



## **Radiotherapy after mastectomy and in BRCA positive patients**

Radioterapia dopo mastectomia e in pazienti BRCA mutate

**Martin Maffei**

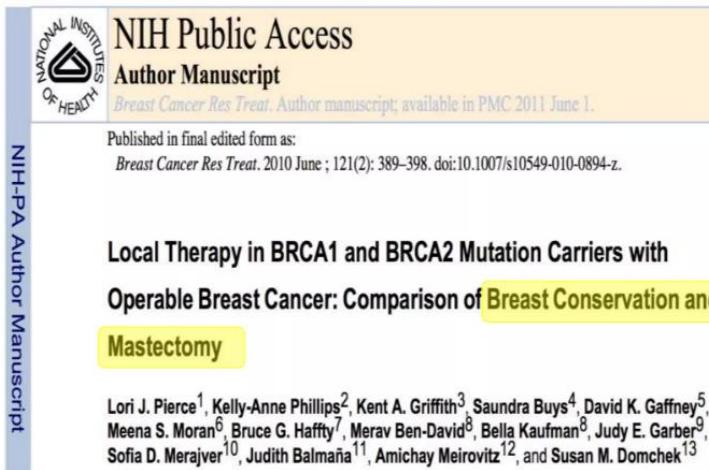
**Mariarosa Di Biase**

**Sarah Reiner**

Dienst für onkologische Strahlentherapie - Servizio di Radioterapia oncologica

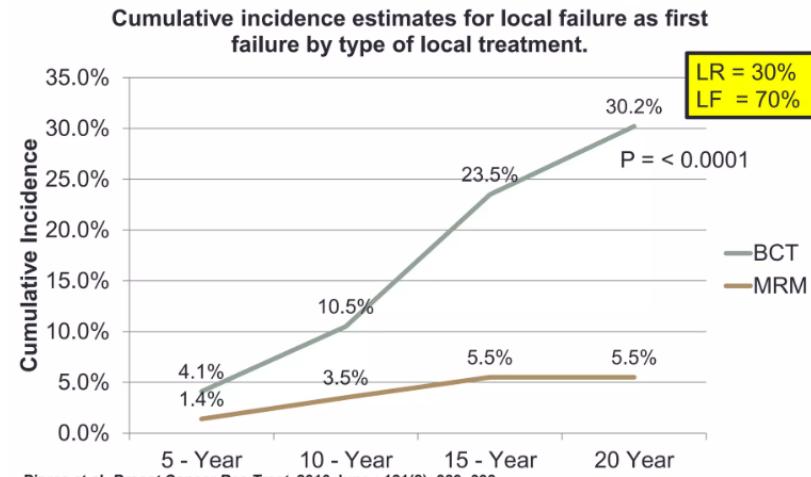


## Breast Cancer with BRCA Mutation: Choice of Loco-Regional Management:

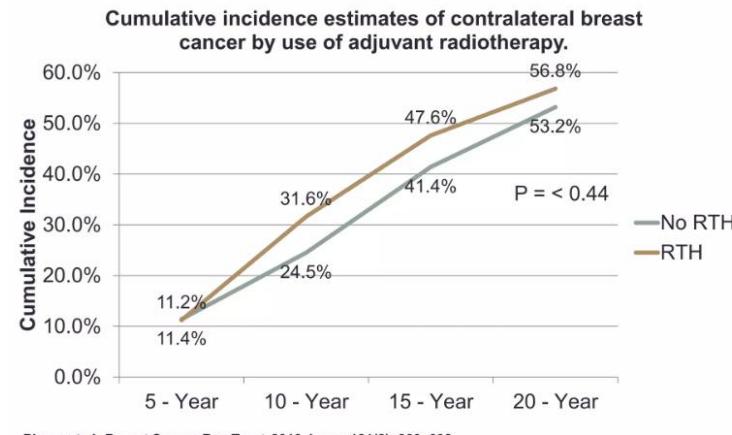


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## Breast Cancer with BRCA Mutation: Choice of Loco-Regional Management:



## Breast Cancer with BRCA Mutation: Choice of Loco-Regional Management:





## Indicazione a RT dopo mastectomia

> 3 linfonodi positivi

1-3 linfonodi positivi (alto rischio)

1-3 linfonodi positivi (basso rischio)

T3 / T4

pT3 pN0 R0 (senza ulteriori fattori di rischio)

Resezione R0 non ottenibile (per tumori invasivi)

In pazienti giovani con un alto rischio di recidiva

Le indicazioni per la PMRT e la RT regionale sono indipendenti dalla terapia sistemica adiuvante  
Carcinoma infiammatorio: RT della parete toracica e delle regioni di drenaggio linfatico

**AIRO Breast Cancer Group  
Best Clinical Practice 2022 Update**





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Guidelines Breast  
Version 2024.1D

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### Radiotherapy of the Chest Wall After Mastectomy (PMRT) in Case of 1-3 Axillary Lymph Node Metastases

PMRT  
can be omitted  
**LoE 3b B AGO +**

ER pos, G1, HER2 neg, pT1  
(at least 3 criteria present)

Kyndi et al. 2009

PMRT  
to be discussed  
**LoE 3b B AGO +/-**

Patients, who  
don't fulfill  
the mentioned  
criteria for  
high or low  
risk

PMRT  
recommended  
**LoE 3b B AGO +**

≥ 45 y. AND > 25% pos. ax. Lnn in case of  
axillary dissection OR  
<45 y. AND (ER neg. OR>25% pos. ax. Lnn in case  
of axillary dissection OR medial tumor location)

Truong et al. 2005

< 40 y. OR  
HER2 pos. OR  
lymphovascular invasion

Shen H et al. 2015

G3 OR  
lymphovascular invasion OR  
triple negative

Different publications

Comment: In case of an indication for radiotherapy of regional lymph nodes,  
radiotherapy of the chest wall should also be administered



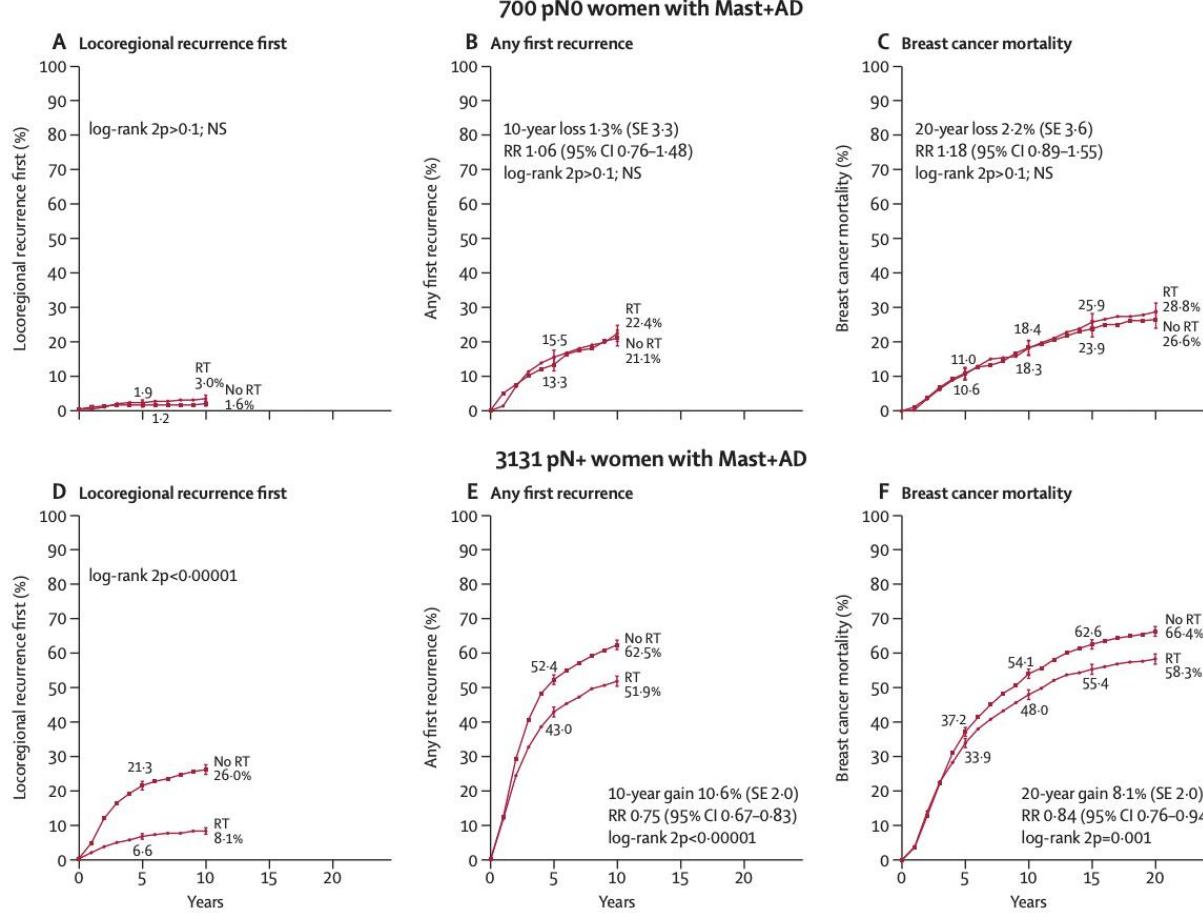
PMRT benefit in 1-3 and  $\geq 4$  nodes

# **Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials**

*EBCTCG (Early Breast Cancer Trialists' Collaborative Group)\**



## PMRT benefit in 1-3 and $\geq 4$ nodes



**pN0** • no benefit with RT for recurrence or BCM

**Any N+** •

5-yr LRR 21% vs. 7% •

10-yr LRR 26% vs. 8% •

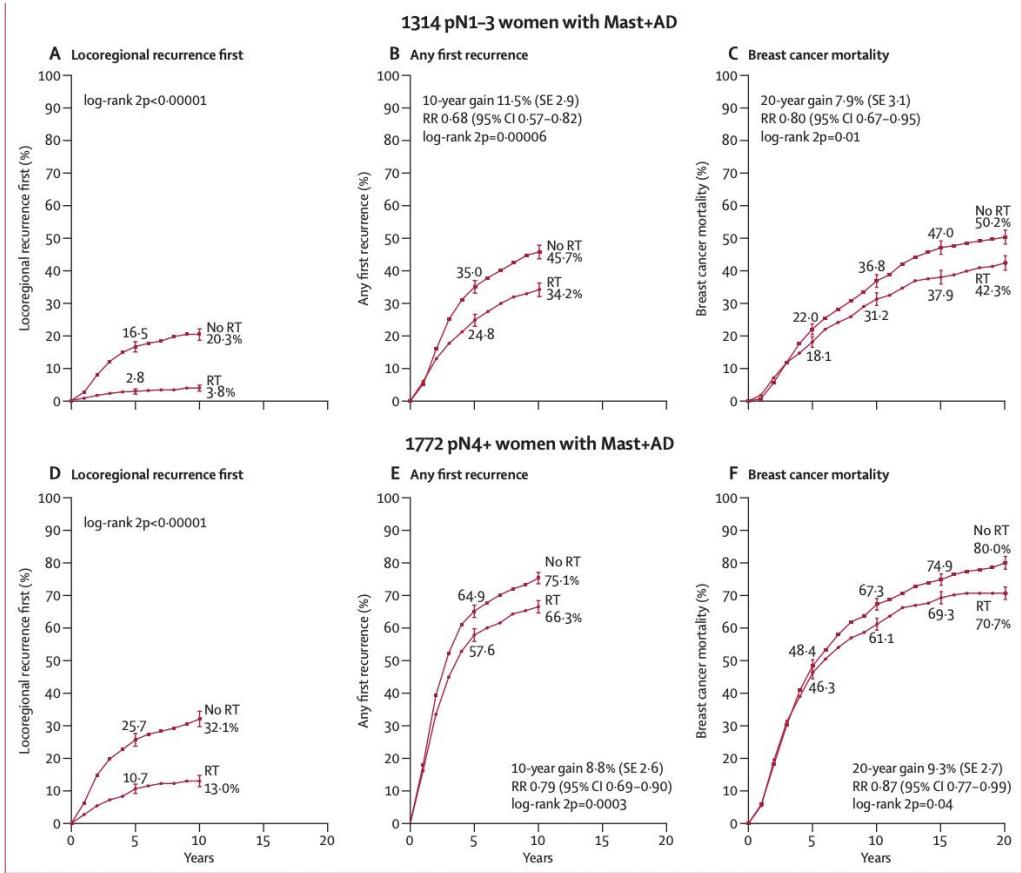
5-yr BCM 37% vs. 34% •

10-yr BCM 54% vs. 48% •

20-yr BCM 66% vs. 58%



## PMRT benefit in 1-3 and $\geq 4$ nodes

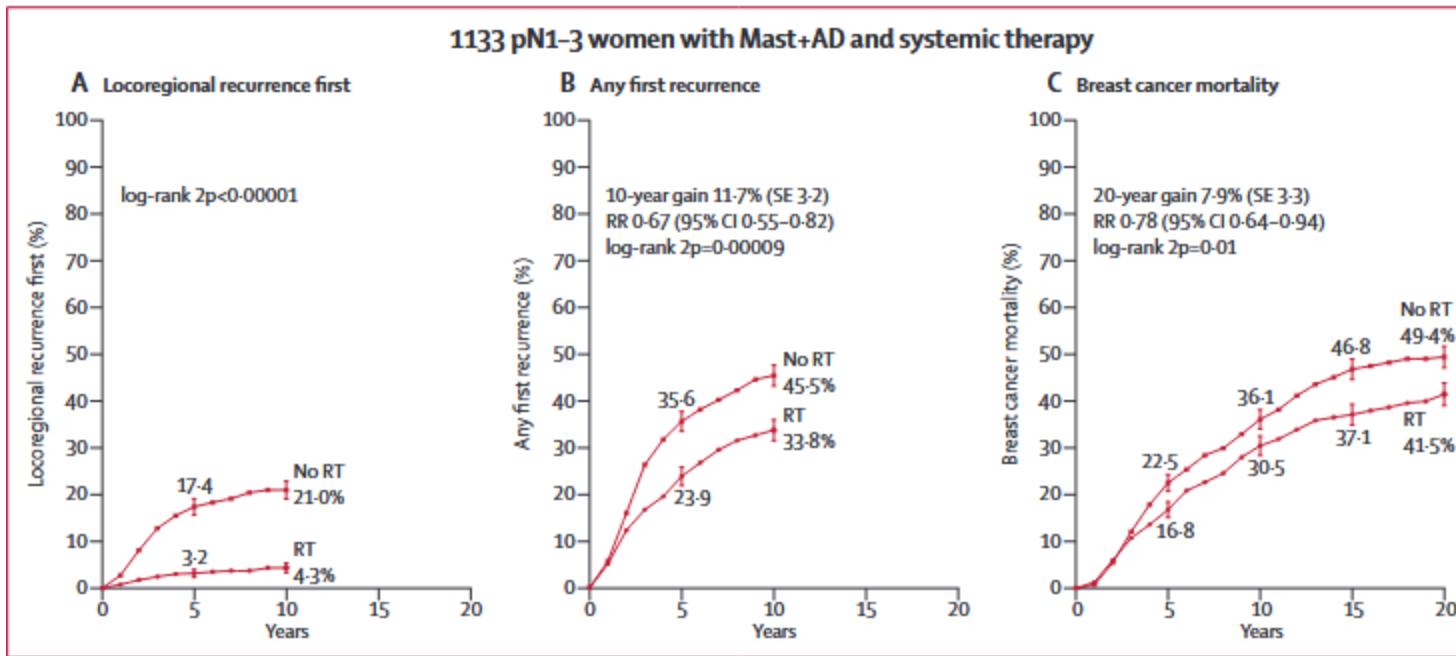


### 1-3 nodes •

- 5-yr LRR 17% vs. 3%
- 10-yr LRR: 20% vs. 4% •
- 5-yr BCM 22% vs. 18% •
- 10-yr BCM 37% vs. 31% •
- 20-yr BCM 50% vs. 42%



## PMRT benefit in 1-3 and $\geq 4$ nodes



**Figure 5:** Effect of radiotherapy (RT) after mastectomy and axillary dissection (Mast+AD) on 10-year risks of locoregional and overall recurrence and on 20-year risk of breast cancer mortality in 1133 women with one to three pathologically positive nodes (pN1-3) in trials in which systemic therapy was given to both randomised treatment groups

Analyses of locoregional recurrence first ignore distant recurrences, see appendix pp 8-9 for details. See appendix p 22 for analyses of both locoregional and distant recurrences, and appendix p 21 for analyses of overall mortality. RR=rate ratio. Vertical lines indicate 1 SE above or below the 5, 10, 15, and 20 year percentages.

- RT also reduces DM
- Results consistent in those who received chemotherapy or ET (CMF or TAM)



## PMRT benefit in 1-3 and $\geq 4$ nodes

La PMRT : > LRR in 1-3 nodi e  $\geq 4$  nodi.

Gli studi erano precedenti all'era di Her2. Gli autori commentano nella discussione che da questi studi le tecniche sono migliorate, anche per quanto riguarda la terapia sistematica mirata, la dissezione e il sezionamento linfonodale, la terapia endocrina e anche le tecniche di RT. Tutte le terapie sono migliorate, compresa la RT, soprattutto per quanto riguarda le tecniche per evitare il cuore.



## PMRT benefit in 1-3 and $\geq 4$ nodes

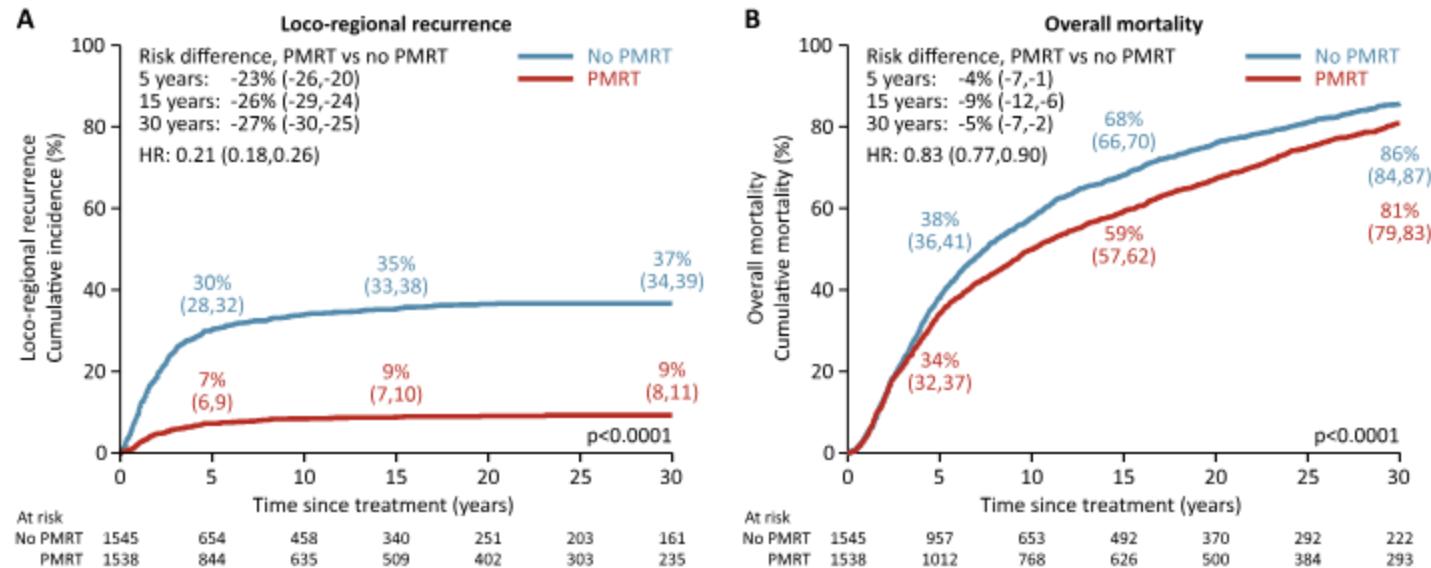
Original Article

Postmastectomy radiotherapy in high-risk breast cancer patients given adjuvant systemic therapy. A 30-year long-term report from the Danish breast cancer cooperative group DBCG 82bc trial <sup>☆</sup>



Marie Overgaard <sup>a</sup>, Hanne Melgaard Nielsen <sup>b</sup>, Trine Tramm <sup>c</sup>, Inger Højris <sup>b</sup>, Trine Lønbo Grantzau <sup>a</sup>, Jan Alsner <sup>a</sup>, Birgitte Vrou Offersen <sup>a,b</sup>, Jens Overgaard <sup>a,\*</sup>, on behalf of the DBCG Radiotherapy Group <sup>1</sup>

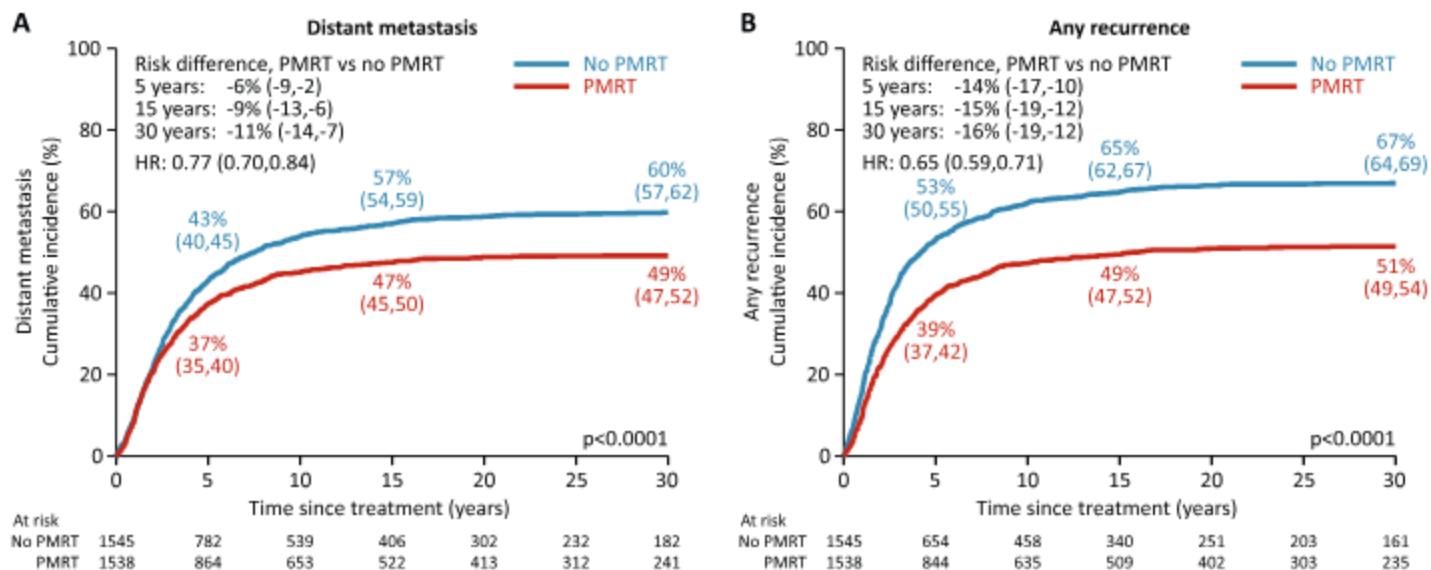
<sup>a</sup>Department of Experimental Clinical Oncology, Aarhus University Hospital, Denmark; <sup>b</sup>Department of Oncology, Aarhus University Hospital; and <sup>c</sup>Department of Pathology, Aarhus University Hospital, Denmark



**Fig. 1.** Effect of radiotherapy on locoregional recurrence (A) and overall mortality (B).

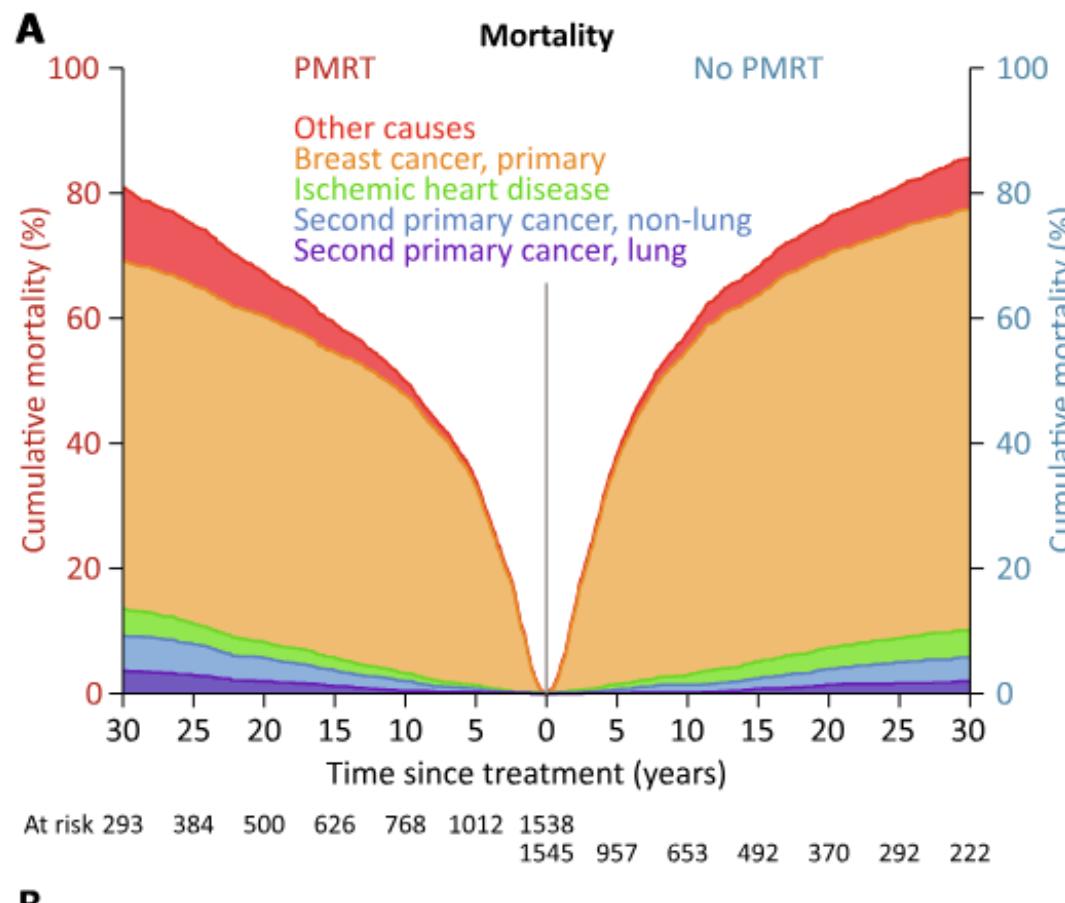


## PMRT benefit in 1-3 and $\geq 4$ nodes





## PMRT benefit in 1-3 and $\geq 4$ nodes





TAILOR RT (protocol)	<a href="#">Canadian Cancer Trials Group protocol</a>	2140	Oncotype <18, ER+, Her2- 1-3 LNs after LND, or 1-2 LNs after SLNB + BCS, or 1 LN after SLNB + mastectomy	→no RT (except WBRT for BCS) vs. →WBRT+RNI or PMRT+RNI  (no neoadj chemo)  16 fx hypofx or 25 fx conventional permitted	Ongoing trial  Primary endpoint: BCRFI  Secondary endpoints: DFS, BCM, OS, LRRFI, toxicity, PROs, QOL, cost effectiveness	<p>RECRUITING <small>i</small></p> <p><b>Regional Radiotherapy in Biomarker Low-Risk Node Positive and T3N0 Breast Cancer (TAILOR RT)</b></p> <p><a href="#">ClinicalTrials.gov ID</a> <small>i</small> NCT03488693</p> <p><b>Sponsor</b> <small>i</small> Canadian Cancer Trials Group</p> <p>Information provided by <small>i</small> Canadian Cancer Trials Group (Responsible Party)</p> <p>Last Update Posted <small>i</small> 2024-06-14</p> <p>indication. Future directions perhaps should include evaluating omission of endocrine therapy in those with low Oncotype.</p> <p>For the RNI arm: Heart, left sided mean <math>\leq</math>3 Gy Heart, left sided V25 <math>\leq</math>10% (variation acc Mean <math>\leq</math>5 Gy, V30 <math>&lt;</math>10%) Ipsi lung V20 <math>\leq</math>35%</p>
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## PMRT benefit after NSCT



Pre terapia	Post terapia	RT-BET	PMRT	RT-LAW*	Oxford	
		AGO	AGO	AGO	LoE	GR
<b>Lokal fortgeschritten</b>	<b>pCR / keine pCR</b>	<b>++</b>	<b>++</b>	<b>++</b>	<b>1a/1a/1a</b>	<b>A/A/A</b>
<b>cT1-3 cN1**</b>	<b>ypT+ ypN0</b>	<b>++</b>	<b>+</b>	<b>+/-<sup>1</sup></b>	<b>1a/1b/1b</b>	<b>A/B/B</b>
<b>cT1-3 cN1**</b>	<b>ypT0/is ypN0</b>	<b>++</b>	<b>+/-<sup>1</sup></b>	<b>+/-<sup>1</sup></b>	<b>1a/1b/1b</b>	<b>A/B/B</b>
<b>cT1-3 cN0 / cN1** (Sonogr. obligat)</b>	<b>ypN+ o. ypT3/4</b>	<b>++</b>	<b>+</b>	<b>+</b>	<b>1a/2b/2b</b>	<b>A/B/B</b>
<b>cT1-3 cN0 (Sonogr. obligat)</b>	<b>ypT0/is ypN0</b>	<b>++</b>	<b>-</b>	<b>-</b>	<b>1a/2b/2b</b>	<b>A/B/B</b>
<b>cT1-3 cN0 (Sonogr. obligat)</b>	<b>ypT1-2 ypN0</b>	<b>++</b>	<b>-</b>	<b>-</b>	<b>1a/2b/2b</b>	<b>A/B/B</b>

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RT moderata ipofrazionata (dose totale circa 40 Gy in circa 15/16 frazioni in circa 3 settimane).

Dopo la ricostruzione del seno

RT ultra-ipofrazionata (dose totale 26 Gy, cioè 5 frazioni in una settimana = 1 frazione)

RT convenzionale frazionata (dose totale circa 50 Gy in circa 25-28 frazioni in circa 5 settimane = 1 frazione/settimana).



## cosa è la radioterapia





## Chi lavora in radioterapia

Radiooncologo



Fisico



Tecnico / infermiera





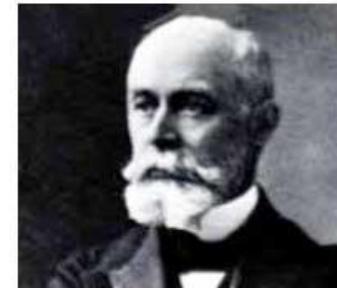
## storia

- 1885 scoperta dei raggi X da Wilhelm Conrad Röntgen



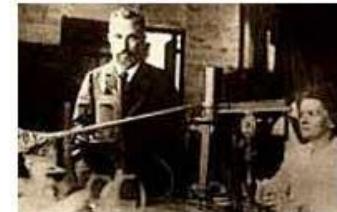
**W.C. Roentgen**

Scoperta dei Raggi X nel 1895  
Premio Nobel per la fisica nel 1901



**H. Becquerel**

Scoperta della radioattività dell'uranio.  
Premio Nobel per la fisica nel 1903



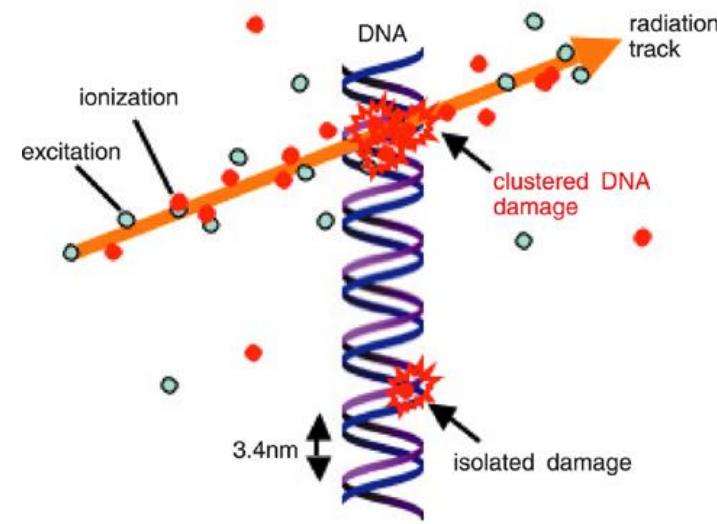
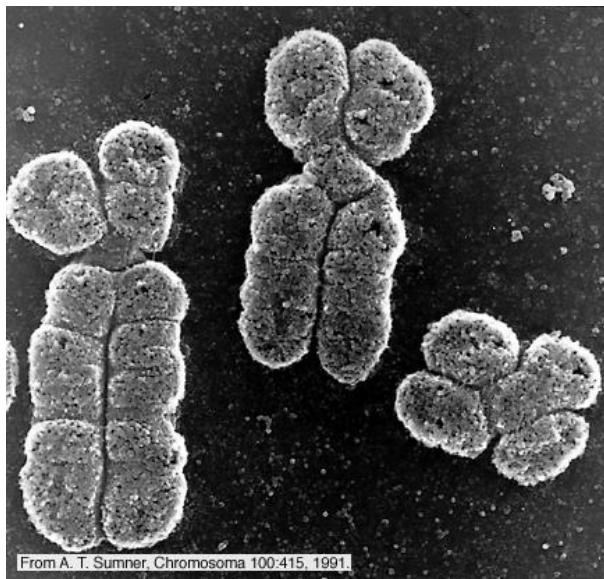
**Marie e Pierre Curie**

nell'hangar di Rue Lhomond (1898). Scoperta della radioattività del polonio e del radio.  
Premio Nobel per la fisica nel 1903





## Come funziona





## Procedura di radioterapia

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presentazione nel tumorboard – la riunione multidisciplinare



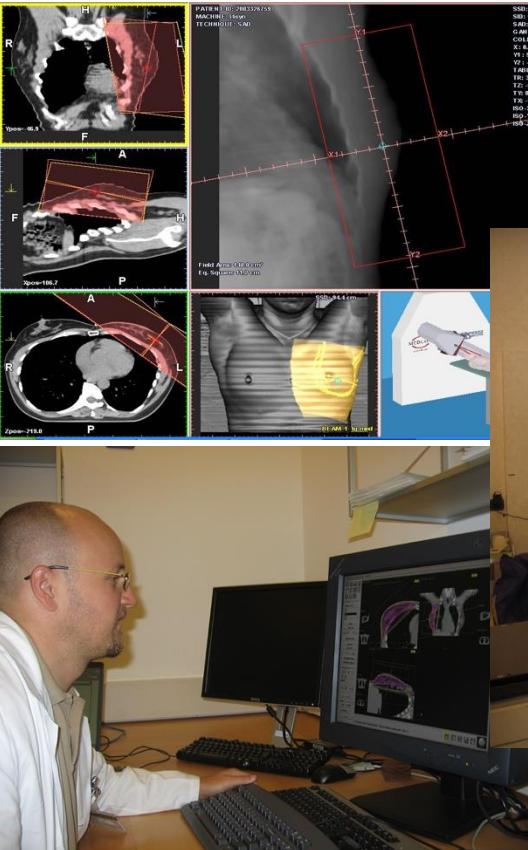


## Procedura di radioterapia



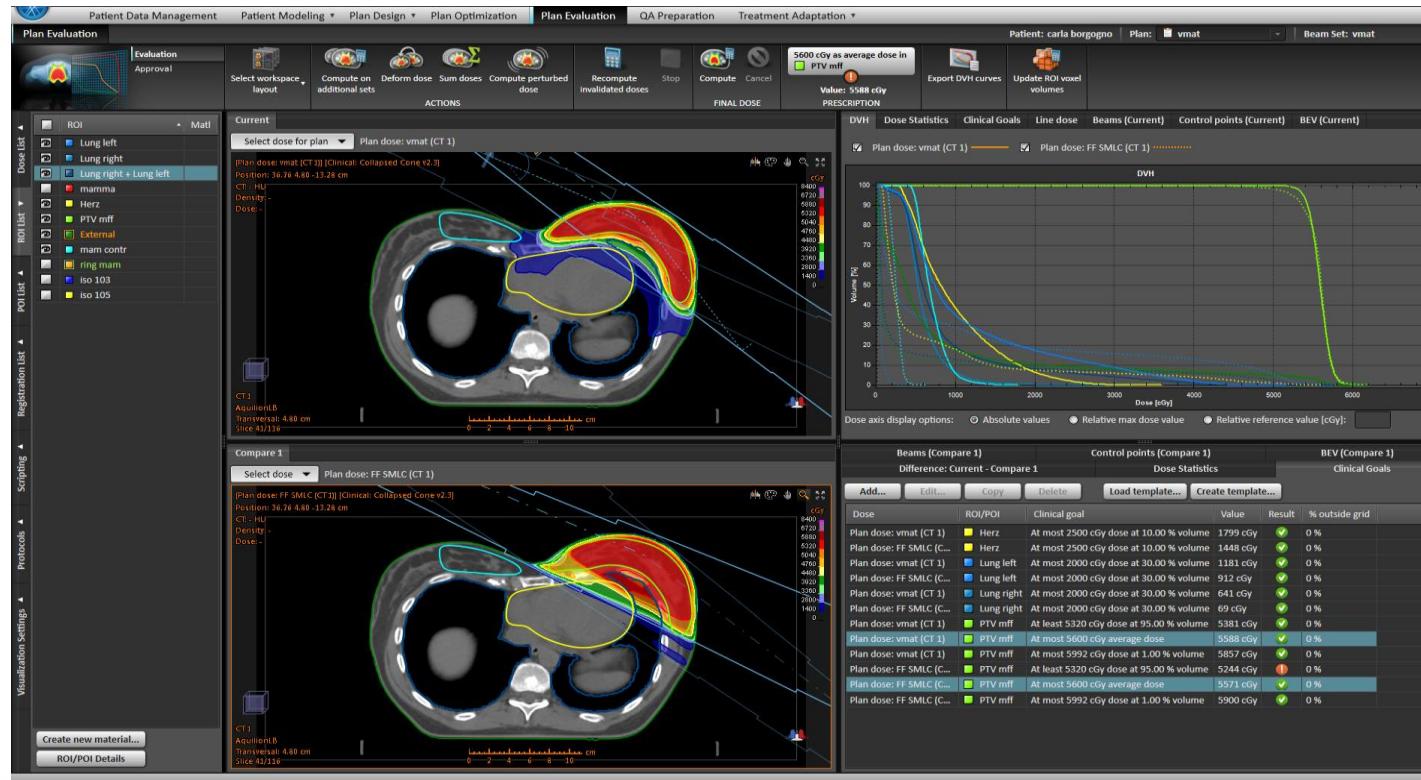


## Procedura di radioterapia





## Tecniche con modulazione della dose: VMAT IMRT





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Original Article

ESTRO ACROP consensus guideline for target volume delineation in the setting of postmastectomy radiation therapy after implant-based immediate reconstruction for early stage breast cancer



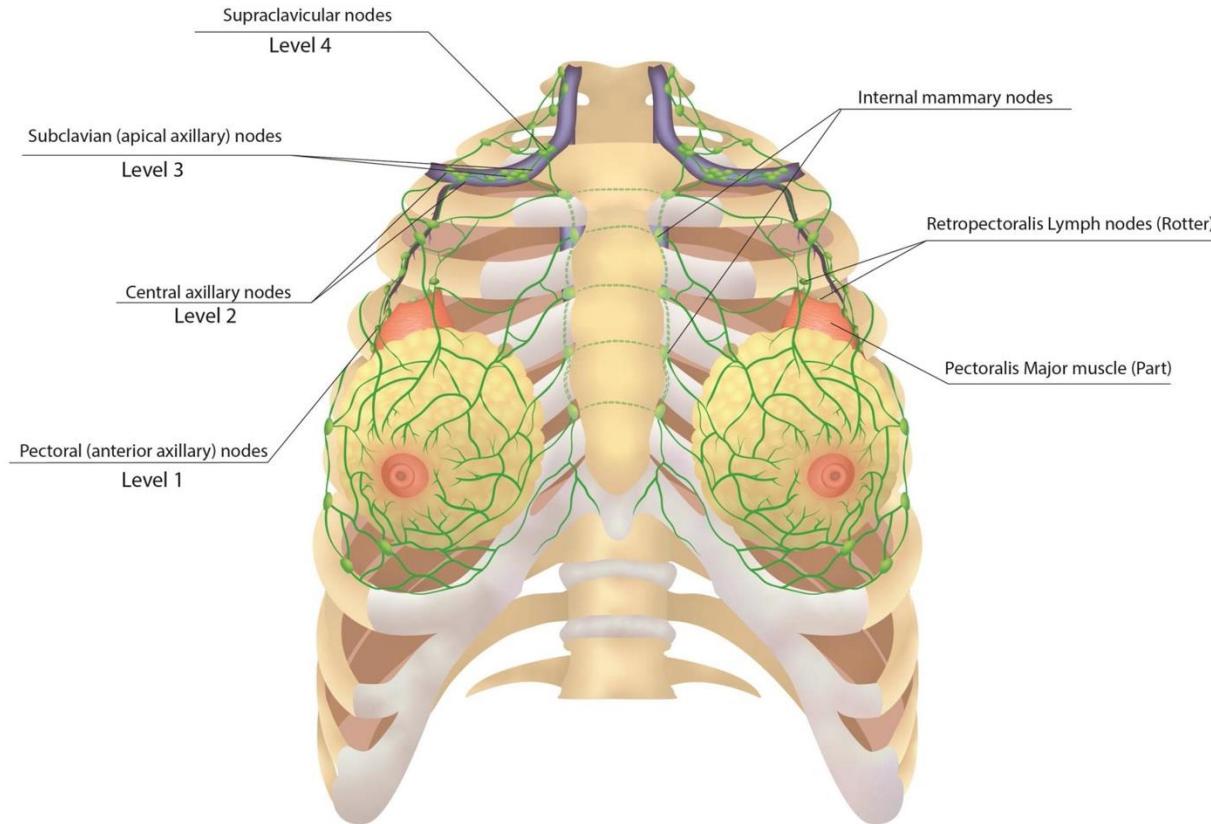
I tassi di ricostruzione immediata del seno (IBR) dopo la mastectomia sono in aumento. Mancano linee guida per il contornamento della radioterapia postmastectomia (PMRT) per i volumi target in caso di IBR. Pertanto, molte pazienti sottoposte a IBR ricevono la PMRT con volumi target simili a quelli dell'irradiazione convenzionale del seno intero con simulatore.

**Lo scopo di questo lavoro è descrivere le linee guida per la delineazione della PMRT dopo IBR con impianto, basate su una comprensione approfondita delle procedure chirurgiche, dello stadio della malattia, dei modelli di recidiva e delle tecniche di irradiazione.**

Esse si basano su un consenso approvato da un gruppo multidisciplinare globale di esperti di cancro al seno.

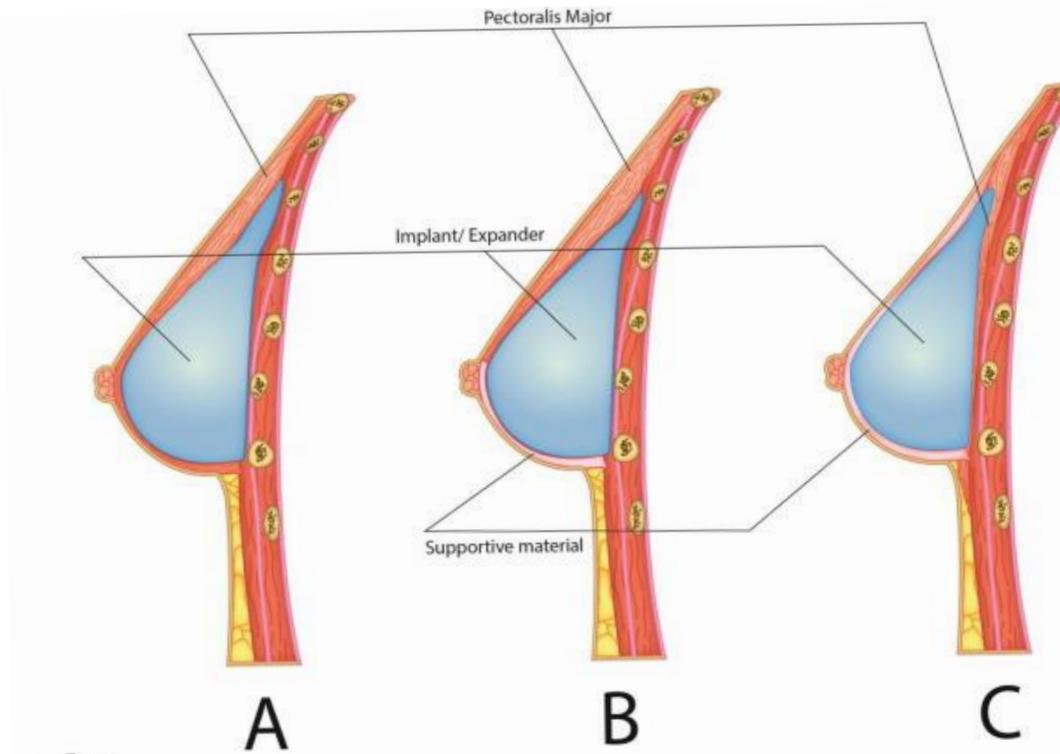


## Linea guida di consenso ESTRO ACROP per la delineazione del volume





## Linea guida di consenso ESTRO ACROP per la delineazione del volume



Alon Person

*Radiotherapy and Oncology* 137 (2019) 159–166

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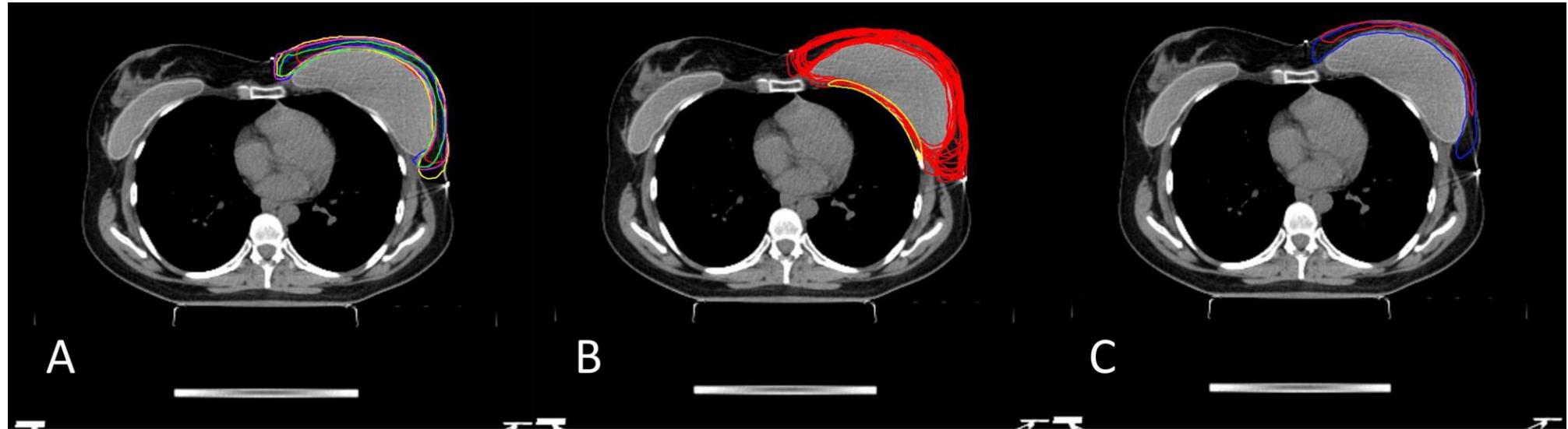
Original Article

ESTRO ACROP consensus guideline for target volume delineation in the setting of postmastectomy radiation therapy after implant-based immediate reconstruction for early stage breast cancer

Orit Kaidar-Person <sup>a,\*</sup>,<sup>1</sup> Birgitte Vrou Ooffersen <sup>b,1</sup>, Sandra Hol <sup>c</sup>, Meritxell Arenas <sup>d</sup>, Cynthia Aristei <sup>e</sup>, Celine Bourgier <sup>f</sup>, Maria Joao Cardoso <sup>g</sup>, Boon Chua <sup>h</sup>, Charlotte E. Coles <sup>i</sup>, Tine Engberg Damsgaard <sup>j</sup>, Dorota Gabrys <sup>k</sup>, Reshma Jagst <sup>l</sup>, Rachel Jimenez <sup>m</sup>, Anna M. Kirby <sup>n</sup>, Carine Kirkove <sup>o</sup>, Youlia Kirova <sup>p</sup>, Vassilis Kouloulas <sup>q</sup>, Tanja Marininko <sup>r</sup>, Icro Meattini <sup>s</sup>, Ingvil Mjaaland <sup>t</sup>, Gustavo Nader Marta <sup>u,v</sup>, Petra Witt Nyström <sup>w</sup>, Elzbieta Senkus <sup>x</sup>, Tanja Skyytä <sup>y</sup>, Tove F. Tvedskov <sup>z</sup>, Karolien Verhoeven <sup>aa</sup>, Philip Poortmans <sup>ab</sup>

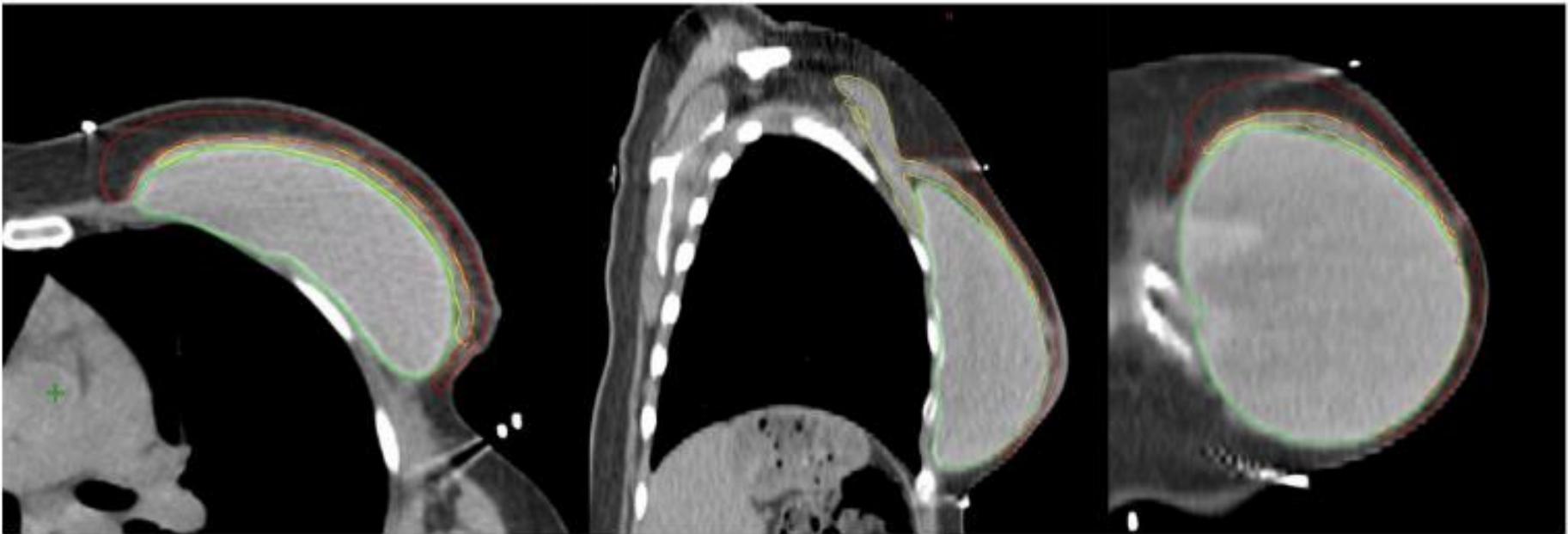


Linea guida di consenso ESTRO ACROP per la delineazione del volume





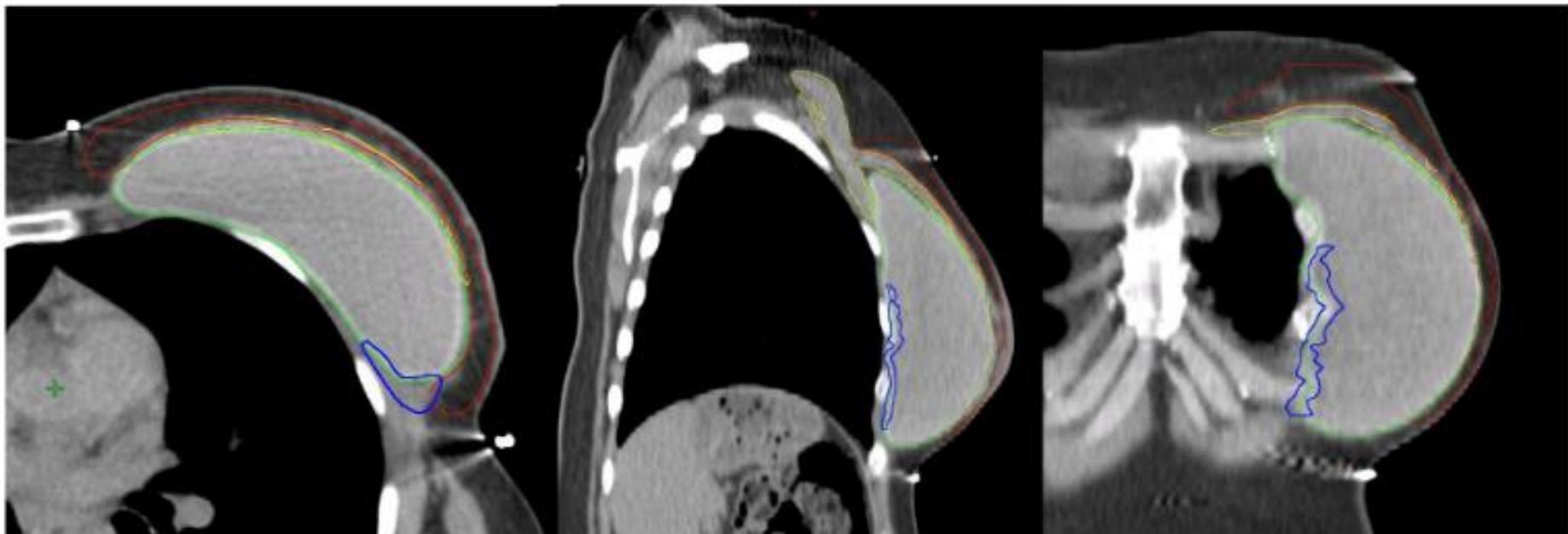
## Linea guida di consenso ESTRO ACROP per la delineazione del volume



**Fig. 4a.** CTVp\_chestwall with only a ventral part (red) in cases for whom only the subcutaneous lymphatic plexus should be irradiated. Pectoral muscles (yellow) and implant (green).



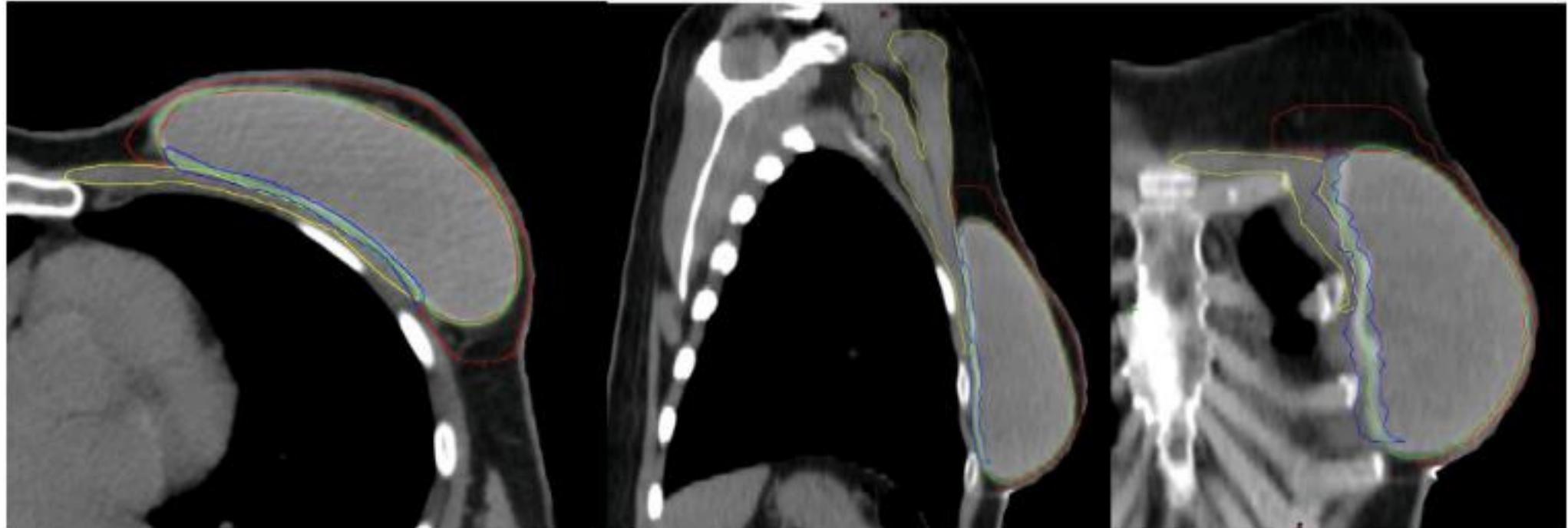
## Linea guida di consenso ESTRO ACROP per la delineazione del volume



**Fig. 4b.** CTVp\_chestwall with a ventral (red) and dorsal (blue) part in cases for whom the subcutaneous lymphatic plexus should be irradiated as well as the part of the chest wall that was initially not covered by the pectoral muscles (yellow). Retropectoral implant (green).



## Linea guida di consenso ESTRO ACROP per la delineazione del volume



**Fig. 4c.** CTVp\_chestwall with a ventral (red) and dorsal (blue) part in cases with a prepectoral implant (green). Pectoral muscles (yellow).

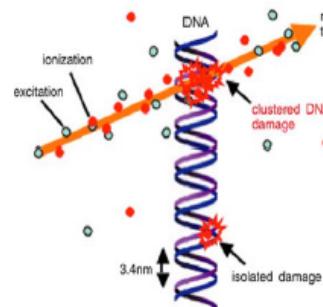


## Funzione di BRCA1 e BRCA2

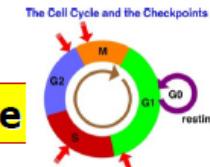
GENI ONCOSOPPRESSORI



**mantenimento stabilità del genoma e  
regolazione proliferazione cellulare**

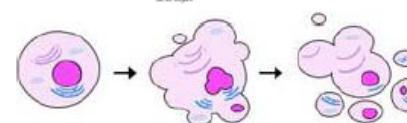


Arresto del ciclo cellulare



Riparo del DNA

Apoptosi





## Radioterapia dopo chirurgia conservativa in pazienti portatrici di mutazione per BRCA1/2

Radiotherapy and Oncology 176 (2022) 59–67



Systematic review

A systematic review exploring the role of modern radiation for the treatment of Hereditary or Familial Breast Cancer



Varshu Goel, Dayanand Sharma, Aman Sharma, Supriya Mallick \*

Department of Radiation Oncology, All India Institute of Medical Sciences, New Delhi, India

E' meno efficace?

**BRCA1/2 Status Does Not Influence Radiation Outcomes in Breast Cancer**

E' più tossica?

Causa nuovi tumori?



## QUESITO CLINICO

Qual è il ruolo della RT nelle donne con cancro al seno che presentano una mutazione germinale BRCA1/2 o una mutazione germinale selezionata a moderata penetranza non BRCA1/2?

Per le donne con carcinoma mammario trattate con BCT o mastectomia per le quali si prende in considerazione la radioterapia post-mastectomia, la radioterapia non deve essere sospesa a causa dello stato di mutazione. Non ci sono prove di un aumento significativo di tossicità o di tumori al seno contralaterali (CBC) legati all'esposizione alle radiazioni tra le pazienti con una mutazione in un gene BRCA1/2 o a moderata penetranza.

