Opto-thermal radiometry for in-vivo nail measurements

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Abstract. We have developed a new method for in-vivo human nail characterization by using opto-thermal transient emission radiometry (OTTER) and condenser-chamber TEWL (transdermal water loss) method – AquaFlux. With OTTER, we can measure nail water content, nail water concentration depth profiles, as well as topically applied solvent penetration through nail. With AquaFlux, we can measure nail transonychial water loss (TOWL). Combining the water content results with TOWL results, we can get the water diffusion coefficient of nail. Measuring the water diffusion coefficients of nail at different nail water concentration levels can also yield information on how nail diffusion coefficients change with water content. We will present the theoretical background, and experimental results on water concentration depth profile in nail, as well as topically applied solvent penetration through nail.

1. Introduction

Human nail is a skin appendage that is made of keratin. Human nail is about 0.5 mm in thickness and grows about 0.1 mm per day. Nail diseases affect many people in their everyday life. Water content and water diffusion coefficient of nails are two key parameters in drug permeation studies through nail tissue [1-3]. However, to measure water content and water diffusion coefficient of in-vivo human nails is very difficult. The traditional gravimetric method [3, 4] and more recently electrical methods [5] are only suitable for in-vitro nail water content measurements, whilst only NIR and Raman spectrometry have been tried for in-vivo nail [6-8]. In this paper, we have developed a new method for in-vivo human nail characterization. It uses opto-thermal transient emission radiometry (OTTER) [9-13] to measure water content, water concentration gradient and water concentration depth profiles within nail, and uses a condenser-chamber TEWL (transdermal water loss) method – AquaFlux [14] to measure the transonychial water loss (TOWL) of nail. Combining the OTTER water content results with TOWL results, we can also get the water diffusion coefficient of nail. By measuring the water diffusion coefficients of nail at different water concentration levels, we can also get information on how the water diffusion coefficient depends on water concentration.

2. Apparatus

OTTER is an infrared remote sensing technique, which uses a pulsed Er:YAG laser (2.94 µm, 100ns pulse width, <4mJ/per pulse) as a heat source to heat up the sample surface, and a fast infrared detector (Mercury Cadmium Tellurium or MCT) to pick up the consequent increase of sample’s blackbody radiation. The detection wavelength is 13.1 µm. By analysing the shape of the signals, we can get information on sample’s water content, the water concentration gradient, and the water...
concentration depth profiles. AquaFlux is a novel closed-chamber TEWL measurement methods, which uses a cylindrical measurement chamber with one end sealed with a condenser, cooled to -7.65°C, and another end open to the sample surface. The water vapour coming out of the sample goes into the chamber, is frozen to ice on the condenser surface, and forms a steady vapour density distribution within the chamber, through which we can work out the water vapour flux density from sample. The closed-chamber makes the measurements independent of external environments (e.g. temperature, relative humidity or RH, and air movements), and the condenser removes excess water vapour within the chamber, and improves the measurement repeatability and accuracy.

3. Theory

In-vivo nail is wet inside and dry outside, and there must exist a water concentration gradient, using a linear water distribution model, the water concentration within nail can be described by:

\[ H(z) = H_0 + W \cdot z \]  

(1)

Where \( H_0 \) is the water concentration at the nail surface (volume ratio of water and nail, %), or surface hydration, \( W \) is nail water concentration gradient (%/\mu m), \( H(z) \) is the water concentration at depth \( z \) underneath nail surface. We understand that \( H(z) \) might saturate and become nonlinear at bottom of the nail, but because OTTER’s detection depth is only limited to top 20\mu m at 13.1\mu m detection wavelength, Eq.(1) is a simple but sufficient expression for the water concentration profile within this range. According to Fick’s law, when there is a water concentration gradient, there will be a water flux,

\[ J = -D \frac{\partial H}{\partial z} = -D \cdot W \]  

(2)

Where \( J \) is the water flux, \( D \) is the water diffusion coefficient of nail. With OTTER, by using a gradient model described in Eq.(1), we can use least squares fitting to fit the OTTER signals and get the best fit \( H_0 \) and \( W \) [10,11], and with AquaFlux, we can measure \( J \), from Eq.(2), we can calculate the water diffusion coefficient \( D \) of nail.

4. Results and Discussions

Three measurements were performed in this study, measurements of different finger nails, finger nail immersive hydration, and penetration of the topically applied solvent - Dimethyl sulfoxide (DMSO). The measurement conditions are 20~21°C in temperature, and 40~50% in relative humidity (RH).

4.1. Different Finger Nails

The measurements of different finger nails were done by performing OTTER measurements and TOWL measurements on centre points of 10 different fingers of both hands of a healthy volunteer. Figure 1A shows the surface water concentration \( H_0 \) and water concentration gradient \( W \) results of 10 different finger nails. The measurements were repeated three times for each finger nail, and each data point of Figure 1A represents the average of three measurements, and the error bars represent the standard deviation of the three measurements. The results show that finger nails from left hand and right hand are similar but slightly different. Generally speaking, the nail surface water concentration tends to increase from thumb nail toward little finger nail, ranging from 17% to 18.8%, with less than 2% difference between all finger nails. Figure 1B shows TOWL results of the 10 different fingers of both hands. In this case, the results are much more symmetrical for both hands, the TOWL values increase steadily from thumb nail toward little finger nail, from about 40g/m²h to 60 g/m²h, about 50% increase. Combining with the water concentration gradient \( W \) results, and using Eq.(2), we can also get the water diffusion coefficients \( D \) of nails, also shown in Figure 1B. The results show that the water diffusion coefficients of nails (~ 10^{-12} m²/s) are much higher than that of normal skin (~ 10^{-13}
m²/s) [10], and again, the water diffusion coefficients generally increase from thumb nail toward little finger nail, 0.8x10⁻¹² m²/s ~ 1.2x10⁻¹² m²/s, also about 50% increase.

![Figure 1](image1)

**Figure 1.** The surface water concentration and water concentration gradient (A), TOWL and water diffusion coefficients (B) of 10 different finger nails.

![Figure 2](image2)

**Figure 2.** The hydration distributions (A) and TOWL distributions (B) on the surface of the same ring finger nail.

Figure 2A shows the surface water concentration distributions on the surface of the same nail, and Figure 2B shows the TOWL distributions of the same nail surface. The results suggest that even on the same nail, water concentration levels and TOWL values are different from point to point, and both tend to increase from the distal part of nail towards the proximal part of nail. Surface water
concentration increases from 17% to 20%, about 18% change, whilst TOWL increases from 39 g/m²h to 54 g/m²h, about 38% change. The water concentration differences within the same nail appear larger than that of different nails at the similar points. The TOWL differences within the same nail appear smaller than that of different nails at the similar points.

4.2. Immersive Hydration
Immersive hydration measurements were performed on the left hand thumb nail, by soaking the nail in room temperature water for 15 minutes, and measurements were performed both before and periodically after the immersive hydration.

**Figure 3.** The surface water concentration and TOWL of thumb nail, before and after a 15 minutes immersive hydration (A). The corresponding water concentration depth profiles before and after the immersive hydration (B).

**Figure 4.** The water diffusion coefficients of thumb nail, before and after a 15 minutes immersive hydration (A), and the water dependent diffusion coefficients (B).

Figure 3A shows the surface water concentration results and TOWL results of thumb nail, before and after the immersive hydration. Both water concentration and TOWL increased significantly
immediately after immersion, indicating that nail is hydrated, then as thumb nail recovered in air, both water concentration and TOWL gradually reduced to their normal level. It is worth to point out that even after 40 minutes of immersion, both water concentration and TOWL are not exactly the same as that of normal nail, water concentration is slightly under shoot, while TOWL is a bit higher, this probably indicates that nail is somehow damaged due to immersive hydration, and not recovered fully even after 40 minutes. By using segmented least squares (SLS) fitting [12], we can also get the corresponding water concentration depth profiles before and after the immersive hydration, shown in Figure 3B. Different from previous least squares fitting, SLS does not need to know the water concentration profiles in nails, it can work out the depth profiles according to mean detection depth. The results in Figure 3B show good linearity, which agree well with the linear model we used in Eq.(1).

From the results shown in Figure 3A, using Eq.(2), we can also get the nail water diffusion coefficients before and after the immersive hydration, see Figure 4A. By plotting the water diffusion coefficients with corresponding water concentrations, we can get information on how the water diffusion coefficients depend on water content, see Figure 4B. It is estimated that dry nail has water diffusion coefficients of 5x10^{-14} m^2/s and fully hydrated nail can go to 5x10^{-12} m^2/s.

4.3. Penetration of Topically applied solvent - DMSO

Dimethyl sulfoxide (DMSO) is a colourless liquid with the formula (CH₃)₂SO. DMSO is a popular penetration enhancer that can penetrate skin very readily. DMSO strongly absorbs water when exposed in air, and has been widely used in many pharmaceutical medicines. In this measurement, a small amount of DMSO was uniformly applied to the index finger nail using a cotton bud, and excess DMSO on nail surface was carefully wiped out with a tissue.

Figure 5. The nail water concentration and TOWL results before and after the DMSO application (A), and corresponding DMSO concentration depth profiles within nail (B). Figure 5A shows the nail water concentration and TOWL results before and after the DMSO application. The nail water concentration decreased after DMSO application, due to DMSO’s weak optical absorption at 13.1µm detection wavelength. The TOWL values increased first then decreased and went undershoot. Both water concentration results and TOWL results suggest that nail has been damaged due to DMSO and did not recover fully even 70 minutes after the application. From the water concentration results in Figure 4A, using optical absorption of dry skin (~10^4 m⁻¹), pure water (2.7x10^5 m⁻¹), and pure DMSO (~10^-7 m⁻¹), we can easily work out the DMSO concentration level...
within nail. Figure 5B shows the DMSO concentration depth profiles within nail before and after application, calculated by using SLS fitting [12].

5. Conclusions and Future Work
We have developed a new method for in-vivo human nail characterization. The combination of OTTER and AquaFlux can provide useful information of nail, e.g. nail surface water concentration, water concentration gradient underneath nail, nail water diffusion coefficients, as well as penetration of topically applied substances through nail. With SLS fitting, we can also get water or externally applied substances concentration depth profiles within nail.

Acknowledgements
The authors thank London South Bank University and EPSRC for the financial support.

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