



The Effect of Aspect Ratio and Layer Thickness on Accuracy of Microneedle Fabrication Using Stereolithography

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Abstract. Microneedle is an innovation in injecting drugs without pain and without leaving damage to skin tissue. Microneedles can be applied to drug injection, biosensing, and biological specimen extraction. In this study, we investigated the effects of material choice, aspect ratio, and layer height on the fabrication parameters of microneedles—specifically focusing on needle height, angle, and base dimensions. Utilizing an ANOVA framework, we analyzed how these factors influence the structural integrity and functionality of microneedles. Our findings reveal that material is the most significant factor affecting both needle height, base dimensions, and needle angle. The aspect ratio was found to primarily affect the needle height and needle base. In general, the best parameters are the aspect ratio of 1.3:1, precision model material, and 0.05 mm layer thickness.

Keywords: 3D Printing, Additive Manufacturing, Stereolithography, Microneedle, Dimension Accuracy.

1 INTRODUCTION

Microneedles (MN) represent a transformative approach in transdermal drug administration by creating microscopic pathways for absorption, offering a minimally invasive method to deliver vaccines and macromolecules [1]. MN has several advantages, one of which is that it can inject drugs painlessly so as to reduce trauma to the syringe [2]. Needle trauma often induces fear and painful experiences, particularly among children. In addition to children, it is reported that about 80% of adults have a phobia of needles and syringes [3]. Beyond drug delivery, microneedles are employed in diverse applications such as biological specimen extraction—where they can gather sweat, blood, or tissue samples—and biosensing, including applications for detecting tumor cells or monitoring glucose levels. This versatility extends to managing chronic conditions like diabetes, where microneedles provide a less painful alternative to traditional syringe-based insulin administration for both type 1 and 2 diabetes [4].

There are four types of microneedles, i.e., solid microneedle, coated microneedle, dissolving microneedle, and hollow microneedle. All these microneedle types can be fabricated using Stereolithography. Among these types, dissolving microneedles has the advantage of being able to inject drugs with just one step [5]. Dissolving

Microneedle has biodegradable properties that will be released when the microneedle is injected into the skin.

Microneedles can be produced using several fabrication processes including micro-molding and drawing lithography (DL), additive manufacturing. Additive manufacturing employs computer-aided design (CAD) to fabricate microneedles layer by layer, offering flexibility in design and enabling rapid prototyping. This technique involves the precise deposition of material, often photocurable resins, according to the digital model. Among additive manufacturing techniques, digital light processing (DLP) and stereolithography (SLA) stand out for their ability to produce microneedles with intricate geometries and varying dimensions using precise light sources to cure the resin. While DLP and SLA share similar concepts, SLA is particularly recognized for its capability to produce objects with more diverse dimensions and shapes [6].

When designing and fabricating microneedles, several critical design criteria must be carefully considered to ensure their accuracy and functionality. The height of the microneedle, which is typically limited to the sub-millimeter range, is crucial as it allows for a largely painless insertion while also controlling the depth of drug delivery. The aspect ratio, defined as the height relative to the base width of the needle, is another vital parameter that influences both the ease of insertion and the mechanical integrity of the microneedle. Higher aspect ratios facilitate easier skin penetration, whereas lower aspect ratios enhance the mechanical strength of the needles, making them less prone to bending or breaking during use. Additionally, both the height and aspect ratio are instrumental in determining the volume of each microneedle, directly impacting the precise dosage of drugs delivered. A previous study utilized a resin known as 3DM-Castable to fabricate a splint equipped with a microneedle, achieving a high aspect ratio and a small tip, which proved essential for precise drug delivery and immobilizing the finger during anti-inflammatory drug injections [7]. Another study employed class I resin—Dental SG—to create pyramid-shaped and flat spear-shaped microneedles, where optimized printing processes significantly improved the accuracy of skin penetration tests compared to those made with metal materials [8].

Layer height is a critical variable in microneedle fabrication that directly affects the accuracy and smoothness of the microneedles' surfaces. Reducing the layer height enhances the surface finish, crucial for minimizing patient discomfort and increasing the precision of drug delivery. However, it also increases build time and the potential for mold failure due to the greater number of layers requiring curing. Conversely, a higher layer height can expedite the fabrication process and reduce the risk of mold failure due to fewer individual layers needing to be cured [9]. This, however, may lead to a ladder effect, potentially increasing the local stress and impacting the microneedle's precision and structural integrity.

Despite the advancements in microneedle fabrication technologies, there remains a gap in understanding the optimal combination of material properties and fabrication parameters, such as aspect ratio and layer height, that best enhance microneedle accuracy. Additionally, there is limited research on how material choices may impact the accuracy of the microneedles. Therefore, this study evaluates the effects of aspect ratio, layer thickness, and materials on the accuracy of microneedles.

2 MATERIAL AND METHODS

2.1 Microneedle Fabrication

Microneedles, as shown in Fig. 1, was designed using Autodesk Inventor 2021. The CAD models were sliced using Prusa software which converted the designs to G-code. Three different materials were used to fabricate microneedles using SLA method (Prusa SL1), i.e., PLA resin, Precision Model, and High Temperature Resin, all of which were sourced from eSUN. Material specifications can be seen in Table 1 Microneedles were cleaned using isopropyl alcohol for 5 minutes post printed, followed by curing at 80°C for 30 minutes.

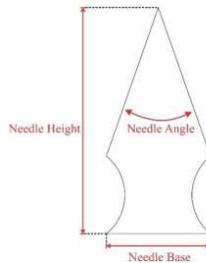


Fig. 1. Microneedle design.

Table 1. Specification material of microneedle.

Description	PLA	Precision Model	High Temperature
Viscosity (mPa-s)	100-270	170-270	180-220
Density (g/cm ³)	1.07-1.10	1.13-1.16	1.09-1.10

2.2 Design of Experiment

This study considered the influence of three factors, namely material choice, aspect ratio and layer height on the accuracy of printed microneedles. The choice of layer height and aspect ratio were inspired by Krieger et al [9]. In this study, we used 25 μm , 35 μm , and 50 μm , to see the effect of layer height without causing a significant ladder effect so that when fabrication still produces precise microneedles. Whereas the aspect ratios tested were 1.625:1, 1.4:1, and 1.3:1, with corresponding needle widths of 800 μm , 900 μm , and 1000 μm , respectively, while maintaining a constant needle height of 1300 μm . Layer heights varied at three levels: 0.025 mm, 0.035 mm, and 0.05 mm. These parameters are tabulated in Table 2. The CAD for each microneedle aspect ratio can be seen in Fig. 2 – Fig. 4.

Table 2. Parameter considered with their level.

Process Parameter	Level		
	1	2	3
Material	High Temp	Precision Model	PLA
Aspect ratio	1.625:1	1.4:1	1.3:1
Layer height	0.025 mm	0.035 mm	0.05 mm

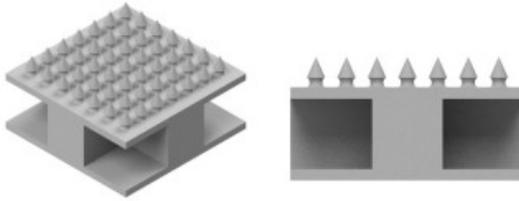


Fig. 2. Microneedle CAD with aspect ratio 1.625:1

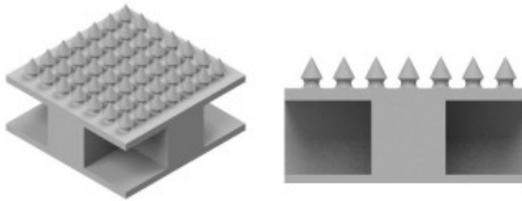


Fig. 3. Microneedle CAD with aspect ratio 1.4:1

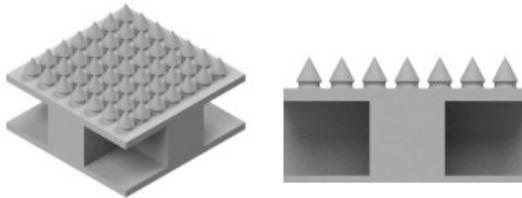


Fig. 4. Microneedle CAD with aspect ratio 1.3:1

Taguchi’s orthogonal array L9 (Table 3) was employed to design the experiment, allowing for the efficient evaluation of the combined effects of these factors with a minimal number of experimental runs. Each run was replicated three times to minimize the impact of random errors or variations in the fabrication process, bringing a total of 27 specimens tested. The response variable in this study is microneedle accuracy comprising of height, base, and angle dimensions.

Table 3. Taguchi orthogonal array L9.

Run	Material	Factor	
		Aspect ration	Layer height (mm)
1	High Temp	1.625:1	0.025
2	High Temp	1.4:1	0.035
3	High Temp	1.3:1	0.05
4	Precision Model	1.625:1	0.035
5	Precision Model	1.4:1	0.05
6	Precision Model	1.3:1	0.025
7	PLA	1.625:1	0.05
8	PLA	1.4:1	0.025
9	PLA	1.3:1	0.035

2.3 Data Analysis

The dimensions of the printed microneedles were measured using an Olympus SZX16 macro microscope with 1x to obtain data for further analysis with arbitrary line feature. The data included height, base width, and angle. The needles measured are each needle on each different side. The measured needle is each needle on each different side. Data analysis was conducted using Minitab software version 20 to assess the main effects and interactions between the factors. The analysis incorporated the Taguchi method's signal-to-noise (S/N) ratio to determine the optimal parameters for achieving the smallest error or highest accuracy. This analysis employed the "smaller is better" approach, as higher accuracy corresponds to a lower error rate. The formula for the smaller-is better S/N ratio using base 10 log is:

$$S/N = -10 \log \left(\frac{1}{n} \sum_{i=1}^n y_i^2 \right) \quad (1)$$

where y_i^2 = responses for the given factor level combination and n = number of responses in the factor level combination.

After calculating the S/N ratios, ANOVA was performed to analyze if differences in material, aspect ratio, or layer height significantly affect the accuracy of the microneedles. ANOVA will be determined using the following equation 2-5.

$$S_T = \sum_{i=1}^N (\eta_i - \eta) \quad (2)$$

Where S_T = total sum of square, N = total number of observation and η = overall mean of S/N ratio

$$SS_j = \sum_{i=1}^l (\eta_{ji} - \eta)^2 \quad (3)$$

Where SS_j = sum of square deviation of j th factor l is level of j th factor.

$$V_j = \frac{SS_j}{f_j} \quad (4)$$

V_j and f_j = variance and degree of freedom respectively of j th parameter.

$$F_j = \frac{V_j}{v_e} \quad (5)$$

3 RESULT AND DISCUSSION

3.1 Printed Microneedles

The results of printed microneedles can be seen in Fig. 5 – Fig. 7. As can be seen from the figures, microneedles with higher aspect ratio resulted in taller microneedles while the smaller aspect ratio created a sturdier structure.



Fig. 5. Microneedle CAD with aspect ratio 1.625:1 using precision model resin.



Fig. 6. Microneedle CAD with aspect ratio 1.4:1 using precision model resin.



Fig. 7. Microneedle CAD with aspect ratio 1.3:1 using precision model resin.

3.2 Normality Data

In this study, data from each response variable will be tested for normality. The data of the response variable height, needle base, and needle angle have a p value > 0.05 so it can be concluded that the data of each response variable is normally distributed. This can be seen in Fig 8.

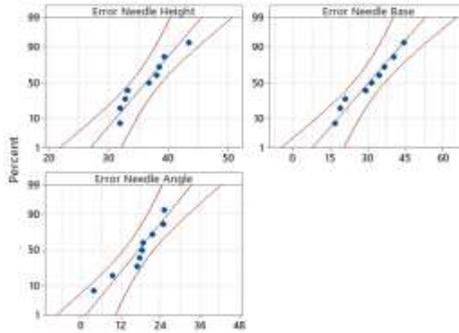


Fig. 8. Normality test graph.

3.3 Needle Height

Needle height is the height formed from the microneedle. The microneedle has a constant theoretical height of 1690 μm . The result is that the microneedle formed from each material has a lower height than the theoretical height. The effect of material, aspect ratio, and layer height on needle height can be seen in Fig 9. In the effect of material, the precision model material has the smallest error value of 34.4 % and SN ratio of 30.7. In the aspect ratio effect, the aspect ratio of 1.4:1 has the smallest error value of 33.96% and SN ratio of -30.6. In the influence of layer height, layer height 0.05 mm has the smallest error value of 34.38% and SN ratio of 30.6. So that the material selection, aspect ratio, and layer height that can produce the closest theoretical height, in order are precision model materials, 1.4: 1, and 0.05 mm. The ANOVA

analysis identified aspect ratio as the most influential factor affecting microneedle height, followed by material choice and layer height. Despite these influences, the statistical analysis, indicated by the P-values, suggests that material and aspect ratio have statistical significance.

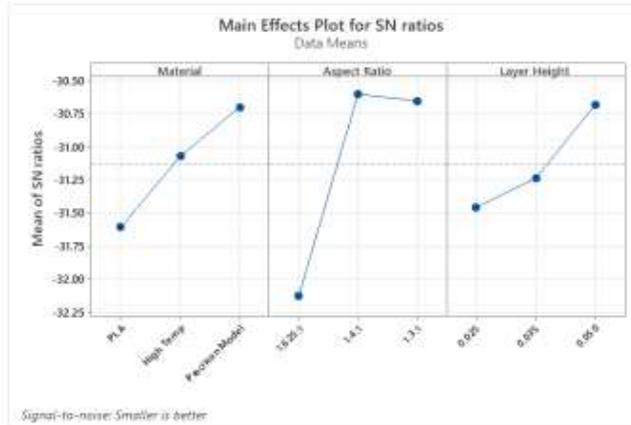


Fig 9. Signal to noise ratio graph of the effect of material, aspect ratio, layer height on needle height.

Table 4. ANOVA assessment on needle height

Analysis of Variance					
Source	DF	Adj SS	Adj MS	F Value	P-Value
Material	2	60.22	30.108	3.78	0.040
Aspect Ratio	2	241.63	120.813	15.18	<0.0001
Layer Height	2	49.49	24.746	3.11	0.067
Error	20	159.20	7.960		
Total	26	510.54			

3.4 Needle Angle

The effect of material, aspect ratio, and layer height on needle angle will also be discussed in this section. A needle angle is the angle formed by the tip of the microneedle. The microneedle has theoretical angles of 49.03°, 54.65°, and 55.29°. The result is that the microneedle formed from each material has an angle greater than the theoretical angle. The effect of material, aspect ratio, and layer height on needle angle can be seen in **Fig 10**. In the effect of material, the precision model material has the smallest error value of 10.18% and SN ratio of -18.5. In the aspect ratio effect, the aspect ratio of 1.625:1 has the smallest error value of 14.59% and SN ratio of -21.15. In the influence of layer height, the layer height of 0.035 mm has the smallest error value of 15.17% and SN ratio of -21.3. So, the material selection, aspect ratio, and layer height that can produce the closest theoretical angle, in order, are precision model material, 1.625:1, and 0.035 mm. The ANOVA results indicate that material had the

most substantial impact on needle angle, followed by layer height and aspect ratio. Despite these influences, the statistical analysis, indicated by the P-values, suggests that material and layer height have statistical significance.

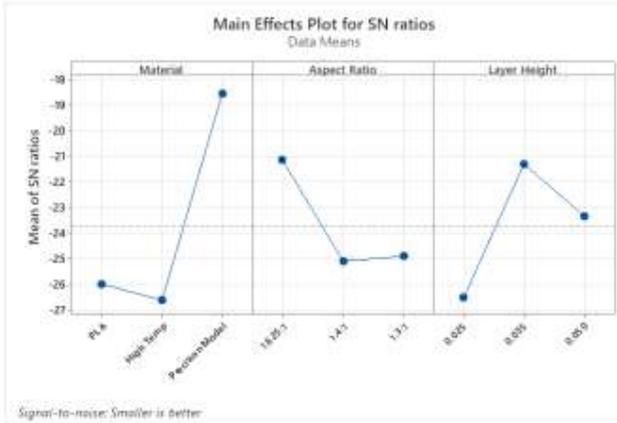


Fig 10. Signal to noise ratio graph of the effect of material, aspect ratio, layer height on needle angle.

Table 5. ANOVA assessment on needle angle

Source	DF	Analysis of Variance			P-Value
		Adj SS	Adj MS	F Value	
Material	2	692.3	346.14	17.9	<0.0001
Aspect Ratio	2	119.8	59.92	3.1	0.067
Layer Height	2	221.4	110.69	5.72	0.011
Error	20	386.8	19.34		
Total	26	1420.3			

3.5 Needle Base

Needle base is the size of the needle diameter on the microneedle array. The effect of material, aspect ratio, and layer height on the needle base will also be discussed in this section. Microneedles have theoretical bases of 800 μm, 900 μm, and 1000 μm. The result is that the microneedle formed from each material has a smaller base than the theoretical base. The effect of material, aspect ratio, and layer height on needle base can be seen in **Fig 11**. In the effect of material, the precision model material has the smallest value error of 26.57% and SN ratio of -28.09. In the aspect ratio effect, the aspect ratio of 1.3:1 has the smallest value error of 18.58% and SN ratio of -25.3. In the influence of layer height, layer height 0.035 mm has the smallest value error 28.78% and SN ratio of -28.8. So, the material selection, aspect ratio, and layer height that can produce the closest theoretical angle, in order are precision model, 1.3:1, and 0.035 mm. The ANOVA analysis identified aspect ratio as the most influential factor affecting microneedle base, followed by material choice and

layer height. Despite these influences, the statistical analysis, indicated by the P-values, suggests that material and aspect ratio have statistical significance.

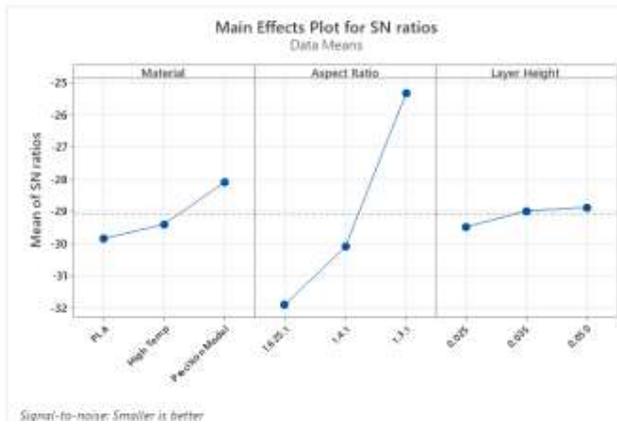


Fig 11. Signal to noise ratio graph of the effect of material, aspect ratio, layer height on needle base.

Table 6. ANOVA assessment on needle base

Analysis of Variance					
Source	DF	Adj SS	Adj MS	F Value	P-Value
Material	2	167.31	83.65	3.92	0.037
Aspect Ratio	2	2019.25	1009.63	47.25	<0.0001
Layer Height	2	65.58	32.79	1.53	0.240
Error	20	427.32	21.37		
Total	26	2679.46			

3.6 Discussion

Best parameters from the most to least influencing are as follows:

1. for needle height: aspect ratio 1.4: 1, precision model material, and 0.05 mm layer thickness
2. for needle angle: precision model material, 0.035 mm layer thickness, and aspect ratio of 1.625:1.
3. for needle base: aspect ratio of 1.3:1, 0.05 mm layer thickness, and precision model material.

In general, the best parameters for fabricating microneedles in this study are aspect ratio of 1.3:1, precision model material, and 0.05 mm layer thickness. Aspect ratio is the primary factor influencing needle height, followed by material and layer height. Significant factors are material and aspect ratio, this means that the choice of material and the dimensional comparison between the height and width of the microneedle can affect the height of the microneedle. Material choice has the most significant impact on needle angle, with layer height and aspect ratio also playing roles. The significant factors are material and layer height, this implies that the combination of material and

layer height influences the formation of the needle angle. The aspect ratio and material are the most critical factor for needle base dimensions, showing statistical significance. This implies that the geometric proportions of the needle are crucial for maintaining its base size. Layer height, while influential, did not show statistically significant effects. The impact of aspects on both needle height and base implies that optimal design proportions are crucial for structural integrity. Since material properties predominantly affect needle angle, selecting the right materials becomes crucial for ensuring the microneedles maintain their desired orientation upon insertion. This finding suggests a potential to explore new materials or composites that might better maintain their structural properties during and after fabrication. The lack of statistical significance for many of the tested factors in influencing needle height and angle suggests that additional variables or manufacturing conditions might be influencing outcomes. Future research could benefit from a multi-factorial approach that examines the interactions between materials, aspect ratios, and layer heights. Additionally, implementing advanced statistical methods or simulation models could provide deeper insights into the subtle effects of these factors.

4 CONCLUSION

The study explored the influence of aspect ratio, material choice, and layer height on microneedle dimensions. The findings indicate that the best parameters are aspect ratio of 1.3:1, precision model material, and 0.05 mm layer thickness. The material emerged as a crucial factor, significantly impacting needle base dimensions, showing a consistent influence on needle height and impacting needle angle. The aspect ratio was found to primarily affect the needle height and needle base. However, the lack of statistical significance for many factors influencing needle height and angle indicates potential areas for further research. This might include exploring additional environmental and process variables or more sophisticated materials and composites. Additionally, the findings suggest that precise control over the manufacturing parameters, especially aspect ratio, can lead to improvements in the reliability and performance of microneedles in clinical applications.

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