Alternatives to Standard Fractionation Radiation Therapy After Lumpectomy

Hypofractionated Whole-Breast Irradiation and Accelerated Partial-Breast Irradiation

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KEYWORDS

• Breast cancer • Breast-conserving therapy • Lumpectomy • Standard fractionation • Hypofractionation • Accelerated partial-breast irradiation

KEY POINTS

- Adjuvant whole-breast irradiation after lumpectomy has been an established standard of care to optimize local tumor control for decades.
- Standard-fractionation whole-breast irradiation delivered over 5 to 7 weeks can achieve durable tumor control with low toxicity and favorable cosmesis but can be inconvenient and cost ineffective.
- Hypofractionated whole-breast irradiation can be completed in 3 to 4 weeks and is the preferred standard of care in appropriately selected patients.
- Accelerated partial breast irradiation can be delivered using even shorter treatment regimens, and early results suggest it is an effective alternative to WBI in select patients.
- Results from ongoing hypofractionated whole-breast irradiation and accelerated partial breast irradiation trials will help establish their roles in the adjuvant management of early stage breast cancer.

INTRODUCTION

Breast-conservation therapy, or breast-conserving surgery (BCS) followed by adjuvant radiation therapy (RT), was established as an acceptable alternative to mastectomy after multiple randomized trials conducted in the 1970s and 1980s demonstrated equivalent high survival rates with both approaches.[1,2] In 2005, the

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Early Breast Cancer Trialists' Collaborative Group meta-analysis further established breast-conservation therapy as the standard of care for early-stage breast cancer. The most commonly used radiation regimen in these randomized trials was 50 Gy in 25 fractions to the whole breast with or without a boost, now referred to as a *standard fractionation whole-breast irradiation* (SF-WBI).[3]

The radiobiological rationale in support of SF-WBI is that smaller doses of radiation per fraction can spare normal tissues, such as the breast, muscle, ribs, and lung, without compromising tumor control. Some of the challenges of SF-WBI, however, include the cost and inconvenience of 5 to 7 weeks of daily radiation treatment. As a result, there has been growing interest in establishing alternate methods of delivering adjuvant RT using shorter and more convenient regimens. This article reviews hypofractionated WBI (HF-WBI) and accelerated partial breast irradiation (APBI) as accepted alternate approaches to SF-WBI in appropriately selected patients with early-stage breast cancer.

HYPOFRACTIONATED WHOLE-BREAST IRRADIATION

HF-WBI refers to the delivery of adjuvant whole-breast RT in a shortened 3- to 4-week course of treatment. The evidence in support of HF-WBI comes from a series of large randomized trials showing equivalence in efficacy, toxicity, and long-term cosmesis compared with SF-WBI. Key features and results of each trial are summarized in **Tables 1** and **2**.

EFFICACY OF HYPOFRACTIONATED WHOLE-BREAST IRRADIATION

One of the earlier HF-WBI trials was initiated in 1986 at the Royal Marsden Hospital and Gloucester Oncology Center (RMH/GOC) in the United Kingdom. This was a pilot trial that included 1410 patients younger than 75 years of age with T1-3, N0-1, M0 breast cancer who underwent BCS with complete macroscopic resection of invasive

Table 1
Key features of randomized breast hypofractionation trials

Variable	RMH/GOC	START A	START B	Canadian
Patients enrolled	1410	2236	2215	1234
Study years	1986–1998	1998–2002	1999–2001	1993–1996
Median follow-up (y)	9.7	9.3	9.9	12.0
Stage	T1-3, N0-1, M0	T1-3a, N0-1, M0	T1-3a, N0-1, M0	T1-2, N0, M0
Surgery				
Lumpectomy, N (%)	1410 (100)	1900 (85)	2038 (92)	1234 (100)
Mastectomy, N (%)	0	336 (15)	117(8)	0
Treatment arms (Gy/fractions)	50/25 (5 wk) 42.9/13 (5 wk) 39/13 (5 wk)	50/25 (5 wk) 41.6/13 (5 wk) 39/13 (5 wk)	50/25 (5 wk) 40/15 (3 wk)	50/25 (5 wk) 42.5/16 (3.2 wk)
Boost				
N (%)	1051 (75)	1159 (61)	875 (43)	0
Dose (Gy/fractions)	14/7	10/5	10/5	
Regional nodal irradiation, N (%)	290 (21)	318 (14)	161 (7)	0
Chemotherapy, N (%)	196 (14)	793 (35)	491 (22)	135 (11)