Equivalence of CBV Measurement Methods in DSC-MRI

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Purpose: Measurements of cerebral blood volume (CBV) from dynamic susceptibility contrast (DSC) MR exams are of high diagnostic value for acute ischemic stroke, chronic vascular diseases as well as for the assessment of tumor vascularization. Currently, two established methods, derived from the indicator dilution theory, are used to determine estimates of relative CBV from DSC signals: (1) CBV_1 — area under residue function, $r(t)$ (Eq. 2); (2) CBV_2 – ratio between the areas under tissue, $c_t(t)$, and arterial curves, $c_a(t)$ (Eq. 3). Existing literature suggests that these two methods might not be equivalent (e.g. [1]), although from conservation of masses one would expect them to be equal. Here, we demonstrate that such discordance is only due to incorrect processing of the data and processing methods.

Methods: The indicator-dilution theory states that:

$$c_t(t) = CBF \int r(\tau) c_a(t-\tau) d\tau \qquad \text{Eq. 1}$$

where CBF is the cerebral blood flow. The CBV can be determined:

$$CBV_1 = CBF \int r(t) dt \qquad \text{Eq. 2}$$

or

$$CBV_2 = \frac{\int c_t(t) dt}{\int c_a(t) dt} \qquad \text{Eq. 3}$$

And we aim to prove that $CBV_1 = CBV_2$, i.e. that

$$CBF \int r(t) dt = \frac{\int c_t(t) dt}{\int c_a(t) dt} \qquad \text{Eq. 4}$$

where $r(t)$ is a normalized residue function $\max(r(t)) = 1$ and $\int r(t) dt = 1$.

Substituting Eq. 1 for $c_t(t)$ in Eq. 2 yields

$$CBF \int r(t) dt = \frac{\int CBF \int r(\tau) c_a(t-\tau) d\tau dt}{\int c_a(t) dt} \qquad \text{Eq. 5}$$

which can be recasted into

$$\int r(t) dt \int c_a(t) dt = \int\int r(\tau) c_a(t-\tau) d\tau dt \qquad \text{Eq. 6}$$

Because the order of integration can be freely chosen or exchanged one can rewrite Eq. 6 so that

$$\int r(t) dt \int c_a(t) dt = \int\int r(\tau) c_a(t-\tau) dt d\tau \qquad \text{Eq. 7}$$

When integrating over dt, τ is an independent variable and $r(\tau)$ can be considered a constant; thus,

$$\int r(t) dt \int c_a(t) dt = \int r(\tau) d\tau \int c_a(t-\tau) dt \qquad \text{Eq. 8}$$

It is key to recognize that the equivalence is true, because when integrating from -∞ to ∞, the value of $\int c_a(t-\tau) dt$ is independent from the auxiliary variable τ, and $\int r(t) dt = \int r(\tau) d\tau$.

Another way to prove our claim is by carrying out in the analysis in the frequency domain in which a convolution in the time domain corresponds to a multiplication in frequency domain and where $C_{t,a}(f)$, $R(f)$ are frequency-domain representations of respective time-domain functions. Fourier transform states that

$$C(f) = \int c(t) e^{-2\pi j f t} dt \qquad \text{Eq. 9}$$

Note that $C(0)$ represents the zero-th component ('DC') of the frequency spectrum and relates to the area under curve expression by $\int c(t) dt = C(0)$ for $f = 0$. Hence

$$CBV_1 = CBF \int r(t) dt = CBF\, R(0) \qquad \text{Eq. 10}$$

and

$$CBV_2 = \frac{\int c_t(t) dt}{\int c_a(t) dt} = \frac{C_t(0)}{C_a(0)} \qquad \text{Eq. 11}$$

Analogously, for equivalence testing we relate Eq. 11 and 12:

$$CBF\, R(0) = \frac{C_t(0)}{C_a(0)} \qquad \text{Eq. 12}$$

Writing out the convolution theorem for $c_t(t)$ in the frequency domain and evaluating it for $f = 0$:

$$C_t(0) = CBF\, R(0)\, C_a(0) \qquad \text{Eq. 13}$$

Substituting Eq. 14 into 13 yields

$$CBF\, R(0) = \frac{CBF\, C_a(0)\, R(0)}{C_a(0)} \qquad \text{Eq. 14}$$

which obviously proofs equivalence. Actual numerical equivalence of both methods is presented on Figure 1.

Results: We conclude that any differences between CBV values obtained from either the area under residue curve (Eq. 2) or the ratio of areas under the tissue and arterial curves (Eq. 3) reported in literature are a misconception. Most likely these differences are caused by errors in post-processing. Interestingly, noise and even more importantly regularization should not play a role in CBV assessment since for both estimation methods only the ratio of mean values ('DC terms') is important as is clearly evident from the frequency-domain explanation. However, this is true only if the regularization filter $G(f)$ (Eq. 15) does not influence the DC term (e.g. as in [2]).

$$R(f) = G(f) \frac{C_t(f)}{C_a(f)} \qquad \text{Eq. 15}$$

Other implementation of regularization filters (e.g. [3], Eq. 16)

$$G(f) = \frac{C_a(f)^2}{C_a(f)^2 + \lambda^2 f^{2k}} \qquad \text{Eq. 16}$$

might bias the computation of $R(0)$ under certain conditions. E.g. $G(f) \neq 1$ for $f = 0$, $k = 0$ (where k represents the order of the filter); in that case such filter violates assumptions of Eq. 1 unless properly rescaled.

Discussion: One possible explanation for discordant values of CBV reported in literature is the use of the delay-sensitive SVD approach [4], in which the matrix model of convolution is inappropriate. Thus, the area under $r(t)$ is also on error. Another possible explanation is that area under the curves is typically computed using *trapz()* function (e.g. in Matlab) which is not circular. Therefore, for residue functions with a peak close to $t = 0$, a considerable part of the area of the regularized $r(t)$ estimate is towards the end of reconstructed $r(t)$ curve. Because *trapz()* does not use circular integration, it does not connect the first and last point. This, of course, violates the -∞ to ∞ integration (typically approximated by the circular processing and zero padding). To mitigate these problems, we suggest that use of circular deconvolution and circular integration rules (or replacement of *trapz()* with simple *sum()* function) is advisable. Yet another explanation for the discordance could be in CBV determination by deliberate integration over bolus first-pass only and not over whole curve (when using Eq. 3) where arbitrary selection of the first-pass cut-off thresholds will violate the required (-∞, ∞) integration that is on the other hand applied when CBV is determined by Eq. 2.

References:

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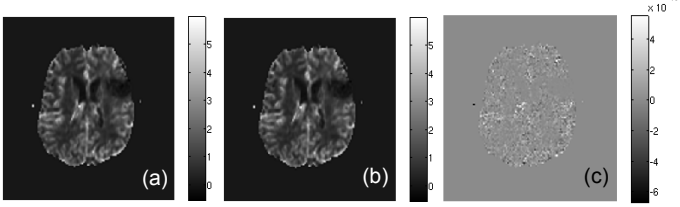

Figure 1: Example of CBV values determined using Eq. 2 (a) and Eq. 3 (b) (with circular deconvolution and circular trapezoid integration rule). (c) shows the difference between the two discussed methods; note that any differences are purely due to rounding errors (~5.10^{-16}).