Utility of High-Dose Contrast Enhancement for Detecting Recurrent Herniated Intervertebral Disks

Canh Nguyen, Howard An, Khang-Cheng Ho, Victor M. Haughton, and Toru Hasegawa

PURPOSE: To study the utility of high-dose contrast enhancement in the detection of recurrent herniated disk fragments. **METHODS:** Recurrent herniated disks were modeled in nine dogs by placing a fragment of normal autologous disk tissue in the epidural space at laminectomy. MR was performed at 30, 60, and 90 days with 0.3 mmol/kg of gadoteridol and repeated 24 hours later with 0.1 mmol/kg of gadopentetate dimeglumine. Contrast enhancement in the disk and scar tissue was measured and conspicuousness of the disk fragments assessed. **RESULTS:** In 70% of the animals, disk fragments were more conspicuous with the larger dose of contrast medium than with the smaller dose. In 30% of animals the conspicuousness was approximately equal. Contrast between disk fragment and scar decreased with time elapsed since surgery, with time elapsed since contrast-medium injection, and with decreasing dose of contrast medium. **CONCLUSION:** In the experimental model, increased conspicuousness of disk fragments was achieved with the larger dose of contrast medium. A clinical study is needed to confirm that a contrast-medium dose of 0.3 mmol/kg improves detection of recurrent herniated disks over a dose of 0.1 mmol/kg.

Index terms: Magnetic resonance, contrast enhancement; Magnetic resonance, experimental; Spine, intervertebral disks, herniation; Spine, magnetic resonance; Animal studies

AJNR Am J Neuroradiol 15:1291–1297, Aug 1994

Magnetic resonance (MR) with intravenous contrast medium is the procedure of choice to evaluate patients after laminectomy (1, 2). The contrast medium is used to improve the conspicuousness of scar tissue, which usually enhances with contrast medium to a variable degree, and to distinguish disk fragments, which normally enhance to a lesser degree (3, 4). Scar tissue is better enhanced and more conspicuous after administration of 0.3 mmol/kg than 0.1 mmol/kg (5). Therefore, in principle, the larger dose may provide greater contrast between scar and disk tissue. The utility of a high contrast-medium dose in the differentiation of scar and disk tissue has not been studied, to our knowledge. The purpose of this study was to compare the conspicuousness of recurrent herniated disks with the conventional 0.1-mmol/kg dose of gadopentetate dimeglumine and the 0.3-mmol/kg dose of gadoteridol, which is also approved for clinical use. We used an animal model of recurrent herniated disk.

Materials and Methods

Twelve mongrel dogs weighing from 11 to 22 kg that completed a 30-day quarantine and testing for mycobacterial and intestinal infections were used. Nine (treated) dogs had a left L-3 to L-4 hemilaminectomy and placement of a fragment of intervertebral disk in the epidural space, and three (control) dogs had a hemilaminectomy without placement of a disk fragment.

For the surgery, the dogs were fasted for 12 hours and then anesthetized with acepromazine (1 mg/kg intramuscularly), atropine (0.05 mg/kg intramuscularly), and phenobarbital (25 mg/kg intravenously). The animals were intubated and ventilated with a respirator (Harvard Instruments, Cambridge, Mass). The skin over the lumbar spine was shaved and surgically disinfected. A vertical midline incision was made at L3–4. The left paraspinal muscles were dissected free of the spinous processes with perios-

Received June 9, 1993; accepted pending revision August 26; revision received October 18.

Supported by a grant from Bristol Meyers-Squibb (Princeton, NJ).

From the Departments of Radiology, Pathology, (C.N., V.M.H., K.-C.H.) and Orthopedic Surgery, (H.A., T.H.) Medical College of Wisconsin, Milwaukee.

Address reprint requests to Victor M. Haughton, MD, Department of Radiology, Froedtert Memorial Lutheran Hospital, 9200 W Wisconsin Ave, Milwaukee, WI 53226.

AJNR 15:1291–1297, Aug 1994 0195-6108/94/1507–1291

teal elevators. Hemostasis was achieved with electrocautery. With a cutting burr drill (Microdrill model 5053–001, Hall Surgical, Santa Barbara, Calif) the inferior half of the left L-3 lamina and the superior half of the left L-4 lamina were removed. Drilling was continued until a defect 2 cm long and 1 cm wide was created. The ligamentum flavum and periosteum in the defect were removed with rongeurs and curettes. The surgical field was irrigated with sterile saline and suction. The intervertebral disk space was located by palpating with a probe. The anulus fibrosus was incised with a number 11 blade, and then the defect was enlarged with a blunt instrument until nucleus pulposus was seen to ooze from the disk. Any bleeding from the epidural venous plexus was controlled with gelfoam and light compression. In control animals, the procedure was terminated at this point, and the wound was closed in layers. In the treated animals, the proximal portion of the tail was shaved, surgically disinfected, and resected. The skin over the proximal tail was sutured to cover the wound. From the distal tail one intervertebral disk was removed aseptically. A cylindrical fragment about 1.5 to 2 mm in height and 6 to 7 mm in diameter was removed from the intact intervertebral disk. The fragment was inserted into the epidural space to the left of the dural sac and slightly cephalad to the laminectomy defect. Hemostasis was rechecked. The wound was then closed in layers.

The dogs were allowed to recover from anesthesia in a humidified, warmed environment (Kirschner, Intensive Care System). The animals were then returned to their cages. For analgesia, fentanyl 0.04 mg/kg and droperidol 2 mg/kg were given as necessary intramuscularly. Cefazolin sodium was given daily for 3 days prophylactically.

Up to the scheduled time of death MR was performed on the 15th, 30th, 60th, and 90th days after surgery. For MR the dogs were sedated with acepromazine, atropine, and phenobarbital and placed supine on a 3-in surface coil in a 1.5-T imager. Axial and sagittal images were obtained through the lumbar spine with 256 256 matrix, 3-mm section thickness, and 600/25/2 (repetition time/echo time/excitations). The axial images were obtained both with and without chemical-shift fat suppression. Gadoteridol (ProHance, Bristol Meyers-Squibb, Princeton, NJ) was then administered intravenously in a dose of 0.3 mmol/kg. The short-repetition-time axial images with fat suppression were repeated at 2, 25, and 45 minutes after injection of contrast medium with identical techniques. Supplementary axial and sagittal images without fat suppression were also obtained at 12 and 35 minutes. When the 1.5-T imager was unavailable, images were obtained on a 0.5-T Signa imager (General Electric Medical Systems, Milwaukee, Wis), with the same parameters, except that variable bandwidth was used.

On the day of death and at least 24 hours after the last MR, each dog had an MR study with gadopentetate dimeglumine (Magnevist, Berlex Laboratories, Secaucus, NJ) in a dose of 0.1 mmol/kg. For this imaging study sagittal and axial images with fat suppression were obtained before contrast medium, and axial images were repeated at 2 minutes after injection of contrast medium. Imaging parameters were the same as in the MR study with gadoteridol.

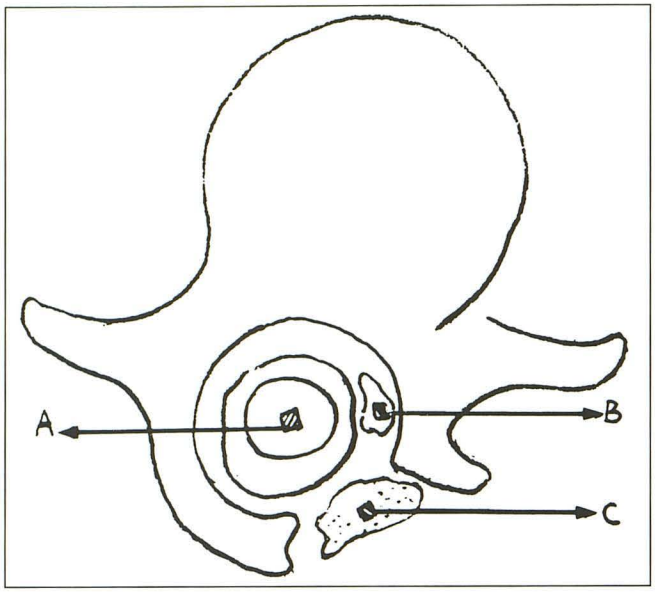


Fig 1. Sketch showing placement of cursor to measure contrast enhancement in epidural scar, disk fragment, and dural sac. *A* indicates spinal cord; *B*, disk fragment; and *C*, scar in laminectomy defect.

Pre- and postenhancement images were compared and the locations of scar and disk fragment determined. Signal intensity in the disk fragment, in the scar tissue in the region of the excised lamina, and in the dural sac (as an internal control) was measured with a cursor (Fig 1) in the baseline and 2-, 25-, and 45-minute images. Signal intensities in baseline and postcontrast images with the cursor position carefully aligned to the same tissue in each image were compared. Contrast enhancement for each of the tissues was calculated as the difference in signal intensity between postcontrast and baseline images divided by the baseline signal intensity. All measurements were entered in a spread-sheet program (Quattro, Borland International) and averages and standard deviations calculated and graphed. Contrast enhancement was plotted as a function of time after injection, as a function of time elapsed since surgery, and as a function of dose.

The animals were killed serially at 30, 60, and 90 days. The lumbar spine was carefully removed en bloc and fixed in 10% formalin, decalcified, embedded in paraffin, sectioned axially, and stained with hematoxylin and eosin. The stained sections were examined to verify the location of the scar tissue and disk fragment in the epidural space.

Results

All animals survived the surgery. No complications were observed. Four animals (three treated and one control) were killed at 31 days, four more at 61 days, and four more at 91 days.

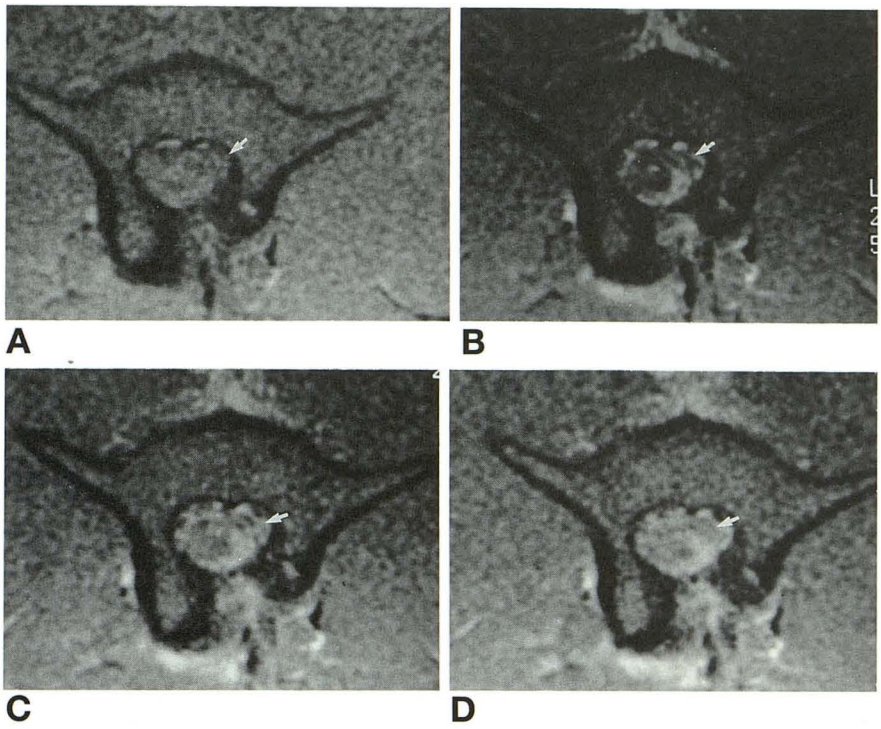


Fig 2. A sequence of axial MR images in a dog with a laminectomy and a disk fragment in the epidural space (*arrow*). All images were obtained at the same location.

A, Before administration of contrast medium, a T1-weighted image does not show the fragment effectively.

Images *B*, *C*, and *D* were obtained at 2, 25, and 45 minutes after 0.3 mmol/kg gadoteridol with the same parameters used in *A*.

In each MR study in the treated animals, a laminectomy defect and an epidural fragment of disk were identified (Fig 2). In none of the control animals were abnormalities in the epidural space suggestive of disk fragments identified. In five animals the disk fragments appeared more conspicuous on the images obtained with 0.3 mmol/kg than in the images with 0.1 mmol/kg of contrast medium (Fig 3) obtained 1 day later. Fat suppression did not appear to affect the contrast between disk fragment and scar in the dogs because of the sparse fat in the epidural space. In two animals, the fragments appeared equally conspicuous with the two doses of contrast medium (Fig 4). In two animals, a 0.5-T Signa imager was used, because the 1.5-T Signa was not available for research. These studies were not included in the tabulations or contrast-enhancement measurements.

The contrast enhancement in disk fragments and scar tissue is shown in the Table and Figures 5 and 6. Contrast enhancement in disk and scar tissue varied with the time elapsed since surgery. Two minutes after the intravenous injection of gadoteridol (0.3 mmol/kg) in dogs that had surgery 15 days previously, the enhancement of the disk fragments was 130%, and the enhancement of scar tissue was 201%. At 30, 60, and 90 days the enhancement of scar tissue was progressively less. The disk fragments also tended to enhance less at 30, 60, and 90 days. The difference between the enhancement of scar tissue and disk fragment was also less at 30, 60, and 90 days than at 15 days (Fig 5). At 25 and 45 minutes, the contrast between scar tissue and disk fragment diminished, because disk tissue tended to show progressive enhancement, and scar tissue tended to decrease in signal intensity by 25 or 45 minutes.

Contrast enhancement in disk fragments and in scar tissue was less after the injection of the gadopentetate dimeglumine (0.1 mmol/kg) (Fig 6). As in the case of gadoteridol injection, the enhancement in scar tissue after gadopentetate dimeglumine tended to decrease with time elapsed since surgery. The difference in enhancement between scar and disk fragment was greater at 15 days than at 30, 60, or 90 days. With the smaller dose of contrast medium, differences between the enhancement in the disk and in the scar tissue were smaller.

Enhancement varied also with the elapse of time since the injection of the contrast medium (Table). Enhancement in both scar and disk fragment tended to increase between 2 and 25 minutes and then decrease between 25 and 45 minutes. The difference between enhancement in the scar tissue and disk fragment was greatest at 2 minutes.

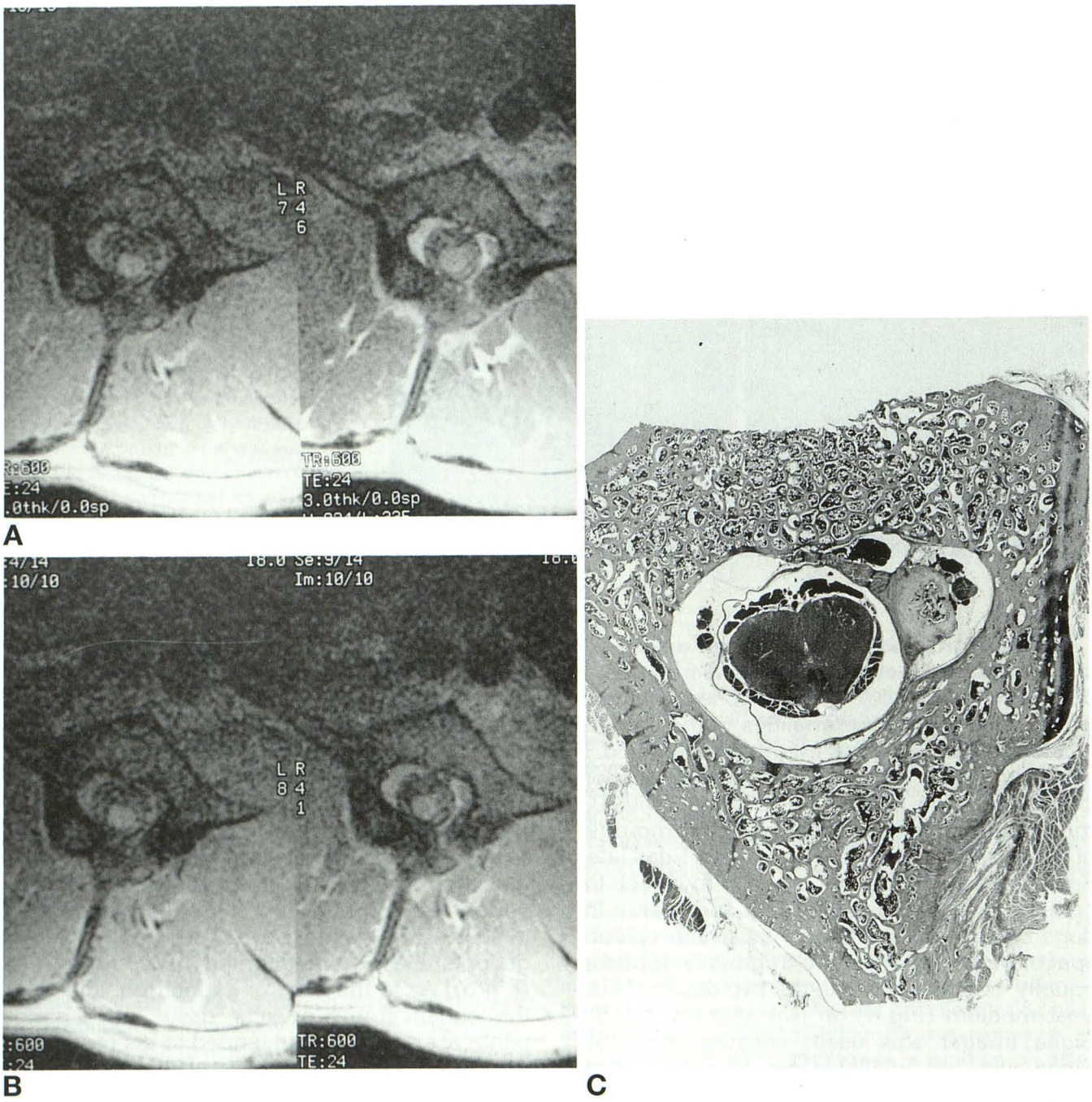
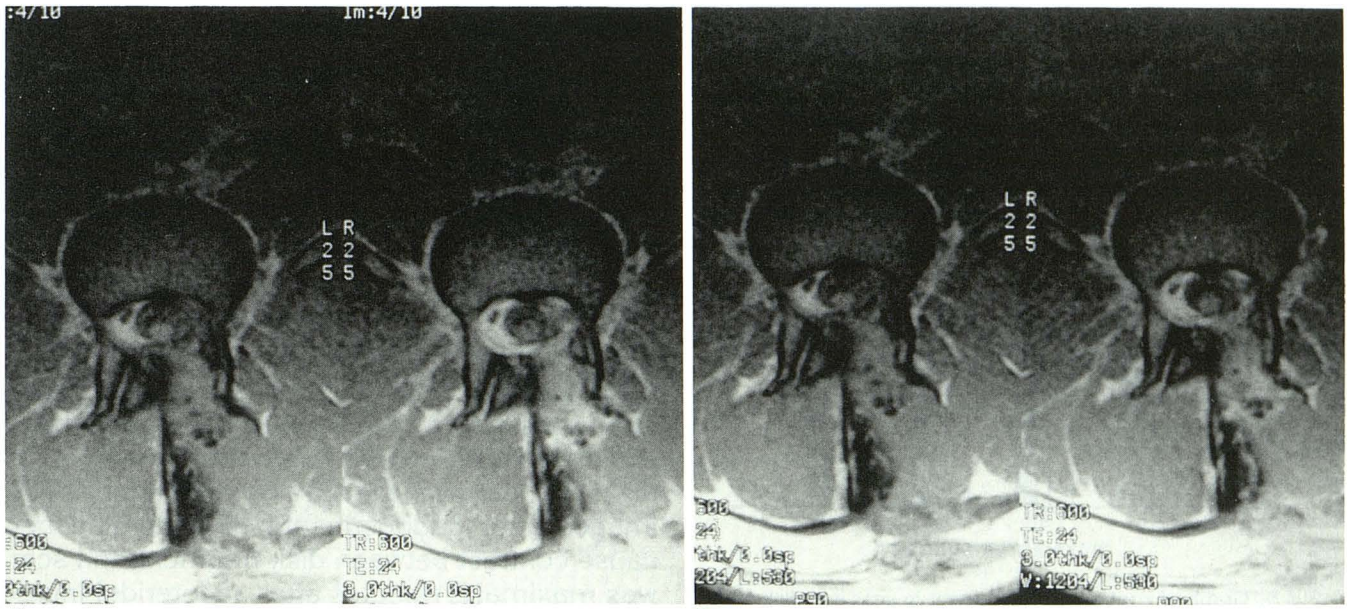


Fig 3. MR obtained at 90 days in a dog with postlaminectomy scar and epidural disk fragment.

A, Images before (*left*) and 2 minutes after (*right*) intravenous contrast medium (0.3 mmol/kg) show the small disk fragment in the left epidural space and the left laminectomy.

B, Images before (*left*) and 2 minutes after (*right*) contrast medium in a dose of 0.1 mmol/kg show less contrast between the disk fragment and the scar tissue (600/24/2, fat suppression).

C, Postmortem axial histologic section shows the fragment of disk infiltrated with small blood vessels and surrounded by scar tissue.



A B

Fig 4. MR images 600/24/2 without (*left*) and with (*right*) intravenous contrast medium obtained from the 0.3-mmol/kg study (*A*) and 0.1-mmol/kg study (*B*). Conspicuousness of the disk fragment to the left of midline was judged about equal in the two studies.

Examination of the postmortem spine sections verified fibrocartilage in the epidural space, where the MR scan showed an epidural abnormality assumed to represent disk fragment (Fig 3C). At 15 days blood vessels were apparent in the fibrocartilage. The number of blood vessels increased at 30, 60, and 90 days. Fibrous tissue surrounded the fibrocartilaginous fragment in the epidural space.

Discussion

This study shows that the contrast enhancement in disk fragments and scar tissue varies with the dose of contrast medium, the age of the scar and disk fragment, and the elapsed time from the injection of contrast medium. Contrast between scar and disk may be increased by increasing the dose of contrast medium used for MR and by obtaining images as soon as possible after the injection of the contrast medium.

For this pilot study not all variables were controlled. An animal model was selected to permit anatomic verification and controls. The epidural space of dogs contains less fat than that of humans. However, the fibrocartilagenous and fibrous constituents of dog and human disks are similar (6, 7). Although the animal model pro-

Percentage of enhancement (standard deviation) in disk fragment and scar tissue after administration of contrast medium

	0.03 mmol/kg							0.1 mmol/kg 2 min	
	2 min		25 min		45 min				
	Disk Fragment	Scar	Disk Fragment	Scar	Disk Fragment	Scar		Disk Fragment	Scar
15 days n=7[a]	130(70)	201(35)	271(65)	174(44)	131(63)	130(41)	15 days n=1	10	60
30 days n=8[b]	137(55)	151(77)	171(71)	158(67)	142(72)	117(59)	30 days n=3	52 (3)	66 (4)
60 days n=6	76(58)	105(65)	115(67)	111(59)	116(63)	100(64)	60 days n=3	32 (30)	47 (14)
90 days n=3	99(70)	91(46)	95(60)	92(88)	113(39)	99(37)	90 days n=3	47 (14)	24 (18)

[a] One measurement at 0.5 T excluded.
[b] Two measurements at 0.5 T excluded.

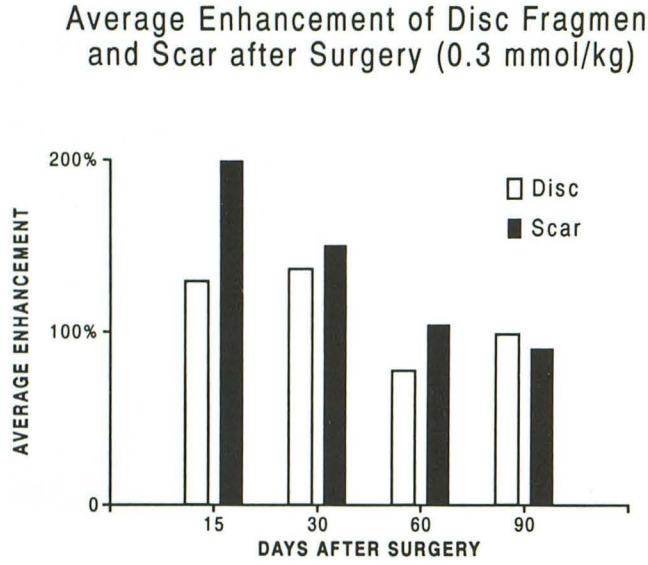


Fig 5. Graph of contrast enhancement in scar and disk fragment (2 minutes after intravenous injection of 0.3 mmol/kg gadoteridol) in dogs 15, 30, 60, and 90 days after surgery.

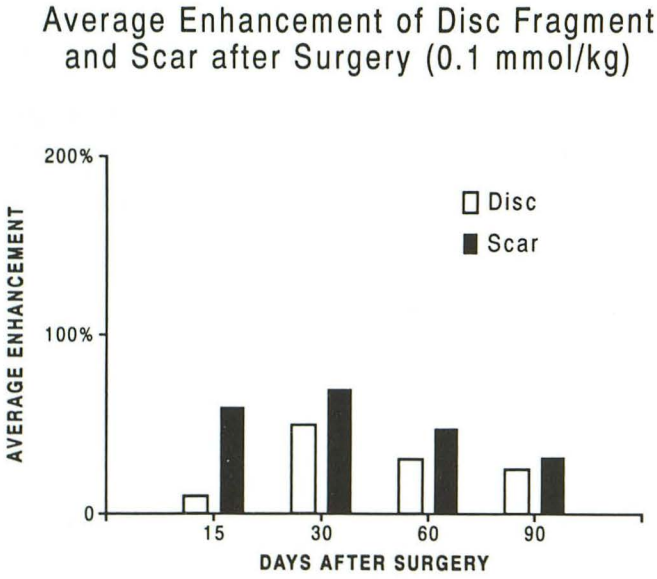


Fig 6. Graph of contrast enhancement (0.1 mmol/kg) in scar and disk fragment 2 minutes after injection in dogs 15, 30, 60, and 90 days after surgery.

duced consistent data, the conditions in the animal model do not duplicate clinical conditions exactly. In the model, normal disk fragments were placed in the epidural space, whereas in patients the fragments escaping into the epidural space may not be normal. In humans the disk fragments may be larger than in our model. We avoided larger fragments to minimize postoperative complications. The recurrent disk herniation and the scar had the same age in the dogs, an unlikely situation in humans. We damaged the anulus fibrosus in control and treated animals to induce mild degeneration of the disk. The MR appearance of these disks will be reported separately. We varied not only the amount of contrast medium, but also the type. This strategy was used because only the nonionic contrast medium is approved for use in higher doses. Because the enhancement of disk fragment per unit dose differed between the ionic and the nonionic medium, we plan to examine the effect of molecular charge on diffusion of contrast medium into the intervertebral disk. We omitted the 25- and 45-minute MR images after gadopentetate dimeglumine because contrast between disk fragment and scar was maximal 2 minutes after gadoteridol injection.

The epidural disk fragment, which vascularizes by 15 days, probably enhances because the contrast medium enters the disk and diffuses readily through it. Vascularization of herniated disk fragment also has been reported in about 40% of routine clinical cases examined microscopically (6–10). The ingrowth of blood vessels may explain the depletion of cartilagenous matrix from herniated disk fragments. The diminishing enhancement of the disk fragment with time probably reflects the gradual resorption of fibrocartilage from the disk fragment.

The measurements of enhancement in scar tissue in this study are in agreement with experimental results previously reported. Contrast enhancement in scar tissue has been reported to vary with the elapse of time from injection (3–5, 11). In this study an inverse relationship between the age of the scar and amount of enhancement was more evident than in previous studies.

This study reveals some of the variables in the enhancement of scar tissue and disk fragments in the epidural space. It suggests that high contrast-medium doses may improve the conspicuousness of recurrent herniated disks because of the greater contrast between disk fragment and scar than with the conventional dose. A clinical trial is needed to determine the efficacy and cost-to-benefit ratio of higher doses of contrast media in the differentiation of recurrent herniated disk and postlaminectomy scar.

References

1. Ross JS, Modic MT, Masaryk TJ, Carter J, Marcus RE, Bohlman H. Assessment of extradural degenerative disease with Gd-DTPA-enhanced MR imaging: correlation with surgical and pathologic findings. *AJNR Am J Neuroradiol* 1989;10:1243–1249
2. Ross JS, Masaryk TJ, Schrader M, Gentili A, Bohlman H, Modic MT. MR imaging of the postoperative lumbar spine: assessment with gadopentetate dimeglumine. *AJNR Am J Neuroradiol* 1990; 11:771–776
3. Ross JS, Blaser S, Masaryk TJ, et al. Gd-DTPA-enhancement of posterior epidural scar: an experimental model. *AJNR Am J Neuroradiol* 1989;10:1083–1088
4. Ross JS, Delamarter R, Hueftle MG, et al. Gadolinium-DTPA-enhanced MR imaging of the postoperative lumbar spine: time course and mechanism of enhancement. *AJNR Am J Neuroradiol* 1989;10:37–46
5. Nguyen CM, Haughton VM, Ho K-C, An H. MR contrast enhancement: an experimental study in postlaminectomy epidural fibrosis. *AJNR Am J Neuroradiol* 1993;14:997–1002
6. Walmsey. The development and growth of the intervertebral disc. *Edinburgh Med J* 1953;60:341–364
7. Ghoshi P, Taylor TKF, Yarrol JM. Genetic factors in the maturation of the canine intervertebral disc. *Res Vet Sci* 1975;19:304–311
8. Fernstrom U, Goldie I. Does the tissue in the intervertebral disc provoke low back pain? *Acta Orthop Scand* 1960;30:202–206
9. Goldie I. Granulation tissue in the ruptured intervertebral disk. *Acta Pathol Microbiol Scand* 1958;42:302–304
10. Holman WL, Duff GL. Pathology of the intervertebral disc. *Am J Med Sci* 1939;198:419–437
11. Bundschuh CV, Stein L, Slusser JH, Schinco FP, LE Ladaga, Dillon JD. Distinguishing between scar and recurrent herniated disk in postoperative patients: value of contrast-enhanced CT and MR imaging. *AJNR Am J Neuroradiol* 1990;11:949–958