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The Effect of Loading Parameters and Dynamic Immersion Time on the Fatigue Life of Magnesium Bone Scaffolds

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Abstract. Bone scaffolding implants are used in orthopedic applications to aid bone growth and regeneration. However, these implants degrade over time and will also be exposed to the burden of physiological activity during use, which can affect their mechanical properties and fatigue life. The aim of this study was to investigate the effect of degradation time and physiological activity load on changes in bone scaffolding implant morphology on fatigue life and determine significant parameters using the ANOVA method. The study was conducted using numerical simulation using finite element method in software Comsol Multiphysics. Bone scaffolding implants are exposed to cyclic fatigue loads and degradation over time as well as loads of different physiological activities. The results showed that degradation time and physiological activity load had a significant effect on changes in bone scaffolding implant morphology and fatigue life. Increased degradation time and physiological activity load lead to decreased implant fatigue life. The results of the analysis using the ANOVA method showed that the degradation time of factors affecting fatigue with a percentage value of 64.56% was significant on morphological changes and the load of physiological activity had an influence of 35.44% on the fatigue life of bone scaffolding implants. This study emphasizes the importance of considering degradation time and physiological activity load in the design and evaluation of bone scaffold implants. Analysis using the ANOVA method can help to determine significant parameters that affect implant performance and improve implant design to extend fatigue life.

Keywords: Bone scaffolding; Time Immersion; Physiological activity; Morphology; ANOVA

INTRODUCTION

Human bones have a natural ability to recover from injury and damage, but in some cases, this natural healing process is ineffective and requires the assistance of implanted bone scaffolding. Bone scaffold implants are medical devices used to strengthen, stabilize, or repair damaged or deformed bones. Bone scaffold implants are made of various types of materials such as metals, polymers, and ceramics. However, although bone scaffold implants have been used extensively in clinical practice, a frequent problem is material fatigue which can lead to implant failure. Loads applied to bone scaffold implants during physiological activities can cause damage to the implant structure and shorten its fatigue life. In addition, the degradation that occurs in the bone scaffold implant material can also affect the performance of the implant and its fatigue life. Implant material degradation can occur over time and can accelerate implant fatigue. Therefore, this study aims to investigate the effect of degradation time and physiological activity load on the morphological changes of bone scaffold implants and their fatigue life.

Through this research, it is expected to provide a better understanding of the performance of bone scaffold implants and assist in the development of bone scaffold implants that are more durable and effective using the analysis of variance (ANOVA) method in Design Expert software to determine significant parameters in the effect of degradation time and load of physiological activity on the morphological changes of bone scaffold implants and their fatigue life.

The results of this study are expected to make an important contribution in the development of more durable and effective bone scaffold implants. This research can also assist in determining optimal parameters to increase the fatigue life of bone scaffold implants so that they can assist patients in recovery and can return to normal activities.

Overall, this study is important for improving the performance of bone scaffold implants and providing greater clinical benefits for patients who require bone scaffold implants.

METHODS

The material that can be used to make commercially available orthopedic implants is magnesium from Goodfellow Inc. in Cambridge, England. The diameter of this magnesium material is 25.4 mm and a purity of 99.9%. This material was used to manufacture orthopedic implants with a porosity diameter of 800 μm using a CNC machine (HAAS, USA). The implant is in the form of a cube measuring 5x5x3 mm (Md Saad et al., 2019), which can be seen in Table 1 shows the porous magnesium geometry.

Table 1. Detailed geometry for porous Magnesium specimens (Md. Saad et al., 2016)(Md Saad et al., 2017)

Porosity	Surface Area	Mass per surface area	Volume
41%	209.81 mm^2	0.34 kg/m^2	44.57 mm^3

After the fabrication process, the porous Mg bone scaffold were subjected to a dynamic immersion test under simulated body fluids (SBF) at a flow rate of 0.025 m/min with pH levels and temperatures of 7.4 and 37 °C ± 1 °C [6][7]. The dynamic immersion test rig is set to have laminar flow. A peristaltic pump was used to provide a constant flow rate of 0.025 ml/min with a Reynolds (Re) number of 5.44 for SBF in all tube passages with a diameter of 2 mm. Specimens were immersion for 24 hours, 48 hours, and 72 hours. The specimens were then cleaned with deionized water and vacuum dried for 1 hour.

Morphological characteristics of samples with 41% porosity can be seen in figure 1. Then immersion with different degradation times (0, 24, 48 and 72 hours) (Md. Saad et al., 2016). Micro-CT images of the specimens were cleaned and acquired (n = 12) using a Skyscan 1172 micro-CT (Kontich, Belgium) at 17.2 μm voxel resolution. The micro-CT images were then exported to ImageJ (US National Institutes of Health, Bethesda, MD, USA, Rasband, W.S., ImageJ). This was then used to calculate the degraded volume to total volume ratio (BV/TV), surface area, and trabecular space (Tb.Sp).

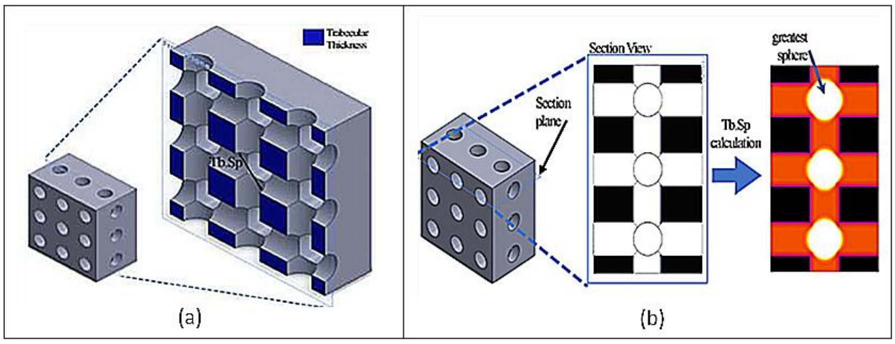

Figure 1. Porous magnesium scaffold morphology in detail (a) cross sectional (b) Tb.Sp (Putra et al., 2023)

Gray scale images of the micro-CT images were used to reconstruct the 3D model of the degraded magnesium implant porous specimen. 2D data set with a slice thickness of 0.172 mm. images imported into Mimics software (Materialize, Belgium) were then processed into a 3D model, shown in Figure 2. The region of interest (ROI) was identified and shrunk as much as feasible so that the specimen was encapsulated with as few black voxels (i.e. air) as possible. A rectangle form of 4 mm x 6 mm (bigger than the cross-sectional area) and 6 mm high is used to identify ROI.

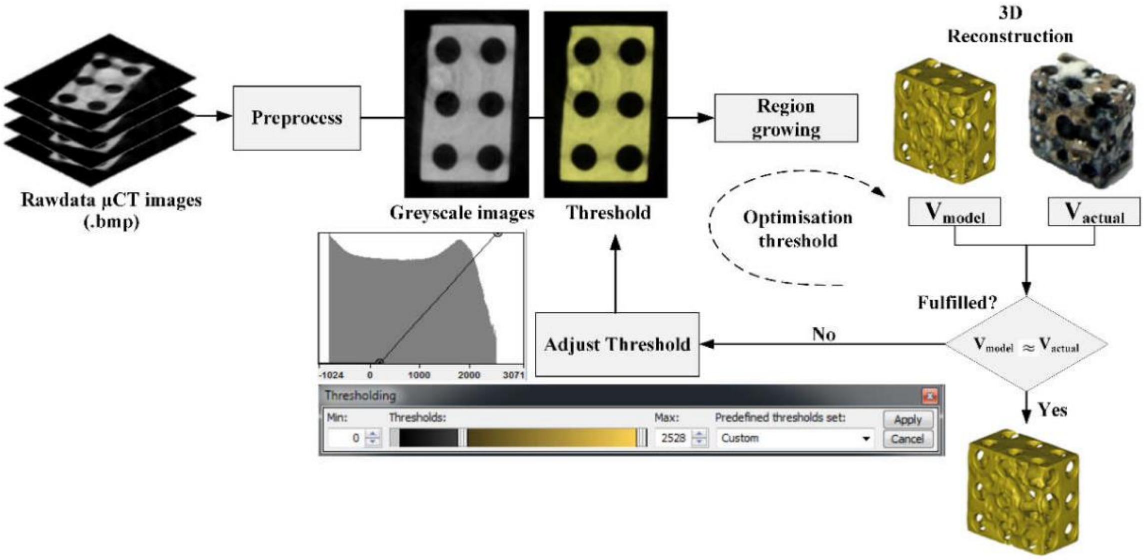

Figure 2. 3D Specimen 3D reconstruction from micro-CT images using Mimics software (Md Saad et al., 2019)

The mechanical properties of magnesium were previously determined using solid samples using a universal testing device (FastTrack 8874, Instron, Norwood, USA) utilized for monotonic compression tests. Compression testing of the mechanical characteristics of porous magnesium specimens was performed using a 25 kN load cell at a strain rate of 0.005/second. (Basri et al., 2020). Techniques that can be used to predict the fatigue life of specimens include fracture mechanics, strain life, and stress life. The strain-based method is effective at predicting low cycle fatigue. In universal testing equipment, strain-controlled cyclic loading is also a possibility. The cyclic loading was carried out using software with strain control (Wave MatrixTM Dynamic Material Testing Software, Instron, USA). Under a typical 1-3 Hz operational condition, samples are compressed and loaded on a 2 Hz sine wave with a loading ratio of R = 0.1.

Homogeneous, isotropic, and plastic-elastic properties are assigned to the porous magnesium 3D model. Before doing numerical analysis, the Young's modulus of solid magnesium was measured by performing a pressure test with solid magnesium. The average of the test findings is then used as the input value for all numerical simulation samples in this study. Poisson's ratio 0.35 (see Table 2) was chosen based on bone tissue trabecular thickness, density 1,74 g/cm3, and Young's modulus of 3.5 GPa.

Table 2. Mechanical properties of magnesium used in FEM.

Mechanical properties	Magnesium
Monotonic Properties	
Young modulus, E (GPa)	3.5
Poisson's ratio	0.35
Kinematic tangent modulus, K_{Tkin}	0.05E
Yield Strength, σ_y (MPa)	147
Fatigue Properties	
Fatigue ductility exponent, c	-1.3
Fatigue ductility coefficient, ε'_f	0.425
Fatigue strength coefficient, $\sigma_f{}'$ (MPa)	180
Fatigue strength exponent, b	-0.09

After obtaining material characteristics, fatigue modeling based on Finite Element Analysis (FEA) is carried out, which is a numerical method for analyzing the mechanical properties of porous scaffolds, such as structural strength and fatigue life. FEA has the benefit of being repeatable and may be used to simulate actual experiments. It may be used frequently to produce many sorts of simulations, which direct experimental studies in people can't do. (Ammarullah et al., 2022). The ability to improve scaffold samples creates many new possibilities.

A computer method known as Finite

Element Analysis (FEA) is very suitable for predicting fatigue life (Bashiri & Alshoaibi, 2020; Gibbons & Chen, 2022; Kashyzadeh et al., 2021; Roda-Casanova et al., 2021; Shah et al., 2022). The benefit of FEA is that it is reproducible and may be used to replicate actual investigations. As an example, it is possible to run many simulations using equivalent models repeatedly, but this cannot be done with damaging experimental tests. The scaffold sample can be increased in a variety of ways with this capability.

Walking, running, and climbing stairs are a few examples of physiological actions performed by people that exert recurrent stresses on their bones. (Thompson et al., 2012). The porous scaffold model's stress distribution and lifetime were simulated in the following stage using industry-standard software created by Comsol Multiphysics. The components of the resulting three-dimensional number are tetrahedral. The boundary conditions employed in this simulation are shown in Figure 3. On the top surface, specific displacement boundary conditions are defined to replicate uniaxial loads brought on by mechanical loads on the bone. (Ahlhelm et al., 2021; Chang et al., 2020; Shokry et al., 2021). Additionally, the zero-state displacement limit is shifted by the surface normal. This boundary condition allows nodes to be multiaxial in the x-z direction while restricting them to being uniaxial in the y direction with regard to the load. Contrary to uniaxial loading, which is dominated by high cycle loading, multiaxial loading is dominated by low cycle fatigue. (Fatihhi et al., 2015). The model is oriented in the y-direction to the bottom, and the top surface receives a physiological strain of 1000–3500 μm/mm load depending on changes in bone mechanical loading (Zargarian et al., 2016). The elastic modulus of magnesium material is 3500 MPa, the Poisson's ratio is 0.35, and the kinematic tangent modulus is 0.05E. To calculate low and high cycle fatigue life, fatigue analysis was done on entire elastoplastic materials using a combination of Basquin and Coffin-Manson equations.

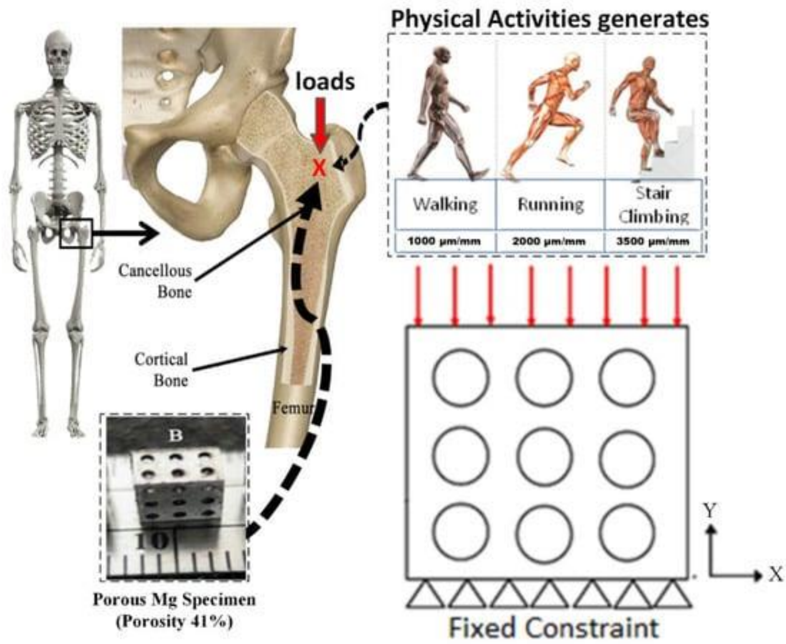

Figure 3. Schematic for boundary conditions (Putra et al., 2023)

After the boundary conditions are determined, Convergent meshing is carried out first to reduce numerical errors during the simulation which can be seen in Figure 4. The tetrahedral element type is used in meshing. Mesh sensitivity analysis shows that the number of elements around 100000-400000 is enough to produce an accurate value.

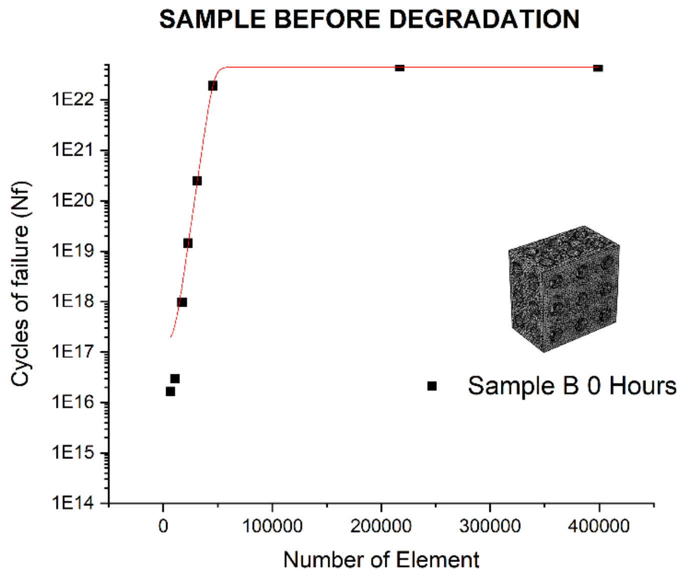

Figure 4. Convergence study for fatigue simulation Sample before degradation

The simulation results shown in figure 5 for a sample with a porosity of 41% for 48 hours show that human activity has a significant effect on the fatigue life of the bone scaffold implant while running, with a low fatigue life value of 1.11995E+09. The lifetime of these implants increases significantly when the activity load is reduced

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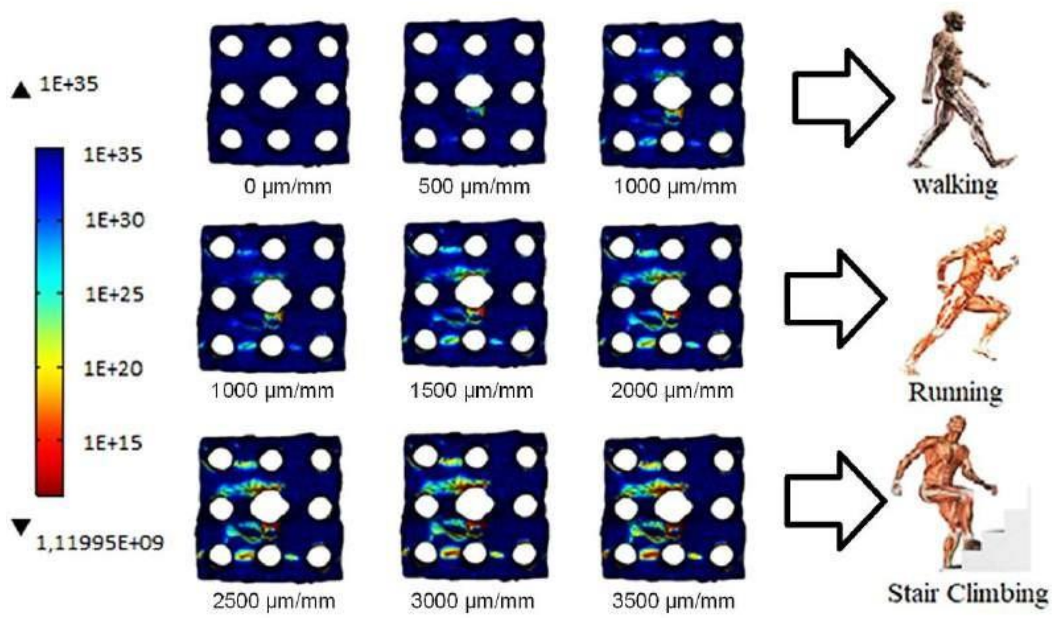

Figure 5. On human physiological activity, effective contour plot of porous magnesium plastic strain with 48 hours of immersion time (Putra et al., 2023)

Fatigue analysis software is used to predict fatigue failure of porous magnesium. Figure 6 shows the failure fatigue degradation rates of porous magnesium before and after 72 h dynamic immersion. With a larger surface area, porous magnesium will have a longer fatigue life. This is due to surface degradation due to the longer immersion. Thus, surface area has a significant impact on fatigue life. It describes the effective strain contours of a porous magnesium plastic at 0, 24, 48 and 72 h of dynamic immersion. This simulation on porous magnesium obtained a maximum fatigue value of 4.5081×10^{22} and a minimum of 2.2856×11^{11} in human physiological activity while walking. As the porous magnesium dynamic immersion time increases, the effective plastic strain will decrease. The specimen's decreased volume and surface area both show this decline. There is an increase in stresses in some places with a decrease in surface area and volume.

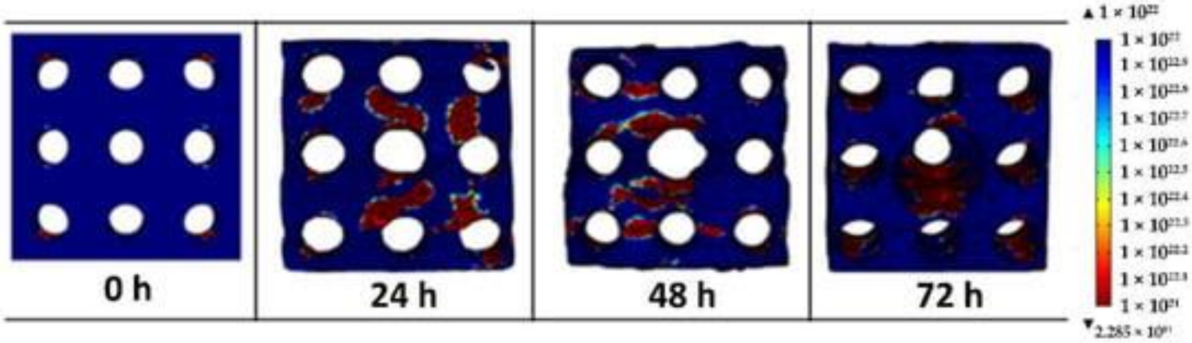

Figure 6. Effective contour plot of magnesium plastic strain for dynamic immersion time on walking activity

In conducting this ANOVA experiment, data was used from previous research by R.U Putra in 2023 (Putra et al., 2023), the selected parameter is Time Immersion; 0 – 72 hours and Load Activity; 1000-3500 με as independent variable. Each independent variable range has four and seven levels in Table 3.

Table 3. Independent Variable

Parameter	Level 1	Level 2	Level 3	Level 4	Level 5	Level 6	Level 7	Unit
Immersion Test	0	24	48	72				
Load Activity	500	1000	1500	2000	-	-	-	Hours

The main objective of this study was to observe the fatigue life of magnesium bone scaffolds on the effect of each parameter combination. The end result of the experiment must have a good fatigue life, then data processing is carried out using the ANOVA method, which is calculated by the equation as shown in Table 4.

Table 4. Anova Formula

Source	Sum of Squares	Degrees of Freedom	Mean Square	F_0
Overall model	SS_{model}	$(k_A.k_B)-1$	$SS_{model}/(k_A.k_B)-1$	MS_{model}/MS_E
Main Effect of A	SS_A	v_A	SS_A / v_A	MS_A/MS_E
Main Effect of B	SS_B	v_B	SS_B / v_B	MS_B/MS_E
Error	SS_E	v_e	SS_E / v_e	
Total	SS_{Total}	v_T		

RESULTS AND DISCUSSION

Analysis of variance was carried out using a multi-level method of two factors and one response which was determined to see the effect of each test parameter. Specimen testing was carried out randomly according to the measurement design matrix in Table 5,

Table 5. Design matrix

STD	RUN	Parameter		Cylces of Failure (Nf)
		Time Immersion (Hours)	Load Activity (με)	
2	1	24	500	2.17771E+21
7	2	48	1000	1.24165E+15
6	3	24	1000	9.86279E+17
15	4	48	2000	5.62341E+11
28	5	72	3500	205873
8	6	72	1000	2.2856E+11
5	7	0	1000	4.50817E+22
26	8	24	3500	8.87156E+11
21	9	0	3000	2.25424E+17
20	10	72	2500	8.65366E+06
23	11	48	3000	6.20869E+09
12	12	72	1500	2.52464E+09
22	13	24	3000	4.9204E+12
4	14	72	500	5.05825E+14
16	15	72	2000	1.03276E+08
14	16	24	2000	4.45656E+14
13	17	0	2000	2.03704E+19
3	18	48	500	2.74789E+18
18	19	24	2500	3.7325E+13
11	20	48	1500	1.37404E+13
10	21	24	1500	1.08893E+16
24	22	72	3000	1.1413E+06
17	23	0	2500	1.70608E+18
1	24	0	500	9.977E+25
27	25	48	3500	1.11995E+09
9	26	0	1500	4.97737E+20
19	27	48	2500	4.70977E+10
25	28	0	3500	4.06443E+16

The simulation generated by the fatigue method is needed to analyze the fatigue of the structure, namely the fatigue cycle. The resulting simulation is based on variations in loading with magnitudes between 0-3500 με. Simulation results will be displayed via graphs and visualized in 2D. Fatigue life prediction on porous magnesium was carried out using Multiphysics 5.4 study fatigue analysis software. Samples before degradation with 500 με loading showed the highest fatigue cycle of 9.977E+25 and the lowest value at 72 hours of immersion time of 205873 so that the greater the loading the failure cycle value on porous magnesium bone scaffolds the lower.

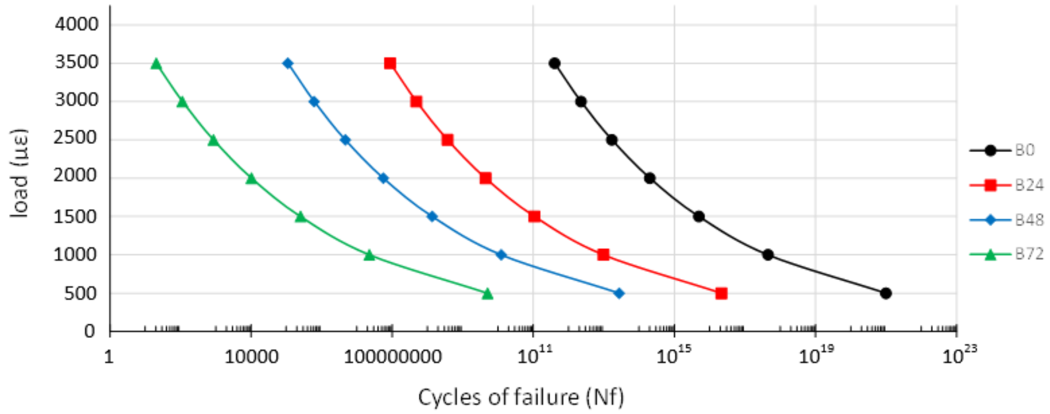

Figure 7. Cycles of failure (Nf) vs Load (με)

On bone scaffold samples, the value of fatigue life has significant effects on loading variations. Figure 7 shows that the implant volume decreases as the load increases and the fatigue value increases. The fatigue life value of the implant will be affected by samples with various variations in immersion duration; the fatigue life value falls with increasing immersion time because the volume of the specimen on the implant is lowered.

Data from the measurement design for the test specimens yielded minimum, maximum, average, standard deviation, and the ratio of each response and element in the test, as shown in Tables 6 and 7.

Table 6. The test results' mean and standard deviation

Factor	Name	Units	Min	Max
A	Immersion Test	Hours	0	72
B	Load Activity	με	500	3500

Table 7. Response testing with the main effect model design

Name	Unit	Observ.	Analysis	Min	Max	Mean	Std. Dev	Ratio
Cycles of failure	Nf	28	Factorial	205873	9,977E+25	3,565+24	1,885E+22	4,846E+20

From the measurement data in Table 6 and Table 7, the following process analyzes the influence of parameters on fatigue life, and the results of the analysis are shown in Table 8, as follows:

Table 8. ANOVA test results

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F	
Model	739,53	9	82,17	9,098E+08	< 0.0001	significant
A-Time Immersion	477,44	3	159,15	1,762E+09	< 0.0001	
B-Load Activity	262,09	6	43,68	4,836E+08	< 0.0001	
Residual	1,626E-06	18	9,032E-08			
Cor Total	739,53	27				

From the results of the ANOVA experiment, as shown in Table 8, it can be seen that the significant F value is Time Immersion which is the main factor affecting Fatigue life of magnesium bone scaffolds.

Table 8 shows the influence of the main factors on fatigue life. By using the equation in Table 4, it is possible to calculate the percentage value of the contribution of each factor that affects fatigue life to the bone scaffold, that is:

A Factor = Time Immersion : (477,44-1,626E-06) / 739,53= 64,56 %
B Factor = Load Activity : (262,09-1,626E-06) / 739,53= 35,44 %

CONCLUSION

The results of the analysis showed that the parameters affecting fatigue life on magnesium bone scaffolds were Time Immersion = 64.56 % and Load Activity = 35.44 %, with the conclusion that time Immersion parameters had the most significant contribution to Fatigue life of magnesium bone scaffolds.

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REFERENCES

Ahlhelm, M., Latorre, S. H., Mayr, H. O., Storch, C., Freytag, C., Werner, D., Schwarzer-Fischer, E., & Seidenstücker, M. (2021). Mechanically Stable β-TCP Structural Hybrid Scaffolds for Potential Bone Replacement. *Journal of Composites Science*, *5*(10), 281. https://doi.org/10.3390/jcs5100281

Ammarullah, M. I., Santoso, G., Sugiharto, S., Supriyono, T., Kurdi, O., Tauviqirrahman, M., Winarni, T. I., & Jamari, J. (2022). Tresca stress study of CoCrMo-on-CoCrMo bearings based on body mass index using 2D computational model. *Jurnal Tribologi*, *33*, 31–38.

Bashiri, A. H., & Alshoaibi, A. M. (2020). Adaptive Finite Element Prediction of Fatigue Life and Crack Path in 2D Structural Components. *Metals*, *10*(10), 1316. https://doi.org/10.3390/met10101316

Basri, H., Prakoso, A. T., Sulong, M. A., Md Saad, A. P., Ramlee, M. H., Agustin Wahjuningrum, D., Sipaun, S., Öchsner, A., & Syahrom, A. (2020). Mechanical degradation model of porous magnesium scaffolds under dynamic immersion. *Proceedings of the Institution of Mechanical Engineers, Part L: Journal of Materials: Design and Applications*, *234*(1), 175–185. https://doi.org/10.1177/1464420719881736

Chang, Z., Zhang, H., Schlangen, E., & Šavija, B. (2020). Lattice Fracture Model for Concrete Fracture Revisited: Calibration and Validation. *Applied Sciences*, *10*(14), 4822. https://doi.org/10.3390/app10144822

Fatihhi, S. J., Harun, M. N., Abdul Kadir, M. R., Abdullah, J., Kamarul, T., Öchsner, A., & Syahrom, A. (2015). Uniaxial and Multiaxial Fatigue Life Prediction of the Trabecular Bone Based on Physiological Loading: A Comparative Study. *Annals of Biomedical Engineering*, *43*(10), 2487–2502. https://doi.org/10.1007/s10439-015-1305-8

Gibbons, M. M., & Chen, D. A. (2022). Bio-Inspired Sutures: Using Finite Element Analysis to Parameterize the Mechanical Response of Dovetail Sutures in Simulated Bending of a Curved Structure. *Biomimetics*, *7*(2), 82. https://doi.org/10.3390/biomimetics7020082

Kashyzadeh, K. R., Rahimian Koloor, S. S., Omidi Bidgoli, M., Petrů, M., & Amiri Asfarjani, A. (2021). An Optimum Fatigue Design of Polymer Composite Compressed Natural Gas Tank Using Hybrid Finite Element-Response Surface Methods. *Polymers*, *13*(4), 483. https://doi.org/10.3390/polym13040483

Md. Saad, A. P., Jasmawati, N., Harun, M. N., Abdul Kadir, M. R., Nur, H., Hermawan, H., & Syahrom, A. (2016). Dynamic degradation of porous magnesium under a simulated environment of human cancellous bone. *Corrosion Science*, 1–12. https://doi.org/10.1016/j.corsci.2016.08.017

Md Saad, A. P., Abdul Rahim, R. A., Harun, M. N., Basri, H., Abdullah, J., Abdul Kadir, M. R., & Syahrom, A. (2017). The influence of flow rates on the dynamic degradation behaviour of porous magnesium under a simulated environment of human cancellous bone.

Materials and Design, *122*, 268–279. https://doi.org/10.1016/j.matdes.2017.03.029

Md Saad, A. P., Prakoso, A. T., Sulong, M. A., Basri, H., Wahjuningrum, D. A., & Syahrom, A. (2019). Impacts of dynamic degradation on the morphological and mechanical characterisation of porous magnesium scaffold. *Biomechanics and Modeling in Mechanobiology*, *18*(3), 797–811. https://doi.org/10.1007/s10237-018-01115-z

Putra, R. U., Basri, H., Prakoso, A. T., Chandra, H., Ammarullah, M. I., Akbar, I., Syahrom, A., & Kamarul, T. (2023). Level of Activity Changes Increases the Fatigue Life of the Porous Magnesium Scaffold, as Observed in Dynamic Immersion Tests, over Time. *Sustainability (Switzerland)*, *15*(1). https://doi.org/10.3390/su15010823

Roda-Casanova, V., Pérez-González, A., Zubizarreta-Macho, Á., & Faus-Matoses, V. (2021). Fatigue Analysis of NiTi Rotary Endodontic Files through Finite Element Simulation: Effect of Root Canal Geometry on Fatigue Life. *Journal of Clinical Medicine*, *10*(23), 5692. https://doi.org/10.3390/jcm10235692

Shah, G. J., Nazir, A., Lin, S.-C., & Jeng, J.-Y. (2022). Design for Additive Manufacturing and Investigation of Surface-Based Lattice Structures for Buckling Properties Using Experimental and Finite Element Methods. *Materials*, *15*(11), 4037. https://doi.org/10.3390/ma15114037

Shokry, A., Mulki, H., & Kharmanda, G. (2021). A Logarithmic Formulation for Anisotropic Behavior Characterization of Bovine Cortical Bone Tissue in Long Bones Undergoing Uniaxial Compression at Different Speeds. *Materials*, *14*(17), 5045. https://doi.org/10.3390/ma14175045

Thompson, W. R., Rubin, C. T., & Rubin, J. (2012). Mechanical regulation of signaling pathways in bone. *Gene*, *503*(2), 179–193. https://doi.org/10.1016/j.gene.2012.04.076

Zargarian, A., Esfahanian, M., Kadkhodapour, J., & Ziaei-Rad, S. (2016). Numerical simulation of the fatigue behavior of additive manufactured titanium porous lattice structures. *Materials Science and Engineering C*. https://doi.org/10.1016/j.msec.2015.11.054