

Supplementary Information

In Vivo Quantum Time-Domain Diffuse Optical Spectroscopy

S1 Acquisition-time dependence of blood-phantom measurements

To quantify the dependence of the Q-DOS measurements on acquisition time, each 60 s blood-phantom acquisition was divided into non-overlapping temporal windows of duration t . For each blood concentration and acquisition time, the absorption coefficient μ_a was independently retrieved from each DTOF.

Measurement precision was quantified through the coefficient of variation,

$$\text{CV}(t) = 100 \frac{\sigma[\mu_a(t)]}{\langle \mu_a(t) \rangle}, \quad (1)$$

where $\langle \mu_a(t) \rangle$ and $\sigma[\mu_a(t)]$ are respectively the mean and standard deviation of the values retrieved from the independent temporal windows of duration t .

Accuracy was quantified through the relative error with respect to the absorption coefficient retrieved from the complete 60 s acquisition,

$$\text{Error}(t) = 100 \frac{\langle \mu_a(t) \rangle - \mu_{a,60\text{ s}}}{\mu_{a,60\text{ s}}}. \quad (2)$$

Supplementary Fig. S1a shows the CV as a function of blood concentration and acquisition time. Shorter acquisition times lead to increased statistical variability because fewer photon-pair coincidences contribute to each reconstructed DTOF. The precision progressively improves with increasing acquisition time; for integration times of 10 s or longer, the CV remains below 13.5% across the investigated blood-concentration range.

The corresponding relative error is shown in Supplementary Fig. S1b. Despite the larger statistical fluctuations at short acquisition times, the mean retrieved absorption coefficient approaches the value obtained from the full 60 s acquisition as the integration time increases. For acquisition times of 10 s or longer, the absolute relative error remains within 2% across all investigated blood concentrations.

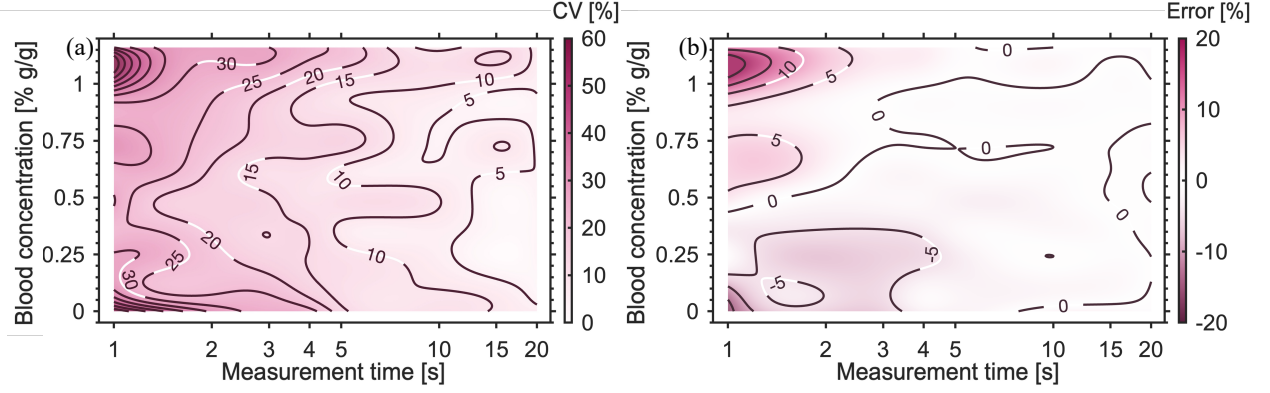


Figure S1: **Precision and accuracy of Q-DOS blood-phantom measurements as a function of acquisition time.** (a) Coefficient of variation (CV) of the retrieved absorption coefficient, μ_a , as a function of blood concentration and acquisition time. The CV is calculated as the standard deviation divided by the mean of the μ_a values retrieved from independent temporal windows of each duration. (b) Relative error of the mean retrieved μ_a with respect to the value obtained from the complete 60 s acquisition, shown as a function of blood concentration and acquisition time. Positive and negative values indicate overestimation and underestimation, respectively. Contour lines indicate constant CV and relative-error levels.

S2 Additional human *in vivo* cuff-occlusion measurements

To assess the reproducibility of the haemodynamic response measured with Q-DOS, the cuff-occlusion protocol described in the main text was performed in four additional healthy volunteers. The participant shown in Fig. 5d of the main text was also measured a second time on a different day, yielding five additional measurement sessions.

For each measurement, the effective absorption coefficient, μ_a , was retrieved from non-overlapping 15 s DTOFs throughout the 15 min protocol, comprising a 6 min resting baseline, 5 min of vascular occlusion at 250 mmHg and a 4 min post-occlusion period. The same reconstruction and fitting procedure described in the Methods was applied to all datasets.

As shown in Supplementary Fig. S2, all five additional measurements exhibit an increase in the retrieved μ_a during vascular occlusion followed by a decrease after cuff release. The magnitude and temporal evolution of the response vary across participants and between repeated measurements, as expected for *in vivo* measurements affected by inter-subject physiological variability and differences in optical coupling and finger positioning. The repeated measurement of the participant presented in the main text shows the same qualitative haemodynamic response on a different measurement day.

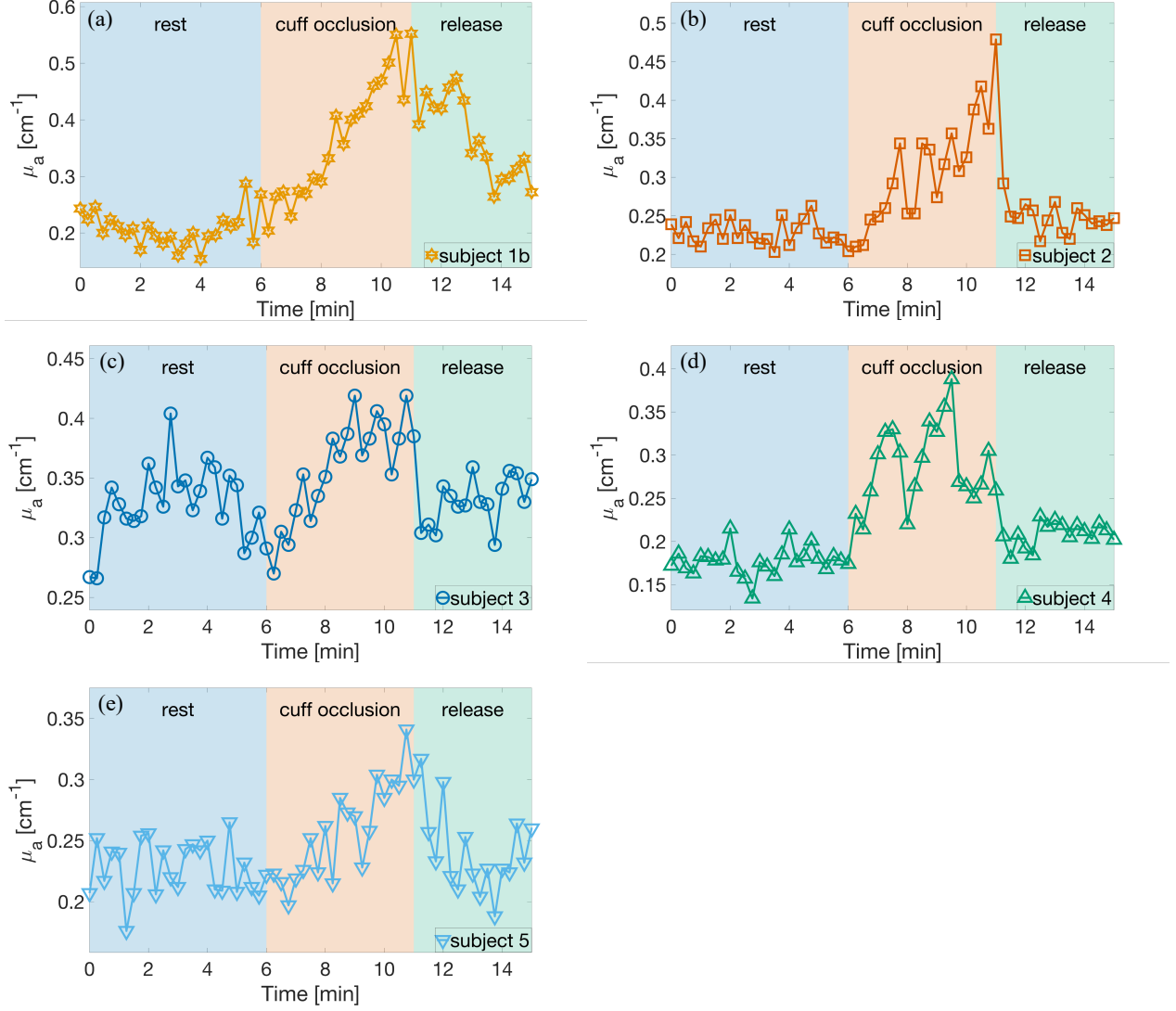


Figure S2: **Additional human *in vivo* cuff-occlusion measurements with Q-DOS.** Temporal evolution of the effective absorption coefficient, μ_a , during vascular cuff occlusion in five additional measurement sessions. (a) Repeated measurement, performed on a different day, of the participant shown in Fig. 5d of the main text. (b–e) Measurements from four additional healthy volunteers. Each point corresponds to μ_a retrieved from a DTOF reconstructed over a non-overlapping 15 s acquisition window. Shaded regions indicate the resting baseline, vascular cuff-occlusion and post-occlusion periods. All measurements show an increase in μ_a during occlusion followed by a decrease after cuff release, with subject-dependent response amplitudes and dynamics.