

# Chapter 17

## Tissue Engineering Scaffolds for Bone Repair: Application to Dental Repair

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**Abstract** Medical implants for bone repair are starting to benefit from advanced design and (micro-) manufacturing technologies that promote a precise control of final geometries and allow for the incorporation of design-controlled and in some cases personalized features for enhanced interaction at a cellular level. Recent advances in additive manufacturing technologies and available materials support solid free-form design and fabrication approaches, hence helping with device personalization and enabling a real 3D control of device geometry. Furthermore, the vast knowledge generated during last decades in the field of tissue engineering can be used as a source for redesigning all types of implants, pursuing improved biomechanical and biomimetic solutions, especially in the area of bone repair. Hybridizations between conventional compact bone implants and trabecular tissue engineering scaffolds can help to adjust the mechanical performance of bone repair solutions to that of real bone, thus promoting long-term stability and preventing bone resorption thanks to a more adequate stress distribution in service. The increased surface to volume ratio of such lattice or trabecular implants, based on the tissue engineering scaffold concept, helps with cellular attachment to the implant, improves cell motility due to the presence of irregularities that help them to “crawl”, enhances osseointegration in the case of implants aimed at bone repair and promotes drug incorporation for disease prevention. The potential of dental scaffolds for the in vitro development of artificial teeth is also remarkable. The general aspects and main design and manufacturing strategies linked to these advanced scaffold-based implants for bone repair have been introduced in previous chapter. Here we focus on the area of dental implants, detailing novel concepts, describing the development process of a scaffold library for dental applications, modeling and discussing dental implant interactions with bone and also analyzing the more remarkable technologies capable of providing adequate results for the manufacture of high-precision dental solutions, when compared with other state-of-the-art manufacturing approaches.

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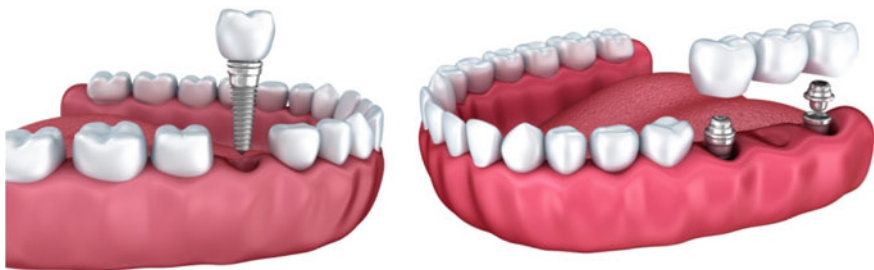
## 17.1 Introduction to Dental Implants and Prostheses

Dental implants are replacements for the root or roots of teeth. They are fixed to the jawbone or to the skull (normally screwed to the jaw or skull after an initial drilling) and are used to support dental prostheses (the visible parts of artificial teeth), including crowns, bridges, dentures, as well as facial prostheses. Usually dental implants are made of titanium and titanium alloys, with are: lightweight, very resistant to stresses and cyclic loadings, and provides a very interesting biological interaction, which normally leads to an adequate osseointegration. Some common types of dental implants and prostheses are included in Fig. 17.1. Due to the very adequate performance of titanium alloys, dental implants have the highest success rate of any implanted surgical device, according to the website: [www.dentalimplants.com](http://www.dentalimplants.com).

In spite of the well-known dental implant techniques and of the related commonly used good-practices, there are risks and possible complications related to dental implant therapy including: nerve injury and excessive bleeding during surgery and post-surgical problems due to a lack of osseointegration, to mechanical failures or to the appearance of chronic infection or inflammation.

Recent design, manufacturing, testing and implantation procedure, aimed at minimizing the required hands-on expertise of prosthetic technicians and maxillo-facial surgeons, are helping to perform these interventions in a more systematic and automated way, as detailed in the next section. The use of novel materials and geometries for improved biological interactions and mechanical performances is also among the main research trends for dental substitutes with enhanced response and is clearly linked to synergistic advances in design technologies, modeling and simulation resource, synthesis, processing, manufacturing and characterization procedures and computer-aided surgical planning and support strategies.

In addition, hybrid concepts based on new combinations of traditional dental implants and tissue engineering scaffolds are gaining momentum and opening new horizons in this field, as will be also discussed along present chapter.



**Fig. 17.1** Examples of dental implants and dental prostheses. *Left* Dental implant and crown. *Right* Dental implants and bridge. Purchased under standard license agreement: [alexmit]© [www.123RF.com](http://www.123RF.com)

## 17.2 Novel Concepts in the Field of Dental Implants

Medical implants for bone repair, including dental implants and prostheses, are starting to benefit from advanced design and (micro-) manufacturing technologies that promote a precise control of final geometries and allow for the incorporation of design-controlled and in some cases personalized features for enhanced interaction at a cellular level. Recent advances in additive manufacturing technologies and available materials support solid free-form design and fabrication approaches, hence helping with device personalization and enabling a real 3D control of device geometry.

Furthermore, the vast knowledge generated during last decades in the field of tissue engineering can be used as a source for redesigning all types of implants, pursuing improved biomechanical and biomimetic solutions, especially in the area of bone repair, and is also starting to have an impact in the fields of odontology and maxillofacial surgery. Hybridizations between conventional compact bone implants and trabecular tissue engineering scaffolds can help to adjust (in fact to define) the mechanical performance of bone repair solutions to that of real bone, thus promoting long-term stability and preventing bone resorption thanks to a more adequate stress distribution in service.

The increased surface to volume ratio of such lattice or trabecular implants, based on the tissue engineering scaffold concept, helps with cellular attachment to the implant, improves cell motility due to the presence of irregularities that help them to “crawl”, enhances osseointegration in the case of implants aimed at bone repair and promotes drug incorporation for disease prevention. The potential of dental scaffolds for the *in vitro* development of artificial teeth is also remarkable: design strategies are covered in Sect. 17.3, *in silico* testing for design validation is covered in Sect. 17.4 and manufacturing procedures are finally analyzed in Sect. 17.5.

These technological breakthroughs act synergistically with improvements in the available biomaterials for the medical industry and with several technologies for micromanufacturing and for surface biofunctionalization detailed in Chaps. 8 and 9, as well as with the more specific resources cited here.

Although the general aspects and main design and manufacturing strategies linked to these advanced scaffold-based implants for bone repair have been introduced in previous chapter, particular details linked to device personalization must be taken into account and are covered in the following paragraphs.

It is necessary to mention that the advances seen in recent decades linked to all medical imaging systems (mainly, computed tomography (CT), Doppler-effect echo scans, nuclear magnetic resonance (NMR) or magnetic resonance imaging (MRI) and positron emission tomography (PET), as well as some more novel combinations PET/CT) have led to a very remarkable increase in the diagnostic capabilities of these tools, as well in the reliability of the diagnoses made based on this information and the therapeutic decisions consequently taken.

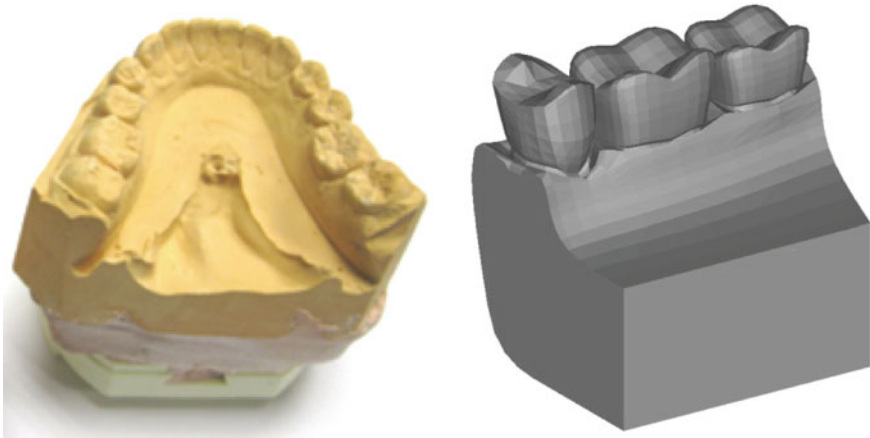
In parallel to the advances of medical imaging resources, during last couple of decades, biomedical device personalization has been greatly promoted by novel ways of combining medical imaging technologies and the related outer/inner-corporal information, with the capabilities of computer-aided design and engineering tools. In short, the information obtained using some of these medical imaging can be almost directly converted in three-dimensional objects (replicating the geometries and structures of the human body and of biological subsystems) and can subsequently be used as input in CAD programs, for designing personalized medical devices adapted to the morphologies of such biostructures (Osuna 2008; Ojeda Diaz 2009; Ojeda Diaz et al. 2009; Díaz Lantada et al. 2010; Díaz Lantada and Lafont Morgado 2011; Díaz Lantada 2013).

There are several software tools, for handling the information obtained from medical imaging technologies, and enabling computer-aided design, engineering and prototyping tasks. They are usually referred to as “MIMICS-like” programs (due to the relevance of MIMICS (Materialise NV)). Among such programs, due to their industrial impact and quality of results, it is important to mention at least:

- MIMICS (Materialise NV), for general purpose applications.
- Implant (Materialise NV) especially oriented to Odontology.
- Surgiguide (Materialise NV) especially oriented to Odontology.
- 3D Doctor, for bone modeling from CT scan and soft tissue from MRI.
- Analyze (Mayo Clinic), for handling images from MR, CT and PET.
- MRIcro Software, for converting medical images to Analyze format.
- Biobuild, for converting volumetric imaging data to RP file formats.
- Volume Graphics, for general purpose applications.

Their applications to the dental field are noteworthy and the employment of medical imaging, combined with the adequate software, as input for the computer-aided design of personalized dental prostheses, mainly the personalized crowns and bridges, which will be supported by standard implanted screws, is now wide-spread. The use of symmetries, Boolean operations, patterns features, among other common operations available in CAD software, allows for a more systematic and rapid development of personalized crowns and bridges, especially as the CAD models can be used as input for CNC machining resources for direct manufacture of final parts in ceramic materials. Surgical planning is also possible and today constitutes one of the more relevant uses of rapid prototyping (Díaz Lantada and Lafont Morgado 2012).

In fact, not just surgical planning is possible, but also enhanced surgical procedures are being continuously developed thanks to the manufacture of guiding splints and other supporting prototypes, which help surgeons to carry out the more aggressive tasks with increased security. The use of stereolithographic templates for guiding the surgeons’ tools and limiting their penetration, hence avoiding the potential damage to intramandibular nerve and helping to place the implants with the desired three-dimensional orientation for optimal performance, is note-worthy (Valente 2009).



**Fig. 17.2** Procedures for obtaining 3D CAD geometries of teeth for carrying out personalized prosthetics and implant design tasks

In order to carry out the aforementioned personalized approaches, it is first of all necessary to obtain a 3D CAD model of patient's jawbone and teeth. There are some alternative procedures, each with its own advantages and drawbacks. One possibility is to obtain a polymeric mold of patient's teeth by traditional processes and subsequently a ceramic or polymeric replica, as the one shown in Fig. 17.2 (left image).

The ceramic or polymeric replica can then be optically digitalized and further incorporated to a computer-aided design program for designing the crowns or bridges, for planning the optimal position and orientation of the different required implants, for designing surgical guides and even for *in silico* assessment of the mechanical performance of the desired reconstruction, as further detailed in the following Sect. 17.3.

Another option, possibly more precise, but more invasive for the patient, is the use of a medical imaging technology for obtaining a 3D model of the patient's jawbone and skull, which can be further processed with MIMICS-like programs and used as design input. In many cases the use of just a small portion of the teeth, as the example from Fig. 17.2 (right image) may be enough for some design tasks.

Apart from being a more dangerous procedure for the patients, due to being exposed to radiation during the medical imaging process, the difficulties related to the three-dimensional reconstruction of the softer tissues surrounding the bones and teeth, which are not always so clearly visualized and whose boundaries are sometimes fuzzy in the Hounsfield grayscale images typical from these imaging resources, must be also taken into account. Therefore, counting with well-trained professionals is a main key towards successful medical imaging-driven prosthetic designs.

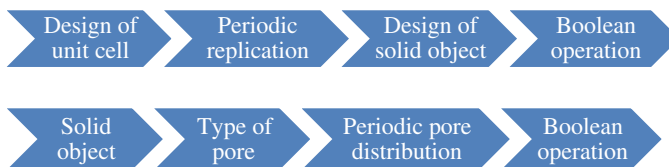
### 17.3 Case Study: Development of a Scaffold Library for Dental Applications

The design of porous and lattice structures with the help of CAD resources is in fact simple and rapid, once a couple of operations are adequately combined. In some previous chapters a set of introductory examples have been provided and main design strategies have been also recently highlighted (Díaz Lantada and Lafont Morgado 2012; Díaz Lantada 2013).

In short, the process, for lattice structures, normally includes combination of solid operations (cylinders, piles...) for obtaining a unit cell and pattern or periodic replication of such solids and unit cells. Intersecting the obtained lattice with a solid implant leads to final device. In the case of porous structures, the process instead of additive is subtractive. It normally begins with a solid cube or cylinder, depending on the overall geometry of the desired implant, from which smaller spheres and cubes are usually subtracted. The porous structure (in fact a design-driven material, a knowledge-based material or a even metamaterial) obtained can additionally be intersected with the geometry of a solid prosthesis or biodevice, for finally obtaining a porous implant. Both processes are schematized in Fig. 17.3 included below.

Even though all conventional CAD programs already commented (Solid Edge, NX-8.5, Catia v.5, Solid Works, Autodesk-Inventor...) include several operations for designing unit cells and replicating them, for applying pores to solid objects and Boolean operations for applying an outer geometry to a lattice structure, novel CAD resources are being specifically developed for promoting the application of meta-materials to product development.

Among ad hoc CAD software oriented to the design of lattice and porous structures, for improved control of aspects such as density, stiffness and resistance of final geometries, we would like to cite “Within” ([www.within-lab.com](http://www.within-lab.com)) and also “Netfabb” ([www.netfabb.com](http://www.netfabb.com)), among the most advanced ones, and with direct application in Biomedical Engineering. Advances in topological optimization, a mathematical approach that optimizes material layout within a given design space, for a given set of loads and boundary conditions, are also helpful for deriving into lattice and porous structures and progressively being incorporated to conventional CAD resources (Bendsoe and Sigmund 2003; Schramm and Zhou 2006).



**Fig. 17.3** Schematic processes for designing biodevices with lattice and porous structures

As application example, this section details the development of a CAD library of dental implants with porous, lattice and trabecular structures for a potentially improved osseointegration and mechanical performance, as the use of trabecular metallic implants helps to match the mechanical properties of bone, as described in previous chapters. Starting from four different common types of solid dental implants, which have been designed using the modeling resources of NX-8.5 (Siemens PLM Solutions), the final porous, lattice and trabecular structures are obtained with the help of “Within” ([www.within-lab.com](http://www.within-lab.com)), thanks to its unique features and with the help of a trial version, which we acknowledge.

In more detail, “Within” is an engineering design software company that has created software and CAD designs with a degree of complexity and functionality oriented to the world of additive manufacturing. They have developed a new set of tools and design rules and implemented several software resources for optimizing component design with the help of tunable porous and lattice geometries to meet design specifications in an unmatched way. The optimized components can be manufactured using additive manufacturing machines to create products which perform beyond the state-of-the-art.

Within’s technologies and software resources allow for the straight-forward development of lightweight materials and devices, flexible or robust structures depending on the desired displacement or loading requirements and truly functional bodies with functional gradients of properties. The osseointegration process may be even promoted from the design stage, thanks to the possibility of controlling main surface features.

Biomimetic approaches are additionally supported by Within’s advanced processes for the generation of variable density lattices, which are ideally suited for mimicking the trabecular and compact structures of bones and the transitions among them. The process is much more direct than the use of Boolean operations with conventional CAD resources.

By means of example Fig. 17.4 shows the result of systematically applying different lattices of interest to develop a CAD library of trabecular dental implants based on the concept of the tissue engineering scaffold applied to conventional prostheses. Figure 17.5 shows the porosity distribution within the lattice core of an advanced porous dental implant.

After having analyzed different strategies for the personalized and biomimetic design of solutions for dental repair (and even regeneration, thanks to the potential of scaffold-based designs for incorporating patient’s cells, growth factors and drugs for enhanced response), Sect. 17.4 focuses design validation by means of in silico assessment resorting to FEM-based modeling, considering the combined performance and the mutual interaction of implant and jawbone.

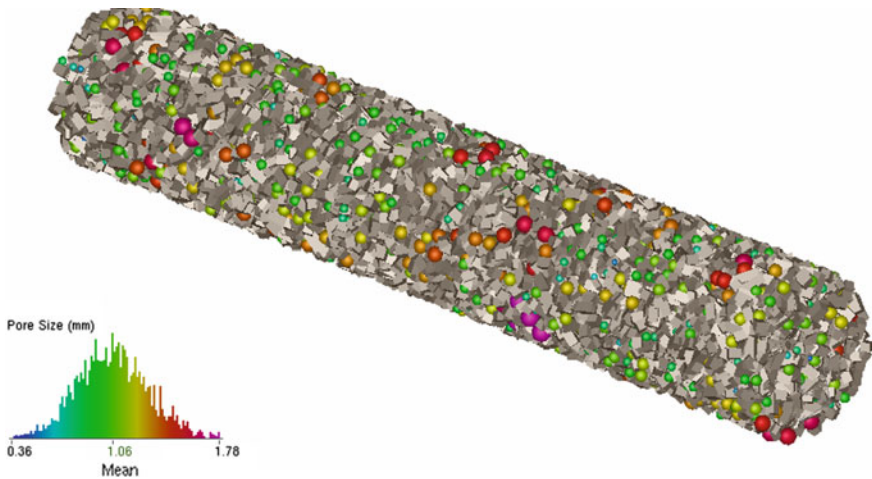
**Fig. 17.4** CAD library of trabecular dental implants based on the concept of the tissue engineering scaffold applied to conventional prostheses (Within Lab software, trial version: <http://www.withinlab.com/>)



## 17.4 Case Study: Modeling the Interaction Between Dental Implants and Jaw Bone

Before investing in the manufacture of prototype series for mechanical testing and *in vitro* assessment of a potentially effective novel design of a dental implant, it is very advisable to carry out a set of systematic *in silico* evaluations, so as to predict the performance of the implant, to assess the influence of the main design parameters, to compare alternative possible solutions and to analyze the effects of the implant on the surrounding biological structures.





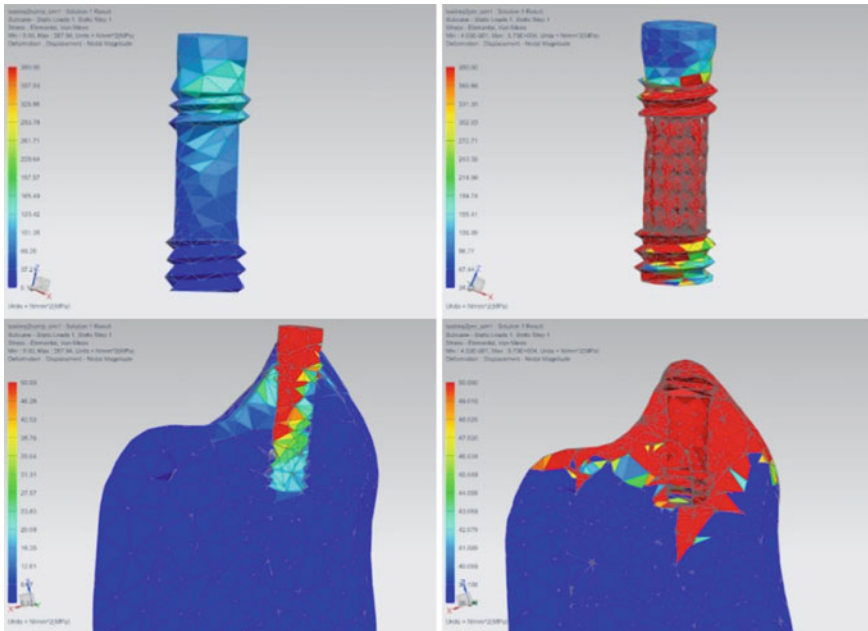
**Fig. 17.5** Porosity distribution of the lattice core of an advanced porous dental implant (Within Lab software, trial version: <http://www.withinlab.com/>)

The complexity of geometries, the anisotropy of the materials involved (such as bone in the case of dental repair or other biological structures), the loading and boundary conditions, among other issues, prevent the use of analytical methods and promote the employment of numerical and computational approaches, such as FEM-based simulations.

In present case of study, we compare the performance of a solid titanium dental implant with that of an alternative implant with a lattice structure for biomimetic response. The implants are loaded axially with 1000 N and transversely with 200 N to simulate them in a very demanding situation. They are simulated screwed to a portion of a jawbone, reconstructed with the help of medical images, in which a trabecular bone nucleus and an outer cortical shell can be appreciated. Both of them are affected by the drilled implants. Bone properties have been applied using commonly used values and differentiating between the cortical and trabecular (or spongy) zones (Hasegawa et al. 2010).

Figure 17.6 helps to summarize the results from these FEM based simulations regarding the impact of using compact and porous implants on the stresses under loading and on the effects upon the jawbone.

Clearly, the lattice structure reaches higher stresses, up to 300 MPa and around a 30 % higher than the values obtained for the solid implant. However the implant is still well below the limit of the material and the presence of porosities may help to load cells from the patient for enhanced integration or drugs for preventing the appearance of disease and inflammation after implantation. Regarding the jaw, the use of a compact implant leads to lower maximal stresses, but also to some stress concentration phenomena in the cortical zone, related with stress-shielding, while the spongy part remains almost unloaded. The use of a lattice implant promotes compatibility of strains between implant and bone and leads to more areas of the



**Fig. 17.6** FEM based simulation of the impact of compact and porous implants on the stresses under loading and on the effects upon the jaw

jawbone under acceptable stresses. The absence of stresses in the spongy bone, when using the compact implant, instead of having positive effects, may lead to bone resorption, loss of density and even implant failure. On the other hand, the lattice implant is more demanding for the jawbone, which may have very positive biomechanical effects for long-term durability of the union and for the mechanical stability of the implant, as bone is a living biomaterial, which regenerates itself taking into account the mechanical demands of the surrounding environment. The cells perceive them and respond accordingly, as the mechanical cues are part of the key aspects of the cell niche, together with other biochemical stimuli and with the presence of certain components within the extracellular matrix, towards gene expression and final tissue development.

## 17.5 Manufacturing Strategies for Dental Scaffolds and Trabecular Dental Implants

State-of-the-art CNC machining, being adequate for the direct manufacture of dental implants and crowns using the information from computer-aided designs, is inadequate for the manufacture of the very complex porous, lattice or trabecular

geometries of dental scaffolds, trabecular dental implants and similar hybrids for dental repair and even for dental regeneration (Zhang et al. 2013). Such more complex geometries must be obtained resorting to layer-by-layer manufacturing approaches or to real 3D printing technologies capable of producing detailed and complex parts with biomaterials including titanium, titanium alloys, (bio-)ceramics and, in the near future, composites, nano-composites, functionally graded materials and multi-layered materials, possibly resorting to combined processes (Park et al. 2010).

Computer-aided personalized dental implants, as well as more complex dental scaffolds and trabecular implants, can be obtained in titanium and titanium alloys, with adequate degrees of precision, using additive manufacturing resources such as selective laser sintering, selective laser melting and electron-beam melting. All these technologies start from a raw material in the form of metallic powder, which is heated with the help of different energy sources (laser-beam or electron-beam) until sintering or melting temperature. The processes are carried out in a layer-by-layer fashion and the final parts are obtained by the superposition of several layers following the desired geometry stored in the 3D CAD files, which drive the movements of the laser or electron beams. Companies such as Stratasys, Realizer GmbH, SLM Solutions GmbH and Arcam provide some of the most interesting machines for metallic additive manufacturing based on different approaches and energy sources.

Regarding the manufacture of design-driven dental scaffolds and trabecular dental implants in ceramic materials, which may prove even more biomimetic and biocompatible than titanium and related Ti-alloys, it is important to highlight the recent development of lithography-based ceramic manufacture (LCM), an additive manufacturing technology initially developed by the group of Prof. Jürgen Stampfl and Prof. Robert Liska at the Technical University of Vienna (TU Wien) and is currently commercialized by Lithoz GmbH ([www.lithoz.com](http://www.lithoz.com)) (Felzmann et al. 2012; Schwentenwein and Homa 2015).

Lithography-based ceramic manufacture provides the highest available degree of precision for the manufacture of highly complex geometries, such as those from dental scaffolds and trabecular dental implants, using a wide set of (bio-)ceramic materials. Attainable precision, as already shown in the examples from Chap. 16, is remarkable indeed. Structural elements with thicknesses down to 200  $\mu\text{m}$  can be obtained, reaching the level of precision required for any biomimetic model of bone and with the possibility of promoting multi-scale and functional gradients of density, porosity and mechanical properties controlled from the design stage.

## 17.6 Main Conclusions and Future Research

The vast knowledge generated during last decades in the field of biomedical materials and tissue engineering is starting to be applied as a source for designing novel types of implants for repair and regeneration tasks, pursuing improved

biomechanical and biomimetic solutions, especially in the area of bone repair and in the very relevant field of dental implants and prostheses.

Hybridizations between conventional compact bone implants and trabecular tissue engineering scaffolds are helping to adjust the mechanical performance of bone repair solutions to that of real bone, thus promoting long-term stability and preventing bone resorption thanks to more adequate distributions of stresses and strains. The increased surface to volume ratios of such porous, lattice or trabecular implants, based on the tissue engineering scaffold concept, help osseointegration thanks to enhanced cellular attachment to the implant, improve cell motility due to the presence of irregularities that help them to “crawl” and promote the use of incorporated drugs for disease prevention. The potential of dental scaffolds for the *in vitro* development of artificial teeth is also remarkable.

This chapter has focused on the area of advanced dental implants, detailing novel concepts, describing the development process of a scaffold library for dental applications, modeling and discussing dental implant interactions with bone (jaw-bone and skull are typically affected) and also analyzing the more remarkable technologies capable of providing adequate results for the manufacture of high-precision dental solutions.

Future challenges linked to optimizing the whole supply chain, from medical imaging and personalized implant design, to rapid manufacture of implantable components, taking account of the normative environment for the a combined promotion of personalized responses, optimal performance and patient security, still need to be addressed.

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