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·专题研究·

术中Sonazoid超声造影在特殊部位肝细胞癌经腹腔镜微波消融中的应用价值

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摘　要

背景与目的：超声常用于引导微波消融（MWA）治疗肝细胞癌（HCC）。部分MWA可经皮完成，对于特殊部位HCC，则常选择通过腹腔镜完成。腹腔镜下MWA亦存在局限，对于小肝癌、等回声结节或合并肝硬化背景等情况，灰阶超声（GSUS）定位靶病灶常存在困难，此时可应用超声造影来增加病灶与肝实质的显影对比，提高靶病灶可视性。但目前临床常用的造影剂如声诺维等增强时间窗较短暂，因而在HCC消融术中的引导作用有限。Sonazoid于2019年在中国上市，相比其他造影剂，Sonazoid的优势在于其能被肝脏Kupffer细胞摄取，在注射造影剂约10 min后进入其特有的枯否相，此期肝脏实质显像增强，且文献报告枯否相可持续至少1 h。HCC因缺乏Kupffer细胞则呈低增强或增强缺失，因此，术中Sonazoid超声造影（S-CEUS）理论上有利于靶病灶的定位，且能为MWA提供充足的时间窗。本研究主要探讨S-CEUS相较于GSUS在针对特殊部位HCC行腹腔镜MWA术中对于肿瘤定位的优势，并分析S-CEUS对于消融治疗的实时引导作用。

方法：连续选取2020年6月—2021年12月湖南省人民医院/湖南师范大学附属第一医院肝胆外科49例靶病灶位于特殊部位行腹腔镜MWA的HCC患者，术中分别行GSUS与S-CEUS，分析术中靶病灶的定位情况，采用5分信心量表法对靶病灶的可视度进行评分，比较GSUS与S-CEUS对靶病灶的可视度差异；同时观察靶病灶枯否相持续时间，以及在枯否相行MWA的效果。

结果：49例患者术前MRI发现病灶56个，术中S-CEUS发现病灶59个，穿刺活检均证实为HCC。GSUS扫描时，靶病灶的可视度评分为2.86±0.96；S-CEUS动脉相，靶病灶的可视度评分为3.90±0.78；S-CEUS枯否相，靶病灶的可视度评分为4.25±0.60。S-CEUS动脉相、枯否相对靶病灶的可视度评分均优于GSUS（均 $P<0.001$）；S-CEUS枯否相对靶病灶的可视度评分优于S-CEUS动脉相（$P<0.001$）。靶病灶枯否相持续时间超过1 h；术前已知多个病灶的病例均只注射1次造影剂即完成所有病灶的定位；3个术前影像学检查未发现的隐匿性病灶均在枯否相发现；所有病灶均在枯否相进行MWA。消融后15 min再次注射Sonazoid即时评估及术后1个月增强MRI检查均显示所有病灶消融完全。

结论：针对特殊部位HCC的腹腔镜MWA，靶病灶在S-CEUS动脉相、枯否相的可视度均优于GSUS，有利于靶病灶的定位；S-CEUS枯否相有利于MWA的实时引导。

关键词　癌，肝细胞；消融技术；超声检查；造影剂

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Application value of intraoperative Sonazoid-enhanced ultrasonography in laparoscopic microwave ablation of hepatocellular carcinoma in special locations

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Abstract

Background and Aims: Microwave ablation (MWA) for the treatment of hepatocellular carcinoma (HCC) is often performed under ultrasound guidance. MWA in some cases can be completed via a percutaneous approach, while a laparoscopic approach is usually chosen for HCC in special locations. However, laparoscopic MWA also has limitations. For small HCC, isoechoic nodules or target lesions within a cirrhotic background, gray-scale ultrasound (GSUS) is sometimes difficult to locate the target lesions. At this time, contrast-enhanced ultrasound can be used to increase the contrast between the lesions and the liver parenchyma and improve the visibility of the target lesions. However, the time window of enhancement imaging with commonly used contrast agents such as SonoVue is relatively short, so its guiding role in HCC ablation is limited. Sonazoid was approved for use in China in 2019. Compared with other contrast agents, the advantage of Sonazoid is that it can be phagocytosed by Kupffer cells in the liver and has its unique Kupffer phase about 10 min after the injection of contrast agent. At this stage, the ultrasonic imaging of liver parenchyma is enhanced, and previous literature has reported that that Kupffer phase can last for at least 1 h. Meanwhile HCC exhibits low enhancement or no enhancement due to the lack of Kupffer cells. Therefore, intraoperative contrast enhanced ultrasound with Sonazoid (S-CEUS) is theoretically helpful for the localization of the target lesions, and can provide a sufficient time window for MWA. This study was performed to investigate the advantages of S-CEUS in tumor localization compared with GSUS in laparoscopic MWA for HCC in special locations, and analyzed the real-time guiding capability of S-CEUS for ablation.

Methods: From June 2020 to December 2021, 49 HCC patients undergoing laparoscopic MWA with target lesions located in special areas in Department of Hepatobiliary Surgery, Hunan Provincial People's Hospital/the First Affiliated Hospital of Hunan Normal University were consecutively selected. GSUS and S-CEUS were respectively performed during laparoscopic MWA. The positioning accuracy of the target lesions was analyzed. The 5-point confidence scale was used to evaluate the visibility of the target lesion and the difference of the visibility of the target lesions between GSUS and S-CEUS was compared. At the same time, the duration of Kupffer phase was observed, and the efficacy of MWA performed in this phase was evaluated.

Results: In the 49 patients, 56 lesions were found by preoperative MRI examination, and 59 lesions were detected by S-CEUS during operation, which were all identified as HCC by aspiration biopsy. The visibility score of target lesions was 2.86±0.96 for GSUS, and was 3.90±0.78 in arterial phase and 4.25±0.60 in Kupffer phase for S-CEUS. The visibility scores of target lesions in both arterial phase and Kupffer phase were better than that in GSUS (both $P<0.001$), and the visibility score of target lesions in Kupffer phase is better than that in arterial phase ($P<0.001$). The Kupffer phase lasted more than 1 h; the localization of all lesions in patients with multiple lesions known before operation was completed by injection of the contrast agent in one session; three occult tumors that were not found by preoperative imaging examination were all found in Kupffer phase; all lesions underwent MWA in Kupffer phase.

　

Both immediate evaluation by Sonazoid injection again 15 min after ablation and enhanced MRI examination one month after operation showed that all lesions were ablated completely.

Conclusion: For laparoscopic MWA of HCC in special locations, the visibilities of target lesions in arterial phase and Kupffer phase of S-CEUS are better than that of GSUS, which is helpful for the localization of target lesions. The Kupffer phase of S-CEUS is helpful for the real-time guidance during performing MWA.

Key words Carcinoma, Hepatocellular; Ablation Techniques; Ultrasonography; Contrast Media

CLC number: R735.7

微波消融（microwave ablation，MWA）被广泛应用于肝细胞癌（hepatocellular carcinoma，HCC）的治疗，在一些早期HCC患者中可以获得与手术切除相类似的疗效[1-2]。超声具有简易、无创、可重复等多重优势[3]，因而常用于MWA术中的实时引导。部分MWA可经皮完成，但特殊部位HCC如肿瘤凸出肝脏表面，靠近膈肌、胆囊、胃、横结肠、心脏等脏器，经皮MWA常存在困难和风险[4-5]，该部分病例的消融治疗常选择通过腹腔镜完成。

然而，腹腔镜MWA亦存在其局限性，对于小肝癌、等回声结节或合并肝硬化背景等，灰阶超声（gray-scale ultrasound，GSUS）常定位困难。而靶病灶的精准定位是保证消融完全的重要因素之一[6]。

近年来，超声造影常用于改善超声的可视性，在HCC的MWA治疗中起到了一定的引导作用[7-8]。但目前临床常用的造影剂如声诺维等增强时间窗较短暂，注射造影剂后5 min左右即失去对比增强效果，其在HCC消融术中的引导作用有限[9]。注射用全氟丁烷微球（Sonazoid）为第二代超声造影剂，于2019年在中国上市。相较于其他造影剂，Sonazoid的优势在于其能被肝脏Kupffer细胞摄取，在注射Sonazoid约10 min后进入其特有的肝实质特异期，亦称为枯否相（Kupffer phase），此期肝脏实质显像增强，而缺乏Kupffer细胞的HCC则呈低增强或增强缺失，提高了HCC与肝实质的显影对比。且文献[10]报告枯否相可持续至少1 h，因此，Sonazoid超声造影（contrast-enhanced ultrasound with Sonazoid，S-CEUS）理论上为靶病灶的定位提供了明确的依据，且为MWA提供了充足的时间窗。

本文通过对比S-CEUS与GSUS针对特殊部位HCC行腹腔镜MWA时术中靶病灶的可视度差异，探讨S-CEUS对于靶病灶的定位优势，同时通过观察枯否相引导MWA，分析S-CEUS对于消融治疗的实时引导作用。

1 资料与方法

1.1 一般资料

连续选取2020年6月—2021年12月湖南省人民医院/湖南师范大学附属第一医院肝胆外科49例不宜或不愿手术切除且肿瘤位于特殊部位考虑经皮MWA存在困难的HCC患者，其中男31例，女18例；平均年龄（54.53 ± 10.81）岁；49例患者，术前增强MRI共发现56个靶病灶。

1.2 纳入及排除标准

纳入标准：(1) 年龄>18岁；(2) 所有病例均符合HCC的临床诊断标准，肿瘤直径<3 cm，肿瘤数目≤3个；(3) 靶病灶至少1个位于特殊部位，如肿瘤凸出肝脏表面，靠近膈肌、胆囊、第一肝门区胆管和血管、胃、横结肠等脏器；(4) 邻近器官无侵犯，无门静脉癌栓。排除标准：(1) 肝外转移；(2) 肝功能差不能耐受消融手术治疗；(3) 伴随其他不能耐受手术的系统性疾病。医生术前与患者充分沟通，告知S-CEUS的优缺点、对手术的价值及相应的并发症等，患者均签署手术知情同意书。本研究通过湖南省人民医院/湖南师范大学附属第一医院伦理委员会批准[伦理批复号：(2020）科研伦审第（101）号]。

1.3 靶病灶定位

患者全麻，术野消毒铺巾，于脐上做1 cm切口，气腹针建立气腹，置入穿刺鞘及腹腔镜，根据靶病灶部位再于上腹分别穿刺置入2~3个穿刺

鞘，用于置入腔镜用超声探头及辅助器械。采用日立ARIETTA 60型号超声诊断仪，选用UST-5418探头，频率2~13 MHz，造影谐波成像软件。GSUS扫描肝脏，对比术前MRI观察能否准确定位靶病灶。再选取超声造影剂Sonazoid，使用前用2 mL注射用水稀释混匀，用量0.015 mL/kg，经中心静脉或上肢外周静脉快速推注，推注后用5 mL生理盐水冲洗静脉给药管路，确保造影剂完全注射。实时全程观察10 min以上，分为动脉相（10~30 s）、门脉相（30~120 s）、枯否相（10 min后），在注射造影剂同时启动超声仪计时器，快速扫描肝脏，观察肝脏实质灌注有无局限性异常显影的造影剂聚集区，发现病灶后存储扫描图并记录位置，与术前MRI对比病灶的位置、大小，以及有无新病灶发现。同时存在两个或以上靶病灶的病例，在S-CEUS动脉相常难以同时观察到所有靶病灶，可在枯否相记录所有靶病灶位置后再重新造影观察各个靶病灶的各相表现。分别观察每个靶病灶在各时相的可视度差异，采用5分信心量表[11]分别在GSUS期、S-CEUS动脉相、S-CEUS枯否相对靶病灶的可视度进行评分：完全看不见，1分；几乎看不见，2分；勉强可见，可视度较差，3分；可视度较好，4分；清晰可见，5分。于枯否相规划穿刺点及穿刺路径，体表标记。超声工作由临床医生和专门从事肝胆超声（造影）的超声科医生共同完成。

1.4　S-CEUS引导靶病灶活检及MWA

S-CEUS实时引导下循规划路径行靶病灶穿刺活检。使用冷循环微波消融治疗仪（南京维京九洲医疗器械研发中心生产，许可证号：苏食药监械生产许20160024号）在实时超声引导下沿规划路径，在枯否相将微波消融针插入靶病灶深面（图1），针尖定位在病灶的前端，启动冷循环系统，开始MWA，依据肿瘤直径设置消融工作功率为60~80 W，按瘤体形状采用单点或多点消融，消融范围超出肿瘤边缘0.5 cm，以达安全边界，若病灶紧邻横膈或大血管、胆囊、结肠等（<0.5 cm），无法获得0.5 cm安全边界，但消融灶其他边缘均达到安全边界，可认为达到安全边界[12]。

1.5　消融效果评估

消融完成后15 min再次S-CEUS评估消融效果（图2）。造影显示原病灶区域无局部高增强灶，且非强化区覆盖肿瘤及其周边0.5 cm视为消融完全，对于靠近包膜边缘、血管或胆囊等的肿瘤，非强化区至其边缘即视为消融完全[13]。若考虑消融不完全，再次消融直至术中即时评估消融完全。术后1个月复查增强MRI再次评估。

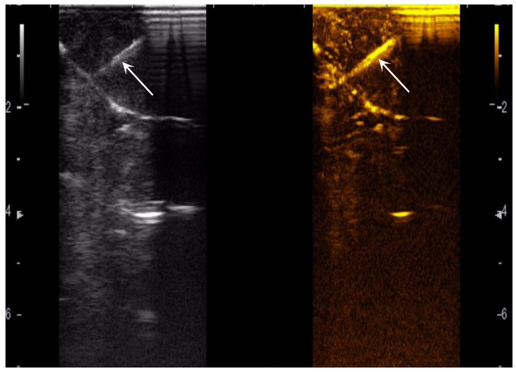

图1　利用枯否相引导微波消融针插入靶病灶（箭头所示为消融针）

Figure 1　Guiding the insertion of the ablation needle into the lesion during Kupffer phase (arrow showing the ablation needle)

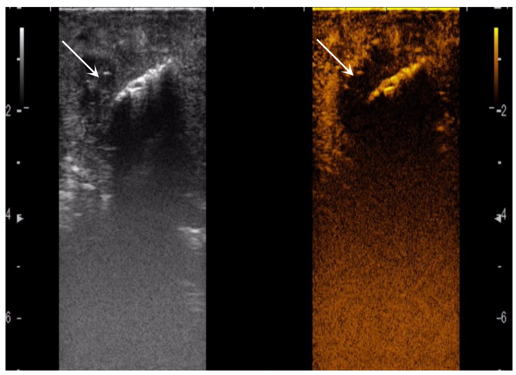

图2　消融术后15 min S-CEUS即时评估消融效果（箭头所示造影显示非强化区覆盖肿瘤及其周边0.5 cm，病灶区域无局部高增强灶，考虑消融完全）

Figure 2　Immediate evaluation of the ablation efficacy by S-CEUS injection 15 min after ablation (coverage of the tumor and surrounding 0.5 cm area by the non-enhancement area shown by the arrow, indicating complete ablation for the absent of highly enhanced foci within the lesion area)

1.6　统计学处理

应用SPSS 20.0进行数据分析，计量资料采用均值±标准差（$\bar{x} \pm s$）表示，GSUS与S-CEUS对靶病灶的可视度差异采用配对样本t检验。P<0.05为差异有统计学意义。

　

2 结 果

2.1 靶病灶定位情况

本组共49例患者，术前MRI发现肿瘤病灶56个，术中S-CEUS发现肿瘤病灶59个，S-CEUS新发现3个肿瘤。肿瘤大小（2.07±0.51）cm，所有靶病灶均通过穿刺活检证实为HCC。GSUS期因肝硬化多结节的干扰而导致不可见的10个靶病灶，有6个靶病灶在S-CEUS动脉相中可视度良好，10个靶病灶在S-CEUS枯否相中均可视度良好（图3）。GSUS期因呈等回声而导致不可见的8个靶病灶，有3个靶病灶在S-CEUS动脉相中可视度良好，7个靶病灶在S-CEUS枯否相中可视度良好（图4）。GSUS期因≤1 cm而导致不可见的4个靶病灶，在S-CEUS动脉相及枯否相中均可视度良好（图5）。S-CEUS动脉相中因呈等增强而导致不可见的3个靶病灶，2个在CEUS枯否相中可视度良好（图6）。各时相靶病灶可视性见表1。

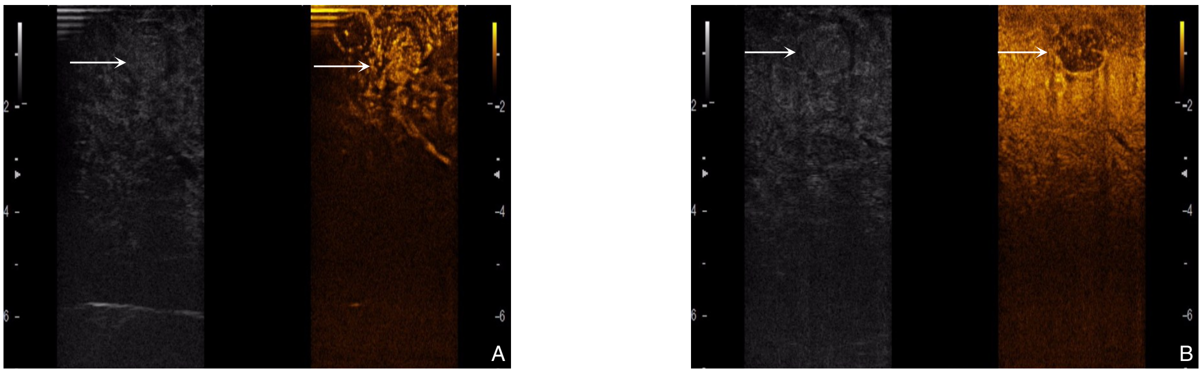

图3 因肝硬化多结节干扰，靶病灶（箭头所示）在GSUS期不可见，而在S-CEUS动脉相及枯否相均可视度良好 A：在动脉相，靶病灶呈快速高增强；B：在枯否相，靶病灶呈增强缺失

Figure 3 Interference by a background of hepatic cirrhosis with multiple nodules, and invisibility of in GSUS, but good visibility in both arterial phase and Kupffer phase of S-CEUS of the target lesion (shown by the arrow) A: The target lesion presenting rapid high enhancement in arterial phase; B: The target lesion showing loss of enhancement in Kupffer phase

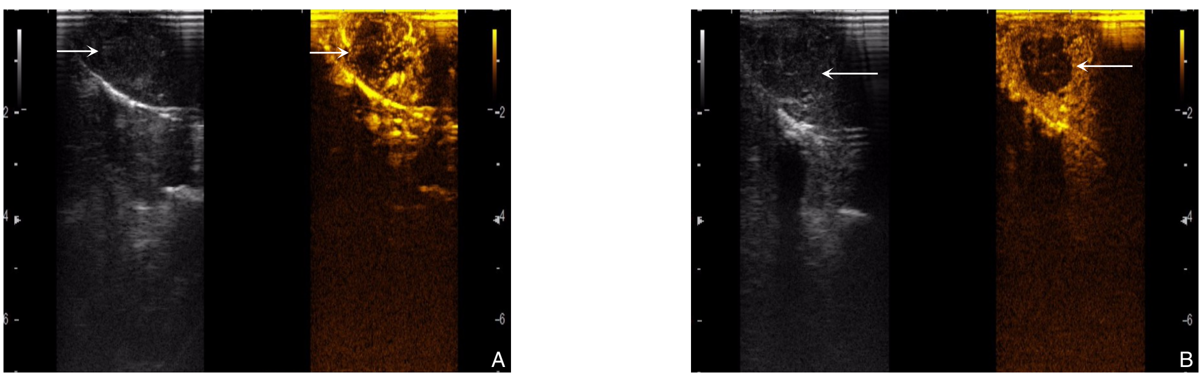

图4 靶病灶（箭头所示）在GSUS期呈等回声而不可见，而在S-CEUS动脉相及枯否相均可视度良好 A：在动脉相，靶病灶呈快速向心性高增强；B：在枯否相，靶病灶呈增强缺失

Figure 4 Isoechoic texture and invisibility in GSUS, but good visibility in both arterial phase and Kupffer phase of S-CEUS of the target lesion (shown by the arrow) A: The target lesion presenting rapid centripetal high enhancement in arterial phase; B: The target lesion showing loss of enhancement in Kupffer phase

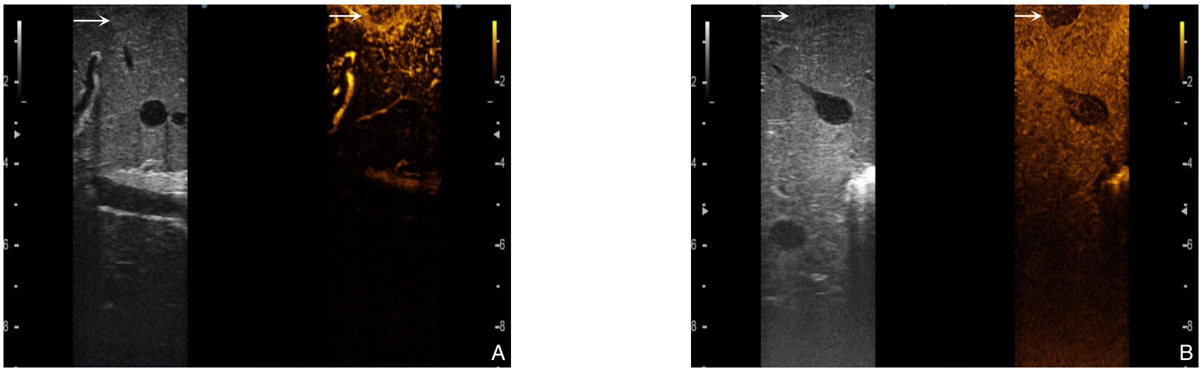

图5 靶病灶（箭头所示）因≤1 cm且在GSUS期呈等回声而不可见，而在S-CEUS动脉相及枯否相均可视度良好 A：在动脉相，靶病灶呈快速向心性高增强；B：在枯否相，靶病灶呈增强缺失

Figure 5 Isoechoic texture and invisibility in GSUS, but good visibility in both arterial phase and Kupffer phase of S-CEUS of the target lesion ≤1 cm (shown by the arrow) A: The target lesion presenting rapid centripetal high enhancement in arterial phase; B: The target lesion showing loss of enhancement in Kupffer phase

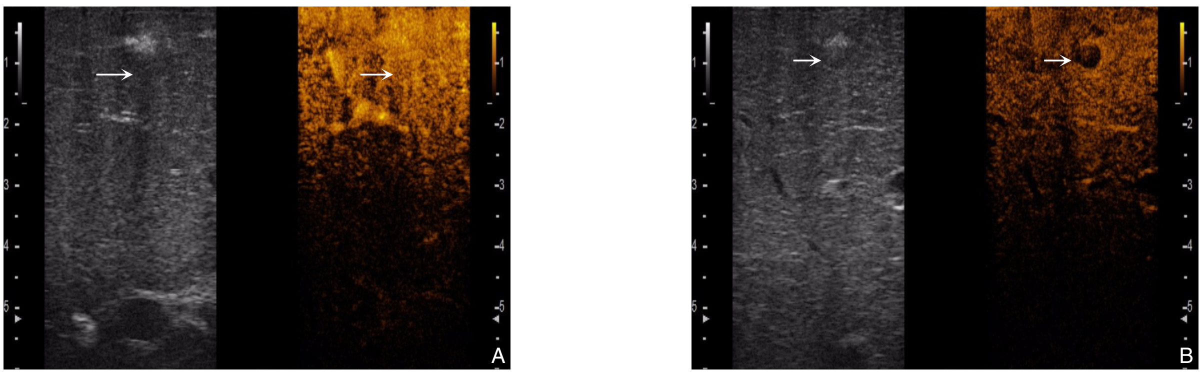

图6 靶病灶（箭头所示）在动脉相中呈等增强而不可见，在枯否相可视度良好 A：靶病灶在动脉相呈等增强；B：靶病灶在枯否相呈增强缺失

Figure 6 Isoenhancement and invisibility in arterial phase, but good visibility in Kupffer phase of the target lesion (shown by the arrow) A: Isoenhancement of the target lesion arterial phase; B: No enhancement of the target lesion in Kupffer phase

表1 各时相靶病灶可视性（*n*）

Table 1 Visuality of the target lesion in each phase (*n*)

时相	靶病灶可视性				
	不可见（1~2分）			可见（3~5分）	
	肝硬化多结节的干扰	靶病灶呈等回声	靶病灶≤1 cm	较差（3分）	良好（4~5分）
GSUS期	10	8	4	20	17
S-CEUS动脉相	—	3	—	12	44
S-CEUS枯否相	—	—	—	5	54

2.2 靶病灶的可视度比较

GSUS期，靶病灶的可视度评分为2.86±0.96；S-CEUS动脉相，靶病灶的可视度评分为3.90±0.78；S-CEUS枯否相，靶病灶的可视度评分为4.25±0.60。S-CEUS动脉相、枯否相对靶病灶的可视度评分均优于GSUS期（图7），差异均有统计学意义（均$P<0.001$）；S-CEUS枯否相靶病灶的可视度评分优于动脉相，差异具有统计学意义（$P<0.001$）。

2.3 S-CEUS对于消融治疗的实时引导作用

术中靶病灶枯否相时间可持续1 h以上（图8），所有靶病灶均在枯否相行MWA，术后15 min即时S-CEUS评估及术后1个月行增强MRI检查，均消融完全。

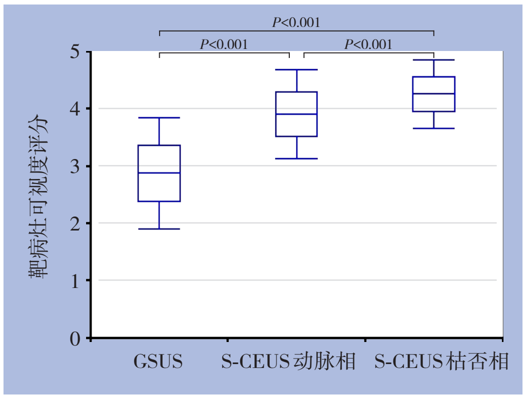

图7　各时相靶病灶评分

Figure 7　Visibility score of target lesions in each phase

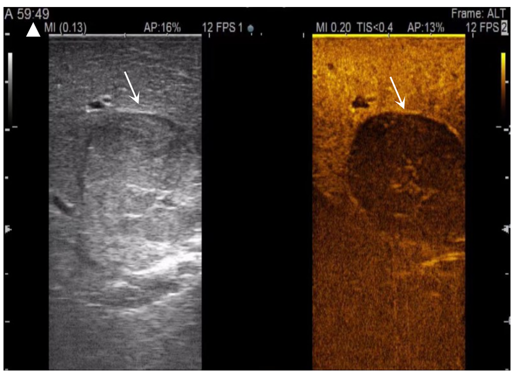

图8　枯否相持续近1 h后（白色三角形所示为注射造影剂后59 min 49 s），靶病灶（箭头所示）仍清晰显示

Figure 8　Clear display of the target lesion (shown by the arrow) in Kupffer phase lasting for approximately 1 h (triangle showing 59 min 49 s after injection of the contrast agent)

2.4　不良反应

1例患者在推注造影剂后出现血压下降，考虑过敏反应，经积极抗过敏性休克处理后迅速恢复，无后续并发症及后遗症出现，其他患者未观察到不良反应发生。

3　讨　论

GSUS因其简易、无创及可重复性等优点，常用于HCC经腹腔镜MWA的病灶定位及实时引导[14-15]。但在以下情况时，GSUS定位靶病灶常存在困难：⑴存在肝硬化背景的肿瘤[6, 16]：肝硬化背景下，肝脏常多发再生结节，这些结节的回声呈多样性，因此HCC结节难以与周边的再生结节及发育不良结节区分。本组数据显示：16.95%（10/59）的靶病灶因肝硬化多发再生结节的干扰，GSUS难以定位。⑵小肿瘤：小的HCC在GSUS时可能被遗漏[17]。Kim等[16]统计有47.8%的直径≤1 cm的HCC难以被GSUS发现。本组数据显示，6.78%（4/59）的靶病灶因直径≤1cm，GSUS难以定位。⑶等回声肿瘤[18]：部分HCC结节呈等回声，与肝实质难以区分。本组数据显示，13.56%（8/59）的靶病灶GSUS期呈等回声，因而定位困难。

靶病灶定位困难，有可能导致消融不完全或异位消融[16]。超声造影因增加了病灶与周边肝实质的显影对比，改善了病灶在超声下的可视性，可提高靶病灶定位的精准性[7-8]。但目前临床常用的造影剂如声诺维等增强时间窗较短暂，注射造影剂后5 min左右即失去对比增强效果，既不能满足多病灶患者的多次定位需要，也不能提供消融治疗时布针所需要的时间窗，因此其在HCC消融治疗中的作用有限[9]。

S-CEUS能较好地克服上述缺陷。HCC在S-CEUS动脉相和门静脉相的显像与其他二代造影剂类似，但在注射Sonazoid约10 min后即进入其特有的枯否相[19]，正常肝脏组织因Kupffer细胞摄取Sonazoid而表现为高增强，而HCC因缺乏Kupffer细胞则表现为低增强或增强缺失，亦称为"洗出"。肿瘤在枯否相的洗出效应提高了其在超声下的可视性。

多项研究[3,11,20-21]表明：S-CEUS动脉相、枯否相对HCC的可视度优于GSUS，差异具有统计学意义，与本研究结果相符。

S-CEUS枯否相可持续1 h以上[22]，为靶病灶的定位和治疗提供了宽裕的时间窗，便于反复扫描及MWA的实时引导、监测[4]。对于同一病例的多个肿瘤病灶，1次造影剂注射即可满足多个病灶的显影和治疗需求，本组术前已知多个病灶的患者均只注射1次造影剂即完成所有病灶的定位和MWA。同时，研究[3, 23-25]表明，相较于动脉相，枯否相肝实质与HCC的增强强度差异性更显著，枯否相尤其有助于消融治疗的穿刺引导。本研究亦显示，动脉相、枯否相靶病灶的可视性均优于GSUS期，枯否相靶病灶的可视度优于动脉相。本组所有患者的消融布针、治疗均在枯否相引导完成，靶病灶显影良好。

同时，国内学者顾炯辉等[25]研究认为，基于枯否相的时间优势，Sonazoid的使用有望提高肝脏隐匿性病灶的检出。本组数据中，S-CEUS共发现了3个术前影像学检查未发现的肿瘤病灶。相较于

CT或MRI的间歇断层扫描成像，S-CEUS的最大优势在于实时动态扫描，可以反复多次扫描肝脏。持续时间达1 h以上的枯否相为反复扫描提供了充裕的时间窗，同时枯否相HCC特征性的洗出效应也为隐匿性病灶的良恶性鉴别提供了依据。对于枯否相新发现的呈低或无增强的病灶，可通过造影剂再灌注成像的方式，进一步判断新检出的结节是否为HCC[26]。

消融后术中即时效果评估是肿瘤消融完全的重要保障，MWA后再次注射Sonazoid可观察肿瘤病灶是否消融完全[24,27-29]。无论是否消融，病灶在枯否相均表现为低或无增强，因此评估消融效果需再次注射造影剂，动脉相观察病灶区域有无局部高增强灶，以判断肿瘤是否消融完全。本组患者均在术中即时行消融效果评估，考虑消融不完全者均再次消融直至术中即时评估消融完全。术后1个月复查增强MRI，原肿瘤区域均显示无活性。

Sonazoid造影剂耐受性良好，不良反应多较轻[30]。Chou等[31]统计54例使用Sonazoid的患者，无严重不良反应发生，最常见的不良反应为腹痛（9.3%），其次是心率不规则（5.6%），除1例严重腹痛持续15 min外，其他所有患者不良反应均是短暂且可耐受的，无需医疗干预。本组患者因均在气管插管全麻后注射造影剂，无法记录患者自觉症状，心电监护未显示心律失常等不良反应。1例患者注射Sonazoid后即出现休克表现，考虑Sonazoid过敏可能性大，予抗休克处理后迅速缓解。因Sonazoid氢化卵磷脂酰丝氨酸外壳的存在，对蛋类和蛋类制品过敏的患者需谨慎使用[23]，本例患者无相关过敏史。

综上所述，针对特殊部位HCC的腹腔镜下MWA，靶病灶在S-CEUS动脉相、枯否相的可视度均优于GSUS，有利于靶病灶的定位；持续时间达1 h以上的枯否相有利于反复扫描及MWA的实时引导，同时有可能发现术前影像学未能发现的隐匿性小病灶。但本研究缺少与其他超声造影剂的随机对照，且因样本数相对较少，部分结论可能存在偏差，尚待进一步的临床数据积累。

利益冲突：所有作者均声明不存在利益冲突。

参考文献

[1] 国家卫生健康委办公厅. 原发性肝癌诊疗指南(2022年版)[J]. 临床肝胆病杂志, 2022, 38(2):288–303. doi: 10.3969/j.issn.1001–5256.2022.02.009.
General Office of National Health Commission. Standard for diagnosis and treatment of primary liver cancer(2022 edition) [J]. Journal of Clinical Hepatology, 2022, 38(2):288–303. doi:10.3969/j.issn.1001–5256.2022.02.009.

[2] 许赟, 王能, 沈强, 等. 经皮微波消融治疗较大原发性肝癌的可行性及疗效研究[J]. 中国普通外科杂志, 2016, 25(1):39–44. doi:10.3978/j.issn.1005–6947.2016.01.007.
Xu Y, Wang N, Shen Q, et al. Efficacy and feasibility of percutaneous microwave ablation for relatively large hepatocellular carcinoma[J]. Chinese Journal of General Surgery, 2016, 25(1):39–44. doi: 10.3978/j.issn.1005–6947.2016.01.007.

[3] Park HS, Kim YJ, Yu MH, et al. Real-time contrast-enhanced sonographically guided biopsy or radiofrequency ablation of focal liver lesions using perflurobutane microbubbles (sonazoid): value of Kupffer-phase imaging[J]. J Ultrasound Med, 2015, 34(3):411–421. doi: 10.7863/ultra.34.3.411.

[4] 洪智贤, 丁同领, 胡雄伟. 合并严重肝硬化的肝癌患者腹腔镜下消融治疗[J]. 中华肝胆外科杂志, 2017, 23(11):750–753. doi:10.3760/cma.j.issn.1007–8118.2017.11.008.
Hong ZX, Ding TL, Hu XW. Laparoscopic ablation of patients with hepatocellular carcinoma in a background of severe cirrhosis[J]. Chinese Journal of Hepatobiliary Surgery, 2017, 23(11):750–753. doi: 10.3760/cma.j.issn.1007–8118.2017.11.008.

[5] 许赟, 王能, 沈强, 等. 经皮热消融治疗极早期肝癌的疗效及预后因素分析[J]. 中国普通外科杂志, 2015, 24(7):945–951. doi:10.3978/j.issn.1005–6947.2015.07.006.
Xu Y, Wang N, Shen Q, et al. Percutaneous thermal ablation for very early stage hepatocellular carcinoma: efficacy and prognostic factors[J]. Chinese Journal of General Surgery, 2015, 24(7):945–951. doi: 10.3978/j.issn.1005–6947.2015.07.006.

[6] Lee SJ, Won HJ, Kim KW, et al. Value of contrast–enhanced sonography of small hepatocellular carcinoma with sonazoid prior to radiofrequency ablation[J]. J Clin Ultrasound, 2017, 45(7):383–390. doi: 10.1002/jcu.22469.

[7] 谢晓燕, 徐作峰, 匡铭, 等. 超声造影在肝癌消融治疗中的作用[J]. 中华肝胆外科杂志, 2008, 14(12):836–839. doi:10.3760/cma.j.issn.1007–8118.2008.12.002.
Xie XY, Xu ZF, Kuang M, et al. Application of contrast ultrasound in ablation treatment of liver cancer[J]. Chinese Journal of Hepatobiliary Surgery, 2008, 14(12):836–839. doi: 10.3760/cma.j.issn.1007–8118.2008.12.002.

[8] 邹瑞, 王一尧, 彭旭, 等. 实时动态超声造影在肝癌 射频消融治疗中的价值分析[J]. 中国普通外科杂志, 2020, 29(8):1023–1028. doi:10.7659/j.issn.1005–6947.2020.08.016.

Zou R, Wang YY, Peng X, et al. Analysis of value of real-time dynamic contrast-enhanced ultrasound in liver cancer radiofrequency ablation[J]. Chinese Journal of Hepatobiliary Surgery, 2020, 29(8): 1023–1028. doi: 10.7659/j. issn. 1005–6947.2020.08.016

[9] Minami Y, Kudo M, Hatanaka K, et al. Radiofrequency ablation guided by contrast harmonic sonography using perfluorocarbon microbubbles (Sonazoid) for hepatic malignancies: an initial experience[J]. Liver Int, 2010, 30(5):759–764. doi: 10.1111/j.1478–3231.2010.02226.x.

[10] Kudo M. Defect reperfusion imaging with sonazoid®: a breakthrough in hepatocellular carcinoma[J]. Liver Cancer, 2016, 5(1):1–7. doi: 10.1159/000367760.

[11] Lee MW, Kim YJ, Park SW, et al. Sequential changes in echogenicity and conspicuity of small hepatocellular carcinoma on gray scale sonography after transcatheter arterial chemoembolization[J]. J Ultrasound Med, 2010, 29(9):1305–1312. doi: 10.7863/jum.2010.29.9.1305.

[12] 刘德林, 黄斌, 孙希希, 等. 人工腹水辅助超声引导下经皮微波消融治疗邻近横膈肝癌的应用价值[J]. 中华医学超声杂志: 电子版, 2020, 17(8): 776–781. doi: 10.3877/cma. j. issn. 1672–6448.2020.08.012.

Liu DL, Huang B, Sun XX, et al. Value of ultrasound-guided percutaneous microwave ablation with artificial ascites in treatment of liver cancer adjacent to the diaphragm[J]. Chinese Journal of Medical Ultrasound: Electronic Edition, 2020, 17(8):776–781. doi: 10.3877/cma.j.issn.1672–6448.2020.08.012.

[13] 许凯豪, 焦德超, 韩新巍, 等. 经肝动脉化疗栓塞联合C臂CT引导微波消融治疗肝癌[J]. 中国介入影像与治疗学, 2021, 18(5): 265–269. doi: 10.13929/j.issn.1672–8475.2021.05.003.

Xu KH, Jiao DC, Han XW, et al. Transcatheter arterial chemoembolization combined with C-arm CT guided microwave ablation for liver cancer[J]. Chinese Journal of Interventional Imaging and Therapy, 2021, 18(5): 265–269. doi: 10.13929/j.issn.1672–8475.2021.05.003.

[14] Minami Y, Kudo M. Review of dynamic contrast-enhanced ultrasound guidance in ablation therapy for hepatocellular carcinoma[J]. World J Gastroenterol, 2011, 17(45):4952–4959. doi: 10.3748/wjg.v17.i45.4952.

[15] 朱天彤, 黄瑛. Sonazoid超声造影剂在肝脏肿瘤诊疗中的应用[J]. 现代肿瘤医学, 2020, 28(20):3624–3627. doi: 10.3969/j.issn.1672–4992.2020.20.035.

Zhu TT, Huang Y. Application of contrast-enhanced ultrasonography with Sonazoid for liver neoplasm[J]. Journal of Modern Oncology, 2020, 28(20): 3624–3627. doi: 10.3969/j.issn.1672–4992.2020.20.035.

[16] Kim PN, Choi D, Rhim H, et al. Planning ultrasound for percutaneous radiofrequency ablation to treat small (≤3 cm) hepatocellular carcinomas detected on computed tomography or magnetic resonance imaging: a multicenter prospective study to assess factors affecting ultrasound visibility[J]. J Vasc Interv Radiol, 2012, 23(5):627–634. doi: 10.1016/j.jvir.2011.12.026.

[17] Zhai HY, Liang P, Yu J, et al. Comparison of sonazoid and SonoVue in the diagnosis of focal liver lesions: a preliminary study[J]. J Ultrasound Med, 2019, 38(9):2417–2425. doi: 10.1002/jum.14940.

[18] Calandri M, Mauri G, Yevich S, et al. Fusion imaging and virtual navigation to Guide percutaneous thermal ablation of hepatocellular carcinoma: a review of the literature[J]. Cardiovasc Intervent Radiol, 2019, 42(5):639–647. doi: 10.1007/s00270–019–02167–z.

[19] Claudon M, Dietrich CF, Choi BI, et al. Guidelines and good clinical practice recommendations for Contrast Enhanced Ultrasound (CEUS) in the liver-update 2012: a WFUMB-EFSUMB initiative in cooperation with representatives of AFSUMB, AIUM, ASUM, FLAUS and ICUS[J]. Ultrasound Med Biol, 2013, 39(2): 187–210. doi: 10.1016/j.ultrasmedbio.2012.09.002.

[20] Eso Y, Takai A, Takeda H, et al. Sonazoid-enhanced ultrasonography guidance improves the quality of pathological diagnosis in the biopsy of focal hepatic lesions[J]. Eur J Gastroenterol Hepatol, 2016, 28(12): 1462–1467. doi: 10.1097/MEG.0000000000000745.

[21] Kang TW, Lee MW, Song KD, et al. Added value of contrast-enhanced ultrasound on biopsies of focal hepatic lesions invisible on fusion imaging guidance[J]. Korean J Radiol, 2017, 18(1):152–161. doi: 10.3348/kjr.2017.18.1.152.

[22] Lee JY, Minami Y, Choi BI, et al. The AFSUMB consensus statements and recommendations for the clinical practice of contrast-enhanced ultrasound using sonazoid[J]. Ultrasonography, 2020, 39(3):191–220. doi: 10.14366/usg.20057.

[23] 陈烁淳, 许敏, 顾炯辉, 等. 超声造影剂Sonazoid的研究进展[J]. 中华超声影像学杂志, 2020, 29(7):636–641. doi: 10.3760/cma.j.cn131148–20191225–00799.

Chen SC, Xu M, Gu JH, et al. Research progress of the ultrasonic contrast agent Sonazoid[J]. Chin J Ultrason, 2020, 29(7):636–641. doi: 10.3760/cma.j.cn131148–20191225–00799.

[24] Dohmen T, Kataoka E, Yamada I, et al. Efficacy of contrast-enhanced ultrasonography in radiofrequency ablation for hepatocellular carcinoma[J]. Intern Med, 2012, 51(1): 1–7. doi: 10.2169/internalmedicine.51.6042.

[25] 顾炯辉, 何蒙娜, 许敏, 等. 基于时间–强度曲线评价SonoVue和Sonazoid在肝癌中的价值[J]. 中国超声医学杂志, 2020, 36(12): 1133–1136. doi:10.3969/j.issn.1002–0101.2020.12.020.

Gu JH, He MN, Xu M, et al. Diagnostic value of SonoVue and Sonazoid in hepatocellular carcinoma based on time intensity curve[J]. Chinese Journal of Ultrasound in Medicine, 2020, 36(12): 1133–1136. doi:10.3969/j.issn.1002–0101.2020.12.020.

[26] Kudo M, Ueshima K, Osaki Y, et al. B-mode ultrasonography versus contrast-enhanced ultrasonography for surveillance of hepatocellular carcinoma: a prospective multicenter randomized controlled trial[J]. Liver Cancer, 2019, 8(4):271–280. doi: 10.1159/000501082.

[27] Maruyama H, Sekimoto T, Yokosuka O. Role of contrast-enhanced ultrasonography with Sonazoid for hepatocellular carcinoma: evidence from a 10-year experience[J]. J Gastroenterol, 2016, 51(5): 421–433. doi: 10.1007/s00535–015–1151–3.

[28] Dietrich CF, Averkiou M, Nielsen MB, et al. How to perform contrast-enhanced ultrasound (CEUS) [J]. Ultrasound Int Open, 2018, 4(1):E2–15. doi: 10.1055/s–0043–123931.

[29] Nishigaki Y, Hayashi H, Tomita E, et al. Usefulness of contrast-enhanced ultrasonography using Sonazoid for the assessment of therapeutic response to percutaneous radiofrequency ablation for hepatocellular carcinoma[J]. Hepatol Res, 2015, 45(4): 432–440. doi: 10.1111/hepr.12370.

[30] Barr RG, Huang P, Luo Y, et al. Contrast-enhanced ultrasound imaging of the liver: a review of the clinical evidence for SonoVue and Sonazoid[J]. Abdom Radiol (NY), 2020, 45(11): 3779–3788. doi: 10.1007/s00261–020–02573–9.

[31] Chou YH, Liang JD, Wang SY, et al. Safety of perfluorobutane (sonazoid) in characterizing focal liver lesions[J]. J Med Ultrasound, 2019, 27(2):81–85. doi: 10.4103/JMU.JMU_44_19.

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本刊对来稿中统计学处理的有关要求

1.统计研究设计：应交代统计研究设计的名称和主要做法。如调查设计（分为前瞻性、回顾性或横断面调查研究）；实验设计（应交代具体的设计类型，如自身配对设计、成组设计、交叉设计、正交设计等）；临床试验设计（应交代属于第几期临床试验，采用了何种盲法措施等）。主要做法应围绕4个基本原则（随机、对照、重复、均衡）概要说明，尤其要交代如何控制重要非试验因素的干扰和影响。

2.资料的表达与描述：用$\bar{x} \pm s$表达近似服从正态分布的定量资料，用M（QR）表达呈偏态分布的定量资料；用统计表时，要合理安排纵横标目，并将数据的含义表达清楚；用统计图时，所用统计图的类型应与资料性质相匹配，并使数轴上刻度值的标法符合数学原则；用相对数时，分母不宜小于20，要注意区分百分率与百分比。

3.统计分析方法的选择：对于定量资料，应根据所采用的设计类型、资料所具备的条件和分析目的，选用合适的统计分析方法，不应盲目套用t检验和单因素方差分析；对于定性资料，应根据所采用的设计类型、定性变量的性质和频数所具备条件以分析目的，选用合适的统计分析方法，不应盲目套用χ^2检验。对于回归分析，应结合专业知识和散布图，选用合适的回归类型，不应盲目套用简单直线回归分析，对具有重复实验数据的回归分析资料，不应简单化处理；对于多因素、多指标资料，要在一元分析的基础上，尽可能运用多元统计分析方法，以便对因素之间的交互作用和多指标之间的内在联系进行全面、合理地解释和评价。

4.统计结果的解释和表达：当$P<0.05$（或$P<0.01$）时，应说明对比组之间的差异有统计学意义，而不应说对比组之间具有显著性（或非常显著性）的差别；应写明所用统计分析方法的具体名称（如：成组设计资料的t检验、两因素析因设计资料的方差分析、多个均数之间两两比较的q检验等），统计量的具体值（如t=3.45, χ^2=4.68, F=6.79等）应尽可能给出具体的P值（如P=0.023 8）；当涉及到总体参数（如总体均数、总体率等）时，在给出显著性检验结果的同时，再给出95%置信区间。

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