DOI: 10.53469/jcmp.2025.07(04).28

De-Escalation of Adjuvant Radiotherapy in Early Breast Cancer: Progress and Perspectives Following Breast-Conserving Surgery

Yu Zhang, Shengchun Liu*

Department of Breast and Thyroid Surgery, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China
**Correspondence Author*

Abstract: ***Clinical evidence has shown that breast-conserving surgery combined with postoperative radiotherapy has become the standard treatment for patients with early-stage breast cancer, significantly reducing the rate of local-regional recurrence. However, conventional radiotherapy protocols require daily treatments over several consecutive weeks, which not only increase the economic burden on patients but also are associated with significant radiotherapy-related adverse effects. Acutely, these adverse effects mainly manifest as skin reactions in the treated area, breast tissue edema, and cancer-related fatigue. In the long term, there may be subsequent tissue damage, including radiation dermatitis, telangiectasia, breast fibrosis, and chronic pain. Notably, existing studies have suggested that some low-risk subgroups of patients (e.g., the elderly, those with favorable tumor biological characteristics, negative surgical margins, and those who have received standardized systemic therapy) have limited survival benefits from adjuvant radiotherapy. Therefore, the safety and feasibility of postoperative radiotherapy exemption for specific low-risk populations urgently need further validation.***

Keywords: Early-stage breast cancer, Breast-conserving surgery, De-escalation therapy, Omission of radiotherapy.

1. Introduction

Data from the 2022 global cancer burden showed that there were approximately 2.3 million new cases of breast cancer, making it the most common cancer among women and a leading cause of cancer-related mortality [1]. Owing to the widespread adoption and innovation of imaging screening technologies, as well as the promotion of multidisciplinary treatment models, the early diagnosis rate and the level of standardized treatment for breast cancer patients have been significantly improved [2]. The current clinical treatment system has established a comprehensive therapeutic strategy centered on radical surgery, combined with radiotherapy, neoadjuvant/adjuvant chemotherapy, endocrine therapy, and molecularly targeted therapy. Evidence-based medical data demonstrate that individualized treatment plans based on tumor molecular subtypes effectively improve patients' 5-year survival rates and quality-of-life indicators. Building on these advancements, the clinical application of genomic testing technologies and the deepening of precision medicine concepts are driving the gradual transition of breast cancer treatment from traditional empirical approaches to individualized, precision therapies guided by molecular subtyping.

Currently, radiotherapy (RT) and endocrine therapy (ET) are the standard treatment modalities following breast-conserving surgery for hormone receptor–positive (HR+) breast cancer. However, many elderly patients face greater risks of treatment-related toxicity and non-cancer-related mortality and are less likely to benefit from these standard treatments [3, 4]. The question of which patients can be adequately treated with breast-conserving surgery without undergoing radiotherapy remains a matter of debate [5-10]. Relevant clinical studies have demonstrated that postoperative radiotherapy can effectively control local recurrence, but it does not impact overall survival [4, 6, 11]. Thus, it is acceptable that some low-risk patients may achieve adequate treatment and maintain a low recurrence rate through surgery alone, without the need for additional therapy. However, the definition of such low-risk populations varies in current clinical practice. Therefore, this review focuses on studies related to the omission of radiotherapy after breast-conserving surgery, aiming to provide a basis for clinical decision-making.

2. Method

2.1 The Role of Radiotherapy in Early-Stage Breast Cancer

Multiple clinical studies have been committed to identifying subgroups of early-stage breast cancer patients who do not derive significant clinical benefits from postoperative radiotherapy (Radiotherapy, RT). Early exploratory studies failed to establish a patient group with consistently low-risk features for recurrence. The EBCTCG meta-analysis further confirmed the clinical value of whole-breast irradiation (Whole-Breast Irradiation, WBI) after breast-conserving surgery (Breast-Conserving Surgery, BCS): the analysis showed that, overall, radiotherapy reduced the 10-year risk of any (i.e., local or distant) first recurrence from 35.0% to 19.3% (absolute reduction of 15.7%, 95% CI 13.7 - 17.7, $p< 0.00001$), and the 15-year risk of breast cancer death from 25.2% to 21.4% (absolute reduction of 3.8%, 1.6 - 6.0, $p= 0.005$); radiotherapy to the conserved breast after breast-conserving surgery halved the rate of disease recurrence and reduced the rate of breast cancer death by about one-sixth. These proportional benefits varied little between different groups of women. The absolute benefit of radiotherapy varied widely according to the clinical and pathological features of patients and could be predicted when treatment decisions needed to be made [12]. The NSABP B-21 trial enrolled 1,009 women with tumors less than 2 cm in size who had undergone breast-conserving surgery and had negative lymph nodes. The study explored various treatment modalities, including radiotherapy plus tamoxifen, tamoxifen alone, or radiotherapy alone after breast-conserving surgery

[13]. Results showed that at 8 years, women treated with tamoxifen alone had the highest rate of breast cancer recurrence (16.5%), whereas those treated with radiotherapy alone (9.3%) or in combination (2.8%) had lower recurrence rates. However, no significant differences were observed in overall survival and distant metastasis. Long-term follow-up data from two landmark randomized controlled trials, CALGB 9343 and PRIME II, demonstrated that in low-risk patient populations, omission of radiotherapy after breast-conserving surgery (BCS) led to a significant increase in local recurrence rates, but overall survival (OS) did not significantly differ between the radiotherapy and observation groups. In the CALGB 9343 trial, the study population comprised 636 women aged ≥70 years with T1N0M0, estrogen receptor (ER)-positive invasive breast cancer, who were randomly assigned in a 1:1 ratio to receive tamoxifen alone or tamoxifen plus radiotherapy. At 10 years, the local recurrence-free rates were 90% (95% CI, 85% - 93%) and 98% (95% CI, 96% - 99%), respectively, while the survival rates were 66% (95% CI, 61% - 71%) and 67% (95% CI, 62% - 72%), respectively [10]. For the experimental group of patients, radiotherapy did not show significant benefits in terms of survival, time to distant metastasis, or overall survival, although it slightly reduced the local recurrence rate. In the PRIME II trial, 1,326 women aged ≥65 years with hormone receptor-positive, axillary node-negative, T1-T2 tumors (<3 cm in size) and clear surgical margins who had undergone breast-conserving surgery and were receiving adjuvant endocrine therapy were randomly assigned in a 1:1 ratio to receive radiotherapy or no radiotherapy. After a median follow-up of 5 years, the 5-year ipsilateral breast tumor recurrence rates were 1.3% (95% CI 0.2-2.3; n=5) in the radiotherapy group and 4.1% (95% CI 2.4-5.7; n=26) in the no-radiotherapy group (p=0.0002). The 10-year overall survival rates were nearly identical between the two groups, with the no-radiotherapy group at 80.8% (95% CI, 77.2-84.3) and the radiotherapy group at 80.7% (95% CI, 76.9-84.3) [6]. Omission of radiotherapy is associated with an increased incidence of local recurrence but has no detrimental effect on overall survival. The results of two randomized controlled trials, PRIME II and CALGB 9343, provide favorable data support for the omission of radiotherapy after breast-conserving surgery. With the advancement of surgical practices and the development of various medications, the decreasing recurrence rates and increasing survival rates of breast cancer patients have enhanced the feasibility of omitting radiotherapy. However, there is still no precise definition for low-risk populations, and clinically, there is a lack of effective tools for predicting low-risk patients.

2.2 The Population Eligible for Omission of Radiotherapy

The National Comprehensive Cancer Network guidelines (NCCN) recommend that patients aged 65 years or older, or 70 years or older, with stage I receptor-positive breast cancer may omit radiotherapy after breast-conserving surgery, provided that they receive full-course endocrine therapy [14]. Similarly, the Guidelines for Diagnosis and Treatment of Breast Cancer by the Chinese Anti-Cancer Association and the Oncology Branch of the Chinese Medical Association also propose that patients meeting the enrollment criteria of the CALGB 43 study (≥70 years old, pT1N0, ER+, negative margins) or the PRIME II study (≥65 years old, ≤3 cm, pN0, HR+, negative margins) may be exempted from radiotherapy, provided that they receive standardized endocrine therapy. However, the low-risk population still cannot be precisely defined. Currently, an increasing number of studies are focusing on this issue, with the hope of finding reliable screening tools to safely exempt patients from radiotherapy.

2.3 Tools for Predicting Low-risk Patients

The use of biomarkers and genetics to guide adjuvant systemic therapy decisions has become a focus. Relevant trials have determined that the Oncotype DX Recurrence Score (RS) can reliably predict the risk of distant recurrence in patients with node-negative, hormone-sensitive breast cancer receiving endocrine therapy, as well as the benefit of chemotherapy [15]. The recently reported LUMINA study is a single-arm prospective study that evaluated a patient population aged ≥55 years with histological grade 1 to 2 tumors, tumor size ≤2 cm, surgical margins ≥1 mm, node-negative status, and a low proliferation index (Ki67 ≤13.25%) [16]. The LUMINA study reported that among the 727 eligible patients, the 5-year local-regional recurrence risk was extremely low at 2.3%. Although Ki67 may be sufficient to identify low-risk tumors, some studies have shown that genomic assays, such as the Oncotype DX Recurrence Score (RS), can also be used to predict local-regional recurrence and assist clinical decision-making [17-19]. A single-arm study named IDEA enrolled 200 postmenopausal breast cancer patients aged 50-69 years. The inclusion criteria were as follows: pathological stage T1N0M0, tumor margin ≥2 mm after breast-conserving surgery, ER+, PR+, HER2-, single-focal lesion, and an Oncotype DX 21-gene recurrence score ≤18. These patients received at least 5 years of endocrine therapy [20]. The results showed that the 5-year overall survival rate and breast cancer-specific survival rate were both 100%. The 5-year recurrence-free rate was 99% (95% CI, 96% - 100%). The 5-year recurrence probability of the IDEA study is consistent with or lower than the 4% risk estimated a priori based on the 5-year outcomes of PRIME II and CALGB 9343, supporting the necessity and appropriateness of ongoing trials assessing the omission of radiotherapy after breast-conserving surgery. The findings also suggest whether the option of avoiding immediate radiotherapy after breast-conserving surgery could be extended to a broader group of women, rather than those currently recommended by guidelines. Following the IDEA study, several additional studies investigating the omission of radiotherapy were initiated; the DEBRA trial (NRG BR007 NCT04852887) uses similar inclusion and exclusion criteria as the IDEA study. Patients are randomized to receive endocrine therapy with or without radiotherapy. Other studies include the PRIMETIME cohort study, which relies on immunohistochemistry to determine biological risk, and the PRECISION and EXPERT trials, which use the PAM50 assay [21]. These results will further inform clinical decision-making. A prospective study combined breast MRI and postoperative pathology to determine whether patients can be exempted from radiotherapy [22]. These findings also offer new insights. Moreover, studies have shown that precision screening strategies based on molecular characteristics can optimize radiotherapy decisions after breast-conserving surgery. Yi Cui and colleagues proposed, through the integration of genomic features, that specific gene

expression patterns can assist in identifying two potential beneficiary groups: one is low-risk patients eligible for treatment de-escalation, and the other is groups with insufficient sensitivity to standard radiotherapy, who may require the addition of radiosensitizers or immunotherapy to improve local control efficiency [23]. The team of Corey Speers further developed and validated a biologically relevant human breast cancer radiation sensitivity signature (RSS). This signature quantitatively assesses the intrinsic radiosensitivity of tumors by integrating postradiation clonogenic survival data with gene expression data across breast cancer cell lines. The RSS can predict the risk of local recurrence and provides a molecular basis for designing individualized radiotherapy regimens [24, 25]. In addition, the single-sample predictor (SSP) constructed by M. Sjöström and colleagues has been proven to independently predict the risk of ipsilateral breast tumor recurrence. Its predictive performance is closely related to the biological heterogeneity of breast cancer molecular subtypes. This suggests that the model may be used for risk stratification to identify radiotherapy-resistant populations, thereby avoiding overtreatment [26, 27]. The combined use of the previously mentioned molecular prediction tools is expected to enable a shift from "empiric radiotherapy" to a "biomarker-based precision exemption" model in clinical practice. This method can further pinpoint individuals who are resistant to radiotherapy, thus preventing overtreatment and promoting individualized therapy in clinical decision-making.

2.4 The Adverse Effects of Radiotherapy and specific Manifestations

Multidimensional analyses of radiotherapy-related toxicities and their risk factors have shown that adjuvant radiotherapy for breast cancer can cause both acute and late health impairments. Short-term follow-up data indicate that the incidence of acute toxicities (such as radiation dermatitis, fatigue, and local edema) can reach 30% to 50%, while late complications (including persistent breast pain and subcutaneous tissue fibrosis) significantly affect patients' quality of life. Notably, the carcinogenic potential of radiotherapy has been confirmed in multiple cohort studies, with the long-term risk of secondary malignancies being positively correlated with cumulative radiation dose and age, especially in younger patient populations with higher radiation sensitivity [28-31]. In addition, specific risk factors may exacerbate the effects of radiotherapy toxicity. Shaitelman et al. confirmed through a prospective cohort study that a history of smoking can increase the risk of late radiotherapy toxicity (≥grade 2) by 2.3 times (95% CI: 1.4 - 3.8), suggesting that nicotine exposure may exacerbate tissue damage through pro-inflammatory mechanisms [32]. Regarding cardiovascular toxicity, the Darby team, based on a dose–effect model, revealed that for every 1-Gy increase in the mean dose to the heart, the risk of developing ischemic heart disease rises by 7.4% (95% CI: 2.9 - 14.5). This risk emerges within 5 years after radiotherapy and persists for over 20 years. Of particular concern is that patients with pre-existing cardiovascular conditions such as hypertension or diabetes mellitus have a 3- to 5-fold increase in the absolute risk of radiotherapy-related cardiovascular events compared with the general population [33].

The current standard treatment in the clinic is the long-course whole-breast irradiation (WBI) regimen lasting 5-7 weeks. However, clinical practice has been shifting towards shorter radiotherapy regimens, including hypofractionated WBI (completed in 1-3 weeks) or accelerated partial breast irradiation (APBI) (completed in 1-5 days). Advances in radiotherapy techniques have significantly reduced the treatment-related burden [34-37]. Many prospective trials and guidelines have now established that partial breast irradiation (PBI) can be an alternative to whole-breast irradiation (WBI) in a selected group of low-risk patients. Multiple clinical studies have provided evidence-based support for optimizing radiotherapy strategies. The phase III trial of accelerated partial breast irradiation (APBI) conducted by the team in Florence, Italy, demonstrated that a 5-fraction regimen (30 Gy/5f) delivered using external beam intensity-modulated radiotherapy had no statistically significant difference in local control rate compared with conventional whole-breast irradiation (WBI) at 10 years of follow-up, and significantly reduced the incidence of acute radiation dermatitis and improved long-term cosmetic scores [38]. The FAST-Forward trial further confirmed that the ultra-hypofractionated whole-breast irradiation regimen of 26 Gy in 5 fractions is non-inferior to the standard regimen of 40 Gy in 15 fractions in terms of 5-year local recurrence rate, providing evidence for the shortened treatment course [39]. However, the conclusions of the aforementioned studies should be interpreted with caution regarding their scope of applicability. First, the inclusion criteria required pathologically negative lymph nodes and safe surgical margins, thus not applicable to subgroups that do not meet surgical quality requirements. Second, the trial populations had strictly selected characteristics (e.g., adherence to endocrine therapy >90%), so the risk-benefit ratio needs to be re-evaluated for patients with poor treatment adherence. It is worth noting that although the new fractionation patterns can reduce the treatment burden, some patients, due to concerns about late toxicities (such as second primary cancers and cardiovascular events), prefer to completely exempt radiotherapy, which highlights the clinical necessity of accurately identifying radiotherapy-sensitive populations [40]. Some studies have demonstrated the feasibility of preoperative radiotherapy and confirmed its efficacy in nearly all analyzed studies. However, the clinical evidence for preoperative radiotherapy in breast cancer remains limited, as it primarily derives from retrospective case series [41]. Patient preferences are also crucial for the implementation of radiotherapy exemption. A retrospective study found that older patients, those with low income, divorced individuals, white patients, those with advanced disease, and those who did not receive chemotherapy were more likely to refuse radiotherapy. [42] This further underscores the urgency of expanding the criteria for low-risk populations.

3. Conclusion

For some patients, omission of radiotherapy does not affect overall survival, and a low rate of local recurrence is acceptable, thus making them potential candidates for radiotherapy exemption. Current clinical guidelines and consensus suggest that older age, hormone receptor positivity,

and small tumor size are characteristics of low-risk populations who may be eligible for radiotherapy exemption. However, precision medicine requires more accurate and effective predictive tools. The results of the DEBRA trial (NRG BR007), IDEA trial, as well as the PRECISION and EXPERT trials, are expected to provide valuable clinical evidence. Advances in radiotherapy techniques have also offered new ways to reduce treatment-related toxicities and de-escalate therapy. In clinical practice, the decision to exempt radiotherapy should also take into account adherence to endocrine therapy, drug side effects, comorbidities and concomitant diseases, life expectancy, and individual treatment preferences, rather than simply being based on clinical pathological factors and molecular subtypes.

References

[1] Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries [J]. CA Cancer J Clin, 2024, 74(3): 229-63.

[2] Dunn J A, Donnelly P, Elbeltagi N, et al. Annual versus less frequent mammographic surveillance in people with breast cancer aged 50 years and older in the UK (Mammo-50): a multicentre, randomised, phase 3, non-inferiority trial [J]. Lancet, 2025, 405(10476): 396-407.

[3] Savard M F, Clemons M, Hutton B, et al. De-escalating adjuvant therapies in older patients with lower risk estrogen receptor-positive breast cancer treated with breast-conserving surgery: A systematic review and meta-analysis [J]. Cancer Treat Rev, 2021, 99: 102254.

[4] Tringale K R, Berger E R, Sevilimedu V, et al. Breast conservation among older patients with early-stage breast cancer: Locoregional recurrence following adjuvant radiation or hormonal therapy [J]. Cancer, 2021, 127(11): 1749-57.

[5] Kunkler I H, Williams L J, Jack W J, et al. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial [J]. Lancet Oncol, 2015, 16(3): 266-73.

[6] Kunkler I H, Williams L J, Jack W J L, et al. Breast-Conserving Surgery with or without Irradiation in Early Breast Cancer [J]. N Engl J Med, 2023, 388(7): 585-94.

[7] Chowdhary M, Chhabra A M, Jhawar S R. Is It Time to Reevaluate Radiotherapy Omission in Older Patients with Favorable Early-Stage Breast Cancer? [J]. JAMA Oncol, 2021, 7(7): 965-6.

[8] Rutter C E, Lester-Coll N H, Mancini B R, et al. The evolving role of adjuvant radiotherapy for elderly women with early-stage breast cancer [J]. Cancer, 2015, 121(14): 2331-40.

[9] Hughes K S, Schnaper L A. Can older women with early breast cancer avoid radiation? [J]. Lancet Oncol, 2015, 16(3): 235-7.

[10] Hughes K S, Schnaper L A, Bellon J R, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343 [J]. J Clin Oncol, 2013, 31(19): 2382-7.

[11] Williams L J, Kunkler I H, Taylor K J, et al. Postoperative radiotherapy in women with early operable breast cancer (Scottish Breast Conservation Trial): 30-year update of a randomised, controlled, phase 3 trial [J]. Lancet Oncol, 2024, 25(9): 1213-21.

[12] Darby S, Mcgale P, Correa C, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials [J]. Lancet, 2011, 378(9804): 1707-16.

[13] Fisher B, Bryant J, Dignam J J, et al. Tamoxifen, radiation therapy, or both for prevention of ipsilateral breast tumor recurrence after lumpectomy in women with invasive breast cancers of one centimeter or less [J]. J Clin Oncol, 2002, 20(20): 4141-9.

[14] Gradishar W J, Anderson B O, Balassanian R, et al. NCCN Guidelines Insights: Breast Cancer, Version 1.2017 [J]. J Natl Compr Canc Netw, 2017, 15(4): 433-51.

[15] Sparano J A, Gray R J, Makower D F, et al. Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer [J]. N Engl J Med, 2018, 379(2): 111-21.

[16] Whelan T J, Smith S, Parpia S, et al. Omitting Radiotherapy after Breast-Conserving Surgery in Luminal A Breast Cancer [J]. N Engl J Med, 2023, 389(7): 612-9.

[17] Mamounas E P, Tang G, Fisher B, et al. Association between the 21-gene recurrence score assay and risk of locoregional recurrence in node-negative, estrogen receptor-positive breast cancer: results from NSABP B-14 and NSABP B-20 [J]. J Clin Oncol, 2010, 28(10): 1677-83.

[18] Solin L J, Gray R, Goldstein L J, et al. Prognostic value of biologic subtype and the 21-gene recurrence score relative to local recurrence after breast conservation treatment with radiation for early stage breast carcinoma: results from the Eastern Cooperative Oncology Group E2197 study [J]. Breast Cancer Res Treat, 2012, 134(2): 683-92.

[19] Sparano J A, Gray R J, Makower D F, et al. Prospective Validation of a 21-Gene Expression Assay in Breast Cancer [J]. N Engl J Med, 2015, 373(21): 2005-14.

[20] Jagsi R, Griffith K A, Harris E E, et al. Omission of Radiotherapy After Breast-Conserving Surgery for Women with Breast Cancer with Low Clinical and Genomic Risk: 5-Year Outcomes of IDEA [J]. J Clin Oncol, 2024, 42(4): 390-8.

[21] Upadhyay R, Bazan J G. Advances in Radiotherapy for Breast Cancer [J]. Surg Oncol Clin N Am, 2023, 32(3): 515-36.

[22] Mann G B, Skandarajah A R, Zdenkowski N, et al. Postoperative radiotherapy omission in selected patients with early breast cancer following preoperative breast MRI (PROSPECT): primary results of a prospective two-arm study [J]. Lancet, 2024, 403(10423): 261-70.

[23] Cui Y, Li B, Pollom E L, et al. Integrating Radiosensitivity and Immune Gene Signatures for Predicting Benefit of Radiotherapy in Breast Cancer [J]. Clin Cancer Res, 2018, 24(19): 4754-62.

[24] Speers C, Zhao S, Liu M, et al. Development and Validation of a Novel Radiosensitivity Signature in

Human Breast Cancer [J]. Clin Cancer Res, 2015, 21(16): 3667-77.
[25] Speers C, Chang S L, Pesch A, et al. A Signature That May Be Predictive of Early Versus Late Recurrence After Radiation Treatment for Breast Cancer That May Inform the Biology of Early, Aggressive Recurrences [J]. Int J Radiat Oncol Biol Phys, 2020, 108(3): 686-96.
[26] Sjöström M, Staaf J, Edén P, et al. Identification and validation of single-sample breast cancer radiosensitivity gene expression predictors [J]. Breast Cancer Res, 2018, 20(1): 64.
[27] Sjöström M, Fyles A, Liu F F, et al. Development and Validation of a Genomic Profile for the Omission of Local Adjuvant Radiation in Breast Cancer [J]. J Clin Oncol, 2023, 41(8): 1533-40.
[28] Taylor C, Correa C, Duane F K, et al. Estimating the Risks of Breast Cancer Radiotherapy: Evidence from Modern Radiation Doses to the Lungs and Heart and From Previous Randomized Trials [J]. J Clin Oncol, 2017, 35(15): 1641-9.
[29] Whelan T J, Julian J A, Berrang T S, et al. External beam accelerated partial breast irradiation versus whole breast irradiation after breast conserving surgery in women with ductal carcinoma in situ and node-negative breast cancer (RAPID): a randomised controlled trial [J]. Lancet, 2019, 394(10215): 2165-72.
[30] Waljee J F, Hu E S, Ubel P A, et al. Effect of esthetic outcome after breast-conserving surgery on psychosocial functioning and quality of life [J]. J Clin Oncol, 2008, 26(20): 3331-7.
[31] Howard K, Norris S, Salisbury A, et al. Women's Preferences for Hypofractionated Radiation Therapy for Treatment of Early-Stage Breast Cancer: A Discrete Choice Experiment [J]. Int J Radiat Oncol Biol Phys, 2024, 119(1): 172-84.
[32] Shaitelman S F, Howell R M, Smith B D. Effects of Smoking on Late Toxicity from Breast Radiation [J]. J Clin Oncol, 2017, 35(15): 1633-5.
[33] Darby S C, Ewertz M, Mcgale P, et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer [J]. N Engl J Med, 2013, 368(11): 987-98.
[34] Haussmann J, Corradini S, Nestle-Kraemling C, et al. Recent advances in radiotherapy of breast cancer [J]. Radiat Oncol, 2020, 15(1): 71.
[35] Shah C, Bauer-Nilsen K, Mcnulty R H, et al. Novel radiation therapy approaches for breast cancer treatment [J]. Semin Oncol, 2020, 47(4): 209-16.
[36] Shah C, Al-Hilli Z, Vicini F. Advances in Breast Cancer Radiotherapy: Implications for Current and Future Practice [J]. JCO Oncol Pract, 2021, 17(12): 697-706.
[37] Chandra R A, Keane F K, Voncken F E M, et al. Contemporary radiotherapy: present and future [J]. Lancet, 2021, 398(10295): 171-84.
[38] Meattini I, Marrazzo L, Saieva C, et al. Accelerated Partial-Breast Irradiation Compared with Whole-Breast Irradiation for Early Breast Cancer: Long-Term Results of the Randomized Phase III APBI-IMRT-Florence Trial [J]. J Clin Oncol, 2020, 38(35): 4175-83.
[39] Murray Brunt A, Haviland J S, Wheatley D A, et al. Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial [J]. Lancet, 2020, 395(10237): 1613-26.
[40] Rodin D, Sutradhar R, Jerzak K J, et al. Impact of non-adherence to endocrine therapy on recurrence risk in older women with stage I breast cancer after breast-conserving surgery [J]. Breast Cancer Res Treat, 2023, 201(1): 77-87.
[41] Corradini S, Krug D, Meattini I, et al. Preoperative radiotherapy: A paradigm shift in the treatment of breast cancer? A review of literature [J]. Crit Rev Oncol Hematol, 2019, 141: 102-11.
[42] Liu J, Zhu Z, Hua Z, et al. Radiotherapy refusal in breast cancer with breast-conserving surgery [J]. Radiat Oncol, 2023, 18(1): 130.