RADIOEMBOLIZATION DOSIMETRY USING GADOXETATE DISODIUM FOR SEGMENTATION OF THE HEALTHY LIVER PARENCHYMA

Hanke J Schalkx[1], Jip P Prince[1], Gerrit H van de Maat[2], Peter R Seevinck[3], Clemens Bos[3], Wouter B Veldhuis[1], Maarten S van Leeuwen[1], Maurice AAJ van den Bosch[1], Marnix GEH Lam[1], and Marijn van Stralen[3]

[1]*Radiology and Nuclear Medicine, University Medical Center Utrecht, Utrecht, Utrecht, Netherlands,* [2]*Quirem Medical BV, Diepenveen, Netherlands,* [3]*Image Sciences Institute, University Medical Center Utrecht, Utrecht, Utrecht, Netherlands*

PURPOSE: Hepatic radioembolization (RE) is a treatment for non-resectable liver cancer, in which microspheres loaded with a radioisotope, such as yttrium-90 and holmium-166 (^{166}Ho), are injected into the hepatic arterial supply to administer a large radiation dose to the target hepatic volume. The injected activity is aimed to achieve a tumoricidal dose, but is limited by its toxic effect on the healthy parenchyma, as radiation-induced liver disease (RILD) needs to be prevented [1]. To evaluate the absorbed dose in the healthy liver parenchyma, it is essential that the non-tumorous parenchymal volume is measured accurately. In current clinical practice the total liver volume and the absorbed dose in that volume are taken into account, with the risk of under- or overdosing [2]. Improved dosimetry and dosimetry-based treatment planning are expected to lead to improved patient outcomes.

Dynamic Contrast-Enhanced (DCE) MRI using the hepatospecific contrast agent gadoxetate disodium (Gd-EOB-DTPA, Primovist or Eovist, Bayer Schering, Germany) results in parenchymal enhancement due to active uptake by hepatocytes. On hepatobiliary phase images (~≥10 min post-injection), the enhanced healthy parenchyma appears hyperintense to intrahepatic vessels and e.g. colorectal metastases.

This study investigates (i) whether segmentation of the healthy liver parenchyma using gadoxetate-enhanced MRI is feasible in a RE population, and whether this can be performed automatically, and (ii) whether gadoxetate-based liver segmentation might be used for healthy liver parenchyma dosimetry in RE. Our study was performed in patients receiving ^{166}Ho-RE, as it benefits from the MRI-based quantification of the paramagnetic holmium microspheres [3].

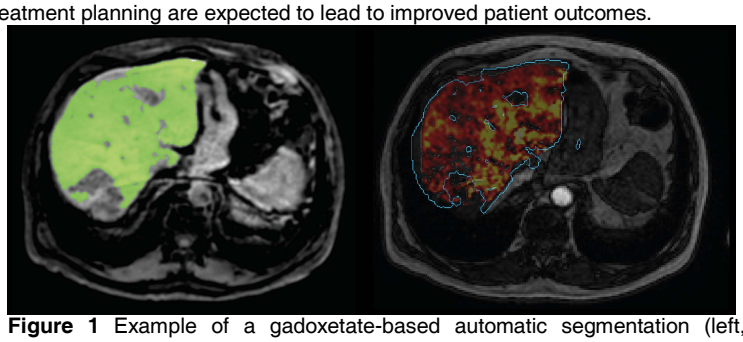

Figure 1 Example of a gadoxetate-based automatic segmentation (left, overlay on 15 min post-contrast T1-w acquisition), excluding vessels and hypointense tumors; and corresponding map of ^{166}Ho microspheres (right).

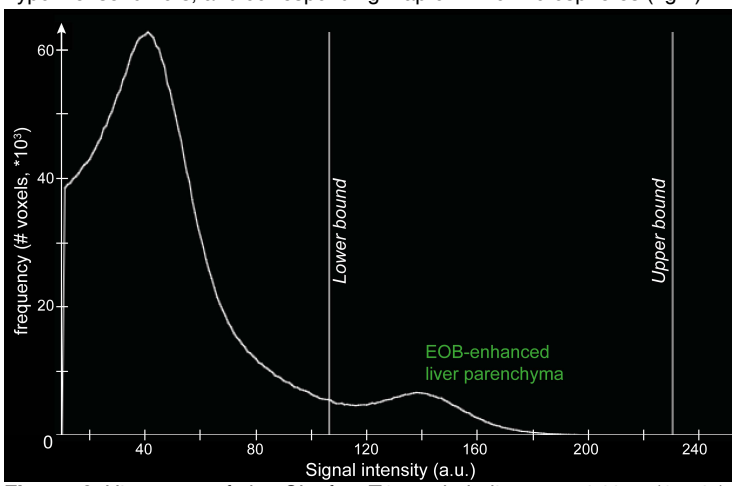

Figure 2 Histogram of the SI of a T1-w whole-liver acquisition (15min), displaying the interval containing the gadoxetate-enhanced parenchyma.

METHODS, *Experiments* 5 noncirrhotic patients (1 female, age mean 71 ± SD 8.5yrs, range 59-83yrs) undergoing 166Ho-RE for liver metastases (primary tumor: 3 colorectal, 1 breast, 1 gastric cardia), received gadoxetate-enhanced MRI on the day before and the day after RE in the HEPAR-II trial (NCT01612325). Written informed consent was obtained. ***Imaging*** All imaging was performed on a 1.5T MR system (Achieva, Philips Healthcare, Best, Netherlands) with a 16-channel body coil. After T1w, T2w, and multi-gradient echo [3] acquisitions, a DCE series was obtained. Gadoxetate (0.025 mmol/kg, 1 ml/s, 25ml saline flush) was administered and, with a keyhole technique [4], 16 whole-liver 3D acquisitions were obtained up to 5 min, completed with one at 10 and 15 min. For 1/5 patients, the post treatment DCE-MRI was only obtained up to 5 min. ***Analysis*** Parenchymal SI were measured on all pre-contrast, 5, 10 and 15 min images, averaged over 3 region-of-interests and expressed relative to the SI of the paraspinal muscle. Using an atlas-based liver segmentation, the bounds of the desired intensity interval were derived. After application of morphology filters (erosion and dilation operations), the hyperintense parenchyma without the hypointense tumors and vessels was segmented. For comparison, the liver was also manually segmented without tumors and large vessels. The dose of ^{166}Ho on the healthy parenchyma was visualized using the imaging-based R2* maps and the automatically obtained segmentations.

RESULTS: Parenchymal SI increased over time (see table 1), as expected, and did not differ significantly between the pre and post treatment MRI. For all patients, the healthy parenchyma was successfully segmented with the automatic intensity-based method, as shown in Figure 1 with its corresponding dosimetric map. Figure 2 shows a histogram of the SI values with the interval containing the hyperintense parenchyma. The segmented healthy parenchymal volume was 1340±261 mL, obtained from the 15 min post treatment MRI. These volumes correlated well (r^2=.98) with those from the pre treatment MRI, and correlated moderately (r^2=.53) with the manual segmentations, which did not exclude all large vessels. The manual segmentations led to higher liver volumes than the automatic method (p=.160).

Table 1: Relative parenchymal signal intensities				
MRI	precontrast	5min	10min	15min
pre treatment	1.43±0.23	1.92±0.20	2.12±0.24	2.21±0.30
post treatment	1.33±0.27	1.84±0.47	2.00±0.56 (b)	2.05±0.55 (b)
No sign diff,(a)	*p=0.843*	*0.866*	*0.765*	*0.584*

Table 2: Gadoxetate-based volumetry	**i**	**ii**
Healthy parenchyma *(mL)*	1480±213	1340±261

Mean ± standard deviation. (a) Paired 2-samples t-test at p<.005, (b) for N=4. (i) Manual segmentation, (ii) automatic on 15 min image

DISCUSSION: Our results show feasibility of automatic gadoxetate-enhanced MRI for segmentation of healthy hepatic parenchyma for MRI-based dosimetry of holmium microspheres, whereby hypointense tumors and vessels were excluded. Both the 10 and 15 min acquisitions were sufficient for automatic segmentation. Visually, the automatic segmentations were deemed more accurate than the manual segmentations, as these excluded too few vessels. With this approach the healthy parenchymal volume was obtained fully automatically and can therefore be easily implemented in clinical practice. Although this study focused on post-treatment dose evaluation, treatment planning based on dosimetry can also be improved using the gadoxetate-based healthy parenchymal volume.

CONCLUSION: Gadoxetate-based automatic segmentation of the healthy hepatic parenchymal volume is feasible and might benefit radioembolization dosimetry and dosimetry-based treatment planning.

References: [1]] Gil-Alzugaray B. et al. Hepatology. 2013;57(3):p1078. [2] Lam MG et al. J Vasc Interv Radiol 2014;25(7):p1085. [3] Van de Maat GH et al. Eur Radiol 2013;23(3);p827. [4] Beck GM et al. JMRI 2008;27(6):p1461.