Comparison of Gd-Bz-TTDA, Gd-EOB-DTPA and Gd-BOPTA in Dynamic MR Imaging of the liver with Rat Models

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Introduction

We have developed and characterized a new lipophilic paramagnetic complex, Gd-Bz-TTDA [4-benzyl-3,6,10-tri (carboxymethyl)-3,6,10- triazado-decanedioic acid], designed for use as liver MR contrast agent [1, 2]. The prelimionary results of our previous study showed an intense liver enhancement in normal rats lasting from 5 minutes to 3 hours. It can also improve tumor conspicuity in late phase images due to intense liver enhancement [3]. Two Gd-chelates, gadobenate dimeglumine Gd-BOPTA and gadoxetate Gd-EOB-DTPA, are recently available for clinical use as hepatobiliary MR contrast agent. The R1 relaxivity of Gd-Bz-TTDA is superior to Gd-BOPTA. Its rotational correlation time is longer than Gd-EOB-DTPA, and its water exchange lifetime is significantly shorter than Gd-EOB-DTPA and Gd-BOPTA[1,2]. To evaluate the competitive potential of this new, potential contrast agent with Gd-EOB-DTPA and Gd-BOPTA, dynamic MR imaging studies of the liver in normal rats and implanted HCC rats with these three agents were performed.

Material and Methods

MR imaging studies for normal, and hepatocellular carcinoma (HCC) rat models were performed using a 1.5-T scanner. Sequential multislice T1-weighted turbofield echo (TFE) (TR/TE/flip angle: 15 ms/6.1 ms/25^0) coronal images of normal rats (n=12) were obtained before and after intravenous injections of 0.1 mmol/kg Gd-Bz-TTDA, Gd-EOB-DTPA or Gd-BOPTA. Similar protocols of MR imaging with additional T2 weighted images were used for the rats with implanted HCC (n=6) before and after intravenous injection of these three contrast agents. MR images were analyzed to evaluate the time-enhancement change (% increase of signal-to-noise ratio, SNR) in normal liver and tumors. The liver-lesion contrast-to-noise ratios (CNR) were also evaluated.

Results

The time-enhancement changes of the normal rats after injection of 0.1 mmol/kg Gd-Bz-TTDA, Gd-EOB-DTPA or Gd-BOPTA are shown in Fig. 1. The enhancement of liver in normal rats rapidly rose during the first five minutes in all groups. After that, in Gd-Bz-TTDA group, the liver enhancement maintained a plateau, then steadily but slowly declined during 2 hours of study. The liver enhancement in normal rats injected with Gd-EOB-DTPA or Gd-BOPTA reached a peak at five minutes after injection followed by a gradual decline. At 5 minutes, there is significantly more intense liver enhancement in Gd-Bz-TTDA and Gd-EOB-DTPA groups than in Gd-BOPTA group (151.0±40.5%, 150.2±32.7% versus 115.3±35.8%, $p<0.05$). After that, Gd-Bz-TTDA produced significantly more intense enhancement in liver than the other two groups in each time points ($p<0.001$). Sequential MR images of a rat with implanted HCC before and after intravenous injection of 0.1 mmol/kg Gd-Bz-TTDA, Gd-EOB-DTPA or Gd-BOPTA are shown in Fig. 2. All agents showed a similar enhancement pattern of the implanted HCCs. Nevertheless, Gd-Bz-TTDA group revealed slightly better and prolonged enhancement of the tumors than the other groups. At 5 minutes, good liver-lesion discrimination was observed in all groups, because tumor enhancement had gradually washed out but intense liver enhancement reached. At 60 minutes, the enhancement of liver faded in rats injected with Gd-EOB-DTPA or Gd-BOPTA, whereas intense liver enhancement persisted and good liver-lesion discrimination remained in rats injected with Gd-Bz-TTDA (Fig.2). Quantitative analyses of the percentage increase of liver-lesion CNR in rats with HCC after injection of Gd-Bz-TTDA, Gd-EOB-DTPA or Gd-BOPTA are compared in Fig.3. The liver-lesion CNRs were also higher in rats injected with Gd-Bz-TTDA than those injected with Gd-EOB-DTPA or Gd-BOPTA after 30 minutes.

Discussion

In this study, an intense and prolonged liver enhancement in normal rats was demonstrated after intravenous injection of 0.1 mmol/kg of Gd-Bz-TTDA. Liver enhancement increased rapidly during the first five minutes reached a plateau, which slowly decreased to 110% at 2 hours after injection. Instead, liver enhancement of rats injected with Gd-EOB-DTPA or Gd-BOPTA peaks at five minutes and decreased steadily. After 60 minutes, the liver enhancement in the later groups was below 50%. The prolonged plateau- like enhancement of Gd-Bz-TTDA has important practical implications because the wide postcontrast imaging window provides flexibility for managing patient work flow.

Conclusion

Our results indicated that Gd-Bz-TTDA is competitive to the commercially available hepatobiliary MR contrast agents, Gd-BOPTA or Gd-EOB-DTPA, by its more intense and prolonged liver enhanced and its better liver-lesion discrimination.

References

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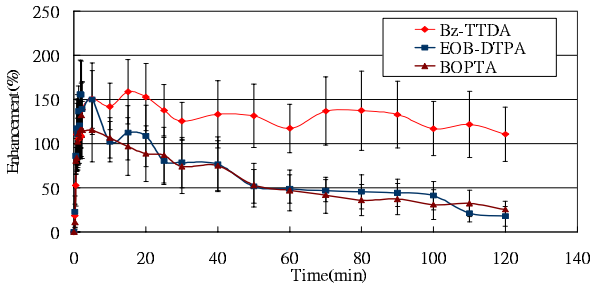

Fig.1. Time-enhancement change of the liver in normal rats after injection of 0.1 mmol/g Gd-Bz-TTDA, Gd-EOB-DTPA or Gd-BOPTA with T1-wegihted images (mean ± standard deviation, n=12 in each group).

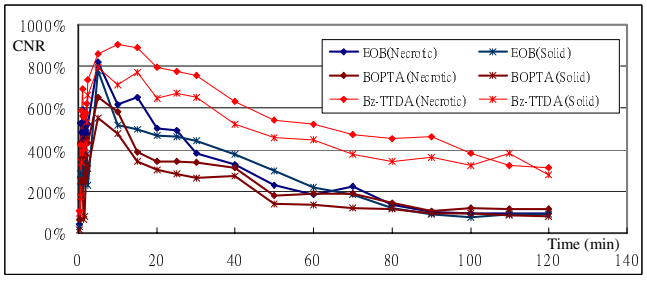

Fig. 3. The percentage increase of liver-lesion CNR in rats with HCC af injection of Gd-Bz-TTDA, Gd-EOB-DTPA or Gd-BOPTA (mean, n=6 i each group, Solid: solid part of tumor, Necrotic: central necrosis of tum

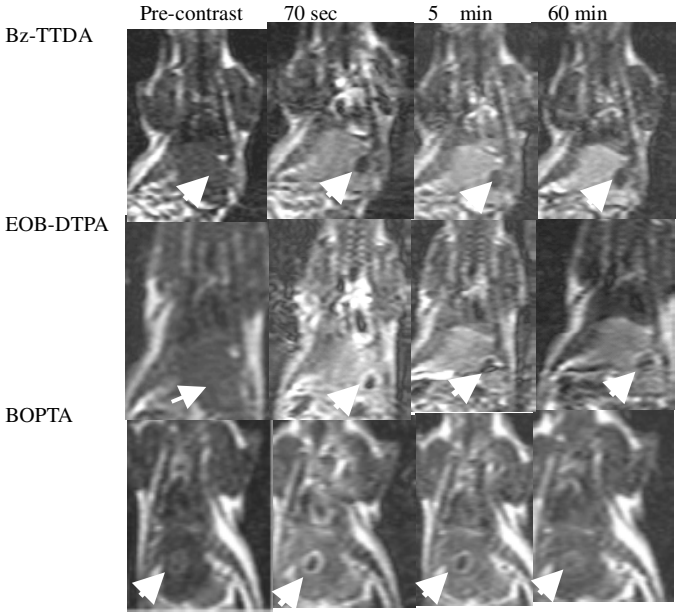

Fig.2 Sequential T1-weighted TFE images of a rat with implanted HCC befor and after injection of 0.1 mmol/kg Gd-Bz-TTDA (A), Gd-EOB-DTPA (B) or Gd-BOPTA (C). In the images at 28 seconds, a similar enhancement of tum is noted in all groups. A 5 minutes, good liver-to-lesion differentiation is demonstrated in all 3 groups to the intense liver enhancement and wash-out o tumor contrast. At 60 minutes, persistent intense liver enhancement with better liver-lesion contrast is noted with injection of Gd-Bz-TTDA, however, only faint enhancement of liver and less discrimination of lesion are demonstrated in the other two groups. Arrows indicate the tumor.