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Structural analysis and simulation of solid microneedle array for vaccine delivery applications

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ABSTRACT

This paper promotes a basic, quick, stature adaptable, and direct approach to selecting exceptionally suitable materials in polyethylene glycol diacrylate (PEGDA) and silicon for microneedle fabrication. Researchers and scientists are facing challenges in readily selecting biocompatible materials for microneedle fabrication. Solid porous silicon and PEGDA microneedles are particularly biocompatible and desirable for vaccine delivery by the transdermal vaccine delivery method if microneedle arrays are fabricated successfully using lithography techniques as they belong to enhanced patient concurrence and well-being. Moreover, silicon and PEGDA microneedles are the ultimate for conveying coronavirus vaccines. In this work, we applied the ANSYS workbench tool to investigate the properties of triangular pyramidal-shaped solid silicon and PEGDA microneedle array to perform structural analysis on microneedle for estimating the capability of an array of needles to enter and convey vaccines along with the skin. These outcomes demonstrated that microneedles of porous silicon are better than polymers such as PEGDA as far as mechanical strength and capacity to convey drugs. Buckling was anticipated as the fundamental method to estimate the failure of microneedles and finally, by analysis, it was clear that buckling does not impact the potential of the silicon microneedle needle array. Silicon and PEGDA microneedles are penetrated against human skin surfaces in explicit dynamics by utilizing the ANSYS tool to select the best material. Along these lines, the current strategy can work with silicon and PEGDA microneedles for useful applications. The von Mises stresses generated by applying loads on silicon and PEGDA arrays were greater than the skin resistance of 3.18 MPa and suitable for skin insertion. Silicon microneedles are sustained due to buckling but PEGDA needles fail if the loading is more than 0.1 N. Vaccination can be provided to humans if needle arrays are fabricated based on this approach and design analysis and considering parameters.

Selection and peer-review under responsibility of the scientific committee of the 2022 International Conference on Materials and Sustainable Manufacturing Technology.

1. Introduction

Microneedle is a needle-like micron-scaled structure with the greatest extreme length of 1 mm. Microneedles are homogeneous in appearance to the hypodermic needles but are normally compact, facilitating pain-free delivery of vaccines into tissues [1]. Microneedles may be utilized to convey macroparticles, such as insulin, DNA, vaccines, proteins, peptides, development hormones, immunobiological, and cosmeceuticals to improve skin tone [2]. Microneedle has many benefits like minimizing pain, low cost and less expensive fabrication, eliminating needle phobia, a faster rate of drug delivery, controlled drug delivery, and self-administered [2].

Transdermal drug delivery deals with the carrying of vaccines through the skin. Transdermal Drug Delivery Systems (TDDS) are stated as self-sufficient, distinct dosage forms that are also recognized as "patches". These patches are applied over the skin to convey the vaccine by the skin at a controlled rate for organized circulation [3]. Transdermal Drug Delivery improves patient pliability, reduces dangerous side effects, and keeps down pain during vaccine delivery, uninterrupted input of vaccines, and [4] sustained

Abbreviations: ANSYS, Analysis of Systems; FEM, Finite element method; PEGDA, Poly(ethylene glycol) diacrylate; TDDS, Transdermal Drug Delivery Systems; DNA, Deoxyribonucleic acid; TB, Tuberculosis; FEA, Finite Element Analysis; CMC, Carboxymethyl cellulose; CAD, Computer Aided Design.

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administration of drugs. TDDS convey vaccines along with the skin as a substitute for subcutaneous, oral, and intravascular, conventional routes.

Porous or pure silicon is a biocompatible, biodegradable, bioinert, and non-toxic material like standard silicon. Porous silicon microneedles might be material to convey drugs when developed as high porosity [5], compact pore-sized silicon, and controlled drug release achievable into the skin. Porous solid silicon microneedle arrays can possess prospective for future microneedle-based vaccine and drug delivery and must be a significant add-on to the other microneedle-based vaccine conveyance [6] approaches.

Vaccination with microneedle array resulted effective over conventional hypodermic needles in humans in respect of vaccine [7] stability, immunogenicity, and dose-affording abilities. Microneedle arrays are coated with vaccines and are utilized to deliver drugs such as [8] smallpox, TB, inactivated virus, antigen vaccines, hepatitis B, influenza A, H_5N_1, insulin, plasmid DNA and Coronavirus vaccine. Conventional vaccine delivery techniques to the skin sacrifice the skin by using a bifurcated [8] needle and causing serious skin reactions and a persistent mark on the skin. Present research work searched alternative delivery methods to overcome these issues.

The finite element analysis is accomplished to evaluate and inspect the capacity of solid porous silicon microneedles array while the penetration of skin across the human [9] skin. In this analysis, the impact of different loads on a solid microneedle array was inspected to forecast the mechanical characteristics of an array of microneedles [10]. Porous silicon microneedles are especially suitable for vaccines and biological entities delivery to patients. Silicon microneedles are a biohazardous waste when used, which contains environmental issues and immunogenic risks [11].

PEGDA Microneedles gives drug inserting within the needle matrix and controlled vaccine release later skin-piercing via polymer dissolution and swelling after degradation and excretion from physiological conditions [11]. Poly (ethylene glycol) diacrylate (PEGDA) was chosen for building the needle shaft, exploiting its high mechanical strength and flexible crosslinking degree [12]. PEGDA biomedical applications are utilized in drug-controlled delivery networks because of their amazing biocompatibility, hydrophilicity, and capacity to forestall protein adsorption and cell bonding [13].

Zhang et al. Proved that the FEA of a 3 × 3 HfO_2 microneedle pressed over the skin well clarifies the skin had broken here first over the activity of these microneedles [14]. Loizidou et al. Performed numerical simulations utilizing the Structural Mechanics module of COMSOL Multiphysics and these investigations revealed the reasons for microneedle failure [15]. Olatunji et al. conducted simulations using AutoFEM on a biopolymer microneedle array where they predicted microneedle failure stresses [16]. Sabitha et al. presented a structural analysis of 3D models of microneedle arrays by applying axial loads to predict deformation for fluid extraction applications [17]. Tayyaba et al. developed dual radii array for extraction of blood applications and conducted structural analyses to predict the structural strength of the array of needles using ANSYS software [18] (Table 1).

The advancement of utilitarian conveyance frameworks for new dynamic drug particles is a difficult assignment. The quest for an economical and dependable method of directing the medication securely over the epidermal layer, not harming the nerve cells, and limiting possibilities of the microbial entrance, prompted the improvement of microneedles. Microneedle-based medication conveyance frameworks can be investigated as a likely instrument for the conveyance of an assortment of macromolecules that are not adequately conveyed by ordinary transdermal methods. The greatest disadvantage of conventional drug delivery is helpless penetrability through the skin's initial layer and it tends to be overwhelmed by utilizing microneedles. Subsequently, analysts paid attention to their consideration of the advancement of various kinds of microneedles for the conveyance of macromolecules, immune-biologicals, and drugs just to pull out tissue liquids. The development of the microneedle is a main complex task for accomplishing effective medication conveyance by the end objective that the microneedle neither breaks nor causes aggravation. The instant selection of biocompatible material to develop the microneedle that can withstand human skin penetration is presently a challenging task for researchers.

An explicit dynamics tool in ANSYS Workbench was utilized to display and reenact the act of the microneedle and the skin while the penetration process. Several parameters must be considered when designing the microneedles, such as strong material and mechanical strength, deformation, and failure analysis to make insertion into the skin easier. Simulation, Structural Analysis, and buckling analysis of solid porous silicon microneedle array were carried out utilizing ANSYS Finite Element Analysis (FEA) tool to evaluate the consequence of developed loads during penetration of microneedle arrays into the skin structure well before fabrication of the device. The current work gives helpful anticipated information to create a reasonable medication conveyance device. Different mathematical investigations have already been led on the development and microneedle analysis. Nonetheless, all past examinations cover either primary investigation as they were. We have performed the structural strength, failure analysis, simulation, skin penetration analysis, and checked the mathematical forecasts in our current work. Up to now, published content has no accurate analysis and simulation for solid microneedles with integration to analytically estimate the structural strength under various boundary conditions. This analysis involving structural and simulation has been conducted to enhance design models before fabrication. We proposed strong microneedles with super sharp tips to accomplish better skin penetration and mechanical strength at wanted rates. This current work talks about just a hypothetical way and analysis of microneedles, we have additionally proposed a suitable microneedle fabrication process, which has not been done yet.

2. Materials and methods

The bio compactable polymer material silicon and PEGDA were utilized in this series of operations of numerical simulation. The

Table 1
Comparison table of previously reported work.

Reference	Materials	Shape of Microneedles	Array size	Analysis Type
Zhang et al. [14]	HfO2	hollow out-of-plane Cylindrical	3 × 3	FEA
Loizidou et al. [15]	CMC/SUC	hollow out-of-plane Cone	6 × 4	FEM
Olatunji et al. [16]	Biopolymer films	hollow out-of-plane Cone	1 × 1	FEM
Sabitha et al. [17]	Titanium	hollow out of a plane	3 × 1	structural analyses
Tayyaba et al. [18]	PGA (polyglicolide acid)	hollow out of a plane tapered tip	5 × 5	Structural and fluidic analyses

triangular pyramidal-shaped solid silicon and PEGDA microneedles array (9 × 9) modeled by CREO CAD Software with pyramid altitude 350 μm and base side 100 μm on top of the surface of the square block (500 μm × 6000 μm × 6000 μm) respectively. The skin structure was designed with 1100 μm thickness with three layers. Skin layers such as stratum corneum, dermis, and epidermis layers were designed in CREO CAD Software with thicknesses of 20 μm, 80 μm, and 1 mm and density of 1.3 g/cm^3, 1.2 g/cm^3, 1.2 g/cm^3. All the three layers are bonded together tightly and considered as a single skin structure similar to human skin and the parameters considered are constant for all skin layers of human. All the layers are having a Modulus of elasticity of 0.75 MPa, 0.48 MPa, and 7.33 MPa with 0.50 Poisson's ratio. Microneedle array was modeled with PEGDA material with a Modulus of elasticity of 40 MPa with Poisson's ratio of 0.3.

Static Structural Analysis and buckling analysis were performed in ANSYS Workbench 2019 R3 software to predict the mechanical strength of the silicon and PEGDA microneedles array. The three-dimensional model of the microneedle has meshed and skin structure networks on the ANSYS Workbench that holds fine for the surface to surface contact and this microneedle inclusion into the human skin is iterated utilizing the previously mentioned bioviable materials. Unanticipated failure of the microneedle during penetration must give rise to buckling. This was predicted by utilizing Eigenvalue linear buckling analysis in ANSYS to predict critical load factors. The critical buckling force for all microneedles arrays may be evaluated by multiplying the obtained critical load factor with the applied force. ANSYS Workbench Explicit dynamics tool was utilized to realize the deformation and equivalent von-mises stresses which are applied on the skin structure or microneedles array by applying some velocity on the array of microneedles (Fig. 1).

3. Results and discussion

3.1. Static structural analysis

FEM is truly reasonable for primary mechanical investigation, particularly for the examination of stresses and deformation in solid bodies. This technique improves on the complex actual models and the more modest FEM network makes the estimation results nearer to genuine qualities. The microneedle is affected by numerous forces in the course of skin insertion, such as bending and buckling. The structural analysis accomplished estimates the impact of these forces on the silicon microneedle array for the microneedle pattern. Initially, the geometry of the silicon microneedle array was imported into ANSYS Workbench 2019 R3. The automatic meshing of the silicon microneedle array was performed by default sizing and smoothing options. Forces of 1 N, 0.7 N, 0.5 N, 0.3 N, and 0.1 N were applied evenly on all silicon and PEGDA microneedles of an array to predict the resistance offered by the silicon and PEGDA material to the applied forces. The bottom portion of microneedles was fixed while performing static structural analysis. By applying the above-said forces ranging from 0.1 N to 1 N on the silicon and PEGDA microneedle array the resistance offered or stress generated on the microneedle developed was the same. This generated equivalent or Von-Mises stress was sufficient to overcome the resistance (=3.18 MPa) offered by the skin during microneedle array penetration and the skin will be pierced during penetration. Total deformation (Fig. 2) and directional deformation (Fig. 3) of microneedles were predicted and are very less than the length of the microneedles (350 μm) in the case of silicon microneedles but it is more than the needle length in the case of PEGDA. Hence, the PEGDA array is only limited to 0.1 N forces, which are suitable where deformation is less than the needle length (Fig. 2). The directional deformation is minimum in both silicon and PEGDA microneedle array (Fig. 3). The outcomes from this analysis give proof that microneedle arrays can be created into a scope of aspects and keep up with adequate structural strength to puncture the skin.

3.2. Eigenvalue buckling analysis

Failure of microneedle array is generally caused by buckling which was employed to estimate the stability of microneedles. Pre-stress for buckling analysis for all loadings is obtained from static structural analysis to generate Load Multipliers (Fig. 5). If the load multiplier (7.2424) is multiplied by the applied load (1 N) and all microneedles in the array i.e., 81, then the calculated value (586.6344) must be greater than that applied load (1 N) and it is called as critical buckling force (N), which is shown in Fig. 4. Hence, for all variations of loading the Silicon microneedles array is acceptable for penetration into the skin without any failure/buckling. Which will the total deformation of silicon and PEGDA microneedles during buckling be the same for all applied loads (equivalent to 1 μm), indicating constant deformation frequency. The triangular pyramidal-shaped Solid Silicon microneedle array had no failure and is safe to use in clinical trials. But buckling is the main mode of failure in PEGDA microneedles where the needle fails due to buckling. When the applied load is less than 0.1 N then the needle sustains the buckling, where the critical buckling force is more than 0.1 N (Fig. 4).

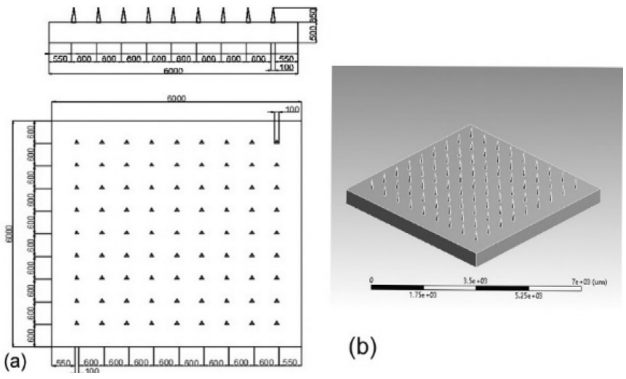

Fig. 1. Silicon Microneedles array. (a) Front and Top View of Microneedles array; (b) Three-dimensional view of microneedle array in ANSYS.

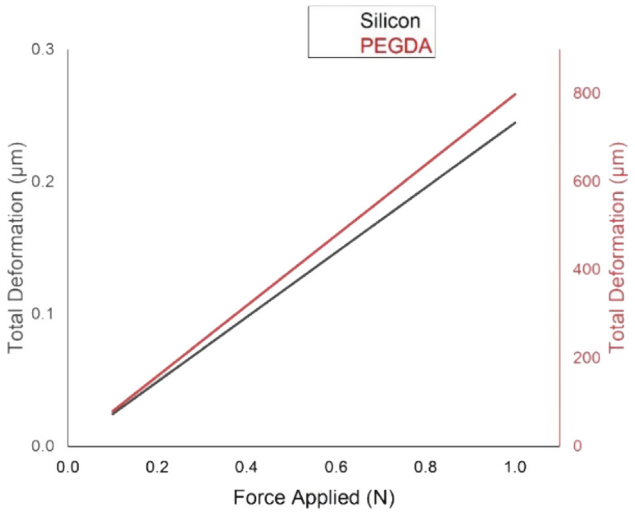

Fig. 2. Total deformation of silicon and PEGDA.

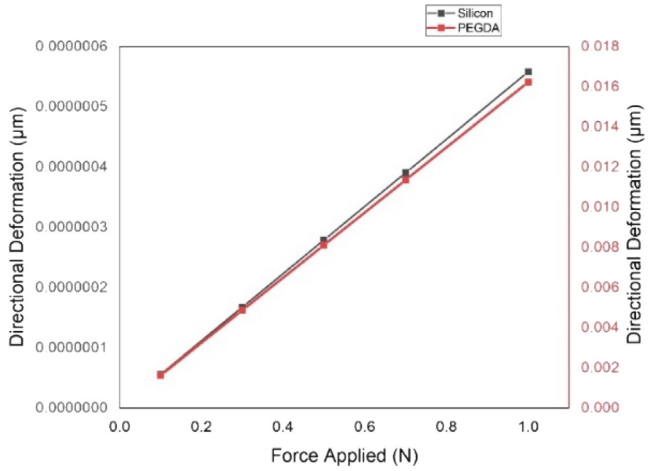

Fig. 3. Directional deformation of silicon and PEGDA.

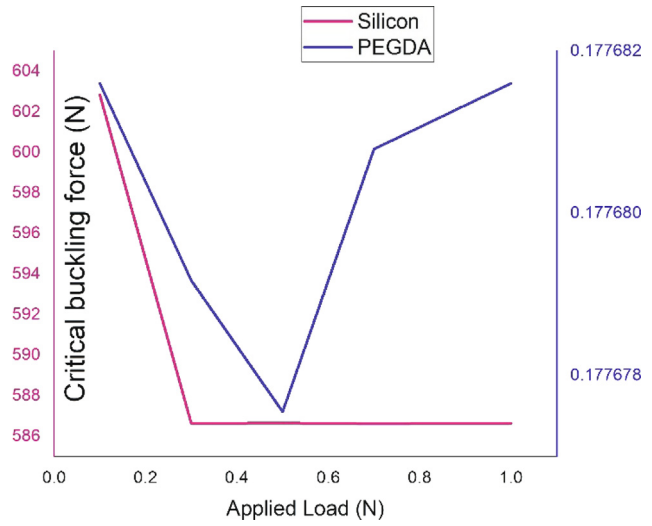

Fig 4. Comparison of critical buckling force (N) in silicon and PEGDA.

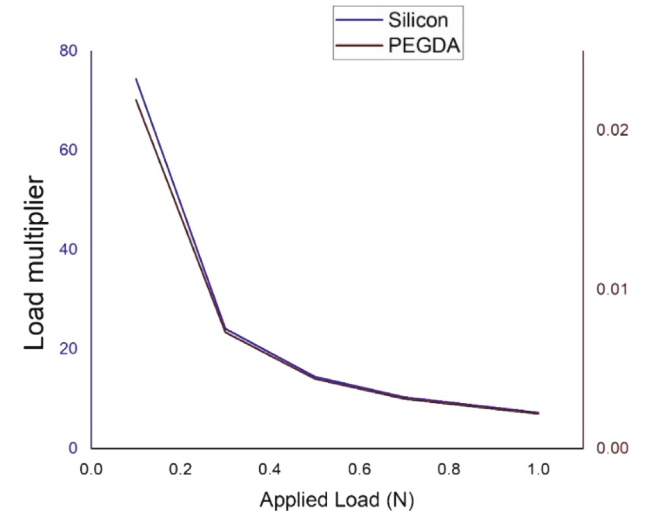

Fig. 5. Comparison of Load multiplier in silicon and PEGDA.

3.3. Microneedle array simulations

Microneedle array developed with silicon was penetrated modeled skin structure by using explicit dynamics tool in ANSYS 2019 R3. This type of skin penetration study is not conducted before. This simulation analysis predicts the Von-Mises stresses generated in the microneedle array within the insertion process whereas the faces of skin structure were fixed. The velocity of 5×10^5 µm/s was applied in a downward direction on the microneedle array which facilitates the microneedles to penetrate the skin structure. Maximum von – Mises stresses (Table.2) induced in silicon and PEGDA microneedles arrays (Figs. 6–7) were high and stress/resistance offered by skin structure (Figs. 8–9) was very less indicating the penetration of microneedles without any barriers. The Von-Mises stresses developed in skin structure against silicon microneedles is 11.004 MPa (Fig. 6). The Von-Mises stresses generated in the solid silicon microneedles array during penetration were equal to 1.2605e+005 MPa (Fig. 7). Accordingly, the Von-Mises stresses developed in skin structure against PEGDA microneedles is 8.7818 MPa (Fig. 8). The Von-Mises stresses generated in the solid PEGDA microneedles array during penetration were equal to 1.2605e+005 MPa (Fig. 9). Hence, it is clear that the microneedle array is suitable for further development (SAMN 1–4 & PEAMN 1–4).

4. Conclusion

The structural, buckling, simulation analysis of solid silicon and PEGDA microneedles array by utilizing ANSYS has been executed to estimate the stress distribution. These estimations and results proved that silicon is superior to the PEGDA in all aspects. The triangular pyramidal-shaped microneedle array is selected for its geometrical configuration which permits the microneedle array to insert into the skin with applied force. The conferred simulations confer that porous silicon and PEGDA are acceptable for the development of a microneedle array for vaccine delivery. Microneedle arrays are a fascinating platform for drug/vaccine delivery and can show a key role in the treatment of a COVID-19 pandemic. Vaccination and clinical trials will be performed using a microneedle array, which is a key factor in increasing vaccination exploration around the world. More investigation is required to use silicon and PEGDA microneedles in drug/vaccine delivery, constituting the bio-compatibility of silicon and PEGDA needle materials.

CRediT authorship contribution statement

S.B.V.J. Chandbadshah: Conceptualization, Methodology, Software, Data curation, Writing – original draft. **Giriraj Mannayee:** Investigation, Supervision, Validation.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: CHANDBADSHAH S B V J reports administrative support, equipment, drugs, or supplies, statistical analysis, and writing assistance were provided by VIT University. CHANDBADSHAH S B V J

Table 2
Stresses after penetration.

Material	Equivalent stress in the skin (MPa)	Equivalent stress in the array (MPa)
Silicon	11.004	1.2605e+005
PEGDA	8.7818	67.674

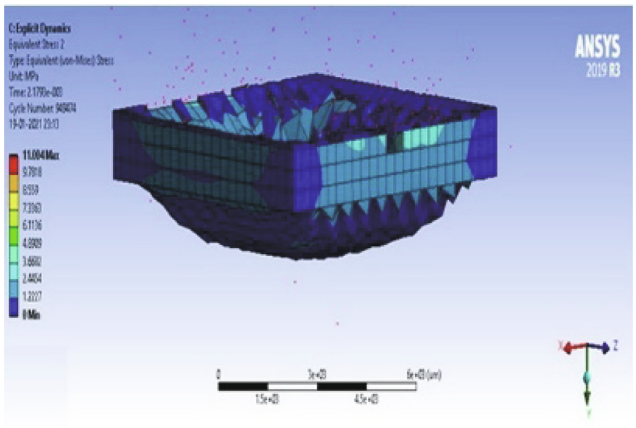

Fig. 6. Stress offered by skin against silicon microneedles.

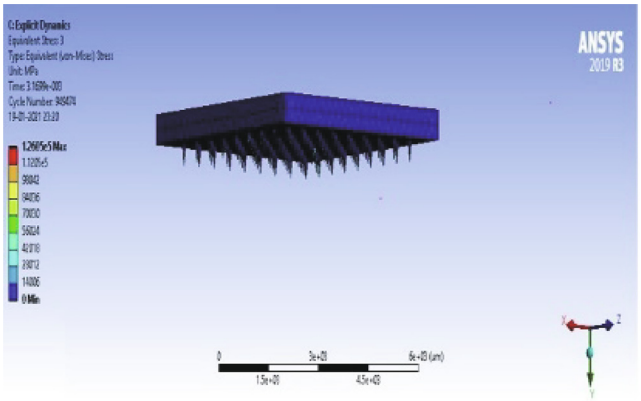

Fig. 7. Stresses induced in silicon microneedles.

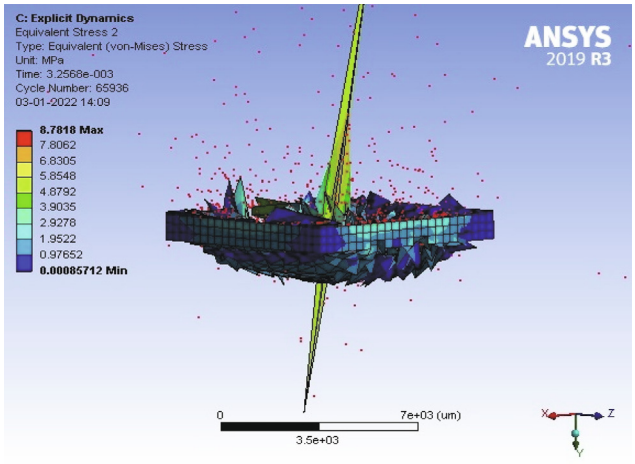

Fig. 8. Stress offered by skin against PEGDA microneedles.

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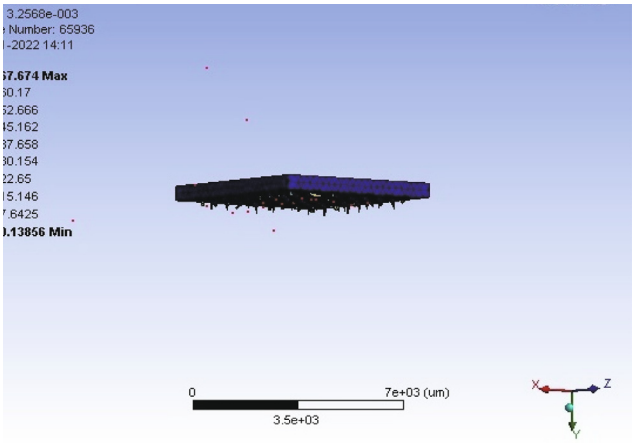

Fig. 9. Stresses induced in PEGDA microneedles.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.matpr.2022.06.483.

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