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Pseudolayering of Gd-DTPA in the Urinary Bladder[1]

When excreted gadolinium diethylenetriaminepentaacetic acid (DTPA) collects in the bladder of a supine patient during magnetic resonance (MR) imaging, a puzzling pattern of signal intensities is noted. A gradual change in urine signal intensity with progressive addition of Gd-DTPA does not occur; instead, three sharply defined "layers" are seen both on T1- and T2-weighted images within the urine-Gd-DTPA mixture. The physical basis for this triple-layering phenomenon was investigated. A bladder phantom was constructed to reproduce the phenomenon. T1 and T2 relaxivities of urine doped with varying concentrations of Gd-DTPA were measured in vitro; measured signal intensities corresponded closely to predicted intensities. Early urine concentrations of excreted Gd-DTPA may be relatively high (10-40 mmol/L), resulting in extremely short T1 and T2 values (less than 30 msec). These extremely short relaxation times cause an artifactual pseudolayering of signal within the urine-Gd-DTPA mixture.

Index terms: Bladder, MR studies, 83.1214 • Diethylenetriaminepentaacetic acid (DTPA) • Gadolinium • Magnetic resonance (MR), contrast enhancement • Phantoms • Urine

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WHEN excreted gadopentetate (gadolinium diethylenetriaminepentaacetic acid [DTPA]) dimeglumine collects in the bladder of a supine patient during magnetic resonance (MR) imaging, a somewhat puzzling pattern of signal intensities is noted. A gradual change in urine signal intensity with progressive addition of Gd-DTPA does not occur; instead, three sharply defined "layers" or "bands" of signal intensity are characteristically seen on both T1- and T2-weighted images within the urine-Gd-DTPA mixture (Fig 1).

The upper layer clearly represents unopacified urine and has the signal intensity expected for each pulse sequence. The origin of the signals from the middle and bottom layers is not so easily explained, however. Do these layers physically exist or are they the result of some curious MR contrast phenomenon? If they are not true anatomic layers, why are they so sharply defined? Why do we not see a gradual and predictable transition from urine to Gd-DTPA as we do with iodinated contrast material in the bladder on pelvic computed tomographic (CT) images (Fig 2)? To answer these questions, a systematic study was undertaken to investigate MR signal intensity changes and relaxation parameters associated with urine-Gd-DTPA mixtures in vitro.

MATERIALS AND METHODS

The spin-lattice (T1) and spin-spin (T2) relaxivities of urine doped with varying concentrations of Gd-DTPA were first determined in vitro. Gadopentetate dimeglumine (Magnevist; Berlex Imaging, Wayne, NJ), was added in a stepwise fashion to samples of fresh urine obtained from a healthy volunteer. This resulted in 12 urine-Gd-DTPA mixtures with a Gd-DTPA concentration ranging from 0 to 9.0 mmol/L. All specimens were thoroughly mixed by gentle swirling in their containers.

Relaxation time measurements of the solutions were initially performed on a clinical MR imager operating at 1.5 T (Vista MR; Picker International, Highland Heights, Ohio). T1 relaxation times were computed with an inversion recovery protocol with a TR of 8,000 msec, a TE of 30 msec, and inversion times (TIs) in 10 separate acquisitions ranging from 100 to 1,000 msec in steps of 100 msec. Field of view was 25 cm, section thickness was 10 mm, and the number of excitations was one. T2 measurements were obtained with a multiecho protocol (8,000/26, 52, 78, 104, 130, 156). Other variables were identical to those for the T1 measurements except that the number of excitations was increased to two. Three measurements of T1 and T2 were made for each sample, with reproducibility of within 5%.

Signal intensities for each sample were measured with circular regions of interest over each specimen bottle. The values were normalized to account for changing signal attenuations set by imager software and then fitted to single exponential curves based on eigenvalue decomposition combined with a nonlinear least-squares algorithm (1).

T1 relaxation times for each specimen were verified by careful measurement in a laboratory nuclear MR spectrometer (Wats65; Waterloo NMR Spectrometers, Waterloo, Ont, Canada) operating at 64 MHz. We measured T1 relaxation times by using an inversion recovery sequence with 30 free induction decay signals recorded for each T1 measurement (2). These data were fitted by means of a single exponential function with use of a linear least-squares method. The accuracy of T1 measurement was better than 8%, and the calculated slopes of the T1 relaxivity curves for the commercial imager and the nuclear MR spectrometer agreed to within 1.6%.

A bladder phantom was constructed to validate the triple layering phenomenon in vitro. This consisted of a Pyrex beaker filled with urine from a normal volunteer into which Gd-DTPA at a concentration of 15 mmol/L was carefully added. The Gd-DTPA was meticulously pipetted into the bottom of the phantom while the phantom lay in the MR scanner to simulate the nonturbulent inflow of excreted Gd-DTPA posteriorly and inferiorly from

Abbreviations: DTPA = diethylenetriaminepentaacetic acid, TE = echo time, TI = inversion time, TR = repetition time, SE = spin echo.

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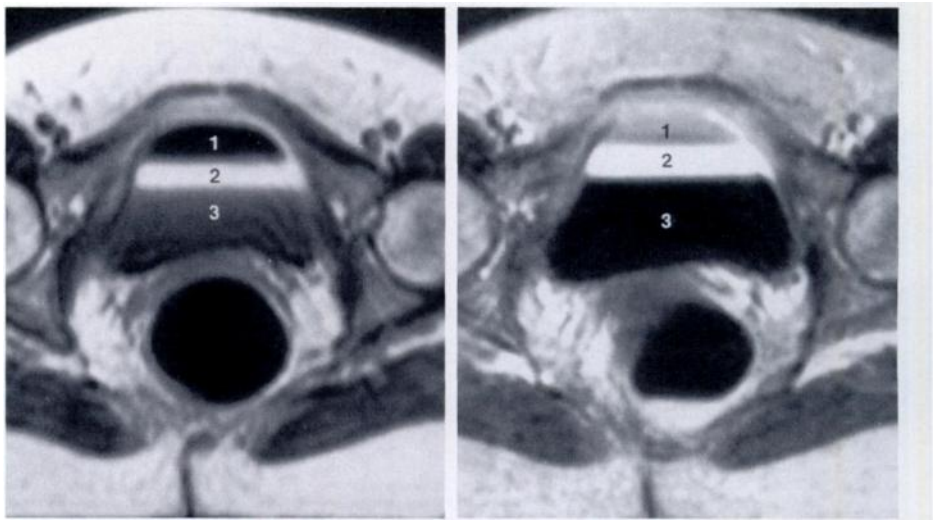
the ureters into a partially filled human bladder. Imaging of the bladder phantom was performed with both short TR/TE (600/16) and long TR/TE (2,000/60) spin-echo (SE) pulse sequences.

RESULTS

The T1 relaxivity of Gd-DTPA in urine was calculated to be 3.74 (mmol/L · sec)$^{-1}$ on the clinical imager and 3.80 (mmol/L · sec)$^{-1}$ on the nuclear MR spectrometer. The T2 relaxivity on the clinical imager was 4.75 (mmol/L · sec)$^{-1}$. These values are in agreement with published data concerning T1 relaxation rates for lanthanide complexes in aqueous solution (3). On the basis of these relaxivity curve data, T1 and T2 values at 1.5 T for a wide range of potential concentrations of Gd-DTPA in urine were computed (Table). For moderately high concentrations of Gd-DTPA (above 5 mmol/L) both T1 and T2 values become extremely short (less than 50–60 msec). As we will subsequently demonstrate, it is this extreme shortening of both T1 and T2 values of urine by excreted Gd-DTPA that contributes to the unusual pseudolayering phenomenon observed visually. Images of the bladder phantom were obtained (Fig 3) with pulse sequences identical to those used to obtain images of the human subject in Figure 1. The same triple-layering phenomenon noted in the human bladder partially filled with Gd-DTPA was consistently reproduced in vitro in this phantom. Measured signal intensities of each layer corresponded closely to signal intensities predicted with use of the T1 and T2 values in the Table. A separate dilution experiment confirmed that concentrations of Gd-DTPA within each range produced MR signal intensities consistent with theory.



a. b.

Figure 1. Axial MR images of the pelvis obtained with 600/16 (repetition time [TR] msec/echo time [TE] msec) **(a)** and 2,000/60 **(b)** sequences show excretion of Gd-DTPA into the partially filled bladder. Three discrete layers or signal regions (1–3) are identified with each sequence.

Predicted Relaxation Times of Urine-Gd-DTPA Mixtures of Various Concentrations

Concentration of Gd-DTPA (mmol/L)	T1 (msec)	T2 (msec)
0.0	7,010	871
0.1	1,930	616
0.2	1,120	476
0.3	790	388
0.4	610	328
0.5	496	284
1.0	257	169
5.0	53	40
10.0	27	21
20.0	13	10
30.0	9	7
40.0	7	5
50.0	5	4

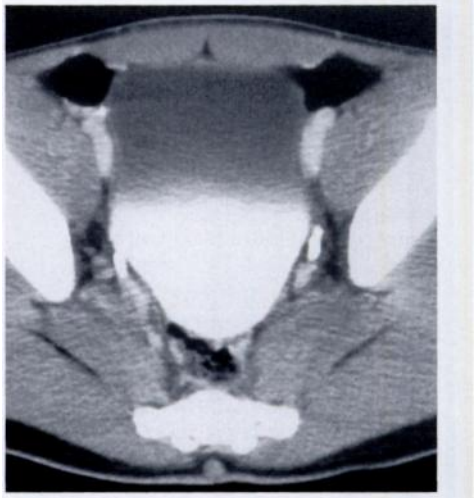


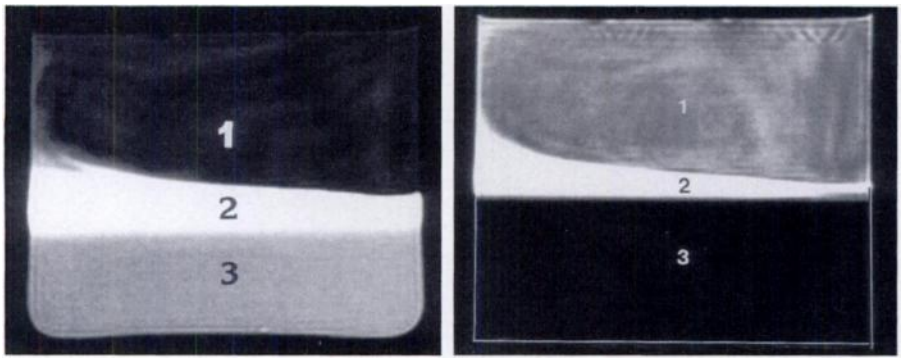
Figure 2. Excretion of iodinated contrast material into the partially filled bladder on CT scan. The transition from pure urine anteriorly into progressively denser contrast material posteriorly is easily understood.

DISCUSSION

The pharmacokinetics of intravenously administered Gd-DTPA in normal subjects conforms to a two-compartment open model with a mean elimination half-life of approximately 1.6 hours (4,5). At injection, the meglumine salt of gadopentetate dimeglumine completely dissociates from the gadopentetate complex. No detectable biotransformation or decomposition occurs. Gd-DTPA is exclusively eliminated in the urine and has a clearance rate similar to that of substances subject to glomerular filtration (5).

The concentration of Gd-DTPA within freshly excreted urine is surprisingly high (6) and can be easily estimated from the pharmacokinetic data (5). Consider a 70-kg man who receives the manufacturer's recommended dose of Gd-DTPA (0.1 mmol/kg) for a certain MR study. The total injected quantity of Gd-DTPA will therefore be 7.0 mmol. If one ignores redistribution time and assumes an elimination half-life of 1.6 hours, the approximate total fraction F excreted in time t after injection can be easily calculated with a classic exponential decay formula (7): $F = 1 - \exp[(-\ln 2/1.6)t] = 1 - \exp(-0.43\,t)$. In the first 30 minutes (t = 0.5 hour), therefore, approximately 19.5% of the total injected dose should appear in the urine. For the 70-kg man, this corresponds to an excreted dose of approximately 1.36 mmol of Gd-DTPA. If one assumes the bladder was initially empty and that the usual urine production rate is 1–2 mL/min, the concentration of Gd-DTPA appearing in the bladder over the first 30 minutes may be as high as 23–45 mmol/L. If mixing with residual unopacified urine in the bladder occurs, or if urinary flow rates are significantly higher, the resultant concentration of Gd-DTPA will be lower. The 15-mmol/L solution used in the bladder phantom (Fig 3) produced MR signal changes of a nature similar to that seen in the human patient (Fig 1).

The apparent segmentation of urine mixed with Gd-DTPA into three layers can easily be understood by plotting calculated signal intensities for each SE pulse sequence based on classic approximated solutions (8) to the Bloch equations (Fig 4). The top layer of fluid represents pure urine with long T1 and T2 values relative to the SE variables TR and TE. The expected levels of signal intensity (dark on SE 600/16 images, brighter on SE 2,000/60 images) are easily understood and represent the



a. b.

Figure 3. MR images obtained with 600/16 **(a)** and 2,000/60 **(b)** sequences show triple-layering phenomenon seen in vivo. Uneven middle "layer" resulted from mixing along edge of container where pipettes were inserted.

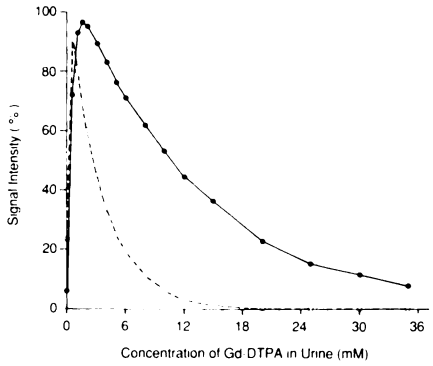


Figure 4. Predicted MR signal intensities for aqueous solutions of Gd-DTPA at 1.5 T. ● = 600/16 sequence, O = 2,000/60 sequence.

normal appearances of urine with these pulse sequences at 1.5 T.

The bottom "layer" of fluid represents urine with a relatively high concentration of Gd-DTPA (greater than 5–10 mmol/L). At these concentrations (see Table), the T1 and T2 relaxation times of the urine–Gd-DTPA mixture are extremely short (less than 50 msec). It is this extreme T2 shortening (possibly coupled with magnetic susceptibility effects) that accounts for the very dark appearance of the bottom layer on the "T2-weighted" 2,000/60 image (9). The muddy gray appearance of the bottom layer on the SE 600/16 image can also be easily understood by reference to the Table and Figure 3. At high Gd-DTPA concentrations, T1 and T2 values of the solution are relatively similar in magnitude, with $T1/T2 \cong 1.3$. (Recall that for most tissues at 1.5 T, T1/T2 ratios [10] are usually on the order of 5–10). The signal intensity of this bottom layer on the SE 600/16 image represents the balanced effects of short T1 (which would increase signal intensity) and short T2 (which decreases signal intensity). As a result, the highly concentrated urine–Gd-DTPA mixture has an intermediate gray appearance with the SE 600/16 pulse sequence.

The origin of the signal from the middle layer of fluid is a little more difficult to understand intuitively. Curiously, this layer is exceedingly bright with both the short TR/TE and long TR/TE sequences. Furthermore, this band of higher signal intensity does not correspond with an anatomically discrete layer of fluid. Rather, it represents an interesting signal contrast phenomenon that occurs at relatively low concentrations of Gd-DTPA (0.5–5.0 mmol/L). We have used the term "pseudolayering" to remind ourselves that this is merely an interesting MR signal phenomenon rather than a true physical layer with distinct margins.

The bright middle pseudolayer can be predicted to occur at concentrations of approximately 0.5–5.0 mmol/L, at which the peak signals in Figure 4 are noted. The Table shows that for urine–Gd-DTPA mixtures of these concentrations, T1 and T2 values are of comparable size and both are on the order of a few hundred milliseconds. The computer simulations described by Davis et al (11) predict high signal intensity with both short TR/TE and long TR/TE pulse sequences for liquid solutions of Gd-DTPA over this range of concentrations.

When the T1 of a urine–Gd-DTPA mixture falls below 400 msec, SE pulse sequences with TRs of more than five times the T1 (ie, greater than 2,000 msec) become relatively independent of T1. Hence the SE 2,000/60 pulse sequence in this example becomes heavily weighted toward the long T2 and high spin density values of the solution. The middle pseudolayer thus appears very bright with long TR/TE pulse sequences such as this (Fig 1a).

Similar reasoning can explain the high signal intensity of this middle pseudolayer with the SE 600/16 sequence. For this sequence the measured T2s are very long compared to TE, while the T1s are slightly shorter than TR. The SE 600/16 sequence can thus be considered reasonably T1 weighted and will have high signal intensity because of the relative T1 shortening that occurs with these low concentrations of Gd-DTPA.

The middle pseudolayer of urine and Gd-DTPA, therefore, exists in the MR image alone. This pseudolayer is seen because of a fortuitous phenomenon involving changes in T1 and T2 values of solutions containing progressively higher concentrations of Gd-DTPA. The inferior edge of this pseudolayer appears sharply defined only because the predicted signal intensity curve is very steep over the corresponding range of Gd-DTPA concentrations. The fact that MR signal intensity may change nonlinearly and even paradoxically with the progressive addition of Gd-DTPA underscores a fundamental difference between the behavior of MR and CT contrast agents as each interacts with its respective imaging process. The daily observation of pseudolayers of Gd-DTPA that appear in the urinary bladder should serve as a constant reminder of the many complex and competing physical processes that determine MR signal intensity. ■

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