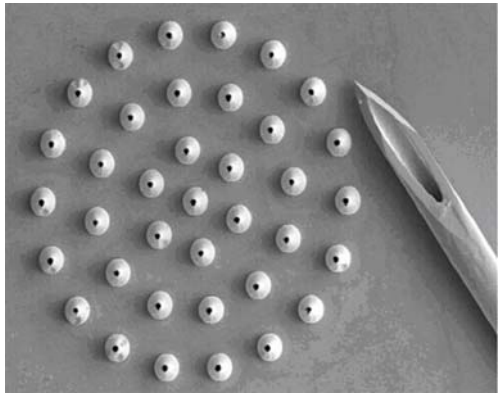
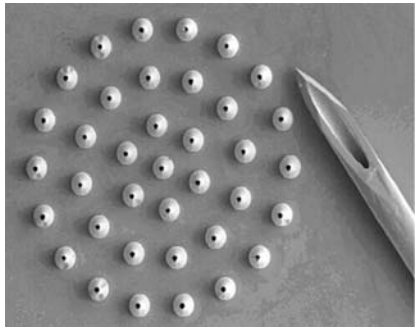


Mechanics of Skin Penetration by Microneedles

Groves, RB (a), Evans, SL (a), Coulman, SA (b), Birchall, J (b)

(a) School of Engineering, Cardiff University

(b) Welsh School of Pharmacy, Cardiff University



Contents

Microneedle arrays

- What are they?
- What are the advantages over other methods of drug delivery?
- Current design issues

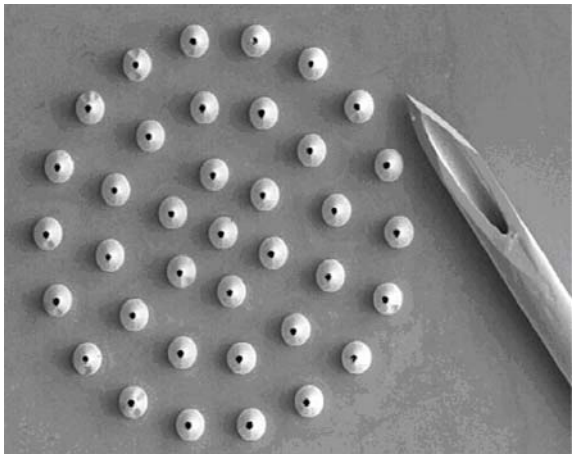
Study Outline: Developing a FEM of human skin

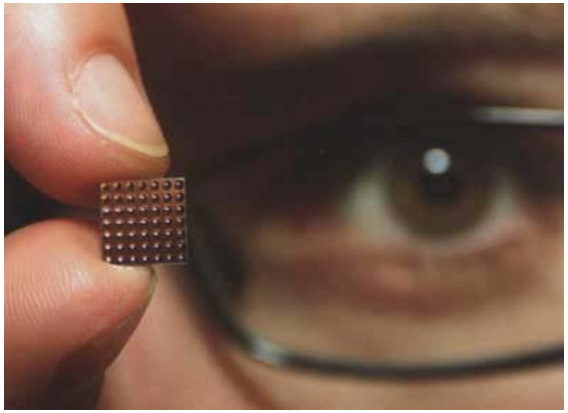
- Preliminary models and experiments
- Incorporation of different layers within the model
- Adding an initial strain and coefficient of friction

Future improvements to the model

Final aims

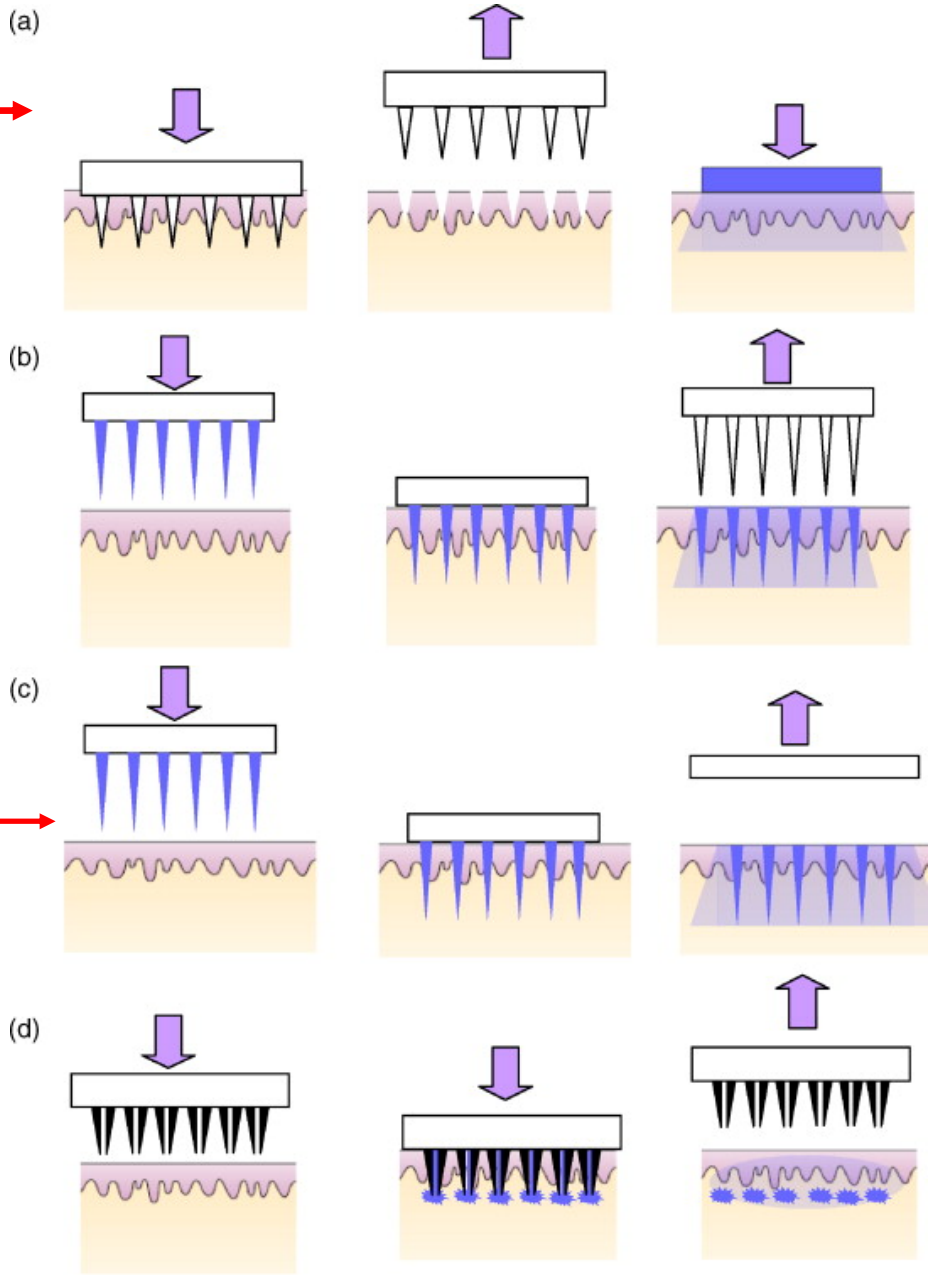
Microneedle Arrays





- A painless and safer alternative to hypodermic needles
- Can be thinner than the diameter of a human hair and have a length of between 150μm and 700μm
- Self administration
- Arrays have been shown to deliver a variety of therapeutic compounds
- Up to 50 times greater immune response when using microneedle arrays, compared with intramuscular injection

Using microneedles to create a pathway through the skin



Coated microneedles

Biodegradable arrays

Hollow microneedles

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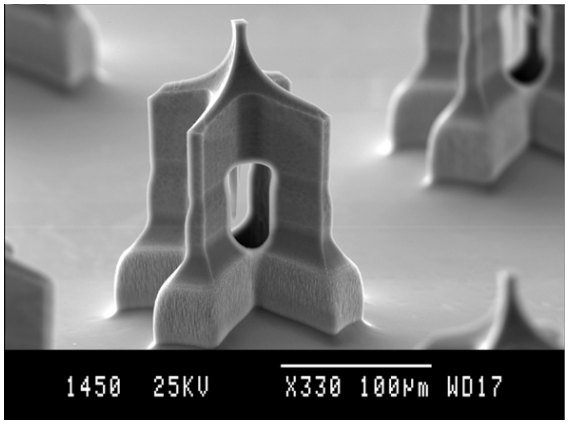
Design Issues



- Due to the wide range of applications, there is no uniform shape, size, material or method of manufacture.
- The only similarity is that the needle must pierce the stratum corneum to deliver the therapeutic compound

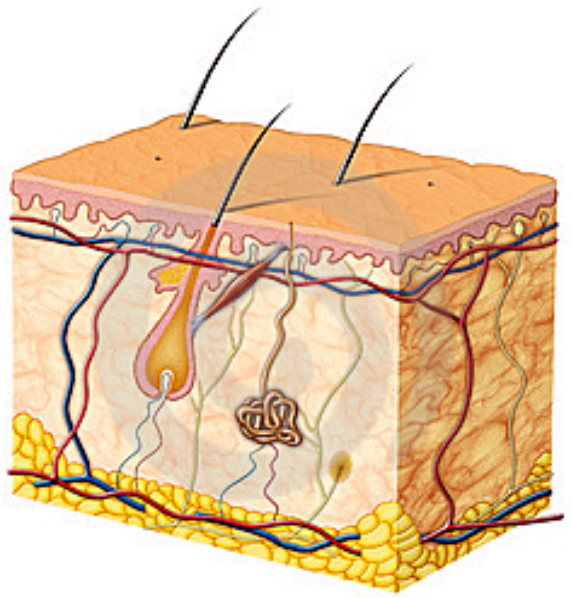
Study Aims:

To quantify the material properties of human skin, *in vivo*, using experimental assessments and computational methods.

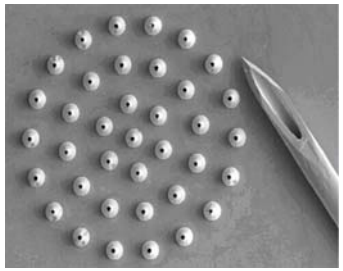
From this the dynamics of skin penetration by microneedles can be assessed.

Identifying the Mechanical Properties of Skin

- Skin is a multilayer structure, subjected to a pre-stress and exhibits anisotropic, non-linear and viscoelastic properties.
- Properties differ due to age, level of hydration and location on the body
- The Ogden material model was chosen to describe the non-linear stress-strain relationship



$$W(\lambda_1,\lambda_2,\lambda_3) = \sum_{P=1}^{N} \frac{\mu_p}{\alpha^2{}_p}\left(\lambda_1^{\alpha_p} + \lambda_2^{\alpha_p} + \lambda_3^{\alpha_p} - 3\right)$$



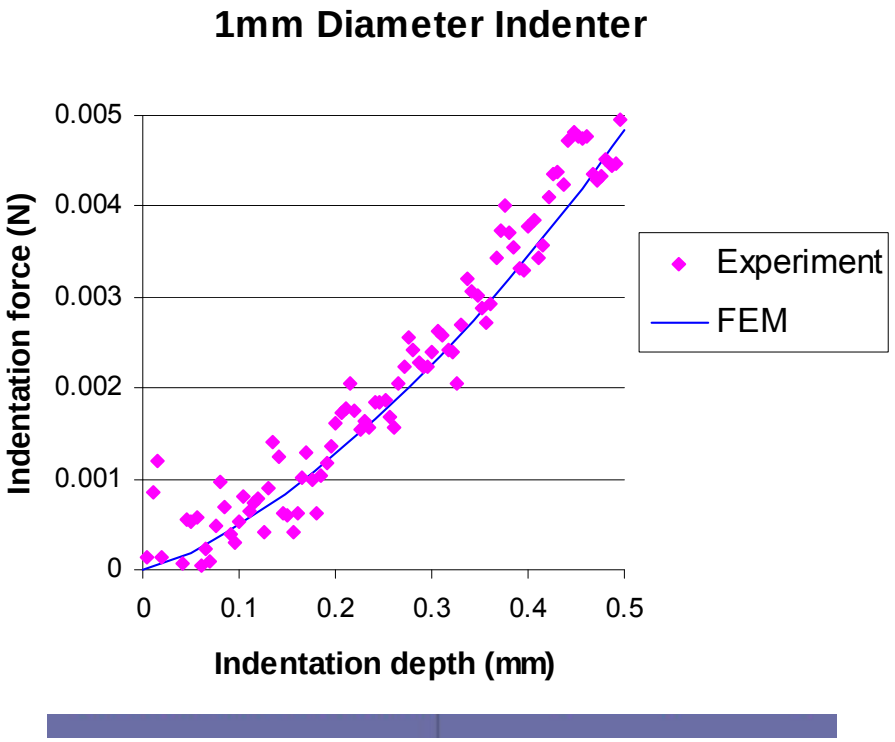
Preliminary Models and Experiments

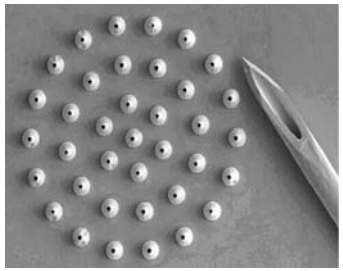
Modelling Silicone

- Series of indentation tests using indenters of various sizes and shapes
- FEA was used to estimate the Ogden parameters of the silicone.

Single layer model of human skin

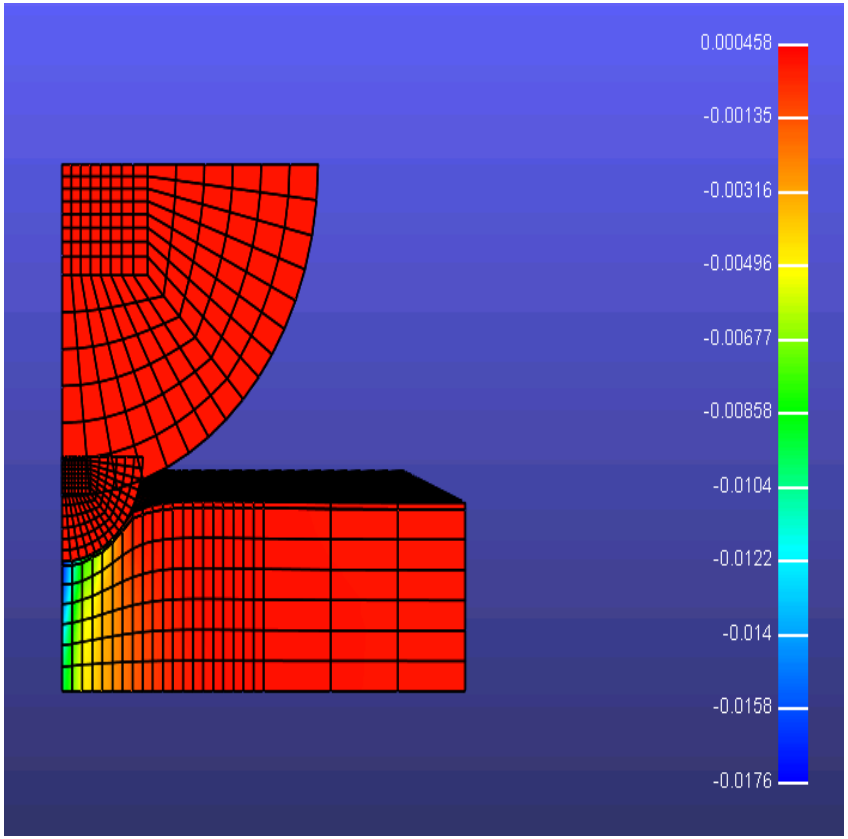
- *In vivo* skin indentation tests were preformed
- FEA was used to estimate the Ogden parameters of the skin



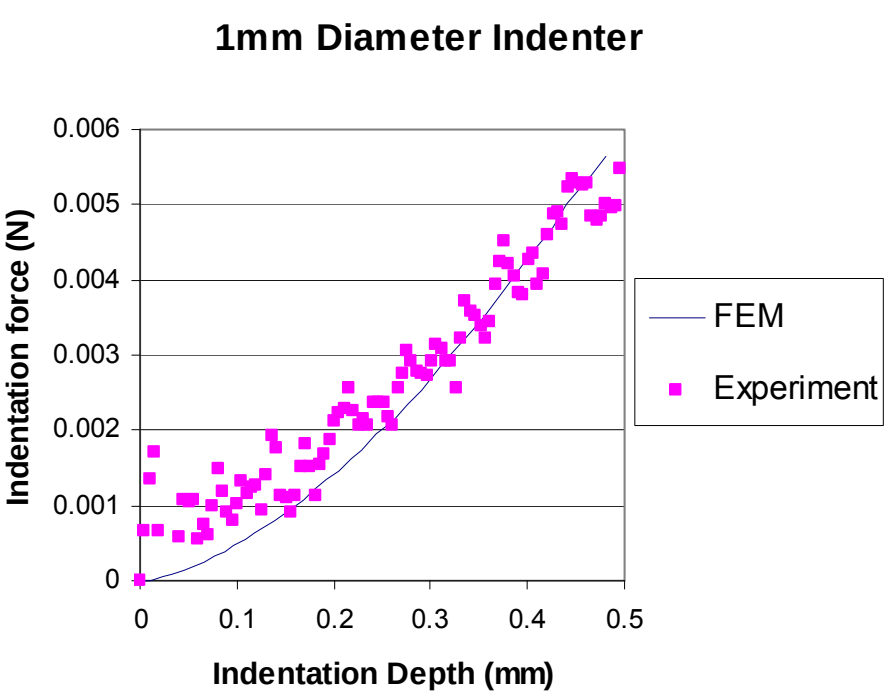


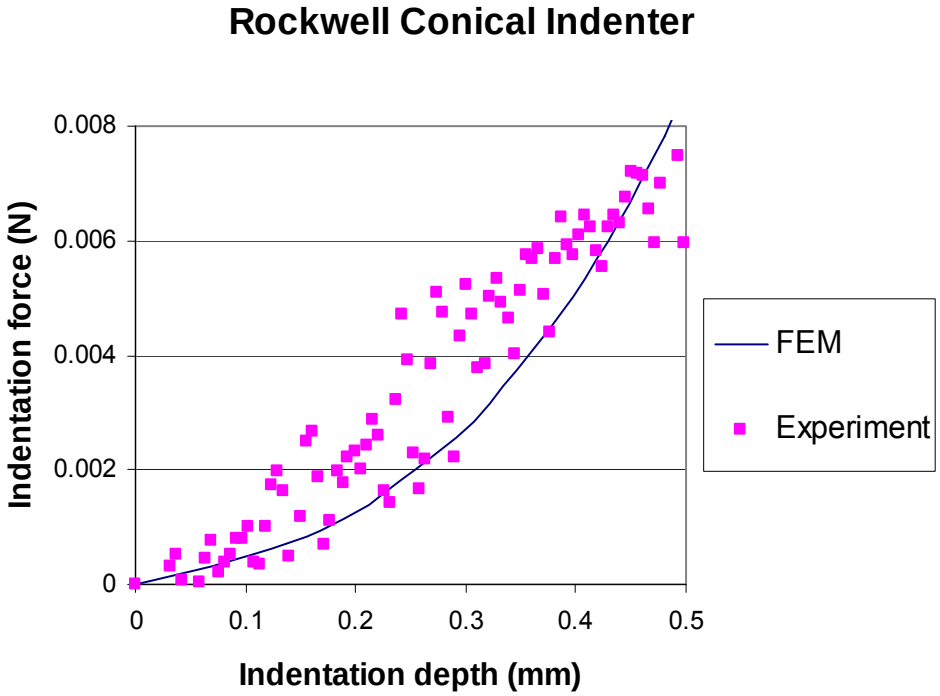
Double layer model of skin indentation

- Same experimental procedure was employed
- Epidermis and dermis thicknesses were set to 0.06mm [1] and 1.74mm [2] respectively
- The epidermis was assumed to be stiffer than the dermis because of the stratum corneum
- Ogden parameters were optimised to match the experiment



Double layer model of skin indentation





Epidermis Ogden parameters:

Bulk modulus=1N/mm²

α = 2, μ = 0.005 MPa

with an initial Young's Modulus of 0.01N/mm²

Dermis Ogden parameters:

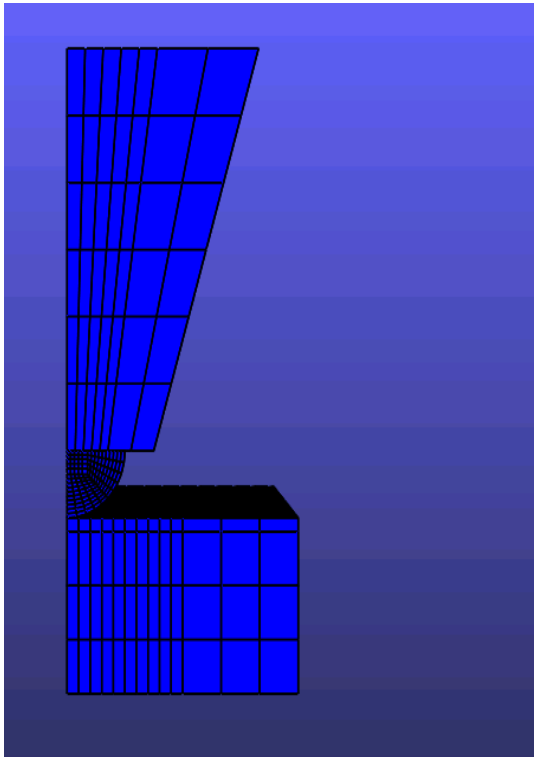
Bulk modulus=0.75N/mm²

α = 1.5, μ = 0.005 MPa

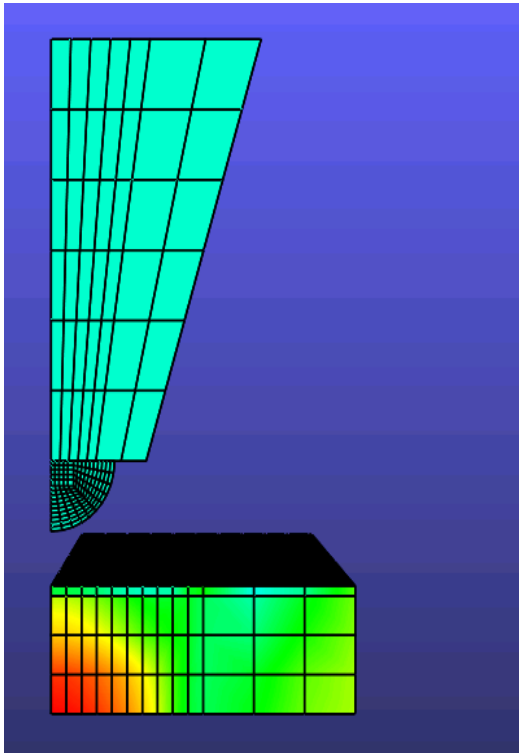
with an initial Young's Modulus of 0.0075N/mm²

Improvements to the FE Model

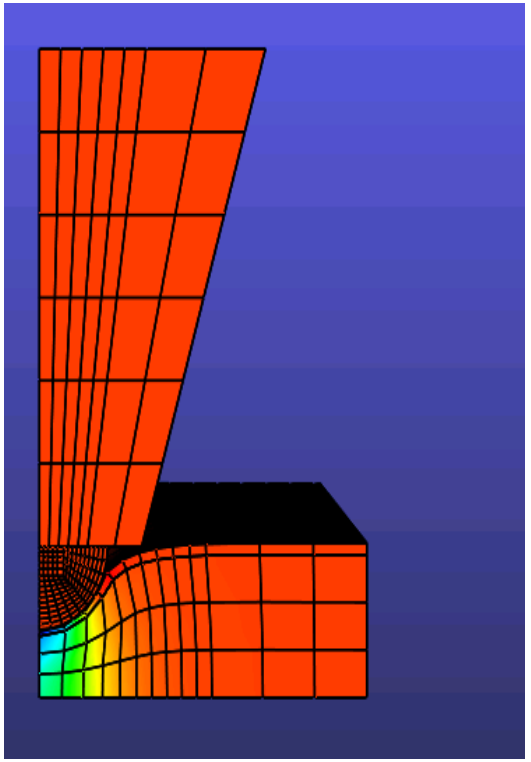
Phase One → **Phase Two** → **Phase Three**



Coefficient of friction of 1.2 [3] acting between the indenter and the surface

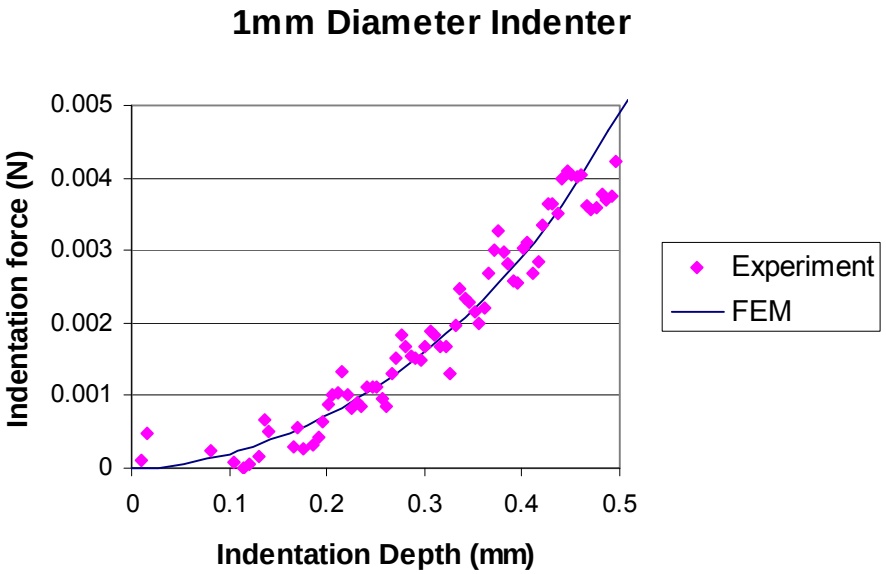


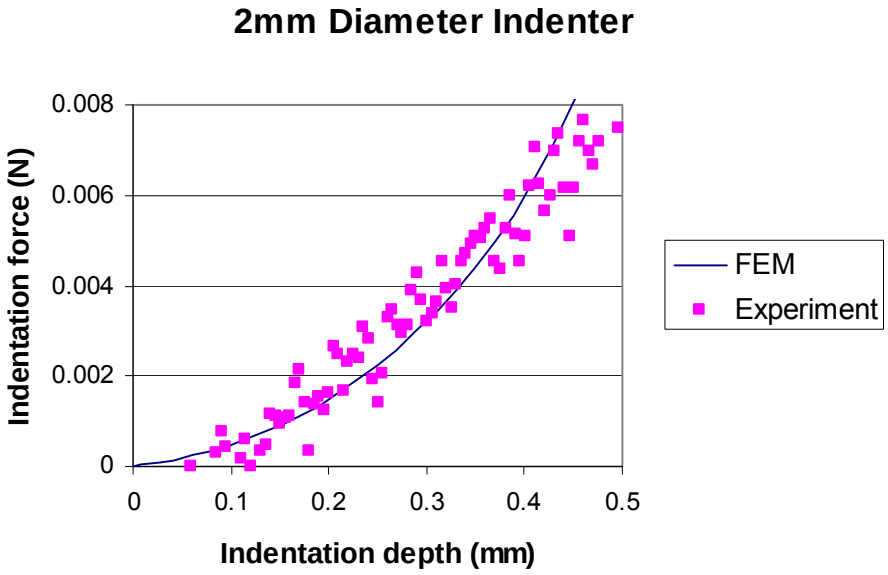
Initial strain of 0.2 [4] is applied. Epidermis and dermis thicknesses are now 0.07mm [5] and 0.84mm respectively [6]



Indenter is pressing on the skin

Improvements to the FE Model





Epidermis Ogden parameters:

Bulk modulus=1.8N/mm²

α = 6, μ = 0.003MPa

with an initial Young's Modulus of 0.018N/mm²

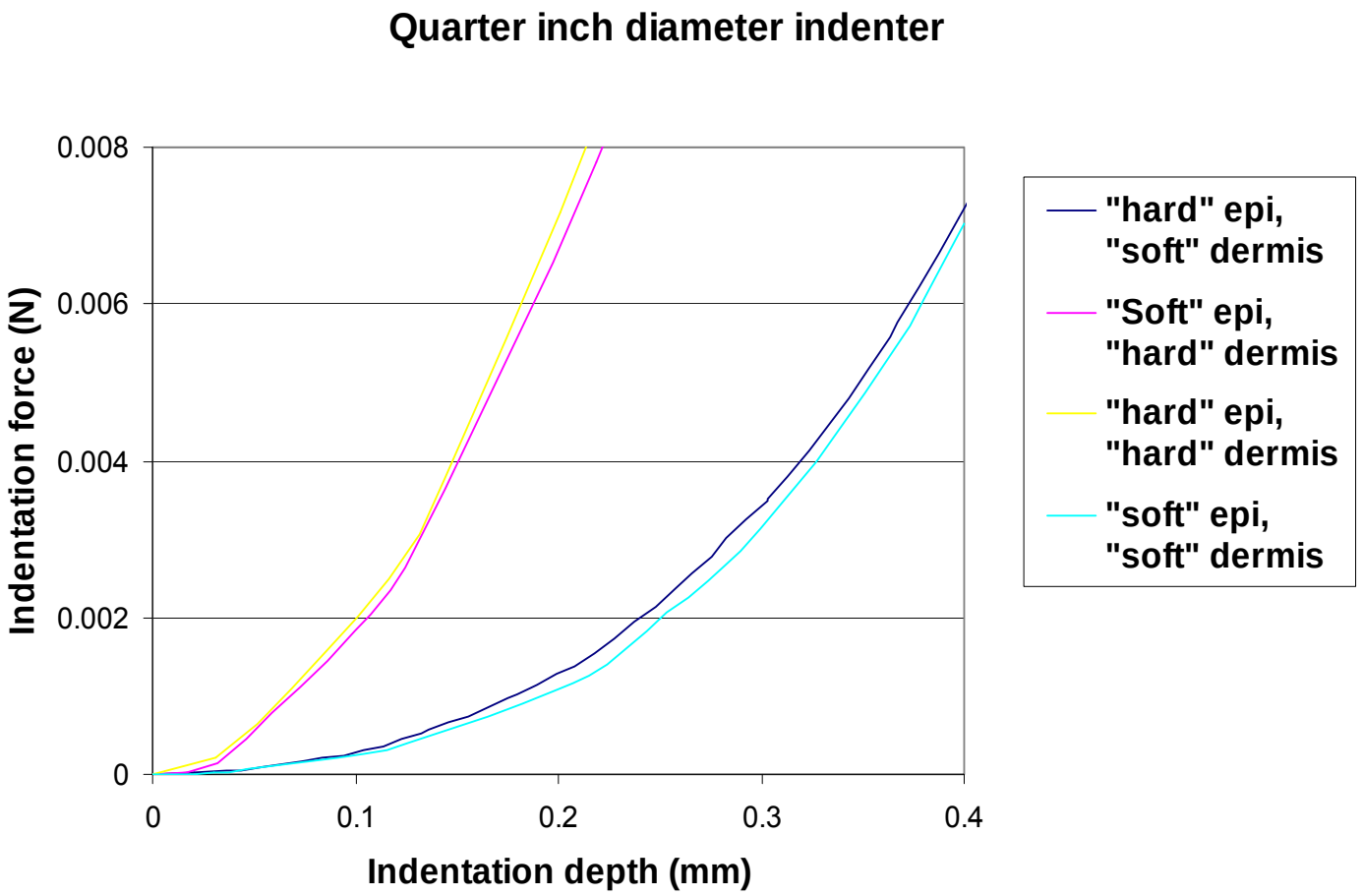
Dermis Ogden parameters:

Bulk modulus=1.25N/mm²

α = 5, μ = 0.0025MPa

with an initial Young's Modulus of 0.0125N/mm²

Further Work



The effect of epidermis stiffness on the overall mechanical properties of the skin FE model.

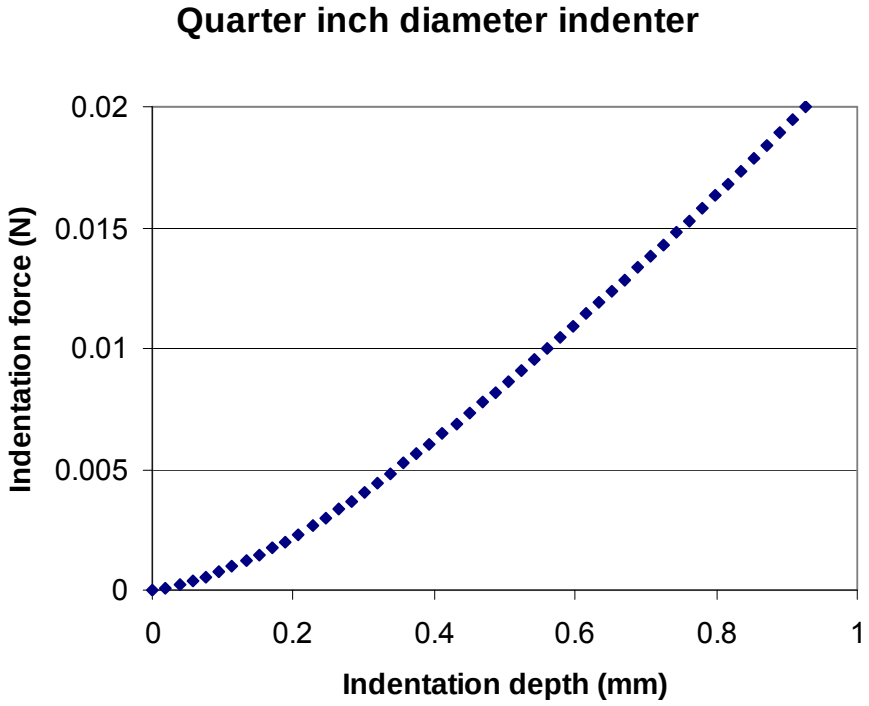
Future Improvements to the model

1. **Hypodermis:**
   Add a layer of fat to the model

2. **Epidermis:**
   Find the properties of the epidermis separately

3. **Improvements to *in vivo* test procedure:**
   Reduction of fluctuations by reducing frequency at which the recordings are made

4. **Increase sample size of skin indentation test.**
   Include people of different age, gender and ethnicity.



Future Work

Improvements to test procedure and finite element model

Ogden constants for skin layers

A finite element analysis of a microneedle piercing the skin can be developed. Further validation of the model can be made from *in vivo* experimental observations

By modelling different microneedle geometries and materials

Suggestions on how to optimise future microneedle designs, to allow for more efficient transdermal drug administration.

References

[1] J. T. Whitton and J.D. Everall: The thickness of the epidermis (1973). British journal of dermatology 89: 467-476

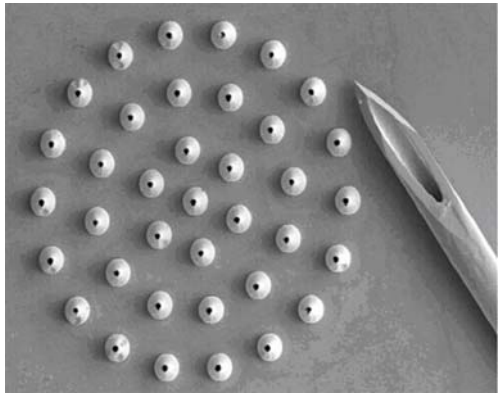
[2] A. Laurent et al. Echographic measurement of skin thickness in adults by high frequency ultrasound to assess the appropriate microneedle length for intradermal delivery of vaccines

[3] Kwiatkowska, M. et al. 2009. Friction and deformation behaviour of human skin. *Wear* 267(5-8), pp. 1264-1273.

[4] Evans, S. L. and Holt, C. A. 2009. Measuring the mechanical properties of human skin in vivo using digital image correlation and finite element modelling. *Journal of Strain Analysis for Engineering Design* 44(5), pp. 337-345.

[5] Gambichler, T et al 2006. In vivo data epidermal thickness evaluated by optical coherence tomography: Effects of age, gender, skin type, and atomic site. *Journal of Dermatological science 44* pp.145-152

[6] Moore, T.L. et al 2003. Seventeen-point dermal ultrasound scoring system – a reliable measure of skin thickness in patients with systemic sclerosis. *Rheumatology.* 42 pp. 1559-1563



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Thank you

Any Questions????!