Supplementary Material

for the Manuscript

" Early Time Points Perfusion Imaging: Theoretical Analysis of Correction Factors for Relative Cerebral Blood Flow Estimation Given Local Arterial Input Function"

Second recipe to apply the correction factor for $\mathbf{C(t)}$

Pre-select a single value S and set all the different correction factors $\int_0^t AIF(\tau)d\tau$ equal to S. For two different AIF's, the question to solve next is to obtain the proper time limit t_1 and t_2 such that

$\int_0^{t_1} AIF_1(\tau)d\tau = \int_0^{t_2} AIF_2(\tau)d\tau = S.$

Given $C(t) \approx f\int_0^t AIF(\tau)d\tau,$ it is clear that if

$$\int_0^{t_1} AIF_1(\tau)d\tau = \int_0^{t_2} AIF_2(\tau)d\tau = S, \qquad then\ \frac{C_1(t_1)}{C_2(t_2)} = \frac{f_1}{f_2}$$

with $C_1(t)$ and $C_2(t)$ from separate regions of tissue fed by AIF_1 and AIF_2. The recovered t_1 and t_2 values are required to be smaller than T, the tissue mean transit time, thereby meeting ET's basic assumption.

Given normalization of the correction factor, the single value S should be a fractional number (less than 1), indicating the percentage of the total integral ($\int_0^\infty AIF(\tau)d\tau$). For AIF_1 and AIF_2, the idea is to find the t_1 and t_2 where the integral of AIF_1 and that of AIF_2 reach the same percentage of their respective total AIF signal. The single value S to be picked for experimental data is somewhat arbitrary with the only requirement being that t recovered would be smaller than T, the tissue mean transit time. Since we do not know the T value *a priori*, one tentative choice could be testing the usefulness of S in the range of values such that t_1 and t_2 recovered are smaller than TMD1.

While the second recipe can be used to set up correction factors to $C(t)$, and similarly to $\frac{d}{dt}C(t)$ and $\frac{d^2}{dt}C(t)$, it cannot be used to set up correction factors for MD1 and MD2. So we will limit our investigation of the correction factor applied to $C(t)$ as a representative study for the second recipe.

Second Recipe of correction factor given the normalized gamma-variate function model for AIF

Since the integral of local AIF is given by $P(t, a)$ when the gamma-variate function $e^{-t}t^{a-1}$ is used as a model for AIF, the second recipe can be demonstrated by pre-selecting a single constant value (a fractional number) S and then identifying the time point t that would set $P(t, a)$ of each local AIF to be equal to S. The value of the time point t can be obtained by the Matlab routine calculating the inverse incomplete gamma function which recovers t from $P(t, a)$. One can also employ a graphical method finding the intersection between the line of S and the plots of various $P(t, a)$. The intersection time points are the desired time results.

If $P(t_1, a) = P(t_2, a) = S,\ then \quad \frac{C_1(t_1)}{C_2(t_2)} = \frac{f_1}{f_2}$

Results of the correction factors generated using the second recipe

For the second recipe, the arbitrary single value S to pick is somewhat tricky. There is no simple guideline on how to come up with the value of S which can guarantee that t from $P(t, a)$ would be shorter than tissue mean transit time T. All we can say is that if such a constant S can be found, than t_1 and t_2 can be determined for $C_1(t_1)$ and $C_2(t_2)$.

We can use TMD1 as a guide for setting up a limit for any t recovered for $P(t, a)$. For example, if we take pre-selected single value S=0.3, the time t obtained from each $P(t, a)$ can be compared with TMD1 (Fig S1),

for a=3, t =1.9138 vs. TMD1=2

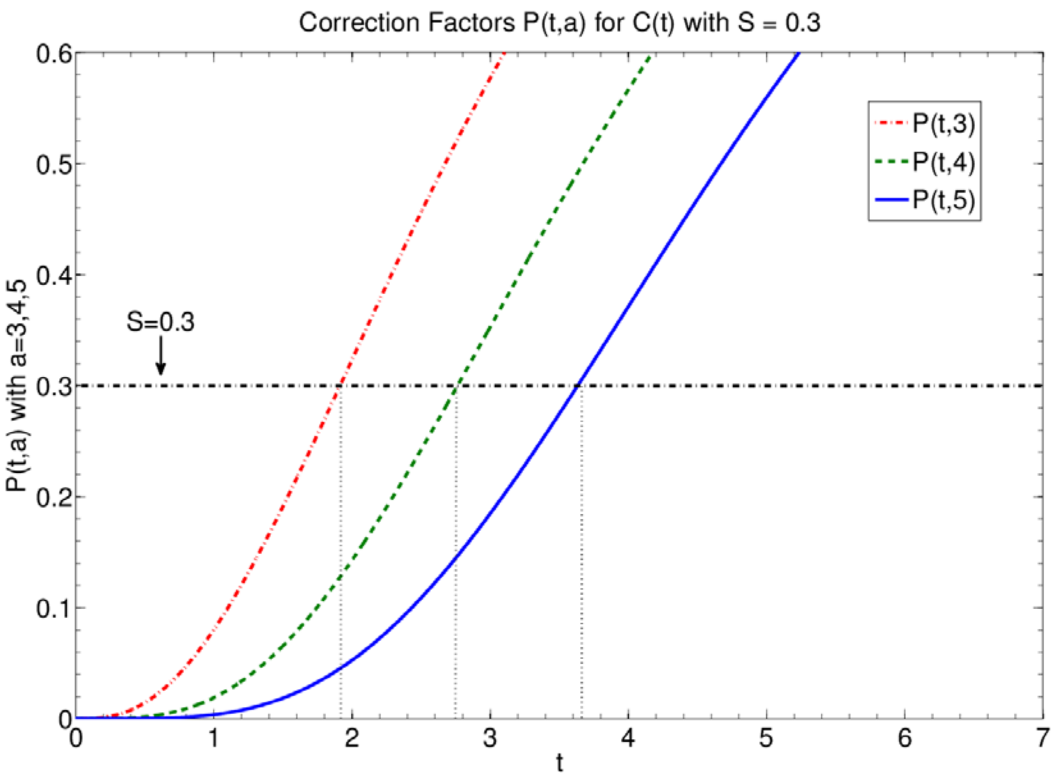
for a=4, t =2.7637 vs. TMD1=3

for a=5, t =3.6736 vs. TMD1=4

So S=0.3 could be considered a reasonable constant value to be used for the second recipe.

Figure Caption

Fig. S1. Graphs of $P(t,3), P(t,4)$ *and* $P(t,5)$, representing correction factors of $C(t)$ given different local AIF's modeled by the normalized version of gamma-variate function $e^{-t}t^{a-1}$ with parameter a equal to 3, 4, and 5. An horizontal line (indicated by arrow) representing a predetermined constant value S=0.3 intersects with $P(t,3), P(t,4)$ *and* $P(t,5)$ and the three time points at the intersection (t =1.9138, 2.7637 and 3.6736) are selected for the respective $C(t)$ associated with each local AIF for the purpose of evaluating rCBF by ET. The three time points, recovered in this figure by a graphic method and with their located indicated by three dotted vertical half lines, can also be obtained by the Matlab routine calculating the inverse incomplete gamma function which recovers t for $P(t,a) = S$ with a equal to 3, 4 and 5. The Matlab approach was described in the text of the Supplementary Material. The constant value S was selected under the condition that the recovered t is smaller than TMD1 of each $P(t,a)$. Given $P(t,a)$, TMD1=2, 3, 4 for $a = 3, 4, 5$.



Correction Factors P(t,a) for C(t) with S = 0.3
P(t,a) with a=3,4,5
t
S=0.3
P(t,3)
P(t,4)
P(t,5)
0
0.1
0.2
0.3
0.4
0.5
0.6
0
1
2
3
4
5
6
7

Fig S1