilino 2008, Deaton and Grandhi 2014). The aim is to determine the material distribution to optimise a specific design space considering a set of load and boundary conditions (Sehmi et al. 2018). In order to find the optimal material distribution, the finite element method is used to divide the design space into a set of
discrete elements (Bendsøe and Sigmund 2004, Al-Tamimi et al. 2017). After this meshing step, the optimisation method is used to determine each element property through a material exists or not strategy. This optimisation scheme that leads to a binary problem that defining different states for each material, is known as the Isotropic Solid or Empty (ISE) elements topology (Rodrigues et al. 2014). The density or solid isotropic with microstructure penalisation (SIMP) method and the homogenisation method are the two main strategies to solve the ISE topology optimisation (Bendsøe and Sigmund 2004, Sigmund and Maute 2013). Initially, topology optimisation algorithms focus on the problem of minimising structural compliance, but new objective and constraint functions have been proposed to investigate other mechanical problems such as natural frequencies, yield stresses and fatigue behaviour, applied to linear and non-linear materials and multi-material structures (Ma et al. 1993, Jung and Gea 2004, Wang and Wang 2004, Suresh and Takalloozadeh 2013, Nabaki et al. 2019).

As mentioned, the aim of topology optimisation is to find the optimal material distribution ($\Omega^*$) of a given design space ($\Omega$), discretising it into a set of small subspaces (N). Usually, topology optimisation focuses on minimising structural compliance (maximising stiffness), and the problem can be formulated as follows:

$$\min_{\rho_e u} f^T \cdot u$$

where $u$ is the displacement vectors and $f$ is the load vector governed by:

$$f = K(k_e) \cdot u = \sum_{e=1}^{N} K_e(k_e)$$

where $K$ is the global stiffness matrix and $K_e$ is the matrices of the element stiffness.

The design stiffness matrix is modified according to the design variable (density, $\rho$). This means that the density of each element ($\rho_e$) defined on $\Omega$ through a binary approach will result in either $\rho_e=1$ (i.e. keeping the element) or $\rho_e=0$ (i.e. removing the element). Solving this problem requires rewriting the initial problem as follows:

$$\min Z(\rho_e) = f^T \cdot u, \text{ subject to } \left\{ \begin{array}{l} V = \sum_{e=1}^{N} \rho_e v_e \leq V^*, \\ \rho_e = 0 \text{ or } 1, \quad e = 1, \ldots, N, \end{array} \right.$$
where \( V \) is the initial volume, \( v_e \) is the volume of each element and \( V^* \) is the desired user-defined volume. Figure 2.1 illustrates a generic topology optimisation scheme.

\[
\text{Objective function: } \int_{\Omega} f \cdot u_f \, d\Omega + \int_{\Gamma} t \cdot u_f \, d\Gamma \\
\text{Sensitivity: } -2\alpha \cdot ESE_{ij} / \rho_{ij}
\]

Figure 2.1 A general topology optimisation scheme.
2.1.3 Tissue engineering scaffolds

Tissue engineering is an emerging research field aiming at restoring, repairing and regenerating the function of tissues and organs (Bártolo et al. 2009, Melchels et al. 2012, Pereira and Bártolo 2015a, Madrid et al. 2019). Three main approaches have been considered. Cell-based therapies corresponds to the classical approach (Pereira and Bártolo 2015b, Pereira et al. 2017). It is a simple but less effective method as it is difficult to keep injected cells in the right position during clinically relevant times. Most recent approaches are based on the use of additive manufacturing to produce scaffolds or cell laden constructs (Pereira et al. 2018a, Pereira et al. 2018b, Koc et al. 2019, Aguilar et al. 2019, Leberfinger et al. 2019, Miri et al. 2019). The scaffold-based approach is the most commonly used approach. Scaffolds are three-dimensional, biocompatible and biodegradable porous structures that provide the physical substrate for cell attachment, proliferation and differentiation (Turnbull et al. 2018, Huang et al. 2019, Wang et al. 2019, Yan et al. 2019, Du et al. 2019). Optimal scaffolds must follow a multitude of requirements. They must present a degradation rate similar to the regeneration of a tissue, appropriate mechanical properties supporting the loads during the regeneration process, high porosity, appropriate pore shape and pore size, and pore interconnectivity to guarantee high permeability allowing oxygen, nutrients and metabolic waste to diffuse promoting tissue ingrowth (Caetano et al. 2016, Vyas et al. 2017). Scaffolds must also present proper surface roughness and surface chemistry to promote cell adhesion, proliferation and differentiation (Wang et al. 2016a, Liu et al. 2018a). Figure 2.2 presents the main steps related to the design, fabrication and assessment of scaffolds. This is a very complex process requiring a multitude of interdependent relationships between material, rheological properties, fabrication system and processing conditions, scaffold architecture and performance as shown in Figure 2.3.
Figure 2.2 Main steps for the design and fabrication of optimal tissue engineering scaffolds.

Figure 2.3 Tissue engineering scaffolds as a multi-dimensional optimisation problem.

The design of scaffolds presenting high porosity and good mechanical properties is challenging. Lin et al. (2004) used topology optimisation to design scaffold microstructures meeting specific requirements (stability, stiffness and porosity) and isotropic elastic constants. The study was further extended by considering permeability as part of the optimisation process (Hollister and Lin...
However, in this study, permeability was not coupled with the mechanical properties and therefore no correlation between permeability and mechanical performance was considered. This was solved by Kang et al. (2010), which used a homogenisation topology optimisation algorithm to design three-dimensional units of tissue engineering scaffolds. In order to avoid numerical instabilities authors considered the Sigmund’s non-linear sensitivity filter (Sigmund 1994). Target properties were selected based on known cross-property bounds between mechanical properties and isotropic diffusivity. Based on the optimisation of scaffolds unit cells, an interbody fusion cage was also designed. Unit cells were designed with porosity values ranging between 30% and 60% (Figure 2.4a). A correlation between bulk modulus and diffusivity for different topologies and 50% of porosity is presented in Figure 2.4b, which clearly shows the effect of the architecture on both mechanical and permeability properties of a scaffold.

**Figure 2.4** (a) Microstructures obtained for 30%, 50% and 60% of porosity. (b) Effective bulk modulus versus effective diffusivity for microstructures with 50% of porosity. K is the bulk modulus of the solid phase, K_1 is the bulk modulus of the void phase, D is the free isotropic diffusion coefficient of a solute in the fluid phase and D_2 is diffusivity of the solid phase (Kang et al. 2010).

Almeida and Bártolo (2010) proposed a computer tool to support the design of scaffolds for additive manufacturing. This tool enables to perform topology optimisation identifying the most appropriate geometries of scaffolds fitting predefined mechanical properties for a specific material.
reduction. Studies were performed considering hydroxyapatite scaffolds and the maximum porosity level achieved was around 70%, after which a lack of integrity of the scaffolds structure was observed. Similarly, Poh et al. (2019), assuming a scaffold as a lego-like structure based on repeated single units, developed a macroscopic optimisation routine to create polycaprolactone (PCL) scaffolds. The routine allowed the optimisation of the volume fraction distribution along the scaffold. A penalty factor was also considered to control the scaffold volume fraction avoiding shapes that potentially could compromise vascularisation. Optimal material distribution allowed to optimise porosity, maximise stiffness and to reduce the risk of mechanical failure.

Hu et al. (2019) used topology optimisation to design poly-lactic acid (PLA) customised mandibular porous scaffolds using an extrusion-based machine. Computer tomography was used to create 3D digital models of the mandible. Scaffolds were printed using different lay down patterns and assessed in terms of ultimate load, failure deflection, yield deflection, strain distribution and porosity. Results show that the combination of numerical simulation and topology optimisation allows the fabrication of scaffolds with improved mechanical properties.

Implicit surface modeling using triply periodic minimal surfaces (TPMS) has been explored to design scaffolds with optimal topology considering both mechanical and permeability properties. A periodic surface is defined as follows (Almeida 2013):

\[
\varphi(r) = \sum_{k=1}^{K} A_k \cos\left[2\pi (h_k \cdot r)/\lambda_k + p_k\right] = C
\]  

(2.10)

where \( r \) is the location vector in the Euclidean space, \( h_k \) is the \( k^{th} \) lattice vector in reciprocal space, \( A_k \) is the magnitude factor, \( \lambda_k \) is the wavelength of periods, \( p_k \) is the phase shift, and C is a constant. Specific periodic structures and phases can be constructed based on this implicit form (Wang 2007, Qi and Wang 2009, Almeida 2013).

In the case of TPMS, the Weierstrass formula describes their parametric form as follows (Wang 2007, Qi and Wang 2009):

\[
\begin{align*}
    x &= \text{Re} \int_{\omega_0}^{\omega_1} e^{i\theta} (1 - \omega^2) R(\omega) d\omega \\
    y &= \text{Im} \int_{\omega_0}^{\omega_1} e^{i\theta} (1 + \omega^2) R(\omega) d\omega \\
    z &= -\text{Re} \int_{\omega_0}^{\omega_1} e^{i\theta} (2\omega) R(\omega) d\omega
\end{align*}
\]  

(2.11)
where $\omega$ is a complex variable, $\theta$ is the so-called Bonnet angle, and $R(\omega)$ is the function which varies for different surfaces.

From a multi-dimensional control parameter space point of view, the geometric shape of a periodic surface is specified by a periodic vector, such as (Wang 2007, Qi and Wang 2009, Almeida 2013):

$$V = \langle A, H, P, \Lambda \rangle_{K \times 6} \tag{2.12}$$

where:

$$A = [A_k]_{K \times 1} \tag{2.12a}$$

$$H = [h_k]_{K \times 3} \tag{2.12b}$$

$$P = [p_k]_{K \times 1} \tag{2.12c}$$

$$\Lambda = [\lambda_k]_{K \times 1} \tag{2.12d}$$

are row concatenations of magnitudes, reciprocal lattice matrix, phases, and period lengths, respectively. Examples of TPMS tissue engineering unit cells are presented in Figure 2.5.

**Figure 2.5** Examples of triply periodic minimal surfaces (Kapfer et al. 2011).
Almeida (2012a,b, 2013) investigated the use of Schwartz and Schoen primitives as unit cells to design scaffolds with improved mechanical and permeability properties. Two important parameters can be used as modelling control constraints: thickness and radius. Figure 2.6 illustrates the effect of these parameters. These units can be easily manipulated from a computational point of view through operations such as union, difference, intersection, modulation and convolution, allowing the design of scaffolds with a thickness gradient. Results show that for both surfaces the porosity decreases by increasing the surface thickness, while the elastic modulus increases. A linear dependence between the scaffold porosity and the elastic modulus was achieved. For the Schwartz surfaces, it was observed that the porosity decreases by increasing the surface radius till a threshold value, from which it starts to increase (Figure 2.7). The elastic modulus decreases by increasing the surface radius. The relationship between porosity and surface radius follows a hyperbolic behaviour and a similar behaviour was observed regarding the relationship between elastic modulus and porosity, so it is possible to decrease or increase the elastic modulus of the scaffold while maintaining high porosity values. In the case of Schoen geometries, the porosity decreases by increasing surface thickness and the elastic modulus increases with thickness and decreases with porosity. In the case of Schoen surfaces, the elastic modulus decreases by increasing either the surface radius or the porosity. Fluid flow studies were also performed considering shear strain rate and the wall shear stress on the surface of the scaffold units. These two parameters strongly contribute to cell proliferation and differentiation. For both Schoen and Schwartz unit cells of scaffolds results show that the shear strain rate decreases with the thickness of the unit and increases with the radius. Results also suggest that the best geometric option is to work with lower thicknesses and higher radius values. Regarding the variation of the wall shear stress as a function of the thickness variation, the author found that the wall shear stress increases with thickness in the case of Schwartz units and decreases in the case of Schoen geometries. A similar behaviour was observed for the variation of the wall shear stress with radius variation.

Panesar et al. (2018) used TPMS geometries and topology optimisation to produce functionally graded porous structure for additive manufacturing. Authors found that functionally grade structures presented 40% to 50% superior stiffness than uniform porous structures. However, the effect of the gradient geometry in terms of permeability was not investigated.
Chapter two: State-of-the-art

Figure 2.6 The effect of thickness and radius on the topology of TPMS. a) Schwartz unit cells obtained through thickness variation with constant surface radius; b) Schwartz unit cells obtained through radius variation with constant surface thickness; c) Shoel unit cells obtained through thickness variation with constant surface radius; d) Schoen unit cells obtained through radius variation with constant surface thickness (Almeida 2012b, 2013).
Figure 2.7 Schwartz surfaces a) variation of the scaffold porosity with the surface radius b) variation of the elastic modulus with the porosity (Almeida 2012b, 2013).

2.1.4 Metal lattice structures
Metallic lattice structures, not considered as tissue engineering scaffolds due to their non degradability nature, are being used for orthopaedic applications. They are lightweight structures presenting good mechanical properties and their porous structure facilitate implant fixation and
proper bonding with the surrounding tissues. Rodgers et al. (2014) developed a topology optimised structural design methodology to obtain lattice structures for orthopaedic applications with optimised stiffness, porosity, volume fraction and surface area. A non-linear optimisation algorithm based on a 3D finite-element beam model was used to determine the structural properties of the lattice structures. An objective function considering porosity, material volume and surface stresses was considered. Porosity described through a non-linear relationship with pore size determines the permeability of the lattice structure. A stress term was considered to avoid stress shielding. Rahimizadeh et al. (2018) developed a computational methodology combining multi-scale mechanics and topology optimisation to design titanium lattice structures aiming to reduce the stiffness mismatch between the structure and the surrounding bone (Figure 2.8). Asymptotic homogenisation theory was used to characterise the mechanics of individual blocks forming the lattice structure while the Soderberg fatigue criterion was used to investigate the fatigue resistance of the lattice structure under multi-axial physiological loading conditions. Using this methodology authors were able to produce lattice structures reducing in 26% the bone loss in comparison to the full dense titanium medical implants. Similarly, Xiao et al. (2012) apply topology optimisation to design titanium scaffolds with 30% volume fraction and minimum mean pore size of 231 μm fabricated using selective laser melting (SLM). Challis et al. (2010) used topology optimisation to create TPMS-based lattice structures for bone applications. By tuning the porosity, it was possible to produce SLM structures presenting stiffness similar to bone. Parts were produced using proprietary materials (EOSINT M Direct Metal 50 and EOSINT M Direct steel 50 powder). Maximum porosity considered was 80%.
Figure 2.8 Computational methodology used to design a lattice structure for tibial-knee applications. (Rahimizadeh et al. 2018).

Significant mandible defects can affect the masticatory function and lead to loss of speech and facial deformity. Luo et al. (2017) used an optimisation method based on the concept of uniform stress to design metallic structures with minimal weight. Tetrahedral structural titanium lattice structures were successfully designed for repairing mandibular defects and produced using SLM. The optimisation scheme allows the design of structures presenting more homogenous stress distribution and eliminating regions of stress concentration. Kang et al. (2012) used topology optimisation to design a porous bone anchor Ti-alloy implant minimising the deformations near the bone-implant interface (Figure 2.9). The implant was produced using SLM, the dimensional accuracy was assessed and differences lower than 10% between physical and digital models were obtained.
Similar to tissue engineering biodegradable scaffolds, metallic lattice structure can be considered as a lego-like structure based on repeated single unit elements. Xiao et al. (2018) used topology optimisation to design 316L stainless steel lattice structures to be produced using SLM as shown in Figure 2.10a. Three different unit elements, face centre cube (FCC), vertex cube (VC) and edge centre cube (ECC), were considered and optimised in terms of mechanical performance for different levels of porosity (Figure 2.10b). The Gibson-Ashby model was used to predict the performance behaviour of these units. Results show that the FCC and VC lattice structures present better mechanical properties (i.e. Young’s modulus) than ECC lattice structures which presents high energy absorption efficiency.
Figure 2.10 a) Topology optimisation iterations for lattice structures. b) The three different lattice structures considering different percentages of porosity (Xiao et al. 2018).

Topology optimisation has been used to create lattice structures with negative Poisson’s ratio (NPR) for additive manufacturing (Figure 2.11) (Schwerdtfeger et al. 2011, Yang et al. 2015, Yuan et al. 2017, Souza et al. 2018, Yang et al. 2019, Zadpoor 2019). These auxetic structures (when deformed in one direction also expand in one or more of the remaining principal directions) present higher flexural bending strength and buckling under bending, being highly relevant for angioplasty stents or annuloplasty rings (Figure 2.12). Soft lattice structures are also relevant for tendons applications, which presents a negative Poisson behaviour.
Figure 2.11 Examples of auxetic structures. a) design of lattice structures and b) EBM produced auxetic lattice structures (Eldesouky et al. 2017, Gao et al. 2019).
Figure 2.12 Negative Poisson’s ratio stent a) design and b) assembled design with vessel (Wu et al. 2018).
2.1.5 Orthopaedic implants

Grujicic et al. (2010) used finite element analysis and design optimisation to create a distal femoral fracture fixation plate with optimal size/thickness ratio as shown in Figure 2.13. The design was supported by realistic functional requirements (strength, bending stiffness and longevity) obtained through a musculoskeletal multibody inverse dynamics analysis considering a human riding a bicycle. Among the different functional requirements considered in this research study it was observed that it is longevity that controls the fixation plate optimal design.

![Figure 2.13 a) Fractured femur fixed with lateral plate and locking screws assembled with adjoining bones and b) fixation plate thickness design optimisation presenting lower and upper bound (Grujicic et al. 2010).](image-url)
Fraldi et al. (2010) designed hip prosthesis minimising the risk of implant failure due to stress shielding. The prosthesis was assessed using a non-linear static finite element analysis on a femur. A maximum stiffness topology optimisation strategy considering different volume reductions (55%, 65%, 75% and 85%) was implemented. A comparison between the actual stress level in the intact femur and the stress level in a femur with optimised implants was estimated. Ti-6Al-4V alloy was considered for the head of the prosthesis and CrCo alloy for the stem. The results show that it was possible to design hip prosthesis with reduced stress shielding. Similarly, Al-Tamimi et al. (2017, 2019a,b) used topology optimisation to redesign bone fixation plates (locking compression plates) considering different geometries in terms of number of screw holes, volume reductions (25%, 45% and 75%) and loading conditions (bending, compression, torsion and combinations of these loads). Optimised plated were printed in Ti-6Al-4V using electron beam melting (EBM). Results showed a decrease on the equivalent stiffness with an increase of volume reduction. It was also possible to obtain some designs where the equivalent Young’s modulus is in the range of cortical bone. Non-polished plates were biologically tested showing a significantly high cell attachment and proliferation compared to commercially available plates.

Peto et al. (2019) used topology optimisation and additive manufacturing to produce a tibia intramedullary implant for an eight-year old osteosarcoma patient. Topology optimisation was used to reduce the weight of the implant and to minimise stress shielding problems. SLM was used to produce the optimised implant using stainless steel powder. Figure 2.14 illustrates the main steps considered to develop the implant. Iqbal et al. (2019) used a multi-objective topology optimisation to design a personalised pelvic prosthesis minimising weight/volume and maximising stiffness. The design was obtained considering physiological loading conditions of different daily routines (e.g. walking, sitting down, stairs ascending and descending). A pelvic design with minimal stress concentration regions and a strength close to pelvic bone was achieved. The personalised pelvic prosthesis was designed considering Ti-6Al-4V, produced using EBM and implanted in a patient suffering from pelvic sarcoma with satisfactory short-term clinical results (see Figure 2.15).
Figure 2.14 Strategy to produce a personalised tibia intramedullary implant through the combination of topology optimisation and additive manufacturing (Peto et al. 2019).

Figure 2.15 Produced prosthesis using EBM before implementation and the prosthesis radiographic image after implementation (Iqbal et al. 2019).

2.1.6 Discussion and challenges
The use of optimisation techniques and additive manufacturing opens new routes to design and fabricate more effective medical designs. Different examples related to biocompatible and biodegradable tissue engineering scaffolds, metallic lattice structures and orthopaedic implants are provided mainly focusing on personalisation, reduce weight/volume and to improve specific
properties (e.g. mechanical properties and permeability). In the case of metallic implants, topology optimisation allows to design plates minimising plate instability and stress shielding.

A wide range of software packages allow to perform topology optimisation (e.g. Simulia Tosca Structure, Altair Optistruct, Ansys, Autodesk Netfabb, ParetoWorks, SolidThinking and Simright). However, these tools were not designed for additive manufacturing and consequently they are not able to link the design optimisation of medical implants with key fabrication issues such as build direction, minimum wall thickness, overhangs and minimal use of support structures. Moreover, topology optimisation tools allow the weight reduction of an implant, but they are not considering the effect of part redesign in terms of minimising distortion during the fabrication process and minimising post-processing steps. Residual stress constraint topology optimisation, particularly for the fabrication of metallic implants using powder bed fusion technologies is also a challenge.

Topology optimisation has been used mainly to optimise the porosity of scaffolds to achieve a good balance between mechanical properties and permeability. However, tissue engineering scaffolds are made of degradable materials which can degrade through hydrolytic, enzymatic or a combination of both mechanisms (Azevedo and Reis 2004). As a consequence of degradation, the shape of the scaffold changes along time and, as a consequence the mechanical performance also changes. Currently, topology optimisation only considers the initial design of the scaffold optimised based on the expected properties after fabrication. The long-term behaviour of the scaffold and the effect of the designed topology on the degradation process and as a consequence on the biomechanical properties must also be considered. Moreover, topology optimisation of tissue engineering scaffolds usually assumes each filament as homogenous and isotropic. The inherent anisotropy is determined by the layout of the scaffold. However, recent studies show a significant impact of processing conditions (e.g. temperature, screw rotation velocity, deposition velocity) on the crystalline formation, crystalline size and crystalline orientation (Liu et al. 2018b, Huang et al. 2019). Crystallisation and crystal orientation influence the mechanical properties, degradation characteristics and the biological performance of the scaffolds. Some authors are attempting to establish correlation models between processing conditions and morphological development during the fabrication process allowing to design the anisotropy in each printed filament (Liu et al. 2018b,c). Currently, topology optimisation models are not able to consider this.
Consequently, they are not able to consider the effect of processing conditions on the morphology and the mechanical properties which may impact the optimisation process.

The performance of topology optimised, and additive manufactured scaffolds, metallic lattice and other orthopaedic implants must be assessed against the mechanical properties of biological tissues (e.g. bone and cartilage). This requires the existence of a database, which can eventually be used as a knowledge-based system, that currently does not exist. A database including mechanical properties of bones and other tissues considering locations, age and gender groups is critical.

Additive manufacturing processes often require support structures to support large overhang areas, to facilitate part removal after fabrication, or to reduce thermal distortion (Jiang et al. 2018). Methods including the sloping wall structures, creating a tree-like structures or cellular structures, have been proposed for support slimming, and different topology optimisation schemes have been developed (Huang et al. 2008, Strano et al. 2013, Gan and Wong 2016, Mirzendehdel and Suresh 2016). However, these methods are computationally expensive and the thermal performance, which is critical particularly for powder bed fusion process, was not fully addressed. As an alternative several researchers proposed methods to totally remove the need for support structures (Leary et al. 2014, Gaynor and Guest 2016). However, these methods strongly depend on the build direction and limited the part design optimisation (Liu et al. 2018d). Therefore, there is a need for more robust algorithms that are able to minimise the need of support structures, considering their thermo-mechanical performance without posing any constraint to the topology optimisation of the part (no difference regarding conventional topology optimisation).
2.2 A review on powder bed fusion additive manufacturing for metallic fixation implants*

Trauma is a major cause of disability and death in both developed and developing countries. The World Health Organisation (WHO) has predicted that by 2020 trauma will be one of the primary cause of years of life loss (Maharaj et al. 2013). Bone fractures are frequently associated to major injuries and are caused by stresses that exceed bone strength.

Bone can heal itself through a complex physiological process comprising acute inflammatory reaction, cartilage callus formation, endochondral ossification, and finally bone remodelling (Bigham-Sadegh and Oryan 2015). However, if the energy of the trauma is high, exceeding bone strength it can cause significant displacement of the bones resulting in a bone fracture or inherently unstable fracture patterns. Often this requires a surgical procedure on the affected bone to stabilise the injury and allow healing to take place. The fractured bone is restored to its original anatomy by bringing the bone ends into apposition and is fixed with either absolute or relative stability to enhance bone healing, reduce pain, and improve the return to full function for the affected patient (Szypryt and Forward 2009). Bone healing is influenced by the fracture site stability (interfragmentary movement). Interfragmentary movement is determined by the mechanical strain (e.g., deformation) that occurs at the fracture site and controlled by the stability process. Two mechanisms of healing have been identified (Marsell and Einhorn 2011):

• Indirect (secondary) bone healing: occurs due to mechanical stimulation (relative stability) of interfragmentary movement (2 – 10% strain)

• Direct (primary) bone healing: occurs in the present of absolute stability (i.e., little or no movement of the fracture fragments - 0 – 2% strain)

The most common methods of bone fracture treatment are based on the use of bone fixation implants by the implementation of the device either internally or externally. The role of these fixators is to stabilise the fractured bone to initiate and assist the healing process. Internal fixation (Figure 2.16) is preferable for minimising the morbidity and inconvenience of management of an

---

external fixation device. Examples of internal fixation implants are intramedullary (IM) nails, plates, and screws. Internal fixations are classified according to design parameters (number, type and location of screws, geometry, etc.), injury location, material type, or type and site of fracture (Tucker et al. 2018).

![Figure 2.16 An x-ray image of an internal fixation implant fixed to a midshaft humerus fracture.](image)

The gold-standard materials for internal fixation implants are biocompatible metallic biomaterials, which are preferred because of their excellent mechanical properties, strength, and good ductility (Tilton et al. 2018). These metallic internal fixators are typically made of stainless steel (e.g. 316L), titanium (e.g. Ti-6Al-4V, CP-Ti), or cobalt chromium (e.g. CoCrMo) and its alloys. However, the current internal fixation is associated with main issues:

- The anatomical fitting of the implant to the complex shape of the bone (e.g., in the case of clavicle fractures, where an unfit implant could result a delay in healing or non-union).
• After the fracture has healed, the internal fixation implant no longer needs to remain in the body. Approximately 30% of metallic internal fixation implants are removed after the healing process through a second surgery (Hanson et al. 2008). However, such procedures present significant risks of bone refracture and nerve damage. Bone refracture is due to the significant mechanical difference between the bone and the fixation implant, which results in insufficient bone density in the area close to the implant (i.e. stress shielding).

• If decided for the implant to be left in-situ, a mismatch in the Young’s modulus between the implant and the bone can lead to a phenomenon known as stress shielding, which is also associated with implant failure and bone loss. For example, the Young’s modulus of Ti-6Al-4V is approximately 120 GPa, while the modulus of cortical bone is between 15 and 25 GPa (Rho et al. 1997, Elias et al. 2008, McNamara 2011).

• Alternatively, the implant can remain in the body after the healing process, but this option also presents problems such as corrosion, release of metal ions, and the risk of allergic and potentially carcinogenic reactions (Hofmann 1992, Inion 2015).

Currently, internal fixation implants are conventionally fabricated by subtractive manufacturing using computer numerical control (CNC) machines and casting (Cronskär 2014). However, these processes have some disadvantages such as material waste and a lack of custom fit for patients. The latter results in mismatched geometry, limitation of design, longer lead times, greater effort required from surgeons, and higher costs. Consequently, these processes can result in delayed or poor fracture healing, fracture healing with residual bone deformity, implant or screw yield, or fatigue failure and screw loosening (Tilton et al. 2018).

Additive manufacturing (AM) offers an efficient solution for the fabrication of medical fixations and implants (Xie et al., 2017). Additive manufacturing has several advantages (see Figure 2.17) including the fabrication of parts with complex geometries, the fact that no tools are needed during the fabrication process, and the reduction in production costs and time (Sing et al., 2016). Currently, surgeons perform bone graft surgeries and use scalpels or manually bend implants to obtain the desired shape, size, and fit. With the help of AM, a custom design can be fabricated for each patient. Additive manufacturing is also a suitable technique for lightweight implant production and individual patient customisation (Parthasarathy 2015). This process eliminates the
most common traditional internal fixation defects such as misalignment by adhering to complex structural bone and fixation pre-shaping requirements.

<table>
<thead>
<tr>
<th>Customisation</th>
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<tbody>
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<td>• Customised fixation/implants involve a shorter and less painful and stressful adaptation phase and improve healing.</td>
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<th>Complex Design</th>
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<td>• It is possible to freely design and produce complex designs.</td>
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<th>Functional Integration</th>
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<td>• The number of components and manufacturing steps is reduced. It is possible to feature both a porous structure and a rough surface, improving bone integration. No further post-process is required.</td>
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<th>Reduced Surgical Cost and Time</th>
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<td>• Customisation allows pre-operative planning, which in turn allows the surgeon to understand the complexity of the patient's condition, and follow-up treatment is reduced.</td>
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<th>Reduced Lead Time</th>
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<td>• The lead time is shortened and three-dimensionally printed medical devices can be applied to patients sooner.</td>
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**Figure 2.17** Additive manufacturing advantages in the medical field.

In this Section, the term ‘internal fixation’ is used to represent the bone fixation plate employed for reconstruction, fracture fixation, and fixation and fusion surgical operations. Bone characteristics and its healing process is detailed (Section 2.2.1) and the most relevant metallic biomaterials presented, and main advantages and disadvantages discussed (Section 2.2.2). Among these materials, titanium and titanium alloys (particularly Ti-6Al-4V) are the most relevant materials and the core materials of this Section. The powder bed fusion techniques, the most suitable additive manufacturing technologies to process these materials, are presented in Section 2.2.3 and a comparison between electron-beam melting (EBM) and selective laser sintering (SLM) is provided at the end of the Section. The effect of the two different melting techniques on the morphology, mechanical and biological properties of printed parts is also discussed. Finally,
Sections 2.2.4 and 2.2.5 provides examples of internal implants produced by EBM or SLM discussing their mechanical and biological performance, stress shielding, personalisation and the reduction of the total surgical procedure.

2.2.1 Bone characteristics

2.2.1.1 Bone as a material

Human bone is a complex rigid organ and its structure results from a combination of inorganic and organic components (Hamill and Knutzen 2006). It protects and supports skeleton and facilitates movement, haematopoiesis, and storage of fats and minerals (Hamill and Knutzen 2006, Clarke 2008, Tortora and Derrickson 2008, Florencio-Silva et al. 2015). Bone is a collagen-based tissue containing organic components such as cells (e.g., osteocytes, osteoblasts, and osteoclasts) and extracellular matrix proteins as well as inorganic components such as hydroxyapatite (HA) (Hamill and Knutzen 2006, Jameson 2014, Zimmermann and Ritchie 2015). The organic components are responsible for providing the corresponding tensile properties, whereas the inorganic components are responsible for compression strength and stiffness (Doblaré et al. 2004). Bones have complex internal and external structures (Maharaj et al. 2013). They consist of two types of tissues: cortical bone and cancellous bone. Cortical bone, or compact bone, is the hard-outer layer, while cancellous bone, also known as trabecular bone or spongy bone, is the soft inner layer of bone tissue situated inside the cortical bone (Khurana et al. 2009). Bone is a linear-elastic material, meaning that the relationship between stress and strain up to the yield point is linear (Jameson 2014). It is also considered to be a heterogeneous, anisotropic material (Natali and Meroi 1989).

Importantly, the mechanical properties of bone changes in relation to the bone structure. Cortical or compact bone is a very dense area around the bone marrow gap (porosity 5–10%) accounting for 80% of the total bone with a Young’s modulus range of 11.4–25 GPa, and compressive strength of 107–146 MPa (McNamara 2011, Jo et al. 2014). In comparison, trabecular bone or cancellous bone is a highly porous structure (porosity 50–95%) composed of a trabecular plate and rod-shaped honeycomb network scattered in the bone marrow and accounts for 20% of bone mass. Cancellous bone has a Young’s modulus of 0.2-12.7 GPa and a compressive strength of 5–10 MPa (Rho et al. 1997, Jo et al. 2014).

Bones differ in shape and can be classified into four main categories: long bones, short bones, flat bones, and irregular bones (Tortora and Derrickson 2008, Umadevi and Geethalakshmi 2011).
2.2.1.2 Bone types

Long bones are cylindrical in shape and formed by a combination of endochondral and membranous bone. Long bones include the femur, tibia, fibula, metatarsal, humerus, ulna, radius, metacarpals, and phalanges. They act as levers to enable body movement. Short bones such as the carpals in the hand and tarsals of the foot are cube-like shapes that provide stability and support and allow for some movement (Tortora and Derrickson 2008, Umadevi and Geethalakshmi 2011). These short bones also play a major role in force transmission and shock absorption. Flat bones such as ribs, scapulae (shoulder blades), the pelvis, and the cranium (skull) are thinner than long bones and curved in places. These bones act as protection for internal organs. Lastly, the fourth type of bone, the irregular bone, is represented by the vertebrae and facial bones, which have complex shapes. They support the spinal cord, resist mechanical compression, support weight, and contribute to movement (Hamill and Knutzen 2006, Tortora and Derrickson 2008, Umadevi and Geethalakshmi 2011).

2.2.1.3 Bone healing

2.2.1.3.1 Indirect bone healing

Indirect fracture healing is a natural form of fracture healing that consists of inflammation, repair (with soft and hard callus formation), and bone remodeling (Marsell and Einhorn 2011). It occurs as a result of interfragmentary movement (2–10% strain) stimulated by either non-surgical treatment (cast) or surgical procedures using fracture fixation implants such as intramedullary nailing, external fixation, or internal fixation.

The inflammatory response involving peripheral, intramedullary blood, and bone marrow cells is critical for fracture healing and tissue regeneration and is characterised by haematoma formation at the end of the fracture and in the medulla (Gerstenfeld et al. 2003). Mesenchymal stem cells (MSCs) and bone morphogenic proteins (BMPs) play a critical role in the regeneration and bone repair process (Tsuji et al. 2006, Granero-Moltó et al. 2009).

Bone healing begins with the formation of a soft callus by replacing the haematoma with fibrocartilage. This is achieved by new blood vessels occupying the haematoma region around the fracture site with the addition of fibroblasts originating from the periosteum. After the haematoma effect, granulation tissue is formed, allowing cells to differentiate into fibrous tissue (Rahn 2002). Two simultaneous ossification processes occur to ensure fracture stability and hard callus.
formation. Inside the granulation tissue, endochondral ossification occurs between the outer region of the periosteal site and the end of the fracture, ensuring the formation of cartilage callus (Marsell and Einhorn 2011). Furthermore, intramembranous ossification occurs at the distal and proximal ends of the fracture, generating a semi-rigid structure that carries hard osteophytes (woven bone) (Gerstenfeld et al. 2006).

The final stage of the fracture healing process corresponds to the bone remodeling of the hard osteophytes into a lamellar bone structure with a central medullary cavity (Gerstenfeld et al. 2003). During this process, the hard osteophytes are absorbed by osteoclasts while the osteoblasts form the lamellar bone on the external callus and the medullar cavity on the internal callus.

2.2.1.3.2 Direct bone healing

Direct healing is surgically initiated through open reduction and internal fixation (ORIF) procedures using orthopaedic implants and by establishing absolute stability (i.e., substantively low interfragmentary movement) (Marsell and Einhorn 2011). Direct healing is achieved through lamellar bone formation, blood vessels and the formation of Haversian canals. This is surgically accomplished through a contact healing or gap healing processes without the formation of callus.

Contact healing requires less than 2% interfragmentary strain, allowing the formation of bone healing and the restoration of the Haversian system. Gap healing occurs under the same conditions as contact healing but requires a gap distance of less than 0.8–1 mm (Kaderly 1991). This healing process requires a secondary osteonal reconstruction to create the correct remodeling procedure (similar to contact healing) to heal fractures (Schenk and Hunziker 1994). Secondary remodeling occurs when osteoblasts form lamellar bone on the interstitial surface through revascularised osteons carrying osteoprogenitor cells (Marsell and Einhorn 2011).

2.2.2 Metallic biomaterials

In general, biomedical materials should meet essential requirements including high strength, corrosion resistance and biocompatibility, low Young’s modulus and density, and good wear resistance. Metals are the most commonly used biomaterials and are currently the gold standard biomaterials for many commercial medical implants in different orthopaedic applications such as osteosynthesis, arthroplasty, and dentistry. The most commonly used metal biomaterials are titanium-based alloys, cobalt-based alloys, and stainless steel (Tucker et al. 2018). Among these materials, titanium-based materials present the most relevant properties for bone applications.
However, stainless steel remains the most commonly used due to its significantly lower cost. In order to guarantee the successful use of these materials as implant materials they must follow specific mechanical (e.g., wear and corrosion resistance) and biological (e.g., biocompatibility and biofunctionality) requirements, which strongly depend on the type of metallic alloy, the fabrication process, and the processing conditions. Additionally, the fabrication process and its conditions will determine the resulting behaviour of the material (i.e., microstructure), which will mostly only affect physical properties such as strength, elongation, hardness, wear resistance, and corrosion resistance. Young’s modulus, tensile strength, compressive strength, and elongation determine the mechanical properties of the material and its mechanical compatibility with human bones. Relevant mechanical properties of commonly used metallic biomaterials are presented in Table 2.1.

Table 2.1 Mechanical properties of metallic biomaterials and cortical bone (Jo et al. 2014; Chen and Thouas 2015; Tucker et al. 2018).

<table>
<thead>
<tr>
<th>Materials</th>
<th>Young’s modulus (GPa)</th>
<th>Ultimate tensile strength (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Titanium alloys</td>
<td>80–125</td>
<td>860</td>
</tr>
<tr>
<td>316L stainless steel</td>
<td>190–200</td>
<td>540–1,000</td>
</tr>
<tr>
<td>CoCrMo alloys</td>
<td>210–240</td>
<td>900–1,540</td>
</tr>
<tr>
<td>Cortical bone</td>
<td>11.4–25</td>
<td>107–146</td>
</tr>
</tbody>
</table>

2.2.2.1 Titanium and its alloys

Titanium and its alloys are popular for their superior biocompatibility and corrosion resistance compared to other metallic biomaterials. They are relatively lightweight with a density approximately 40% lower than iron’s and 50% lower than cobalt’s, and the Young’s modulus is about half of the modulus of other metal materials. Titanium alloys present two crystallographic allotropes: the low temperature (below β transus) hexagonal close-packed (HCP) α-phase and the high temperature (above β transus) body-centered cubic (BCC) β-phase as shown in Figure 2.18 (Kolli and Devaraj 2018). At room temperature titanium alloys can be classified as α phase, α-β phase and β phase. The α phase alloys mainly consist of HCP with possible margins of the other
Chapter two: State-of-the-art

This is typically the structure of commercially pure titanium (CP-Ti; >99% Ti), used for applications where low strength and adequate corrosion resistance are required. In this phase, alloys often contain aluminium (Al) and marginal quantities of other elements such as oxygen, nitrogen and carbon. Oxygen can increase the yield strength and tensile strength but decreases the ductility of the alloy. Alpha-beta alloys, such as Ti-6Al-4V, comprise both α and β phases. These alloys are used for applications requiring high strength, excellent corrosion resistance and adequate toughness and fatigue behaviour. Usually they consist of Al as an α phase stabiliser and a β phase stabiliser such as vanadium (V) or molybdenum (Mo). As shown in Figure 2.18, the phase transformation is dependent on the cooling process. Rapid cooling could lead to an α’ martensitic transformation while a slow cooling rate results in a α-β structure. Finally, β alloys can be divided into three different categories such as near-beta, metastable beta and stable beta alloys (see Kolli and Devaraj 2018 for a further review). This Section focus only on the α and α-β alloys. CP-Ti and Ti-6Al-4V alloys are the most attractive titanium alloys in the field of orthopaedics. However, due to their relatively poor tribological properties, they have proven to produce unfavourable tissue reactions, particularly in implants with high friction (Sumita et al. 2003). However, this may not be an issue because fretting is always intended to be limited to an internal fixation environment compared to the joint replacement applications. The α-β alloys exhibit poor bending ductility due to the availability of the α phase HCP structure (Hussam 2002). Titanium and its alloys (e.g., Ti-6Al-4V) are one of the gold standard metallic biomaterials used for multiple internal fixation systems. For instance, DePuy Synthes uses CP-Ti and Zimmer Biomet uses Ti-6Al-4V alloy.
2.2.2 Stainless steel

Stainless steel is an iron-based alloy that has a percentage of nickel and chromium ranging between 11 and 30 wt.%. Based on its microstructure, stainless steel can be divided into four main groups: martensitic, ferritic, deplex, and austenitic. Currently, only the latter is used for medical implants (Davis 2003). The most commonly used stainless steel alloy is the 316L, due to its acceptable biocompatibility, ease of fabrication, and relatively low cost (Chen and Thouas 2015). 316L stainless steel is rarely used for long-term load-bearing applications due to its high mechanical properties, relatively poor wear and corrosion resistance, and low fatigue properties. In some patients these limitations have been shown to cause stress shielding, allergic reactions, and toxicity, besides exhibiting carcinogenic effects (Mudali et al. 2003, Tavares et al. 2010, Chen and Thouas 2015). Therefore, it has been replaced by metallic biomaterials with better biocompatibility, fatigue, wear, and corrosion properties such as cobalt alloys and titanium alloys. Stainless steel is much cheaper than other alloys and is still employed for internal fixation implants in fixation systems such as DePuy Synthes’ locking compression plates.

2.2.2.3 Cobalt chromium

Cobalt-based alloys were first introduced to the medical field in the 1930s and have been used as orthopaedic implant biomaterials since the 1940s. Currently, there are eight ASTM standards for different compositions of CoCr alloys for either long-term or short-term implants (Davis 2003).
Only two cobalt-based compositions (i.e., Co-20Cr-15W-10Ni and Co-Ni-Cr-Mo-W-Fe) are used for short-term implantation such as internal fixations due to corrosion resistance and possible nickel toxicity if left for a long-term. Cobalt-based alloys are characterised by better corrosion resistance and mechanical properties than stainless steel. However, they are not used for internal fixation applications (except for internal fixation screws) due to their high cost, stress shielding, and metal toxicity. Their high stiffness (i.e., 220–230 GPa) will result in an uneven stress distribution. Additionally, the presence of Ni, Cr, and Co was found to be toxic and may cause systemic allergic reactions (Chen and Thouas 2015). Cobalt alloys are popular for long-term orthopaedic applications.

2.2.3 Powder bed fusion techniques

Powder bed fusion is an additive manufacturing process in which thermal energy is used to selectively fuse regions of a powder material (Emelogu et al. 2016, Murr 2016, Brunello et al. 2016). It comprises two main techniques: electron beam melting using an electron beam to selectively melt the powder, and selective laser sintering using a laser beam (Murr et al. 2012a, Murr et al. 2012b, Suska et al. 2016). Both techniques comprise the following steps:

- Powder is dispensed;
- Parts are selectively melted via laser or an electron beam;
- Build station is lowered and new powder is dispensed.

2.2.3.1 Electron beam melting

The EBM process uses a high energy electron beam to melt layers of metallic powder to a desired geometry (Milberg and Sigl 2008). It operates under vacuum and high processing temperatures allowing the fabrication of parts with low residual stresses, near-full density and without internal defects (Gao et al. 2015, Galarraga et al. 2016, Riedlbauer et al. 2017). The main components of a typical EBM machine are the electron beam unit and the build chamber as shown in Figure 2.19 (Galati and Iuliano 2018). The electron beam unit consists of an upper column that contains an electron generating part and a lower column that contains a magnetic lens used to form and deflect the electron beam (Galati and Iuliano 2018). The heated filament, or the cathode, emits electrons in the upper column (Galati and Iuliano 2018). The electric potential between the cathode and anode is approximately 60kV (Murr et al. 2012b, Galati and Iuliano 2018). The shape and
deflection of the electron beam are controlled by magnetic lenses (Mallik et al. 2014, Galati and Iuliano 2018). The entire process takes place in vacuum (Galati and Iuliano 2018). The build chamber comprises a steel build tank, powder feeder, and a raking system (Mahale 2009, Galati and Iuliano 2018). The steel build tank contains the process platform that constitutes the XY build plane and can be moved along the Z-axis (Galati and Iuliano 2018). A preheated base plate is used as a build platform. The powder storing system consists of two hoppers in the upper left and right sides of the build chamber (Galati and Iuliano 2018). The powder is distributed over the XY build plane by the rake, which collects powder from both sides and moves over the surface build platform (Galati and Iuliano 2018). The layer thickness ranges between 0.05 mm and 0.20 mm depending on the powder material (Galati and Iuliano 2018).

![Figure 2.19 Schematic setup of an EBM system.](image)

EBM can be used to process different metallic materials such as titanium and titanium alloys, stainless steel, tool steel, Ni-based super alloys, Co-based super alloys, low-expansion alloys, hard metals, intermetallic compounds, aluminium, copper, beryllium, and niobium (Biamino et al. 2011, Galati and Iuliano 2018).
2.2.3.1.1 Microstructure

Murr et al. (2009a) investigated the Ti-6Al-4V microstructure of EBM parts. Results show a homogenous and primarily acicular α-phase with Widmanstätten patterns (Figure 2.20a). Authors also show a slight difference regarding the variance of α-plate microstructures between the top (~1 cm) and the bottom (~1 cm). The top average α-plate thickness was 2.1 μm (Figure 2.20a), and the bottom was 1.4 μm (Figure 2.20b). Figure 2.20b exhibits a finer α-microstructure and, when closer to the bottom of the structure, it is more lamellar-like than acicular. In addition, the optical micrographs of EBM-produced Ti-6Al-4V show that the microstructure is mainly composed of α phase and a small amount of β within the prior β columnar grains oriented along the build direction (Rafi et al. 2013). The α phase possesses a lamellar morphology with β surrounding the α lamellae boundary. The scanning electron microscopy (SEM) image presented in Figure 2.21 shows that α lamellae are arranged in a Widmanstätten/basket-weave structure with different sizes and orientations and forms alpha platelet colonies within the columnar grains.

![Figure 2.20](image_url)  

**Figure 2.20** Optical metallographic images comparing acicular α-plates in the top section (~1 cm) of EBM fabricated samples (a) and the bottom section (~1 cm) (b) (Murr et al. 2009a).
2.2.3.1.2 Mechanical and physical properties

Galarraga et al. (2016) have examined the mechanical properties of Ti-6Al-4V alloy fabricated by EBM. Figure 2.22 shows the microhardness graphs for various built conditions. A similar average value of 368 HV was observed for both vertical and horizontal directions. Table 2.2 shows the tensile strength and relative standard deviations for vertically oriented specimens fabricated in three different locations (diagonally) of the build platform. As observed, tensile properties (ultimate tensile strength, yield stress and elongation) are greater in locations where porosity is lower.

**Figure 2.21** Scanning electron microscopy showing Widmanstatten structure in Ti-6Al-4V EBM produced part (Rafi et al. 2013).

**Figure 2.22** Microhardness values for (a) vertical and (b) horizontal directions (Galarraga et al. 2016).
Table 2.2 Mechanical properties and relative standard deviations for vertically oriented specimens at different locations (Galarraga et al. 2016).

<table>
<thead>
<tr>
<th></th>
<th>Rear Corner</th>
<th>Centre</th>
<th>Front Corner</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultimate tensile strength (MPa)</td>
<td>1065±2.2</td>
<td>1050±1.0</td>
<td>1102±1.0</td>
</tr>
<tr>
<td>Yield strength (MPa)</td>
<td>993±2.3</td>
<td>983±1.0</td>
<td>1026±1.5</td>
</tr>
<tr>
<td>Elongation (%)</td>
<td>10.7±26.7</td>
<td>10.4±10.3</td>
<td>11.3±19.8</td>
</tr>
</tbody>
</table>

2.2.3.1.3 Biological properties

Li et al. (2012) seeded osteoblast cells on Ti-6Al-4V EBM constructs. After 14 days of cell culture, it was found that the cells adhered, diffused, and proliferated into a multi-layered structure. The osteoblasts achieved confluence and completely covered the surface with a large amount of extracellular matrix formation (see Figure 2.23). In vivo studies were also performed in rabbit’s critical size calvaria defects. Histological analysis shows a rapid ingrowth of bone tissue from the calvarial margins towards the centre of the bone defect in 12 weeks (Li et al. 2012).

Figure 2.23 Scanning electron microscopy morphologies of cells on titanium after 14 days of culture (Li et al. 2012).

Palmquist et al. (2013) presented a long-term in vivo study using EBM porous and non-porous Ti-6Al-4V implants implanted in the femur and dorsum of a sheep. After 26 weeks of implantation, the surrounding tissue were successfully retrieved with no signs of intolerance from either implant.
type. Authors claims that both porous and non-porous exhibited excellent long-term soft tissue biocompatibility with high degree of osseointegration.

2.2.3.2 Selective laser melting

A selective laser melting (SLM) system (Figure 2.24) includes a control system, a processing laser, an automatic powder feeder container, inert gas system protection, roller/scrapper, and overflow container. The fabrication process occurs under a controlled environment (e.g., argon) to minimise unwanted chemical reactions especially from oxygen. Prior the printing process, the working environment is heated to minimise shrinkage (Kruth 2005, Zhang and Attar 2016).

![Selective laser melting system](image)

**Figure 2.24** Selective laser melting system.

2.2.3.2.1 Microstructure

Selective laser melting studies involving (α–β) Ti materials mainly focused on Ti–6Al–4V. Figure 2.25 shows the microstructure of a Ti–6Al–4V component produced by SLM process. The typical SEM microstructure exhibits a similar fine acicular α’ martensite as in the pure titanium CP-Ti samples due to the high temperature gradient (rapid cooling) occurring in the SLM process (Thijs et al. 2010, Gorsse et al. 2017).
2.2.3.2.2 Mechanical and physical properties

Different authors investigated the mechanical properties of Ti-6Al-4V biomedical parts fabricated by SLM (Vandenbroucke and Kruth 2007, Murr et al. 2009b). Regarding the strength and hardness, results show that the tensile strength and microhardness of SLM parts are higher than those produced by EBM. This can be explained by the different microstructures presented by SLM and EBM parts (Sing et al. 2016). Table 2.3 shows the ultimate tensile strength (UTS), yield strength (YS), elongation and microhardness of Ti-6Al-4V SLM parts.

Table 2.3 UTS, YS, elongation, and microhardness (Yap et al. 2015).

<table>
<thead>
<tr>
<th>Material</th>
<th>UTS (MPa)</th>
<th>YS (MPa)</th>
<th>Elongation (%)</th>
<th>Microhardness (HV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP-Ti</td>
<td>654</td>
<td>522</td>
<td>17.0</td>
<td>308</td>
</tr>
<tr>
<td>Ti-6Al-4V</td>
<td>1,250</td>
<td>1,125</td>
<td>6.00</td>
<td>613</td>
</tr>
</tbody>
</table>

2.2.3.2.3 Biological properties

Wang et al. (2016d) compared the biocompatibility characteristics of Ti-6Al-4V EBM and SLM parts, including cytocompatibility, haemocompatibility, skin irritation, and skin sensitivity. Both EBM and SLM parts exhibited good cytobiocompatibility, and the haemolytic ratios of SLM and EBM were 2.24% and 2.46%, respectively, demonstrating good haemocompatibility (Wang et al. 2016d).
Animal tests (rabbits and guinea pigs) show no dermal irritation or any allergic skin reaction (Wang et al. 2016d).

Kawase et al. (2014) conducted cell proliferation studies on the surface of Ti-6Al-4V parts fabricated by SLM. Two types of cells – fibroblast-like cells (L929 cells) and osteoblast-like cells (MC3T3-E1 cells) – were used. In both cases the SLM part was able to support cell attachment and proliferation.

2.2.4 Additive manufactured internal bone fixation implants

Liu et al. (2014) used EBM to produce a commercial locking compression plate (DePuy Synthes’ clavicle plate). The commercial plate was initially scanned, and the digital model tessellated and sliced and printed using Ti-6Al-4V and the EBM A1 system (Arcam, Sweden). The mechanical properties of both commercial and EBM clavicle plate (based on the F382 ASTM standard), as well as surface roughness and macrohardness, were evaluated. As observed, the EBM plates presented significantly higher bending stiffness and hardness than the commercial LCPs. Smith et al. (2016) used SLM to develop an FDA (Food and Drug Administration) approved internal fixation (FastForward™ Bone Tether Plate, MedShape, Inc.). The device was designed to reduce the first/second intercondylar angle in a bunion correction procedure with successfully corrected hallux valgus deformity during short-term and mid-term follow-up. Authors also demonstrated that the combination of SLM and surface post-treatment improves fatigue strength and allows the fabrication of devices with properties comparable to traditionally manufactured bone fixations. Results also suggest that the FastForward™ preserves structural integrity by reducing the short- and long-term stress concentrations of the second metatarsal supported by bone tissue ingrowth.

Al-Tamimi et al. (2019b) combined topology optimisation and EBM to design and fabricate internal fixations with reduced stress shielding. Ti-6Al-4V fixations were mechanically assessed using quasi-static tensile tests and biologically tested with osteosarcoma bone cells. EBM fixations topology optimised considering 75% of volume reduction present Young’s modulus similar to cortical bone. Moreover, EBM fixations presented significantly higher cell-affinity than commercial fixations being able to support cell attachment and proliferation. Xie et al. (2017) used a laser sintering M290 machine (EOSINT, Germany) to produce Ti-6Al-4V reconstruction fixations for large skull defects and compared them to machined fixations in terms of hardness and mechanical properties. Authors found that SLM fixations presented significantly higher hardness,
static torsion, and bending than machined fixations. Koptyug et al. (2013) investigated the use of EBM to produce a surgically planned bone fixation plate to treat comminuted fractures of the distal radius. In addition, the same technique was used to produce fixation plates for mandible reconstruction. Lima et al. (2017) used EBM (LENS, USA) to produce functionally graded Ti alloy fixation plates designed to reduce the risk of stress shielding. Authors successfully produced a graded block component containing a low modulus Ti-35Nb-15Zr (wt%) and a high modulus CP-Ti near the centre.

Mazzoni et al. (2015) used an EOSINT M270 system (EOS, Germany) to produce a fixation plate for the maxilla in the setting of reconstructive surgery. The accuracy of the SLM replication and its assistance in the surgical plan were evaluated. They demonstrated that in 10 patients the implant accuracy was 92.7%. These results indicated that surgical splints for repositioning of the maxilla were no longer needed. Cronskär et al. (2015) used EBM to fabricate patient-specific titanium fixation plates for clavicular reconstruction. The authors investigated the EBM internal fixation fit on the complex structure of the clavicle and compared the results with commercial fixations. EBM fixations were post-treated to have a smoother surface. Results show that EBM reconstruction fixations have a better fit, and contrary to commercial fixations they did not require additional pre-shaping. Wang et al. (2017) used a DiMetal-100 (SCUT, China) SLM system to produce a patient-specific bone fixation plate for a complex pelvic fracture as shown in Figure 2.26. Post-processing included heat treatment and surface treatment to eliminate residual stresses and produce a smoother disinfecting surface. Surgical rehearsal and clinical evaluation indicated that the fixation plate fit the fractured pelvis and the operation time was shortened by two hours. Similarly, Harrysson and Cormier (2006) used EBM to produce custom-designed bone plates, eliminating the shape mismatch between fixations and damaged bones; and Yang et al. (2018) used SLM to successfully produce patient-specific CP-Ti bone fixations for head and neck reconstruction.
Figure 2.26 An SLM produced bone fixation for a complex pelvic fracture (a), (b) after post-processing and surface treatments, and (c) the bone fixation implementation on the CT scanned pelvic model (Wang et al. 2017).

2.2.5 Conclusions and research challenges

Different metallic biocompatible materials have been explored for medical applications and the most commonly used were detailed in this review. Among these materials, titanium and titanium alloys (particularly Ti-6Al-4V) are the most relevant for the fabrication of internal fixation systems. However, Ti-6Al-4V fixations present stress shielding problems and if left inside the body after the healing process present also other problems such as corrosion, release of metal ions, and the risk of allergic and potentially carcinogenic reactions (Hofmann 1992, Inion 2015). If the
implant is removed after healing process a second surgery is required increasing the healthcare costs.

Commercial fixations are available in standard shapes and sizes. In a significant number of cases their use requires a significant amount of time to pre-shaping them according to the patient-specific defect. The use of additive manufacturing can solve this problem through the fabrication of fully customised fixations. In this case medical imaging is used to obtain an image of the defect area allowing to design a personalised device. Additive manufacturing comprises a group of different techniques that produces objects adding material layer-by-layer contrary to the material removal approach that characterises most conventional processes. Powder bed fusion is the ideal technique to produce Ti-6Al-4V fixations. Two methods, EBM and SLM, were presented allowing the fabrication of fixations with different microstructures and consequently different mechanical properties:

- Due to the slow cooling process of EBM, the Ti-6Al-4V microstructure results in an α and β phases and Widmanstatten/basket-weave structure. Contrary, SLM presenting fast cooling induces the formation of α’ martensitic needles.
- The developed microstructure of EBM and SLM parts, explains the superior mechanical properties and high hardness of SLM parts.

Powder bed fusion was successfully used to produce personalised fixations for different applications allowing to reduce the surgical time in around two hours accelerating the recovery time of the patient (Cronskär et al. 2015, Wang et al. 2017). This has a significant impact not only in terms of the quality of the clinical procedure but also in terms of cost savings.

An important research question related to the use of powder bed fusion for the fabrication of fixations is: would it be possible to commercialise fixation devices using powder bed fusion without the need for costly post-processing procedures? Results presented in this review seems to suggest that it is possible. Despite the surface roughness that characterises both EBM and SLM processes printed fixations present better biological properties than commercial polished fixations, being able to support cell attachment and proliferation. However, long-term studies are still required.
The combination of topology optimisation and additive manufacturing also allows to create lightweight fixations, using less material (cost reduction) and presenting reduced stiffness (minimising stress shielding and bone loss). It is also possible to create gradient fixations with mechanical properties varying according specific directions. This opens new routes to design advanced and more effective fixations. However, there is still a need to use other material than Ti-6Al-4V. A wide range of polymeric, ceramic, and polymer/ceramic materials has been investigated for bone tissue engineering, but they do not present adequate mechanical properties for load bearing applications (Prakasam et al. 2017). More recently, the use of degradable metallic materials such as magnesium has gained significant attention, but they are highly reactive, difficult to process, and have a very fast degradation process (Zhao et al. 2017).

Fixation plate design for additive manufacturing represents an emerging research area as there is no standard procedure for fixation design. The only so-called standard currently available is related to the fixation technique (conventional or locking head screwing). Other design specifications such as fixation dimensions (length, width, and thickness) and dimensional correlations or screw hole designs (combi-hole or single-hole) require further investigation in terms of the overall performance of the fixations.
Chapter Three

Metallic bone fixation implants: a novel design approach for reducing the stress shielding phenomenon
Chapter Three  

Metallic bone fixation implants: a novel design approach for reducing the stress shielding phenomenon*

Fixation devices are commonly used for bone fracture treatments. These implants are made of biocompatible materials such as stainless steel, cobalt, titanium and its alloys (e.g. CoCrMo and Ti6Al4V). However, metallic medical implants present higher stiffness compared to bone, contributing to the stress shielding phenomena compromising bone integrity. This Chapter explores the use of 2D topology optimisation to create novel bone fixation designs with reduced material volumes. Results show that for certain levels of volume reductions, which depends on the load condition, it is possible to obtain designs that minimise the stress shielding phenomena.

3.1 Introduction

Bone is a vascular and highly specialised form of connective tissue which is able to heal and remodel without leaving any scars in cases of very limited damage or fracture. However, in pathological fractures, traumatic bone loss or primary tumour resection, where the bone defect exceeds a critical size (around 5 mm), bone is no longer able to heal itself (Lichte et al. 2011, Lee et al. 2014).

In highly traumatised bones, metallic orthopaedic repair implants such as plates, screws, wires, and intramedullary pins are commonly used to support and stabilise the healing of the broken bone (Alsop 2013, Jardini et al. 2014). After a fracture has healed bone fixation implants are no longer needed. In a number of patients, the implant can be left in situ with no adverse consequences. However, the persistence of implants beyond the heal time can cause adverse reactions such as stress shielding effects, and release of metallic ions, which can be toxic or even carcinogenic (Hofmann 1992, Matusiewicz 2014). Although, implant design and quality have been improved, there is substantial evidence of implant failure due to the large stiffness mismatch (stress shielding) between plates and bone (Chanlalit et al. 2012, Sumner 2015, Goshulak et al. 2016). Metallic implants have much higher elastic moduli than bone, e.g. Ti-6Al 4V has a modulus of around 110 GPa and CoCrMo has a modulus of around 210 GPa (Andani et al. 2014, Shibata et al. 2015).

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However, cortical bone has elastic moduli ranging from 3 to 30 GPa, while trabecular bone has lower elastic moduli ranging from 0.02 to 2 GPa (Shibata et al. 2015).

The stress shielding phenomena are particularly critical in osteoporotic bones. Osteoporosis (OP) (Strømsøe 2004, Reginster and Burlet 2006) is a disorder of unbalanced bone remodeling, which occurs when bone resorption exceeds bone formation resulting in low density bones with poor mechanical properties. Patients with osteoporosis are at a greater risk of bone fracture after minimal trauma leading to high healthcare expenses and decreased quality of life. Additionally, advanced stages of OP may also lead to bone mass decrease and a consequent risk of fragility fractures (Kylloenen et al. 2015). In such cases, surgical treatment is generally under-taken with metallic plates that act as fracture stabilisers to enable bone healing.

Removal of implants after a period of time is a common surgical procedure and accounts for up to 30% of planned orthopaedic operations (Chanlalit et al. 2012). However, complications are not infrequent with infection, nerve damage, risk of refracture and increased pain at the site of surgery being common.

In order to overcome the above-mentioned drawbacks, it is expected that new therapeutic strategies can be developed and clinically implemented. This is the aim of a project entitled ‘Osteofix-novel biodegradable composite implants for osteoporotic bone fractures’ partially funded by the government of Saudi Arabia and the UK Royal College of Surgeons. As part of this project, this Chapter investigates the use of topology optimisation to reduce the stress shielding phenomena by reducing the equivalent stiffness of the metallic implants. Optimised designs are suitable to be produced using additive manufacturing (AM), which is the ideal technology to fabricate lightweight implants, with adjusted stiffness, customised to the patient, minimising the use of material particularly critical in the case of titanium. The potential of additive manufacturing for medical applications has been extensively explored. Vat-photopolymerisation, extrusion-based and binder jetting systems have been used to create highly porous polymeric, ceramic and composite scaffolds for regenerative medicine (Bartolo et al. 2012, Melchels et al. 2012, Santos et al. 2013, Wang et al. 2016a, Wang et al. 2016b). Several authors also used powder bed fusion systems to create porous metallic for bone and spinal fusion applications. Other authors used AM to fabricate metallic implants (Serra et al. 2016, Sing et al. 2016, Wang et al. 2016c). The benefits of combining topology optimisation with additive manufacturing are significant as additive manufacturing provides high design flexibility for fabrication with improved part performance.
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being ideal for lightweight part production of custom-fit medical design (Abouel Nasr et al. 2015, Popovich et al. 2016).

This Chapter focuses on the use of topology optimisation, to redesign an existing bone fixation plate minimising the stress shielding phenomena. A commercially available bone fixation implant is considered as a case study. Due to the small thickness of the plate, two-dimensional (2D) topology optimisation is considered and different design solutions assessed considering different loads and material volume reduction conditions.

3.2 Topology Optimisation

Structural optimisation is a decision-making computational tool for structural design, which defines the material distribution of a structure according to specific constraints and objective functions. Depending on the design variables, structural optimisation is classified into: sizing, shape and topology optimisation. Sizing optimisation is the simplest method, commonly used to optimise truss-like structures. In this case, the structure layout is prescribed and the only parameter that can be modified is the size of the component. In shape optimisation, the topology of the component is not modified. The modified design variables are for example the thickness of the walls or the radius of holes. Topology optimisation (TO) (Hassani and Hinton 1998a, Rozvany 2009, Sigmund and Maute 2013, Deaton and Grandhi 2014), which is the most common structural optimisation technique, seeks to find the optimal load path for a specific load and boundary condition, fulfilling imposed requirements for the stiffness, weight or volume reduction.

In order to find the optimal distribution of material and voids for a structure, the finite-element (FE) method is used to discretise the structure’s initial design domain as a set of material discrete divisions corresponding to the design variables (Figure 3.1). After meshing, TO is used to identify the element property through a ‘material exist or not’ strategy. This leads to a binary 0 (void) or 1 (full material) problem for each element.

The most widely used algorithms are based on the search for the minimum compliance design (maximising the stiffness) with constraining volume and assumes a continuous optimisation approach, introducing a continuous function density as a design variable. Usually, the optimisation is performed using the solid isotropic microstructure with the penalisation (SIMP) approach, proposed by Bendsøe (1989) and further improved by Zhou et al. (2001) and Bendsøe and Sigmund (2004).
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Figure 3.1 A two-dimensional (a) initial design domain and (b) discretised design domain for a topology optimisation problem.

3.2.1 Problem Formulation

In this work the SIMP approach is used to solve the topology optimisation problem. This is the most common strategy for topology optimisation, used by several authors to solve structural problems (Long et al. 2016). In the medical field, the SIMP method was also used by Wang et al. (2016c) for tissue engineering scaffolds and by Sutradhar et al. (2016), to design a craniofacial implant. The SIMP follows a continuous convergence algorithm for the material element density between 0 (no material) and 1 (full of material). This gradient-based approach distributes the relative density as a constant for each element \( \rho(x, y, z) \) of the FE mesh and it is associated with the distribution of the Young’s modulus, \( E \), according to the following power law:

\[
E(x, y, z) = [\rho(x, y, z)]^p \cdot E^o
\]  

(3.1)

where \( p \) is the penalisation factor and \( E^o \) is the solid material Young’s Modulus of \( \rho = 1 \).

The mathematical formulation presented in this section is based on the work of Sigmund (2001), Bendsøe and Sigmund (2004) and Nana et al. (2016).

The topology optimisation problem is to minimise the objective function (C) which here corresponds to the strain energy for a given load (the work of the external loads), with a constraint on the volume fraction (f). This problem can be stated according to Equation (3.2) where volume (V) is a function of the density \( \rho(x, y, z) \) and (Vi) is the initial design domain volume,

\[
\min \: C: \quad U^T F = \sum_{e=1}^{N_1} [\rho_e(x, y, z)]^p [u_e]^T [k_e][u_e] \quad (3.2) \]

(3.2a)
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subject to \[
\begin{align*}
    f &= \frac{V}{V_i} \\
    F &= [K] \cdot [U] \\
    0 &< \rho_{\text{min}} \leq \rho_e \leq 1
\end{align*}
\] (3.2b) (3.2c) (3.2d)

The constraint (3.2c) corresponds to the equilibrium equation discretised by the FE method where F, U and K are the force vectors, the global displacement and the global stiffness, respectively. $k_e$, $u_e$, $\rho_e$ and $\rho_{\text{min}}$ are the element stiffness matrix, displacement vector, the relative density of the element e and the minimum relative densities (non-zero for FE analysis stability), respectively.

In order to describe the implementation of the basic SIMP approach, let us consider that the initial design domain density distribution is developed towards the optimal design through iterative steps. For each numerical iteration, the first step corresponds to the evaluation of the sensitivity in each element according to the derivative of Equation (3.2a) with respect to the design variable (relative density):

\[
\frac{\partial c}{\partial \rho_e} = -\frac{p}{\rho_e} [u_e]^T [k_e] [u_e]
\] (3.3)

Filtering formulas are imposed to update the sensitivity calculations and average each element’s sensitivity within a filtering radius in order to obtain a checkerboard-free solution. In the SIMP approach, the sensitivity and density values are determined using mathematical optimisation methods such as the optimality criteria (OC), sequential linear programming (SLP) and method of moving asymptotes (MMA) (Svanberg 1987, Bendsøe 1995, Hassani and Hinton 1998b).

3.3 **Computer implementation**

3.3.1 **Finite Element Analysis**

The locking compression plate narrow model #423.591 (Synthes, US) (Figure 3.2) is considered as a case study. This plate is commonly used for the fixation of long bones such as the humerus, femur and tibia. For simulation purposes, plates with 180 mm length, 30 mm width and thickness of 3 mm with different numbers of holes (four, six and eight) were considered (Table 3.1).
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Figure 3.2 Synths #423.591 Locking Compression Plate for bone fractures. Dimensions in mm.

Table 3.1 Design domain of bone fixation plates.

<table>
<thead>
<tr>
<th>Name</th>
<th>Number of Holes</th>
<th>Design Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plate 1</td>
<td>Four</td>
<td></td>
</tr>
<tr>
<td>Plate 2</td>
<td>Six</td>
<td></td>
</tr>
<tr>
<td>Plate 3</td>
<td>Eight</td>
<td></td>
</tr>
</tbody>
</table>

The initial design of each plate was discretised using 2D plane elasticity elements with three-node triangular elements using a regular mesh size (a total of 7430 elements for Plate 1, 7070 elements for Plate 2 and 6948 elements for Plate 3). Three different loading conditions were considered: ‘End Load’ (Figure 3.3(a)), ‘Screw Load’ (Figure 3.3(b)) and ‘Combined Loads’ (Figure 3.3(c)). The End Load is a static tension force with a magnitude of 70 N applied on both far-end sides of the plate. The Screw Load is a multi-directional force with a magnitude of 70 N applied on the screw holes simulating the forces of the screws. The Combined Loads are the combination of both End Load and Screw Load. In all cases, the structure is constrained in the centre of the plate. Although, the SIMP technique is not sensitive to the magnitude of the load, the magnitudes of the loads considered in this research are based on that of a 70 kg patient walking with crutches (Wehner et al. 2009, Kim et al. 2011). The plates were considered to be made from biocompatible Ti-6Al-4V with a Young’s modulus of 120 GPa and Poisson’s ratio of 0.3.
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Figure 3.3 Boundary and loading conditions (a) End Load model, (b) Screw Load model and (c) Combined Load model.

3.3.2 Topology Optimisation
The SIMP topology optimisation was performed for solving a stiffness optimisation problem for the plate structure indicated in Table 3.1 subject to volume constraints ranging between 25% and 75% (Table 3.2). For simulation purposes, two geometrical constraints were imposed to the screw holes and force regions (Figure 3.4) to avoid any change of shape during the optimisation process. The goal is to use TO to produce a lightweight plate with reduced equivalent stiffness, minimising the stress shielding phenomena.

Table 3.2 Objective function and constraints.

<table>
<thead>
<tr>
<th>Design Response</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objective function</strong></td>
<td>Strain Energy</td>
</tr>
<tr>
<td><strong>Performance constraint</strong></td>
<td>Volume</td>
</tr>
<tr>
<td></td>
<td>25% - 75%</td>
</tr>
<tr>
<td><strong>Geometric Constraints</strong></td>
<td>Frozen Region is shown in Figure 3.4</td>
</tr>
<tr>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Force region</td>
</tr>
<tr>
<td></td>
<td>N/A</td>
</tr>
</tbody>
</table>
Figure 3.4 Design and frozen regions of an initial design domain. In this figure, the frozen region corresponding to the force region was not represented as this region varies according to the loading conditions.

The TO was performed using the Abaqus Topology Optimisation Module (ATOM) (Dassault Systems, Vélizy-Villacoublay, France). The default value of the initial density is 0.5, meaning that 50% of the design domain volume material is available for developing the final structure and the $\rho_{\text{min}}$ (no material) was assumed to be 0.001 due to the non-zero condition of $0 < \rho_{\text{min}} \leq \rho_e \leq 1$ to avoid singularities. The density-based methods of TO determine the design domain element density by either eliminating the material element density or keeping the material element density. Reducing the density of an element will reduce the stiffness of that particular element, and its contribution to the overall stiffness will decrease. Figure 3.5 illustrates the optimisation workflow considered in this research work.
Figure 3.5 Topology optimisation workflow.

3.3.3 Equivalent Stiffness and Work of the external loads
To assess the mechanical performance of the optimised designs both the equivalent stiffness and the work of the external loads were calculated. In both cases the plates were assumed to be homogeneous and isotropic. For the numerical computation of the equivalent stiffness, a uniform longitudinal displacement (displacement in the x direction) was considered (Almeida and Bartolo 2014). This is equivalent to the strain in the same direction ($\varepsilon_{xx}$) in Equation (3.4), imposed on Face A of the plate (Figure 3.6):

$$\varepsilon_{xx} = \frac{\Delta L}{L_i}$$  \hspace{1cm} (3.4)

where $\Delta L$ is the displacement (final length – initial length) and $L_i$ is the initial length of the plate.
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The opposite face, Face B (Figure 3.6) of the plate is constrained and unable to have any displacement. The average reaction force produced on Face A is used to determine the equivalent stiffness (E), due to the imposed displacement:

\[ \sigma_{xx} = \frac{F_{xx}}{A} \]  
\[ E = \frac{\sigma_{xx}}{\varepsilon_{xx}} \]  

where \( F_{xx} \) is the average reaction force and \( A \) is the cross sectional area of the plate.

Similarly, the work of the external loads was calculated considering the average displacement occurred on Face A according to the following equation:

\[ W_{xx} = \sum_{i=1}^{n} F_{xxi} \cdot U_{xxi} \]  

where \( F_{xx} \) is the longitudinal force at node \( i \) and \( U_{XX} \) the longitudinal displacement of node \( i \).

**Figure 3.6** Loads and Constraints for the numerical calculation of the equivalent stiffness and the work of the external load. a) initial design domain and b) optimised design domain.

### 3.4 Results and Discussion

Figure 3.7 illustrates, for the case of Plate 1 under Combined Loads and a volume reduction of 75%, the TO procedure. Firstly, the initial model is defined and an FE mesh created (Figure 3.7a). Then, for specific load and boundary conditions the FE determines the stress distribution (Figure 3.7b). Finally, the TO follows the load path identifying the highly sensitive elements, corresponding to the high stress values, by applying the sensitivity filter formulas, keeping the density equal to 1 (solid) in high sensitivity elements (Figure 3.7c). The optimised design domains considering different volume reduction (75, 65, 45, 35 and 25%) for Plate 3, Plate 2 and Plate 1 are presented in Figures 3.8 to 3.10, respectively. Maximum volume reductions of 75% were considered to guarantee a structural integrity of each plate under different loading conditions. Figure 3.11 illustrates the typical variation of strain energy during the minimisation process and
the volume changes till the constraint value, for Plate 3, considering a screw load and a volume reduction of 65%. Similar trends were observed for the other cases. The increase in the strain energy at the beginning of the optimisation process is caused by an abrupt reduction of volume. After the initial iterations as the volume tends to the constraint value, the strain energy converges to an almost constant value.

Figure 3.7 Optimisation process following the Von-Misses stress path, a) initial design domain; b) stress distribution; c) optimised design.
Figure 3.8 Design optimisation for Plate 3 under different loads and volume reductions.
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Figure 3.9 Design optimisation for Plate 2 under different loads and volume reductions.
Figure 3.10 Design optimisation for Plate 1 under different loads and volume reductions.
Figure 3.11 The historical evolution of the strain energy (red) and volume (blue) constraint along the optimisation process.

Tables 3.3 to 3.5 present the equivalent stiffness of the different optimised domains obtained for Plate 1, Plate 2, Plate 3 at different loading conditions. The works of the external loads calculated for each optimised design are presented in Tables 3.6 to 3.8. The results show that for the different loading conditions the equivalent stiffness decreases by increasing the volume reduction. It is also possible to observe that for the same load condition and volume reduction the equivalent stiffness is always lower in the cases of plates with high number of holes. However, the equivalent stiffness reduction trend depends on the load condition. According to the results, a fast decrease in the equivalent stiffness was observed for the Screw Load condition compared to the End Load case. Tables 3.3 to 3.5 also show the equivalent stiffness values of the original plates. As the TO procedure seeks to find the optimal load path for a particular load and boundary condition, searching for a minimum compliance design, it is not a surprise to observe that the equivalent stiffness of some optimised design is higher than the equivalent stiffness of the original design. This is the case of all optimised designs obtained for an End Load condition or the optimised design obtained for a Screw Load and Combined Loads condition and volume reductions lower than 75%. However, the equivalent stiffness of the optimised plates considering both Screw Loads
and Combined Loads conditions is lower than the original design. In these cases, reducing the density of an element, which reduces the stiffness of that particular element becomes the dominant effect, contributing to the decrease in the overall equivalent stiffness. These observations are also corroborated by the variation of the work of the external loads (Tables 3.6 to 3.8) that follow the same trend. The results show that through TO it is possible to obtain a design that can minimise the stress shielding phenomena.

**Table 3.3** Equivalent stiffness values for different optimised designs considering a Screw Load condition.

<table>
<thead>
<tr>
<th>Volume reduction (%)</th>
<th>Implants (MPa)</th>
<th>Plate 1</th>
<th>Plate 2</th>
<th>Plate 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>22155</td>
<td>17072</td>
<td>13724</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>20296</td>
<td>11693</td>
<td>13703</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>17065</td>
<td>11818</td>
<td>10915</td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>10835</td>
<td>7547</td>
<td>6459</td>
<td></td>
</tr>
<tr>
<td>75</td>
<td>7744</td>
<td>5621</td>
<td>5219</td>
<td></td>
</tr>
<tr>
<td><strong>Original design</strong></td>
<td><strong>8387</strong></td>
<td><strong>7529</strong></td>
<td><strong>6563</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Table 3.4** Equivalent stiffness values for different optimised designs considering a End Load condition.

<table>
<thead>
<tr>
<th>Volume reduction (%)</th>
<th>Implants (MPa)</th>
<th>Plate 1</th>
<th>Plate 2</th>
<th>Plate 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>23185</td>
<td>21576</td>
<td>18260</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>21089</td>
<td>19974</td>
<td>16481</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>19367</td>
<td>17623</td>
<td>15056</td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>13989</td>
<td>13212</td>
<td>11922</td>
<td></td>
</tr>
<tr>
<td>75</td>
<td>11052</td>
<td>9506</td>
<td>8474</td>
<td></td>
</tr>
<tr>
<td><strong>Original design</strong></td>
<td><strong>8387</strong></td>
<td><strong>7529</strong></td>
<td><strong>6563</strong></td>
<td></td>
</tr>
</tbody>
</table>
### Table 3.5 Equivalent stiffness values for different optimised designs considering a Combined Load condition.

<table>
<thead>
<tr>
<th>Volume reduction (%)</th>
<th>Plate 1 (MPa)</th>
<th>Plate 2 (MPa)</th>
<th>Plate 3 (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>21373</td>
<td>19698</td>
<td>16866</td>
</tr>
<tr>
<td>35</td>
<td>18781</td>
<td>17517</td>
<td>15252</td>
</tr>
<tr>
<td>45</td>
<td>16049</td>
<td>14645</td>
<td>13742</td>
</tr>
<tr>
<td>65</td>
<td>10844</td>
<td>9883</td>
<td>9067</td>
</tr>
<tr>
<td>75</td>
<td>7895</td>
<td>7002</td>
<td>6319</td>
</tr>
</tbody>
</table>

*Original design* 8387 7529 6563

### Table 3.6 The work of external loads for different optimised designs considering a Screw Load condition.

<table>
<thead>
<tr>
<th>Volume reduction (%)</th>
<th>Implants (mJ)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Plate 1</td>
</tr>
<tr>
<td>25</td>
<td>1.33</td>
</tr>
<tr>
<td>35</td>
<td>1.45</td>
</tr>
<tr>
<td>45</td>
<td>1.72</td>
</tr>
<tr>
<td>65</td>
<td>2.72</td>
</tr>
<tr>
<td>75</td>
<td>3.80</td>
</tr>
</tbody>
</table>

*Original design* 3.51 3.92 4.49
Chapter Three: Metallic bone fixation implants: a novel design approach for reducing the stress shielding phenomenon

Table 3.7 The work of external loads for different optimised designs considering a End Load condition.

<table>
<thead>
<tr>
<th>Volume reduction (%)</th>
<th>Implants (mJ)</th>
<th>Plate 1</th>
<th>Plate 2</th>
<th>Plate 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td></td>
<td>1.27</td>
<td>1.37</td>
<td>1.61</td>
</tr>
<tr>
<td>35</td>
<td></td>
<td>1.40</td>
<td>1.47</td>
<td>1.81</td>
</tr>
<tr>
<td>45</td>
<td></td>
<td>1.52</td>
<td>1.67</td>
<td>1.98</td>
</tr>
<tr>
<td>65</td>
<td></td>
<td>2.11</td>
<td>2.23</td>
<td>2.49</td>
</tr>
<tr>
<td>75</td>
<td></td>
<td>2.66</td>
<td>3.10</td>
<td>3.48</td>
</tr>
<tr>
<td><strong>Original design</strong></td>
<td></td>
<td>3.51</td>
<td>3.92</td>
<td>4.49</td>
</tr>
</tbody>
</table>

Table 3.8 The work of external loads for different optimised designs considering a Combined Load condition.

<table>
<thead>
<tr>
<th>Volume reduction (%)</th>
<th>Implants (mJ)</th>
<th>Plate 1</th>
<th>Plate 2</th>
<th>Plate 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td></td>
<td>0.93</td>
<td>1.00</td>
<td>1.75</td>
</tr>
<tr>
<td>35</td>
<td></td>
<td>1.05</td>
<td>1.68</td>
<td>1.93</td>
</tr>
<tr>
<td>45</td>
<td></td>
<td>1.23</td>
<td>2.02</td>
<td>2.14</td>
</tr>
<tr>
<td>65</td>
<td></td>
<td>2.73</td>
<td>2.99</td>
<td>3.26</td>
</tr>
<tr>
<td>75</td>
<td></td>
<td>3.74</td>
<td>4.22</td>
<td>4.67</td>
</tr>
<tr>
<td><strong>Original design</strong></td>
<td></td>
<td>3.51</td>
<td>3.92</td>
<td>4.49</td>
</tr>
</tbody>
</table>

3.5 Conclusion

Currently, the market manufacturers of bone fixation medical devices are recognising that the stress shielding phenomenon is a key problem to be solved. To address this problem researchers are focusing on selecting different materials rather than changing the design. As a consequence, there are no metallic bone fixation implants on the market that are able to avoid the stress shielding phenomena. This Chapter shows that through TO it is possible to obtain optimised designs with
Chapter Three: Metallic bone fixation implants: a novel design approach for reducing the stress shielding phenomenon

reduced equivalent stiffness compared to the original designs. Results also show that this reduction is highly sensitive to the load conditions and the initial design (number of holes). As noted, the combined use of TO and additive manufacturing technologies appears to be an effective and viable approach to produce metallic implants with reduced equivalent stiffness, thus minimizing material consumption during the fabrication process.
Chapter Four

Topology optimisation of bone plates to reduce stress shielding
Chapter Four  **Topology optimisation of bone plates to reduce stress shielding**

Fractured bones are treated with metallic bone fixation plates. However, despite being the gold standard clinical approach the use of metallic plates presents several problems including the stiffness mismatch between the bone and plates (stress shielding) resulting in bone resorption and plate failure. This Chapter investigates the use of topology optimisation as a design tool to create fixation plates with reduced stress shielding effects. A standard locking compression plate was used as a reference and the optimisation process conducted considering different plate configurations (four-, six- and eight-screw holes), different loading conditions (bending, compression, torsion and combined loads), and different volume reductions (25%, 45% and 75%). The optimised bone plates stiffness was assessed by finite element analysis and the results obtained for the optimised plates compared with the initial designs. Results show that by increasing volume reduction it is possible to reduce the overall plate stiffness creating also lightweight plates. It is also possible to observe that up to 75% of volume reduction the structural stability of the designed plates is maintained. Results also show that topology optimisation is a viable design tool to create metallic plates with optimised mechanical performance.

The topology optimised designs obtained in this Chapter were used for further analyses in **Chapters Five to Eight**: in **Chapter Five**, the bone mass change was studied considering the bone remodeling problem; in **Chapter Six**, the load transfer across a bone fracture is assessed by a stress analysis; in **Chapters Seven and Eight**, the mechanical, biological and tribological characteristics of the optimised designs produced using EBM and SLM powder bed fusion techniques are investigated. Additional results are presented in Appendix A.

---

4.1 Introduction

The current bone fixations (plates and screws), used to stabilise fractured bones, are made of metallic biocompatible materials such as 316L stainless steel, cobalt chrome alloys and titanium alloys (Ti-6Al-4V). However, these materials present significantly higher stiffness than natural bone, resulting in a stiffness mismatch called stress shielding that leads to bone resorption and delay in healing (Prasad et al. 2017). For example, titanium and its alloys present Elastic Modulus ranging between 80 and 120 GPa, stainless steel has an Elastic Modulus of around 190 GPa and the Elastic Modulus of CoCr is around 210 GPa, while the Elastic Modulus of cortical bone ranges between 15-25 GPa (Currey 2004, Elias et al. 2008, Hermawan et al. 2011, McNamara 2011).

Different approaches have been considered to address this problem by reducing the stiffness of the bone fixation implant. Some studies redesigned the plates creating a porous structure through a manual iterative procedure, costly and requiring high level of expertise (Fousová et al. 2017). Other researchers explored also the use of alternative materials (e.g. biocompatible and biodegradable composites) but failing in achieving appropriate mechanical performance (Prakasam et al. 2017, Zhao et al. 2017). This Chapter proposes an alternative route based on the use of topology optimisation, an automatic iterative design optimisation approach that considers an objective function (e.g. minimise compliance), constraints (e.g. reducing the overall volume) and loading conditions to create a lightweight structure with reduced equivalent stiffness.

4.2 Design and optimisation

4.2.1 Bone fixation plate designs

Three locking compression fixation plates were designed. These plates present 180 mm of length, 14 mm of width, 5 mm of thickness and different number of screw holes (four, six and eight) as shown in Figure 4.1. Fixation plates are assumed to be made of Ti-6Al-4V with 120 GPa of Elastic Modulus and 0.3 of Poisson’s ratio. Numerically, fixation plates were modelled using 8-node linear hexahedral elements. The finite element mesh is formed by around 50,000 elements.
Chapter Four: Topology optimisation of bone plates to reduce stress shielding

Figure 4.1 Initial fixation plate designs consisting of (a) four holes, (b) six holes and (c) eight holes.

4.2.2 Topology optimisation

Topology optimisation was performed using the Solid Isotropic Microstructure with Penalisation (SIMP) approach and performed using the software Abaqus (Dassault Systèmes, France). SIMP is a gradient-based approach that is used to penalise the design variable (i.e. density, $\rho_e$) for better convergence of the solution (Bendsøe 1989, Bendsøe and Sigmund 2004) and can be mathematically described as follows:

$$0 < \rho_0 \leq \rho_e \leq 1$$  \hspace{1cm} (4.1)

$$E(x,y,z) = [\rho(x,y,z)]^p \cdot E^i$$  \hspace{1cm} (4.2)

$$K(\rho) = \sum_{e=1}^{N} \rho_e^p \cdot K_e$$  \hspace{1cm} (4.3)

where $\rho_0$ is the non-zero minimum density, $p$ is the penalisation factor (recommended to have a value of 3 for a better convergence), $K_e$ is the elemental stiffness and $E^i$ is the initial Elastic modulus at $\rho=1$ of the material.

The SIMP is used to solve the minimum compliance ($Z$) considering a constraint the volume ($V$) according to the:

$$\min_{\rho_e} Z(\rho_e) = f^T \cdot u$$  \hspace{1cm} (4.4a)
Chapter Four: Topology optimisation of bone plates to reduce stress shielding

\[
\begin{align*}
\sum_{e=1}^{N} \rho_e v_e & \leq V, \quad (4.4b) \\
\sum_{e=1}^{N} \rho_e^p K_e u &= f, \quad (4.4c) \\
0 &< \rho_0 \leq \rho_e \leq 1, \quad (4.4d)
\end{align*}
\]

subject to

where \( f \) is the force vector and \( u \) is the displacement vector.

Topology optimisation initiates with identifying the user-defined geometry and material. The geometry is discretised into a set of finite elements with each element consisting of a density value contributing to the overall design density. Sensitivity of each element (strains) determines how the density of each element is updated towards optimality. Hence, with each density update, the optimisation scheme will decide either to keep the element (\( \rho = 1 \)) or to remove it (\( \rho = 0 \)), updating the overall stiffness. The sensitivity for each element in each iteration is evaluated considering the derivative of equation (4.4a) with respect to the density as follows:

\[
\frac{\partial z}{\partial \rho_e} = -\frac{p}{\rho_e^p} [u]^T [k_e] [u] \quad (4.5)
\]

Sensitivities of the elements go through filtering techniques to avoid checkerboarding.

In this Chapter, three volume reductions were imposed (25, 45 and 75%). A geometric constraint (frozen region) was considered for the screw holes to preserve their shape.

4.2.3 Loading conditions

Similar to the physiological conditions, four different loading conditions (compression, bending, torsion and/or a combination of all three cases) were considered. Compression load considers two forces applied on both end of the plate along the longitudinal axis of the plate (x-axis), constraining six nodes in the middle of the model. Bending load considers a four-point bending setting following the standards for mechanically testing a bone plate (BS 3531-23.1:1991 ISO 9585:1990), where two equally distributed loads are applied, vertically acting on the plate (z-axis) with two supports applied on the opposite face. Other supports were considered for other axis to avoid the plate from moving. Torsion considers a moment along the x-axis applied on one end of plate where the other end of the plate’s face was pinned. Combined corresponds to the combination of the compression, bending and torsion using the constraints defined for the compression case.

4.2.4 Equivalent stiffness

The stiffness of the bone plate is the main criteria to determine the stress shielding effect. The stiffness of both the initial and optimised bone plates were determined corresponding the loading
Chapter Four: Topology optimisation of bone plates to reduce stress shielding

conditions used for topology optimisation. All models were considered isotropic and homogeneous.

For the compression case, and similarly for the combined one, the equivalent stiffness is measured considering a uniaxial force \( F_{xx} \) applied to one end of the plate along the longitudinal axis while supporting the opposite end:

\[
K_{Ten} = \frac{F_{xx}}{D_{xx}}
\] (4.6)

where \( K_{Ten} \) is the equivalent stiffness and \( D_{xx} \) is the resulted displacement.

For the bending optimised plates, the equivalent stiffness was evaluated based on the BS standard which defines the bending equivalent stiffness \( E_B \) as follows:

\[
E_B = \frac{(4h^2 + 12h\xi + \xi^2)Sh}{24}
\] (4.7)

where \( h \) is the distance between the load and support points, \( \xi \) is the distance between the load points and \( S \) is the slope of the load-deflection curve.

In the case of torsion optimised plates, the equivalent stiffness \( K_{Tor} \) is determined according to the following equation:

\[
K_{Tor} = \frac{T_{xx}}{\varphi_{xx}}
\] (4.8)

where \( T_{xx} \) is the torsion moment and the \( \varphi_{xx} \) is the angle of twist.

4.3 Results and discussion

All optimised designs are shown in Figures 4.2 to 4.5. The equivalent stiffness values of both initial and optimised plates considering compression, bending, torsion and combined loads are presented in Tables 4.1 to 4.4, respectively. Results show that by increasing volume reduction the equivalent stiffness decreases. These results are in agreement with previously reported results presented for 2D geometries (Al-Tamimi et al. 2017). In all cases reducing the density of an element, which reduces the stiffness of that particular element becomes the dominant effect, contributing to the decrease in the overall equivalent stiffness. It is also possible to observe, that in general for the same volume reduction the equivalent stiffness decreases by increasing the number of holes.
Chapter Four: Topology optimisation of bone plates to reduce stress shielding

<table>
<thead>
<tr>
<th>Volume reduction</th>
<th>Four hole</th>
<th>Six hole</th>
<th>Eight hole</th>
</tr>
</thead>
<tbody>
<tr>
<td>25%</td>
<td>(a)</td>
<td>(d)</td>
<td>(g)</td>
</tr>
<tr>
<td></td>
<td>(b)</td>
<td>(e)</td>
<td>(h)</td>
</tr>
<tr>
<td>45%</td>
<td></td>
<td>(f)</td>
<td>(i)</td>
</tr>
<tr>
<td>75%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 4.2** Topology optimisation under compression conditions of (a) four hole plate and 25% of volume reduction, (b) four hole plate and 45% of volume reduction, (c) four hole plate and 75% of volume reduction, (d) six hole plate and 25% volume reduction, (e) six hole plate and 45% of volume reduction, (f) six hole and 75% volume reduction, (g) eight hole plate and 25% of volume reduction, (h) eight hole plate and 45% of volume reduction, (i) eight hole plate and 75% of volume reduction.
Chapter Four: Topology optimisation of bone plates to reduce stress shielding

<table>
<thead>
<tr>
<th>Volume reduction</th>
<th>Four hole</th>
<th>Six hole</th>
<th>Eight hole</th>
</tr>
</thead>
<tbody>
<tr>
<td>25%</td>
<td>(a)</td>
<td>(d)</td>
<td>(g)</td>
</tr>
<tr>
<td>45%</td>
<td>(b)</td>
<td>(e)</td>
<td>(h)</td>
</tr>
<tr>
<td>75%</td>
<td>(c)</td>
<td>(f)</td>
<td>(i)</td>
</tr>
</tbody>
</table>

Figure 4.3 Topology optimisation under bending loading conditions for (a) four hole plate and 25% of volume reduction, (b) four hole plate and 45% of volume reduction, (c) four hole plate and 75% of volume reduction, (d) six hole plate and 25% volume reduction, (e) six hole plate and 45% volume reduction, (f) six hole plate and 75% of volume reduction, (g) eight hole plate and 25% of volume reduction, (h) eight hole plate and 45% of volume reduction, and (i) eight hole plate and 75% of volume reduction.
## Figure 4.4

Topology optimisation under torsion loading conditions for (a) four hole plate and 25% of volume reduction, (b) four hole plate and 45% of volume reduction, (c) four hole plate and 75% of volume reduction, (d) six hole plate and 25% volume reduction, (e) six hole plate and 45% volume reduction, (f) six hole plate and 75% of volume reduction, (g) eight hole plate and 25% of volume reduction, (h) eight hole plate and 45% of volume reduction, and (i) eight hole plate and 75% of volume reduction.
<table>
<thead>
<tr>
<th>Volumre reduction</th>
<th>Four hole</th>
<th>Six hole</th>
<th>Eight hole</th>
</tr>
</thead>
<tbody>
<tr>
<td>25%</td>
<td>(a)</td>
<td>(d)</td>
<td>(g)</td>
</tr>
<tr>
<td>45%</td>
<td>(b)</td>
<td>(e)</td>
<td>(h)</td>
</tr>
<tr>
<td>75%</td>
<td>(c)</td>
<td>(f)</td>
<td>(i)</td>
</tr>
</tbody>
</table>

Figure 4.5 Topology optimisation under combined loading conditions for (a) four hole plate and 25% of volume reduction, (b) four hole plate and 45% of volume reduction, (c) four hole plate and 75% of volume reduction, (d) six hole plate and 25% volume reduction, (e) six hole plate and 45% volume reduction, (f) six hole plate and 75% of volume reduction, (g) eight hole plate and 25% of volume reduction, (h) eight hole plate and 45% of volume reduction, and (i) eight hole plate and 75% of volume reduction.
**Table 4.1** Equivalent stiffness for the compression case.

<table>
<thead>
<tr>
<th>Plate configuration</th>
<th>Volume reduction (%)</th>
<th>Equivalent stiffness (kN/mm)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Initial design</td>
<td>306</td>
</tr>
<tr>
<td>Four-holes</td>
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<td>264</td>
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<tr>
<td></td>
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<tr>
<td></td>
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<td>122</td>
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<tr>
<td></td>
<td>Initial design</td>
<td>247</td>
</tr>
<tr>
<td>Six-holes</td>
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<td>229</td>
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<tr>
<td></td>
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<tr>
<td></td>
<td>75</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>Initial design</td>
<td>237</td>
</tr>
<tr>
<td>Eight-holes</td>
<td>25</td>
<td>228</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>227</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>55</td>
</tr>
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</table>

**Table 4.2** Equivalent stiffness for the bending case.

<table>
<thead>
<tr>
<th>Plate configuration</th>
<th>Volume reduction (%)</th>
<th>Equivalent stiffness (N.m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial design</td>
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</tr>
<tr>
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<td>17.54</td>
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<tr>
<td></td>
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<td>15.52</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>13.51</td>
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<td>18.68</td>
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<td>Six-holes</td>
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<td>17.49</td>
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<tr>
<td></td>
<td>45</td>
<td>15.61</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>12.33</td>
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<tr>
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<td>Initial design</td>
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<td>Eight-holes</td>
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<td>14.31</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>8.55</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>7.24</td>
</tr>
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</table>
Table 4.3 Equivalent stiffness for the torsion case.

<table>
<thead>
<tr>
<th>Plate configuration</th>
<th>Volume reduction (%)</th>
<th>Equivalent stiffness (N.mm/rad)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial design</td>
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</tr>
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<td>Four-hole</td>
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<tr>
<td></td>
<td>45</td>
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<tr>
<td>Initial design</td>
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<tr>
<td>Six-holes</td>
<td>25</td>
<td>25442</td>
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<tr>
<td></td>
<td>45</td>
<td>23302</td>
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<td>75</td>
<td>13632</td>
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<tr>
<td>Initial design</td>
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<tr>
<td>Eight-holes</td>
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<td>20183</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>18823</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>11831</td>
</tr>
</tbody>
</table>

Table 4.4 Equivalent stiffness for the combined case.

<table>
<thead>
<tr>
<th>Plate configuration</th>
<th>Volume reduction (%)</th>
<th>Equivalent stiffness (kN/mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial design</td>
<td>306</td>
</tr>
<tr>
<td>Four-holes</td>
<td>25</td>
<td>244</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>169</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>41</td>
</tr>
<tr>
<td>Initial design</td>
<td>247</td>
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</tr>
<tr>
<td>Six-holes</td>
<td>25</td>
<td>233</td>
</tr>
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<td></td>
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<td>176</td>
</tr>
<tr>
<td></td>
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<td>75</td>
</tr>
</tbody>
</table>
4.4 Conclusion

Stress shielding is a major limitation of the current standard bone fixation plate due to their built-up material and their rigid design. This Chapter employed topology optimisation to optimally redesign different locking compression bone plate configurations considering minimising compliance, under different loading conditions and volume reductions. For all considered cases, the optimised bone plates presented lower stiffness in comparison to the initial designs, showing that topology optimisation is a viable tool to design fixation plates with reduced stress shielding effects. In the future, the effect of mesh size will be considered, and the optimised designs will be produced using additive manufacturing and further characterised.
Chapter Five

Bone remodeling analysis using locking compression fracture plates designed to reduce stress shielding
Chapter Five: Bone remodeling analysis using locking compression fracture plates designed to reduce stress shielding

Fracture plates used to treat fractured bones are built with metallic materials such as stainless steel, titanium and their alloys. This will lead to stress shielding due to the stiffness mismatch when comparing to the cortical bone. In this Chapter, a new concept to design bone fracture plates to reduce the effect of stress shielding is proposed, using topology optimisation and finite element analysis. Three different fracture plates (four-, six- and eight-screw holes) are considered for redesigning by imposing different volume reductions (25%, 45% and 75%) and loading conditions (bending, compression, torsion and the combination of all these loading cases). To evaluate the changes in stress shielding, bone remodeling was performed for a humerus digital model treated with the different fracture plates. Six load cases, including muscle and joint reaction forces, were considered. Fracture plates with high volume reduction resulted in a less bone mass loss. Topology optimised plates is a viable technique to redesign fracture plates reducing the risk of stress shielding and bone loss. The topology optimised designs obtained in Chapter Four were used in this Chapter for further analysis.

5.1 Introduction

Locking compression plate (LCP) composed of plate and screws is the current gold standard used to surgically treat fractured bones by mechanically restoring the integrity of the bone structure whilst the bone fragments heal. The LCP consists of a locking screw head which has the capability of leaving a gap between the plate and the bone, promoting relative stability (Szypryt and Forward 2009). Relative stability is defined as an interfragmentary movement, inducing secondary bone fracture healing (enchondral ossification) by callus formation. This type of healing initiates with hematoma formation, followed by inflammation and fibrous tissue formation (Marsell and Einhorn 2011). In due course, new cartilaginous callus is formed through the differentiation of mesenchymal stem cells which finally leads to bone ossification. The advantages of such stability are that, with each healing step, the motion at the fracture gap is reduced until the appropriate environment is created for the cortical bone to form and the amount of callus formation increases.

which will support the implant role of load bearing and reduce the risk of early implant failure (Egol et al. 2004).

Nevertheless, there are drawbacks with current implants, mainly due to the mechanical properties mismatch between the plate and the bone. Locking compression plates are built with metallic biocompatible materials such as Ti-6Al-4V and Stainless steel (316L) with Young’s modulus varying between 120 GPa and 200 GPa (Elias et al. 2008, Parsad et al. 2017), whereas for the human cortical bone Young’s modulus ranges between 15 and 25 GPa (Rho et al. 1997, McNamara 2011). Therefore, and according to the Wolff’s law, the load distribution during the healing process will be uneven, shielding the bone from the stress stimulus required to provide adequate bone healing and eventually cause bone resorption and implant loosening, through a phenomenon known as “stress shielding” (Parsad et al. 2017).

New implants are being developed and proposed in the literature to address stress shielding by creating porous structures to reduce the overall design stiffness (Parthasarathy et al. 2011, Prasad et al. 2017). However, the current design methodology of such fracture plates has no current standard and requires experience and high computational cost, showing the need for a new methodology. Topology optimisation is an automatic iterative design methodology that allows the development of optimised designs considering the user-defined objective function, constraints and mechanical conditions (i.e. loads and boundaries). Topology optimisation has already presented promising results in medical implant designing (Parthasarathy et al. 2011, Kang et al. 2013, Almeida and Bártolo 2015). In this Chapter, a new design approach is proposed to optimally redesign bone fracture plates aiming to reduce bone mass loss and to minimise stress shielding. Thirty-six fracture plate designs were considered and obtained using topology optimisation, three initial designs (four, six and eight hole plate), four different loading conditions (bending, compression, torsion and combination of these loads) and three different volume reductions (25%, 45% and 75%).

5.2 Simulation procedure

5.2.1 Fracture plates optimisation

Three fracture plate designs (Figure 5.1) with 180 mm of length, 14 mm of width and 5 mm of thickness and different screw-holes (four-, six- and eight-screw holes) were considered as the initial design plates and further optimised considering bending, compression or torsional loads, or
Chapter Five: Bone remodeling analysis using locking compression fracture plates designed to reduce stress shielding

a combination of all these loads. The topology optimisation was performed considering the Solid Isotropic Microstructure with Penalisation (SIMP) method using the software Abaqus 6.14 (Dassault Systèmes, France) (Bendsøe and Sigmund 2004):

\[
\min_{\rho_e} \mathbf{C}(\rho_e) = f^T \cdot u 
\]

subject to

\[
\begin{align*}
\sum_{e=1}^{N} \rho_e v_e & \leq V^*, \\
\sum_{e=1}^{N} \rho_e p K_e & = f, \\
0 & < \rho_0 \leq \rho_e \leq 1,
\end{align*}
\]

where \(\mathbf{C}\) is the compliance, \(p\) is the penalisation factor, \(u\) is the displacement vector, \(f\) is the force vector, \(\rho_e\) is the element density, \(\rho_0\) is the initial density, \(V^*\) is the volume fraction, \(v_e\) is the volume of each element and \(K_e\) is the element stiffness matrix. A frozen region was considered on the screw hole region to keep their shape. Three volume reductions were considered (25%, 45% and 75%). Fracture plates are considered to made of the Ti-6Al-4V (120 GPa of Young’s modulus and 0.3 of Poisson’s ratio). Table 5.1 summarises the different cases being considered and corresponding reference names.

**Figure 5.1** The initial fracture plate designs considering (a) four-, (b) six- and (c) eight-screw holes.
Chapter Five: Bone remodeling analysis using locking compression fracture plates designed to reduce stress shielding

Table 5.1 Fracture plate references.

<table>
<thead>
<tr>
<th>Load conditions</th>
<th>Volume reduction, %</th>
<th>Four-hole plate</th>
<th>Six-hole plate</th>
<th>Eight-hole plate</th>
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</tr>
<tr>
<td>25</td>
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<td>Torsion</td>
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</table>

5.2.2 Density analysis on a humerus model

To evaluate the impact of the different fracture plate designs on bone remodeling, the plates were considered to stabilise a fractured humerus assuming also the locking screw head technique. The 3D geometry of the humerus was generated from the Visible Human Male dataset (Spitzer et al. 1996) using Mimics 20.0 (Materialise NV, Leuven, Belgium). The fixation of the plates into the humerus was virtually assembled using Solidworks (Dassault Systèmes, France), following the recommendations from the AO Foundation and discussed with an orthopedic surgeon, which is also co-author of this manuscript. Solidworks was used to model screws and initial fracture plates. Each screw has a head of a 5 mm in diameter and a main body with 3.5 mm of diameter and 34 mm of total length.
A model of the native humerus, without any implant, and models with implanted fracture plates were considered. Numerical simulations were performed using the software Abaqus 6.14 (Dassault Systèmes, France) with linear tetrahedral (C3D4) elements. Assumed properties for the cortical bone were a Young’s modulus of 18 GPa and a Poisson’s ratio of 0.3 (Santos et al. 2018).

To simulate the complex in vivo loading of the humerus, 6 load cases including muscle and joint reaction forces were applied. The magnitude and direction of the applied forces were estimated through inverse dynamics using a musculoskeletal model of the upper limb (Quental et al. 2015, Quental et al. 2018). Selected load cases represent the loading conditions of the upper limb for arm elevations of 10º, 60º and 90º in the frontal and sagittal planes. In Abaqus, muscle forces were applied at different attachment points, defined according to the anatomical data of the musculoskeletal model of the upper limb used, and distributed over the humeral surface to better replicate the actual distribution of forces from the muscles to bone. For the distribution of muscle forces at their origin or insertion attachment sites, coupling constraints were defined between the attachment points and the sets of nodes on the surface of the humerus closest to them. If the muscle force to be applied resulted from the wrapping of a muscle over the humerus, the force was projected onto the surface of the humerus and distributed over the surface nodes closest to the projection point. A similar procedure was considered for the distribution of the glenohumeral joint reaction force considering its application at the glenohumeral joint centre. Figure 5.2 highlights the nodes to which forces are distributed. To eliminate rigid body motion, nodes at the articulating surface of the elbow joint were constrained in all directions.
5.2.3 Bone remodeling model

The bone remodeling used is a node-based approach of the mathematical model proposed by (Fernandes et al. 1999). In this model, bone is a linearly elastic orthotropic material obtained through the periodic repetition of cubic unit cells with rectangular holes. The orientation of the microstructure, given by the angles $\theta$, and the dimensions of the rectangular holes, given by $a$, define the local properties of bone. Considering $\theta$ and $a$ as design variables, the bone remodeling process is formulated as an optimisation problem that maximises the structural stiffness while considering a biological term related to the cost of bone maintenance ($\kappa$ and $m$). The stationary conditions of the optimisation problem with respect to the design variables provide the bone remodeling law, expressed as:

$$
\sum_{P=1}^{NC} \left[ \alpha^P \frac{\partial E^H_{ijkl}}{\partial a} \varepsilon_{ij} \varepsilon_{kl} \right] - \kappa \frac{\partial \mu}{\partial a} = 0
$$

(5.2)

$$
\sum_{P=1}^{NC} \left[ \alpha^P \frac{\partial E^H_{ijkl}}{\partial \theta} \varepsilon_{ij} \varepsilon_{kl} \right] = 0
$$

(5.3)

where $NC$ is the number of applied load cases, $\alpha^P$ is the load weight factor, $E^H$ are the homogenised bone material properties (Guedes and Kikuchi 1990), $\mu$ is the bone density and $\varepsilon$ is the strain field.
Briefly, for a given set of design variables, the material properties of the bone are computed by the homogenisation method and provided to the finite element code. The solution of the finite element analysis yields the strain field that allows the updating of the design variables according to Equations 5.2 and 5.3. Once these equations are satisfied bone is in equilibrium and the remodeling process stops. Considering the relative frequencies of arm movements during daily activities, the weight factors $\alpha$ were defined as 0.251, 0.056 and 0.012 for abduction, and 0.537, 0.119 and 0.025 for flexion (Coley et al. 2008, Coley et al. 2009). The parameters $\kappa$ and $m$, defined as $1.5 \times 10^{-4}$ and 2, respectively, based on Santos et al. (2018), control the bone remodeling process by defining the cost of bone maintenance. These parameters were selected based on their ability to reproduce the actual bone density distribution of the humerus under analysis (Santos et al. 2018).

The finite element model of the native humerus, without any implant, was applied to define an initial bone density distribution to be considered for the remaining bone remodeling simulations. Starting from a homogeneous bone density distribution of approximately 1 g/cm$^3$, iterations were run until bone reached an equilibrium condition. 400 iterations were run. The final bone density distribution was mapped into the finite element meshes of the remaining models to be considered as the initial solution. For the implanted fracture plate models, all bone remodeling simulations were run until bone reached an equilibrium condition. For the implanted models, all bone remodeling simulations were run for 200 iterations.

5.2.3.1 Bone remodeling post-osteosynthesis

The humerus remodeling process post-analysis was quantitatively and qualitatively performed by comparing bone density distributions between the implanted and intact humerus models. The qualitative assessment was based on the visual changes between the post-analysis of the bone density distributions of different fracture plates. The density of bone tissue was defined as 1.8 g/cm$^3$. A cross-section of the region of interest was also considered to observe the qualitative differences of the humerus remodeling and categorised as bone apposition, equilibrium and bone resorption. The equilibrium condition is considered for absolute bone density differences below 0.2 g/cm$^3$. For the quantitative evaluation, changes in the bone mass were computed for a region of the humerus that is opposite to the plate’s mid-region (i.e. between the mid two screws), as illustrated in Figure 5.3, assuming this region as the fracture (e.g. transverse fracture) site. The change in bone mass ($\Delta bm$) was quantified as follows:
Chapter Five: Bone remodeling analysis using locking compression fracture plates designed to reduce stress shielding

\[ \Delta bm(\%) = \frac{\sum_{i=1}^{n}(\rho_i^{\text{implanted}} - \rho_i^{\text{intact}}) \times V_i}{\sum_{i=1}^{n} \rho_i^{\text{intact}} \times V_i} \]  

(5.4)

where \( n \) is the number of nodes within the interest region, \( \rho_i^{\text{intact}} \) and \( \rho_i^{\text{implanted}} \) are the bone densities for the intact and implanted models for node \( i \), respectively, and \( V_i \) is the volume associated at node \( i \) (Quental et al. 2014).

![Figure 5.3 The region of interest, highlighted in red, for the evaluation of the change in bone mass of the humerus.](image)

**5.3 Results**

Thirty-six fracture plate designs were obtained through topology optimisation (Figures B.1 to B.3 in Appendix B) and considered for the bone remodeling study. The bone mass changes in the region of interest for all fracture plates are presented in Table 5.2. For all simulation models, the fracture plates effect on bone mass changes showed a trend related to the volume reduction imposed on the fracture plates. For fracture plates with higher volumes reduced (i.e. reduced stiffness), lower bone mass changes were observed. The bone mass distribution and magnitude at the region of interest are also presented in Figure 5.4, for the initial designs and the 75% volume reduction fracture plate which is the case that corresponds to the minimum bone mass change at the region of interest. The lowest bone mass changes were obtained for the least stiff (higher volume reduced) plates optimised under compression and combined loads (i.e. 4Cp75 and 4Cb75;
Chapter Five: Bone remodeling analysis using locking compression fracture plates designed to reduce stress shielding

6Cp75 and 6Cb75; 8Cp75 and 8Cb75), indicating a better distribution of loads into the bone. The least presented bone loss among these plates was observed for the four-holes plate, which can be explained by the reduced number of screw-holes that directly affects the rigidity of the fixation of the plate. The highest bone mass changes were observed for the stiffest plates (i.e. the initial plates). The qualitative assessment shows no significant change in the bone mass between the initial and the optimised plates. However, a small increasing shift can be observed of bone apposition and bone equilibrium in the least stiff plates, particularly between the eight-hole initial design and 8Cb75.

Table 5.2 Bone mass changes at the fracture site between the implanted and intact bone in the humerus.

<table>
<thead>
<tr>
<th>Plate</th>
<th>Hole Numbers</th>
<th>Four-hole plate</th>
<th>Six-hole plate</th>
<th>Eight-hole plate</th>
<th>Volume reduction, %</th>
<th>Bone mass change, %</th>
</tr>
</thead>
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<td>Initial designs</td>
<td>/</td>
<td>-10.94</td>
<td>-13.71</td>
<td>-15.44</td>
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</tr>
<tr>
<td></td>
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<td>-14.58</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>-8.82</td>
<td>-10.38</td>
<td>-11.22</td>
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<td></td>
</tr>
<tr>
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<td>-12.87</td>
<td>-14.95</td>
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<td></td>
</tr>
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<td>-14.87</td>
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</tr>
<tr>
<td></td>
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<td>-7.04</td>
<td>-6.84</td>
<td>-8.63</td>
<td></td>
<td></td>
</tr>
<tr>
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<td>-13.63</td>
<td>-15.32</td>
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<td></td>
</tr>
<tr>
<td></td>
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<td>-13.20</td>
<td>-14.82</td>
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<td></td>
<td>75</td>
<td>-8.84</td>
<td>-13.03</td>
<td>-13.48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined</td>
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<td>-14.75</td>
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<td></td>
</tr>
<tr>
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<td>-10.06</td>
<td>-14.09</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>-5.13</td>
<td>-8.35</td>
<td>-8.62</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Chapter Five: Bone remodeling analysis using locking compression fracture plates designed to reduce stress shielding.

**Figure 5.4** Bone mass distributions for the initial designs and all load cases considering 75% of volume reduction. Blue is bone apposition, green is equilibrium and red is bone resorption.
5.4 Discussion and Conclusion

The stiffness mismatch between the bone and fracture plate will lead the bone to resorb and possible plate loosening and failure due to stress shielding. In addition, the use of high stiff metallic materials with a solid (non-porous) structure promotes the stress shielding effect (Elliott and Goswami 2012). Instead of finding a better suitable material that matches the bone stiffness, porous implants have been developed (Parthasarathy et al. 2011). This will reduce the rigidity of the implant, hence the implants’ structural stiffness and decrease the risk of stress shielding. Topology optimisation showed promising potential in designing porous bone implants (Ridzwan et al. 2007), and to the authors best knowledge this is the first study to address shielding by implementing topology optimisation to optimally reduce the stiffness of a generic fracture plate. The mass of the bone post-operation is a major indicator of whether stress shielding is occurring or not, as the existence of bone mass indicates the rate of callus formation which is a clear sign that proper stresses are being induced (Ridzwan et al. 2007, Quental et al. 2014). Moreover, influences the screw stability and reduces the risk of plate failure (Egol et al. 2004).

Bone remodeling results at the region of interest (fracture site), beneath the fracture plate, show less bone mass changes with the implantation of less stiff plates produced by topology optimisation compared to their initial and stiffer counterparts. Results also show that topology optimisation can be a useful tool to design less stiff fracture plates thus minimising stress shielding, reducing bone loss and improving the bone healing process. In this Chapter, the bone remodeling model of the humerus was not evaluated for all bone regions. Nonetheless, the region of interest studied is one of the most affected regions by the fracture plate.
Chapter Six

Stress analysis in a bone fracture fixed with topology optimised plates
The design of commercially available fixation plates and the materials used for their fabrication lead to the plates being stiffer than bone. Consequently, commercial plates are prone to stress shielding and failure. In this study, novel three-dimensional fixation plates are designed using topology optimisation to reduce the risk of stress shielding. Fixation plate designs were optimised by minimising the strain energy for three levels of volume reduction (i.e. 25%, 45% and 75%). To evaluate stress shielding, changes in stress due to the different fixation plate designs were determined on the fracture plane of an idealised shaft of a long bone under a four-point bending load considering the effect of a patient walking with crutches of a transverse fractured tibia. Topology optimisation is a viable approach to design less stiff plates with adequate mechanical strength considering high volume reductions, which consequently increased the stress transferred to the bone fracture plane and promoted the reduction of stress shielding with the ability to withstand the stresses. The topology optimised designs obtained in Chapter Four were used in this Chapter for further analysis.

6.1 Introduction

Stress shielding is an important phenomenon that must be considered during design optimisation of fracture fixation plates to minimise the risk of bone resorption and plate failure (Prasad et al. 2017). It is the result of the stiffness mismatch between the most commonly used metallic fracture fixation plates and bones, which strongly determines the bone remodelling process whereby, according to Wolff’s law, bone adapts to the forces acting upon it (Ridzwan et al. 2007, Quental et al. 2014).

Stress shielding is a common problem for mild to high load-bearing medical implants and can be reduced by redesigning the medical implant (Ramakrishna et al. 2004, Galbusera et al. 2008). The use of topology optimisation is gaining significant attention due to the ability to automatically generate optimal redesigns for a given design, considering different loading conditions and volume reduction constraints. Several authors demonstrated the feasibility of topology optimisation for the

redesign of femur hip joints to minimise stress shielding (Rizdwan et al. 2006, Fraldi et al. 2010, Saravana Kumar and George 2017). In these cases, results showed improved load transfer in the case of optimised implants. Similarly, Liu et al. (2017) used topology optimisation to design mandible fixation plates with adequate biomechanical performance.

A valid concern when reducing stiffness of implants is whether the change in biomechanical characteristics has a negative effect on the stability at the fracture site which might affect bone healing. In order to ensure appropriate stresses imposed on the bone, fixation plates stiffness should be optimised whilst maintaining plate stability during the healing process.

Therefore, this paper investigates the use of topology optimisation to design fixation plates that minimise stress shielding and promote load transfer to the bone fracture plane, thus stimulating bone remodeling. Two different fixation plates were considered (four- and eight-screw holes) and were optimised for different loading conditions (bending, compression, torsion and a combined load) and three volume reductions (25%, 45% and 75%). The optimised plates were evaluated using finite element analyses considering a tibia-like bone shape model under a bending loading condition to study the induced stresses on the defined bone fracture plane.

### 6.2 Modelling and simulation

#### 6.2.1 Optimisation and mechanical evaluation

The Solid Isotropic Microstructure with Penalisation (SIMP) method, was applied to redesign two different fixation plates with four and eight screw holes. Initial designs were created in Solidworks (Dassault Systèmes, Waltham, MA, USA) considering generic locking compression fixation systems for treating long bones for midshaft fractures with a length of 180 mm, width of 14 mm and thickness of 5 mm. Three volume reductions (25%, 45%, and 75%), and different loading conditions (bending, compression, torsion and a combination of all these loads), were considered as shown in Figure 6.1. A frozen region was considered on the screw hole region to keep their shape. Simulations were performed considering quadratic hexahedral meshes with around 50,000 elements.

Mathematically, the SIMP formulation can be described as follows (Bendsøe and Sigmund 2004):

\[
\min_{\rho_e} C(\rho_e) = f^T \cdot u
\]  

(6.1)
subject to\[
\sum_{e=1}^{N} \rho_e v_e \leq V^*,
\]
subject to\[
(\sum_{e=1}^{N} \rho_e^p K_e) u = f,
\]
subject to\[
0 < \rho_0 \leq \rho_e \leq 1,
\]
where \( C \) is the compliance, \( p \) is a penalisation factor \((p = 3)\), \( u \) is the displacement vector, \( f \) is the force vector, \( \rho_e \) is the element density, \( \rho_0 \) is the initial density, \( V^* \) is the volume fraction, \( v_e \) is the volume of each element and \( K_e \) is the element stiffness matrix. The topology optimisation problem was run using the TOSCA module in Abaqus (Dassault Systèmes, Waltham, MA, USA).

**Figure 6.1** Load and boundary conditions considered for the fixation plate optimisation of (a) four-point bending load, (b) uniaxial compression, (c) torsional and (d) combination of the bending, compression and torsion loads.
Figure 6.1 (cont.) Load and boundary conditions considered for the fixation plate optimisation of (a) four-point bending load, (b) uniaxial compression, (c) torsional and (d) combination of the bending, compression and torsion loads.

The mechanical behaviour of both initial and optimised designs was investigated through finite element analyses, assuming elastic behaviour and homogeneous and isotropic plates. Numerical simulation was used to determine the equivalent stiffness in a four-point bending setting according to the British standards (BS 3531-23.1:1991 ISO 9585:1990). In this case, the equivalent bending stiffness is determined according to the following equation:
Chapter Six: Stress analysis in a bone fracture fixed with topology optimised plates

\[ E_B = \frac{(4h^2+12ha+a^2)K\cdot h}{24} \quad \text{(N.m}^2) \quad \text{(6.2)} \]

where \( h \) is the distance between the force points, \( a \) is the span between the force and support points and \( K \) is the stiffness calculated as follows:

\[ K = \frac{RF}{D} \quad \text{(N/m)} \quad \text{(6.3)} \]

where \( RF \) is the average reaction force in the z-axis (along with the fixation plate thickness) at the constraint points and \( D \) is the maximum displacement.

Changes in the equivalent stiffness between the optimised fixation plates and the initial designs were calculated using the following equation:

\[ \Delta \text{equivalent stiffness(\%)} = \frac{\text{Plate stiffness}^{\text{Optimised}} - \text{Plate stiffness}^{\text{Initial}}}{\text{Plate stiffness}^{\text{Initial}}} \quad \text{(6.4)} \]

### 6.2.2 Stress analysis of a bone model

In order to determine the stresses in the fracture plane of a bone, which provides an indication of the stress shielding effect of the plates, a bone-plate construct (i.e. the assembly of the fracture plate to the bone with screws) was considered. For simplicity, no fracture gap was imposed, and the plate was assumed to fixate a transverse fractured tibia bone. Only the cortical bone region was considered, and a hollow cylinder region with an external diameter of 24 mm and an internal diameter of 12 mm was assumed for simulation purposes.

All 3D geometric parts, i.e., cortical bone, screws and initial fixation plates, were modelled in Solidworks (Dassault Systèmes, Waltham, MA, USA). Each screw has a 5 mm diameter head and a main body with 3.5 mm of diameter and 34 mm of total length. Both fracture plates and screws were assumed to be made of Ti-6Al-4V. For the cortical bone, a Young’s modulus of 18 GPa and a Poisson’s ratio of 0.3 was assumed (Santos et al. 2018). In order to avoid high computational costs, only half of the bone-plate construct was considered, as illustrated in Figure 6.2. To simulate the Locking Compression Plate technique, the finite element model considered the bone-plate construct with a gap of 0.5 mm between the bone and plate (i.e. no contact). The screw heads were securely locked to the plate and the screws tied to the bone. Quadratic hexahedral elements were considered for the bone model region of interest (i.e. fracture plane) and quadratic tetrahedron elements for the plates, screws and the bone region outside of the fracture plane. Two equally
distributed moments of 20 Nm were applied along the horizontal axis of the bone, simulating the moment load happening on the tibia during the swing phase (i.e. 10% of the body weight) in patients walking with crutches (Ramakrishna et al. 2004, Wehner et al. 2009, Kim et al. 2011). To prevent rigid body motion, the extremity faces of the bone were fully constrained.

In addition, since the mechanical strength of the topology optimised fixation plates is important to assess their stability during healing, a mechanical strength analysis was performed based on the materials yield strength, considering the yield strength of the Ti-6Al-4V as ~860 MPa (Elias et al. 2008). The Von Mises stresses on the topology optimised fixation plates were used to determine their mechanical strength and, consequently, to investigate their stability.

![Figure 6.2 Bone-plate construct considered to determine stresses at the fracture plane.](image)

### 6.3 Results

The changes in the equivalent stiffness between the optimised and initial designs are shown in Table 6.1. Optimised designs obtained through topology optimisation are presented in Appendix C (Figures C.1 and C.2). The equivalent bending stiffness change increases as the volume reduction increases. For the same volume reduction and plates with different number of holes there is no clear trend in terms of the equivalent stiffness change. Also, as expected, plates optimised considering bending loading conditions exhibit the least reduced equivalent stiffness change. The highest decreases were observed for the 75% volume reduction with combined load for the four-hole and eight-hole.
Table 6.1 Change in the equivalent bending stiffness in comparison to the initial values for four and eight-hole plates (19.27 and 16.22 N.m², respectively).

<table>
<thead>
<tr>
<th>Plate</th>
<th>Hole Numbers</th>
<th>Volume reduction (%)</th>
<th>Equivalent stiffness change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Four-hole plate</td>
<td>Eight-hole plate</td>
<td></td>
</tr>
<tr>
<td>Bending</td>
<td>25</td>
<td>-3</td>
<td>-2</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>-5</td>
<td>-5</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>-20</td>
<td>-61</td>
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<tr>
<td>Compression</td>
<td>25</td>
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<td>-15</td>
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<td></td>
<td>45</td>
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</tr>
<tr>
<td></td>
<td>75</td>
<td>-49</td>
<td>-71</td>
</tr>
<tr>
<td>Torsion</td>
<td>25</td>
<td>-3</td>
<td>-31</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>-9</td>
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</tr>
<tr>
<td></td>
<td>75</td>
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<td></td>
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<tr>
<td></td>
<td>75</td>
<td>-92</td>
<td>-87</td>
</tr>
</tbody>
</table>

The maximum Von Mises stresses from the bone-plate construct at the fracture plane, considering both the initial and topology optimised fixation plates are presented in Table 6.2. The stress distribution and magnitude at the bone fracture plane are presented in Figure 6.3, for the initial designs and only for the 75% volume reduction optimised plates, which is the case causing the maximum Von Mises stresses on the bone at the fracture plane. Overall, the stresses in the bone increase when topology optimised plates are used. The most substantial increase of stresses at the fracture plane was observed for the combined loading conditions and 75% volume reduction plates. In comparison to the initial designs, the maximum stresses at the fracture plane increased by 31% for the four-hole plate and 37% for the eight-hole plate in the combined case with a 75% of volume reduction. The stress distribution shows that less stiff plates produce higher compressive...
stresses (in the plate-bone interface due to the bending load) at the fracture plane. Moreover, the neutral axis with the less stiff plates becomes closer to that of the bone’s when compared with high stiff plates. In terms of plate mechanical stability (i.e. mechanical strength), the stresses among the least stiff fixation plates (75% of volume reduction) are shown in Figure 6.4. The maximum stresses occur on both four-hole and eight-hole designs with a combined load and 75% of volume reduction. Minimum values of the Von Mises stresses for all plates occur for compression loads and 75% of volume reduction.

Table 6.2 Maximum Von Mises stresses on the bone at the fracture plane for all considered designs.

<table>
<thead>
<tr>
<th>Hole Numbers</th>
<th>Plate</th>
<th>Four-hole plate</th>
<th>Eight-hole plate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Volume reduction (%)</td>
<td>Von Mises stress (MPa)</td>
<td></td>
</tr>
<tr>
<td>Initial designs</td>
<td>N/A</td>
<td>17.59</td>
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Figure 6.3 Von Mises stresses at the bone fracture plane resulted from the initial designs and all of the 75% volume reduction optimised plates.
Chapter Six: Stress analysis in a bone fracture fixed with topology optimised plates

Figure 6.4 Stress distribution on the optimised four and eight screw hole plates with 75% volume reduction and different loading conditions (a) bending, (b) compression, (c) torsion, and (d) a combined load.
6.4 Discussion and conclusions

Results show that through topology optimisation it is possible to design less stiff fixation plates, resulting in higher loads being transferred to the bone fracture plane, while maintaining the plate’s ability to withstand stresses. By considering a maximum of 75% of volume reduction for plates containing different screw holes, it is possible to increase the load transfer to up to 37% in comparison to the initial plates. This reduces stress shielding, and likely bone loss, to promoting secondary healing, that promotes callus formation and bone formation (Woo et al. 1977, Goodship and Kenwright 1985, Claes et al. 1997).

Maximum Von Mises stresses were observed in plates optimised for combined loading conditions and 75% of volume reduction. This can be explained by stress concentrations induced by the plate design presenting thin features. However, as observed, the highest stresses are still 50% lower than the yield strength of the material, guaranteeing the plate mechanical stability.

For the four-hole plates, the best performance was observed for plates with 75% of volume reduction and optimised for bending loading conditions, which enable 22% of load transfer to the bone, presenting also low Von Mises stresses (221 MPa). While for the eight-hole plates, a maximum load transfer of 29% and 240 MPa of Von Mises stresses was observed for compression load optimised plates.

As shown, topology optimisation allows to design less stiff and lightweight fixation plates, reducing the stress shielding effect, promoting load transfer to the bone and thus contributing to bone remodeling. However, further analysis is still required, considering for example a fracture gap and measuring the gap strains to correlate the resulted strains (i.e. relative or absolute stability) with the healing process (i.e. secondary or primary healing). Furthermore, screw threads were not considered in the simulation and their role on load transfer must be also considered.
Chapter Seven

Topology optimised metallic bone plates produced by electron beam melting: a mechanical and biological study
Chapter Seven  

**Topology optimised metallic bone plates produced by electron beam melting: a mechanical and biological study**

Metallic bone plates are commonly used as a medical implant to treat bone fractures. The gold standard materials for these implants are biocompatible 316L stainless steel, cobalt chromium, titanium and its alloys (e.g. CoCrMo and Ti6Al4V). However, the main disadvantage of these implants is the material stiffness mismatch between the implant and bone. This mismatch may negatively affect the biological processes in bone healing. This Chapter investigates topology optimisation to produce plates with reduced equivalent stiffness and the fabrication of optimised plate designs using an electron beam melting (EBM) system. Non-post-processed EBM plates were assessed against commercially available bone fixation plates in terms of mechanical and biological characteristics. Results show that some redesigned produced plates present mechanical properties similar to the cortical bone and that there is no need to post-process the produced plates in order to establish a good biological bonding with the surrounding tissue. The designs of topology optimised for compression loads obtained in **Chapter Four** were used in this Chapter for further analysis.

### 7.1 Introduction

Bone is a highly vascular and specialised tissue responsible for maintaining the shape of the skeleton, protecting soft tissues, transmitting the force of muscular contraction during movement, serving as a reservoir for ions and contributes to the regulation of the extracellular matrix, blood cell production and blood pH regulation (Dorati et al. 2011). Bone is prone to traumatic injuries as well as diseases. In the case of minor fractures, bone heals and remodels with little detectable scarring. However, in the case of pathological and traumatic fractures, traumatic bone loss or primary tumour resection, bone is not able to heal itself (Marsell and Einhorn 2011, Lee et al. 2014, Bigham-Sadegh and Oryan 2015). Bone fractures that are displaced or unstable are frequently surgically treated with bone fixation implants such as internal
fixation devices, external fixators and intramedullary pins. In the case of internal fixation devices, the locking compression plate (LCP) is widely used to treat various types of fractures due to its hybrid screw system containing two means of fixation techniques. This allows the application of absolute stability or relative stability leading to both primary healing and secondary healing (Szypryt and Forward 2009). Similar to other internal fixation plates (e.g. dynamic compression plate and periarticular locking plate system), LCP is made from an inert and biocompatible metal. The most commonly used metallic materials are titanium and its alloys, stainless steel, or cobalt chrome and its alloys (Elias et al. 2008, Prasad et al. 2017).

The role of the internal fixation plates is to stabilise the fractured bone during the union/healing process. After the fracture is healed, the implant is no longer required to stay in the body. Currently, around 30% of the metallic implants have to be surgically removed after the healing process (Hanson et al. 2008). However, this procedure presents significant risks of bone refracture and nerve damage. Bone refracture is due to the lack of density of the bone in the close vicinity of the implant due to the significant mechanical differences between bone and fixation plates. For example, the Young’s modulus of Ti6Al4V is around 120 GPa whilst the Young’s modulus of trabecular bone ranges between 50 and 100 MPa and between 15 and 25 GPa in the case of cortical bone (Rho et al. 1997, McNamara 2011, Prasad et al. 2017). This Young’s modulus mismatch results in a phenomenon named stress shielding which is usually associated with implant loosening and bone loss. Alternatively, the implant can be left in the body, but this option also presents problems such as risks of periprosthetic fracture due the stress risers at the cortical bone and implant junctions, corrosion, release of metal ions and the risk of allergic and potentially carcinogenic reactions (Hofmann 1992, Inion 2015).

Several researchers also explored the use of novel additive manufacturing technologies to produce fully personalised metallic implants. A notable example was the fabrication of a metallic complex jaw implant coated with bioceramic and implanted in an 83-year-old lady. Partners in Belgium and the Netherlands (universities of Leuven and Hasselt, AM bureau LayerWise) designed the implant to guarantee good attachment of muscles and space for nerves and used a powder bed fusion system to produce it (Bartolo et al. 2012). Other research groups also explored powder bed fusion techniques (selective laser melting and electron beam melting) to produce personalised metallic bone plates without any concerns regarding the stress shielding effect (Sing et al. 2016). Very few studies addressed this problem by changing the plate design (e.g. plate thickness) to improve its
Chapter Seven: Topology optimised metallic bone plates produced by electron beam melting: a mechanical and biological study

performance through a trial and error approach (Anitha et al. 2015). A systematic approach is still required. This Chapter presents a combined approach linking computer modelling, simulation and optimisation together with additive manufacturing to address this problem. The following research questions are addressed:

- Is it possible to use topology optimisation to produce plates with reduced equivalent stiffness?
- Is it possible to automatically produce optimised plate designs using an electron beam system?
- Are the mechanical properties of the produced plates similar to the designed ones and similar to the cortical bone?
- Is it necessary to post-process the produced plates in order to establish a good biological bonding with the surrounding tissue?

7.2 Initial bone plate design

There are no standard dimensions (i.e. length, width and thickness) or number of screw holes for commercially available bone fixation plates. Different commercial companies are also commercialising plates of the same type (e.g. locking compression plates) with different dimensions. Commercial bone plates from the same company present the same width and thickness but different lengths. Therefore, the number of distinct topologies (geometry and number of holes) is high. In this research, the DePuy Synthes narrow locking compression plate (DePuy Synthes, Synthes GmbH, Switzerland) was considered as the reference design. Plates containing four, six and eight holes, with 180 mm in length, 14 mm in width and 5 mm in thickness, were defined (see Table 7.1) and considered for redesigning.
Table 7.1 The design domain of the bone plates.

<table>
<thead>
<tr>
<th>Plate name</th>
<th>Number of holes</th>
<th>Plate design</th>
</tr>
</thead>
<tbody>
<tr>
<td>ID4</td>
<td>Four</td>
<td><img src="image" alt="Plate ID4" /></td>
</tr>
<tr>
<td>ID6</td>
<td>Six</td>
<td><img src="image" alt="Plate ID6" /></td>
</tr>
<tr>
<td>ID8</td>
<td>Eight</td>
<td><img src="image" alt="Plate ID8" /></td>
</tr>
</tbody>
</table>

7.3 Computer modelling, simulation and optimisation

Plates were initially designed using Solidworks (Dassault Systèmes, France). Optimisation was conducted using the Abaqus Topology Optimisation Module (ATOM) software (Dassault Systèmes, France), and the Solid Isotropic Microstructure with Penalisation (SIMP) method proposed by Bendsøe (1989). Mathematically topology optimisation is described as follows (Bendsoe and Sigmund 2004):

\[
\min_{\rho_e} C(\rho_e) = f^T \cdot u \quad (7.1)
\]

subject to

\[
\begin{align*}
\sum_{e=1}^{N} \rho_e v_e &\leq V^*, & (7.1a) \\
\sum_{e=1}^{N} \rho_e^p K_e u &= f, & (7.1b) \\
0 < \rho_0 &\leq \rho_e \leq 1, & (7.1c)
\end{align*}
\]

where \(C\) is the compliance, \(f\) is the force vector, \(K_e\) is the element stiffness matrix, \(u\) is the displacement vector, \(V^*\) is the user-defined fraction volume, \(p\) is the penalisation factor, \(\rho_e\) is the element density, \(\rho_0\) is the initial density and \(v_e\) is the volume of each element.

The iterative process to achieve the optimal design starts with the definition of a design domain, \(\Omega\), discretised into a set of elements with specific density (\(\rho\)) and Young’s modulus (\(E\)) values. Loading and boundary conditions are imposed, generating stresses and strains at each element,
determining the corresponding sensitivity, i.e. the element that will have their density updated. Filtering techniques are implemented to restrict the optimisation from common disadvantages such as checkerboarding. The density is distributed along the design domain and updated after each iteration toward optimality according to the derivative of equation (7.1), considering for each element the value of $\rho = 1$ for full element stiffness and $\rho=0$ for a void. The density update process is repeated until reaching the optimal solution.

Even though topology optimisation is a load magnitude independent process, a post-operative case of a 70-kg patient was considered. Post-operation, patients suffering from a fractured tibia walk with crutches and their gait induces an overall load on the legs equivalent to 10% of the bodyweight (Kim et al. 2011). Therefore, we assume a static compression force of 70 N applied on both far-end sides of the bone plate. Screw holes were considered a frozen design region. Ti6Al4V (Young’s modulus of 120 GPa and 0.3 Poisson’s ratio) was considered as the bone plates’ material. Different volume reductions (25, 45 and 75%) were considered and a mesh of approximately 50,000 8-node linear hexahedral elements was used for all considered geometries.

The redesigned plates were computationally assessed considering a static mechanical tensile test to determine their equivalent stiffness. In this case, a longitudinal force ($F_{xx}$) in the x-axis direction is applied to one side of the plate constraining the movement of the opposite side. Following a previously reported procedure Almeida and Bartolo (2014), the equivalent stiffness of the designed plates can be determined as follows:

$$K = \frac{RF_{xx}}{U_{xx}}$$

where $K$ is the structural stiffness, $RF_{xx}$ is the reaction force on the constraint face and $U_{xx}$ is the displacement.

### 7.4 Fabrication process

Bone fixation plates were prepared (e.g. part orientation, design of support structures and position in the building platform) using the software Magics (Materialise, Belgium) and exported as STL files to the Build Assembler software where the models were sliced and uploaded to the machine. Support structures were designed considering part stability and to reduce both thermal stresses and warping. The EBM Arcam A2 model (Arcam, Sweden) was used for producing the plates. Its schematic configuration is shown in Figure 7.1a. The machine consists on an electron beam emitted from a hot tungsten filament, operates at 60 kV under vacuum pressure of $2.0 \times 10^{-3}$ mBa,
scanning speed of 4530 mm/s, beam focus offset of 3 mA, line offset of 0.1 mm and layer thickness of 50 μm. The substrate plate temperature was kept at ~ 600 °C and the build temperature was defined to be ~ 750 °C. Parts were produced using standard Ti6Al4V powder supplied by the machine manufacturer. The powder material consists of spherical gas atomised particles with a size ranging between 45 and 100 μm (see Figure 7.1b), composed of 6.04% of aluminium, 4.05% of vanadium, 0.013% of carbon, 0.0107% of iron, 0.13% of oxygen and balanced titanium.

The EBM fabrication process initiates with the entire titanium powder being scanned and preheated to 750 °C (80% of its melting temperature) with a low beam current of approximately 0.2 mA and high scanning speed up to 8000 m/s to minimise residual stresses. After fabrication, the powder recovery system was used to remove all trapped powder through blasting a stream of high-pressure air and the support structures were removed using pliers. Parts were not submitted to any post-processing operation or thermal treatment.

![Figure 7.1 a) The Arcam A2 EBM system schematic; b) Scanning electron microscopy of the Ti6Al4V powder.](image)

### 7.5 Characterisation of produced plates

#### 7.5.1 Mechanical testing

Bone plates were mechanically assessed against the mechanical properties of cortical bone and compared to four commercially available titanium Depuy Synthes LCP 4.5/5.0 narrow bone plates with different screw holes (ten, nine, eight and six holes) purchased from DePuy Synthes (DePuy Synthes, Synthes GmbH, Switzerland). The test is a displacement controlled quasi-static tension
using the Instron® 8862 system (Instron, MA, USA) with a maximum force of 100 kN and an accuracy of ±0.002% of load cell capacity or 0.5% of indicated load. All tests were performed at room temperature until plate failure. Failure is determined by either plate crack, breakage or extreme plastic deformation, whichever occurred first. The test considered a 0.5 mm/min displacement rate. Strains and displacements were measured using a standard straight profile knife edged extensometer (2630-106, Instron, USA). Tests were performed in duplicate. Force and displacement histories were documented at a sampling rate of 10 Hz, and the mean slope of the curve (i.e. stiffness) measured. The equivalent Young’s modulus was obtained through the following procedure:

i. From the tensile test, and considering the linear elastic region, the following correlation between applied force (F) and associated displacement (δ) determined by the extensometer can be established as follows:

\[ F = \kappa \delta \]  

(7.3)

where \( \kappa \) is the stiffness.

ii. Knowing the cross-section area and the initial length of each plate equation (7.3) can be transformed into:

\[ \sigma = E \varepsilon \]  

(7.4)

where \( \sigma \) is the stress, \( \varepsilon \) is the strain and \( E \) is the equivalent Young’s modulus determined from the slope of the stress-strain curve. The yield stress was calculated by measuring the slope of the stress-strain curve from a 0.2% strain offset.

7.5.2 Surface roughness

Surface roughness was determined using a coaxial laser confocal microscope (Keyence, VK-X200, Japan) by scanning a zone of 500 × 750 μm². The arithmetic average of the surface roughness, Ra, and the average arithmetic height of the surface, Sa, of both produced EBM plates and commercial plates were calculated considering 10 measurements with an area of 100 × 100 μm² over a length of 500 μm using the VK Analyser 3.3 software (Keyence, Japan).

7.5.3 Hardness

Hardness was measured using the Vickers hardness (HV) tester-Armstrong Pedestal considering a normal load of 10 kgf applied for 12 s as shown in Figure 7.2a. Previously, the surface of the EBM bone plate was prepared using silicon carbide paper with a grid of 400, 800, 1200 and 2400 grits and polished with 1-μm diamond particle paste. A total of 5 indentations were taken as shown in
Figure 7.2b: measurements 1, 4 and 5 along the y-axis and measurements 1, 2 and 3 along the x-axis. The Vickers hardness was calculated replacing the average length of the diagonal, measured by optical microscopy from all the indentations in millimetres according to the following equation (Denry and Holloway 2004):

\[ H_v = \frac{18.55F}{d^2} \]  

(7.5)

where \( F \) is the load and \( d \) is the arithmetic mean of the diagonals.

7.5.4 Morphological characterisation
The morphology of the EBM plates was investigated using scanning electron microscopy (SEM) with a Hitachi S300N microscope (Hitachi, Japan), using an accelerating voltage of 15.0 kV.

7.5.5 In vitro biological testing
Biological tests were conducted to understand the impact of the surface characteristics of the EBM plates and to investigate the potential need for any post-process in order to establish a good biological bonding with the surrounding tissue. A commercial plate was used as a reference.

7.5.5.1 Sample preparation
EBM and commercial bone plates were cut into samples to fit a 12-well plate using an electron discharge machine. Samples were sterilised by sonication whilst the samples were immersed within 80% ethanol for 30 min, rinsed with distilled water and then autoclaved for 30 min at 121 °C.
7.5.5.2 Cell culture and seeding

*In vitro* tests were performed using human osteosarcoma cells Saos-2 (ATCC® HTB-85™) (ATCC, Manassas, VA, USA). Cells were cultured in T75 tissue culture flasks (Sigma-Aldrich, Dorset, UK) with McCoy’s 5A Medium (ATCC® 30-2007™) (ATCC, Manassas, Virginia, USA) based media containing 15% foetal bovine serum, supplemented with penicillin and streptomycin (1%) until 80% confluence and harvested using 0.05% trypsin-EDTA solution (Thermo Fisher Scientific, Waltham, MA, USA) (Huang et al. 2018). Cells were seeded on the samples at a density of $5 \times 10^4$ cells in 200 μL of media per sample, and the cell-seeded samples incubated at standard conditions (37 °C, 5% CO$_2$ and 95% humidity) for 3 h to allow cell attachment, before the addition of 2 mL fresh media (Huang et al. 2018). Seeded samples were transferred into a new well plate after 24 h. Cell culture media was changed every 3 days.

7.5.5.3 Cell viability and morphology

EBM and commercial samples were cultured up to 14 days to assess cell morphology and attachment through SEM. Samples were fixed with a 3% glutaraldehyde solution (Sigma-Aldrich, UK) for 30 min at room temperature, rinsed twice with phosphate-buffered saline (PBS) solution, dehydrated with a graded ethanol series (50%, 60% 70%, 80%, 90% and 100% (twice)), in 50:50 ethanol/hexamethyldisilazane (HMDS, Sigma-Aldrich, Dorset, UK) and then in 100% HMDS, for 15 min at each step, and allowed to evaporate overnight to remove HMDS (Huang et al. 2018). Laser confocal microscopy was employed to examine cell viability through a Live/Dead stain kit (Thermo Fisher Scientific, Waltham, MA, USA) for days 4 and 14. The Live/Dead staining solution was prepared according to manufacturer’s instruction. Briefly, a 4 μm M EtHD-1 and of 2 μm M calcein AM working solution was prepared in PBS. The samples were washed with PBS prior to the addition of the staining solution and incubated for 45 min at room temperature. Cell viability images were obtained using an inverted Leica TCS SP5 confocal microscope (Leica Microsystems, Germany).

7.5.6 Statistical analysis

The statistical analysis was performed using Minitab 18 software (PA, USA) considering one-way analysis of variance (ANOVA) with Tukey test. Differences were considered statistically significant at p < 0.05.
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7.6 Results

7.6.1 Topology optimisation and produced bone plates

For the three different plate designs (four, six and eight holes), nine designs were obtained as shown in Figure 7.3. The EBM produced bone plate after support structure removal are shown in Figure 7.4. Parts were not submitted to any post-processing operation or thermal treatment.

![Figure 7.3](image_url)

**Figure 7.3** Topology optimised plates. Four-hole plates considering a) 25% volume reduction, b) 45% volume reduction and c) 75% volume reduction; Six-hole plates considering d) 25% volume reduction, e) 45% volume reduction, f) 75% volume reduction; Eight-hole plates considering g) 25% volume reduction, h) 45% volume reduction and i) 75% volume reduction.
Figure 7.4 EBM produced bone plates. Four-hole designs considering a) 75% of volume reduction, b) 45% of volume reduction, c) 25% of volume reduction; Six-hole designs considering d) 75% of volume reduction, e) 45% of volume reduction, f) 25% of volume reduction; Eight-hole designs considering g) 75% of volume reduction, h) 45% of volume reduction and i) 25% of volume reduction; and initial designs considering j) four-holes, k) six-holes and l) eight-holes.
7.6.2 Surface roughness
Surface roughness of the EBM plates are presented in Figure 7.5. Results showed arithmetic average of the surface roughness, Ra of 19.15 ± 4.94 μm and average arithmetic height of the surface, Sa of 12.42 ± 1.11 μm for the EBM plates, whereas the commercial plates presented an average Ra of 0.37 ± 0.03 μm and Sa of 0.42 ± 0.03 μm. Significant difference was observed (p < 0.05) between the samples for both Ra and Sa.

![Figure 7.5](image)

**Figure 7.5** a) Surface of EBM produced bone plate and b) the surface roughness height across a line of the EBM surface.

7.6.3 Hardness
EBM-produced plates presented a high hardness compared to commercial plates. Results showed that the EBM plates mean hardness is 326.9 HV 10 ± 3.35 and the mean hardness of the commercial plates is 275.98 HV 10 ± 7.75. The hardness between the samples showed significant difference (p < 0.05).

7.6.4 Tensile tests
A comparison between experimental and numerically predicted tensile results are presented in Figures 7.6 to 7.8. A good approximation was obtained with differences not higher than 7%. The highest equivalent stiffness values were observed for the initial designs. Results also show high values of stiffness in plates containing a smaller number of holes (293,810N/mm for four-hole plate, 242,634 N/mm for six-hole plate and 226,132 N/mm for eight-hole plate). Moreover,
stiffness decreases by increasing volume reduction (228,050 N/mm for four-hole plate, 228,418 N/mm for six-hole plate and 216,226 N/mm for eight-hole plate and 25% of volume reduction; 152,648 N/mm for four-hole plate, 118,970 N/mm for six-hole plate, 216,147 N/mm for eight-hole plate and 45% of volume reduction; 103,674 N/mm for four-hole plate, 52,011 N/mm for six-hole plate, 55,824 N/mm for eight-hole plate and 75% of volume reduction).

A comparison of the equivalent Young’s modulus values of all considered plates is provided in Figure 7.9. Results show a decrease in the equivalent Young’s modulus in the optimised plates. However, optimised plates considering 25% of volume reduction are three times stiffer than the cortical bone. The commercial plates resulted in an equivalent Young’s modulus of around 40 GPa. Optimised six- and eight-hole plates considering 75% of volume reduction present values within the cortical bone region.

Table 7.2 presents the yield stress values from the tensile tests for all considered plates. In the case of commercially available plates, it was considered the maximum value between the four commercial plates investigated in this Chapter. The yield stress values of the initial plates, four-hole 25% and 45% volume reduction and eight-hole 25% volume reduction are 1.5 to 3 times higher than the commercial plates, whilst the four-hole 75% volume reduction and six-hole 25% volume reduction plate showed approximately similar values. The two optimised bone plates that resulted with similar cortical bone modulus, the 75% volume reduction for the six- and eight-hole bone plates, resulted in around half of the yield of the commercial plates and the maximum force reached before yield was around 4191N and 5481 N, respectively. The equivalent stiffness of the four-hole plates (75%, 45% and 25% volume reductions) were significantly different (p < 0.05) than the four-hole initial plates. Six-hole plates (75% and 45% volume reductions) showed significant difference between the six-hole initial plate with no significance when comparing with the 25% volume reduction. Similar, significant difference was observed in the eight-hole plates. In terms of the equivalent Young’s modulus, the four-hole 45% and 75% volume reduction, six-hole 75% volume reduction and eight-hole 45% and 75% volume reduction plates were significantly different (p < 0.05) comparing with the commercial plates. Similarly, the EBM (six-hole bone plates and 45% and 75% of volume reduction and eight-hole plates with 75% of volume reduction) presented significant lower yield stress than commercial plates (p < 0.05).
Figure 7.6 Four-hole bone plates; a) initial design, b) 25% reduction, c) 45% reduction and d) 75% reduction.
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Figure 7.7 Six-hole bone plates; a) initial design, b) 25% reduction, c) 45% reduction and d) 75% reduction.
Figure 7.8 Eight-hole bone plates; (a) initial design, (b) 25% reduction, (c) 45% reduction and (d) 75% reduction.
Figure 7.9 Summary of the equivalent Young’s modulus values for the considered commercial and EBM plates and their position with respect to the cortical bone. ID4: Four-holes initial design; 4H 25%: Four-holes 25% volume reduction; 4H 45%: Four-holes 45% volume reduction; 4H 75%: Four-holes 75% volume reduction; ID6: Six-holes initial design; 6H 25%: Six-holes 25% volume reduction; 6H 45%: Six-holes 45% volume reduction; 6H 75%: Six-holes 75% volume reduction; ID8: Eight-holes initial design; 8H 25%: Eight-holes 25% volume reduction; 8H 45%: Eight-holes 45% volume reduction; 8H 75%: Eight-holes 75% volume reduction.
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Table 7.2 Yield stresses of all bone plates.

<table>
<thead>
<tr>
<th>Plate</th>
<th>Volume reduction, %</th>
<th>Yield stress, MPa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial</td>
<td>300</td>
</tr>
<tr>
<td>Four holes</td>
<td>25</td>
<td>281</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>250</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>160</td>
</tr>
<tr>
<td></td>
<td>Initial</td>
<td>346</td>
</tr>
<tr>
<td>Six holes</td>
<td>25</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>91</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>Initial</td>
<td>368</td>
</tr>
<tr>
<td>Eight holes</td>
<td>25</td>
<td>359</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>279</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>104</td>
</tr>
<tr>
<td>DePuy Synthes plate</td>
<td></td>
<td>170</td>
</tr>
</tbody>
</table>

7.6.5 Cell morphology and viability
SEM images of the surface of both EBM and commercial plates are shown in Figure 7.10a and b, respectively. The cell seeded EBM plates after days 7 and 14 are shown in Figure 7.10c and e, respectively, whilst cells seeded on commercial plates after days 7 and 14 are presented in Figure 7.10d and f, respectively. Cell viability results are presented in Figure 7.11 for both EBM and commercial plates after days 4 and 14 of cell seeding. Results show that cells are proliferating and are viable on the EBM plates whilst in the case of commercial plates, fewer cells attached with a higher number of dead cells.
Figure 7.10 The SEM images before seeding of the surface topography of a) EBM bone plate and b) commercial bone plate. Cell morphology on c) EBM after 7 days of cell culture, d) commercial after 7 days of cell culture, e) EBM after 14 days of cell culture, and f) commercial after 14 of cell culture.
Figure 7.11 Cell viability images of the EBM a) after day 4 and b) after day 14; and c) the commercial plates after day 4 and d) day 14, presenting red for dead cells and green for live cells. Scale bar 200 μm.

7.7 Discussion

The topology optimisation method is based on the material redistribution, eventually leading to a material reduction whilst optimising stiffness. As also previously reported, topology optimisation can be used to create lightweight structures capable of keeping satisfactory mechanical performance (Sutradhar et al. 2016, Wang et al. 2016c). By imposing high volume reduction, the effect of material removal becomes the significant contributing factor to an overall reduction in the stiffness of the plates. This was previously reported by the authors with 2D designed plates (Al-Tamimi et al. 2017). Different volume reductions were considered (25%, 45% and 75%) but the obtained volume reduction was not always exactly the same as the imposed value. In the case of eight-hole bone plates and imposed volume reductions of 25% and 45%, no significant
differences were observed on the optimised shapes in terms of equivalent stiffness as the optimisation procedure stopped at relatively similar volume reductions. This is due to the fact that the optimisation procedure stops once it reaches a local optimal value, which is not necessarily the global one. It can also be explained by equation 7.1a, which shows that the optimisation process approximates to the user-defined volume, and to the fact that the optimisation process is mesh-dependent. However, the effect of the mesh on the topology optimisation is not considered here. An automatic mesh generation procedure was considered.

The function of a bone plate is to resist the stresses occurring in the physiological environment whilst stabilising the fractured bone. Therefore, avoiding mechanical failure as well as plastic deformation is critical. In this research, both the elastic and plastic deformations were considered. The elastic linear region was analysed to measure both the equivalent stiffness and equivalent Young’s modulus. Equivalent stiffness values were used to characterise each family of bone plates (four, six and eight holes). Results show, for all cases, a reduction on the equivalent stiffness by increasing the volume reduction. A good approximation between numerical and experimental results was also obtained, showing that the computational tools considered in this research represent a viable approach to design and simulate their behaviour before expensive fabrication and experimental steps. Results also show that topology optimisation is a viable tool to redesign bone plates, reducing their equivalent stiffness and consequently the stress shielding effect. The equivalent Young’s modulus was used to position the mechanical properties of produced plates and commercial ones against cortical bone. Initial designed plates present higher equivalent Young’s modulus values than commercial plates. These differences are reduced through topology optimisation. Although as mentioned earlier, taking into consideration that the dimensions of the bone plates defer from one another, the EBM plates containing six holes (45% of volume reduction) and four holes (75% of volume reduction) show equivalent Young’s modulus similar to commercial plates. However, produced plates containing six and eight holes (75% of volume reduction) show a significant reduction in the equivalent Young’s modulus, presenting values in the cortical bone region, which is not possible to achieve with the commercially available plates. This confirms that topology optimisation can be used to create lightweight plates (less material volume) with reduced equivalent stiffness and sufficiently strong without impairing the plate’s mechanical performance, thus minimising the stress-shielding phenomena.
Chapter Seven: Topology optimised metallic bone plates produced by electron beam melting: a mechanical and biological study

This Chapter is limited in terms of considering the mechanical stability of the topology optimised bone plates, assuming that a significant decrease in the material volume could result in stress concentration and plate failure, leading to a delay of bone healing. However, the authors are addressing this limitation by analysing the plastic region of the mechanical tests, considering the commercial plate (i.e. DePuy Synthes LCP, the gold standard for bone fracture healing) as a reference to base the stability of the bone plates in terms of the yield stress results. Most of the bone plates presented a higher yield stress with two plates (four-hole 75% volume reduction and six-hole 25% volume reduction plates) showing similarity with the commercial ones in terms of yield behaviour. The resulting yield stresses for the two bone plates that have similar equivalent Young’s modulus to the cortical bone showed approximately half of the commercial bone plate yield. However, if we consider that the maximum force required to yield the two bone plates are 4191 N (six holes and 75% of volume reduction) and 5481 N (eight hole and 75% of volume reduction), this is still clinically acceptable as it corresponds to 6 to 8 times the bodyweight of a 70-kg patient.

EBM-produced plates were not submitted to any postprocessing treatment (e.g. elimination of residual stresses, surface finishing and polishing). This was decided to avoid the use of any additional time, consumables and costly steps and to avoid any additional effects of the post-processing on the topography, microstructure and properties of the plates, partially answering the question: is it necessary to perform any post-processing to produce plates with adequate physical and biological characteristics? Due to the nature of the EBM process (powder bed fusion technique), rough parts were produced. As observed by Karlsson et al. (2013) and Tong et al. (2017), the surface characteristics of EBM parts are influenced by the raw powder characteristics (e.g. particle size) and processing conditions (e.g. scan speed) that result in the presence of both partially melted particles and fully melted ones (flattest zones aligned with the build direction). Despite presenting high surface roughness compared to commercial plates, produced plates were not polished to understand if the rough values were within an acceptable range to allow cell attachment and cell-cell communication. This was investigated by accessing the in vitro response of osteosarcoma cells seeded on both EBM and the commercial plates. Contradictory results were previously reported regarding the biological influence of smooth and rough surfaces. According to de Wild et al. (2013), EBM implants should be surface treated as their study showed improved biological response on acid-etched and sand-blasted implants.
Pattanayak et al. (2011) showed that heat treated smoother implants improve the osteo-integration of the implants. However, Thomsen et al. (2009) and Bertollo et al. (2012) did not observe significant differences between no postprocessed implants and conventionally wrought machined and plasma-sprayed implants. Ponader et al. (2008) observed high cell attachment and proliferation in EBM parts with Ra values lower than 24.9 μm and reduced cell proliferation values in rough parts (Ra higher than 56.9 μm), surprisingly showing that the highest proliferation rate and cell viability were obtained with highly smooth surfaces (Ra of 0.07 μm). In contrast, the results presented in this Chapter showed that surface roughness of the produced plates (19.15 ± 1.56 μm) allowed a high level of cell attachment and proliferation suggesting that no polishing post-processing step is required after the plate printing phase. Results also show high cell attachment on the EBM rough plates than in the commercial plates with a smooth surface (0.37 ± 0.01 μm). Cell viability studies also show a significant number of dead cells in the commercial plates after 14 days of cell seeding compared to the EBM plates. This can be partially explained by the surface topography of the commercial bone plates. However, further investigation is required to elucidate the role that ion release and wettability have on cell interactions.

Surface hardness also has an important role on cell attachment and proliferation and differentiation. Several studies reported that harder substrates promote osteogenesis and increase cell attachment (Park et al. 2011, Kuo et al. 2014). The results show that EBM plates present higher surface hardness (326.9 ± 3.35) than commercial plates (275.98 ± 7.75), both exhibiting significantly higher values compared to cortical bone hardness (i.e. ~ 50 HV) (Evans et al. 1990).

### 7.8 Conclusion

This Chapter presents an integrated strategy combining topology optimisation and additive manufacturing to produce bone fixation plates minimising the stress-shielding phenomena. From the results, it is possible to conclude the following:

- Topology optimisation can be used to design plates minimising the stress-shielding effect. For high values of volume reduction, the effect of material removal strongly contributes to an overall reduction of the equivalent stiffness of the designed bone fixation plates.
- Designed plates were successfully produced using EBM.
- No significant mechanical differences were observed between produced and designed, showing a good accuracy between numerical and experimental results. It was also possible to design plates with equivalent Young’s modulus values in the region of cortical bone.
Chapter Seven: Topology optimised metallic bone plates produced by electron beam melting: a mechanical and biological study

- No post-processing seems to be required to establish a good biological bonding with the surrounding tissue. High cell attachment and proliferation was observed on rough EBM plates, which also presents higher surface roughness than commercial plates. Contrary to other studies, results also show that EBM parts with no postprocessing present higher biocompatibility than commercially available plates.
Chapter Eight

Mechanical, biological and tribological behaviour of fixation plates 3D printed by Electron Beam and Selective Laser Melting
Chapter Eight  Mechanical, biological and tribological behaviour of fixation plates 3D printed by Electron Beam and Selective Laser Melting*

Commercially available fixation plates are built using metallic biocompatible materials such as titanium and its alloys and stainless steel. However, these plates show a stiffness mismatch comparing to bone, leading to stress shielding and bone loss. In this Chapter, we investigate the combined use of topology optimisation and additive manufacturing to print fixation plates with reduced stiffness and improved biological performance. Ti-6Al-4V plates were topology optimised for different loading conditions and volume reductions and printed using electron beam melting and selective laser melting. The effect of processing conditions on mechanical properties, hardness, wear resistance and surface roughness were analysed. Results show acceptable wear resistance values for a medical device and a reduction of stress shielding by increasing volume reduction. It is also shown that no polishing is required as 3D printed plates are able to support cell attachment and proliferation. In comparison to commercial plates, 3D printed ones show significantly better biological performance. For the same design, SLM plates present higher mechanical properties while EBM plates present better cell attachment and proliferation. The topology optimised designs obtained in Chapter Four were used in this Chapter for further analysis. The EBM manufactured plates in this Chapter are the same as those in Chapter Seven.

8.1 Introduction

Bone fracture due to accidents or diseases represent an important healthcare problem. Worldwide, due to age population problems the number of hip fractures is expected to be 6.3 million in 2050 with an estimated cost of $13.15 billion (Johnell 1997). In 2016, in the UK 11,000 patients required revision operations due to implant failure and this number will significantly increase in the next decade (Green et al. 2016).

In most cases, fixation devices are used to return the fractured bone to its original anatomy and stabilise it. These fixation devices are commercially available as either pins, rods, plates and

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screws. However, they were not properly designed and, consequently, stress shielding and bone loss problems are common.

Previously we demonstrated that topology optimisation is a viable tool to redesign fixation plates, minimising equivalent stiffness and consequently the stress shielding effect (Al-Tamimi et al. 2017).

Topology optimisation minimises the compliance (C) of a structure considering a volume constraint and is mathematically described as follows (Bendsøe and Sigmund 2004):

$$\min_{\rho_e} C(\rho_e) = f^T \cdot u$$

$$\sum_{e=1}^{N} \rho_{e} v_{e} \leq V^*,$$  \hspace{1cm} (8.1a)

subject to
$$\left( \sum_{e=1}^{N} \rho_{e} p_{e} K_{e} \right) u = f,$$ \hspace{1cm} (8.1b)

$$0 < \rho_{0} \leq \rho_{e} \leq 1,$$ \hspace{1cm} (8.1c)

where \( f \) is the force vector, \( K_{e} \) is the element stiffness matrix, \( u \) is the displacement vector, \( V^* \) is the user-defined fraction volume, \( p \) is the penalisation factor, \( \rho_{e} \) is the element density, \( \rho_{0} \) is the initial density and \( v_{e} \) is the volume of each element. As observed topology optimisation seeks to find the optimal load path for a particular load and boundary conditions searching for a minimum compliance design. However, as previously reported reducing the density of an element which reduces the stiffness of that particular element becomes the dominant effect, contributing to the reduction of the overall equivalent stiffness.

The two most common powder bed fusion techniques are electron beam melting (EBM) and selective laser melting (SLM) consist of the same nature but different in their processing conditions (Murr 2015, Khorasani et al. 2019). These conditions affect the surface and microstructure characteristics. Consequently, the mechanical, biological and tribological performances of the built part are affected.

In a previous paper authors used Electron Beam Melting to 3D print topology optimised fixation plates considering different geometries and volume reduction (Al-Tamimi et al. 2019b). Results show that some redesigned printed plates present mechanical properties similar to the cortical bone able to withstand physiological loads and that there is no need to post-process the EBM plates in order to establish a good biological bonding with the surrounding tissue. This paper investigates two different powder bed fusion techniques, electron beam melting and selective laser melting, to 3D print topology optimised plates. Key research questions being addressed are:
Chapter Eight: Mechanical, biological and tribological behaviour of fixation plates 3D printed by Electron Beam and Selective Laser Melting

- How the different processing conditions, influencing the microstructure, surface hardness and roughness affect the biological performance of the printed plates?
- What is the impact of the fabrication technique on a strategy to reduce the stress shielding?
- Are the plates 3D printed using standard powder bed fusion operating conditions and corresponding Ti-6Al-4V powder suitable for medical applications without post-processing?

Printed fixation plates are compared to two commercially available plates, the DePuy Synthes 4.5/5.0 narrow locking compression plates (in commercial pure Titanium) and Zimmer Biomet anatomic locked plating system plates (in Ti-6Al-4V).

### 8.2 Design of the fixation plates

Two different locking compression plates with four- and eight-screw holes were designed in Solidworks (Dessault Systems, France) as shown in Figure 8.1. All plates have a length of 180 mm, a width of 14 mm and a thickness of 5 mm. Plates were redesigned using the Solid Isotropic Microstructure with Penalisation (SIMP) approach assuming different loading conditions (compression, bending, torsion and combination of all these loads) and volume reductions (45% and 75%) following the procedure previously described (Al-Tamimi et al. 2017). Topology optimised designs were exported to the Magics software (Materialise, Belgium), where they were tessellated (STL file generation) and exported to the additive manufacturing machines.

![Figure 8.1 Design domains of fixation plates considered for optimisation; a) four screw hole and b) eight screw hole.](image)

### 8.3 Fixation plates fabrication

Two powder bed fusion techniques were used to 3D print the plates: electron beam melting (EBM) (Arcam A2 model, Arcam, Sweden) and selective laser melting (SLM) (250HL, SLM Solutions)
Lübeck, Germany). Ti-6Al-4V powders were supplied by Arcam for the EBM system and TLS Technik GmbH (Bitterfeld, Germany) for the SLM system.

The chemical composition of the initial powders is presented in Table 8.1. The powders are spherical in shape, having a size distribution between 45 and 100 µm (EBM powder) and between 25 to 45 µm (SLM powder).

**Table 8.1** Chemical composition of the initial Ti-6Al-4V powders.

<table>
<thead>
<tr>
<th>Element</th>
<th>Chemical Composition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ti</td>
<td>89.607</td>
</tr>
<tr>
<td>Al</td>
<td>6</td>
</tr>
<tr>
<td>V</td>
<td>4</td>
</tr>
<tr>
<td>C</td>
<td>0.03</td>
</tr>
<tr>
<td>Fe</td>
<td>0.1</td>
</tr>
<tr>
<td>O</td>
<td>0.15</td>
</tr>
<tr>
<td>N</td>
<td>0.01</td>
</tr>
<tr>
<td>H</td>
<td>0.003</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Element</th>
<th>Chemical Composition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ti</td>
<td>89.866</td>
</tr>
<tr>
<td>Al</td>
<td>5.9</td>
</tr>
<tr>
<td>V</td>
<td>3.9</td>
</tr>
<tr>
<td>C</td>
<td>0.01</td>
</tr>
<tr>
<td>Fe</td>
<td>0.19</td>
</tr>
<tr>
<td>O</td>
<td>0.12</td>
</tr>
<tr>
<td>N</td>
<td>0.01</td>
</tr>
<tr>
<td>H</td>
<td>0.004</td>
</tr>
</tbody>
</table>

The printing process, using a powder bed fusion technique starts with the powder being spread in the working platform, scanned (based on the sliced pattern), and melted into a molten pool using a heat source (i.e. a laser beam controlled by two rotating lenses above a certain angle lens for the SLM or an electron beam for the EBM). Once the scanning is completed, a new layer is deposited above the scanned layer and the steps are repeated until the part is built.

The EBM system consists of an electron beam emitted via a hot tungsten filament, operated at 60 kV under vacuum pressure of 2.0 x10⁻³ mBa, scanning speed of 4530 mm/s, beam focus offset of 3 mA, line offset of 0.1 mm and layer thickness of 50 µm. The substrate plate temperature was kept around 600 °C and the build temperature was defined to be around 750 °C. The SLM processing conditions were: spot size of around 80 µm, laser power of 100W, scanning speed of 375 mm/s, hatching distance of 130 µm, and a layer thickness of 30 µm. The substrate plate was preheated to 200 °C. In both cases, support structures were removed manually using pliers, and parts were not submitted to any further post-processing operation.

### 8.4 Fixation plate characterisation

#### 8.4.1 Plate preparation

Fixation plates were cut using electron discharge machine (EDM) (FI 440 CC, GF machining solutions, Switzerland) using the parameters shown in Table 8.2. All plates were cleaned in an
ultrasonic bath submerged in 80% ethanol and then washed thoroughly by distilled water. Plates for the biological study were sterilised in an autoclave for 30 minutes at 121 °C.

**Table 8.2** EDM parameters used for cutting the fixation plates.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy duration of the pulse (μs)</td>
<td>0.50</td>
</tr>
<tr>
<td>Average voltage (V)</td>
<td>35.0</td>
</tr>
<tr>
<td>Wire speed (mm/min)</td>
<td>10.0</td>
</tr>
<tr>
<td>Time between 2 pulses, μs</td>
<td>23.0</td>
</tr>
<tr>
<td>Wire tension (g)</td>
<td>1.30</td>
</tr>
<tr>
<td>Wire material</td>
<td>AC Brass 900</td>
</tr>
</tbody>
</table>

8.4.2 Density

The density was measured according to the standard Archimedes method (ASTM B962 – 17) immersing the fixation plates in water.

8.4.3 Surface roughness

Surface roughness ($R_a$) was determined using a coaxial laser confocal microscope (VK-X200, Keyence, Japan) by scanning a zone of 500 x 750 μm$^2$. The average surface roughness, $R_a$, was calculated considering 10 measurements over a length of 500 μm using the VK Analyser 3.3 software (Keyence, Japan).

8.4.4 Hardness, microstructure and XRD

In order to determine the microhardness and microstructure the surface of the fixation plates was prepared using Silicon carbide paper with a grid of 400, 600, 800, 1200 and 2400 grits and polished with 9 and 1 μm diamond particle paste. At least five indentations were considered. Vickers microhardness (Indentec, UK) was measured considering a normal load of 0.3 Kgf applied for 10 seconds. The Vickers hardness (HV) was measured by optical microscopy from all the indentations according to the following equation:

$$HV = \frac{1.8544F}{d^2}$$  \hspace{1cm} (8.2)

where F is the load and d is the arithmetic mean of the diagonals.
The grinded and polished plates were examined using the FE-SEM (Jeol, Japan) scanning electron microscopy (SEM), equipped with an Energy-Dispersive X-ray (EDX) with a voltage of 15.0 kV. Additionally, the plates were used to reveal the microstructure by etching in Kroll’s reagent (300 mL H$_2$O, 100 mL HNO$_3$ and 100 mL HF). The phase analysis was performed using an X-ray diffraction (XRD) with Cu-K$_\alpha$ radiation ($\lambda$=0.145nm) and scan speed 2 deg/min using X-Ray diffractometer (Bruker, Germany).

8.4.5 Mechanical performance

Topology optimised fixation plates were mechanically evaluated considering tensile, torsion and bending tests. Each optimised plate was tested considering the load case assumed for the topology optimisation i.e. four-point bending for plates optimised for bending loading conditions; torsion for plates optimised for torsion loading conditions; and tensile for plates optimised for compression and combined loading conditions. All tests were performed at room temperature until plate failure. Failure was determined by either plate crack, breakage or permanent plastic deformation, whichever occurred first.

8.4.5.1 Tensile test

Tensile tests were performed using the Instron® 8862 system (Instron, MA, USA) with a maximum force of 100 kN, with a controlled displacement rate of 0.5 mm/min. Strains and displacements were measured using a standard straight profile knife edged extensometer (2630-106, Instron, USA). Tests were performed in duplicate. Force and displacement histories were documented at a sampling rate of 10 Hz, and the mean slope of the curve (i.e. equivalent stiffness) measured. The equivalent stiffness was obtained through the following procedure:

i) From the tensile test, and considering the linear elastic region, the following correlation, between applied force ($F$) and associated displacement ($\delta$) determined by the extensometer, can be established as follows:

$$F = \kappa \delta \quad (8.3)$$

where $\kappa$ is the equivalent stiffness.

ii) Knowing the cross-section area and the initial length of each plate, equation (8.3) can be transformed into
\[ \sigma = E \varepsilon \]  

(8.4)

where \( \sigma \) is the stress, \( \varepsilon \) is the strain and \( E \) is the equivalent elastic modulus determined from the slope of the stress strain curve.

### 8.4.5.2 Torsion test

Torsion tests were performed using a servo-hydraulic tension/torsion Instron® 8862 (Instron, United States) machine with a maximum torque capacity of 1000 Nm and 45° deflection with a controlled deflection of 5°/min. The strain was measured by a torsional Epsilon (Model 3350, Epsilon, USA) extensometer with a gauge length of 25 mm and a shear strain angle of +/- 3°. Tests were performed in duplicate. Moment and deflection histories were documented, and the mean slope of the curve (i.e. equivalent stiffness in Nmm/rad) measured.

### 8.4.5.3 Four-point bending test

Four-point bending tests were performed following the British Standard (BSI) for determining the stiffness of a fixation plate (BS 3531-23.1: 1991 ISO 9585:1990) using the Instron 5969 (Instron, United States) machine fitted with a 10kN load cell with displacement rate of 1 mm/minute. This test considers four rollers of 10 mm in diameter as shown in Figure 8.2. The distance between the load and support rollers (\( h \)) and the load rollers span (\( k \)) values were 30.5 mm and 75 mm for the four-hole plate and 22.5 mm and 45 mm for the eight-hole plate. The displacement was measured using an Imetrum universal video extensometer (Flax Bourton, UK) and three replicas were considered. The equivalent bending stiffness was measured as follows:

\[ S_B = \frac{(4h^2 + 12hk + k^2)Sh}{24} \text{ (N.m}^2) \]  

(8.5)

where \( S_B \) is the bending stiffness and the slope (\( S \)) was measured from the load-displacement curve.

The equivalent bending elastic modulus was calculated as follows:

\[ E_B = 0.17L^3S/bd^3 \]  

(8.6)

where \( E_B \) is the equivalent bending elastic modulus, \( L \) is the support span, \( b \) is the plate’s width and \( d \) is the plate’s thickness.
Chapter Eight: Mechanical, biological and tribological behaviour of fixation plates 3D printed by Electron Beam and Selective Laser Melting

8.4.6 Tribological study

Wear rate and coefficient of friction of both EBM and SLM plates were analysed using a pin-on-disc test (Pod-2, Teer Coatings Ltd, UK). An alumina bearing ball (Al₂O₃) with a 5 mm diameter, was used as the friction pin (Ceratec Technical Ceramics, The Netherlands). The pin-on-disk experiment was conducted for 9000 s, at a constant sliding speed of 5.24 cm/s and a constant load of 2, 6, 10 and 14 N. Tests were performed in triplicate, in a lubricated condition using Phosphate Buffered Saline (PBS) (Sigma Aldrich, USA), under a controlled temperature of 37 °C. The coefficient of friction was recorded as function of time during the experiments.

The wear rates were calculated using the following equation:

\[ W = \frac{v}{F_{\text{applied}}} \times \frac{1}{\nu \times t} \]  \hspace{1cm} (8.7)

where \( W \) is the wear rate, \( F \) is the applied load, \( \nu \) is the sliding speed and \( t \) is the duration of the experiment. The wear volumes (\( V \)) of the plates after testing were estimated from surface scanners taken out by confocal microscopy (VHX-500, Keyence, Japan). The wear tracks were observed by scanning electron microscopy (Q-250, Thermo Fisher, Waltham, USA) in back-scattering electron mode (BSE) and their chemical composition was analysed by energy dispersive x-ray spectroscopy (EDS), using an acceleration voltage of 20 kV.
8.4.7 Biological study

8.4.7.1 Cell culture/cell seeding

In vitro tests were performed using human adipose-derived bone osteosarcoma cells, Saos-2 (ATCC® HTB-85™) (ATCC, Manassas, Virginia, USA). Cells were cultured in T75 tissue culture flasks (Sigma-Aldrich, Dorset, Uk) with McCoy's 5A Medium (ATCC® 30-2007™) (ATCC, Manassas, Virginia, USA) based media containing 15% fetal bovine serum, supplemented with penicillin and streptomycin (1%) until 80% confluence and harvest using 0.05% trypsin-EDTA solution (Thermo Fischer Scientific, Waltham, USA) (Huang et al. 2018). After cell counting, cells were seeded on the fixation plates (200 μL of media containing around 5x10⁴ cells per plate), and incubated at standard conditions (37°C under 5% CO2 and 95% humidity) for 3 hours to allow cell attachment, before the addition of 5 mL fresh based media.

8.4.7.2 Cell proliferation

Cell proliferation was assessed at 1, 4 and 7 days after cell seeding using the resazurin assay, also known as the Alamar Blue assay (reagents from sigma-Aldrich, Dorset, UK) (Huang et al. 2018). The media was changed every 3 days. At each time point the cell-seeded plates were placed in a new 6-well plate and 5 μL Alamar Blue solution 0.001% (v/v) in culture media was added to each well. The plates were incubated for 4 hours under standard conditions. After incubation 150 μL of each plate was transferred to a 96-well plate and the fluorescence intensity measured at 530 nm excitation wavelength and 590 nm emission wavelength with a spectrophotometer (sunrise, Tecan Mannedorf, Zurich, Switzerland). Tests were performed in triplicate.

8.4.7.3 Cell viability

Laser confocal microscopy was employed to further examine cell viability through a Live/Dead stain kit (Thermo Fischer Scientific, Waltham, MA, USA) at day 4 and 7. The live/dead stain was prepared through adding 20 μL of 2 mM EtHD-1 stock solution to 10 mL of sterile Phosphate Bovine Serum (PBS) and the reagents were combined via transferring 5 μL of 4 mM calcein AM stock solution to the 10 mL EthD-1 solution (Huang et al. 2018). The resulted solution was then added directly to the plates. Confocal images were obtained using a Leica TCS SP5 (Leica, Milton Keynes, UK) confocal microscope.
8.4.8 Statistical analysis
All results were analysed using Minitab 18 software (Pennsylvania, USA). All studies were analysed using ANOVA to compare between the results. The data were also analysed using the Tukey post hoc test by specific pairwise comparisons. Significance was set at $p<0.05$ with a confidence interval of 95%.

8.5 Results
8.5.1 Printed fixation plates and its characterisation
The EBM and SLM fixation plates were vertically 3D printed to maximise the use of the working platform as shown in Figure 8.3. The surface map and surface profile of the fixation plates are presented in Figure 8.4. The results of the surface roughness ($R_a$), density, chemical composition and microhardness of the EBM, SLM and commercial Synthes and Biomet fixation plates are shown in Table 8.3.

![Figure 8.3](image_url) 3D printed fixation plates on the build platform of a) EBM (150x150 mm) and b) SLM (280x280 mm).
As observed EBM fixation plates present higher surface roughness and hardness compared to SLM and commercial Synthes and Biomet plates. Statistical analysis show that all plates were significantly different (p<0.05) regarding the surface roughness. However, regarding the hardness, there is no statistical significance (p>0.05) between the EBM, SLM and Biomet. The EDX results presented in Table 8.3 confirmed the initial powder composition provided by the suppliers. Results also show that commercial Synthes plates are 100% made of Titanium while the Biomet plates are made of Ti-6Al-4V alloy with a composition similar to the printed plates.

Figure 8.4 Surface map of 500 x 750 µm² and surface profile of 500 µm for a) EBM and b) SLM, c) Biomet and d) Synthes.
Table 8.3 Characteristics of the EBM, SLM and Commercial parts.

<table>
<thead>
<tr>
<th></th>
<th>EBM</th>
<th>SLM</th>
<th>Synthes</th>
<th>Biomet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density (%)</td>
<td>99.0</td>
<td>98.0</td>
<td>98.0</td>
<td>96.0</td>
</tr>
<tr>
<td>Surface roughness R_{a} (µm)</td>
<td>19.16±4.94</td>
<td>15.11±2.25</td>
<td>0.37±0.04</td>
<td>0.45±0.06</td>
</tr>
<tr>
<td>Overall composition (wt.%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Al</td>
<td>5.9</td>
<td>5.82</td>
<td>0</td>
<td>5.65</td>
</tr>
<tr>
<td>V</td>
<td>4.19</td>
<td>3.77</td>
<td>0</td>
<td>4.08</td>
</tr>
<tr>
<td>Ti</td>
<td>90.12</td>
<td>90.00</td>
<td>100</td>
<td>90.27</td>
</tr>
<tr>
<td>Hardness</td>
<td>337.40±17.60</td>
<td>312.60±7.37</td>
<td>268.20±13.42</td>
<td>310.80±7.79</td>
</tr>
</tbody>
</table>

The microstructure of the EBM and SLM plates are shown in Figure 8.5. The EBM plates consist of α and β alloys with the beta phase appearing at the grain boundaries. The SLM plates present martensitic α’ needles. The XRD patterns of the fixation plates (Figure 8.6) present similar diffraction patterns. However, it is possible to observe in the EBM and Biomet pattern, a peak of body centered cubic β structure as pointed in Figure 8.5a for EBM, whilst the other peaks are identified as α/α’, which cannot be differentiated as they show the same hexagonal close-packed structure. EBM plates show higher peak intensities than the SLM, which can be attributed to the rougher structure of the EBM fixation plates and a finer α’ phase in the SLM fixation plates.

![Image of microstructure](image1)

**Figure 8.5** Microstructure of a) EBM and b) SLM.
8.5.2 Mechanical performance of printed fixation plates

8.5.2.1 Tensile test

Tensile test results for both EBM and SLM plates are presented in Figure 8.7. Results show that the equivalent stiffness decreases by increasing the volume reduction. As observed for plates optimised for compression loads and 45% of volume reduction, SLM plates present high equivalent stiffness. Differences between SLM and EBM plates tend to decrease by increasing the number of holes. In the case of plates containing eight-holes and optimised for 75% of volume reduction, the SLM plates present slightly high equivalent stiffness. For the four-hole plates optimised for 75% of volume reduction, EBM plates present slightly high equivalent stiffness. In the case of plates optimised for combined loads, SLM plates present high equivalent stiffness, except for four-hole plates and 45% of volume reduction in which the equivalent stiffness of both EBM and SLM plates is similar.
Figure 8.7 Tensile equivalent stiffness of compression and combined optimised for both EBM and SLM plates. 4H45: Four-hole plate with 45% reduction and 4H75: Four-hole plate with 75% reduction; 8H45: Eight-hole plate with 45% reduction and 8H75 and Eight-hole plate with 75%.

8.5.2.2 Torsion test

The equivalent torsional stiffness results are presented in Figure 8.8. Results show that the equivalent torsional stiffness decreases by increasing volume reduction. SLM plates present high equivalent torsional stiffness, except for four-hole plates and 45% of volume reduction in which the equivalent torsional stiffness of both EBM and SLM plates is similar. The equivalent torsional stiffness differences between EBM and SLM plates tend to increase by increasing the volume reduction.
Figure 8.8 Equivalent torsional stiffness of the torsion optimised EBM and SLM plates. 4H45: Four-hole plate with 45% reduction and 4H75: Four-hole plate with 75% reduction; 8H45: Eight-hole plate with 45% reduction and 8H75 and Eight-hole plate with 75% reduction.

8.5.2.3 Bending test

The resulted equivalent bending stiffness for both EBM and SLM fixation plates is shown in Figure 8.9. The equivalent bending stiffness decreases by increasing the volume reduction. In all cases, SLM fixation plates present high equivalent bending stiffness. Results also show that by increasing the volume reduction, the equivalent bending stiffness differences between EBM and SLM plates increases.
Chapter Eight: Mechanical, biological and tribological behaviour of fixation plates 3D printed by Electron Beam and Selective Laser Melting

Figure 8.9 Equivalent bending stiffness of initial and bending optimised cases of EBM and SLM plates considering a volume reduction. 4H45: Four-hole plate with 45% reduction and 4H75: Four-hole plate with 75% reduction; 8H45: Eight-hole plate with 45% reduction and 8H75 and Eight-hole plate with 75% reduction.

8.5.3 Tribological study

The wear rate values of both the EBM and SLM plates are presented in Figure 8.10. The highest wear rates (0.22 ± 0.02 \times 10^{-3} \text{ mm}^3/\text{Nm} for EBM plates and 0.19 ± 0.01 \times 10^{-3} \text{ mm}^3/\text{Nm} for SLM plates) are observed for the 2N load. For 6N, the wear rate values decrease (0.15 ± 0.01 \times 10^{-3} \text{ mm}^3/\text{Nm} for both plates) and increase again by increasing the load. At 14N the wear rate values are 0.18 ± 0.01 \times 10^{-3} \text{ mm}^3/\text{Nm} for EBM plates and 0.17 ± 0.01 \times 10^{-3} \text{ mm}^3/\text{Nm} for SLM plates.

Figure 8.11 shows a view-map of the wear tracks obtained by optical microscopy. The wear mechanisms stages comprise delamination, ploughing, grooving and oxidation. The delamination is shown as the perpendicular lines of the wear direction. These lines are larger for lower loads and decrease in size with the increase of the load value. The wear tracks of both EBM and SLM plates tested under the same load present similar profiles and track width. At lower loads, higher depth of penetration is observed in the EBM plates. At the highest load, 14N, the EBM fixation plates present a lower depth of penetration of 125 ± 5 \mu m and for the SLM the depth of penetration is 136 ± 4 \mu m. From the wear tracks, it is possible to observe that the worn surfaces of loads higher
than 2 N displayed plastic deformation (ploughing) highlighted by the presence of grooves. These grooves on the plates shown as lines marked parallel to the sliding direction are a result of the hard Alumina ball being in contact against the plates. The grooves increase and became more visible when the load increases. The EDS spectrums for the EBM and SLM plates at all considered loads are presented in Figure 8.12. An oxide debris was found on both plates between 40-70 at. %. Plates conveyed small traces of Na and Cl due to the PBS solvent.

![Figure 8.10](image)

**Figure 8.10** Wear rate of EBM and SLM plates for different loads.
Figure 8.11 Wear track of the EBM and SLM plate tested at 2, 6, 10 and 14 N obtained in the optical microscope.
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![Figure 8.12](image)

**Figure 8.12** BSE images of the wear track of the EBM and SLM plates tested at 2, 6, 10 and 14 N at x1000 magnifications with the EDS spectrums.

The variation of the coefficient of friction considering different loading values (2, 6, 10 and 14N) applied for 9000s are shown in Figure 8.13a,b. Four stages are observed. First, the coefficient of friction exhibits an initial increment until a local maximum, due to the contact between the ball and the plates surface. Then, the coefficient of friction values decreases reaching a minimum due to the formation of an oxide layer. In the third stage, the coefficient of friction increases resulting from the elimination of the oxide layer due to the erosion and the stresses caused by the surface...
plastic deformation produced during the wear tests. Finally, the coefficient of friction values reaches a steady state after ~ 4,000 s. The SLM fixation plates present lower oscillations and better stability of coefficient of friction than EBM plates. However, there are no significant differences (p > 0.05) between the EBM and SLM steady state coefficient of friction.

**Figure 8.13** Evolution of the coefficient of friction with the time for the a) EBM and b) SLM, and c) mean of coefficient of friction at the steady state of EBM and SLM plates.
8.5.4 Biological properties

Figure 8.14 presents the live/dead assay results showing live (green) and dead (red) cells on the fixation plates after 4 and 7 days of cell seeding. Results show that cells were not able to attach and proliferate on the commercial plates while in the case of both EBM and SLM fixation plates, cells are proliferating creating cell-cell network with very few cells dying. These results are confirmed by the Alamar blue assay (Figure 8.15) showing an increase in fluorescence intensity (measuring the metabolic activity of cells) with time in the case of EBM and SLM plates. At day 7, higher fluorescence intensity values are observed for the EBM plates in comparison to the SLM ones. This can be explained by the high surface roughness of the EBM plates that promotes cell attachment and proliferation, yet not high enough to compromise cell-cell interaction. High metabolic cell activity (fluorescence intensity) is also observed in EBM and SLM fixation plates in comparison to commercial ones.

Figure 8.14 Live and dead assays of EBM, SLM, Synthes and Biomet plates on day 4 and day 7. Scale bar is 200 μm.
Figure 8.14 (cont.) Live and dead assays of EBM, SLM, Synthes and Biomet plates on day 4 and day 7. Scale bar is 200 μm.
Discussion

As a consequence of the fabrication procedure, 3D printed plates present higher surface roughness. The surface roughness depends on the raw powder properties (e.g. particle size) and processing conditions (e.g. scan speed and layer thickness). Results show that EBM fixation plates present high surface roughness compared to the SLM fixation plates. This is due to the larger powder particle size (45 to 100 µm for EBM and 25 to 45 µm for SLM), higher scan speed (4530 mm/s for EBM and 375 mm/s for SLM) and higher layer thickness (50 µm for EBM and 30 µm for SLM).

The same raw powder composition was used for both EBM and SLM process. However, EBM and SLM fixation plates present different microscopic structure due to the different heating and cooling cycles. In the case of EBM plates, printed under vacuum, the slow cooling rates due to the high temperature of the substrate is responsible for the presence of the α phase instead of the α’. In the case of SLM plates, printed in an inert environment using Argon, the low temperature of the substrate plate causes a faster solidification leading to the α’ martensitic transformation. In the case of SLM plates, the fast cooling rates also induces a superior growth orientation of the α’ plates as observed from Figure 8.5b, showing the martensitic needles mostly inclined towards the build direction at ~40°. Moreover, the microstructure significantly alters the hardness of the manufactured parts. However, contrary to what was expected, results presented in Table 8.3 shows
that EBM fixation plates present slightly high microhardness than SLM fixation plates. This can be explained by the grain boundary and size (Figure 8.5a) and to the fact that the EBM α needles are smaller and more compact than the ones observed in the SLM fixation plates.

The tensile, torsion and bending tests show that the SLM fixation plates present higher equivalent stiffness than the EBM plates. This can be explained by the α’ presence in the microstructure of the SLM plates and the α lamellar structure of the EBM (Khorasani et al. 2019). Mechanical tests also show that topology optimised plates present significantly reduced equivalent stiffness for high volume reductions. As observed, the mechanical performance of the optimised plates tends to approach the mechanical properties of natural bone. This was observed in the case of the fixation plate optimised using compression load with 75% of volume reduction and eight-screw holes, 3D printed using both EBM and SLM, with an equivalent elastic modulus of 22 GPa like natural cortical bone (15-25 GPa) (McNamara 2011). Other designs also tend to the cortical bone region such as the eight-hole plate optimised for combined loads with 75% of volume reduction 3D printed by EBM. However, the equivalent bending modulus of the bending optimised plates (28 GPa for the eight-hole with 75% of volume reduction) are slightly higher than the bending modulus of the natural cortical bone (9.82-15.7 GPa) (Keller et al. 1990).

Wear results show that the highest wear rates occur for the lowest load (2N), due to the rubbing of the counter part on the plate surface, resulting in insignificant plastic deformation. As reported by Hisakado (1977), for low loads the wear rate is mainly affected by the surface roughness with the hardness and microstructure not playing a significant role. This explains the higher wear rate observed for the EBM and the high coefficient of friction at 2N. However, Hutchings (1992), shows that for higher loads the surface hardness plays a major role on the wear resistance. This can explain the similar wear rate values of both EBM and SLM plates for higher loads (6N, 10N and 14N). For high load regimes, the wear rate increases with the load increase as more volume is removed is from the plate. All printed plates present acceptable wear resistance values (Toh et al. 2016).

As reported by Sing et al. (2016), cell to cell network is significantly affected by the surface characteristics such as the surface roughness. In this paper, the EBM and SLM plates were not post-processed in order to investigate if further post-processing is necessary to acquire adequate cell attachment and proliferation. This is to circumvent costly procedures such as surface finishing
and polishing. Therefore, cell proliferation studies using osteosarcoma cells, show the contrary to commercial plates, both EBM and SLM plates are able to sustain cell attachment and proliferation. It is possible to observe that the surface roughness of printed plates is acceptable not compromising the establishment of cell-cell interaction. Live/dead results also show that due to limited cell attachment to commercial plates cells tend to die.

### 8.7 Conclusion

This Chapter shows that the combined use of topology optimisation with powder bed fusion is a viable approach to produce metallic fixation plates with improved mechanical performance (i.e. reduced equivalent stiffness and consequently bone loss problems). This approach allows to obtain lightweight fixation plates (a maximum of 75% of volume reduction was successfully considered) reducing also the costs of the plates. SLM plates present high mechanical properties, while EBM plates high wear resistance, hardness and surface roughness. Biological results also confirm that the obtained surface roughness values of both EBM and SLM plates are acceptable with 3D printed plates showing a significantly better capability to support cell attachment and proliferation.
Chapter Nine

Conclusion and Future work
Chapter Nine  Conclusion and Future work

This Chapter presents the main conclusions of this Thesis. The novelty and contribution of this research work to science is also highlighted.

9.1 Conclusions

As presented in Chapter One, this research focus on the design of fixation plates avoiding the mismatch between the properties of fracture fixation plates and bone properties (stress shielding). This is achieved using topology optimisation and additive manufacturing to produce optimised plates for further assessment. Research findings and novelty was assessed against the current state-of-the-art presented in Chapter Two. The initial computational methodology was developed considering 2D geometries and was detailed in Chapter Three and further extended in Chapter Four. Due to the lack of standards regarding the design of plates (e.g. dimensions, number of holes), for the same application (LCP plates) different companies have different plate designs. The only common characteristics, which were considered in this research as the starting design parameters, are the plate shape and the type of screw hole system (combi- or single-hole). The number of screw holes are determined by the application and fracture type. In order to circumvent this lack of standards, the procedure considered in this research was to fix the plate dimensions and separate the screw holes according to equal distances along the plates’ length. This creates a generic design model that can be used in the future to simulate/optimise different commercially available plate or to consider new designs. It is also important to mention that, non-published results performed with some commercially available LCP plate design (Zimmer Biomet and DePuy Synthes) showed that these plates present geometric characteristics that do not allow the optimisation process considering relevant volume reductions without compromising their structural integrity (an example is presented in Figure 9.1). The distance between holes is fixed to ensure the screw fixation to the bone without interfering on the bone fractured fragments if used for complex/comminuted fractures. All the designs considered in this Thesis can be clinically applied without interfering to the fractured fragments. Further investigation is required to address the limitation of the uncertainty of the bone plate geometry and features.
Figure 9.1 Structural integrity compromised considering the topology optimisation of an LCP DePuy Synthes commercial plates. This topology optimisation was performed considering a volume reduction of 25% and compression loading conditions.

Chapter Five evaluates the changes in stress shielding by considering a bone remodeling model of a humerus treated with the different optimised fracture plates. Six loading cases, including muscle and joint reaction forces were considered. Bone remodeling results at the bone-plate interface (i.e. fracture site), beneath the fracture plate, show less bone mass changes with the implantation of less stiff plates produced by topology optimisation in comparison to their initial and stiffer counterparts. These results show that topology optimisation is a useful tool to design less stiff fracture plates, minimising stress shielding, reducing bone loss and improving the bone healing process. Chapter Six evaluates the stress shielding by considering the changes in stress (the load transfer at the bone-plate interface) of different topology optimised plates fixated on a long bone shaft considering a four-point bending load, which simulates a patient walking with crutches after treated to transverse fractured mid-tibia. These results show that through topology optimisation, it is possible to design less stiff fixation plates, resulting in higher loads being transferred to the bone fracture plane, while maintaining the plate's ability to withstand stresses. By considering a maximum of 75% of volume reduction for plates containing different screw holes, it was possible to increase the load transfer to up to 37% in comparison to the initial plates. This reduces bone loss, promoting secondary healing. Additional results are presented in Appendix C.

Topology optimisation results, for both 2D and 3D geometries, show that significant volume reductions lead to designs with reduced mechanical strength. Moreover, some of the optimised 3D plates present specific features prone to stress concentration, which must be avoided in the future.
through a modification of the optimisation algorithm. Post-processing could also be a possibility, but one of the aims of this research is also to investigate if it is possible to minimise post-processing steps on the fabricated plates in order to reduce costs and production times. Nevertheless, the mechanical tests described in Chapters Six and Seven do not indicate any critical failure for the considered conditions.

The mechanical strength is a major indicator of the stability of the plates during healing process. Adequate mechanical strength of bone plates avoids any healing delays and plate failure. This was partially (dynamic loading conditions were not considered) addressed in Chapter Six from a computational point of view and experimentally investigated in Chapter Seven. The mechanical strength characteristics of fixation plates were experimentally obtained and compared to commercially available plates (DePuy Synthes narrow locking compression plates). In this Chapter only the fixation plates optimised for compression load cases are considered. The mechanical strength of other optimised plates (bending, torsion and combined load cases), determined under the standard testing (BS 3531-23.1: 1991 ISO 9585:1990) of static conditions are presented in Appendix D. Results presented in Chapter Seven and Eight show that it was possible to obtain designs with equivalent Young’s modulus and equivalent bending modulus in the range of natural cortical bone values.

Ti-6Al-4V optimised plates were produced using EBM and SLM and the results presented in Chapters Seven and Eight. These processes operate under different conditions and use different methods to melt metallic powder. SLM process is based on the heat produced by the absorption of photons of light while EBM is based on the kinetic energy transmitted due to the collision of electron. Results presented in these Chapters show that for the same design, SLM plates present higher mechanical properties, lower hardness and lower surface roughness in comparison to EBM plates. Results show acceptable wear resistance values for a medical device and a reduction of stress shielding by increasing volume reduction. No significant differences were observed in terms of wear resistance. Microstructure studies show that SLM plates are characterised by a martensitic α’, while EBM plates consist of both α and β phases. Microstructure differences are related to the different cooling rates (high cooling rates for SLM). Biological tests (Live/Dead and Alamar Blue assay) using osteosarcoma cells were conducted on EBM, SLM and a two commercial LCP plates (Zimmer Biomet – Ti-6Al-4V; and DePuy Synthes – CP-Ti). Results seems to suggest that both EBM and SLM plates present acceptable surface roughness as they are able to support cell
attachment and proliferation. Alamar Blues results after seven days of cell seeding suggest high cell metabolic activity in the EBM plates, but the differences are not statistically significant. Additive manufactured plates also present significantly better biological performance than commercial plates. Further studies must be conducted to investigate the acceptability of the obtained surface roughness particularly considering potential harmful effects once implanted (i.e. potential risk of tendon to rip).

This research work presents several contributions to knowledge which can be summarised as follows:

❖ This is the first research using topology optimisation to reduce stress shielding in bone fixation plates;

❖ Topology optimisation is combined for the first time with both bone remodeling and stress analysis, allowing to numerically confirm that the results from topology optimisation are effectively reducing the stress shielding. This validation is based on assessment of load transfer to bone and bone loss/remodel which is an indicator of potential bone healing. Computational results also show that the plates are mechanically stable under static physiological loading conditions;

❖ Topology optimised fixation plates were produced using two different powder bed fusion techniques and extensively characterised. Mechanical tests show that it was possible to obtain designs with equivalent Young’s modulus and bending modulus in the range of cortical bone. These results demonstrate the success of the proposed methodology;

❖ EBM, SLM and commercial plates were biologically assessed. Significantly high cell metabolic activity was observed in additive manufactured plates. Seven days after cell seeding, live/dead results show that cells were not attaching to commercial plates and the few cells attached died. Results seems to suggest that the surface roughness of the additive manufactured plates is acceptable as cells were able to attach and proliferate. Moreover, results suggest that additive manufactured plates present high potential for tissue integration.
9.2 Future Work

Despite the contributions to the current knowledge, this research opened also new research questions that must be addressed in the future. Major future research activities will focus on:

❖ Improve the topology optimisation scheme in order to obtain optimal designs not only in terms of minimising the stress shielding, but also producing designs minimising stress concentration regions and considering the long-term mechanical performance of the fixation plates by including fatigue analysis;

❖ Additive manufactured plates must also be tested in dynamic loading conditions;

❖ Due to the lack of standards in terms of plate design, it will be important to consider the effect of each individual parameter (length, width, thickness, number of screw-holes, space between screw-holes, design curvature and the screwing system) in terms of mechanical and clinical performance. Initial studies must be performed through numerical simulation and the Theory of Inventive Problem Solving (TRIZ) method along with Design of Experiments (DOE) will be used to identify the most relevant parameters;

❖ Long term biological studies must be performed. Additionally, ions release and media characterisation (e.g. detection of eventual carcinogenic elements) will be performed, which complemented with animal tests (sheep model is a suitable model) will provide a complete description of the plate performance. Histological analyses performed during the \textit{in vivo} tests will allow to assess the bone remodelling process and bone organisation;

❖ Additional investigations must be conducted to assess how suitable are the surface roughness values obtained for both EBM and SLM plates. In this case a new testing setup will be considered allowing the fixation plate to move in a cyclic movement to rub the rough plate against a cadaveric tendon;

❖ The effect of processing conditions and fabrication technique must be taken into consideration during the topology optimisation phase. Powder bed fusion techniques characterised by a phase change transformation of the material (Solid – Melt – Solid) induces shrinkage and internal residual stresses that must be considered;

❖ Alternative materials to the conventional metallic materials must also be considered. Future research will focus on the use of biocompatible materials aiming to produce biodegradable
fixation plates, which will disappear after the bone healing (see Figure A.1 in Appendix A). In this case, the major research challenge is the relatively poor mechanical properties of these materials, not suitable for load-bearing applications. Numerical simulation will be used to determine suitable combinations of biodegradable polymers, ceramics and metals (e.g. magnesium). The topology optimisation scheme will be modified considering material addition into specific areas rather than material removal. This approach, called Bi-directional Evolutionary Structural Optimisation (BESO) was recently proposed for the design of tissue engineering scaffolds (Chen et al. 2011). Plates will be designed considering their degradation behaviour and the optimal processing conditions will be investigated. Mechanical and biological tests will be also performed.
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Appendix A

Topology optimisation of 3D fixation plates

Appendix A

Topology Optimisation on reducing the stress shielding effect for orthopedic applications

Orthopedic problems are significantly increasing posing pressure to healthcare systems. Traditional clinical procedures for traumatic bone fracture applications comprise the use of high stiffness metallic implants caused by the built-up material and implant design. These implants show a high mechanical mismatch comparing to bone properties resulting in stress shielding phenomena that leads to less dense and fragile bone. This paper follows a design phase by exploring the use of 3D Topology Optimisation to create lightweight metallic implants with reduced stiffness, thus minimising stress shielding and bone loss problems.

Introduction

Bone is one of the few tissues that has the ability to heal itself, through a complex physiological process comprising acute inflammatory responses, cartilage callus formation, endochondral ossification and bone remodelling, without developing a scar (Bigham-Sadegh and Oryan 2015). However, in bone fracture events such as high traumatic or pathological fractures, exceeding a critical size defect, bone fracture healing capabilities becomes limited causing delays or non-union problems and requires further interventions (e.g. bone fixation implants) (May et al. 1989, Aho et al. 2013, Vorys et al. 2015). In the United States of America, an estimated 15 million fractures occur annually costing over 60 billion dollars.

Bone fixation is a routine orthopedic procedure. Fracture fixation devices stabilise and immobilise the fracture segments initiating the fracture healing process (Nieto and Baroan 2017). Commercially available bone fixation implants (i.e. external fixators, internal fixators and intramedullary pins) are built up with metallic biomaterials like stainless steel, titanium, cobalt and its alloys (e.g. Ti6Al4V and CoCrMo). a large number of cases (Choudhury et al. 2017, Wang et al. 2017, Longhofer et al. 2017), these implants are left permanently in the body leading to long term problems such as possible release of metal ions, inflammatory reactions, risk of infection, screw loosening and most importantly bone resorption due to stress shielding effects.

Additionally, metallic biomaterials have high elastic moduli (e.g. CoCrMo Young’s Modulus is around 210 GPa, Ti6Al4V Young’s Modulus is around 110 GPa and, Stainless Steel 316 L SS is around 190 GPa) than natural bone (the Young’s Modulus of trabecular bone ranges from 0.02 to
2 GPa while for cortical bone the Young’s Modulus ranges from 3 to 30 GPa) (Murr 2017, Li et al. 2017, Martin et al. 2017). This large mismatch in mechanical properties between bone and metallic materials causes bone stress shielding, bone instability and bone loss. Stress concentration in the fixation device, which may lead to cracking of plates or screw pullout, is another consequence of the high stiffness of metallic implants.

Removal of implants after the healing process is an alternative approach, accounting for up to 30% of planned orthopedic operations (Bostman et al. 1996), but often associated with complications like infection, nerve damage, risk of refracture and increased pain at the site of surgery being common.

In order to overcome the current limitations of metallic implants, authors are starting a new research project entitled “Osteofix-novel biodegradable composite implants for osteoporotic bone fractures” partially funded by the government of Saudi Arabia and the UK Royal College of Surgeons. The project aims to reduce the stress shielding phenomena by reducing the equivalent stiffness of the metallic implants through the use of Topology Optimisation (TO), and to avoid the need of a second surgery to remove the implant by replacing metallic materials with biocompatible and degradable materials (polymers, ceramics, metals or composites). Figure A.1. illustrates the major research activities behind this research program.
Figure A.1 Research activity flowchart for a novel bone fixation implant.

In a previous paper (Al-Tamimi et al. 2017), authors showed that, despite TO seeks to find the optimal load path for a particular load and boundary condition, searching for a minimum compliance design, it is possible to use this mathematical optimisation method to obtain implant designs with reduced “equivalent stiffness”. Preliminary results were obtained for a Locking Compression Plate (LCP) simulated as a 2D plate. LCP is the most recent developed fracture fixator design with a capability of treating fractures with different healing processes (i.e. secondary bone healing and primary healing) intending to treat juxta-articular fractures (e.g. distal tibia, fibula, olecranon) and in osteoporotic bones (Wagner 2003). Based on these preliminary results, this paper focus on the topology optimisation of 3D LCP plates, considering different loads, boundary conditions and volume reductions. New designs were obtained with reduced “equivalent stiffness” minimising the stress shielding phenomena.
Computer Optimisation

A constrained optimisation problem is mathematically described as the minimisation of cost functions subjected to a set of constraints as follows:

\[
\begin{align*}
\text{Find} & \quad x = \begin{bmatrix} x_1 \\ x_2 \\ \vdots \\ x_n \end{bmatrix} \text{ which minimises } f(x) \\
\text{Subject to} & \quad \begin{cases} 
  g_i(x) \leq o, i = 1, 2, \ldots, m \\
  h_j(x) = 0, j = 1, 2, \ldots, n
\end{cases}
\end{align*}
\] (A.1)

where \(x\) is the vector of design parameters and \(f(x)\) is the cost function. The functions \(g_i(x)\) and \(h_j(x)\) are called the inequality constraint function and the equality constraint function respectively, and they define the constraints of the problem.

Structural optimisation is a decision making tool which defines the material distribution according to specific constraints and objective functions. Three methods can be identified. Sizing optimisation is the simplest method to optimise truss-like structures including bridges, support bars and frames. In sizing optimisation, the structure layout has been defined and the only parameter that can be modified is the size of the component itself or the size of structure element. Shape optimisation will not change the topology of the structure and the modified design variables could be the thickness of the wall, radius of holes, width of slot or other complex geometry shape changes. Topology optimisation, the most commonly used structural optimisation method, seeking to find the best material distribution for specified Computer Aided Engineering (CAD) structure following the load path from the Finite Element (FE) analysis (i.e. loading and boundary conditions), subject to the objective function (e.g. minimising strain energy), and constraints (e.g. volume).

In TO, the initial CAD structure is discretised into discrete divisions (elements) by the FE method (Figure A.2). Each element is analysed and given a certain value of stiffness/strain which defines the stress/displacement of the CAD structure. The TO considers each element of the structure as a design variable (e.g. density \(\rho_e\)) and updates the distribution of the material on the structure through a binary strategy, either 1 keeping the material (i.e. solid) or 0 removing the material (i.e. void).
For the TO computations, this paper uses the widely and popular Solid Isotropic Microstructure with Penalisation (SIMP) method with minimising the strain energy (maximising the stiffness), constraining the volume and specifying the density of each element (Bendsoe 1989, Sutradhar et al. 2015).

**Figure A.2** (a) Initial CAD structure and (b) discretised CAD structure with loading and boundary conditions.

### Solid Isotropic Microstructure with Penalisation (SIMP)

The SIMP method developed by (Bendsoe 1989, Zhou et al. 2001, Bendsoe and Sigmund 2004) is a gradient-based method with a continuous converging algorithm controlled by the penalising factor \( p \). In the initial design, each element \( e \) corresponds to the design variable which is generally considered as the relative density \( \rho_e \). The density in each element is associated with a Young’s Modulus \( E \), as follows:

\[
E = [\rho_e]^p \cdot E^o
\]  
(A.2)

where \( E^o \) is the initial Young’s Modulus of the material.

### Problem formulation

The problem is formulated as follows: i) objective function \( Z \) definition, which minimises the strain energy; ii) constraint the volume fraction \( f \) and the relative density \( \rho_e \) to be non-zero for analysis stability. Mathematically, the TO problem can be formulated according to the following equations:

\[
\min Z: U^T F = \sum_{e=1}^{N} [\rho_e]^p [u_e]^T [k_e][u_e]
\]  
(A.3)
subject to
\[
\begin{align*}
  f &= \frac{V}{V_i} \\
  F &= [K] \cdot [U] \\
  0 < \rho_{\text{void}} &\leq \rho_e \leq 1
\end{align*}
\]

where $\rho_e$, $u_e$, $k_e$ and $\rho_{void}$ are the relative density, displacement vector, element stiffness matrix and minimal relative density (i.e. $\rho_{\text{void}}=0.001$ by default), respectively. The equation (B.3b) explains the equilibrium equations for discretised elements where $F$, $K$ and $U$ are the force vectors, the global stiffness and the global displacement, respectively.

The information flowchart of the SIMP algorithm is presented in Figure A.3. In each iteration the density of the design elements is measured and updated whilst affecting the sensitivity. The sensitivity filtering defines how and where the material is to be distributed along the given design structure. The density in each element can be correlated to the element stiffness, with full stiffness for $\rho_e=1$ and no stiffness for $\rho_{\text{void}}$. Thus, stiffness changes in each iteration as the structure is developed with new densities.

Figure A.3 SIMP method flowchart.
Computational methods

As a case study, a Locking Compression Plate (LCP) is considered (Figure A.4). The plate has 170 mm of length, 14 mm of width and 5 mm of thickness. The 3D plate was modelled using ABAQUS (Dassault Systèmes, France) software using 8-node hexahedral elements and a mesh with a total of 62894 elements. The built-up material for the plate is the biocompatible Titanium (Ti-6Al-4V) with a Young’s Modulus of 120 GPa and a Poisson’s ration of 0.3.

![Figure A.4 Bone plate CAD design](image)

Finite element analysis

The finite element analysis follows the ISO 9585:1990 standard for testing an internal bone fixation implant considering a 4-point bending loading condition as shown in Figure A.5a. Additionally, the plate was simulated under a torsion loading (Figure A.5b) and tensile loading conditions as illustrated in Figure A.5c. It is also important to note that the SIMP technique is not sensitive to the load magnitude.

Design optimisation

The optimisation procedure seeks to minimise the strain energy for the design region shown in Figure A.4, considering two different values of volume reduction (65% and 75%) for two loading conditions (i.e. bending and torsion) and 55% and 65% for tensile loading condition. The criteria used to select these upper values is related to the lack of structural integrity for higher volume reductions. It is also clear that the maximum volume reduction depends on the load type. Other volume reductions were considered but not presented in this space as the aim was to obtain plates with reduced “equivalent stiffness” compared to the initial design. A geometric constraint (i.e. non-design region) is considered on the shape of the holes in order to keep the integrity of the standardised screw geometry.
Design mechanical performance

The resulted optimal designs were mechanically evaluated using finite element analysis in order to determine their equivalent stiffness and strength (i.e. work of external load). The initial implant and the optimised designs were assumed to be homogeneous and isotropic. The strength of the plates was determined by applying a uniform longitudinal force ($F_{xx}$) in the x-axis direction, applied on Face A of the plate as shown in Figure A.6, while keeping Face B fixed in all directions. The average displacements in the x-axis direction ($U_{xx}$) on Face A was used to determine the work of the external loads ($W$), as follows:

$$W_{xx} = \sum_{i=1}^{n} F_{xx_i} \cdot U_{xx_i}$$  \hspace{1cm} (A.4)

Similarly, the stiffness of the plate was assessed by imposing a displacement on Face A, equivalent to the strain in the x-axis direction ($\varepsilon_{xx}$):

$$\varepsilon_{xx} = \frac{\Delta L}{L_i}$$  \hspace{1cm} (A.5)
where \( L_i \) is the initial plate length and \( \Delta L \) is the difference between the final and initial length. Then, the equivalent stiffness (E) is calculated by considering the average reaction forces \( (RF_{xx}) \) occurred on Face A, as follows:

\[
\sigma_{xx} = \frac{RF_{xx}}{A} \quad \text{(A.6)}
\]

\[
E = \frac{\sigma_{xx}}{\varepsilon_{xx}} \quad \text{(A.7)}
\]

where \( \sigma_{xx} \) and \( A \) is the stress in x-axis direction and the plate cross-sectional area, respectively.

**Results and discussion**

Optimum designs for torsion and bending loading conditions considering the specified volume reductions (65% and 75%) are presented in Figures A.7 and A.8, respectively. Additionally, Figure A.9 illustrates the optimal design attained from the tensile loading for 55% and 65% volume reductions. Table A.1 shows the equivalent stiffness values for different loading conditions and volume reduction values. The work of the external are indicated in Table A.2.

![Figure A.7 Optimised bone plates for torsion conditions and (a) 65% and (b) 75% of volume reduction.](image)

![Figure A.8 Optimised bone plates for bending conditions and (a) 65% and (b) 75% of volume reduction.](image)
Figure A.9 Optimised bone plates for tensile loading conditions and (a) 55% and (b) 65% of volume reduction.

Table A.1 Equivalent stiffness.

<table>
<thead>
<tr>
<th>Volume reduction (%)</th>
<th>Equivalent Stiffness (MPa)</th>
<th>Equivalent stiffness variation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original plate</td>
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<td>3958</td>
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<td>2031</td>
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<td>1080</td>
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<td></td>
<td>75</td>
<td>1021</td>
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<tr>
<td>Tensile load</td>
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<td>7850</td>
</tr>
<tr>
<td></td>
<td>65</td>
<td>5649</td>
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Table A.2 The work of the external loads.

<table>
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<th>Volume reduction (%)</th>
<th>Work of external loads (N.mm)</th>
<th>Variation of the Work of external loads (%)</th>
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</thead>
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<td></td>
</tr>
<tr>
<td>Torsion load</td>
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<td>23</td>
<td>667%</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>48</td>
<td>1500%</td>
</tr>
<tr>
<td>Bending load</td>
<td>65</td>
<td>73</td>
<td>2333%</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>104</td>
<td>3467%</td>
</tr>
<tr>
<td>Tensile load</td>
<td>55</td>
<td>11</td>
<td>267%</td>
</tr>
<tr>
<td></td>
<td>65</td>
<td>16</td>
<td>433%</td>
</tr>
</tbody>
</table>

Results show that by increasing volume reduction it was possible to obtain plate designs with reduced equivalent stiffness and an increase in the work of the external loads (higher values of the work results in less-stronger plates). This proves that Topology Optimisation is capable of producing an optimal material distribution resulting in weaker plate designs comparing to the initial plate design with using the same material properties. Plates under torsion considering volume reductions of 65% and 75% presented a stiffness reduction of 56% and 78%, and a work increment of 667% and 1500%, respectively. Plates under bending conditions for volume reductions of 65% and 75% exhibited a stiffness reduction of 88.1% and 88.7%, and a work increment by 2333% and 3467%, respectively. Similarly, plates under tensile loading conditions showed a decrease in stiffness of 13% and 38%, and an increase in work of 267% and 433% for 55% and 65% volume reductions, respectively.

It is important to mention that the SIMP method used for Topology Optimisation intends to decrease the strain energy (increase the stiffness) of each element. However, due to the high percentage of volume reduction we observed that the lightweight effect is the prevalent one, contributing to decrease the equivalent stiffness of the plate.
Conclusion

The design of metallic fracture fixation devices is one of the major factors of controlling the stiffness of the device that causes stress shielding which induces bone loss and instability due to the high stiffness of metallic properties comparing to bone properties. Topology Optimisation is employed considering different loading and boundary conditions to find the best material allocation for the design of a metallic bone fracture fixation. The optimal designs obtained and through a tensile test by finite element showed a decrease in the equivalent stiffness comparing to the initial design. This decrease occurred due to the large volume reduction that was constrained in the optimality criteria. The decrease of the stiffness leads to a minimisation of the stress shielding occurring during bone fracture healing.

Reference


Appendix B

Design of fixation plates using topology optimisation and stress analysis

Figure B.1 Topology optimisation results of four-hole fracture plate. Under bending load: (a) 25% of volume reduction, (b) 45% of volume reduction and (c) 75% of volume reduction. Under compression load: (d) 25% volume reduction, (e) 45% of volume reduction and (f) 75% volume reduction. Under torsion load: (g) 25% of volume reduction, (h) 45% of volume reduction and (i) 75% of volume reduction. Under combined load: (j) 25% of volume reduction, (k) 45% of volume reduction and (l) 75% of volume reduction.
Figure B.2 Topology optimisation results of six-hole fracture plate. Under bending load: (a) 25% of volume reduction, (b) 45% of volume reduction and (c) 75% of volume reduction. Under compression load: (d) 25% volume reduction, (e) 45% of volume reduction and (f) 75% volume reduction. Under torsion load: (g) 25% of volume reduction, (h) 45% of volume reduction and (i) 75% of volume reduction. Under combined load: (j) 25% of volume reduction, (k) 45% of volume reduction and (l) 75% of volume reduction.
Figure B.3 Topology optimisation results of eight-hole fracture plate. Under bending load: (a) 25% of volume reduction, (b) 45% of volume reduction and (c) 75% of volume reduction. Under compression load: (d) 25% volume reduction, (e) 45% of volume reduction and (f) 75% volume reduction. Under torsion load: (g) 25% of volume reduction, (h) 45% of volume reduction and (i) 75% of volume reduction. Under combined load: (j) 25% of volume reduction, (k) 45% of volume reduction and (l) 75% of volume reduction.
Appendix C

Stress analysis in a bone fracture fixed with topology optimised plates

This Appendix is based on the Supplementary material of the paper: Al-Tamimi, A.A., Quental, C., Folgado, J., Peach, C. and Bartolo, P. (2019). Stress analysis in a bone fracture fixed with topology optimised plates. Biomechanics and Modeling in Biomechanics. (Submitted). It includes also two extra tables describing the stiffness change of the six-hole plate calculated in Section 6.2.1 (Table C.1) and the Von Mises stresses at the fracture plane (Table C.2), due to load transfer from the plate; and two extra figures showing the stress distribution at the fracture plane (Figure C.3) and the stress distribution at the six-hole optimised plate considering 75% volume reduction (Figure C.4).
Figure C.1 Topology optimisation results of four-hole fracture plate. Under bending load: (a) 25% of volume reduction, (b) 45% of volume reduction and (c) 75% of volume reduction. Under compression load: (d) 25% volume reduction, (e) 45% of volume reduction and (f) 75% volume reduction. Under torsion load: (g) 25% of volume reduction, (h) 45% of volume reduction and (i) 75% of volume reduction. Under combined load: (j) 25% of volume reduction, (k) 45% of volume reduction and (l) 75% of volume reduction.
Figure C.2 Topology optimisation results of eight-hole fracture plate. Under bending load: (a) 25% of volume reduction, (b) 45% of volume reduction and (c) 75% of volume reduction. Under compression load: (d) 25% volume reduction, (e) 45% of volume reduction and (f) 75% volume reduction. Under torsion load: (g) 25% of volume reduction, (h) 45% of volume reduction and (i) 75% of volume reduction. Under combined load: (j) 25% of volume reduction, (k) 45% of volume reduction and (l) 75% of volume reduction.
Table C.1 Change in the equivalent bending stiffness in comparison to the initial value for six-hole plates (18.68 N.m²).

<table>
<thead>
<tr>
<th>Plate</th>
<th>Volume reduction (%)</th>
<th>Equivalent stiffness change (%)</th>
</tr>
</thead>
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<tr>
<td></td>
<td>25</td>
<td>-6</td>
</tr>
<tr>
<td>Bending</td>
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<td>-19</td>
</tr>
<tr>
<td></td>
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<td>-47</td>
</tr>
<tr>
<td>Compression</td>
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<td>-21</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>-59</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>-78</td>
</tr>
<tr>
<td>Torsion</td>
<td>25</td>
<td>-12</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>-14</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>-30</td>
</tr>
<tr>
<td>Combined</td>
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<td>-10</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>-40</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>-65</td>
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</table>
Table C.2 Maximum Von Mises stresses on the bone at the fracture plane for six-hole optimised designs.

<table>
<thead>
<tr>
<th>Plate</th>
<th>Volume reduction (%)</th>
<th>Von Mises stress (MPa)</th>
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</thead>
<tbody>
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<td>Initial designs</td>
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<td></td>
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<td>19.12</td>
</tr>
<tr>
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</table>
Figure C.3 Von Mises stresses at the bone fracture plane resulted from the six-hole initial design and all of the 75% volume reduction optimised plates.
Figure C.4 Stress distribution on the optimised six screw hole plates with 75% volume reduction and different loading conditions.
Appendix D

Four-point bending tests of topology optimised plates according to the standard (BS 3531-23.1: 1991 ISO 9585:1990)

This Appendix provided additional information to Chapter Seven considering the BS 3531-23.1: 1991 ISO 9585:1990 standard to test metallic bone plates.
Table D.1 The equivalent bending stiffness of 3D printed topology optimisation plates.

<table>
<thead>
<tr>
<th>Holes</th>
<th>Volume reduction (%)</th>
<th>Bending</th>
<th>Compression</th>
<th>Torsion</th>
<th>Combined</th>
<th>Initial</th>
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Table D.2 The equivalent bending strength of 3D printed topology optimisation plates.

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<th>Compression</th>
<th>Torsion</th>
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Table D.3 The equivalent bending modulus of 3D printed topology optimisation plates.

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