Comparison of Contrast-enhanced Ultrasonography Images by Sonazoid® and Levovist® in Hepatic Tumors

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Purpose:
We compared imaging characteristics of hepatic tumors on contrast-enhanced ultrasonography between using Sonazoid® and using Levovist® in patients with hepatocellular carcinoma (HCC).

Materials and Methods:
We investigated 26 patients who underwent contrast-enhanced ultrasonography with both Levovist® and Sonazoid®. All patients had hypervascular HCC. Contrast-enhanced sonographic images were obtained using Aplio-XG (Toshiba) imaging equipment. The dose of injected Levovist® was fixed at 8 mL and that of Sonazoid® were adjusted to the recommended dose or half of it according to the weight of patients. We analyzed differences in blood vessel enhancement and perfusion of the tumor during the vascular phase (arterial phase and portal-venous phase). Also we compared detectability of tumors during the postvascular phase (Kupffer phase).

Results:
During the arterial phase, Sonazoid® was superior in detecting tumor blood vessels in 8 patients and equivalent in 15 patients compared with Levovist®.

During the portal venous phase, tumor perfusion was observed more clearly by Sonazoid® in 1 patient and equivalent in 22 patients compared with Levovist®.

In 3 patients in whom Levovist® was superior to Sonazoid® in depicting both tumor blood vessels in the arterial phase and tumor perfusion the in portal venous phase, tumor was located in the deep part of the liver in 2 patients and marked attenuation of ultrasound was occurred due to fat deposit of subcutaneous layer in the other patient.

During the postvascular phase, the number of tumors increased in 3 patients with contrast-enhanced US with Sonazoid® compared with plain US, whereas no increase in tumor number was observed by contrast-enhanced US with Levovist®. Sonazoid® was more sensitive than Levovist® in detecting minute tumors.

Conclusion:
Based on these findings, Sonazoid® is useful in diagnosing HCC and is expected to become a major contrast agent in ultrasonography.
S1-2 The Initial Experience of Contrast-enhanced Ultrasonography of Pancreatic Tumor

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PURPOSE: To study contrast-enhanced ultrasonography (CEUS) for pancreatic tumor.

MATERIALS AND METHODS: Seventeen patients with pancreatic tumor were examined by CEUS with Perfluorutane Microbubble (Sonazoid™/DD723/NC100100). Diagnosis was confirmed by biopsies and/or surgical resection of the tumors. Twelve patients had pancreatic ductal carcinoma, two metastatic tumors, one endocrine tumor, one autoimmune pancreatitis and one intraductal papillary mucinous carcinoma. After 10 seconds of contrast media injection, early vascular phase was captured until about 25 sec and parenchymal phase was captured from the following time of early vascular phase to 50 - 90 seconds. We visually assigned the intratumoral enhancement pattern of the tumor into two groups in each enhancement phase, one is linear and the other spotty diffuse enhancement pattern in early vascular phase, one is hypo and the other iso/hyper echoic enhancement pattern in parenchymal phase. Two board certified radiologists analyzed the enhancement pattern individually without any patient’s information. Intratumoral microvessel density (IMD) was calculated by means of CD 34 immunostaining. Enhancement pattern in parenchymal phase was compared to IMD. Statistically significant differences were evaluated by Kappa coefficient, and Mann Whitney U-test. A p<0.05 was defined as being statistically significant.

RESULTS: The Kappa coefficients of two radiologists analysis were 1.0 in vascular phase, while 0.89 in parenchymal phase. When linear enhancement pattern in vascular phase and hypo echoic enhancement pattern in parenchymal phase was defined as pancreatic ductal carcinoma, sensitivity were 66.7% and 83.3%, accuracy were 64.7% and 75.6%, respectively. Significant difference of IMD was found between hypo echoic and iso/hyper enhancement pattern (p<0.05).

CONCLUSION: We suggest that CEUS is useful in differentiating pancreatic tumors.
Objective: We evaluated the usefulness of contrast-enhanced harmonic gray-scale sonography with a newly developed sonographic contrast medium of guidance for percutaneous ablation therapy of hepatocellular carcinoma lesions not detected by conventional sonography.

Methods: We examined 85 patients with 108 hepatocellular carcinoma lesions that were indentified as hypervascular by multi-detector row CT, by using contrast-enhanced harmonic gray-scale sonography after injection of Sonazoid, a lipid-stabilized suspension of a perfluorobutane gas microbubble contrast agent. In the late phase of contrast-enhanced harmonic gray scale sonography, we scanned the whole liver using this modality at a low mechanical index without destroying the Sonazoid microbubbles, and this method allowed detection of small hepatocellular carcinoma lesions as perfusion defects. When we scanned the tumor lesion with the higher acoustic power of contrast-enhanced harmonic gray-scale sonography, the Sonazoid microbubbles within and around the tumor has been destroyed at once and the tumor vessels and vascular spaces. We also performed percutaneous ablation therapy guided by this modality to treat viable hepatocellular carcinoma lesions that couldn’t be detected by conventional sonography.

Results: Conventional sonography identified 90 (83%) of 108 hepatocellular carcinoma lesions, and additional 15 (14%) viable lesions not detected by conventional sonography were detected in the late phase of contrast-enhanced harmonic gray-scale sonography at low mechanical index. Contrast-enhanced harmonic gray-scale sonography diagnosed 105 (97%) of the 108 viable hepatocellular carcinoma lesions. Contrast-enhanced harmonic gray-scale sonography was a more sensitive means of detecting hepatocellular carcinoma lesions than conventional sonography (p < 0.01 by chi-squared test). 14 (93%) of the 15 lesions not detected by conventional sonography were successfully treated by percutaneous ablation therapy guided by this modality.

Conclusion: Contrast-enhanced harmonic gray-scale sonography is useful for guidance for percutaneous ablation therapy of hepatocellular carcinoma lesions not detected by conventional sonography.
Usefulness of Sonazoid-enhanced contrast ultrasonography

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Sonazoid is a new ultrasound contrast agent which was introduced for the first time to Japan in January of this year. Levovist®, a generally used contrast agent, collapses easily when exposed to ultrasound pulse. Sonazoid® is, however, stabler than Levovist®, and real-time imaging is available under low acoustic power of ultrasound. We can observe vascular phase imaging about 120 seconds following an intravenous bolus injection of 0.0075 – 0.015mL/kg of Sonazoid®, and post-vascular phase imaging can be observed after 10 minutes. The detection rate of arterial tumor vascularity for hepatocellular carcinoma (HCC) by the Sonazoid-enhanced contrast ultrasonography (US) is almost equivalent to that of dynamic CT. Moreover we can observe real-time imaging for a long time in the post-vascular phase. Therefore the Sonazoid-enhanced contrast US is clinically useful, especially for assessing the therapeutic effect of radiofrequency ablation (RFA) of HCC and guiding RFA therapy when the HCC nodules are poorly defined in B mode US. Recently Real-time Virtual Sonography (RVS) has been used for the guidance of RFA against nodules can not be visualized clearly by conventional sonography. This RVS is supposed to be effective for detection of ultrasound ill-defined HCC nodules and local recurrence of HCC. It is also used to recognize insufficient ablated margins after initial RFA session when adding secondary sessions. Sonazoid can help to ablate HCC accurately in these difficult cases instead of RVS. Moreover we can elevate the accuracy by using Sonazoid alongside RVS. This new ultrasound contrast agent, Sonazoid is extremely useful modality in the clinical practice of HCC.
Evaluation of hepatic Nodule hemodynamics using contrast-enhanced ultrasonography (CEUS) with Sonazoid in comparison to Levovist

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Levovist has been the only intravenous contrast material available in Japan for the last 9 years. It allows detailed visualization of hemodynamics and has a diagnostic rate for hepatic nodules superior to those of CT and MRI in our institute. This study was designed to analyze hepatic nodule hemodynamics using CEUS with Sonazoid, a new contrast agent, and to clarify any differences from Levovist.

METHODS: Among 258 hepatic nodules examined by Sonazoid CEUS since February 2007, 31 hepatic nodules in 30 cases were selected for this study because Levovist CEUS and pathological findings were also available. There were 21 HCC nodules (16 moderately differentiated: 4 well-differentiated: 1 mixed), 9 hyperplastic nodules including 4 focal nodular hyperplasia, and 1 angiomyolipoma. The Levovist (1 vial; 300 mg/ml) and Sonazoid (0.01ml/kg) were administered intravenously. Arterial phase imaging from 1 to 45 seconds after the injection, and subsequent enhancement at 1, 2, 3, 5 and 7 minutes for Levovist and at 1, 2, 3, 5, 10 and 30 minutes for Sonazoid was observed. ADI (Sequoia 512) was used for Levovist, and ePHD (Prosound α 10), CPS (Sequoia 512) and CHI (Aplio XG) for Sonazoid.

RESULTS:
In the arterial phase, feeding arteries were better visualized with Levovist, while nodule enhancement was more clearly seen with Sonazoid. Capture mode is useful for analyzing feeding arteries in Sonazoid CEUS. About 70% of nodules showed negative enhancement during the subsequent phases. These findings were exhibited within the first 5 min. in all of the nodules with Levovist, but were prolonged for up to 30 min. with Sonazoid. Most malignant nodules showed negative enhancement, while 50% of the benign nodules remained iso-enhanced during the subsequent phase.

Conclusion:
Sonazoid allowed clear, though prolonged, visualization of hemodynamics. Vascular structure was observed in detail using capture mode. Further improvement of this protocol is currently ongoing.