Dynamic contrast-enhanced MR imaging in rectal cancer: study of inter-software accuracy and reproducibility using simulated and clinical data

Luc Beuzit[1], Pierre-Antoine Eliat[2], Elise Bannier[1,3], Jean-Christophe Ferré[1,3], Yves Gandon[1], Vanessa Brun[1], and Hervé Saint-Jalmes[4,5]

[1]Radiology, CHU Rennes, Rennes, France, [2]PRISM-Biosit CNRS UMS 3480, INSERM UMS 018, University of Rennes I, Rennes, France, [3]Neurinfo MR imaging platform, University of Rennes I, Rennes, France, [4]Radiology, Eugène Marquis Cancer Institute, Rennes, France, [5]LTSI, UMR 1099, INSERM, University of Rennes I, Rennes, France

Purpose: T1-weighted dynamic contrast-enhanced (DCE) MRI has been recognized as a biomarker of early therapeutic response in various clinical applications, including rectal cancer (1-3). Nevertheless, Heye and al. (4) showed a considerable variability among software packages (SPs) for pharmacokinetic parameters of uterine fibroids, either extracted from Tofts and Kermode's model (volume transfer constant K^{trans}, extravascular extracellular volume fraction v_e) (5) or model-free (initial area under the gadolinium curve iAUGC). A new method of Dicom files processing was developed in this study to test both reproducibility and accuracy of pharmacokinetic parameter measurements on five analysis software packages (SPs) for DCE-MR imaging, using clinical images of rectal cancer and simulated data.

Methods: Institutional review board approval was obtained. Thirty-one DCE-MR scans were performed between November 2012 and February 2014 with a 3T Siemens scanner on 23 patients treated for locally advanced rectal cancer. Acquisitions included a dynamic pre- and post-contrast T1-weighted, three-dimensional spoiled gradient-echo sequence whose parameters were: matrix 192x192, FOV 240x240 mm², slice thickness 3 mm, TR 4.1 ms, TE 1.4 ms, flip angle 15°, 24 slices, temporal resolution of 5.2 s for an acquisition time of 3.5, 4.5 or 6 minutes. Dual-flip-angle (2° and 15°) pre-contrast T1 mapping was performed. Since some SPs provided by MR scanner vendors do not allow analysis of DCE-MR images acquired on the scanners of rival vendors, additional acquisitions with the same parameters were performed on General Electric and Philips scanners using a physical phantom (water container). A Mathematica-based software (Wolfram Research Inc., v8.0.1) was developed to substitute these phantom images with clinical images without changing the Dicom header. Simulated tissues consisted of calculated dynamic signal changes for 18 combinations of K^{trans}, v_e and T1, then converted into pixel clusters for three Gaussian noise levels and inserted into Dicom dynamic images (**Fig 1**). All images were post-processed with five SPs applying the Tofts' model in order to measure K^{trans}, v_e and iAUGC: Tissue 4D v.40A (Siemens) [**A**], GenIQ v.11.3 (GE) [**B**], T1 Permeability v.6.0.1 (Philips) [**C**], DCE Tool v.2.0 (K. Sung, UCLA) [**D**] and UMM perfusion v.1.5.1 (F. Zöllner et al., University of Mannheim) [**E**].

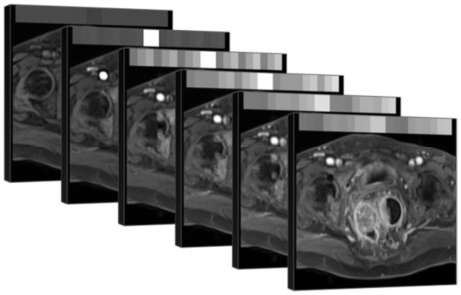

Fig 1: selection of DCE MR images of a large rectal tumor with inserted pixel clusters corresponding to simulated tissues

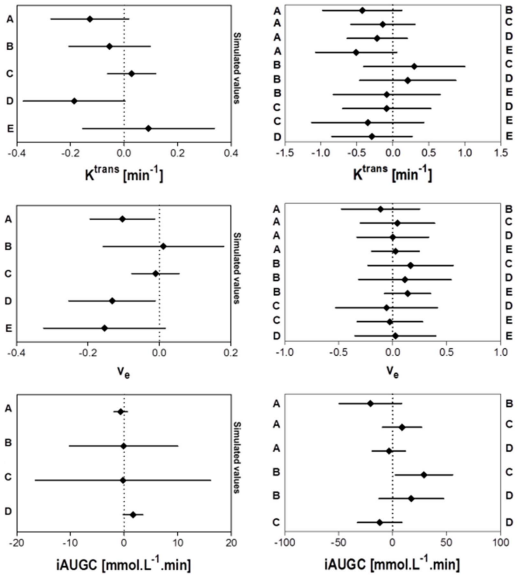

Fig 2: Bland-Altman analysis. ♦ bias (mean of the differences). The length of the horizontal bar is proportional to the dispersion.

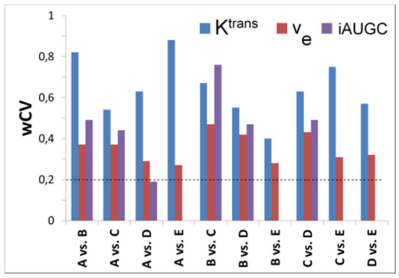

Fig 3: within-subject coefficient of variation (wCV) among SPs on clinical data

Results: A graphical representation of the Bland-Altman analysis is given in **Fig 2**, plotting the difference between the value of a parameter measured by an SP and its simulated "true" value (left graphs) or between the values measured by a pair of SPs on clinical data (right graphs). Measurement errors were observed on the simulated data for all the pharmacokinetic parameters and SPs, with a bias ranging from -0.19 min^{-1} to 0.09 min^{-1} for K^{trans}, -0.15 to 0.01 for v_e, and -0.65 to 1.66 $mmol.L^{-1}.min$ for iAUGC. The within-subject coefficient of variation for a pairwise comparison of all SP combinations on clinical data is given in **Fig 3**.

Discussion: Our results yielded significant errors in calculated DCE-MR imaging pharmacokinetic parameters among perfusion analysis SPs, resulting in poor inter-software reproducibility. The inter-software variability was higher in all comparisons but one than the upper limit of 20%, which is the goal of current quantitative imaging initiatives (6).

Table 1	Tissue 4D [**A**]	GenIQ [**B**]	T1 permeability [**C**]	DCE Tool [**D**]	UMM perfusion [**E**]
T_1 relaxation time estimation	Variable flip angle map or user input	Reference value	Variable flip angle map	Variable flip angle map or user input	None
Arterial Input Function	Population based	Population or patient based	Population or patient based	Population or patient based	Population or patient based
Time to peak measurement	User input	Automatic	Automatic	User input	User input

Several perfusion analysis SP characteristics listed in **Table 1** can explain these results. The use of different curve-fitting algorithms, although not explicitly mentioned in the SPs' documentation, is likely. Using the same simulation tool but with lower K^{trans} values, Cron et al. observed a high percentage of unphysical values when comparing the reaction of three DCE-MR SPs to increasing noise levels (7). A potential bias in our study may have been caused by an additional source of variability due to the organ of interest, which can be affected by technical difficulties such as peristaltism. Nevertheless, the technique we used was approved by several authors (2,3) and variation among pharmacokinetic parameters was observed both on clinical and simulated data.

Conclusion: There is a need for standardization of post-processing tools to enable the use of DCE-MR imaging as a biomarker in multicenter trials and clinical practice. For now, a single SP should be used in a given study and absolute values of parameters provided in the literature should be viewed with caution.

References: **1.** Hylton *et al. J Clin Oncol* 2006;24:3293–3298. **2.** Gollub *et al. Eur Radiol* 2012;22:821–831. **3.** Kim *et al. J Magn Reson Imaging* 2014;40:730-737. **4.** Heye *et al. Radiology* 2013;266:801–811. **5.** Tofts, Kermode *Magn Reson Med* 1991;17:357–367. **6**. Quantitative Imaging Biomarkers Alliance - http://www.rsna.org/QIBA **7.** Cron *et al. Abstract from the ISMRM meeting* 2014 **Target audience**: radiologists, MR physicists, MR vendors