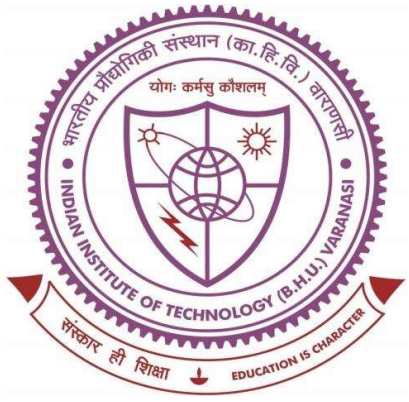
Design and Optimization of Triply Periodic Minimal Surfaces based Porous Scaffolds for Bone Applications: A Conceptual Prosthetic Design for Restoration of Large Bone Defects



Thesis submitted in partial fulfillment
for the Award of Degree

Doctor of Philosophy

by

Rati

SCHOOL OF BIOMEDICAL ENGINEERING
INDIAN INSTITUTE OF TECHNOLOGY (BHU)
(BANARAS HINDU UNIVERSITY)
VARANASI – 221005, (U.P.), INDIA

ROLL NO: 15021001

2022

CERTIFICATE

It is certified that the work contained in the thesis titled **"Design and Optimization of Triply Periodic Minimal Surfaces based Porous Scaffolds for Bone Applications: A Conceptual Prosthetic Design for Restoration of Large Bone Defects"** by **"Rati"** has been carried out under my supervision and this work has not been submitted elsewhere for a degree.

It is further certified that the student has fulfilled all the requirements of Comprehensive Examination, Candidacy and SOTA for the award of Ph.D. Degree.

(Dr. Sanjay Kumar Rai)
Supervisor
Associate Professor,
School of Biomedical Engineering,
Indian Institute of Technology (BHU),
Varanasi - 221005, (U.P.), India

SUPERVISOR

DECLARATION BY THE CANDIDATE

I, **Rati**, certify that the work embodied in this Ph.D. thesis is my own bona fide work and carried out by me under the supervision of **Dr. Sanjay Kumar Rai** from **21st July 2015 to 30th June 2022** at the School of Biomedical Engineering, Indian Institute of Technology (BHU), Varanasi. The matter embodied in this thesis has not been submitted for the award of any other degree/diploma.

I declare that I have faithfully acknowledged and given credits to the research workers wherever their work has been cited in my work in this thesis. I further declare that I have not wilfully copied any other's work, paragraphs, text, data, results, etc., reported in journals, books, magazines, reports dissertations, theses, etc., or available at websites and have not included them in this thesis and have not cited as my own work.

Rati

Date: 30/06/2022

Place: Varanasi

Signature of the Student
(Rati)

CERTIFICATE BY THE SUPERVISOR

It is certified that the above statement made by the student is correct to the best of our knowledge.

Sanjay Kumar Rai

(Dr. Sanjay Kumar Rai)
Supervisor
Associate Professor,
School of Biomedical Engineering,
Indian Institute of Technology (BHU),
Varanasi - 221005, (U.P.), India

SUPERVISOR

Sanjeev Kumar Mahto 30.06.22

(Dr. Sanjeev Kumar Mahto)
Coordinator
Associate Professor
School of Biomedical Engineering,
Indian Institute of Technology (BHU),
Varanasi - 221005, (U.P.), India

समन्वयक/CO-ORDINATOR
जैव चिकित्सा अभियांत्रिकी स्कूल
SCHOOL OF BIOMEDICAL ENGG
भारतीय प्रौद्योगिकी संस्थान (का.हि.वि.)
INDIAN INSTITUTE OF TECHNOLOGY (B.H.U.)
वाराणसी-221005/VARANASI-221005

COPYRIGHT TRANSFER CERTIFICATE

Title of the Thesis: Design and Optimization of Triply Periodic Minimal Surfaces based Porous Scaffolds for Bone Applications: A Conceptual Prosthetic Design for Restoration of Large Bone Defects

Name of the Student: Rati

Copyright Transfer

The undersigned hereby assigns to the Indian Institute of Technology (BHU), Varanasi all rights under copyright that may exist in and for the above thesis submitted for the award of the Doctor of Philosophy.

Date: 30/06/2022

Place: Varanasi

Signature of the Student
(Rati)

Note: However, the author may reproduce or authorize others to reproduce material extracted verbatim from the thesis or derivative of the thesis for author's personal use provided that the source and the Institute's copyright notice are indicated.

ACKNOWLEDGEMENTS

It is my greatest pleasure to have this opportunity to express my sincere appreciation to everyone who helped me during my Ph.D. program at the Indian Institute of Technology (Banaras Hindu University), Varanasi. First, I want to thank my supervisor Dr. Sanjay Kumar Rai, for his valuable guidance, encouragement, and paternal behavior throughout the work. His inspiring and excellent guidance is the key reason that I could successfully finish each of the research objectives. Without his guidance as a great mentor, this work would not have been possible.

A very special thanks to my external advisor Prof. Dr. Shekhar Madhukar Kumta (expert- Orthopedics, and Traumatology, CUHK, Hong Kong) for guiding me at each and every step throughout my thesis and beyond. My words will never be enough to thank you for your immense support, guidance, and trust in my work.

I offer my special thanks to Dr. Sanjeev Kumar Mahto, Coordinator of the School of Biomedical Engineering for providing all the necessary facilities for the School. I would like to express my appreciation to my research progress evaluation committee (RPEC) members, Dr. S.K. Mahto and Prof. S.K. Panda, for their kind cooperation during the course of my work.

I would like to thank the Institute of Medical Sciences, Banaras Hindu University, for providing the necessary data, without which the completion of this work was not possible. I also wish to express thankfulness to all other respected faculty members of the School for their kind support and valuable suggestions. I would like to sincerely thank all the supporting staff of the School for their kind help whenever I required it.

I would like to thank my wonderful lab mates and juniors for their stimulating discussions and for creating a cheerful environment in the lab. I would also like to thank my batch mates and friends for their extended support. This thesis would not have been possible

without their cooperation. I thank all my beloved friends across the globe for sharing my happy and sorrowful moments at all times.

I can never forget my parents Mr. Shobh Nath & Mrs. Chandrwati, my In-laws Dr. Nehru Singh & Dr. Kalawati, my (late) brother Mr. Mahendra Pratap, brother in law Mr. K.S Mohan, sisters Archana and Vandana, sister in law Dr. Pooja Singh, whose boundless love, constant inspiration, emotional support, and blessings have provided me encouragement at every step of life. My parents' everlasting shower of blessings kept me moving easily with all hazards vanishing miraculously. I am especially thankful to my husband Dr. Nishant Singh whose consistent guidance, support, and love throughout this journey made this dream come true. My word power fails to express my feelings of gratitude to my loving son Ridant for his unconditional love and sacrifice during my work.

Lastly, I would like to thank Almighty, for having made everything possible by giving me the strength and courage to do this work.

Date: 30/06/2022

Place: Varanasi **(Rati)**

Dedicated
To
My Loving Family

Table of Contents

Page No.

LIST OF FIGURES

LIST OF TABLES

PREFACE

Musculoskeletal disorders and associated bone diseases are one of the major causes of pain and disability, resulting in a social and economic burden for our society. Due to the rapidly changing lifestyles of individuals, orthopedic conditions are considered to be the most affected. Joint diseases, like osteoarthritis and rheumatoid arthritis; bone diseases, like osteoporosis and consequent fragility fractures and trauma-related fractures; bone tumors i.e. osteosarcoma, frequently observed at the physis of the bones often lead to the problem of large segmental bone defects (LSBD). These are severe injuries affecting individuals of all generations causing continuous discomfort that limits motion, flexibility, and complete functional strength, significantly decreasing work efficiency and making their treatment and outcomes difficult. 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 of orthopedics. When the joint function is impaired or bone defects are too large to be treated with bone grafts, prosthetic implants are the gold standard to replace the defective location or fill the gap.

Engineering and medical technology breakthroughs in recent years have offered the resources to design and implement novel medical methods to overcome these challenges. However, despite the tremendous progress in the field of orthopedic implant devices (material and design), a reasonable proportion of patients undergoing bone reconstruction or limb salvage surgery with conventional/standard metal prosthetics are continuously experiencing a variety of postoperative complications which compromises the overall outcomes causing residual pain due to these off-the-shelf implants. Pathophysiologic, mechanical, or a combination of both conditions are responsible for such complications, due to which the developed implants are still not completely marked as optimum. However,

the long-term success of a prosthesis is directly or indirectly dependent on the biomaterials used and the shape of the prosthesis. To date, medical-grade titanium and its alloys (Ti6Al4V) are considered one of the most biocompatible metals and are used to fabricate implants due to their outstanding outcomes and long-term stability. However, due to its high elastic modulus of ≈110 GPa as compared to natural bone (≈ 0.02-30 GPa), stiffness mismatch between bone and implant results in the stress-shielding phenomena. It occurs due to inefficient stress transfer to the bone surrounding the implant causing bone weakening and implant loosening thereby resulting in the ultimate failure of the implant. Additionally, conventional fabrication methods such as gas injection molding, hot isostatic pressing, etc. are used to provide porous coatings on the implant surface to enhance the biological properties. These coatings are simply made up of arbitrarily distributed and shaped pores with uncontrolled sizes, making it difficult to achieve quantitatively adjusted stiffness around the bone anatomy and no possibility of bone ingrowth and nutrient transport. Hence, these traditional implants are not sufficient for generating complex geometrical cellular structures that can vary the strength of Ti6Al4V implants to mimic the natural bone properties. Furthermore, due to the dynamic variability of bone structure, the traditionally manufactured implants used for the treatment of SBD usually lead to maladaptation resulting in the ultimate failure of the prosthesis in the postoperative period.

To address these issues, the present study focuses on the computational design and development of patient-specific porous implants inspired by advanced additive manufacturing (3D printing) techniques that can provide the advantages of customized fit being patient-specific (PS) in nature; lightweight porous geometry enables better mechanical performance by reducing stiffness gap between bone and implant and facilitates the possibility of bone ingrowth thereby being permeable to body fluids and nutrient exchange. The global objective of this research is to computationally analyze and evaluate

the morphological, mechanical, and permeable performance characteristics of the designed and developed porous structures for the treatment of large segmental bone defects. The porous implant geometry is typically based on the nature-inspired triply periodic minimal surfaces (TPMS), which have unique properties of sustaining extensive loads with extremely lightweight geometry.

The study includes four sequential stages. First stage deals with the efficient mathematical modeling and design of TPMS-based porous structures which are parameterized for robustness. The selection criterion for TPMS structures specifically, Schwarz primitive (P) and diamond (D), and Schoen's gyroid (G) and I-graph wrapped package (IWP), included in this research work are based on previous in vivo studies on the effect of shape and size of porous structures. The effect of morphological parameters like thickness constant on volume fraction; the size of a unit cell on stress distribution; pore size, as well as the effect of the number of unit cells on the change in elastic modulus of TPMS structures is evaluated to select an optimum criterion for the study of lattice TPMS structures that uniquely patterned in three coordinates. Based on this criterion, robust analytical (implicit) and CAD-based modeling approaches are employed to obtain an optimized unit cell structure that can be effectively used for FEA purposes. An algorithm to convert the STL model into a solid model is developed that enables easy implementation of these models for finite element studies (FEA). TPMS lattices for each of the P, D, G, and IWP structures are then modeled by repeating the unit cells in three independent (x, y, and z) Cartesian coordinates. At the end of this stage, four TPMS lattice structures of 2x2x2 are obtained to evaluate the mechanical performance for their possible applications depending on the bone quality of the application area.

The second stage deals with the preparation of FE models of the TPMS lattice structures for evaluating the morphological properties such as thickness, pore size porosity, and

surface-to-volume ratio to assess the suitability of structures for bone replacement accounting for cell adhesion, migration, and bone ingrowth. The mechanical performances of these lattices were numerically analyzed by assigning additively manufactured Ti6Al4V nonlinear material properties and applying boundary conditions with appropriate meshing parameters and loading steps in accordance with IS0 13314:2011. This enables the establishment of a unique structural-mechanical relationship for the structures included in this study. The assessment was done to study the effect of the design, pore size, porosity, and strut thickness on the mechanical, and morphological properties of these structures. Finite element structural analysis was performed to study the stress distribution pattern, elastic modulus, compressive strength, and energy absorption properties to assess the mechanical performance characteristics of TPMS lattice structures. Additionally, computational fluid dynamics (CFD) analysis was also performed to study the mass-transport properties such as permeability, and wall shear stress (WSS) of the fluid, to access the vascularization and cell attachment thresholds on the following parameters included in the mechanical evaluation.

The third stage demonstrates the development of a 3D femur model obtained from CT scan data of healthy femur bone providing key insights into anatomical features. The developed 3D femur model was used to create an intentional segmental bone defect of 50 mm size that was surgically fixed with a TPMS-based (P) porous scaffold of 80% porosity, to access the performance on account of stress shielding. The porous scaffold is implanted at the defect location and physiological boundary conditions are applied to the assembly to study the stress transfer pattern from the implant to surrounding bone tissue.

Lastly, the fourth and final stage deals with the development of patient-specific prostheses to treat tumor-infected femur bone. Surgical resection of the tumor-infected segmental defect was performed virtually and a morphologically controlled PS prosthesis particularly

signifying large segmental bone defects was developed with the conceptualization of the insertion of the implant to the final outcomes. To this, a complete strategy was demonstrated to develop a conceptual prosthesis enabling porous structures with controlled morphological features that mimic the host bone. Lastly, the approach of porous mapping on the solid implant is well represented which helps to obtain an anatomically matched lightweight structure to bridge the gap between the mechanical performances and ultimate outcomes of the treatment of large segmental bone defects.

Overall, the results indicated that the TPMS-based porous structures have the potential to be used as porous scaffolds for the treatment of large segmental bone defects in orthopedic applications. Due to their outstanding load-bearing abilities with extremely lightweight geometry and dynamically variable morphological and mechanical properties, the TPMS-based porous scaffolds fabricated with Ti6Al4V inspired by additive manufacturing technology can be applied at different anatomical locations of bone depending on the bone quality. Also, the novel concept of anatomically matched porous implant design presents its potential to be used in the real scenario of applications in orthopaedics subjected to experimental and clinical validations.