Role of Diffusion Weighted MRI in differentiating benign and malignant focal liver lesions

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Aims and objectives

Liver is one of the common sites of haematogenous metastases of most of the primary malignancies in the body. Gastrointestinal, breast, melanoma, neuroendocrinal and lung cancers are the most common primary cancers responsible for metastatic liver involvement [1,2]. The differentiation between malignant and benign focal liver lesions always remains a diagnostic challenge for a radiologist. For detection and characterisation of focal liver lesions, various imaging modalities are being used, including US, multi-phase contrast enhanced CT, CT portography, MRI and perfusion studies using dedicated contrast media. Of these, MRI with contrast is considered the most accurate modality as it has high resolution for soft tissue on T1, T2 and post contrast images[3].

Diffusion is the Brownian movement of water molecules which is thermally induced randomized microscopic movement in biological tissue. Diffusion is known to be a sensitive parameter of microscopic tissue characterisation. It is a marker of cellularity and its quantitative analysis can be obtained by means of apparent diffusion coefficient (ADC) measurements. A high ADC indicates that water can move more freely, suggesting low cellularity and a low ADC implies that there is restriction of water movement, suggesting high cellularity [4]. With the development of fast MRI techniques like echo-planar imaging (EPI) and better coil systems, diffusion weighted (DW) MR imaging is now available for qualitative and quantitative assessment of diffusivity of water molecule within different liver lesions without injecting the contrast media, which becomes even more important in Indian patients where cost is one of the main factors in patient management and also in patients with renal dysfunction who are at risk for developing nephrogenic systemic fibrosis [5,6].

The purpose of this study was to evaluate the role of diffusion-weighted MR imaging in differentiating benign and malignant focal liver lesions.
Methods and materials

Patients:

This was a prospective study done on 80 lesions in 59 patients over a period of 6 months during September 2013 to March 2014. These patients were referred for MRI of abdomen in the Department of Radiology of our hospital from different oncology units. Only those lesions, which underwent FNAC or biopsy under US or CT guidance or had excision done during the abdominal surgery or had typical imaging features on MR or other imaging modalities, were included in the study. Atypical lesions were correlated with pathological diagnosis.

Informed consent was taken from all the patients after explaining the entire procedure, its benefits and risks. All patients were subjected to full clinical evaluation, laboratory investigations and radiological assessment using conventional MRI and Diffusion-weighted MRI with or without post contrast imaging.

MRI protocol for liver:

MRI studies were performed on 1.5 T unit (GE Signa HDx1.5T MRI, GE Healthcare system) by using body phased-array coil with patient in supine position.

1. Axial T1-weighted (TR/TE of 600/30ms; non fat sat) and T2-weighted (TR/TE of 200/100ms; Fat sat). For both T1 &T2 the slice thickness was 6mm, FoV of 34 cm and an acquisition matrix of 256 x 256. These images were used for assistance in lesion detection and characterization.

2. Diffusion-weighted Imaging was performed using respiratory triggered protocol at b value 0 and 800, with the single shot echo-planar imaging (EPI) technique in axial plane, matrix=128 x 128; slice thickness 6mm and interslice gap of 1mm.

   Qualitative assessment at different b values and quantitative assessment by measuring ADC values were done.

3. Dynamic post contrast (Gd-DTPA) T1-weighted axial 3D fat suppressed GRE were performed in some of the cases. Images were acquired in all 3 phases after bolus injection at the rate of 0.2mmol/kg body weight of Gd-DTPAflushed with 20ml of sterile 0.9% of saline. Arterial phase at 20 sec, portal venous phase at 60sec and delayed at 180sec after contrast injection.
Diagnosis of malignant liver lesions (primary or metastatic) were confirmed by histopathological diagnosis. The diagnosis of benign liver lesions were confirmed either by histopathological diagnosis or with typical imaging findings on US, CT or MRI or if they remained stable on follow up scans.

Statistical analysis:

Data were analyzed using statistical software R version 3.1.2 with \( p<0.001 \). Quantitative data of different variables were expressed as mean \( \pm \) standard deviation (SD).

Receiver operating characteristics (ROC) was drawn to identify cut off values for the ADC that best classified the liver lesions as benign and malignant.
Results

Patients:

A total of 80 focal liver lesions in 59 patients fulfilled the inclusion criteria. Mean age of these patients was 53 years (range, 4-83 years) with 37 male (63%) and 22 female (37%).

Liver lesions:

There were 40 benign and 40 malignant lesions which included 9 hepatocellular carcinoma (11.25%), 30 metastases (37.5%), 1 hepatoblastoma (1.25%), 19 hemangiomas (23.75%), 14 hepatic cysts (17.5%), 2 adenomas (2.5%), 2 FNH (2.5%) and 3 regenerating or degenerating hepatic nodules (3.75%).

Qualitative assessment on DW imaging:

All cystic lesions and hemangiomas showed facilitated diffusion with significant or near complete loss of signal intensity on increasing b value, and lesions which did not show reduction of signal intensity, showed high signal intensity on ADC map.

Solid benign hepatic lesions showed facilitated diffusion with mild loss of signal intensity on increasing b value. On ADC map, there was lower signal intensity compared to surrounding normal liver parenchyma.

All malignant liver lesions (primary or metastases) showed restricted diffusion with increase in signal intensity on increasing b value. On ADC map, they were much darker than the surrounding normal liver parenchyma.

Quantitative (ADC) evaluation:

The average ADC values were $3.07 \times 10^{-3}$ mm$^2$/s for hepatic cysts, $1.86 \times 10^{-3}$ mm$^2$/s for hemangiomas, $1.71 \times 10^{-3}$ mm$^2$/s for benign hepatocellular lesions, $0.98 \times 10^{-3}$ mm$^2$/s for hepatocellular carcinoma and $0.97 \times 10^{-3}$ mm$^2$/s for metastases (Table 1).
<table>
<thead>
<tr>
<th>Focal hepatic lesions</th>
<th>Number of cases</th>
<th>Mean ADC value (x $10^{-3}$ mm$^2$/s)</th>
<th>Range of ADC values (x $10^{-3}$ mm$^2$/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic cyst</td>
<td>14</td>
<td>3.07</td>
<td>1.6 - 4</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>19</td>
<td>1.86</td>
<td>1.1 - 3.3</td>
</tr>
<tr>
<td>Benign hepatocellular lesion</td>
<td>7</td>
<td>1.71</td>
<td>1.5 - 2.2</td>
</tr>
<tr>
<td>HCC</td>
<td>9</td>
<td>0.98</td>
<td>0.2 - 1.5</td>
</tr>
<tr>
<td>Metastases</td>
<td>30</td>
<td>0.97</td>
<td>0.5 - 1.5</td>
</tr>
</tbody>
</table>

Table 1. Focal liver lesions with their ADC values.

ADC values of benign hepatic lesions ($2.25 \times 10^{-3}$ mm$^2$/s ± 0.81) were significantly higher than the malignant hepatic lesions (0.97 $\times 10^{-3}$ mm$^2$/ ± 0.30).

The ROC curve was generated to determine the cut off point for ADC value that best differentiated the malignant and benign liver lesions.

The cut off ADC value of $1.5 \times 10^{-3}$ mm$^2$/s was best able to differentiate malignant focal lesion from all benign lesions including hepatic cysts with accuracy of 96.5%, sensitivity of 87.5% and specificity of 92.5% (Fig. 1).
Fig. 1: ROC curve to determine the cut off point of ADC to discriminate malignant and benign liver SOL's including hepatic cysts: $1.5 \times 10^{-3}$mm$^2$/s with accuracy of 96.5% 

References: Basvatharkam Indo-American Cancer Hospital, Hyd/In.

When ROC curve was generated for only solid benign and malignant lesions (excluding hepatic cysts), the cut off ADC value was $1.4 \times 10^{-3}$mm$^2$/s with accuracy of 94.7%, sensitivity of 88.5% and specificity of 85% (Fig. 2).
Fig. 2: ROC curve to determine cut off point of ADC value to distinguish malignant and solid benign liver lesions: $1.4 \times 10^{-3}$mm$^2$/s with accuracy of 94.7%.

References: Basvatarkam Indo-American Cancer Institute Hyd, India

Cases:
Fig. 3: 60 year male with Hepato-cellular carcinoma: (a.) CECT arterial phase showed an enhancing mass in the liver with neovascularity and central necrosis. (b & c.) DWI at b0 and b800 revealed increase in signal intensity on increasing b value. (d.) Very low ADC value

References: basvatharkam Indo-American Cancer Hospital, Hyd/In.
Fig. 4: 62-year female with hepatic metastasis from carcinoma cervix: (a.) Well defined hyperintense SOL on T2WI in right lobe of liver. (b.) Restriction on DWI. (c.) low ADC value.

References: Basvatharkam Indo-American Cancer Hospital, Hyd/In.
Fig. 5: 55 year old female with liver hemangioma in known c/o carcinoma ovary: (a.) Intensely hyperintense lesion on T2WI. (b &c.) Persistence of hyperintense signal on increasing b value. (d.) High ADC value compared to surrounding liver parenchyma. (e.) Peripheral nodular enhancement in arterial phase of CECT, typical of hemangioma. 

References: Basvatharkam Indo-American Cancer Hospital, Hyd/In.
**Fig. 6**: 70 year old male with degenerating nodule in right lobe of liver in a known c/o rectosigmoid carcinoma: (a.) Mildly hypointense on T1WI compared to normal liver parenchyma. (b.) Hypointense on T2WI. (c.) Mild restriction on DWI. (d.) ADC value of 2.2 x 10^-3 mm²/sec. (e.) Metabolically inactive on PET-CT.

**References**: Basvatharkam Indo-American Cancer Hospital, Hyd/In.
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Fig. 2: ROC curve to determine cut off point of ADC value to distinguish malignant and solid benign liver lesions: 1.4 x 10^-3 mm²/s with accuracy of 94.7%.

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Conclusion

Diffusion-weighted imaging is a fast MR based sequence (single-shot EPI) which adds only 3 to 4 minutes to the entire examination and has proven very useful for the detection, further characterization and subsequent differentiation between benign and malignant lesions without the administration of contrast media, by quantifying diffusion effects via ADCs measurement.

This is even more useful in the setting when post Gadolinium-images can not be obtained due to poor renal function or history of allergy.

Since solid benign lesions are more difficult to differentiate from malignant liver lesions, the cut off value obtained with exclusion of hepatic cysts in the analysis should be utilized for differentiation.
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References