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肝细胞癌超声造影研究热点与进展

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摘要: 肝细胞癌是最常见的原发性肝癌类型,整体预后较差。超声造影在肝细胞癌的诊断、疗效评估及预后判断等方面具有重要价值。本文系统梳理了超声造影在肝细胞癌领域的文献特征、研究热点与前沿进展。该领域年发文量总体呈稳步增长趋势,中国在发文总量上居全球首位。高被引文献高度集中于临床指南与标准化规范。关键词分析结果显示,该领域研究热点主要包括肝细胞癌诊断与标准化评估、鉴别诊断、局部治疗后疗效评价及预后预测。同时,微血管侵犯、人工智能及超分辨超声等可能成为当前领域的前沿方向。其中,人工智能可应用于肝细胞癌辅助诊断、肿瘤生物学特征评估及预后预测,而超分辨超声可突破衍射极限,实现肝脏微血管精确成像。当前,肝细胞癌超声造影已有坚实的研究基础,具有较强的临床实践导向。未来基于超声造影的人工智能模型及超分辨超声等新技术有望进一步推动肝细胞癌精准诊疗的发展。

关键词: 癌, 肝细胞; 超声造影; 文献计量学; 人工智能; 超分辨超声

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Research hotspots and advances in contrast-enhanced ultrasound for hepatocellular carcinoma

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Abstract: Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer and has a poor overall prognosis. Contrast-enhanced ultrasound (CEUS) plays a crucial role in the diagnosis, treatment response evaluation, and prognostic evaluation of HCC. This article systematically reviews the literature characteristics, research hotspots, and frontier advances of CEUS in the field of HCC. There has been a gradual increase in annual publication volume in this field, with China ranking first globally in the total number of publications. Highly cited articles mainly focus on clinical guidelines and standardized protocols. Keyword analysis shows that the main research hotspots in this field include the diagnosis and standardized assessment of HCC, differential diagnosis, treatment response evaluation after local therapy, and prognostic prediction. Meanwhile, microvascular invasion, artificial intelligence (AI), and super-resolution ultrasound (SRUS) may be emerging as cutting-edge frontiers in this field. Specifically, AI can be used for the auxiliary diagnosis of HCC, the evaluation of tumor biological characteristics, and prognostic prediction, and SRUS can overcome the acoustic diffraction limit to achieve precise microvascular imaging of the liver. Currently, a solid foundation has been established for the research on CEUS in HCC, showing a strong orientation toward clinical practice. In the future, emerging technologies such as CEUS-based AI models and SRUS are expected to further promote the development of precise diagnosis and treatment for HCC.

Key words: Carcinoma, Hepatocellular; Contrast Enhanced Ultrasound; Bibliometrics; Artificial Intelligence; Super Resolution Ultrasound

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肝细胞癌（hepatocellular carcinoma，HCC）是最常见的原发性肝癌，主要风险因素包括慢性乙型或丙型肝炎病毒感染[1]。全球每年新增约68万HCC病例，造成死亡约59万例，发病数与死亡数的接近提示该病整体预后较差[2]。此外，HCC临床症状常不典型导致早期诊断困难[3]。尽管近年来HCC的局部及系统治疗均取得了一定进展，但仍有较多患者可能无应答[1]。因此，加强HCC的早期诊断、疗效监测及预后评估具有重要临床意义。

超声造影（contrast enhanced ultrasound，CEUS）是在常规超声基础上通过注射微泡造影剂，动态显示病灶血流灌注的影像技术。HCC具有典型的动脉期高增强及晚发廓清等强化模式，CEUS可为HCC的诊断及局部治疗后评估提供重要依据[1-2]。目前，国内外多部指南均肯定了CEUS在HCC诊疗中的应用价值。欧洲肝病学会在2025年指南中指出CEUS可作为肝硬化等高危人群的HCC非侵入性诊断的影像方法之一，同时作为计算机体层成像（computed tomography，CT）和磁共振成像（magnetic resonance imaging，MRI）结果不确定时的二线检查[3]。美国肝病学会、世界超声医学与生物学联合会同样强调了CEUS在HCC诊断中的补充价值，并指出其可用于消融治疗前评估及围手术期疗效评价[4-5]。我国《原发性肝癌诊疗指南（2026年版）》进一步提及了基于CEUS的超分辨超声（super resolution ultrasound，SRUS）成像技术的潜在价值[6]。此外，相较于CT和MRI，CEUS具有实时、无辐射、便捷、造影剂无肾毒性等优势[7]。

在CEUS临床价值逐渐受到指南关注、相关研究不断积累的背景下，对HCC超声造影领域的研究系统梳理具有重要意义。本研究通过文献计量学手段概览该领域的文献发展特征，并根据关键词揭示当前研究热点与研究进展，综述CEUS在HCC诊断标准化、鉴别诊断、疗效评价、预后预测及新兴技术应用等方面的进展。

本文基于Web of Science核心合集中的科学引文索引扩展版，对1900年1月1日—2026年4月26日的文献进行检索，检索式设定为TS=（HCC OR HCCs OR “hepatocellular carcinoma*” OR “hepatocellular cancer*” OR “hepatocellular neoplasm*” OR hepatoma* OR “liver cell carcinoma*”） AND TS=（“CEUS” OR “contrast enhanced sonograph*” OR “contrast enhanced ultrasonography” OR “contrast enhanced ultrasound” OR “contrast enhanced US”）。文献类型限定为论著和综述，排除会议、摘要、信件和评论等其他形式的文献。语言限定为英语。此外，为补充未来可能迁移于HCC的潜在技术方向，单独针对CEUS进一步开展了二次检索，检索式如下：TS=（“CEUS” OR “contrast enhanced sonograph*” OR “contrast enhanced ultrasonography” OR “contrast enhanced ultrasound” OR “contrast enhanced US”）。本文采用VOSviewer 1.6.20、Microsoft Office Excel 2019、Adobe Illustrator 2025及Datawrapper（https://www.datawrapper.de/）等软件及网站进行分析和绘图。

1 HCC CEUS的文献计量学概况

1.1 文献分布情况 本研究最终纳入Web of Science核心合集中的相关文献1 905篇。该领域文献累计被引66 382次，篇均被引34.96次，施引文献共32 942篇。该检索集合的H-index为97，提示该领域已形成一定规模的研究积累和学术影响力。文献产出随年度变化总体呈稳步增长趋势。在Web of Science学科分类体系中，逾半数文献隶属于“放射学、核医学与医学影像学”领域，其次为“胃肠病学与肝脏病学”及“声学”领域（附录A）。不同国家/地区的发文情况各异，其中中国在发文量与总被引次数上均居首位，发文量达792篇，总被引次数达15 682次，且中国同样具有最紧密的国际合作关系（附录B～C）。在全球主要研究机构中，中山大学发文量最高，共发表文献184篇，复旦大学及近畿大学次之；加利福尼亚大学圣迭戈分校、梅奥诊所等总被引次数位居前列（附录D）。作者发文量按照全计数原则进行统计，即一篇文献中出现的所有作者均被计入相应作者的发文量中（附录E）。

1.2 热门期刊及高被引文献 期刊的发文量可反映不同期刊对HCC CEUS研究主题的关注程度。*Ultrasound in Medicine and Biology*在HCC超声造影领域的发文量最高，*Abdominal Radiology*与*Journal of Ultrasound in Medicine*位列第二与第三，且不同期刊之间存在较为密切的引用关系（附录F～G）。此外，本领域的高被引文献主要集中于国际指南、专家共识等（附录H）。

2 基于关键词挖掘HCC CEUS的研究热点与进展

本领域文献关键词主要分为4个簇：HCC的预后评估、HCC影像诊断与标准化评估、HCC的局部治疗疗效评估、肝脏局灶性病变的鉴别诊断。这些簇反映着当前这一领域的研究现状。近3年的关键词时间叠加图进一步聚焦研究前沿，结果显示“microvascular invasion”“deep learning”“artificial intelligence”等关键词平均发表年份较新，提示研究前沿正在向微血管侵犯（microvascular invasion，MVI）及人工智能（artificial intelligence，AI）辅助方向扩展（附录I）。

为补充未来可能迁移于HCC的潜在技术，从CEUS技术演进角度对关键词进行人工筛查与归纳（表1）。结果显示，在平均发表年份较新的技术相关关键词中，以SRUS为代表的微血管成像相关的关键词较为集中，包括 microvascular imaging、localization microscopy、ultrasound localization microscopy、super-resolution ultrasound 和 tracking 等。其中，SRUS相关关键词虽然总体出现频次仍有限，但多个关键词出现次数均超过5次，可能代表CEUS微血管成像方向中初步形成的新兴技术。SRUS通常依赖微泡造影剂，能够在CEUS基础上进一步提高微血管显示能力，可作为CEUS技术延伸的重要方向。

3 HCC CEUS领域的研究热点

关键词聚类结果提示，HCC CEUS研究主要围绕诊断与标准化评估、局灶性肝脏病变的鉴别诊断、局部治疗后疗效评价以及预后评估展开。

3.1 *诊断与标准化评估* CEUS在HCC诊断中的价值主要来自其对病灶血流的实时观察[8]。HCC在CEUS中通常表现为动脉期高增强与延迟出现的轻度廓清[3]。在HCC诊断中，当首次CT或MRI结果不确定后，CEUS可作为二线检测，具备极高的特异度[9-10]。美国放射学会引入肝脏影像报告与数据系统（liver imaging reporting and data system，LI-RADS），为HCC的CEUS诊断提供了标准化评估，其仅适用于高风险HCC患者（肝硬化、慢性乙型病毒肝炎患者等）。LI-RADS综合评估病灶的大小、动脉期增强和廓清情况，将局灶性肝脏病变分为8类，包括LR-NC（无法分类），LR-1（明确良性）至LR-5（明确HCC），同时包含LR-M（提示恶性但非HCC特异性病变）和LR-TIV（脉管内癌栓）等特殊类别[11-12]。多项荟萃分析持续证实了CEUS LI-RADS的临床诊断效能，其对HCC诊断的敏感度、特异度和准确度分别达到了73%、92%和78%，与CT/MRI相仿[13-15]。此外，一项纳入1 000余项肝硬化背景下肝脏病灶的回顾性研究显示，符合CEUS典型HCC模式的LR-5类病灶，其诊断HCC的阳性预测值可接近99%[16]。

3.2 *局灶性肝脏病变的鉴别诊断* 在临床中，HCC通常需要与肝内胆管癌（intrahepatic cholangiocarcinoma，ICC）、混合型肝细胞-胆管癌（combined hepatocellular-cholangiocarcinoma，CHC）及肝转移瘤等肝脏病变进行鉴别诊断。CEUS在非侵入性HCC诊断中仍存争议，其核心原因之一便在于理论上存在的误诊风险。尤其是ICC，其病发率占肝硬化所有新结节的2%～5%[17]，并且同样也会出现动脉期高增强与随后出现的廓清。HCC与ICC可根据廓清出现时间与程度进行区分，大多数ICC的廓清会在造影剂注射后60 s以内即开始出现，而HCC通常超过60 s。此外，ICC的廓清程度通常更明显[8, 18]。CEUS LI-RADS中定义为LR-M类的特征，包括周边环状高增强、早期廓清及显著廓清，为ICC与HCC的鉴别提供了重要标准，依据该标准鉴别二者的曲线下面积可达0.92[19]。另一方面，CHC由于其复杂的组织病理特征，使得影像学特征与HCC较难区分，通常需要联合血清肿瘤标志物，例如甲胎蛋白、糖类抗原等提高鉴别诊断效能[20-21]。

3.3 *局部治疗后疗效评价* 除诊断外，局部治疗后疗效评价也是CEUS的重要研究方向[22-23]。消融治疗和经导管动脉化疗栓塞术（transcatheter arterial chemoembolization，TACE）等局部治疗方式均需要准确判断病灶是否存在残余活性或早期复发[24, 25]。与CT或MRI相比，CEUS能够更加便捷地描绘肿瘤灌注动态，更适合进行短间隔

表1 超声造影相关技术方向及代表性关键词

Table 1 CEUS-related technical directions and representative keywords

技术方向	相关关键词
造影剂	contrast agent、ultrasound contrast agents、Sonazoid、SonoVue、nanobubbles
多模态评估	Doppler、elastography、multiparametric ultrasound、fusion imaging
人工智能算法应用	artificial intelligence、deep learning、machine learning、radiomics、segmentation、prediction model
超分辨超声	microvascular imaging、localization microscopy、ultrasound localization microscopy、super-resolution ultrasound、tracking

的重复评估[22]。在消融治疗中，CEUS可引导HCC的消融治疗，且接受CEUS引导的患者的术后并发症、复发率远低于仅经常规超声引导者[26]。临床通常在术后1周或1个月内行CEUS以评估消融效果，其敏感度通常可超过80%，特异度接近100%。然而，由于存活肿瘤与术后反应性充血难以区分，所以CEUS通常不作为极早期评估[27]。在TACE中，CEUS可观察动脉期是否存在残余强化进而判断有无肿瘤残留，并且因不受碘油沉积伪影的影响，可较CT/MRI更早地评估TACE术后情况[27]。

目前，LI-RADS体系已进一步拓展并提出CEUS非放射性治疗反应评估2024版，为评估TACE、消融治疗及手术切除等治疗后病灶提供了标准。其分别评价病灶内和病灶周肿瘤活性，病灶内的活性主要看动脉期是否存在残余强化，而病灶周边活性因需与术后反应性充血相鉴别，故需综合评估动脉期、门静脉期及延迟期。如果病灶内或病灶周任一处提示“有活性”即被评估为LR-TR viable[11]。目前已有多项临床研究对这一标准进行了评估，结果显示其诊断效能与阅片者间一致性均表现良好[28-29]。

3.4 预后预测 近年来，CEUS在HCC中的应用已不再局限于病灶检出，其在患者预后预测中显示出一定价值。目前多项研究将LI-RADS类别、增强模式及廓清时间等影像特征纳入模型，用以评估HCC手术切除后的早期复发风险，并且其通常联合临床特征、血清学指标等，可进一步提高预测能力[30-31]。除常规特征外，动态CEUS定量分析能够提取峰值强度、达峰时间、曲线下面积等参数，可作为预后评估的补充量化指标[32]。随着AI的发展，基于CEUS的影像组学及深度学习模型进一步提高了预后预测的准确度，利用CEUS图像或视频构建的模型可预测HCC切除或消融后的早期复发、无进展生存和总生存，提示多维影像特征可弥补传统肉眼评估的不足[33-35]。然而，现阶段基于CEUS的预后预测研究大多仍局限于单中心、回顾性设计，样本量有限，模型外部验证不足，未来仍需进一步明确CEUS预后模型在HCC个体化治疗决策中的临床转化价值。

4 HCC CEUS领域研究进展

根据关键词时间叠加图及针对CEUS技术演进的关键词分析提示，AI、MVI及SRUS是值得关注的前沿方向。

AI通常包含影像组学、机器学习及深度学习技术，现已应用于HCC辅助诊断、肿瘤生物学特征评估及预后预测。研究表明，通过整合局灶性肝脏病变的CEUS视频，免疫组化生物标志物及临床信息，利用双流深度学习模型分析空间和时间信息，可实现HCC与肝转移瘤等六种肝脏病变的精准分类[36]。此外，AI也可辅助HCC的鉴别诊断，例如区分LR-M分类中的HCC与非HCC恶性病变等[37-38]。术前无创评估HCC的生物学行为对临床决策具有指导作用。因此，当前诸多研究尝试挖掘CEUS影像学特征以无创评估肿瘤特性[39-41]，MVI是最受关注的研究热点之一，是HCC复发和不良预后的重要病理学指标[42]。现有研究多基于CEUS图像，结合深度学习算法构建HCC MVI的预测模型。一项研究联合CEUS图像与临床信息进行MVI的预测，其外部验证集曲线下面积达0.81[43]。此外，多项研究也证明了CEUS对MVI的预测效能[41,44-45]。近年来，研究也进一步扩展到肿瘤包绕型血管等更细化的病理结构[40]，旨在通过整合早期影像及临床数据预测HCC预后，从而优化个体化治疗方案[46]。

在对CEUS技术前沿评估中，SRUS这一新兴微血管成像方式值得关注。SRUS通过定位和追踪微泡，可突破传统超声成像的衍射极限，实现微血管结构的超分辨率显示（附录J）[47-48]。目前已有HCC相关研究发现，血管复杂度、面积比值和灌注指数等SRUS参数与MVI高风险相关[49]。需要指出的是，SRUS并非单纯用于MVI预测，其为HCC微血管研究提供了一项新的技术。目前SRUS可利用其血管密度参数，对HCC、肝转移瘤及肝脏局灶性结节增生进行鉴别诊断，结果显示HCC与肝实质的血管密度相仿，肝转移瘤的血管密度显著低于肝实质，肝脏局灶性结节增生的血管密度则较高[50]。同时，SRUS还可检测TACE的疗效，完全反应组的血管密度低于部分反应组及对照组[51]。鉴于肝脏作为富血管器官，HCC的生长、转移及侵袭性等均与异常血管生成、血管拟态、血管共选择等血管特性密切相关[52]。因此，基于这一趋势，SRUS可作为新兴微血管成像技术被纳入未来研究展望，为HCC诊疗提供新的影像学思路。

5 小结与展望

本研究通过文献计量学分析，系统描绘了HCC CEUS领域的文献特征，并基于关键词分析挖掘该领域的研究热点与前沿进展。当前，该领域的研究热点正经历从早期的应用探索逐渐拓展至HCC的诊断与标准化评估、局灶性肝脏病变的鉴别诊断、局部治疗后疗效评价以及预后评估。其中，LI-RADS体系已覆盖诊断及局

部治疗后疗效评价的标准化。展望未来，基于CEUS的AI技术应用及SRUS等将为HCC的诊疗提供全新的技术方向，进一步拓展HCC诊疗的影像学思路。

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附录A~J见二维码

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