Two non-linear parametric models of enhancement for breast DCE-MRI that can be fitted using linear least squares

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Introduction

The interpretation of dynamic contrast enhanced (DCE) MR images of the breast is predicated on the assessment of tissue enhancement kinetics. Both pharmacokinetic (PK) and empirical parametric (EP) models have been developed to quantify this change in enhancement. The former aim to measure physiologically meaningful parameters while the latter seek to measure the shape of the enhancement curve. Given that different PK models can yield markedly different estimates of the same physiological parameter (because of model assumptions) and that such models need to be fitted using non-linear least squares (NLS) which is in itself problematic (need to specify starting values, convergence issues), EP models remain of interest. Herein we propose two such models—linear-slope [1] and Ricker [2]—which have the advantage that they can be fitted using linear least squares (LS) meaning that fitting is quick and that there is no need to specify initial parameter estimates. Furthermore, if desired, the LS fit can be used to provide parameter estimates for a subsequent NLS fit. The results of an empirical evaluation of the goodness-of-fit (GoF) of these two models relative to the pharmacokinetically-inspired Hayton model [2], and the simplified gamma-variate model [4] are also presented.

Materials and methods

The DCE-MRI data used in this study originate from routine clinical breast MRI examinations of 22 women performed by Queensland X-Ray, Queensland, Australia over the last five years. The data were acquired on a 1.5T Signa Echospeed (GE Medical Systems) scanner using a 3D FSPGR sequence (typically TR=5.072 ms, TE=2.424 ms, FA=10°). Gadopentate dimeglumine, 0.2 mmol/kg, was administered manually at a rate of about 1 ml/s. Pixel spacing is from 0.644-0.742 mm, slice thickness from 1.4-3 mm, number of post-contrast volumes is from 5-7, and the temporal resolution is around 90 s. The 22 cases were selected because the reporting radiologist identified one or more suspiciously enhancing lesions. In total 33 lesions were identified. A 3D segmentation, hereinafter referred to as VOI, of each was performed by a radiographer using the region growing tool in OsiriX (http://homepage.mac.com/rossetantoine/osirix). Each model listed in Table 1 was fitted to each VOI in turn both voxel-wise and to the VOI mean intensity. The models were fitted to values $E(t) = \big(S(t) - S(0)\big)/S(0)$ where $S(t)$ represents the observed MR signal at time t after injection. In the voxel-wise case a 3×3 mean filter was applied to each resulting slice image to mitigate noise and motion artifacts. The linear-slope model was fitted using the method of [5] which involves evaluating a fixed number of LS solutions. The Ricker model was fitted using LS by first writing it in the form $\log(C(t)) - \log t = \log a - bt$. The Ricker model was also fitted using NLS. All of the remaining models were fitted using NLS. NLS fitting was performed using *lsqcurvefit* (Trust-Region-Reflective optimization) in MATLAB (The MathWorks, Inc.).The GoF of each model was assessed in terms of $R^2 = 1 - SS_{\text{err}}/SS_{\text{tot}}$ and mean squared error (MSE).

Table 1: Proposed and reference parametric models

Linear-slope	$C(t) = \begin{cases} \beta_1 t & \text{if } t \le \alpha \text{ and} \\ \beta_1 \alpha + \beta_2 (t - \alpha) & \text{if } t > \alpha \end{cases}$
Ricker	$C(t) = at \exp(-bt)$
gamma-variate	$C(t) = At^{\alpha} \exp(-t/\beta)$
Hayton	$C(t) = \dfrac{A}{a-b}(\exp(-bt) - \exp(-at))$

Results and discussion

Fig. 1 and Fig. 2 show box plots of the fitting results (note: the trimmed mean ignores 5% of the lowest and highest values). The gamma-variate model demonstrates the better fit (higher R^2 or smaller MSE) and smaller spread than the other models. However the linear-slope model comes a close second. The Hayton model is then the next best followed by the Ricker model fitted by NLS. A Friedman test was performed for each GoF measure in turn (R^2, MSE, trimmed mean R^2, and trimmed mean MSE) with the models as column effects and the VOIs as row effects. In each case the test was significant (p-value < 0.0000) providing evidence at the $\alpha = 0.05$ level of significance that the models do not fit equally well. Next, for each GoF measure in turn four paired-sample Wilcoxon tests were performed to test the null hypothesis that the linear-slope model fits equally well as the other model versus the alternate hypothesis that the linear-slope model fits better. For each model except the gamma-variate all of the tests were significant (p-value < 0.0125) providing evidence at the $\alpha = 0.05$ level of significance (with Bonferroni correction) that the linear-slope model fits the data better than all but the gamma-variate model.

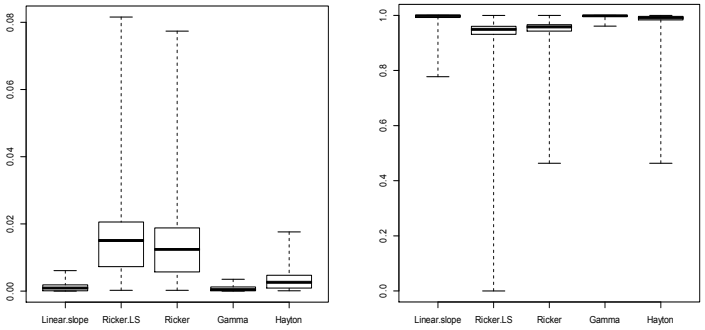

Fig. 1: MSE (left) and R^2 (right) of the mean enhancement curve of each VOI

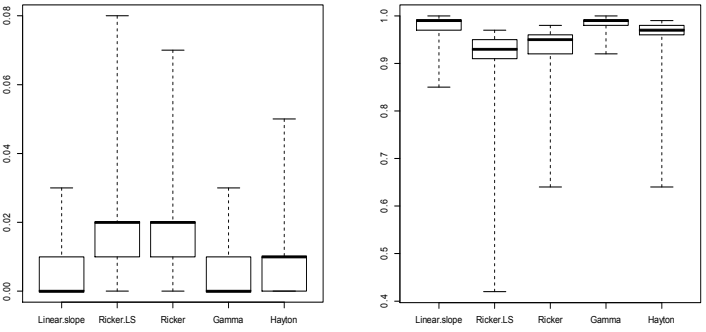

Fig. 2: Trimmed mean of voxel-wise MSE (left) and R^2 (right) values for each VOI

Conclusions

The results show that the proposed linear-slope model fits routine clinical DCE-MRI data better than the pharmacokinetically-inspired Hayton model and the Ricker model. Moreover they show that it fits almost as well as the more complex gamma-variate model. They also show that the Ricker model provides a remarkably good degree of fit given that, in contrast to the other models, it has only two rather than three free parameters. The advantage of the two proposed models is that they have a parsimonious form and can be fitted using LS.

References

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