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# MEMS Based Microneedles in the Field of Drug Delivery

**Shilpa Nagod, S. V Halse**

***Abstract*: The technology of MEMS has paved way for many biomedical applications where a lot of new devices at microscale have emerged making the diagnosis and treatment of diseases more easy and efficient. Microneedles are one such example which have been used in drug delivery, vaccines as well and also in the field of cosmetology for skin treatments for scars, pigmentation, acne etc. Apart from penetration into the skin, the microneedles are also used in treating eye with some insertion of bioactives and also in the treatment of cells. The success of microneedles design and its application would depend solely on how it gets infused into the skin, skin recovery post the microneedle removal, how the drug stays stable during manufacturing and the delivery as well. Microneedle can pierce into the skin only when required amount of pressure is put for the insertion. This paper reviews on inception and the evolution of MEMS based microneedles and a microneedle is designed to show through the simulation that the force of 1.29N is required to break through the human skin for the reliable delivery of the drug.***

***Keywords: Microneedle, Drug Delivery, MEMS, Biomedical Applications***

## I. INTRODUCTION

**MEMS** (Micro Electro Mechanical System) devices have gained a lot of interest in past decades and are rapidly growing in the field of biomedical applications to improve the efficacy of disease diagnosis and treatments. In the recent years MEMS has given large contribution towards drug delivery. The drug delivery is generally done via oral and parenteral routes. Majority of the drug is administered orally [1]. Oral route is the most conventional and easy ones to deliver drugs [2,3] since in it, there is ease of portability, pre-determined dosage and patient's self-administration without any need of expertise, however most therapeutic drugs comprise of polymers and peptides that cannot be given orally. Hence injections are used for delivering such drugs with macromolecules. But these have their own limitations of pain, allergy and infections in some cases [4]. Thus a need of painless and efficient delivery was attained with the advent of Microneedles. In contradiction to the conventional needles, the microneedles are minimally invasive and carry no risk of infections.

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MEMS has come up with "lab on chip" mechanism for diagnosis and treatment at the same time, where these microneedles would play a pivotal role by delivering microvolumes of the drug as and when required.
Micro needles use human skin as the route for drug delivery and this way of administering the drug has more advantages in comparison with the conventional drug delivery techniques because here the first-pass metabolism can be avoided and small volume of drug would suffice. It is painless, minimally invasive and can easily be administered and the release rate can be controlled [5, 6]. In order to understand the concept of microneedle based drug delivery, its interaction with the skin is to be understood which requires understanding of the anatomy of human skin.

## II. ANATOMY OF HUMAN SKIN

The outermost part of our body is the skin which comprises 16% of the total average mass of any person. It has total surface area of about 1.7 m² [7-9]. There are three layers in the human skin, the epidermis, dermis and hypodermis which is the subcutaneous tissue. Fig. (1) Shows the component layers of the skin [10]. The external layer is called Stratum Corneum (SC) which functions like a strong barrier for the foreign bodies like microorganisms and prevents them from entering into the body [11-12]

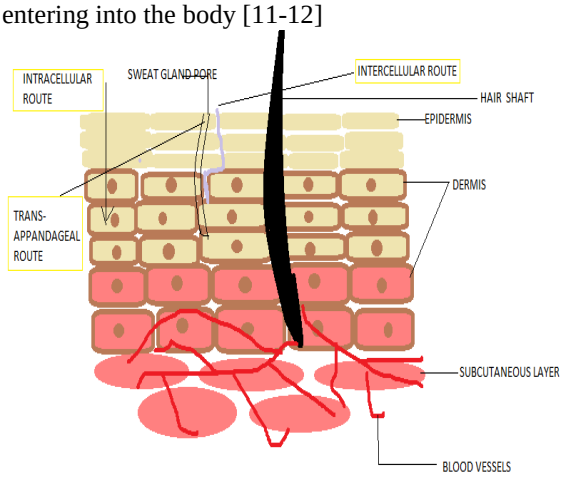


**Fig. (1) Human Skin Structure.**

For the efficacy of the drug and appropriate drug release through the skin there is necessity of physical and/or chemical boosters which would basically improve the drug permeability. Microneedle is a physical booster which enhances the drug permeability through the skin to the degree of three times. The micro needle doesn't puncture the nerves and it diffuses well under the skin layer and hence it is painless [11, 13-15]

## III.ROUTES OF DRUG PENETRATION THROUGH THE SKIN

It has been studied that the drug delivery through skin is advantageous since it avoids the first-pass metabolism. The drug that penetrates through the surface of skin that goes into SC layer basically passes to the delivery site through these 3 routes namely.

- Intercellular route
- Intra-cellular route
- Trans-appendegeal route,

These above mentioned routes are depicted in Fig. (1)

**Intercellular route** is the route for lipophilic drugs since they are impermeable through the dense packing of proteins in the corneocytes of stratum corneum [16, 17]. They do pass between the gaps of cells in the epidermis layer as shown in the above Fig. (1)

**Intracellular route** is the route for hydrophilic drugs which are permeable through the dense packed proteins of corneocytes of the SC. The drug gets driven based on its partition co-efficient [16-18].

**Trans-appendegal route** is mainly for the drugs that cannot pass through SC layer. They get transported via the pores that are associated with the sweat glands or the hair follicles. This however is not that vastly used channel since the number of hair follicles and the sweat glands is only about 0.1% of the entire surface of the skin [18,19].

Microneedles enhance the skin permeability so that the efficacy of drug penetration is improved.

## IV.MICRONEEDLES- HISTORY AND CLASSIFICATION

Microneedle technology for drug delivery was invented by Gerstel and Place in the year 1971 [20,21] but they gained significance in mid 1990s when they got advanced with the improvement and development in the field of MEMS. The permeability of the skin was increased with the help of solid microneedles. Drug coated microneedles were manufactured which on piercing would help in the administration of the required drug. Dissolvable polymer microneedles came into existence. Hollow microneedles for drug infusion into the skin are being used. [6, 20]. Microneedles should have appropriate mechanical strength, toughness to disrupt SC layer without getting fractured and buckled. Irrespective of any end application or the type, the drug delivery efficiency of the microneedle is of utmost importance [22].

**Table (1): Microneedle Classification**

| Material | Applications | Manufacturing Technique | Design |
|---|---|---|---|
| Silicon | Medicine | Etching | Solid |
| Metal | Pharmacy | Injection Molding | Hollow |
| Glass | Cosmetology | Micro-molding | Coated |
| Polymer | | Lithography | Dissolving |
| Ceramic | | Micromachining | |

**Silicon Microneedles**: Silicon microneedles have good hardness but they are fragile too hence they are sensitive to fracture. Manufacturing should be done in clean room and hence they are complex and expensive [20-23].

**Metal Microneedles**: Metal used in manufacturing of microneedles are stainless steel, nickel, titanium, and palladium. Their strength is good, they are tough and hard hence they are resistant to mechanical failure .These can be manufactured with relatively a low cost. Titanium is widely used for biomedical applications. The metal microneedles produce waste at their tip which could be hazardous [23].

**Glass Microneedles**: Silica can be used to make microneedles since the flow would be transparent however they are brittle and hence have a tendency to break. Borosilicate glass features good elasticity but these would require longer time to manufacture [23].

**Polymer Microneedles**: The polymer microneedles are the ones most widely used because of their toughness, and they are not brittle hence less prone to mechanical failure. Polymers would be of two types. Biodegradable polymer microneedles used are poly-lactide-co-glycolide acid (PLGA), poly-Llactic acid (PLA). Drugs can also be encapsulated in the microneedles that get dissolved into the skin. Advantages of such biodegradable microneedles is that they are very safe and have no side effects. They are preferred due to their biocompatibility and low cost. Polymers used for this are poly (methyl vinyl ether-comaleic anhydride) and poly methyl vinyl ether-comaleic acid, poly carbonate, poly vinylpyrrolidone (PVP), poly vinyl alcohol (PVA) [20-23].

**Ceramic Microneedle**: Material used for ceramic microneedle are calcium sulfate dihydrate and calcium phosphate dihydrate. These materials have good mechanical and drug-loading properties [21-23].

**Solid Microneedles**: Solid microneedles puncture the surface of the skin and applies the drug to the skin layer which slowly diffuses through the holes. It resists the pathogenic infections but the drug effect is low [24-26].

**Hollow Microneedle**: Hollow microneedles work in similar fashion as that of conventional syringes, allowing the liquid medication to flow into the skin layer [24-26].

**Coated Microneedle**: Coated Microneedle as the name goes, are coated with a layer of water soluble drug. When the microneedle is inserted into the skin the coat dissolves and then the microneedle is taken out. Coating has to done properly for efficacy of the drug delivery. These carry some risk of infection when inserted into other person and they are capable of delivering small quantity of drug [24-26].

**Dissolving Microneedle**: The dissolving microneedles when pushed into the skin, gets dissolved and the drug gets released. These microneedles can deliver large quantity of drug and hence are can address the issue of coated microneedles [24-26].

## V. INSERTION TECHNIQUES OF MICRONEEDLE INTO THE SKIN

There are many ways of releasing drugs through microneedles. They are mainly segregated as:

1) Poke with Patch

2) Coat and Poke (/Dip and Scrape)
3) Poke and Flow
4) Poke and Release

These insertion techniques are shown in the Fig. 2

**Poke and Patch**- is the technique where the solid microneedle is poked to create microchannels and then the transdermal patch is applied which would release the drugs by diffusion [13,14].

**Coat and Poke**- is the technique where the needles are coated with the drug to be diffused and then they are inserted into the skin for drug release [27,28]. There is one alternative to this and that is **Dip and Scrape**- Here the microneedles would be immersed in a solution containing the drug and then the entire surface of the skin is scraped to introduce the drug into micro-abrasions created by the needles [14, 25]

**Poke and Flow**- This mechanism is for hollow microneedles where the injections where the microneedles are inserted and drug flows through the micro channels [29].

**Poke and Release**- This mechanism is meant for dissolving microneedles, drug gets released during dissolution of microneedles [30-32].

## VI. APPLICATIONS

Microneedles are used in various applications pertaining to the health. They have proven to be very good members for drug delivery, they are used in cosmetology.

Hollow Microneedles are used in treatment of Glaucoma without any side effects by delivering apt dosage of medicine [33]. Microneedles can be used in glucose monitoring where they operate at lower potential than that of conventional ones hence reducing interferences [34].

Continuous glucose monitoring can be done using hollow microneedles [35].

## VII. SIMULATION

Currently there is a large focus on the biomedical applications of MEMS based microneedles. An array of microneedles can be designed which can be used to deliver different drugs at same time.

There are various factors that need to be considered while designing a microneedle. A microneedle would be successful in delivery of the drug only if it can pierce the skin with the pressure between 3-14Mpa.

This is the ultimate stress to break through the skin. The average insertion force of a microneedle patch into the skin is about 1.29N [36].

In this work we have designed a model to show that a 1.29N total force is enough to break through the human skin.

**Geometry**

A cylindrical block represents the skin and a circular patch shows the microneedle with the diameter of 80 microns

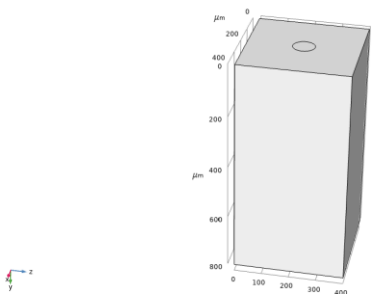

**Fig. (2) Microneedle within a block of human skin**

The above model is being simulated using Comsol Multiphysics. Solid Mechanics study is done.

**Design Parameters**

**Table (2): Design Parameters**

| Parameters | Values |
|---|---|
| Width of the skin | 400 um |
| Length of the skin | 400 um |
| Depth of the skin | 800 um |
| Poisson's Ratio | 0.3 |
| Young's Modulus | 4.5Mpa |
| Density | 1100 kg/m3 |
| Diameter of the microneedle | 80um |

Here we are considering a single microneedle out of 60 microneedle's patch hence the insertion force 0.02158N which is applied downwards towards the skin.

**Assumption**

Insertion force of 1.29N is being evenly distributed on the patch of 60 microneedles that is used for drug delivery.

**Mesh**

A physics controlled mesh with the normal size is being used for meshing the geometry. Complete mesh consists of 4517 domain elements, 744 boundary elements, and 92 edge elements. Number of degrees of freedom in meshing is 20418.

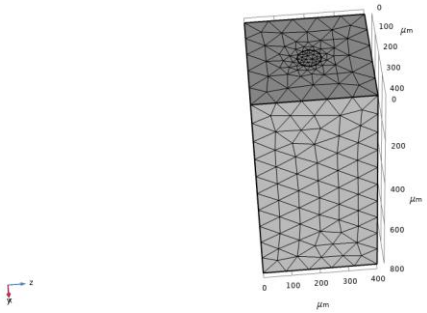

**Fig. (3) Meshing**

## VIII. RESULTS

The highest insertion force of the microneedle was felt in the tip of microneedle itself as per the results obtained from the simulation. It can be observed that the highest stress is 8.49 Mpa which is in the range of 3-14Mpa.

Thus the microneedle breaks through the human skin and the drug delivery takes place as per the simulation results.

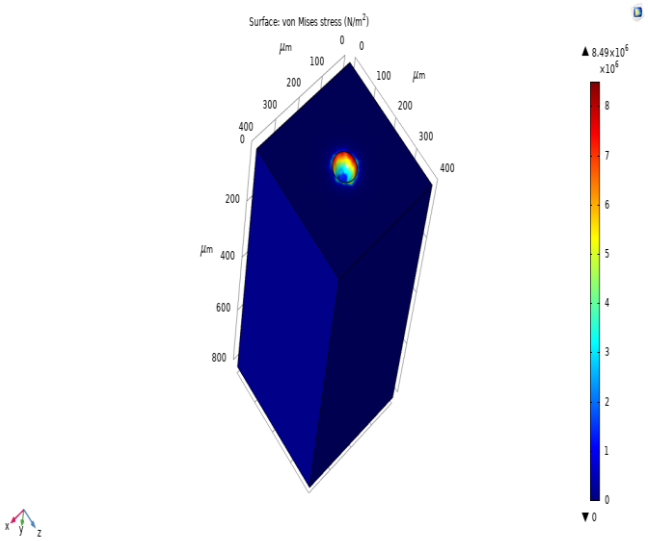


**Fig. (4) Results showing stress of 8.5Mpa which is within the range of 3-14Mpa implying microneedles break through the human skin.**

## IX. CONCLUSION

A glance of microneedles from its inception to its development till date has been seen in this paper. Also the types of microneedles and how it is pierced into skin is studied through showing the anatomy of human skin structure. A microneedle is designed in Comsol Multiphysics tool and simulated to check for the stress at needle-human skin interface. The simulation study is done to prove that for the needle designed a force of 1.29 Newton is enough to break the skin and thus the drug can be administered.

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