Assessment of Microneedle Intradermal Penetration Depth using Terahertz Pulsed Imaging

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Abstract - **Terahertz Pulsed Imaging (TPI) has been used successfully to image microneedles in human skin *ex-vivo*. By applying the Fresnel equations to the time domain reflected pulse one can obtain an estimate for the refractive index of skin and thereafter calculate the skin penetration depth of the microneedle from time of flight calculations.**

INTRODUCTION

Terahertz rays (T-rays) lie between the far-infrared and the microwave band, and cover a frequency range of 300 GHz up to 3 THz, which equals a wavelength of 1mm to 100µm. Given that T-rays are able to penetrate the skin and have energies of approximately 10µW (which is lower than natural black body radiation) they offer the opportunity to develop a non-ionising, safe imaging technique for measurements both in-vivo and ex-vivo. The purpose of this study was to visualise microneedles in human skin (ex-vivo) and to measure the penetration depth of the microneedle. To our knowledge this is the first attempt to use terahertz imaging to monitor a drug delivery device in the skin and specifically a microneedle.

MATERIALS AND METHODS

A microneedle was inserted into freshly excised human skin from the cheek and placed on a quartz window. Sample data was gathered using Terahertz Pulsed Imaging (TPI) module of a Teraview TPS 3000™ which fires a terahertz pulsed beam within an angle of 30°. The beam reflected from the sample detects the electrical field as well as the phase change and thus allows one to collect 3D data from the sample. Depending on absorption and reflectance of the material to be examined the reflected pulse shows differences in media of different refractive indices which results in a phase change and a delay of the maximum peak (see Figure 1). Using the reflection amplitude coefficient (r_p) from the Fresnel equations, it is possible to calculate the refractive indices of air (n_1) and skin (n_2). Given a normal incidence of 1, the refractive index of skin (n_2) can be calculated using Eq.1.

$$r_p = \frac{E_{\max\_sample}}{E_{\max\_reference}} = \frac{n_2 - n_1}{n_2 + n_1} \qquad (1)$$

where r_p is calculated from the maximum peak from the sample (E_{max_sample}) and a reference (maximum reflectance) peak ($E_{max\_reference}$), measured with a mirror on the quartz window.

Having estimated the refractive index of skin, the following formula (time of flight) is then used to determine the thickness of the skin between the quartz window and the microneedle,

$$d = \frac{optical\ delay * c}{n_2 - 1} \qquad (2)$$

where d is the thickness. n_2 the refractive index of skin and c the speed of light.

RESULTS AND DISCUSSION

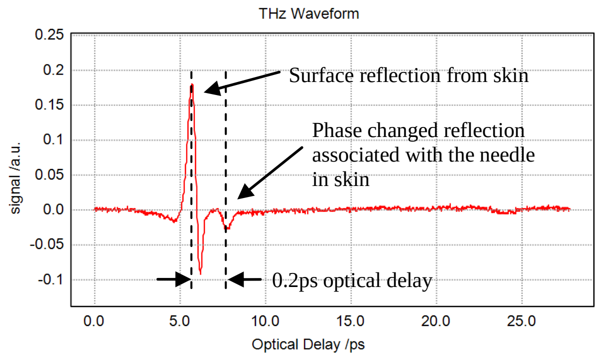

Fig. 1. Raw Terahertz reflected pulse of microneedle in skin.

Assuming the first incidence to be the reflected pulse of the skin / air interface, with n_1=1 and r_p=0.25 the refractive index of the skin is calculated to be n2=1.67, which is in an agreement with Fitzgerald et al [1]. Using Eq.2 and an optical delay of 0.2 ps (as specified in Fig.1), the thickness of the skin and hence penetration depth of the needle was calculated to be 90µm (+/- 10 µm).

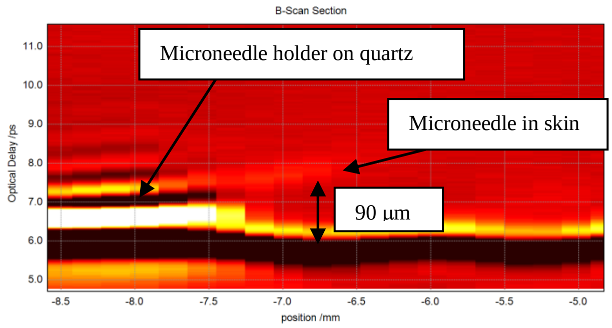

Figure 2: B-Scan image of microneedle in skin.

CONCLUSIONS

It is shown that TPI successfully images a microneedle in skin, where the spatial resolution is limited to 200µm laterally and 20µm axially, and that penetration depth information can be obtained using the Fresnel equations.

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[1] A. Fitzgerald, E. Berry, N. Zinov'ev, S. Homer-Vanniasinkam, R. Miles, J. Chamberlain, M. Smith, "Catalogue of human tissue optical properties at terahertz frequencies" Journal of Biological Physics, **29** (2003) 123-128.