

# Case Report: Functional, Volumetric, Treatment Response Assessment Using MR OncoTreat

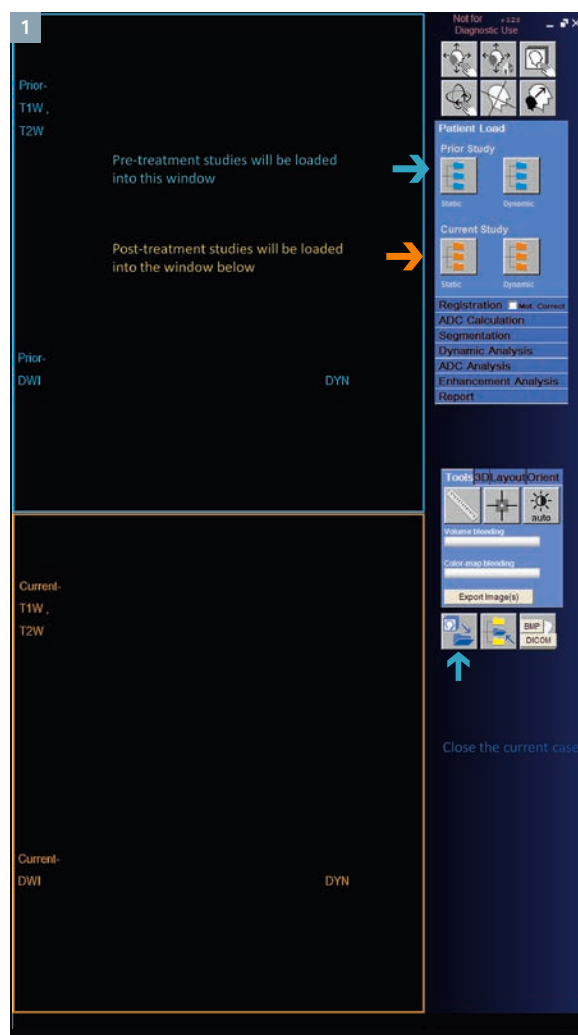
Susanne Bonekamp; Ihab R. Kamel

The Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins Hospital, Baltimore, MD, USA

## Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide and is associated with a very low survival rate [1]. Because the majority of HCC lesions are diagnosed at an advanced stage, few patients qualify for surgical resection or liver transplantation [2]. Loco-regional treatment methods, most commonly transarterial chemoembolization (TACE), are considered the standard of care in patients with unresectable HCC [3, 4]. Response to treatment is often assessed using cross-sectional imaging. Current guidelines include EASL (European Association for the Study of Liver Disease) and modified RECIST (Response Evaluation Criteria in Solid Tumors). Both metrics rely on the measurement of viable tumor burden in a single axial plane [5, 6]. However, assessment of a single axial slice can be misleading and may have low reproducibility. Furthermore, residual enhancement assessed by contrast-enhanced MRI or CT can be difficult to evaluate owing to the presence of changes in signal intensity (hyperintensity on unenhanced T1-weighted images) related to a combination of iodized oil injection and hemorrhagic necrosis.

Several recent publications have highlighted the advantage of volumetric assessment of tumor anatomy and function as a method of response assessment. Functional volumetric assessment of diffusion-weighted MRI (DWI) using apparent diffusion coefficient (ADC) maps and post-contrast-enhancement MRI have been successfully applied in the brain and liver [7, 8]. Using a prototype software



Overview of MR OncoTreat. First patient DICOM data is loaded. The pre-treatment data is loaded into the window outlined in blue, while the follow-up MRI data is loaded into the window outlined in orange. After loading patient data an automatic data classification is done after loading which classifies data into six categories: T1W, T2W, DWI, ADC, DIFF and OTHER based on the protocol settings stored in the DICOM header. These settings can be manually overwritten.

(MR OncoTreat\*; Fig. 1) developed by Siemens Corporation; Corporate Technology, USA and Siemens Healthcare, Erlangen, Germany we have published several recent manuscripts that outline the feasibility of a volumetric, functional assessment of treatment response in patients with primary

and metastatic liver cancer [8-13]. This case report outlines the functional, volumetric analysis of response to TACE in a patient with HCC.

\* Work in progress: The product is still under development and not commercially available yet. Its future availability cannot be ensured.

## Patient history

The patient is a 61-year-old male with a history of hepatitis B, liver cirrhosis, and hepatocellular carcinoma. After diagnosis of a large lesion in the liver (14 cm in diameter) on CT imaging, he underwent one session of hepatic artery chemoembolization to the right lobe of the liver. MR imaging was performed one day before TACE to more accurately assess the lesion. Follow-up MRI was done one month after TACE.

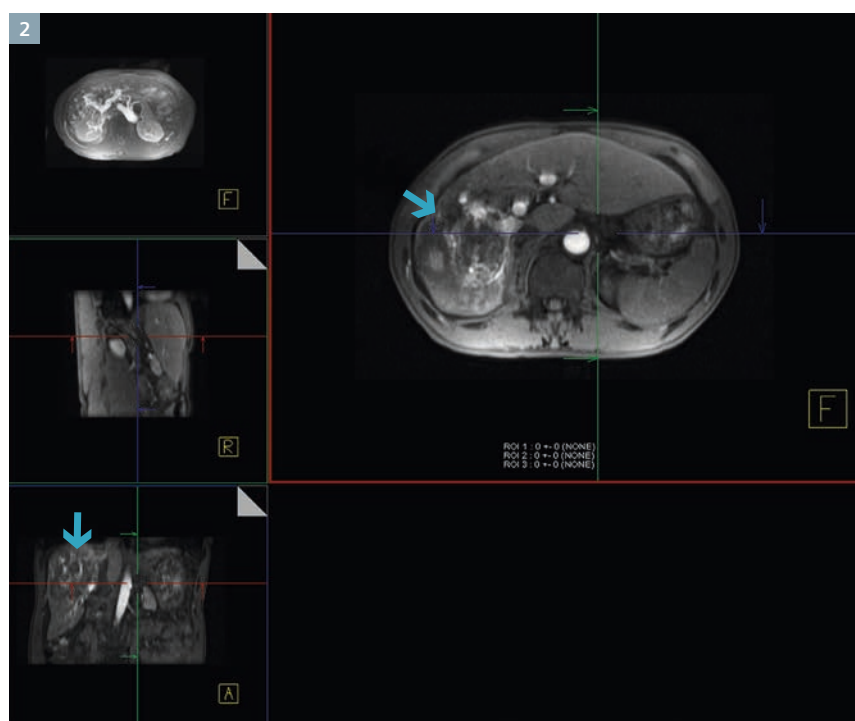
## Sequence details

All images have been acquired on a 1.5T MAGNETOM Avanto (Siemens Healthcare, Erlangen, Germany). The patient underwent our standard clinical imaging protocol. Which included breath-hold diffusion-weighted echo planar images (matrix,  $128 \times 128$ ; slice thickness 8 mm; interslice gap, 2 mm; b-value,  $0 \text{ s/mm}^2$ ,  $750 \text{ s/mm}^2$ ; repetition time (TR) 3000 ms; echo time (TE) 69 ms; received bandwidth 64 kHz) as well as breath-hold unenhanced and contrast-enhanced ( $0.1 \text{ mmol/kg}$  intravenous gadobenate dimeglumine; Multihance; Bracco Diagnostics, Princeton, NJ, USA) T1-weighted three-dimensional fat suppressed spoiled gradient-echo images (field-of-view 320–400 mm; matrix  $192 \times 160$ ; slice thickness 2.5 mm; TR 5.77 ms; TE 2.77 ms; received bandwidth 64 kHz; flip angle  $10^\circ$ ) in the hepatic arterial phase (AE) (20 s), and portal venous phase (VE) (70 s).

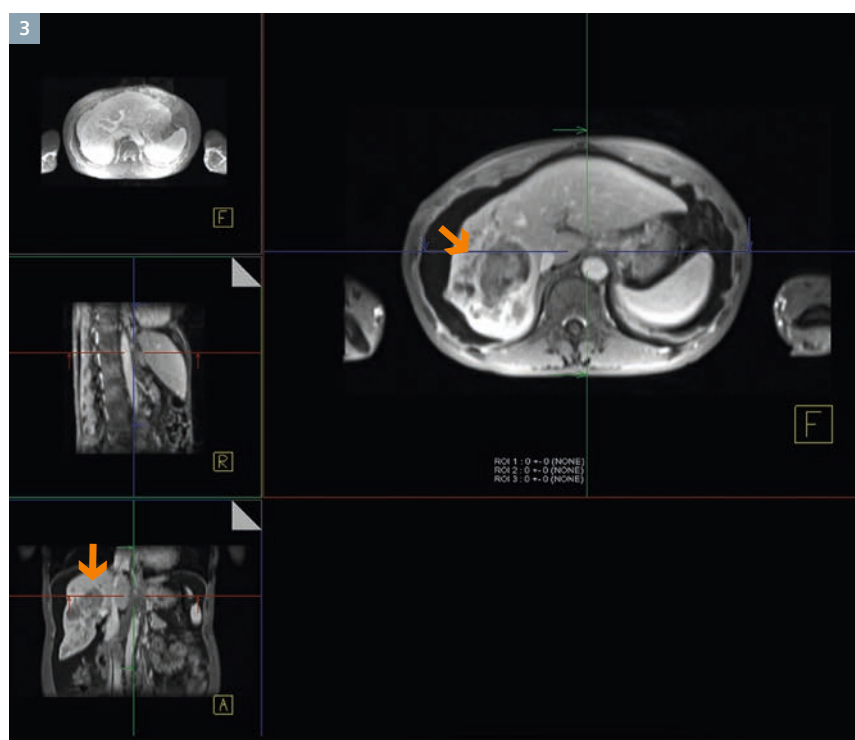
## Volumetric functional MRI response

Image analysis was performed by an MRI researcher (S.B.) with 8 years experience in MR imaging using proprietary, non-FDA approved software, MR OncoTreat (Siemens Healthcare, Erlangen, Germany). A single, treated HCC index lesion was selected as the representative index lesion for the patient. Figure 2 shows the arterial phase images of the lesion (arrow) before treatment. Figure 3 shows the same lesion after treatment.

Lesion segmentation is shown in figure 4 (pre-treatment) and figure 5

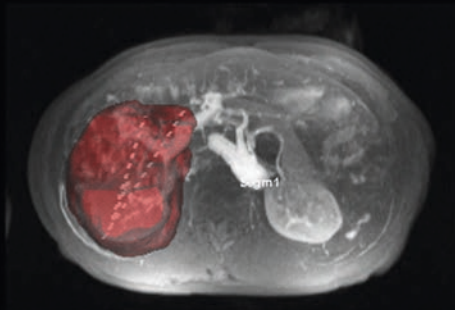


**2** Arterial phase images of a liver with a large heterogeneously enhancing HCC lesion (arrows) in a 61-year-old male with a history of hepatitis B before loco-regional therapy.



**3** Arterial phase images of a liver with a large heterogeneously enhancing HCC lesion (arrows) of the same patient after loco-regional therapy.

4

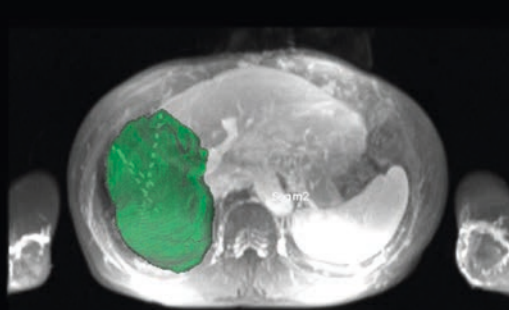


Total Volume : 547.5 0 cm3  
Total Surface : 32.3 0 cm2  
Total Diameter : 137.2 0 mm  
Total RECIST : 115.1 0 mm

F

- 4 Segmentation of the HCC lesion before treatment performed using seed placement and 'Random Walker', a semi-automatic 3D segmentation technique.

5

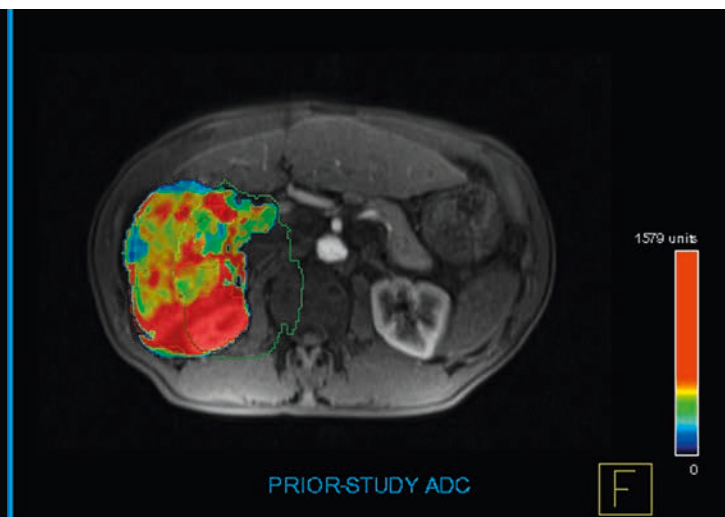


Total Volume : 0 420.7 cm3  
Total Surface : 0 26 cm2  
Total Diameter : 0 149.5 mm  
Total RECIST : 0 105.7 mm

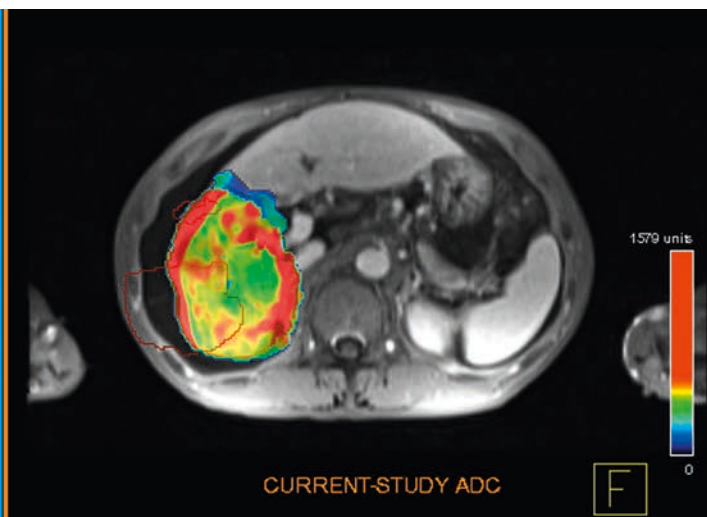
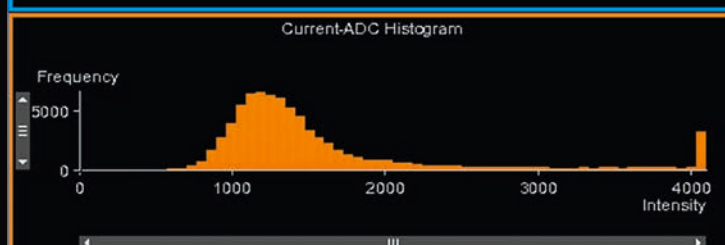
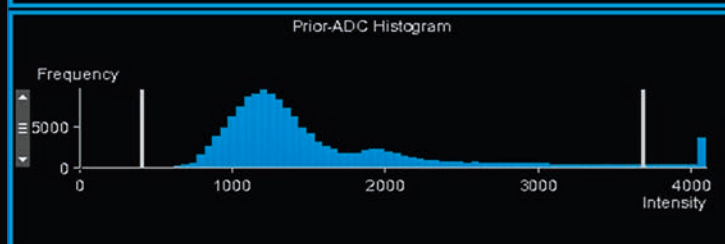
F

- 5 Segmentation of the HCC lesion after treatment performed using seed placement and 'Random Walker', a semi-automatic 3D segmentation technique. No co-registration of the HCC lesion was performed due to the change in size and structure.

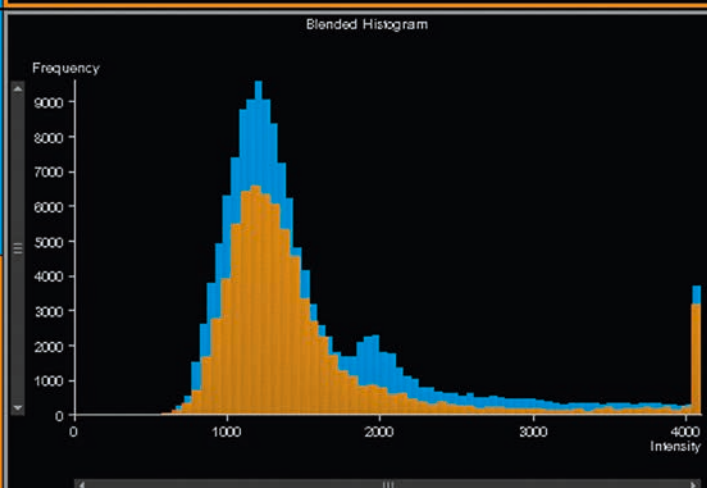
6



ADC: 1320 ± 760.536 [0 , 4095] units

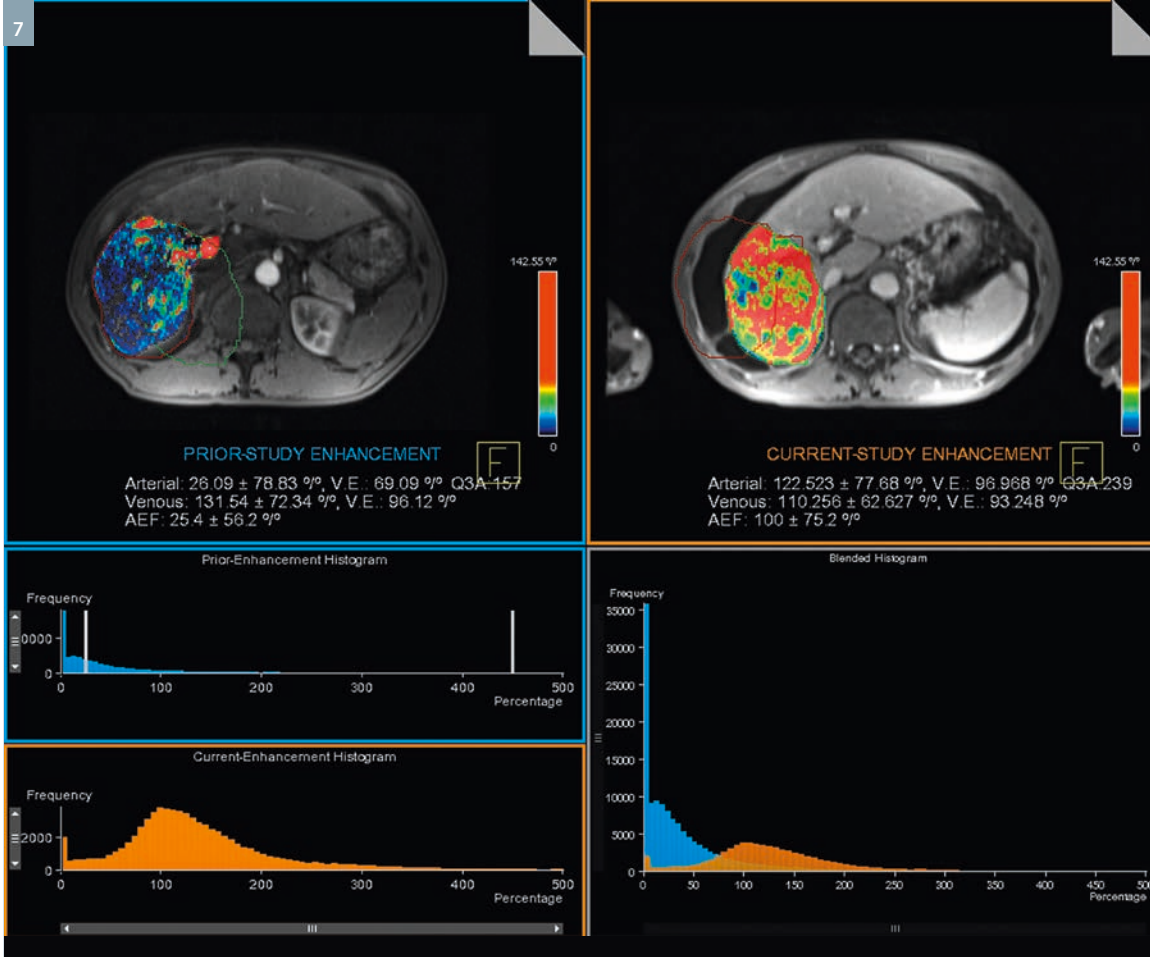


ADC: 1318 ± 780.47 [81 , 4095] units



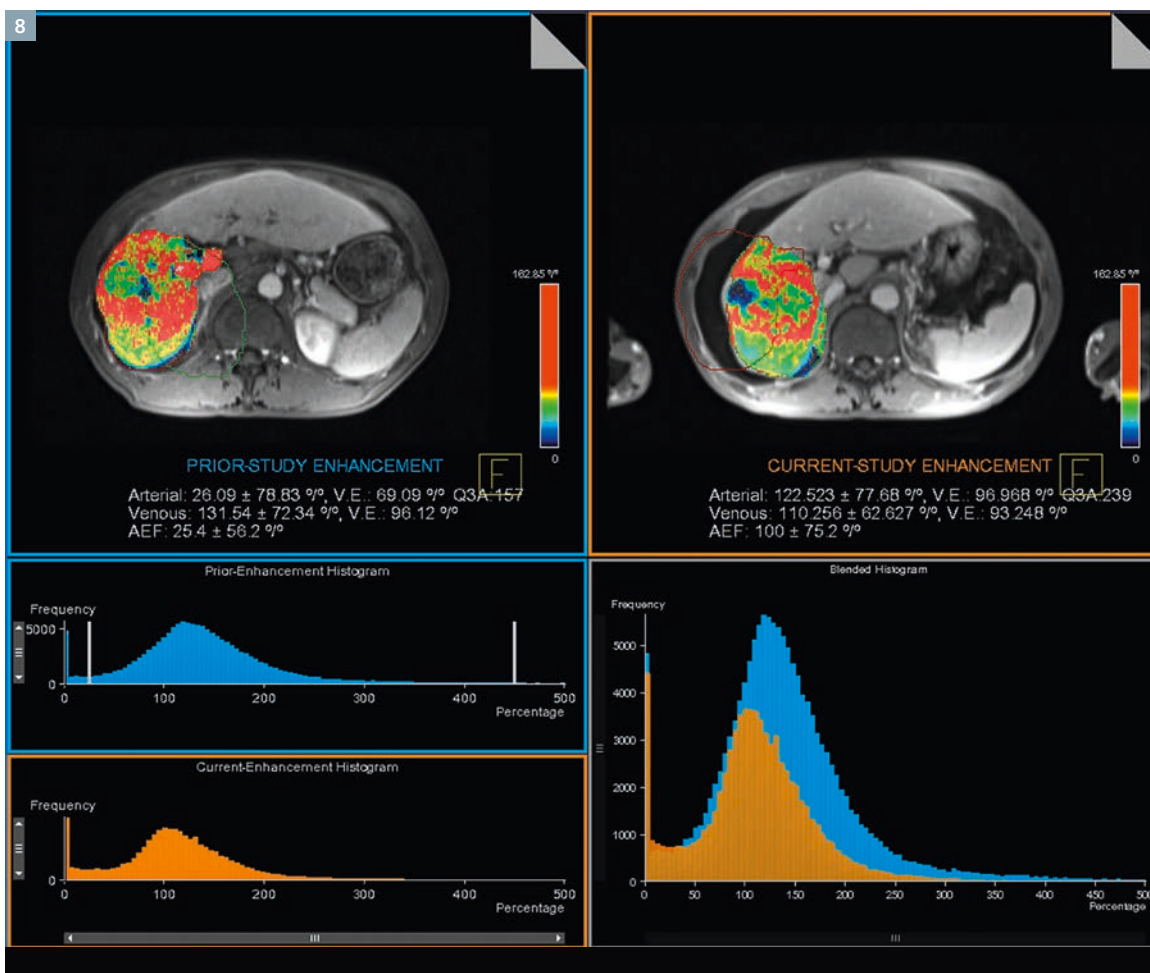
- 6 Comparison of the ADC values before and after TACE within the entire segmented tumor volume. The upper left window and the blue histogram show the heterogeneous distribution of ADC values before treatment, the upper right window and the orange histogram show the distribution of ADC values after treatment. The window in the lower left shows an overlay of the pre- and post-treatment ADC values and their distribution, allowing for easy visual assessment of treatment induced changes in ADC.





**7**

Comparison of the arterial enhancement (AE) values before and after TACE within the entire segmented tumor volume. The upper left window and the blue histogram show the heterogeneous distribution of AE values before treatment, the upper right window and the orange histogram show the distribution of AE values after treatment. The window in the lower left shows an overlay of the pre- and post-treatment AE values and their distribution, allowing for easy visual assessment of treatment induced changes in AE.



**8**

Comparison of the portal venous enhancement (VE) values before and after TACE within the entire segmented tumor volume. The upper left window and the blue histogram show the heterogeneous distribution of VE values before treatment, the upper right window and the orange histogram show the distribution of VE values after treatment. The window in the lower left shows an overlay of the pre- and post-treatment VE values and their distribution, allowing for easy visual assessment of treatment induced changes in VE.

(post-treatment). The software automatically generated tumor diameter, tumor volume, volumetric ADC and volumetric enhancement in the arterial (AE) and portal venous phase (VE).

ADC maps were reconstructed using a monoexponential fit between two b-values of 0 and 750 s/mm<sup>2</sup>. Figure 6 depicts a comparison of the ADC values of the pre-treatment lesion (segment 1), along with the pre-treatment ADC histogram in blue, and the post-treatment lesion (segment 2), with the post-treatment ADC histogram in orange.

For the assessment of treatment response the percent change in volumetric tumor ADC at follow-up compared with baseline values can be calculated using the formula  $\{(ADC_{post} - ADC_{pre})/ADC_{pre}\} \times 100$ , where  $ADC_{pre}$  is the mean baseline volumetric ADC value and  $ADC_{post}$  is the mean follow up volumetric ADC value.

Enhancement in the portal venous phase was calculated by subtracting the native phase signal intensity from the venous phase signal intensity multiplied by 100 to obtain percentage change. Similar to the ADC results, figures 7 (AE) and 8 (VE) show a comparison of the pre-treatment enhancement values (segment 1, blue histogram) compared to the post-treatment enhancement values (segment 2, orange histogram).

Again, for the assessment of response to treatment the percent change in volumetric tumor AE or VE at follow up compared with baseline values can be calculated using the formula  $\{(E_{post} - E_{pre})/E_{pre}\} \times 100$ , where  $E_{pre}$  represents the mean baseline volumetric enhancement value and  $E_{post}$  represents the mean 3–4 weeks follow up volumetric enhancement value.

## Diagnosis

Figures 4–8 show the large, heterogeneously enhancing HCC lesion before and after treatment. ADC values did not change significantly after TACE ( $1.320 \times 10^{-3}$  mm<sup>2</sup>/s to  $1.318 \times 10^{-3}$  mm<sup>2</sup>/s, fig. 6). Enhancement values in the hepatic arterial phase were highly variable with

a standard deviation of 79% and increased after treatment (26.09% to 122.52%, fig. 7), while portal venous enhancement was also highly variable (standard deviation of 72%) and showed a slight decrease after TACE (131.54% to 110.26%, fig. 8). Together these functional parameters indicate that the lesion did not respond to treatment. The patient subsequently underwent treatment with doxorubicin eluting microspheres (DEB-TACE) which resulted in a more favorable outcome than the initial TACE.

## Conclusion

The case shows how functional, volumetric analysis of MR imaging data using MR Oncotreat can assist diagnostic and interventional radiologist in the assessment of treatment response and planning of follow-up treatment.

## Acknowledgement

We would like to thank Atilla Kiraly, Mehmet Akif Gulsun, and Li Pan (Siemens Corporation, Corporate Technology, USA), Peter Gall and Berthold Kiefer (Siemens Healthcare, Erlangen, Germany) for the development and the help and support with the MR OncoTreat software used for image processing.

### References

- 1 Altekruse SF, McGlynn KA, Reichman ME. Hepatocellular carcinoma incidence, mortality, and survival trends in the United States from 1975 to 2005. *J Clin Oncol* 2009;27(9):1485-1491.
- 2 Jemal A, Siegel R, Xu J, Ward E. Cancer Statistics, 2010. *CA Cancer J Clin* 2010
- 3 Llovet JM, Bruix J. Systematic review of randomized trials for unresectable hepatocellular carcinoma: Chemoembolization improves survival. *Hepatology* 2003;37(2):429-442.
- 4 Camma C, Schepis F, Orlando A, et al. Transarterial chemoembolization for unresectable hepatocellular carcinoma: meta-analysis of randomized controlled trials. *Radiology* 2002;224(1):47-54.
- 5 Suzuki C, Jacobsson H, Hatschek T, et al. Radiologic measurements of tumor response to treatment: practical approaches and limitations. *RadioGraphics* 2008;28(2):329-344.

- 6 Suzuki C, Torkzad MR, Jacobsson H, et al. Interobserver and intraobserver variability in the response evaluation of cancer therapy according to RECIST and WHO-criteria. *Acta Oncol* 2010;49(4):509-514.
- 7 Moffat BA, Chenevert TL, Lawrence TS, et al. Functional diffusion map: a non-invasive MRI biomarker for early stratification of clinical brain tumor response. *Proc Natl Acad Sci U S A* 2005;102(15):5524-5529.
- 8 Bonekamp S, Jolepalem P, Lazo M, Gulsun MA, Kiraly AP, Kamel IR. Hepatocellular Carcinoma: Response to TACE Assessed with Semiautomated Volumetric and Functional Analysis of Diffusion-weighted and Contrast-enhanced MR Imaging Data. *Radiology* 2011;260(3):752-761.
- 9 Bonekamp S, Li Z, Geschwind JF, et al. Unresectable Hepatocellular Carcinoma: MR Imaging after Intraarterial Therapy. Part I. Identification and Validation of Volumetric Functional Response Criteria. *Radiology* 2013.
- 10 Bonekamp S, Halappa VG, Geschwind JF, et al. Unresectable Hepatocellular Carcinoma: MR Imaging after Intraarterial Therapy. Part II. Response Stratification Using Volumetric Functional Criteria after Intraarterial Therapy. *Radiology* 2013.
- 11 Gowdra Halappa V, Corona-Villalobos CP, Bonekamp S, et al. Neuroendocrine Liver Metastasis Treated by Using Intraarterial Therapy: Volumetric Functional Imaging Biomarkers of Early Tumor Response and Survival. *Radiology* 2012.
- 12 Halappa VG, Bonekamp S, Corona-Villalobos CP, et al. Intrahepatic cholangiocarcinoma treated with local-regional therapy: quantitative volumetric apparent diffusion coefficient maps for assessment of tumor response. *Radiology* 2012;264(1):285-294.
- 13 Li Z, Bonekamp S, Halappa VG, et al. Islet cell liver metastases: assessment of volumetric early response with functional MR imaging after transarterial chemoembolization. *Radiology* 2012;264(1):97-109.

## Contact

Ihab R. Kamel, M.D., Ph.D.  
The Johns Hopkins Hospital  
Department of Radiology  
600 N. Wolfe St, MRI 143  
Baltimore, MD 21287  
USA  
Phone: +1 410-955-4567  
ikamel@jhmi.edu