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Usefulness of contrast-enhanced phase-inversion harmonic power Doppler imaging in the diagnosis of hepatic hemangiomas

Przydatność szarokopasmowego odwróconego w fazie obrazowania harmonicznego z wykorzystaniem Dopplera mocy w diagnostyce naczyniaków wątroby.

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Summary

Background: The purpose of this study was to assess the sensitivity of echo-enhanced phase-inversion power Doppler sonography (PI) in depicting the vascular enhancement of hemangiomas, thus confirming the exact diagnosis.

Material/Methods: Twenty patients were examined. The presence of hemangioma was confirmed by surgical resection (n=2), two-phase (hepatic arterial and portal phases) contrast-enhanced spiral computed tomography (n=8), or sonographic follow-up, which showed no change in lesion size for at least 6 months (n=10). Prior to enhanced sonography, all patients had undergone both native B-mode and tissue harmonic imaging mode sonography, color Doppler, and power Doppler helical CT examinations. After injection of 2.5 g of Levovist intravenously, analysis of the arrival of contrast agent was performed by phase-inversion power Doppler sonography.

Results: Evaluation of the 20 patients revealed 37 hemangiomas. Color and power Doppler sonography were non-specific for hemangioma in our examination. However, based on the phase-inversion power Doppler sonography findings, the 20 patients with the 37 hemangiomas were diagnosed. Typical features of hemangioma, such as peripheral globular and rim-like enhancement followed by a slow centripetal fill-in, were clearly visible. In 3 cases of small hemangiomas, computed tomography had failed to disclose the pathology, while phase-inversion sonographic images were completely suggestive of what was later confirmed at 6 months follow-up.

Conclusions: Based on our results, we can recommend phase-inversion power Doppler sonography in the differential diagnosis of hemangioma by visualizing the characteristic rim-like enhancement pattern followed by a slow centripetal fill-in as an excellent diagnostic modality.

Key words: liver • hemangioma • contrast media

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Background

Hepatic hemangiomas are the most frequent benign liver tumor, of still unknown etiology. Several factors like specific liver-hemangioma gene, endogenous proliferative factors, pharmacological agents have been postulated to promote tumor growth. Hepatic hemangiomas are mesenchymal in origin, usually solitary and composed of atypical, irregular blood vessels [1]. Hemangiomas can be divided: capillary constituted by vascular ducts, cavernous with wide and tortuous vascular spaces, hemangiomas with degenerative changes, microvascular, macrovascular and avascular pattern hemangiomas. The incidence rate is higher amongst women and increasing with age. Hemangiomas present a diagnostic challenge because they can be diagnosed as hypervascular or hypovascular malignancies of the liver and can coexist or even mimic other benign and malignant hepatic lesions as focal nodular hyperplasia, hepatic adenoma, hepatic cyst, hemangioendothelioma, hepatic metastasis, hepatocellular carcinoma [2]. Sonography is still considered as only initial diagnostic tool with the accuracy that can not match that of CT or MRI. Improvement in US diagnostic technology has drawn much attention to differential diagnosis of hepatic focal lesions. The cavernous hemangiomas are the most often found in general population. They may reach very large size although in majority they are rather small. The accurate diagnosis can be very difficult in case of small and medium sized ones but is very important for further treatment. Failure to proper assesses the nature of the lesion might exposure patient to dangerous biopsy or lead to harmful treatment regiment. For the exact differential diagnosis usually data collected by power Doppler has been satisfactory. In difficult cases, dynamic CT is still considered the final resort. The 2nd harmonic power Doppler filtering has been a huge lap forward in sonographic technology but still a need to use filters lowers the accuracy and quality of imaging [3]. A new potentially excellent diagnostic method is contrast-enhanced, phase-inversion harmonic power Doppler imaging which is presently investigated. It is a very simple examination therefore, it may prove to represent a new area in the ultrasonic screening, confirmation, and differentiation of hepatic lesions. What more, contrast agent-Levovist (Schering, Berlin, Germany) has the unique characteristic of remaining in liver parenchyma even after blood-pool clearance thus enabling recognition of subcentimeter lesions [4,5].

The purpose of this study was to assess the sensitivity of echo-enhanced, phase-inversion (PI) power Doppler sonography in depicting the vascular enhancement of hemangiomas thus confirming the exact diagnosis.

Materials an methods

This study is a part of a project assessing performance of pulse inversion contrast-enhanced power Doppler sonography in the differential diagnosis of hepatic masses and comparing it with the results of unenhanced color, power Doppler sonography, dynamic computed tomography and magnetic resonance imaging. Our institutional review board approved this study. The patients were enrolled over a – 12-month period. All patients gave full informed consent for our study. In the present study, all patients previously diagnosed of having hemangiomas were evaluated. From January to December 2002, 20 patients were investigated. Fourteen were female, six were men, aged 26 to 82, mean age 48,7 years. A routine diagnostic approach was utilized in every single case which consisted of B-mode gray scale and harmonic US, color and power Doppler US, enhanced power Doppler US, dynamic helical CT and in some cases dynamic MRI. PI mode imaging was performed by a single senior radiologist who was blinded to the patient?s identity and the results of other methods at the time of examination. Final diagnosis was made based on at least two positive imaging examination (e.g. sonography, dynamic helical CT or MRI) or histologic examination by means of surgical resection. The CT scans were obtained by using a dynamic serial hemangiona protocol with complete or near-complete fill with contrast agent on delayed scans obtained 5–10 minutes after bolus [6].

Imaging

All sonographic examinations were performed by one senior radiologist using Siemens SONOLINE Elegra with multihertz convex probe (2.5 to 4 MHz) equipped with Ensemble™ Contrast Imaging (ECI) using Phase Inversion technology developed by Siemens Medical Systems, Inc., Ultrasound Group. All patients underwent gray scale sonography and size, localization, echogenicity, homogeneity, were assessed. After this examination, vascularity and vascular architecture of the lesions were assessed with unenhanced and echo-enhanced power Doppler sonography.

Before echo-enhanced power Doppler sonography a galactose-based blood pool contrast agent, SHU 508A (Levovist, Schering AG, Berlin, Germany), was administrated in an antecubital (2,5 g) vein by bolus injection during 5 seconds. Levovist consists of granules of D-galactose microparticles (99.9%) and palmitic acid (0.1%) and has to be shaken for 10 s after adding 7 ml of distilled water. The microbubbles size of 2–8 μm, mean 3 μm lets them to cross freely through capillary beds. This results in concentrations 300 mg/ml galactose respectively. Prior to injection, the suspension must be allowed to stand for 2 min. Eight seconds after the start of the injection echo enhancement has been visible in the arterial phase of the liver. At this point, fine-tuning of the gain settings, size of the color window and position of the focal point was performed. Consecutive images were taken in after every 3–5 seconds periods in arterial, capillary, and 5–10 seconds in portal and late phases.

The phase-inversion technology uses two consecutive US pulses that are 180° out of phase. The resulting echoes are added to form the final ultrasound image line. Linear signals, such as tissue, are cancelled whereas non-linear echoes from microbubbles summate to produce a signal. Non-linearity is caused by a different way in which microbubbles compress and decompress. As these particles are strong non-linear scatterers, the technique is extremely sensitive to US contrast agents.

Results

The 20 patients' evaluation revealed the existence of 37 hemangiomas. Seven patients had multiple hemangiomas.

Table 1. The localization of the lesions in the liver in accordance with Couinaud's Topography in B-mode US (N=37).
Tabela 1. Lokalizacja zmian w wątrobie w odniesieniu do topografii Couinaud`a w badaniu B-mode US.

	Right part (n=26)				Left part (n=11)			
Segment	VIII	VII	VI	V	IV	III	II	I
n of hemangiomas	2	2	1	1	2	1	0	0
real n of lesions	10	6	6	4	4	4	2	1
Size of lesions (mean in mm)	21.3	19.7	25.3	14	8.5	30	20.5	12.6

Table 2. The localization of the hemangiomas in the liver in accordance with Couinaud's topography in PI scans and in CT (N=37).
Tabela 2. Lokalizacja naczyniaków w wątrobie w odniesieniu do topografii wg Couinaud`a w badaniu PI i CT (n=37).

	Right part (n=26)				Left part (n=11)			
Segment	VIII	VII	VI	V	IV	III	II	I
n of hemangiomas in CT	10	6	6	4	2	4	2	0
n of hemangiomas in PI	10	6	6	4	4	4	2	1

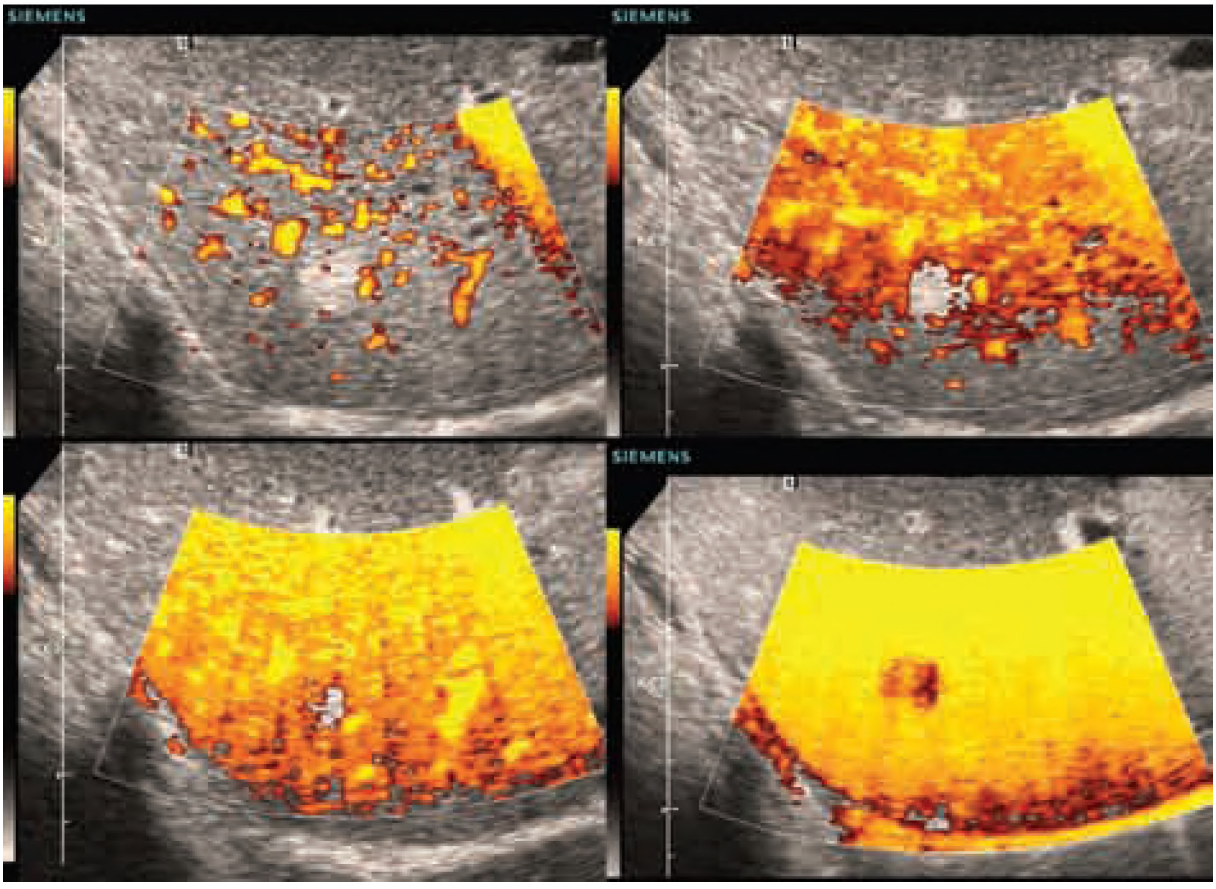

Figure 1. Consecutive phases: arterial, capillary, portal I, and portal II. Centripetal fill-in of hemangioma.
Rycina 1. Kolejne fazy: tętnicza, włośniczkowa, wrotna I i wrotna II. Dośrodkowe zakontrastowanie naczyniaka.

The diameters of the hemangiomas as measured on gray scale US were 4.1 to 61.8 mm (mean 23.04 mm). All lesion locations were described in accordance with the Couinaud's segmental anatomy of the liver (table 1). The classic finding of hemangioma that of a well defined, echogenic mass was seen only in 15 cases (40,5%). The echogenity of remaining lesions to the adjacent liver was, hypoechoic in 8 cases (5 homogenous and 3 in-homogenous) (21,6%) and mixed in 14 cases (37,8%) – all inhomogeneous, compared to surrounding liver parenchyma.

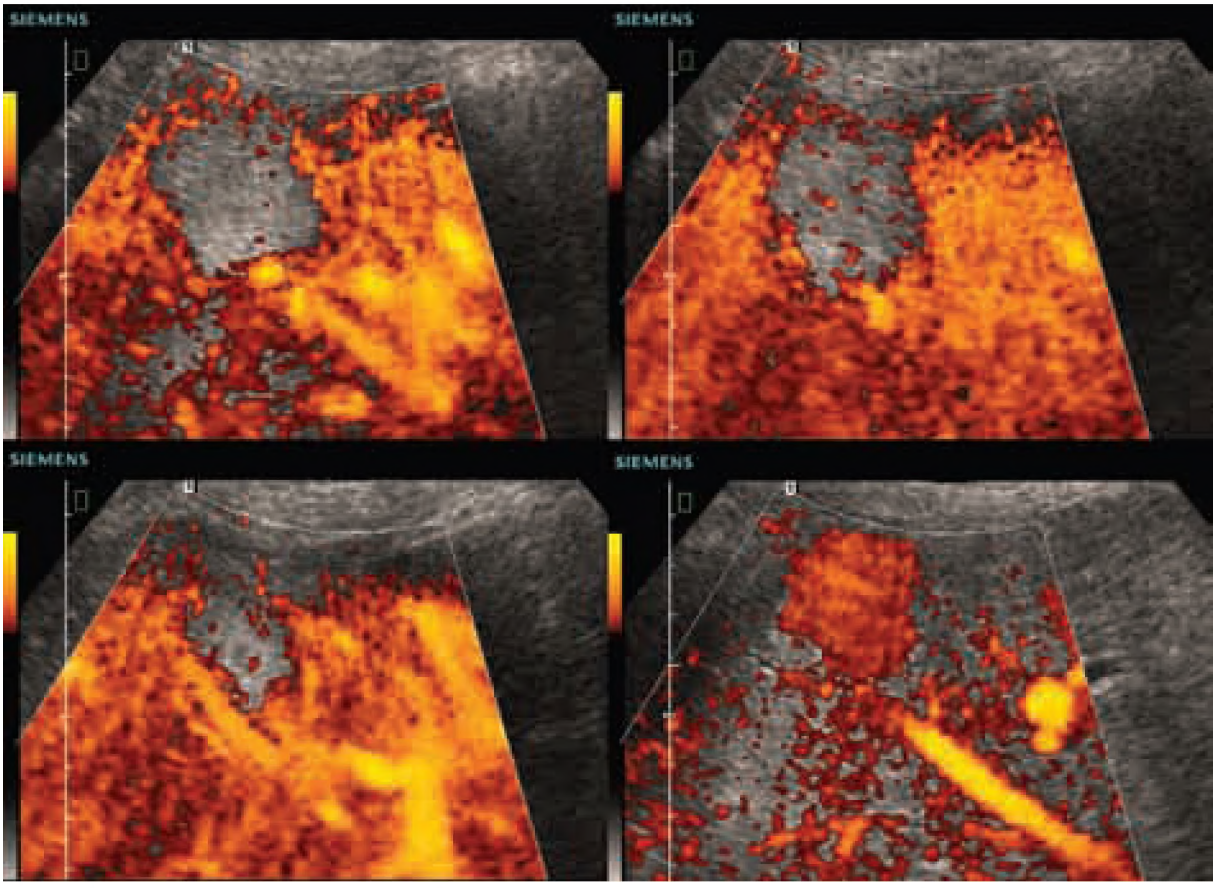

Figure 2. Consecutive phases: arterial, capillary, portal, and late. Hemangioma was remarkably longer enhanced than adjacent liver parenchyma.
Rycina 2. Kolejne fazy: tętnicza, włośniczkowa, wrotna i późna. Wzmocnienie w naczyniaku utrzymywało się dłużej niż w miąższu watroby.

There were no typical features of hemangiomas seen in unenhanced color and power Doppler sonography. Only occasionally arteries and veins were traced and in two cases good visualization of arteries with low flow resistance were observed. Addiction of contrast agent to power Doppler examination has worsened imaging considerably. The presence of hemangioma was positively diagnosed in 37 (100%) lesions by contrast-enhanced, wide-band phase-inversion harmonic power Doppler imaging (table 2). Typical enhancement of the hemangioma was prominent in all cases. Enhancement of lesions happened noticeably later than liver parenchyma. Apart from two cases during early arterial phase there were (up to 15s) no peritumoral signals at all. In capillary phase in two cases centripetal spread of contrast was seen, in 19 cases peripheral globular enhancement was obvious, in 3 cases complete homogenous fill-in was observed, rim-like enhancement was pronounced in 13 cases. In portal and late phase centripetal fill-in was clearly visible in 32 cases (fig 1) and the rest of cases spot-like peritumoral enhancement "blood pools". These 32 lesions were then remarkably longer enhanced than adjacent parenchyma (fig 2). In three cases, CT has failed to disclose beyond any doubt the nature of shown lesions (91%). All three were located in left lobe seg. II. No adverse effects occurred after administration of SH U 508A. Duration of echo enhancement was sufficient and lasted up to 8 minutes after bolus injection of Levovist.

Final diagnosis of hemangiomas was made at histologic examination by means of ultrasound-guided fine-needle biopsy in 1 patient, surgical resection in 2 patients with progressive thrombocytopenia and in 17 patients was made by dynamic helical CT or MRI.

Discussion

Resection means the total or partial removal of an organ. For people diagnosed with liver cancer, liver resection offers the best chance for cure or long-term survival. Removal of a liver tumor is the surest method of eradicating the cancer and preventing its spread to other parts of the body. Although surgical techniques have improved enormously lately, the proper differential diagnosis, especially of small lesions still poses great challenge. Both sides of a misfortunate coincidence can be catastrophic for the patient either exposing him for unnecessary surgery or delaying life-saving treatment [7]. In our study we have tried to evaluate the accuracy of the phase-inversion power Doppler US in depicting the characteristic features of hemangiomas.

Hemangiomas are the most common benign tumor of the liver. According to post mortem records up to 7% of patients had them. In 20% they are multiple. More common in females [8]. They are usually localized at the periphery of the organ. Microscopic view demonstrates an overgrowth

of enlarged endothelial lined vascular spaces. While generally asymptomatic, these tumors have been associated with abdominal pain, fullness and belching. The complications are similarly rare. The clinical problem with these incidentally discovered tumors is to distinguishing them from malignancies, especially metastases [9]. Apart from this fatal hemorrhage after needle biopsy of hemangioma is very well documented [10].

Among imaging modalities used to evaluate hemangiomas are US, CT, MRI and Tc-99m RBC single photon emission CT (SPECT).

Until recently sonographic Doppler methods have not been much appreciated in the differential diagnosis of hepatic tumors. It is generally due to inability to acquire a proper signal-to-noise ratio, both background noise and clutter. This is partly because the flow signals from small vessels or those located deep tissues cannot be sufficiently separated from the background noise.

In our institution, as everywhere else, all modern diagnostic techniques are sometimes used. All have advantages and shortcomings.

B-mode US is quick, cheap, and free from ionizing radiation. In our study, topography of all lesions was clearly visualized on conventional scans. Well-defined, echogenic mass is the mark of hemangioma. However, this appearance can also be seen in adenomas, hepatocellular carcinomas and metastases. Therefore, generally conventional US are used to assess localization, size but not specific features of hemangioma [11]. In our study the correct diagnosis was possible only in 15 cases (after the exclusion of cancer disease and after reassuring of non-enlargement for 3 months of the periodical observation). The mixed echogenity in 16 cases (43%)-all inhomogeneous can be considered atypical for a hemangioma.

Color and power Doppler sonography is considered of no use in diagnosing slow blood flows, which are typical for hemangiomas. The lowest detectable flow velocity of power Doppler US (about 0,5 cm/s) is much over the range of human capillary flow (max 0,1 cm/s). Recent reports indicate that most signals within hemangiomas most likely represent artifacts produced from stationary strong echoes of hemangiomas rather than true capillary flow [12]. In our paper no typical pattern of enhancement of hemangiomas was observed. Only some nonspecific features as low flow resistance arteries were visualized in two cases (AV shunts?). We have noted high levels of artifacts associated with the microbubble contrast agent. Blooming artifacts are nearly impossible to prevent or minimize successfully. Another problem is tissue motion, especially caused by the heart, which degrades visualization in the left lobe. Therefore specific features like centripetal fill-in and persistent enhancement could not be shown in color nor power Doppler sonography, enhanced or not [13].

Introduction of contrast agents has improved the performance of power Doppler sonography.

The limitation of 2nd harmonic contrast-enhanced power Doppler sonography is its susceptibility to tissue motion artifacts called "blooming". Thus, implementation of this method in patients with poor breath-holding ability and close to great vessels becomes prohibitive. Furthermore frequency-filtering using in this method results in losing much information because non-linear backscatter is distributed through a board spectrum of frequency.

None mentioned above limitations had appeared with contrast-enhanced, wide-band phase-inversion harmonic power Doppler imaging. In recent papers some authors found enhancement of liver lesions to insufficient. We are of opinion that it is extremely important to overcome this obstacle to interrupt the scanning process for a sufficient time (interval-delay imaging) to allow the agent to wash into the capillary bed. Then all US pulses should produce the best harmonic signals because they will arouse intact microbubbles that have flown into the microvasculature. Therefore, continuos scanning can only decrease the accuracy of the method! In our study, all images of hemangiomas were very evident. All have filled-in latter and enhancement have been visible longer than normal liver parenchyma. Apart from 2 cases in which the high-flow hemangiomas were diagnosed, the rest have shown typical pattern of enhancement-peripheral globular, rim-like or homogeneous with progressive centripetal fill. In no case the visualization of the blood vessel inside of hemangioma was achieved. The enhancement pattern in two high-flow hemangiomas was a bit different in time. The centripetal contrast uptake was over in capillary phase and decreasing during portal venous phase. Our observations are similar to other authors using pulse-inversion US [14,15].

Although in these papers lower sensitivities obtained can be explained. The gray-scale US could not deliver so many details as power Doppler US. Another reason is that analyzing just one or two characteristic feature of hemangioma self-restrict the accuracy.

By contrast, based on CT helical scan results it was sometimes hard to diagnosis hemangioma. The classic finding of a round, low attenuation lesion with peripheral puddling is not always evident. In our study, three lesions had not attenuation greater or equal to the liver causing the radiologist to fail to recognize it as hemangioma. Leslie et al had noted similar problems with CT scans [16].

Conclusions

According to our results, contrast enhanced, phase-inversion harmonic US allows demonstration of typical enhancement patterns in hemangiomas, thus providing useful diagnostic information for their characterization. It is superior to conventional, color, power Doppler US. It is comparable with CT lacking its main disadvantages like iodinated contrast, ionizing radiation, not mention costs and availability. We are of opinion that further technological development can introduce this method into the modern radiology further more.

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