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自动全乳腺超声在乳腺癌中的应用进展

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摘 要

自动全乳腺超声是一种新型高分辨率乳腺三维超声成像技术，可以克服常规手持超声对操作者依赖性大、缺乏标准化操作、可重复性差等缺点，其特有的冠状面视角可以提供额外的影像资料，在鉴别诊断乳腺良恶性病变方面表现出较高的价值。本文将对自动全乳腺超声辅助乳腺癌诊断的应用现状进行综述。

关键词

自动全乳腺超声，乳腺癌

Application Progress of Automated Breast Ultrasound in Breast Cancer

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Abstract

Automated breast ultrasound is a new high-resolution breast three-dimensional ultrasound imaging technology that can overcome the disadvantages of conventional hand-held ultrasound, such as high operator dependence, lack of standardized operation, and poor repeatability. Its unique coronal view angle can provide additional imaging data, showing high value in the differential diagnosis of benign and malignant breast lesions. This article will review the application status of automated breast ultrasound assisted diagnosis of breast cancer.

Keywords

Automated Breast Ultrasound, Breast Cancer

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1. 引言

近年来，乳腺癌发病率日益上升，已成为女性癌症性死亡的首要原因[1]，在过去 20 年中，中国的乳腺癌发病率以每年 3%~5%的速度增长，远远快于世界平均每年 0.5%的增长速度[2]，对多为致密性乳腺的中国女性，超声检测乳腺病变的能力可能优于 MG (mammography, MG) [3]。ABUS (automated breast ultrasound, ABUS)是一种能够克服传统 HHUS (hand-held ultrasound, HHUS)受操作者经验和主观判断限制，通过标准化的扫描方法，提高扫描的一致性和可重复性的检查方法[4]，本文旨在概述 ABUS 在乳腺癌中的临床应用价值。

2. ABUS 设备简介

自动乳腺超声的概念可以追溯到 70 年代[5]，最初被提出的目的是克服 HHUS 的操作员依赖性，提高检查的可重复性。GE 公司研发的最新一代 Invenia ABUS 超声诊断仪，配备特有的大尺寸高频探头(15 × 17 cm)，扫查速度更快，分辨率更高，与旧系统相比，弯曲探头和乳房曲面之间产生的耦合伪影更少[6]。扫查时患者取仰卧位，双手置于头顶，移动机械臂，将探头放置在乳房上给予一定压力后开始采集。通常，三次 1 分钟的扫描可扫描整个乳房，不包括腋窝。图像采集后，将数据存储在系统的硬盘上，然后传输到专用工作站，在该工作站中，可以查看原始轴向平面和重建的冠状面和矢状面中显示的图像，以进行进一步的分析。冠状面，也称为“手术视图”，引入了新的诊断信息，即汇聚征[7]。

3. ABUS 的诊断效能

3.1. 与 HHUS 相比

最近，各种研究对 ABUS 诊断方面的应用进行了评价。然而，ABUS 的诊断能力仍然存在争议，特别是与 HHUS 相比。Liu 等人[8]的研究表明，ABUS 和 HHUS 诊断乳腺癌的灵敏度分别为 92.8%和 96.3%，特异度为 93.0%和 89.6%，ABUS 的特异度较 HHUS 更高($P < 0.01$)，而 HHUS 的灵敏度更高($P = 0.01$)。在 Zhang 等人[9]的研究中，HHUS 与 ABUS 的灵敏度、特异度、准确性分别为 97.33% vs 90.67%、89.79% vs 92.49%、90.74% vs 92.26%，ABUS 的特异度明显优于 HHUS ($P = 0.024$)，HHUS 的 AUC 高于 ABUS (0.936 vs 0.916)，但差异无统计学意义($P > 0.05$)。在 2019 年的一篇纳入 9 项研究、1376 名患者的 mate 分析中[10]，Zhang 等人认为 ABUS 在检测癌症方面与 HHUS 具有相同的检出率(100%)，ABUS 在数值上具有更高的灵敏度(93% vs 90%)和特异度(86% vs 82%)，但差异无统计学意义($P = 0.0771$)。综上所述，在包含上文的共 8 项研究中[11]-[15]。ABUS 和 HHUS 的灵敏度范围分别为(93.3%~84.2%)和(84.2%~100%)，特异度范围分别为(80.5%~93.0%)和(81.0%~89.8%)，并且以上文章均得出了 ABUS 与 HHUS 具有相当的诊断效能的结论。然而也有研究表明[16] [17] ABUS 诊断非肿块型乳腺癌的敏感度、特异性和准确性均显著优于 HHUS ($P < 0.05$)。在宋灿许等人[18]的研究中，在诊断触诊阴性乳腺癌患者时，ABUS 的灵敏度高于 HHUS，可减少肿块较小引起的漏诊，特别是当病灶直径 < 5 mm 时，其诊断效能显著提升[19]。

3.2. 与其他检查联合诊断

在乳腺癌的实际诊断中，使用 ABUS 联合 HHUS、彩色多普勒血流技术、弹性成像技术等可提高对

乳腺病变分类判断的准确性[20]，有利于良恶性肿瘤的鉴别。Li [21]等人将 ABUS、弹性成像和彩色多普勒血流技术联合用于鉴别诊断硬化性腺病和浸润性导管癌时表现出了最高的准确率，AUC (area under the ROC curve, AUC)为 0.895，显著高于单独使用 3 种影像学方法($P < 0.05$)。Wang 等人[22]证明，声触诊组织量化技术(virtual touch tissue quantification, VTQ)和 ABUS 的联合使用可能提高乳腺癌诊断的准确性和特异性。

ABUS 还可与 MG 联用提升对乳腺肿块的诊断效能。在一项多中心临床研究中[23]，937 名乳房致密的女性分别接受了 ABUS、HHUS 和 MG 检查，结果显示在乳腺组织致密且 MG 结果阴性的情况下，联合 ABUS 筛查可提高癌症的检出率为 42.8/1000 次。Ren 等人[24]也得出了相似的结论，他们评估了第二眼 ABUS 检查辅助 MG 与单独使用 MG 在无症状女性中的作用，并将其与 HHUS 进行了比较，结果显示 HHUS 和 ABUS 联合筛查 MG 阴性病例时，病变检出率为 3.66/1000，高于单独使用 MG 的检出率(2.69/1000)。故而认为 ABUS 能有效弥补 MG 的不足，提高 MG 的病灶检出率，降低其假阴性结果[19] [25] [26]。

3.3. ABUS 冠状面成像优势

与 HHUS 相比，ABUS 不能使用彩色多普勒成像、弹性成像等技术，之所以能获得与 HHUS 相当的诊断效能，这归功于其独特的冠状面视角，后者引入了新的诊断信息，即汇聚征[27]。有研究表明[16] ABUS 的汇聚征比 MG 更敏感地揭示结构异常。Liu 等人[28]的研究表明，汇聚征在检测乳腺癌中具有 100.0%的特异度和 80.0%的灵敏度，在区分乳腺良恶性病变中具有 91.4%的高准确性。Amir 等人[29]的研究表明，HHUS 联合 ABUS 的特异度与单独使用“汇聚征”无显著性差异($P > 0.05$)，但灵敏度优于单纯应用“汇聚征“($P = 0.002$)。然而，有文献表明[30] [31]，汇聚征的特异度可能在 98.4%到 100%之间，而其灵敏度可能只有 39.1%到 70%，这意味着大多数冠状面上具有汇聚征的乳腺病变是恶性的，而只有部分恶性乳腺病变表现出汇聚征。Zhang 等人[27]也提出，ABUS 在鉴别诊断中的独立价值限制是由汇聚征的低灵敏度(37.0%)引起的。究其原因，一方面，这种低灵敏度是由汇聚征的非特异性引起，少部分良性乳腺病变如硬化性腺病、手术疤痕、导管内乳头状瘤等也可出现汇聚征[32]，在 Nakhlis 等人[33]的研究中，硬化性腺病在冠状面显示汇聚征的可能性虽然显著低于浸润性导管癌($P < 0.05$)，但其增殖组织挤压小叶出现假浸润现象，仍然可能被误诊为浸润性导管癌；另外一方面，汇聚征在影像学上的主观性和缺乏标准化定义可能会影响其敏感度[34]。

4. ABUS 预测乳腺癌分子亚型的能力

乳腺癌蛋白分子标志物的表达与患者的治疗及预后密切相关[35]。MRI 定量分析已被尝试应用于预测乳腺癌的分子分型[36]，但是其价格昂贵且费时并未在临床普及。ABUS 冠状面声像图可为术前预测乳腺癌分子分型提供重要信息[37]。黄思等人[38]的研究显示汇聚征是 Luminal A 型乳腺癌的独立相关因素。Xu 等人[39]认为生长缓慢，预后较好的 Luminal A 型有充足的时间累积出汇聚征。范莉芳等人[40]认为 Luminal B 型乳腺癌在肿瘤增殖速率和恶性程度方面均高于 Luminal A 型，所以更易出现汇聚征。Chen 等人[41]表明，汇聚征与高回声晕较少出现在三阴型和人表皮生长因子受体-2 (Human epidermal growth factor receptor 2, Her-2)阳性型乳腺癌中，而肿块内微钙化是 Her-2 阳性型乳腺癌的独立相关因素。Giuliano [42]提出乳腺癌边缘毛刺征与雌、孕激素受体阳性呈正相关，而肿块内微钙化与 Her-2 阳性呈正相关。综上所述，Luminal 型乳腺癌更易出现汇聚征，究其原因可能是，Luminal 型乳腺癌组织学分级低，肿瘤细胞容易与相邻正常组织交错浸润，而三阴型乳腺癌肿瘤组织学分级高，肿瘤较少诱发周边反应，因此较少出现汇聚征[43]。然而也有研究证明[44]采用汇聚征预测分子分型的平均准确率仅为 40.6%。

5. ABUS 预测腋窝淋巴结转移

脉管浸润(Lymphovascular invasion, LVI)阳性与腋窝淋巴结(Axillary lymph node, ALN)状态和远处转

移的风险增加有关[45]。LVI 可促进乳腺癌局部复发[46]，ALN 是决定乳腺癌患者 N 分期、判断其预后及决定后续治疗方案的重要参考指标[47]，故而术前了解 LVI 与 ALN 状态有助于临床决策。

Li 等人[48]基于 ABUS 的放射组学特征开发用于确定乳腺癌中 LVI 状态的模型，在验证队列中，融合模型达到了 0.879 的最高 AUC 和 85.00%的准确度，在乳腺癌术前无创预测 LVI 方面表现出良好的性能，与范莉芳[49]等人研究结果一致。王美晨等人[50]发现汇聚征是乳腺癌腋窝淋巴结转移的独立危险因素，并且病灶距乳头与距皮肤距离越近，转移负荷越高，而 ABUS 可自动获得病灶距乳头距离与距皮肤距离，定位客观准确，故而 ABUS 对乳腺癌腋窝淋巴结转移有一定临床预测价值。Yang 等人[51]提出以上结论可能与乳腺中央区淋巴管丰富有关。然而，Li 等人[52]的研究结果与上述研究有差别：他认为肿瘤距皮肤距离是腋窝淋巴结转移的独立预测因子，但病灶接近乳头不会增加腋窝淋巴结转移的风险，这与 Lewis 等人[53]研究结果一致。除此之外，乳腺肿瘤的大小与腋窝淋巴结转移密切相关[54]。在 Li 等人[52]的研究中，乳腺肿瘤的体积在非转移组为 3.42 cm^3，在转移组为 8.78 cm^3，差异有统计学意义($P < 0.05$)。故认为乳腺肿瘤越大，发生腋窝淋巴结转移风险越高，这可能是因为：乳腺癌越大，浸润到周围淋巴管的可能性就越大，最终导致腋窝淋巴结转移的风险就越高。

6. ABUS 在评估新辅助治疗中的应用

新辅助治疗(Neoadjuvant therapy, NAT)通过促进肿瘤体积缩小，将不可手术病灶转化为可手术病灶，增加保乳手术的机会，在治疗乳腺癌中起着至关重要的作用[55]。然而，NAT 的治疗效果对许多患者来说并不理想，只有 20%~40%的患者在治疗后达到病理完全缓解(Pathologic complete response, pCR)。超声检查在 NAT 评估中具有较多优势，在测量肿瘤大小方面比临床触诊或 MG 更准确[56]，有研究表明，ABUS 在测量肿瘤大小方面与 MRI 相当[57]。

ABUS 通过生成对病变的完整体积分析，消除了一些 HHUS 的可变性，在评估 NAT 疗效方面比 HHUS 具有更高的准确率[58]，Elen 等[59]研究表明，ABUS 在预测 pCR 方面的特异度达到 100%，能够准确预测 NAT 后最终病理肿瘤大小。Wei 等人[60]提出两个 NAC 周期后 ABUS 图像的放射组学特征可提供最有效的预测。使用基于 MRI 的放射组学也报告了类似的发现[61] [62]。Wang 等人[63]发现，NAC 治疗后 ABUS 最大肿瘤直径减少 50%可以高度预测 pCR，该研究的 AUC 为 0.89。Xie 等人[64]研究结果显示，在 NAT 前后 pCR 组和非 pCR 组之间的直径变化和体积变化存在统计学上的显著差异($P < 0.001$)。然而，将这两个参数纳入二元 logistic 回归分析后，只有体积变化是 pCR 的独立预测因子，故而他们认为体积变化反映了整个肿块的减少，而直径的变化只影响肿瘤内的特定部分，并且更难测量。然而，Murakami 等人[65]表明，ABUS 在三阴型乳腺癌中预测残余肿瘤大小和 pCR 的可靠性低，且有低估残余肿瘤的倾向，这提示 ABUS 在鉴别 NAC 后化疗诱导的纤维化和低回声肿瘤时可能不够敏感。除此之外，病灶周围存有导管原位癌将影响 ABUS 对肿瘤变化的评估[66]，并且 ABUS 在某些情况下可能会出现误判，在病理检查中显示为 pCR 或最小残留病变的情况下，超声通常会显示为残留肿块[67]。

7. 未来展望

相较 HHUS，ABUS 在临床实践中会导致更多的召回、随访和活检[68]，未来需要统一 ABUS 图像的诊断标准，减少人为因素造成的误诊。

8. 总结

ABUS 作为一种三维超声，在克服 HHUS 局限性的同时拥有与其相当的诊断效能，在联合其他检查时可表现出更出色的诊断能力。此外，ABUS 在预测乳腺癌的分子分型、腋窝淋巴结转移以及评估新辅助治疗疗效方面表现出了极大的潜能。

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