The microvascular characteristics of cervical cancer: Limitations of the modified-Tofts tracer kinetic model for the analysis of DCE-MRI data

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1. Purpose/Introduction
The modified-Tofts tracer kinetic model (standard Tofts + plasma volume, v_p) is often used to analyse DCE-MRI data. It represents a particular case of the general 2-compartment exchange model (2CXM) with two simplifying assumptions: a) negligible plasma mean transit time (MTT) and b) plasma flow, F_p, much greater than microvascular permeability-surface area, PS (F_p >> PS). The 2CXM provides separate estimates of PS and F_p, while the mod.-Tofts model only provides an estimate of the transfer constant, K^trans. K^trans reflects PS if the simplifying assumptions are met but may also be sensitive to F_p if they're not. The aim of this work was to compare the 2 models in patients with carcinoma of the cervix and to assess whether the assumptions made in the mod.-Tofts model are valid in this cervix tumour dataset.

2. Subjects and Methods
Twenty-seven patients with cervical cancer (stages IIB – IVA) were scanned prior to external-beam radiotherapy. MRI studies were performed on a 1.5 T Siemens Magnetom Avanto using a phased-array pelvic coil. A sagittal 3D T1-w VIBE sequence (TR/TE 5.6/1.1 ms, 96 x 128 x 16 matrix, 240 x 320 x 80 mm FOV, acquisition time 3 s) was used for pre-contrast T1 estimation (α = 5°, 10°, 35°) and the dynamic acquisition (α = 25°). Individual arterial input functions (AIFs) were obtained from the descending aorta. Whole tumour ROIs were defined and concentration-time curves were analysed using: a) mod.-Tofts model to obtain estimates of K^trans, v_p, interstitial volume, v_e and bolus arrival time, t_b; b) 2CXM model to obtain estimates of F_p, PS, v_p, v_e & t_b. A paired t-test was used to compare equivalent parameters obtained with the two models.

3. Results
The 2CXM provided excellent fits to all datasets while fits using the mod.-Tofts model were significantly poorer (e.g. Fig. 1). The table shows parameter estimates obtained using both models averaged over all 27 patients. The results of paired t-tests are shown. K^trans correlated poorly (fig. 2) with PS (r = 0.36, p < 0.01) but correlated strongly with F_p (r = 0.95, p < 0.01).

![Fig. 1: Whole tumour concentration-time curve (circles) with fits using mod.-Tofts (gray) and 2CXM (black) along with patient-specific AIF (inset).](image1)

![Fig. 2: Scatterplot showing correlation of K^trans with F_p and PS for all 27 patients. Lines of best fit are also shown.](image2)

<table>
<thead>
<tr>
<th>Model</th>
<th>F_p (ml/ml/min)</th>
<th>K^trans (ml/min)</th>
<th>PS (ml/ml/min)</th>
<th>v_p</th>
<th>v_e</th>
<th>t_b (s)</th>
<th>Chisq</th>
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<tr>
<td>Mod.-Tofts</td>
<td>-</td>
<td>0.31 ± 0.23</td>
<td>-</td>
<td>0.03 ± 0.02</td>
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<td>2CXM</td>
<td>0.56 ± 0.42</td>
<td>-</td>
<td>0.14 ± 0.08</td>
<td>0.20 ± 0.13</td>
<td>0.20 ± 0.11</td>
<td>3.7 ± 1.3</td>
<td>1.5 ± 0.9</td>
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<tr>
<td>P-value</td>
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<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01*</td>
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</table>

Table 1: Values obtained with 2 models averaged over 27 patients. Where comparable, the result of a paired t-test on the 2 groups is shown. Blank cells - parameter not estimated with this model. * - compared using the F-test.

4. Discussion/Conclusion
Our estimates of F_p and PS compare well with those of Haider et al. who used DCE-CT to assess cervical cancer, and demonstrate the highly vascular nature of cervical tumours. The 2CXM provided a better fit than mod.-Tofts in all patients and significantly different estimates were obtained for all comparable parameters. K^trans did not reflect 2CXM estimates of PS or F_p despite correlating well with F_p. Average plasma MTT was 19 s suggesting that the assumption of negligible MTT made in the mod.-Tofts model is not valid in this dataset. Taken together, these results suggest that the 2CXM is more suitable for the analysis of this DCE-MRI dataset than the mod.-Tofts model.

References: