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Evaluation of renal function by dynamic MR imaging: effect of water load.

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Abstract

The aim of this study was to investigate the usefulness of magnetic resonance (MR) imaging in the evaluation of renal function, with particular attention to the effects of water load. Ten healthy volunteers underwent dynamic MR imaging after an injection of gadolinium diethylene-triaminepenta-acetic acid (Gd-DTPA) as a contrast agent to evaluate renal function by the following four methods: the positive method [longitudinal relaxation time (T1) shortening is the dominant effect], the negative method [transverse relaxation time (T2) shortening is the dominant effect] and two intermediate methods by switching the Gd-DTPA concentrations used in the positive and negative methods. A prolonged cortical peak time and a reduced medullary peak level were observed by the positive method under a dehydrated condition, suggesting that these variables were slightly influenced by Gd-DTPA concentrated in the medulla. By the negative method, low signals due to T2* (T2* is the effective transverse relaxation time, typically shorter than T2) shortening appeared in the medulla under normal conditions, but these signals were unclear when the subject was under an overhydrated condition. These results indicate that water metabolism, in addition to imaging parameters and Gd-DTPA dose levels, should be considered when renal function is evaluated by dynamic MR imaging. Analysis of both the pattern of MR images and the time-signal intensity curves may be useful in the evaluation of renal function. The results also indicate that the positive method is preferred when the patient is overhydrated as it allows the evaluation of the local renal kinetic function by recording changes in the regional contrast agent levels.

KEYWORDS: dynamic MRI, renal function, water load, negative enhancement, time-signal intensity curve

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The aim of this study was to investigate the usefulness of magnetic resonance (MR) imaging in the evaluation of renal function, with particular attention to the effects of water load. Ten healthy volunteers underwent dynamic MR imaging after an injection of gadolinium diethylene-triaminepenta-acetic acid (Gd-DTPA) as a contrast agent to evaluate renal function by the following four methods: the positive method [longitudinal relaxation time (T1) shortening is the dominant effect], the negative method [transverse relaxation time (T2) shortening is the dominant effect] and two intermediate methods by switching the Gd-DTPA concentrations used in the positive and negative methods. A prolonged cortical peak time and a reduced medullary peak level were observed by the positive method under a dehydrated condition, suggesting that these variables were slightly influenced by Gd-DTPA concentrated in the medulla. By the negative method, low signals due to T2 * (T2 * is the effective transverse relaxation time, typically shorter than T2) shortening appeared in the medulla under normal conditions, but these signals were unclear when the subject was under an overhydrated condition. These results indicate that water metabolism, in addition to imaging parameters and Gd-DTPA dose levels, should be considered when renal function is evaluated by dynamic MR imaging. Analysis of both the pattern of MR images and the time-signal intensity curves may be useful in the evaluation of renal function. The results also indicate that the positive method is preferred when the patient is overhydrated as it allows the evaluation of the local renal kinetic function by recording changes in the regional contrast agent levels.

Key words: dynamic MRI, renal function, water load, negative enhancement, time-signal intensity curve

W e investigated the usefulness of magnetic resonance (MR) imaging in the evaluation of renal function. Gadolinium diethylenetriaminepenta-acetic acid (Gd-DTPA), a paramagnetic MR imaging contrast agent is freely filtered at the glomerulus and has no known nephrotoxicity. It is, therefore, recommended as a renal MR imaging agent (1-4). The usefulness of dynamic Gd-DTPA-enhanced MR imaging has already been demonstrated in the evaluation of renal function (1-4). While Gd-DTPA always shortens both longitudinal relaxation time (T1) and transverse relaxation time (T2), T1 shortening predominates at lower concentrations, resulting in tissue enhancement on T1-weighted images; we call this phenomenon positive enhancement. At higher concentrations, the effect of shortened T1 is maximal and T2-dependent contrast becomes dominant; we call this phenomenon negative enhancement (1, 2).

In previous studies, we attempted to evaluate renal function by dynamic MR imaging (5-7). In these studies, healthy volunteers showed low signal intensity (SI) in the renal pelvic region because Gd-DTPA is concentrated by normal kidneys. Patients with renal dysfunction sometimes showed higher SI in the pelvic region, indicating a reduced concentrating function. Because the concentrating and diluting ability of the normal kidney is normally affected by water load (dehydration or overhydration), concomitant changes in MR images of the kidney can be expected. However, several studies reported that healthy volunteers showed higher SI in the renal pelvic region, while in patients with renal dysfunction the appearance of low SI in the medulla was either delayed or absent (1, 2). There were two major differences between the reports of Semelka et al. (1) and Kikinis et al. (2) and our method

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in the flip angle (FA) and the dose of Gd-DTPA. Therefore, we investigated various hydration states and pulse sequences in this study to determine the usefulness of dynamic Gd-DTPA-enhanced MR imaging in the evaluation of renal function.

Subjects and Methods

Subjects and imaging technique.   A total of 10 healthy volunteers were examined, aged from 23–36 years (mean, 27.3 years). They had no disease (*i.e.*, hypertension) or medication that affects renal function. Informed consent was obtained from all volunteers verbally.

MR images were obtained on a 0.5 T superconducting imager (Resona; Yokogawa Medical Systems, Tokyo, Japan). Images were rapidly recorded with the use of gradient recalled acquisition in the steady state (GRASS) during the span of a held breath. We combined the use of presaturation toward the head and gradient moment nulling in the axial, coronal and sagittal planes.

The method of dynamic MR imaging was slightly modified from the method we used in previous experiments (5–7). The 5 sec that were required until steady state free precession (SSFP) could be achieved and signal collection started were recently shortened by modification of the software. Therefore, in the present study, the time required for a scan was 8 sec, and the minimum interval from the start of a scan to the start of the next scan was 15 sec.

The method of dynamic MR imaging used a larger flip angle (FA), and T1-dependent contrast shortening was the dominant effect (5–7). The dose of Gd-DTPA was lower than that used in several other studies (1–4). We called this method positive enhancement weighting (positive method). The methods of several studies that used a smaller FA and larger doses of Gd-DTPA (1–4) showed T2 * (T2 * is the effective transverse relaxation time, typically shorter than T2) shortening as the dominant effect and the negative enhancement was weighted (negative method).

Phantom study.   First, we performed a phantom study to determine the optimum parameters before measurement of the water load in healthy volunteers.

An acrylic phantom for MR imaging was used (Data Spectrum Corporation, NC, USA). A uniform volume (25 ml) of human plasma (plasmanate cutter; Miles Inc, San Francisco, CA, USA) was combined in a series of

units that contained 0, 0.25, 0.5, 1.0, 1.5, 2.0, and 2.5 mmol/l of Gd-DTPA. Each unit was set in the phantom. The phantom was injected with a solution of nickel chloride (5 mmol/l). A GRASS sequence, fixed with a repetition time (TR) of 50 msec and an echo time (TE) of 20 msec, was obtained for an FA series of 10, 20, 30, 40, 50, 60, 70, 80, and 90 degrees. Then we examined the SI of each FA to determine the optimum parameters. Other conditions of radio frequency (RF) tuning, receiving gain, *etc.* were constant throughout the study.

Protocol.   The pulse sequence of the positive method was TR = 50 msec, TE = 20 msec, and FA = 70 degrees. The dose level of Gd-DTPA was 0.05 mmol/ kg of body weight. The pulse sequence of the negative method was TR = 50 msec, TE = 20 msec, and FA = 30 degrees. The dose level of Gd-DTPA was 0.1 mmol/ kg of body weight. Four healthy volunteers (eight kidneys; all men; 23–36 years of age; mean, 27 years) were studied by the positive method. Four other healthy volunteers (eight kidneys; all men, 23–29 years; mean 27.5 years) were studied by the negative method. To allow a comparison under similar conditions, MR imaging was performed three times for every subject in the positive method group: one time each under a normal, a dehydrated and an overhydrated conditions. Every subject in the negative method group was examined twice each under a normal and an overhydrated conditions.

Dehydration and overhydration were achieved according to the Fishberg concentration and dilution tests. For MR imaging under a dehydrated condition, the subjects were given dinner before 8 p. m. on the day before testing and were allowed no food or water until MR imaging was performed at 8 a. m. the following morning. For MR imaging under an overhydrated condition, the subjects were given 1l of water within 30 min after they rose in the morning on the day of testing.

In an additional experiment to compare the effects of water kinetics, two of the subjects in the positive method group were studied under an overhydrated condition induced by intravenous injection of 500 ml water. MR imaging under a dehydrated condition was not performed by the negative method because low SI would appear in the renal medulla due to the concentrated contrast agent, making it impossible to estimate changes of the SI in the renal medulla.

We attempted two other experiments for the remaining two volunteers (four kidneys) by two intermediate methods between the positive and negative methods. One

pulse sequence was TR = 50 msec, TE = 20 msec, FA = 30 degrees, and Gd-DTPA 0.05 mmol/kg. The other was TR = 50 msec, TE = 20 msec, FA = 70 degrees, and Gd-DTPA 0.1 mmol/kg. These two methods included an intravenous injection of 500 ml water to induce the overhydrated condition. Both subjects were men, aged 26 and 29 years (mean, 27.5 years). Every subject was examined four times for each method and condition.

The results for each condition were compared by Student's t-test. The level of significance was set at 0.05.

Results

Phantom study.   Fig. 1 shows the results of the phantom study. The SI for each plasma unit gradually increased with the concentration of Gd-DTPA, but thereafter the rise in the SI gradually leveled off. When the FA was small, SI increased to a maximum at lower concentrations of Gd-DTPA and they began to decrease

gradually with higher concentrations. When a larger FA (from 70 to 90 degrees) was used, the maximum SI could not be obtained with our concentrations. The SI increased with the concentration of Gd-DTPA, but the rate of elevation was slight. The exact value of T1 and T2 of the kidney tissue differed from that of human plasma. The effect of concentration of Gd-DTPA on SI in renal parenchyma did not match the phantom study, but it was expected to have a similar pattern.

When we determined the optimum parameters of this MR imager, we considered the contrast enhancement effect, the incline of the curves, and the quality of each MR image represented by the SI of each material. The optimum pulse sequence of the positive method was an FA of 70 degrees and a Gd-DTPA dose of 0.05 mmol/kg, and that of the negative method was an FA of 30 degrees and a Gd-DTPA dose of 0.1 mmol/kg.

Positive method.   Table 1 shows the mean values of the respective parameters under three conditions
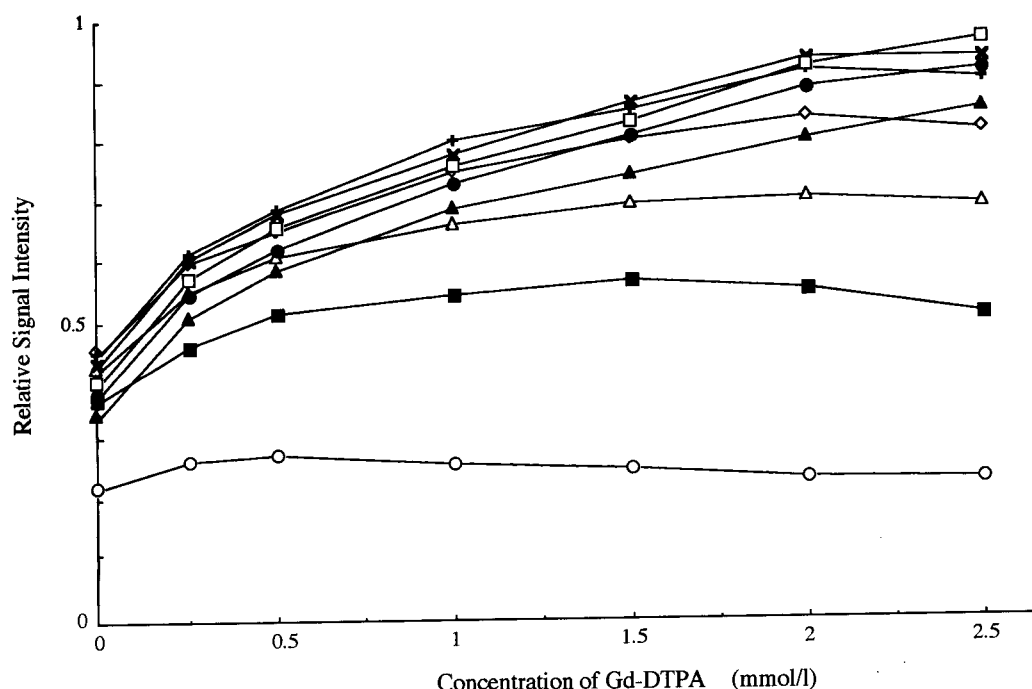

Fig. 1   The effect of concentration of Gd-DTPA on relative signal intensity (SI) observed with nine flip angles (FAs). This phantom study indicated that the smaller FAs exhibited maximum SI at lower Gd-DTPA concentrations. The larger FAs lacked a maximum SI within these concentrations. FAs: 10 (○), 20 (■), 30 (△), 40 (◇), 50 (+), 60 (×), 70 (□), 80 (●), 90 (▲) degrees.
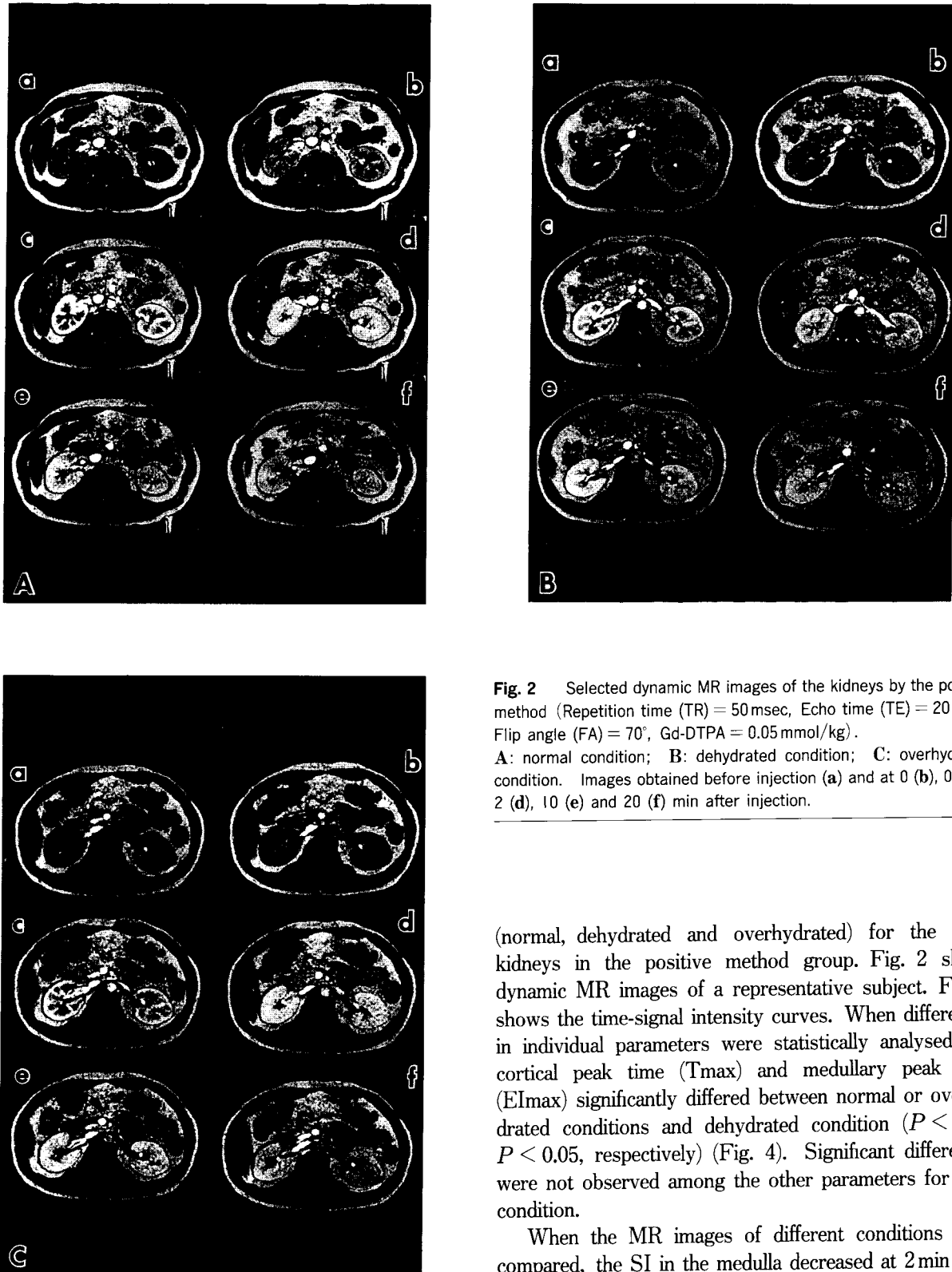
Fig. 2 Selected dynamic MR images of the kidneys by the positive method (Repetition time (TR) = 50 msec, Echo time (TE) = 20 msec, Flip angle (FA) = 70°, Gd-DTPA = 0.05 mmol/kg).
A: normal condition; **B**: dehydrated condition; **C**: overhydrated condition. Images obtained before injection (**a**) and at 0 (**b**), 0.5 (**c**), 2 (**d**), 10 (**e**) and 20 (**f**) min after injection.

(normal, dehydrated and overhydrated) for the eight kidneys in the positive method group. Fig. 2 shows dynamic MR images of a representative subject. Fig. 3 shows the time-signal intensity curves. When differences in individual parameters were statistically analysed, the cortical peak time (Tmax) and medullary peak level (EImax) significantly differed between normal or overhydrated conditions and dehydrated condition ($P < 0.01$, $P < 0.05$, respectively) (Fig. 4). Significant differences were not observed among the other parameters for each condition.

When the MR images of different conditions were compared, the SI in the medulla decreased at 2 min after

injection of Gd-DTPA under a dehydrated condition (Fig. 2 Bd). The low SI under the dehydrated condition can be due to concentrated Gd-DTPA as a result of reduced water elimination. This difference was evident when these images were compared carefully. However, the difference was not clear at first glance or on the time-signal intensity curves, nor were there significant differences in any parameters between oral and intravenous overhydration (Table 1).
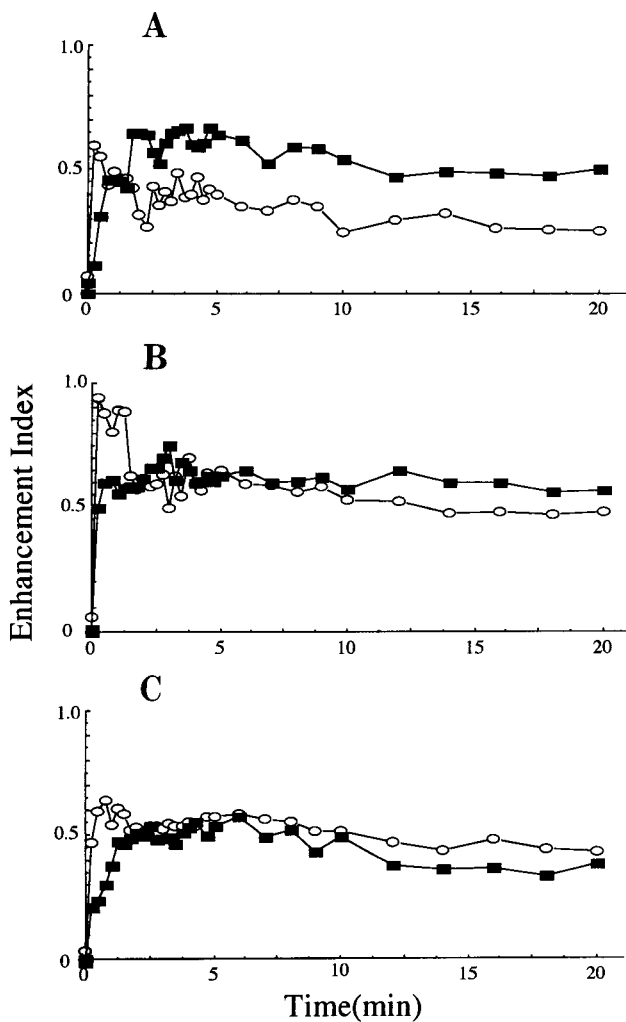
Negative method.   The test results of the eight kidneys in the negative method group are illustrated in

Fig. 3   Time-signal intensity curves by the positive method. A: normal condition; B: dehydrated condition; C: overhydrated condition. Enhancement index was expressed as the signal intesity (SI) of the precontrast image minus the SI of the postcontrast image, divided by the SI of the percutaneous fat. ○: Cortex, ■: Medulla
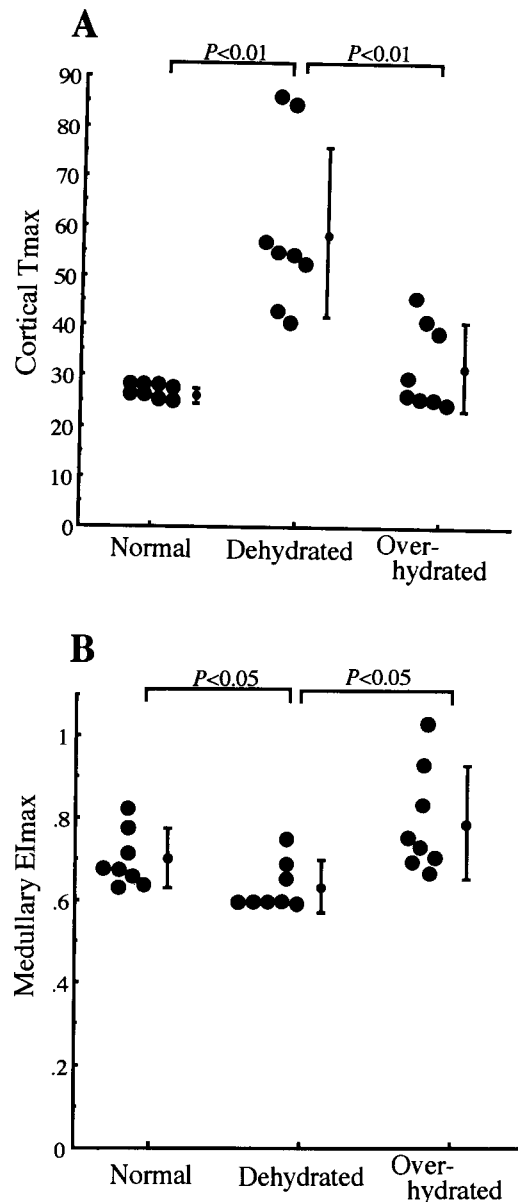
Fig. 4   The cortical peak time (Tmax) and medullary peak level (EImax) under normal, overhydrated and dehydrated conditions. A; The significant difference in the cortical Tmax among normal or overhydrated condition and dehydrated condition determined by Student's t-test ($P < 0.01$). B; The significant difference in the medullary EImax between the normal or overhydrated condition and the dehydrated condition determined by Student's t-test ($P < 0.05$).

Table I Mean values of parameters under three conditions by the positive method

		Normal (n = 8)	Dehydrated (n = 8)	Overhydrated (oral) (n = 8)	Overhydrated (intravenous) (n = 4)
Aorta					
	EI^a max	1.59 ± 0.25	1.37 ± 0.23	1.42 ± 0.18	1.36 ± 0.06
	EI (5 min)–EI (20 min)^b	0.223 ± 0.101	0.278 ± 0.042	0.268 ± 0.075	0.205 ± 0.017
Cortex					
	EI max	0.780 ± 0.138	0.278 ± 0.112	0.850 ± 0.092	0.843 ± 0.108
	T max^c	26.0 ± 1.6 (sec)	58.8 ± 17.5 (sec)	31.9 ± 8.7 (sec)	40.0 ± 17.3 (sec)
	T 3/4^d	180 ± 172 (sec)	300 ± 320 (sec)	120 ± 48 (sec)	109 ± 70 (sec)
	EI (5 min)–EI (20 min)	0.158 ± 0.070	0.140 ± 0.043	0.177 ± 0.091	0.165 ± 0.034
CMJT^e		76.3 ± 24.1 (sec)	92.5 ± 20.0 (sec)	90.6 ± 20.5 (sec)	83.7 ± 7.0 (sec)
Medulla					
	EI max	0.711 ± 0.078	0.636 ± 0.065	0.788 ± 0.14	0.773 ± 0.222
	T max	168 ± 58 (sec)	154 ± 99 (sec)	156 ± 57 (sec)	130 ± 35 (sec)
	EI (5 min)–EI (20 min)	0.167 ± 0.055	0.175 ± 0.663	0.151 ± 0.058	0.180 ± 0.583

a: Enhancement index
b: Reduced EI values at 20 min from those at 5 min
c: Time at maximal EI
d: Time when values are 3/4 of EI max
e: Cortico-medullary junction time
n expresses the number of kidneys.

All values are expressed as mean ± SD

Table 2 Mean values of parameters under two conditions by the negative method

	Normal (n = 8)	Overhydrated (n = 8)
Aorta		
EI max	1.26 ± 0.09	1.20 ± 0.09
EI (5 min)–EI (20 min)	0.315 ± 0.341	0.251 ± 0.143
Cortex		
EI max	0.538 ± 0.036	0.562 ± 0.065
T max	77.5 ± 8.7 (sec)	17.5 ± 18.4 (sec)
T 3/4	108 ± 25 (sec)	109 ± 36 (sec)
EI (5min)–EI (20min)	−0.246 ± 0.333	0.008 ± 0.033
CMJT	40.8 ± 21.9 (sec)	36.4 ± 22.0 (sec)
Medulla		
EI max	0.568 ± 0.097	0.667 ± 0.056
T max	670 ± 317 (sec)	295 ± 286 (sec)
EI (5min)–EI (20min)	−0.823 ± 0.753	0.268 ± 0.037

Abbreviations: See Table I.
All values are expressd as mean ± SD
n expresses the number of kidneys.

Fig. 5 which shows dynamic MR images of a representative subject. Under a normal condition, the SI in the medulla did not increase at about 1.5 min after injec-

tion, indicating that the Gd-DTPA did not become concentrated, but the SI in the cortex did increase. The disparity in corticomedullary enhancement allowed excellent differentiation (Fig. 5 Ac). Thereafter, the SI in the medulla increased gradually as the SI in the cortex decreased, resulting in loss of the corticomedullary boundary (Fig. 5 Ad). Under an overhydrated condition, the SI decrease in the medulla differed, and the corticomedullary differentiation was not enhanced (Fig. 5 Bc). Fig. 6 shows one representative time-signal intensity curve by the negative method. Under a normal condition, the SI in the medulla approached the preinjection level at 1.5 to 2 min after Gd-DTPA injection. Thereafter, the SI in the medulla rose again and hardly decreased for 20 min. The degree of SI reduction in the cortex was also small. The decrease in medullary SI, which was observed under a normal condition at 1.5 to 2 min after Gd-DTPA injection, was also absent on the curves under this condition. The overall degree of SI reduction under an overhydrated condition was similar to that under a normal condition. Table 2 shows the mean values of the respective parameters. Cortical peak time (Tmax) and medullary peak level (EImax) significantly differed between normal and overhydrated conditions ($P < 0.05$, $P < 0.01$, respectively). The degree of cortical and medullary intensity reduction, which was obtained by deducting EI (20 min) from EI (5 min), was
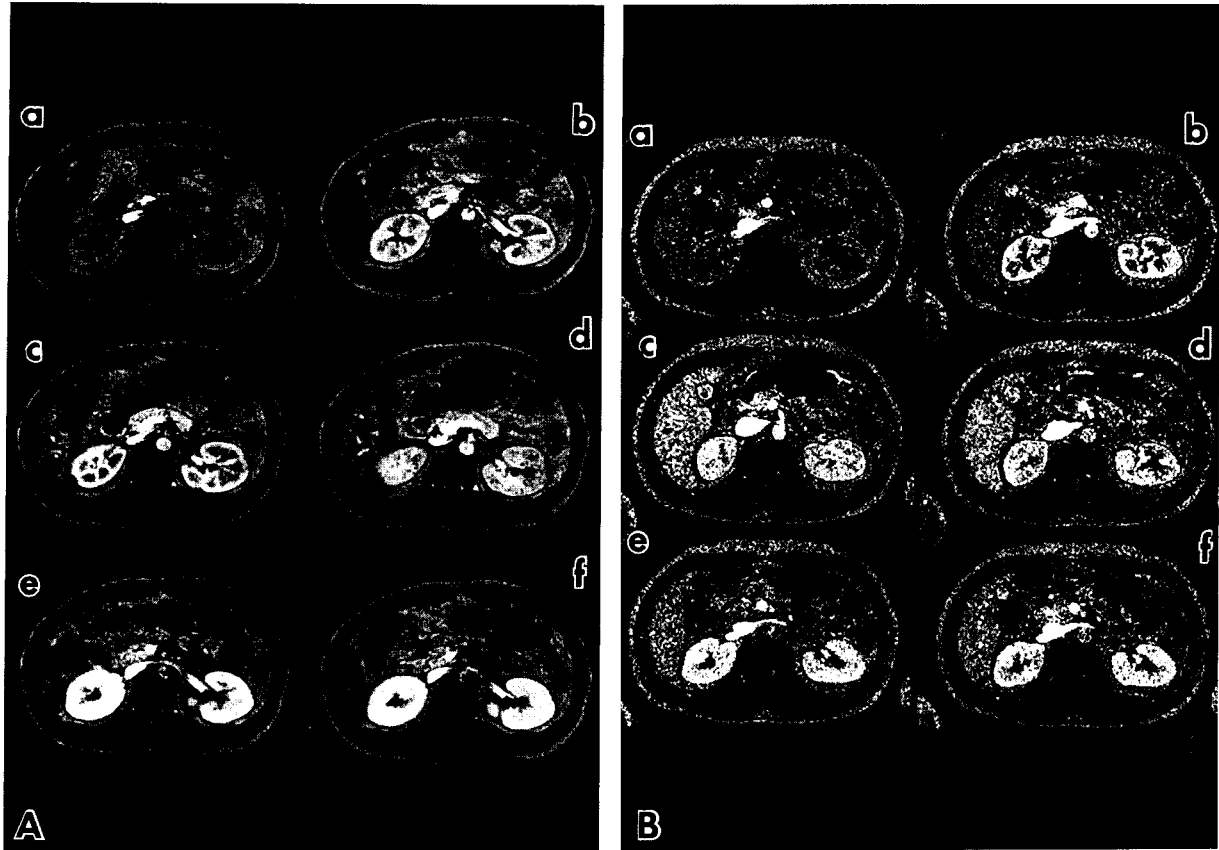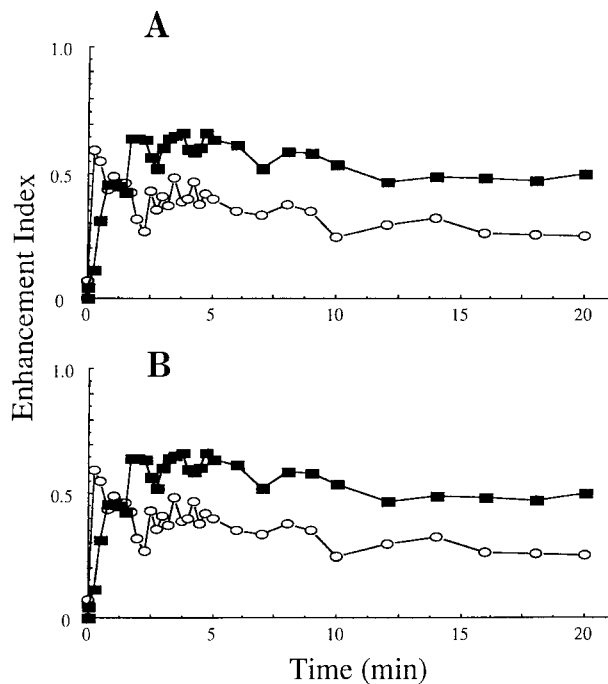
Fig. 5   Selected dynamic MR images of the kidneys by the negative method (TR = 50 msec, TE = 20 msec, FA = 30°, Gd-DTPA = 0.1 mmol/ kg). **A**: normal condition; **B**: overhydrated condition. Images obtained before injection and at 0.5, 1.5, 2.5, 10 and 20 min after injection (a–f, respectively). TR, TE and FA: See Fig. 2.

Table 3   Mean values of parameters under two conditions by two other intermediate methods

	Normal (n = 4) FA = 30° Gd-DTPA = 0.05 mmol/kg	Overhydrated (n = 4) FA = 30° Gd-DTPA = 0.05 mmol/kg	Normal (n = 4) FA = 70° Gd-DTPA = 0.1 mmol/kg	Overhydrated (n = 4) FA = 70° Gd-DTPA = 0.1 mmol/kg
Cortex				
EI max	0.515 ± 0.007	0.630 ± 0.136	0.720 ± 0.014	0.625 ± 0.021
T max	32.5 ± 10.6 (sec)	17.5 ± 10.6 (sec)	32.5 ± 10.6 (sec)	32.5 ± 10.6 (sec)
T 3/4	86.5 ± 0.1 (sec)	144 ± 4 (sec)	149 ± 27 (sec)	104 ± 10 (sec)
EI (5 min)–EI (20 min)	0.016 ± 0.015	0.022 ± 0.001	0.104 ± 0.023	0.125 ± 0.035
CMJT	62.1 ± 3.8 (sec)	62.2 ± 3.8 (sec)	84.4 ± 5.9 (sec)	445.9 ± 3.8 (sec)
Medulla				
EI max	0.590 ± 0.283	0.730 ± 0.042	0.655 ± 0.021	0.785 ± 0.007
T max	340 ± 127 (sec)	93 ± 11 (sec)	243 ± 53 (sec)	183 ± 11 (sec)
EI (5 min)–EI (20 min)	0.145 ± 0.212	0.065 ± 0.002	0.097 ± 0.004	0.235 ± 0.035

FA: flip angle; other abbreviations: See Table I.
All values are expressed as mean ± SD. n expresses the number of kidneys.

Fig. 6 Time-signal intensity curves by the negative method. **A**: normal condition; **B**: overhydrated condition. (□) Cortex; (■) Medulla.

much smaller by the negative method (frequently a negative value) than by the positive method.

Intermediate methods. A low SI did not appear on the images of the negative method. However, a detailed comparison between individual images disclosed regional differences in concentrating ability of the medulla, resulting in an inhomogeneous distribution of the SI. Fig. 7 shows one representative time-signal intensity curve, and Table 3 shows the mean values of the respective parameters. Under a normal condition, with an FA of 30 degrees and a Gd-DTPA dose of 0.05 mmol/kg, the medullary SI began to fall at about 2 min after Gd-DTPA injection (Fig. 7A), but this change did not occur under
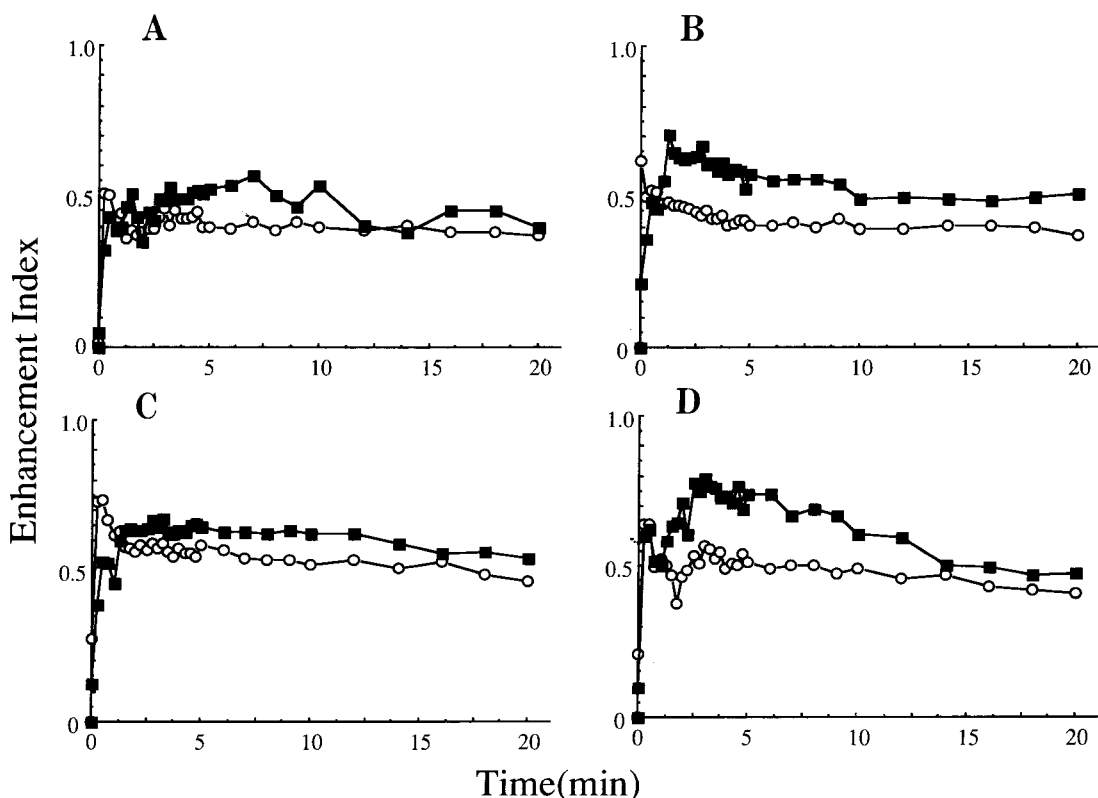

Fig. 7 Time-signal intensity curves. **A**: normal condition (TR = 50 msec, TE = 20 msec, FA = 30°, Gd-DTPA = 0.05 mmol/kg); **B**: overhydrated condition (TR = 50 msec, TE = 20 msec, FA = 30°, Gd-DTPA = 0.05 mmol/kg), **C**: normal condition (TR = 50 msec, TE = 20 msec, FA = 70°, Gd-DTPA = 0.1 mmol/kg), **D**: overhydrated condition (TR = 50 msec, TE = 20 msec, FA = 70°, Gd-DTPA = 0.1 mmol/kg). TR, TE, FA: See Fig. 2. (□) Cortex; (■) Medulla.

an overhydrated condition (Fig. 7B). With an FA of 70 degrees and a Gd-DTPA dose of 0.1 mmol/kg, no such change was observed under any condition, but the overall degree of SI reduction tended to be smaller under a normal condition than under an overhydrated condition (Fig. 7C, D). The differences between each condition were not significant.

Discussion

Four different methods of dynamic MR imaging using Gd-DTPA were used to study renal kinetic function (1-4). Unlike iodine-containing contrast materials which have been used for dynamic computed tomography (CT) (8, 9), the Gd-DTPA level is not in direct proportion to SI. Increasing the level of Gd-DTPA causes negative enhancement due to T2 shortening, resulting in a reduction in SI (1, 2). This is one of the remaining problems in the evaluation of renal function by dynamic MR imaging.

In the present study, we used positive enhancement weighting of the pulse sequence for dynamic MR imaging (5-7). Assuming that negative enhancement could be ignored, changes in regional levels of the contrast agent could be assessed directly, and the time-signal intensity curves were analyzed.

There have been many attempts to analyze renal function based on the presence/absence of concentration induced by negative enhancement (1-4). Most of these methods were MR fast imaging techniques during a breath holding, although the magnetic field strength differed among the instruments used. Our method differed only in the two respects, the FA and the dose level of contrast agent. The other parameters (TR and TE) are difficult to compare between studies because they are related to the capacity of the instruments used (both hardware and software). A relatively small FA was used for T2 weighting (2-4). The dose level of contrast agent was 0.1 mmol/kg (1-4).

In this study, we determined the optimum parameters of this MR imager with a phantom. Because a small increase in the concentration of the contrast agent was correlated with a rise in the SI, the positive method was used with a larger FA. Based on the signal-to-noise ratio (SNR), we considered an FA of 70 degrees and a dose level of Gd-DTPA 0.05 mmol/kg to be optimum. With this concentration of Gd-DTPA, negative enhancement could be ignored. Before the development of MR fast imaging techniques, Ikehira et al. (10-13) and Torii

et al. (14, 15) reported that a dose of 0.05 mmol/kg allowed accurate assessment of regional renal function. After the longitudinal relaxation rate was determined, changes in the regional concentrations of contrast agents could be assessed directly.

A lower concentration of contrast agent showed the maximum SI when a smaller FA was used. As expected, the SI decreased quickly with each increase of the concentration of contrast agent. By the negative method, we determined the optimum FA to be 30 degrees and the dose of contrast agent to be 0.1 mmol/kg.

We compared MR images and the time-signal intensity curves between the positive and negative methods. The positive method was applied to normal, dehydrated and overhydrated conditions, while the negative method was applied to normal and overhydrated conditions only because low SI make it impossible to estimate SI changes in the renal medulla.

By the positive method, there were no apparent differences among normal, dehydrated and overhydrated conditions. However, the statistical test of parameters showed significant differences in a prolonged cortical peak time (Tmax) and a reduced medullary peak level (EImax) between the normal or overhydrated condition and the dehydrated condition. The reduction in the medullary peak level under the dehydrated condition that occurred with Gd-DTPA concentrated in the medulla seemed to be caused by suppression of renal elimination of water (due to the antidiuretic hormone) and promotion of water reabsorption via the urinary tubule. These results suggest that the prolongation of cortical peak time under a dehydrated condition may represent delayed renal elimination. By the positive method, it seemed that the effect of T2 shortening was inevitable under a dehydrated condition because Gd-DTPA was concentrated. The other parameters showed no significant differences. These results suggest that the changes in water metabolism evaluated hardly affect the renal concentrating and diluting function of Gd-DTPA in healthy individuals.

Semelka et al. (1) reported that Gd-DTPA reached the collecting tubule of the renal medulla about 1.5 to 2 min after injection, and very similar results were obtained in the present study. In the present study, the SI in the medulla decreased at about 1.5 min after injection, when examined by the negative method. The disappearance of SI under an overhydrated condition when examined by the negative method seems to be the result of suppressed water reabsorption in the medulla which diluted the

concentrated Gd-DTPA in the collecting tubule. It has been reported that the negative enhancement due to T2 weighting was not seen in patients with renal dysfunction (1, 2). Based on this finding, the presence/absence of negative enhancement has been utilized to assess renal function. Indeed, the disappearance of medullary low SI is expected in patients with impaired concentrating function, because the Gd-DTPA level in the collecting tubules is decreased in such patients. However, because Gd-DTPA levels in the collecting tubules can also be changed by water kinetics, care is needed in assessing renal function based on the presence/absence of negative enhancement.

In the present study, we depicted the time-signal intensity curves by both the positive and negative methods. Analysis of parameters using the curves obtained by the negative method disclosed significant differences between normal and overhydrated conditions, and these differences were similar to those observed by the positive method between dehydrated and normal conditions. The fall of SI in the cortex and medulla was less marked by the negative method, and some cases were elevated. It therefore seems likely that SI by the negative method is not proportional to the concentration of Gd-DTPA because of the influence of T2 * shortening.

The disappearance of medullary low SI differed between healthy volunteers under an overhydrated condition measured by the negative method and patients with renal dysfunction. In normal kidneys, the disappearance of low SI represents a relative reduction of the concentrating ability while the diluting function remains intact. In diseased kidneys, the disappearance of low SI reflects a reduction in the concentrating ability. By inference, blood levels of the contrast agent are expected to be higher in patients with renal dysfunction due to impaired elimination, and the influence of recirculation is expected to be stronger in them. For this reason, observation of the medullary SI reduction (a change in the images) and analysis of the time-signal intensity curves is required. If the negative method does not show regional differences in the levels of contrast agent, the difference between them has to be analyzed using the time-signal intensity curves by the positive method.

By the negative method, a dramatic change appeared relatively early (about 1.5 to 2 min after contrast agent injection) and lasted for a short period. We believe that a single scan time of MR imaging is too long to allow evaluation of sudden changes. For this reason, we have not analyzed the early patterns of the parameters (such as early rising of parameters) on dynamic CT as attempted by Ishikawa et al. (8). However, such analysis should be done once the scan time is shortened through improvement of the software. Satoh et al. (9) reported that a new parameter, the CA (cortico-aortic) ratio, correlates best with creatinine clearance in the examination for renal parenchymal dysfunction based on the time-density curves (by dynamic CT). In the future, new parameters useful in the analysis of the time-signal intensity curves (by dynamic MR imaging) must be explored. We plan to compare the results of this study with other renal function tests in a large population.

Some investigators have reported that individuals with normal renal function also showed high signals within the renal pelvis some time after Gd-DTPA injection (1). Such high signals were not observed in this study either by the positive or negative methods. In our opinion, such high signals by the positive method indicate some disturbance of the renal function.

The results of the experiments by the two intermediate methods between positive and negative methods have diagnostic implications. These findings suggest that it is necessary to consider water kinetics in addition to imaging parameters, Gd-DTPA dose levels and imaging method. For analysis of the time-signal intensity curves from MR imaging renograms, regional changes in contrast agent levels have to be determined directly. The positive method seems to be superior to the negative method in this device because the former allows more direct determination of changes in regional contrast agent levels. Water overload reduced the influence of negative enhancement and improved the accuracy in determining regional changes in contrast agent levels. Thus, the application of water overloading seems promising. This method may be of value when assessment of subsegmental function of the kidneys is required. By evaluating both the temporal changes in renal parenchymal SI and the morphologic appearance of the kidneys, dynamic Gd-DTPA-enhanced MR imaging will make it possible to determine the glomerular filtration ratio (GFR) value without blood sampling, and the GFR pattern may be visualized with an MR GFR functional image (13).

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