

EXPERIMENTALLY MEASURED OPTICAL PATHLENGTHS FOR THE ADULT HEAD, CALF AND FOREARM AND THE HEAD OF THE NEWBORN INFANT AS A FUNCTION OF INTER OPTODE SPACING

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INTRODUCTION

The technique of near infrared spectroscopy (NIRS) is being increasingly used in clinical measurements of blood and tissue oxygenation (Wyatt et al 1986, Edwards et al 1990), and there are now several commercially produced instruments undergoing clinical testing. Whilst early NIR measurements were solely of a qualitative nature (Brazy et al 1985,1986, Fox et al 1985, Ferrari et al 1986), techniques have now been developed to quantitate some parameters such as cerebral blood flow (Edwards et al 1988a), cerebral blood volume (Wyatt et al 1990a) and muscle oxygen consumption (Cheatle et al 1990).

All these quantitative techniques require a knowledge of the pathlength travelled by the light as it traverses the tissue. Due to the effects of scattering of light by the tissue, this distance is greater than the geometrical spacing between the optodes by an amount which depends upon the optical properties of the tissue and the measurement geometry (Delpy et al 1989). We have previously shown that for measurements in the near infra red region, it is possible with reasonable accuracy to apply a modified Beer Law to the measured changes in attenuation (Cope et al 1988). The modification involves the addition of a simple constant differential pathlength factor (DPF) to the inter optode spacing. The DPF can be determined from time of flight measurement of an ultrashort optical pulse through the tissues (Delpy et al 1988). Monte Carlo modelling and experimental measurements have shown that this method of deriving the DPF is valid both for slab and spherical tissue geometries (Delpy et al 1988, van der Zee 1990). For spherical geometries, the inter optode spacing is the length of the chord between the optodes. Values for the DPF have been derived for the transilluminated rat head (Delpy et al 1988), adult wrist (Edwards et al 1988b) and post mortem pre term infant head (Wyatt et al 1990b). Several alternative methods have been suggested for determining the DPF. These include derivation from the absorption of light by tissue water (Wray et al 1988, Cope et al 1989), measurement of the log slope of a transmitted ultra short light pulse (Chance et al 1988, Wilson et al 1989) or by measurement of the phase shift of amplitude modulated light (Lakowicz et al 1990). However, none of these alternative techniques has yet been validated by experimental measurement.

When NIRS measurements are made on large objects, it is often not possible to transilluminate the tissues and measurements must be made in partial transmission or reflection mode. In these cases, data are needed for the value of the DPF as a function of optode spacing. We report here values of the DPF derived from time of flight measurements in reflection mode from the adult head, calf and forearm and post mortem on the head from the newborn infant.

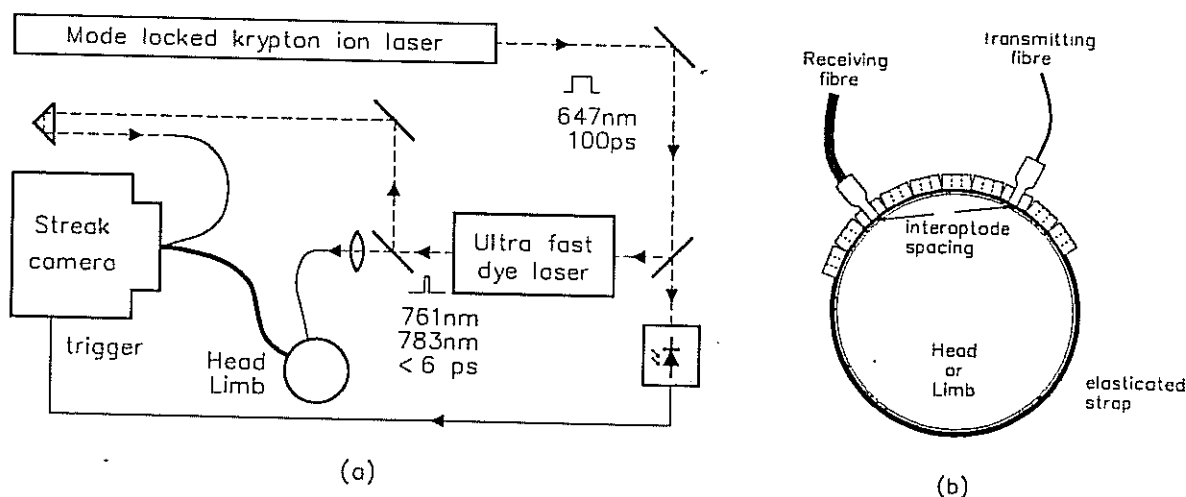


Figure 1. (a) Experimental system for time of flight measurement. (b) Method for attachment of the optical fibres.

EXPERIMENTAL METHOD

Equipment

The measurement system is shown schematically in Figure 1a. Ultra short light pulses (<6ps duration, 76 MHz repetition rate, wavelength 761nm or 783nm) were generated by a synchronously pumped dye laser (Coherent 701-3) pumped by a mode locked Krypton laser (Coherent KR3000). These pulses were coupled into a single 125 μm diameter, 60 cm long low dispersion optical fibre (Corning SDF). This permitted flexible positioning of the input light onto the tissue surface. Light emerging from the tissue was collected in an optical fibre bundle of the same low dispersion fibre. This fibre bundle consists of 100 fibres each exactly one metre long, arranged in a 1.9 mm diameter circle at the proximal end, but aligned in a single row at the distal end. This single row of fibres formed the input slit of the synchroscan streak camera (Hamamatsu Photonics C1587) which was used to detect the emerging light. A single additional fibre was used to couple a reference light pulse into the streak camera. This pulse was used to time the photons emerging from the tissue.

Subjects

Measurements of the DPF for the adult forearm were made on a group of 11 subjects, six male, five female aged 22 - 54 years (median 30). For the calf, measurements were made on 10 subjects, five male, five female aged 22 - 54 years (median 31) and for the head studies, 10 subjects, six of whom were male and four female, aged 22 - 54 years (median 26). All subjects were in good health. The measurements were made at a laser wavelength of 761nm.

The heads of ten infants were studied after death. They all had been admitted to the Neonatal Unit at University College Hospital. Five were male and five female. Their birthweights varied from 494 to 3220 (median 1720) grams. The principle clinical details are given in Table 1. Death occurred at a postnatal age of 0.75 to 384 (median 145) hours, and they were studied 12 to 55 (median 36) hours after death. These measurements were made at a wavelength of 783nm, except for infant 10 where a wavelength of 761nm was employed.

Measurement Procedure

To couple the transmitting and receiving fibres to the tissues, a flexible elasticated strap was placed around the object (see Figure 1b). Attached to the strap was an array of one centimetre wide black plastic blocks. Holes in these enabled the fibres to be held against the tissue at intervals of

Table I. Principle clinical details of the infants studied. Ultrasound images were obtained in life and confirmed on the day of study.

Infant No.	Sex	Gestation (weeks)	Age at death (hours)	Time at study, post mortum (hours)	Diagnosis	Ultrasound appearance	Biparietal diameter (cm)	Birth weight (g)
1	F	37	32	48	Diaphragmatic hernia	Normal	9.1	3220
2	F	38	0.75	25	Cerebral birth trauma	Normal	8.9	2850
3	M	28	19	32	Pulmonary interstitial emphysema	Bilateral periventricular echos	6.8	1260
4	F	26	30	37	Pulmonary interstitial emphysema	Haemorrhagic parenchymal infarction	6.7	1140
5	M	24	14	48	Pulmonary interstitial emphysema	Normal	5.3	600
6	M	35	384	12	Truncus arteriosus	Normal	9.0	2530
7	F	33	14	12	Pulmonary hypoplasia	Normal	6.6	1299
8	M	24	8	12	Extreme prematurity	Normal	5.0	494
9	M	34	16	32	Polycystic kidneys	Normal	7.7	1420
10	F	27	2.5	55	Rhesus isoimmunisation, hyaline membrane disease	Normal	7.6	1020

approximately one centimetre. During measurements, the receiving fibre bundle was usually held fixed in one block while the more flexible transmitting fibre was moved. At the end of the measurements, the fibres were removed and the positions of the holes in the blocks marked on the skin surface using a felt tip pen. The elasticated strap was then removed and the inter optode spacing measured using callipers. The accuracy of the measurement, allowing for possible skin movement was ± 2 mm.

Measurements from the forearm were made at a point mid way between the wrist and elbow, the arm being supported in a relaxed position. The optical fibres were positioned over the muscles on the medial aspect of the forearm away from any palpable bone. Measurements from the calf were made on the rear surface of the muscle at the broadest part of the leg. The subjects were seated with the leg muscles relaxed. Measurements from the adult head were carried out on the upper part of the forehead just below the hair line. The receiving fibre was positioned over the temple, and the transmitting fibre moved outward along the forehead. For the studies on the head of the newborn infant, the elasticated strap was not used, the fibres being held in movable clamps. The receiving fibre was positioned over the coronal suture midway between the anterior fontanelle and the external auditory meatus. The transmitting fibre was positioned successively at approximately one centimetre intervals along the medial portion of the coronal suture.

As a final study to assess the repeatability of the DPF measurement, a series of five separate measurements were made on the forearm of one adult subject at an inter optode spacing of 3 cm. The elasticated band was left in position on the arm, but the transmitting and receiving fibres were removed and then replaced between each measurement.

RESULTS

Measurement Repeatability

The DPF calculated from the repeated measurements from the adult forearm showed a standard deviation (S.D.) σ_r of 0.07. This is much smaller than the S.D. that arose from errors in the measurement of d , the inter optode spacing: $\sigma_d = 2$ mm. The vertical error bars in the subsequent data for the DPF were determined as follows:

$$S.D._{total} = \sqrt{\frac{DPF^2}{d^2} \sigma_d^2 + \sigma_r^2}$$

Adult Forearm

The results are shown in Figure 2. It can be seen that the DPF was almost constant beyond an inter optode spacing of 2.5 cm. The mean value of 3.59 ± 0.32 was the same for both male and female subjects

Adult Calf

Figure 3 shows that the DPF of the adult calf was almost constant beyond an inter optode spacing of 2.5 cm, but that there was a considerable difference in the DPF between males and females. The mean value for all the subjects was 4.65 ± 0.73 , the values for the males was 3.98 ± 0.46 and for females 5.14 ± 0.43 .

Adult Head

The DPF of the adult head was almost constant beyond an inter optode spacing of 2.5 cm as shown in Figure 4 and no difference between males and females was observed. The mean value of the DPF was 5.93 ± 0.42 , which is considerably higher than the value observed in either the forearm or the calf.

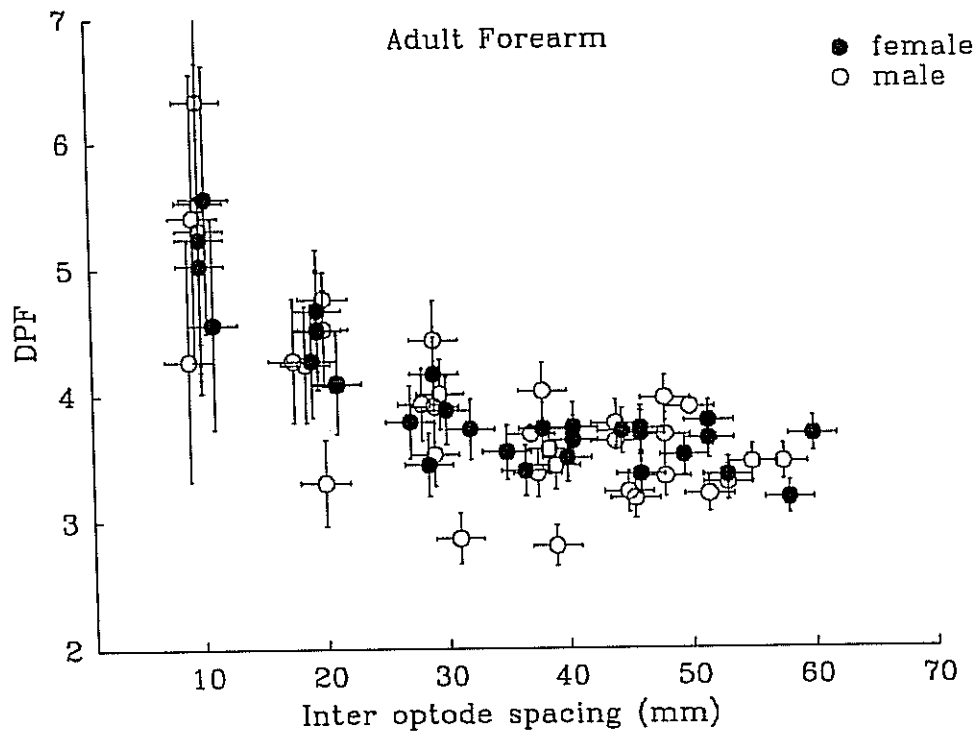


Figure 2. Experimentally derived values for the DPF in the adult forearm. The error bars indicate one standard deviation.

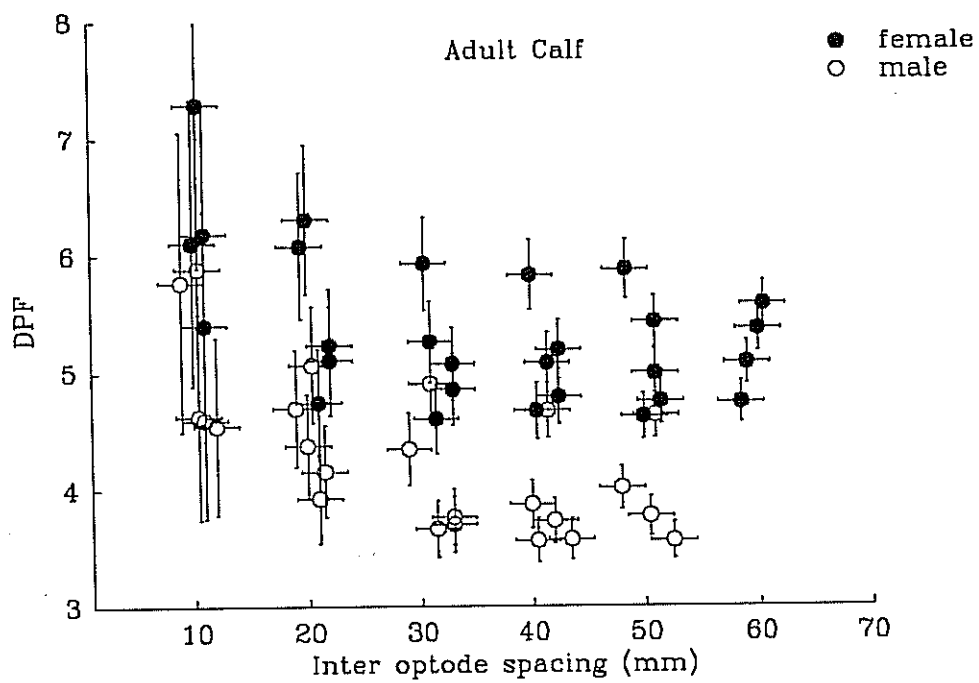


Figure 3. Experimentally derived values for the DPF in the adult calf. The error bars indicate one standard deviation.

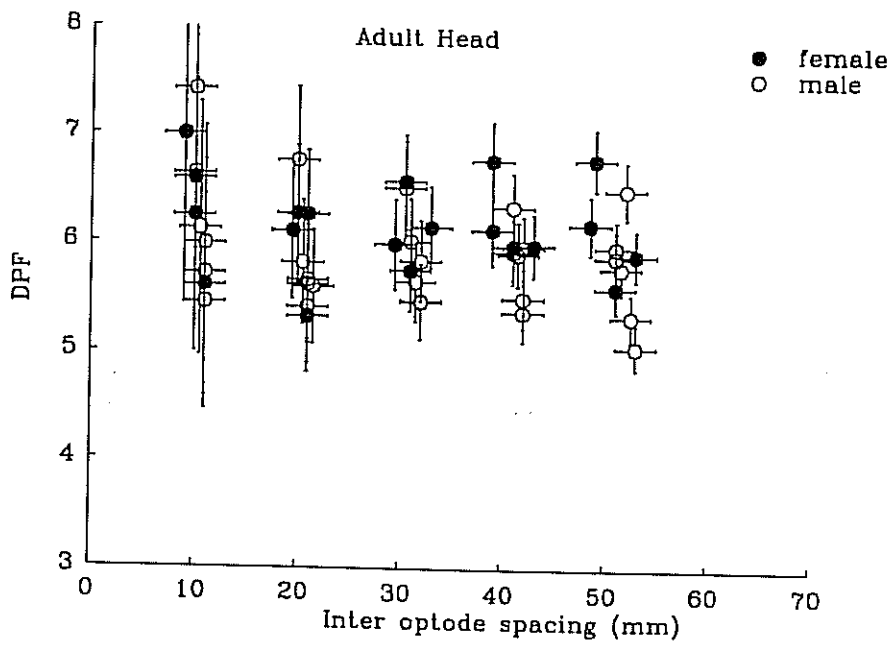


Figure 4. Experimentally derived values for the DPF in the adult head. The error bars indicate one standard deviation.

Baby Head

The results are shown in Figure 5, the data being displayed for two gestational age ranges, 24 - 30 and 33 - 38 weeks gestation. In common with the previous data, the DPF was almost constant beyond an inter optode spacing of 2.5 cm. The mean value of the DPF for all the infants was 3.85 ± 0.57 . There was a statistically insignificant tendency for the DPF to increase with gestation.

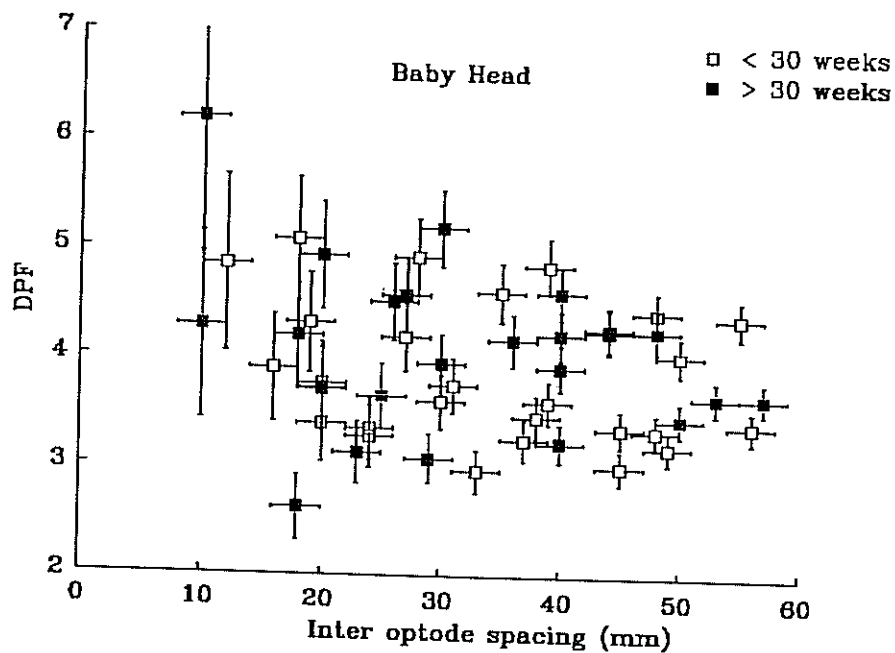


Figure 5. Experimentally derived values for the DPF in the baby head. The error bars indicate one standard deviation.

DISCUSSION

The results obtained in these studies reveal features which require discussion both in terms of the variations in tissue type and geometry, and the differences between observed and theoretically predicted behaviour.

The first general point of importance was that in all tissues the DPF fell with increasing inter optode spacing, the value becoming almost constant beyond 2.5cm. The absolute magnitude of the final DPF was dependent on the tissue being examined. These results are at variance with predictions based upon Monte Carlo modelling of light transport in a homogeneous sphere (van der Zee 1990). The model predicted that the DPF should increase with inter optode spacing in the manner shown in Figure 6. There are three possible explanations for this discrepancy. The first is that the model is incorrect in its treatment of light transport in tissue. This is considered unlikely since for slab geometries, the results obtained from the model have been verified against both experimentally measured light distributions and theoretical calculations. (Delpy et al 1988). Also, model predictions for cylindrical geometries are in qualitative agreement with experimental data (Arridge et al 1990). The second explanation is that the increase in DPF at shorter fibre spacings is a result of the inhomogeneity of real tissue and in particular the presence of superficial layers of skin, fat and bone. Although this may account for some of the observed differences, it is not thought to be the major cause of the discrepancy. If it were, the effects should be most marked in the DPF measurements on inhomogeneous tissues such as the adult and neonatal head, and less so on the more homogeneous tissues of the arm and leg. The experimental data tend if anything to show the reverse. The third explanation is that the difference is caused by the limited acceptance angle of the receiving fibre/streak camera in the measurement system (approximately 7° half angle). The modelled results were obtained for an imaginary receiving fibre, capable of accepting light emerging at any angle. Thus, in the model, light which is scattered obliquely as it first enters the tissue may be detected by the receiving fibre with a high relative intensity (since its pathlength is short). These detected photons

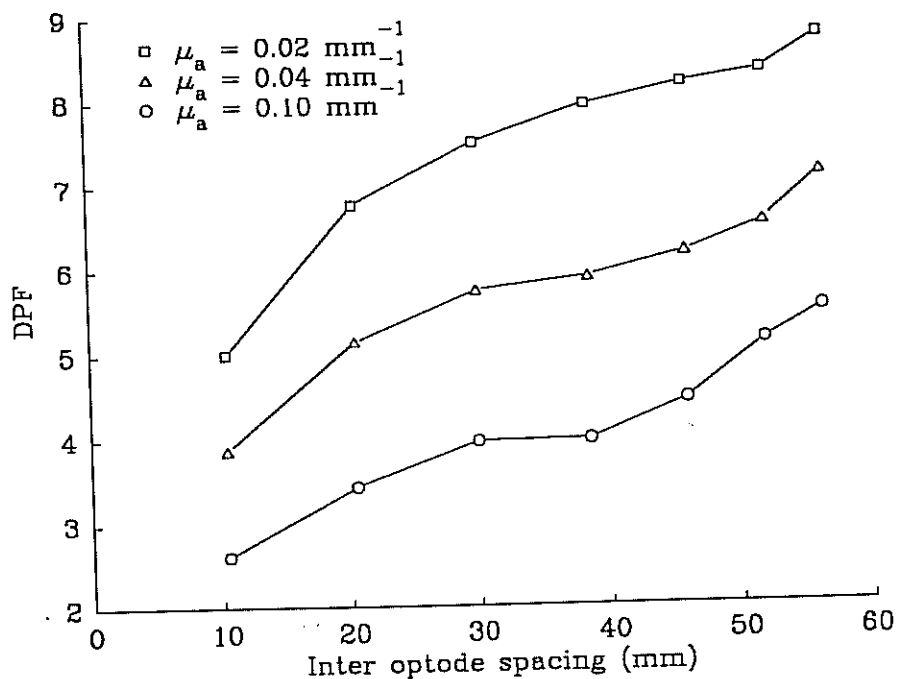


Figure 6. Monte Carlo predictions for the change in the DPF with inter optode spacing on a sphere of six centimetre diameter. The data are shown for three different absorption coefficients, the scattering coefficient being 5 mm^{-1} .

will tend to weight the calculated DPF towards lower values. In the measurement system these photons would not be detected. To check this supposition, the Monte Carlo model will be modified to take into account the acceptance angle of the receiver and the previous calculations repeated.

The second general feature of the measured DPF's is that the absolute value differed with tissue type. This is in general attributable to the differences in the absorption coefficient (μ_a) and reduced scattering coefficient $\mu_s(1-g)$. The predictions of the Monte Carlo model show that the DPF increases with scattering and decreases with absorption, with the absorption dependence being the dominant factor (see Figure 6). A higher absorption will tend to attenuate photons which have travelled a greater distance thus shortening the DPF. There are few data available on the absorption and scattering coefficients for the various tissues at 760 - 800nm. Values reported at 630nm for the brain lie in the range $\mu_a = 0.02 - 0.18 \text{ mm}^{-1}$ and $\mu_s(1-g) = 0.64 - 5.7 \text{ mm}^{-1}$ (Patterson et al 1987, Sterenborg et al 1989, Karagiannes et al 1989, van der Zee - unpublished observations). For muscle, the reported values are $\mu_a = 0.15 - 0.17 \text{ mm}^{-1}$ and $\mu_s(1-g) = 0.44 - 0.7 \text{ mm}^{-1}$ (Wilson et al 1986). Although there are no data on the absorption and scattering coefficients for the brain of the preterm infant, it is known that the attenuation is lower than for adult brain (Svaasand et al 1983). This is thought to be due to the lesser degree of myelination in the immature brain, myelin being an important contributor to scattering.

The DPF's from the arm were lower than for any other tissue (3.59 ± 0.32), (with no difference between males and females), probably because the highly absorbing muscle at this point on the arm is close to the surface with, in these subjects, only a thin layer of surface fat. The corresponding data for the calf of men is slightly higher (3.98 ± 0.49), and for females it is much higher (5.14 ± 0.43). This finding presumably reflects differences in fat-muscle ratio, and possibly differences in the thickness of the superficial fat layers. The size of this difference is rather surprising since all these subjects were of normal weight, and the majority took regular exercise. If the difference arose for the reasons given above, then it is likely that the DPF will be significantly different for sedentary subjects or those with specific pathologies.

The adult head gave the largest values for DPF (5.93 ± 0.42). This was not unexpected, since the relatively high albedo of adult brain tissue would lead to a longer pathlength. The relatively low value for the standard deviation was surprising. The adult head is an extremely heterogeneous structure containing many differing tissue types and convoluted tissue boundaries which vary from subject to subject. These could be expected to give rise to scattering which might be subject dependent. However this was not the case, the S.D. being only 7.1% of the mean DPF, and of this, almost 6% can be explained by the inaccuracy in the measurement of the inter optode spacing.

Results for the head of the newborn infant gave a mean value for the DPF of 3.85 ± 0.57 . Although this is lightly less than the value of 4.39 ± 0.28 previously obtained for the transilluminated infant head (Wyatt et al 1990b), the difference does not reach statistical significance. The value is lower than that for the adult head, and presumably this reflects the lower scattering coefficient for the newborn infant brain. This explanation would be consistent with the small difference in the DPF that appears to exist between those infants <30 weeks gestation and those >30 weeks. The fact that these measurements were made post mortem should not have caused a large error in the DPF. Previous studies in the rat brain have shown that the DPF changed by less than 4% before and after death. In the only other reported study of pathlength in infants, using the as yet unvalidated phase shift technique (Benaron et al 1990), values for the DPF in the range 3.96 - 6.13 were obtained at inter optode spacings of 1.8 - 3.0 cm.

SUMMARY

The Differential Pathlength Factor (DPF) has been measured for several different tissues. The results showed that the DPF varied with the type of tissue studied, and in the case of the adult calf with sex. However, the DPF for all tissues studied was constant once the inter optode spacing exceeded 2.5 cm.

Thus, measurements can be made by NIR spectroscopy at a range of inter optode spacings, and a single DPF used in the calculation of chromophore concentration. The results also showed that the major source of error in the DPF lay in the measurement of the inter optode spacing. To improve accuracy, two options are possible. Firstly, some means of continuous measurement of inter optode spacing could be incorporated in the NIR instrumentation. The better alternative would be an instrument incorporating a method of directly measuring the optical pathlength at each wavelength. This could be done either by time of flight measurement, or if it can be validated, by phase shift measurement.

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