Magnetic Resonance Imaging of Rat Head with a High-Strength (4.7 T) Magnetic Field

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ABSTRACT. This study was designed to seek the appropriate scanning parameters for T_1 and T_2 weighted images of rat head by use of a high (4.7 T) magnetic field strength magnetic resonance imaging unit. The optimum values of variables for T_1 weighted images were considered to be a time of repetition of 1,000 msec, and for T_2 weighted images, 8 echoes. When the sagittal images of a healthy rat head were scanned using these optimum values, the cerebrum, cerebellum, olfactory bulb, pituitary gland, pineal gland, spinal cord, tongue, nasopharynx, nasal conchae, vermis and cerebrospinal fluid were clearly observed in either T_1 or T_2 weighted images. Moreover, a primary brain tumor induced by ethylnitrosourea was depicted as a high signal intensity mass in T_2 and contrast-enhanced T_1 weighted images. — KEY WORDS: ethylnitrosourea, MRI, rat.

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A high field strength magnetic resonance imaging (MRI) unit can produce a strong signal, so that high-resolution images can be obtained. Furthermore, the sensitivity of signal intensity required for obtaining clear MR images depends on the use of a strong magnetic field, but it is difficult to attain the high contrast. The present study was designed to seek the optimum scanning variables for T_1 and T_2 weighted images of the rat head by use of a high (4.7 T) magnetic field strength MRI unit. After selecting appropriate scanning variables, we have diagnosed brain primary tumors induced by ethylnitrosourea (ENU).

Ten-week-old male Sprague-Dawley (SD) rats weighing about 300 g (Charles River Japan, Kanagawa, Japan, n=10) were used in the study in order to find the optimum values for variables. Brain tumors were induced in 12-week-old female Fischer 344 (F344) rats weighing 217–237 g (Charles River Japan, Kanagawa, Japan, n=5), in the following manners: the rats were injected intravenously with a dose of 50 mg/kg of ENU on the 20th day of gestation [1]. Offspring (n=47) whelped by the mother were raised for 6 months under standard conditions. Rats were housed in 5 animals per wire-mesh cages in a ventilated room (temperature: 23 ± 2°C, relative humidity: 55 ± 15%, light/dark cycle: 12 hr). They were allowed free access to commercial laboratory chow (F-2, Funabashi Farm, Chiba, Japan) and tap water. Images were obtained with a 4.7 T super-conductive magnet MRI unit (Biospec CSI 47/40, Bruker Japan, Tsukuba, Japan) for this investigation, and the maximum strength of the gradient coil was 200 mT/m for the slice selection. Prior to imaging, the rats were anesthetized by the inhalation of 1.0–2.0% halothane (Halothane Hoechst®, Hoechst Japan, Tokyo, Japan), maintained throughout experiment and were placed in the supine position inside the radio frequency coil. T_1 and T_2 weighted images were obtained with the spin echo (SE) pulse sequence and the rapid acquisition relaxation enhancement (RARE) pulse sequence, respectively. On investigation of the appropriate values for variables in T_1 and T_2 weighted images, the slice thickness of the image was fixed at 2 mm since anatomical information without partial-volume effects had been obtained. First, T_1 weighted images were examined using various combinations of time of repetition (TR; 500, 1,000, 1,500 and 2,000 msec) and time of echo (TE; 15, 20, 25 and 30 msec). Second, T_2 weighted images were evaluated with different combinations of TR (2,000, 3,000, 4,000, 5,000 and 6,000 msec) and number of echoes (2, 4 and 8) with TE fixed at 20 msec. In T_1 weighted images, a TR of 500 msec gave a poor signal-to-noise ratio (S/N), and a TR of 1,500 msec or more yielded a high S/N and low T_1 contrast. In T_2 weighted images, longer TRs produced higher S/N, and increased number of echoes provided better T_2 contrast. The optimum scanning values were considered to be TR/TE=1,000/15 or 20 msec in T_1 weighted images and TR/TE=6,000/20 msec with 8 echoes in T_2 weighted images. Figure 1 shows sagittal images of a healthy rat head using the following variables [TR/TE=1,000/18.9 msec for T_1 weighted images, TR/TE/echo=6,000/20 msec/8 times for T_2 weighted images, 70 mm field of view (FOV), 2 mm slice thickness, 512 × 512 matrix]. The resolution of the images is under 0.14 mm. The cerebrum, cerebellum, olfactory bulb, pituitary gland, pineal gland, spinal cord, tongue, nasopharynx and nasal conchae were distinctly observed in T_1 weighted image (top), and the vermis and cerebrospinal fluid were clearly identified in T_2 weighted image (bottom).

Using the optimum values described above (TR/TE=1,000/15 msec for T_1 weighted images, TR/TE/echo=6,000/20 msec/8 times for T_2 weighted images, 50 mm FOV, 2 mm slice thickness, 256 × 256 matrix), the usefulness of these images for diagnosing ENU-induced primary brain tumors was evaluated. Experiments were performed on following three steps; T_1 weighted images, T_2 weighted images and then contrast-enhanced T_1 weighted images. Gadodiamide injection (Omniscan®, Daiichi Pharmaceutical Co.) consisting of gadodiamide hydrate and caldiamide sodium [3, 5], used as a contrast agent, was injected at a dose of 0.2 mmol/kg into the tail vein through a 24 gauge indwelling needle. Figure 2 presents representative images. The resolution of these images is under 0.20 mm. No lesion was observed, but the left cerebral hemisphere seemed to be swollen in T_1 weighted image (A). In T_2 weighted image, on the other hand, a

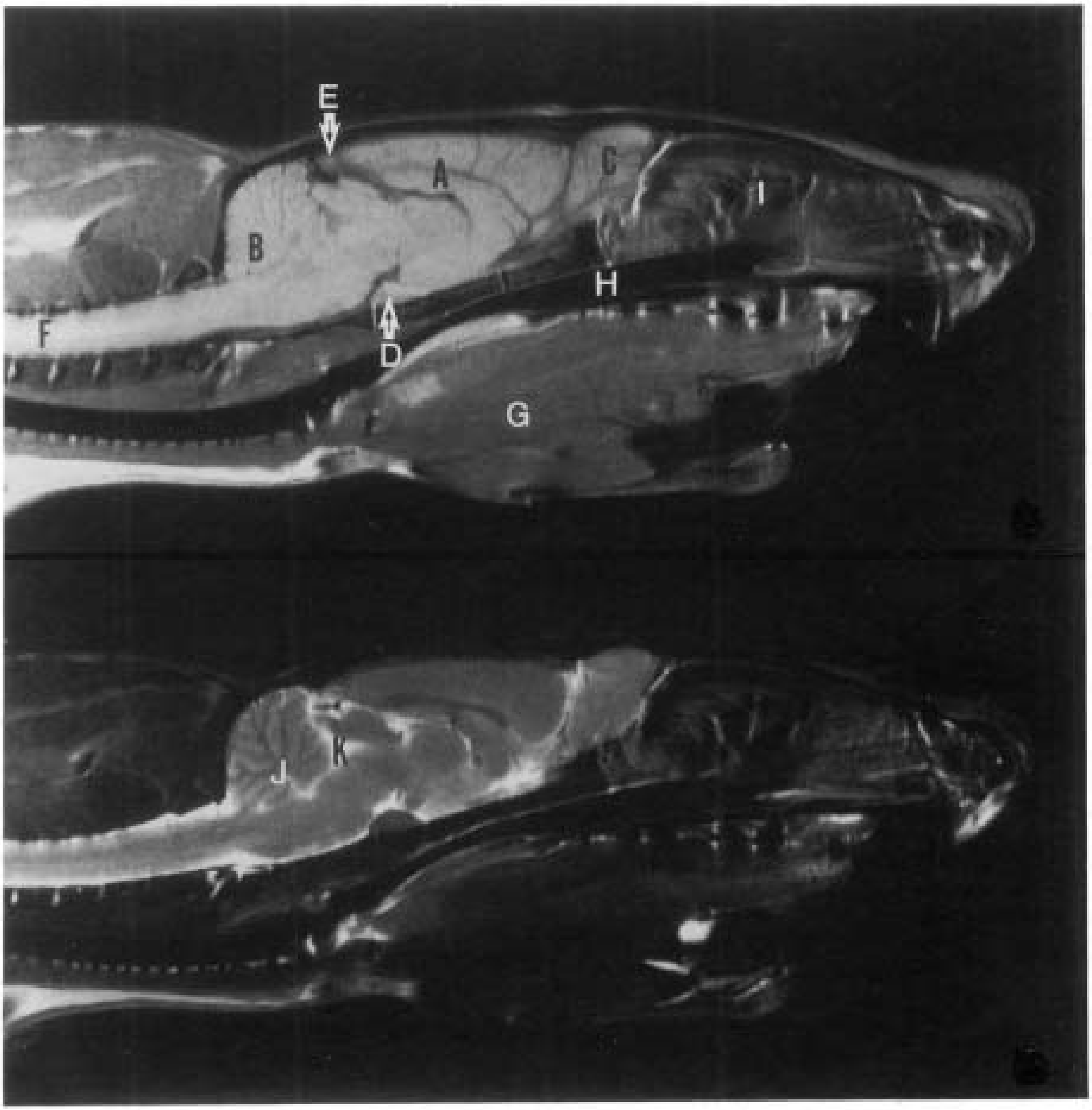

Fig. 1. Sagittal T_1 weighted image (top, SE, TR/TE=1,000/18.9 msec) and sagittal T_2 weighted image (bottom, RARE, TR/TE=6,000/20 msec, 8 echoes) of the head of a healthy SD rat, obtained using the optimum parameters. Both images are scanned in 512 × 512 matrix, 70 mm FOV, 2 mm slice. A: cerebrum; B: cerebellum; C: olfactory bulb; D: pituitary gland; E: pineal gland; F: spinal cord; G: tongue; H: nasopharynx; I: nasal conchae; J: vermis; K: cerebrospinal fluid.

tumor with edema was depicted as a high signal intensity area (B). This implies that the use of a contrast agent in MRI may not be necessary, because of the high sensitivity of MRI to water. However, the signal intensity of the tumor was even greater in contrast-enhanced T_1 weighted image (C). The tumor margin of contrast-enhanced T_1 weighted image was clearer than that of T_2 weighted image. This enhanced area is due to disruption of the blood-brain barrier by tumor invasion, and contrast agent was transported into the cerebral tissue [3, 5]. After completion of the imaging protocol, the animals were subjected to euthanasia by exsanguination. The intracranial tissue samples were fixed in 10% buffered formalin and embedded in paraffin wax. Thin sections 4 μm thick were prepared, stained with hematoxylin and eosin (H.E.). Histological examination revealed schwannoma of the trigeminal nerve exhibiting the Antoni type A pattern of growth and consisting of parallel bundles of spindle-shaped cells with indistinct cytoplasmic boundaries and an eosinophilic fibrillar cytoplasm (D). Enhanced area in contrast-enhanced T_1 weighted image

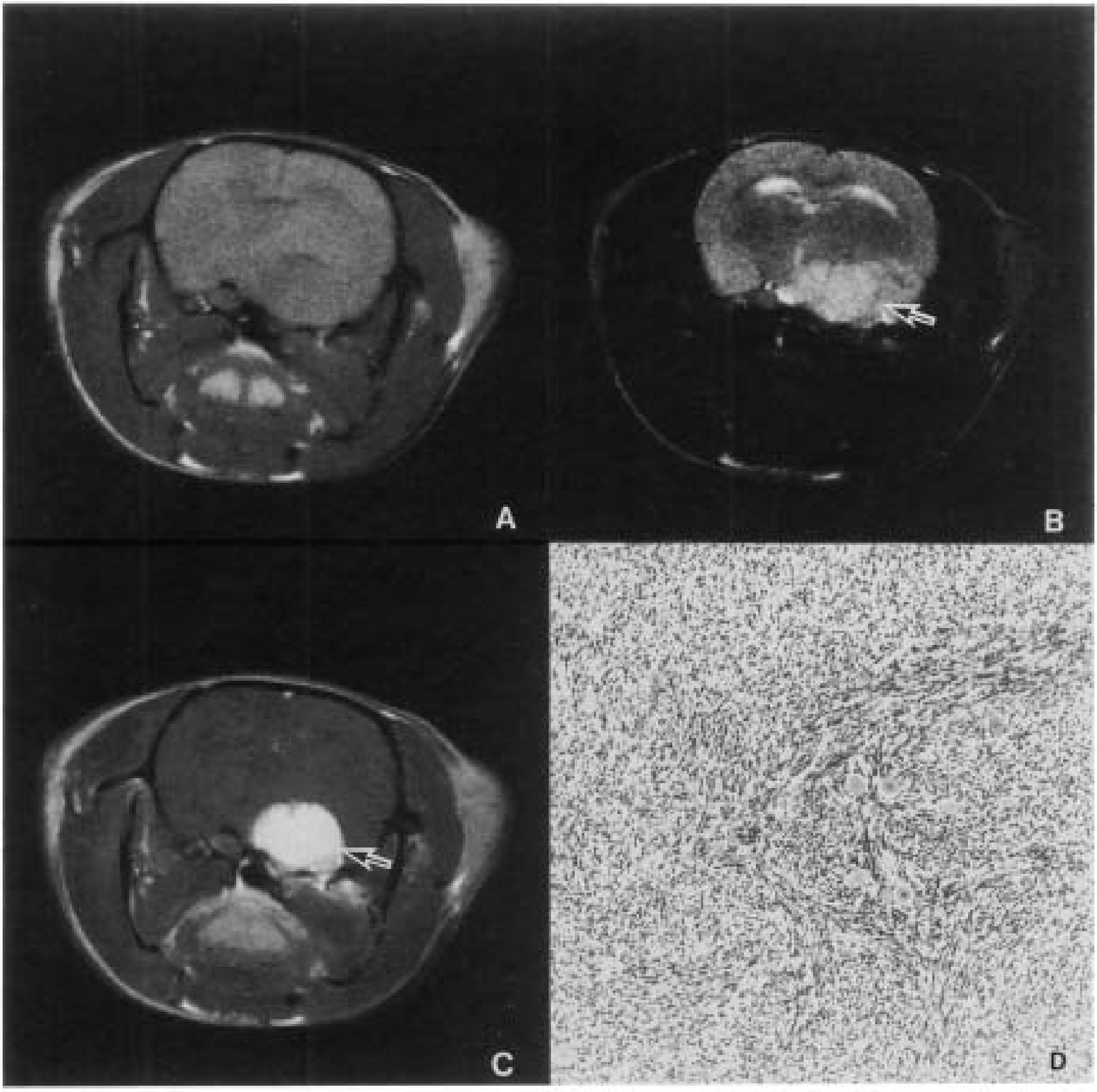

Fig. 2. Transverse images of a primary brain tumor induced by ethylnitrosourea (ENU) in a F344 rat. Both images are scanned in 256 × 256 matrix, 50 mm FOV, 2 mm slice. A: T_1 weighted image (SE, TR/TE=1,000/15 msec); B: T_2 weighted image (RARE, TR/TE=6,000/20 msec, 8 echoes); C: contrast-enhanced T_1 weighted image (SE, TR/TE=1,000/15 msec); D: histological appearance (H.E. stain, × 75). Arrows show the lesion site.

corresponded with microscopic findings.

We reported previously that the optimum values for a 0.2 T MRI unit [4] with a low magnetic field MRI are 400/38 msec and 1,800/110 msec in T_1 and T_2 weighted images, respectively. The differences between the two studies may have resulted from the difference in the magnetic field strength, because relaxation time depends on the field strength. It is possible to obtain images of the rat brain in a low or medium strength magnetic field MRI [2, 4]. However, the image quality of those provided by a high magnetic field is much better than that obtainable with a low or medium strength magnetic field as a result of the high S/N. The use of optimum values for MR imaging conditions led to the acquisition of high-contrast images in high magnetic field MRI.

REFERENCES

1. Swenberg, J. A., Koestner, A., Wechsler, W., and Denlinger, R. H. 1972. *Cancer Res.* 32: 2656–2660.
2. Wolf, R. F. E., Lam, K. H., Mooyaart, E. L., Bleichrodt, R. P., Nieuwenhuis, P., and Schakenrad, J. M. 1992. *Lab. Anim.*

26: 222–227.
3. Yamada, K., Jinbo, T., Miyahara, K., Sato, M., Hirose, T., Tateno, Y., Ikehira, H., Sugihara, H., and Furuhama, K. 1996. *J. Vet. Med. Sci.* 58: 389–396.
4. Yamada, K., Miyahara, K., Sato, M., Hirose, T., Yasugi, Y., Matsuda, Y., and Furuhama, K. 1995. *Vet. Radiol. Ultrasound.* 36: 523–527.
5. Yamada, K., Miyahara, K., Sato, H., Nakayama, W., Sato, M., Hirose, T., Tateno, Y., Ikehira, H., Sugihara, H., and Furuhama, K. 1996. *J. Vet. Med. Sci.* 58: 291–295.