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Analysis of Signal Intensity Curve on Dynamic Contrast-Enhanced MR Imaging of Postoperative Scars in Rabbits:

Comparison of Gadopentetate Dimeglumine and 24-gadolinium-tetraazacyclododecane tetraacetic acid (DOTA)-dendrimer

Joon Woo Lee, M.D., Woo Kyung Moon, M.D., Kee Hyun Chang, M.D., Soo Jeoung Kim, MSC., Jong Hyo Kim, PhD., Tae Jung Kim, M.D., Joon-il Choi, M.D., Se Hyung Kim, M.D., Chong Won Kwon, M.D., Bo Yoon Choi, M.D., Hyo-Cheol Kim, M.D., Hanns-Joachim Weinmann, PhD.,[2]

Purpose: To compare the enhancement patterns of 24-gadolinium-tetrazacyclododecane tetracetic acid (DOTA)-dendrimer (Gadomer-17) with those of gadopentetate dimeglumine (Magnevist) in postoperative scars in rabbits.

Materials and Methods: Twelve rabbit thighs with experimentally induced postoperative scars underwent dynamic contrast-enhanced MR imaging with both Gadomer-17 and gadopentetate dimeglumine at a 24-hr interval at one (n = 10), two (n = 8) and three months (n=4) after scar induction. The enhancement and the ratios of lesions at each time point, peak enhancement ratios, and the slope and shape of curves were assessed.

Results: At all time points, enhancement ratios were significantly lower after the injection of Gadomer-17 than with gadopentetate dimeglumine ($p<0.05$). Peak enhancement ratios were significantly lower with Gadomer-17 (1.29 ± 0.15) than with gadopentetate dimeglumine (1.61 ± 0.31) ($p<0.01$). The slope values were 2.99%/min $\pm$2.72 after Gadomer-17 injection and 8.99%/min$\pm$7.32 after gadopentetate dimeglumine injection ($p<0.01$). The enhancement ratio curves showed mostly the plateau pattern with Gadomer-17 (90.9%), while for gadopentetate dimeglumine, the curve pattern was either plateau (50%) or washout (50%). Difference in enhancement characteristics between the two contrast agents were most pronounced for one-month scars.

Conclusion: With Gadomer-17, weaker enhancement and the plateau pattern were found in postoperative scars, whereas stronger enhancement and either washout or the plateau pattern were found with gadopentetate dimeglumine.

Index words : Magnetic resonance (MR), experimental studies
Magnetic resonance (MR), contrast enhancement
Animals

[1]Department of Radiology, Seoul National University College of Medicine and the Institute of Radiation Medicine, SNUMRC
[2]Contrast Media Research, Schering, Mullerstra. 178, 13353 Berlin, Germany
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Address reprint requests to : Woo Kyung Moon, M.D., Department of Radiology, Seoul National University College of Medicine and the Institute of Radiation Medicine, SNUMRC
28 Yongon-dong, Chongno-gu, Seoul 110-744, Korea.
Tel. 82-2-760-2584 Fax. 82-2-743-6385 E-mail: moonwk@radcom.snu.ac.kr

Differentiation between post-therapeutic change and residual or recurrent tumor is of major importance in the follow-up of patients with most treated cancers. In the differential diagnosis between fibrotic and tumorous tissues, both CT and sonography suffer certain limitations, and several studies have assessed the value of high signal intensities on T2 weighted magnetic resonance (MR) imaging for this purpose (1 - 8). Later studies, however, indicated that high signal intensity on T2 weighted images is not specific for recurrent tumor and that low signal intensity can be due to both fibrosis and tumors (4 - 8).

For distinguishing late fibrosis (over 6 months) from malignancy, MR imaging with a conventional extracellular agent, gadopentetate dimeglumine, has been evaluated by several authors, and the results were promising (4, 8, 9 - 10). Late fibrosis showed no substantial enhancement on postcontrast T1-weighted images, wherease recurrent tumors demonstrated early enhancement. However, early fibrosis (less than 6 months) showed occasional enhancement due to different permeability partly due to leaky junctional complexes (4, 8, 11 - 12). Low-molecular-weight (546 d) gadopentetate dimeglumine not only enhances the vascular space but also diffuses rapidly into the interstitial space (13).

In order to minimize the problems associated with extracellular contrast agents, blood-pool contrast agents that remain exclusively within the intravascular space are currently under investigation (14). A 24-gadolinium-tetrazacyclododecane tetracetic acid (DOTA)-dendrimer (Gadomer-17; Schering, Berlin, Germany), a new macromolecular contrast agent, has an apparent molecular weight of 35,000 d, low enough to guarantee renal excretion and high enough to reduce diffusion through the endothelial cells of intact blood vessels (15). Potential clinical applications for this class of contrast agent include MR angiography and the determination of tissue perfusion, angiogenesis, and capillary integrity (16 - 19). Comparative studies of blood-pool and extracellular contrast agents, the former involving animals, have demonstrated improved lesion conspicuity and tumor characterization (20, 21). Where tumors are malignant, the hyperpermeability of tumor microvessels to macromolecular contrast agents has been demonstrated (22).

We hypothesized that postoperative scars may be less enhanced using a blood-pool contrast agent than when a small molecular contrast agent is used, and this might be new application for blood-pool contrast agents in postoperative conditions. The purpose of this experimental study was to compare the enhancement patterns of a new blood-pool contrast agent, Gadomer-17, and a conventional extracellular agent, gadopentetate dimeglumine, in postoperative scars in rabbits.

Materials and Methods

Animals and Experimental Models

For the experiments, 12 New Zealand white rabbits weighing 2 - 3kg were used. The animals were sedated with an intramuscular injection of 50 mg of ketamine hydrochloride (Ketalar; Yuhan Yanghang, Seoul, Korea) and 20 mg of xylazine hydrochloride (Rompun; Bayer Korea, Seoul, Korea). Experimental procedures were approved by the animal care committee at our institution.

Scars were induced in the (mainly right) thigh of each rabbit. After aseptic vertical incision of the skin of the lateral thigh, the underlying muscles were exposed. These were incised and dissected, and a 4-in. gauze square was folded and packed between muscle the bellies. Layer by layer closure from the muscle to the skin was then performed. Two weeks later, the gauze was removed under aseptic conditions, and after reincision of the skin, the muscle along the previous suture sites was incised and the gauze was removed. To avioe infection, 500 mg of cefazoline sodium (Cefazoline; Chongkeun Dang Pharmacy, Seoul, Korea) and 10 mg of gentamicin sulfate (Gentamicin; Korea United Pharmacy Inc., Seoul, Korea) were injected into the (mainly left) contralateral buttock daily for four weeks after initial gauze packing. On the basis of the interval between scar induction and sacrifice, the 12 rabbits were assigned equally to a 1-, 2-, or 3- month group, and in each group, MR studies were performed at one-month intervals after scar induction. An exception was that two of four rabbits in the 3-month group were not studied at one month because MR equipment was not available at that time and a total of 22 sets of MR images were thus obtained.

MR Imaging

All examinations were performed on a 1.5-T system (Magnetom Vison Plus; Siemens, Erlangen, Germany) using a CP-extremity coil. All images were acquired in the transaxial plane, with animals in the prone position. After routine localization and axial T2-weighted spin-echo imaging (TR/TE, 4000/96; 4-mm slice thickness), two sets of dynamic T1-weighted images were acquired.

For this two types of contrast agent were administrated via the aural vein by manual fast bolus injection in each animal: one injection of 0.1 mmol/kg gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany), followed by another, 24 hrs later, of 0.05 mmol/kg Gadomer -17 (supplied as an aquous formulation with a concentration of 500 mmol/l) (15). Dynamic T1-weighted MR imaging was performed with a fast spin-echo sequence (TR/TE, 450/16; echo train length, 10; bandwidth, 16 kHz; slice thickness, 4mm; field of view, 15 cm; acquisition matrix 256×128) before and 1, 2, 3, 4, 5, 10, 15, 20, 25 and 30 min after bolus injection of the contrast agent.

Image Analysis

MR imaging signal intensities were measured with the region-of-interest method in the most enhancing area of each scar. The enhancement ratio, determined by dividing the signal intensity seen on postcontrast scan by that seen on precontrast scan, was calculated for each time point. Peak enhancement ratio and the enhancement ratio at each time point were compared between the two contrast agents. In all studies enhancement ratios (postcontrast / precontrast signal intensities) for scars were plotted against time as mean values±standard deviation and the ratios were compared between the two contrast agents. In all cases, the slope of the curve (percentage increase in enhancement ratio per minute over baseline value) was derived using the following equation (15, 23, 24): slope = (ERmax-ERpre)×100 / (ERpre×Tmax), where ERpre represents the enhancement ratio of a given region of interest before the injection of contrast agents. The maximum enhancement ratio (ERmax) was determined as the value at a time point (Tmax) beyond which the sum of slopes measured for the two intervals between three consecutive time points on each curve was 10%/min or less. The slope of the curve was also compared between both contrast agents.

Enhancement ratio curves were classified on the basis of shape as either type I (steady enhancement), type II (plateau of enhancement ratio), or type III (washout of enhancement ratio)(25 - 26). Two radiologists blinded to the contrast agent employed determined the type of each curve, decisions being reached by consensus, and curve types were statistically analyzed.

At each maturation interval (one, two and three months) we compared enhancement ratio, peak enhancement ratio, slope and pattern, according to the contrast agent employed, and for each agent also compared enhancement ratios according to scar maturation interval.

Histologic Analysis

Animals were sacrificed with a lethal dose (90 mg/kg) of IV sodium pentobarbital (Pentothal; Choong Wae Pharmacy, Seoul, Korea), and the lateral muscle group of the thigh was excised and fixed in formaline solution. The scar area was then sectioned and stained with hematoxylin-eosin for light microscopic evaluation. Pathological review of the slides focused on the presence of fibrosis and differences in this according to scar maturation interval. A pathologist blinded to this interval reviewed the slides of the 12 scars, analysing collagen laydown, cellularity, extent of muscle involvement, vascularity and inflammation. By comparing the slides, these features were graded 0 to 3+, and the vessels (seen under 100- fold magnification) were counted.

Statistical Analysis

An SPSS software package version 9.0 (SPSS, Chicago, Ill., U.S.A.) was used for statistical data analysis. The Mann-Whitney U-test was employed to assess the statistical significance of differences between the contrast agents in terms of peak enhancement ratio, enhancement ratios at each time point and slope values, as well as that of differences in enhancement ratios at each scar maturation interval (one, two and three months). To determine the difference in curve type between the two agents, Fisher's exact test was used. For all tests, a p value of less than 0.05 was deemed significant.

Results

The enhancement ratios of scars varied substantially according to the contrast agent used (Fig. 1). In all studies (n = 22) and at all time points, ratios were consistently lower with Gadomer-17 than with gadopentetate dimeglumine (Magnevist), and all differences were statistically significant ($p < 0.05$) (Fig. 2). Peak enhancement ratios were significantly lower with Gadomer-17 (1.29± 0.15) than gadopentetate dimeglumine (1.61±0.31) ($p < 0.01$). For the former, the enhancement ratio peaked at 14.3±8.36 (3 - 30) mins, while for gadopentetate dimeglumine, the peak occured at 9.77±6.19 (1 - 30) mins. Peak enhancement occurred before five minutes in eight of 22 cases (36.4%) where gadopentetate dimeglumine was used, and five of 22 (22.7%) where Gadomer-17 was used. Slope values for scars were

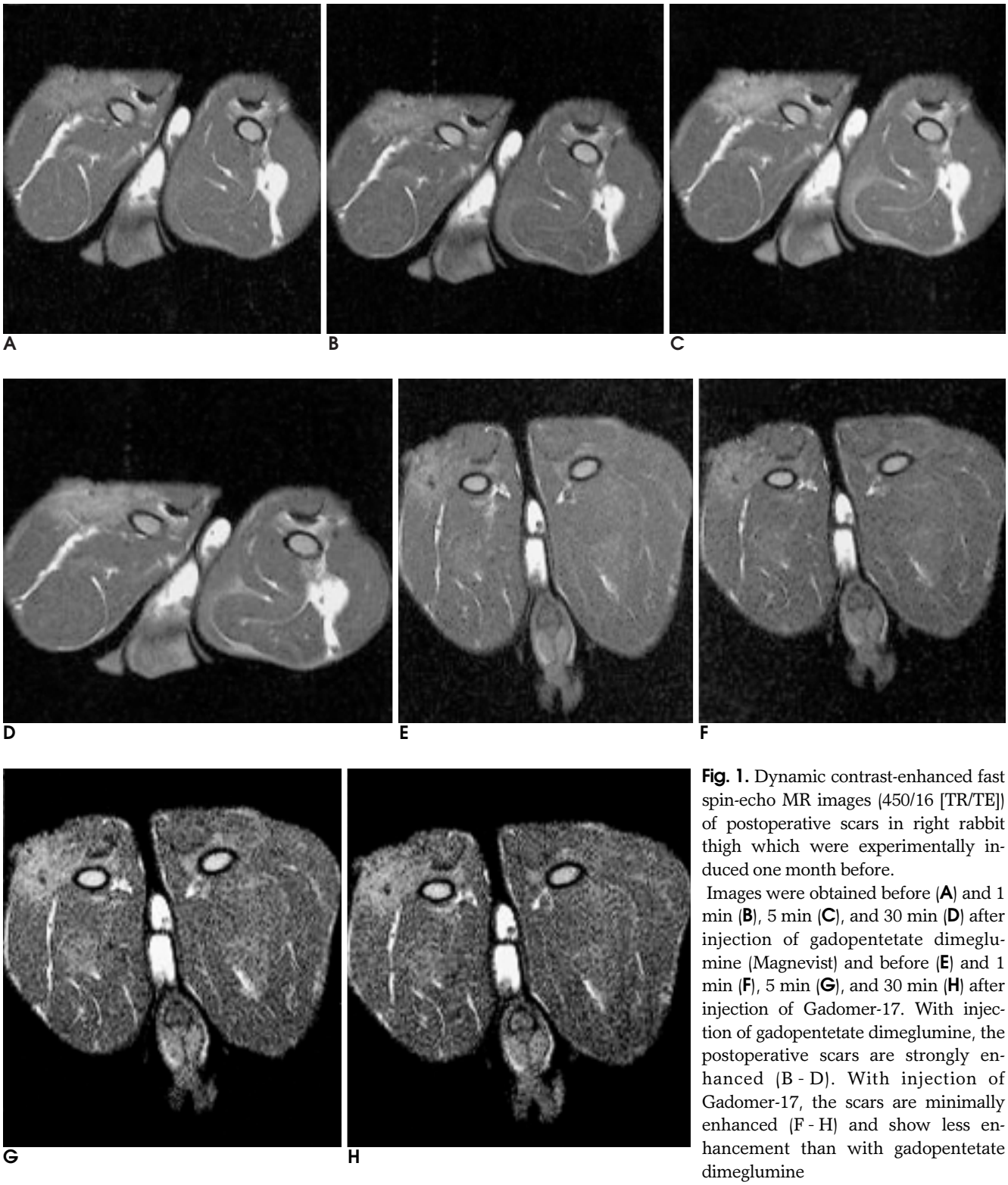

Fig. 1. Dynamic contrast-enhanced fast spin-echo MR images (450/16 [TR/TE]) of postoperative scars in right rabbit thigh which were experimentally induced one month before.
Images were obtained before (**A**) and 1 min (**B**), 5 min (**C**), and 30 min (**D**) after injection of gadopentetate dimeglumine (Magnevist) and before (**E**) and 1 min (**F**), 5 min (**G**), and 30 min (**H**) after injection of Gadomer-17. With injection of gadopentetate dimeglumine, the postoperative scars are strongly enhanced (B - D). With injection of Gadomer-17, the scars are minimally enhanced (F - H) and show less enhancement than with gadopentetate dimeglumine

0.79 - 9.57% (mean, 2.99%) /min±2.72 with Gadomer-17, and 0.97-30% (mean, 8.99%) /min±7.32 with gadopentetate dimeglumine. The difference was statistically significant ($p < 0.01$), and the shapes of the curves differed significantly ($p < 0.01$). With Gadomer-17, the predominant enhancement ratio curve was type II (plateau pattern), being found in 90.9% of cases (20 of 22). A type-I curve (steady enhancement) was identified in 4.54% of cases (1 of 22) while a type-III curve (washout pattern) was obtained in only 4.54% (1 of 22).

With gadopentetate dimeglumine, a type-II and a type III curve each occurred in 50% of cases (11 of 22).

When enhancement ratios were compared between 1-, 2- and 3-month scars after the injection of gadopentetate dimeglumine, they were consistently higher for 1-month scars (n = 10) than for 2- (n = 8) or 3-month scars (n = 4). Other than at 4, 25 and 30 mins, the difference was statistically significant at all time points ($p < 0.05$). With Gadoomer-17, however, enhancement ratios were not significantly higher for 1-month scars (n = 10) than for 2- (n = 8) or 3-month scars (n = 4) ($p > 0.01$) (Fig. 3).

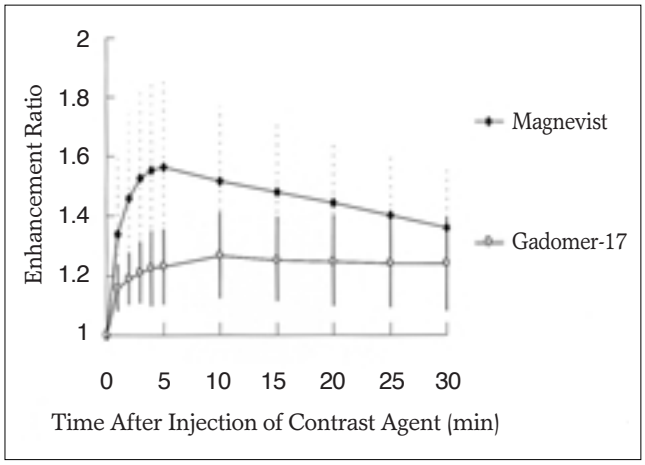

Fig. 2. Graphic shows mean enhancement ratio after injection of gadopentetate dimeglumine (0.1 mmol/kg) and Gadomer-17 (0.05 mmol/kg) in postoperative scars. Compared with plateau pattern of Gadomer-17, remarkable enhancement and washout pattern are seen after injection with gadopentetate dimeglumine. Enhancement ratios of scars are significantly higher at all time points with gadopentetate dimeglumine than with Gadomer-17 ($p < .05$). Error bars represent two standard deviation. Open circles represent enhancement curves with Gadomer-17. Solid diamonds represent enhancement curves with gadopentetate dimeglumine.

For one-month scars (n = 10), peak enhancement ratios were significantly lower with Gadomer-17 (1.34±0.17) than with gadopentetate dimeglumine (1.71±0.23) ($p < 0.01$) For Gadomer-17, the enhancement ratio peaked at 16.1±8.88 (1-30) / mins, while for gadopentetate dimeglumine, the ratio peaked at 8.80±3.62 (4 - 15) / mins. The enhancement ratios of these scars were consistently lower with Gadomer-17 than with gadopentetate dimeglumine, and the difference was statistically significant at all time points except 30 minutes ($p < 0.05$). Slope values were 0.98 - 9.57% (mean, 2.68%) / min± 2.72 with Gadomer-17 and 3.32-21.14% (mean, 10.39%) / min±6.13 with gadopentetate dimeglumine; the difference was statistically significant ($p < 0.01$).

For two-month scars (n = 8), peak enhancement ratios were significantly lower with Gadomer-17 (1.28±0.12) than with gadopentetate dimeglumine (1.61±0.40) ($p < 0.05$). For Gadomer-17, the enhancement ratio peaked at 12.25±8.21 (2-20) mins, while for gadopentetate dimeglumine the peak occurred at 8.38±5.53 (3 - 20) mins. Enhancement ratios at each time point were consistently lower with Gadomer-17 than with gadopentetate dimeglumine, though the difference was statistically significant only during the early phase (2, 3,

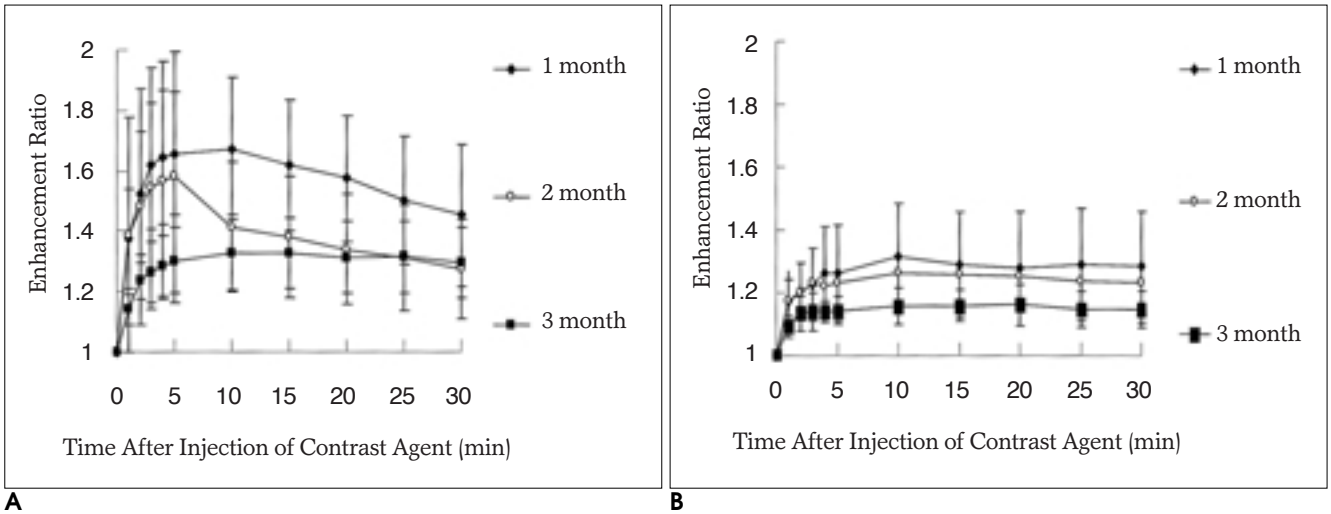

Fig. 3. Graphic presentation of mean enhancement ratio after injection of gadopentetate dimeglumine (**A**) and Gadomer-17 (**B**) in scars according to scar maturation interval. With injection of gadopentetate dimeglumine, there are significant decrease in three month scars compared with one month at all time point except 4, 25, 30 min ($p < 0.05$) (A). However, with injection of Gadomer-17, there are no significant decrease in three month scars compared with one month at all time point ($p > 0.05$) (**B**). Solid diamond represent enhancement curves in one month scars. Open circles represent enhancement curves in two month scars. Solid rectangles represent enhancement curves in three month scars.

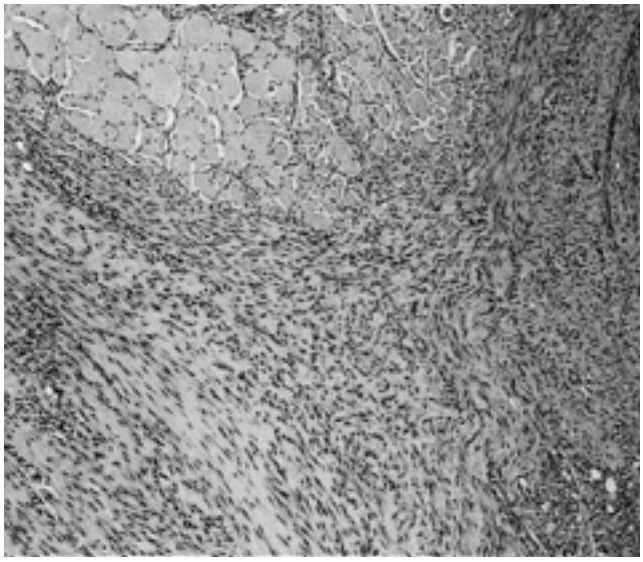

Fig. 4. Light microscopic view of 2-month scars.
On 40 fold magnification view (H & E staining), there are extensive collagens and fibroblasts between muscular bundles.

4 and 5 minutes) ($p<0.05$). Slope values were 0.79 - 2.20% (mean, 1.55%) / min±0.69 with Gadomer-17 injection and 0.97 - 4.34% (mean, 2.67%) / min±1.39 with gadopentetate dimeglumine; the difference was statistically significant ($p<0.05$).

For three-month scars (n=4), peak enhancement ratios were significantly lower with Gadomer-17 (1.17± 0.05) than with gadopentetate dimeglumine (1.35±0.10) ($p<0.05$). For Gadomer-17, the enhancement ratio peaked at 13.75±8.54 min (5 - 25) mins, while for gadopentetate dimeglumine the peak occurred at 16.25 ±9.46 (10 - 30) mins. Enhancement ratios at each time point were slightly lower with Gadomer-17 than with gadopentetate dimeglumine, but the difference was not statistically significant except at ten minutes ($p>0.05$). Slope values were 0.79 - 2.20% (mean, 1.55%) / min± 0.69 with Gadomer-17 and 0.97 - 4.34% (mean, 2.67%) / min±1.39 with gadopentetate dimeglumine (n=8), though the difference was not statistically significant ($p>0.05$).

Light microscopic pathologic findings were consistent with fibrosis in all cases. Light microscopic examination revealed no differences in grade of collagen laydown, cellularity, muscle involvement or vessel count between 1-, 2- and 3-month scars (Fig. 4).

Discussion

Dynamic contrast-enhanced MR imaging is a method of physiologic imaging method which provides information on the early sequential enhancement kinetics of a water-soluble contrast agent after IV bolus injection (23, 27, 28). After IV injection of gadopentetate dimeglumine, a conventional extracellular agent, the contrast agent diffuses rapidly from the intravascular into the interstitial space and the enhancement pattern results from various properties of the lesion including blood volume, blood supply, vascular and extracellular spaces, and endothelial permeability (13). A blood-pool contrast agent confined to the vascular space, on the other hand, reflects the size of that space, except under certain abnormal conditions such as malignancy and inflammation (18, 21, 29).

In general, the contrast enhancement of any tissue with gadopentetate dimeglumine requires (1) a vascular supply, (2) a route for the contrast material out of the vasculature, and (3) an interstitial space for sequestering the contrast material. Scars have all of these attributes. They have an abundant vascular supply (especially in early fibrosis), and the leaky junctions and intercellular gaps observed in the endothelium and large interstitial space (4, 11 - 12). Thus, when a small molecular contrast agent is used, a scar exhibits contrast enhancement. In this study, scars showed better contrast enhancement with an agent containing small molecules than with one containing large ones; since the latter is able to reduce diffusion through the endothelial cells of intact blood vessels, this was as expected.

Nguyen-minh et al. (17) described the signal intensity changes observed in recurrent herniated disk and scars in dogs after the injection of Gadomer-17 and gadopentetate dimeglumine. In their study, MR imaging involved the use of gadopentetate dimeglumine at 20 and 50 days and Gadomer-17 at 22 and 52 days, and changes in signal intensity from baseline in the disk and scar tissue were measured at 2, 22 and 45 minutes. The average signal intensity change in a scar at 20 or 22 days was lower with Gadomer-17 than with gadopentetate dimeglumine. The difference in signal intensity between the two agents was, however, statistically significant only at 2 minutes. The average signal intensity change observed in a scar at 50 or 52 days was slightly lower with Gadomer-17 than with gadopentetate dimeglumine at 2 and 22 minutes, and slightly higher at 45 minutes. There was, though, no significant difference. With both agents, scar enhancement was greater at 20 days than at 50 days. Because their study was not a dynamic one, the enhancement pattern and other parameters such as peak enhancement ratios or slope could not be evaluated.

In our study, the injected dose of Gadomer-17 was 0.05 mmol/kg, which was half of that of gadopentetate dimeglumine (0.1 mmol/kg). However, the T1 relaxivity of Gadomer-17 was 11.9 l*mmol-1*sec-1 , more than twice than that of gadopentetate dimeglumine (4.9 l*mmol-1*sec-1). With regard to the injected dose, our study therefore involved no bias.

Moon et al. (15) described the enhancement pattern of Gadomer-17 and gadopentetate dimeglumine in bacterial abscess and VX2 carcinoma in rabbits. For the latter condition, enhancement curves demonstrated a washout pattern with both contrast agents; peak enhancement occurred later with Gadomer-17 (at 10 mins) than with gadopentetate dimeglumine (at 3 mins). Thus, with Gadomer-17, enhancement patterns differ significantly between scars (plateau pattern) and VX2 carcinomas (washout pattern), while with gadopentetate dimeglumine, there is substantial overlap of the washout pattern between scars and VX2 carcinomas. Previous reports also showed that in breast cancer, a type-III washout pattern is a strong indicator of malignancy (25, 26). In our study, the enhancement curves of scars in rabbits were predominantly plateau pattern with Gadomer-17 (90.9%), whereas with gadopentetate dimeglumine, half (50%) showed washout patterns. For a direct comparison of enhancement characteristics between fibrosis and malignant tumors using large molecular contrast agents, further investigation is needed.

The leaky junctions and intercellular gaps observed in the endothelium of fibrosis appear to provide a basic structure-function correlation with enhancement by gadopentetate dimeglumine. Early fibrosis or young scar (defined clinically as less than 6 months or 1 year) most probably has leaky junctional complexes, and on the basis of many different criteria-including basement membrane thickness-differs in permeability relative to old scar. Early fibrosis or young scar thus enhances more intensely after gadopentetate dimeglumine contrast enhancement (4, 11 - 12). These features correlated closely with our results showing that with gadopentetate dimeglumine, the enhancement ratios of scars decreased significantly during the maturation of fibrosis from one month to three months. With Gadomer-17, on the other hand, enhancement ratios showed no significant decrease during this same period. These results reflect the fact that with Gadomer-17, enhancement ratios correlated with vascularity, independent of minor change of permeability according to scar maturation. Thus, differences in enhancement patterns between the two contrast agents are most pronounced one month after scar induction. These results suggest that during early postoperative periods when it is difficult to differentiate the early stage of fibrosis from recurrent tumor using gadopentetate dimeglumine, the use of Gadomer-17 would be useful. A limitation of our study, however, is that light microscopic analysis was not enough to reveal differences according to scar maturation interval. Early or immature fibrosis is defined clinically as requiring a six-moth or one-year maturation interval in humans (4, 6, 12), and definite criteria for early fibrosis was not revealed by light microscopic rather than electron microscopic studies, which-for practical reasons-were not performed in the present study. It may be that 1-month scars are earlier or more immature than 2- or 3-month scars.

Because we were unable to find postoperative models for rabbit thigh in the literature, the successful induction of fibrosis required many trials. These involved scar induction by ethanol injection, muscle ablation by bovie, and numerous muscle incisions and intramuscular microbarium injections: pathologic examination showed that in all instances little or no fibrosis resulted, and a pilot study indicated that temporary gauze packing was the most reliable method inducing fibrosis in rabbit thigh.

In conclusion, the observed enhancement patterns of Gadomer-17 and gadopentetate dimeglumine after scarring were quite different. With Gadomer-17, a lower enhancement ratio and plateau curves were found, whereas with gadopentetate dimeglumine there was a higher enhancement ratio, and washout or plateau curves were observed. This difference in enhancement patterns between the two contrast agents is most pronounced during the earlier stages of fibrosis, and can help differentiate between early postoperative scars and recurrent tumors.

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가토에 유발한 수술 후 반흔에 대한 역동적 조영 증강 자기공명영상 Signal Intensity Curve: Gadopentetate Dimeglumine 와 24 - gadolinium - tetraazacyclododecane tetraacetic acid (DOTA) - dendrimer 의 비교[1]

[1]서울대학교 의과대학 방사선과학교실, 서울대학교 의학연구원 방사선의학연구소
[2]Contrast Media Research, Schering, Germany

이준우 · 문우경 · 장기현 · 김수정 · 김종효 · 김태정 · 최준일 · 김세형 · 권종원
최보윤 · 김효철 · Hanns - Joachim Weinmann, PhD[2]

목적: 가토에서 실험적으로 유발한 수술후 반흔에 대해 24 - gadolinium - tetraazacyclododecane tetraacetic acid (DOTA) - dendrimer (Gadomer - 17; Schering, Berlin, Germany) 과 gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany)를 이용한 역동적 조영증강 자기공명영상에서의 조영 증강 행태를 비교해 보고자 하였다.

대상과 방법: 12 마리의 가토에 한쪽 다리에 수술적 방법으로 반흔을 만든 후 24시간 간격으로 두 가지 조영제인 Gadomer - 17과 gadopentetate dimeglumine를 이용하여 조영제 주입 후 1, 2, 3, 4, 5, 10, 15, 20, 25, 30분에 영상을 얻는 역동적 자기공명영상을 시행하였다. 한달 째 열 마리, 두달 째 여덟 마리, 세달 째 네 마리, 총 22 번의 실험을 시행하였으며, 각 시간당 조영비를 이용해 그래프를 그린 후, 각 시간 당 조영비, 최대조영비, 경사, 조영 곡선의 모양 등을 분석하였다.

결과: Gadomer - 17을 이용한 역동적 자기 공명 영상에서 각 시간 당 조영비는 모든 시간대에서 gadopentetate dimeglumine 에 비해서 통계적으로 유의하게 낮았다 ($p<0.05$). 최대 조영비도 Gadomer - 17의 경우 gadopentetate dimeglumine 에 비해서 통계적으로 유의하게 낮았다 (1.29±0.15 vs 1.61±0.31, $p<0.01$). Gadomer - 17의 경우 경사비는 2.99%/min±2.72였고, gadopentetate dimeglumine 의 경우는 8.99%/min±7.32 였다 ($p<0.01$). Gadomer - 17의 경우에는 대부분 plateau 양상 (90.9%) 의 조영 증강 곡선 모양이었으나 gadopentetate dimeglumine 의 경우에는 plateau 양상과 washout 양상이 반반씩이었다. 두 조영제 간에 역동적 자기공명 영상에서의 조영비의 차이는 1 개월째 반흔에서 가장 현저하였다.

결론: Gadomer - 17을 이용한 경우는 수술 후 반흔에 대한 역동적 자기공명영상에서 gadopentetate dimeglumine 보다 조영 정도가 약하며 최대치가 낮고 보다 늦게 최대치에 도달하며 주로 plateau 양상이지만 gadopentetate dimeglumine의 경우에는 보다 조영 정도가 강하며 washout 이나 plateau 양상이었다.