ACTUAL RADIODIAGNOSIS TECHNOLOGIES OF HEPATIC CANCER

UDC 616.36–006.6–073.75
Received 10.04.2012

© **I.S. Cheremisinova,** Head of Radiology Department[1];
B.E. Shakhov, D.Med.Sc., Professor, Head of the Department of Radiodiagnosis, the Faculty of Doctors' Advanced Training, Rector[2]

[1]Kirov Regional War Veterans Hospital, Karl Marx St., 113, Kirov, Russian Federation, 610027;
[2]Nizhny Novgorod State Medical Academy, Minin and Pozharsky Square, 10/1, Nizhny Novgorod, Russian Federation, 603005

The aim of the investigation was to study the possibilities of computer tomography with intravenous contrast and multiphase scanning and magnetic resonance tomography using hepatospecific contrast substance — gadoxetic acid — in hepatic cancer diagnostics.

Materials and Methods. Within the period of 2008–2011 on the basis of Kirov Regional War Veterans Hospital and Kirov Regional Clinical Hospital there was carried out the complete clinical and radiological examination of 60 patients with hepatic cancer. Primary liver tumors were diagnosed in 23 patients. Metastatic tumors were revealed in 37 patients.

Abdominal multispiral computed tomography (CT) was performed in 45 patients (75%). 31 patients (52%) underwent magnetic resonance tomography (MRT) of abdominal and retroperitoneal organs.

Conclusion. Actual CT and MRT technologies with intravenous contrast and multiphase scanning are high-quality and informative in topical and differential diagnosis of liver tumors. The application of hepatospecific contrast substance — gadoxetic acid — expands MRT opportunities in detection and recognition of small (less than 1 cm) liver metastases.

Differential radiodiagnosis of focal liver lesions (using CT and MRT) should be based on multicentre study of morphological structure, the character of lesion vascularity, and their dynamic and organ-specific (in MRT — in hepatocyte phase) contrast.

Key words: hepatic cancer; computer tomography (CT); magnetic resonance tomography (MRT); gadoxetic acid.

In Russia hepatocellular carcinoma (HCC) ranks eighth among all malignancies [1]. When detected, most patients (52%) with liver cancer are considered inoperable [2]. Liver is most frequently involved in metastasis of tumors of various localizations: according to autopsy findings, 36% of oncologic patients have metastases in liver [1–4].

The treatment results to a large extent depend on early detection and precise diagnosis of liver cancer, correct assessment of intact parenchyma condition. Despite rampant development of high tech imaging methods, it is difficult to detect small-sized tumors, especially if there are diffuse hepatic changes [5, 6]. There are reports on difficulties of differential radiodiagnosis of focal hepatic lesions [1, 2, 5, 6].

The aim of the investigation was to study the possibilities of computer tomography with intravenous contrast and multiphase scanning and magnetic resonance tomography using hepatospecific contrast substance — gadoxetic acid — in hepatic cancer diagnostics.

Materials and Methods. Within the period of 2008–2011 on the basis of Kirov Regional War Veterans Hospital and Kirov Regional Clinical Hospital there was carried out the complete clinical and radiological examination of 60 patients with hepatic cancer, among them 28 female (47%) and 32 male (53%). Mean age of patients was 52.6±3.9 years (from 38 to 71 years). Primary liver tumors were diagnosed in 23 patients including 19 patients with HCC, and 4 patients with cholangiocellular carcinoma. Metastatic tumors were revealed in 37 patients. Primary tumor were localized in large intestine — in 15 patients (40%), in pancreas — in 5 (14%), in stomach — in 3 (8%), in breast — in 4 (11%), in lungs — in 3 (8%), in other organs (kidneys, thyroid, ovaries) — in 7 (19%) patients.

Abdominal multispiral computed tomography (CT) was performed in 45 patients (75%) on "Asteion Super-4" (Toshiba, Japan). Intravenous contrast by iohexol (Omnopaque) — 350 mg of iodine/ml, iopromide (Ultravist) — 370 mg of iodine/ml and multiphase scanning were used in 39 patients (65%).

31 patients (52%) underwent magnetic resonance tomography (MRT) of abdominal and retroperitoneal organs on "Gyroscan T 5-II" (Philips, Netherlands) with superconducting magnet with magnetic field intensity of 0.5 T. 25 patients underwent contrast MRT. Gadodiamide (Omniscan) was used in 11 patients, gadoxetic acid (Primovist), organotropic preparation, was used in 14 patients. The investigation included survey scanning, reconstruction of axial and front sections with T1- and T2-weighted images, as well as the examination in atypical, oblique planes along hepatic, portal veins and inferior vena cava. Magnetic resonance cholangiopancreatography was performed in 7 patients (12%).

All CT- and MRT-investigations were carried out according to standard techniques [5, 6]. The analysis of the obtained data enabled to assess hepatic anatomic features, characterize lesions and determine their localization and

For contacts: Cheremisinova Irina Sergeevna, tel. +7 912-728-55-32; e-mail: irina.cheremisinova@gmail.com

relationship with porta hepatic and vascular secretory structures. We estimated the condition of intact parenchyma and the intensity of compensatory hypertrophy. There were observed the changes in lower lungs, diaphragm, abdominal and retroperitoneal organs, enlargement of lymph nodes, and ascites.

Results and Discussion. Clinical symptoms of hepatic tumors were various, low-specific, and caused by hepatic lesions, extrahepatic extension of pathological process, and the presence of complications.

According to CT and MRT, HCC in 74% of cases, and cholangiocellular carcinoma — in 25% of cases were associated with diffuse hepatic changes. The signs and hepatic cirrhosis revealed by radiology were torous contour of the liver, the enlargement of the left caval lobe and hepatic segment I, reduction of hepatic segments VI and VII, the organ heterogeneous structure, reduced density of liver parenchyma on CT. Splenomegaly with venous dilatation around the spleen and stomach was the most common (67%) sign among other symptoms of portal hypertension.

HCC development against the background of liver cirrhosis is a multistep process [6, 7]. Most commonly the following evolution is observed: regeneration nodes — low atypical dysplastic nodes — high atypical dysplastic nodes with cancer foci — small HCC and large HCC. Tumor progression in affected nodes leads to blood supply changes: arterializations of blood flow and neoangiogenesis. Regeneration and dysplastic nodes mainly have portal blood supply, while HCC lesions — predominantly arterial blood supply [7, 8]. We considered HCC development possible in intense contrast of dysplastic node in arterial phase. HCC characteristic contrast type was intense non-uniform trap of contrast substance in arterial phase with its following “outwashing” in portal and delayed phases. The results of our survey corresponded to diagnostic criteria of American Association for the Study of Liver Disease (AASLD), 2010 [8] and contributed to early HCC detection in patients with hepatic cirrhosis. The characteristics of HCC with no preceded hepatic cirrhosis were acute clinical manifestations of the disease, high level of oncomarkers in blood serum.

The sizes of lesions in HCC varied from 27 to 96 mm. In 12 cases (63%) the lesions of the right anatomic part of the liver were observed. In most cases (52%) large HCC mass was visualized on CT and MRT, when the tumor was determined as a solitary node in the liver. In nodular cancer type (32% of cases) a tumor consisted of nodular conglomerate. Moreover, we revealed disseminated areas in adjacent hepatic sections in 2 patients, and metastases in other anatomic part of the liver — in 1 patient. 16% of cases had diffuse tumors with no well-defined boundaries on CT and MRT. HCC was characterized by indistinct irregular contours of the lesion, and heterogeneous structure in 16 patients (84%).

HCC heterogeneous structure was due to the presence of intra-tumor septa, small hemorrhages, areas of adipose degeneration, necrotic foci. CT revealed calcified lesions in tumors in 2 cases (10%). Pseudocapsule around the tumor was revealed in 6 patients (32%) with HCC masses. Invasion of vascular secretory structures was characteristic of large tumors, over 5 cm in size. CT and MR imaging revealed intrahepatic metastases in 3 patients, metastases in lymph nodes of hepatoduodenal junction in 6 patients. Distant metastases in adrenals and the lungs were found in 3 patients.

Cholangiocellular carcinoma on CT and MRT was visualized as nodular and periductal infiltrative tumor. Tumor contours were indistinct on native tomograms, and after contrast became well-defined, irregular. In all patients cholangiocellular carcinoma was characterized by significant fibrous components and was hypovascular. After contrast there was slight peripheral enhancement of cholangiocellular carcinoma in arterial and portal phases. More intense contrast enhancement of tumors was observed in late delayed phases, 10–15 min after contrast injection. The most informative MR images were T2-weighted images: cholangiocellular carcinoma was visualized as hyperintense, especially in peripheral areas. The zones of low MRT-signal in central tumor part corresponded to scar zone. In all cases we revealed dilated intrahepatic bile ducts proximally to the tumor.

Patients with metastatic hepatic lesions examined by CT and MRT were divided into three groups according to Wood (1991) [4]. Group 1 consisted of 4 patients (11%) with solitary metastases, group 2 — 9 patients (24%) with multiple metastases in one hepatic lobes, group 3 — 24 patients (65%) with lesions in both hepatic lobes. Right hepatic lobe lesions were diagnosed most frequently (69%) in group 1 and 2 patients. The sizes of metastatic lesions varied from 5 to 98 mm in diameter.

Characteristic features of hepatic metastases on native CT and MR images were the following: indistinct contours and nonhomogeneous structure. The maximum changes of density/intensity were found in central parts of metastatic lesions. Computer tomograms of 4 patients revealed calcifications in colorectal cancer metastases. Unlike cholangiocellular carcinoma with larger calcifications, metastatic nodes were found to have punctuate, amorphous calcifications.

Hepatic metastases are known to have predominantly arterial blood supply [4]. Hypervascular and hypovascular metastases are distinguished depending on the intensity of contrast in arterial phase in relation to the surrounding liver parenchyma [5].

In most patients (84%) hepatic metastases of gastrointestinal, pulmonary, breast, and ovarian tumors were hypovascular. Such metastases were poorly enhanced in CT and MRT arterial phase, predominantly in peripheral parts (“target symptom” [5]), and in portal phases they became hypodense/hypointense and were well-defined against the background of well-enhanced hepatic parenchyma.

Hypervascular metastases (16%) of renal cell carcinoma, neuroendocrine tumors, pancreatic cancer compared to hepatic parenchyma were enhanced more intensely in arterial phase. In portal phase such metastases were less visible (“vanishing lesions” [9]), since they kept some contrast media delivered from hepatic artery, and liver parenchyma was enhanced from portal vein. Arterial

phase of contrast was the most informative to detect and characterize hypervascular liver metastases [10, 11].

MRT with organ specific contrast media — gadoxetic acid — enables to detect hepatic metastatic lesions less than 1 cm in diameter. In dynamic contrast phases hepatic lesions are characterized according to their perfusion as

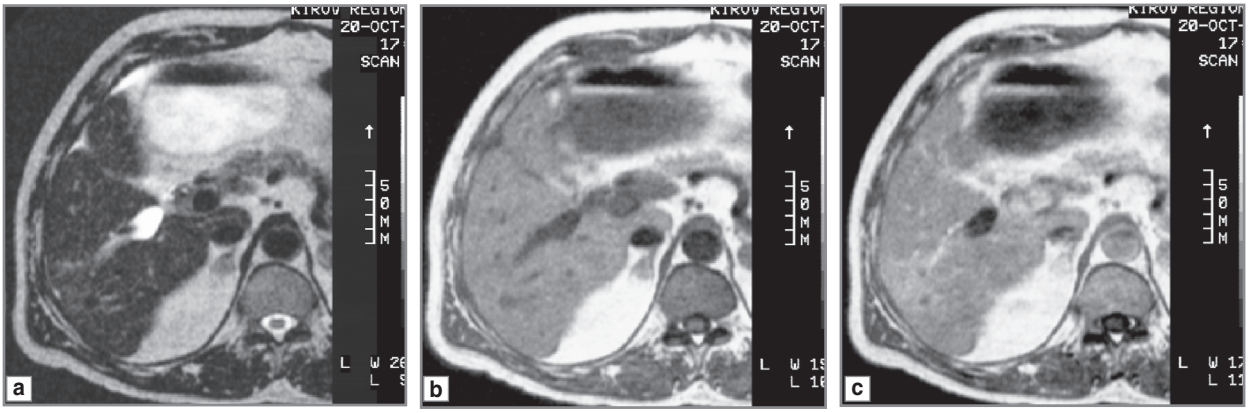

Fig. 1. Hepatic metastases of colorectal cancer in patient K., 52 years: *a, b* — fragments of native MRT; T2- and T1-weighted images. In S_{VI} of liver there is seen one round lesion with pathological signal, insignificant data for differential diagnosis; *c* — fragment of gadoxetic acid-enhanced MR-imaging, hepatocyte phase; T1-weghted image. In S_{VI} of the liver there are two round hypointense lesions, 4 and 6 mm in diameter, non-accumulating hepatospecific contrast that is the characteristic of metastases

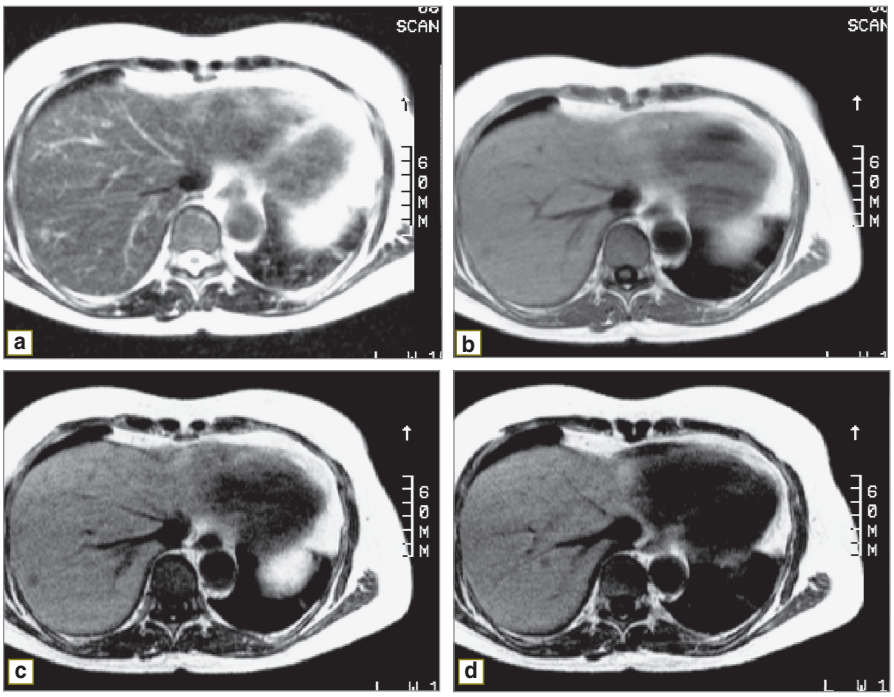

Fig. 2. Hepatic metastases from pancreatic adenocarcinoma in patient K, 55 years. Native MRT: *a* — T2-weighted axial images; *b* — T1-weighted axial images; *c, d* — gadoxetic acid-enhanced MR-imaging, hepatocyte phase; T1-weighted images; two metastatic lesions, less than 1 cm in diameter, in S_{VII} of the liver

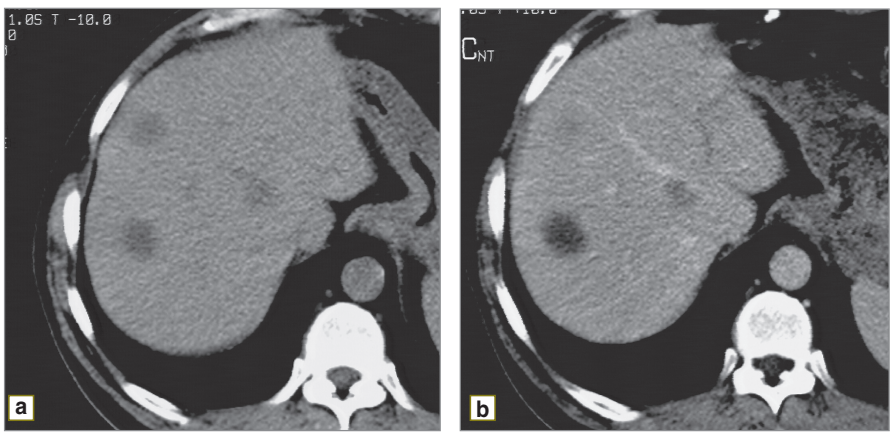

Fig. 3. Multiple hypovascular metastases of colorecral cancer in the liver (S7, S6, S5, S8, S4) with median hepatic vein entry extension, congenital "small caval lobe" syndrome in patient D, 52 years. CT fragments: native (*a*) and with intravenous contrast (predominantly, venous phase) (*b*)

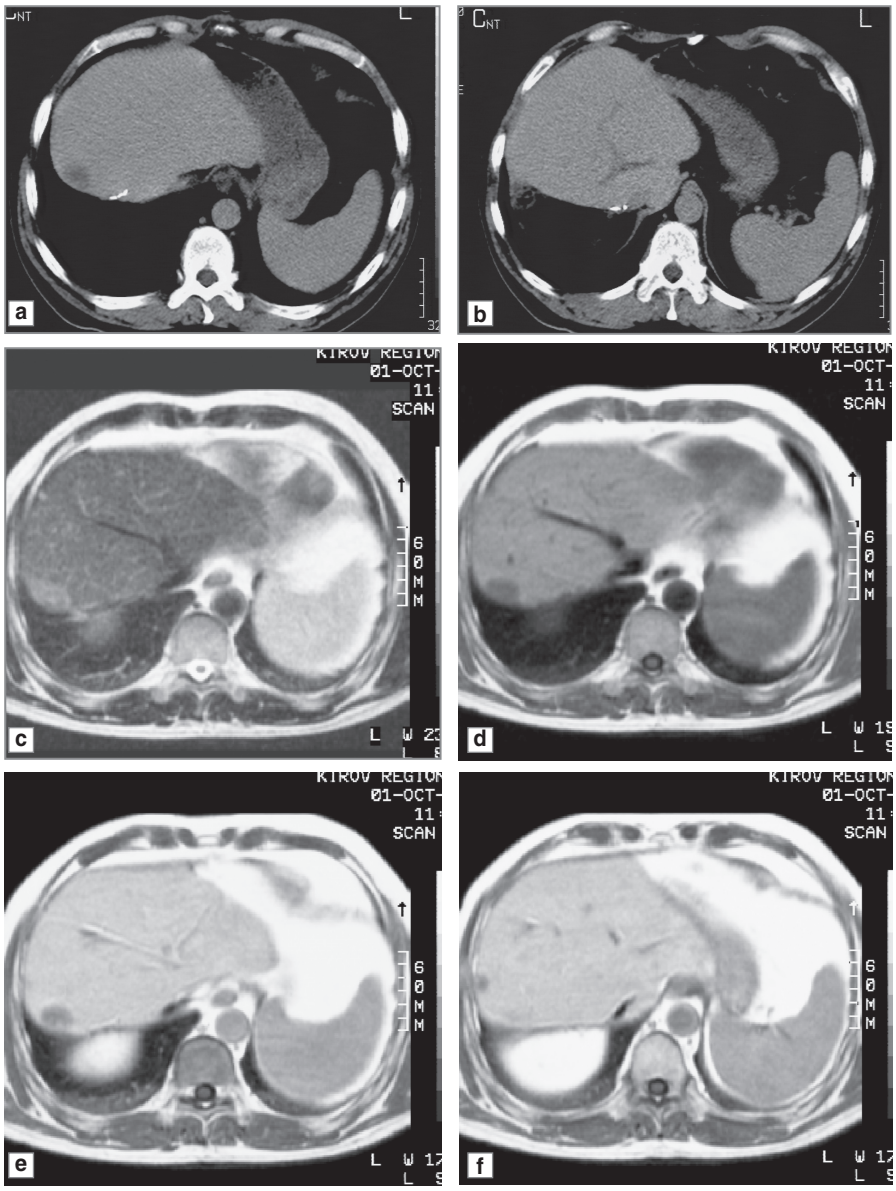

Fig. 4. Recurrence, the same patient D, 52 years. Metastatic lesion of hepatic stump after ligation of the right branch of portal vein to induce hypertrophy of the left caval lobe, the following extended right hemihepatectomy with S_{IVa} resection, and resection of median hepatic vein: *a, b* — contrast CT (predominantly, parenchymatous phase); *c, d* — native MRT, T1- T2-weighted images; *e, f* — gadoxetic acid-enhanced MR-imaging, hepatocyte phase; T1-weighted images; two metastatic lesions along the edge of hepatic stump are seen

hyper- or hypovascular masses [10, 12]. In hepatocyte phase gadoxetic acid enhances liver parenchyma [11, 13, 14]. In our situation, all hepatic metastases did not accumulate organotropic contrast media, and therefore, were hypointense on T1-weighted images (Fig. 1, 2).

The analysis of MR gadoxetic acid-enhanced tomograms obtained in hepatocyte phase enabled to reveal in 3 patients hepatic metastases less than 1 cm undetected by other modalities.

Complex radiological investigation revealed recurrences of malignant tumors after hepatectomy in 4 patients (Fig. 3, 4).

Conclusion. Actual CT and MRT technologies with intravenous contrast and multiphase scanning are high-quality and informative in topical and differential diagnosis of liver tumors. The application of hepatospecific contrast substance — gadoxetic acid — expands MRT opportunities in detection and recognition of small (less than 1 cm) liver metastases.

Differential radiodiagnosis of focal liver lesions (using CT and MRT) should be based on multicentre study of morphological structure, the character of lesion vascularity, and their dynamic and organ-specific (in MRT — in hepatocyte phase) contrast.

References

1. Zhuravlev V.A. *Aktual'nye, spornye i nereshennye voprosy khirurgii pecheni* [Relevant, disputable and open issues of hepatic surgery]. Kirov; 2008; 277 p.

2. Patyutko Yu.I. *Khirurgicheskoe lechenie zlokachestvennykh opukholey pecheni* [Operative therapy of hepatic cancer]. Moscow: Prakticheskaya meditsina; 2005; 312 p.

3. Bosch F.X., Ribes J., Diaz M., Cleries R. Primary liver cancer: worldwide incidence and trends. *Gastroenterology* 2004; 127: S5–S16.

4. Bosetti C., Levi F., Boffetta P., Lucchini F., Negri E., La Vecchia C. Trends in mortality from hepatocellular carcinoma in Europe, 1980–2004. *Hepatology* 2008; 48: 137–145.

5. Karmazanovskiy G.G. *Spiral'naya komp'yuternaya tomografiya: bolyusnoe kontrastnoe usilenie* [Spiral computer tomography: bolus contrast enhancement]. Moscow: Vidar-M; 2005; 376 p.

6. Bolog N., Andreisek G., Oancea I., Mangrau A. CT and MR imaging of hepatocellular carcinoma. *J Gastrointestin Liver Dis* 2011; 20(2): 181–189.

7. Efremidis S.C., Hytiroglou P. The multistep process of hepatocarcinogenesis in cirrhosis with imaging correlation. *European Radiology* 2002; 2: 753–764.

8. Bruix J., Sherman M. Management of hepatocellular carcinoma: an update. Alexandria (VA): American Association for the Study of Liver Diseases; 2010; 35 p.

9. Karmazanovskiy G.G., Shimanovskiy N.L. *Meditsinskaya vizualizatsiya — Medical Imaging* 2007; 6: 135–143.

10. Burns P.N., Wilson S.R. Focal liver masses: enhancement patterns on contrast-enhanced images — concordance of US scans with CT scans and MR images. *Radiology* 2007; 242(1): 162–174.

11. Ichikawa T., Saito K., Yoshioka N., et al. Detection and characterization of focal liver lesions a Japanese phase III, multicenter comparison between gadoxetic acid disodium-enhanced magnetic resonance imaging and contrast-enhanced computed tomography predominantly in patients with hepatocellular carcinoma and chronic liver disease. *Investigative Radiology* 2010; 45(3): 1–9.

12. Huppertz A., Yariada S., Kraus A., et al. Enhancement of focal liver lesions at gadoxetic acid-enhanced MR-imaging: correlation with histopatologic findings and spiral CT — initial observations. *Radiology* 2005; 234(2): 468–478.

13. Luca A., Grazioli L., Caruso S., et al. A two-centre study for the comparison of Gd-EOB-STPA (Primovist)-enhanced MRI versus triple-phase MDCT for the detection of hepatocellular carcinoma in cirrhosis. *European Radiology* 2009; 19(Suppl 1): S162.

14. Zech C.J., Grazioli L., Jonas E., et al. Health-economic evaluation of three imaging strategies in patients with suspected colorectal liver metastases: Gd-EOB-DTPA-enhanced MRI vs. extracellular contrast media-enhanced MRI and 3-phase MDCT in Germany, Italy and Sweden. *European Radiology* 2009; 19(Suppl 3): S753–S763.