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影像新技术在乳腺疾病筛查中的应用

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摘　要

乳腺癌是全世界女性最常见的恶性肿瘤。目前国内外常用的乳腺癌筛查手段包括乳房X线摄影术、超声成像和磁共振成像技术等。这篇综述中，我们主要对近几年来出现的乳腺癌筛查的新技术进行描述分析，并总结这些筛查方法的优缺点以及在临床的应用价值。

关键词

乳腺筛查，影像技术，乳腺肿瘤，综述

Application of New Imaging Technology in Breast Disease Screening

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Abstract

Breast cancer is the most common malignant tumor in women worldwide. The most commonly used methods for breast cancer screening in China and other countries include mammography, ultrasound, and magnetic resonance imaging. In this review, we mainly describe and analyze the new technologies for breast cancer screening in recent years, and summarize the advantages and disadvantages of these screening methods and their clinical application value.

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Keywords

Breast Screening, Imaging Technology, Breast Tumor, Review

1. 前言

乳腺癌是全世界妇女最常见的癌症，据统计 2020 年约有 230 万女性被确诊为乳腺癌，占新发癌症比例的 11.7%，初次超越肺癌，成为发病率最高的癌症[1]；其死亡率全球排名第五，在中国排名第四[2]。目前乳腺癌仍缺乏有效的预防手段，因此实现乳腺癌早发现、早诊断及早治疗是公认的能够有效提高女性乳腺癌生存率的主要方法，以期进一步提高患者生活质量。已证实通过乳腺 X 线摄影术可降低乳腺癌的死亡率，然而乳腺 X 线摄影具有众所周知的局限性，在 9%的乳腺腺体致密的女性中，患乳腺癌的风险是腺体不致密型乳腺的 2.5~4 倍，敏感性较低仅为 60% [3]。在过去 20 年里，突破了传统的乳腺 X 线摄影技术，乳腺癌筛查的影像学方法正在与时俱进，包括对比增强 X 线摄影、触觉及微波传感器成像、简化的磁共振序列以及超声新技术已被用作辅助筛查工具。

2. 对比剂增强型数字化乳腺 X 线摄影术 (Contrast Agent-Enhanced Digital Mammography, CEDM)

对比增强数字乳腺摄影术(CEDM)将使用碘对比剂的双能量减影技术与全视野数字乳房 X 线摄影术(FFDM)相结合。融合了 X 线摄影术的高空间分辨率与恶性肿瘤由于血管通透性增加，导致其对造影剂快速摄取形成高对比度的优势。CESM 的辐射剂量是标准 2D 数字乳腺 X 线摄影的 1.2 到 1.8 倍，但完全符合乳腺 X 线检查质控标准[4]，可用于乳腺腺体致密的女性行传统乳腺 X 线摄影的补充筛查方式。研究发现 CEDM 具有显著高于乳腺 X 线摄影术的灵敏度、特异性、阳性预测值、阴性预测值和准确度[5]，CEDM 有望成为 FFDM 的替代筛查技术[6]。另有研究在比较 CEDM 和 MRI 在评估新诊断乳腺癌患者的病灶方面的研究表明[7] [8]，MRI 和 CEDM 在发现继发性病灶方面的敏感性相似(57% vs 61%)，但 CEDM 始终显示出较低的假阳性率和较高的阳性预测值。Patel 等人[9]研究，用 CEDM 代替 MRI 作为乳腺筛查的成像技术，每次检查最多可节省 750 美元，每年可节省 11 亿美元的医疗费用，从而有助于降低乳房成像成本。对比剂增强型数字化乳腺 X 线摄影术特别是针对乳腺腺体致密患者对病灶的显示更清晰，但同时得注意对比剂过敏问题。

3. 简化的乳腺磁共振成像(Abbreviated Breast MRI, ABB-MRI)与非增强序列的研究

乳腺的磁共振成像(MRI)对癌症的早期检测具有最高的敏感性，一般被用在高危或乳房腺体致密患者的补充筛查工具[10] [11]，然而，只有 6.6%的高危女性在乳房 X 线筛查后的 2 年内进行了补充乳腺 MRI 检查[12]，因 MRI 成像时间长、成本高、患者耐受性差以及诸多禁忌症限制 MRI 在临床的广泛应用。为了克服 MRI 检查时间长及检查的高成本，Kuhl 等人[13]首次报道了 ABB-MRI 作为筛查的研究，简化序列包括 T1 平扫、第一期增强 T1 加权、减影图像和最大信号投影图像，时间分辨力显著提高而不会对诊断准确性产生负面影响。另一篇对简化 MRI 序列的综述[14]，序列包括 T1 平扫和第一期对比增强的 T1 加权序列，而其中一些还包括 T2 加权、压脂、第二期 T1 对比增强、减影和最大信号投影图像，结论是

在时间分辨力显著提高的前提下，仍可以检测到64%~97%的早期浸润性癌症和大部分中高级别的导管原位癌(DCIS)。

然而，简化的MRI序列，通常只包含第一期增强，不能对时间信号强度曲线进行评估。为了克服这一缺陷，一些研究探索了多种成像加速序列[15] [16] [17]，包括时间分辨随机轨道成像(TWIST)和采用SENSE (Sensitivity Encoding)加速因子的加速技术在保持高空间分辨率的同时减少了采集时间。最近，已经证实钆造影剂(GBCA)在大脑的沉积，因此，研究人员正努力开发与乳腺增强MRI筛查具有同等敏感性的非增强MRI技术[18]。此外，简化的非增强MRI序列被证实在检测病灶的敏感性方面甚至优于乳房X线摄影[18] [19]。这些研发可能使MRI能更广泛地用作针对目前筛查尚不符合成本效益的中低风险女性中。简化的MRI序列有望成为一种补充筛查工具，旨在检测乳腺X线上呈隐匿性的乳腺癌。

4. 触觉传感器成像(Tactile Sensor Imaging)

此成像仪器像小型的掌上血压仪，通过无辐射、无痛的电池式机械手持式乳房触诊仪(IBreastExam, IBE)进行乳房检查，特别适合在医疗条件较落后的地区实行乳腺疾病的初步筛查。其基本原理为压电探测器原理，该压电探测器可产生有关组织压缩和硬度的定量信息，通过配备专有软件的平板电脑，将结果信息实时显示在屏幕上，红色区域表示异常组织，绿色区域为正常组织。用以评估正常乳腺组织和坚硬的肿块之间弹性模量的变化。Broach小组等人[20]对78名患者纳入研究，结果经诊断性影像检查已确认有77个病变，IBE正确识别出66个病变，灵敏度为86%，特异性为89%。新的触觉成像技术正在不断的开发中[21] [22]。

5. 微波无线电波雷达乳腺成像系统 (MICRIMA Radio-Wave Radar Breast Imaging System, MARIA)

MARIA系统作为新技术，它包含安装在扫描单元的半球无线电波阵列，仪器位于检查床的下方，患者俯卧在检查床上，乳房通过扫描床孔自然悬垂。MARIA扫描每个乳房时间不到5分钟，通过捕获不同腺体组织在阻抗、介电常数和电导率这三个参数的变化，使该设备能够构建乳房的3D图，可显示出乳房的体积，并附有强度标尺，使得临床医生能够区分正常组织和病变组织[23] [24]。已知在腺体致密的女性中乳腺X线检查存在局限性，Shere等人[24]对进行MARIA检查且符合评估标准的225名患者进行研究，结果表明MARIA系统在不同乳房密度及不同年龄段诊断的敏感性相当。MARIA系统无电离辐射、无需压迫检查、无MRI检查昂贵的成本；尤其在腺体致密的年轻女性或年龄太小而无法行乳腺X线摄影的一般人群的筛查方面具有广阔的应用前景。

6. 超声技术

6.1. 自动乳腺超声检查(ABUS)

手持式超声(hand-held ultrasound, HHUS)在国外被用作乳房X线摄影的辅助筛查技术，但是存在局限性，如特异性较低、操作者依赖性强、重复性差、视野相对狭窄等局限性。自动乳房超声检查(ABUS)是一种很有前途的技术，特别是在乳腺组织较密的年轻女性中。通过宽传感器实现整个乳房的连续扫查，获取的图像自动进行冠状面及矢状面的重建，降低对操作者的依赖性，同时可实现远程读片。研究显示[25]，作为数字化乳腺X线摄影的补充筛查，癌症的检出率提高1.9/1000。Giuliano研究了[26] 3418名在乳房X线照片上腺体密集的女性，结果表明相对于仅实行FFDM，在添加ABUS检查后可导致乳腺癌的检出率从4.6/1000提高到12.3/1000，敏感性从76.0%增加到97.7%。最近开发了一种用于3D-ABUS的计算机辅助检测软件(QVCAD, QView Medical) [27]，对筛查结果的解释时间可减少高达35%，并减少假阳

性的召回率。Evans 等人建议[28]，在乳腺密度中等或中等风险的女性中，于乳房 X 线摄影检查阴性后，将 HHUS 或 3D ABUS 用作补充筛查方式。ABUS 实现乳腺三维成像，最大程度展现肿块的形状与周围组织的关系，但对腋窝淋巴结的探测是其一大局限性。

6.2. 光声超声(OAUS)

光学超声也称为光声断层扫描和光声成像，利用光学分辨率和穿透力深的优点，利用内源性造影剂(如水、血红蛋白、脂质及黑色素)可提供结构、功能、分子和动力学信息的能力[29]。通过使用激光脉冲使血管可视化并检测肿瘤新生血管，同时监测返回的声波，以产生光声信号。光声成像基于血液中脱氧血红蛋白和氧合血红蛋白的光学对比度差异，与良性病变相比，癌症组织代谢活跃，产生更多的脱氧血红蛋白。用不同波长的激光脉冲可使光声 US 区分脱氧血红蛋白与氧合血红蛋白，并对其进行颜色编码[30]。光超特别适用于检测肿瘤微脉管系统，具有区分缺氧组织和正常含氧组织的固有能力。在一项前瞻性多机构研究中[31]，共有 1972 名女性接受了穿刺活检前灰阶超声及光学超声检查，结论为联合光声超声成像及灰阶超声特征助于区分乳腺癌的病理亚型。几项研究[32] [33]，对乳腺切除标本行光学超声实验，与无肿瘤区域相比，肿瘤病灶内几乎没有脂肪信号，而肿瘤的边缘具有强烈的脱氧血红蛋白信号，当切除的肿块标本的边缘表现为连续的脂质信号时证明肿块切除完全。光声成像可作为快速、有效的评估术中肿瘤切除出现阴性边缘的潜在工具。光学超声于还可用于对可疑恶性肿块的 BIRADS 降级处理[34] [35]，提高乳房肿块病灶评估的特异性。但光学超声在临床作为乳腺疾病的筛查应用仍然有限，常见于科研研究中。

7. 小结与展望

总之，随着设备仪器的更新换代，乳腺癌的筛查将超越传统的成像工具，特别是针对乳腺腺体致密、年龄偏小不适合乳腺钼靶、磁共振检查禁忌症、检查耗时以及医疗条件较落后的国家，新的筛查方法都能提供很好的补充，甚至在降低召回率方面表现显著。提倡精准医疗的时代，通过制定个性化筛查方案，结合新颖的体液筛查技术有望进一步提高术前的诊断效能。

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