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FULL PAPER

Magnetic resonance imaging of hepatocellular carcinoma in Long-Evans Cinnamon rats under a magnetic field of 7.05 T

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Abstract

Magnetic resonance (MR) images of livers in 3-, 12- and 29-month-old Long-Evans Cinnamon(LEC) rats (male) were taken under a magnetic field of 7.05 T. MR images of sagittal and transversal sections were obtained in 1-mm-thick slices by T_1-weighted and two-dimensional Fourier transformation techniques. The data matrix size was 256 phase-encoded steps. Each image was obtained through four acquisitions. Three-month-old rats gave MR images with low signal intensity over the liver probably due to the shorting of its T_1 and T_2 relaxation times. However, 12-month-old rats gave hyperintense regions around hepatic veins in right hepatic lobe, which was assigned to hepatocellular carcinoma. In 29-month-old rats, MR images with hyperintensity throughout the hepatic lobe were observed. These MR images, therefore, suggested that hepatocellular carcinoma in LEC rats developed from the restricted regions surrounding hepatic veins. In the present study, T_1-weighted MR imaging under a magnetic field of 7.05 T was shown to be applicable to the diagnosis of hepatic cancer in LEC rats.

Key words : hepatocellular carcinoma, Long-Evans Cinnamon rat, MRI

Introduction

The theory of nuclear magnetic resonance (NMR) suggests that the higher magnetic field the stronger are NMR signals obtained[2)3)8)]. This means that MR imaging under a high magnetic field is favored over imaging under a low magnetic field for small animals like mice and rats. Our previous studies showed that MR imaging of rat brains under a magnetic field of 7.05 T, which was higher than that of usual human MRI (0.5–2.0 T), was successful to visualize the age-dependent morphological changes in brains[7)11)].

Recent MR imaging studies proved that this method was useful for the diagnosis of not only human brain cancer but also human hepatocellular carcinoma (HCC)[9)]. Since LEC rats are known as a good animal model for studying chronic hepatitis as well as hepatic cancer[5)10)12)], it is natural to consider that the MR imaging method

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should be applicable to the diagnosis of hepatic cancer of LEC rats. However, LEC rats contain several paramagnetic ions in the liver at high concentrations (40–50 times higher than those of normal rats). Generally, the higher the concentrations of paramagnetic ions and the higher magnetic field, the relaxation times (T_1 and T_2) of MRI become shorter[1)14)]. The shorting of T_1 and T_2 relaxation times results in the decrease of MR signal intensities and gives hypointense MR images. In the present study, T_1-weighted MR images of the livers of 3-, 12- and 29-month-old LEC rats were taken under a magnetic field of 7.05 T to know whether or not T_1-weighted MR imaging at high magnetic field was applicable to hepatic pathogenesis in LEC rats.

Materials and Methods

Animals

LEC rats which are maintained under conventional conditions at the Institute for Animal Experimentation, Hokkaido University School of Medicine were used. They fed a regular diet and water *ad libitum* in an air-conditioned animal room at 22 ± 3°C with a relative humidity of 55 ± 5%. Male rats aged at 3, 12 and 29 months old were used in the present experiments. Hepatitis with jaundice was once observed at 12- and 29-months of age[15)].

MRI

T_1-weighted MR images were obtained on an Oxford 7.05 T superconducting magnet equipped with a Toshiba workstation with an SIS 300/183 imaging system using a two-dimensional Fourier transformation technique. LEC rats were anesthetized with pentobarbital sodium solution (40 mg/kg) diluted 2.5 times with a mixed solution of propylene glycol/ethanol/H_2O (2/1/7, w/w). The saddle-shaped coil (89 mm in diameter) designed for MR imaging of whole body of rat was used. Each rat was positioned supination in the probe running parallel to z-axis of the magnet, and fixed to a cradle using adhesive tape to minimize the artifacts due to respiratory motions. After adjusting the coils, sagittal sections of body were roughly imaged under a T_1-weighted condition (repetition time (TR) / echo time (TE) = 500 ms / 20 ms) to determine the positions of transversal sections in the hepatic region. Then, T_1-weighted images were taken using a spin echo (SE) sequence with 4 acquisitions and pulse width of 4 kHz. In addition to these parameters, the followings were employed[7)11)]; the gradient magnetic field, 3 mT/cm ; the field of view (FOV), 10×10 cm^2 for sagittal sections and 6×6 cm^2 for transversal section ; the slice thickness, 1.0 mm ; data matrix size, 256×256 ; reconstructed images, 512×512 pixel matrix.

Results

Typical T_1-weighted MR image of the transversal section at about 10 mm from the top of xiphoid process to head in a 3-month-old male LEC rat is shown in Fig. 1a. Hepatic veins, muscle and spinal cord were clearly imaged, though whole liver showed hypointensity on T_1-weighted image. Shortening of T_1 and/or T_2 relaxation times of the liver due to the presence of excess metal ions is thought to be responsible for hypointensity (unpublished results).

MR image of the transversal section at about 5 mm from the top of xiphoid process to head in a 12-month-old rat is shown in Fig. 1b. The MR signal intensity in the normal hepatic region was the same as that of a 3-month-old rat, but the hyperintense regions (2–6 mm in diameter) were observed around hepatic veins in right hepatic lobe. These hyperintense regions were assigned to HCC regions because the hyperintense regions were proved to be HCC in T_1-weighted MR imaging of the livers in human[4)6)13)].

MR image of the transversal section at about 15 mm from the top of xiphoid process to tail in 29-month-old rat is shown in Fig. 1c. A number of hyperintense regions (6–10 mm in diameter) with irregular shapes were observed all over

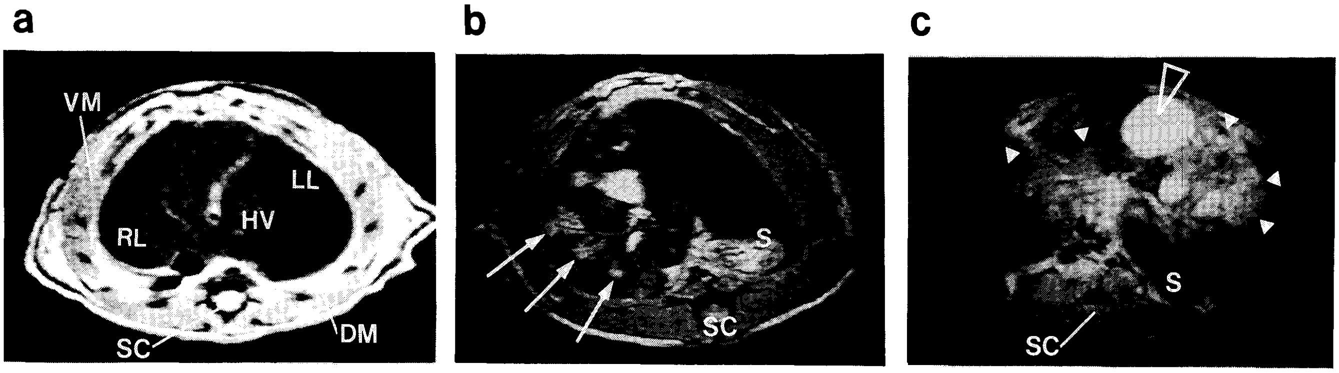

Fig. 1 (a) T_1-weighted MR image of the transversal section at about 10 mm from the top of xiphoid process to head of 3-month-old LEC rat abdomen. LL : left hepatic lobe, RL : right hepatic lobe, SC : spinal cord, DM : dorsal muscle, VM : ventral muscle, HV : hepatic vein. (1b) T_1-weighted MR image of the transversal section at about 5 mm from the top of xiphoid process to head of 12-month-old LEC rat abdomen. S : stomach. Arrows show abnormal hyperintense regions around hepatic veins. These regions were assigned to HCC. (1c) T_1-weighted MR image of the transversal section at about 15 mm from the top of xiphoid process to tail of 29-month-old LEC rat abdomen. Solid arrow heads show hyperintese regions (6–10 mm in diameter) with obscured borders gathering with one another. An open arrow head shows hyperintese region with egg-like structure consisting of the viscous liquid.

hepatic lobe. Additionally, several hyperintese regions with unclear border were observed to gather with one another. A large egg-like structure was observed as the hyperintense region in the left hepatic lobe. The pathological dissection after MR imaging revealed that a viscous liquid cyst was present at the surface of left hepatic lobe (Fig. 2). The egg-like structure was, therefore, assigned to the liquid cyst but not HCC.

Discussion

T_1-weighted MR imaging technique was applied to visualize the livers of 3-, 12- and 29-month-old LEC rats under a high magnetic field of 7.05 T. Before experiments, there was a fear that T_1-weighted MR images of LEC rat livers under the high magnetic field, as a whole, become hypointense due to the shortening of T_1 and T_2 relaxation times arising from the presence of excess paramagnetic ions. However, anatomical and pathological information of the livers could be obtained in 1-mm-thick slices by MR images. A number of hyperintense regions in the 12- and 29-month-old rat livers were observed in T_1-weighted images. These regions were assigned to HCC because the hyperintense regions were identified as HCC in T_1-

Fig. 2 Macroscopic observation of 29-month-old LEC rat liver. The cystic hypertrophy of liver by HCC was observed in upper abdominal cavity (arrow). This cyst corresponded to the egg-like structure in Fig. 1c.

weighted MR imaging of the livers in human[4)6)13)]. The interesting finding in 12-month-old rat livers was the fact that the hyperintense regions corresponding to HCC were distributed at the circumference of hepatic veins. Furthermore, it was found that hyperintense regions were distributed over the livers in 29-month-old rats. These results indicated that HCC in LEC rats developed from the regions surrounding the hepatic veins.

From these results, it was concluded that T_1-weighted MR imaging at high magnetic field was applicable to hepatic pathogenesis in LEC rats.

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