

# 乳腺癌放射性皮炎的风险识别、诊断技术及防治策略研究进展

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## 摘 要

放射性皮炎(radiation dermatitis, RD)是乳腺癌患者放疗期间最常见的急性不良反应,发生率高达95%,其不仅会降低患者治疗依从性,还会严重影响生活质量。本文围绕RD的风险识别、新型诊断技术及防治策略展开综述,梳理相关研究进展:在风险识别方面,已明确身体质量指数  $\geq 25 \text{ kg/m}^2$ 、吸烟、糖尿病及特定基因多态性为宿主风险因素;在新型诊断技术领域,反射式共聚焦显微镜、皮肤反射光谱法、光声成像与弹性成像技术,以及分子与血清标志物检测技术的应用,实现了RD的早期、定量及客观诊断,诊断效能显著优于传统视觉评估方法;在防治策略上,调强放疗、大分割放疗等放疗技术可有效降低皮肤受照剂量,局部屏障保护措施与糖皮质激素、细菌去定植等药物干预均为临床证实的有效防治手段。未来需依托精准风险识别体系与新型诊断技术,进一步优化个体化防治方案,持续提升RD的临床管理效果。

## 关键词

乳腺癌, 放射性皮炎, 风险识别, 新型诊断技术, 防治策略, 去细菌定植

# Research Progress on Risk Identification, Diagnostic Techniques, and Prevention and Management Strategies for Radiation Dermatitis in Breast Cancer

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## Abstract

Radiation dermatitis (RD) is the most common acute adverse reaction in breast cancer patients undergoing radiotherapy, with an incidence rate as high as 95%. It not only reduces patients' treatment compliance but also severely impairs their quality of life. This article reviews the research progress focusing on RD's risk identification, novel diagnostic techniques, and prevention and management strategies: In terms of risk identification, body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup>, smoking, diabetes mellitus, and specific gene polymorphisms have been identified as key host risk factors. In the field of novel diagnostic technologies, the application of reflectance confocal microscopy, skin reflectance spectrophotometry, photoacoustic imaging, elastography, as well as molecular and serum marker detection technologies has enabled early, quantitative, and objective diagnosis of RD, with diagnostic efficacy significantly superior to traditional visual assessment methods. Regarding prevention and management strategies, radiotherapy techniques such as intensity-modulated radiation therapy (IMRT) and hypofractionated radiotherapy can effectively reduce skin radiation dose, while local barrier protection measures and pharmacological interventions including glucocorticoids and bacterial decolonization have been clinically proven as effective prevention and treatment approaches. Future efforts should rely on precise risk identification systems and novel diagnostic technologies to further optimize individualized prevention and treatment regimens, continuously improving the clinical management outcomes of RD.

## Keywords

Breast Cancer, Radiation Dermatitis, Risk Identification, Novel Diagnostic Technologies, Prevention and Management Strategies, Bacterial Decolonization

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## 1. 引言

放射性皮炎(Radiation Dermatitis, RD)是乳腺癌患者接受放疗期间最常见的急性不良反应, 发生率高达 95%, 严重程度从轻微红斑、干燥脱屑、湿性糜烂至溃疡不等[1][2]。其不仅引发疼痛、瘙痒等不适症状, 还可能导致放疗中断, 影响肿瘤控制效果, 同时显著降低患者生活质量, 部分患者甚至面临迟发性色素沉着、纤维化等长期损伤风险[3][4]。因此, 识别能够预测放射性皮炎风险的因素, 采取预防和治疗措施, 使患者在放疗过程中减少放射性皮炎的发生与发展, 有利于乳腺癌患者的生存结局。本文就放射性皮炎的高风险患者识别、新型诊断技术、预防和治疗进展进行综述。

## 2. 识别发生放射性皮炎的高风险患者

患者自身因素决定皮肤对放疗的固有耐受性。年龄是 RD 易感性的重要影响因素, 老年患者(>60 岁)由于皮肤厚度变薄、胶原蛋白含量减少、修复能力下降, 因此, 面临较高 RD 风险[5]。研究发现, 身体质量指数(BMI)  $\geq 25$  kg/m<sup>2</sup> 是明确的高危因素, 肥胖患者(BMI  $\geq 30$  kg/m<sup>2</sup>)发生  $\geq 2$  级急性放射性皮炎的风险较正常体重患者升高 2.33 倍, 其机制与肥胖导致乳房组织厚度增加、皮肤受压摩擦加剧, 以及局部血供减少、氧化应激水平升高密切相关[5][6]。同时, 乳房体积本身(罩杯  $\geq$  C 杯或胸围  $\geq 40$  英寸)独立增加 RD 风险, 其与脂肪组织丰富导致的皮肤剂量分布不均密切相关, 且乳房下垂形成的皮肤皱褶易造

成剂量蓄积, 进一步加重皮肤损伤[7]。吸烟患者通过尼古丁抑制皮肤微循环、破坏胶原蛋白合成, 增加晚期皮肤纤维化和慢性疼痛风险[8] [9]; 糖尿病患者因高血糖抑制成纤维细胞活性、延缓皮肤修复, 使  $\geq 2$  级放射性皮炎风险提升 2.7 倍[5] [10]。皮肤色素类型(Skin of Color, SOC)是影响患者发生 RD 的重要因素, 研究显示 IV~VI 型患者急性皮炎发生率较低, 但迟发性色素沉着风险高( $OR = 3.658$ ), 这与黑色素细胞对放疗诱导的 DNA 损伤修复能力较弱、炎症后色素沉着通路激活相关[11] [12]; 此外, 患者基因型与放射性皮炎的发生相关联, 如 GSTA1 rs3957356-CT、MAT1A rs2282367-GG 基因型通过影响抗氧化酶活性、甲基化代谢, 增加严重放射性皮炎风险, PTTG1 rs2961952-GG 基因型通过调控细胞凋亡通路降低发病风险[13]。手术类型同样影响皮肤反应。临床数据表明, 乳房重建术后放疗, 皮瓣组织血供较原生皮肤差, 对放疗耐受性更低, 发生 RD 的风险高[14] [15]; 改良根治术较保乳手术对皮肤屏障的破坏更明显, 术后皮肤厚度减少, 增加了放疗损伤风险[15]。放疗同步系统治疗通过“协同损伤”也会放大 RD 风险, 如曲妥珠单抗(T-DM1)联合放疗时  $\geq 2$  级皮炎发生率达 62.9%, 双 HER2 阻断治疗(曲妥珠单抗 + 帕妥珠单抗)也需警惕协同效应[16] [17]。

### 3. 新型诊断技术: 从“临床可见”到“早期预警”

传统放射性皮炎诊断依赖美国放射治疗肿瘤组标准(RTOG)或常见不良事件评价标准(CTCAE)视觉分级, 存在主观性强、预警滞后(症状出现后才诊断)的局限。近年来, 多模态成像与量化检测技术的发展, 实现了皮炎的早期识别与评估, 为“主动预防”提供技术支撑。

#### 3.1. 多模态成像技术

光声成像与弹性成像技术通过检测皮肤氧饱和度、真皮厚度及弹性变化, 可在临床症状(如红斑)出现前 1 周识别早期放射性损伤。研究显示, 当放疗剂量达 20Gy 时, 光声成像已能检测到照射区域皮肤氧饱和度显著下降(从 65%降至 48%), 这与放疗诱导的皮肤微血管损伤、局部缺血相关; 弹性成像则发现真皮层硬度增加(弹性模量升高 35%), 反映胶原纤维早期变性, 这些变化的准确性优于传统 RTOG 分级[18] [19]。皮肤反射光谱法(SRS)通过监测红斑指数(EI)、黑色素指数(MI), 提前预警皮炎风险: 放疗 3 周后, EI 升高 2 倍以上的患者, 后续发生  $\geq 2$  级皮炎的风险增加 3.8 倍, 尤其适用于 SOC 患者, 可规避视觉评估偏倚[20]。反射共聚焦显微镜(RCM)则从细胞层面实现早期诊断, 放疗 2 周后即可观察到表皮细胞间隙增宽(增加 40%)、角质形成细胞凋亡率升高(从 2%升至 15%), 这些微观变化与后续皮炎严重程度高度相关( $r=0.76$ ), 可作为预测指标[21]。此外, 超声弹性成像能评估皮肤皮下组织的弹性模量变化, 放疗后 3 周即可出现显著差异, 为判断皮肤修复潜力提供依据[19]。

#### 3.2. 分子与血清标志物识别技术

分子与血清标志物通过反映皮肤炎症、修复状态, 展现出重要预测价值。皮肤微生物组动态变化可作为预警信号: 放疗期间皮肤细菌总负荷异常增高( $\geq 10^6$  CFU/cm<sup>2</sup>)早于临床症状出现 1 周, 基线时表皮葡萄球菌、痤疮丙酸杆菌等共生菌丰度  $< 5\%$  的患者, 发生严重放射性皮炎的风险显著升高( $OR = 4.2$ ) [22] [23]; 此外, 血清细胞因子 IL-4 ( $\geq 10$  pg/mL)、IL-17 ( $\geq 8$  pg/mL)、干扰素- $\gamma$  (IFN- $\gamma$ ,  $\geq 15$  pg/mL)的水平变化与皮炎严重程度呈正相关, 可纳入人工智能(AI)预测模型, 提升风险评估精准度[24]。

### 4. 预防放射性皮炎的策略

#### 4.1. 优化放疗技术与方案

患者治疗技术与方案的选择决定了皮肤毒性的发生风险与严重程度。在放疗技术方面, 调强放疗

(IMRT)通过逆向计划优化剂量分布,减少皮肤高剂量区体积,避免皮肤局部剂量叠加,减少发生 RD [25] [26];质子放疗需通过“皮肤优化”技术调整布拉格峰位置,将皮肤表面剂量控制在  $\leq 90\%$  处方剂量,避免升高皮炎风险[27] [28]。部分乳腺照射(PBI)适用于早期低风险乳腺癌患者(T1N0M0),通过仅照射肿瘤床及周围 1~2 cm 区域,避免全乳腺照射导致的广泛皮肤损伤,其 RD 发生率(9.9%)显著低于全乳腺照射(23.5%) [29]。剂量分割方案中,选用大分割(MHF, 2.65~3.3Gy/13~16 次)和超大分割(UHF, 5 次)  $\geq 2$  级急性放射性皮炎发生率显著低于常规分割(CF, 50~50.4Gy/5~6 周),这与大分割方案可减少皮肤细胞累积损伤、降低炎症反应相关[30] [31];但 UHF(如 26Gy/5 次)与 MHF 的直接对比证据仍不足,且 UHF 的长期美容效果需 10 年以上随访验证[32]。此外,放疗计划优化与剂量约束是降低 RD 风险的重要技术保障,治疗计划设计时应严格控制皮肤剂量,推荐皮肤最大剂量(Dmax)  $< 55$  Gy,皮肤 V30Gy  $< 50$  cm<sup>2</sup>,对于高风险患者,可进一步降低剂量约束(Dmax  $< 52$  Gy, V30Gy  $< 40$  cm<sup>2</sup>) [33]。

## 4.2. 保护皮肤屏障

适宜的皮肤环境与局部护理可以保护皮肤屏障、减少外在刺激。皮肤清洁方式与放射性皮炎改善效果相关,过度清洁(如使用肥皂、热水  $> 40$  °C)会破坏皮肤角质层,导致经表皮水分流失增加,使皮炎风险升高 2.1 倍,推荐采用 37°C 温水轻柔冲洗,避免摩擦[34] [35];衣物材质选择需以纯棉、透气为原则,减少皮肤摩擦刺激,尤其对大乳房或肥胖患者,可降低局部皮肤受压损伤,减少湿性脱屑发生率;此外,放疗期间避免使用含酒精、香料的护肤品,可减少皮肤刺激,降低瘙痒、红斑发生率[34]。

## 4.3. 预防性药物干预

屏障膜类制剂和保湿剂的使用可以起到防护效果。屏障膜类制剂通过在皮肤表面形成保护膜,减少放疗射线对皮肤的直接损伤,同时减少摩擦与水分流失。研究证实, Mepitel Film (硅酮材质)可将  $\geq 2$  级放射性皮炎发生率从 45.6%降至 15.5%,湿性脱屑发生率从 19.2%降至 8.0% [36] [37];Hydrofilm 等聚氨酯膜同样能改善患者报告结局(疼痛评分降低 2.3 分、瘙痒评分降低 2.1 分),且长期使用未发现增加晚期毒性(如色素异常、纤维化),适合保乳术与乳房重建术后患者[38]。此类屏障膜建议从放疗第 1 天开始全程使用,每 1~2 周更换 1 次,避免频繁撕扯损伤皮肤。保湿修复制剂需贯穿放疗全程,从放疗前 14 天开始使用,持续至放疗后 2 周,以维持皮肤屏障功能。研究显示,保湿剂(如 0.2%透明质酸乳膏、Sanyrene®、多活性润肤剂、角蛋白基外用乳膏等)通过补充皮肤脂质,增强屏障完整性,减少水分流失,尤其适用于干燥皮肤患者(基线经表皮水分流失  $\geq 20$  g/(m<sup>2</sup>·h)),可使 RD 发生率降低[20] [39]~[41];维生素 E 纳米制剂则通过抗氧化作用减轻放疗诱导的氧化应激损伤,降低炎症反应,适合合并吸烟、糖尿病的高风险患者[42]。传统草药制剂如 henna 软膏、silymarin 凝胶也显示出一定防护效果( $\geq 2$  级皮炎发生率降低 35%),但需注意过敏风险,使用前建议进行斑贴试验[43] [44]。

# 5. 治疗放射性皮炎的药物

## 5.1. 外用糖皮质激素

外用糖皮质激素通过抑制 NF- $\kappa$ B 炎症通路,减少红斑、瘙痒等症状,适用于  $\geq 1$  级皮炎或高风险人群。莫米松(0.1%)、倍他米松(0.1%)是常用中强效激素,meta 分析显示其可降低  $\geq 2$  级皮炎风险[45] [46];但使用需遵循“分级原则”:轻度皮炎(1 级,仅红斑)可选择弱效激素(如氢化可的松 1%),每日 2 次;中度皮炎(2 级,干燥脱屑)推荐中强效激素(如莫米松),每日 1 次。另外,应避免长期(超过 4 周)使用外用糖皮质激素,以防皮肤萎缩、毛细血管扩张[45] [47]。对于乳房下皱襞等易摩擦区域,可联合屏障膜使用,减少激素对皮肤的直接刺激。



## 5.2. 新型药物

表没食子儿茶素没食子酸酯(EGCG)是绿茶提取物的主要活性成分, 可通过抗氧化、抑制 NF- $\kappa$ B 通路减轻炎症。随机对照试验显示其可将  $\geq 2$  级皮炎发生率从 72.2% 降至 50.5%, 且安全性良好(不良反应发生率  $< 5\%$ ), 适合合并氧化应激升高的患者(如吸烟、老年) [43] [48]。褪黑素乳膏通过调节氧化应激与睡眠质量, 降低放疗全程皮肤反应评分(从 2.8 分降至 1.5 分), 尤其对合并睡眠障碍的患者, 可同时改善生活质量(PSQI 评分降低 3.2 分) [49] [50]。依克多因(ectoin)则通过稳定皮肤屏障(角质层含水量提升 25%)、抑制炎症因子(IL-6、TNF- $\alpha$  降低 30%)释放, 减轻患者疼痛和瘙痒( $P < 0.001$ ), 适用于敏感皮肤患者 [51]。

## 5.3. 细菌去定植药物

皮肤细菌定植(尤其是金黄色葡萄球菌)是皮炎加重的重要诱因, 可使湿性脱屑发生率增加 2.8 倍, 细菌去定植可有效降低感染风险。鼻腔莫匹罗星软膏(每日 2 次)联合氯己定全身清洁(每日 1 次)的方案, 可完全预防湿性脱屑型  $\geq 2$  级皮炎, 其机制与减少金黄色葡萄球菌定植(从  $10^5$  CFU/cm<sup>2</sup> 降至  $10^3$  CFU/cm<sup>2</sup>)、降低继发感染相关 [52]; 但需注意, 过度使用抗菌药物可能导致耐药, 需严格掌握适应证(如糖尿病、反复皮肤感染史患者) [52] [53]。

## 6. 结论

本文综述了乳腺癌放疗相关放射性皮炎的防治策略。基于现有证据, 我们认为, RD 的临床管理应从被动的毒性处理, 转向“精准风险评估-动态早期诊断-个体化干预”的前瞻性、全周期管理体系。在放疗前, 应建立风险分层模型, 综合评估患者年龄、BMI、乳房体积、合并症(如糖尿病)、患者基因型等多维度因素, 识别出高危患者, 并实施针对性预处理(如优化放疗技术与方案、保护皮肤屏障、预防性使用药物干预)。在放疗过程中, 应积极应用客观评估与早期诊断技术(如多模态成像技术、分子与血清标志物识别技术), 实现 RD 的客观量化与亚临床期识别, 为早期干预提供依据。对于已发生的 RD, 应实施个体化治疗: 使用糖皮质激素药物、新型药物、去细菌定植药物, 以加速愈合, 最大限度维持患者生活质量。然而, 该领域的高级别证据仍显匮乏, 未来还需要依托大样本前瞻性临床试验来提供确凿结论, 以头对头比较不同预防方案(如各类新型敷料、药膏)及治疗药物的疗效; 深入探索 RD 的分子与免疫机制, 鉴定可用于预测风险的生物标志物(如特定细胞因子、基因多态性、皮肤微生物组特征); 并利用人工智能技术开发基于临床与影像学数据的风险预测模型, 以推动 RD 管理迈向真正的精准医学。总之, 乳腺癌患者的放疗成功, 不仅在于肿瘤的根治, 也在于治疗相关毒性的最小化。通过构建并实践上述整合管理路径, 我们有望在确保疗效的同时, 显著减轻患者痛苦, 改善其治疗体验与远期生活质量。

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