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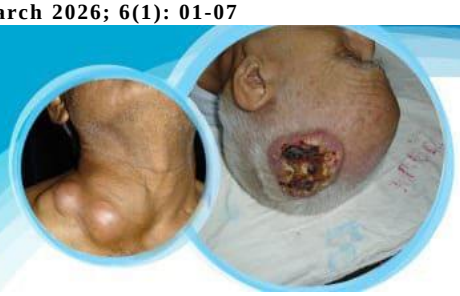

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Feasibility and early toxicity in hypofractionated adjuvant breast radiotherapy with simultaneous integrated boost: A prospective study

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Abstract
Background: Breast-conserving surgery (BCS) followed by whole breast irradiation (WBI) is the standard of care for early-stage breast carcinoma. Hypofractionated radiotherapy with simultaneous integrated boost (SIB) offers potential advantages in treatment duration and efficacy. This study evaluates the feasibility and early toxicity profile of hypofractionated adjuvant breast radiotherapy with SIB.
Methods: A prospective study was conducted on 30 patients with invasive breast cancer post-BCS between 2022-2023. Patients received 40.05 Gy in 15 fractions to the whole breast with a concomitant boost of 48.0 Gy in 15 fractions to the lumpectomy cavity over 3 weeks. Treatment was delivered using volumetric modulated arc therapy (VMAT). Dosimetric parameters and acute toxicity profiles were assessed.
Results: The treatment regimen achieved satisfactory dosimetric parameters with mean ipsilateral lung dose of 9.84±1.49 Gy, V20 of 14.9±3.67%, and mean heart dose of 3.45±1.0 Gy. Acute skin toxicity was acceptable, with 36.67% of patients experiencing no change from baseline, 53.33% experiencing Grade 1 toxicity, and 10% experiencing Grade 2 toxicity. No Grade 3 or 4 toxicities were observed. No cardiac or pulmonary toxicities were noted during the follow-up period.
Conclusion: Hypofractionated whole breast irradiation with simultaneous integrated boost delivering 40.05 Gy/48.0 Gy in 15 fractions is feasible with acceptable dosimetry and favorable early toxicity profile. This regimen reduces overall treatment time while maintaining safety standards.

Keywords: Breast cancer, hypofractionation, simultaneous integrated boost, radiotherapy, toxicity, VMAZ

1. Introduction

1.1 Background

Breast cancer remains one of the most prevalent malignancies affecting women worldwide. Breast-conserving surgery (BCS) combined with adjuvant whole breast irradiation (WBI) has become the established standard of care for the majority of patients with early-stage breast carcinoma, offering equivalent survival outcomes to mastectomy while preserving cosmetic appearance and quality of life [1, 2].

Conventional radiotherapy following BCS typically employs two tangential fields to deliver doses of 45-50 Gy at 1.8-2.0 Gy per fraction to the whole breast. Subsequently, a boost irradiation using electron or photon beams is administered to the tumor bed to achieve a total dose of 60-66 Gy [3]. While this approach has demonstrated excellent local control rates, the extended treatment duration of 6-7 weeks poses logistical challenges for patients and healthcare systems, potentially affecting treatment compliance and resource utilization.

1.2 Rationale for Hypofractionation

The radiobiological foundation for hypofractionated breast radiotherapy stems from the estimated alpha/beta (α/β) ratio of breast cancer tissue, which is approximately 4 Gy [4]. This relatively low α/β ratio, comparable to that of late-responding normal tissues, suggests that hypofractionated regimens delivering larger doses per fraction over a shorter period may be more effective than conventional fractionation schedules.

The biological rationale is further supported by the principle that shorter overall treatment times reduce the opportunity for accelerated repopulation of tumor cells, potentially improving local control [5].

1.3 Clinical Evidence for Hypofractionation

Multiple landmark randomized controlled trials have established the non-inferiority of hypofractionated whole breast radiotherapy compared to conventional fractionation:

START Trials (A and B): The UK Standardisation of Breast Radiotherapy (START) trials demonstrated that hypofractionated schedules (39-40 Gy in 13-15 fractions over 3-4 weeks) achieved similar rates of locoregional relapse compared to conventional 50 Gy in 25 fractions [6, 7]. Long-term follow-up data exceeding 10 years confirmed equivalent breast cosmesis and toxicity profiles between treatment arms.

Canadian Trial (Whelan *et al.*): This study compared 42.5 Gy in 16 fractions over 22 days versus 50 Gy in 25 fractions, demonstrating comparable local recurrence rates and cosmetic outcomes [8].

RMH/GOC Trial: The Royal Marsden Hospital/Gloucestershire Oncology Centre trial further validated the safety and efficacy of hypofractionated regimens [9].

These trials collectively established that 13-16 fraction regimens delivered over 3-4 weeks are as safe and effective as 50 Gy in 25 fractions, leading to widespread adoption of hypofractionated schedules as standard practice.

1.4 Simultaneous Integrated Boost Concept

While hypofractionation reduces treatment duration, the addition of a sequential boost to the tumor bed extends the overall treatment time by an additional 1-2 weeks. The concept of simultaneous integrated boost (SIB) addresses this limitation by delivering differential doses to the whole breast and tumor bed concurrently within the same treatment session [10].

Based on published literature, acceptable boost doses range from 10-16 Gy in 2.0 Gy fractions or 10 Gy in 2.5 Gy fractions [11]. A concurrent boost delivering 48.0 Gy in 15 fractions at 3.2 Gy per fraction to the tumor bed, combined with 40.05 Gy in 15 fractions at 2.67 Gy per fraction to the whole breast, results in an equivalent tumor bed dose of approximately 63-66 Gy in 2-Gy fractions when corrected for α/β ratio of 4 and proliferation effects [12].

1.5 Evidence for 40.05 Gy/48 Gy in 15 Fractions

Several studies have investigated the specific dose schedule of 40.05 Gy to the whole breast and 48 Gy to the lumpectomy cavity in 15 fractions:

Scorsetti *et al.* (2012): This Phase I-II study evaluated hypofractionated SIB using volumetric modulated arc therapy (VMAT) for adjuvant breast radiotherapy, demonstrating feasibility and acceptable acute skin toxicity profiles [13].

De Rose *et al.* (2016): A Phase II trial of hypofractionated VMAT-based treatment for early-stage breast cancer reported that the 3-week VMAT-SIB course following breast-conserving surgery was well tolerated and associated with optimal local control at 2-year follow-up [14].

NRG RTOG 1005 (2022): This landmark Phase III trial compared hypofractionated whole breast irradiation with concurrent boost versus conventional WBI with sequential boost in high-risk early-stage breast cancer. The study demonstrated non-inferior breast recurrence rates for the concomitant boost approach while significantly reducing overall treatment time. Importantly, no differences in toxicity or cosmetic outcomes were observed between the concurrent versus sequential boost approaches or between fractionation regimens [15].

1.6 Study Rationale and Objectives

Despite growing evidence supporting hypofractionated SIB approaches, real-world feasibility data and toxicity profiles in diverse clinical settings remain valuable for guiding clinical practice. This prospective study aims to evaluate:

1. The feasibility of delivering hypofractionated whole breast radiotherapy with simultaneous integrated boost (40.05 Gy/48.0 Gy in 15 fractions)
2. Dosimetric parameters and plan quality for target volumes and organs at risk
3. Early acute toxicity profile, particularly skin reactions
4. Technical challenges and limitations in implementation

2. Methods

2.1 Study Design and Patient Selection

This prospective observational study was conducted between 2022 and 2023 at our institution. The study included 30 patients with histologically confirmed invasive breast carcinoma who underwent breast-conserving surgery with clear surgical margins.

Inclusion Criteria

- Histologically confirmed invasive breast cancer
- Status post breast-conserving surgery with negative margins
- Presence of surgical clips marking the lumpectomy cavity
- Age ≥18 years
- Eastern Cooperative Oncology Group (ECOG) performance status 0-2
- Adequate organ function for radiotherapy

Exclusion Criteria

- Positive surgical margins requiring re-excision
- Distant metastatic disease
- Previous radiation therapy to the chest wall
- Pregnancy or lactation
- Connective tissue disorders affecting radiation tolerance

Patients were permitted to receive systemic therapy in either the neoadjuvant or adjuvant setting according to standard institutional protocols. All patients provided informed consent prior to enrollment.

2.2 Simulation and Immobilization

All patients underwent CT simulation using standardized positioning protocols. Patients were positioned supine on a breast board with both arms abducted above the head at approximately 90-120 degrees to ensure reproducible setup and minimize arm positioning variability. A CT dataset was

acquired with 5 mm thick contiguous slices without intravenous contrast administration, covering the entire thorax from the level of the mandible to the upper abdomen. Respiratory gating techniques were not employed in this study due to equipment limitations. Patients were instructed to breathe normally during CT acquisition and treatment delivery.

2.3 Target Volume Delineation
Target volumes and organs at risk were delineated according to established contouring guidelines:

Clinical Target Volume - Whole Breast (CTV_WB)
The CTV_WB encompassed the entire palpable mammary gland, extending from the sternal border medially to the mid-axillary line laterally, from the inferior border of the clavicle superiorly to the inframammary fold inferiorly, and from the skin surface anteriorly to the pectoralis muscles and chest wall posteriorly.

Clinical Target Volume- Boost (CTV_Boost)
The CTV_Boost was defined as the surgical bed identified by surgical clips placed during lumpectomy, with a 1 cm three-dimensional expansion to account for microscopic disease extension and surgical bed changes post-operatively.

Planning Target Volumes (PTVs):
- **PTV_WB:** Created by adding a 5 mm uniform expansion to CTV_WB, limited to 5 mm from the skin surface and excluding the chest wall (ribs) and lung parenchyma
- **PTV_Boost:** Created by adding a 5 mm uniform expansion to CTV_Boost, with similar constraints excluding skin, ribs, and lung

Organs at Risk (OARs): The following organs at risk were contoured:
- Ipsilateral and contralateral lungs
- Heart
- Contralateral breast
- Spinal cord (when applicable)

2.4 Treatment Planning and Dose Prescription
Treatment planning was performed using volumetric modulated arc therapy (VMAT) technique with simultaneous integrated boost approach. The prescribed doses were:
- **PTV_WB:** 40.05 Gy in 15 fractions (2.67 Gy per fraction)
- **PTV_Boost:** 48.0 Gy in 15 fractions (3.2 Gy per fraction)

Treatment was delivered over 3 weeks with 5 fractions per week.

Dose-Volume Objectives
Target Coverage
- At least 95% of PTV_WB should receive at least 95% of the prescribed dose (≥38.0 Gy)
- At least 95% of PTV_Boost should receive at least 95% of the prescribed dose (≥45.6 Gy)
- Maximum dose to target volumes should not exceed 107% of prescribed dose

Organs at Risk Constraints
Ipsilateral Lung
- Mean dose: <10 Gy (primary objective)
- V20Gy: <10% (acceptable up to 20% based on NRG RTOG 1005 protocol) [15]
- V5Gy: As low as reasonably achievable

Heart
- V40Gy: <3%
- V18Gy: <5%
- Mean dose: As low as reasonably achievable (based on Formenti *et al*. 2007) [16]

Contralateral Lung and Breast
- Mean dose: Minimize to the extent possible
- No specific dose constraints, but minimize exposure

2.5 Treatment Delivery and Quality Assurance
All treatments were delivered using linear accelerators equipped with VMAT capability. Patient-specific quality assurance was performed prior to treatment initiation for all plans, including:
- Pre-treatment verification using portal dosimetry or phantom measurements
- Daily image guidance using orthogonal kilovoltage imaging or cone-beam CT
- Weekly physician review during treatment course

2.6 Toxicity Assessment
Acute toxicity was assessed using the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Skin toxicity was evaluated weekly during treatment and at follow-up visits. The grading system for skin toxicity was:
- **Grade 0:** No change over baseline
- **Grade 1:** Follicular, faint or dull erythema, epilation, dry desquamation, decreased sweating
- **Grade 2:** Tender or bright erythema, patchy moist desquamation, moderate edema
- **Grade 3:** Confluent moist desquamation other than skin folds, pitting edema
- **Grade 4:** Ulceration, hemorrhage, necrosis

Cardiac and pulmonary toxicity assessments were performed through clinical evaluation during follow-up visits.

2.7 Statistical Analysis
Dosimetric parameters were analyzed using descriptive statistics. Continuous variables are presented as mean±standard deviation (SD). Toxicity rates are presented as frequencies and percentages. Subgroup analyses were performed comparing right-sided versus left-sided breast treatments.

3. Results
3.1 Patient Characteristics
A total of 30 patients with invasive breast cancer following breast-conserving surgery were enrolled in the study between 2022 and 2023. All patients completed the prescribed radiotherapy course without interruption. The distribution included both right-sided and left-sided breast

cancers, allowing for comparative analysis of laterality-specific dosimetric parameters.

3.2 Dosimetric Outcomes

3.2.1 Target Volume Coverage

All treatment plans successfully met the prescribed dose coverage objectives:

- PTV_WB: ≥95% of the volume received ≥95% of the prescribed dose (≥38.0 Gy)
- PTV_Boost: ≥95% of the volume received ≥95% of the prescribed dose (≥45.6 Gy)

The dose-volume histograms demonstrated steep dose gradients between the boost volume and whole breast, with adequate sparing of organs at risk while maintaining target coverage.

3.2.2 Organs at Risk Dosimetry

Detailed dosimetric parameters for organs at risk are presented in Table 1.

Table 1: Dosimetric Parameters for Organs at Risk (Mean ±SD)

Structure	Parameter	All patients	Right	left
Lung ipsi	Mean	9.84±1.49	9.7±1.4	9.93±1.5
	V20	14.9±3.67	15.6±3.4	13.78 ±3.77
	V5	56.9±14.02	54.7±13	60.3±14.57
Lung contra	Mean	3.43±1.28	3.65±1.12	3.08±1.41
Heart	Mean	3.45±1.0	2.89±0.67	4.29±0.83
	V18	1.59±2.19	0.11±0.26	3.8±1.93
	V40	0±0	0±0	0±0
Breast contra	mean	2.67±0.82		

Ipsilateral Lung

The mean dose to the ipsilateral lung was 9.84±1.49 Gy, which met the primary objective of <10 Gy. The V20 parameter (volume receiving ≥20 Gy) was 14.9±3.67%, which is within the acceptable range of <20% as per NRG RTOG 1005 protocol criteria. No significant differences were observed between right-sided (9.70±1.40 Gy) and left-sided (9.93±1.50 Gy) treatments for mean lung dose.

Heart

The mean heart dose was 3.45±1.0 Gy for all patients. As expected, left-sided breast treatments resulted in higher mean heart doses (4.29±0.83 Gy) compared to right-sided treatments (2.89±0.67 Gy). The V18 parameter was 1.59±2.19% overall, with left-sided treatments showing 3.80±1.93% compared to 0.11±0.26% for right-sided treatments. Notably, V40 was 0% for all patients, indicating excellent cardiac sparing. All cardiac dose parameters remained well within established safety thresholds.

Contralateral Structures: The mean dose to the contralateral lung was 3.43±1.28 Gy, and the contralateral breast received a mean dose of 2.67±0.82 Gy, demonstrating effective sparing of contralateral structures.

3.3 Acute Toxicity Profile

3.3.1 Skin Toxicity

Acute skin toxicity was systematically assessed during treatment and early follow-up. The toxicity profile was favorable, with the majority of patients experiencing minimal to mild reactions (Table 2).

Table 2: Acute Skin Toxicity Profile

Grade	Toxicity Description	Number of cases	Percentage of cases
0	No change over baseline	11/30	36.67
1	Follicular, faint or dull erythema/epilation/dry desquamation/decreased sweating	16/30	53.33
2	Tender or bright erythema, patchy moist desquamation/moderate edema	3/30	10
3	Confluent, moist desquamation other than skinfolds, pitting edema	0/30	0
4	Ulceration, hemorrhage, necrosis	0/30	0

Key Findings

- 36.67% of patients (11/30) experienced no change from baseline skin condition throughout treatment
- 53.33% of patients (16/30) developed Grade 1 toxicity, characterized by mild erythema and dry desquamation
- Only 10% of patients (3/30) experienced Grade 2 toxicity with bright erythema and patchy moist desquamation
- No patients developed severe toxicity (Grade 3 or 4)
- All skin reactions were manageable with standard supportive care measures

3.3.2 Cardiac and Pulmonary Toxicity

No clinically evident cardiac or pulmonary toxicities were observed in any patient during the follow-up period. All patients remained asymptomatic with respect to cardiac symptoms (chest pain, dyspnea, palpitations) and pulmonary symptoms (cough, dyspnea, pneumonitis). However, longer follow-up is required for comprehensive assessment of late cardiac and pulmonary effects.

3.4 Treatment Feasibility and Technical Challenges: The hypofractionated SIB regimen was successfully implemented in the majority of patients. However, several technical challenges were encountered:

Medial Quadrant Tumors: In some patients with medial quadrant tumors, achieving the desired dosimetric objectives for both target coverage and cardiac sparing proved challenging. The proximity of the boost volume to the heart necessitated careful optimization to balance target dose coverage with cardiac dose constraints. In cases where simultaneous integrated boost planning could not me*et al*l dosimetric objectives, a sequential electron boost approach was adopted as an alternative strategy.

Respiratory Motion Management: The absence of deep inspiration breath-hold (DIBH) or respiratory gating techniques represented a limitation in this study. These advanced techniques, which can significantly reduce cardiac exposure particularly in left-sided breast treatments, were unavailable at our institution during the study period. Implementation of DIBH could potentially further improve cardiac dosimetry, especially for left-sided cases.

Planning Complexity: VMAT-based SIB planning required greater optimization time and expertise compared to

conventional tangential field techniques. However, once established workflows were in place, planning efficiency improved substantially.

4. Discussion

4.1 Principal Findings

This prospective study demonstrates that hypofractionated adjuvant whole breast radiotherapy with simultaneous integrated boost, delivering 40.05 Gy in 15 fractions to the whole breast and 48.0 Gy in 15 fractions to the tumor bed, is feasible and associated with an acceptable acute toxicity profile. The treatment regimen achieved satisfactory dosimetric parameters for target coverage and organs at risk protection, with the majority of patients experiencing minimal to mild acute skin reactions.

4.2 Comparison with Existing Literature

Our findings align with and extend previous studies investigating hypofractionated SIB approaches in breast radiotherapy:

Dosimetric Feasibility: The mean ipsilateral lung dose of 9.84±1.49 Gy and V20 of 14.9±3.67% in our study compare favorably with published reports. Scorsetti *et al*. (2012) reported similar pulmonary dosimetric parameters in their Phase I-II study of hypofractionated VMAT-SIB, demonstrating the reproducibility of these results across different institutions [13]. The mean heart dose of 3.45±1.0 Gy, with higher values for left-sided treatments (4.29±0.83 Gy), is consistent with expected patterns and remains well within safety thresholds established by Formenti *et al*. [16].

Acute Toxicity: Our acute skin toxicity profile, with 90% of patients experiencing Grade 0-1 toxicity and only 10% experiencing Grade 2 toxicity, compares favorably with the literature. De Rose *et al*. (2016) reported similar low rates of acute toxicity in their Phase II trial of hypofractionated VMAT-SIB, with no Grade 3 or higher toxicity observed [14]. The absence of severe acute toxicity in our cohort supports the safety of this approach for routine clinical practice.

The landmark NRG RTOG 1005 trial, which compared hypofractionated WBI with concurrent boost versus conventional WBI with sequential boost, demonstrated non-inferior outcomes for the concurrent boost approach with no differences in toxicity profiles [15]. Our study adds real-world feasibility data supporting the implementation of this approach in diverse clinical settings.

4.3 Clinical Implications

Treatment Time Reduction: The primary advantage of the hypofractionated SIB approach is the substantial reduction in overall treatment time from 6-7 weeks (conventional fractionation with sequential boost) to 3 weeks. This reduction offers multiple benefits:

- Improved patient convenience and quality of life
- Reduced transportation burden and associated costs
- Enhanced treatment compliance
- Increased radiotherapy capacity and resource utilization
- Potential reduction in tumor cell repopulation during treatment

Economic Considerations: Shorter treatment courses reduce healthcare costs through decreased resource utilization, fewer treatment sessions, and reduced staffing requirements. For patients, the reduced treatment duration translates to fewer days of work absence and lower transportation costs, particularly beneficial for those traveling long distances for treatment.

Patient Selection

While the hypofractionated SIB approach proved feasible for most patients in our cohort, careful patient selection remains important. Patients with medial quadrant tumors, particularly in the left breast, require meticulous planning to ensure adequate cardiac sparing. In cases where dosimetric objectives cannot be met with SIB, alternative approaches such as sequential boost or consideration of advanced techniques like DIBH should be considered.

4.4 Technical Considerations

VMAT Planning

The use of VMAT technique facilitated the delivery of differential doses to the whole breast and boost volumes while maintaining excellent conformity and organs at risk sparing. VMAT offers advantages over conventional tangential field techniques, including:

- Improved dose homogeneity
- Better target coverage for complex geometries
- Enhanced organs at risk sparing through inverse planning optimization
- Capability to deliver SIB effectively

However, VMAT planning requires greater expertise, longer planning time, and more sophisticated quality assurance compared to conventional techniques. Institutions implementing this approach should ensure adequate training and quality assurance infrastructure.

Respiratory Motion Management

The absence of DIBH or respiratory gating in our study represents a limitation, particularly for left-sided breast cancer patients. DIBH has been shown to significantly reduce cardiac exposure by increasing the distance between the heart and chest wall during inspiration [17]. Future implementation of DIBH at our institution could further improve cardiac dosimetry, especially for patients with medial or central tumors in the left breast.

4.5 Radiobiological Considerations

The hypofractionated SIB schedule employed in this study is based on sound radiobiological principles. With an estimated α/β ratio of approximately 4 Gy for breast cancer, the biological effective dose (BED) delivered by 48 Gy in 15 fractions (3.2 Gy per fraction) to the tumor bed is:

$BED = nd[1 + d/(\alpha/\beta)] = 15 \times 3.2 \times [1 + 3.2/4] = 86.4$ Gy

This is equivalent to approximately 63-66 Gy in conventional 2 Gy fractions when accounting for proliferation effects, matching the standard boost dose for breast cancer [12].

The lower α/β ratio of breast cancer compared to many other tumor types provides a therapeutic advantage for hypofractionation, as larger fraction sizes have a greater biological effect on tumor cells while remaining within the tolerance of late-responding normal tissues.

4.6 Limitations

Several limitations of this study should be acknowledged:

Sample Size and Follow-up: The relatively small sample size of 30 patients limits the statistical power for detecting rare toxicities or subgroup differences. Additionally, the early follow-up period is insufficient for assessing late toxicity, local control, and long-term cosmetic outcomes. Extended follow-up of at least 5-10 years is necessary to fully evaluate the safety and efficacy of this approach.

Absence of Advanced Techniques: The unavailability of DIBH and respiratory gating techniques represents a technical limitation, particularly for cardiac dose reduction in left-sided breast cancer patients. Implementation of these techniques could further improve the therapeutic ratio.

Single Institution Experience: As a single-institution study, the generalizability of our findings may be limited by institution-specific practices, patient populations, and technical capabilities. Multi-institutional validation would strengthen the evidence base.

Lack of Control Group: The absence of a control group receiving conventional fractionation or sequential boost limits direct comparative analysis. However, the extensive literature on conventional approaches provides a reasonable benchmark for comparison.

Tumor Location Challenges: Some patients with medial quadrant tumors required conversion to sequential electron boost due to dosimetric constraints, indicating that the SIB approach may not be universally applicable. This highlights the importance of individualized treatment planning.

4.7 Future Directions

Several avenues for future research and clinical improvement are apparent:

Long-term Outcomes: Extended follow-up is essential to evaluate:

- Late toxicity profiles (cardiac, pulmonary, cosmetic)
- Local control rates
- Overall survival and disease-free survival
- Patient-reported quality of life outcomes
- Comparative cosmetic assessment using validated scales

Advanced Motion Management: Implementation of DIBH or respiratory gating techniques should be prioritized to further reduce cardiac exposure, particularly for left-sided breast cancer patients. Prospective evaluation of cardiac dosimetry improvements with these techniques is warranted.

Comparative Studies: Randomized controlled trials or large prospective cohort studies comparing hypofractionated SIB versus conventional sequential boost approaches would provide higher-level evidence for clinical decision-making, although the NRG RTOG 1005 trial has already established non-inferiority [15].

Predictive Modeling: Development of predictive models to identify patients most likely to benefit from SIB versus those requiring alternative approaches (e.g., based on tumor location, breast size, cardiac position) could optimize patient selection.

Partial Breast Irradiation

For highly selected patients with favorable tumor characteristics, further investigation of accelerated partial breast irradiation (APBI) techniques may offer even shorter treatment courses while maintaining oncologic safety.

Biomarker Studies

Investigation of molecular and genetic biomarkers that predict radiation response and toxicity could enable personalized treatment selection and dose adaptation.

5. Conclusion

This prospective study demonstrates that hypofractionated adjuvant whole breast radiotherapy with simultaneous integrated boost, delivering 40.05 Gy to the whole breast and 48.0 Gy to the tumor bed in 15 fractions over 3 weeks, is feasible with respect to dosimetric parameters and early toxicity profile. The treatment regimen achieved excellent target coverage, maintained organs at risk doses within acceptable limits, and was associated with predominantly mild acute skin toxicity with no severe reactions observed.

The key findings of this study include:

1. **Dosimetric Feasibility:** Mean ipsilateral lung dose of 9.84±1.49 Gy and mean heart dose of 3.45±1.0 Gy demonstrate effective organs at risk sparing
2. **Favorable Acute Toxicity:** 90% of patients experienced Grade 0-1 skin toxicity, with no Grade 3 or 4 reactions
3. **Treatment Time Reduction:** The 3-week treatment course represents a 50% reduction compared to conventional fractionation with sequential boost
4. **Clinical Applicability:** The approach is implementable in routine clinical practice with VMAT capability, though careful planning is required for medial quadrant tumors

These results support the adoption of hypofractionated whole breast radiotherapy with simultaneous integrated boost as a safe and efficient alternative to conventional fractionation schedules for appropriately selected patients with early-stage breast cancer following breast-conserving surgery. The substantial reduction in treatment duration offers significant advantages in terms of patient convenience, healthcare resource utilization, and cost-effectiveness without compromising safety.

However, long-term follow-up is essential to comprehensively evaluate late toxicity, local control, cosmetic outcomes, and survival endpoints. Future implementation of advanced motion management techniques such as deep inspiration breath-hold could further optimize cardiac sparing, particularly for left-sided breast cancer patients.

As breast cancer treatment continues to evolve toward personalized, efficient, and patient-centered approaches, hypofractionated radiotherapy with simultaneous integrated boost represents an important advancement that balances oncologic efficacy, safety, and quality of life considerations.

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