Effect of accurate T1 calculation on pharmacokinetic analysis of primary breast cancer.

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\textbf{INTRODUCTION}

Dynamic contrast-enhanced MRI (DCE-MRI) is frequently used to detect, diagnose and stage breast cancer\textsuperscript{1}. Several methods of analysing the dynamic data-sets obtained using this technique are still being assessed and compared\textsuperscript{2,3}. One promising method is the use of pharmacokinetic analysis of the contrast agent uptake curve\textsuperscript{4}.

\textbf{MATERIALS AND METHODS}

DCE-MRI was performed on one woman (age 44 years) who presented with a breast cancer in the upper outer quadrant of her right breast exhibiting heterogeneous, spiculated enhancement after contrast administration (see fig. 1). The MR dynamic acquisition consisted of a set of nine 2D fast gradient-echo slices positioned to cover the lesion (which had been previously identified using a 3D hi-res acquisition of both breasts) in the coronal plane with; α = 35\textdegree, TR/TE = 8.3/4.2, bandwidth = 31.2 kHz, FoV = 34x17 cm, 5.0 mm slice thickness (zero spacing), matrix size of 256x256/1 NEX. Forty time points were acquired with a temporal resolution of approximately 10 seconds, an injection of Gd-DTPA being administered at a dose of 0.2 mmol/kg on the fifth temporal frame. The 2D acquisition was chosen in order to give adequate temporal resolution for the model being fitted\textsuperscript{1}. Prior to the dynamic acquisition a set of the same 2D slices were acquired with flip angles of 6, 10 and 35\textdegree in order to calculate an accurate T1 map of the lesion and surrounding tissue. All MR images were obtained using a 1.5 T GE NV/CVi scanner.

T1 values were calculated using the three signal intensity values acquired for the 6, 10 and 35\textdegree scans to perform a Levenberg Marquardt least squares fit to the FLASH equation. Assuming the 6\textdegree image is essentially PD-weighted, the intrinsic T1 value of each pixel may be determined. A gaussian smooth matrix was applied to each of the source images before T1 fitting to compensate motion effects. Firstly, T1 fitting was performed using the assumption that the 2D slice profile was approximately rectangular, therefore simply using 6, 10 and 35\textdegree substituted directly into the FLASH equation. T1 was then recalculated, taking into account any possible effects of a non-rectangular slice profile on the effective flip angle, by numerically integrating the FLASH equation across 100 points through a simulated slice profile. The slice, each of which was fitted to the FLASH equation and then integrated. The slice profile was confirmed using an oscilloscope to be a single lobe truncated sinc pulse with Hanning windowing applied.

\textbf{RESULTS}

Sample T1 maps for both methods are presented in Fig 2. Sample ROI’s were drawn on the T1 maps as shown and the mean T1 values for the ROIs calculated for fat and tumour (as identified using the subtraction image shown in Fig 1) with both methods. These values are presented in table 1. Both T1 maps were used to independently calculate k\textsubscript{trans} and V pixel maps of the breast and tumour. A 3x3x3 search matrix was applied to the 2D nine slice dynamic data set to determine the 3x3x3 pixel volume of mean maximum enhancement. The mean k\textsubscript{trans} and V values were then calculated for this volume for both sets of results and are also presented in table 1. The pharmacokinetic parameters were calculated using a Levenberg Marquardt fitting algorithm implemented in the IDL software package using Toft’s three compartment approach to model contrast uptake\textsuperscript{1}.

\textbf{DISCUSSION}

Using the simple assumption of a rectangular slice profile leads to an underestimation of T1 in fat when compared with the numerical integration method (the expected value is approx. 270 ms\textsuperscript{7}), and a large underestimation of T1 in tumour compared with the numerical integration method. The tumour k\textsubscript{trans} and V values calculated for the 3x3x3 pixel volume show a 32\% increase in k\textsubscript{trans} and a 45\% increase in V using the numerical integration method when compared with the more simple method.

\textbf{CONCLUSION}

Assessing tumour characteristics by assessing changes in pharmacokinetic parameters is now common. An accurate calculation of T1 is shown to be important when assessing tumours using the Tofts approach, however the method of T1 calculation is not commonly quoted in work discussing pharmacokinetic analysis. We have shown that even whilst performing a robust least squares fit to calculate T1, making simple assumptions of slice profile can result in large variations in pharmacokinetic parameters. Without confirming an accurate T1 calculation, one cannot therefore reliably compare pharmacokinetic parameters quoted by different research groups.

\textbf{REFERENCES}


<table>
<thead>
<tr>
<th>Method</th>
<th>Mean T1 of fat (ms)</th>
<th>Mean T1 of tumour tissue (ms)</th>
<th>Mean $k_{\text{trans}}$ (min\textsuperscript{-1})</th>
<th>Mean tumour V (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple method</td>
<td>102</td>
<td>359</td>
<td>0.540</td>
<td>48.1</td>
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<tr>
<td>Numerical integration</td>
<td>231</td>
<td>1060</td>
<td>0.797</td>
<td>73.4</td>
</tr>
</tbody>
</table>

Table 1. Mean T1 relaxation times for fat tissues and tumour tissues (selected using ROIs shown in figure 2) for rectangular slice profile assumption and numerical integration method. Mean $k_{\text{trans}}$ and V values calculated for tumour for both methods.