Chapter-1

Introduction

1.1 The clinical significance of Patient-Specific Implants (PSI) and the requirement of porous structures

Global life expectancy has been increasing with continuous advancements in technology. From 1960 to 2020, global life expectancy has improved significantly. It increased by 19.8 years for men from 50.7 years in 1960 to 70.6 years in 2020. Whereas, for women, it has increased by 20.5 years i.e., from 54.6 years in 1960 to 75.1 years in 2020 (life expectancy by worlddata.info). The average lifespan in advanced nations is significantly greater (over 80 years). Despite these advancements, a considerable amount of the population suffers and dies due to the effects of organ failure. Body organ failure can be caused by a variety of circumstances such as trauma, severe diseases, drugs, and the like. Many of these failures may now be resolved thanks to recent advances in medical research, by either treatments or replacements of defective organs with clinical substitutes that perform associated functions.

Among all the factors mentioned above, one of the major problems experienced includes the orthopedic conditions of a person. Due to the rapidly changing lifestyles of individuals, orthopedic conditions are considered to be the most affected. Traumatic and several other pathophysiological conditions together cause bone deformities affecting individuals of all generations. One such factor includes the problem of large segmental bone defects (LSBD) that are severe injuries making their treatment and outcomes difficult. Infections, tumor resection, osteonecrosis as well as open fractures that may be segmental, occur post debridement, or due to blast injury are the main causes of these defects (Mauffrey et al. 2015). Osteosarcoma, the most common reason for segmental defects is frequently observed at the physis of long bones. Limb ablation was formerly the only acceptable means for attaining disease eradication. Restoration and joint preservation for high-risk patients suffering from significant traumatic bone injuries continue to be a major problem for orthopedics (Kumta et al. 1999). Patients undergoing limb salvage surgery with conventional/standard metal prosthetics are continuously experiencing residual pain due to these off-the-shelf implants (Schwarzkopf et al. 2015). An overly stiff implant material could result in subsidence, which would preclude the benefits of motion restoration. Conversely, an overly compliant material would transfer most of the load to the center, accelerating its degeneration.

Humans have a wide range of physical characteristics. Average humans might be about 4 feet to 7 feet tall, weighing between 100 and 500 pounds. There are variations in skeletal morphologies, from externally evident changes like alignment deformities (varus/valgus) of the lower extremity to internal defects in shape (femur neck angle or femur head diameter) as shown in Figure 1.1. With so many variations, designing well-fitted implants for the general market is difficult. Since an average short human is not simply a reduced size of a taller one, it is important to study the variations in shapes and sizes of the available conventional implants.

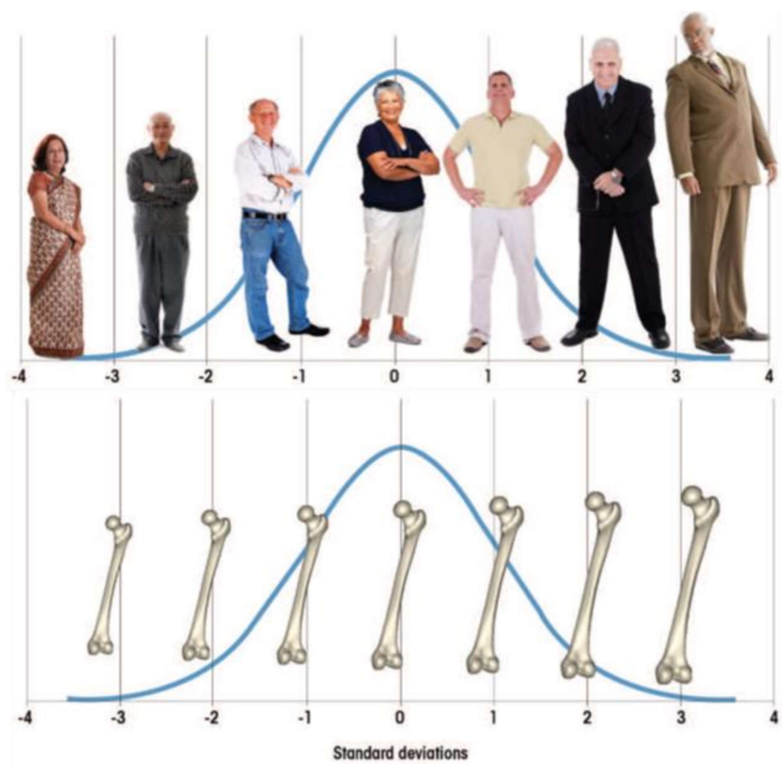

Figure 1.1: Variations in human populations and their respective femur bone anatomy.

Research from the literature report that implants developed for certain racial or ethnic population (like males or females, Asians, Europeans, and North Americans) or physical attributes (taller or shorter, slim or overweight) may not be suitable for others.

In general, several studies suggest that implants developed to benefit a specific group may not provide an appropriate fit and even result in high failure rates for other populations (Bischoff et al. 2014). As a result, a regular off-the-shelf implant may not be considered appropriate. Therefore, patient-specific implants (PSI) are a promising approach for the treatment of segmental bone defects in human long bones (DeVasConCellos et al. 2012). Where standard implants are developed using "population average" models, a patient-specific/custom-made implant is developed particularly for patients using the self-anatomy, enabling the patients to obtain a significantly better fit.

Reducing the stiffness mismatch of implants with neighboring bone tissues for minimizing the effect of stress shielding is still considered crucial for the implant's clinical effectiveness (Herrera et al. 2014). Porous scaffolds, therefore, are an excellent solution for this problem as they are designed to reduce the stiffness of an implant due to the presence of pores (Chen et al. 2020, Krishna et al. 2007, Van der Stok et al. 2013). Porous scaffolds designed in accordance with triply periodic minimal surfaces (TPMS) are considered extremely beneficial in the treatment of large segmental bone defects (LSBD) (Feng et al.2022, Li et al. 2019, Yánez et al. 2018, Ma et al. 2020, Dong and Zhao 2021).

They have been studied for over a decade and the available literature to date shows that the modifications in porosity, pore size as well as wall thickness of porous structure together contribute to obtaining desired implant models to resemble the properties of host bones (Zaharin et al. 2018). The elastic modulus of these porous structures can therefore be obtained in ranges of cortical and cancellous bones that reduce stiffness thereby reducing the problem of stress shielding (Dalaq et al. 2016). Their lightweight and highly porous structure support bone ingrowth and nutrient transportation within the implant which is not possible with solid implants (Santos et al. 2020). Additionally, this lightweight structure is capable of providing excellent load-bearing capacity which enables early mobilization, and freedom of flexibility. Patient-specific porous implants are, therefore, specifically designed in particular to match the structural requirements and are particularly customized for individuals to overcome the osseous defects that may either be natural, pathological, or traumatic in a person.

The present study is aimed at developing a framework that helps the manufacturer and the surgeon to adapt the type of implant and associated characteristics best suitable for an urgent resection, providing insight into the patient-specific parameters. To this aim, the proposed work focuses on the design of patient-specific porous (TPMS-Triply periodic minimal surface-based) Ti6Al4V implants and further carries out optimization to reduce stress shielding and enhance implant osseous integration and promote cell ingrowth. The TPMS-based porous implants are fabricated with medical-grade titanium alloy (Ti6Al4V) using SLM technology. Further, finite element simulations are performed to evaluate the mechanical performance and permeability of TPMS-based porous implants. Experimental observations compared with FE results to evaluate the suitability of each model for its application in different anatomical locations.

1.2 Modeling porous PSI: Role of multiple parameters

The present scenario shows interesting improvements in the application of 3D radiology, particularly computed tomography (CT) as well as magnetic resonance imaging (MRI), and simultaneous advances in the application of advanced manufacturing technology, that enables the possibility of three-dimensional analysis of patient's anatomical features, patterns (Zadpoor 2017). This can be used to develop novel customized patient-specific implants or to enhance the topology of conventional implants. Observations that were formerly acquired by 2-D X-ray radiography may now be obtained via 3-D techniques using CT or MRI, with greater precision. Therefore, a “patient-specific model” can be directly designed using patient-specific CT/MRI data, allowing engineers to develop implants with improved fixation possibilities.

Interestingly, specific morphological parameters like unit cell topology, porosity, and wall thickness can be beneficial for designing and optimizing porous implants (Al-Ketan et al. 2020). To begin with the porous implant design- a basic unit cell structure is created, which could be used to optimize the pore size and shape, porosity as well as wall thickness to obtain a set of porous structures (scaffolds) as shown in Figure 1.2. These structures are scaled and mapped on the resected bone with defects to develop customized porous scaffolds which are further analyzed to evaluate their morphological, mechanical, and permeable behavior.

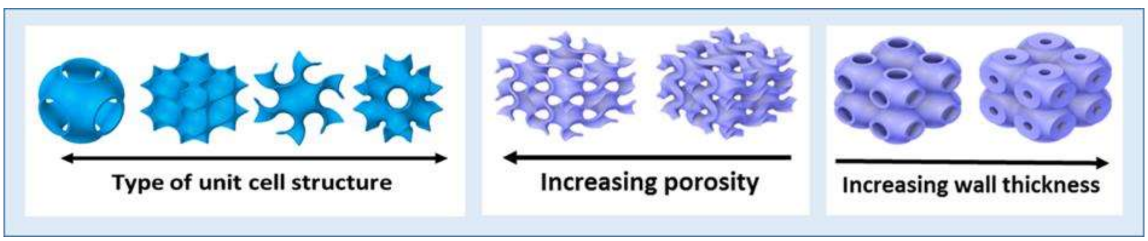

Figure 1.2: Parameters affecting the mechanical and biological responses of a porous implant.

The study provides pre-clinical in-depth knowledge about the performance characteristics of porous implants to ensure a customized fit. The three-dimensional data may be designed and analyzed in improved ways using methods like computer-aided design (CAD) and finite element simulations (FEA) to study the mechanical and biological performance, enabling the most essential parameters of modification to be reported.

1.3 Purpose of study: Motivation

Repairing load-bearing segmental bone defects efficiently is a significant problem in orthopedic and trauma surgery. To enhance bone regeneration, this frequently calls for the use of bone grafts or bone graft replacements. The autologous approach is still the gold standard for a bone graft, however, the amount of bone that can be extracted is restricted and accompanied by 10-40% comorbidities.

Additionally, defects exceeding 3cm in length require traditional weighted implants which have shown poor outcomes in retrospective studies. These limitations encourage the development of porous scaffolds that may be utilized as a material alternative on big implants to lighten their weight and improve their biomechanical and fluid transport capabilities.

1.4 Research problem: Gap

1. Parameterization of TPMS structures is not uniquely achieved to develop porous implants in an effective way to meet patient-specific demands.
2. Biological requirements such as cell attachment, ingrowth, and differentiation are not uniquely achieved from previous reports either by strut-based porous structures or porous structures fabricated by conventional methods.
3. Fluid responses are not uniquely achieved in previous reports in contrast to bone application with TPMS structures.
4. Conventionally developed implants have anatomical mismatch problems which give poor outcomes when used for treating LSBD as reported in previous literature.
5. Modulus (stiffness) mismatch is a serious concern in implants. Very little work is addressed and implemented.

6. A dual approach i.e., the use of patient-specific implants for long bones with porous TPMS implementation for the reduction of weight with optimal bio-mechanical parameters with the surrounding bone to compatibly withstand the physiological load has not been reported.
7. An on-demand virtual preoperative systemic approach for customized development of prostheses with controlled porosity has not been reported.

1.5 Research Objectives: Aim and Contributions

1. Solve the parameterization problem on the conversion of STL to SOLID complex TPMS porous structures when numerically analyzing its outcomes.
2. Reduce the elastic properties of a solid implant by introducing TPMS pores and minimize the risk of stress shielding.
3. Introduce an approach for integrating the geometric and biological properties of additively built lattice structures to achieve optimal scaffold parameters for direct application.
4. Investigate the role of morphological features on scaffold performances.
5. Develop novel patient-specific implants (PSI) for large segmental bone defect treatment.
6. Porous mapped PSI for the reduction of weight with optimal mechanical parameters to withstand the physiological load.

1.6 Novel Aspects of the Proposed Work

This work proposes a framework for developing a complex triply periodic minimal surface-based scaffold. The work shows the potential benefits of using morphologically controlled porous structures in prosthesis development on account of additive manufacturing. This work can be a comprehensive basis for the novel generation of a patient-specific prosthesis for the treatment of large segmental bone defects with superiorly enhanced biomechanical properties.

Also, it can be a novel template for virtual surgical planning (VSP) that might help the surgeons for managing high-critical in conjunction with CAD & AM and for bioengineers as facilitators.

The main aim is to develop a system that helps the Manufacturer & the surgeon decide which type of implant and what characteristics are best suitable for a given resection, given bone size, and patient-specific parameters.

1.7 Thesis structure