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# The Effect of Repetition Time on the Maximum Linear Relationship Between Contrast Agent Concentration and Signal Intensity on T1-Weighted Image Using Inversion Recovery (IR) Sequence

**Background/Objective:** The relaxation time T1 depends on the concentration of paramagnetic contrast agent. To calculate perfusion parameters from dynamic contrast-enhanced MRI acquisitions, measurement of the concentration is necessary. At low concentrations, the relationship between changes in 1/T1 and concentration can be considered to be linear. To maximize the concentration, and hence the signal to noise ratio (SNR) in perfusion images, the range of this linearity should be known. This work studied the effect of two repetition times (TR) on the linearity using inversion recovery Turbo Fast Low Angle Shot (TurboFLASH) sequences at different effective inversion times (TI).

**Patients and Methods:** To assess the relationship between signal intensity (SI) and concentration, a water-filled phantom containing vials of different concentrations of Gd-DTPA (0 to 19.77 mmol/L) was used. The mean SI was obtained in the region of interest using T1-weighted images. Coil non-uniformity was corrected on SI.

**Results:** This study shows that an increase in TR is associated with a decrease in the maximum linear relationship between effective TI and concentration where the square correlation ($R^2$) between corrected SI and concentration were equal to 0.95 or 0.99.

**Conclusion:** In spite of TR = 2 or 3s and $r^2$= 0.95 or 0.99 at a typical effective TI = 800ms, which is normally used for in vivo perfusion, the maximum linearity is about twice that previously reported (i.e. 0.8mmol/L) for measuring the perfusion parameters. The higher dose will improve the SNR in perfusion images.

Keywords: Inversion Recovery, T1-Weighted Image, Signal Intensity, Inversion Time, Repetition Time

## Introduction

Different investigations suggest that perfusion parameters may be assessed by studying signal intensity (SI) changes after the first pass of a paramagnetic contrast medium through tissue.[1-2]

Changes in signal intensity depend on the magnetic susceptibility of contrast agent, the magnetic field strength, the pulse sequence parameters, the dose of contrast agent, the injection rate and bolus volume, the cardiac output and blood volume, and the topology of tissue.[3]

MRI is not able to measure the concentration of contrast agent directly; it is measured indirectly from signal intensity. Therefore, the resulting signal intensity time curves should be converted into concentration time curves.[4]

At low concentrations, the relationship between changes in signal intensity and concentration may be considered to be linear. To maximize the

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concentration, and hence signal to noise ratio in perfusion images, the range of this linearity must be known. Different papers suggested different values for maximum linearity between SI and concentration in the stationary state.[5-7]

The effect of inversion time (TI) on maximum linearity on T1 weighted images for measuring perfusion with MRI was investigated in the previous study by use of the center-out phase-encoding acquisition.[8] This work studied the effect of two repetition times (TR) on the maximum linearity using the linear phase-encoding acquisition[9] on IR turbo fast low-angle shot (TurboFLASH) sequence at different effective TIs.

## Materials and Methods

For T1-weighted monitoring of contrast agent a number of T1-weighted sequences are available.[10] The standard inversion recovery sequence, which is dependent on TI and repetition time (TR), is described by the following equation[8]

$$S(t) = S_0\left(1 - 2\exp\left(-TI\left(\frac{C(t)}{K} + \frac{1}{T1_{Pre}}\right)\right) + \exp\left(-TR\left(\frac{C(t)}{K} + \frac{1}{T1_{Pre}}\right)\right)\right) \quad (1)$$

in which S(t) is the signal intensity after administration of contrast agent and $S_0$ is the observed signal intensity in the absence of any magnetization preparation pre pulses or contrast agent. T1(t) is the longitudinal relaxation time at time t after contrast application and $T1_{Pre}$ is the longitudinal relaxation time at time t before contrast application. C(t) is the concentration of contrast agent at time t. K is a constant that depends on the contrast media.Figure 1 shows schematic representation of the inversion recovery gradient-echo TurboFLASH sequences.

To assess the relationship between signal intensity (SI) and concentration in stationary vials, a phantom was designed to hold vials containing either different or constant concentrations of the contrast agent (Fig. 2).

One of the major sources of image non-uniformity in the MR scanner is the radio frequency (RF) coil inhomogeneity.[11] Therefore, for measuring the accurate SI of an image, the response of the RF coils should be uniform. The vials of constant concentration were used to measure coil non-uniformity. The vials of different concentrations were used to measure the relationship between SI and concentration.

The phantom of different concentrations consisted of 25 vials (glass tube, inner diameter approximately 15 mm filled with different concentrations of Gd-DTPA (Magnevist, Schering Health Care Ltd, West Sussex, UK). The concentration of Gd-DTPA varied between 0 and 19.77 mmol/L (0.00, 0.30, 0.45, 0.60, 0.75, 0.90, 1.20, 1.50, 1.80, 2.10, 2.39, 2.69, 2.99, 3.28, 3.58, 3.98, 4.96, 5.95, 7.93, 9.90, 13.85 and 19.77 mmol/L).

Clinical head and neck coil was used with the phantom. The vials were set vertically and the axes of the vials were perpendicular to the image plane (coronal image).

Two experiments were performed, one using the vials with different concentrations and one using the vials of constant concentration.

The vials in the phantom with constant concentration (1.20 mmol/L) were placed in exactly the same positions of the vials with different concentrations.

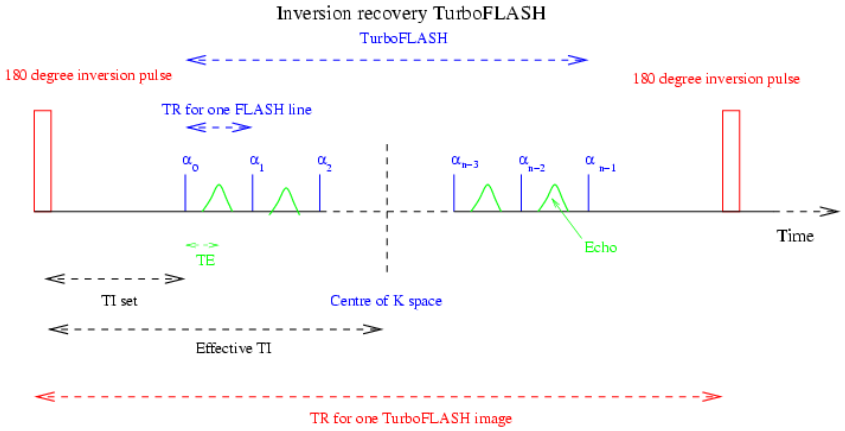


**Fig. 1.** Inversion recovery gradient-echo TurboFLASH for one image. This is an inversion recovery TurboFLASH with n α pulses, where the n/2th line traverses the centre of K space (for Linear Phase-Encoding). "TI set" is the time between 180° inversion pulse and the first α excitation pulse. The effective TI is the time from the inversion pulse to the mid line of K space n/2th). TE and TR are the echo time and repetition time respectively. Imaging gradients are not shown in this diagram.

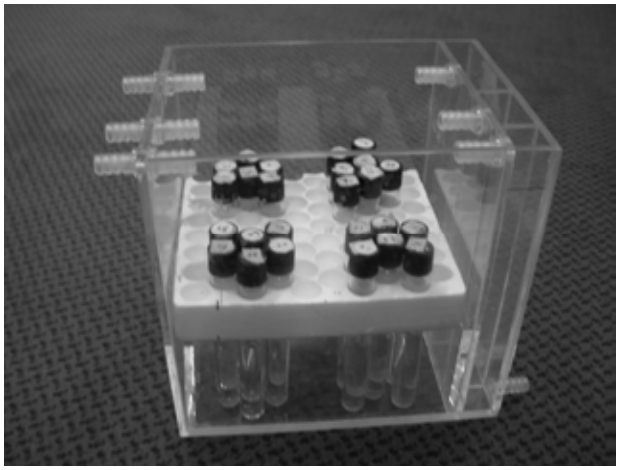

**Fig. 2.** Phantom with different concentrations placed inside the head and neck coil.

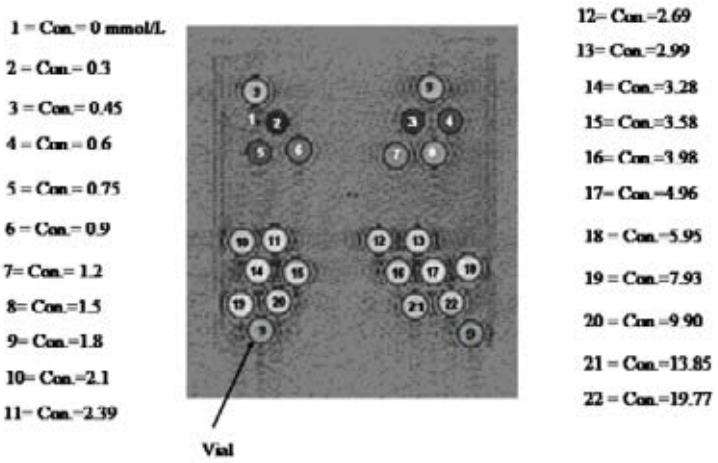


**Fig. 3.** Coronal image of the phantom. The position of different concentrations inside the vials are evident.

The non-uniformity of the coil was calculated from each vial with constant concentration and it was normalized to give a correction factor. To calculate the corrected SI for different concentrations, the SI of each vial was multiplied by its correction factor.

The phantom was positioned within the coil. All studies were carried out using a 1.5-T clinical MR scanner (Vision, Siemens Medical, Erhlangen, Germany). T1-weighted TurboFLASH images were used to measure signal intensity in the vials with different and constant concentration.

The TurboFLASH imaging parameters were as follows:

matrix size, 128×128; time for one FLASH line, 8.5 ms; echo time [TE], 4 ms; effective inversion time [TI] was varied between 644 and 1944 ms; pixel size, 2×2 mm. The images were acquired (TR) every 2 and 3 seconds with a slice thickness of 10 mm and a flip angle of 15˚.

The image data were transferred from the MR scanner to a Unix workstation. The image processing software interactive data language (IDL, Research Systems, Inc. http://www.rsinc.com) was used for processing.

Programs were written to automatically find:

1- The correction factors of the coil non-uniformity from vials with constant concentration. The SI of the vials with different concentration was then multiplied by these factors.

2- To draw the best fit curve of concentration versus SI curve using equation 1.

3- To find the maximum concentration, where the square correlation coefficient ($r^2$) between corrected SI and concentration were equal to 0.95 or 0.99 from the best fit curve. The square correlation coefficient ($r^2$) gives the strength of the linear relationship between SI and concentration. When $r^2$ is 0.95, it indicates that 95% of the variation in SI is explained by the variation of concentration.[12]

These programs could be run from either a Unix workstation or a personal computer.

## Results

Figure 3 shows the coronal image of the phantom. The position of different concentrations inside the vials can be seen in the figure.

Figure 4 shows a typical result of corrected SI versus concentration of the contrast agent. The maximum linear relationship between concentrations and corrected SI that gave a square correlation ($r^2$) equal to 0.95 and 0.99 were 3.92 and 2.25 mmol/L, respectively at effective TI =644 ms at TR=2 s.

Figure 5 shows that the maximum linear relationship between SI and concentration is up to 3.92 and 2.84 mmol/L for short effective TI (644 ms) and long effective TI (1944 ms), respectively ($r^2$ = 0.95). In addition, these values reduced to 2.25 and 1.23 mmol/L for these effective inversion times where $r^2$ = 0.99 at TR = 2 s.

The figure indicates that an increase in effective TI is associated with a decrease in the maximum concentration. The $R^2$ was measured from the best fit curve for each TI similar to that obtained from Figure 4.

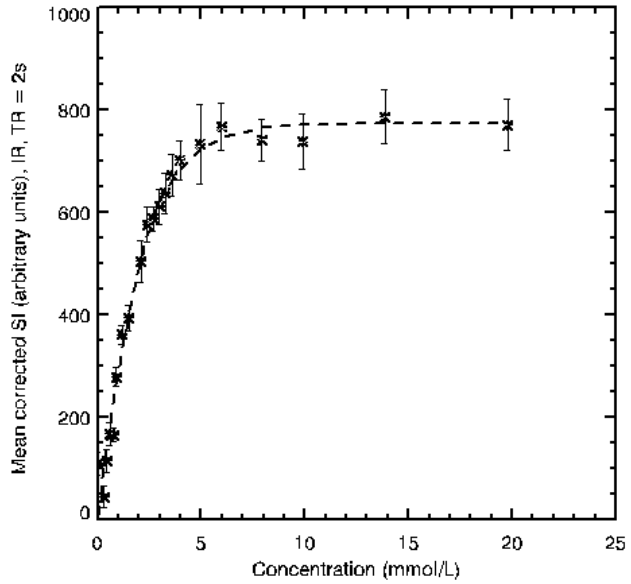


**Fig. 4.** A typical result of mean corrected SI from the 9 innermost pixels of the vials versus concentration of contrast agent. The maximum linear relationship between concentrations and corrected SI that gave a square correlation ($r^2$) equal to 0.95 and 0.99 were 3.92 and 2.25 mmol/L, respectively at effective TI = 644 ms (TI set = 100 ms). The error bars show the standard deviation of each vial (TR = 2 s).

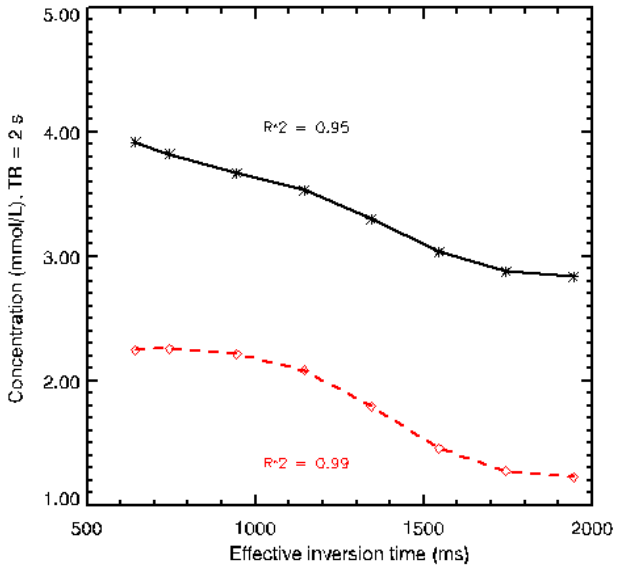


**Fig. 5.** The maximum concentration that gives $r^2$ = 0.95 and 0.99 versus effective TI. The linear relationship between SI and concentration is up to 3.92 and 2.84 mmol/L for short effective TI (644 ms) and long effective TI (1944 ms), respectively ($r^2$ = 0.95). In addition, these values reduce to 2.25 and 1.23 mmol/L for these effective inversion times where $r^2$ = 0.99 (TR = 2 s).

Figure 6 shows a typical result of corrected SI versus concentration of the contrast agent. The maximum linear relationship between concentrations and corrected SI that gave a square correlation ($r^2$) equal to 0.95 and 0.99 were 3.50 and 1.84 mmol/L, respectively at effective TI = 644 ms at TR=3 s.

Figure 7 illustrates that the maximum linear relationship between SI and concentration is up to 3.50 and 1.66 mmol/L for the short effective TI (644 ms) and long effective TI (1944 ms), respectively where $R^2$ = 0.95. In addition, these values reduced to 1.84 and 0.87 mmol/L for these effective inversion times where $r^2$ = 0.99 at TR = 3 s.

## Discussion

The concentration of contrast agent in CT or radioisotope scintigraphy linearly correlates with CT number or radioactivity, but in MRI, the concentration of Gd-DTPA does not necessarily correlate linearly with SI. Gd-DTPA has both a T1 shortening effect and T2 shortening effect. The T1 shortening effect is dominant at low concentrations of Gd-DTPA as modeled by equation 1, and the T2 shortening effect is dominant at high concentrations.[6] At high concentrations, both T1 and T2 can be affected as the SI response became non-linear with an unsteady plateau.

MRI is unable to measure the concentration of contrast within the ROI; therefore, it is measured indirectly from the SI. Consequently, in order to calculate concentration from SI, the maximum concentration for this linearity should be measured.

Correlation between MR signal intensity values on T1-weighted TurboFLASH and concentration of Gd-DOTA (Gadoterate, 0.5 mol/mL) was reported by Canet et al.[5] They investigated a broad range of in-vitro concentrations (0-5.0 mmol/L, Gd-DOTA diluted in saline). MR images were obtained using a 1.5-T MR scanner (Vision, Siemens Medical, Erhlangen, Germany) with an inversion time of 300 ms. They showed that the SI increase on T1-weighted images was linearly proportional to the Gd chelate concentration at lower concentrations (≤ 0.8 mmol/L); however, SI response became non-linear at higher concentrations. In this study, SI was corrected by the correction factor of the coil non-uniformity.

The present results, using the inversion recovery TurboFLASH sequence from the vials indicate that an increase in TI is associated with a decrease in the maximum linear concentration, where $r^2$ is equal to 0.95 or 0.99. The result also shows that at long TI (1944 ms) the maximum linear relationship between SI and concentration is up to 2.84 mmol/L where $r^2$ is 0.95 or up to 1.23 mmol/L where $r^2$ is 0.99 at TR =2s.

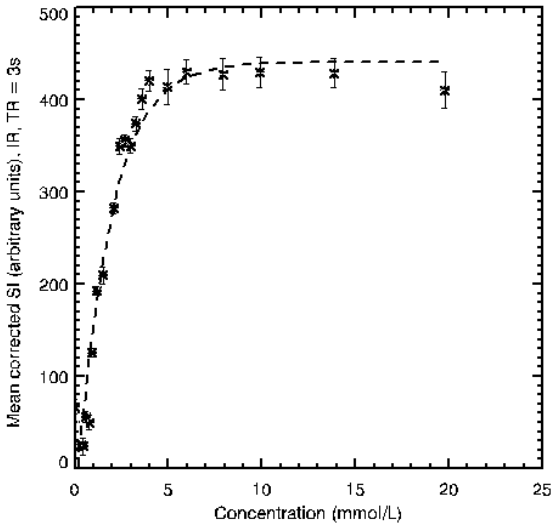


**Fig. 6.** A typical result of mean corrected SI from the 9 innermost pixels of the vials versus concentration of contrast agent. The maximum linear relationship between concentrations and corrected SI that gave a square correlation ($r^2$) equal to 0.95 and 0.99 were 3.50 and 1.84 mmol/L, respectively at effective TI = 644 ms (TI set = 100 ms). The error bars show the standard deviation of each vial (TR = 3 s).

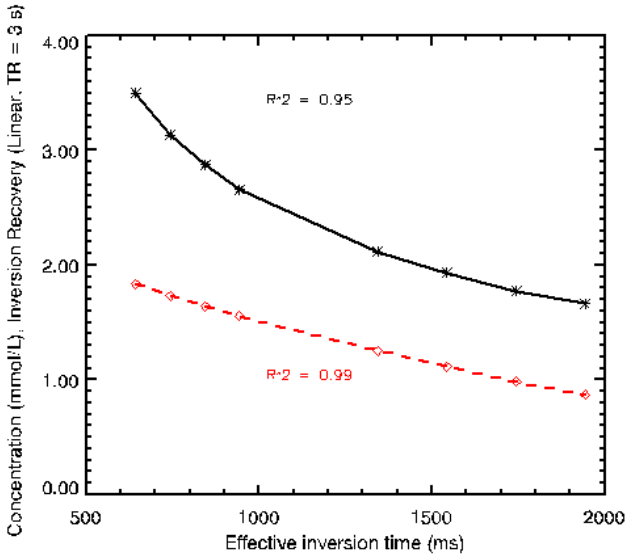


**Fig. 7.** The maximum concentration that gives $r^2$ = 0.95 and 0.99 versus effective TI. The linear relationship between SI and concentration is up to 3.50 for the short effective TI (644 ms) and 1.66 mmol/L for the long effective TI (1944 ms) where $r^2$ = 0.95. In addition, these values reduce to 1.84 and 0.87 mmol/L for these effective inversion times where $R^2$ = 0.99 (TR = 3 s).

These values can increase at short TI.

Although Canet et al.[5] found a linear relationship up to 0.8 mmol/L using Gd-DOTA contrast agent at TI = 300 ms (effective TI = 716 ms), our results using Gd-DTPA contrast agent under similar conditions were about 3.75 mmol/L ($r^2$ = 0.95) or 2.25 mmol/L ($r^2$ = 0.99) at TR=2s. It should be noted that the two contrast agents have roughly the same relaxivity.[3]

As was mentioned before, the non-uniformity of the coils can affect SI and this contributes to a large error in measuring the SI. Since Canet did not mention the correction of the non-uniformity of the coil, the difference between the present study and that of Canet et al.'s report may be due to non-uniformity of the coil. Another reason may be due to using different TR, or a different value of $r^2$ used to find the maximum linear relationship between SI and concentration. Neither of these values was quoted by Canet.

In addition, Fritz-Hansen et al.[13] found linearity between signal changes and tracer concentrations up to 1.0 mmol/L ($r^2$=0.999), an effective TI of 720 ms using IR TurboFLASH sequence (Linear Phase-Encoding) (TR, Time for one FLASH line = 6.5 ms, TE = 3.0 ms, flip angle = 12˚, effective TI varied between 170 and 2000 ms). They did not mention the actual TR.

Our image parameters are slightly different from the Fritz-Hansen's image parameters. The present study (Figs. 4 and 5) shows the maximum linearity is about 2.25 and 1.70 for TR =2 and 3 ms, respectively where $r^2$ is 0.99 at the effective TI of 720.

Dean et al.[14] and Evan et al.[3] reported that this linearity is up to 1 mmol/L, but they did not mention how they found this value in detail to compare with the results of this study.

Vallee et al.[7] reported the relationship between signal intensity and 1/T1 (in $s^{-1}$) up to 11 $s^{-1}$ was linear in FAST sequence. The 1/T1 ratio linearly related to the Gd concentration. Nevertheless, they did not mention the exact Gd concentration to compare with this study.

As mentioned above, different papers have reported different values for the maximum linear relationship between SI and the concentration of contrast agent in T1-weighted imaging. These values varied between concentrations of 0.8 (inversion recovery)[5] and 3 mmol/L (saturation recovery sequence).[6]

For finding this linearity, the value of the square correlation ($r^2$) which gives the strength of linear relationship between SI and concentration is important. The use of $r^2$ to measure the linearity is mentioned with different values in different papers. Takeda et al.[6] accepted the value of 0.76 for the linearity and Bourke et al.[15] also stated that an $r^2$ equal to 0.74 shows a reasonably strong association between two

variables. In this study, the maximum linearity was calculated for both 0.95 and 0.99 $r^2$, which indicates a far higher degree of linearity.

This study shows that not only TI but also TR is an important parameter when measuring SI. These parameters can have an effect on the maximum linearity. An increase in TI and TR leads to a decrease in the range of linearity.

Using T1-weighted images for perfusion study needs about 1/10th of the contrast agent that is normally used for a T2-weighted acquisition. Using a low dose of contrast agent was previously a disadvantage of using the T1-weighted technique for measuring blood flow because the changes in SI due to the contrast agent are small; it makes SI time curves very noisy.

The results of this study show that the maximum linearity will be increased in short TI and TR, which will improve the perfusion measurement in clinical studies.

This study indicates that in spite of TR=2 or 3s and $r^2$=0.95 or 0.99, at a typical effective TI=800ms, which is normally used for in vivo perfusion, the blood signal is nulled at 1.5-T, the maximum linearity for measuring the perfusion parameters on T1-weighted imaging is about twice that previously reported (i.e. 0.8mmol/L).[16-17] The higher dose will improve the signal to noise ratio in perfusion images.

## Conflict of interest

The author has no financial and personal relationship with other people or organizations that could inappropriately influence this work.

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