Journal of Biological Physics **129:** 123–128, 2003.

Catalogue of Human Tissue Optical Properties at Terahertz Frequencies

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Abstract. Recently published studies suggest that terahertz pulsed imaging will have applications in medicine and biology, but there is currently very little information about the optical properties of human tissue at terahertz frequencies. Such information would be useful for predicting the feasibility of proposed applications, optimising acquisition protocols, providing information about variability of healthy tissue and supplying data for studies of the interaction mechanisms. Research ethics committee approval was obtained, and measurements made from samples of freshly excised human tissue, using a broadband terahertz pulsed imaging system comprising frequencies approximately 0.5 to 2.5 THz. Refractive index and linear absorption coefficient were found. Reproducibility was determined using blood from one volunteer, which was drawn and measured on consecutive days. Skin, adipose tissue, striated muscle, vein and nerve were measured (to date, from one individual). Water had a higher refractive index (2.04 ± 0.07) than any tissue. The linear absorption coefficient was higher for muscle than adipose tissue, as expected from the higher hydration of muscle. As these samples came from a single subject, there is currently insufficient statistical power to draw firm conclusions, but results suggest that *in vivo* clinical imaging will be feasible in certain applications.

Key words: absorption, human tissue, medical imaging, refractive index, terahertz pulsed imaging

1. Introduction

In existing medical imaging techniques it is possible to predict the feasibility of imaging in particular applications. This can be done because there is sufficient information available about the relevant attenuation characteristics of tissue for determination of radiation penetration and image contrast. There is currently little such information available about the optical properties of human tissue at terahertz frequencies, although differences between tissues have been demonstrated [1, 2]. In this study, measurements will be made from a range of freshly excised healthy human tissue samples from a five donors. Results are presented here only for the first set of samples, but once more data are collected, the data will also provide information about variability of the optical properties in healthy tissue and data for studies of the interaction mechanisms.

2. Methods

Local research ethics committee approval was obtained to collect small samples of skin, adipose tissue, striated muscle, artery, vein and nerve following vascular surgery; and blood from volunteers. Informed consent was obtained. For comparison, measurements were made also from de-ionised water. All measurements were made in transmission, using a terahertz pulsed imaging system similar to that described by Fitzgerald et al. [3]. Terahertz frequency radiation with a bandwidth approximately from 0.5 to 2.5 THz was generated by optical rectification, and an optical delay line used to sample the time domain data, to give 256 points at 80 fs separations.

The soft tissue samples were cut approximately to one of four thicknesses (50, 100, 150 and 200 μm), then placed between two TPX (poly-4-methylpent-1-ene) windows and compressed by spacers to the exact thickness required. TPX was chosen because it has low absorption and constant refractive index over the frequency range of interest [4]. Reference pulse measurements were made for each sample thickness using the sample holder with air in place of the sample. Measurements were made within 48 hours of excision. The liquid samples were held in a polyethylene bag, which was compressed between two slices of polystyrene. This material was chosen because in the terahertz band it has low attenuation and a refractive index equal to that of air [5]. A mechanical translation stage was used to change the path length by 25 μm, 50 μm, 75 μm and 100 μm. Reference pulse measurements were acquired using the path through the liquid cell before changes were made to the path length. Each blood measurement was made within five hours of donation.

For the soft tissues and water, the mean and standard deviation of the broadband refractive index, n, were found for each tissue using the relation

$$t = \frac{(n-1)x}{c} \tag{1}$$

where t is the time delay for the transmitted pulse peak relative to the reference pulse peak, c is the velocity of light in vacuo and x is the sample thickness. This broadband result included all the frequencies present in the incident pulse; the range was approximately 0.5 to 2.5 THz. A two sample t-test was used to determine if differences in measured mean values between tissues were statistically significant ($p < 0.05$).

For all samples, the mean and standard deviation for the linear attenuation coefficient, $\mu(\omega)$, for frequencies from 0.5 to 1.5 THz, were found for each material by assuming that the Beer-Lambert law was obeyed

Table I. Broadband refractive index results. N is the number of samples, <n> the mean refractive index and σ the standard deviation of the refractive index. ✓ indicates significant differences between the mean refractive indices (p <0.05), × indicates a non-significant difference (p >0.05)

		N	<n>	σ	H_2O	Sk	AT	SM	V	N
H_2O	De-ionised water	16	2.04	0.07	–	✓	✓	×	✓	×
Sk	Skin	24	1.69	0.39	✓	–	×	×	✓	×
AT	Adipose tissue	25	1.58	0.58	✓	×	–	×	✓	×
SM	Striated muscle	25	1.79	0.54	×	×	×	–	✓	×
V	Vein	25	0.71	0.53	✓	✓	✓	✓	–	✓
N	Nerve	12	1.95	0.46	×	×	×	×	✓	–

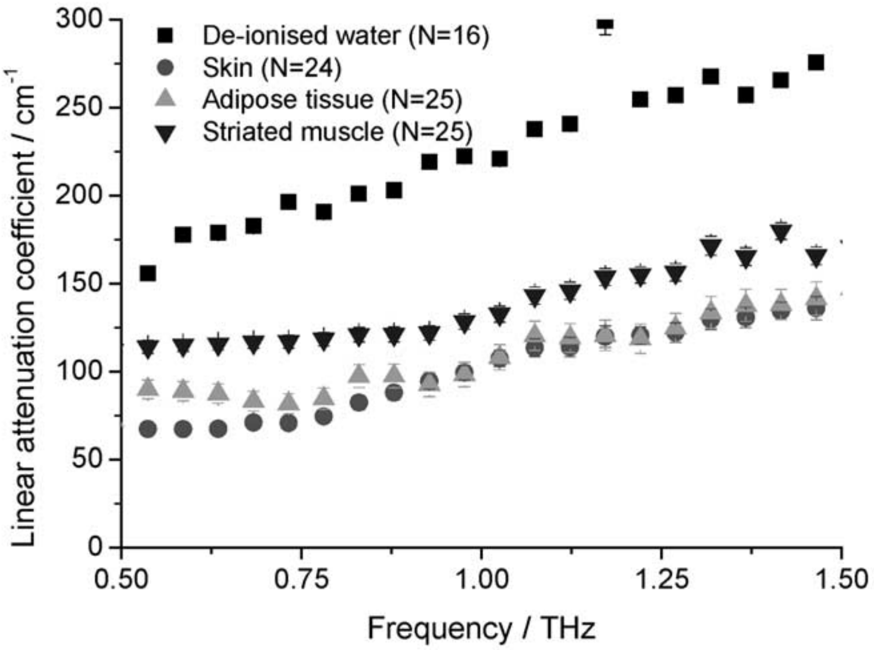

Figure 1a. Measured linear attenuation coefficient as a function of frequency for samples of de-ionised water, skin, adipose tissue and striated muscle. Error bars indicate ± one standard error of the mean, N is the number of samples.

$$I(\omega)/I_0(\omega) = \exp[-\mu(\omega)x] \quad (2)$$

where $I(\omega)$ is the transmitted pulse intensity, $I_0(\omega)$ is the incident pulse intensity and x is the sample thickness. The upper frequency limit was set to 1.5 THz because the amplitude of higher frequency components after transmission was found to be comparable to that of noise. To assess repeatability of the measurement of the linear

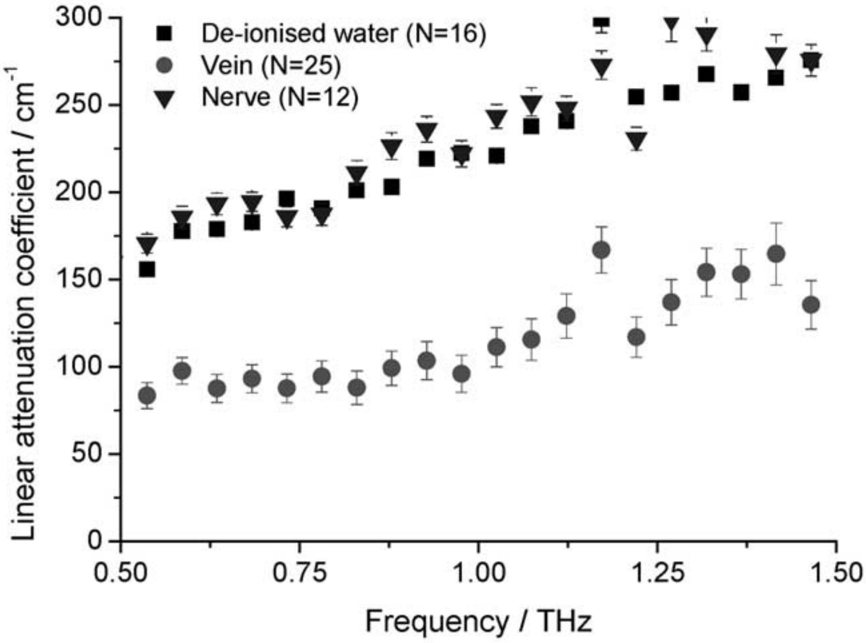

Figure 1b. Measured linear attenuation coefficient as a function of frequency for samples of de-ionised water, vein and nerve. Error bars indicate ± one standard error of the mean, N is the number of samples.

attenuation coefficient, two donations of blood, separated by a day, were obtained from a volunteer. Comparison was made by the Bland Altman technique [6].

3. Results

Results for soft tissues obtained from one male (age 64) undergoing vascular surgery, and 16 samples of de-ionised water are presented in Table I and Figure 1. It was not possible to obtain healthy artery tissue from this subject.

The results of the repeatability analysis on blood are shown in Figure 2. A total of 20 samples of blood were used. 95% of the measurements lie within two standard deviations of the mean difference, however, there is a dependence between the error and the true value, and the mean difference is non-zero.

4. Discussion

These are the first systematic measurements of the optical properties of human tissue in the terahertz region (0.5 to 1.5 THz). The work presented here represents the first tranche of a larger study, and includes measurements from only one subject and with a limited number of samples (Table I), especially for nerve tissue or fibres. Measurements will be made from further samples of these healthy tissues,

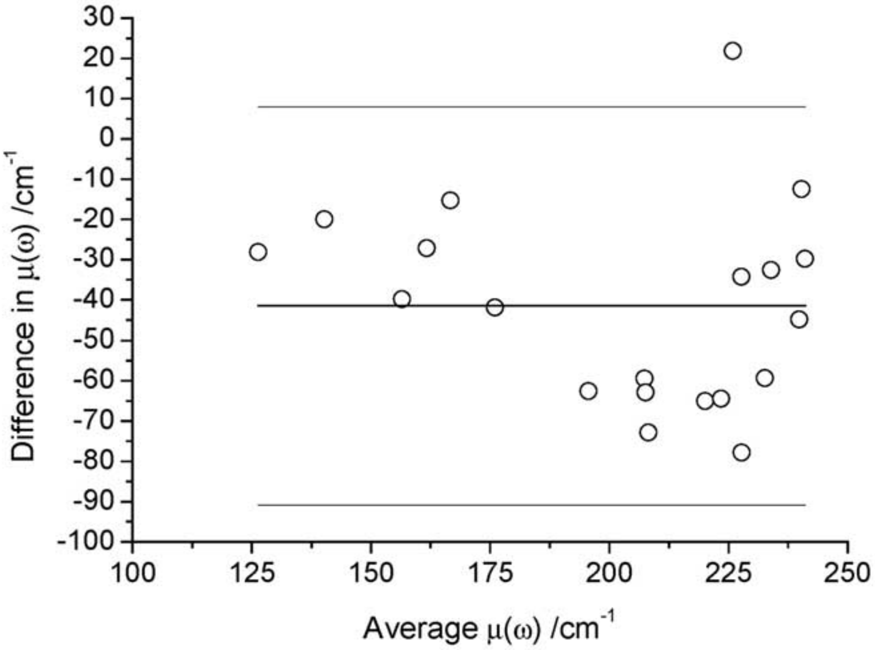

Figure 2. Repeated measurements of linear attenuation coefficient of blood in an individual. A 24 hour period elapsed between donations.

from samples of cortical bone, tooth enamel and dentine and from diseased tissue. Even in this preliminary set, statistically significant differences in the values of the optical properties were found between a number of healthy tissues. This is encouraging with regard to imaging, both in transmission and reflection modes. In the latter, differences in refractive index at boundaries will be essential to generate the strong echoes required for image formation. As expected, the hydration of a tissue has a strong effect on its absorption characteristics, with lower attenuation coefficients measured for tissues known to have lower water content. For example, note the lower attenuation coefficient for adipose tissue in comparison with striated muscle. Much previous work on demonstrating tissue contrast in terahertz imaging has involved samples that have undergone histopathological preparation and as a result are dehydrated compared with living tissue [7, 8]. The soft tissue samples here will have properties closer to those of living tissue. The samples were measured within 48 hours and were stored at 4 °C, but it is recognised that their properties will differ from that of living tissue, not least through uptake of the saline in which they were stored. Other methods of preparation are being investigated. Whilst the repeatability was satisfactory, we shall also investigate further ways of reducing variability. Although liquid cells are widely available, they proved unsuitable for the liquid measurements presented here because of their high attenuation of terahertz radiation. Instead, a technique was devised using a polyethylene bag compressed between two pieces of polystyrene known to have low terahertz attenuation [5]. We assumed that attenuation was described by a linear attenuation coefficient, but further investigation will be necessary to gain an understanding scattering of terahertz radiation in tissue and thus determine the conditions under which that assumption is valid. The results confirm the well-known advantage of the coherent detection scheme used in terahertz pulsed imaging; measurement of amplitude rather than intensity means that both attenuation and time delay (or phase) parameters are available to differentiate tissue. These early results suggest that *in vivo* clinical imaging will be feasible in certain applications, and are useful for the development of clinical protocols and for advancing the understanding of contrast mechanisms in biological terahertz images. When further data are available they will be used to predict the likely penetration depth of terahertz radiation in simple models of clinical applications such as those in dermatology, wound assessment and dentistry.

Acknowledgements

This research was supported under the European Union Teravision Project (IST-1999-10154). Associated support was from EPSRC (GR/N39678). Our thanks to S.L. Thornton, C.D. Sudworth, G.C. Walker, P. Jackson, M. Whitaker, D.J. Wood, F. Carmichael, S. Strafford, B.B. Seedhom, M. Cuppone, R. Soames, P. Day, W. Merchant, J. Bull, M. Fletcher.

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