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Comparing the Diagnostic Value of Superb Microvascular Imaging With Color and Power Doppler in Primary and Secondary Liver Tumors

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Abstract

Background: To evaluate the ability of superb microvascular imaging to differentiate benign from malignant liver tumors and to compare it with color and power Doppler ultrasonography.

Methods: Patients scheduled for core biopsy of a liver mass were evaluated with superb microvascular imaging, color, and power Doppler, and their vascularity grades were determined. Vascularity grades of malignant and benign tumors were compared.

Results: Vascularity grades were significantly higher in superb microvascular imaging compared to color and power Doppler in both benign and malignant liver lesions ($P < .001$). However, no statistical difference in vascularity grades between benign and malignant tumors on superb microvascular imaging, power, and color Doppler was found. The area under the ROC curve was 0.642 for SMI ($P = .127$), 0.514 for color Doppler ($P = .153$), and 0.653 for power Doppler ($P = .144$).

Conclusion: Superb microvascular imaging is superior to color and power Doppler techniques in terms of depiction of liver tumor vascularity. However, superb microvascular imaging vascularity grade is not reliable at identification of malignant from benign tumors.

Keywords: Biopsy, Doppler, liver tumor, SMI, ultrasound

Introduction

Radiologists frequently encounter liver lesions in daily practice. Although history, physical examination, and laboratory tests are important in the evaluation of liver lesions, radiologic imaging is considered the most important modality in its evaluation.[1] However, a reliable diagnosis may not be achieved based on the radiologic appearances, and biopsy is often required to make an accurate diagnosis.

The biopsy of liver lesions is highly accurate (98.6%), and most patients tolerate the procedure well. Despite the application of local anesthesia, pain is the most common complication of this procedure, and anesthetics may often be required to manage moderate to severe pain.[2,3] Death due to hemoperitoneum is also well recognized, but fortunately, it is a rare complication of liver biopsy occurring in 9/100 000 biopsies.[4]

Superb microvascular imaging (SMI) was developed by Toshiba Medical Systems as a new ultrasound Doppler technique, and it has been available since 2014. Superb microvascular imaging employs algorithms that allow visualization of slower blood flow, with less motion artifacts, higher image resolution, and higher frame rates. Doppler shift is generated by moving blood in vessels as well as by tissue motion (clutter). To avoid displaying clutter, conventional color Doppler and power Doppler techniques apply wall filters that exclude all Doppler shift below certain thresholds. Thus, conventional wall filters sacrifice valuable Doppler shift data that originated from blood moving at a slow velocity in order to exclude clutter from the final image. SMI algorithm is able to analyze Doppler data and differentiate Doppler shift from actual blood flow from clutter which provides more clinically relevant images of slow vascular flow.[5,6]

The purpose of this study is to compare SMI with color and power Doppler and investigate their ability to depict vascularity of

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liver lesions and evaluate their ability to differentiate benign from malignant liver lesions.

Materials and Methods

After institutional review board approval, patients scheduled to undergo a biopsy for a liver lesion between October 2018 and January 2019 were recruited in the study. Biopsies performed for diffuse liver disease (e.g., unexplained elevated transaminase, primary biliary cirrhosis, and liver fibrosis) were excluded from the study. All patients signed an informed consent form.

All patients were scanned with an Aplio500 Platinum Series ultrasound (Toshiba America Medical Systems) using a curvilinear 1-6 MHz transducer. B-mode grayscale images, color Doppler, power Doppler, and SMI images were obtained. Scale (pulse repetition frequency) was decreased, gain was increased, and wall filter was decreased as much as possible to obtain the best quality images with as little artifacts as possible. Dimensions of the lesions and depth of the lesions from the skin were recorded. All ultrasound scans were performed by 2 radiologists with 4 and 6 years of experience in liver ultrasonography within 1 hour before the biopsy was obtained. Both radiologists were present on-site during the scan, and both agreed on the final vascularity grade. When in doubt whether an observed signal was a true vascular flow or an artifact, pulsed wave (spectral) Doppler was used to verify the observation. The scanning radiologists were not blinded to prior imaging studies.

Vascularity grade was assigned on a scale from 0 to 3. The presence of single or multiple peripheral vessels was given 1 point only. One point was given if a single internal vessel was observed and 2 points were given if 2 or more vessels were observed. The absence of peripheral or internal vessels was given no points. The sum of points for each lesion was used to determine the vascularity grade as follows: 0 point was considered grade 0, 1 point was given grade 1, 2 points were given grade 2, and ≥3 points were assigned as grade 3.

The same radiologists who performed the ultrasound scan targeted that lesion on ultrasound-guided biopsy. Disposable 16-gauge or 18-gauge spring-loaded automatic core biopsy instruments were used. Touch imprint cytology was performed by an on-site cytologist, and biopsy was repeated if the sample was inadequate. Lesions were biopsied up to 3 times. Tissue samples were sent to the pathology laboratory for histopathologic evaluation.

Statistical analysis was performed using SPSS v22.0 (IBM SPSS Corp.; Armonk, NY, USA). Categorical data were expressed as numbers (percentage). Continuous data were expressed as median (min-max). Receiver operating curves (ROC) were generated, and the area under the curve (AUC) was calculated for each of the modalities to evaluate how well vascular grades could identify benign from malignant lesions. Friedman's test was used to evaluate for statistical difference between the malignant and benign liver lesion groups; and if it existed, Wilcoxon-signed rank test was used to compare paired modalities. The data were stratified according to lesion size and depth from skin, and statistical analysis was repeated for these strata. $P < .05$ was considered statistically significant. Bonferroni correction was used to determine the cut-off P for comparing the 3 Doppler modalities using Wilcoxon signed-rank test which was <0.017 (Bonferroni correction: $a^* = a/k = 0.05/3$).

Results

Thirty patients (18 male and 12 female) with 30 lesions were included in this study. Six benign lesions and 24 malignant lesions were pathologically diagnosed on core biopsy. The benign lesions were as follows: 3 regeneration nodules, 1 dysplastic nodule, 1 focal nodular hyperplasia, and 1 scar tissue/fibrosis (probably secondary to a previous hydatid (echinococcal) cyst). The malignant tumors consisted of 18 metastases, 4 cholangiocarcinomas, 1 hepatocellular carcinoma, and 1 stromal epithelial tumor/teratoid hepatoblastoma. The 18 liver metastases consisted of 6 colon adenocarcinomas, 4 breast ductal adenocarcinomas, 2 neuroendocrine tumors, 1 lung adenocarcinoma, 1 pancreatic ductal adenocarcinoma, 1 stomach adenocarcinoma, 1 clear cell renal cell carcinoma, 1 medullary thyroid carcinoma, and 1 ovarian serous adenocarcinoma. The anatomic location of the lesions along with the patients' demographic data and ultrasonographic characteristics are summarized in Table 1.

At least 1 blood vessel (central or peripheral) could be visualized in all lesions on SMI. No blood vessels could be visualized in 11 (36.7%) lesions with color Doppler and in 4 (13.3%) lesions with power Doppler (Figures 1 and 2). Friedman's test showed a significant difference between vascularity scores of all 3 modalities ($P < .001$). Significantly higher vascularity grades were scored with SMI compared to power Doppler and color Doppler ($P < .001$ and $P = .002$, respectively). A significantly higher vascularity grade was obtained with power Doppler compared with color Doppler ($P < .001$) (Table 2).

The vascularity grades of benign and malignant lesions are compared in Table 3. No significant difference in vascularity grades was found between benign and malignant groups. Receiver operating curves curves yielded an AUC of 0.514 for color Doppler ($P = .917$), 0.653 for power Doppler ($P = .254$), and 0.642 for SMI ($P = .288$).

Table 1. Patients' Demographic Data, the Anatomic Location, and the Sonographic Characteristics of the Lesions

	Malignant	Benign
Gender		
Male, n	14	4
Female, n	10	2
Age, median (min-max)	58 (21-83)	61 (24-69)
The largest dimension of the lesion, median mm (min-max)	35 (17-170)	18 (13-77)
Distance of the lesion from the probe, median mm (min-max)	26 (6-90)	49 (21-65)
Location of the lesion		
Right lobe, n	21	2
Left lobe, n	3	4
Echogenicity of the lesion		
Hypoechoic, n	10	1
Isoechoic, n	4	2
Hyperechoic, n	10	3

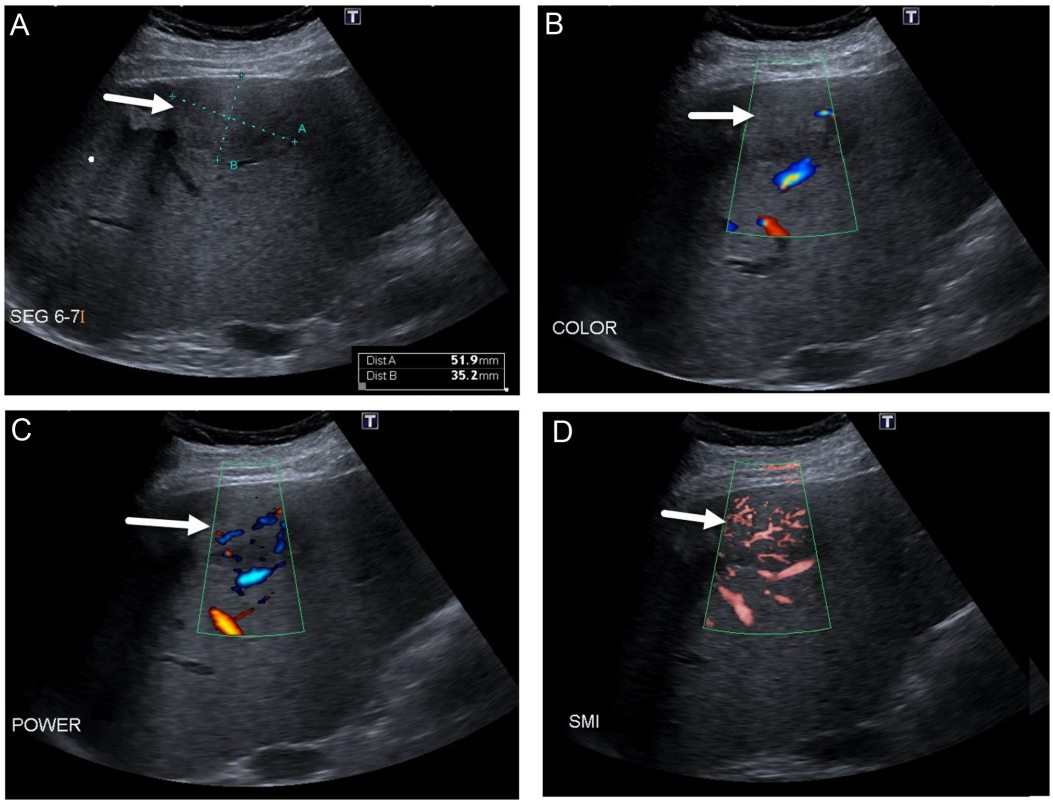

Figure 1. (A) A 5.2 cm subcapsular iso-hypoechoic hepatocellular carcinoma (arrow). On color Doppler (B) it had one internal and one peripheral vessels, thus it was scored as grade 2 tumor. Power Doppler (C) and SMI (D) images show multiple internal and external vessels. This tumor was given grade 3 on both power Doppler and SMI. SMI, superb microvascular imaging.

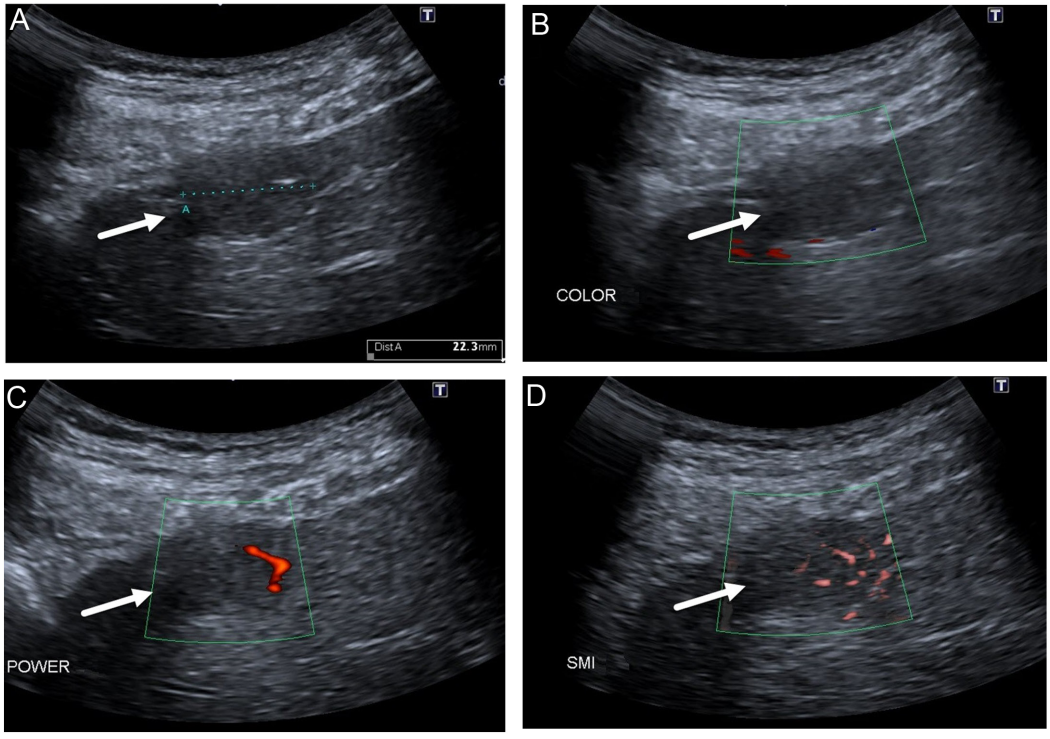

Figure 2. (A) A 2.2 cm isoechoic renal cell carcinoma metastasis (arrow). On color Doppler (B) no internal or peripheral vessel is seen. On power Doppler (C) 2 internal vessels were visualized; thus it was scored as grade 2. On SMI (D) multiple internal and peripheral vessels were seen. It was graded as grade 3 on SMI. SMI, superb microvascular imaging.

Table 2. Vascularity Grades in Color Doppler, Power Doppler, and SMI

Vascularity Grade*	Modality			Friedman Test, *P*	*P***		
	Color Doppler	Power Doppler	SMI		SMI versus Color Doppler	SMI versus Power Doppler	Color versus Power Doppler
0	11 (36.7)	4 (13.3)	0 (0.0)				
1	12 (40.0)	8 (26.7)	10 (33.3)				
2	5 (6.7)	6 (20.0)	3 (10.0)				
3	2 (6.7)	12 (40.0)	17 (56.7)				
Median grade (min-max)	1 (0-3)	2 (0-3)	3 (1-3)	<.001	<0.001	0.002	<0.001

*Data are shown as numbers (percentage). **The modalities were compared using Wilcoxon ranked test. SMI, superb microvascular imaging.

The median distance between the probe and the lesion was 3 cm. A subgroup analysis was made comparing the vascularity scores of lesions according to their distance from the probe using 3 cm as the cut-off value. Friedman's test yielded a significant difference between the subgroups ($P < .001$). Comparison of paired modalities in both subgroups showed no significant difference in vascularity grades between SMI and power Doppler in lesions within 3 cm from the probe ($P = .052$). However, statistically significant differences were found in all other groups as demonstrated in Table 4.

The median lesion size was 3 cm. A subgroup analysis was made comparing the vascularity scores of lesions smaller and larger than 3 cm. Friedman's test yielded a significant difference between both subgroups ($P < .001$). Comparison of paired modalities in both subgroups showed no significant difference in vascularity grades between SMI and power Doppler in lesions larger than 3 cm. Statistically significant differences between all other groups were present as demonstrated in Table 5.

Discussion

Superb microvascular imaging is a relatively new Doppler technique that allows visualization of slow blood flow. To date, only a few studies assessed the role of SMI in the evaluation of liver lesions.[7-10] Different methodologies were used to evaluate liver lesions in these studies; some evaluated liver lesions based on various classifications of flow patterns,[8-10] whereas other studies classified liver lesions according to the number of vessels.[7,9] The authors of the present study chose to use a methodology similar—but not identical—to that utilized by Dubinsky et al. All liver lesions included in the present study were biopsy proven.

In the present study, SMI showed significantly higher vascularity grades compared to color and power Doppler techniques in both benign and malignant liver tumors. However, the ability of vascularity grades to differentiate benign from malignant tumors was not statistically significant. Dubinsky et al[7] who used a similar methodology to that utilized in this study obtained comparable AUC values for SMI in their study. Yang et al[9] used Alder's semi-quantitative grading system to classify vascularity of liver lesions with color Doppler and SMI. In their study, significantly higher vascularity grades were obtained with SMI compared to color Doppler. The area under the curve value for SMI differentiating hepatocellular carcinoma (HCC) from non-HCC was 0.760 (74.3% sensitivity and 85.4% specificity).[9] Therefore, although SMI is clearly superior to other Doppler techniques in terms of depiction of blood vessels, the authors believe that SMI vascularity grades are not sufficient to differentiate benign from malignant lesions.

The present study additionally sub-categorized and analyzed lesions according to their distance from the probe and according to their largest diameter. As demonstrated in Tables 4 and 5, both SMI and power Doppler had significantly higher vascularity grades compared to color Doppler. Comparing SMI with power Doppler, SMI had significantly higher vascularity grades only in tumors less than 3 cm large in diameter and in tumors more than 3 cm far from the probe. Thus, SMI may be especially better at depiction of vascularity in deeper and smaller tumors. Validation of this finding in future studies with larger patient populations is necessary.

The authors believe that future research on the role of SMI in pathologic entities in which the depiction of vascular flow is

Table 3. Vascularity Grade Compared Between Benign and Malignant Lesions

Modality	Vascularity Grade	Diagnosis		AUC	95% CI	Median (Min-Max)	Standard Error	Cut-off Value	Sensitivity	Specificity	*P*
		Malignant	Benign								
Color Doppler	0	8 (33.3)	3 (50.0)	0.514	0.213-0.815	1 (0-3)	0.153	≥1	66.7%	50.0%	.917
	1	11 (45.8)	1 (16.7)								
	2	4 (16.7)	1 (16.7)								
	3	1 (4.2)	1 (16.7)								
Power Doppler	0	2 (8.3)	2 (33.3)	0.653	0.370-0.935	2 (0-3)	0.144	≥1	92.7%	66.7%	.254
	1	6 (25.0)	2 (33.3)								
	2	6 (25.0)	0 (0.0)								
	3	10 (41.7)	2 (33.3)								
SMI	0	0 (0.0)	0 (0.0)	0.642	0.394-0.891	3 (1-3)	0.127	≥2	70.8%	50.0%	.288
	1	7 (29.2)	3 (50.0)								
	2	2 (8.3)	1 (16.7)								
	3	15 (62.5)	2 (33.3)								

Table 4. Vascularity Scores Compared Between Lesions Less and More Than 3 cm Far From the Transducer

Vascularity Grade	Modality*			Friedman Test, *P*	*P***		
	Color Doppler	Power Doppler	SMI		SMI versus Color Doppler	SMI versus Power Doppler	Color Doppler versus Power Doppler
Lesions < 3 cm from the transducer							
0	4 (25.0)	0 (0.0)	0 (0.0)				
1	8 (50.0)	5 (31.3)	3 (18.8)				
2	4 (25.0)	4 (25.0)	3 (18.8)				
3	0 (0.0)	7 (43.8)	10 (62.5)				
Median vascularity grade (min-max)	1 (0-3)	2 (0-3)	3 (1-3)	<.001	0.001	0.059	0.001
Lesions > 3 cm from the transducer							
0	7 (50.0)	4 (28.6)	0 (0.0)				
1	4 (28.6)	3 (21.4)	7 (50.0)				
2	1 (7.1)	2 (14.3)	0 (0.0)				
3	2 (14.3)	5 (35.7)	7 (50.0)				
Median vascularity grade (min-max)	1 (0-3)	2 (0-3)	2 (1-3)	<.001	0.002	0.014	0.014

*Data are shown as numbers (percentage). **The modalities were compared using Wilcoxon ranked test. SMI, superb microvascular imaging.

crucial for making the diagnosis (e.g. testicular torsion, ovarian torsion, and ovarian lesions) may yield more promising results.

Limitations of this study include the small sample size, small number of benign tumors, and absence of certain benign entities (e.g., hepatocellular adenoma). Inter-reader agreement was not evaluated because both readers agreed on the vascularity grade at the time of the scan. Although the vascularity grading system utilized in this study yielded similar values to other grading systems used in the literature, grading systems are not identical and authors did not seek to specify vascularity patterns as reported in other studies.

In conclusion, SMI is superior to color and power Doppler techniques in terms of depiction of tumor vascularity. However, SMI vascularity grade is not reliable at identification of malignant from benign tumors. Superb microvascular imaging seems to be especially better at the depiction of vascularity in smaller lesions and in lesions furthest from the probe.

Table 5. Vascularity Scores Compared Between Lesions Less and More Than 3 cm in Largest Diameter

Vascularity Grade	Modality*			Friedman Test, *P*	*P***		
	Color Doppler	Power Doppler	SMI		SMI versus Color Doppler	SMI versus Power Doppler	Color Doppler versus Power Doppler
Lesions < 3 cm in diameter							
0	10 (66.7)	4 (26.7)	0 (0.0)				
1	5 (33.3)	5 (33.3)	8 (53.3)				
2	0 (0.0)	3 (20.0)	3 (20.0)				
3	0 (0.0)	3 (20.0)	4 (26.7)				
Median vascularity grade (min-max)	0 (0-1)	1 (0-3)	1 (1-3)	<.001	0.001	0.014	0.007
Lesions > 3 cm in diameter							
0	1 (6.7)	0 (0.0)	0 (0.0)				
1	7 (46.7)	3 (20.0)	2 (13.3)				
2	5 (33.3)	3 (20.0)	0 (0.0)				
3	2 (13.3)	9 (60.0)	13 (86.7)				
Median vascularity grade (min-max)	1 (0-3)	3 (1-3)	3 (1-3)	<.001	0.003	0.059	0.002

*Data are shown as numbers (percentage). **The modalities were compared using Wilcoxon ranked test. SMI, superb microvascular imaging.

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Conflict of Interest: The authors have no conflict of interest to declare.

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