

# **Robust and fast characterization of OCT-based optical attenuation using a novel frequency-domain algorithm for brain cancer detection**

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## Supplemental information

### Method to Remove the Influence of Depth-dependent Effects of Laser Beam Profiles

In order to extract  $\mu_{ext}$ , we proposed to first image a reference phantom of known optical properties before imaging the sample of interest. In our experiments, the reference phantom was constructed with home-made mono-dispersive silica nanospheres of  $180 \pm 20 \text{ nm}$  and a concentration of  $12.5 \text{ mg/ml}$ . Our previous study indicated that the attenuation coefficient of the silica phantom matched very well with predictions by the *Mie* theory. OCT imaging of both the reference phantom and the sample were performed under the same experimental conditions, *i.e.*, with the same incident power, focused spot size, and focusing depth. The corresponding OCT signals for the sample of interest (with a subscript or superscript *s*) and the reference phantom (with a subscript or superscript *r*) can be written as:

$$I_s(z) = A \cdot \sqrt{\frac{\mu_{bs}^s}{4\pi}} \cdot e^{-\mu_{ext}^s \cdot (z-z_0)} \cdot h(z) \cdot U(z-z_0), \quad (5)$$

$$I_r(z) = A \cdot \sqrt{\frac{\mu_{bs}^r}{4\pi}} \cdot e^{-\mu_{ext}^r \cdot (z-z_0)} \cdot h(z) \cdot U(z-z_0). \quad (6)$$

Dividing the sample OCT signal  $I_s(z)$  in equation (5) by the reference phantom OCT signal  $I_r(z)$  in equation (6) and assuming the point spread function  $h(z)$  is almost identical for the sample and reference phantoms, we will get the following depth-dependent function with a single exponential decay:

$$I(z) = \frac{I_s(z)}{I_r(z)} = \sqrt{\frac{\mu_{bs}^s}{\mu_{bs}^r}} \cdot e^{-(\mu_{ext}^s - \mu_{ext}^r) \cdot (z-z_0)} \cdot U(z-z_0). \quad (7)$$

### Simple Linear Regression Algorithm in the LF Method

For simplicity, equation (7) can be rewritten as:

$$I(z) = \frac{I_s(z)}{I_r(z)} = C \cdot e^{-\mu \cdot (z-z_0)} \cdot U(z-z_0), \quad (8)$$

where  $C = \sqrt{\frac{\mu_{bs}^s}{\mu_{bs}^r}}$  is a constant,  $\mu = \mu_{ext}^s - \mu_{ext}^r$  is the attenuation coefficient difference,  $z$  is the imaging depth and  $z_0$  is the sample surface. When assuming  $z_0 = 0$ , equation (8) can be further simplified to:

$$I(z) = C \cdot e^{-\mu \cdot z}. \quad (9)$$

The LF method uses the logarithm of equation (9) to obtain a linear equation:

$$\ln(I(z)) = \ln(C) - \mu \cdot z, \quad (10)$$

where  $-\mu$  is the slope of the linear equation. For discrete A-line data, *i.e.*,  $I(n \cdot \Delta z)$ , equation (10) can be rewritten as:

$$y_n = \alpha + \beta \cdot z_n, \quad (11)$$

where  $y_n = \ln(I(z_n))$ ,  $\alpha = \ln(C)$ ,  $\beta = -\mu$ ,  $z_n = n \cdot \Delta z$ ,  $n = 0$  to  $N-1$  represents the sequential index of the discrete data for a given A-line,  $\Delta z$  is the pixel size along the imaging depth, and  $N$  is the total number of data points (*i.e.*, pixels) per A-line.

Then  $\beta$  can be derived using the simple linear regression (least squares) algorithm, *i.e.*:

$$\beta = \frac{\sum_{n=0}^{N-1} z_n \cdot y_n - \frac{1}{N} \cdot \sum_{n=0}^{N-1} z_n \cdot \sum_{n=0}^{N-1} y_n}{\sum_{n=0}^{N-1} z_n^2 - \frac{1}{N} \cdot (\sum_{n=0}^{N-1} z_n)^2}. \quad (12)$$

### Robustness of the FD Method to Incorrect Surface Detection

To derive  $\mu$  with the FD method, we can calculate the Fourier transform of equation (8):

$$F(\kappa) = \int_{-\infty}^{\infty} C \cdot e^{-\mu \cdot (z-z_0)} \cdot e^{-j \cdot \kappa \cdot z} \cdot U(z-z_0) dz = \begin{cases} \frac{C}{\mu + j \cdot \kappa} \cdot e^{-j \cdot \kappa \cdot z_0} & \text{if } z_0 \geq 0 \\ \frac{C}{\mu + j \cdot \kappa} \cdot e^{-\mu \cdot |z_0|} & \text{if } z_0 < 0 \end{cases}, \quad (13)$$

where  $\kappa$  is the frequency in space,  $z$  is the imaging depth of OCT signal. Please note that for OCT data analysis, the depth by default cannot be negative. Thus  $z \geq 0$  is assumed for deriving the above equation.

Then the optical attenuation coefficient  $\mu$  can be derived by comparing the DC component with the modulus of the first harmonic coefficient of equation (13), which leads to:

$$\frac{|F(\kappa=0)|}{|F(\kappa=\frac{2\pi}{N\Delta z})|} = \frac{\sqrt{(\frac{2\pi}{N\Delta z})^2 + \mu^2}}{\mu}, \quad (14)$$

where  $\Delta z$  is the pixel size along depth and  $N$  is the total number of data points (*i.e.*, pixels) per A-line.

Clearly, equation (14) is independent of  $z_0$ , *i.e.*, the sample surface position; thus in theory the FD method is not sensitive to the accuracy of surface detection.