Value of diffusion weighted MR imaging assessment in differentiation of hemangiomas and metastases in liver

Poster No.: C-0057  
Congress: ECR 2010  
Type: Scientific Exhibit  
Topic: Abdominal Viscera (Solid Organs)  
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Keywords: DWI-MR, ADC, liver  
DOI: 10.1594/ecr2010/C-0057

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**Purpose**

Diagnostic value evaluation of Diffusion Weighted MR Imaging (DWI-MR) in differentiation of hemangiomas and metastases in liver. ADC value assessment of hemangiomas and metastases.

**Methods and Materials**

83 focal lesions in liver was analysed at 43 patients. 15 of 83 were hemangiomas, 68 of 83 metastases.

32/68 - large intestine cancer metastases, 10 (at 2 patients) - pancreas cancer, 9 (at 1 patient) - medullary carcinoma, 8 (at 2 patients) stomach cancer, 4 (at 1 patient) - kidney cancer, 2 (at 1 patient) - adrenal cancer, 2 (at 1 patient) FPI adenocarcinoma, 1 - breast cancer.

MR examinations were performed at the Radiodiagnostic Department for Maria Sklodowska - Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, using 1,5T scanner (Siemens Avanto) between June 2006 and December 2008.

Besides standard MR examination of liver DWI was performed with EPI-SE sequence using 5 or 6 mm slice thickness. Diffusion sequences were performed in three axial planes using at 4 b values. Maximum b value was 1000 and minimum was 0. ADC maps were automatically calculated using MR manufacturer program.

Final recognition of focal lesion type in liver was stated on the basis of:

1. Histopathological verification - 46 lesions
   - 43 metastases(large intestine -28, pancreas -10, FPI-2, adrenal-2, breast-1)
   - 3 hemangiomas

2. Observation lasting at least 18 months and results of examinations
   -15 lesions was recognized metastatic on the basis of criteria:

   Recognized neoplastic disease + progression of number and size of focuses in liver + increased level of neoplastic markers + clinical progression of disease
-10 lesions was recognized as metastatic on the basis of criteria:

Recognized neoplastic disease + high (SUV>2.5) 18FDG uptake in FDG PET examination + increased level of neoplastic markers + clinical progression of disease

-12 hemangiomas was recognized on the basis of criteria:

Stable picture in imaging examinations during at least 18 months without oncological treatment + proper level of neoplastic markers and in 5/12 lesions: negative result of 18FDG PET/CT examination.

Methods ROI determination:

1. In heterogenic lesions ROI was situated on ADC maps in the area of the lowest ADC value, except necrosis area and normal hepatic parenchyma.

2. In homogenic lesions ROI was including the whole field of lesion at its biggest section, without crossing the border of lesion.

2. ADC measurement of parenchyma of liver and spleen was performed in the area of propes IS in T2-weighted images with fat suppresion, ROI was bigger than 1 cm$^2$ and didn't include vessels.

Results

Fig.1: Histogram -ADC hemangiomas

Mean ADC of hemangiomas = $1,640 \times 10^{-3}$ mm$^2$/s (SD = $0,642 \times 10^{-3}$ mm$^2$/s).

Max ADC of hemangiomas = $3,379 \times 10^{-3}$ mm$^2$/s,

Min ADC of hemangiomas = $0,772 \times 10^{-3}$ mm$^2$/s

Median ADC of hemangiomas=$1,412 \times 10^{-3}$ mm$^2$/s

Fig.2: Histogram - ADC metastases

Mean ADC of metastases = $0,908 \times 10^{-3}$ mm$^2$/s (SD= $0,239\times 10^{-3}$ mm$^2$/s)
Max ADC of metastases = 1,914 x10^{-3} \text{mm}^2/\text{s},

Min ADC of metastases = 0, 573 x10^{-3} \text{mm}^2/\text{s}.

Median ADC of metastases = 0,874 x10^{-3} \text{mm}^2/\text{s}.

**Fig.3: mean ADC**

Mean ADC value for hemangiomas is statistically higher than for metastases (1,64 x10^{-3}\text{mm}^2/\text{s} vs 0,90x10^{-3}\text{mm}^2/\text{s}; p<0,0001).

**Fig.4:**

**ROC analysis for obtaining cut-off value of ADC for differentiation between hemangiomas and metastases**

Area under the ROC curve =0.92353

**Mean ADC value**

<table>
<thead>
<tr>
<th>Cut-off value</th>
<th>sensitivity</th>
<th>specificity</th>
<th>Cut-off value for ADC</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Similar benefit point</td>
<td>94,1%</td>
<td>86,7%</td>
<td>1,22 x10^{-3}\text{mm}^2/\text{s}</td>
<td>97%</td>
<td>76%</td>
</tr>
<tr>
<td>Optimal sensitivity and specificity</td>
<td>88%</td>
<td>87%</td>
<td>1,12 x10^{-3}\text{mm}^2/\text{s}</td>
<td>97%</td>
<td>62%</td>
</tr>
</tbody>
</table>
The most optimal ADC value differentiating hemangiomas from metastases in liver is $\text{ADC} = 1.22 \times 10^{-3} \text{mm}^2/\text{s}$, value $> 1.22 \times 10^{-3} \text{mm}^2/\text{s}$ - hemangiomas, $< 1.22 \times 10^{-3} \text{mm}^2/\text{s}$ - metastases. Taking this cut-off value into consideration 13 of 15 hemangiomas and 64 of 68 metastases were correctly qualified.

Fig.5: ROC analysis for obtaining cut-off value of ADC normalised to normal appearing liver

Area under the ROC curve $= 0.92353$

ADC ratio normalised to normal appearing liver

<table>
<thead>
<tr>
<th>Cut-off value</th>
<th>sensitivity</th>
<th>specificity</th>
<th>Cut-off value for ADC</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Similar benefit point</td>
<td>90%</td>
<td>86.7%</td>
<td>1.09</td>
<td>97%</td>
<td>65%</td>
</tr>
<tr>
<td>Optimal sensitivity and specificity</td>
<td>87%</td>
<td>87%</td>
<td>1.05</td>
<td>97%</td>
<td>59%</td>
</tr>
</tbody>
</table>
Optimal sensitivity 97% 50% 1.31 90% 80%

Optimal specificity 50% 93% 0.83 97% 29%

The most optimal normalised to normal appearing liver ADC ratio differentiating hemangiomas from metastases in liver is \(1.09 \times 10^{-3}\text{mm}^2/\text{s}\) (sensitivity 90% specificity 87%, high PPV 97% and quite low NPV 65%). If normalised ADC \(\leq 1.09 \times 10^{-3}\text{mm}^2/\text{s}\) the lesion with high probability is metastasis.

### ADC ratio normalised to normal appearing spleen

<table>
<thead>
<tr>
<th>Cut-off value</th>
<th>sensitivity</th>
<th>specificity</th>
<th>Cutoff value for ADC</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Similar benefit point</td>
<td>90%</td>
<td>66.7%</td>
<td>1.44</td>
<td>92%</td>
<td>63%</td>
</tr>
</tbody>
</table>

| Optimal sensitivity and specificity | 73% | 73% | 1.25 | 92% | 38% |

| Optimal sensitivity | 90% | 50% | 1.50 | 90% | 67% |

| Optimal specificity | 50% | 87% | 1.06 | 94% | 28% |

The most optimal normalised to normal appearing spleen ADC ratio differentiating hemangiomas from metastases in liver is \(1.27 \times 10^{-3}\text{mm}^2/\text{s}\) (sensitivity 90% specificity 67%, PPV 92% and NPV 63%).

Normalization to spleen parenchyma is less effective than normalization to liver. Area under the ROC curve for spleen is \(= 0.81\) and for liver is 0.92.
Fig. 6: 55 year-old woman with hepatic hemangioma a-fat suppressed T2 #.

Fig. 7: 50 year-old woman with hepatic metastasis a- lesion is hyperintense on ...

Images for this section:
Fig. 1: Histogram - ADC hemangiomas
Fig. 2: Histogram - ADC metastases
**Fig. 3:** mean ADC
**Fig. 4:** ROC analysis for obtaining cut-off value of ADC for differentiation between hemangiomas and metastases
Fig. 5: ROC analysis for obtaining cut-off value of ADC normalised to normal appearing liver
**Fig. 6:** 55 year-old woman with hepatic hemangioma. 
- a-fat suppressed T2-weighted shows high signal of hemangioma.
- b-ADC maps of hemangioma is $1.44 \times 10^{-3}$ mm$^2$/s (ROI was drawn covering entire lesion).
- c-diffusion weighted MR image obtained with a $b$ max of 1000 s/mm$^2$ shows high signal of hemangioma.

**Fig. 7:** 50 year-old woman with hepatic metastasis. 
- a- lesion is hyperintense on fat suppressed T2-weighted.
- b-ADC maps of metastasis is $0.75 \times 10^{-3}$ mm$^2$/s (ROI was drawn covering peripheral part of lesion).
- c-diffusion weighted MR image obtained with a $b$ max of 1000 s/mm$^2$ shows high signal of metastasis.
Conclusion

Differential diagnosis (Ddx) of focal liver lesions is still being difficult. One of the common problem is to differentiate atypical hemangiomas from metastases. Diffusion weighted MR imaging (DWI) has been considered recently as helpful, non-invasive method in differentation between these two entities.

DWI provides image contrast that depends on the molecular motion of water in extracellular and intravessel compartment. The shape and spread of extracellular compartment depend on cellularity and its relationship therefore it shows indirectly microenvironment.

Provided that inner structure of hemangiomas and metastases is quite different, parameters obtained in DWI might be helpful in Ddx. When measuring molecular motion with DWI, the apparent diffusion coefficient (ADC) can be calculated. ADC is quantitative parameter accomplished by obtaining at least two image sets, one with a very low b value and one with higher (1, 2, 3, 13, 14, 15, 16).

Comparison between ADC values reported by different authors is difficult because of methodology, for instance region of interest (ROI) placement or bmax value usage for calculation of ADC maps. It is recomended to always report bmax value. Structure of the lesion is also important. Most of the lesions are heterogenous, contain necrosis, hemosiderin, thrombosis or sclerosis.

Our results show that mean ADC value for hemangiomas is statistically higher than for metastases (1,64 x10^{-3} mm^2/s vs 0,90x10^{-3}mm^2/s; p<0,0001). Vossen et al. (5) also reported statistically different values (haemangiomas 2,29x10^{-3} mm^2/s vs metastases 1,43x10^{-3} mm^2/s).

Our results might be different from these reported by Vossen et al. because of bmax used for ADC calculation and ROI placement. We placed ROI in solid part of the lesion except necrosis and measured minimal value ADC, whereas Vossen et al. measured mean ADC in the whole lesion. Quite similar with our results for haemangiomas obtained Goshim et al. (4) 1,86 x10^{-3} mm^2/s and 1,71x10^{-3} mm^2/s. Bruegel et al. (7)1,92 x10^{-3}mm^2/s and Parikh et al. (10) 2,04 x10^{-3} mm^2/s reported higher values.

We obtained 0,90x10^{-3}mm^2/s mean ADC value for metastases which is comparable to results of Taouli et al. (8) 0,94 x10^{-3}mm^2/s, Gourtsoyianni et al. (6) 0,99x01-3mm2/s, , and Kim et al. (9) 1,06 x10^{-3}mm^2/s. Bruegel et al. (7) 1,22 x10^{-3}mm^2/s and Parikh et al. (10). 1,50 x10^{-3}mm^2/s showed higher results.
The most comparable to our results obtained Gourtsoyianni et al. who placed ROI's within the lesion in the same way and obtained ADC maps with bmax=1000 like we did. Gourtsoyianni et al. presented 0.99 x10^{-3} \text{mm}^2/\text{s} for metastases and slightly higher 1.9 x10^{-3} \text{mm}^2/\text{s} for hemangiomas, which might be result of small amount of hemangiomas included to analysis.

We found optimal cut-off value, by means of ROC analysis, for differentiation between hemangiomas and metastases as mean ADC=1.22 x10^{-3} \text{mm}^2/\text{s} (sensitivity 94%, specificity 87%, PPV 97%, NPV 76%). Quite similar cut-off value obtained Gourtsoyianni et al. ADC =1.26 x10^{-3} \text{mm}^2/\text{s} with sensitivity and specificity 100%.

Whereas Vossen et al. the best quality obtained for ADC= 2.3 x10^{-3} \text{mm}^2/\text{s} (sensitivity 55% and specificity 100%, PPV 100%, NPV 89%).

Lack of publication considered ADC ratio normalised to a normal appearing liver or spleen exist. We found that cut-off value for mean ADC is similar to cut-off value for ADC ratio normalised to normal appearing liver in differentiation between hemangiomas and metastases and equals 0.923x10^{-3} \text{mm}^2/\text{s}

Diffusion weighted MR imaging (DWI) is effective method in differentiation between hemangiomas and metastases.

References


