Logan Reference Tissue Model

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1 Summary

The Logan reference tissue model (LoganRTM) [1] has the following features:

- A reference model. That is, it does not require arterial input.

- A graphical model with linear fitting. That is, it works with transformed TACs, not the original TACs.

- For reversible receptor ligands.

- Does not assume a specific compartment model structure of the target tissue and reference tissue. This is because it is derived from the Logan plot, which assumes no specific compartment model. However, its operational usage often assumes a 1TCM for the reference tissue.

- It outputs the distribution volume ration (DVR) for the target tissue, which is the ratio between the DV of the target tissue and that of the reference tissue. With the assumption that $\frac{K_1}{k_2} = \frac{K_1'}{k_2'}$ (the level of nonspecific binding is the same in the target and reference tissues), $\mathrm{DVR} = \mathrm{BP_{ND}} + 1$.

Operational equation:

$$\underbrace{\frac{\int_0^T C_T(t)\,\mathrm{d}t}{C_T(T)}}_{y(T)} = \mathrm{DVR} \underbrace{\left[\frac{\int_0^T C'(t)\,\mathrm{d}t + \frac{C'(T)}{k_2'}}{C_T(T)} \right]}_{x(T)} + b\,, \tag{1}$$

where

- $C_T(t)$ is the TAC of the target tissue

- $C'(t)$ is the TAC of the reference tissue

- k_2' is the tissue-to-plasma clearance rate of the reference tissue.

For T sufficiently large, the curve $y(T)$ vs. $x(T)$ becomes linear, with DVR as the slope and b as the intercept.

About k_2':

- According to [2], k_2' in the original publication [1] was the population average for the reference tissue determined using blood sampling, but using the subject's own k_2' may be preferable; the k_2' resulting from SRTM or MRTM method might be a reasonable estimate to use in Eq. (1).

- According to [1], reasonable variation in k_2' does not cause big changes in the output value of DVR.

2 Derivation

According to the Logan graphical analysis (Logan plot) of reversible receptor ligands, for the target tissue, we have

$$\frac{\int_0^T C_T(t)\,dt}{C_T(T)} = V_T \frac{\int_0^T C_p(t)\,dt}{C_T(T)} + b\,, \tag{2}$$

where $C_p(t)$ is the plasma TAC after metabolite correction, V_T is the distribution volume of the target tissue. Assuming 2TCM for the target tissue, $V_T = \frac{K_1}{k_2}\left(1 + \frac{k_3}{k_4}\right)$. (Note that there are three usages of letter T in the above equation, with different meanings.)

For the reference tissue, we have

$$\frac{\int_0^T C'(t)\,dt}{C'(T)} = V_T' \frac{\int_0^T C_p(t)\,dt}{C'(T)} + b'\,. \tag{3}$$

Assuming 1TCM for the reference tissue (due to absence of target receptors), $V_T' = \frac{K_1'}{k_2'}$, $b' = -\frac{1}{k_2'}$.

Combining Eq. (2) and Eq. (3) by canceling the $\int_0^T C_p(t)\,dt$ term and re-arranging, we obtain the operational equation

$$\frac{\int_0^T C_T(t)\,dt}{C_T(T)} = \frac{V_T}{V_T'}\left[\frac{\int_0^T C'(t)\,dt + \frac{C'(T)}{k_2'}}{C_T(T)}\right] + b\,. \tag{4}$$

Here DVR $= \frac{V_T}{V_T'}$. With the above assumptions, DVR $= 1 + \frac{k_3}{k_4} = 1 + \text{BP}_{\text{ND}}$.

References

[1] Jean Logan, Joanna S Fowler, Nora D Volkow, Gene-Jack Wang, Yu-Shin Ding, and David L Alexoff. Distribution volume ratios without blood sampling from graphical analysis of pet data. *Journal of Cerebral Blood Flow & Metabolism*, 16(5):834–840, 1996.

[2] PMOD. Logan's reference tissue model based on average k2'.