OBJECTIVE. We conducted a prospective study to compare sonography, color Doppler sonography, and contrast-enhanced sonography for the detection and characterization of portal and hepatic vein thrombosis complicating hepatic malignancies.

SUBJECTS AND METHODS. Three hundred sixteen patients with biopsy-proved hepatic tumors were studied at baseline and 3 months later with sonography, color Doppler sonography, and contrast-enhanced sonography. Thrombosis was defined as the presence of intraluminal echogenic material at sonography, absence of intraluminal color signals at color Doppler sonography, and presence of nonenhancing intraluminal area at contrast-enhanced sonography. Thrombi were considered malignant if they displayed continuity with tumor tissue at sonography, intrathrombus color signals at color Doppler sonography, and enhancing signals at contrast-enhanced sonography, both having arterial waveforms at Doppler spectral examination. Definitive diagnoses were obtained by sonographically guided biopsy except for thrombi displaying at conventional sonography unequivocal continuity with tumor tissue.

RESULTS. Thrombosis was detected in 79 (25.0%) of 316 patients at baseline and in 83 (26.3%) of 316 patients after 3 months. Eighty-one (97.6%) of the 83 thrombi were malignant. Definitive diagnosis was performed by imaging in 60 (72.3%) of the 83 cases and by biopsy in 23 cases (27.7%). For thrombus detection, contrast-enhanced sonography displayed significantly higher sensitivity than color Doppler sonography (p = 0.004) and borderline superiority over sonography (p = 0.058). For thrombus characterization, contrast-enhanced sonography was significantly more sensitive than color Doppler sonography (p < 0.0005) and conventional sonography (p = 0.02).

CONCLUSION. Contrast-enhanced sonography is superior to sonography and color Doppler sonography for the detection and characterization of portal and hepatic vein thrombosis complicating hepatic malignancies.
Subjects and Methods

Subjects

The study protocol, which was fully concordant with the ethical principles of the Declaration of Helsinki, was approved by the institutional ethics committee. Each participant provided written informed consent for all study procedures.

Between January 2002 and June 2003, sonography, color Doppler sonography, and contrast-enhanced sonography studies of the hepatic and portal veins were performed on 324 consecutive patients with malignant hepatic tumors. All diagnoses of malignancy had been confirmed by sonographically guided biopsy using a 21-gauge cutting needle (Biomol, Hospital Service), and all patients underwent abdominal helical CT for tumor staging. The latter was done using a third-generation single-detector CT scanner (Somatom Plus, Siemens Medical Solutions) with conventional technique [21].

Eight patients whose livers could not be adequately visualized because of anatomic peculiarities (n = 2) or substantial fatty degeneration (n = 6) were excluded from the study. The study population was composed of the remaining 316 patients. They included 199 men and 117 women who ranged in age from 26 to 88 years (mean ± SD, 67 ± 10 years). Of these patients, 220 had hepatocellular carcinoma (HCC), 14 had cholangiocarcinoma, and 82 had hepatic metastases. The latter were from colorectal cancer (n = 52), breast cancer (n = 10), stomach cancer (n = 6), carcinoid tumors (n = 3), or other epithelial tumors (n = 11). Multiple tumor nodules were detected in 169 (53.5%) of the 316 patients, and the maximum nodule diameter was greater than 3.0 cm in 162 patients (51.3%). At recruitment and during their participation in the study, none of the patients was taking any drugs that affected coagulation.

Sonography Techniques and Diagnostic Criteria

All sonography examinations were performed on a Prosound SSD 5500 ePHD (extended Pure Harmonic Detection) scanner (Aloka) and multifrequency convex array transducers (3.0–6.0 MHz) with suitable technology for microbubble detection—for example, mechanical index (MI) settings of 0.04 or lower, second harmonic filtering, and phase detection. Each examination was digitally recorded (Premium Digital Videocassettes and DVCAM model DSR-20 DMP recorder, both from Sony).

The examination began with a preliminary gray-scale sonography examination of the upper abdomen. Sonography scans were obtained in the sagittal, transverse, oblique, and intercostal planes using conventional technique and second harmonic filtering. The intrahepatic branches of the portal vein, splenic and mesenteric veins, hepatic veins, and inferior vena cava were then examined with color Doppler sonography. The color Doppler sonography images, in which red and blue indicated flow toward and away from the transducer, respectively, were displayed on-screen with simultaneous B-mode gray-scale or Doppler spectral examination images. A number of flow settings were used depending on the underlying flow velocity, and color gain was adjusted during each examination to select the highest value allowing artifact-free images. If a thrombus was detected, the Doppler-encoded area was restricted to maximize color sensitivity and frame rate, and the thrombus was carefully examined for internal color signals. Any signal detected was subjected to Doppler spectral examination using a sample volume of 1.5–3.0 mm without angle correction.

Each patient then underwent contrast-enhanced sonography using an aqueous suspension of stabilized sulfur fluoride microbubbles (SonoVue, Bracco) as a contrast agent, in accordance with the manufacturer’s instructions. The product consists of 25 mg of lyophilized powder, which is reconstituted in 5.0 mL of 0.9% sodium chloride solution to produce a solution containing sulfur hexafluoride microbubbles at a concentration of 8 µL/mL. Shortly after preparation, this solution was administered as a 2.4-mL bolus via a 19-gauge IV cannula in an antecubital vein. The injection was immediately followed by a bolus of 5.0 mL of 0.9% sodium chloride solution. A chronometer displayed on the screen was used to determine the temporal characteristics of flow enhancement. Contrast-enhanced sonography scans were obtained in a harmonic mode with an MI of 0.04 or less. If a thrombus was detected (Fig. 1), up to two
Sonography of Portal and Hepatic Venous Thrombosis

Fig. 2—Doppler spectral examination in 52-year-old man of enhancing intrathrombotic signals detected during contrast-enhanced sonography. A, Oblique subcostal scan with longitudinal view of common trunk of portal vein during portal phase of contrast-enhanced sonography. Within enhanced lumen, nonenhancing area (thrombus) measuring about 4.0 mm in diameter can be seen adhering to wall of vein. At center of thrombus, pulsating punctate enhancing signal reflects intrathrombotic vascularization. B, Doppler spectral examination of pulsating punctate enhancing signal within thrombus reveals arterial waveform. C–E, Helical CT scans. In arterial phase (C), hyperdense area that represents hepatocellular carcinoma (HCC) nodule is seen in segment IV of liver. On same scan, in portal (D) and late (E) phases, branch of portal vein adjacent to HCC nodule appears to be fully patent, with no sign of small neoplastic thrombus seen on contrast-enhanced sonography.
additional boluses of SonoVue were injected, and the thrombus was examined more closely for pulsating, enhancing signals within its boundaries (Fig. 2A). When present, these signals were subjected to Doppler spectral examination, as described (Fig. 2B).

At the end of the baseline examination, digitally recorded images obtained with each of the three sonography techniques were subjected to independent frame-by-frame review by a team of two reviewers who have been trained in and are experienced with Doppler techniques. For each method, a diagnosis of thrombosis or nonthrombosis was recorded; in the former case, the thrombus was also diagnosed as benign or malignant. All diagnoses represent consensus decisions reached by the two reviewers and were based on the criteria shown in Table 1.

In cases with sonographic diagnoses of thrombosis at baseline, we also analyzed the helical CT scans obtained for tumor-staging purposes. This analysis was limited to those cases in which the baseline sonography studies and the helical CT examination had been performed within 5 days of one another. The scans that satisfied these criteria were reviewed by two experienced radiologists. Using the criteria recommended by Tublin et al. [22], the reviewers classified each CT scan as positive or negative for thrombosis (Fig. 3). The sole purpose of this analysis was to obtain a preliminary estimate of the relative sensitivity of CT in detecting portal or hepatic vein thrombosis. The CT diagnoses had no impact on the diagnoses of thrombosis made by sonography, color Doppler sonography, or contrast-enhanced sonography or on the definitive diagnoses.

Three months after the baseline examinations, sonography, color Doppler sonography, and contrast-enhanced sonography were repeated on all patients to verify the initial diagnosis. The second examination was performed and evaluated as described.

### Definitive Diagnoses of Thrombosis and Thrombus Malignancy

At the end of the study, patients were definitively classified as negative for thrombosis if none of the three sonography techniques had revealed any evidence of thrombosis at the baseline or 3-month study. In the remaining cases, one or more of the baseline or 3-month examinations was positive for thrombi. In these cases, the definitive diagnoses of thrombosis and thrombus malignancy were based on sonographically guided aspiration biopsy performed using a 21-gauge Chiba needle (Ecoject, Hospital Service) [16] (Fig. 4). The exception to this rule was for thrombi that showed unequivocal evidence of continuity with the tumor tissue (Fig. 5). In these cases the nature of the thrombus was assumed to be the same as that of the biopsied tumor. This feature is widely accepted in CT and MRI studies as sufficient proof of portal thrombus malignancy [14, 15].

### Statistical Calculations

The sonography, color Doppler sonography, and contrast-enhanced sonography diagnoses regarding thrombus detection and characterization made using the criteria in Table 1 were checked against the definitive diagnoses performed as described, and the sensitivity [true-positives / (true-positives + false-negatives)] and specificity [true-negatives / (false-positives + true-negatives)] of each technique was computed. In both cases, exact 95% confidence intervals (CIs) were calculated using software (version 7.0, Stata Statistical Software 2002, Stata Corp.). Chi-square and Fisher’s exact tests were used to evaluate differences in the sensitivity and specificity of the different techniques, as appropriate [23]. A p value of less than 0.05 was considered indicative of statistical significance. All tests were two-sided.

### TABLE 1: Diagnostic Criteria Used for Detection and Characterization of Portal and Hepatic Vein Thrombosis by Different Sonography Techniques

<table>
<thead>
<tr>
<th>Diagnosis of Portal and Hepatic Vein Thrombosis</th>
<th>Gray-Scale Sonography</th>
<th>Color Doppler Sonography</th>
<th>Contrast-Enhanced Sonography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection: definition of thrombosis</td>
<td>Intraluminal echogenic material</td>
<td>Complete or partial absence of color signals within the vessel lumen</td>
<td>Complete or partial absence of enhancement within the vessel lumen</td>
</tr>
<tr>
<td>Characterization: criteria for diagnosis of malignancy</td>
<td>Continuity between thrombus and tumor tissue</td>
<td>Intrathrombus color signals with arterial waveforms at Doppler spectral examination</td>
<td>Intrathrombus pulsating enhanced signals with arterial waveforms at Doppler spectral examination</td>
</tr>
<tr>
<td>With Spectral Doppler Examination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alone</td>
<td>With Spectral Doppler Examination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Only</td>
<td>Alone</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| For the four thrombi involving the hepatic veins: three (5.9%) of 76 found in patients with HCC; one (33.3%) of three patients with cholangiocarcinoma, and one (25.0%) of four in patients with metastases. Fifty-five (66.3%) of the 83 thrombi were occlusive and 60 (72.3%) were continuous with the tumor tissue. Seventy-nine (95.2%) of the 83 thrombi were detected during the baseline examination, using the diagnostic criteria listed in Table 1: 72 (86.7%) of the 83 thrombi were detected on sonography; 67 (80.7%) of the 83, on color Doppler sonography; and 79 (95.2%) of the 83, on contrast-enhanced sonography. The remaining four thrombi (4.8%) were first detected on one or more of the sonography studies performed during the 3-month examination. On the hypothesis that these thrombi might have been present at the baseline examination in a smaller, less detectable form, we classified these four cases as false-negative detections for all three sonog-
Sonography of Portal and Hepatic Venous Thrombosis

Fig. 3—Helical CT scan shows malignant portal vein thrombus in 69-year-old man. During arterial phase, thrombus appears as iso- to hypodense intraluminal area with dense linear enhancement.

Fig. 4—Sonographically guided fine-needle aspiration biopsy of portal vein thrombus in 69-year-old man. Sonography scan shows tip of needle is within hypoechoic thrombus.

Fig. 5—Intercostal sonography scan reveals direct extension of hepatocellular carcinoma tissue into main portal vein in 71-year-old man. This finding represents unequivocal evidence of continuity between thrombus and tumor tissue and is a reliable indicator of thrombus malignancy.

Contrast-enhanced sonography was more sensitive in thrombus detection than either color Doppler sonography (p = 0.004) or sonography (p = 0.058), although the latter displayed only borderline significance. With respect to color Doppler sonography, contrast-enhanced sonography provided significantly higher sensitivity for the detection of thrombi with and without continuity with the tumor tissue (p < 0.05) and occluding and nonoccluding thrombi (p < 0.05). All three sonography techniques were characterized by 100% specificity.

As shown in Figure 6, contrast-enhanced sonography was more sensitive in thrombus detection than either color Doppler sonography (p = 0.004) or sonography (p = 0.058), although the latter displayed only borderline significance. With respect to color Doppler sonography, contrast-enhanced sonography provided significantly higher sensitivity for the detection of thrombi with and without continuity with the tumor tissue (p < 0.05) and occluding and nonoccluding thrombi (p < 0.05). All three sonography techniques were characterized by 100% specificity.

Forty-eight of the 79 patients whose thrombi were detected at the baseline sonography examination had undergone helical CT within 5 days of sonography studies. Review of these 48 CT scans revealed evidence of thrombosis in only 20 (41.7%). The thrombi visualized on the CT scans included two (11.1%) of 18 that had appeared to be nonocclusive on sonographic studies; 18 (60%) of 30 that were fully occlusive; 13 (35.1%) of 37 that showed clear continuity with the tumor tissue; and seven (63.6%) of 11 that were non-continuous with the tumor tissue.

Thrombus Characterization

Eighty-one (97.6%) of the 83 thrombi were definitively classified as malignant. In 60 (74.1%) of 81 cases, this diagnosis was based on clear sonography evidence of thrombus continuity with the tumor tissue. In these 60 thrombi, color Doppler sonography revealed intrathrombus vascular signals in 52 cases (86.7%) but Doppler spectral examination visualization of arterial waveforms was possible in only 47 (78.3%) of 60 cases. In contrast, contrast-enhanced sonography detected pulsating enhanced signals whose arterial waveforms were confirmed by Doppler spectral examination in 60 of 60 cases. In the remaining 21 (25.9%) of 81 cases, the diagnosis of thrombus malignancy was based on sonographically guided biopsy. All 21 of these thrombi were visualized on contrast-enhanced sonography and 14 (66.7%) of 21 on color Doppler sonography, but only four (19.0%) of 21 met the criteria for malignancy on both sonography studies. In the other 17 (81.0%) of 21 cases, color Doppler sonography failed to reveal any color signals within any of the 10 thrombi it detected; in contrast, contrast-enhanced sonography detected enhancing pulsating signal within 11 (64.7%) of 17 thrombi and no enhancing pulsating signals in the remaining six (35.3%).
The other two (2.4%) of 83 thrombi were ultimately classified as benign. In both cases, the definitive diagnosis was based on cytologic examination of sonographically guided biopsies because neither of these thrombi had presented continuity with the tumor tissue on gray-scale sonography. In one case, the color Doppler sonography and contrast-enhanced sonography findings at baseline and 3 months were also negative for thrombus malignancy. In contrast, the second benign thrombus met both the color Doppler sonography and contrast-enhanced sonography criteria for malignancy (Table 1) on the baseline examination, in clear contradiction with the biopsy, which showed no cytologic evidence of tumor cells. Three months later, a repeat contrast-enhanced sonography examination revealed that the vascular signals, which had previously appeared to be intrathrombotic, were actually related to a small branch of the left hepatic artery crossing the portal vein at the site of the thrombus. This case was thus classified as a false-positive characterization for color Doppler sonography and contrast-enhanced sonography.

The relative sensitivities of the three sonography techniques in thrombus characterization are shown in Figure 7. Contrast-enhanced sonography was significantly superior to color Doppler sonography for the characterization of malignant thrombi \( p < 0.0005 \). Compared with sonography, it displayed higher sensitivity for identifying malignancy in all thrombi \( p = 0.02 \) and in those without continuity with tumor tissue \( p < 0.001 \). Because only two thrombi proved to be benign, the specificities of the three sonography techniques could not be determined in this study.

**Thrombus Patterns on Contrast-Enhanced Sonography**

Figure 8 shows schematic representations of the different thrombus patterns detected on contrast-enhanced sonography both in patients with liver tumors and in those with long-standing benign portal thrombosis. Clinical examples of each pattern are provided in Figures 9–13. Pattern 1 is typical of thrombi without internal vascularization—that is, benign thrombosis (Figs. 9 and 10). Thrombus enhancement is absent in all three phases. Pat-
tern 2 (blooming) consists of diffuse thrombus enhancement that is visible only during the early arterial phase. It reflects diffuse vascularization of a thrombus similar to that of the tumor tissue from which it originates (Fig. 11). Patterns 3 (linear or punctate) and 4 (multilinear or multipunctate) can be observed during either the arterial or portal and late phases of contrast-enhanced sonography and are indicative of thrombus vascularization (Figs. 12 and 13). The linear-versus-punctate appearance depends on the orientation of the intrathrombotic...
vessel or vessels with respect to the scan angle. Patterns may be combined: For example, in the arterial phase, certain areas of a thrombus may display diffuse enhancement (pattern 2), whereas other areas present linear or punctate enhancement (patterns 3 or 4). The latter enhancement generally persists during the portal and late phases after the blooming has disappeared. In all patterns, during the portal and late phases, luminal enhancement appears around the thrombus if the latter is nonocclusive (Fig. 1); if the thrombus is occlusive, only the proximal lumen will be enhanced (Fig. 13C).

All 10 patients with long-standing benign thrombi presented pattern 1 in both the arterial and portal phases of the contrast-enhanced sonography examination. However, this pattern was also detected in six cases of malignant thrombosis (false-negative contrast-enhanced sonography characterizations). The other 75 thrombi definitively classified as malignant presented pattern 2, 3, or 4. Their relative frequencies in the arterial and portal phases are reported in Table 2.

Contrast-Enhanced Sonography Characteristics and Complications

The mean duration of the contrast-enhanced sonography examination, including Doppler spectral examination when possible, was 15 min (range, 11–21 min), and each patient received from one to three boluses of SonoVue (mean, 2.5 boluses). The mean estimated cost of each contrast-enhanced sonography study was €140, including the costs of contrast medium and digital cassettes, use of the sonography room, and medical and nursing staff and the amortization of sonography and recording equipment.

Portal blood flow enhancement was evident $22 \pm 4$ sec (mean $\pm$ SD) after injection of the contrast agent and remained at useful levels for a mean of $240 \pm 30$ sec; enhanced flow in the hepatic veins appeared after $22 \pm 5$ sec and remained useful for a mean of $180 \pm 25$ sec.
**Fig. 12**—Pulsating linear or punctate contrast-enhanced sonography pattern in occlusive malignant thrombus in 63-year-old woman.

A, Oblique color Doppler sonography scan with longitudinal view of left branch of portal vein. Vessel lumen is completely filled with hypoechoic material. No color signals were detected within lumen of portal vein or within thrombus.

B, Oblique contrast-enhanced sonography scan with longitudinal view of left branch of portal vein during arterial phase. Thrombus appears as predominantly nonenhancing area that reproduces shape of vessel lumen; within its borders is pulsating linear signal, which is indicative of arterial neovascularization.

**Fig. 13**—Pulsating multilinear or multipunctate contrast-enhanced sonography pattern in occlusive malignant thrombus in 68-year-old man.

A, Simultaneous oblique subcostal (left) and color Doppler (right) sonography scans show longitudinal views of right branch of portal vein. Sonography scan reveals isoechoic area within vessel lumen (arrow) representing thrombus; on color Doppler sonography, some color signals are visible within boundaries of thrombus.

B, Oblique subcostal contrast-enhanced sonography scan with longitudinal view of right branch portal vein during initial portal phase. Thrombus (arrow) appears as predominantly nonenhancing area reproducing shape of vessel lumen. Multiple pulsating punctate and linear signals indicative of arterial neovascularization are visible within its borders. Only proximal lumen of portal vein appears enhanced.
TABLE 2: Patterns Displayed on Contrast-Enhanced Sonography by the 81 Malignant Portal or Hepatic Vein Thrombi Detected in Patients with Hepatic Tumors

<table>
<thead>
<tr>
<th>Pattern of Enhancement</th>
<th>No. (%) of Thrombi with Pattern Displayed During</th>
<th>Arterial Phase</th>
<th>Portal and Late Phases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6 (7.4)%</td>
<td>9 (11.1)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>15 (18.6)%</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>13 (16.0)%</td>
<td>18 (22.2)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>47 (58.0)%</td>
<td>54 (66.7)</td>
<td></td>
</tr>
</tbody>
</table>

*False-negative characterizations by contrast-enhanced sonography.

In these thrombi, pattern 2 evolved into pattern 3 or 4 during the portal and late phases.

Three (23.1%) of 13 thrombi were characterized by the simultaneous presence of patterns 2 and 3 in the arterial phase.

Twenty (42.6%) of 47 thrombi were characterized by the simultaneous presence of patterns 2 and 4 in the arterial phase.

When present, enhanced pulsating intrathrombus signals appeared 14 ± 5 sec after SonoVue injection and persisted for 175 ± 30 sec.

No major complications were observed. One patient experienced mild transient hyperemia at the site of IV cannula (antebrachial vein) that was probably due to accidental extravasation of contrast medium.

Discussion

Our findings in the present study confirm that portal vein thrombosis is a frequent complication of primary liver tumors, especially those with diameters larger than 3.0 cm [24]. In patients with HCC, these thrombi are almost always malignant and, in most cases, direct invasion of the veins by neoplastic tissue can be sonographically shown.

In this preliminary clinical experience, contrast-enhanced sonography appears to be a reliable technique for evaluating the patency of the veins of the portal and hepatic systems. It was significantly more sensitive than color Doppler sonography for both the detection and characterization of thrombi, and it was also more sensitive than conventional sonography for thrombus characterization. In overall thrombus detection, the superiority of contrast-enhanced sonography over sonography displayed only borderline significance. Nonetheless, it allowed detection of thrombi that were missed on conventional sonography (n = 7) and on color Doppler sonography (n = 12). In fact, contrast-enhanced sonography was significantly more sensitive for the detection of nonocclusive thrombi, which represented fewer than 30% of those found in our study population. In a larger patient series, it is thus likely that the superiority of contrast-enhanced sonography over sonography would have been more significant. Furthermore, the detection sensitivity of contrast-enhanced sonography reported here may well be underestimated. For the four thrombi detected for the first time during the second examination, the baseline diagnoses were classified as false-negatives, although it is possible that some of these delayed diagnoses were actually new thrombi that had not been present 3 months earlier. When these four cases were reclassified as true-negatives for all three techniques, contrast-enhanced sonography still proved to be superior to both color Doppler sonography and conventional sonography.

The high sensitivity of contrast-enhanced sonography in thrombus detection has already been noted with the use of first-generation microbubble contrast agents [15, 25]. Second-generation agents, such as SonoVue, produce an even better optical gradient between vessel lumens, which are strongly enhanced, and thrombi, which appear as nonenhancing areas. Furthermore, because the signals are generated by the oscillation, rather than the rupture, of the bubbles induced by low-MI insonation, real-time imaging can be achieved. The useful enhancement lasts for 3–4 min, during which an experienced sonographer can easily examine all portal and hepatic veins. No other imaging technique currently offers an observation period of this length. These factors markedly improve diagnostic yield, allowing detection of thrombi with diameters of approximately 3.0 mm and of hypoechoic thrombi, which are difficult to visualize with conventional sonography and are not always detectable even with Doppler techniques. In addition, the absence of artifacts caused by heart-related movement greatly facilitates exploration of vessels in the left hepatic lobe and segment VIII of the liver, which cannot be adequately studied with color Doppler sonography [26].

As for thrombus characterization, the main advantage of contrast-enhanced sonography over conventional sonography techniques is its ability to detect even tiny vessels within tissue. Arterial neovascularization within a neoplastic thrombus appears as enhancing signals, which are easily distinguishable from those of venous flow by their pulsation. The high visibility of these signals also facilitates Doppler spectral examination confirmation of their arterial nature. In fact, Doppler spectral examination during color Doppler sonography was sometimes impossible because of the location of the thrombus (e.g., left hepatic lobe or deep in the right hepatic lobe); in other cases, it was difficult because of a lack of patient cooperation. Doppler spectral examination during contrast-enhanced sonography was successful in a significantly higher percentage of cases. The only false-positive contrast-enhanced sonography characterization was caused by the presence of vascular signals from a small branch of the left hepatic artery overlaying the thrombosed segment of the portal vein, and the same error was also made on color Doppler sonography. Errors of this type have also been reported by other groups [5].

Helical CT is frequently proposed for noninvasive assessment of the portal venous system [22], although its sensitivity in thrombus characterization is reportedly low and its comparative efficacy has never been evaluated, to our knowledge, in large-scale prospective studies [27]. Our experience in this study suggests that helical CT may be less sensitive than contrast-enhanced sonography or even sonography for the detection of venous thrombosis in the liver. However, it is important to recall that, although state-of-the-art sonography equipment was used in this study, the CT studies were performed using a third-generation single-slice helical CT scanner, and in any case the two methods were compared in only a limited number of cases.

One of the main limitations of our study is the absence of pathologic confirmation for some diagnoses. Sonographically guided biopsy is undoubtedly the best method for characterizing malignant thrombosis [16]. It was deferred in those 60 cases in which gray-scale sonography revealed unequivocal evidence of continuity between thrombus and tumor tissue on both the baseline and 3-month studies. CT or MRI visualization of thrombus–tumor continuity is widely accepted as a reliable indicator of thrombus malignancy [14, 15], and we think that there is no reason to assume that the significance of this finding is different when it is clearly shown by sonography. Furthermore, in most cases, thrombus–tumor continuity was accompanied by clear color Doppler sonography–Doppler spectral examination evidence of intrathrombus vascularization, which is associated with a specificity of close to 100% [5, 14]. For these reasons, we think that all of the definitive diagnoses reported in this study can be considered fully reliable.
Sonography of Portal and Hepatic Venous Thrombosis

Our results were obtained with state-of-the-art equipment, which may not be available in many centers. This factor might explain the excellent performance of gray-scale sonography and second harmonic filtering, which, in our study, was surprisingly almost as informative as color Doppler sonography. Moreover, the success of the contrast-enhanced sonography examinations, like other sonographic studies, depends on the skill, experience, and motivation of the sonographers and on the characteristics of the patient. Used correctly, however, the technique we evaluated seems to offer several potential advantages. It not only improves detection of small thrombi, but can also be used to reliably identify malignant thrombi even when there is no continuity with tumor tissue. Intrahepatic neovascularity can certainly be shown with conventional color Doppler sonography and Doppler spectral examination, and if this is the case, there is no indication for contrast-enhanced sonography. However, this process is considerably easier in the presence of contrast enhancement. Furthermore, the absence of artifacts related to heart movements facilitates exploration of thrombi located in left hepatic lobe, which are notoriously difficult to examine with color Doppler sonography. With respect to Doppler spectral examination performed during color Doppler sonography, Doppler spectral examination performed during contrast-enhanced sonography can thus eliminate the need for biopsy in a considerably higher percentage of cases.

Preliminary studies have already highlighted the potential value of contrast-enhanced sonography in diagnosing primary hepatic tumors and in detecting liver metastases [18–20]. Although thrombosis is less common with the secondary hepatic lesions, contrast-enhanced sonography exploration of the portal and hepatic veins could also be used in cases of this type to provide more complete staging. The higher cost of contrast-enhanced sonography should therefore be weighed against potential benefits in terms of the elimination of additional diagnostic procedures, particularly invasive ones such as liver biopsy, and also the avoidance of inappropriate therapies.

In conclusion, our preliminary findings are promising and suggest an important future role for contrast-enhanced sonography in staging hepatic tumors. However, further prospective blinded studies are necessary to confirm its apparent superiority to conventional sonography studies and to compare it with helical CT and MRI, which also appear to be promising tools [28] for the assessment of the veins of the portal and hepatic systems.

References