# Model Parameter Correlation for DCE-MRI in Advanced Cervical Cancer

Jesper Folsted Kallehauge[1], Erik Moore Pedersen[2], Kari Tanderup[1], Finn Rasmussen[2], Jacob Lindegaard[1], Lars Fokdal[1], Søren Haack[1], and Thomas Nielsen[1]

[1]*Department of Oncology, Experimental Clinical Oncology, Århus, Denmark,* [2]*Department of Radiology, Department of Radiology, Århus, Denmark*

## Purpose

Recently it has been shown that stratifying patients by certain DCE-MRI parameters can distinguish between patients with better and poorer outcome for advanced cervical cancer. The results from Yuh et al. [1] showed the lowest 10$^{th}$ percentile of the RSI (Relative Signal Increase) to be the best stratifyer. Recent results from Halle et al. [2] have shown the 20-30$^{th}$ percentile of $A_{Brix}$ to be the best stratifyer. A number of these derived model parameters are highly correlated [3] and may thus be redundant. If such a correlation can be determined the computationally fastest and most robust approach could be chosen to enhance clinical use of these functional estimates for improving therapy.

## Materials and Methods

In total 24 DCE-MRI scans in 11 different patients were included in the study. A 3T Philips Achieva was used with the following DCE protocol: 20-24 slices, 5mm slice thickness, TE/TR: 1.4ms/2.9 ms , 10$^{o}$ Flip Angle (FA) , 2,27mm isotropic in-plane resolution . The bolus injected was 0.1 mmol/kg Dotarem at 4ml/s, followed by a 5 ml saline flush. 120 dynamics equidistantly spaced by 2.1 sec were acquired. Tumor delineation was performed by an experienced oncologist on T2W images. The models tested and parameters estimated were: the Tofts model ($k_{ep,std}$ and $K^{trans,std}$), the extended Tofts model ($v_p$, $k_{ep,extend}$ and $K^{trans,extend}$), the Brix-Hoffman model ($A_{Brix}$, $k_{ep,Brix}$ and $k_{el}$), the Relative Signal Increase of the first 90 seconds ($RSI_{90}$) and initial Area under the Curve ($iAUC_{90}$) . $R^2$ and Normalized Mutual Information (NMI) were determined for sets of parameter pairs.

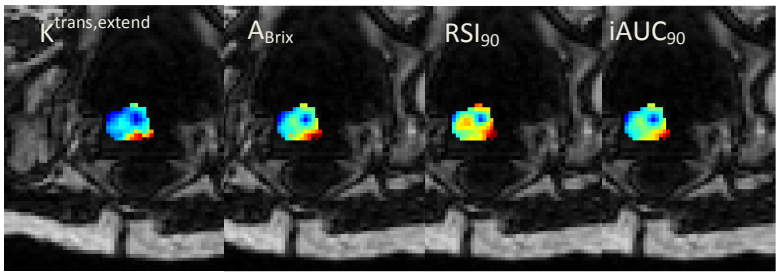


Figure 1A: Four different DCE parameter estimates

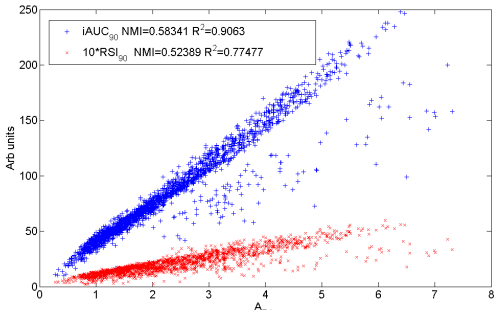


Figure 1B: Woxelvise scatterplot for $iAUC_{90}$ vs $A_{Brix}$ (blue) and $10*RSI_{90}$ vs $A_{Brix}$ (red)

## Results

In Figure 1A an example of the spatial distribution of different modeling parameter is shown. A voxelwise scatterplot of the same data are shown in figure 1B. The $R^2$ value indicates that the 91% of variability of the $iAUC_{90}$ is explained by the $A_{Brix}$ factor if assuming a linear relation between parameters. $R^2$ and NMI for the 24 scans for a subset of parameter are shown in table 1.

| Table 1 | $iAUC_{90}/K^{trans,extend}$ | $A_{Brix}/K^{trans,extend}$ | $iAUC_{90}/A_{Brix}$ | $RSI_{90}/A_{Brix}$ | $A_{Brix}/RSI_{max}$ | $K^{trans,std}/A_{Brix}*k_{ep,Brix}$ |
|---|---|---|---|---|---|---|
| $R^2$ | 0.59±0.19 | 0.58±0.17 | 0.82±0.15 | 0.73±0.17 | 0.83±0.13 | 0.55±0.15 |
| NMI | 0.58±0.15 | 0.57±0.16 | 0.64±0.11 | 0.61±0.13 | 0.61±0.12 | 0.53±0.14 |

## Discussion

The parameters that best describe the same mechanism are $iAUC_{90}$ and $A_{Brix}$ followed by RSI and $A_{Brix}$. The latter correlation might explain the consistent results from [1] and [2]. Also worth noticing is that the often cited correlation [4] between $K^{trans,std}$ and $A_{Brix}*k_{ep,Brix}$ only reaches $R^2$=0.55 in these tumors of advanced cervical cancer. $K^{trans}$ describes the permeability/leakage from the vessels into the interstitium and is determined mostly by the initial slope of the tissue curve. The $A_{Brix}$ and similarly RSI mostly describe the maximum buildup of contrast in the tissue and is related to the extracellular extravascular fraction. Both $K^{trans}$ and $A_{Brix}$ have been shown to correlate with hypoxia and thus radioresistance though they describe different aspects of tumor blood flow.

## Conclusion

Estimation of outcome in patients with advanced cervical cancer by measuring $A_{Brix}$ [2] can potentially be replaced by estimating the much less computationally intensive parameter $iAUC_{90}$ or $RSI_{max}$. This could stimulate broader clinical use of DCE-MRI for estimating outcome in patients with advanced cervical cancer.

[1] Yuh, W., et al, Predicting control of primary tumor and survival by DCE MRI during early therapy in cervical cancer, Invest Radiol, 2009, 44 [2] Halle, C., et al., Hypoxia-induced gene expression in chemoradioresistant cervical cancer revealed by dynamic contrast enhanced MRI, Cancer Res, 2012. 72 [3] Donaldson, S. A comparison of tracer kinetic models for T1-weighted dynamic contrast-enhanced MRI: application in carcinoma of the cervix. Magn Reson Med, 2010, 63 [4] Cho, H. et al, Noninvasive Multimodality Imaging of the Tumor Microenvironment: Registered Dynamic Magnetic Resonance Imaging and Positron Emission Tomography Studies of a Preclinical Tumor Model of Tumor Hypoxia, Neoplasia, 2009, 11.