Quantification Techniques to Minimize the Effects of Native $T_1$ Variation and $B_1$ Inhomogeneity in Dynamic Contrast-Enhanced MRI of the Breast at 3 T

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The variation of the native $T_1$ ($T_{10}$) of different tissues and $B_1$ transmission-field inhomogeneity at 3 T are major contributors of errors in the quantification of breast dynamic contrast-enhanced MRI. To address these issues, we have introduced new enhancement indices derived from saturation-recovery snapshot-FLASH (SRSF) images. The stability of the new indices, i.e., the SRSF enhancement factor ($EF_{\text{SRSF}}$) and its simplified version ($EF_{\text{SRSF}}^0$) with respect to differences in $T_{10}$ and $B_1$ inhomogeneity was compared against a typical index used in breast dynamic contrast-enhanced MRI, i.e., the enhancement ratio (ER), by using computer simulations. Imaging experiments with Gd-DTPA-doped gel phantoms and a female volunteer were also performed. A lower error was observed in the new indices compared to enhancement ratio in the presence of typical $T_{10}$ variation and $B_1$ inhomogeneity. At changes of relaxation rate ($\Delta R_1$) of 8 s$^{-1}$, the differences between a $T_{10}$ of 1266 and 566 ms are $<1, 12,$ and 58%, respectively, for $EF_{\text{SRSF}}, EF_{\text{SRSF}}^0, \text{and } \text{ER}$, whereas differences of 20, 8, and 51%, respectively, result from a 50% $B_1$ field reduction at the same $\Delta R_1$. These quantification techniques may be a solution to minimize the effect of $T_{10}$ variation and $B_1$ inhomogeneity on dynamic contrast-enhanced MRI of the breast at 3 T. Magn Reson Med 67:531–540, 2012. © 2011 Wiley Periodicals, Inc.

Key words: DCE-MRI; high-field MRI; native $T_1$; $B_1$ inhomogeneity

Quantitative analysis may be performed using multi-compartment pharmacokinetic modeling of the DCE-MRI enhancement. To account for the effects of native $T_1$ ($T_{10}$) on enhancement pharmacokinetic modeling, the $T_{10}$ may be measured before the dynamic MRI scanning and incorporated into the pharmacokinetic model (4). However, the disadvantage of performing $T_{10}$ measurements in vivo is that it can be challenging to implement especially in MR centers with little research expertise. Hence, the technique is rarely incorporated into routine clinical breast DCE-MRI. Another drawback of this technique is significant errors can also be introduced into...
the parameters calculated through errors in the $T_{10}$ measurement (5,6). As such a method of measuring signal enhancement that is independent of $T_{10}$ would be beneficial.

At 1.5 T and lower fields, DCE-MRI is typically performed by using a FLASH pulse sequence. This technique produces a good tissue contrast and spatial resolution within an acceptable clinical scanning duration. 3-T MRI is becoming more commonly used in clinical MRI. The main advantage of these high-field scanners is that improvement in image signal-to-noise ratio (SNR). However, the drawback of these scanners is that $B_1$ transmission-field inhomogeneity is increased in the field-of-view (FOV) (7), which causes a significant error in the calculated ER (8) and pharmacokinetic quantifications (9). To minimize the effect of the $B_1$ inhomogeneity in DCE-MRI, a saturation-recovery snapshot-FLASH (SRSF) pulse sequence is used (rather than a pulse sequence (10) for this purpose. Hoffmann et al. (10) used this pulse sequence to improve the temporal resolution of breast DCE-MRI. The technique has also been used to measure the $T_{10}$ of breast tissues (11). At 3 T, this approach has been used by Kim et al. (12) in cardiac imaging. It also has been shown that the SRSF pulse sequence is much less sensitive to the $B_1$ inhomogeneity when calculating ER (13).

The aim of this study was to develop and evaluate enhancement indices that are insensitive both to the variation of tissues’ $T_{10}$ and $B_1$ transmission-field inhomogeneity in DCE-MRI of the breast at 3 T. We propose SRSF using Hoffmann’s method of saturation as the pulse sequence (10) for this purpose.

THEORY

To minimize the effect of $T_{10}$ variations in DCE-MRI quantification, Hittmair et al. (14) proposed an enhancement factor as the index quantified from images acquired using a FLASH pulse sequence. The Hittmair’s enhancement factor (EFHITTMAIR) is given by

$$EF_{HITTMAIR} = \frac{1}{K \cdot TR} \ln \left( \frac{S_{\text{MAX}} - S_{\text{PRE}}}{S_{\text{MAX}} - S_{\text{POST}}} \right),$$  

where $\alpha$ is flip angle, $K$ is a correction factor dependent on $\alpha$, $TR$ is repetition time, $S_{\text{PRE}}$ is precontrast signal, $S_{\text{POST}}$ is postcontrast signal, $k$ is the scanner’s signal amplification factor, and $M_0$ is equilibrium magnetization. This index was derived by approximating the signal intensity ($S$) to the FLASH equation

$$S \approx S_{\text{APPROX}} = S_{\text{MAX}} \left[ 1 - \exp \left( -K \frac{TR}{T_1} \right) \right].$$  

Alternatively, a similar argument can be applied in the case where an SRSF sequence is used (rather than a FLASH sequence as per EFHITTMAIR). In this case, the SRSF signal intensity can be simplified to be

$$S = k \cdot M_0 \left[ 1 - \exp \left( -\frac{T_{\text{REC}}}{T_1} \right) \right] \sin \alpha,$$

where $T_{\text{REC}}$ is the duration between the end of the saturation pulse and the first acquisition pulse in the pulse sequence. For SRSF, a proton density signal ($S_{\text{PD}}$) can be obtained with $T_{\text{REC}} > T_1$. Hence, the signal can be applied as an approximation of the maximum signal intensity, i.e., $S_{\text{PD}} \approx S_{\text{MAX}}$. By comparing Eq. 4 with Eq. 3, the enhancement factor using SRSF (EF_SRSF) can now be determined as follows:

$$EF_{SRSF} = \frac{1}{T_{\text{REC}}} \ln \left( \frac{S_{\text{PD}} - S_{\text{PRE}}}{S_{\text{PD}} - S_{\text{POST}}} \right).$$  

The linear relationship between EF_SRSF and $\Delta R_1$ can be shown as follows. By using the SRSF pulse sequence, precontrast and postcontrast signals are given by

$$S_{\text{PRE}} = S_{\text{MAX}} \left[ 1 - \exp \left( -T_{\text{REC}} \cdot R_{1,\text{PRE}} \right) \right]$$  

and

$$S_{\text{POST}} = S_{\text{MAX}} \left[ 1 - \exp \left( -T_{\text{REC}} \cdot R_{1,\text{POST}} \right) \right].$$

The difference between the maximum signal and precontrast and postcontrast signals are given by

$$S_{\text{MAX}} - S_{\text{PRE}} = S_{\text{MAX}} \cdot \exp \left( -T_{\text{REC}} \cdot R_{1,\text{PRE}} \right)$$  

and

$$S_{\text{MAX}} - S_{\text{POST}} = S_{\text{MAX}} \cdot \exp \left( -T_{\text{REC}} \cdot R_{1,\text{POST}} \right).$$

By substituting Eqs. 8 and 9 into Eq. 5

$$EF_{SRSF} = \left( R_{1,\text{POST}} - R_{1,\text{PRE}} \right) = \Delta R_1.$$

Equation 10 shows that EF_SRSF can be directly used to quantify $\Delta R_1$ (and thus contrast agent uptake) in a manner which is independent of $T_{10}$.

This enhancement factor and $\Delta R_1$ relationship can be further simplified. By expanding with a Taylor series, for $T_{\text{REC}} < T_1$, we have

$$\exp \left( -\frac{T_{\text{REC}}}{T_1} \right) \approx 1 - \frac{T_{\text{REC}}}{T_1} = 1 - T_{\text{REC}} \cdot R_1.$$  

Thus, by substituting Eq. 11 into Eq. 4, the signal intensity can be approximated as follows:

$$S \approx k \cdot M_0 \frac{T_{\text{REC}}}{T_1} \sin \alpha.$$  

For $T_{\text{REC}} < T_1$, $\Delta R_1$ can be determined by normalizing the signal enhancement to the proton density signal. This index that is denoted as EF’_SRSF in this article is a simplified version of the EF_SRSF and given by

$$EF’_{SRSF} = \frac{1}{T_{\text{REC}}} \left( \frac{S_{\text{POST}} - S_{\text{PRE}}}{S_{\text{PD}}} \right) \approx \Delta R_1.$$  

In theory, this simple index could be implemented on a typical image viewing workstation. The indices evaluated in this article are summarized in Table 1.

For the SRSF pulse sequence to work efficiently in the presence of $B_1$ transmission-field inhomogeneity, the
Table 1
Enhancement Indices with Their Respective Pulse Sequence

<table>
<thead>
<tr>
<th>Index</th>
<th>Equation</th>
<th>Pulse sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enhancement ratio</td>
<td></td>
<td>FLASH</td>
</tr>
<tr>
<td>Hittmair’s enhancement factor</td>
<td>( \text{ER} = \frac{\text{S}<em>{\text{POST}} - \text{S}</em>{\text{PRE}}}{\text{S}_{\text{PRE}}} )</td>
<td>FLASH</td>
</tr>
<tr>
<td>SRSF enhancement factor</td>
<td>( \text{EF}<em>{\text{HITTMAIR}} = \frac{1}{\text{TR}} \ln \left( \frac{\text{S}</em>{\text{MAX}} - \text{S}<em>{\text{PRE}}}{\text{S}</em>{\text{PRE}} - \text{S}_{\text{POST}}} \right) )</td>
<td>SRSF</td>
</tr>
<tr>
<td>Simplified SRSF enhancement factor</td>
<td>( \text{EF}<em>{\text{SRSF}} = \frac{1}{\text{REC}} \ln \left( \frac{\text{S}</em>{\text{POST}} - \text{S}<em>{\text{PRE}}}{\text{S}</em>{\text{POST}} - \text{S}_{0}} \right) )</td>
<td>SRSF</td>
</tr>
</tbody>
</table>

The effects of \( B_1 \) inhomogeneity on enhancement index were performed by simulating DCE-MRI data, as above, and using RF pulses that were 50 and 150% of their nominal pulse angles. This was done for the imaging pulses and for, the SRSF sequence, the saturation pulses. Again, ER, EF_{SRSF}, and EF’_{SRSF} were calculated.

For the quantification of EF_{SRSF} and EF’_{SRSF} using the SRSF pulse sequence, a longer scanning time is expected. To minimize the scanning time by using this pulse sequence, a short \( T_{\text{REC}} \) both in the \( T_1 \)-weighted proton density–weighted image acquisitions is desirable. Hence, the relationship between the indices and \( D_R \) was evaluated by using different \( T_{\text{REC}} \). All computer simulations were performed using Matlab (Mathworks, Inc., Natick, USA).

**Imaging Experiments**

To validate the computer simulations, a series of imaging experiments were performed on a set of \( T_1 \) gel phantoms, which were prepared using methods used by Walker et al. (18) and Waiter and Foster (19). These phantoms represent typical \( T_1 \) values of the precontrast and postcontrast breast tissues at 3 T (20). \( T_1 \) values were determined using inversion-recovery fast spin-echo (IR-FSE) pulse sequence. Values of \( T_1 \) and \( S_0 \) were estimated by fitting the following function to the observed signal intensity:

\[
S = S_0 \left[ 1 - 2 \exp \left( - \frac{T_{\text{REC}}}{T_1} \right) \right],
\]

where \( S_0 \) is the signal for \( T_{\text{REC}} > T_1 \).

To achieve the effective saturation effect in the presence of \( B_1 \) inhomogeneity in the SRSF pulse sequence, Hoffmann’s method of saturation pulses (10) was used. The technique uses a series of six nonselective 90° hard RF pulses separated by a decreasing duration of delays and spoiling gradients. The saturation scheme was applied immediately after the readout pulses.

Using ImageJ (National Institute of Health, Bethesda, USA), signal intensity values were measured from regions-of-interest in each gel phantoms in the central (10th) slice of a 3D data set. Measurement of the effect of \( T_{10} \) variation on the enhancement indices was done by assuming that different \( T_{10} \) (and hence \( S_{\text{PRE}} \)) correspond to the gel phantoms with the longer \( T_1 \) values and then assuming that the remaining phantoms with \( T_1 < T_{10} \) represent tissues with shorter postcontrast \( T_1 \) values. The proton density signal (\( S_{100} \)) was determined by averaging the signal intensities of all the gel phantoms in the proton density signal–weighted images. From these signal values, ER (using \( T_1 \)-weighted FLASH), EF_{SRSF}, and EF’_{SRSF} (using \( T_1 \)-weighted and proton density–weighted SRSF) were calculated. Changes in relaxation rate (\( D_R \)) for the gel phantoms were calculated using Eq. 14. The effect of \( B_1 \) inhomogeneity on the measurement of ER,
EF$_{SRSF}$ and EF$^0_{SRSF}$ was then evaluated. This was done by imaging the same phantoms using RF pulses that were 50 and 150% of their nominal pulse angles as for the simulations (i.e., 35° for FLASH, and 90° preparation and 12° read-out pulses for SRSF sequences).

For comparison, SRSF with a 90° hard RF pulse followed by spoiling gradients before the read-out scheme was also performed. For this study, the $B_1$ inhomogeneity was applied only in the read-out scheme. Hence, an SRSF sequence with completely effective saturation was assumed being acquired. Again, ER, EF$_{SRSF}$, and EF$^0_{SRSF}$ were calculated. All imaging experiments were performed using a Philips Achieva X-series 3.0-T scanner and a transmit-receive birdcage quadrature head coil (Philips

Table 2
Imaging Parameters Used in the Imaging Experiments on Gel Phantoms

<table>
<thead>
<tr>
<th>Parameter</th>
<th>IR-FSE</th>
<th>SRSF</th>
<th>FLASH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technique</td>
<td>2D</td>
<td>3D</td>
<td>3D</td>
</tr>
<tr>
<td>$T_{REC}$ (ms)</td>
<td>50, 150, 350, 700, and 1400</td>
<td>100 ms</td>
<td>Nil</td>
</tr>
<tr>
<td>$T_{1}$-weighted and 2000 (PD-weighted)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\alpha$ (°)</td>
<td>90</td>
<td>12</td>
<td>35</td>
</tr>
<tr>
<td>TR (ms)</td>
<td>7000</td>
<td>4.1</td>
<td>10</td>
</tr>
<tr>
<td>TE (ms)</td>
<td>18</td>
<td>2.3</td>
<td>2.3</td>
</tr>
<tr>
<td>Voxel size (mm)</td>
<td>$1 \times 1 \times 1$</td>
<td>$1 \times 1 \times 1$</td>
<td>$1 \times 1 \times 1$</td>
</tr>
<tr>
<td>FOV (mm)</td>
<td>200 $\times$ 200</td>
<td>200 $\times$ 200</td>
<td>200 $\times$ 200</td>
</tr>
<tr>
<td>No. of slices</td>
<td>1</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Echo-train-length</td>
<td>6</td>
<td>50</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 3
Imaging Parameters Used in the Imaging on a Volunteer and the Respective Imaging Time

<table>
<thead>
<tr>
<th>Parameter</th>
<th>$T_{1}$-w SRSF</th>
<th>PD-w SRSF</th>
<th>$T_{1}$-w FLASH</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_{REC}$ (ms)</td>
<td>100</td>
<td>2000</td>
<td>Nil</td>
</tr>
<tr>
<td>$\alpha$ (°)</td>
<td>12</td>
<td>12</td>
<td>35</td>
</tr>
<tr>
<td>TR (ms)</td>
<td>4.4</td>
<td>4.4</td>
<td>11</td>
</tr>
<tr>
<td>TE (ms)</td>
<td>2.3</td>
<td>2.3</td>
<td>2.3</td>
</tr>
<tr>
<td>Voxel size (mm)</td>
<td>$1 \times 1 \times 1$</td>
<td>$1 \times 1 \times 1$</td>
<td>$1 \times 1 \times 1$</td>
</tr>
<tr>
<td>FOV (mm)</td>
<td>340 $\times$ 340</td>
<td>340 $\times$ 340</td>
<td>340 $\times$ 340</td>
</tr>
<tr>
<td>No. of slices</td>
<td>150</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>Echo-train-length</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>SENSE</td>
<td>Yes$^a$</td>
<td>Yes$^a$</td>
<td>Yes$^a$</td>
</tr>
<tr>
<td>Imaging time</td>
<td>51 s</td>
<td>5 min 18 s</td>
<td>1 min 8 s</td>
</tr>
</tbody>
</table>

$^a$A SENSE factor of 2 was applied in both the right-left and foot-head directions.

FIG. 1. The effect of different native $T_1$s ($T_{10}$) on enhancement indices, where (a) ER ($\alpha = 35°$ and TR = 10 ms), (b) EF$\text{HITMAIR}$ ($\alpha = 35°$, TR = 10 ms, and $K = 3.05$), (c) EF$_{SRSF}$ and (d) EF$^0_{SRSF}$. For (c) and (d), $\alpha = 12°$, $T_{REC}$ ($T_1$-weighted) = 100 ms, and $T_{REC}$ (PD-weighted) = 2000 ms were used.
Healthcare, Best, The Netherlands). The head coil was used instead of breast coil because of its ability to produce a homogeneous $B_1$ transmission field across a transaxial section through its center (8). Hence, all phantoms were assumed to be subject to the same amplitude of $B_1$ transmission field. The parameters used in the imaging experiments are given in Table 2. To determine the noise (uncertainty) for the images produced using different imaging techniques, the standard deviation from four regions-of-interest was measured outside the gel phantoms in the image (i.e., in air). The SNR was calculated by dividing the mean signal intensity of the shortest $T_1$ gel phantom with the average noise value across the four regions-of-interest. The ratios between the enhancement indices and the uncertainty were then calculated.

To simulate the clinical situation, the $T_1$-weighted SRSF, proton density–weighted SRSF, and $T_1$-weighted FLASH 3D imaging were also performed on a healthy female volunteer after ethical approval by a local ethics committees, and informed consent was obtained. The subject was positioned prone and head first inside the scanner and imaged axially with a seven-channel sensitivity-encoding (SENSE) breast coil (Philips Healthcare, Best, The Netherlands). Imaging parameters used are given in Table 3.

**RESULTS**

**Computer Simulations**

The effect of $T_{10}$ variation on ER, $E_{HITTMAIR}$, $E_{FRS}$, and $E_{SRSF}$ is shown in Fig. 1. Here, $\Delta R_1$ was assumed to be directly proportional to the contrast agent uptake within the tissue. In theory, an enhancement index that is insensitive to the $T_{10}$ variation will have the same curve of enhancement versus $\Delta R_1$ regardless of the value of $T_{10}$. The closer the curves lay to each other on Fig. 1, the less the index is influenced by the $T_{10}$ variation. Hence, from the figure, $E_{HITTMAIR}$ (both using a FLASH sequence) are significantly influenced by the $T_{10}$ variation compared to ER. The range of $\Delta R_1$ was chosen to cover a wide range of $\Delta R_1$ expected in breast cancers.

The effect of $B_1$ inhomogeneity on the enhancement indices is shown in Fig. 2. The closer the curves lay to each other on Fig. 2, the less the index is affected by the $B_1$ inhomogeneity. Hence, $ER$ and $E_{HITTMAIR}$ (both using $T_{REC}$) are much less sensitive to $T_{10}$ variation compared to ER. The range of $\Delta R_1$ was chosen to cover a wide range of $\Delta R_1$ expected in breast cancers.

Figure 3 shows the relationship between the SRSF enhancement factors and $\Delta R_1$ by using different proton density–weighted $T_{REC}$. The closer the curve to the identity line shows more similarity between the index and
1. In general, a better index and \( \Delta R_1 \) value similarity can be obtained by using a longer \( T_{REC} \) in proton density image acquisition. However, for the range of the proton density \( T_{REC} \) used in the simulation, the effect of shorter \( T_{REC} \) to the index-\( \Delta R_1 \) identity is minimal especially in the calculation of \( EF^0_{SRSF} \). The index-\( \Delta R_1 \) mismatch is more prevalent at a smaller \( \Delta R_1 \) range.

The effect of using different \( T_1 \)-weighted \( T_{REC} \) is shown in Fig. 4. A very small difference was observed when different \( T_1 \)-weighted \( T_{REC} \) were used to calculate \( EF_{SRSF} \). However, for \( EF_{SRSF} \), a significant decrease in index-\( \Delta R_1 \) identity was observed for a longer \( T_{REC} \).

Imaging Experiments

By using 2D IR-FSE pulse sequence, the \( T_1 \) values for the gel phantoms were found to be 89, 180, 366, 559, 800, 962, and 1266 ms. These values have a good correlation with breast tissue \( T_1 \) at 3 T (19).

Figure 5a,b shows the effect of a variation of \( T_{10} \) on \( EF_{SRSF} \) and \( EF^0_{SRSF} \). Both indices were calculated from images acquired by using Hoffmann’s SRSF. ER calculated by using FLASH images is shown in Fig. 5c as a comparison. The figures show that the effect of a variation in \( T_{10} \) on \( EF_{SRSF} \) and \( EF^0_{SRSF} \) is minimal, whereas ER is significantly affected by the \( T_{10} \) variation. For example at \( \Delta R_1 \) of 8 s\(^{-1} \), the difference between ER calculated using \( T_{10} \) values of 1266 and 566 ms is 58%. However, \(<1\) and 12% differences were observed for \( EF_{SRSF} \) and \( EF^0_{SRSF} \), respectively.

Figure 6a,b, respectively, shows the effect of \( B_1 \) inhomogeneity on the \( EF_{SRSF} \) and \( EF^0_{SRSF} \) calculated using Hoffmann’s SRSF images. The indices calculated using SRSF with an effective 90° saturation pulse are shown in Fig. 6c,d, whereas ER using FLASH sequence images is shown in Fig. 6e as comparison. From the figures, the effect of \( B_1 \) inhomogeneity on \( EF_{SRSF} \) and \( EF^0_{SRSF} \) calculated from images obtained by using Hoffmann’s SRSF is much less in comparison to the common ER (with FLASH sequence). At a \( \Delta R_1 \) of 8 s\(^{-1} \), a 50% reduction in the \( B_1 \) field reduces the ER by 51%, whereas for \( EF_{SRSF} \) and \( EF^0_{SRSF} \) the index increases by 20 and 8%, respectively. Theoretically, the enhancement indices are unaffected by the \( B_1 \) error if a perfect saturation can be achieved in the saturation scheme of the SRSF sequence (Fig. 6c,d). Note that the values of ER, \( EF_{SRSF} \) and

\[ EF^0_{SRSF} \]
EF\textsubscript{SRSF} at \( \Delta R_1 = 8 \text{ s}^{-1}, T_{10} = 1266 \text{ ms} \) and \( B_1 = 100\% \) are 7.1, 8.2 and 5.2 respectively.

The means and uncertainties of the signal intensities and \( \text{EF}_{\text{SRSF}}, \text{EF}^{'}_{\text{SRSF}}, \) and \( \text{ER} \) are given in Table 4. By using the parameters used in the phantom experiments, the SNR (given by the mean/uncertainty ratio) for \( T_1\)-weighted imaging using Hoffmann’s SRSF sequence is slightly lower compared to imaging using FLASH sequence. However, the mean/uncertainty ratios of \( \text{EF}_{\text{SRSF}} \) and \( \text{EF}^{'}_{\text{SRSF}} \) are substantially higher compared to \( \text{ER} \). This is due to the higher SNR of the \( S_{PD} \) signals acquired using the SRSF pulse sequence.

Figure 7 shows typical images of the breast for \( T_1\)-weighted SRSF, proton density–weighted SRSF, and FLASH pulse sequences acquired on a healthy volunteer.

DISCUSSION

In DCE-MRI of the breast, \( \text{ER} \) calculated using a FLASH pulse sequence is a commonly used enhancement index to evaluate breast cancers. We have shown that this index is significantly affected by the variation of tissue’s \( T_{10} \). Tissues with a short \( T_{10} \) have a low \( \text{ER} \) values and vice versa (Fig. 1a). This index can be minimized by using \( \text{EF}_{\text{HITTMAIR}} \), which is an alternative index introduced by Hittmair et al. (Fig. 1b) (14). Like \( \text{ER} \), \( \text{EF}_{\text{HITTMAIR}} \) is also calculated on images acquired using a FLASH pulse sequence. However, the main limitation of this index is that it is significantly affected by \( B_1 \) inhomogeneity (Fig. 2b), which is a significant problem at 3 T. It has been shown that the \( B_1 \) field can be reduced to about one-half of the nominal field in one side of the breast at 3 T (7,8). However, contrary to the \( \text{ER} \), a lower \( B_1 \) increases the \( \text{EF}_{\text{HITTMAIR}} \) and vice versa.

To minimize the effect of both the variation of tissue’s \( T_{10} \) and the \( B_1 \) inhomogeneity in DCE-MRI at 3 T, we propose a new approach to quantify the contrast agent uptake. This technique involves new enhancement indices namely \( \text{EF}_{\text{SRSF}} \) and \( \text{EF}^{'}_{\text{SRSF}}, \) which were calculated on images acquired using an SRSF pulse sequence. \( \text{EF}_{\text{SRSF}} \) is a modification of \( \text{EF}_{\text{HITTMAIR}} \) specifically developed to be used with SRSF pulse sequence. Like Hittmair’s index, the \( \text{EF}_{\text{SRSF}} \) requires the calculation of natural log, which may be difficult to perform using a standard clinical workstation. Therefore, this index is more likely to be used by the manufacturer as part of their analysis product or by research personnel in the viewing or independent workstation. As an alternative, we also introduced another index called \( \text{EF}^{'}_{\text{SRSF}}, \) which is simpler to implement on a typical viewing workstation. Both of these indices have much less sensitivity to the variation of \( T_{10} \) and \( B_1 \) inhomogeneity compared to the \( \text{ER} \). This is demonstrated in this work by computer simulation (Figs. 1 and 2) and imaging experiments (Figs. 5 and 6). Like \( \text{EF}_{\text{HITTMAIR}}, \) both indices require the acquisition of \( T_1\)-weighted and proton density–weighted images.

We used Hoffmann’s method of preparation scheme (10) to produce saturation in the presence of \( B_1 \) inhomogeneity. By using this technique much less error in the \( \text{EF}_{\text{SRSF}} \) and \( \text{EF}^{'}_{\text{SRSF}} \) was observed (Fig. 6a,b) compared to the \( \text{ER} \) acquired using the FLASH sequence (Fig. 6e) in the presence of \( B_1 \) inhomogeneity. The error in \( \text{EF}_{\text{SRSF}} \) and \( \text{EF}^{'}_{\text{SRSF}} \) is mainly contributed by the imperfection in Hoffmann’s saturation technique in producing a perfect saturation in the presence of \( B_1 \) inhomogeneity. Less error in both indices can be obtained if a better saturation scheme is used in the SRSF pulse sequence (Fig. 6c,d).
Another advantage of EF SRSF and EF' SRSF compared to EF HITTMAIR is that the indices do not require the correction factor $K$ in the calculation (Eq. 2). Because the factor is dependent on the flip angle (and hence the $B_1$), less error in the indices can be obtained in the presence of $B_1$ inhomogeneity by omitting the $K$ factor. Furthermore, although it was not investigated in this article, a similar argument indicates that EF SRSF and EF' SRSF will not be affected by slice profile effects in 2D implementations of the methods, as compared to EF HITTMAIR which may be. As shown by the simulations of Figs. 1c and 2c, EF SRSF equals $\Delta R_1$. This is confirmed to a good approximation by the experimental data of Figs. 5a and 6a. Hence, the index can be used as a direct quantification of the contrast agent uptake. This is a major benefit of EF SRSF. However, unlike EF SRSF, EF' SRSF is not linear with the

![Image of graphs showing the effect of $B_1$ transmission-field inhomogeneity on the enhancement indices using two different pulse sequences, where (a) EF SRSF using Hoffmann's SRSF, (b) EF' SRSF using Hoffmann's SRSF, (c) EF SRSF using SRSF with an effective 90° saturation pulse, (d) EF' SRSF using SRSF with an effective 90° saturation pulse, and (e) ER using FLASH. The dotted lines are the fitted lines of the plotted enhancement indices.](image-url)
\( \Delta R_1 \) (Figs. 1d and 2d). Hence, \( E \) \( F \) \( S \) \( R \) \( S \) \( F \) \( S \) \( F \) \( S \) should be used like ER and \( E \) \( F \) \( H \) \( T \) \( M \) \( A \) \( R \) (with \( \alpha = 35^\circ \)) where standard acquisition parameters must be used during imaging so that the index can be compared between different patients, scanners, and imaging centers.

Images acquired on a volunteer show that the \( T_1 \)-weighted image quality is comparable to that obtained with typical FLASH parameters (see Fig. 7). Even though the SNR produced in the \( T_1 \)-weighted images was slightly lower compared to the FLASH, the ratio between the enhancement index and the uncertainty calculated from the noise levels is substantially higher than the ER (see Table 4). This is due to the higher SNR of the proton density images acquired using SRSF pulse sequence. From our experience of imaging on several volunteers, the image quality in the proton density images is not substantially affected by the patient motion (assuming that the subject lies in prone position).

The main drawback of the new DCE-MRI quantification approach is the longer total scanning time is required compared to the common technique, i.e., ER with FLASH. This time penalty is contributed by an additional scanning protocol to acquire the proton density–weighted images for the calculation of the indices. Furthermore, the SRSF pulse sequence requires a delay between the saturation pulse and the image acquisition. A much longer recovery time is needed for the acquisition of proton density–weighted images (\( T_{REC} \geq T_1 \)) compared to \( T_1 \)-weighted images (\( T_{REC} < T_1 \)).

The SRSF imaging time can be reduced by optimizing the acquisition parameters of the pulse sequence, e.g., by using a very short TR. This is performed by using a very low flip angle in the image acquisition. Because the contrast in the SRSF pulse sequence is mainly contributed by the \( T_1 \) and \( T_{REC} \) (Eq. 4), multiple signal acquisitions (echo train) can be performed after a saturation pulse. This is useful to reduce the imaging time. For example, we performed 50 signal acquisitions (echo-train-length) after the saturation scheme in the SRSF experiment. A longer echo-train-length will reduce the time further at the cost of increasing the index error.

Another time reduction approach is to use the shortest \( T_{REC} \) as possible both in the \( T_1 \)- and proton density–weighted image acquisitions. By using the imaging parameters used in this work (see Table 3), the scanning time for the \( T_1 \)-weighted imaging using the SRSF pulse sequence is shorter (by a quarter) than the typical FLASH. However, a much longer time is required for the proton density–weighted imaging (>5 min). This is due to the long \( T_{REC} \) is necessary to produce the proton density–weighted signals. Decreasing \( T_{REC} \) in proton density image acquisition will reduce the index-\( \Delta R_1 \) identity relationship (see Fig. 3). This effect is caused by the fact that there is more \( T_1 \) weighting component introduced in the image and so will also influence the indices calculated. A shorter \( T_{REC} \) in the \( T_1 \)-weighted image acquisition will improve the index-\( \Delta R_1 \) identity relationship (Fig. 4), but it will reduce the SNR. Therefore, an optimum \( T_{REC} \) for both the \( T_1 \)- and proton density–weighted

<table>
<thead>
<tr>
<th>Pulse sequence</th>
<th>Signal or enhancement index</th>
<th>Mean</th>
<th>Uncertainty</th>
<th>Mean/Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoffmann’s SRSF</td>
<td>( S_{PRE} )</td>
<td>( 1.25 \times 10^5 )</td>
<td>( 1.32 \times 10^4 )</td>
<td>9.53</td>
</tr>
<tr>
<td></td>
<td>( S_{POST} )</td>
<td>( 1.09 \times 10^6 )</td>
<td>( 1.32 \times 10^4 )</td>
<td>83.28</td>
</tr>
<tr>
<td></td>
<td>( S_{PD} )</td>
<td>( 1.60 \times 10^6 )</td>
<td>( 1.35 \times 10^4 )</td>
<td>118.14</td>
</tr>
<tr>
<td></td>
<td>( E_{FRSFS} )</td>
<td>10.80</td>
<td>0.10</td>
<td>103.85</td>
</tr>
<tr>
<td></td>
<td>( E_{FRSF} )</td>
<td>6.07</td>
<td>0.04</td>
<td>151.75</td>
</tr>
<tr>
<td>FLASH</td>
<td>( S_{PRE} )</td>
<td>( 1.84 \times 10^4 )</td>
<td>( 1.48 \times 10^3 )</td>
<td>12.37</td>
</tr>
<tr>
<td></td>
<td>( S_{POST} )</td>
<td>( 1.77 \times 10^5 )</td>
<td>( 1.48 \times 10^3 )</td>
<td>119.25</td>
</tr>
<tr>
<td></td>
<td>( ER )</td>
<td>8.60</td>
<td>0.70</td>
<td>12.30</td>
</tr>
</tbody>
</table>

FIG. 7. Typical images of the breast acquired on a volunteer using: (a) \( T_1 \)-weighted Hoffmann’s SRSF, (b) proton density–weighted Hoffmann’s SRSF, and (c) \( T_1 \)-weighted FLASH pulse sequences.
image acquisitions should be used. For example, in this work, we used $T_{REC}$ of 100 and 2000 ms for the T$_1$-weighted and proton density–weighted imaging, respectively.

The extra time penalty due to performing the proton density–weighted imaging is compensated by avoiding imaging to measure the tissues’ $T_{10}$ as commonly performed in pharmacokinetics studies. Note that it is possible to improve the index/uncertainty ratio for ER to the same level of EF$_{SRSF}$ and EF$^{SRSF}$ with this extra time. This can be done by improving the SNR in the precontrast $T_1$-weighted FLASH, e.g., by using several numbers of signals averaging in the imaging. Other fast MRI approaches such as SENSE (21) (as implemented in the in vivo imaging), dynamic keyhole (22), and compressed sensing (23) may also be beneficial to reduce the scanning time even further.

**CONCLUSION**

New enhancement indices, i.e., EF$_{SRSF}$ and EF$^{SRSF}$, to quantify contrast agent uptake in DCE-MRI of the breast have been tested. These indices were calculated from $T_1$ and proton density–weighted images acquired using a SRSF pulse sequence. Compared to conventional enhancement indices that compare signal change against pre-enhancement signal values, these new indices are considerably less affected by errors caused by variations in the $T_{10}$ of different tissues and by $B_1$ transmission-field inhomogeneity. The methods are also expected to have applications in other organs and at field strengths at 3 T and above.

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