Comparison of diagnostic efficacy of CE-MDCT and dynamic MRI after i.v. administration of hepatotropic contrast agent in detection and evaluation of focal liver lesions.

Poster No.: C-2303
Congress: ECR 2013
Type: Educational Exhibit
Authors: K. Markiet, E. Szurowska, T. Nowicki, E. Izycka-Swieszewska, P. Naumczyk, K. Gwozdziewicz, D. Zadrozny; Gdansk/PL
Keywords: Efficacy studies, MR, CT, Liver, Abdomen, Metastases
DOI: 10.1594/ecr2013/C-2303
Learning objectives

A growing attention to dynamic nuclear resonance imaging with intravenous administration of hepatobiliary contrast media in differentiation and characterization of focal liver lesions (FLLs) is recently observed. Hepatobiliary phase allows differentiation of FLLs consisting of healthy hepatocytes from those deprived of them.

Our main objective is to illustrate enhancement patterns of most commonly encountered focal liver lesions (FLLs) in multi-detector computed tomography (MDCT) after intravenous administration of iodine contrast media (CM) versus dynamic magnetic resonance imaging (MRI) with i.v. administration of hepatobiliary CM.

We would also like to shortly compare the efficacy of contrast enhanced MDCT and magnetic resonance imaging (MRI) with hepatotropic CM in differentiation of FLLs, outline the role of dynamic magnetic resonance imaging after i.v. administration of hepatotropic contrast media in differential algorithm of FLLs and stress the impact of clinical data on the diagnostic effectiveness of FLLs.
Background

Clinical manifestations, laboratory results, tumor markers and ultrasound (US) findings often show limited value in detection and differentiation of FLLs. Therefore, MDCT and MRI are required in order to establish the correct diagnosis. Despite the rapid development in MDCT technique, a great attention is payed to MRI, especially with i.v. administration of organ-specific CM. Hepatocyte-specific contrast agents combine the properties of extracellular gadolinium chelates that allow hepatic arterial and portal venous phase imaging with delayed hepatocyte uptake and partial excretion into the biliary system. Therefore, we can observe an increase in the signal intensity of the liver, bile ducts and some hepatocyte-containing lesions at T1-weighted imaging. Two gadolinium-based hepatocyte-specific contrast agents are commercially available at the moment: gadoxetic acid (Eovist - U.S.A, Primovist - elsewhere worldwide; Bayer Schering Pharma, Germany) and gadobenate-dimeglumine (MultiHance; Bracco, Italy). The protocol of the examination should be adjusted accordingly to the contrast agent of use - hepatobiliary phase images are acquired approx. 20-40 minutes after gadoxetic acid injection and approx. 1-2 hours after gadobenate-dimeglumine injection.

The majority of FLLs in non-cirrhotic livers are benign, and the most common solid ones are: hemangiomas, focal nodular hyperplasias and adenomas.

The most frequently encountered malignant lesions in noncirrhotic livers are metastases. Hepatocellular carcinoma and intrahepatic cholangiocarcinoma usually occur in due course of chronic liver disease.
Imaging findings OR Procedure details

We retrospectively analyzed 177 Patients (94 female Patients, 89 male Patients), mean age 63yo, with equivocal FLLs revealed in greyscale ultrasound, who underwent CE-MDCT and subsequently dynamic MRI with i.v. application of liver-specific CM (gadobenate dimeglumine, Gd-BOPTA) within three weeks from initial examination.

After intravenous administration of CM arterial (HAP), venous-portal (PVP), equilibrium (EP) phases in both CT and MR and additionally, a hepatobiliary phase (HBP) in MR were obtained.

MR study was performed with 1.5 T MR system using phased-array flex coil. The protocol included: T1-weighted SE sequence (TR/TE ms - 303/12, scan time 17sec) in axial and coronal planes, with and without contrast enhancement in EP and HBP, T2-weighted axial Express sequence (18000/92, scan time 17sec), T2-weighted coronal FSE sequence (6500/116.8, scan time 20sec), also with fat saturation and T1-weighted out of phase sequence (150/2.24, flip angle of 90°, scan time 12sec) without and after contrast administration in HAP, PVP, EP and HBP. Slice thickness was 5mm, with intersection gap of 0.5, matrix 256 × 256. Dynamic MRI was obtained immediately after a bolus injection of gadobenate-dimeglumine (Gd-BOPTA, 0.1 mmol per kilogram of body weight), followed by saline flush of 25mL through a 20G venous catheter in the antecubital vein. HAP, PVP, and EP were performed with a delay time of 25, 60 and 180 seconds respectively; HBP was acquired 60min after contrast agent (Gd-BOPTA) administration. The phase-encoding direction was anterior-posterior for all sequences. All images were acquired during breath-hold.

Multi-phase multi-detector (6 and 32-row) CT examination of the liver has been conducted first unenhanced, then after application of a iodine contrast agent in HAP, PVP and EP. We administrated 100ml of iodinated contrast agent at a flow rate of 4mL/sec through an 20G venous catheter positioned in an antecubital vein using a power injector. The CT section thickness was 2.5mm, image interval - 2.5mm and pitch - 1.0.

Inclusion criteria: presence of a FLL that did not present typical features consisting with a simple cyst (anechoic focus with posterior acoustic enhancement) or a hemangioma (hyperechoic, round or oval, homogeneous or slightly inhomogeneous echotexture, well-defined margins and posterior wall shadowing) in greyscale US. The atypical hemangiomas included in the study were characterized by at least partial hypoechoic (to total hypoechoic) pattern in US.
Exclusion criteria included any contraindications to MDCT or NMR examination, amongst them contraindications to iodine contrast agents or Gd-BOPTA administration and lack of Patient's consent.

Final diagnosis was based on the result of the histopathological examination and on grounds of clinical and imaging follow-up in case of benign lesions in Patients, who had not been operated on and in Patients with metastatic hepatic lesions treated with chemotherapy.

Examinations were evaluated by three independent radiologists with at least 5-year experience in abdominal imaging, first with no prior knowledge of clinical data, then supported with clinical insight. The number, size and enhancement pattern of lesions were analyzed. The differentiation of FLLs was based on the enhancement pattern in CE-MDCT and CE-MRI with inclusion of HBP.

Study was approved by Independent Bioethic Committee for Scientific Research of Medical University of Gdansk. All patients gave their written consent to participate.

High interobserver agreement (kappa values of 0.66 - 0.80) confirmed the methodology as reliable and reproducible.

Amongst all analyzed FLLs - the total number of 404, we have found and confirmed: 149 metastatic lesions, 99 haemangiomas (HHs), 96 hepatocellular carcinomas (HCCs), 44 lesions consistent with focal nodular hyperplasia (FNH) and 16 other FLLs (including 4 adenomas and 5 cholangiocarcinomas) - Table 1.

Typical enhancement patterns for the most frequently encountered focal liver lesions are as follows:

**Haemangioma (Fig. 1, Fig. 2)**

Hepatic hemangiomas (HHs) are the most common solid benign focal liver lesions with the incidence of 2% - 20%. It is estimated that about 40% of hemangiomas are of atypical appearance in US.

NE-CT (non-enhanced CT):

- small (less than 2 cm in diameter) and typical HHs (2-10cm) - well-circumscribed, ovoid or spherical mass isodense to blood
- giant HH (more than 10 cm in diameter) - heterogenous, hypodense mass, central low-density scar or calcifications (approx. 10% of cases) may be present
CE-CT (contrast-enhanced CT):

- HAP: early peripheral, nodular or globular interrupted enhancement
- PVP: progressive centripetal filling to uniform filling
- EP: persistent complete filling
- in case of giant HHs an incomplete centripetal filling in PVP and EP may be observed (the scar if present, it does not enhance)
- in case of atypical HHs an "inside to outside" pattern may be observed with no significant enhancement in HAP and gradual centrifugal filling in PVP

Dynamic MRI:

- T1WI: hypointense or isointense to blood
- T2WI and heavily T2WI: hyperintense
- central scar if present is of decreased signal intensity
- CE-MRI (T1WI +CM)
  - small HH: homogeneous enhancement in HAP and PVP; flash-filling may be present in arterial phase
  - typical and giant HH: HAP - peripheral nodular, interrupted enhancement, PVP - progressive centripetal filling; isointense to blood; central scar if present: no enhancement, remains hypointense
  - HBP: hypointense

Focal Nodular Hyperplasia (Fig. 3, Fig. 4)

Focal nodular hyperplasia (FNH) comprises 8% of all primary liver tumors. It is common in asymptomatic patients, consists of nonneoplastic hepatocytes in a disorganized array surrounding a central scar with anomalous vessels.

NE-CT:

- iso- or hypodense to adjacent liver parenchyma

CE-CT:

- HAP: intense, usually homogeneous, transient enhancement
- PVP: iso- or hypodense to liver parenchyma
- EP: isodense to adjacent liver parenchyma
- central scar visible in approx. 2/3 of large and 1/3 of small FHNs is hyperdense in delayed scanses

Dynamic MRI:

- T1WI: iso- or hipointense; hypointense central scar
- T2WI: iso- to hyperintense; hyperintense central scar
- CE-MRI
Adenoma (Fig. 5)

Hepatocellular adenoma (HCA) is a rare, usually encapsulated benign liver tumor, consisting of proliferating hepatocytes, linked to exogenous hormone exposure.

NE-CT:
- iso- or hypodense (if containing lipids)
- calcifications or signs of hemorrhage may be present
- well-defined

CE-CT:
- HAP: heterogeneous, hyperdense enhancement
- PVP: hypo-, iso-, hyperdense to liver parenchyma
- EP: enhancement does not persist, hypodense

Dynamic MRI:
- T1WI:
  - heterogeneous signal intensity
  - increased signal due to fat and recent hemorrhage
  - decreased signal in case of necrosis, calcifications and old hemorrhage
  - fibrous pseudocapsule (rim): hypointense
- T2WI:
  - increased signal intensity: necrosis, old hemorrhage
  - decreased signal: fat, recent hemorrhage
  - fibrous pseudocapsule (rim): hypointense
- CE-MRI:
  - HAP: heterogeneous enhancement
  - PVP: slightly hyperintense; rim - of higher signal intensity to liver parenchyma and adenoma itself
  - HBP: hypointense (no substantial uptake or retention of hepatobiliary CM)

Hepatocellular Carcinoma (Fig. 6, Fig. 7)
Hepatocellular carcinoma (HCC) is the fifth most common malignant neoplasm in the world and there is a tendency of frequency increase being observed. It may occur as a single tumor (50-60%), as multiple lesions (40%) and as a diffuse lesion (less than 10%). Almost exclusively it is encountered in the setting of chronic liver disease.

NE-CT:

- in cirrhotic liver: hypodense to liver (regenerative nodules may be hyperdense)
- in noncirrhotic liver:
  - solitary mass: hypodense, rounded, well-defined
  - multifocal: multiple hypodense lesions
  - may be encapsulated
  - may include signs of degenerative changes, such as areas of necrosis

CE-CT:

- HAP: heterogeneous hypervascular enhancement
- PVP: isodense or early washout of CM
- EP: washout of contrast medium to hypodense

Dynamic MRI:

- heterogenous signal intensity depending of degree of lipid inclusion, fibrosis or necrosis
- T1WI: hypo-, iso- or hyperintense; hyperintense areas of fat or hemorrhage
- T2WI: hyperintense; "nodule within nodule" pattern may sometimes be observed - small focus of high signal intensity within a hypointense dysplastic nodule
- HAP: heterogeneous hyperintense enhancement
- PVP, EP: washout of CM
- delayed enhancing of pseudocapsule may be present (approx. 50% of cases)
- HBP: usually hipointense

Fibrolamellar carcinoma (Fig. 8)

Fibrolamellar carcinoma (FLC) is a primary liver tumor, originating from hepatic cell, which usually occurs in young patients. FLC frequently develops in previously unchanged liver, with the prevalence to the left lobe. No correlation with viral inflammation or cirrhosis has been found. In ultrasound examinations it is often faulty recognized as a hemangioma, in CT as FNH.
NE-CT:

- hypodense mass, well-defined, polycyclic outline; central scar and septa may be seen, as well as calcifications and areas of necrosis (more than 50%)

CE-CT:

- HAP: heterogeneous, hyperdense
- PVP: hypo- to isodense
- EP: mass - isodense, scar and septa - hyperdense

Dynamic MRI:

- T1WI: heterogeneous, hypointense; scar and septa - hypointense
- T2WI: heterogeneous, hyperintense; scar and septa - hypointense
- HAP and PVP: strong, heterogeneous enhancement with the exclusion of the scar
- HBP: lower signal intensity in comparison to adjacent liver parenchyma

**Cholangiocarcinoma**

Cholangiocarcinoma (ICC) represent 10% of primary hepatic malignant tumours. ICC tends to arise in the background of chronic liver disease.

NE-CT:

- large, heterogeneous mass of lower density

CE-CT:

- HAP: rim-like peripheral enhancement
- PVP: slight enhancement

Dynamic MRI:

- T1WI: irregular, hypointense mass
- T2WI: heterogeneous, hyperintense mass; a hypointense scar may be visible (reflecting central fibrosis)
- HAP: early rim enhancement, usually continuous; the rim of arterial enhancement may show a peripheral washout in further phases
- PVP: progressive centripetal heterogeneous enhancement
- HBP:
  - capsular retraction, peripheral biliary dilatation and satellite nodules may be observed
  - HBP: delayed contrast material uptake
Metastases (Fig. 9, Fig. 10)

Liver is the most frequent site of development of metastases among parenchymal organs due to its dual blood supply from hepatic artery and portal vein and the presence of humoral factors influencing the cell growth. In 90% metastases are multiple foci. However, in 30% of patients with known neoplastic disease foci observed in the liver may be of benign character.

The most common primary site in case of liver metastases is the gastrointestinal tract and approximately 90% of those metastases are hypovascular lesions.

Hypervascular metastases derive from neuroendocrine tumors, RCC, sarcomas, GIST, choriocarcinomas, thyroid carcinomas and melanomas.

NE-CT:

- hypo-, iso or hyperdense (melanin, hemorrhage, calcifications)

CE-CT:

- hypovascular metastases: hypodense with peripheral rim enhancement
- hypervascular metastases:
  - late HAP: hyperdense
  - PVP, EP: hypo- to isodense

Dynamic MRI:

- T1WI: hypointense or hiperintense (if containing melanin)
- T2WI: hyper - to isointense
- hypovascular metastases: hypointense with peripheral rim enhancement
- hypervascular metastases: HAP - hyperintense enhancement, PVP - washout
- HBP: hypointense
**Images for this section:**

<table>
<thead>
<tr>
<th>Final diagnosis</th>
<th>Number of foci</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastases</td>
<td>149</td>
</tr>
<tr>
<td>Haemangiomas (HHs)</td>
<td>99</td>
</tr>
<tr>
<td>Hepatocellular carcinomas (HCCs)</td>
<td>96</td>
</tr>
<tr>
<td>Focal nodular hyperplasia (FNH)</td>
<td>44</td>
</tr>
<tr>
<td>Other FLLs:</td>
<td></td>
</tr>
<tr>
<td>Adenomas</td>
<td>4</td>
</tr>
<tr>
<td>Cholangiocarcinomas (CCCs)</td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
</tr>
</tbody>
</table>

**Table 1:** The number and type of focal liver lesions found and confirmed in Patients included in the study.

© II Department of Radiology, Medical University of Gdansk - Gdansk/PL
**Fig. 1:** Small hemangioma, 6th segment of the liver, CT. a. A non-enhanced image shows a hypodense lesion. b. Typical nodular, peripheral interrupted enhancement is seen in HAP. c. Progressive centripetal filling of the lesion is observed in PVP. d. The lesion is almost homogeneously enhanced in EP. In each of the phases hemangioma is isodense to vessels.

© II Department of Radiology, Medical University of Gdansk - Gdansk/PL

![Image of CT scan of a small hemangioma](image1)

**Fig. 2:** Large cavernous hemangioma (segment 6th), MRI. a. Out-of-phase T1-weighted image presents a large, hypointense lesion. b. T2-weighted image shows marked hyperintensity - a typical radiological feature of hemangioma. c. Globular, peripheral enhancement in PVP. d. Out-of-phase T1-weighted image shows a weaker enhancement of the lesion in comparison to the adjacent liver parenchyma in HBP.

© Szurowska E et al. MR imaging including hepatocyte-specific contrast enhanced MR study and diffusion-weighted sequence in characterisation of hypervascular liver tumors: A pictorial essay. EPOS ECR 2010
Fig. 3: Focal nodular hyperplasia, CT. a. The lesion is isodense to the adjacent liver parenchyma in a non-enhanced image. b. Lesion shows marked hyperdensity in HAP; the central scar is visible. c. PVP - lesion is hyperdense; central scar is clearly visible. d. Higher density of the lesion is seen in EP.

© II Department of Radiology, Medical University of Gdansk - Gdansk/PL
**Fig. 4:** Focal nodular hyperplasia, MR - the same case as in Fig. 3. a. T1-weighted image shows an isointense lesion in the 4th segment. b. Marked enhancement of the lesion in HAP; a non-enhancing central scar is visible. c. Lesion shows higher signal intensity in comparison to adjacent liver parenchyma in PVP. d. T1-weighted image with fat saturation shows hyperintensity of the lesion in HBP.
Fig. 5: Two cases of hepatocellular adenomas. a. Axial CT image in HAP shows a strong, slightly heterogeneous enhancement of the lesion within the left lobe of the liver. b. The same lesion as a. - CT image in PVP shows a lesser enhancement - the lesion is heterogeneous, iso- to hypodense. c. Out-of-phase T1-weighted MRI image presents strong homogenous enhancement of the second lesion in HAP. d. The same lesion as c. - HBP shows higher peripheral enhancement of lesion with hypointense central area (MRI).

© Szurowska E et al. MR imaging including hepatocyte-specific contrast enhanced MR study and diffusion-weighted sequence in characterisation of hypervascular liver tumors: A pictorial essay. EPOS ECR 2010
Fig. 6: Hepatocellular carcinoma, CT. a. A non-enhanced image shows a large, hypodense lesion. b. Heterogenous enhancement is observed in HAP. c. Lesion is heterogeneously enhancing in PVP, areas of necrosis are visible as well as signs of malperfusion in the surrounding liver parenchyma. d. A washout of the CM is seen in EP.

© II Department of Radiology, Medical University of Gdansk - Gdansk/PL
Fig. 7: Hepatocellular carcinoma, 8th segment of the liver, under the dome of the diaphragm, MR. a. Strong, heterogenous enhancement of the lesion in HAP. b. HBP shows a focus of lower signal than the remaining liver parenchyma.

© Szurowska E et al. MR imaging including hepatocyte-specific contrast enhanced MR study and diffusion-weighted sequence in characterisation of hypervascular liver tumors: A pictorial essay. EPOS ECR 2010
Fig. 8: Fibrolammelar carcinoma in segment 3 of the left lobe of the liver; MRI. a. T1-weighted image presents heterogenous, hypointense lesion. b. Heterogenous enhancement in HAP; large central scar is seen. c. Lesion is heterogenous in PVP. d. HBP (sequence with fat-saturation) shows a large heterogenous mass.

Fig. 9: Multiple hepatic metastatic foci, CT. a. Lesions show low density in a non-enhanced scan. b. Slight, peripheral, rim-like enhancement in HAP. c. and d. Lesions remain hypodense to adjacent liver parenchyma in both PVP and EP.

© II Department of Radiology, Medical University of Gdansk - Gdansk/PL
Fig. 10: Large metastatic focus with satellite nodules - coronal T1-weighted image in HBP shows marked hypointensity of observed lesions.

© II Department of Radiology, Medical University of Gdansk - Gdansk/PL
Conclusion

From the introduction of gadolinium-based hepatocyte-specific contrast media, their use in MR imaging of FLLs has become vital. A familiarity with typical and atypical appearances of both benign and malignant FLLs in dynamic CE-MR examination with the use of hepatobilary CM is required to achieve optimal diagnostic accuracy.

HBP is of significant value in detection and differentiation of small FNH (especially with no visible central scar) and metastatic disease. A focus may correspond to FNH when it is not presenting hypointensity in HBP. The only limitation of this method are foci of HCC characteristics with high grade cell differentiation, but they are rare in patients with no clinical history of liver cirrhosis or chronic liver inflammation type B or C, hemochromatosis or autoimmune liver disease, what makes clinical information such a valuable tool.

Weak contrast medium uptake by adenomas is seen in HBP, nevertheless lesions still remains of lower signal intensity in comparison to adjacent liver parenchyma (due to the lack of bile ducts). Lower enhancement of adenomasa in hepatocyte selective phase is a differentiating factor between adenoma and FNH.

Metastatic disease presents as hypointense foci in HBP. The hepatocyte phase alone does not allow certain differentiation of metastases, hemangiomas and low grade HCCs, as they all show as hypointense foci, however, hypointensity of FLL in hepatocyte-selective phase (with the exception of hemangiomas) is a criterion suggesting malignancy.

In case of HCC, arterial enhancement, although nonspecific, is an essential diagnostic feature, followed by the presence of washout and delayed enhancement of the pseudocapsule.

Hepatocyte selective phase is of no application in differentiating hemangiomas from other focal liver lesions.

In conclusion, the patterns of contrast enhancement provide well-described criteria for detection and characterization of FLL. MRI is a highly specific and accurate modality for FLLs detection and given the lack of ionizing radiation it becomes a modality of choice in FLLs characterization, demonstrating similar if not superior performance to CT, as proven also in our results. It needs to be stressed that in our experience the awareness of clinical information significantly increases specificity and diagnostic accuracy, especially in case of HCC and FNH, in both CT and MR examinations. The pharmacokinetics of hepatobiliary contrast media provide extended opportunities for FLLs assessment.
References