

Liver cancer: Evaluation of the hemodynamic features and correlation with response to therapy using Arterial Enhancement Fraction based on tri-phasic MRI

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TARGET AUDIENCE - Clinical researchers and radiologists

Purpose of Study Hepatocellular carcinoma (HCC) is the most common primary malignant disease of the liver.

Assessing early response to therapy using objective criteria is paramount for clinical care. The aim of this study was to investigate the feasibility of using the arterial enhancement fraction (AEF) to predict response to intra-arterial treatment (IAT) in patients with unresectable HCC.

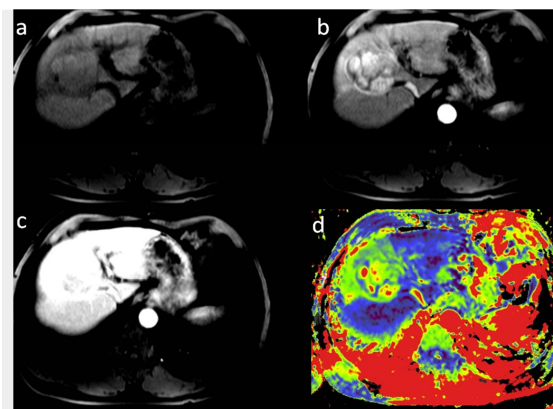
Materials, Methods and Procedures 131 patients (108 male, mean age 56.6 years) with liver cancer were included. Tri-phasic MR images (native, arterial phase at 20 seconds, portal venous phase at 70 seconds) were acquired at baseline and 3-4 weeks after IAT using a 1.5 T scanner. Quantitative AEF color maps were generated using a research software tool. The AEF of tumor and tumor-free hepatic parenchyma was measured by placing 6 ROIs on axial images. RECIST and EASL parameters as well as clinical measures and patient survival (until August 31st 2012 or time of death) were assessed as well. Change in tumor AEF was calculated and descriptive statistical analysis was performed. Kaplan-Meier plots and Cox proportional hazards model were used to assess whether change in tumor AEF can be used to predict patient survival.

Results: The mean AEF of the tumor at baseline ($66.7\% \pm 20.0$) was significantly higher than that of tumor-free parenchyma ($27.2\% \pm 11.8$, $p < 0.0001$). After IAT the mean AEF of the tumor decreased by 35% on average (mean AEF = $66.7\% \pm 20.0$ to mean AEF = $44.0\% \pm 26.7$, $P < 0.0001$), while the mean AEF of the tumor-free parenchyma remained unchanged ($27.2\% \pm 11.8$ to $26.4\% \pm 10.9$, $p = 0.41$). According to mean tumor AEF patients were stratified into AEF responders if they had an AEF decrease of 35% after IAT ($n = 66$). AEF responders survived longer than non-responders (35.2 months vs. 10.8 months, Hazard Ratio (HR) = 0.37, $P < 0.0001$). These results were only minimally influenced when clinical information (age, gender, BCLC stage, number of treatments, presence of cirrhosis, multifocality of liver cancer) was included in the statistical model (HR = 0.28, $p = 0.001$).

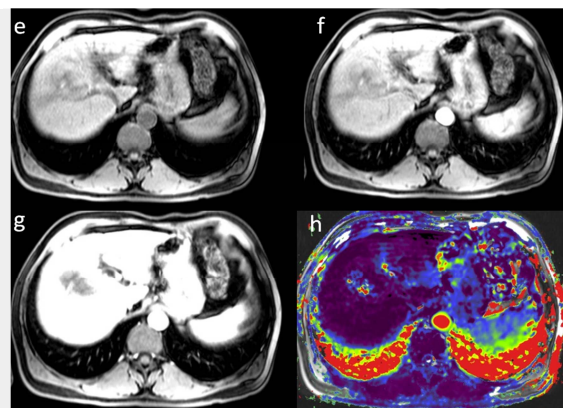
Discussion: Previous studies of AEF based on triple phase CT imaging have shown that AEF correlates strongly with HPI obtained at cine mode perfusion CT¹, and that the addition of AEF color maps to regular CT imaging can increase HCC detection from 71.7% to 88.8%². A third study determined that pre-treatment AEF values in patients with metastatic liver cancer could predict treatment response³. In our study we investigated the response to treatment 3-4 weeks after IAT using tri-phasic MRI. We found that AEF response provided a better stratification of patients into responders and non-responders than RECIST or EASL at this early stage.

Conclusion: Evaluating the AEF values based on tri-phasic MRI may be helpful for predicting tumor response in patients with unresectable primary liver cancer treated with IAT before a change in size can be observed.

References: 1. Kim, K. W. *et al.* CT. *AJR Am. J. Roentgenol.* **196**, 102-108 (2011). 2. Kim, K. W. *et al.* *Radiology* **250**, 425-434 (2009). 3. Joo, I. *et al.* *L. Eur. J. Radiol.* (2011).



HCC lesion **before** targeted therapy. Mean AEF of the tumor was 95%. (a) unenhanced, (b) hepatic arterial phase, (c) portal venous phase, and (d) resulting color map images.



HCC lesion **after** targeted therapy. Mean AEF of the tumor decrease to 12%. (e) unenhanced, (f) hepatic arterial phase, (g) portal venous phase, and (h) resulting color map images.