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Assessment of liver tumor response by high-field (3 T) MRI after radiofrequency ablation: Short- and mid-term evolution of diffusion parameters within the ablation zone

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ABSTRACT

Purpose: To compare the apparent diffusion coefficient (ADC) values of malignant liver lesions on diffusion-weighted MRI (DWI) before and after successful radiofrequency ablation (RF ablation).

Materials and methods: Thirty-two patients with 43 malignant liver lesions (23/20: metastases/hepatocellular carcinomas (HCC)) underwent liver MRI (3.0 T) before (<1 month) and after RF ablation (at 1, 3 and 6 months) using T2-, gadolinium-enhanced T1- and DWI-weighted MR sequences. Jointly, two radiologists prospectively measured ADCs for each lesion by means of two different regions of interest (ROIs), first including the whole lesion and secondly the area with the visibly most restricted diffusion (MRDA) on ADC map. Changes of ADCs were evaluated with ANOVA and Dunnett tests.

Results: Thirty-one patients were successfully treated, while one patient was excluded due to focal recurrence. In metastases ($n = 22$), the ADC in the whole lesion and in MRDA showed an up-and-down evolution. In HCC ($n = 20$), the evolution of ADC was more complex, but with significantly higher values ($p = 0.013$) at 1 and 6 months after RF ablation.

Conclusion: The ADC values of malignant liver lesions successfully treated by RF ablation show a predictable evolution and may help radiologists to monitor tumor response after treatment.

1. Introduction

For several years magnetic resonance imaging (MRI) has been used for the evaluation of treatment response in malignant liver lesions [1]. However, after certain loco-regional treatments such as radiofrequency ablation (RF ablation), the assessment of tumor response remains difficult. The usual morphological criteria primarily based on the lesional maximal size (RECIST) cannot be used with confidence, as the induced ablation zones comprise the tumor and a safety margin. Residual contrast enhancement (European Association for the Study of the Liver, EASL) [2] may also be difficult to appreciate, since some types of secondary tumors (e.g. colo-rectal metastases) are hypovascular without strong contrast medium enhancement. Furthermore, focal liver lesions treated by RF ablation often contain a hypersignal on T1-weighted MR sequences, corresponding to coagulation necrosis, which makes any residual tumoral contrast enhancement difficult to be differentiated [3].

Diffusion-weighted MRI (DWI), primarily performed in neuroradiology for acute stroke, has then been introduced into abdominal imaging. Representing a supplementary tool for detecting and characterizing hepatic lesions [4,5], DWI is now increasingly being used to evaluate tumors' response to various treatments [6].

DWI evaluates the random diffusion of water molecules. Restriction of this diffusion depends on the extracellular matrix and the cellularity of the tissue. Some authors have postulated that diffusion and its quantitative representation, the apparent coefficient of diffusion (ADC), may increase in hepatic lesions after successful treatment with chemoembolization (TACE) [7,8]. This response seems to reflect the passage of water molecules from the intracellular compartment to the extracellular matrix, due to the induced tumoral cell necrosis. Thus, ADC may be used to assess metabolic tumor response after loco-regional treatment. Additionally to the ADC measurement in the whole lesion, some authors have tried to determine whether the intra-lesional measurement of the lowest ADC might be helpful in the monitoring of tumor recurrence, because this value could reflect the persistence of viable and residual tumor cells [9].

The first purpose of this study was to evaluate the ADC values of primary and secondary hepatic malignancies, before and after successful treatment by RF ablation, using high-field MRI (3.0 T). The second objective was to observe the mid-term evolutional pattern of these ADC values.

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2. Materials and methods

2.1. Study population

Since 23 April 2008, diffusion sequences have been added to our standard liver protocol (Section 2.2), permitting the prospective collection of our patients. From April 23, 2008 to February 16, 2011, 32 consecutive patients were evaluated for the study. Inclusion criteria were: (1) more than 18 years old, (2) being investigated with pre-treatment MRI for liver malignancy, (3) treatment by RF ablation within one month of the initial MRI evaluation, (4) undergoing three MRI examinations after RF ablation treatment, the first one at 1 month, the second one at 3 months, and the last one at 6 months. There were 26 men and 6 women. Age ranged from 24 to 76 years. Mean and median age were 59 and 60 years, respectively. Exclusion criteria were if (a) the patient had focal tumor recurrence (irregular and nodular peripheral enhancement followed by post-contrast washout in case of HCC or/and newly appeared hypersignal on T2-weighted MR images in case of metastases), (b) the lesion was poorly identified due to artifacts, (c) the lesion was too small (<1 cm in short diameter) to be correctly delineated, or (d) patient missed a post-treatment assessment within the pre-defined period of time. Hence, one lesion in one patient was excluded because of focal metastatic recurrence at 14 months (histopathologically proven).

We ended up including 31 patients with 20 hepatocellular carcinomas and 22 liver metastases (due to 6 colon cancers, 2 breast cancers, 1 gastric cancer, 2 carcinoid tumors, 2 GIST, 4 ocular melanoma, 1 retroperitoneal liposarcoma and 4 neuroendocrine pancreatic tumors). Six patients had 2 lesions, one had 3 three lesions and one four lesions. There were one lesion in the segment 1, one lesions in the segment 2, four lesions in the segment 3, nine lesions in the segment 4, five in the segment 5, six in the segment 6, six in the segment 7 and 10 in the segment 8. All the lesions were biopsied before the RF ablation procedure (one biopsy per patient). Mean follow-up was 24.3 ± 8.7 months (from 13 to 39 months, median 24 months).

This study complies with the local ethical guidelines and it was approved in its present form by our institutional ethics board. Informed written consent was obtained from each patient during an informative consultation before treatment.

2.2. MRI protocol

Data were acquired on a 3.0 Tesla MR unit (Trio, Siemens Healthcare, Erlangen, Germany).

The maximum gradient strength was 40 mT/m. For abdominal imaging, we used a 12-channel phased-array body coil with a field of view of 38 cm × 28 cm. Bandwidth was 1602 Hz. Our standard liver protocol consisted of a breath-hold T2-weighted transverse half-Fourier acquisition single-shot turbo spin echo sequence (HASTE, repetition time/echo time ms: 1200/89, echo train length: 211, number of excitations (NEX) 1, matrix: 320 mm × 211 mm, slab thickness/gap mm: 3/0.8), a T1-weighted transverse spoiled gradient-recalled-echo sequence (in-phase: 115/2.5, out-phase: 115/3.7, 320 × 180, 6/1.5), a respiratory-triggered T2-weighted transverse fat-suppressed fast spin echo sequence (4040.6/121, echo train length: 23, NEX 1, 512 × 188, 6/1.8), and a breath-hold T1-weighted transverse fat-suppressed GE sequence (VIBE, 3.7/1.4, 384 × 236, flip angle 10°, NEX 1, 4/0.8,). The latter was performed before and after intravenous (IV) dynamic Gadolinium (Dotarem, Guerbet SA, Zürich, Switzerland) 0.1 mmol/kg injection (arterial, portovenous, and equilibrium phase).

Diffusion-weighted MR sequences were acquired before the IV contrast injection. During free but shallow breathing, we acquired a transverse single-shot spin-echo echo-planar sequence (7700/66, 6/0, FatSat, receiver bandwidth 1750 Hz/pixel) in three orthogonal directions (frequency-encoding, phase-encoding, and slice-selection) with three *b*-values (50, 300, 600 s/mm^2). These *b*-values were chosen in order to acquire images with a sufficient contrast-to-noise ratio. The number of excitations was 6. A parallel acquisition technique (GRAPPA GeneRalized Auto-calibrating Partially Parallel Acquistion) was used with an acceleration factor 2. The duration of the sequence was 7 min 20 s. The ADC map was then automatically computed with vendor-provided software. Voxel volume was 3.4 mm × 2.7 mm × 6.0 mm. Window width and level were set to adequately visualize the whole liver.

2.3. RF ablation protocol

Radiofrequency ablations were performed either under ultrasound (US) guidance alone or under combined US and CT guidance by two interventional radiologists. Patients were treated under general sedation. A Covidien/Valley Lab RF ablation system (RF Ablation System, E series, Covidien/Valley Lab, Boulder CO, USA) was used to deliver RF ablation energy to the targeted lesions. Single, clustered, or multiple cooled electrodes (Cool-Tip Ablation Electrodes, Covidien/Valley Lab, Boulder CO, USA) were used according to the size and shape of the tumor to be treated. Radiofrequency energy was applied during 12 min, according to the manufacturer's recommendations, with automated control of the impedance. When the ablation zone was thought to be insufficient after one application, additional applications were performed until the ablation zone appeared to be sufficient on US imaging. Radiofrequency ablations were considered successful when the temperature in the lesion was 70 °C or higher. In some cases where the lesion was located near a great hepatic vein or portal vein branch, occlusion balloons were used to limit the heat sink effect caused by the circulating blood. All patients were controlled by a post-procedural CT 24 h after RF ablation to confirm that the target lesion had been adequately treated and to rule out early complications. Patients were discharged the day following the procedure.

2.4. MR image analysis and ADC measurements

Two readers (observer 1, with seven years of experience in liver MR, and observer 2, with four years of experience in liver MR) jointly reviewed the 31 patients' MR examinations. Using an Argus workstation with version VB17 software (Siemens, Erlangen, Germany), the two readers agreed which DWI images best depicted the lesions. The observers were different from the interventional radiologists, who performed the RF ablation, and were blinded to any clinicopathological results. Therefore, they were not biased regarding the evaluation of the lesions. In cases with multiple treated lesions, each lesion larger than 1 cm in short axis was included in the image analysis. The area that visibly had the most restricted diffusion (MRDA) on the ADC map was also determined. A free-hand region of interest (ROI) was drawn on the DWI sequences, first including the whole of each lesion (i.e. the zone of ablation), and second including the MRDA only. These ROIs were then paste-copied onto the ADC maps (Figs. 1 and 2). The ADC measurements were performed by the two observers in consensus. The ADCs of the whole lesion and of the MRDA were assessed, as well as the surface of the ROI.

To evaluate the heterogeneity of the lesions, the standard deviations of both ADC measurements ($SD_{computed}$), automatically computed by the workstation, were also recorded [9].

Finally, the ADC of the normal hepatic parenchyma (background) within segment VI if possible, otherwise within segment V, was measured with a circular ROI of 0.5 cm^2 to evaluate the intersession reproducibility. The background ADC value was also used to normalize ADC values in the whole lesion and in MRDA.