Educational Course
Body MRI: How We Do It

Cirrhotic Liver & HCC

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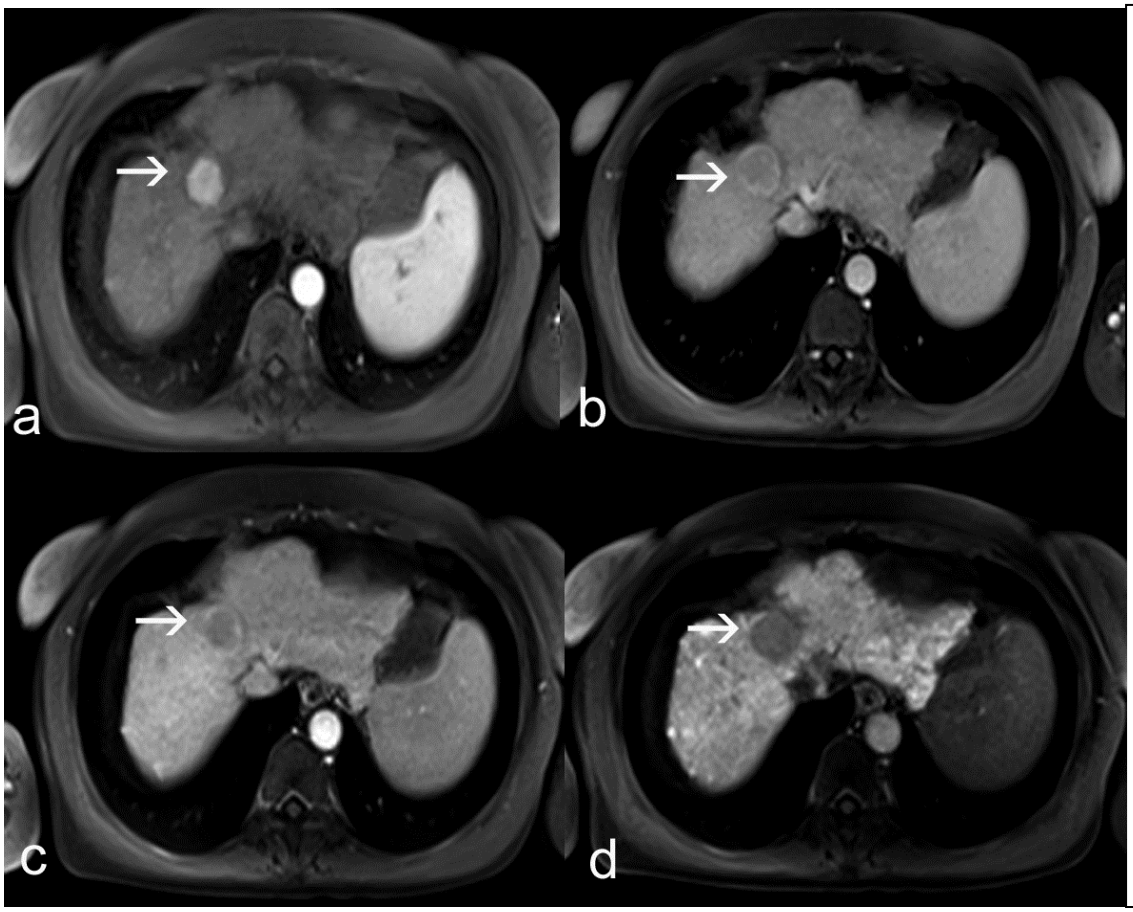
This lecture aims at physicians and technicians who are interested in liver MRI in patients with liver cirrhosis. A suitable MR protocol will be introduced and the information added by new technologies (DWI, hepatobiliary MRI) will be discussed. Diagnostic criteria for HCC and its most important differentials will be explained and demonstrated on imaging examples.

- HCC is the most important differential diagnosis for focal liver lesions in the cirrhotic liver
- Detection of HCC is crucial to ensure early therapy and proper patient management
- Challenging differential diagnoses for HCC are mainly regenerative nodules and pre-neoplastic nodules
- MRI provides a multiparametric approach to detect and characterize HCC – including MR signal in T2w images and DWI, vascularity of the lesions and uptake behaviour with hepato-biliary contrast agents

HCC is a very frequent tumor worldwide with an incidence rate of 20-150/100.000/year in high risk areas in Asia and Africa, of 5-20/100.000/year in the areas with intermediate risk in Japan and the Mediterranean countries and of 5/100.000 and less in areas with low risk in northern Europe and US [1]. Its incidence is linked to the distribution of liver cirrhosis and viral hepatitis, which are the main risk factors for the development of HCC. For the evaluation of the cirrhotic liver and for the diagnosis of HCC, multidetector computed tomography (MDCT) proved to be a robust and reliable tool. In MDCT the diagnosis of HCC can be made based on neo-vascularisation with increased arterial and decreased portal venous supply [2]. With modern magnetic

resonance imaging (MRI) spatial resolution and robustness increased dramatically. Beside the evaluation of neo-vascularisation by means of Gadolinium-enhanced early dynamic MRI, the main advantage of MRI are additional information on tissue composition and liver specific function. With diffusion-weighted imaging or plain T1- and T2-weighted sequences, different tissue elements like fat, haemorrhage, glycogen, edema and cellular density can be evaluated [3]. Liver-specific contrast agents give insight into the hepatocellular function. The integration of all these parts into the MR examination allows for a very high detection rate for overt HCC nowadays, although very small HCCs and pre-neoplastic nodules are still a challenge. Moreover, insight into the different stages of hepatocarcinogenesis can be possible with MRI [4]. Despite its limited availability in some countries, MRI has rendered to be modality of choice for the distinct evaluation of lesions in the cirrhotic liver [3, 4].



MR scan of a 62 y/o female patient with liver cirrhosis Child-Pugh A based on a chronic hepatitis C. T1w GRE sequence with fat-saturation in arterial (a), porto-venous (b) and equilibrium phase (c) after bolus injection of Gd-EOB-DTPA; (d) liver-specific phase 20 minutes after injection. Note the lesion (arrow) with the typical enhancement pattern of a HCC with arterial hyper-vascularity and rapid wash-out, which can be seen best in the transitional phase (2 min) scan (c). As an additional criterion for a HCC missing hepato-biliary uptake with high tumor-to-liver contrast is seen in the liver-specific phase (d). Note multiple small nodules (< 5mm) with hepato-biliary uptake representing regenerative nodules.

Source:
Zech et al. Imaging of hepatocellular carcinoma by computed tomography and magnetic resonance imaging: state of the art. Dig Dis. 2009;27(2):114-24.

MRI has made dramatic changes with regard to artifact robustness, spatial resolution and speed in the abdominal area. The use of phased-array multi-channel coils and fast imaging techniques like gradient recalled echo (GRE) or fast spin echo (FSE) techniques are now established since many years as a standard for abdominal MR imaging. The introduction of parallel imaging, diffusion-weighted imaging DWI, 3D GRE techniques with interpolation and ultra-short repetition times and the navigator-techniques of respiratory triggering have been introduced recently and are by now already in broad use. A liver MR study usually comprises a T1w 2D GRE sequences in-phase and opposed phase, a T2w single shot FSE and/or T2w multi-

shot FSE with fat-saturation, a DWI echoplanar imaging (EPI) sequence and a dynamic T1w 3D GRE sequence with fat-sat prior and after contrast agent injection. Depending on the type of contrast medium additional sequences for the liver-specific phase are performed.

The contrast agents used for liver MRI are on one hand extracellular, unspecific gadolinium agents, on the other hepatobilary contrast agents, which are targeted directly to the hepatocyte and are excreted via the bile. There are currently two approved liver-specific contrast agents available on the market.

Non-enhanced MRI plays an important role in the characterization of different tissue components. The signal intensity of hepatic nodules in the cirrhotic liver can vary in T1w and T2w plain sequences. It has been demonstrated that copper deposition, glycogen, intratumoral bleeding or fat within a nodule causes hyperintensity on plain T1w sequences. Since hyperintensity occurs in dysplastic nodules as well as in approximately one third of moderately differentiated HCC, it seems impossible to distinguish the nature of a hepatic nodule based on T1w signal alone. For the signal behavior in T2w sequences hyperintensity with depiction of a mosaic pattern has been described to be typical for HCC. Overall over 90% of HCC are hyperintense lesions in T2w images. A nodule that is hyperintense on T1w images and iso- or hypointense on T2w images usually indicates that the lesion is at a high risk for ongoing malignant transformation (high-grade dysplastic nodule). In contrast nodules that are hyperintense on T1w images and iso- or hyperintense on T2w images usually represent an overt HCC. A nodule being isointense on T1w images and hypo- or isointense on T2w images exhibits the typical signal behavior of a regenerative nodule. Other typical morphological features of HCC that can be seen on pre-contrast (and contrast-enhanced) MR images include a pseudocapsule and a mosaic pattern.

Diffusion-weighted imaging has for long played only a minor role in abdominal imaging, however, with new scanner generations with homogenous magnetic fields and with the introduction of parallel imaging DWI with echo-planar images is feasible with a high image quality and robustness. DWI can help to increase the detection rate of focal liver lesions especially due to the black-blood effect, which helps to percept even very small lesions or lesions directly adjacent to vessels easily and fast. Moreover, the quantification of restricted diffusion with the apparent diffusion coefficient (ADC) helps to differentiate between benign and malignant lesions. However, up to now there is no evidence in the literature in how far DWI might be a feasible approach to differentiate between regenerative nodules, dysplastic nodules and HCC. An other interesting application for DWI in the cirrhotic liver is the quantification of liver fibrosis in chronic hepatitis, which shows very promising results in the literature.

The dynamic MR examination with Gadolinium-based contrast agents provides information on the changes of vascular supply within different hepatic nodules in the cirrhotic liver and is a crucial part of the evaluation of patients with suspected HCC. With regard to the criteria for the diagnosis of overt HCC the same contrast agent behavior as described for CT is used for MRI, which means hypervascularity in the arterial-dominant

phase and pathological wash-out in the venous or delayed phase. Overall, MRI showed superior results to spiral CT in the detection of HCC in most studies. Beside the higher detection rate of MRI, it is also considered to be more specific with less false-positive lesions than CT in the differentiation between HCC and regenerative nodules. This can be explained by the additional diagnostic criteria (e.g. T2w signal intensity) for the diagnosis of HCC in MRI.

The use of liver-specific contrast agents aims to increase the sensitivity and specificity of MRI in the cirrhotic liver. The two hepatobiliary contrast agents with also extracellular properties, Gd-BOPTA and Gd-EOB-DTPA can be injected as a bolus and provide both a sufficient vascular phase as well as a hepato-biliary phase. Their main difference is the dose of Gadolinium (Gd-EOB-DTPA: 0.025 mmol / kg bodyweight compared to Gd-BOPTA 0.05 mmol / kg BW) and the higher amount of liver specific uptake of Gd-EOB-DTPA (50% versus 5%) compared to Gd-BOPTA. For the hepato-biliary contrast agents, HCC typically presents as a hypointense lesion in the hepatobiliary phase [3, 4]. Uptake with depiction as hyperintense lesions in malignant HCCs in the liver-specific phase has been demonstrated, but usually the frequency of this finding is low (<5%) and confined to well-differentiated HCC. Generally, the presence of typical changes of the vascular supply will help to correctly characterize these lesions. Up to know no exact thresholds for the uptake of regenerative nodules, dysplastic nodules and HCC have been defined. However, the potential value of showing impaired biliary uptake for the evaluation of nodules in the cirrhotic liver has been appreciated [4]. In this respect it has been pointed out that hepato-biliary MRI helps to detect hepatic nodules “at risk” for transformation into well-differentiated HCC (e.g. high grade dysplastic nodules) prior to neo-vascularization and prior to development of overt HCC.

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