

RAPID

Randomized Trial of Accelerated Partial Breast Irradiation using 3-Dimensional Conformal Radiotherapy (3D-CRT)

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for the RAPID Trial Investigators

Ontario Clinical Oncology Group



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Disclosures

No relevant disclosures

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Whole Breast Irradiation

- **WBI** following breast conserving surgery (BCS) reduces risk of local recurrence, avoiding mastectomy
- Daily fractions of 2-2.7 Gy over 3-6 weeks

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Accelerated Partial Breast Irradiation

- **APBI** is based on rationale that most local recurrences occur at primary site
- Delivered to the surgical cavity with a margin of normal tissue and is given in one week or less
- Several techniques exist, many are resource intensive
- 3D conformal RT (3D-CRT) or Intensity modulated RT (IMRT) are non-invasive and use modern technology

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Primary Objective of the RAPID trial

To determine if **APBI** using 3D-CRT was non-inferior to **WBI** following BCS in terms of **Ipsilateral Breast Tumor Recurrence (IBTR)**

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Secondary Objectives

To compare **APBI** with **WBI** for:

- **Disease-free Survival (DFS)**
Recurrence in ipsilateral breast, regional nodes or distant sites
- **Event-free Survival (EFS)**
Any recurrence, contralateral breast cancer, 2nd primary or death
- **Overall Survival (OS)**
- **Radiation Toxicity**
- **Cosmetic Outcome**

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Patient Population

Inclusion Criteria:

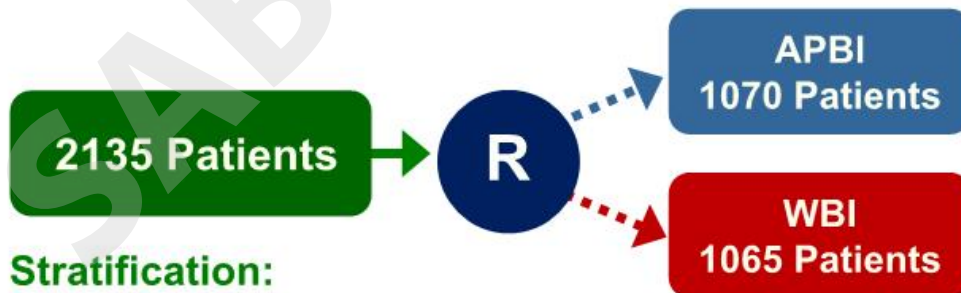
- Invasive breast cancer or DCIS
- ≤ 3 cm in size
- Microscopically clear margins post-BCS
- Node negative

Exclusion Criteria:

- < 40 years of age
- Lobular histology only
- Multi-centric disease

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Trial Design



Stratification:

- **Age** (<50, ≥50)
- **Histology** (DCIS only, Invasive disease)
- **Tumor Size** (<1.5, ≥1.5 cm)
- **ER Status** (Pos, Neg)

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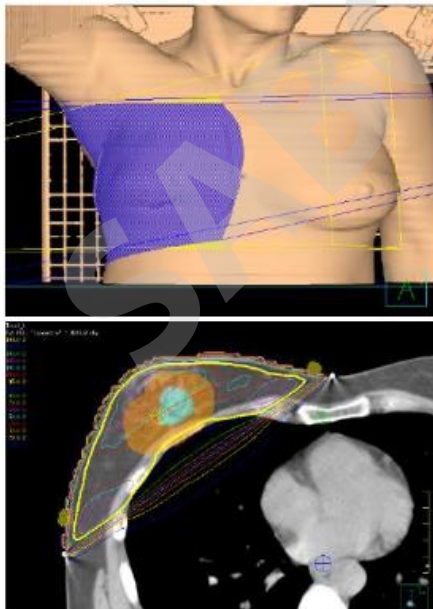


APBI



- 3-5 non-coplanar fields using 3D -CRT or IMRT
- Treat surgical cavity + 1cm margin of surrounding breast tissue
- **Dose: 38.5 Gy/10 fractions given BID (>6h between fractions)**
- Dosimetric restrictions
- RTQA program

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WBI



- Standard tangential fields
- **Dose: 50 Gy/25 fractions or 42.5 Gy/16 fractions**
- **Boost: 10 Gy/4-5 fractions for moderate-to-high risk cases**

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Toxicity

- **Toxicity** assessed using **NCI-CTCAE v3**
- At 1-2 weeks, 12 weeks, 6 months, then yearly by trial nurses

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Cosmesis

- **Cosmesis** assessed using EORTC Cosmetic Rating System
- At baseline, 3, 5, 7 years by nurse and by **patient self-assessment**
- Compare treated with untreated breast
- Score on 4-point scale for size, shape, location of areola/ nipple, telangiectasia and scar
- Global cosmetic outcome (0=excellent, 1=good, 2=fair, 3=poor)
 - **Analyzed as Fair/Poor vs. Excellent/Good**

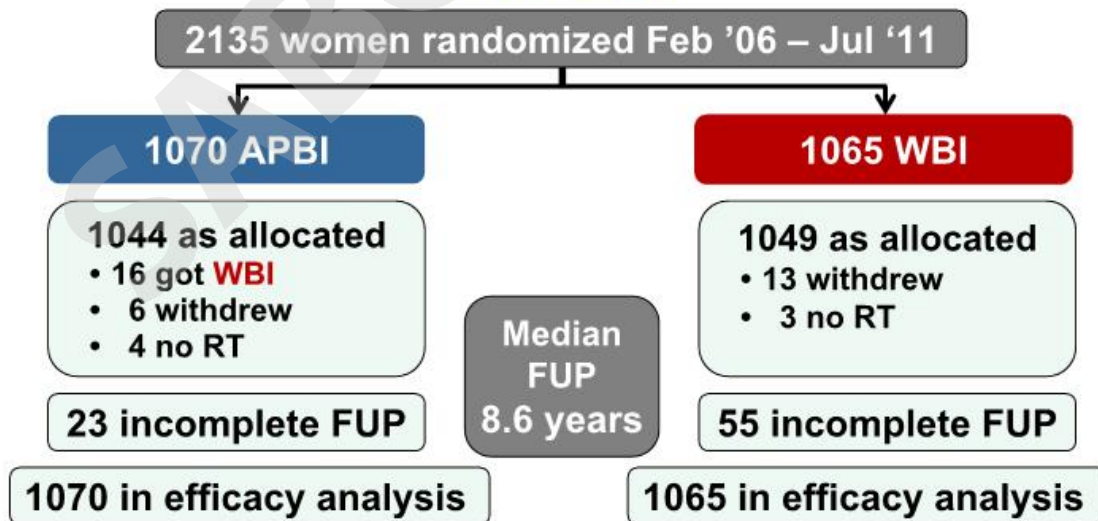
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Statistical Issues

- Sample Size based on risk of IBTR=1.5% at 5 years, non-inferiority margin=1.5% (HR<2.02): **64 events in 2128 patients**
- Stratified Cox PH model
- Non-inferiority declared if upper bound of the **90% CI** for Hazard Ratio for IBTR < 2.02

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Results



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Patient Characteristics

Characteristic	APBI	WBI
Age, median	61	61
Invasive Disease	82%	82%
DCIS only	18%	18%
Tumor Size < 1.5 cm	70%	68%
ER Positive, invasive only	85%	83%
Endocrine Therapy, invasive only	69%	67%
Chemotherapy, invasive only	15%	16%

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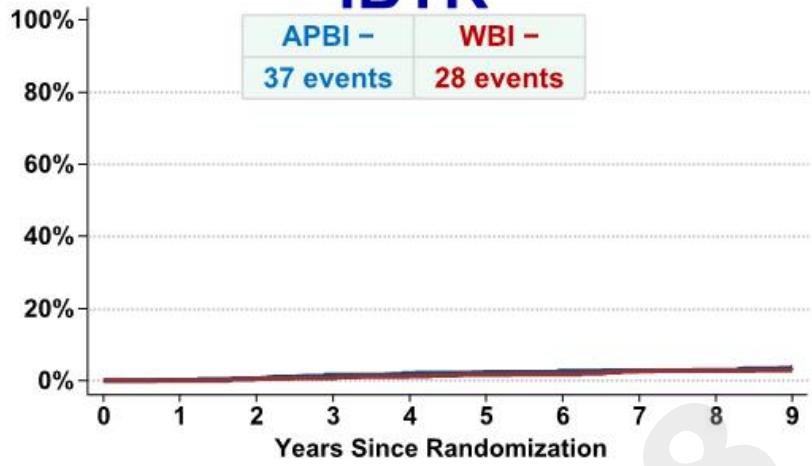
Radiation Treatment

APBI: 90% treated with 3D-CRT
 10% treated with IMRT

WBI: 83% treated with 42.5 Gy/16 fractions
 21% treated with Boost

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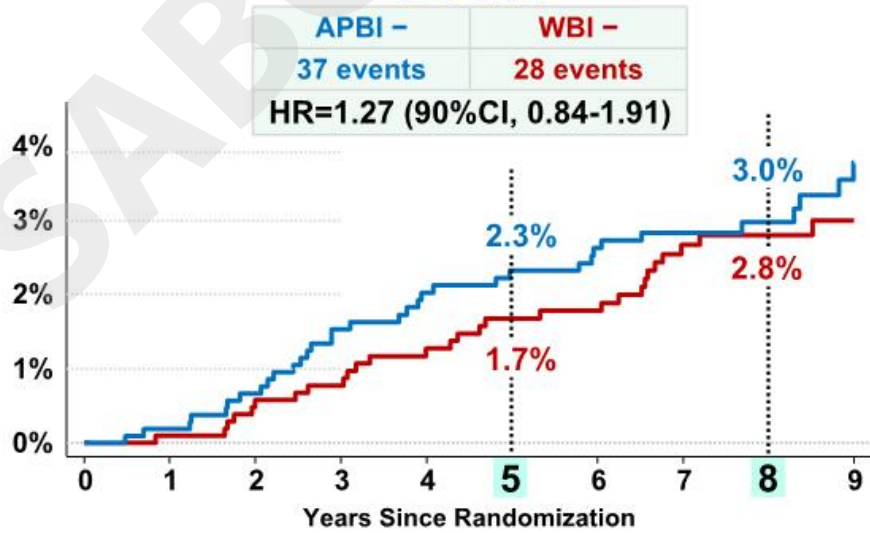
IBTR



APBI	1070	1048	1034	1016	998	979	954	827	609	407
WBI	1065	1040	1025	1002	978	960	930	809	591	389

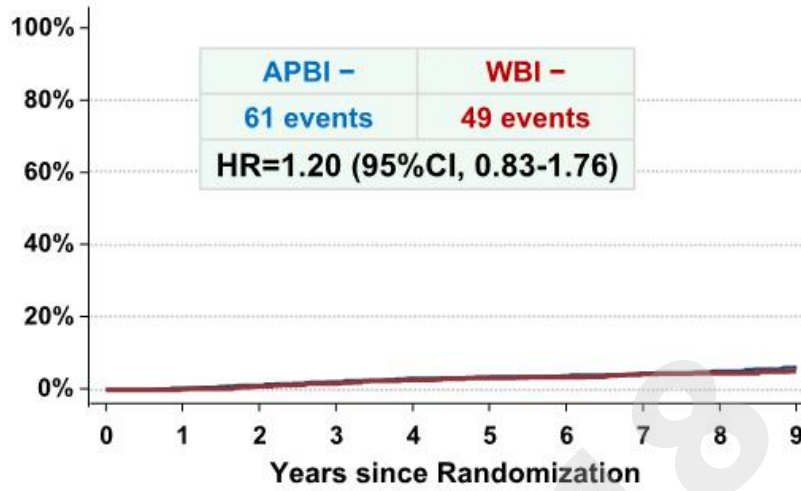
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IBTR



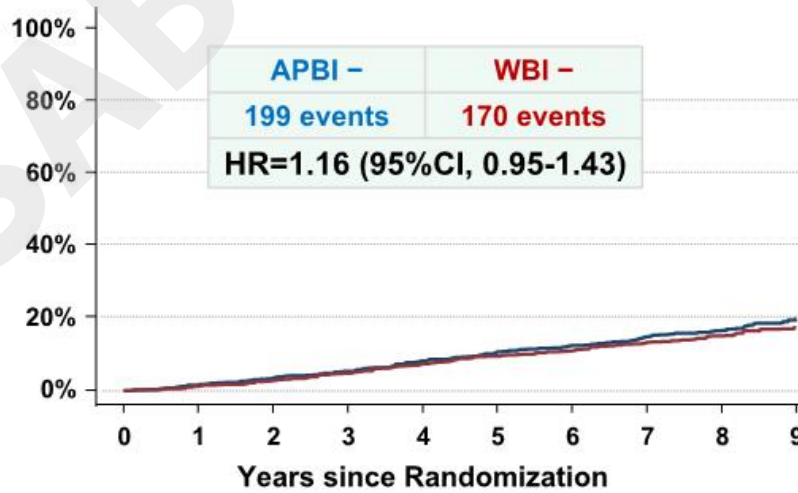
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DFS



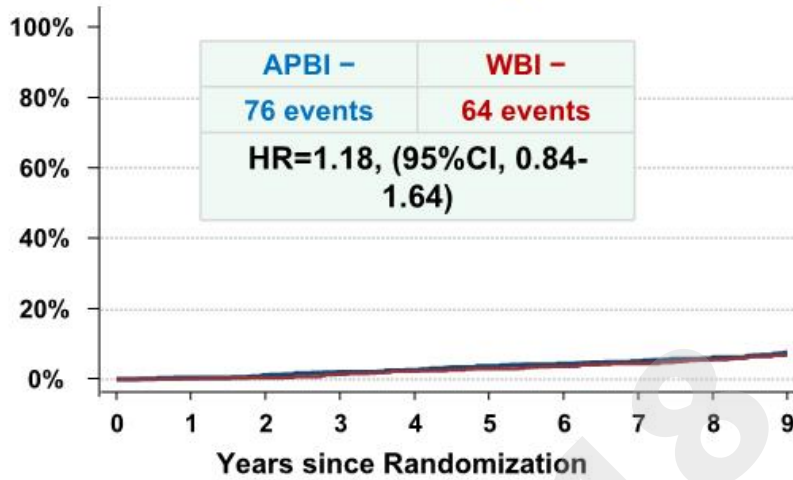
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EFS



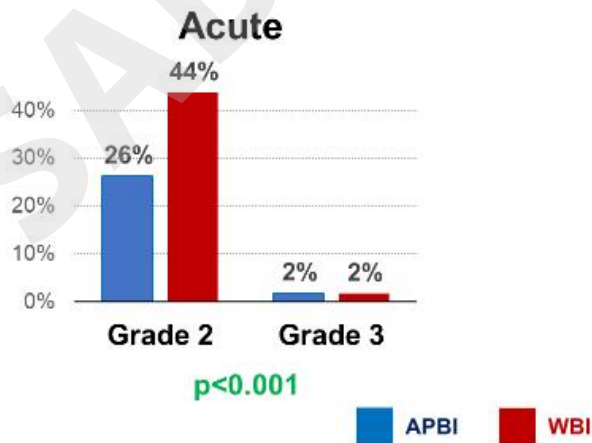
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Mortality



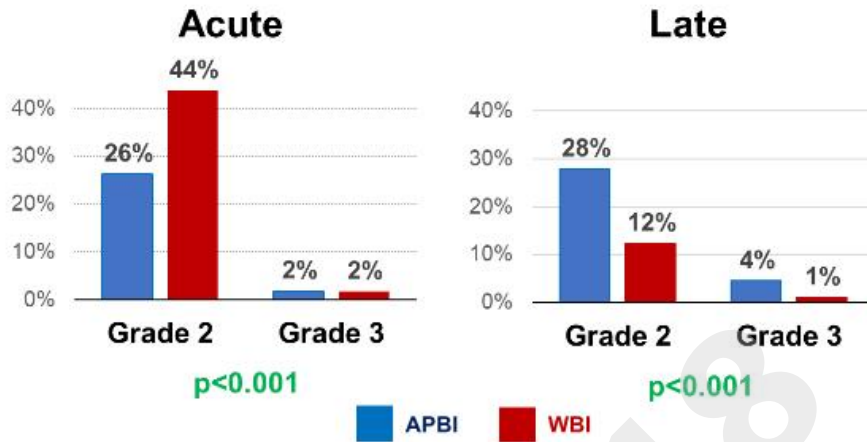
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Radiation Toxicity (Grade ≥ 2)



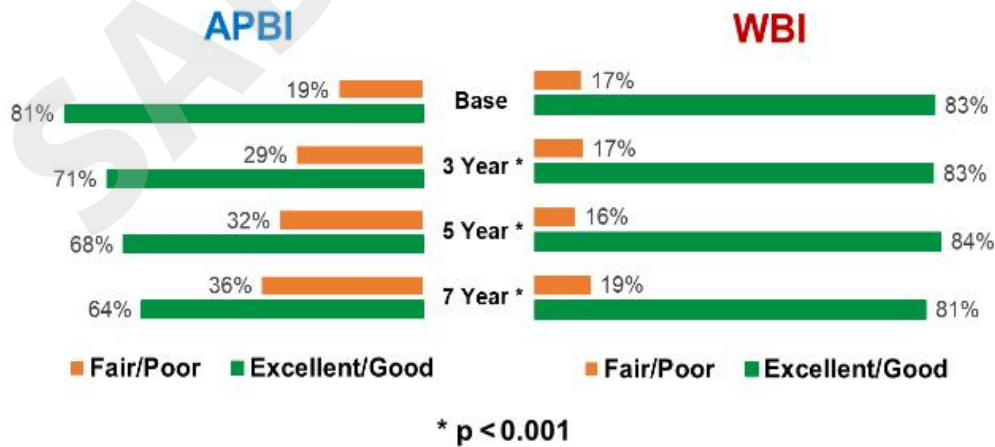
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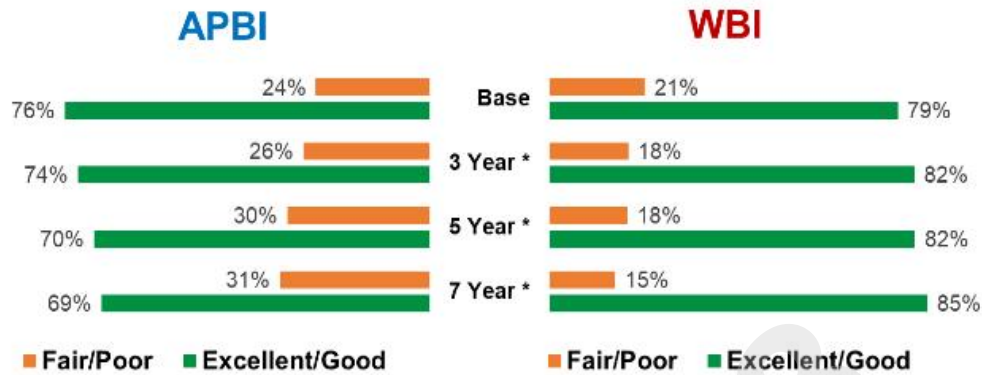
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Cosmesis Rating (Nurse) by Tmt and Time



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Cosmesis Rating (Patient) by Tmt and Time



* $p < 0.001$

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Conclusions

- **APBI** non-inferior to **WBI** in preventing local recurrence
- IBTR rate very low; Absolute differences very small
- **APBI** associated with less acute toxicity but increased late toxicity and adverse cosmesis
- Unable to recommend the *twice-a-day* regimen
- *Once-a-day* treatment may not adversely affect cosmesis, and is being investigated

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Thank You



- ❖ Patients
- ❖ Co-investigators
- ❖ Trial Nurses



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