Assessment of the Mechanical Properties of Transdermal Devices

S. McIntyre[1a], I. Ichim[2], H. Arora[1], R. Bamsey[2], S. Sharma[1] and O. Guy[1]

[1]College of Engineering, Swansea University

Fabian Way, Crymlyn Burrows, Bay Campus, Swansea SA1 8EN (UK)

[2]Innoture Ltd, Singleton Campus, Swansea University
Swansea SA2 8PP (UK)

[a]824456@swansea.ac.uk

Abstract.
Rapid diagnostic testing is a useful tool to confirm or indicate hidden medical conditions enabling healthcare professionals to deliver appropriate treatment regimens based on the result. Quick and effective indication of disease or a condition improves patient outcomes and monitoring other diseases like diabetes (glucose) through constant feedback allows dynamic management of the disease. Transdermal diagnostics are a minimally invasive technique employing methods to bypass the skin barrier with microneedles (MNs) to access skin's interstitial fluid (ISF) for analytes, such as metabolites (glucose, lactate), drugs (for monitoring) and biomarkers. This study investigates the mechanical properties of MNs in response to axial and transverse forces to assess the impact during insertion and determine the safety margin.

Introduction

Biofluid matrices such as urine, stools, blood (via hypodermic syringe) and suction blister fluid face challenges in compliance due to disdain, perceived/actual pain or fear. Transdermal access to target analytes is a convenient solution to achieving better compliance, and potentially, a more accurate and rapid diagnostic interface. MNs are one such transdermal technology in use to overcome these challenges. MN patches can be applied to the skin and are minimally invasive; designed to painlessly penetrate to the dermis. The absence of nerves in the stratum corneum and the small size of the MNs reducing chance of nerve stimulation causing pain [1]. MNs of heights 480 to 1450 µm, as seen in the study by Gill et al [2], were reported to be significantly less painful than a hypodermic needle. Fig 1 shows a schematic of MNs inserted into the skin.

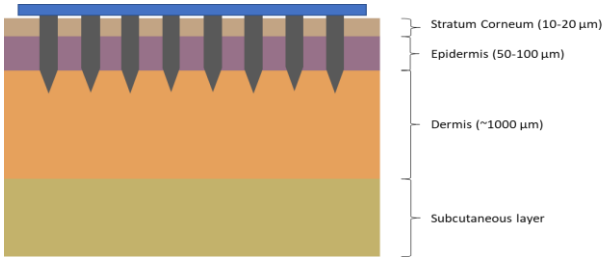

Fig. 1, Diagram of microneedles inserted into skin, penetrating to the dermis layer

MN array platforms can be used to create a transdermal biosensing device to test the ISF in the skin for analytes of clinical significance. It is a relatively new technology and the current most prevalent application is the sensing of glucose and lactate, this is because of the large industry related to diabetes and sports science [3]. They have the ability to be adapted to detect analytes such as metabolites, drugs and biomarkers using specific antibodies or enzymes immobilised on the MN sensor surface therefore they have the potential to detect any condtion which presents an analyte in the ISF.

An effective MN array needs a design which is optimal for penetration, pain free and biocompatible. Design parameters to be considered when fabricating MNs are listed in Table 1 alongside ideal MN parameters [4].

Major MN Parameters	***Ideal Parameters [4]***
Material	Biocompatible and dependant on application and budget, generally high mechanical strength to prevent deformation upon insertion. Polymers, Metals and Ceramics can be used but each has limitations
MN shape	Pyramid or cylindrical with sharp tip
Tip radius [µm]	30 – 80 or as sharp as possible
Length [µm]	500 – 800 to match the depth of viable dermis
Force of insertion [N]	0.1 – 10 dependent on outer diameter of needle

Velocity of insertion	Dependent on tip radius and density of MN array – too high and the MNs may break
Density of MN array (Pitch) [μm]	Ideal pitch is dependent on the height and diameter of the MNs. Higher density gives a higher contact surface area with ISF but too high a density creates a 'bed of nails' effect which may cause pain and require greater insertion force

Table 1. Ideal Microneedle Design Parameters

Microlithographic Manufacture

The arrays used in these were manufactured using a patented microlithographic 3D printing method (ML3DP) to create functional microstructures (MSt) as used by Innoture Ltd [5]. A UV curable polymer is deposited onto a base substrate using a perforated template and cured in layers until the desired height is reached. Heights of the MSts have been varied from 400 – 900 μm. Below in Fig 2a and Fig 2b the solid MSts can be found imaged with a 3D Keyence VHX-950F Series Optical Microscope in Fig 2a and using a Scanning electron microscope (SEM) in Fig 2b.

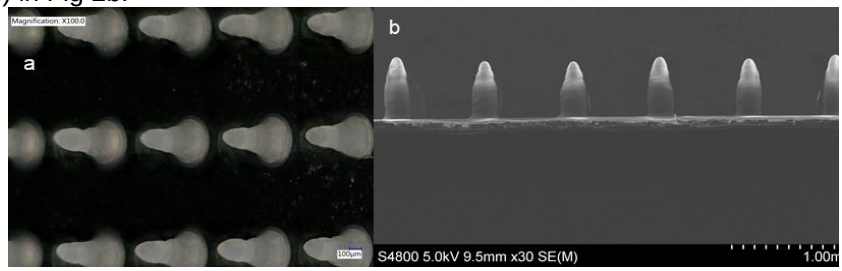

Fig. 2, showing SEM and 3D microscope images of the MSt arrays; 2a. 3D microscope image of the ML3DP solid MSts; 2b, SEM image of the ML3DP solid MSts

Mechanical testing methods

Using a Tinius-Olsen force testing machine and either 1kN or 25N load cell, different force measurements are taken with the MNs in different orientations.

Measurement of axial compression force. The axial compression load effect on the MN array is assessed. The microneedles are placed facing up and force is applied at a slow rate using the moving probe of the Tinius-Olsen system in compression mode to ascertain the fracture/deformation force of the MN arrays. Arrays with different pitch diameters have different fracture/deformation forces. These measurements are to investigate the effects of the axial forces the MN can withstand from insertion.

Measurement of transverse fracture force. To measure transverse fracture force, the MN array is rotated and fixed perpendicular to the fixed plate. The force is applied at a slow rate at varying magnitudes to fracture/deform the first row of the MN array. These measurements are to investigate the forces a MN array can withstand when inserted into skin and moved transversely.

Measurement of insertion force in a skin model. To measure insertion force, the MN array is fixed to the moving probe and a basic skin model like Dragon Skin™ silicone or PDMS is placed on the fixed plate. The force is applied at a slow rate until after the MN array has penetrated the skin model.

Conclusion

Investigating the forces that MN arrays can withstand is important so that painless and effective insertion can be achieved. MNs also need to keep their shape, retain functionality and not break off into the skin post use. Additional investigation can be conducted for MNs with more variation in design and alternative more advanced skin models. MN based diagnostic devices can transform patient care, and the mechanical assessment of the device is essential to ensure accurate and reproducible testing.

References

[1] D. Prausnitz MR. Microneedles for transdermal drug delivery. Adv Drug Deliv Rev. 2004;56(5):581-7.
[2] Gill HS, Denson DD, Burris BA, B.S., Prausnitz MR. Effect of microneedle design on pain in human subjects. Clin J Pain. 2008;24(7):585–94..
[3] Howells O, Rajendran N, Mcintyre S, Amini-asl S, Henri P, Liu Y, et al. Microneedle Array-Based Platforms for Future Theranostic Applications. ChemBioChem. 2019;20:2198–2202.
[4] Davis SP, Landis BJ, Adams ZH, Allen MG, Prausnitz MR. Insertion of microneedles into skin : measurement and prediction of insertion force and needle fracture force. 2004;37:1155–63
[5] De Mello N, Eng C, Bexon J, Hughes A, Dukes M, Bamsey R, et al. Developing and optimising a screen printing technique for microneedle production on flexible substrates. Int J Cosmet Sci. 2015 Feb 1;37:162–163, Febr. 2015.