# Reference free Localization and Quantification of Contrast Agents using Relaxivity Dispersion at 1.5T

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**Introduction:** Unambiguous localization and quantitative concentration measurements of MR contrast agents in tissue or blood are highly desired. Many applications, especially with labeled contrast agents, can benefit from this information. However conventional methods always require reference scans to separate contrast agent signal from tissue signal making robust localization and quantification difficult and tedious.
In this work we present a new method PINPOINT which allows for unambiguous localization and quantification without the need for a reference scan. The technique is based on relaxivity dispersion imaging [1,2]. In contrast to conventional measurements this method does not determine relaxivities ($R_1$) but exploits the dependence of relaxivity on the magnetic field strength (relaxivity dispersion $dR_1/dB$). This quantity is independent from tissue within the limits of the experiment and is directly linked to the concentration of the contrast agent. The resulting images show pure contrast agent intensity and suppress any other signal.

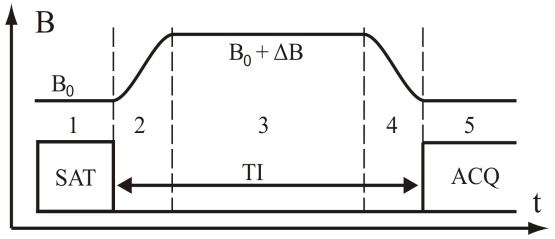


Fig. 1: Scheme of experiment with phases: saturation (1), ramp (2), evolution time at $B_0 \pm \Delta B$ (3), ramp (4) and acquisition (5).

**Methods:** In our experiments we employed a commercial, PINPOINT active contrast agent. Gadofluorine M (Schering, LOT N2044 A01) was calibrated at a temperature of $T$=25°C and a magnetic field strength of $B_0$=1.5T allowing for localization and concentration measurements in any medium. Contrast agents usually become PINPOINT active by bonding to macromolecules such as large biological molecules, polymers or dendrimers resulting in a strong $R_1$ dependence on the magnetic field strength around 1.5T.
We used a home build field cycling system to acquire MR images with contrast from different magnetic field strengths. A $B_0$ offset coil was inserted into a 1.5T clinical scanner to cycle the $B_0$ field by ±90mT. For rf transmitting and receiving the scanner needs to be at the Larmor frequency corresponding to 1.5T. During relaxation times the $B_0$ field can be increased or decreased to tailor desired image contrasts. Fig. 1 shows a schematic of the sequence design: saturation at $B_0$ (1), field ramp to $B_0 \pm \Delta B$ (2), evolution time at $B_0 \pm \Delta B$ (3), field ramp to $B_0$ (4) and multi spin echo acquisition module (5).
Specially processed subtraction of two images [1] – one with contrast from increased $B_0$ field and one from decreased $B_0$ field – yields a PINPOINT image with $dR_1/dB$-contrast. Tissue without contrast agent does not change its relaxivity $R_1$ in both images, hence signal vanishes after subtraction. Tissue with PINPOINT active contrast agent changes its relaxivity $R_1$ and shows signal in the image [1,2]. Consequently PINPOINT images serve as mask for regions with contrast agent.
Measurements to demonstrate unambiguous localization were carried out with a raspberry in which Gadofluorine M (179µM) was injected into some compartments of the berry marked in Fig. 2 (A). A PINPOINT image (shown in Fig. 2 (B)) was acquired with a saturation time of TI=350ms.
Quantitative concentration measurements were carried out with a phantom containing three different concentrations of Gadofluorine M in NaCl and a reference sample. PINPOINT images were acquired after saturation times TI of 70ms, 150ms and 250ms. Sample intensities for the three acquired PINPOINT images were normalized and further processed with information about change in magnetic field $B_0$ and TI times. Plotting the signal as function of TI times shows a linear function (signal=$dR_{1,sample}/dB \cdot TI = c \cdot r_1 \cdot TI$) displayed in Fig. 3.

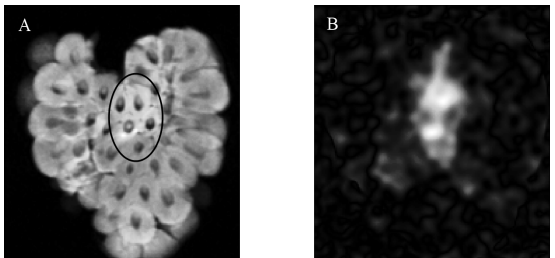


Fig. 2: (A) Conventional, $T_1$ weighted image of raspberry, region with injection of Gadofluorine M is marked; (B) PINPOINT image showing unambiguously the location of the contrast agent.

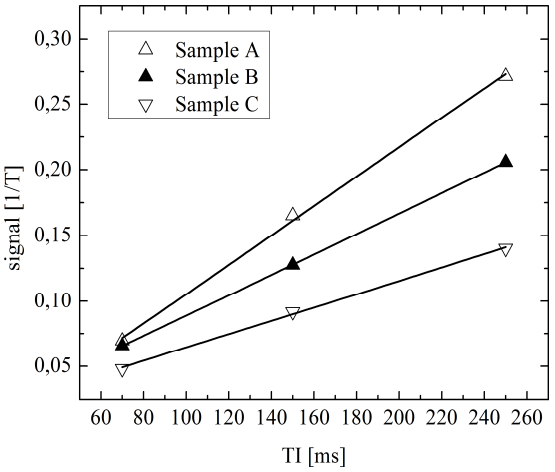


Fig. 3: Intensity from three PINPOINT images with TI=70ms, 150ms and 250ms for three Gadofluorine M samples. The slopes of the lines are proportional to the concentration of the contrast agent.

**Results:** In Fig. 2 (A) the region with contrast agent injected is slightly brighter that the surrounding areas but a robust localization is not possible. However the PINPOINT image in Fig. 2 (B) gives an unambiguous indication for the location of the contrast agent.
Slopes of the data fits in Fig. 3 are proportional to the concentration of the samples. We extracted the concentration for all three Gadofluorine M samples and compared them to their known concentrations from sample preparation. The reference sample in the phantom does not show any significant signal above noise level in all three PINPOINT images. The following table shows good agreement of the figures:

| | Sample A | Sample B | Sample C |
|---|---|---|---|
| Concentration prepared [µM] | 179±15 | 139±15 | 114±15 |
| Concentration measured via DREMR [µM] | 211±30 | 145±10 | 96±10 |

**Conclusion:** We have demonstrated localization and concentration measurements of a contrast agent without reference scans. The method is based on relaxivity dispersion and provides images showing pure contrast agent information without background intensity from tissue, blood or solvent. Its signal can be used as mask for regions with contrast agent and can be processed to determine the concentration of the contrast agent. After having shown a proof of principle we plan to adopt this method to medical small animal problems.

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**References:** [1] Hoelscher et al., ISMRM Poster # 4939, 2010
[2] Alford et al., Delta relaxation enhanced MR, Mag Res Med, 2009, 61, 796-802