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Differentiation of focal hepatic lesions in MR imaging with the use of combined quantitative and qualitative analysis

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Summary

Background: To evaluate the efficacy of the protocol of combined quantitative-qualitative analysis for the differentiation of focal hepatic lesions.

Material/Methods: The study group included 168 patients with 292 hepatic lesions confirmed by histology (n =138) or follow-up (n =154). Lesions were divided into: benign lesions treated conservatively (group A, 120 lesions), malignant tumors and benign lesions treated surgically (group B, 172 lesions). MR imaging (1.5-T) consisted of sequences: T2 double-echo TSE, T2 STIR, T1 GRE and of dynamic study. During the first part of differentiation process, quantitative analysis, based on lesions T2 relaxation times (derived from T2 double-echo TSE sequence), was performed in order to discriminate non-solid lesions (hemangiomas, cysts, abscesses; n = 88) from solid tumors (n = 204). Subsequently, all tumors defined as solid underwent qualitative evaluation based on visual assessment of lesions signal intensities in all sequences and patterns of their contrast enhancement. The aim of this part of analysis was to discriminate benign lesions (FNH and focal fatty infiltration) from other solid tumors. The remaining tumors were characterized as group B lesions.

Results: Statistically significant difference between mean T2 relaxation time of solid tumors (84.1 ms) and non-solid lesions (250.5 ms) was noted, allowing diagnosis of solid tumors with sensitivity of 96% and specificity of 93% (at the threshold of 116 ms). Overall 202 lesions were defined as solid (196 true positive, 8 false negative, 6 false positive results). Qualitative analysis of these lesions was performed allowing correct characterization of all 7 focal fatty infiltrations and 21 of 24 FNH. Six lesions were falsely diagnosed as FNH. Remaining 168 lesions were defined as group B lesions. Both parts of differentiation protocol yielded sensitivity and specificity of 92%, allowing correct characterization of 158 of 172 group B lesions. Fourteen false negative and 10 false positive results (3 FNH, 1 focal inflammation, 6 hemangiomas) were obtained.

Conclusions: Combined protocol of quantitative and qualitative analysis enabled discrimination of group B lesions (malignant tumors and benign lesions treated surgically) with high sensitivity and specificity of 92%.

Key words: focal liver lesions • magnetic resonance imaging • liver • neoplasms

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Background

Computed tomography (CT) and magnetic resonance (MR) are the most commonly performed examinations for differentiation of focal liver lesions. The first enables differentiation of focal lesions within the liver based on evaluation of their vascularization and helps to define whether the lesion is well or poorly vascularized [1–5]. However, only some focal lesions can be explicitly characterized by means of typical CT image (lack of enhancement – cyst or typical contrast enhancement in multiphase exam-most hemangiomas, FNH) [5–6].

In comparison with other imaging techniques, the magnetic resonance is a complex examination which allows analysis of various useful parameters in differential diagnostics of liver tumors, such as: signal intensity in T1 and T2-weighted images, dynamics of their contrast enhancement (evaluated after extracellular contrast agent injection), presence or lack of active hepatocytes and Kupffer cells in visualized lesions after hepatropic or Kupfer cells-related contrast agent administration. Overall analysis of these parameters enables a more precise differentiation of hepatic tumors.

In order to improve the efficacy of MR examination in evaluation of the type of hepatic tumors we applied our own diagnostic algorithm of quantitative and qualitative analysis. The quantitative analysis carried out in the first phase was based on calculations of T2 relaxation times of focal lesions with the use of double-echo TSE sequence. The aim was to distinguish lesions of long T2 relaxation times which include cysts, abscesses and hemangiomas. The second phase of differential algorithm was the qualitative evaluation of signal intensity of lesions in T1 and T2-weighted images after extracellular contrast agent administration in different phases of enhancement. Its aim was to distinguish the lesions with signal (in T1 and T2-weighted images) typical for adipose tissue (focal fatty liver) and those matching criteria for focal nodular hyperplasia (FNH).

Aim of study

To evaluate the efficacy of diagnostic algorithm based on combined quantitative-qualitative analysis differentiation of hepatic tumors.

Material

The analysis included 292 nodules in 168 patients (80 men/88 women) aged 17 to 83 (mean 53). The lesions were multiple in 69 cases, solitary in 99; 13 patients were diagnosed with more than one type of tumor. Lesions are specified in table 1.

Diagnoses of 86 patients were verified at the histopathologic examinations of material collected during surgical procedure (n=64), biopsy (n=19) or diagnostic laparoscopy (n=3). The remaining 82 patients, including cases of inoperable lesions and focuses of image typical for benign lesions confirmed by at least 2 imaging modalities, the definite diagnosis was based on correlation with other imaging procedures, control examinations and clinical assessment.

Table 1. Analyzed focal lesion.

Diagnosis	Number of lesions	Number of patients
Metastases	78	42
Cholangiocarcinoma	59	40
Hemangioma	59	35
hepatocellular carcinoma	27	13
FNH	24	15
Cyst	19	19
Abscess	9	8
Hemangiosarcoma	5	1
Focal fatty degeneration	7	3
Adenoma	2	2
Mixed tumor	1	1
hydatiform cyst	1	1
Inflammation	1	1
Total	**292**	**181**

The sum in „number of patients" column amounts to 181 (instead of 168) as 13 patients were diagnosed with more than one type of lesion (e.g. hemangioma and metastasis)

128 patients were referred for MR scanning from Department of General, Transplant and Hepatic Surgery of Warsaw Medical University, others were referred from other departments of Central Clinical Hospital (n=29) or within the ambulatory procedure (n=11).

Method

Examinations were performed on 1.5 T scanner (Gyroscan ACS NT, Philips), with the use of body coil. The following sequences in transverse plane were performed in all patients: T2-weighted TSE sequence, T2 Dual Echo TSE, T2-weighted Inversion recovery with fat saturation (T2 STIR), T1-weighted gradient echo sequence (fast spoiled multiplanar gradient echo, T1 FSMPGRE) and dynamic multiphase examination of T1 FSMPGRE (for parameters of sequence – see table 2) after quick hand intravenous administration of 0.1 – 0.15 mmol/kg (0.2 – 0.3 ml/kg) of Gd-DTPA. After the injection IV cannula was immediately rinsed with 10 ml of physiological saline. Contrast

Table 2. Selected parameters of the applied sequences.

Name of sequence	images	TR/TE (or Teeff)	Flip	TI	NE	TF	NSA	RG	TL (mm)	matrix
T2 Dual TSE	T2W	1800/(40/120)	90	-	2	12	2	+	5-7	256
T2 STIR	T2W	1800/100	90	150	1	16	3	+	5-8	256
T1 FSMPGRE	T1W	183/1.8	80	-	1	-	1	-	7	256

TR – time of repetition, TE – time of echo, TEeff – time of echo effective, flipangle, TI –time of inversion , NE – number of echoes, TF – turbo factor, NSA – number of signal averages, RG – respiratory gating, TL – slice thickness

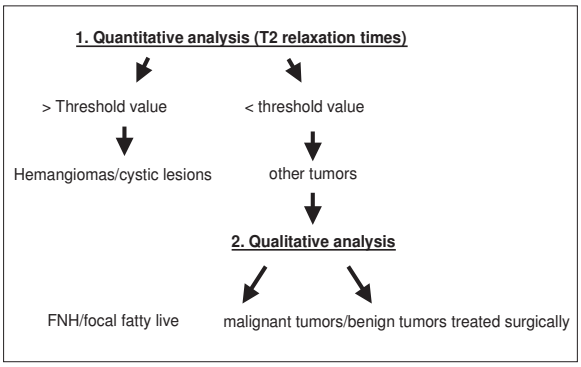

Figure 1. Protocol for the differentiation of focal liver lesions.

enhancement was assessed in following phases: arterial (20–50 sec after the injection), portal vein (55–80 sec), equilibrium (90–120 sec) and delayed (3–5 min).

Evaluation criteria for results of examinations

In order to differentiate the hepatic nodules the observed lesions were divided into 2 groups – group A consisted of benign lesions treated conservatively and inflammatory or parasitic lesions, while group B – of malignant and benign lesions, their treatment of choice being the surgical procedure. Differentiation consisted of discrimination of A-group lesions; other lesions were automatically qualified for group B. Table 3 shows classification of focal lesions that we used.

The process of differentiation consisted of 2 phases – quantitative analysis and qualitative analysis.

Quantitative assessment based on analysis of T2 relaxation times of focal lesions

In order to quantitatively analyze the focal lesions, they were divided into two groups – solid tumors (characterized by T2 relaxation times) and other tumors: hemangiomas and liquid lesions including cysts and abscesses (characterized by longer T2 relaxation times) (table 4).

Quantitative analysis consisted of calculations of transverse relaxation times (T2) of tumors made on the basis of measurements of their signal intensity in T2 Dual Echo TSE sequence. For each of the echoes two measurements were taken and then averaged. Region of interest (ROI) covered the possibly largest part of tumor. In solid-liquid lesions ROI was limited to the solid part of tumor. The following equation was used for calculations:

$$T2\ (ms) = (TE\ 2 - TE\ 1) / (ln\ SI\ 1 - ln\ SI\ 2)$$

TE 1 stands for time of the first echo (40ms), *TE 2*-for time of the second echo (120 ms), and *In SI 1* and *In SI 2* are the natural logarithms of signal intensity obtained in the first and second echo. Calculations were made using the Excell spreadsheet (Microsoft Office software).

Next, optimal threshold value was determined in order to discriminate solid tumors (characterized by short T2 times) from other lesions (long T2 times) with the highest possible sensitivity and specificity. Moreover, solid lesions with shortest T2 relaxation times indicating focal nodular hyperplasia (FNH) were also distinguished. According to our hypothesis, lesions built of normal hepatocytes ought to be characterized by short T2 relaxation times, similar to hepatic parenchyma. The second additional threshold value was determined to discriminate FNH from other lesions with optimal sensitivity and specificity.

Statistic analysis was carried out with the use of t-student test in order to evaluate statistical significance of mean T2 relaxation times of: (1) solid tumors, angiomas and cystic lesions, (2) FNH and other solid tumors.

Qualitative analysis

It was the second stage of differentiating focal lesions and included 202 lesions qualified at the quantitative stage to the group of solid tumors (on the basis of T2 relaxation times shorter than threshold value). The aim of the qualitative analysis was to discriminate focal fatty liver and focal nodular hyperplasia from the group of solid benign lesions. Qualitative analysis consisted of visual assessment of signal of focal lesions in particular sequences, before and after intravenous administration of Gd-DTPA. It was carried out by two radiologists and the final result was based on the principle of unanimity of observers.

The only diagnosis criterion for focal fatty liver was the detection of lesion characterized by elevated or

Table 3. Established classification of focal hepatic lesions.

Group A (n = 120)	Group B (n = 172)
Hemangioma	Metastases
Cyst	Hepatocellular carcinoma
Hydatiform cyst	Cholangiocarcinoma
Abscess	Hemangiosarcoma
Focular nodula hyperplasia (FNH)	Adenoma
Focal fatty liver	
Inflammation	

Table 4. Classification of focal lesions by their solid or non-solid character.

Solid tumors (n = 204)	Other types of lesions (n = 88)
Metastases	Hemangioma
Hepatocellular carcinoma	Cyst
Cholangiocarcinoma	Hydatiform cyst
Hemangiosarcoma	Abscess
Focal nodular hyperplasia (FNH)	
Adenoma	
Focal fatty liver	
Inflammation	

moderate signal in T1-weighted images which presents weakening of the signal in sequence with fat saturation.

For FNH recognition the following criteria were taken into account: (1) short T2 time, below the threshold value of FNH, (2) isointensity or moderate hypointensity in T1-weighted images, (3) strong homogenous enhancement in the arterial phase, (4) isointensity in equilibrium and delayed phases. Three matching criteria out of four were considered as FNH recognition. Additionally, incidence of central scar was also analyzed in FNH cases although its presentation was not a necessary condition for focal nodular hyperplasia diagnosis.

Lesions which did not match the criteria for focal fatty liver or FNH diagnosis and were not previously (in the quantitative phase) qualified for cyst and angioma group, were diagnosed as malignant or benign tumors treated surgically (group B). For outline of differential process – see table 1.

Statistic analysis

Statistic analysis of results was based on parametric t-Student tests for independent samples. The significance level was $p<0.05$. All calculations and analyses were conducted using statistic software package of STATISTICA 6.0 (StatSoft Poland).

Results

Quantitative analysis of T2 relaxation times of focal lesions

T2 relaxation times of liver, solid tumors and other lesions (angiomas, cysts, abscesses) in the analyzed group of 292 lesions in 168 patients are depicted in table 5.

Statistically significant difference was noted between mean T2 relaxation time of solid tumors and mean T2 time of hemangiomas, cysts and abscesses analyzed together ($p<0.0000001$).

Optimal threshold value discriminating solid tumors from other lesions proved to be the T2 time – 116 ms for which the sensitivity amounted to 96% and specificity to 93% (accuracy 95%, positive prognostic value 97%, negative prognostic value 91%).

Figure 2 shows T2 relaxation times of solid tumors and other lesions (hemangiomas, cysts, abscesses).

In the examined group of 292 focal lesions in 168 patients, 8 of 204 solid tumors were falsely qualified to the group of other lesions (hemangiomas, cysts, abscesses) based on transverse relaxation time (T2) longer than threshold value (116 ms). All 8 tumors were focuses with dimensions of 8 to 180 mm which derived from large intestine carcinoma (3 focuses), melanoma, carcinoid, praganglioma, neuroendocrinal carcinoma or neoplasm of unknown source. The dimensions of 2 of the tumors exceeded 100 mm (180 mm and 150 mm), the next measured 87 mm and the remaining 5 did not exceed 30 mm.

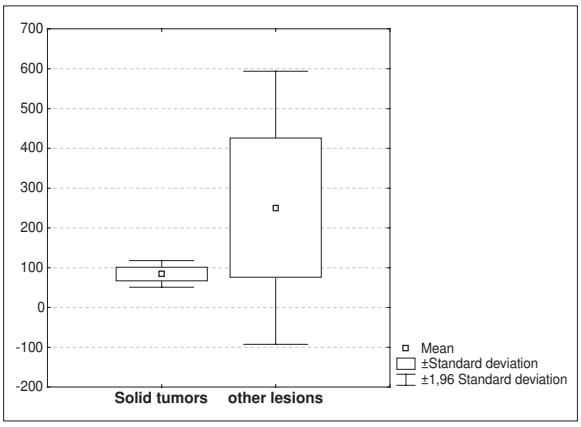

Figure 2. Mean T2 times of solid lesions (84 ms) and other tumors (250.5 ms).

As for the 3 biggest tumors (2 metastases of large intestine carcinoma and 1 carcinoma of an unknown source) necrosis occupying most of the altered area was the reason for longer transverse relaxation time. In spite of measuring the signal intensity in their peripheral solid part, the relaxation times were longer and typical for hemangiomas or cystic lesions. Among 5 smaller tumors 3 presented rich vascularization in multiphase examination after paramagnetic contrast agent administration (metastases of carcinoid, paranglioma, or neuroendocrine tumor). Such vascularization could be the reason why their T2 relaxation times were elongated, although other 18 well-vascularized metastases in the examined population were characterized by relaxation times shorter than threshold value (116 ms). In the analyzed group of 78 metastatic lesions mean T2 relaxation time of well-vascularized metastases was longer (97 ms) than mean time of T2 relaxation times of poorly vascularized metastases (91.8 ms) but the difference was not statistically significant ($p<0.22$). The remaining 2 (metastases of large intestine carcinoma and melanoma) out of 8 falsely qualified to the group of lesions other than solid, were characterized by poor vascularization.

Among 88 tumors other than solid, transverse relaxation times of 6 hemangiomas were shortened and fit in the range typical for solid tumors. The size of the biggest hemangioma was 202 mm; sizes of other 5 varied from 7 to 14 mm (mean – 10 mm). in the first case massive hemangioma of the liver imitated a malignant tumor with central necrosis in MR examination. The peripheral part of the lesion was characterized by lower signal intensity (shorter T2 time), typical for solid lesions. Histopathologic examination revealed that this part of the hemangioma was covered with hyalinization and fibrosis which shortened T2 relaxation time. In 5 other cases of small hemangiomas (mean 10 mm) the most

Table 5. Mean T2 relaxation times of liver and focal hepatic lesions.

	Mean T2 time (ms)	Range (ms)
Liver	54	41 – 74
Solid tumors	84.1	54 – 148
Other lesions	250.5	82 – 1241

* hemangiomas, cysts, abscesses

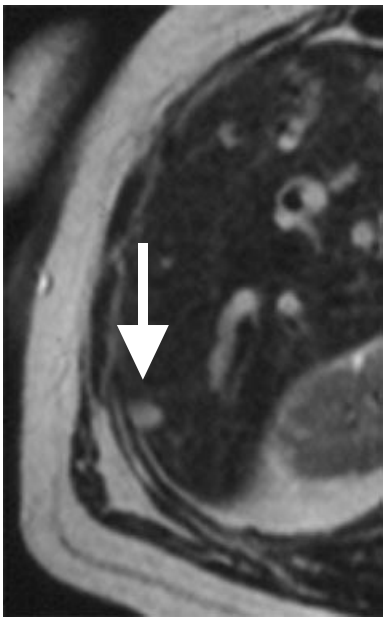

Figure 3. Small hemangioma (arrow) with short, T2 time (103 ms), due to volume averaging effect.

probable reason of false classification was the effect of volume averaging effect – the coil embraces the parts of hepatic parenchyma which are adjacent to lesions and have shorter T2 times (fig. 3). Generally, 19 of 24 small hemangiomas with the maximum size smaller than 15 mm were correctly classified to the group of lesions other than solid (including 10 out of 13 angiomas smaller than 11 mm).

T2 relaxation times of particular types of focal lesions are depicted in table 6.

In the group of solid lesions, nodular hyperplasia was characterized by weakest signal and mean T2 relaxation time closer to the liver (63.7 ms), but shorter compared to other solid tumors (86.8 ms). The difference was statistically significant ($p < 0.0000001$). Threshold value of 68 ms enabled recognition of FNH with sensitivity of 83%, specificity of 93% and accuracy of 92%.

The differences between mean T2 relaxation times were also found in cases of solid tumors such as hepatocellular carcinoma, cholangiocarcinoma and metastases. However, we failed to define a threshold value which would enable its discrimination with satisfying sensitivity and specificity, the reason being wide scope of T2 relaxation times of the aforementioned tumors which hindered their differentiation.

In general, quantitative analysis of transverse relaxation times of 292 focal lesions (204 solid tumors, 88 lesions of other type) with threshold value of 116 ms, enabled accurate diagnosis of 82 of 88 hemangiomas, cysts and abscesses with 8 false positive results (sensitivity 83%, specificity 93%). Moreover, determination of second threshold value of 68 ms allowed accurate diagnosis of 20 of 24 FNH with 12 false positive recognitions (sensitivity 83%, specificity 93%).

Qualitative analysis of focal lesions

This analysis included 202 focal lesions with relaxation times shorter than 116 ms (196 solid lesions, 6 hemangiomas) qualified to the group of solid lesions based on quantitative analysis.

Diagnostics of focal fatty infiltration

All 7 focuses of fatty infiltration found in 3 patients matched the diagnostic criteria for this type of lesion (elevated

Table 6. T2 relaxation times of focal lesions in analyzed material.

Recognition	Number of lesions	Number of patients	Mean T2 time (ms)	Range (ms)
SOLID TUMORS				
Metastases	78	42	**93.2**	56 – 148
Cholangiocarcinoma	59	40	**85**	64 – 110
Hepatocellular carcinoma	27	13	**75.3**	56 – 91
FNH	24	15	**63.7**	54 – 75
Hemangiosarcoma	5	1	**89**	76 – 113
Fatty infiltration	7	3	**78.7**	68 – 85
Adenoma	2	2	**74**	62 – 86
Mixed tumor	1	1	**68**	68
Inflammation	1	1	**69**	69
OTHER LESIONS				
Hemangioma	59	35	**151.3**	82 – 249
Cyst	19	19	**576.6**	180 – 1241
Abscess	9	8	**238.6**	145 – 301
Hydatiform cyst	1	1	**117**	117

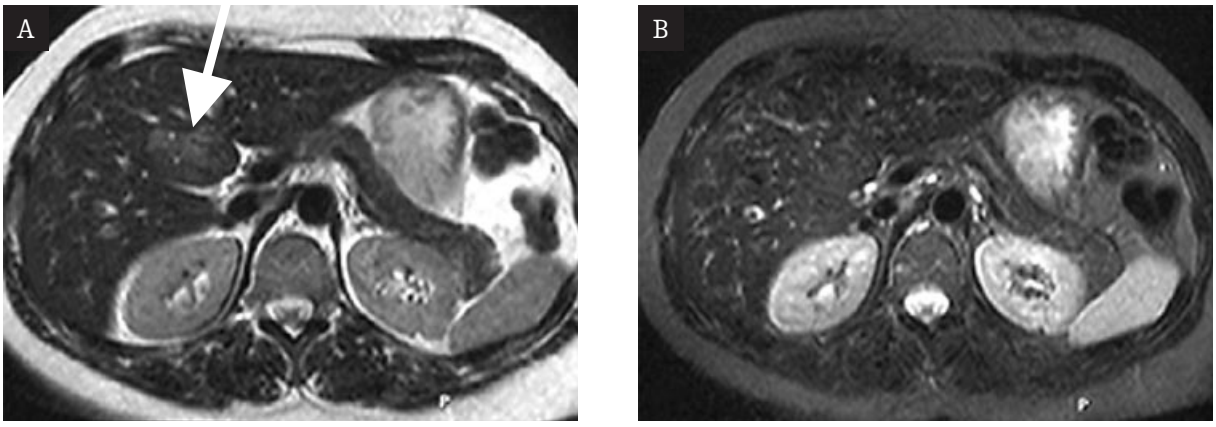

Figure 4. Focal fatty infiltration liver of liver hilum, with slightly increased signal intensity (arrow) in T2 Dual Echo TSE sequence (**A**), isointense sequence with fat saturation – T2 STIR (**B**).

or moderate signal intensity in T1-weighted images and its lowering in sequence of adipose tissue saturation) (fig. 4). False positive results were not stated (sensitivity, specificity, accuracy – 100%).

Diagnostics of focal nodular hyperplasia

After depiction of 7 lesions with typical MR features of focal fatty infiltration the analyzed group consisted of 195 focal lesions (24 FNH, 165 other solid tumors, 6 hemangiomas).

Twenty one of 24 FNH cases matched at least 3 criteria for its recognition (14 matched 4 diagnostic criteria for FNH) (fig. 5). Another 3 lesions matched only 2 of 4 criteria and were therefore the false negative results. The analyzed group included 6 lesions other than FNH which agreed with at least 3 diagnostic criteria for this type of lesion (false positive results): 4 metastases (including 1 secondary focus of cholangiocarcinoma), 1 primary focus of hepatocellular carcinoma, 1 adenoma). Two of these lesions (metastases of melanoma, focus of hepatoma) matched 4 criteria for FNH diagnosis. The sensitivity was 88%, specificity – 97%, positive prognostic value – 78%, negative prognostic value – 98%, accuracy – 95%.

The symptom most frequently observed in FNH focuses (22 out of 24 cases – 95%) was early homogenous enhancement of lesion in the arterial phase which did not include central scar (provided the scar was noticeable). Isointensity

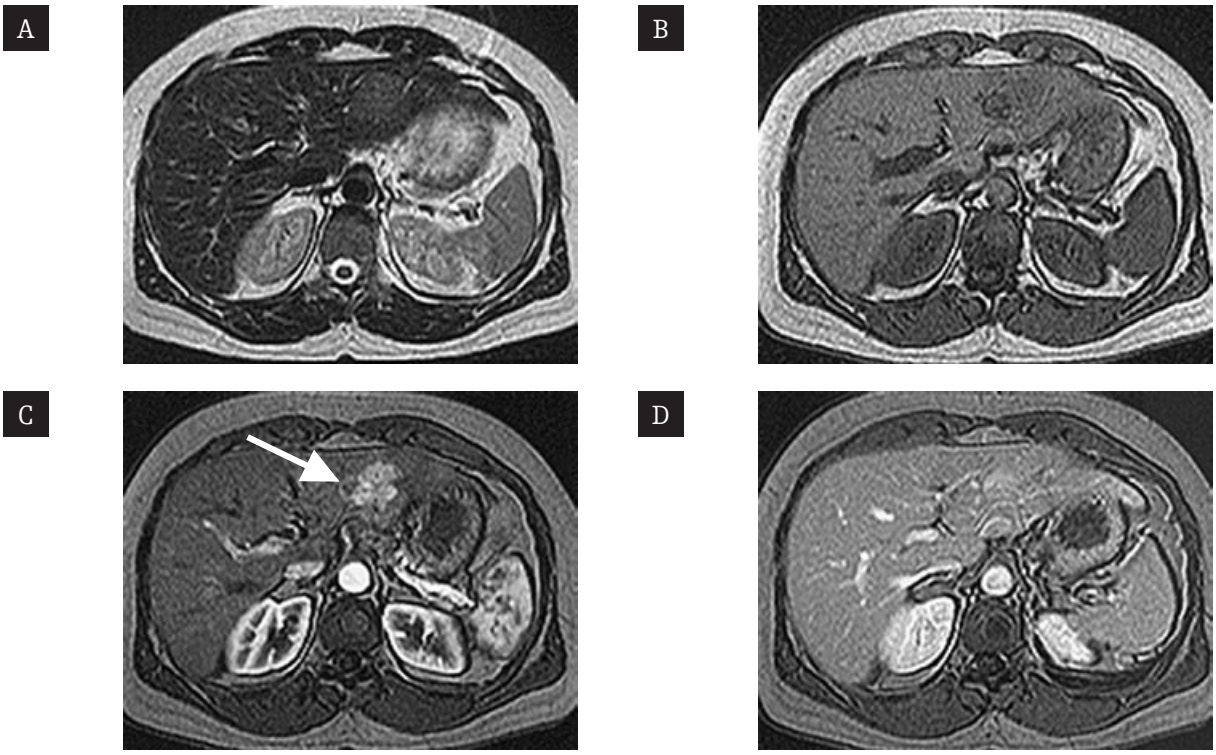

Figure 5. Focal nodular hyperplasia of the liver in sequences: T2 Dual Echo TSE (**A**), T1 GRE (**B**), T1 GRE – arterial phase (**C**), T1 GRE – parenchymal phase (**D**). This lesion is seen only in arterial phase of contrast enhancement (arrow – **C**).

in equilibrium and delayed phases was observed in 88% of cases (21 cases). T1–weighted images showed FNH isointensive in relation to the liver in 62% and hypointensive in 38% of cases. On T2-weighted images tumors were hyperintensive in 58% and isointensive in 42% of cases.

The central scar was observed equally often on T2-weighted images as in the arterial phase of contrast enhancement (each in 9 cases – 38%), but less frequently on T1-weighted images and in delayed phase (each in 7 cases – 29%) and also on T1-weighted images (6 cases – 25%). The scar was hipointensive on T2-weighted images but in the arterial phase an unenhanced (hipointensive) structure was visible. In 6 of 7 cases the scar was noticeable in parenchyma/delayed phases as an area accumulating the contrast agent (hiperintensive), while in 1 case – as a hipointensive structure.

Therefore, in the group of 202 tumors classified as solid lesions (196 true positive results and 6 falsely positive) correct diagnosis was made for all 7 cases of focal fatty liver (sensitivity and specificity – 100%), 21 of 24 FNH cases (sensitivity – 88%, specificity – 97%) and FNH was falsely diagnosed in 6 cases. The remaining 168 lesions of T2 relaxation times shorter than 116 ms, which were neither recognized as focuses of fatty infiltration nor FNH, were qualified to the B group (malignant or benign tumors treated surgically). This group consisted of 158 true positive and 10 false positive results.

In general, the use of presented quantitative-qualitative analysis system for recognition of B group tumors (malignant and benign lesions treated surgically) allowed us to obtain 158 true positive diagnoses, 110 true negative diagnoses (82 lesions other than solid with T2 relaxation times > 116 ms, 7 fatty liver focuses, 21 FNH), 10 false positive results (6 hemangiomas with shortened T2 relaxation times < 116 ms, 3 FNH, 1 inflammation) and 14 false negative results (8 metastatic tumors with elongated T2 relaxation times >116 ms, 6 solid tumors fulfilling FNH recognition criteria). Sensitivity, specificity and accuracy of the B group tumor recognition amounted to 92%, positive prognostic value – 94% and negative prognostic value – 89%.

Discussion

The optimal technique for hepatic focal lesions imaging ought to be characterized by high sensitivity and specificity of detection, as well as accuracy in assessment of character of the lesions. High specificity is especially significant for recognition of most common benign lesions (hemangioma, cyst, FNH), as it enables to cancel out the presence of malignant tumor and complete the imaging diagnostics. Among imaging techniques, MR is the one that helps to obtain the best possible contrast between normal hepatic parenchyma and pathologic tissues, especially on T2 –weighted images.

Hemangioma is the most common focal lesion in the liver and occurs in 2–20% of population [7–9]. MR examination is especially significant in cases of angiomas which do not present typical features in USG (20%) and CT (30–35%) examinations. In MR the diagnosis of angioma consists in assessment of two parameters: typical enhancement after intravenous paramagnetic contrast administration and strong hiperintensity on T2-weighted images [10–13]. Both, qualitative and quantitative analyses of T2-weighted images are also possible. Qualitative analysis is used more frequently as it does not require additional calculations. Such approach is justified by convenience and shorter time needed for qualitative analysis rather than by rationale. Fenlon et al. compared the efficacy of qualitative and quantitative analyses in differentiation of focal lesions in liver with the use of strongly T2-weighted sequences of spin echo and proved a higher efficacy of quantitative analysis in assessment of lesions of the type [14].

Until recently T2 weighted sequences (TE 150 ms) were used for qualitative and quantitative analyses as they were considered best for differentiating angiomas and solid tumors [10, 14–16]. However, sequences of lower T2 weight (TE ≤ 120 ms) are more precise in recognition of solid hepatic tumors due to optimal contrast between the lesion and parenchyma [10]. Until recently it has been believed that including both – moderately and strongly T2-weighted sequences in the protocol of examination was necessary for accurate assessment of number and character of focal lesions in liver [10, 15]. Obtained results seem to negate the above reason as they prove that precise differentiation of focal lesions is possible with the use of moderate T2-weighted TSE sequence (T2 Dual Echo TSE), which was also successfully used to detect tumors in liver.

Quantitative analysis seems necessary in order to assure efficacy of this sequence in differential diagnostics of hepatic tumors. In the examined group of 168 patients (out of 292) with focal lesions located in liver the T2 dual echo TSE sequence showed high accuracy (95%) in differentiation between solid tumors and angiomas or cystic lesions. Another advantage of this technique is the simplification and shortening of MR examination protocol in patients with hepatic tumors, which is achieved by means of omitting strong T2 sequence that was supposed to discriminate cysts and hemangiomas from solid tumors.

In the described material 6 of 59 hemangiomas (10%) were falsely qualified to the group of solid tumors the basis being their untypical short T2 relaxation times (<116 ms). On the other hand, quantitative analysis enabled differentiation of cysts and abscesses from solid tumors with 100% specificity. No cases of lesions with shortened transverse relaxation times were stated in the cysts/abscesses group and their average T2 times (abscesses – 238.6 ms, cysts – 576.6) were significantly longer than T2 of hemangiomas (151.3 ms).

Solid hepatic tumors are in most cases malignant lesions. The most significant exceptions from this rule are benign solid tumors, such as adenoma and focal nodular hyperplasia or malignant cystic tumors, e.g. cystic adenocarcinoma of biliary ducts. Adenoma is a rare tumor, in some cases complicated with life-threatening hemorrhage or far less frequently – with transformation into malignant neoplasm

[7–8, 17–18]. Differentiation between this kind of tumor and malignant lesions does not significantly influence the way of treatment as both – the adenoma and operative malignant tumors – are treated by means of surgical resection [18]. Focal nodular hyperplasia, although more frequent in population, does not carry risks like the adenoma and does not require treatment.

Therefore, it is incredibly important to differentiate FNH from other solid tumors which require surgical treatment (adenoma, malignant tumors). On T1 and T2-weighted images the FNH is characterized by signal intensity similar or same as the liver. T2 relaxation times of FNH are in most cases shorter than T2 relaxation times of other solid tumors. In the analyzed material of 204 solid lesions the mean T2 relaxation time of FNH (63.7 ms) was significantly shorter than mean T2 relaxation time of other solid tumors (86.8 ms) ($p < 0000001$). With the threshold value of 68 ms 4 false negative and 12 false positive recognitions were noted (sensitivity 83%, specificity 93%, accuracy 92%).

Quantitative analysis of transverse relaxation times of focal lesions in liver also carries certain potential disadvantages which can lead to improper recognitions. Hemngioma can be falsely classified as solid tumor in two situations.

First, in case of small lesions (<11 mm) T2 relaxation time can be shortened as a result of partial occupancy which consists in covering not only the hemangioma (with long T2 relaxation time) in the examined section but also a part of hepatic parenchyma (with short T2 relaxation time). As a result mean T2 time, often shorter than the threshold value (116 ms in the examined group) is obtained. The use of thin layers (5–6 mm) in most cases helps to reduce the partial occupancy effect to minimum with simultaneous lack of noticeable worsening in quality of the obtained images. Among 24 analyzed small angiomas (<15 mm) true positive recognitions were made for 19 of them while the T2 relaxation times of the remaining 5 fit into the range of solid lesions (fig. 3).

The second, less frequent reason of misdiagnosis, was hemangioma covered with fibrosis or hyalinization. These regions can imitate solid parts of malignant tumors covered by decomposition what took place in case of a solitary large angioma in which the histopathologic examination showed regions of fibrosis and hyalinization.

The inverse situation – false recognition of hemangioma – is possible with malignant tumors almost entirely covered with decomposition or richly vascularized metastases, often characterized by elongated T2 relaxation times. In cases of tumors which were decomposed the measurements ought to be taken in the peripheral parts which often keep the solid character. In 3 cases of large metastases altered with necrosis the obtained T2 relaxation times were typical for angiomas in spite of taking the measurements in the marginal parts which did not contain enough solid tissue.

According to some authors, several richly vascularized tumors are characterized by elongated T2 relaxation times [19–20]. In the analyzed material, 3 of 21 well vascularized metastases presented transverse relaxation times typical for hemangiomas. Moreover, small, statistically insignificant differences concerning T2 relaxation times of richly vascularized metastases (97 ms) and poorly vascularized (91.8 ms) were also indicated.

Apart from the mentioned 6 false negative results of solid lesions the studied material also contained 2 small (<30 mm), poorly vascularized tumors (metastases of large intestine carcinoma and melanoma) with longer T2 times (>116). In case of these lesions it was not possible to determine the possible reason of their T2 times elongation.

Despite these disadvantages of the method, the results proved that quantitive analysis of hepatic lesions is a very useful technique for assessment of their character. Similar conclusions were presented by authors of other reports on evaluation of utility of quantitive analysis in differentiation of focal lesions [14, 21–23].

In the second phase of hepatic tumors differentiation based on qualitative analysis all 7 focuses of fatty infiltration were confirmed on the basis of applied evaluation criterion – the signal identical or similar to adipose tissue (subcutaneous, retroperitoneal) signal in all examined sequences (sensitivity 100%). Other lesions of identical signal were not observed (specificity 100%).

Focal nodular hyperplasia (FNH) is the third most frequent (after cyst and hemangioma) benign lesion which occurs in liver and constitutes 8% of all primary hepatic lesions. It is far more often found in women than in men, especially between 3rd and 5th decade of life. It is a nodular formation with no capsule created by normal hepatocytes focused around fibrous central scar. FNH contains all elements of normal liver parenchyma but their organization and architecture diverges from the standard [7–8, 17].

The CT and USG image of the FNH is not specific. Although the presence of central scar is considered to be a typical symptom for this lesion, it is only noticeable in 33–50% of imaging examinations (USG, CT, MR) [5–6, 24]. However, even in case of its detection it is not possible to definitely differentiate FNH from malignant solid tumors which can contain central scar as well (hepatocellular carcinoma, especially its fibrolamellar form, cholangiocarcinoma, large hemangiomas). In the examined material the central scar was found only in about 1/3 of cases. It was characterized by hiperintensity on T2-weighted image and typical contrast enhancement – unlike the remaining part of the tumor, it was saturated by the contrast agent after the delayed phase due to the presence of connective tissue. Considering the low sensitivity and specificity of this symptom, it was not included in FNH diagnostic criteria. Detection of scar, as well as typical age and sex of a patient (women aged 20 – 50) can be the additional factor which suggests correct diagnosis.

The FNH recognition in MR examination requires complex analysis of several parameters (T2 relaxation time, signal intensity on T1-weighted images, contrast enhancement in

particular phases of dynamic examination). In the examined group of patients the most common FNH features included homogenous and temporary enhancement in arterial phase (92% of lesions) and isointensity in equilibrium and delayed phases (88% of cases). Such image is not specific for FNH and can also be observed in other tumors – richly vascularized metastases and primary tumors (early HCC) [17, 25]. The specificity of FNH recognition significantly increased when other criteria, such as T2 relaxation times (below threshold value of 68 ms) and signal intensity on T1-weighted images, were taken into consideration. Signal intensity identical or similar to liver on T1 and T2-weighted images is a distinctive feature of FNH.

In the examined group of patients the lesions were isointensive in relation to liver on 62% of T1-weighted images and 42% of T2-weighted images. Most of the remaining FNH lesions, although not isointensive, were characterized by slight hipointensity (on T1-weighted images) or hiperintensity (on T2-weighted images) and short T2 relaxation times (mean 63.7 ms) [26]. The system of complex qualitative analysis that we introduced, based on completion of 3 of 4 criteria set for recognition of this lesion, showed high sensitivity, specificity and accuracy (respectively 88%, 97%, 95%).

Adenoma is a lesion which occurs in population of patients identical to FNH (young women), but less frequently. Differentiation of these benign lesions is significant when we consider different ways of their treatment – adenomas are treated surgically as there is a risk of hemorrhage and sporadic malignant transformation [18,27]. Differentiation of both lesions is not problematic in most cases – adenomas are usually larger tumors (>5 cm), heterogeneous (they contain hemorrhage regions and/or necrosis), well-vascularized and prone to mosaic contrast enhancement [8, 17]. Misdiagnosis is possible in case of smaller adenomas, not altered with hemorrhage or decomposition.

The smaller of 2 adenomas that we examined (dimensions: 28 mm and 56 mm), matched the criteria typical for FNH recognition. Discrimination of such lesions from FNH by means of imaging techniques can be difficult. The report of Grazoli et al. published recently gives hope for improvement as the authors suggest to use the delayed phase of contrast enhancement after Gd-BOPTA administration (after 1–3 hours) in differentiation of both types of lesions. In that phase 96.9% of FNH focuses were characterized by hiper- or isointensity, while all adenomas were hipointensive (sensitivity 96.9%, specificity 100%) [28].

One of the limitations of his study is that final diagnoses of most of benign lesions were stated based on results of control examinations which neither showed their growth nor change of morphology, and on correlation with other imaging techniques, e.g. the recognitions of FNH were made on the basis of histopathologic examinations only in 4 of 15 patients. Verification of the remaining lesions (in 11 patients) which was carried out does not guarantee complete exclusion of small adenomas imitating focal nodular hyperplasia in the group of tumors diagnosed as FNH.

Conclusion

The protocol of qualitative-quantitative analysis proved to be very useful for presurgical differentiation of focal lesions in liver, as it enabled discrimination of malignant and benign tumors group treated surgically with high sensitivity (95%) and specificity (91%).

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