In vivo evaluation of Gd-BOPTA and Gd-DTPA in a rat liver tumor model of a solitary colorectal cancer metastasis at 9.4T

Poster No.: C-1485
Congress: ECR 2014
Type: Scientific Exhibit
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Keywords: Multidisciplinary cancer care, Image registration, Technology assessment, Experimental investigations, MR, Oncology, Liver, Animal (veterinary) studies
DOI: 10.1594/ecr2014/C-1485

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Aims and objectives

The investigation of contrast and perfusion properties in liver metastases in the context of tumor targeted therapies are major aspects for the evaluation of therapeutic effects. At higher field strengths above 1.5 T contrast properties of Gd-based contrast agents (CA) decrease and in vivo data of contrast properties at 9.4 T define a new basis for tumor characterization [1,2]. Since the physical conditions for MR imaging change especially considering the use of well known Gadolinium based CA new standards for the contrasting properties have to be established [3-5].

The aim of this study was to compare signal to noise (SNR) and contrast to noise (CNR) properties of Gd-BOPTA compared to Gd-DTPA in a rat liver tumor model.

Methods and materials

In 10 WAG rats liver tumors were induced by intraparenchymal injection of a colon cancer cell suspension into the left liver lobe. 12 and 14 days after induction all animals were subjected to MRI. We acquired a retrospectively self-gated FLASH (RSG-FLASH) sequence (IntraGate®: TR/TE: 45/2.5 ms, flip angle: 25°, field of view: 50 x 50 mm2, matrix: 256x256, pixel size: 195x195 mm, slice thickness: 1 mm) in axial orientation covering the area of the liver tumor. In addition, we acquired a FLASH sequence with external gating (EG-FLASH) with the same imaging parameters at the same position using an external transducer trigger device obtaining the respiratory signal. After intravenous injection of 0.1mmol / kg BW of Gd-BOPTA or 0.2 mmol / kg BW of Gd-DTPA respectively alternating acquisitions of both sequences at five consecutive time points were performed. Measurements for RSG-FLASH sequences included 2, 5, 9, 13 and 17 minutes after injection of CA as well as 3, 7, 10, 14 and 18 minutes for EG-FLASH sequences respectively.

SNR and CNR were detected on corresponding regions of interest (ROI) drawn within the liver and the tumor and correlated to subtracted noise images. SNR was calculated according to the formula

$$\text{SNR} = \frac{\text{SI}}{\text{noise}} \times 2$$

with SI as the mean signal intensity (SI) measurement of the placed ROI. Each ROI was aimed to cover the tumor with a diameter of at least 3 mm and the liver in a homogeneous area avoiding vascular structures (Fig. 6 on page 3 ). Noise was calculated subtracting two unenhanced pictures of corresponding orientation with a ROI copied in corresponding position and size for the evaluated area.
For the calculation of the CNR the SNR of the liver was subtracted from the SNR of the tumor.

Images for this section:

**Fig. 6:** EG-FLASH image 7 minutes after Gd-BOPTA with implanted tumor tissue (long arrow). A ROI measurement is placed in the tumor area and into adjacent liver tissue (short arrow). These ROIs were copied into unenhanced subtraction images for noise correlation.
Results

On EG-FLASH imaging Gd-BOPTA presented statistically significant ($p<0.05$) higher SNR of liver tissue on all five measurements compared to Gd-DTPA (Fig. 1 on page 4), whereas on RSG-FLASH imaging this was only the case with acquisition 3 and 4 (Fig. 2 on page 4). No significant difference was found in SNR of the tumor with tendency of higher values for Gd-BOPTA (Fig. 3 on page 5). CNR was significantly higher after Gd-BOPTA on all acquisitions of EG-FLASH imaging and acquisition 3 and 4 on RSG-FLASH imaging respectively (Fig. 4 on page 6 Fig. 5 on page 6). Nevertheless SNR of tumor tissue presented varied signal increase after CA administration resulting in different lesion to liver contrast (Fig. 7 on page 7, Fig. 8 on page 7, Fig. 9 on page 8, Fig. 10 on page 9). For Gd-BOPTA an overall negative contrast between tumor and liver tissue was found.

Images for this section:

![BOPTA-DTPA-EG-SNR liver](image)

**Fig. 1:** SNR within the liver on the basis of EG-FLASH sequences on different time points starting with unenhanced (ue) measurements for both tested CA. All contrasted measurements presented significant (asterisks) higher values for GD-BOPTA.
Fig. 2: SNR acquisition in the liver on basis of RSG-FLASH sequences for different time points. Gd-BOPTA presented higher SNR values with a significant difference for time point 3 and 4 (asterisks).
**Fig. 3:** SNR values of tumor tissue on the basis of RSG-FLASH sequences were not significantly different.

![Graph showing SNR values for BOPTA-DTPA-EG-CNR](image)

**Fig. 4:** CNR values for EG-FLASH imaging were all significantly different for the tested CA (asterisks). Gd-BOPTA presented overall negative contrast between tumor and liver.

![Graph showing CNR values for BOPTA-DTPA-EG-CNR](image)

**Fig. 5:** CNR values calculated from RSG-FLASH imaging for both CA. A significant difference was found for time point 3 and 4 (asterisks).
**Fig. 7:** EG-FLASH image 7 minutes after Gd-BOPTA with pronounced tumor delineation (long arrow) within the liver lobe (short arrows).
**Fig. 8:** EG-FLASH image 7 minutes after Gd-DTPA with less pronounced tumor delineation (long arrow) within liver lobe compared to the imaging following Gd-BOPTA.
Fig. 9: EG-FLASH image 7 minutes after Gd-BOPTA with "negative" tumor delineation (long arrow) within the liver (short arrows)- in contrast to the "positive" tumor contrast in the previous case presented (Fig.7).
**Fig. 10:** EG-FLASH image 7 minutes after Gd-DTPA. The tumor presents a CA uptake comparable to liver tissue (long arrow) and is - in contrast to the imaging after Gd-BOPTA - difficult to delineate.
Conclusion

Gd-BOPTA provides higher liver tissue signal and lesion to liver contrast for liver and tumor imaging at 9.4 T compared to Gd-DTPA. This effect is caused by a higher SI for tumor surrounding liver presumably due to active hepatic intracellular uptake of the CA. Since relaxivities of the applied CA decrease with field strengths above 1.5T an additional mechanism for better tumor detection promises a characterisation benefit for future experimental and clinical studies [6,7].

CA uptake within tumor tissue during early and late scanning phases was comparable between the two tested CA with only a tendency of higher values for Gd-BOPTA in earlier perfusion phases. This effect might be useful for future perfusion studies. A better tumor delineation and characterisation might be of great value especially for the evaluation of tumor targeted therapies [8].

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References


