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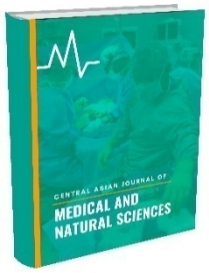

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Possibilities of MRI Diagnostics of Focal Liver Defeats

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Abstract: As you know, in recent decades, along with the trend towards an increase in the overall incidence of various malignant neoplasms, the number of patients with tumor lesions of the liver (primary and secondary), as well as mortality from them, has also increased.

Keywords: liver, MRI, defeats, radiation diagnostics.

The liver is the “target organ” for metastasis of most malignant neoplasms of various localizations. In particular, primary malignant tumors in the area drained by the portal vein metastasize to the liver in about 50% of cases. In general, metastases account for more than 90% of all malignant neoplasms of the liver, and the liver itself is considered the most frequently affected organ by metastases.

As you know, the most frequently detected focal lesions in the liver include simple cysts, hemangiomas, focal nodular hyperplasia, hepatocellular adenomas, primary (hepatocellular, cholangiocellular and combined cancer) and secondary (metastatic) tumors. At the same time, timely and correct diagnosis of focal lesions in the liver (especially small focal ones) continues to be among the complex problems of clinical oncology. The most common primary method for examining the patients concerned is ultrasound, which in modern oncological practice has become a generally available, reliable and widely used diagnostic method. Modern technologies for obtaining an ultrasound image make it possible not only to reliably identify certain focal changes in the liver, but also to characterize them, especially when using special (appropriate) contrast agents.

Along with ultrasound techniques, X-ray computed and magnetic resonance imaging (MRI) continues to be among the leading diagnostic methods for examining various groups of patients, including for examining the liver in cancer patients. However, the often encountered complex diagnostic situations require the use of both standard and new, still being developed techniques. A possible way to improve the accuracy of diagnosing various liver neoplasms can be considered the introduction of new methodological approaches to its study, in particular, the use of diffusion-weighted MRI (DW MRI), which has already convincingly proven its value and effectiveness in the diagnosis of lesions of a number of other organs, in particular the head brain.

The first work on the use of DW MRI was published by D. Le Bihan et al. in 1986. It highlighted the possibilities of its application both for the diagnosis of lesions of the brain substance (strokes, trauma, epilepsy, dementia), and for visualization of pathological changes in other tissues even before the

appearance of any visible morphological disorders. Artifacts from physiological movements (intestinal peristalsis, cardiac contractions) limited the use of DW MRI in extracranial pathology. However, with the advent of multichannel phase coils, as well as ultrafast MR sequences, DW MRI for the diagnosis of abdominal and pelvic lesions has become possible. In recent years, a significant number of works have appeared in the literature devoted to studying the capabilities of this technique in the diagnosis of various diseases of various organs and systems, in particular, focal liver lesions.

The physical principles of DW MRI are based on the possibility of recording the mobility of water molecules. As you know, in the space surrounding us, all molecules are in constant free (Brownian) motion - free diffusion. In biological tissues, their unlimited movement is impossible due to intermembrane interaction and the presence of macromolecules (lipophilic membranes are a barrier in intra- and extracellular spaces). Thus, in tissues with a high content of cells (for example, in tumors), the intercellular spaces are more tortuous, and the hydrophobic membranes are denser, which limits the movement of water molecules. Under such conditions, their diffusion is considered limited.

The sensitivity of DW sequences to diffusing water molecules can vary depending on the so-called "" factor (b-value) or gradient amplitude, its duration, and the time interval between two gradients. The unit of measurement of the factor "b" is s / mm2.

The signal intensity of molecules moving over longer distances per unit time (with blood flow) decreases at low b-values (<100-150 s / mm2). At the same time, when using high b-values (> 500 c / mm2), the signal is attenuated to a lesser extent from high-density (high cellularity) foci containing molecules that are limited in the degree of their mobility compared to normal liver parenchyma. It is important to note that due to the rapid attenuation of the signal from the vascular structures, it is possible It is important to obtain so-called black-blood images, which make it easier to detect a number of focal liver lesions, and the use of higher b-values can differentiate some of them.

Differential diagnosis of individual liver neoplasms can be carried out using both a visual assessment of the degree of signal attenuation, and by quantifying the values of the true diffusion coefficient (ADC map = ADC-map), which is a measured value of the signal intensity in each voxel, depending on the applied b- value.

The ICD values are calculated using the following formula:

ADC = ln [SI1-SI2] / b2-b1

where b1, b2 are diffusion factors, SI, is the signal intensity at low values (factor b, Sl2 is the signal intensity at high values of factor b.

As you know, to calculate the ICD indicators, at least two b-values are required, but the more there are, the more correct the corresponding ones will be.

The disadvantages of visual assessment of DW images include the fact that the signal intensity depends not only on the movement of water molecules, but also on the T2 relaxation time or the so-called “T2-shine through” effect. Consequently, an area with a longer T2 relaxation time will also be hyperintense in DW images and can simulate a diffusion-limited focus.

It should be noted that the degree of attenuation of the signal from the unchanged parenchyma and focal formations of the liver with an increase in the b-value is nonlinear. In the range of low b-values (0-200 s / mm2), a rapid attenuation of the measured signal intensity is observed, while in the range of high b-values (> 200 s / mm2), the signal attenuates more evenly. The initial decrease in signal intensity is thought to be due to vascular capillary perfusion, where the signal from fast moving water molecules is rapidly attenuated by low diffusion weights. This effect is called pseudodiffusion, the relative contribution of which becomes significant only at very low b-values. The phenomenon of

pseudodiffusion makes it possible to separate diffusion and perfusion. Understanding this phenomenon is important for the selection of b-values as they are influenced by tissue perfusion (i.e., low b-values = 0-200 s / mm2) when measuring the true diffusion coefficient (ADC).

The acquisition of DV images is possible both with holding the breath and synchronizing with the breath. Breath-sync images undoubtedly have a number of advantages: better signal-to-noise ratio (especially at high b-values), the ability to use more "b" values, which provides more accurate ICD values. The average duration of such a study is on average 3-7 minutes.

Receiving LW images while holding the breath requires less time, but they are characterized by a suboptimal signal-to-noise ratio and are more sensitive to artifacts. The number of applied b-factors in such cases does not exceed 2-3.

Among the undoubted advantages of the DW MRI technique, several can be noted:

- the technique does not require intravenous contrasting, and, accordingly, additional economic costs;
- obtaining DV-images can be carried out both before and after intravenous contrasting;
- the technique can be performed in patients with systemic kidney disease who have contraindications for intravenous administration of contrast agents;
- the ability to obtain additional and significant diagnostic information in 3-7 minutes.

Among the disadvantages of the technique, it is important to note the following:

- high sensitivity to artifacts (respiratory, cardiac contractions, air in the adjacent gastrointestinal tract);
- the lack of standardization of the method (different manufacturers of MR systems use different b-values, which determines the variability of the CDI indicators).

In recent years, the DW MRI technique has gained particular popularity due to the fact that it has become possible to use it in extracranial pathology, including in the diagnosis of oncological diseases. However, it is believed that the DW MRI technique is largely auxiliary and cannot be used as an independent research method, with the exception of certain cases, which we will mention a little later.

The possibility of detecting tumors with DW MRI is due to the fact of their relatively higher cellularity relative to the surrounding unchanged tissues (in particular, in the liver); therefore, tumor foci usually have an increased signal intensity at various b-values and a low signal intensity on ICD maps.

It is believed that the use of DW MRI improves the detection of small (up to 1 cm) subcapsular and intraparenchymal metastases, which can be difficult to distinguish from the section of vessels or bile ducts.

At the same time, the assessment of the intensity of signal attenuation at different b-values can be used not only to identify foci, but also to assess women of their character.

In particular, T. Parikh et al. the following criteria for benign and malignant lesions are proposed:

- lesions were regarded as malignant (in particular, metastases and hepatocellular carcinoma) if they had a moderately increased signal on T2 images and at low b-values (b = 50), while remaining hyperintense with an increase in b-values (b = 500), but hypointense on ICD maps;
- lesions were considered benign (cysts and hemangiomas) if they had a hyperintense signal on T2-images and at low b-values (b = 50), but with an increase in b-values, the intensity of display of

these foci decreased (partially or completely), and on ICD maps they were of increased intensity or hyperintense relative to the surrounding liver parenchyma;

- the rest of the foci that did not meet the above criteria were regarded as undefined.

The features of the display of the most common focal lesions in the liver during standard MRI studies are described in a number of relevant works. It is well known that the assessment of the peculiarities of their blood supply in different phases of intravenous contrasting is of decisive importance for the correct diagnosis of neoplasms in the liver.

On MRI, simple cysts appear round formations with smooth and clear contours, a homogeneous internal structure, usually hypointense in T1 and hyperintensive in T2. On DW MRI, cysts are hyperintense at low b-values (b = 50), but with an increase in these values (up to b = 400 or b = 800), the intensity of cysts display rapidly decreases, while on ICD maps they retain their hyperintensity. It is important to mention that cystic metastases of some mucinous tumors can have a display similar to simple cysts in DW MRI, in which case it is very important to take into account the patient's history, as well as the histological type of the primary tumor.

Hemangiomas on standard MRI are usually hypointense at T1 and hyperintense at T2, while on DV-MRI they have an increased signal intensity at low and high b-values; on ICD maps, their display is moderately increased in relation to the surrounding liver parenchyma.

Focal nodular hyperplasia (FNG) nodes on MRI are more often iso-intensive or slightly increased in T2, hypointense in T1 with a hyperintense central scar in T2 (if present) in typical cases. On DW MRI (according to single reports), the nodes have an increased signal intensity at different b-values and are predominantly iso-intensive on ICD maps with a hyperintense central scar (if any).

Hepatocellular adenomas (HCA) on MRI can manifest themselves in different ways, depending on their belonging to a particular subgroup according to the classification of P. Bioulac-Sage et al. In MRI studies with hepatospecific contrast agents, HCA is characterized by hypointensity of the internal structure in the delayed (after 20 min) phase of the study, which is due to the absence of proliferating bile ducts in the adenomas and the impossibility of excretion of the hepatotropic drug.

With DW MRI, according to some data, small (up to 2 cm) HCA are practically iso-intensive at different b-values and on ICD maps. However, larger GCA nodes may have slightly increased signal strength at different b-values and on the ICD maps.

For malignant neoplasms of the liver (in particular, for hepatocellular cancer and untreated metastases), the characteristic manifestations are: iso-intensity or moderately increased intensity of their display in T2, increased display intensity at low and high b-values, hypointensity on ICD maps. However, “high-density” benign liver tumors, in particular, HCA and FNG nodes, can have a similar display, in the latter case, due to elements of the fibrous stroma and malformed vessels.

F. Agnello et al. on material from 54 FNG and 36 HCA showed that 87% of all lesions (78 out of 90) were hyperintense with high b-values (b = 600) and hypointense on ICD maps, which formally (externally) did not allow distinguishing them from corresponding manifestations of malignant tumors. It is interesting to note that according to the criteria of benignity and malignancy proposed by T. Parikh et al. [25], 49% of all these lesions would be regarded as malignant, and the remaining 51% as indeterminate. In other words, none of these 90 lesions (54 FNG and 36 HCA) would be considered benign.

When calculating the CDI values in the HCA and VNG nodes, it was noted that their values did not differ significantly from the CDI values in the HCC nodes and metastases. Similar results allowed a

number of authors to believe that the use of DW sequences does not add significant additional information to standard MR sequences in the diagnosis of solid benign and malignant liver tumors.

At the same time, high ICD rates in cysts and hemangiomas are well known, which allows both use them for differential diagnosis.

The observed false-negative results on DW MRI are most often associated with the peculiarities of displaying highly differentiated variants of tumors, in particular, hepatocellular carcinoma, which (against the background of the surrounding parenchyma) can be isointense at different b-values and on ICD maps.

Liver abscesses (of various nature) with DW MRI can be difficult to differentiate from malignant tumors due to the high cellularity of the inflammatory substrate. As is known, the assessment of the effectiveness of treatment of a number of tumor processes is traditionally based on measuring the size of the tumor, in particular, according to the criteria of WHO, RECIST, RECIST 1.1, EASL, mRE-CIST. The emergence of new interventional methods for the treatment of tumor lesions of the liver, such as radiofrequency thermoablation and chemoembolization, led to significant limitations in the application of the RECIST and WHO criteria, given the impossibility of assessing changes in the internal structure of tumors after treatment. In particular, a reduction in the size of a primary liver tumor (according to RECIST criteria) in patients with unresectable forms of hepatocellular cancer during conservative treatments (for example, transarterial chemoembolization) is rarely observed, which in some cases does not allow determining and adjusting the optimal treatment regimen in each specific case. ... In addition, the presence of tumor necrosis - one of the reliable indicators of the effectiveness of treatment - cannot be assessed either by the RECIST criteria or by any other criteria based only on the change in tumor size. Numerous studies confirm insufficient correlation between the degree of tumor necrosis caused by exposure to new agents (for example, yttrium microspheres) and standard methods for assessing the effectiveness of treatment.

Undoubtedly, this situation leads to a revision of the applied and the search for new criteria for assessing the effectiveness of the planned treatment.

According to a number of studies on the use of DW MRI to assess the effectiveness of chemotherapy or radioembolization in patients with HCC, there were significant differences in CDI values in live and necrotic fragments of tumor substrate after treatment, as well as measurable differences in these values before and after treatment. In particular, it was noted that the true diffusion coefficient in tumor nodes can increase during antitumor treatment (chemotherapy or radiation therapy, chemoembolization, ablation), which in some cases allows predicting and evaluating the effectiveness of the treatment. Thus, CDI indices can be used to assess the metabolic activity of a tumor after locoregional treatment. There was a clear correlation between CDI indices and the degree of tumor necrosis in histological studies.

The currently limited number of publications devoted to assessing the effectiveness of treatment of liver malignant neoplasms after radiofrequency thermal ablation (RFA) indicates that the RECIST criteria in the respective patients are not informative enough, and the identification of areas of "residual" contrast (according to the EASL criteria) may be difficult in hypo- vascular tumor nodes. Moreover, neoplasms in the liver after RFA usually contain areas of coagulative necrosis of hyperintense in T1, which can also complicate the visualization of residual tumor tissue. It is noted that the determination of the ICD values at once for the entire volume of the focus is not entirely correct; it is necessary to assess the state of its constituent elements, in particular, the areas with minimal CDI values, which may reflect residual tumor tissue. In patients with liver metastases, the CDI values in the entire focus increased significantly (1 and 3 months after RFA) compared to its values before the start of treatment, and then (after 6 months) these values could slightly decrease (but

not lower than the initial level) ... In patients with HCC, a significant increase in CDI values (in the entire focus) was observed only 1 and 6 months after RFA, although after 3 months (after RFA) these values did not differ significantly from the initial values. A similar increase in CDI values after transarterial chemoembolization was noted by other authors.

It should be noted that in the literature available to us, the rational (justified) interval for conducting repeated (dynamic) MRI studies in the course of the discussed treatment options for the respective patients has not yet been determined. To date, there are only a limited number of publications in the literature concerning the results of the use of DW MRI for preliminary assessment of the possible efficacy of chemotherapy in patients with primary and secondary liver tumors. The effectiveness of chemotherapy is monitored at different times (usually after 2-6 months), however, in patients with aggressive forms of cancer, even 1 month of ineffective chemotherapy can lead to an irreversible decrease in the quality of life and a corresponding prognosis. That's why We need the earliest possible, easily reproducible and non-invasive method for assessing the effectiveness of treatment.

It was noted that in patients with metastases of colorectal cancer in the liver, the average CDI values increased in the foci, even with a partial response to chemotherapy (according to RECIST criteria). Such an increase was not observed in foci without signs of any dynamic changes or in foci with signs of progression (according to RECIST criteria).

Thus, indicators of CDI in metastatic foci can be considered as potential diagnostic biomarkers to determine the possible effectiveness of chemotherapy and to detect early signs of a response to it. Relatively recently, it was proved that the effectiveness of chemotherapy in patients with liver metastases is expressed in an increase in the fibrous component in the tumor nodes, and not in a reduction in their size. However, it can be extremely difficult to differentiate between "living" tumor tissue and areas of fibrosis in DW MRI, since they can all be hypointense on ICD maps. It is believed that the solution to this problem is possible using the technique of intravenous contrasting.

An unsolved problem is also the assessment of the effectiveness of treatment and the completeness of remission in the presence of multiple small (up to 1 cm) metastases in the liver. It is well known that in the course of treatment of patients with liver metastases, the contrasting nature of metastatic foci changes somewhat. There is a prolonged retention of the contrast agent in the mass of the focus, which may resemble the features of contrasting hemangiomas. At the same time, there are a number of circumstances in which visualization and correct interpretation of such metastatic foci can be difficult, in particular:

- when the size of the foci is less than 1 cm;
- with their localization in the left lobe of the liver, or subphrenic divisions;
- with a decrease in the degree of vascularization of metastases and as a result of their indistinct visualization of foci against the background of contrasting liver parenchyma;
- due to respiratory artifacts.

In our opinion, the DW MRI technique can be a solution to this problem, and can also allow avoiding the use of intravenous contrasting in certain groups of cancer patients, and, consequently, reduce the economic costs of a medical institution. Thus, our review of modern scientific literature shows that most studies devoted to the application of the DW MRI technique in the diagnosis of focal liver lesions do not sufficiently detail and convincingly highlight the problems of their differential diagnosis. The issues of evaluating the effectiveness of treatment and monitoring of patients with metastatic liver damage are presented rather sparingly and contradictory. Considering the high sensitivity of the DW MRI technique, the question of the possibility of its isolated use in certain groups of oncological patients is of undoubted interest (we have not come across corresponding works

in the domestic and foreign literature). The possibility of excluding in certain situations the repeated use of intravenous contrasting in cancer patients has undoubted prospects in the diagnostic and economic aspects. It is these circumstances that determine the relevance of further research in this direction.

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