

## 肝局灶性病变非侵入性影像评估意大利指南： 发展和结论(全译)

### Italian guidelines for noninvasive imaging assessment of focal liver lesions: development and conclusions

Carlo Filice<sup>a</sup>, Fabrizio Calliada<sup>b</sup>, Salvatore De Masi<sup>c</sup>, Letizia Sampaolo<sup>d</sup>, Cristina Morciano<sup>d</sup>, Alfonso Mele<sup>d</sup>, Maria Franc Meloni<sup>e</sup>, Chiara Sileo<sup>b</sup>, Mara Scabini<sup>b</sup>, Paolo Ricci<sup>f</sup>, Vito Cantisani<sup>f</sup> and Giovanna Ferraioli<sup>g</sup>  
代表本多学科指南编写组

#### 简介

成像技术的进步极大改善了肝局灶性病变(FLLs)的非侵入性检测和成像。由于良性 FLLs 的发病率极高,因此病变成像极其重要。相对而言,包括原发性肝癌和转移癌在内的肝癌是最常见的肿瘤疾病<sup>[1]</sup>。

有多种诊断成像技术可以用于 FLLs 检测和成像,包括常规超声、彩色多普勒超声、超声造影成像(CEUS)、计算机断层扫描(CT)、磁共振成像(MRI)、正电子放射断层造影术(PET)等。很少使用较具侵入性的成像技术,如血管造影。不断出现的新造影剂和更新、更精密的诊断成像技术提高了这些技术的诊断能力。

选择检测 FLLs 最合适的成像技术,判定属于恶性还是良性,并进行分类,这些工作程序极为复杂。

在日常临床实践中,由于在具体的临床情境中这些成像方式的诊断准确性仍不确定,因此选择最适合 FLLs 研究的成像方式仍然很困难。

医疗资源是有限的,因此必须考虑与程序相关的成本。一方面,医疗资源不足,另一方面,人们对医疗资源的质量和数量要求不断提高,要进行选择需要在决策过程中引入经济性标准。

对于在研究和临床创新前沿中日渐成为焦点的领域,必须要有明确的治疗策略,因此意大利国家卫生研究院(Italian National Institute of Health, SNLG)的意大利国家指南系统(Sistema Nazionale Linee Guida)最近制定了“肝局灶性病变诊断成像”指南,旨在确认当前非侵入性诊断技术的有用性和有效性。

DOI:10.3760/cma.j.issn.1004-4477.2014.02.026

本文首次发表在 European Journal of Gastroenterology & Hepatology, 2011, 23:343-353.

作者单位:<sup>a</sup>Ultrasound Unit, Infectious Diseases Department, <sup>b</sup>Institute of Radiology, IRCCS Fondazione Policlinico S. Matteo, University of Pavia; <sup>c</sup>Dipartimento di Prevenzione, ASL 6 Livorno; <sup>d</sup>National Institute of Health (Istituto Superiore di Sanità), Rome; <sup>e</sup>Institute of Radiology, S. Gerardo Hospital, Monza and <sup>f</sup>Department of Radiology, Umberto I Hospital, University of Roma, Italy

通信作者: Professor Carlo Filice, MD, Ultrasound Unit, Infectious Diseases Department, IRCCS Fondazione Policlinico S. Matteo, University of Pavia, Via Taramelli 5, 27100 Pavia, Italy; Tel: + 39 382 502887/799; Fax: + 39 382 502296; Email: carfil@unipv.it

这些指南的焦点在于:评价超声、CEUS、CT、MRI 和 PET 成像技术在评估 FLLs 中的性能和有效性并制定将这些成像技术应用于(需要进行定向诊断成像的)肝局灶性病变患者的标准程序。成像技术评价指标包括:①诊断准确度;②在肿瘤患者管理中的角色;③良性病变跟踪。

本研究中提出的建议以大范围的文献评估为基础,考虑了 FLLs 成像技术选择的适当性。就我们所知,由政府机构推动制定的这些指南在世界上第一次解决了上述问题。

#### 资料和方法

##### 多学科指南编写组

多学科指南编写组(Multidisciplinary guidelines development group, MGDG)的成员包括重要利益相关者和相关学科的专家,例如结肠直肠外科、内窥镜检查手术、肠胃病学、流行病学、肝病、感染性疾病、内科、肿瘤外科、肿瘤、放疗、肿瘤放疗专家、超声专家和全科医学专家,还包括指南编写专家。每个成员都签署了无利益冲突声明书,并同意所提出的指南编写战略方针。

MGDG 于 2007 年 7 月和 2008 年 6 月召开了会议,讨论并确定了重要的方法问题,认定了研究战略关键词,定义了采纳/排除标准,并就最终版本的方针达成了一致。对指南编写过程的监控以及起草指南的相关协商均通过电子邮件和电话联系,在项目最终阶段通过在意大利国家指南系统(Italian national Guidelines System, SNGL)网站(www.snlg-iss.it/og)上开设网络社区进行协商和讨论。

收集的信息和证据按照 SNGL 要求的方法进行了总结<sup>[2]</sup>。

#### 临床问题

委员会成员提出了 5 个有关判定和对 FLLs 成像的关键问题,这些问题如下:

- (1)癌症患者和慢性肝病患者的 FLLs 的检测。
- (2)未知病理、慢性肝病和肿瘤疾病患者 FLLs 的成像。
- (3)原发性肝癌的局部分期,包括判定病变数量、大小、部位、与功能性解剖结构的关系以及是否涉及淋巴结。
- (4)接受肿瘤治疗患者的并发症、短期和长期(跟踪)治疗反应,这些癌症治疗方法如化疗、射频热消融(RFTA)、经皮酒精注射、激光、微波、肝动脉化疗栓塞、经导管动脉栓塞术、冷冻疗

法、手术等。

(5) 良性 FLLs 患者的跟踪。

### 文献搜索

使用明确的搜索策略,系统查阅 2000 年 1 月至 2007 年 10 月的英文文献(表 1);搜索范围涵盖 PubMed、Embase、Pascal、SciSearch 和 Cochrane Library 数据库。

将搜索术语互相组合,获得各个关键问题针对性的答案,然后对每个关键问题实施不同的搜索策略。

### 纳入标准

全面系统的综述文献,随机受控的实验和评价诊断成像技术所发挥作用的前瞻性/回顾性研究。选入的这些研究评价了超声、CEUS、CT、MRI 和 PET 成像技术在 FLLs 检测、成像、分期,以及短期和长期肿瘤治疗反应评估,和良性 FLLs 跟踪方面的有效性和可重复性。

### 排除标准

若研究未针对于诊断成像技术,未使用标准参照,属于病例分析、述评、信函和叙述性综述,则排除。

### 方法学评价选择标准和手段

由经过培训的人员使用苏格兰学院间指南网络(Scottish Intercollegiate Guidelines Network)中的方法学列表<sup>[3]</sup>(根据意大利国家国家指南系统调整过),对上述大范围搜索到的文献进行临床评估。

使用证据列表对评估结果进行总结,并给出建议。

指南草案由独立的专家组进行审核,专家组成员包括外科医生、内部医学专家和肝病超声扫描专家。

## 结果

### 文献

在线搜索共获得 4 960 条标题和摘要,其中 922 条适用。这些标题做进一步选择,只有 213 篇研究文献真正用于数据评价。只有 176 篇研究文献用于最终的指南相关主题评估<sup>[4-180]</sup>。

在最终讨论阶段,在指南草案演示中,许多 MGDG 成员给出了

文献搜索未发现的文献材料。一些研究虽然不符合给定的纳入标准,但委员会仍认为它们可以纳入文献目录<sup>[181-184]</sup>。

### 评级系统

MGDG 决定不适用证据评级系统,因为所收集信息的多样性和指南主题并不适合当前所用的证据层级结构。因此,在对这些证据进行评价和讨论之后,专家组给出了许多建议,在提出每条建议前都对所收集的研究进行了简要说明和充分讨论,并考虑了每种诊断技术的临床适用性。

因此,证据层级考虑了研究设计,但仅对其进行了叙述性说明而非图示性说明。

### 问题 1

基于文献搜索得到的适用的研究<sup>[4-101]</sup>,表 2 给出了最终的建议。

在肿瘤患者中,对比 PET、CT 或 MRI 结果进行了三项元分析。Wiering 等<sup>[4]</sup>综合了 32 项研究中 1 843 例患者的数据,发现 PET 结果的灵敏度和特异性分别为 88% 和 96.1%,CT 的总和灵敏度和特异性分别为 82.7% 和 84.1%。在 Bipat 等<sup>[5]</sup>的元分析中,该分析综合了 61 项研究 3 187 例患者的数据,与其他成像方式相比,PET 的患者诊断灵敏度显著更高,但病变特征判定的灵敏度并不高。非螺旋 CT、螺旋 CT、1.5-T MRI 和 PET 的患者诊断灵敏度估测值分别为 60.2%、64.7%、75.8% 和 94.6%;在这些成像技术中,PET 的准确性最高。在病变特征判定方面,非螺旋 CT、螺旋 CT、1.5-T MRI 和 PET 的灵敏度估测值分别为 52.3%、63.8%、66.1%、64.4% 和 75.9%。造影 MRI 的灵敏度估测值显著高于螺旋 CT。Kinkel 等<sup>[6]</sup>的元分析综合了 3 080 例患者的数据,比较了超声、CT、MRI 和 PET 检测这些患者结肠、胃和食道癌的肝转移的灵敏度,平均加权灵敏度超声为 55%,CT 为 72%,MRI 为 76%,PET 为 90%。在其他的多项研究中,PET 评估肝转移的灵敏度和特异性随原发癌的部位不同而有所差异<sup>[7-20]</sup>。在胰腺癌患者<sup>[7-8]</sup>中灵敏度和特异性分别为 70%~77% 和 94%~100%,在消化道癌症患者<sup>[9]</sup>中分别为 67% 和 81.3%,在结肠癌患者中分别为 54%~100% 和 58%~100%<sup>[10-18]</sup>。在所有研究中,患者诊断研究结果都比病变特征判定结果好。

表 1 文献搜索策略主要搜索词

#1	'Echography'(回波)
#2	'Tomography'(X 射线断层成像)、'emission - computed'(X 射线计算机断层成像)或'diagnostic imaging'(诊断成像)或'magnetic resonance imaging'(磁共振成像)或'MRI'或'PET'或'positron emission tomography'(正电子放射断层成像)或'positron emission computed'(正电子放射计算机断层成像)或'tomography emission computed'(放射计算机断层)或'computer - assisted emission tomography'(计算机辅助放射断层成像)或'positron emission tomography'(正电子放射断层成像)
#3	'Contrast - enhanced'(对比增强成像)和'ultrasonography'(超声扫描)
#4	'Contrast - enhanced'(对比增强成像)和'ultrasound sonography'(超声扫描成像)
#5	'US'(超声)和'sonography'(超声扫描术)
#6	'CEUS'(超声造影成像)
#7	'Computed tomography'(计算机断层成像)
#8	'Ultrasonography'(超声扫描术)或'ultrasound sonography'(超声扫描成像)或'contrast - enhanced ultrasound sonography'(对比增强超声扫描成像)或'contrast - enhanced ultrasound sonography'(对比增强超声扫描成像)或'contrast - enhanced ultrasonography'(对比增强超声扫描)
#9	'CT'(计算机断层扫描成像)和'tomography'(断层成像)
#10	#1 或 #2 或 #3 或 #4 或 #5 或 #6 或 #7 或 #8 或 #9

**表 2 关键问题、所选研究和对肿瘤患者及慢性肝病患者的建议**

关键问题	研究	建议
US、CEUS、CT、MRI 和 PET 在 FLLs 检测中的作用： ① 肿瘤患者； ② 慢性肝病者	发现 2 407 项， 选择 460 项， 对 110 项进行了评价， 纳入 98 项	①目前关于肿瘤患者 FLLs 检测的知识建议将 CEUS 用作一种筛选方法。此外，对元分析(特别是有关结肠癌 FLLs 检测的元分析)回顾得到的证据表明，在需要进行外科手术或消融术治疗的患者中和得到阴性 CEUS 结果的病例中，如有必要，可以将 PET 和使用肝脏专用造影剂的 CECT 或 CEMRI 作为诊断性确认检查手段 ②建议有可能发展成肝癌的慢性肝病者使用 US 成像。若结果为阳性或不确定，或肝癌高度疑似患者，必须在进行这项检查之后使用肝脏专用造影剂的 CECT 或 CEMRI

MRI 结果的不一致主要是因为所用的造影剂。若使用肝专用造影剂，MRI 检查结果之间的差异最低。使用细胞外造影剂，MRI 的灵敏度为 82%~94%<sup>[21,22]</sup>，使用顺磁氧化铁灵敏度为 66%~93.5%<sup>[23-26,29-31]</sup>，使用肝专用造影剂的特异性和灵敏度分别为 81%~93%和 67%~98%<sup>[32-39]</sup>。

在 FLLs 检测中，CEUS 的灵敏度和特异性分别为 80%~98%和 66%~98%<sup>[43-52,100]</sup>。与 CECT 相比，两种成像技术无显著差异。手术中 CEUS 的灵敏度大于 95%，高于 CT 或 MRI<sup>[58-59]</sup>。

在慢性肝病者中，诊断研究的三篇综合性综述指出很多研究的方法不正确<sup>[71-73]</sup>。这些综述文献的结果表明，超声和 CT 的灵敏度和特异性浮动很大，分别为 30%~100%和 73%~100%。两项研究证明，MRI 的灵敏度和特异性非常优异(分别为 81%和 85%)。没有研究对 PET 的作用进行测试。未发现足够的证据支持将 CEUS 用于这种情况。

**多学科指南编写组的观点**

在肿瘤患者中，CEUS 在检测 FLLs 中的表现优于超声。对由于身体肥胖或有受限制(如心脏病和儿童患者)而很难进行诊断的患者，最好使用 PET、CT 和 MRI。

在慢性肝病者中，CECT 和 CEMRI 虽然是最有效的技术，但价格最为高昂，因此不适合大规模使用。超声是最佳的筛选检查手段，虽然 CECT 和 CEMRI 对于患肿瘤疾病风险高的患者更佳(例如 HIV-HCV 共同感染患者)或特殊生理特征(如肥胖)患者。甲胎蛋白含量高或高度疑似罹患肝癌，且超声结果阴性患者，更适合使用 CECT 和 CEMRI 做进一步诊断。

**问题 2**

基于文献搜索得到的适用的研究<sup>[14,21,52,69,86-87,95,100,102-137]</sup>和 MGDG 成员建议纳入的研究<sup>[181-183]</sup>，表 3 给出了最终的建议。

超声在确定 FLLs 特征中的灵敏度和特异性较低。在区分良性和恶性 FLLs 中，CEUS 的灵敏度和特异性较高(分别为 >80%和 >90%)<sup>[108-112]</sup>。只有在胆管细胞癌中灵敏度较低(<60%)<sup>[108]</sup>。CEUS 判定偶发 FLLs 特征的准确度为 96%<sup>[116]</sup>。

**表 3 关键问题，所选研究，和对病理未知、慢性肝病或肿瘤疾病患者的建议**

关键问题	研究	建议
US、CEUS、CT、MRI 和 PET 在判定病理未知、慢性肝病或肿瘤疾病患者 FLLs 特征中发挥的作用	发现 913 项，选择 252 项， 对 110 项进行了评价，纳入 44 项	对于 FLLs 特征判定和使用其他成像技术得到的 FLLs 诊断结果的确认，建议使用 CEUS 若 CEUS 未得到充分明确的结果，可使用 CEMRI 和肝脏专用造影剂。不适合进行 CEUS 或 CEMRI 的患者，建议使用 CECT

CEUS 的灵敏度和特异性接近 16 排多层 CT，优于 4 排多层 CT<sup>[121]</sup>。

在病变特征判定分析中，MRI 优于 CT；在患者诊断分析中两种成像技术无显著差异<sup>[87]</sup>。

无造影剂 MRI 在区分良性和恶性病变方面的表现优于 CT(两种技术的灵敏度分别为 83.3%和 81.2%，特异性分别为 97.5%和 77.3%)；在检测肿瘤微小转移方面，无造影剂 MRI 也优于 CT，灵敏度分别为 97%和 93%，特异性分别为 97%和 82%)。

与不使用造影剂的 MRI 相比，使用造影剂的 MRI 检测肝硬化和非肝硬化患者 FLLs 的效果更佳。

很少有研究 PET 确定 FLLs 特征的公开文献。

**多学科指南编写组的观点**

可得到的证据在研究对象群体大小、治疗和比较方面差异相当大。实际上，这些诊断成像技术的有效性研究针对的是良性/恶性以及原发/转移病变的特征判定和确认。因此，很难定义每种成像技术在肝病或非肝病者体内 FLLs 鉴别诊断中的作用。最近美国肝病研究协会公布的实践操作指南，提供了一种得到数据支持的诊断、分期和治疗 HCC 患者的方法，并指出病变廓清相的重要性，即使动脉相无富血供表现<sup>[181]</sup>。该指南和另一项研究<sup>[182]</sup>已纳入最终分析中，即使它们在搜索中因其高度针对性而未被发现。此外，委员会选择将另一项研究<sup>[183]</sup>纳入分析中，虽然它公布的数据并不在文献搜索时间范围内，因为它定义了针对病变大小而确定的诊断成像技术最佳使用方法。MGDG 同意美国肝病研究协会发布的指南中关于同时使用两种不同诊断成像技术来准确诊断 1 cm 和 2 cm 的原发性肝癌的建议。许多专家知道，在任何情况下，要获得明确的诊断结果，成像引导的活检都是最佳的标准操作方法。因此可以得出结论，CEUS 的高灵敏度和特异性使其可以作为区分恶性/良性以及原发/转移 FLLs 的推荐方法。然而由于 CEUS 是一种超声成像技术，所以受到患者体型的限制。在这种情况下，CEMRI 结合肝专用造影剂可作为最佳成像技术。

### 问题 3-5

基于文献搜索得到的适用研究<sup>[40,88,138-180]</sup>和 MGDG 成员建议纳入的研究<sup>[84]</sup>,表 4 给出了这些问题的最终建议。

与手术中超声和 MRI 相比,所有研究都表明,在原发肝癌的局部分期中 CT 的准确度较低。

在以 404 位患者为研究对象,评估 CEMRI 检测、判定或排除 FLLs 有效性的研究中,结果与 CECT 相近。在 48% 的患者中,CEMRI 提供了更多诊断信息,在 6% 的病例中修正了患者管理<sup>[40]</sup>。

在以 41 位患者为研究对象,评估 PEI 或 RFTA 治疗刚结束和 1 个月以后的反应,CEUS 与 CECT 相比灵敏度、特异性和准确度更高(分别为 90.9%、96.6% 和 95%),两种技术在评估治疗刚结束后疗效方面略占优势<sup>[149]</sup>。在三项观察研究中,CEUS 检测治疗刚结束和 1 个月后疗效的灵敏度较低(53.8%~83.3%)但特异性较高(90.9%~100%)<sup>[150-152]</sup>。其他研究报告,在经皮治疗刚结束的疗效评估中,CEUS 的特异性为 99%~100%<sup>[153-154]</sup>。

CEMRI 在这种应用中的研究很少,因为检测结果不可重复<sup>[170-172]</sup>。大部分评估 CECT 诊断准确度的研究都在 2000 年以前发表,即文献搜索策略的时间段较早。

PET 只用于少数患者,且结果不确定<sup>[173-178]</sup>。

因为相关研究只有一项<sup>[180]</sup>,第 5 号问题的建议仅基于专家的意见。

#### 多学科指南编写组的观点

关于病变分期,需要多种技术来检查病变的血管化程度、血管结构以及包括周围组织和淋巴结压迫情况。虽然 CECT 是一种常规程序,但能否用作标准的诊断成像技术现在仍未确认。此外,与 CECT 相比,CEMRI 是检测需要外科手术或消融术治疗患者 FLLs 准确度最高的成像技术。相比较而言,超声腹腔镜检查、手术中超声和手术中 CEUS 的灵敏度和特异性高于 CEMRI,且其可靠性更高,因为它们产生的假阳性结果更少。

关于第 4 号问题,通常认为大部分研究的方法不合理,因为样本数不够或方法不明确。诊断技术的选择高度依赖所用的治

疗方法,临床实践的证据确认了这一猜测。搜索得到的研究并未充分研究将诊断技术用于并发症跟踪评估的可能性;几乎所有的研究都针对诊断成像在治疗有效性评估中发挥的作用,忽略了并发症。因此,委员会参考了一项研究 RFTA 并发症的多中心研究。虽然该研究并不是通过搜索得到的,但它定义了 CT 在这种情况下能发挥的作用<sup>[184]</sup>。

目前尚无诊断成像技术用于转移评估的充分证据。CEUS 表现出不同程度的灵敏度,但在肿瘤治疗刚结束和长期治疗反应评估中有良好的特异性。由于它不是一种全身诊断技术,它在病变特征判定方面与 CECT 和 CEMRI 相近,但在患者诊断方面有效性不高。然而,CEUS 很容易重复且对患者侵害性低。虽然目前意大利的大部分医院都在使用 CEUS 评估疗效,目前文献尚未给出参照标准,缺乏专门证据,特别是用于治疗刚结束后的疗效评估。专家们一致同意推荐,在治疗后第 30~40 d 使用 CEUS,在 3 个月后使用 CECT 或 CEMRI 进行跟踪。

专家们同意,对于已确定为良性的病变不应再进行跟踪。仅推荐将诊断成像用于已确诊肝腺瘤的患者,因为它有可能退化为 HCC,虽然这种情况很罕见。相较而言,临床实践中如有必要跟踪已确定为良性的 FLL,超声似乎是最有效的技术。

### 讨论

本研究在一个指南编写国家机构(SNGL)中展开,该机构受意大利卫生部门的管理。在不同临床情境中,需要对成像技术的各种选择进行评价。其中,非常重要的就是诊断成像技术在 FLLs 评估中的应用。实际上,由于级数的巨大进步,成像在 FLLs 的诊断、分期、治疗规划和跟踪中发挥了核心作用。在大部分情况下,只需要以成像技术为基础就可以取得正确的诊断结果。

文献搜索并未得到任何随机、受控的实验可以对特定诊断策略的临床结果进行评估,例如对特定病例使用专用的成像技术。更多的是关于各种成像技术诊断准确性的信息。这些研究中给出的灵敏度和特异性数值经常是属于特定患者群体,如肝硬化患者,因此一种成像技术的应用前景取决于具体的应用环境。

表 4 关键问题、所选研究和对接受肿瘤治疗患者的建议

关键问题	研究	建议
US,CEUS,CT,MRI 和 PET 在:		
①原发肝癌局灶分期	①发现 219 项,选择 118 项,对 13 项进行了评价,纳入 13 项	①虽然当前已有的证据不足以提供 UC、CEUS、CT、MRI 和 PET 在原发肝癌局灶分期中所扮演角色的清晰、可靠观点,但委员会专家建议使用 CT 和 MRI 进行局灶分期。侵入性技术只能用于接受外科手术的患者
②接受肿瘤治疗患者的并发症、短期和长期(跟踪)治疗反应(如化疗、RFTA、经皮酒精注射、激光、微波、肝动脉化疗栓塞、经导管动脉栓塞术、冷冻疗法、手术等)的评估	②发现 1266 项,选择 58 项,对 31 项进行了评价,纳入 31 项	②现有的知识不允许我们为接受肿瘤治疗患者的并发症和治疗刚结束及长期治疗反应跟踪评估推荐专门的参照成像技术。因此建议做进一步的研究。此外,对接受肿瘤治疗 24 h 的患者,现有的发现并不能为诊断成像有效性评估提供充分证据。虽然这种技术的灵敏度和特异性也取决于具体的治疗类型,但 CEUS 的灵敏度仍不确定且特异性低。因此谨慎推荐使用这种技术。在肿瘤治疗的 1 个月跟踪中,CEUS 的有效性仅比 CECT 略高,但特异性良好。因此,考虑到 CEUS 比 CECT 的生物风险低,推荐使用 CEUS。在 3 个月时推荐使用 CECT 或 CEMRI,特别是在 PEI 或 RFTA 治疗后。
③良性 FLLs 患者的跟踪	③发现 56 项,选择 35 项,对 3 项进行了评价,纳入 1 项	③现有的知识并不允许为良性 FLLs 患者推荐专门的诊断成像技术

文献搜索的时间间隔设置可能更偏重选择较新的研究,这样可以得到更先进诊断成像技术的研究数据。然而,MGDG 的观点一定程度上纠正了这种倾向。

为了便于读者充分理解指南的起草过程,在报告中给出了每条建议提出前编写组成员的辩论内容。出于同样的原因,在给出建议时,并未使用评级系统而是使用叙述的形式。这样做的目的是为读者提供所有可用信息,避免因使用简要的内容总结而失去问题研究的深度,虽然从沟通的角度来讲这样更有效。

委员会讨论的一个关键原则是,给出的建议要尽可能符合临床实践的要求。因为诊断成像技术会在今后几年取得重大进步,考虑到目前最先进成像技术及其在意大利全国范围内的广泛使用,所以委员会同意就此应给出明确建议。

MGDG 认为,现在的有效证据有可能在不久的将来遭到淘汰或受到质疑。对于尚未取得清晰可靠的实验证据的诊断成像新技术而言,确实是这样,因此计划于 2011 年对指南进行更新。与此同时,采用下面多种宣传和实施促进策略:① 通过媒体和新闻宣传这项工作;② 向区域级、省级和地区性卫生部门、医院、医疗专家、全科医生和意见领袖发送信函;③ 在网站上发布;④ 发表科学论文;⑤ 在职培训课程;⑥ 推动在意大利境内的医院中采用该指南;⑦ 在全国或国际会议上演示;⑧ 支持卫生部门整合临床渠道,促进地方性医疗机构实施指南,破除指南实施的障碍。实施结果在很大程度上取决于诊断成像技术在当地的应用情况。

#### 多学科指南编写组成员包括:

Mario Angelico, Società Italiana di Gastroenterologia ed Endoscopia Digestiva, SIGE; Vincenzo Arienti, Società Italiana di Medicina Interna, SIMI; Carlo Bartolozzi, Società Italiana di Radiologia Medica, SIRM; Luigi Bolondi, Esperto in Epatologia ed Ecografia, Dipartimenti Malattie Apparato Digerente e Medicina Interna, Policlinico S. Orsola Malpighi-Università di Bologna; Elisabetta Usarini, Associazione Italiana Gastroenterologia ed Endoscopisti Ospedalieri, AIGO; Roberto Buzzoni, Associazione Italiana di Oncologia Medica, AIOM; Fabrizio Calliada, Istituto di Radiologia, Università di Pavia; Vito Cantisani, Dipartimento di Scienze Radiologiche, Università La Sapienza, Roma; Lorenzo Capussotti, Associazione Chirurghi Ospedalieri Italiani, ACOI; Antonella Ciabattini, Associazione Italiana di Radioterapia Oncologica, AIRO; Salvatore De Masi, Dipartimento di Prevenzione, ASL 6 Livorno; Carlo Filice, Società Italiana di Malattie Infettive e Tropicali, SIMIT; Alfredo Garofalo, Società Italiana di Chirurgia Oncologica, SICO; Luigi Grazioli, Esperto in Imaging Epatico, Dipartimento di Radiologia, Spedali Civili di Brescia; Pasquale Ialongo, Società Italiana di Chirurgia, SIC; Luigi Lupo, Società Italiana di Chirurgia Colo-Rettale, SICCR; Maria Franca Meloni, Società Italiana di Ultrasonologia in Medicina e Biologia, SIUMB; Alessandro Maria Paganini, Società Italiana di Chirurgia Endoscopica e Nuove Tecnologie, SICE; Gian Ludovico Rapaccini, Associazione Italiana per lo Studio del Fegato, AISF; Paolo Ricci, Dipartimento di Scienze Radiologiche, Università La Sapienza, Roma; Letizia Sampaolo, Istituto Superiore di Sanità; Angelo Sangiovanni, Esperto in Gestione Clinica delle lesioni focali epatiche, Unità Operativa Gastroenterologia I, Fondazione IRCCS Ospedale Maggiore Policlinico, Mangiagalli-Regina Elena, Milano.

#### 参考文献

- [1] Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin*, 2005, 55: 74-108.
- [2] Programma Nazionale per le Linee Guida - PNLG, Istituto Superiore di Sanità, Agenzia per i Servizi Sanitari Regionali, Manuale metodologico. How to produce, spread and update recommendations for the clinical practice [Italian]. Milano: Zadig, 2002.
- [3] SIGN Publication No 50. A guideline developers' handbook. Published February 2001. Last updated March 2004. ([www.sign.ac.uk/guidelines/fulltext/50/index.html](http://www.sign.ac.uk/guidelines/fulltext/50/index.html)).
- [4] Wiering B, Krabbe PF, Jager GJ, Oyen WJ, Ruers TJ. The impact of fluor-18-deoxyglucose-positron emission tomography in the management of colorectal liver metastases. *Cancer*, 2005, 104: 2658-2670.
- [5] Bipat S, Van Leeuwen MS, Comans EF, Pijl ME, Bossuyt PM, Zwinderman AH, et al. Colorectal liver metastases: CT, MR Imaging, and PET for diagnosis-meta-analysis. *Radiology*, 2005, 237: 123-131.
- [6] Kinkel K, Lu Y, Both M, Warren RS, Thoeni RF. Detection of hepatic metastases from cancers of the gastrointestinal tract by using noninvasive imaging methods (US, CT, MR imaging, PET): a meta-analysis. *Radiology*, 2002, 224: 748-756.
- [7] Diederichs CG, Staib L, Vogel J, Glasbrenner B, Glatting G, Brambs HJ, et al. Values and limitations of 18F-fluorodeoxyglucose-positron-emission tomography with preoperative evaluation of patients with pancreatic masses. *Pancreas*, 2000, 20: 109-116.
- [8] Nishiyama Y, Yamamoto Y, Yokoe K, Monden T, Sasakawa Y, Tsutsui K, et al. Contribution of whole body FDG-PET to the detection of distant metastasis in pancreatic cancer. *Ann Nucl Med*, 2005, 19: 491-497.
- [9] Kalva SP, Sahani DV, Ryan D, Fischman AJ, Hahn PF, Mueller P, et al. Detection of liver metastases from gastrointestinal cancer: comparison of high resolution MnDPDP enhanced MRI and FDG-PET. *Acad Radiol*, 2005, 12: S17-S20.
- [10] Rappeport ED, Loft A, Berthelsen AK, Von der Recke P, Larsen PN, Mogensen AM, et al. Contrast-enhanced FDG-PET/CT vs. SPIO-enhanced MRI vs. FDG-PET vs. CT in patients with liver metastases from colorectal cancer: a prospective study with intraoperative confirmation. *Acta Radiol*, 2007, 48: 369-378.
- [11] Rohren EM, Paulson EK, Hagge R, Wong TZ, Killius J, Clavien PA, et al. The role of F-18 FDG positron emission tomography in preoperative assessment of the liver in patients being considered for curative resection of hepatic metastases from colorectal cancer. *Clin Nucl Med*, 2002, 27: 550-555.
- [12] Ruers TJ, Langenhoff BS, Neeleman N, Jager GJ, Strijk S, Wobbes T, et al. Value of positron emission tomography with [F-18] fluorodeoxyglucose in patients with colorectal liver metastases: a prospective study. *J Clin Oncol*, 2002, 20: 388-395.
- [13] Topal B, Flamen P, Aerts R, D'Hoore A, Filez L, van Cutsem E, et al. Clinical value of whole-body emission tomography in potentially curable colorectal liver metastases. *Eur J Surg*

- Oncol, 2001, 27; 175-179.
- [14] Yang M, Martin DR, Karabulut N, Frick MP. Comparison of MR and PET imaging for the evaluation of liver metastases. *J Magn Reson Imaging*, 2003, 17; 343-349.
- [15] Arulampalam T, Costa D, Visvikis D, Boulos P, Taylor I, Ell P. The impact of FDG-PET on the management algorithm for recurrent colorectal cancer. *Eur J Nucl Med*, 2001, 28; 1758-1765.
- [16] Arulampalam T, Francis DL, Visvikis D, Taylor I, Ell P. FDG-PET for the pre-operative evaluation of colorectal liver metastases. *Eur J Surg Oncol*, 2004, 30; 286-291.
- [17] Willkomm P, Bender H, Bangard M, Decker P, Grunwald F, Biersack HJ. FDG-PET and immunoscintigraphy with <sup>99m</sup>Tc-labeled antibody fragments for detection of the recurrence of colorectal carcinoma. *J Nucl Med*, 2000, 41; 1657-1663.
- [18] Imdahl A, Reinhardt MJ, Nitzsche EU, Mix M, Dingeldey A, Einert A, et al. Impact of <sup>18</sup>F-FDG-PET for decision making in colorectal cancer recurrence. *Langenbecks Arch Surg*, 2000, 385; 129-134.
- [19] Krug B, Dietlein M, Groth W, Stützer H, Psaras T, Gossmann A, et al. Fluor-18-fluorodeoxyglucose positron emission tomography (FDG-PET) in malignant melanoma. Diagnostic comparison with conventional imaging methods. *Acta Radiol*, 2000, 41; 446-452.
- [20] Ghanem N, Althehoefer C, Högerle S, Nitzsche E, Lohrmann C, Schäfer O, et al. Detectability of liver metastases in malignant melanoma; prospective comparison of magnetic resonance imaging and positron emission tomography. *Eur J Radiol*, 2005, 4; 264-270.
- [21] Semelka RC, Martin DR, Balci C, Lance T. Focal liver lesions: comparison of dual-phase CT and multisequence multiplanar MR imaging including dynamic gadolinium enhancement. *J Magn Reson Imaging*, 2001, 13; 397-401.
- [22] Tanimoto A, Yuasa Y, Jinzaki M, Nakatsuka S, Takeda T, Kurata T, et al. Routine MR imaging protocol with breath-hold fast scans; diagnostic efficacy for focal liver lesions. *Radiat Med*, 2002, 20; 169-179.
- [23] Del Frate C, Zuiani C, Londero V. Comparing Levovist-enhanced pulse inversion harmonic imaging and ferumoxides-enhanced MR imaging of hepatic metastases. *Am J Roentgenol*, 2003, 180; 1339-1346.
- [24] Raman SS, Lu DS, Chen SC, Sayre J, Eilber F, Economou J. Hepatic MR imaging using ferumoxides; prospective evaluation with surgical and intraoperative sonographic confirmation in 25 cases. *Am J Roentgenol*, 2001, 177; 807-812.
- [25] Ward J, Robinson PJ, Guthrie JA, Downing S, Wilson D, Lodge JP, et al. Liver metastases in candidates for hepatic resection; comparison of helical CT and gadolinium- and SPIO-enhanced MR imaging. *Radiology*, 2005, 237; 170-180.
- [26] Furuhata T, Okita K, Tsuruma T, Hata F, Kimura Y, Katsuramaki T, et al. Efficacy of SPIO-MR imaging in the diagnosis of liver metastases from colorectal carcinomas. *Dig Surg*, 2003, 20; 321-325.
- [27] Onishi H, Murakami T, Kim T, Hori M, Iannaccone R, Kuwabara M, et al. Hepatic metastases; detection with multi-detector row CT, SPIO-enhanced MR imaging, and both techniques combined. *Radiology*, 2006, 239; 131-138.
- [28] Said B, McCart JA, Libutti SK, Choyke PL. Ferumoxide-enhanced MRI in patients with colorectal cancer and rising CEA; surgical correlation in early recurrence. *Magn Reson Imaging*, 2000, 18; 305-309.
- [29] Van Etten B, van der Sijp J, Kruyt R, Oudkerk M, van der Holt B, Wiggers T. Ferumoxide-enhanced magnetic resonance imaging techniques in pre-operative assessment for colorectal liver metastases. *Eur J Surg Oncol*, 2002, 28; 645-651.
- [30] Vogl TJ, Schwarz W, Blume S, Pietsch M, Shamsi K, Franz M, et al. Preoperative evaluation of malignant liver tumors; comparison of unenhanced and SPIO (Resovist)-enhanced MR imaging with biphasic CTAP and intraoperative US. *Eur Radiol*, 2003, 13; 262-272.
- [31] Kondo H, Kanematsu M, Hoshi H, Murakami T, Kim T, Hori M, et al. Preoperative detection of malignant hepatic tumors; comparison of combined methods of MR imaging with combined methods of CT. *Am J Roentgenol*, 2000, 174; 947-954.
- [32] Kuwatsuru R, Kadoya M, Ohtomo K. Comparison of gadobenate dimeglumine with gadopentetate dimeglumine for magnetic resonance imaging of liver tumors. *Invest Radiol*, 2001, 36; 632-641.
- [33] Peterseini J, Spinazzi A, Giovagnoni A, Soyer P, Terrier F, Lencioni R, et al. Focal liver lesions; evaluation of the efficacy of gadobenate dimeglumine in MR imaging—a multicenter phase III clinical study. *Radiology*, 2000, 215; 727-736.
- [34] Kim YK, Lee JM, Kim CS. Gadobenate dimeglumine-enhanced liver MR imaging; value of dynamic and delayed imaging for the characterization and detection of focal liver lesions. *Eur Radiol*, 2004, 14; 5-13.
- [35] Bluemke DA, Sahani D, Amendola M, Balzer T, Breuer J, Brown JJ, et al. Efficacy and safety of MR imaging with liver-specific contrast agent; US multicenter phase III study. *Radiology*, 2005, 237; 89-98.
- [36] Oudkerk M, Torres CG, Song B, König M, Grimm J, Fernandez-Cuadrado J, et al. Characterization of liver lesions with mangafodipir sodium enhanced MR imaging; multicenter study comparing MR and dual-phase spiral CT. *Radiology*, 2002, 223; 517-524.
- [37] Bartolozzi C, Donati F, Cioni D, Procacci C, Morana G, Chiesa A, et al. Detection of colorectal liver metastases; a prospective multicenter trial comparing unenhanced MRI, MnDPDP-enhanced MRI, and spiral CT. *Eur Radiol*, 2004, 14; 14-20.
- [38] Regge D, Campanella D, Anselmetti GC, Cirillo S, Gallo TM, Muratore A, et al. Diagnostic accuracy of portal-phase CT and MRI with mangafodipir trisodium in detecting liver metastases from colorectal carcinoma. *Clin Radiol*, 2006, 61; 338-347.
- [39] Kim MJ, Kim JH, Lim JS, Oh YT, Chung JJ, Choi JS, et al. Detection and characterization of focal hepatic lesions; mangafodipir vs. superparamagnetic iron oxide-enhanced magnetic resonance imaging. *J Magn Reson Imaging*, 2004, 20; 612-621.
- [40] Federle M, Chezmar J, Rubin DL, Weinreb J, Freeny P, Schmiedl UP, et al. Efficacy and safety of mangafodipir

- trisodium (MnDPDP) injection for hepatic MRI in adults; results of the US multicenter phase III clinical trials. Efficacy of early imaging. *J Magn Reson Imaging*, 2000, 12:689-701.
- [41] Nasu K, Kuroki Y, Nawano S, Kuroki S, Tsukamoto T, Yamamoto S, et al. Hepatic metastases; diffusion-weighted sensitivity-encoding versus SPIO-enhanced MR imaging. *Radiology*, 2006, 239:122-130.
- [42] Obuz F, Oksuzler M, Secil M, Sagol O, Karademir S, Astarcioglu H. Efficiency of MR imaging in the detection of malignant liver lesions. *Diagn Interv Radiol*, 2006, 12:17-21.
- [43] Quaia E, D'Onofrio M, Palumbo A, Rossi S, Bruni S, Cova M. Comparison of contrast-enhanced ultrasonography versus baseline ultrasound and contrast-enhanced computed tomography in metastatic disease of the liver; diagnostic performance and confidence. *Eur Radiol*, 2006, 16:1599-1609.
- [44] Albrecht T, Hoffmann CW, Schmitz SA, Schettler S, Overberg A, Germer CT, et al. Phase-inversion sonography during the liver-specific late phase of contrast enhancement; improved detection of liver metastases. *Am J Roentgenol*, 2001, 176:1191-1198.
- [45] Albrecht T, Blomley MJ, Burns PN, Wilson S, Harvey CJ, Leen E, et al. Improved detection of hepatic metastases with pulse-inversion US during the liver-specific phase of SHU 508A; multicenter study. *Radiology*, 2003, 227:361-370.
- [46] Larsen LP, Rosenkilde M, Christensen H, Bang N, Bolvig L, Christiansen T, et al. The value of contrast-enhanced sonography in detection of liver metastasis from colorectal cancer; a prospective double-blinded study. *Eur J Radiol*, 2007, 62:302-307.
- [47] Konopke R, Kersting S, Bergert H, Bloomenthal A, Gastmeier J, Saeger HD, et al. Contrast-enhanced ultrasonography to detect liver metastasis. *Int J Colorectal Dis*, 2007, 22:201-207.
- [48] Catala V, Nicolau C, Vilana R, Pages M, Bianchi L, Sanchez M, et al. Characterization of focal liver lesions; comparative study of contrast-enhanced ultrasound versus spiral computed tomography. *Eur Radiol*, 2007, 17:1066-1073.
- [49] Dietrich CF, Kratzer W, Strobe D, Danse E, Fessl R, Bunk A, et al. Assessment of metastatic liver disease in patients with primary extrahepatic tumors by contrast-enhanced sonography versus CT and MRI. *World J Gastroenterol*, 2006, 12:1699-1705.
- [50] Bernatik T, Strobel D, Hahn EG, Becker D. Detection of liver metastases; comparison of contrast-enhanced wide-band harmonic imaging with conventional ultrasonography. *J Ultrasound Med*, 2001, 20:509-515.
- [51] Oldenburg A, Hohmann J, Foert E, Skrok J, Hoffmann CW, Frericks B, et al. Detection of hepatic metastases with low MI real time contrast enhanced sonography and SonoVue. *Ultraschall Med*, 2005, 26:277-284.
- [52] Von Herbay A, Vogt C, Willers R, Haussinger D. Real-time imaging with the sonographic contrast agent SonoVue; differentiation between benign and malignant hepatic lesions. *J Ultrasound Med*, 2004, 23:1557-1568.
- [53] Leen E, Angerson WJ, Yarmenitis S, Bongartz G, Blomley M, Del Maschio A, et al. Multi-centre clinical study evaluating the efficacy of SonoVue (BR1), a new ultrasound contrast agent in Doppler investigation of focal hepatic lesions. *Eur J Radiol*, 2002, 41:200-206.
- [54] Quaia E, Bertolotto M, Forgacs B, Rimondini A, Locatelli M, Mucelli RP. Detection of liver metastases by pulse inversion harmonic imaging during Levovist late phase; comparison with conventional ultrasound and helicalCT in 160 patients. *Eur Radiol*, 2003, 13:475-483.
- [55] Rabenandrasana HA, Furukawa A, Furuichi K, Yamasaki M, Takahashi M, Murata K. Comparison between tissue harmonic imaging and liver-specific late-phase contrast-enhanced pulse-inversion imaging in the detection of hepatocellular carcinoma and liver metastasis. *Radiat Med*, 2004, 22:90-97.
- [56] Yarmenitis SD, Karantanas A, Bakantaki A, Papantoniou Y, Gourtsoyannis N. Detection of colorectal cancer hepatic metastases with contrast-enhanced ultrasound; comparison with conventional B-mode ultrasound. *Dig Dis*, 2007, 25:86-93.
- [57] Gultekin S, Yucel C, Ozdemir H, Celik H, Oktar SO, Arac M. The role of late-phase pulse inversion harmonic imaging in the detection of occult hepatic metastases. *J Ultrasound Med*, 2006, 25:1139-1145.
- [58] Leen E, Ceccotti P, Moug SJ, Glen P, MacQuarrie J, Angerson WJ, et al. Potential value of contrast-enhanced intraoperative ultrasonography during partial hepatectomy for metastases. *Ann Surg*, 2006, 243:236-240.
- [59] Zacherl J, Scheuba C, Imhof M, Zacherl M, Längle F, Pokieser P, et al. Current value of intraoperative sonography during surgery for hepatic neoplasms. *World J Surg*, 2002, 26:550-554.
- [60] Dromain C, De Baere T, Lumbroso J, Caillet H, Laplanche A, Boige V, et al. Detection of liver metastasis of endocrine tumors; a prospective comparison of somatostatin receptors scintigraphy, computed tomography and magnetic resonance imaging. *J Clin Oncol*, 2005, 23:70-78.
- [61] Zimmerman P, Lu DS, Yang LY, Chen S, Sayre J, Kadell B. Hepatic metastases from breast carcinoma: comparison of noncontrast, arterial-dominant, and portal-dominant phase spiral CT. *J Comput Assist Tomogr*, 2000, 24:197-203.
- [62] Ashraf K, Ashraf O, Haider Z, Rafique Z. Colorectal carcinoma, preoperative evaluation by spiral computer tomography. *J Pak Med Assoc*, 2006, 56:149-153.
- [63] Soyer P, Pocard M, Boudiaf M. Detection of hypovascular hepatic metastases at triple-phase helical CT; sensitivity of phases and comparison with surgical and histopathologic findings. *Radiology*, 2004, 231:413-420.
- [64] Scott DJ, Guthrie JA, Arnold P, Ward J, Atchley J, Wilson D, et al. Dual phase helical CT versus portal venous phase CT for the detection of colorectal liver metastases; correlation with intraoperative sonography, surgical and pathological findings. *Clin Radiol*, 2001, 56:235-242.
- [65] Glover C, Douse P, Kane P, Karani J, Meire H, Mohammadtaghi S, et al. Accuracy of investigations for asymptomatic colorectal liver metastases. *Dis Colon Rectum*, 2002, 45:476-484.
- [66] Varshney S, Hacking CN, Johnson CD. CT arterial portography in the staging of pancreatic malignancy. *Int J Pancreatol*, 2000, 28:59-65.

- [67] Schwartz L, Brody L, Brown K, Covey A, Tuorto S, Mazumdar M, et al. Prospective, blinded comparison of helical CT and CT arterial portography in the assessment of hepatic metastasis from colorectal carcinoma. *World J Surg*, 2006, 30: 1892-1899.
- [68] Bhattacharjya S, Bhattacharjya T, Baber S, Tibballs JM, Watkinson AF, Davidson BR. Prospective study of contrast-enhanced computer tomography, computer tomography during arteriography and magnetic resonance imaging for staging colorectal liver metastasis for liver resection. *Br J Surg*, 2004, 91: 1361-1369.
- [69] Hosch WP, Schmidt SM, Plaza S, Dechow C, Schmidt J, Ley S, et al. Comparison of CT during arterial portography and MR during arterial portography in the detection of liver metastases. *Am J Roentgenol*, 2006, 186: 1502-1511.
- [70] Satoi S, Yamamoto H, Takai S, Tanigawa N, Komemushi A, Yanagimoto H, et al. Clinical impact of multidetector row computed tomography on patients with pancreatic cancer. *Pancreas*, 2007, 34: 175-179.
- [71] Colli A, Fraquelli M, Casazza G, Massironi S, Colucci A, Conte D, et al. Accuracy of ultrasonography, spiral CT, magnetic resonance, and alpha-fetoprotein in diagnosing hepatocellular carcinoma: a systematic review. *Am J Gastroenterol*, 2006, 101: 513-523.
- [72] Fung KT, Li FT, Raimondo ML, Maudgil D, Mancuso A, Tibballs JM, et al. Systematic review of radiological imaging for hepatocellular carcinoma in cirrhotic patients. *Br J Radiol*, 2004, 77: 633-640.
- [73] De Masi S, Tosti ME, Mele A. Screening for hepatocellular carcinoma. *Dig Liver Dis*, 2005, 37: 260-268.
- [74] Simon G, Link TM, Wörtler K, Doebereiner F, Schulte-Frohlinde E, Daldrup-Link H, et al. Detection of hepatocellular carcinoma: comparison of Gd-DTPA- and ferumoxides-enhanced MR imaging. *Eur Radiol*, 2005, 15: 895-903.
- [75] Marrero JA, Hussain HK, Nghiem HV, Umar R, Fontana RJ, Lok AS. Improving the prediction of hepatocellular carcinoma in cirrhotic patients with an arterially-enhancing liver mass. *Liver Transpl*, 2005, 11: 281-289.
- [76] Matsuo M, Kanematsu M, Itoh K, Ito K, Maetani Y, Kondo H, et al. Detection of malignant hepatic tumors: comparison of gadolinium- and ferumoxide-enhanced MR imaging. *Am J Roentgenol*, 2001, 177: 637-643.
- [77] Limanond P, Raman SS, Sayre J, Lu DS. Comparison of dynamic gadolinium-enhanced and ferumoxides-enhanced MRI of the liver on high- and low-field scanners. *J Magn Reson Imaging*, 2004, 20: 640-647.
- [78] Kim YK, Kwak HS, Kim CS, Chung GH, Han YM, Lee JM. Hepatocellular carcinoma in patients with chronic liver disease: comparison of SPIO-enhanced MR imaging and 16-detector row CT. *Radiology*, 2006, 238: 531-541.
- [79] Giorgio A, Ferraioli G, Tarantino L, De Stefano G, Scala V, Scarano F, et al. Contrast-enhanced sonographic appearance of hepatocellular carcinoma in patients with cirrhosis: comparison with contrast-enhanced helical CT appearance. *Am J Roentgenol*, 2004, 183: 1319-1326.
- [80] Iannaccone R, Laghi A, Catalano C, Rossi P, Mangiapane F, Murakami T, et al. Hepatocellular carcinoma: role of unenhanced and delayed phase multi-detector row helical CT in patients with cirrhosis. *Radiology*, 2005, 234: 460-467.
- [81] Zhao H, Yao JL, Wang Y, Zhou KR. Detection of small hepatocellular carcinoma: comparison of dynamic enhancement magnetic resonance imaging and multiphase multirow-detector helical CT scanning. *World J Gastroenterol*, 2007, 13: 1252-1256.
- [82] Reimer P, Jahnke N, Fiebich M, Schima W, Deckers F, Marx C, et al. Hepatic lesion detection and characterization: value of nonenhanced MR imaging, superparamagnetic iron oxide-enhanced MR imaging, and spiral CT-ROC analysis. *Radiology*, 2000, 217: 152-158.
- [83] Lim JH, Kim CK, Lee WJ, Park CK, Koh KC, Paik SW, et al. Detection of hepatocellular carcinomas and dysplastic nodules in cirrhotic livers: accuracy of helical CT in transplant patients. *Am J Roentgenol*, 2000, 175: 693-698.
- [84] Lim JH, Kim JM, Park KK, Kang SS, Lee WJ, Lim HK. Dysplastic nodules in liver cirrhosis: detection with triple phase helical dynamic CT. *Br J Radiol*, 2004, 77: 911-916.
- [85] Scaife CL, Ng CS, Ellis LM, Vauthey JN, Charnsangavej C, Curley SA. Accuracy of preoperative imaging of hepatic tumors with helical computed tomography. *Ann Surg Oncol*, 2006, 13: 542-546.
- [86] Bartolozzi C, Donati F, Cioni D, Crocetti L, Lencioni R. MnDPDP-enhanced MRI vs. dual-phase spiral CT in the detection of hepatocellular carcinoma in cirrhosis. *Eur Radiol*, 2000, 10: 1697-1702.
- [87] De Lédinghen V, Laharie D, Lecesne R, Le Bail B, Winnock M, Bernard PH, et al. Detection of nodules in liver cirrhosis: spiral computed tomography or magnetic resonance imaging? A prospective study of 88 nodules in 34 patients. *Eur J Gastroenterol Hepatol*, 2002, 14: 159-165.
- [88] Valls C, Cos M, Figueras J, Andía E, Ramos E, Sánchez A, et al. Pretransplantation diagnosis and staging of hepatocellular carcinoma in patients with cirrhosis: value of dual-phase helical CT. *Am J Roentgenol*, 2004, 182: 1011-1017.
- [89] Yukisawa S, Okugawa H, Masuya Y, Okabe S, Fukuda H, Yoshikawa M, et al. Multidetector helical CT plus superparamagnetic iron oxide-enhanced MR imaging for focal hepatic lesions in cirrhotic liver: a comparison with multi-phase CT during hepatic arteriography. *Eur J Radiol*, 2007, 61: 279-289.
- [90] Numminen K, Isoniemi H, Halavaara J, Tervahartiala P, Makisalo H, Laasonen L, et al. Preoperative assessment of focal liver lesions: multidetector computed tomography challenges magnetic resonance imaging. *Acta Radiol*, 2005, 46: 9-15.
- [91] Bhattacharjya S, Bhattacharjya T, Quaglia A, Dhillon AP, Burroughs AK, Patch DW, et al. Liver transplantation in cirrhotic patients with small hepatocellular carcinoma: an analysis of pre-operative imaging, explant histology and prognostic histologic indicators. *Dig Surg*, 2004, 21: 152-159.
- [92] Fracanzani AL, Burdick L, Borzio M, Roncalli M, Bonelli N, Borzio F, et al. Contrast-enhanced Doppler ultrasonography in the diagnosis of hepatocellular carcinoma and premalignant

- lesions in patients with cirrhosis. *Hepatology*, 2001, 34: 1109-1112.
- [93] Kim CK, Lim JH, Lee WJ. Detection of hepatocellular carcinomas and dysplastic nodules in cirrhotic liver; accuracy of ultrasonography in transplant patients. *J Ultrasound Med*, 2001, 20: 99-104.
- [94] Lim JH, Kim SH, Lee WJ, Choi D, Kim SH, Lim HK. Ultrasonographic detection of hepatocellular carcinoma; correlation of preoperative ultrasonography and resected liver pathology. *Clin Radiol*, 2006, 61: 191-197.
- [95] Tanaka S, Oshikawa O, Sasaki T, Ioka T, Tsukuma H. Evaluation of tissue harmonic imaging for the diagnosis of focal liver lesions. *Ultrasound Med Biol*, 2000, 26: 183-187.
- [96] Ren FY, Piao XX, Jin AL. Efficacy of ultrasonography and alpha-fetoprotein early detection of hepatocellular carcinoma. *World J Gastroenterol*, 2006, 12: 4656-4659.
- [97] Caturelli E, Bartolucci F, Biasini E, Vigliotti ML, Andriulli A, Siena DA, et al. Diagnosis of liver nodules observed in chronic liver disease patients during ultrasound screening for early detection of hepatocellular carcinoma. *Am J Gastroenterol*, 2002, 97: 397-405.
- [98] Chen TH, Chen CJ, Yen MF, Lu SN, Sun CA, Huang GT, et al. Ultrasound screening and risk factors for death from hepatocellular carcinoma in a high risk group in Taiwan. *Int J Cancer*, 2002, 98: 257-261.
- [99] Trevisani F, Cantarini MC, Labate AM, De Notariis S, Rapaccini G, Farinati F, et al. Surveillance for hepatocellular carcinoma in elderly Italian patients with cirrhosis; effects on cancer staging and patient survival. *Am J Gastroenterol*, 2004, 99: 1470-1476.
- [100] Tanaka S, Hamada Y, Ioka T, Sugiyama T, Akamatsu I, Takakura R, et al. Contrast-enhanced multiphase dynamic ultrasonography for characterization of liver tumors. *J Med Ultrasonics*, 2005, 32: 57-63.
- [101] Selzner M, Hany TF, Wildbrett P, McCormack L, Kadry Z, Clavien PA. Does the novel PET/CT imaging modality impact on the treatment of patients with metastatic colorectal cancer of the liver? *Ann Surg*, 2004, 240: 1027-1034.
- [102] Srivastava DN, Mahajan A, Berry M, Sharma MP. Color Doppler flow imaging of focal hepatic lesions. *Australas Radiol*, 2000, 44: 285-289.
- [103] Ramnarine KV, Kyriakopoulou K, Gordon P, McDicken NW, McArdle CS, Leen E. Improved characterisation of focal liver tumors; dynamic power Doppler imaging using NC100100 echo-enhancer. *Eur J Ultrasound*, 2000, 11: 95-104.
- [104] Gaiani S, Casali A, Serra C, Piscaglia F, Gramantieri L, Volpe L, et al. Assessment of vascular patterns of small liver mass lesions; value and limitation of the different Doppler ultrasound modalities. *Am J Gastroenterol*, 2000, 95: 3537-3546.
- [105] Sodhi KS, Sidhu R, Gulati M, Saxena A, Suri S, Chawla Y. Role of tissue harmonic imaging in focal hepatic lesions; comparison with conventional sonography. *J Gastroenterol Hepatol*, 2005, 20: 1488-1493.
- [106] Caturelli E, Pompili M, Bartolucci F, Siena DA, Sperandeo M, Andriulli A, et al. Hemangioma like lesions in chronic liver disease; diagnostic evaluation in patients. *Radiology*, 2001, 220: 337-342.
- [107] Rapaccini GL, Pompili M, Caturelli E, Covino M, Lippi ME, Beccaria S, et al. Hepatocellular carcinomas <2 cm in diameter complicating cirrhosis; ultrasound and clinical features in 153 consecutive patients. *Liver Int*, 2004, 24: 124-130.
- [108] Xu HX, Liu GJ, Lu MD, Xie XY, Xu ZF, Zheng YL, et al. Characterization of focal liver lesions using contrast-enhanced sonography with a low mechanical index mode a sulfur hexafluoride-filled microbubble contrast agent. *J Clin Ultrasound*, 2006, 34: 261-272.
- [109] Wen YL, Kudo M, Zheng RQ, Ding H, Zhou P, Minami Y, et al. Characterization of hepatic tumors; value of contrast-enhanced coded phase-inversion harmonic angio. *Am J Roentgenol*, 2004, 182: 1019-1026.
- [110] Quaia E, Calliada F, Bertolotto M, Rossi S, Garioni L, Rosa L, et al. Characterization of FLL with specific US modes and a sulphur hexafluoride-filled microbubble contrast agent; diagnostic performance and confidence. *Radiology*, 2004, 232: 420-430.
- [111] Furuse J, Nagase M, Ishii H, Yoshino M. Contrast enhancement patterns of hepatic tumors during the vascular phase using coded harmonic imaging and Levovist to differentiate hepatocellular carcinoma from other focal lesions. *Br J Radiol*, 2003, 76: 385-392.
- [112] D'Onofrio M, Rozzanigo U, Masinielli BM, Caffarri S, Zogno A, Malagò R, et al. Hypoechoic focal liver lesions; characterization with contrast enhanced ultrasonography. *J Clin Ultrasound*, 2005, 33: 164-172.
- [113] Dai Y, Hua MH, Yin SS, Yan K, Fan ZH, Wu W, et al. Can SonoVue enhanced ultrasound be used to differentiate malignant from benign lesions? *Invest Radiol*, 2007, 42: 596-603.
- [114] Karabacakoglu A, Karakose S, Cil AS, Kaya A. Contrast media-enhanced power Doppler sonography for evaluation of hemangiomas and malignant tumors in the liver. *J Gastroenterol Hepatol*, 2003, 18: 92-99.
- [115] Youk JK, Kim CS, Lee JM. Contrast-enhanced agent detection imaging. Value in the characterization in focal hepatic lesions. *J Ultrasound Med*, 2003, 22: 897-910.
- [116] Bleuzen A, Tranquart F. Incidental liver lesions; diagnostic value of cadence contrast pulse sequencing (CPS) and SonoVue. *Eur Radiol*, 2004, 14: P53-P62.
- [117] Kim SH, Lee JM, Lee JY, Han JK, An SK, Han CJ, et al. Value of contrast-enhanced sonography for the characterization of focal hepatic lesions in patients with diffuse liver disease; receiver operating characteristic analysis. *Am J Roentgenol*, 2005, 184: 1077-1084.
- [118] Li R, Guo Y, Hua X, He Y, Ding J, Guo A, et al. Characterization of focal liver lesions; comparison of pulse-inversion harmonic contrast-enhanced sonography with contrast-enhanced CT. *J Clin Ultrasound*, 2007, 35: 109-117.
- [119] Bleuzen A, Huang C, Olar M, Tchienbou J, Tranquart F. Diagnostic accuracy of contrast-enhanced ultrasound in focal liver lesions of the liver using cadence contrast pulse sequencing. *Ultraschall Med*, 2006, 27: 40-48.

- [120] Celik H, Ozdemir H, Yucel C, Gultekin S, Oktar SO, Arac M. Characterization of hyperechoic focal liver lesions. Quantitative evaluation with pulse inversion harmonic imaging in the late phase of Levovist. *J Ultrasound Med*, 2005, 24: 39-47.
- [121] Krix M, Kiessling F, Essig M, Herth F, Karcher A, Le-Huu M, et al. Low mechanical index contrast-enhanced ultrasound better reflects high arterial perfusion of liver metastases than arterial phase computer tomography. *Invest Radiol*, 2004, 39: 216-222.
- [122] Numata K, Isozaki T, Morimoto M, Sugimori K, Kunisaki R, Morizane T, et al. Prospective study of differential diagnosis of hepatic tumors by pattern-based classification of contrast-enhanced sonography. *World J Gastroenterol*, 2006, 12: 6290-6298.
- [123] Tanaka S, Ioka T, Oshikawa O, Hamada Y, Yoshioka F. Dynamic sonography of hepatic tumors. *Am J Roentgenol*, 2001, 177: 799-805.
- [124] Wang JH, Lu SN, Hung CH, Chen TY, Chen CH, Changchien CS, et al. Small hepatic nodules ( $\leq 2$  cm) in cirrhosis patients: characterization with contrast-enhanced ultrasonography. *Liver Int*, 2006, 26: 928-934.
- [125] WeiHuang C, Bleuzen A, Bourlier P, Roumy J, Bouakaz A, Pourcelot L, et al. Differential diagnosis of focal nodular hyperplasia with quantitative parametric analysis in contrast-enhanced sonography. *Invest Radiol*, 2006, 41: 363-368.
- [126] Leoni S, Piscaglia F, Righini R, Bolondi L. Management of small hepatocellular carcinoma. *Acta Gastroenterol Belg*, 2006, 69: 230-235.
- [127] Farrarher SW, Jara H, Chang K, Ozonoff A, Soto JA. Differentiation of hepatocellular carcinoma and hepatic metastasis from cysts and hemangiomas with calculated T2 relaxation times and T1/T2 relaxation times ratio. *J Magn Reson Imaging*, 2006, 24: 1333-1341.
- [128] Holalkere NS, Sahani DV, Blak Halpern EF, Hahn PF, Mueller PR. Characterization of small liver lesions; added role of MR after MDCT. *J Comput Assist Tomogr*, 2006, 30: 591-596.
- [129] Marti-Bonmati L, Fog AF, De Beeck BO, Kane P, Fagertun H. Safety and efficacy of mangafodipir trisodium in patients with liver lesions and cirrhosis. *Eur Radiol*, 2003, 13: 1685-1692.
- [130] Kim KW, Kim AY, Kim TK, Park SH, Kim HJ, Lee YK, et al. Small ( $< 2$  cm) hepatic lesions in colorectal cancer patients: detection and characterization on mangafodipir trisodium-enhanced MRI. *Am J Roentgenol*, 2004, 182: 1233-1240.
- [131] Pirovano G, Vanzulli A, Marti-Bonmati L, Grazioli L, Manfredi R, Greco A, et al. Evaluation of the accuracy of gadobenate dimeglumine-enhancement MR imaging in the detection and characterization of focal liver lesion. *Am J Roentgenol*, 2000, 175: 1111-1120.
- [132] Bennet GL, Petersein A, Mayo-Smith WW, Hahn PF, Schima W, Saini S. Addition of gadolinium chelates to heavily T2-weighted MRI; limited role in differentiating hepatic hemangioma from metastases. *Am J Roentgenol*, 2000, 174: 477-485.
- [133] Paley MR, Mergo PJ, Torres GM, Ros PR. Characterization of focal hepatic lesions with ferumoxides-enhanced T2-weighted MR imaging. *Am J Roentgenol*, 2000, 175: 159-163.
- [134] Kim HJ, Kim KW, Byun JH, Won HJ, Shin YM, Kim PN, et al. Comparison of mangafodipir trisodium and ferucarbotran-enhanced MRI for detection and characterization of hepatic metastases in colorectal cancer patient. *Am J Roentgenol*, 2006, 186: 1059-1066.
- [135] Schneider G, Maas R, Schultze Kool L. Low-dose gadobenate dimeglumine versus standard dose gadopentetate dimeglumine for contrast-enhanced magnetic resonance imaging of the liver. *Invest Radiol*, 2003, 38: 85-94.
- [136] Yoshikawa T, Mitchell DG, Hirota S, Ohno Y, Oda K, Maeda T, et al. Gradient- and spin-echo T2-weighted imaging for SPIO-enhanced detection and characterization of FLE. *J Magn Reson Imaging*, 2006, 23: 712-719.
- [137] Demir OI, Obuz F, Sagol O, Dicle O. Contribution of diffusion-weighted MRI to the differential diagnosis of hepatic masses. *Diagn Interv Radiol*, 2007, 13: 81-86.
- [138] Zacherl J, Pokieser P, Wrba F, Scheuba C, Prokesch R, Zacherl M, et al. Accuracy of multiphasic helical computed tomography and intraoperative sonography in patients undergoing orthotopic liver transplantation for hepatoma: what is the truth? *Ann Surg*, 2002, 235: 528-532.
- [139] Stoker J, Romijn MG, De Man RA, Brouwer JT, Weverling GJ, Van Muiswinkel JM, et al. Prospective comparative study of spiral computer tomography and magnetic resonance imaging for detection of hepatocellular carcinoma. *Gut*, 2002, 51: 105-107.
- [140] Kamel IR, Choti MA, Horton KM, Braga HJ, Birnbaum BA, Fishman EK, et al. Surgically staged focal liver lesions; accuracy and reproducibility of dual-phase helical CT for detection and characterization. *Radiology*, 2003, 227: 752-757.
- [141] Jang HJ, Lim JH, Lee SJ, Park CK, Park HS, Soo Y. Hepatocellular carcinoma: are combined CT during arterial portography and CT hepatic arteriography in addition to triple-phase helical CT all necessary for preoperative evaluation? *Radiology*, 2000, 215: 373-380.
- [142] Burrell M, Llovet JM, Ayuso C, Iglesias C, Sala M, Miquel R, et al. MRI angiography is superior to helical CT for detection of HCC prior to liver transplantation; an explant correlation. *Hepatology*, 2003, 38: 1034-1042.
- [143] Freeman RB, Mithoefer A, Ruthazer R, Nguyen K, Schore A, et al. Optimizing staging for hepatocellular carcinoma before liver transplantation: a retrospective analysis of the UNOS/OPTN database. *Liver Transpl*, 2006, 12: 1504-1511.
- [144] Li S, Beheshti M, Peck-Radosavljevic M, Oezer S, Grumbeck E, Schmid M, et al. Comparison of  $^{11}\text{C}$ -acetate positron emission tomography and  $^{67}\text{Ga}$  citrate scintigraphy in patients with hepatocellular carcinoma. *Liver Int*, 2006, 26: 920-927.
- [145] Berber E, Garland AM, Engle KL, Rogers SJ, Siperstein AE. Laparoscopic ultrasonography and biopsy of hepatic tumors in 310 patients. *Am J Surg*, 2004, 87: 213-218.
- [146] Carrella G, Sortini D, Basaglia E, Marcello D, Carcoforo P. Impact of laparoscopy and ultrasonography in gastrointestinal malignancies. *Epatogastroenterology*, 2005, 52: 139-142.
- [147] Slupski M, Włodarczyk Z, Dąbrowiecki S, Szczesny W, Thabit

- Sinjab A, Kuziemski A, Pacholska M. Value of laparoscopic ultrasonography in the assessment of liver tumor respectability. Single center experience. *Polsky Przegląd Chirurgiczny*, 2003, 75; 723-731.
- [148] Torzilli G, Olivari N, Moron E, Del Fabbro D, Gambetti A, Leoni P, et al. Contrast-enhanced intraoperative ultrasonography in surgery for hepatocellular carcinoma in cirrhosis. *Liver Transpl*, 2004, 10; S34-S38.
- [149] Vilana R, Bianchi L, Varela M, Nicolau C, Sánchez M, Ayuso C, et al. Is microbubble-enhanced ultrasonography sufficient for assessment of response to percutaneous treatment in patients with early hepatocellular carcinoma? *Eur Radiol*, 2006, 16: 2454-2462.
- [150] Vallone P, Gallipoli A, Izzo F, Fiore F, Delrio P. Local ablation procedures in primary liver tumors; Levovist US versus spiral CT to evaluate therapeutic response. *Anticancer Res*, 2003, 23: 5075-5079.
- [151] Wang JH, Lu SN, Tung HD, Changchien CS, Hung CH, Chen CH, et al. Flash-echo contrast sonography in the evaluation of response of small hepatocellular carcinoma to percutaneous ablation. *J Clin Ultrasound*, 2006, 34; 161-168.
- [152] Morimoto-M, Nozawa-A, Numata-K, Shirato K, Sugimori K, Kokawa A, et al. Evaluation using contrast-enhanced harmonic gray scale sonography after radio frequency ablation of small hepatocellular carcinoma-sonographic-histopathologic correlation. *J Ultrasound Med*, 2005, 24; 273-283.
- [153] Kim CK, Choi D, Lim HK, Kim SH, Lee WJ, Kim MJ, et al. Therapeutic response assessment of percutaneous radiofrequency thermal ablation for hepatocellular carcinoma; utility of contrast-enhanced agent detection imaging. *Eur J Radiol*, 2005, 56; 66-73.
- [154] Ding H, Kudo M, Onda H, Suetomi Y, Minami Y, Maekawa K. Contrast enhanced subtraction harmonic sonography for evaluating treatment response in patients with hepatocellular carcinoma. *Am J Roentgenol*, 2001, 176; 661-666.
- [155] Meloni MF, Goldberg SN, Livraghi T, Calliada F, Ricci P, Rossi M, et al. Hepatocellular carcinoma treated with radiofrequency ablation; comparison of pulse inversion contrast-enhanced harmonic sonography, contrast-enhanced power Doppler sonography, and helical CT. *Am J Roentgenol*, 2001, 177; 375-380.
- [156] Vilana R, Llovet JM, Bianchi L, Sanchez M, Pagés M, Sala M, et al. Contrast-enhanced power Doppler sonography and helical computer tomography for assessment of vascularity of small hepatocellular carcinomas before and after percutaneous ablation. *J Clin Ultrasound*, 2003, 31; 119-128.
- [157] Cioni D, Lencioni R, Rossi S, Garbagnati F, Donati F, Crocetti L, et al. Radiofrequency thermal ablation of hepatocellular carcinoma; using contrast-enhanced harmonic power Doppler sonography to assess treatment outcome. *Am J Roentgenol*, 2001, 177; 783-788.
- [158] Fiore F, Vallone P, Ricchi P, Tambaro R, Daniele B, Sandomenico F, et al. Levovist enhanced Doppler sonography versus spiral computed tomography to evaluate response to percutaneous ethanol injection in hepatocellular carcinoma. *J Clin Gastroenterol*, 2000, 31; 164-168.
- [159] Kim HJ, Kim TH, Kim PN, Kim AY, Ko EY, Kim KW, et al. Assessment of the therapeutic response of the hepatocellular carcinoma treated with transcatheter arterial chemoembolization. *J Ultrasound Med*, 2006, 25; 477-486.
- [160] Kono Y, Lucidarme O, Choi SH, Rose SC, Hassanein TI, Alpert E, et al. Contrast-enhanced ultrasound as a predictor of treatment efficacy within 2 weeks after transarterial chemoembolization of hepatocellular carcinoma. *J Vasc Interv Radiol*, 2007, 18; 57-65.
- [161] Shima T, Mizuno M, Otsuji H, Mizuno C, Obata H, Park H, et al. Evaluation of transcatheter arterial chemoembolization therapy on hepatocellular carcinomas using contrast-enhanced harmonic power-Doppler sonography: comparison with CT, power-Doppler sonography and dynamic MRI. *J Med Ultrasonics*, 2005, 32; 107-113.
- [162] Shimizu M, Iijima H, Horibe T, Yamada M, Suzuki S, Yanagisawa K, et al. Usefulness of contrast-enhanced sonography with a new contrast mode, agent detection imaging, in evaluating therapeutic response in hepatocellular carcinoma treated with radio-frequency. *Hepatol Res*, 2004, 29; 235-242.
- [163] Kisaka Y, Hirooka M, Kumagi T, Uehara T, Hiasa Y, Kumano S, et al. Usefulness of contrast-enhanced ultrasonography with abdominal virtual sonography in assessing therapeutic response in hepatocellular carcinoma treated with radiofrequency ablation. *Liver Int*, 2006, 26; 1241-1247.
- [164] Sato S, Shiratori Y, Imamura M, Teratani T, Obi S, Koike Y, et al. Power Doppler signals after percutaneous ethanol injection therapy for hepatocellular carcinoma predict local recurrence of tumors; a prospective study using 199 consecutive patients. *J Hepatol*, 2001, 35; 225-234.
- [165] Koito K, Namieno T, Ichimura T, Hirokawa N, Syonai T, Hareyama M, et al. Power Doppler sonography; evaluation of hepatocellular carcinoma after treatment with transarterial embolization or percutaneous ethanol injection therapy. *Am J Roentgenol*, 2000, 174; 337-341.
- [166] Shirato K, Numata K, Mitsui K, Kitamura T, Morita K, Saito S, et al. Color-Doppler sonography for evaluating response to transcatheter arterial embolization and percutaneous ethanol injection therapy and for detecting recurrence of hepatocellular carcinoma. *J Ultrasound Med*, 2000, 19; 807-814.
- [167] Castroagudin JF, Delgado M, Martinez SM, Abdulkader I, Bustamante M, Martinez J, et al. Doppler ultrasonography for the assessment of tumor necrosis after percutaneous ethanol injection prior to liver transplantation as adjuvant therapy of hepatocellular carcinoma. *Transplant Proc*, 2005, 37; 1493-1495.
- [168] Kim YS, Rhim H, Lim HK, Park CK, Lee WJ, Do YS, et al. Completeness of treatment in hepatocellular carcinomas treated with image-guided tumor therapies; evaluation of positive predictive value of contrast enhanced CT with histopathologic correlation in the explanted liver specimen. *J Comput Assist Tomogr*, 2006, 30; 578-582.
- [169] Kim SH, Lee WJ, Lim HK, Lim JH. Prediction of viable tumor in hepatocellular carcinoma treated with transcatheter arterial

- chemoembolization; usefulness of at tenation value measurement at quadruple-phase helical computed tomography. *J Comput Assist Tomogr*, 2007, 31:198-203.
- [170] Kamel IR, Bluemke DA, Ramsey D, Abusedera M, Torbenson M, Eng J, et al. Role of diffusion-weighted imaging in estimating tumor necrosis after chemoembolization of hepatocellular carcinoma. *Am J Roentgenol*, 2003, 181:708-710.
- [171] Tsui EY, Chan JH, Cheung YK, Cheung CC, Tsui WC, Szeto ML, et al. Evaluation of therapeutic effectiveness of transarterial chemoembolization for hepatocellular carcinoma; correlation of dynamic susceptibility contrast-enhanced echoplanar imaging and hepatic angiography. *Clin Imaging*, 2000, 24:210-216.
- [172] Zhao JG, Feng GS, Kong XQ, Li X, Li MH, Cheng YS. Assessment of hepatocellular carcinoma vascularity before and after transcatheter arterial chemoembolization by using first pass perfusion weighted MR imaging. *World J Gastroenterol*, 2004, 10:1152-1156.
- [173] Anderson GS, Brinkmann F, Soulen MC, Alavi A, Zhuang H. FDG positron emission tomography in the surveillance of hepatic tumors treated with radiofrequency ablation. *Clin Nucl Med*, 2003, 28:192-197.
- [174] Blokhuis TJ, van der Schaaf MC, van den Tol MP, Comans EF, Manoliu RA, van der Sijp JR. Results of radio frequency ablation of primary and secondary liver tumors; long-term follow up with computed tomography and positron emission tomography-18F-deoxyfluoroglucose scanning. *Scand J Gastroenterol Suppl*, 2004, 241:93-97.
- [175] Langenhoff BS, Oyen WJ, Jager GJ. Efficacy of fluorine-18-deoxyglucose positron emission tomography in detecting tumor recurrence after local ablative therapy for liver metastases; a prospective study. *J Clin Oncol*, 2002, 20:4453-4458.
- [176] Donckier V, van Laethem JL, Goldman S, van Gansbeke D, Feron P, Ickx B, et al. [F-18] fluorodeoxyglucose positron emission tomography as a tool for early recognition of incomplete tumor destruction after radiofrequency ablation for liver metastases. *J Surg Oncol*, 2003, 84:215-223.
- [177] Veit P, Antoch G, Stergar H, Bockisch A, Forsting M, Kuehl H. Detection of residual tumor after radiofrequency ablation of liver metastasis with dualmodality PET/CT; initial results. *Eur Radiol*, 2006, 16:80-87.
- [178] Goshen E, Davidson T, Zwas ST, Aderka D. PET/CT in the evaluation of response to treatment of liver metastases from colorectal cancer with bevacizumab and irinotecan. *Technol Cancer Res Treat*, 2006, 5:37-43.
- [179] Gopinath G, Ahmed A, Buscombe JR, Dickson JC, Caplin ME, Hilson AJ. Prediction of clinical outcome in treated neuroendocrine tumours of carcinoid type using functional volumes on 111In-pentetreotide SPECT imaging. *Nucl Med Commun*, 2004, 25:253-257.
- [180] Herman P, Costa ML, Machado MA, Pugliese V, D'Albuquerque LA, Machado MC, et al. Management of hepatic hemangiomas; a 14-year experience. *J Gastrointest Surg*, 2005, 9:853-859.
- [181] Bruix J, Sherman M. Practice Guidelines Committee, American Association for the Study of Liver Diseases. *Hepatology*, 2005, 42:1208-1236.
- [182] Bolondi L, Gaiani S, Celli N, Golfieri R, Grigioni WF, Leoni S, et al. Characterization of small nodules in cirrhosis by assessment of vascularity; the problem of hypovascular hepatocellular carcinoma. *Hepatology*, 2005, 42:27-34.
- [183] Forner A, Vilana R, Ayuso C, Bianchi L, Solé M, Ayuso JR, et al. Diagnosis of hepatic nodules, 20mm or smaller in cirrhosis; prospective validation of the noninvasive diagnostic criteria for hepatocellular carcinoma. *Hepatology*, 2008, 47:97-104.
- [184] Livraghi T, Solbiati L, Meloni MF, Gazelle GS, Halpern EF, Goldberg SN. Treatment of focal liver tumors with percutaneous radio-frequency ablation; complication encountered in a multicenter study. *Radiology*, 2003, 226:441-451.

(收稿日期:2013-08-01)