Assessment of the Dynamic Contrast Enhanced Imaging Data Fitting Regarding the Equilibrium Transcytolemmal Water Exchange Using Chi-Values

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Synopsis

BOLus Enhanced Relaxation Overview (BOLERO) model has been proposed to analyze the dynamic contrast enhanced (DCE) MRI data. The model can work under the assumption of fast-exchange-limit (FXL) and fast-exchange-regime (FXR) regarding the equilibrium transcytolemmal water exchange. To compare FXL analysis and FXR analysis, we used Chi-value in tumor center and in tumor rim of the human melanoma xenografts in mice. Chi-values indicating the reliability of the results were smaller using FXR analysis than using FXL analysis in the tumor rim region. The effect of equilibrium transcytolemmal water exchange was important in tumor rim region.

Introduction

In dynamic contrast enhanced (DCE) MRI study of tumor perfusion, it is controversial that whether or not the effect of equilibrium transcytolemmal water exchange should be considered. Bolus Enhanced Relaxation Overview (BOLERO) method [1] allows data fitting to be constrained in the fast-exchange-limit (FXL, the conventional assumption) or allowed the fitting transiently go into the fast-exchange (FXR). We compare these two analyses using their Chi-values on the DCE MRI data in the different tumor region (center and rim) of the human melanoma. Chi-value indicates the quality of fits and reliability of the results parameters, such as permeability and volume fraction of extracellular, extravascular space (EES). Chi-values were obtained from longitudinal relaxation rate (R1)-time curve fitting individually. Comparing Chi-values using each analysis would suggest which one yields more reliable fitting result.

Methods

Animal: Highly (C8161) and poorly metastatic (A375P) human melanoma cells were implanted subcutaneously in the back of 6-7 weeks old male nude mice. The tumors were used 27-34 days (C8161, n=3) and 31-45 days (A375P, n=4) after implanting, when the volume of the tumors were within the range 200 to 700 mm^3. **MRI**: All MR experiments were performed with a 4.7 T Unity INOVA console (Varian, Palo Alto, CA). MR images were acquired using a home-built birdcage RF coil. All MR acquisitions were gated on the R-wave of the ECG. T One by Multiple Read Out Pulses (TOMROP) sequence was used to obtain a pre-contrast T1 map [2]. DCE MR images were acquired with a saturation recovery GRE sequence. (TE=2.2ms, TR=9ms, ts~1 heart beat, matrix=128*16, FOV ~2.4*3 cm). Gadodiamide (Omniscan, Nycomed, Princeton, NJ) was diluted to 10 mM and 0.2 mL of this solution was injected i.v. in 3-5 sec after acquiring 20 pre-contrast images. The time resolution of the first 60 images was about 2 sec/image. The following 120 images were acquired with 4 signal averages. **Image Analysis**: Region of interest (ROI) for the arterial input function (AIF, R1 of blood) was placed in the left ventricle as described previously [3]. Tumor ROIs were placed on center and rim of the each tumor. R_1versus time curves were obtained using Eq. [1] for FXL analysis and using Eq.[2] for FXR analysis.

$$R_1(T) = r_{1o} \cdot p_o \cdot L \int_0^T \frac{R_{1b}(t) - R_{1b0}}{r_{1p}(1-h)} \exp(-L(T-t))\,dt + R_{10} \qquad \text{Eq .[1]}$$

$$R_1(T) = \frac{1}{2}\left[\left\{2R_{1i} + r_{1o} \cdot L \int_0^T \frac{R_{1b}(t) - R_{1b0}}{r_{1p}(1-h)} \exp(-L(T-t))\,dt + \frac{R_{10} - R_{1i} + 1/\tau_i}{p_o}\right\} - \left\{\left(\frac{2}{\tau_i} + \frac{R_{10} - R_{1i} + 1/\tau_i}{p_o} - r_{1o} \cdot L \int_0^T \frac{R_{1b}(t) - R_{1b0}}{r_{1p}(1-h)} \exp(-L(T-t))\,dt\right)^2 + \frac{4(1-p_o)}{\tau^2 p_o}\right\}^{1/2}\right] \qquad \text{Eq .[2]}$$

Where r is the contrast agent relaxivity, p is the fraction of tissue water, τ is the mean water molecule life time and h is the hematocrit. The subscript 'b' is for blood, 'i' for intracellular, 'o' for extracellular and '0' for pre-contrast agent. The constant L $(= E \cdot F_K(1-h)/(f_w \cdot p_o))$ is defined as described previously[1] . FXL analysis and FXR analysis were processed using a program based on Interactive Data Language (IDL; Research Systems Inc., Boulder, CO, USA).

Results

R_1-time curve was obtained for tumor center and rim and was analyzed under FXL or FXR assumption. Fig. 1 was a representive R_1-time curve in tumor rim (A375P-2 mouse) and respective FXL and FXR fitting curves. FXR analysis gave better fitted curve (solid line) than FXL analysis (dashed line). The quality of fits was appeared as Chi-value. Chi-values acquired on each R_1-time curve were shown in Fig. 2. Chi-values from FXL analysis were smaller than those from FXR analysis especially in tumor rim of both two tumor cells and in tumor center of A375P tumor.

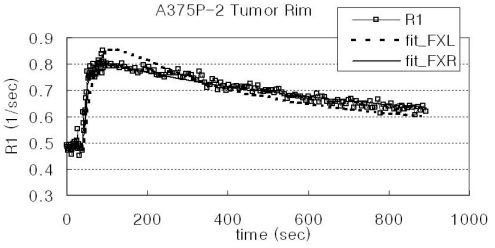
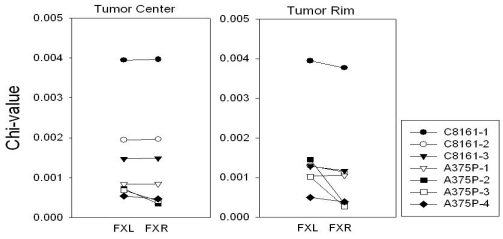


Fig.1 Longitudinal relaxation rate (R1)-time curve and FXL analysis fitting curve using Eq.[1] and FXR analysis fitting curve using [2].



mouse	Tumor Center		Tumor Rim	
	FXL	FXR	FXL	FXR
C8161-1	3.95E-03	3.97E-03	3.95E-03	3.77E-03
C8161-2	1.95E-03	1.96E-03	1.30E-03	1.14E-03
C8161-3	1.48E-03	1.49E-03	1.29E-03	1.17E-03
A375P-1	8.44E-04	8.49E-04	1.04E-03	1.05E-03
A375P-2	7.21E-04	3.48E-04	1.46E-03	3.37E-04
A375P-3	6.87E-04	4.24E-04	1.02E-03	2.66E-04
A375P-4	5.43E-04	4.67E-04	5.02E-04	3.86E-04

Fig.2 Chi-value of FXL analysis and those of FXR analysis in tumor center and in tumor rim.

Discussion

Chi-value provides reliability of the fitting result. There was a limitation on comparing Chi-value between FXL analysis and FXR analysis. They should be compared individually on each R_1-time curve. Chi-values obtained of the FXR fitting were smaller than those of FXL fitting in the tumor rim on 6 of 7 mice (one was almost same). While in the tumor center the two fittings yielded almost identical Chi-values on 4 of 7 mice or smaller different Chi-values. FXR analysis provided more reliable results in tumor rims. These results were consistent with previous observations [3] and suggested FXR analysis played a more important role in tumor rim than in tumor center.

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References [1] Yankeelov, Rooney, Li, Springer MRM 50:1151-1169 (2003). [2] Pickup, Zhou, Glickson Acad Radiol 10:963-968 (2003). [3] Zhou, Pickup, Yankeelov, Springer, Glickson MRM 52:248-257 (2004)