Radioterapia dopo chirurgia conservativa: WBI oppure PBI?

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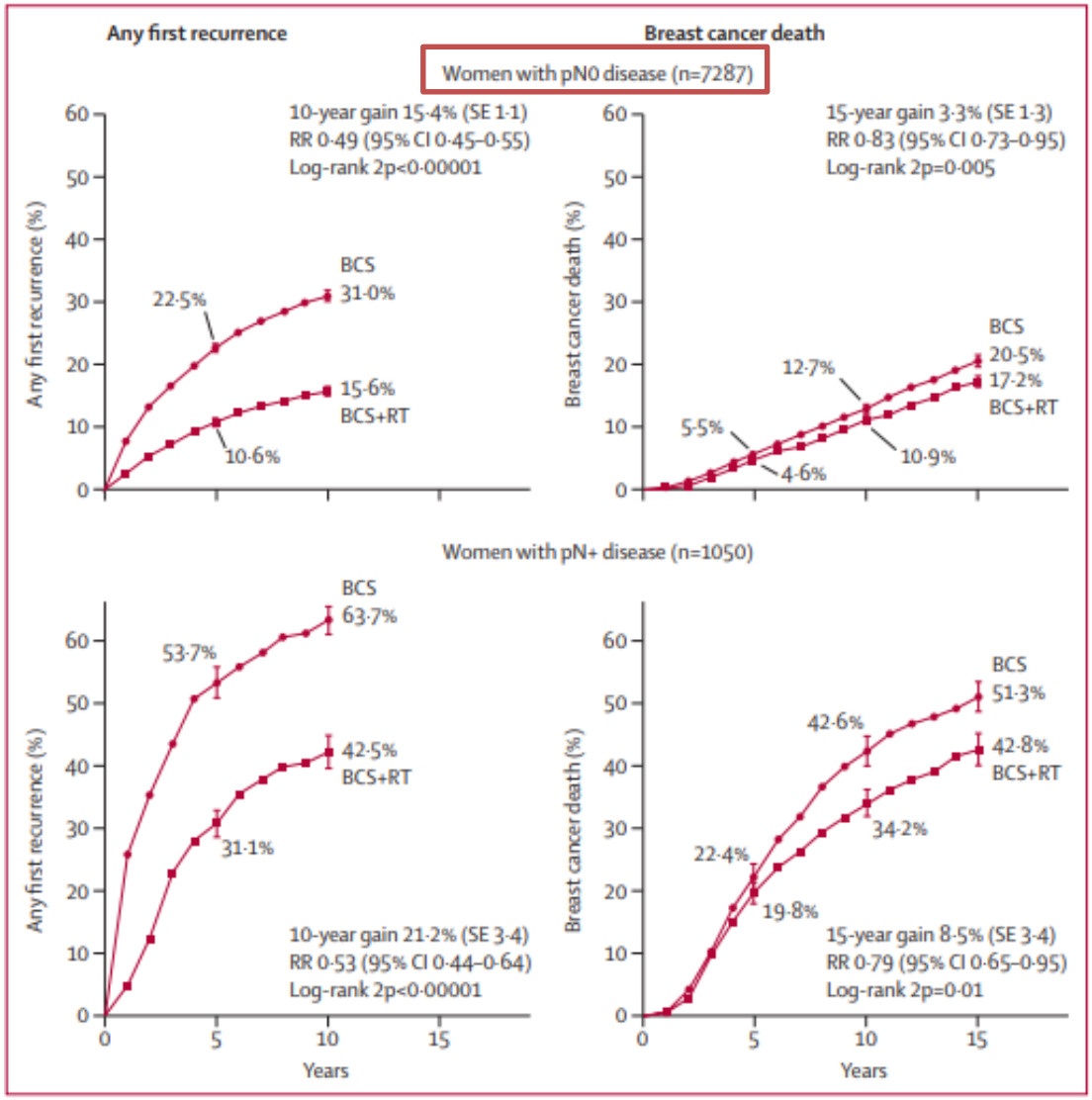
Background



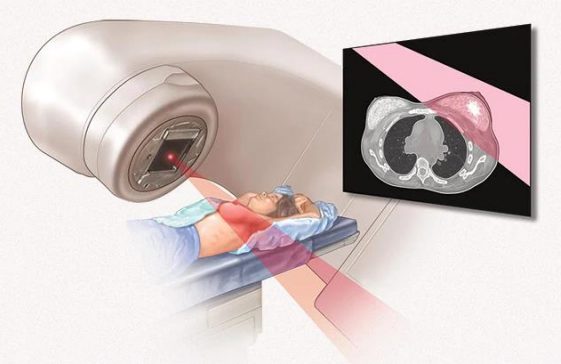
Meta-analysis of individual patient data for **10 801 women in 17 randomized trials**

WBI+BCS vs **BCS**

RT halves the rate at which the disease recurs and **reduces the breast cancer death rate by about a sixth**

Early Breast Cancer Trialists' Collaborative Group, Lancet 2011

Background



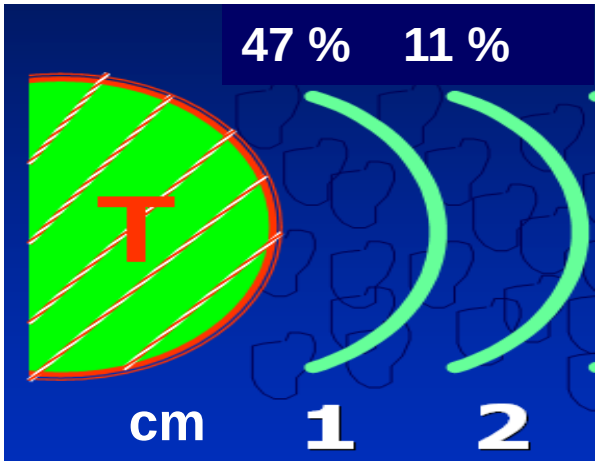
WBI may cause **side effects**
(larger volumes of irradiated organ at risk)

WBI is also associated with

logistical issues
costs
radiation department workload

Meattini et al. The Breast 2023

Background



Results from the BCT trials suggest that the **risk for ipsilateral breast cancer recurrence** resides within **close proximity to the original tumor site**

Ipsilateral breast recurrences in areas other than the tumor bed ("**elsewhere relapse**") occurred in **3–4% of the cases**
Elsewhere relapse are similar to the recurrences of contra-lateral breast cancer

For selected patients **WBI** could be an

over-treatment

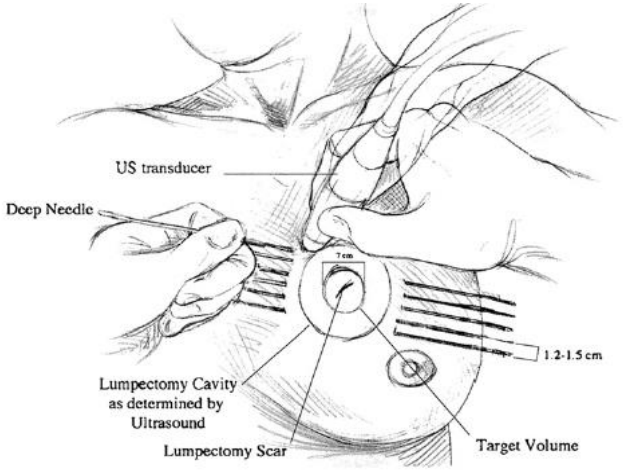
This leads investigators to consider the role of an accelerated and more **tumor bed–focused course of radiotherapy**

SandersME. J Clin Oncol 2007

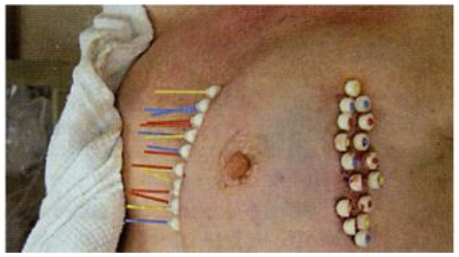
Outline

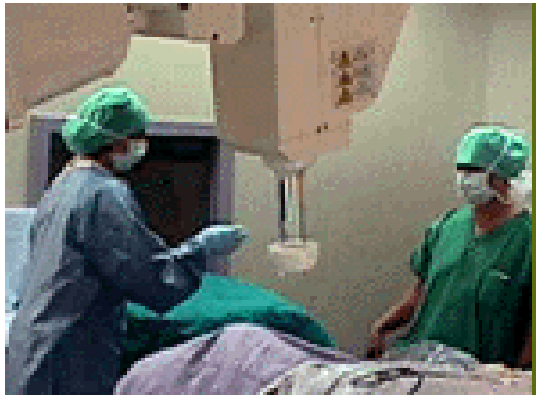
- PBI techniques
- Literature data: Results from RCTs
- International guidelines and recommendations
- Future perspectives: preoperative radiotherapy

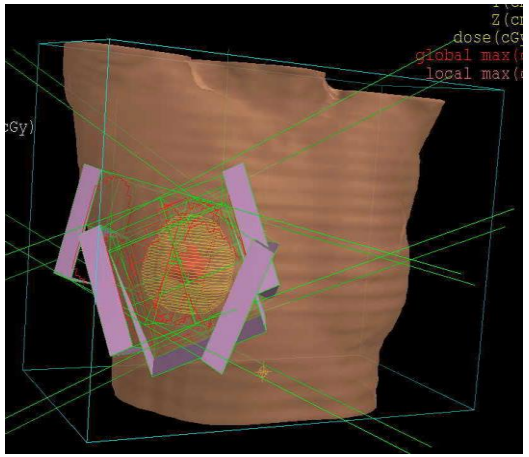
PBI techniques

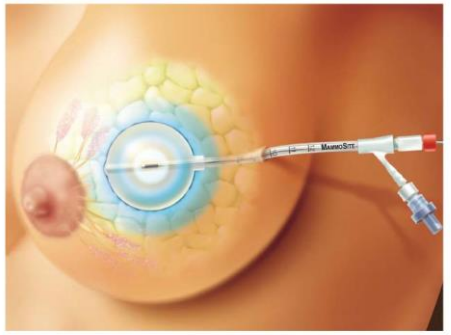


- Interstitial brachytherapy with HDR or LDR
- Intracavitary brachytherapy with Mammosite
- Intraoperative radiotherapy
- External beam radiation therapy









PBI techniques

Table 5 Comparison of the current available APBI techniques (adapted from Sarin [135]), MIB = multicatheter Interstitial brachytherapy, IORT = intraoperative radiation therapy, RCT = randomized Clinical trials, OAR organ at risk

	MIB	Balloon based brachytherapy			Hybrid based brachytherapy		External beam				IORT
		Mammosite	Axxent Electronic	Contura	SAVI	ClearPath	Photons	Electrons	Protons	electrons	Photons
Prescription point	1.5 - 2 cm	1 cm	1 cm	1 cm	1 cm	1 cm	1.5 - 2 cm	1.5 - 2 cm	1.5-2 cm	10- 30 mm	2 mm
Coverage of target volume	Variable	Good	Good	Good	Good	Good	Best	Good	Best	Good	Good
Dose Homogeneity	Fair	Fair	Fair	Fair	Fair	Fair	Best	Fair	Best	Fair	Fair
Sparing of OAR	Good	Good	Better	Better	Better	Better	Least	Varies	Good	Good	Best
Skin Dose	Least	Variable	variable	variable	variable	variable	Least	maximum	Least	Least	Least
Expertise required	High	Average	Average	Average	Average	Average	Average	Least	High	Very High	High
Suitability for various tumor size, location and shape	Not suitable if inadequate tissue or near axilla	Not suitable for large/irregular cavities or at the periphery	Not suitable Large cavities	Not suitable Large cavities	Not suitable Large cavities	Not suitable Large cavities	May not be suitable for small breast	Not suited for deep seated cavities in large breast	Superficial tumor	Not suitable for tumors near brachial plexus/ axilla or skin	Not suitable for large irregular cavities or at the periphery of breast
Potential for wide spread use	Fair	Very good	Very good	Very good	Very good	Very good	Very good	Very good	Limited	limited	fair
Clinical outcome data	11 years case studies	5 years case studies	None	Limited	Limited	None	4.5 years case studies	8 years case studies	Limited	4 years Case studies	4 years RCT
Main drawback	High expertise required and QA	Stringent QA is required Cavity, shape and size	Cavity shape and size	Cavity shape and size	Treatment planning complex	Treatment planning complex	Setup and breathing errors	High skin Dose	Expensive and 2nd neutrons	Pathology not available	Pathology not available

Njeh et al. Radiation Oncology 2010

Outline

- PBI techniques
- Literature data: Results from RCTs
- International guidelines and recommendations
- Future perspectives: preoperative radiotherapy

Results from RCTs: IBR

	GEC-ESTRO	IMPORT LOW	RAPID	RTOG 0413	University of Florence	ELIOT	TARGIT-A
N° pts	1184	2018	2135	4216	520	1305	3451
Primary Endpoint	LR/non-inferiority	IBTR/non-inferiority	IBTR/non-infer	IBTR/	IBTR/ equivalence	IBTR/non-inferiority	IBTR/non-inferiority
Median FUP (years)	10.36	6			10.7	12.4	2.5
PBI technique Dose/fr	**HDR** 32 Gy/8 fr	**EBRT (IMRT)** 40.05 Gy/15	**3D** 38		**EBRT (IMRT)** 30 Gy in 5 fr	**IOERT** 21 Gy/1 fr	**IORT** Low energy 0 KV 1 fr
LC (WBIvsPBI)	1.58% vs. 3.51% p = 0.074	1.1% vs. 0.5% p = 0.016	2.8% vs. 3.0% HR 1.27	3.9% vs. 4.6% HR 1.22	2.5% vs. 3.7% HR 1.56	2% vs. 11% HR 4.62	1.3% vs. 3.3% p = 0.042

IRMA

Session Details

Session type: **Proffered Papers**
Session title: **Late-breaking clinical trials**
Presentation title: **APBI with 3D-CRT vs. WBI: primary endpoint results of the prospective randomised phase 3 IRMA trial**
Session date and time: **6 May 2024 at 16:35-17:45 CEST**

Strnad V et al. Lancet Oncol 2023
Coles CE et al. The Lancet 2017
Whelan TJ et al. Lancet 2019
Vicini FA et al. Lancet 2019
Meattini I et al. J Clin Oncol 2020
Orecchia R et al. Lancet Oncol 2021
Vaidya JS et al. Lancet 2010

Results from RCTs: Toxicity

Trial	Dose/fr	Reported toxicities
IRMA	38.5 Gy/10 twice daily fr	G3-4 late soft tissue: 2.8 % PBI vs 1% WBI G3-G4 late bone toxicity: 1.1% PBI vs 0% WBI
RAPID	38.5 Gy/10 twice daily fr	G>2 induration: 22.9% PBI vs 4.6% WBI G>2 telangiectasi: 9.3% PBI vs 3.7% WBI G>2 breast pain: 4.8% PBI vs 1.9% WBI
RTOG 0413	38.5 Gy/10 twice daily fr (EBRT) 34 Gy/10 twice daily fr (BRT)	No detailed data published
University of Florence	30 Gy in 5 fr (2 weeks)	G>2 overall late toxicity: 0% PBI vs 7% WBI

ELIOT:
Information about side-effects *not available for all patients*
Skin side-effects: significant difference in favour of the IORT group (p=0·0002)
Higher occurrence of fat necrosis in IORT group (p=0·04)

Whelan TJ et al. Lancet 2019
Vicini FA et al. Lancet 2019
Meattini I et al. J Clin Oncol 2020
Meduri B et al. JCO 2023
Orecchia R et al. Lancet Oncol 2021

Results from RCTs: Meta-Analysis

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CLINICAL INVESTIGATION

A Meta-Analysis of Trials of Partial Breast Irradiation

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15 trials
16474 patients
Studies from 1982 to 2015
Most of patients: >60 y, T1N0, Grade 1-2, receiving Hormone therapy
Meta-analysis based on aggregate data from published randomized trials
To assess effectiveness of PBI and to compare different techniques

Goldberg M et al. Int J Radiation Oncol Biol Phys 2023

Results from RCTs: Meta-Analysis

Table 2 Randomized trials of partial versus whole breast irradiation: Radiation therapy details

	PBI				WBI		
Trial	**Technique**	**TV**	**PTV**	**Dose/fraction/time***	**Dose/fraction/time**	**Boost**	**Dose/fraction/time**
External beam without CT guidance							
Manchester (1993)[7,8]	Direct field 8-14 MeV	Tumor bed	NA	40-42.5 Gy/8 qd/10 d	40 Gy/15 qd/3 wk	None	
Yorkshire BCG (2005)[9]	Direct field or tangent electrons/Co^{60}/cesium	Tumor bed	NA	55 Gy/20 qd/28 d	40 Gy/15 qd/3 wk	Required	15 Gy/5 qd/1 wk
Brachytherapy							
NIO Budapest (2020)[14–17]	Multicatheter HDR (69%) Overall electron field (31%)	Tumor bed + 2 cm tumor bed + 2 cm	As per TV As per TV	36.4 Gy/7 bid/4 d 50 Gy/25 qd/25 d	50 Gy/25 qd/5 wk	None	
GEC-ESTRO (2016)[18,19]	Multicatheter HDR or PDR	Tumor bed + 2 cm		32 Gy/8 bid/4 d or 30.1 Gy/7 bid/4 d 50 Gy/0.6-0.8 Gy per h	50 Gy/25 qd/5 wk or 50.4 Gy/28 qd/5.5 wk	Required	10 Gy/5 qd/1 wk
Intraoperative							
ELIOT (2021)[20,21]	Electron applicator 6-9 MeV	Tumor bed	As per TV	21 Gy to 90% isodose	50 Gy/25 qd/5 wk	Required	10 Gy/5 qd/1 wk
TARGIT-A adaptive (2020)[11,12,22] TARGIT-A delayed (2020)[11,12,23]	Cylindrical orthovoltage 50 kV applicator + WBI if high-risk (adaptive)	Tumor bed	As per TV	20 Gy at surface/20-45 min (5-7 Gy at 1-cm depth) 40-56 Gy/15-28 qd/3-5.5 wk	40-56 Gy/15-28 qd/3-5.5 wk	Optional	10-11 Gy/4-8 qd/1-1.5 wk
External beam with CT planning							
Barcelona (2021)[24,25]	3D-CRT	Involved quadrant	NA	37.5 Gy/10 bid/5 d	48 Gy/24 qd/5 wk	Optional	10 Gy/5 qd/1 wk
Florence (2020)[26–28]	IMRT	Tumor bed + 1 cm	1 cm	30 Gy/5 qod/14 d	50 Gy/25 qd/5 wk	Required	10 Gy/5 qd/1 wk
NSABP B-39 (2019)[30,31]	Multicatheter brachytherapy HDR Single catheter brachytherapy HDR 3D-CRT	Tumor bed + 1.5 cm	1 cm	34 Gy/10 bid/5-8 d 34 Gy/10 bid/5-8 d 38.5 Gy/10 bid/5-8 d	50 Gy/25 qd/5 wk	Optional	10-14 Gy/5-7 qd/1-1.5 wk
RAPID (2019)[32,33]	3D-CRT or IMRT	Tumor bed + 1 cm	1 cm	38.5 Gy/10 bid/5-8 d	42.5 Gy/16 qd/3 wk or 50 Gy/25 qd/5 wk	Optional	10 Gy/4-5 qd/1 wk
IMPORT LOW (2017)[29]	IMRT	Tumor bed + 1.5 cm	1 cm	40 Gy/15 qd/3 wk	40 Gy/15 qd/3 wk	None	
Chandigarh (2020)[34]	3D-CRT	Tumor bed + 1 cm	1 cm	34 Gy/10 bid/5 d	40 Gy/16 qd/3 wk	Optional	10-16 Gy/5-8 qd/1-1.5 wk
HYPAB (2020)[36]	VMAT	Tumor bed + 1 cm	0.5 cm	30 Gy/5 qod/2 wk	40 Gy/15 qd/3 wk	Required	Simultaneous 8 Gy/15 qd/3 wk
DBCG PBI (2022)[35]	IMRT	Tumor bed + 1.5 cm	0.5 cm	40 Gy/15 qd/3 wk	40 Gy/15 qd/3 wk	None	

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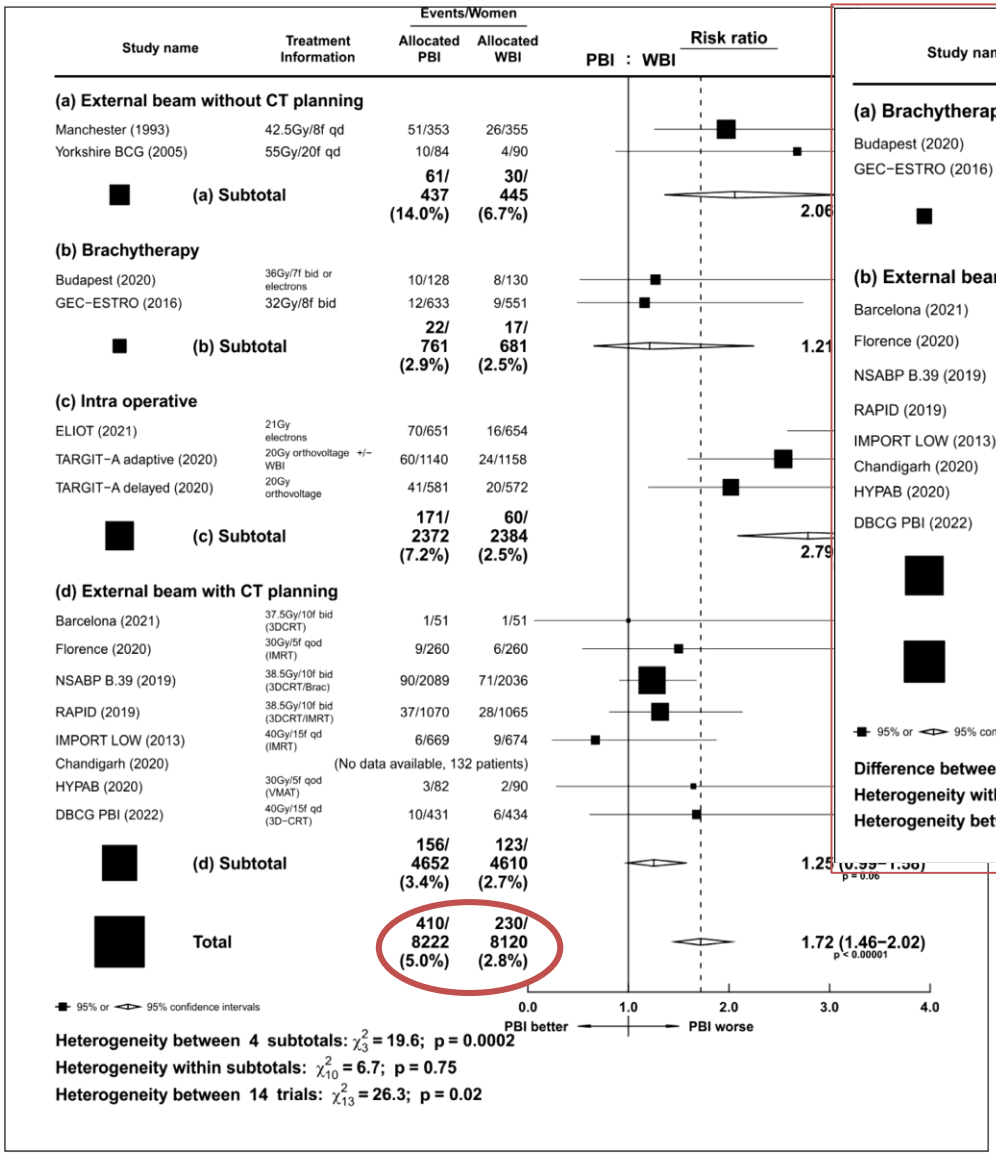
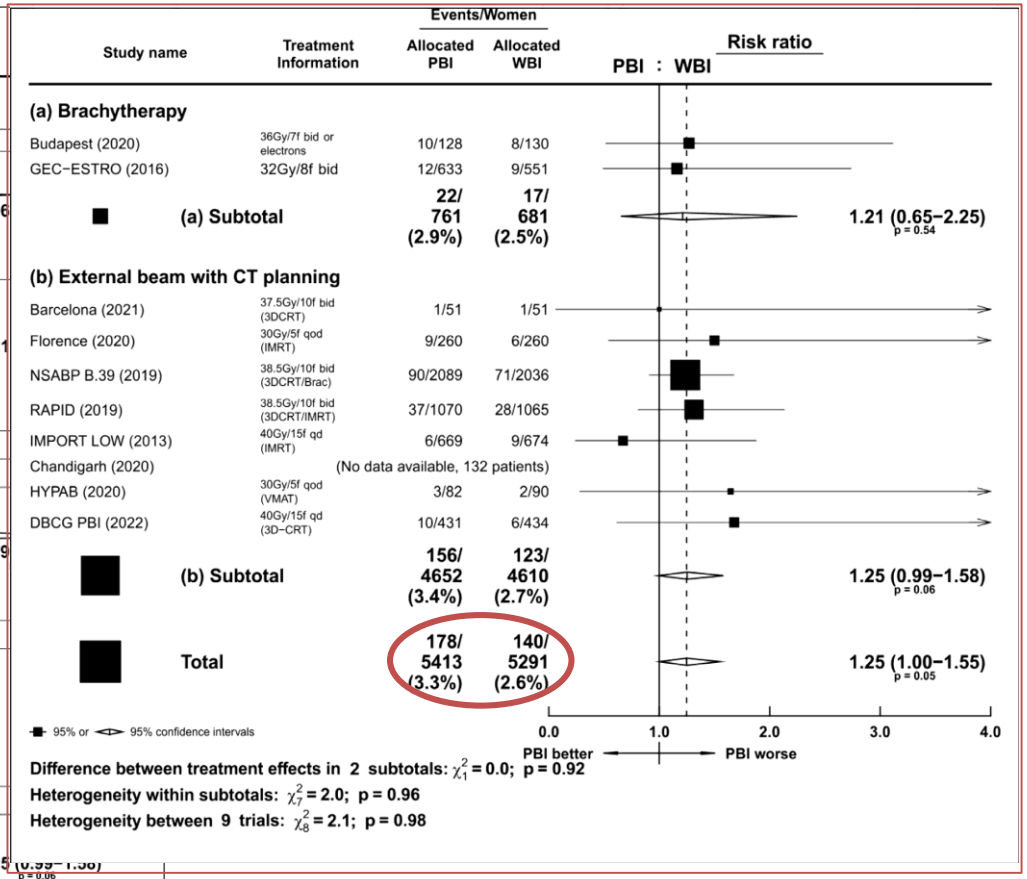
Results from RCTs: Meta-Analysis

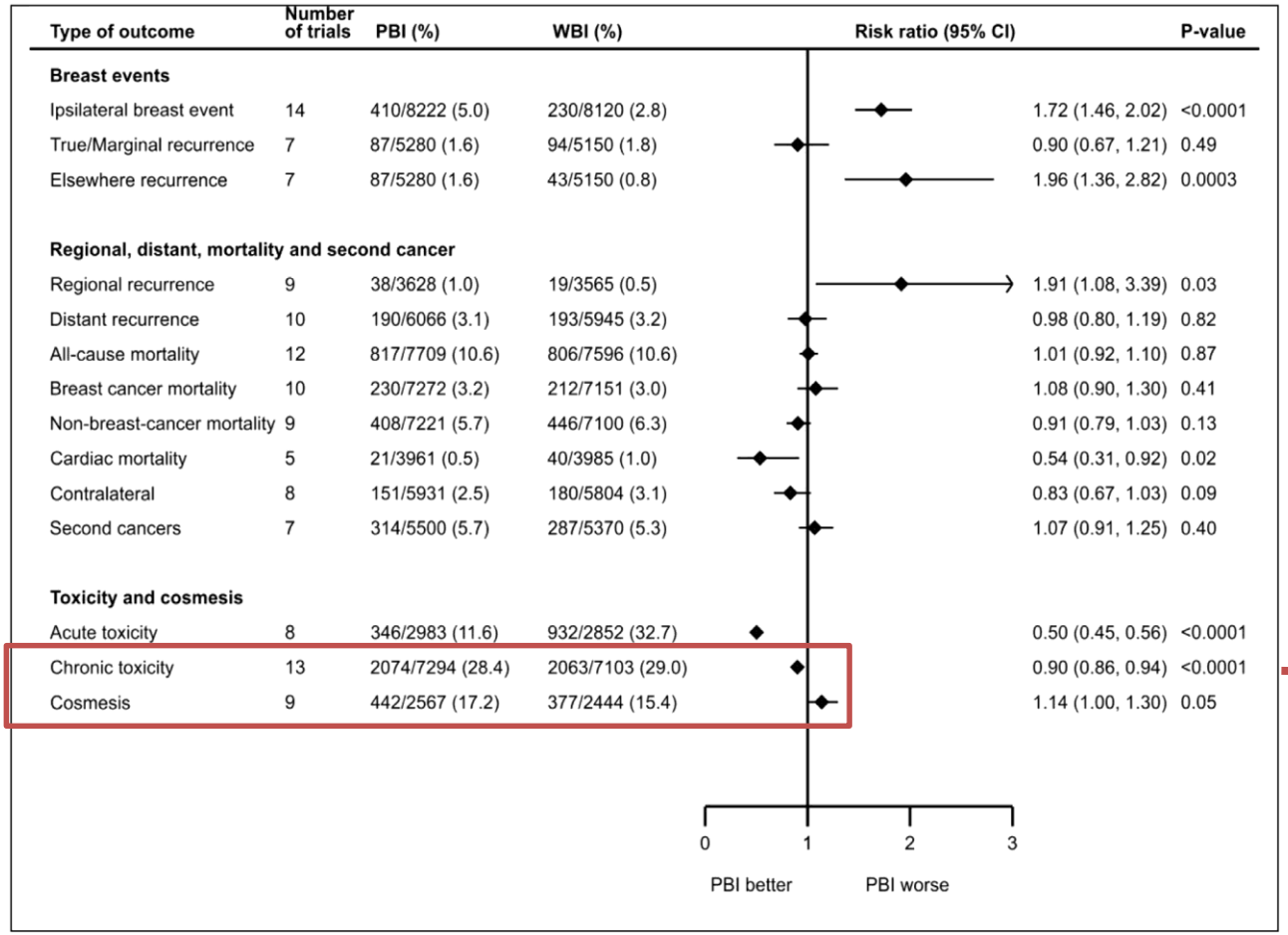




The absolute difference between groups for ipsilateral breast events was very small (<1%), supporting these approaches for women considering PBI

Goldberg M et al. Int J Radiation Oncol Biol Phys 2023

Results from RCTs: Meta-Analysis



Type of outcome	Number of trials	PBI (%)	WBI (%)	Risk ratio (95% CI)	P-value
Breast events					
Ipsilateral breast event	14	410/8222 (5.0)	230/8120 (2.8)	1.72 (1.46, 2.02)	<0.0001
True/Marginal recurrence	7	87/5280 (1.6)	94/5150 (1.8)	0.90 (0.67, 1.21)	0.49
Elsewhere recurrence	7	87/5280 (1.6)	43/5150 (0.8)	1.96 (1.36, 2.82)	0.0003
Regional, distant, mortality and second cancer					
Regional recurrence	9	38/3628 (1.0)	19/3565 (0.5)	1.91 (1.08, 3.39)	0.03
Distant recurrence	10	190/6066 (3.1)	193/5945 (3.2)	0.98 (0.80, 1.19)	0.82
All-cause mortality	12	817/7709 (10.6)	806/7596 (10.6)	1.01 (0.92, 1.10)	0.87
Breast cancer mortality	10	230/7272 (3.2)	212/7151 (3.0)	1.08 (0.90, 1.30)	0.41
Non-breast-cancer mortality	9	408/7221 (5.7)	446/7100 (6.3)	0.91 (0.79, 1.03)	0.13
Cardiac mortality	5	21/3961 (0.5)	40/3985 (1.0)	0.54 (0.31, 0.92)	0.02
Contralateral	8	151/5931 (2.5)	180/5804 (3.1)	0.83 (0.67, 1.03)	0.09
Second cancers	7	314/5500 (5.7)	287/5370 (5.3)	1.07 (0.91, 1.25)	0.40
Toxicity and cosmesis					
Acute toxicity	8	346/2983 (11.6)	932/2852 (32.7)	0.50 (0.45, 0.56)	<0.0001
Chronic toxicity	13	2074/7294 (28.4)	2063/7103 (29.0)	0.90 (0.86, 0.94)	<0.0001
Cosmesis	9	442/2567 (17.2)	377/2444 (15.4)	1.14 (1.00, 1.30)	0.05

Strongly influenced by the RAPID trial

Cardiac mortality LESS with PBI but the number of events was small
A trend for fewer contralateral breast cancers but not statistically significant

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Outline

- PBI techniques
- Literature data: Results from RCTs
- International guidelines and recommendations
- Future perspectives: preoperative radiotherapy

International guidelines and recommendations

European Society for Radiotherapy and Oncology Advisory Committee in Radiation Oncology Practice consensus recommendations on patient selection and dose and fractionation for external beam radiotherapy in early breast cancer

Icro Meattini, Carlotta Becherini, Liesbeth Boersma, Orit Kaidar-Person, Gustavo Nader Marta, Angel Montero, Birgitte Vrou Offersen, Marianne C Aznar, Claus Belka, Adrian Murray Brunt, Samantha Dicuonzo, Pierfrancesco Franco, Mechthild Krause, Mairead MacKenzie, Tanja Marinko, Livia Marrazzo, Ivica Ratosa, Astrid Scholten, Elżbieta Senkus, Hilary Stobart, Philip Poortmans, Charlotte E Coles**

A consensus to harmonise expert opinions about hypofractionation

It addresses dose and fractionation for whole and partial breast irradiation, chest wall irradiation, and regional nodal irradiation

Recommendations for Ultrafractionation (five fractions) and well-defined selection criteria for PBI were reported

Meattini I al. Lancet Oncol 2022

International guidelines and recommendations

	Consensus agreement	Strength
(Continued from previous column)		
4. Partial breast irradiation–suitable patient selection for external beam radiotherapy		
I. Luminal-like subtypes small tumour (≤3 cm)	91·3%	Strong consensus
II. Clear surgical margins (>2 mm)	95·6%	Strong consensus
III. Nodal status	..	..
IIIa. Node negative	100%	Unanimous consensus
IIIb. Node negative (including isolated tumour cells)	82·6%	Consensus
IV. Absence of lymph vascular space invasion	87·0%	Consensus
V. Non-lobular invasive carcinoma	87·0%	Consensus
VI. Tumour grade 1–2	91·3%	Strong consensus
VII. Low-to-intermediate grade DCIS, sized ≤2·5 cm, clear surgical margins (≥3 mm)	78·2%	Consensus
VIII. Age 50 years or more	87·0%	Consensus
IX. Unicentric or unifocal	100%	Unanimous consensus
X. Primary systemic therapy and neoadjuvant chemotherapy is considered an exclusion criterion for partial breast irradiation	78·2%	Consensus
5. Partial breast irradiation–dose and fractionation		
5a. Moderate hypofractionation (40 Gy in 15 fractions) and ultrahypofractionation (26–30 Gy in five fractions) represent acceptable schedules for external beam partial breast irradiation	91·6%	Strong consensus
5b. Twice a day external beam partial breast irradiation dose and fractionations similar to those used in the RAPID trial should not be offered	86·9%	Consensus

DCIS=ductal carcinoma in situ.

Table 1: **Final statements voting agreement and strength of consensus**

Panel: **Final consensus statements**

1. Whole breast irradiation

a Moderate hypofractionated whole breast irradiation should be offered regardless of age at breast cancer diagnosis, pathological tumour stage, breast cancer biology, surgical margins status, tumour bed boost, breast size, invasive or pre-invasive ductal carcinoma in situ (DCIS) disease, oncoplastic breast conserving surgery, and use of systemic therapy

b Ultrahypofractionated (26 Gy in five fractions) whole breast irradiation can be offered as (1) standard of care or (2) within a randomised controlled trial or prospective registration cohort

2. Chest wall irradiation

a Moderate hypofractionation can be offered for chest wall irradiation without breast reconstruction

b Moderate hypofractionation can be offered for chest wall irradiation regardless of time and type of breast reconstruction

c Ultrahypofractionation (26 Gy in five fractions) for chest wall irradiation without breast reconstruction can be offered as (1) standard of care or (2) within a randomised controlled trial or prospective registration cohort

d Ultrahypofractionation (26 Gy in five fractions) for chest wall irradiation after breast reconstruction can be offered within a randomised controlled trial or prospective registration cohort

3. Nodal irradiation

a Moderate hypofractionation should be offered for nodal irradiation

b Ultrahypofractionation (26 Gy in five fractions) should not be offered for nodal irradiation until ongoing trials results are reported

4. Partial breast irradiation–patient selection for external beam radiotherapy

Low risk-features suitable for partial breast irradiation are: luminal-like subtypes small tumour (≤3 cm), absence of lymph vascular space invasion, non-lobular invasive carcinoma, tumour grade 1–2, low-to-intermediate grade DCIS (sized ≤2·5 cm with clear surgical margins ≥3 mm), age at diagnosis 50 years or more, unicentric or unifocal lesion, clear surgical margins (>2 mm), node negative (including isolated tumour cells), and no use of primary systemic therapy and neoadjuvant chemotherapy

5. Partial breast irradiation–dose and fractionation

a Moderate hypofractionation (40 Gy in 15 fractions) and ultrahypofractionation (26–30 Gy in five fractions) represent acceptable schedules for external beam partial breast irradiation

b Twice a day external beam partial breast irradiation dose and fractionations similar to those used in the RAPID trial should not be offered

DCIS=ductal carcinoma in situ.

Meattini I al. Lancet Oncol 2022

International guidelines and recommendations

Practice Guideline

Partial Breast Irradiation for Patients With Early-Stage Invasive Breast Cancer or Ductal Carcinoma In Situ: An ASTRO Clinical Practice Guideline

Simona F. Shaitelman, MD, EdM,[a,*] Bethany M. Anderson, MD,[b] Douglas W. Arthur, MD,[c] Jose G. Bazan, MD,[d] Jennifer R. Bellon, MD,[e] Lisa Bradfield, BA,[f] Charlotte E. Coles, MRCP, FRCR, PhD,[g] Naamit K. Gerber, MD,[h] Madeera Kathpal, DO,[i] Leonard Kim, MS, AMusD,[j] Christine Laronga, MD,[k] Icro Meattini, MD,[l] Elizabeth M. Nichols, MD,[m] Lori J. Pierce, MD,[n] Matthew M. Poppe, MD,[o] Patricia A. Spears, BS,[p] Shaveta Vinayak, MD,[q] Timothy Whelan, BM BCh,[r] and Janice A. Lyons, MD[s]

ASTRO convened a task force to address **4 key questions** focused on the **appropriate indications and techniques for PBI** as an alternative to whole breast irradiation (WBI) to result in similar rates of ipsilateral breast recurrence (IBR) and toxicity outcomes.

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International guidelines and recommendations

3-dimensional conformal radiation therapy
Intensity modulated radiation therapy
Multicatheter brachytherapy
Single-entry brachytherapy

Daily or every-other-day external beam PBI regimen

Table 5 Appropriate PBI dose-fractionation regimens

KQ3 Recommendations	Strength of Recommendation	Quality of Evidence (refs)
1. For patients with early-stage invasive breast cancer or DCIS receiving external beam PBI, 3000 cGy in 5 once daily fractions delivered on nonconsecutive days within 2 weeks is recommended.	Strong	Moderate [12,14]
2. For patients with early-stage invasive breast cancer or DCIS receiving external beam PBI, 4005 cGy in 15 once daily fractions over 3 weeks is recommended.	Strong	Moderate [9]
3. For patients with early-stage invasive breast cancer or DCIS receiving PBI with HDR brachytherapy, 3010 cGy in 7 fractions, 3200 cGy in 8 fractions, 3400 cGy in 10 fractions delivered twice daily or 5000 cGy with 160-180 cGy/hour PDR is recommended. Implementation remark: Single-entry PBI trials used 3400 cGy in 10 fractions delivered twice daily.	Strong	Moderate [7,18]

Intraoperative radiation therapy alone

Twice-daily external beam PBI regimens

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International guidelines and recommendations

Table 3 Indications for PBI as an alternative to WBI

KQ1 Recommendations	Strength of Recommendation	Quality of Evidence (refs)
Early-stage invasive breast cancer*		
1. PBI is recommended for patients with early-stage invasive breast cancer with all of the following factors: • Grade 1-2 disease • ER-positive histology • Age ≥40 years • Tumor size ≤2 cm	Strong	High (for grade, histology, & age ≥50 years) Moderate (for age 40-49 years & size) 7-9,12-15,18
2. PBI is conditionally recommended for patients with early… cancer with the following factors: • Grade 3 disease or • ER-negative histology or • Size >2 - ≤3 cm Implementation remark: PBI may not be appropriate wh… factors are present, given the possibility of a higher recur…		
3. PBI is conditionally **not** recommended for patients with … breast cancer with any of the following factors: • HER2-positive tumors not receiving anti-HER2 thera… • Lymphovascular invasion • Lobular histology Implementation remark: Given low patient numbers acc… risk of recurrence with PBI is possible.		
4. PBI is **not** recommended for patients with early-stage inv… with any of the following factors: • Positive lymph nodes • Positive surgical margins • Known germline BRCA1/2 mutation • Age <40 years		
DCIS		
5. PBI is recommended for patients with DCIS with all of the following factors: • Low-to-intermediate grade • Age ≥40 years • Size ≤2 cm Implementation remark: While represented in the RCTs, there was a lack of subgroup analyses for pathologic and clinical features of patients treated with DCIS.	Strong	Expert Opinion
6. PBI is conditionally recommended for patients with DCIS with the following factors: • High grade or • Size >2 - ≤3 cm Implementation remark: PBI may not be appropriate when both of these factors are present, given the possibility of a higher recurrence risk.	Conditional	Expert Opinion
7. PBI is **not** recommended for patients with DCIS with any of the following factors: • Positive surgical margins • Known germline BRCA1/2 mutation • Age <40 years	Strong	Expert Opinion

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Future perspectives: preoperative radiotherapy

Pre-operative partial breast irradiation: revolutionizing radiation treatment for women with early stage breast cancer

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Early data show similar local control without evidence of increased toxicity or worsening cosmesis, as compared to postoperative PBI or standard whole breast irradiation

Possible clinical advantages:
-reducing the treatment field
-increasing the number of patients eligible for PBI
-identifying biomarkers of response to radiation
-improving the rates of breast conservation and treatment compliance

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Future perspectives: preoperative radiotherapy

Published preoperative PBI/SBRT trials.

Study (year)	Eligibility	N	Follow-up (months)	RT schedule	Surgery timing	pCR	Efficacy	Toxicity
Bondiau et al. (2013) [81]	Not suitable for BCS, unifocal, HER2 negative	26	30	19.5–31.5Gy/3 fractions (robotic SBRT)	4–8 weeks after the last CT	36%	96% ORR, 92% BCS rate	None
Horton et al. (2015) [82]	Age >55 years, T1 or low-intermediate DCIS ≤2 cm, cN0, ER+ and/or PgR+, HER2-	32	23	15–21Gy/1 fraction (IMRT)	within 10 days after RT	NR	Increase in post-radiation vascular permeability, decreased cellular density	13 grade 2; 2 grade 3
Nichols et al. (2017) [80]	<3 cm, cN0, unifocal invasive	27	43.2	38.5Gy/10 fractions (3DCRT)	>3 weeks after RT	15%	Ki-67 decrease after RT in 70.4%, ORR 88.9%	1-year PRCO fair and poor in 17% and 5%, respectively
van der Leij et al. (2015) [78]	Age >60 years, ≤3 cm, invasive, unifocal, non-lobular, negative SNB	70	23	40Gy/10 fractions (3DCRT or IMRT or VMAT)	6 weeks after RT	NR	2 IBTR	At 12 months: 70-11% mild-moderate induration At 24 months: 46% mild-moderate fibrosis
Guidolin et al. (2019) [83]	≤3 cm, ductal, any grade, unifocal ER+, cN0, postmenopausal status	27	16.2	21Gy/1 fraction	1 week after RT	NR	All patients free from relapse	No significant differences in HRQoL and PRCO
Meattini et al. (2022) [32]	Age ≥50 years; hormone receptor positive and HER2-; any grade; unifocal; maximum size 25 mm; clinically node negative	22	18	21Gy/1 fraction (robotic radiosurgery)	2 weeks after RT	9%	No patients have locoregional neither distant recurrence	No acute toxicity greater than G2 was recorded, cosmetic results were scored excellent/good in 14 patients

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Future perspectives: preoperative radiotherapy

Summary of ongoing and recently accrued postoperative and postoperative APBI studies

Institution (TRIAL)	Phase	APBI	Dose	Clinical Trials.gov ID	Notes	Study start date	Primary outcomes
Juravinski Cancer Center	Phase I	Pre-operative	8 Gy ×5 EOD	NCT02065960	SBRT	February 2014	Feasibility
Georgetown University	Phase I–II	Adjuvant	6 Gy ×5	NCT02365714	CK SBRT	February 2015	Feasibility
Laurentian University Jewish General Hospital	Phase II	Pre-operative	21 Gy ×1	NCT02212860	SBRT	March 2015	Toxicity
Georgetown University (SIGNAL TRIAL)	Multi-institutional registry trial	Adjuvant	5 fractions	NCT02457117	CK SBRT	May 2015	Local failure
Duke University	Phase II	Pre-operative	21 Gy ×1	NCT02482376	SBRT	October 2015	Cosmesis
University of Texas Southwestern	Phase I	Adjuvant dose escalation	22.5–30 Gy ×1	NCT02685332	SBRT	March 2016	Dose tolerance
The Netherlands Cancer Institute, Institut Gustave Roussy, Karolinska Institut, University Medical Centre Utrecht (PAPBI Trial)	Phase II	Pre-operative	4 Gy ×10 or 5 Gy ×6	NCT01024582	3-DCRT, IMRT	April 2010	Local failure
Maisonneuve-Rosemont Hospital (SPORT TRIAL)	Phase I	Pre-operative	15, 18, or 20 Gy ×1	NCT01717261	SBRT	August 2012	Acute toxicity
University Medical Center Utrecht (ABLATIVE TRIAL)	Phase I	Pre-operative → BCS (months	15-20 Gy ×1	NCT02316561	Partial breast IMRT	October 2014	pCR
Ohio State University	Phase I, pilot	Pre-operative	10 fractions BID for 5 days	NCT02186470	IMRT, prone	June 2015	Acute toxicity
Medical College of Wisconsin	Phase II	Pre-operative	5 fractions	NCT02728076	3-DCRT, MRI guided	May 2016	Postoperative complications
The Netherlands Cancer Institute (PAPBI-2)	Phase III	Pre *vs.* postoperative APBI	28.5 Gy in 5 fractions	NCT02913729	Partial breast IMRT	November 2016	Cosmesis
University Hospital, Grenoble (NeoAPBI 01)	Phase II randomized	Chemo *vs.* chemo + postoperative APBI	25 Gy in 10 BID fractions	NCT02806258	Partial breast 3-DCRT	March 2016	pCR

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Conclusions

- WBI+BCS reduces the risk of local recurrence and the breast cancer death rate compared with BCS alone
- PBI represents an alternative to whole breast irradiation (WBI) **to reduce radiation exposure to the whole breast and surrounding organs**
- Following **well-defined selection criteria**, PBI showed similar local control and survival outcomes and a significant reduction of acute toxicity
- The effect on late toxicity varied by **technique and dose/fractionation**
- **Pre-operative accelerated PBI (P-APBI)** appears to be safe and has a number of advantages as compared to APBI (adjuvant setting), especially in traslational research (biomarkers of response to radiation) in association with oncoplastic surgery

GRAZIE PER L'ATTENZIONE