DESIGN, 3D PRINTING, & EXPERIMENTAL ANALYSIS OF LATTICE-BASED BIODEGRADABLE METAL IMPLANTS FOR BONE REGENERATION IN SEGMENTAL BONE DEFECTS

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Abstract

Bones naturally self-repair in the case of fracture or minimal bone loss. However, issues such as misalignment, considerable bone loss, and size of the fracture site can hamper this process, especially for load-bearing bones below the waist. Existing procedures can correct misalignment, yet more complex cases require highly invasive permanent solutions like rods or plates. Thus, a suitable temporary alternative is needed.

This study covers the design, simulation, fabrication, and evaluation of a lattice-based degradable metal implant for load-bearing fracture sites requiring such intervention. It is designed to meet the load-bearing requirements while minimizing the amount of material used. The implant gradually degrades as the bone is repaired, with implanted stem cells accelerating the process. Furthermore, this study discusses various experiments performed to evaluate biocompatibility, tissue-metal interface, and mechanical performance. Along with previously performed material characterization and biocompatibility studies, these investigations are essential to developing a functional degradable metal implant.

Introduction

The human body is equipped to repair a variety of tissues when there is loss or damage. This is especially critical for connective tissues due to the wear and tear they undergo [1]. To accomplish bone repair, the fracture site induces granular tissue growth from each end of the fracture, and these then extend into the fracture area and come together to form a connection known as *bridging* [2]. However, bridging has its limitations when it comes to large sections of bone loss or complex fractures. This limitation in bridging due to the gap being too big is defined as a critical defect [3], and external help is needed for the correct alignment and repair of the bone in question [4]. This is most seen in the case of bone breakage and bone loss, with external or internal help needed to facilitate the repair. This can occur in partial or segmental fractures due to excessive or unbalanced loading on the bone, or when the bone must be voluntarily removed due to scenarios such as cancer or necrosis [5].

External repair and alignment techniques for simpler fracture cases such as braces and casts are in use for sites where loading is not necessary for movement (such as arm fractures) [6], but there are additional issues when it comes to fractures below the waist, as the techniques need to deal with the repair, alignment, and load from body weight and movement, as the mechanical requirements are still present despite the fracture [2,4]. External help is needed to mitigate the

loading requirements. Current Methods like casts, rods, and plates do ensure that the foot is arrested in the correct alignment and load is transferred, but there are several disadvantages to these methods. These fixtures are permanent in the case of rods and plates and may cause toxicity issues [7,8]. In some cases, while arresting the foot, such measures tend to overcompensate for the load. This is known as stress shielding and can cause bone loss [9]. In some cases, especially with pediatric or geriatric patients, conditions such as rapid growth or osteoporosis may hamper bone growth and repair, as well as cause further bone damage when internal devices like plates and rods have been used that need to be attached to the bone surface [10]. Additionally, dealignment during fracture healing is also a possibility with any external method and should also be considered before it's too late in the healing process, this can cause incorrect healing and permanent misalignment [11].

Current regenerative therapeutic approaches for bone repair such as autogenous bone grafts [12], allogeneic banked bone [13], demineralized bone matrix (DBM) pastes [14], polymeric scaffolds [15] and ceramics grafts [16], do offer alternatives that do not use metallic implants, but they are not well suited to the repair of load-bearing bone defects; primarily due to the structural demands of such bones [17]. Autogenous bone grafts and allogeneic banked bones have insufficient mechanical properties and the restricted volume of usable bone for autografts limits their use for load-bearing applications, especially in the case of segmental defects [18,19].

Although metallic implants composed of medical-grade steels and titanium have been widely used in the repair of segmental bone defects such as craniofacial reconstruction, dentistry, total joint replacement, and limb lengthening, their long-term residence in the body can result in complications such as corrosion/wear and metal toxicity, mechanical failure of the implant, stress shielding, and limited engraftment of the implant with the hard tissue [20]. There is considerable research in this area but focused more on the degradation and biological performance aspects rather than design, even for AM cases [21]. The focus of this paper is to combine such desired features and incorporate them into a single implant. However, combining biocompatibility, degradability, and AM leads to limited choices in materials considering the functional requirements [22]. AM-based implants have mechanical properties that are like current steel and titanium orthopedic implants, but they offer customizable form factors and variable degradation rates that can be patient-specific allowing for the design of personalized interventions [23]. This convergent approach will enable the development of new hybrid metal/organic therapeutics for personalized/precision orthopedic interventions in load-bearing segmental bone defects.

This design-focused research works in conjunction with research on material selection and characterization [24] by the authors to prepare and evaluate an implant that would be adequate and sustainable for *in vivo* studies in the future. Furthermore, with the several types of experimental analysis performed for this research, some have been established as the platform on which further such experiments can be performed, either with a broader focus, more data points, or both, giving us a well-tested functional lattice-based biodegradable implant. The novelty of this research is establishing a bridge for existing research and bone repair techniques and leveraging the potential to combine them for a novel future clinical application, with existing research in literature focused on either lattice-based design, extensive biological studies, or *in vivo* evaluation of material performance.

Materials & Methods

The issues faced by segmental defects discussed in the previous section can be mitigated with the use of implants designed and implanted in the body to address one or more of the points. Bone repair with implants requires three primary aspects:

- The size and geometry that meets the physical requirements of the fracture site, and in the case of load-bearing location, also contribute to mitigating the loading requirements [25], [26]
- Seeding the implant with stem cells, that would grow and aid with bridging [27]
- Providing signaling molecules to convert stem cells to bone, also known as osteoblasts [27], [28]

Considering the various shortcomings in each of these approaches, novel approaches are needed that can promote tissue regeneration while providing sufficient mechanical strength and stability to the defect area during the load-bearing bone regeneration process. Thus, a viable solution would be to use degradable surgical implants that result in endogenous bone regeneration and tissue repair. To be a comprehensive solution, it is imperative to address the shortcomings of the previously discussed approaches. Figure 1 summarises the various features that are needed in an implant of such scope and functionality, as well as outlines the various experimental techniques that must be utilized to evaluate the performance of such an implant and establish its robustness. With the focus of this paper in mind, only the factors that play a direct role in design are discussed below, with additional features and experimental evaluation discussed in a prior publication [24], while detailed comprehensive results and discussions are planned for publications in the future.

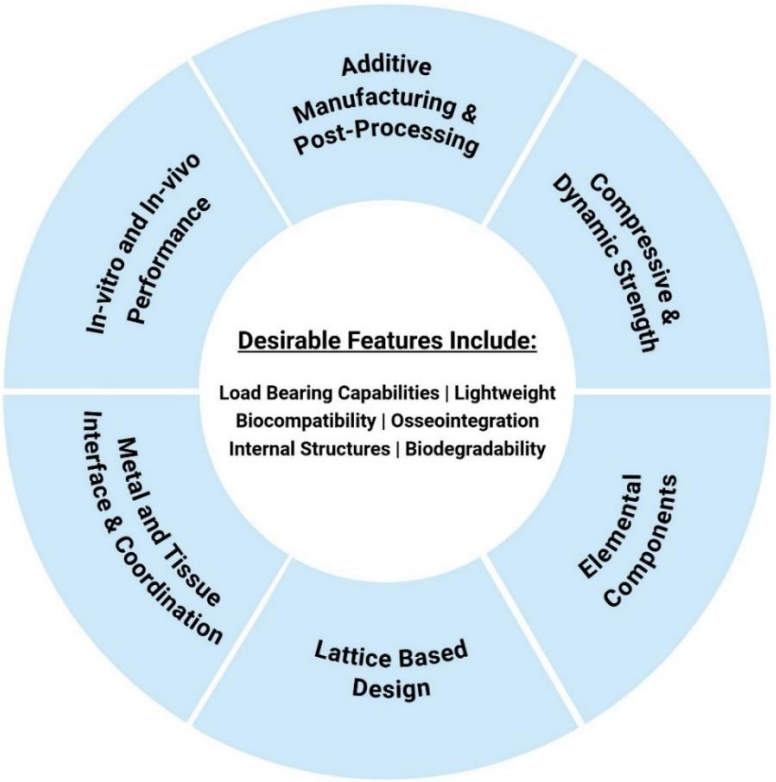

Figure 1: Desirable Features in a biodegradable metal implant for segmental bone defect repair

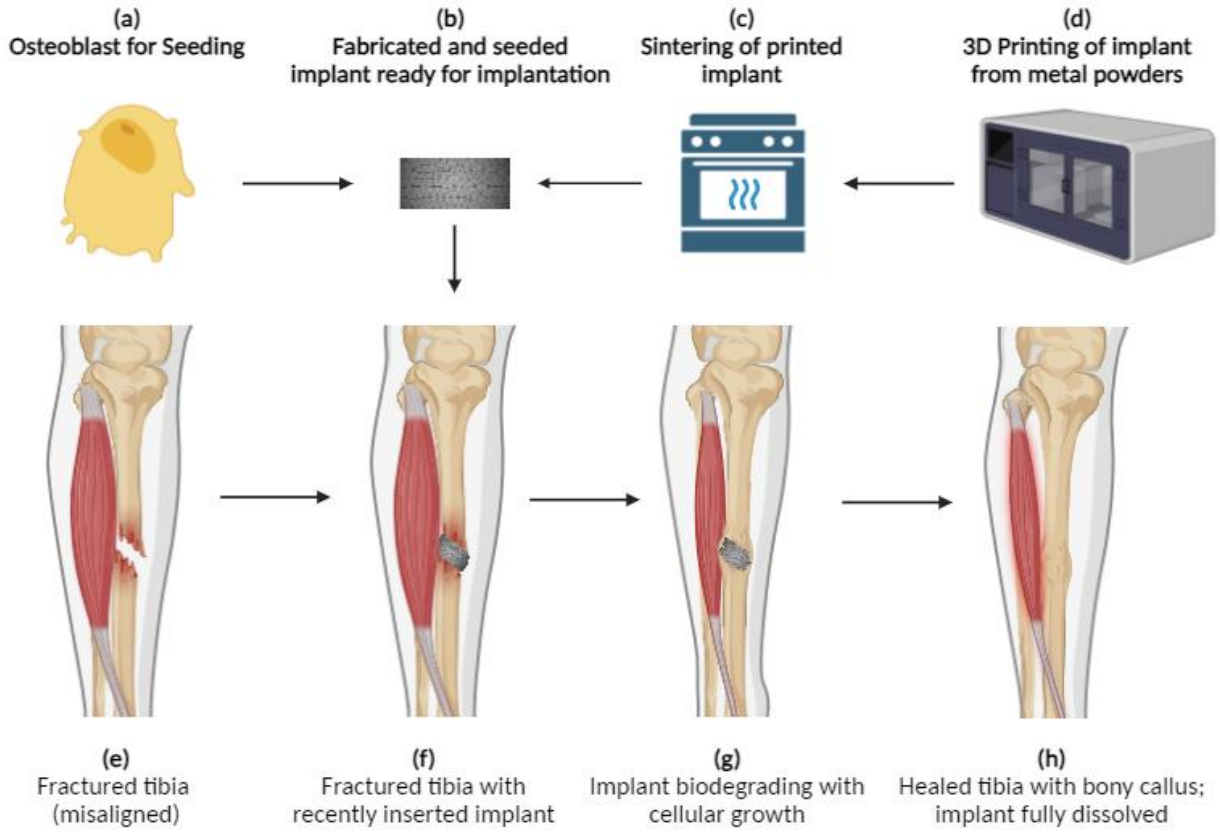

Figure 2: Implant Design, Fabrication, & Application Workflow (Made using Biorender)

With the requirements of the implant established, the overall workflow for the design, fabrication, and evaluation of the implant was conceptualized, as shown in Figure 2. The design portion of the workflow, which this study primarily focuses on, is limited to steps (b), (c), and (d) shown in the figure, with design working hand in hand with printing and evaluation, with several iterations and changes needed before designs were finalized, with several designs failing due to printability issues. However, additional factors that play a major role in the design of the implant that also falls in other sections need to be considered as well and are discussed in detail below as part of the methods followed for this study. Based on the material studies conducted before this phase of the research, the printing method selected for this study to balance degradation and implant strength is binder jetting, while the materials used for this design study are limited to two different material mixture compositions (% compositions by weight):

- Iron (Fe): 69%, Manganese (Mn): 30%, Silicon (Si): 0.5%, Copper (Cu): 0.5%
- Iron (Fe): 68%, Manganese (Mn): 30%, Silicon (Si): 0.5%, Silver (Ag): 1.5%

With material selection and characterization with *in vitro* experimentation completed, the focus shifts to the design stage. Most research in the literature related to degradable metal implants is centered around material selection and characterization, with few even going as far as *in vivo* evaluation [29], [30]. The newer research focuses on process selection and development for AM process production of biodegradable metal implants but does not evaluate functionality, especially from a mechanical properties perspective [31]. Other specific cases such as research on binder jetting done by Chou et al, evaluate bone performance for tensile testing, where the

actual application would be for compressive testing [32]. This research investigates incorporating lattice-based design into such implants, increasing the robustness of the implants beyond what is available in the literature. Evaluation of designs is three-fold:

- They must pass simulation requirements (performed on nTop™, formerly nTopology™) of meeting the desired mechanical properties, while not indicating high stress zones that may lead to stiffness and subsequent stress shielding. Considering the material limitations of nTop, with the mechanical properties of such metal mixtures not easily simulated accurately, it is necessary to evaluate them using mechanical testing as well.
- After passing the simulation, the designs must be printable. Any failure at printability, including during the extraction of the print as green state is considered a failure (except in the case of human error, in which case the specific print is repeated). The print must be repeated 3 times. This is achieved with more than 15 prints in each selected final design as they are needed for various experiments.
- With the design steady in a green state, it must also be passable if it doesn't show any signs of fracture, cracking, or failure after sintering. Internal beam failure that is not easily visible is also a possibility, but it is expected that cases of visually inaccessible catastrophic failure may be rejected during mechanical testing.

Loading & Design Considerations

The Design stage was done in three steps. The first and simplest step was fabricating a 2.5D part for process selection and alloy printability (1-2mm). This was done keeping the ASTM E 09 standard for compression testing for short specimens (Table 1) in mind primarily the length-to-diameter ratio. However, experimental evaluation also must be considered in this case, including the *in vitro* studies and the final application. A major restriction with utilizing the current standards is that it does not accurately evaluate the loading capability of the implant as it is not expected to be that long. Furthermore, once lattice-based designs are introduced into the base implant, this will become a more significant problem as the taller test piece will provide more ductility than the implant should.

Table 1: ASTM E 09 standards for compressive testing samples

Specimens	Diameter		Length		Approx *L*/*D* Ratio
	in.	mm	in.	mm	
Short	1.12 ± 0.01	30.0 ± 0.2	1.00 ± 0.05	25 ± 1	0.8
	0.50 ± 0.01	13.0 ± 0.2	1.00 ± 0.05	25 ± 1	2.0

Considering that binder jetting and sintering facilitate the construction of the resulting complex porous architecture with controlled porosity, and custom structural and mechanical properties, without causing microstructure changes in other laser-based printing processes, it also provides lesser density and more shrinkage during sintering. While this has been previously discussed, it is now needed to evaluate it experimentally and take it into account for design and fabrication. Simulation sizes, however, do remain the same, with test samples kept consistent throughout with a height of 0.5mm and a diameter of 100mm.

Density Analysis

Evaluation of density was performed using the Archimedes test. The Archimedes test is a fundamental technique for determining the density of an object that leverages the principle of buoyancy. For this research, this principle can be used to find the density of the sample by comparing its weight in air and its apparent weight when submerged in DI water. This analysis was done for Fe-Mn and Fe-Mn-Si samples, with the silver and copper samples giving similar results as the latter, and they weren't repeated in the interest of sample preservation, as samples used for this test cannot be utilized for any other experimentation due to contamination and fluid absorption issues. The valuation for each was found to be as follows:

- Temperature: 22.5°C
- Humidity: 32%
- The density of DI Water: 0.99766 gm/cc
- No. of Samples: 10 each

Table 2: Density and Porosity Analysis

Composition	Exterior Volume of Sample (cc)	Bulk Density (gm/cc)	Volume of Pores (cc)	Apparent Porosity (%)
Fe-Mn	0.1201	5.1598	0.0822	22.5876
Fe-Mn-Si (0.5%)	0.0752	5.7784	0.1018	44.7040

Based on these results shown in Table 2, we see that the Fe-Mn samples are 65.53% dense compared to what is expected for the volume, with the introduction of silicon increasing the density to 73.3%. Though this does not impact design directly, it will impact mechanical performance, as the density will cause significant compression and absorption of the mechanical load during the initial part of the application. This analysis also allows one to evaluate apparent porosity (Table 2), which would make the implant more hydrophobic and provide the possibility of cells being integrated deeper into the structure as well. Porosity also plays a significant role in internal properties, with such data indicating that grain growth will not be possible due to low densification, as corroborated by the EDS.

Shrinkage Analysis

During the density experiment in the previous section, the shrinkage was estimated based on a change in volume from the target sample dimensions and volume to the average values seen after sintering (dry samples only). Due to the weak green state of the printed samples, this evaluation could only be performed after sintering was completed. The theoretical volume was calculated based on what was expected and compared with the actual volume of the sample. Table 3 indicates the results obtained, with both samples showing a similar shrinkage of 38.8% for Fe-Mn, and 36.15% for Fe-Mn-Si, which is significant and now must be incorporated into design, especially in later cases when designs are made with implantation for *in vivo* or clinical application in mind.

Table 3: Shrinkage Analysis

Composition	Calculated Theoretical Volume (cc)	Actual Volume (cc)	Shrinkage (%)
Fe-Mn	0.12008	0.19625	**38.80**
Fe-Mn-Si (0.5%)	0.07518	0.11775	**36.15**

Static and buckling analysis on a solid model

Before delving into lattice-based modeling, the solid basic model was first evaluated on nTopology to evaluate the stresses on the implant and evaluate the displacement and the distortion in the implant. The worst-case loading case from the literature is considered for this [24], with 1.5 kN force on the top face and the bottom face being constrained. This load provides a simplified load version of bone loading. Bone loading is highly dynamic, with variations in both magnitude and direction, with additional factors such as jerk and changes in direction also applicable to how the bone is loaded [33]. Though this load application is governed by a complex system of muscles and tendons, it can be simplified to compressive and shear stress that is applied to the various sections of the bone. An implant such as this is not designed with shear stress in mind due to the relatively low thickness, however, it is necessary to make sure that the implant does show good buckling properties without stress points. Once the part was meshed and simulated with the correct normal force and constraints the preliminary results discussed [24] were obtained. The implant was found to have extensive loading on the load face with poor dissipation due to excessive stiffness. This indicates that the lattices used need to be less stiff and buckle more to be able to dissipate the load. This was corroborated by the buckling analysis, which showed a localized region of potentially excessive buckling and sectional failure of the implant, which can be avoided with better dissipation of the load. These results have some critical bearing on the application of such an implant. A stiff implant induces stress shielding, which can cause bone loss from the affected region. This is detrimental to osseointegration and bone growth from that region, if the implant degrades from that area without adequate growth and integration, the implant may fail. Since an entire surface is giving an issue here, it is even possible that the integration of the implant fails as soon as the load is applied, as such a large section being affected can cause implant slippage. This phenomenon is also seen in bulking analysis, with stress concentration on the edge indicating that stress shielding can occur on the edges and grow inward.

Thus, the use of lattice-based implants would reduce stiffness and increase ductility, improving the functionality of the implant and reducing the chances of issues such as stress shielding. Furthermore, it also allows one to maintain structural properties while reducing material, ensuring the implant degrades faster, giving the body fewer by-products to deal with, and providing even greater surface area for stem cell implantation and osseointegration.

Implementation of lattices in the model

With the emphasis on lattice-based implants established due to the results seen in the previous section, it is necessary to establish the key factors that need to be considered from a design perspective and incorporated into designs with their augmentative impact on the application in mind. Based on the experimentation done so far, three key factors were isolated for this purpose, the impact of which has been covered in previous sections:

- **Lattice Cell:** Different cells will have different properties and limitations. Based on the lattice cells available in nTop, samples were populated and evaluated. 18 different unit cells have been utilized, with different orientations depending on the type of cell, and 4 different lattice structure populating methods, giving rise to 56 designs. This approach is an expansive version of examples discussed in prior research, with more designs evaluated and simulated.
- **Node Location:** Variations in the location of nodes for the same cell and structure can alter how the implants respond to manufacturability and functionality. In the case of the nodes

being on the edge of the implant, it promotes better structural stability and printability, as the surface area is greater, giving better print bed adherence and a lesser chance of breams fracturing and breaking off during fabrication. However, when the nodes are present in a more internal position, the exposed and incomplete beams stick out. Though this makes it harder to fabricate them, it would give better roughness and osseointegration for the cells growing from the native bone into the implant and reduce the chance of slippage.

- **Beam Thickness:** There can be significant variation in how thick beams are for an implant, which plays a critical role in implant microporosity, which in turn affects implant strength and cell adhesion. The thicker the beam, the better the strength, but the harder it is for cells that are seeded into the implant to penetrate through and adhere to the internal structures of the implant for uniform cellular growth. Furthermore, an increase in beam thickness means more material that needs to be degraded, however, the flipside of this is that thinner beams may show sudden and unexpected failure due to premature degradation.

Mechanical Testing

With the simulation results-based selection of designs, along with classification based on printability and sintering assessment, along with the alterations in design to establish an appropriate implant for tissue and metal integration, the designs must also be tested for mechanical performance. The implants will be tested using compressive testing using the strain rates and loads obtained from published literature. ASTM Standard: E9 – 09 (Compression Testing of Metallic Materials at Room Temperature) has been used for the testing, with the modifications to consider implant functionality and dynamic loading discussed earlier. With the optimal loading at 1.5kN, 2 kN was used to load the sample to create a buffer and provide additional compression as the bone is initially loaded with body weight with a strain rate of 0.1/s. The maximum load possible from the setup is 10 kN. The basic sample size of diameter 10mm and height 5mm was used as samples were tested on an Instron 599 system (Instron, Norwood, MA, USA) with two 1 kN load cells and pneumatic compression grips. Samples were subjected to tension at a rate of 1 mm/min until failure or to 90% strain as the system cannot be programmed to pause after the required compressive stress of 10MPa is reached.

Cellular Confocal Imaging

As mentioned earlier, this is needed to corroborate the results obtained in the study, as well as to investigate the effect of cell growth on a lattice-based 3D printed implant, as the current study is limited to manually pressed and sintered implants with negligible porosity. Lattice-based implants provide much greater surface area and penetration, allowing for better cell adhesion, but may be a challenge when it comes to fluorescent imaging. To evaluate the design performance using confocal imaging, the lattice-based designs were seeded with osteoblasts and viewed on Day 4 and Day 10. The distribution of cells on each sample was assessed after 6 h using a Leica SP8 DIVE multiphoton microscope (Leica Microsystems, Germany) with a 16× water immersion lens. Dead cells were assessed by staining with ethidium homodimer-1 (EthD-1, 4 µM) for 30 min in the incubator, which was then imaged using the Zeiss Axio Observer microscope. Images were analyzed using ImageJ to determine the red fluorescence intensity and the cellular viability was quantified by dividing the fluorescence intensity of dead cells (red) by the combined fluorescent intensity of both dead (red) and live (green) cells.

Results & Discussion

Lattice-Based Implant Design

With the mechanical and application-related factors taken into consideration, we can now establish the overall approach for introducing and populating lattice cells. The outer shell design is fixed to the 10mm diameter and 2.5mm height of the implant that has been used for experimentation so far. Though it is expected that in practical use this will never stay the same, customization of implants is beyond the scope of the current research, The population of lattice cells is determined primarily by the type of cell and the method of lattice population. To be successful, a design must be able to succeed in the following criteria:

- **Simulation:** There must be no significant stress concentration areas.
- **Printability:** The part must be printable with no issues due to feature size-related limits and the possibility of cleaning the part after curing without breaking or cracking
- **Sintering:** The part must not fail or crack after sintering

Each design was printed with varying beam sizes, ranging from 1 mm to 5 mm in diameter, with edge and center nodes in each case. Though some cubic graph unit cells gave good results in the simulation stage, ultimately there were major fabrication failure issues with such designs, with them either failing due to the features being too thin to print, or walls cracking during the sintering phase. The TPMS and vornoid cells showed a lot more promise in comparison, with most variations in diameters providing successful prints. A majority of the edge node lattice also failed due to the concentration of stresses.

5 designs were finalized after the fabrication process was completed, listed in Table 4, with Figure 3 showcasing the schematic for the design workflow and approach taken for eliminating designs, along with the number of eligible designs at each stage. For each case, it is possible that some designs are not fabricable for certain thicknesses. This plays an even more critical role once ramping is introduced. Furthermore, it is possible that some thicknesses are not possible to generate on nTop in the first place as they cause deprecated lattices structured with intersecting surfaces and beams. A key inference here is that design selection is based on the performance of the settings and design features taken into consideration. It is indeed possible to fabricate other successful designs. Furthermore, it is also possible to fabricate designs eliminated by this study based on printability issues, as it is possible that certain designs can be fabricated based on alteration of print parameters and disregarding print time considerations.

Table 4: Finalized Lattice Structures and Thicknesses

Design No.	Lattice Cell	Successful Thickness(es)
1	Vornoid Thickened Lattice	2, 3 and 5 mm
2	TPMS: Schwartz	2, 3, 4, and 5 mm
3	TPMS: Neovius	2 and 3 mm
4	TPMS: Gyroid	3, 4 and 5 mm
5	TPMS: Split	4 and 5 mm

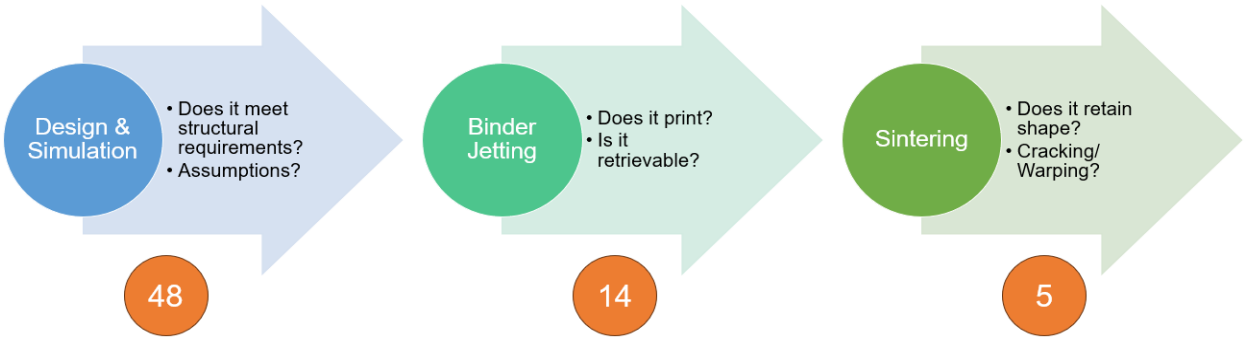

Figure 3: Design Workflow and Successful Designs at Each Stage

The various lattices were populated and structured within the implant using random point generation. Though highly geometric with a well-defined unit cell, such lattices make it difficult to control the pore size and may be difficult to print, especially when the strut diameter or the thickness of the TMPS surface is reduced. Thus, starting with a thin wall and thickening it would be a better option (also known as implicit modeling). The thickness can be controlled and varied with the part. In this case, the nodes and their positions become a critical choice. Porosity can be controlled on nTopology by generating random points on the solid model, with more points reducing the pore size, dictated by the point spacing input. Based on these points, the software can be used to generate a lattice wireframe. This must be thickened to generate the completed lattice. The strut or surface thickness will affect the pore size as well. To ensure that the strut or surface thickness is considered during pore size calculation, it should be included as a variable, rather than thickening the lattice wireframe.

Keeping the cylindrical design as an exterior shell (no customization), the design work focuses on developing lattice-based implant designs that offer light-weighting features without compromising strength, as well as increasing the surface area for degradation of the implant, preventing localized degradation and non-uniform weakening. The designs also consider the minimum feature size for binder jetting with such material, and shrinkage arising sintering. Furthermore, finite element analysis and design optimization for relevant loading conditions are being performed to obtain designs with adequate strength and stiffness on nTop [34], based on the mechanical parameters discussed earlier and in [24].

Figure 4 displays the stress vs strain curves obtained from comparing the 5 designs with each other and with the base (non-lattice) implant for Ag and Cu. The graphs shown extend into the high stress-strain region, whereas the performance is evaluated at 10 MPa. From the results, we see that the lattice-based samples have extensive compression without any significant stress, almost like foam compression, whereas this doesn't show that well in the solid implants (blue). Thus, compression due to initial pressure must be considered during design if the implant needs to be loaded with body weight initially. Being not dense, the implants also show further strain, however, this is not as significant as it would be in the case of solid samples as well. Overall, the lattice-based samples give a much better mechanical performance than the solid samples, showing adequate ductility to deal with stiffness issues. Certain designs such as Design 2 do show dips in stress, indicating slippage or sudden localized failure during testing, which would be an issue for the functionality of the implant.

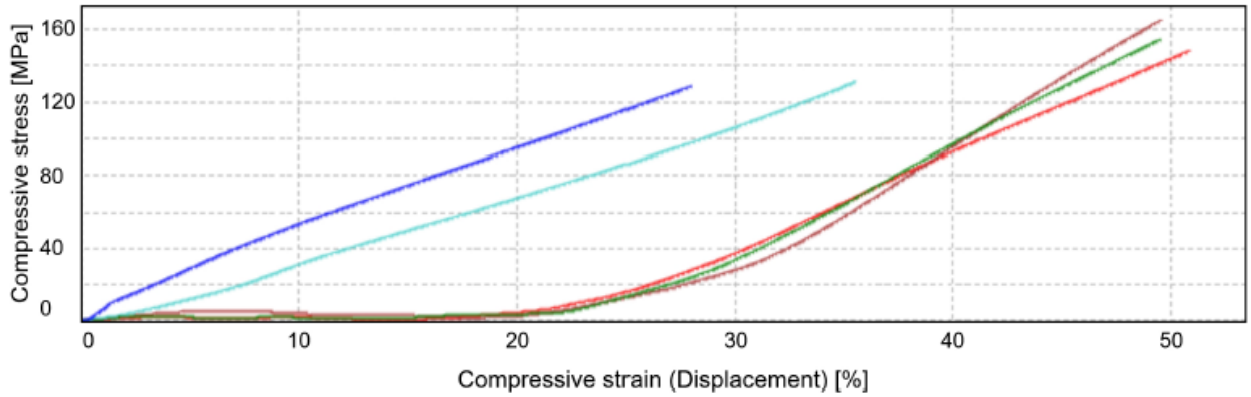

Figure 4: Compressive Testing Stress vs Strain Graph for Lattice-based designs & control sample

Osteoblast Growth and Confocal Imaging of Lattice-based Designs

As mentioned earlier, this is needed to corroborate the results obtained in the study, as well as to investigate the effect of cell growth on a lattice-based 3D printed implant, as the current study is limited to manually pressed and sintered implants with negligible porosity. Lattice-based implants provide much greater surface area and penetration, allowing for better cell adhesion, but may be a challenge when it comes to fluorescent imaging. The experiment provides some interesting and unexpected results, as it was not expected that changes in designs would impact cell viability, as the causes for variation in it were expected to be limited to material properties and biological factors. Again, performance compared to the negative control overall is poor, but toxicity, up to an acceptable level, is considered an acceptable compromise as long as the implant can provide an overall improvement. Designs 1, 3, and 4 show promising results, especially design 3 with good improvement in viability on day 10 compared to day 4. Design 2 is extremely toxic, possibly due to rapid degradation induced by the design of the implant, and design 5 showcases an interesting phenomenon where the toxicity becomes unbearable for the cells after day 10. Thus, based on these results, it's preferable to utilize the neovius design for implant fabrication.

Future Work

A primary focus of future work is integrating this work with the materials and biological performance research done earlier, with additional experimental analysis needed to evaluate the combined performance of the two. This this regard, the development and performance evaluation of this proposed implant design and workflow resulted in the identification of several limitations that can be addressed in future research:

- **Process Limitations and Alternatives:** It may even become feasible for processes such as vat photopolymerization, which is discounted as a viable method for making even metallic implants, to become a favorable choice for fabrication. Additionally, design for AM can also be leveraged more to modify the internal structure and porosity, the elastic modulus, mechanical properties, and biological properties of implants and tailor them for improved performance. There is still an extensive gap in the incorporation of organic and inorganic materials into bone implants, and they may further improve the mechanical and biological performance of the bone implants or their surfaces.
- **Degradation Analysis and matching with cellular growth rate:** A critical part of this research, this was not implemented in the current research due to the variation in results

between in vitro and in vivo performance of cellular growth and implant degradation. Higher animals have a much better regulation of ions in their system, which will play a key role in determining the rate of degradation. Furthermore, even with a setup like perfusion, it will not be possible to get anywhere close to the results of the body to fabricate cells and remove degradation byproducts. Thus, it is hoped that this is something that can be evaluated during *in vivo* experimentation, and the data used to simulate the performance of an implant and introduce design changes accordingly. It will be possible to alter the design of the implant to increase or decrease its degradation rate, to ensure that it matches well with the growth rate of the bone tissue. Porosity control is important to achieve this: namely, the balance between strength and surface area for degradation and adhesion. Additionally, the structure must degrade so there is no structural failure within the implant; critical beams need to be identified and designed to not degrade prematurely.

Summary

Fracture healing in load-bearing bones has evolved dramatically and is now starting to incorporate modern materials, manufacturing, and simulation techniques. Today, the emphasis has shifted towards advanced internal support through innovative medical devices. This paper presents a novel approach to implant design by incorporating lattice-based design into the base implant design and compiling a design workflow for such a fabrication process. With the approach involving the elimination of lattice cell types and variation in population based on node locations, this study provides a streamlined method of selection based on elimination, intending to find the ideal design(s), based on the designer's priorities and selection criteria, as well as limitations related to fabrication such as those seen in printing and sintering. This design-oriented approach seeks to develop implants that not only balance fabrication efficiency with biocompatibility but also hold promise for advancing current techniques in repairing critical bone defects. Through continuous refinement, these implants could eventually surpass existing solutions for load-bearing bone injuries.

References

[1] K. P. Krafts, “Tissue repair: The hidden drama,” Oct. 2010, *Taylor & Francis*. doi: 10.4161/org.6.4.12555.

[2] S. Morshed and A. Ding, “Fracture healing,” *Nonunions: Diagnosis, Evaluation and Management*, pp. 45–74, Sep. 2017, doi: 10.1007/978-1-4939-7178-7_2/COVER.

[3] J. J. Li *et al.*, “A Novel Bone Substitute with High Bioactivity, Strength, and Porosity for Repairing Large and Load-Bearing Bone Defects,” *Adv Healthcare Mater*, vol. 8, no. 8, p. 1801298, Apr. 2019, doi: 10.1002/adhm.201801298.

[4] E. Roddy, M. R. DeBaun, A. Daoud-Gray, Y. P. Yang, and M. J. Gardner, “Treatment of critical-sized bone defects: clinical and tissue engineering perspectives,” Oct. 28, 2018, *Springer*. doi: 10.1007/s00590-017-2063-0.

[5] R. Marti, “Fractures of the Lower Leg,” in *Treatment of Fractures in Children and Adolescents*, Springer, Berlin, Heidelberg, 1980, pp. 330–349. doi: 10.1007/978-3-642-67271-2_20.

[6] J. L. Kelsey and E. J. Samelson, “Variation in risk factors for fractures at different sites,” Nov. 29, 2009, *Springer*. doi: 10.1007/s11914-009-0022-3.

[7] M. L. Wolford, K. Palso, A. Bercovitz, and Ph. D. Monica L. Wolford, M.A.; Kathleen Palso, M.A.; and Anita Bercovitz, M.P.H., “Hospitalization for Total Hip Replacement Among Inpatients Aged 45 and Over: United States, 2000–2010,” *Nchs*, no. 186, p. 8, 2015, doi: ISSN 1941–4935.

[8] N. Sudarmadji, J. Y. Tan, K. F. Leong, C. K. Chua, and Y. T. Loh, “Investigation of the mechanical properties and porosity relationships in selective laser-sintered polyhedral for functionally graded scaffolds,” *Acta Biomaterialia*, vol. 7, no. 2, pp. 530–537, 2011, doi: 10.1016/j.actbio.2010.09.024.

[9] B. Hanks, S. Dinda, and S. Joshi, “Redesign of the femoral stem for a total hip arthroplasty for additive manufacturing,” in *ASME International Design Engineering Technical Conferences and Computers and Information in Engineering Conference*, 2018, pp. 1–13.

[10] J. R. Denning, “Complications of Pediatric Foot and Ankle Fractures,” Jan. 01, 2017, *W.B. Saunders*. doi: 10.1016/j.ocl.2016.08.010.

[11] U. Spiegl, R. Pätzold, J. Friederichs, S. Hungerer, M. Militz, and V. BüHren, “Clinical course, complication rate and outcome of segmental resection and distraction osteogenesis after chronic tibial osteitis,” *Injury*, vol. 44, no. 8, pp. 1049–1056, Aug. 2013, doi: 10.1016/j.injury.2013.05.003.

[12] S. N. Khan, F. P. Cammisa, H. S. Sandhu, A. D. Diwan, F. P. Girardi, and J. M. Lane, “The biology of bone grafting.,” 2005. doi: 10.5435/00124635-200501000-00010.

[13] C. H. Hou, R. S. Yang, and S. M. Hou, “Hospital-based allogenic bone bank-10-year experience,” *Journal of Hospital Infection*, vol. 59, no. 1, pp. 41–45, Jan. 2005, doi: 10.1016/j.jhin.2004.03.017.

[14] S. A. Bender, J. B. Rogalski, M. P. Mills, R. M. Arnold, D. L. Cochran, and J. T. Mellonig, “Evaluation of Demineralized Bone Matrix Paste and Putty in Periodontal Intraosseous Defects,” *J Periodontol*, vol. 76, no. 5, pp. 768–777, May 2005, doi: 10.1902/jop.2005.76.5.768.

[15] X. Liu and P. X. Ma, “Polymeric scaffolds for bone tissue engineering,” *Ann Biomed Eng*, vol. 32, no. 3, pp. 477–486, Mar. 2004, doi: 10.1023/B: ABME.0000017544.36001.8e.

[16] S. K. Ghosh *et al.*, “In vivo response of porous hydroxyapatite and β-tricalcium phosphate prepared by aqueous solution combustion method and comparison with bioglass scaffolds,” *J Biomed Mater Res B Applied Biomaterials*, vol. 86, no. 1, pp. 217–227, Jul. 2008, doi: 10.1002/jbm.b.31009.
[17] Z. Sheikh, S. Najeeb, Z. Khurshid, V. Verma, H. Rashid, and M. Glogauer, “Biodegradable materials for bone repair and tissue engineering applications,” 2015, *MDPI AG*. doi: 10.3390/ma8095273.
[18] G. Fernandez de Grado *et al.*, “Bone substitutes: a review of their characteristics, clinical use, and perspectives for large bone defects management,” Jun. 02, 2018, *SAGE Publications Ltd*. doi: 10.1177/2041731418776819.
[19] P. Chocholata, V. Kulda, and V. Babuska, “Fabrication of scaffolds for bone tissue regeneration,” Feb. 14, 2019, *MDPI AG*. doi: 10.3390/ma12040568.
[20] K. Prasad *et al.*, “Metallic biomaterials: Current challenges and opportunities,” Jul. 31, 2017, *MDPI AG*. doi: 10.3390/ma10080884.
[21] D. Hong *et al.*, “Binder-jetting 3D printing and alloy development of new biodegradable Fe-Mn-Ca/Mg alloys,” *Acta Biomaterialia*, vol. 45, pp. 375–386, 2016, doi: 10.1016/j.actbio.2016.08.032.
[22] M. Prakasam, J. Locs, K. Salma-Ancane, D. Loca, A. Largeteau, and L. Berzina-Cimdina, “Biodegradable materials and metallic implants-A review,” Sep. 26, 2017, *MDPI AG*. doi: 10.3390/jfb8040044.
[23] L. Bai *et al.*, “Additive manufacturing of customized metallic orthopedic implants: Materials, structures, and surface modifications,” Sep. 01, 2019, *MDPI AG*. doi: 10.3390/met9091004.
[24] S. Dinda, D. Banerjee, D. Shaffer, I. T. Ozbolat, and T. W. Simpson, “Material Selection & Design for Lattice-based Biodegradable Metal Implants for Bone Regeneration in Load-Bearing Bone Defects.”
[25] R. M. Pilliar, J. E. Davies, and D. C. Smith, “The Bone-Biomaterial Interface for Load-Bearing Implants,” *MRS Bull*, vol. 16, no. 9, pp. 55–61, 1991, doi: 10.1557/S0883769400056074.
[26] T. Wehner, L. Claes, and U. Simon, “Clinical Biomechanics Internal loads in the human tibia during gait,” *Clinical Biomechanics*, vol. 24, no. 3, pp. 299–302, 2009, doi: 10.1016/j.clinbiomech.2008.12.007.
[27] A. R. Amini, C. T. Laurencin, and S. P. Nukavarapu, “Bone tissue engineering: Recent advances and challenges,” *Crit Rev Biomed Eng*, vol. 40, no. 5, pp. 363–408, 2012, doi: 10.1615/CritRevBiomedEng.v40.i5.10.
[28] G. Fernandez de Grado *et al.*, “Bone substitutes: a review of their characteristics, clinical use, and perspectives for large bone defects management,” Jun. 02, 2018, *SAGE Publications Ltd*. doi: 10.1177/2041731418776819.
[29] N. Cubo, M. Garcia, J. F. Del Cañizo, D. Velasco, and J. L. Jorcano, “3D bioprinting of functional human skin: Production and in vivo analysis,” *Biofabrication*, vol. 9, no. 1, p. 015006, Dec. 2017, doi: 10.1088/1758-5090/9/1/015006.
[30] D. Anton, H. Burckel, E. Josset, and G. Noel, “Three-dimensional cell culture: A breakthrough in vivo,” Mar. 11, 2015. doi: 10.3390/ijms16035517.
[31] M. Prakasam, J. Locs, K. Salma-Ancane, D. Loca, A. Largeteau, and L. Berzina-Cimdina, “Biodegradable materials and metallic implants-A review,” Sep. 26, 2017, *MDPI AG*. doi: 10.3390/jfb8040044.

[32] D. Chou *et al.*, “Novel processing of iron–manganese alloy-based biomaterials by inkjet 3-D printing,” *Elsevier, DT Chou, D Wells, D Hong, B Lee, H Kuhn, PN Kumta, Acta Biomaterialia, 2013•Elsevier*, Accessed: Aug. 01, 2024. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S1742706113001888

[33] W. C. Carter, D. R., & Hayes, “The Compressive Behavior Porous of Bone Structure as a Two-Phase,” *J Bone Joint Surg*, vol. 59, no. 7, pp. 954–962, 1977, [Online]. Available: https://doi.org/10.1007/978-1-4471-5451-8_116

[34] R. Home, “Engineering Software Designed for Advanced Manufacturing | nTopology.” Accessed: Jun. 17, 2020. [Online]. Available: https://ntopology.com/