Neoplasie della mammella: stato dell'arte, problematiche attuali e prospettive future

Alessandra Huscher e Nadia Pasinetti

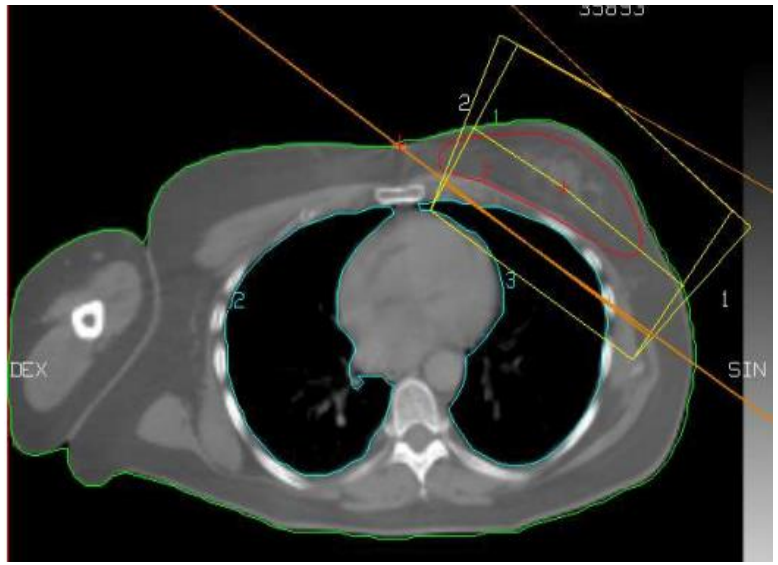
Lecco, 27 Settembre 2021

Sistema Socio Sanitario
Regione Lombardia
ASST Valcamonica

UNIVERSITAS STUDIORUM BRIXIAE

FONDAZIONE POLIAMBULANZA
Istituto Ospedaliero

L’inizio



2D/ 3D
Cuneo di compensazione
Allineamento dorsale fasci

MLD
MHD

L’evoluzione

Biologia

Terapia sistemica

Breast-Unit

L’evoluzione

Analisi di tossicità

THE LANCET
Oncology
Volume 6, Issue 8, August 2005, Pages 557-565

Fast track — Articles

Long-term mortality from heart disease and lung cancer after radiotherapy for early breast cancer: prospective cohort study of about 300 000 women in US SEER cancer registries

Prof Sarah C Darby PhD [a], Paul McGale PhD [a], Carolyn W Taylor FRCR [a], Prof Richard Peto FRS [a]

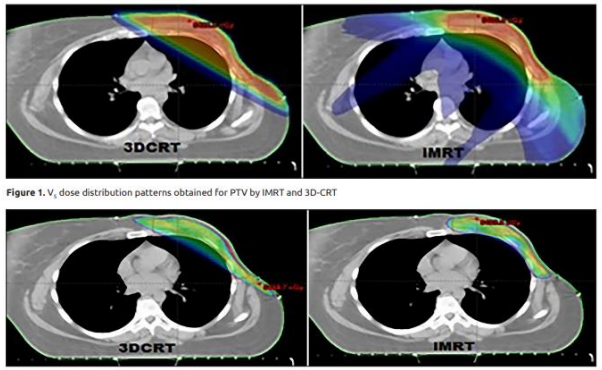
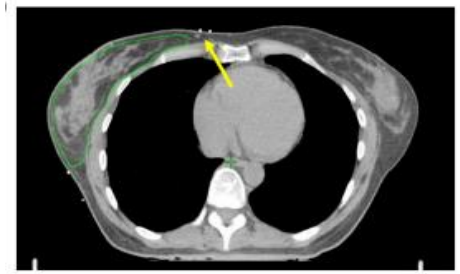


Figure 1. V_t dose distribution patterns obtained for PTV by IMRT and 3D-CRT

Evoluzione tecnologica e conformazione della dose



Definizione 3D dei volumi di trattamento

Avevamo pensato che fosse semplice ma…

Eterogeneità Biologica

Trattamento Sistemico con profili di tossicità differenti

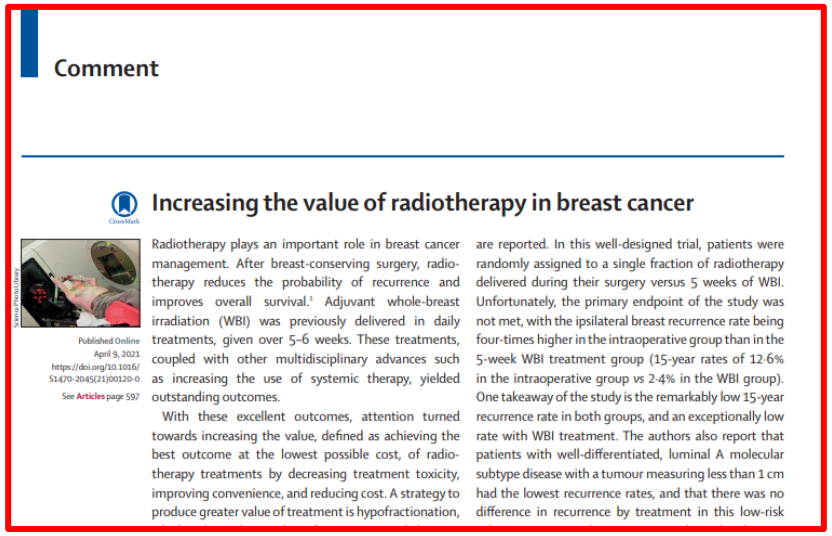
Elevata sopravvivenza

QoL / Tossicità concerns

Prima patologia neoplastica per incidenza
55 k nel 2021

Patient engagement

Increasing the value



Comment

Increasing the value of radiotherapy in breast cancer

Published Online
April 9, 2021
https://doi.org/10.1016/
S1470-2045(21)00120-0

See Articles page 597

Radiotherapy plays an important role in breast cancer management. After breast-conserving surgery, radiotherapy reduces the probability of recurrence and improves overall survival.[1] Adjuvant whole-breast irradiation (WBI) was previously delivered in daily treatments, given over 5–6 weeks. These treatments, coupled with other multidisciplinary advances such as increasing the use of systemic therapy, yielded outstanding outcomes.

With these excellent outcomes, attention turned towards increasing the value, defined as achieving the best outcome at the lowest possible cost, of radiotherapy treatments by decreasing treatment toxicity, improving convenience, and reducing cost. A strategy to produce greater value of treatment is hypofractionation, are reported. In this well-designed trial, patients were randomly assigned to a single fraction of radiotherapy delivered during their surgery versus 5 weeks of WBI. Unfortunately, the primary endpoint of the study was not met, with the ipsilateral breast recurrence rate being four-times higher in the intraoperative group than in the 5-week WBI treatment group (15-year rates of 12·6% in the intraoperative group vs 2·4% in the WBI group). One takeaway of the study is the remarkably low 15-year recurrence rate in both groups, and an exceptionally low rate with WBI treatment. The authors also report that patients with well-differentiated, luminal A molecular subtype disease with a tumour measuring less than 1 cm had the lowest recurrence rates, and that there was no difference in recurrence by treatment in this low-risk

Risultato clinico ↑

Tempo trattamento ↓

Tossicità acuta e tardiva ↓

Increasing the value

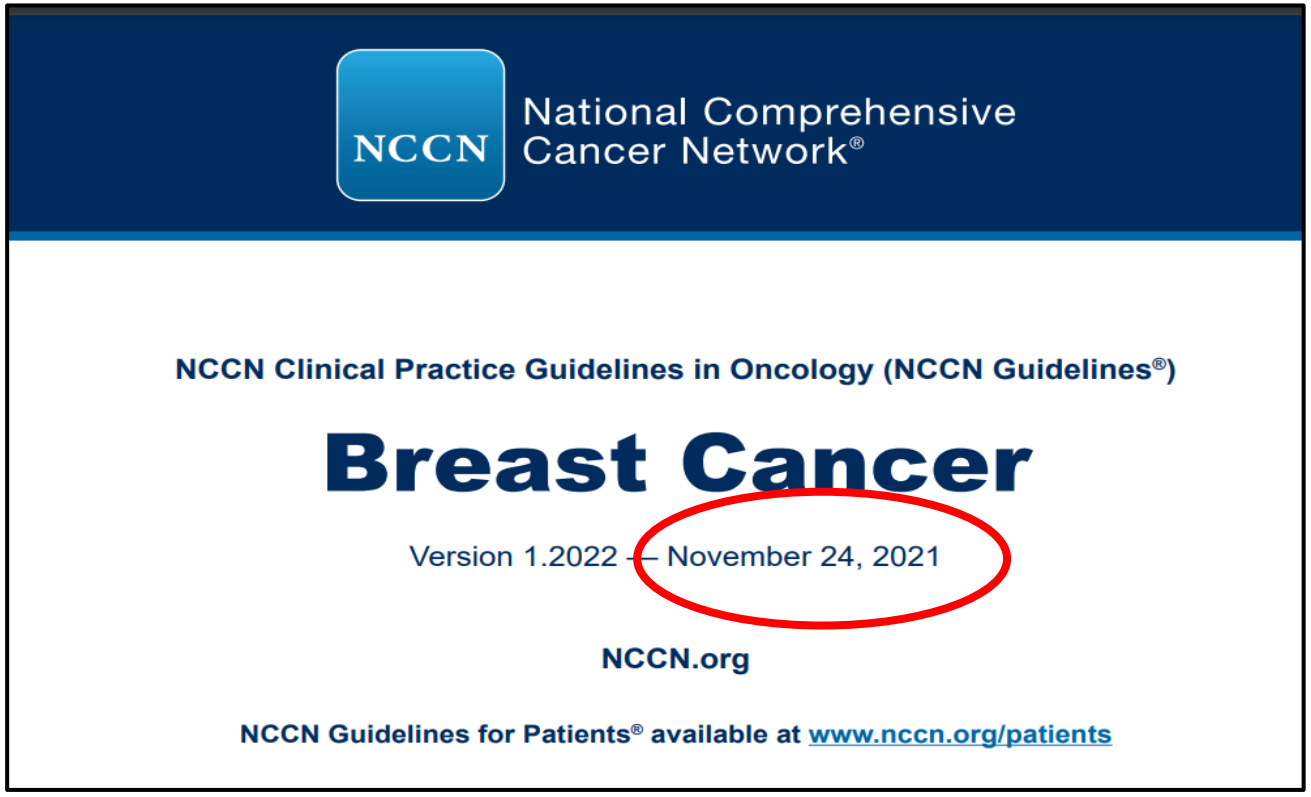
Miglioramento del risultato clinico

Tecnologie

Risorse

Appropriatezza

State of the art



State of the art - DCIS

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022
Ductal Carcinoma in Situ (DCIS)

NCCN Guidelines Index
Table of Contents
Discussion

DIAGNOSIS	WORKUP	PRIMARY TREATMENT		
DCIS Tis,N0,M0 →	• History and physical exam • Diagnostic bilateral mammogram • Pathology review[a] • Determination of tumor estrogen receptor (ER) status • Genetic counseling for patients at risk[b] of hereditary breast cancer • Breast MRI[c,d] as indicated	Breast-conserving surgery[e] (BCS) without lymph node surgery[f] →	Whole breast radiation therapy (WBRT) (category 1) with or without boost to tumor bed[g,h,i,j] or Accelerated partial breast irradiation (APBI)[g,h,i,j] or No RT[g,h,i,j] (category 2B)	→ See Postsurgical Treatment (DCIS-2)
		Total mastectomy with or without sentinel lymph node biopsy (SLNB)[f,h] + reconstruction (optional)[k]	→	See Postsurgical Treatment (DCIS-2)

original reports

Hypofractionated Versus Standard Fractionated Radiotherapy in Patients With Early Breast Cancer or Ductal Carcinoma In Situ in a Randomized Phase III Trial: The DBCG HYPO Trial

Birgitte V. Offersen, MD, PhD[1,2]; Jan Alsner, PhD[1]; Hanne M. Nielsen, PhD[2]; Erik H. Jakobsen, MD[3]; Mette H. Nielsen, PhD[4]; Mechthild Krause, MD, PhD[5]; Lars Stenbygaard, MD[6]; Ingvil Mjaaland, MD[7]; Andreas Schreiber, MD, PhD[8]; Unn-Miriam Kasti, MD[9]; and Jens Overgaard, MD, DMSc[1]; on behalf of the Danish Breast Cancer Group Radiation Therapy Committee

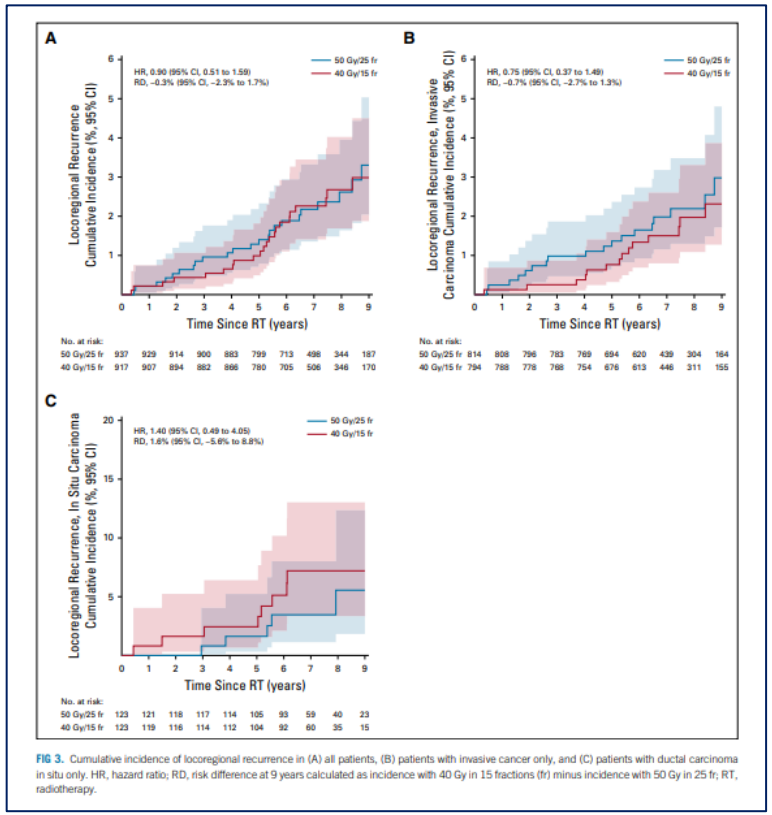


FIG 3. Cumulative incidence of locoregional recurrence in (A) all patients, (B) patients with invasive cancer only, and (C) patients with ductal carcinoma in situ only. HR, hazard ratio; RD, risk difference at 9 years calculated as incidence with 40 Gy in 15 fractions (fr) minus incidence with 50 Gy in 25 fr; RT, radiotherapy.

State of the art - DCIS

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022
Ductal Carcinoma in Situ (DCIS)

NCCN Guidelines Index
Table of Contents
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		Total mastectomy with or without sentinel lymph node biopsy (SLNB)[f,h] + reconstruction (optional)[k]		→ See Postsurgical Treatment (DCIS-2)

Articles

External beam accelerated partial breast irradiation versus whole breast irradiation after breast conserving surgery in women with ductal carcinoma in situ and node-negative breast cancer (RAPID): a randomised controlled trial

Timothy J Whelan, Jim A Julian, Tanya S Berrang, Do-Hoon Kim, Isabelle Germain, Alan M Nichol, Mohamed Akra, Sophie Lavertu, Francois Germain, Anthony Fyles, Theresa Trotter, Francisco E Perera, Susan Balkwill, Susan Chafe, Thomas McGowan, Thierry Muanza, Wayne A Beckham, Boon H Chua, Chu Shu Gu, Mark N Levine, Ivo A Olivotto, for the RAPID Trial Investigators*

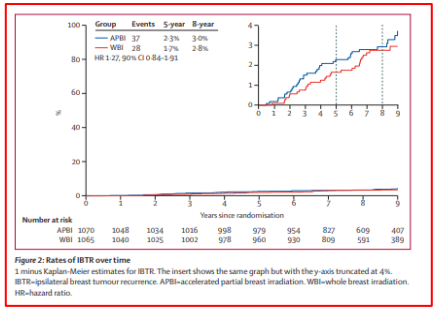


Figure 2: Rates of IBTR over time
1 minus Kaplan-Meier estimates for IBTR. The insert shows the same graph but with the y-axis truncated at 4%. IBTR=ipsilateral breast tumour recurrence. APBI=accelerated partial breast irradiation. WBI=whole breast irradiation. HR=hazard ratio.

APBI

< 2,5 cm Screening detected
G1-2
3 mm margins

Articles

Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial

Frank A Vicini, Reena S Cecchini, Julia R White, Douglas W Arthur, Thomas B Julian, Rachel A Rabinovitch, Robert R Kuske, Patricia A Ganz, David S Parda, Michael F Scheier, Kathryn A Winter, Soonmyung Paik, Henry M Kuerer, Laura A Vallow, Lori J Pierce, Eleftherios P Mamounas, Beryl McCormick, Joseph P Costantino, Harry D Bear, Isabelle Germain, Gregory Gustafson, Linda Grossheim, Ivy A Petersen, Richard S Hudes, Walter J Curran Jr, John L Bryant*, Norman Wolmark

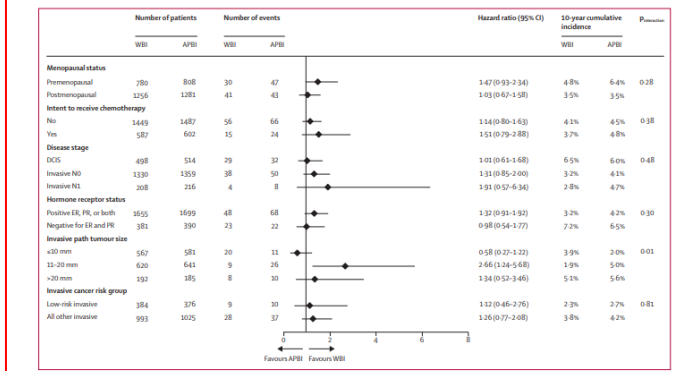
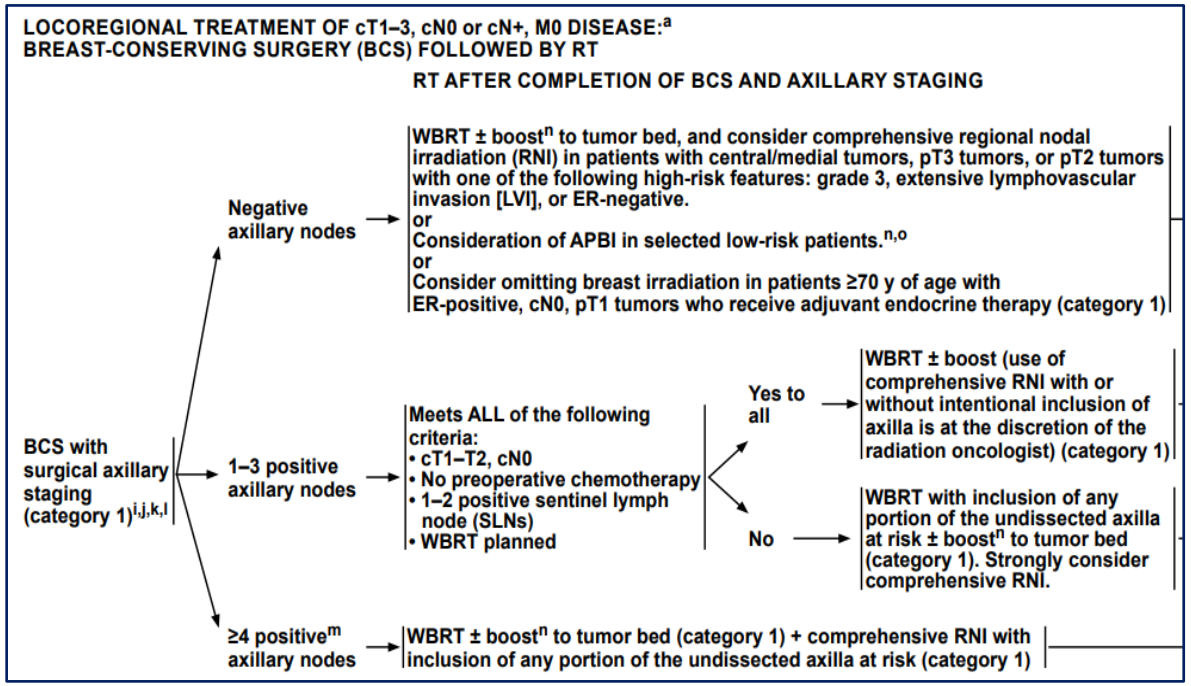


Figure 4: Exploratory post-hoc analysis using forest plots for IBTR
DCIS=ductal carcinoma in situ. IBTR=ipsilateral breast-tumour recurrence. APBI=partial breast irradiation. WBI=whole-breast irradiation.

State of the art - Invasive - BC Surgery



Fractionation

APBI

RNI

State of the art - Invasive - RNI

EORTC

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AMAROS

OTOASOR

MA 20

Breast Care

Review Article

Breast Care 2020;15:128–135
DOI: 10.1159/000507040

Received: December 30, 2019
Accepted: March 9, 2020
Published online: April 9, 2020

An Update on Regional Nodal Irradiation: Indication, Target Volume Delineation, and Radiotherapy Techniques

Marciana Nona Duma

Department of Radiotherapy and Radiation Oncology, University Hospital of the Friedrich Schiller University, Jena, Germany

Differenze significative nelle definizione dei volumi

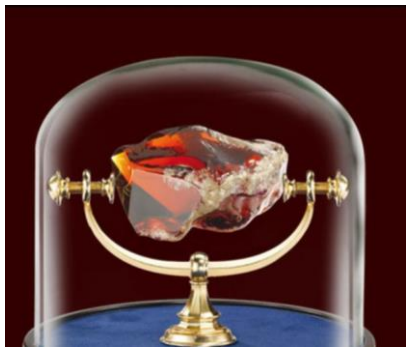
Strahlenther Onkol (2021) 197:820–828
https://doi.org/10.1007/s00066-021-01808-y

REVIEW ARTICLE

Incidental axillary dose delivery to axillary lymph node levels I–III by different techniques of whole-breast irradiation: a systematic literature review

Martin Schmitt[1] · Yvan Pin[2] · Carole Pflumio[2] · Carole Mathelin[4] · Xavier Pivot[3] · Georges Noel[1]

Dose con rilevanza clinica incerta



State of the art - Invasive - RNI

Breast Care

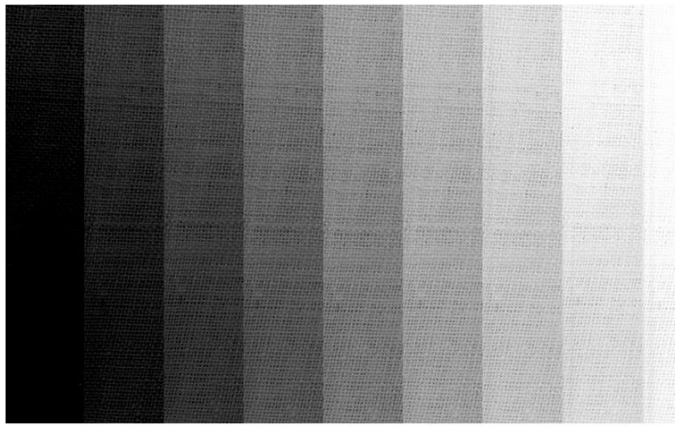
Review Article

Breast Care 2021;16:135–143
DOI: 10.1159/000516114

Received: March 25, 2021
Accepted: March 25, 2021
Published online: April 7, 2021

St. Gallen/Vienna 2021: A Brief Summary of the Consensus Discussion on Customizing Therapies for Women with Early Breast Cancer

Escluso da St.Gallen come quesito specifico



Adam Ansel's Zones/ Kurt Zoglmann

The panel showed uncertainty when asked whether radiotherapy can replace surgery (when 2 of 3 nodes are positive – 38%; 1 out of 3 positive – 52%), demonstrating some movement in this area. However, Philip Poortmans warned specifically against "sloppy" radiotherapy extensions ("high tangents") since this would give away modern technological achievements (better tailoring) of contemporary radiotherapy.

The panel was much more inclined to allow axillary radiotherapy instead of ALND in initially clinically negative axilla in patients without macroscopic nodal involvement (1 of 3 SLN with micrometastasis: 72%; 1 of 3 SLN with ITCs: 88%).

State of the art - Invasive - RNI IMN

OXFORD

JNCI J Natl Cancer Inst (2021) 113(10): djab113

doi: 10.1093/jnci/djab113
First published online July 28, 2021
Article

Side Effects 15 Years After Lymph Node Irradiation in Breast Cancer: Randomized EORTC Trial 22922/10925

Philip M. Poortmans, MD, PhD,[1,2,*] Henk Struikmans, MD, PhD,[3] Peter De Brouwer, MD,[4] Caroline Weltens, MD, PhD,[5] Catherine Fortpied, MSc,[6] Carine Kirkove, MD,[7] Volker Budach, MD,[8] Karine Peignaux-Casasnovas, MD,[9] Femke van der Leij, MD, PhD,[10] Ernest Vonk, MD,[11] Mariacarla Valli, MD,[12] Geertjan vanTienhoven, MD, PhD,[13] Nicola Weidner, MD,[14] Georges Noel, MD, PhD,[15] Matthias Guckenberger, MD,[16] Eveline Koiter, MD,[17] Erik vanLimbergen, MD, PhD,[5] Antoine Engelen, MD,[4] Alain Fourquet, MD,[18] Harry Bartelink, MD, PhD [19] for the EORTC Radiation Oncology and Breast Cancer Groups

Table 1. Cumulative incidence rates at 15 years of late side effects for all patients in the per-protocol population according to the allocated treatment and laterality

	Treatment		
Late side effect	No IM-MS (n = 1944) Rate (95% CI), %	IM-MS (n = 1922) Rate (95% CI), %	P
Clinical evidence of lung fibrosis	2.9 (2.2 to 3.8)	5.7 (4.7 to 6.9)	<.001[a]
Clinical evidence of cardiac fibrosis	1.1 (0.7 to 1.7)	1.9 (1.3 to 2.6)	.07[a]
Right-sided breast cancer	0.6 (0.2 to 1.3)	1.9 (1.1 to 3.1)	.07[b]
Left-sided breast cancer	1.6 (0.9 to 2.6)	1.8 (1.1 to 2.9)	
Any evidence of cardiac diseases	9.4 (8.0 to 10.8)	11.1 (9.6 to 12.7)	.04[a]
Right-sided breast cancer	8.3 (6.5 to 10.3)	10.8 (8.8 to 13.1)	.04[b]
Left-sided breast cancer	10.5 (8.5 to 12.7)	11.3 (9.2 to 13.6)	

[a]Two-sided Gray test. CI = confidence interval; IM-MS = internal mammary-medial supraclavicular irradiation.
[b]Two-sided *P* value for treatment effect, obtained using a Fine and Gray model adjusted for left and right side. Test of treatment by left- and right-side interaction: 2-sided *P* value = .33 and .35 for cardiac fibrosis and cardiac diseases, respectively.

RNI - Shared decisions

Treweek et al. Implementation Science 2013, 8:6
http://www.implementationscience.com/content/8/1/6

IMPLEMENTATION SCIENCE

STUDY PROTOCOL Open Access

Developing and evaluating communication strategies to support informed decisions and practice based on evidence (DECIDE): protocol and preliminary results

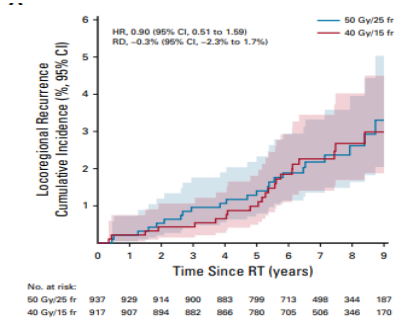
Shaun Treweek[1*], Andrew D Oxman[2], Philip Alderson[3], Patrick M Bossuyt[4], Linn Brandt[2], Jan Brożek[5], Marina Davoli[6], Signe Flottorp[2], Robin Harbour[7], Suzanne Hill[8], Alessandro Liberati[9], Helena Liira[10], Holger J Schünemann[5,11], Sarah Rosenbaum[2], Judith Thornton[3], Per Olav Vandvik[2], Pablo Alonso-Coello[12] and the DECIDE Consortium

State of the art – BCS - Fractionation

original reports

Hypofractionated Versus Standard Fractionated Radiotherapy in Patients With Early Breast Cancer or Ductal Carcinoma In Situ in a Randomized Phase III Trial: The DBCG HYPO Trial

Birgitte V. Offersen, MD, PhD[1,2]; Jan Alsner, PhD[1]; Hanne M. Nielsen, PhD[2]; Erik H. Jakobsen, MD[3]; Mette H. Nielsen, PhD[4]; Mechthild Krause, MD, PhD[5]; Lars Stenbygaard, MD[6]; Ingvil Mjaaland, MD[7]; Andreas Schreiber, MD, PhD[8]; Unn-Miriam Kasti, MD[9]; and Jens Overgaard, MD, DMSc[1]; on behalf of the Danish Breast Cancer Group Radiation Therapy Committee



original reports

Hypofractionated Versus Conventional Fractionated Radiotherapy After Breast-Conserving Surgery in the Modern Treatment Era: A Multicenter, Randomized Controlled Trial From China

Shu-Lian Wang, MD[1]; Hui Fang, MD[1]; Chen Hu, PhD[2]; Yong-Wen Song, MD[1]; Wei-Hu Wang, MD[1]; Jing Jin, MD[1]; Yue-Ping Liu, MD[2]; Hua Ren, MD[1]; Juan Liu, MD[2]; Gao-Feng Li, MD[4]; Xiang-Hui Du, MD[2]; Yu Tang, MD[1]; Hao Jing, MD[1]; Yu-Chao Ma, MD[1]; Zhou Huang, MD[1]; Bo Chen, MD[1]; Yuan Tang, MD[1]; Ning Li, MD[1]; Ning-Ning Lu, MD[1]; Shu-Nan Qi, MD[1]; Yong Yang, MD[1]; Guang-Yi Sun, MD[1]; Xin-Fan Liu, MD[1]; and Ye-Xiong Li, MD[1]

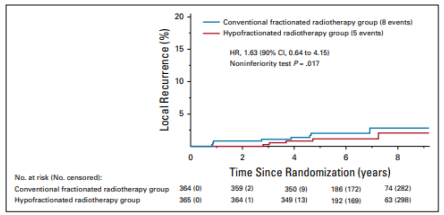


FIG 2. Cumulative local recurrence Kaplan-Meier curves of local recurrence in patients with T1-2N0-3M0 breast cancer who received hypofractionated radiotherapy, compared with those who received conventional fractionated radiotherapy. The intention-to-treat population included all the patients who underwent randomization. HR, hazard ratio.

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Hypofractionated radiation therapy for breast cancer: Preferences amongst radiation oncologists in Europe – Results from an international survey

Ivica Ratosa[a,b,*], Monica Emilia Chirilă[c], Mateja Steinacher[d], Elvisa Kozma[e], Radovan Vojtíšek[f], Pierfrancesco Franco[g,i], Philip Poortmans[h,i,1]

[a] Division of Radiation Oncology, Institute of Oncology Ljubljana; [b] Faculty of Medicine, University of Ljubljana, Slovenia; [c] Radiation Oncology Department, Oncology Institute, Cluj-Napoca, Romania; [d] Department of Oncology, University Medical Centre Maribor, Slovenia; [e] Oncology Service, University Hospital, Tirana, Albania; [f] Department of Oncology and Radiotherapy, University Hospital in Pilsen, Czech Republic; [g] Department of Oncology, University of Turin, Turin, Italy; [h] Iridium Kankernetwerk; and [i] University of Antwerp, Faculty of Medicine and Health Sciences, Wilrijk-Antwerp, Belgium

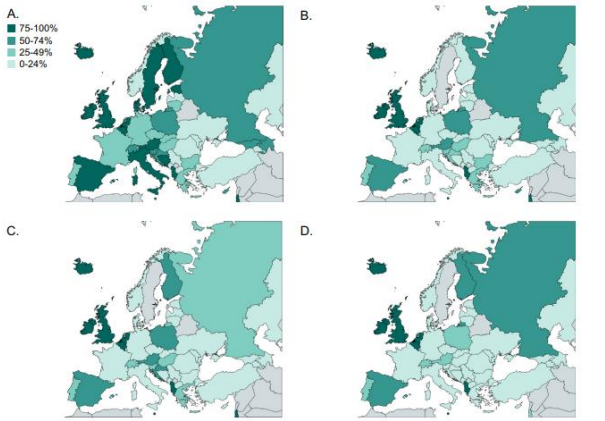


Fig. 1. The proportion of participating radiation oncologists preferring hypofractionated fractionated schedule as their first choice in four different clinical settings. (A) Whole breast irradiation; (B) whole breast and regional nodes irradiation; (C) postmastectomy radiation therapy without reconstruction; (D) postmastectomy radiation therapy with reconstruction.

frontiers in Oncology

SYSTEMATIC REVIEW

Comparing Hypofractionated With Conventional Fractionated Radiotherapy After Breast-Conserving Surgery for Early Breast Cancer: A Meta-Analysis of Randomized Controlled Trials

Lihu Gu[1,2†], Wei Dai[3†], Rongrong Fu[4], Hongfeng Lu[5], Jingyi Shen[3], Yetan Shi[3], Mengting Zhang[3], Ke Jiang[3] and Feng Wu[1*]

editorials

Hypofractionated Whole-Breast Irradiation: Case Closed?

Abram Recht, MD[1]

In summary, the two well-designed and conducted trials reported by Wang et al and Offersen et al. in this issue dispel any doubts that HF-WBI should be the default for the great majority of patients undergoing BCS

State of the art – BCS - Fractionation

Breast Care

Review Article

Breast Care 2021;16:135–143
DOI: 10.1159/000516114

Received: March 25, 2021
Accepted: March 25, 2021
Published online: April 7, 2021

St. Gallen/Vienna 2021: A Brief Summary of the Consensus Discussion on Customizing Therapies for Women with Early Breast Cancer

….the panel endorsed hypofractionation….

Indipendente da

Biologia

Clinical Trial > Int J Radiat Oncol Biol Phys. 2021 Jan 1;109(1):281-287.
doi: 10.1016/j.ijrobp.2020.08.038. Epub 2020 Aug 24.

Breast Cancer Molecular Subtype as a Predictor of Radiation Therapy Fractionation Sensitivity

Nafisha Lalani [1], K David Voduc [2], Rachel B Jimenez [3], Nathalie Levasseur [4], Lovedeep Gondara [5], Caroline Speers [5], Caroline Lohrisch [4], Alan Nichol [2]

Breast size

Medical Oncology (2021) 38:107
https://doi.org/10.1007/s12032-021-01550-6

ORIGINAL PAPER

Hypofractionated whole-breast radiotherapy in large breast size patients: is it really a resolved issue?

Riccardo Ray Colciago[1,2] · Anna Cavallo[3] · Maria Chiara Magrì[4] · Angelo Vitullo[1,5] · Eliana La Rocca[1,5] · Carlotta Giandini[1,5] · Francesca Bonfantini[3] · Serena Di Cosimo[6] · Paolo Bailli[4] · Milena Sant[4] · Emanuele Pignoli[3] · Riccardo Valdagni[1,5,7] · Laura Lozza[1] · Maria Carmen De Santis[1]

Received: 20 May 2021 / Accepted: 5 July 2021 / Published online: 3 August 2021

Contents lists available at ScienceDirect
The Breast
journal homepage: www.elsevier.com/brst

Original article

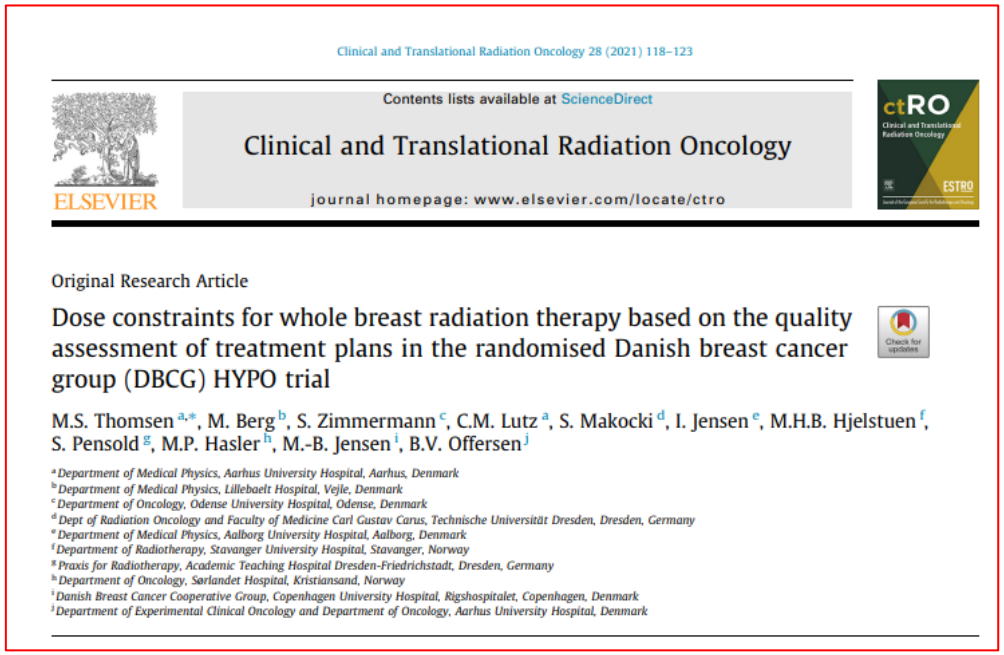
Impact of molecular subtype on 1325 early-stage breast cancer patients homogeneously treated with hypofractionated radiotherapy without boost: Should the indications for radiotherapy be more personalized?

Andrei Fodor [a,*], Chiara Brombin [b,c], Paola Mangili [d], Fulvio Borroni [a], Marcella Pasetti [a], Roberta Tummineri [a], Flavia Zerbetto [a], Barbara Longobardi [d], Lucia Perna [d], Italo Dell'Oca [a], Chiara L. Deantoni [a], Aniko M. Deli [a], Anna Chiara [a], Sara Broggi [d], Roberta Castriconi [d], Pier Giorgio Esposito [d], Najla Slim [a], Paolo Passoni [a], Simone Baroni [a], Stefano L. Villa [a], Paola M.V. Rancoita [b,c], Claudio Fiorino [d], Antonella Del Vecchio [d], Giampaolo Bianchini [a], Oreste D. Gentilini [a], Mariaclelia S. Di Serio [b,c], N.G. Di Muzio [a,c]

Boost

Safe for large breasts
V105%
Comorbidities

State of the art – BCS - Fractionation



Clinical and Translational Radiation Oncology 28 (2021) 118–123

Contents lists available at ScienceDirect

Clinical and Translational Radiation Oncology

journal homepage: www.elsevier.com/locate/ctro

Original Research Article

Dose constraints for whole breast radiation therapy based on the quality assessment of treatment plans in the randomised Danish breast cancer group (DBCG) HYPO trial

M.S. Thomsen [a,*], M. Berg [b], S. Zimmermann [c], C.M. Lutz [a], S. Makocki [d], I. Jensen [e], M.H.B. Hjelstuen [f], S. Pensold [g], M.P. Hasler [h], M.-B. Jensen [i], B.V. Offersen [j]

[a] Department of Medical Physics, Aarhus University Hospital, Aarhus, Denmark
[b] Department of Medical Physics, Lillebaelt Hospital, Vejle, Denmark
[c] Department of Oncology, Odense University Hospital, Odense, Denmark
[d] Dept of Radiation Oncology and Faculty of Medicine Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany
[e] Department of Medical Physics, Aalborg University Hospital, Aalborg, Denmark
[f] Department of Radiotherapy, Stavanger University Hospital, Stavanger, Norway
[g] Praxis for Radiotherapy, Academic Teaching Hospital Dresden-Friedrichstadt, Dresden, Germany
[h] Department of Oncology, Sørlandet Hospital, Kristiansand, Norway
[i] Danish Breast Cancer Cooperative Group, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark
[j] Department of Experimental Clinical Oncology and Department of Oncology, Aarhus University Hospital, Denmark

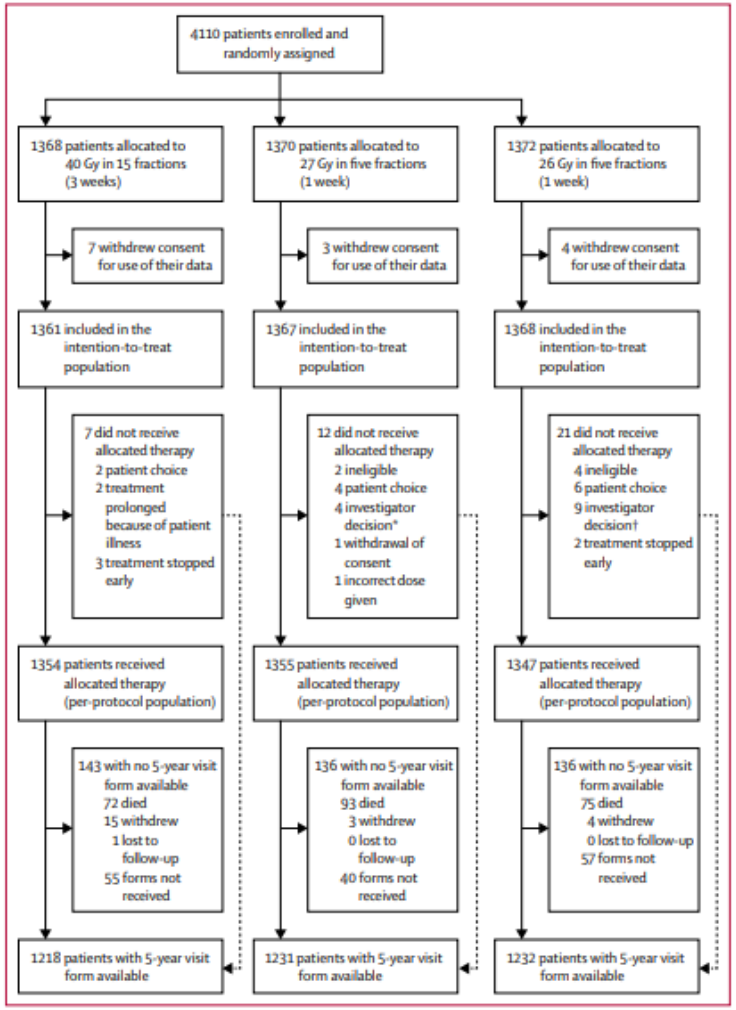
Protocol constraint	
$V_{95\%} \geq 95\%$	
$V_{105\%}$-$V_{107\%} \leq 2\%$	
$V_{107\%}$-$V_{110\%} < 2cm^3$	
$D_{max} \leq 110\%$	
Lung $V_{20Gy}/V_{17Gy} \leq 25\%$	
Heart $V_{20Gy}/V_{17Gy} \leq 10\%$	Right
	Left
Heart $V_{40Gy}/V_{35Gy} \leq 5\%$	Right
	Left
LADCA $D_{max} \leq 20$ Gy/17 Gy	Right
	Left

Vincoli di dose rispettati
Possibilità tecnica di ulteriore riduzione di dose

Hypo Moderate or…FAST?

Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial

Adrian Murray Brunt, Joanne S Haviland*, Duncan A Wheatley, Mark A Sydenham, Abdulla Alhasso, David J Bloomfield, Charlie Chan, Mark Churn, Susan Cleator, Charlotte E Coles, Andrew Goodman, Adrian Harnett, Penelope Hopwood, Anna M Kirby, Cliona C Kirwan, Carolyn Morris, Zohal Nabi, Elinor Sawyer, Navita Somaiah, Liba Stones, Isabel Syndikus, Judith M Bliss†, John R Yarnold†, on behalf of the FAST-Forward Trial Management Group*

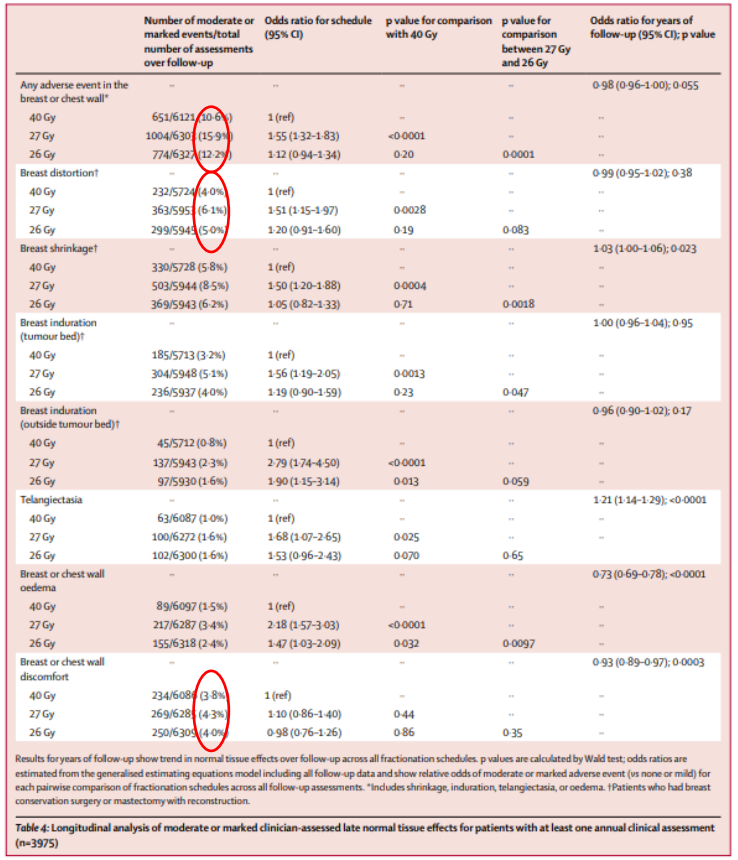


	Cumulative number of events	Estimated cumulative incidence by 5 years (95% CI)	Hazard ratio (95% CI); p value	Estimated absolute difference vs 40 Gy at 5 years (95% CI)
Ipsilateral breast tumour (local) relapse*				
40 Gy (n=1361)	31 (2·3%)	2·1% (1·4 to 3·1)	1 (ref)	..
27 Gy (n=1367)	27 (2·0%)	1·7% (1·2 to 2·6)	0·86 (0·51 to 1·44); 0·56	−0·3% (−1·0 to 0·9)
26 Gy (n=1368)	21 (1·5%)	1·4% (0·9 to 2·2)	0·67 (0·38 to 1·16); 0·15	−0·7% (−1·3 to 0·3)
Locoregional relapse†				
40 Gy (n=1361)	43 (3·2%)	2·8% (2·0 to 3·9)	1 (ref)	..
27 Gy (n=1367)	35 (2·6%)	2·3% (1·6 to 3·3)	0·80 (0·51 to 1·25); 0·33	−0·5% (−1·4 to 0·7)
26 Gy (n=1368)	29 (2·1%)	1·8% (1·2 to 2·7)	0·66 (0·41 to 1·06); 0·083	−0·9% (−1·6 to 0·2)
Distant relapse				
40 Gy (n=1361)	59 (4·3%)	3·8% (2·9 to 5·0)	1 (ref)	..
27 Gy (n=1367)	69 (5·0%)	4·7% (3·7 to 6·0)	1·16 (0·82 to 1·64); 0·41	0·6% (−0·7 to 2·3)
26 Gy (n=1368)	76 (5·6%)	5·1% (4·0 to 6·4)	1·27 (0·90 to 1·79); 0·17	1·0% (−0·4 to 2·9)
Any breast cancer-related event‡				
40 Gy (n=1361)	119 (8·7%)	7·8% (6·5 to 9·4)	1 (ref)	..
27 Gy (n=1367)	112 (8·2%)	7·2% (5·9 to 8·7)	0·93 (0·71 to 1·20); 0·56	−0·6% (−2·2 to 1·5)
26 Gy (n=1368)	114 (8·3%)	7·5% (6·2 to 9·0)	0·94 (0·73 to 1·22); 0·65	−0·4% (−2·1 to 1·6)
All-cause mortality				
40 Gy (n=1361)	92 (6·8%)	5·4% (4·3 to 6·8)	1 (ref)	..
27 Gy (n=1367)	105 (7·7%)	6·9% (5·7 to 8·4)	1·12 (0·85 to 1·48); 0·42	0·6% (−0·8 to 2·5)
26 Gy (n=1368)	90 (6·6%)	5·6% (4·5 to 7·0)	0·96 (0·72 to 1·28); 0·78	−0·2% (−1·5 to 1·5)

Hazard ratios less than 1 favour five-fraction schedules. p values were calculated by log-rank test (two-sided). *Includes three patients with angiosarcoma in ipsilateral breast (one in the 40 Gy group and two in the 26 Gy group). †Defined as ipsilateral breast tumour relapse or regional relapse (axilla, supraclavicular fossa, and internal mammary chain). ‡Includes local, regional, or distant relapse, breast cancer death, or contralateral breast cancer (disease-free survival).

Table 2: **Relapse and mortality by fractionation schedule: time-to-event analysis (n=4096)**

Fast Forward - Clinicians vs Patients



	Number of moderate or marked events/total number of assessments over follow-up	Odds ratio for schedule (95% CI)	p value for comparison with 40 Gy	p value for comparison between 27 Gy and 26 Gy	Odds ratio for years of follow-up (95% CI); p value
Any adverse event in the breast or chest wall*	..	..	..	..	0·98 (0·96–1·00); 0·055
40 Gy	651/6121 (10·6%)	1 (ref)	..	..	..
27 Gy	1004/6303 (15·9%)	1·55 (1·32–1·83)	<0·0001	..	..
26 Gy	774/6327 (12·2%)	1·12 (0·94–1·34)	0·20	0·0001	..
Breast distortion†	..	..	..	..	0·99 (0·95–1·02); 0·38
40 Gy	232/5724 (4·0%)	1 (ref)	..	..	..
27 Gy	363/5957 (6·1%)	1·51 (1·15–1·97)	0·0028	..	..
26 Gy	299/5945 (5·0%)	1·20 (0·91–1·60)	0·19	0·083	..
Breast shrinkage†	..	..	..	..	1·03 (1·00–1·06); 0·023
40 Gy	330/5728 (5·8%)	1 (ref)	..	..	..
27 Gy	503/5944 (8·5%)	1·50 (1·20–1·88)	0·0004	..	..
26 Gy	369/5943 (6·2%)	1·05 (0·82–1·33)	0·71	0·0018	..
Breast induration (tumour bed)†	..	..	..	..	1·00 (0·96–1·04); 0·95
40 Gy	185/5713 (3·2%)	1 (ref)	..	..	..
27 Gy	304/5948 (5·1%)	1·56 (1·19–2·05)	0·0013	..	..
26 Gy	236/5937 (4·0%)	1·19 (0·90–1·59)	0·23	0·047	..
Breast induration (outside tumour bed)†	..	..	..	..	0·96 (0·90–1·02); 0·17
40 Gy	45/5712 (0·8%)	1 (ref)	..	..	..
27 Gy	137/5943 (2·3%)	2·79 (1·74–4·50)	<0·0001	..	..
26 Gy	97/5930 (1·6%)	1·90 (1·15–3·14)	0·013	0·059	..
Telangiectasia	..	..	..	..	1·21 (1·14–1·29); <0·0001
40 Gy	63/6087 (1·0%)	1 (ref)	..	..	..
27 Gy	100/6272 (1·6%)	1·68 (1·07–2·65)	0·025	..	..
26 Gy	102/6300 (1·6%)	1·53 (0·96–2·43)	0·070	0·65	..
Breast or chest wall oedema	..	..	..	..	0·73 (0·69–0·78); <0·0001
40 Gy	89/6097 (1·5%)	1 (ref)	..	..	..
27 Gy	217/6287 (3·4%)	2·18 (1·57–3·03)	<0·0001	..	..
26 Gy	155/6318 (2·4%)	1·47 (1·03–2·09)	0·032	0·0097	..
Breast or chest wall discomfort	..	..	..	..	0·93 (0·89–0·97); 0·0003
40 Gy	234/6086 (3·8%)	1 (ref)	..	..	..
27 Gy	269/6285 (4·3%)	1·10 (0·86–1·40)	0·44	..	..
26 Gy	250/6309 (4·0%)	0·98 (0·76–1·26)	0·86	0·35	..

Results for years of follow-up show trend in normal tissue effects over follow-up across all fractionation schedules. p values are calculated by Wald test; odds ratios are estimated from the generalised estimating equations model including all follow-up data and show relative odds of moderate or marked adverse event (*vs* none or mild) for each pairwise comparison of fractionation schedules across all follow-up assessments. *Includes shrinkage, induration, telangiectasia, or oedema. †Patients who had breast conservation surgery or mastectomy with reconstruction.

Table 4: **Longitudinal analysis of moderate or marked clinician-assessed late normal tissue effects for patients with at least one annual clinical assessment (n=3975)**

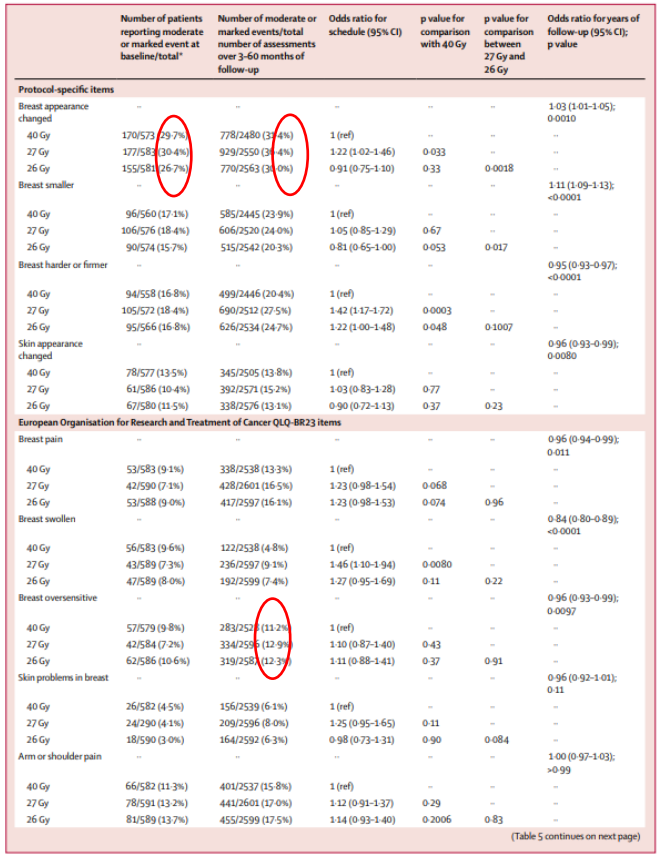
PROMS

› Radiother Oncol. 2021 Jun;159:98-105. doi: 10.1016/j.radonc.2021.03.020. Epub 2021 Mar 23.

How do patient-reported outcomes compare with clinician assessments? A prospective study of radiation dermatitis in breast cancer

Tara Behroozian [1], Lauren Milton [1], Liying Zhang [2], Julia Lou [2], Irene Karam [1], Emily Lam [1], Gina Wong [1], Ewa Szumacher [1], Edward Chow [3]

PRO ≠ CRO



	Number of patients reporting moderate or marked event at baseline/total*	Number of moderate or marked events/total number of assessments over 3–60 months of follow-up	Odds ratio for schedule (95% CI)	p value for comparison with 40 Gy	p value for comparison between 27 Gy and 26 Gy	Odds ratio for years of follow-up (95% CI); p value
Protocol-specific items						
Breast appearance changed	..	..	..	..	..	1·03 (1·01–1·05); 0·0010
40 Gy	170/573 (29·7%)	778/2480 (31·4%)	1 (ref)	..	..	..
27 Gy	177/583 (30·4%)	929/2550 (36·4%)	1·22 (1·02–1·46)	0·033	..	..
26 Gy	155/581 (26·7%)	770/2563 (30·0%)	0·91 (0·75–1·10)	0·33	0·0018	..
Breast smaller	..	..	..	..	..	1·11 (1·09–1·13); <0·0001
40 Gy	96/560 (17·1%)	585/2445 (23·9%)	1 (ref)	..	..	..
27 Gy	106/576 (18·4%)	606/2520 (24·0%)	1·05 (0·85–1·29)	0·67	..	..
26 Gy	90/574 (15·7%)	515/2542 (20·3%)	0·81 (0·65–1·00)	0·053	0·017	..
Breast harder or firmer	..	..	..	..	..	0·95 (0·93–0·97); <0·0001
40 Gy	94/558 (16·8%)	499/2446 (20·4%)	1 (ref)	..	..	..
27 Gy	105/572 (18·4%)	690/2512 (27·5%)	1·42 (1·17–1·72)	0·0003	..	..
26 Gy	95/566 (16·8%)	626/2534 (24·7%)	1·22 (1·00–1·48)	0·048	0·1007	..
Skin appearance changed	..	..	..	..	..	0·96 (0·93–0·99); 0·0080
40 Gy	78/577 (13·5%)	345/2505 (13·8%)	1 (ref)	..	..	..
27 Gy	61/586 (10·4%)	392/2571 (15·2%)	1·03 (0·83–1·28)	0·77	..	..
26 Gy	67/580 (11·5%)	338/2576 (13·1%)	0·90 (0·72–1·13)	0·37	0·23	..
European Organisation for Research and Treatment of Cancer QLQ-BR23 items						
Breast pain	..	..	..	..	..	0·96 (0·94–0·99); 0·011
40 Gy	53/583 (9·1%)	338/2538 (13·3%)	1 (ref)	..	..	..
27 Gy	42/590 (7·1%)	428/2601 (16·5%)	1·23 (0·98–1·54)	0·068	..	..
26 Gy	53/588 (9·0%)	417/2597 (16·1%)	1·23 (0·98–1·53)	0·074	0·96	..
Breast swollen	..	..	..	..	..	0·84 (0·80–0·89); <0·0001
40 Gy	56/583 (9·6%)	122/2538 (4·8%)	1 (ref)	..	..	..
27 Gy	43/589 (7·3%)	236/2597 (9·1%)	1·46 (1·10–1·94)	0·0080	..	..
26 Gy	47/589 (8·0%)	192/2599 (7·4%)	1·27 (0·95–1·69)	0·11	0·22	..
Breast oversensitive	..	..	..	..	..	0·96 (0·93–0·99); 0·0097
40 Gy	57/579 (9·8%)	283/2524 (11·2%)	1 (ref)	..	..	..
27 Gy	42/584 (7·2%)	334/2596 (12·9%)	1·10 (0·87–1·40)	0·43	..	..
26 Gy	62/586 (10·6%)	319/2587 (12·3%)	1·11 (0·88–1·41)	0·37	0·91	..
Skin problems in breast	..	..	..	..	..	0·96 (0·92–1·01); 0·11
40 Gy	26/582 (4·5%)	156/2539 (6·1%)	1 (ref)	..	..	..
27 Gy	24/290 (4·1%)	209/2596 (8·0%)	1·25 (0·95–1·65)	0·11	..	..
26 Gy	18/590 (3·0%)	164/2592 (6·3%)	0·98 (0·73–1·31)	0·90	0·084	..
Arm or shoulder pain	..	..	..	..	..	1·00 (0·97–1·03); >0·99
40 Gy	66/582 (11·3%)	401/2537 (15·8%)	1 (ref)	..	..	..
27 Gy	78/591 (13·2%)	441/2601 (17·0%)	1·12 (0·91–1·37)	0·29	..	..
26 Gy	81/589 (13·7%)	455/2599 (17·5%)	1·14 (0·93–1·40)	0·2006	0·83	..

(Table 5 continues on next page)

Fast Forward – The Future

Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial

Adrian Murray Brunt, Joanne S Haviland*, Duncan A Wheatley, Mark A Sydenham, Abdulla Alhasso, David J Bloomfield, Charlie Chan, Mark Churn, Susan Cleator, Charlotte E Coles, Andrew Goodman, Adrian Harnett, Penelope Hopwood, Anna M Kirby, Cliona C Kirwan, Carolyn Morris, Zohal Nabi, Elinor Sawyer, Navita Somaiah, Liba Stones, Isabel Syndikus, Judith M Bliss†, John R Yarnold†, on behalf of the FAST-Forward Trial Management Group*

Dati di follow up da confermare

Esclusione del basso rischio >65 pT1 G1-2 ER+ HER- pN0

State of the art – BCS - APBI

cancers

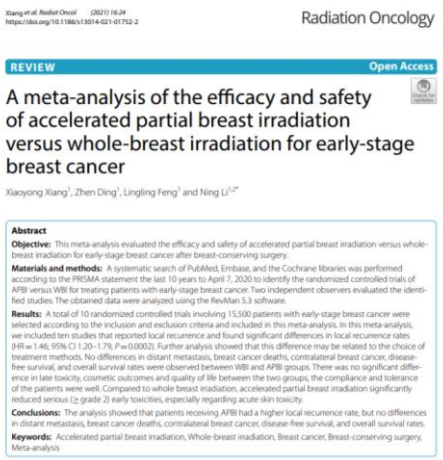
MDPI

Article

Comparing Local and Systemic Control between Partial- and Whole-Breast Radiotherapy in Low-Risk Breast Cancer—A Meta-Analysis of Randomized Trials

Jan Haussmann [1], Wilfried Budach [1], Vratislav Strnad [2], Stefanie Corradini [3], David Krug [4], Livia Schmidt [1], Balint Tamaskovics [1], Edwin Bölke [1,*], Ioannis Simiantonakis [1], Kai Kammers [5] and Christiane Matuschek [1]

Our analysis of IBTR revealed a significant heterogeneity in the comparison, which might be attributable to either difference in risk groups in the selected patients or PBI techniques. The analysis by PBI methods suggests that PBI by EBRT achieved similar local control,



Radiation Oncology

REVIEW Open Access

A meta-analysis of the efficacy and safety of accelerated partial breast irradiation versus whole-breast irradiation for early-stage breast cancer

Xiaoyong Xiang, Zhen Ding, Lingling Feng and Ning Li

Abstract

Objective: This meta-analysis evaluated the efficacy and safety of accelerated partial breast irradiation versus whole-breast irradiation for early-stage breast cancer after breast-conserving surgery.

Materials and methods: A systematic search of PubMed, Embase, and the Cochrane libraries was performed according to the PRISMA statement the last 10 years to April 7, 2020 to identify the randomized controlled trials of APBI versus WBI for treating patients with early-stage breast cancer. Two independent observers evaluated the identified studies. The obtained data were analyzed using the RevMan 5.3 software.

Results: A total of 10 randomized controlled trials involving 15,500 patients with early-stage breast cancer were selected according to the inclusion and exclusion criteria and included in this meta-analysis. In this meta-analysis, we included ten studies that reported local recurrence and found significant differences in local recurrence rates (HR = 1.46, 95% CI 1.20–1.79, $P = 0.0002$). Further analysis showed that this difference may be related to the choice of treatment methods. No differences in distant metastasis, breast cancer deaths, contralateral breast cancer, disease-free survival, and overall survival rates were observed between WBI and APBI groups. There was no significant difference in late toxicity, cosmetic outcomes and quality of life between the two groups, the compliance and tolerance of the patients were well. Compared to whole breast irradiation, accelerated partial breast irradiation significantly reduced serious (≥ grade 2) early toxicities, especially regarding acute skin toxicity.

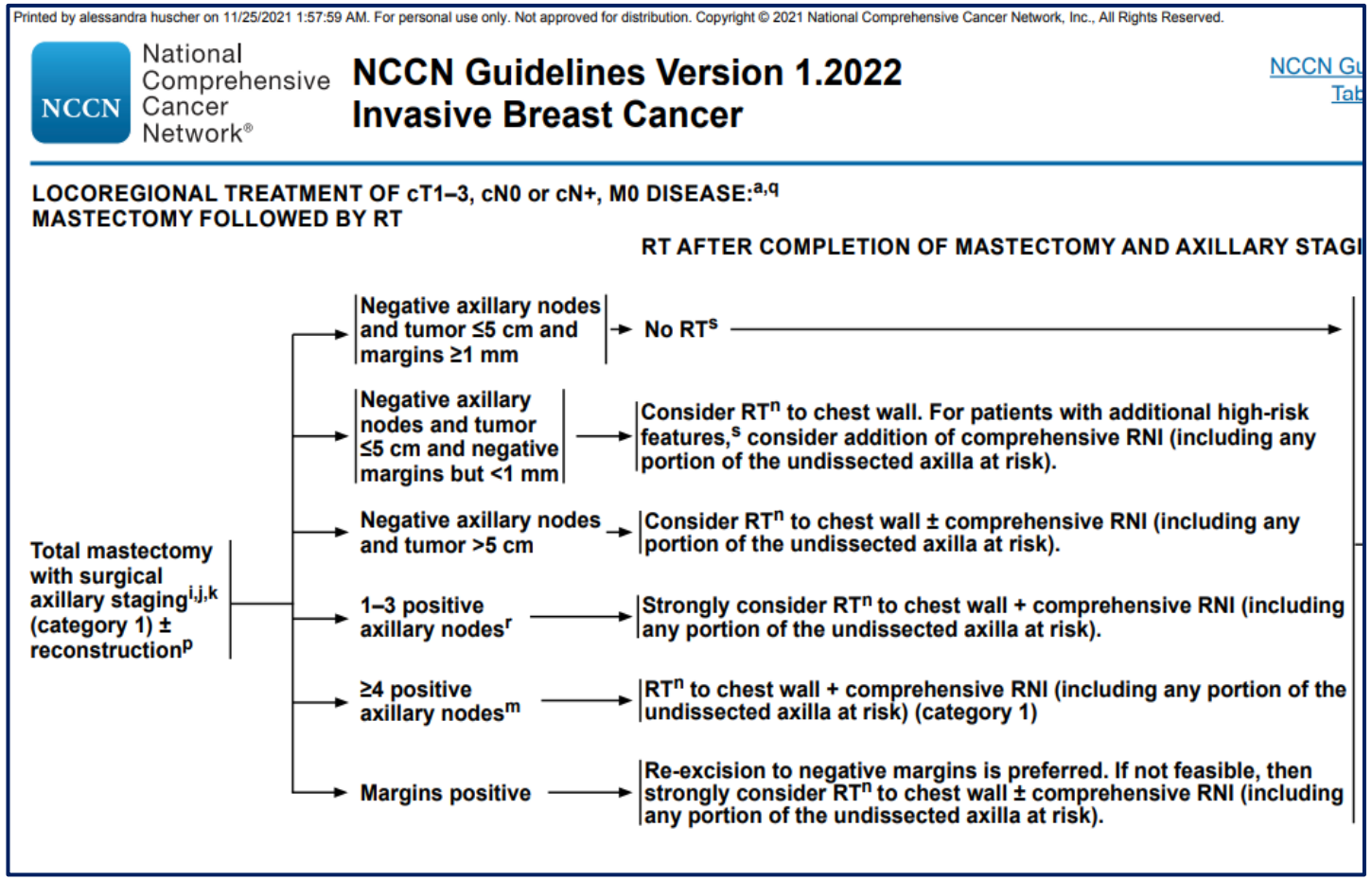
Conclusions: The analysis showed that patients receiving APBI had a higher local recurrence rate, but no differences in distant metastasis, breast cancer deaths, contralateral breast cancer, disease-free survival, and overall survival rates.

Keywords: Accelerated partial breast irradiation, Whole-breast irradiation, Breast cancer, Breast-conserving surgery, Meta-analysis

Partial-breast radiotherapy achieves equivalent oncological outcomes to those of whole-breast radiotherapy when selecting low-risk patients and using appropriate techniques.

The appropriateness of limiting the target volume to a partial treatment of the breast depends on the individual risk profile

State of the art - PMRT



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022
Invasive Breast Cancer

NCCN Gu
Tab

LOCOREGIONAL TREATMENT OF cT1–3, cN0 or cN+, M0 DISEASE:[a,q]
MASTECTOMY FOLLOWED BY RT

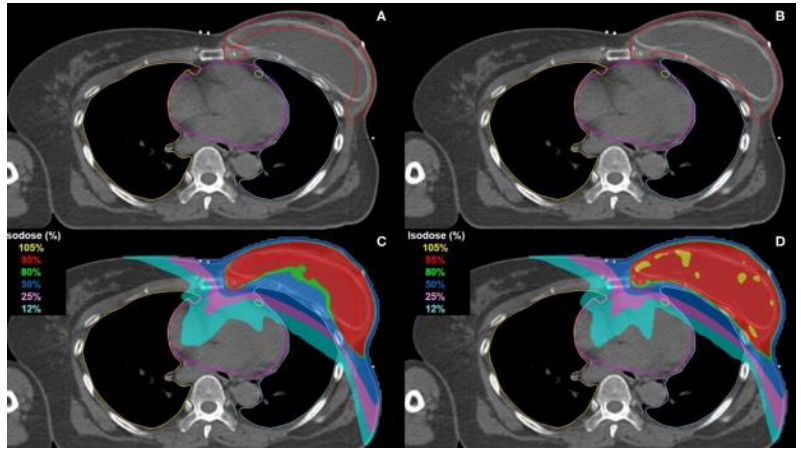
RT AFTER COMPLETION OF MASTECTOMY AND AXILLARY STAGI

Total mastectomy with surgical axillary staging[i,j,k] (category 1) ± reconstruction[p]

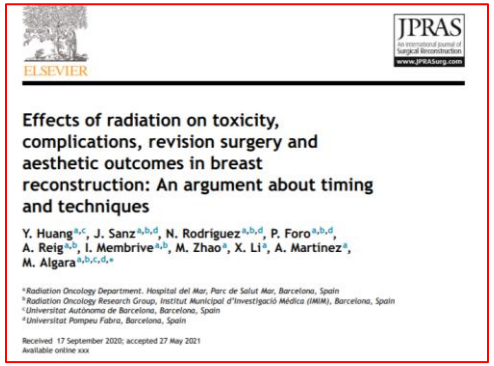
- **Negative axillary nodes and tumor ≤5 cm and margins ≥1 mm** → **No RT[s]**
- **Negative axillary nodes and tumor ≤5 cm and negative margins but <1 mm** → **Consider RT[n] to chest wall. For patients with additional high-risk features,[s] consider addition of comprehensive RNI (including any portion of the undissected axilla at risk).**
- **Negative axillary nodes and tumor >5 cm** → **Consider RT[n] to chest wall ± comprehensive RNI (including any portion of the undissected axilla at risk).**
- **1–3 positive axillary nodes[r]** → **Strongly consider RT[n] to chest wall + comprehensive RNI (including any portion of the undissected axilla at risk).**
- **≥4 positive axillary nodes[m]** → **RT[n] to chest wall + comprehensive RNI (including any portion of the undissected axilla at risk) (category 1)**
- **Margins positive** → **Re-excision to negative margins is preferred. If not feasible, then strongly consider RT[n] to chest wall ± comprehensive RNI (including any portion of the undissected axilla at risk).**

State of the art - PMRT - Volumi

2019 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



Collaborazione tra Chirurgo/Chirurgo Plastico/ Radioncologo



ELSEVIER

JPRAS

Effects of radiation on toxicity, complications, revision surgery and aesthetic outcomes in breast reconstruction: An argument about timing and techniques

Y. Huang[a,c], J. Sanz[a,b,d], N. Rodriguez[a,b,d], P. Foro[a,b,d], A. Reig[a,b], I. Membrive[a,b], M. Zhao[a], X. Li[a], A. Martinez[a], M. Algara[a,b,c,d,*]

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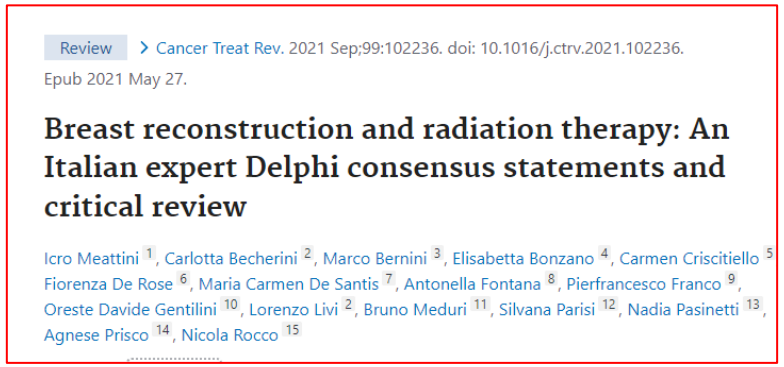

Review > Cancer Treat Rev. 2021 Sep;99:102236. doi: 10.1016/j.ctrv.2021.102236. Epub 2021 May 27.

Breast reconstruction and radiation therapy: An Italian expert Delphi consensus statements and critical review

Icro Meattini [1], Carlotta Becherini [2], Marco Bernini [3], Elisabetta Bonzano [4], Carmen Criscitiello [5], Fiorenza De Rose [6], Maria Carmen De Santis [7], Antonella Fontana [8], Pierfrancesco Franco [9], Oreste Davide Gentilini [10], Lorenzo Livi [2], Bruno Meduri [11], Silvana Parisi [12], Nadia Pasinetti [13], Agnese Prisco [14], Nicola Rocco [15]

PMRT – Hypofractionation

Breast Care

Review Article

Breast Care 2021;16:135–143
DOI: 10.1159/000516114

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St. Gallen/Vienna 2021: A Brief Summary of the Consensus Discussion on Customizing Therapies for Women with Early Breast Cancer

The panel endorsed hypofractionation for postmastectomy radiotherapy (PMRT; 90%) and RNI (76%)

Radiotherapy and Oncology 163 (2021) 105–113

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Implant risk failure in patients undergoing postmastectomy 3-week hypofractionated radiotherapy after immediate reconstruction

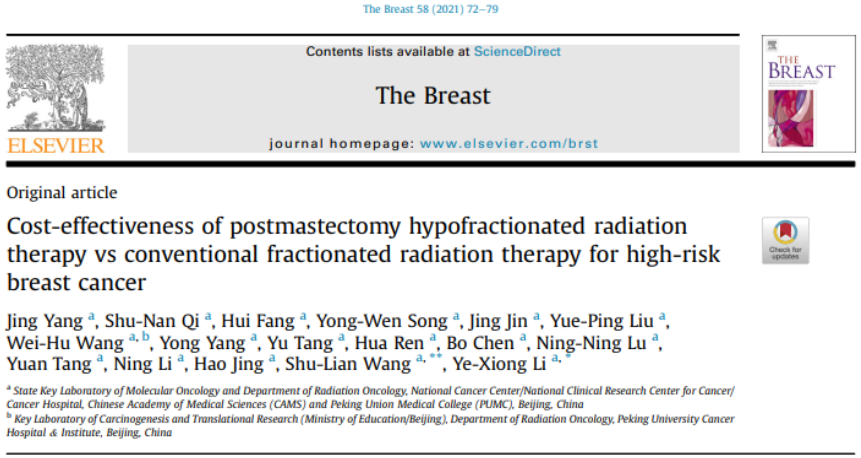
Damaris Patricia Rojas [a], Maria Cristina Leonardi [a,1], Samuele Frassoni [b], Anna Morra [a], Marianna Alessandra Gerardi [a,*], Eliana La Rocca [a,f], Federica Cattani [c], Rosa Luraschi [c], Cristiana Fodor [a], Mattia Zaffaroni [a], Mario Rietjens [d], Francesca De Lorenzi [d], Paolo Veronesi [e,f], Viviana Enrica Galimberti [e], Mattia Intra [e], Vincenzo Bagnardi [b], Roberto Orecchia [g], Samantha Dicuonzo [a,2], Barbara Alicja Jereczek-Fossa [a,f]

[a] Division of Radiation Oncology, IEO, European Institute of Oncology IRCCS, Milan; [b] Department of Statistics and Quantitative Methods, University of Milan-Bicocca, Italy; [c] Unit of Medical Physics, IEO, European Institute of Oncology IRCCS, Milan, Italy; [d] Division of Plastic and Reconstructive Surgery; [e] Division of Breast Surgery, IEO, European Institute of Oncology IRCCS, Milan; [f] Department of Oncology and Hemato-oncology, University of Milan, Italy; [g] Scientific Direction, IEO, European Institute of Oncology IRCCS, Milan, Italy

…safety and feasibility of delivering PMRT on implant-based IBR, with an overall RF rate of 10.2%...

The RF rate in irradiated TE/I patients 12.9% before the exchange for permanent implant

PMRT – Hypofractionation



The Breast 58 (2021) 72–79

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

Cost-effectiveness of postmastectomy hypofractionated radiation therapy vs conventional fractionated radiation therapy for high-risk breast cancer

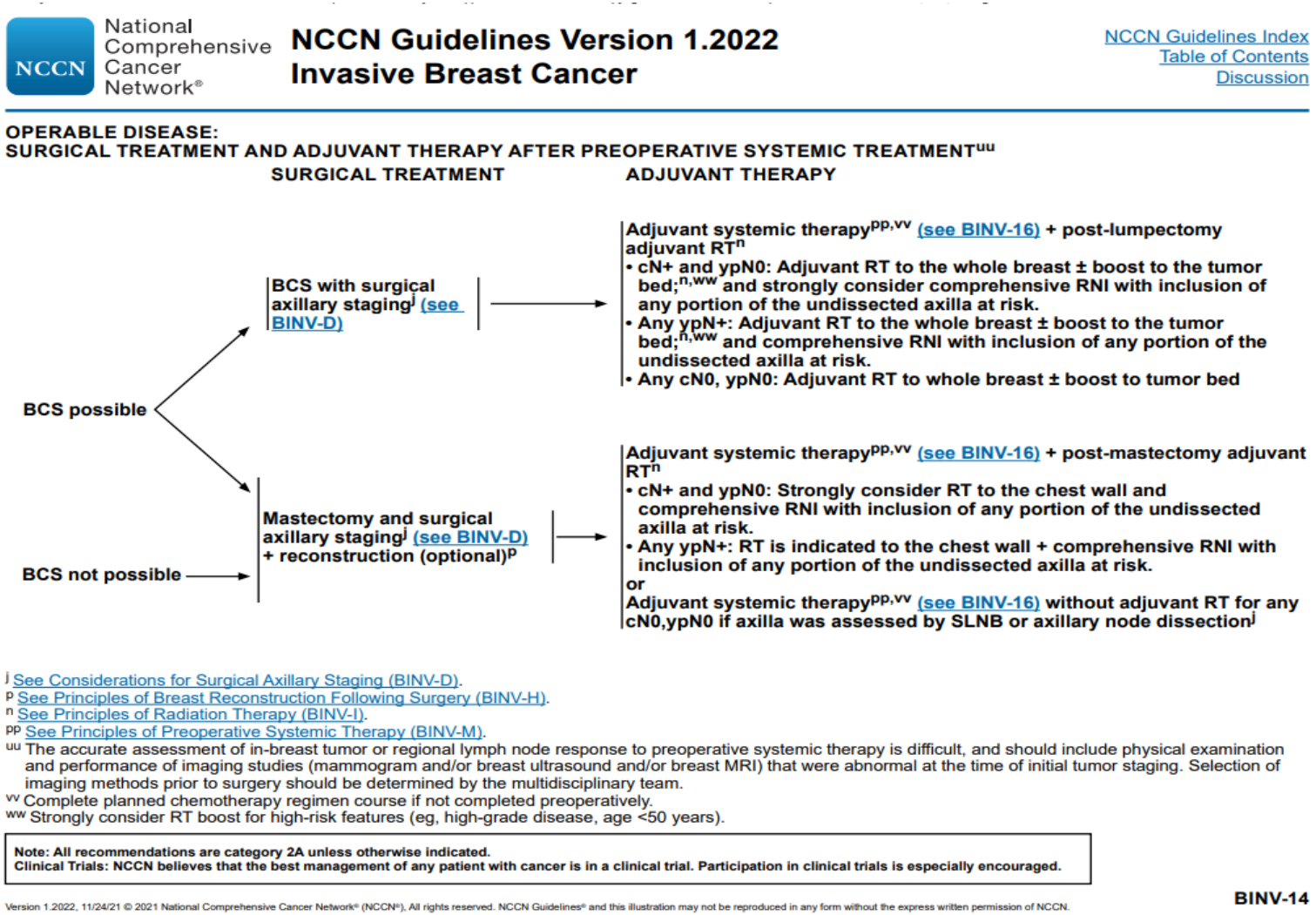
Jing Yang [a], Shu-Nan Qi [a], Hui Fang [a], Yong-Wen Song [a], Jing Jin [a], Yue-Ping Liu [a], Wei-Hu Wang [a, b], Yong Yang [a], Yu Tang [a], Hua Ren [a], Bo Chen [a], Ning-Ning Lu [a], Yuan Tang [a], Ning Li [a], Hao Jing [a], Shu-Lian Wang [a, **], Ye-Xiong Li [a, *]

[a] State Key Laboratory of Molecular Oncology and Department of Radiation Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences (CAMS) and Peking Union Medical College (PUMC), Beijing, China
[b] Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Radiation Oncology, Peking University Cancer Hospital & Institute, Beijing, China

QUALYs

HFRT could be used as a cost-effective substitute for CFRT without compromising clinical outcomes. This finding supports the clinical use of HFRT and enhances the range of its applications.

RT after PST



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022
Invasive Breast Cancer

NCCN Guidelines Index
Table of Contents
Discussion

OPERABLE DISEASE:
SURGICAL TREATMENT AND ADJUVANT THERAPY AFTER PREOPERATIVE SYSTEMIC TREATMENT[uu]

SURGICAL TREATMENT | **ADJUVANT THERAPY**

BCS possible

BCS with surgical axillary staging[j] (see BINV-D) →

Adjuvant systemic therapy[pp,vv] (see BINV-16) + post-lumpectomy adjuvant RT[n]
- **cN+ and ypN0: Adjuvant RT to the whole breast ± boost to the tumor bed;[n,ww] and strongly consider comprehensive RNI with inclusion of any portion of the undissected axilla at risk.**
- **Any ypN+: Adjuvant RT to the whole breast ± boost to the tumor bed;[n,ww] and comprehensive RNI with inclusion of any portion of the undissected axilla at risk.**
- **Any cN0, ypN0: Adjuvant RT to whole breast ± boost to tumor bed**

BCS not possible →

Mastectomy and surgical axillary staging[j] (see BINV-D) + reconstruction (optional)[p] →

Adjuvant systemic therapy[pp,vv] (see BINV-16) + post-mastectomy adjuvant RT[n]
- **cN+ and ypN0: Strongly consider RT to the chest wall and comprehensive RNI with inclusion of any portion of the undissected axilla at risk.**
- **Any ypN+: RT is indicated to the chest wall + comprehensive RNI with inclusion of any portion of the undissected axilla at risk.**

or

Adjuvant systemic therapy[pp,vv] (see BINV-16) without adjuvant RT for any cN0,ypN0 if axilla was assessed by SLNB or axillary node dissection[j]

[j] See Considerations for Surgical Axillary Staging (BINV-D).
[p] See Principles of Breast Reconstruction Following Surgery (BINV-H).
[n] See Principles of Radiation Therapy (BINV-I).
[pp] See Principles of Preoperative Systemic Therapy (BINV-M).
[uu] The accurate assessment of in-breast tumor or regional lymph node response to preoperative systemic therapy is difficult, and should include physical examination and performance of imaging studies (mammogram and/or breast ultrasound and/or breast MRI) that were abnormal at the time of initial tumor staging. Selection of imaging methods prior to surgery should be determined by the multidisciplinary team.
[vv] Complete planned chemotherapy regimen course if not completed preoperatively.
[ww] Strongly consider RT boost for high-risk features (eg, high-grade disease, age <50 years).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

… la tossicità …..

cancers

MDPI

Review

Breast Radiotherapy-Related Cardiotoxicity. When, How, Why. Risk Prevention and Control Strategies

Ana Aurora Díaz-Gavela [1,2,3,*,†], Lourdes Figueiras-Graillet [4,†], Ángel Montero Luis [5], Juliana Salas Segura [6,7], Raquel Ciérvide [5], Elia del Cerro Peñalver [1,2,3], Felipe Couñago [1,2,3,*], Meritxell Arenas [8,9,‡] and Teresa López-Fernández [10,11,‡]

DIBH
Modulazione di intensità
Set up prono
Set up laterale
Sistema di immobilizzazione

Clinical and Translational Radiation Oncology 28 (2021) 10–16

Contents lists available at ScienceDirect

Clinical and Translational Radiation Oncology

journal homepage: www.elsevier.com/locate/ctro

Prolonging deep inspiration breath-hold time to 3 min during radiotherapy, a simple solution

Vincent Vakaet [a,b,*], Hans Van Hulle [a], Max Schoepen [a,c], Els Van Caelenberg [d], Annick Van Greveling [b], Jeroen Holvoet [b], Chris Monten [a,b], Luc De Baerdemaeker [d,e], Wilfried De Neve [a,b], Marc Coppens [d,e], Liv Veldeman [a,b]

[a] Department of Human Structure and Repair, Ghent University, Belgium
[b] Department of Radiation Oncology, Ghent University Hospital, Belgium
[c] Department of Industrial Systems Engineering and Product Design, Kortrijk, Belgium
[d] Department of Anesthesia, Ghent University Hospital, Belgium
[e] Department of Basic and Applied Medical Sciences, Ghent University, Belgium

Allen et al. Radiation Oncology (2020) 15:59
https://doi.org/10.1186/s13014-020-01505-7

Radiation Oncology

RESEARCH Open Access

CPAP (Continuous Positive Airway Pressure) is an effective and stable solution for heart sparing radiotherapy of left sided breast cancer

Aaron M. Allen*, Yasmin Korzets Ceder, Tzippy Shochat, Eyal Fenig, Aron Popovtzer, Dimitry Bragilofsky, Adi Alfassy and Helena Allon

… la tossicità …..

cancers

MDPI

Review

Breast Radiotherapy-Related Cardiotoxicity. When, How, Why. Risk Prevention and Control Strategies

Ana Aurora Díaz-Gavela [1,2,3,*,†], Lourdes Figueiras-Graillet [4,†], Ángel Montero Luis [5], Juliana Salas Segura [6,7], Raquel Ciérvide [5], Elia del Cerro Peñalver [1,2,3], Felipe Couñago [1,2,3,*], Meritxell Arenas [8,9,‡] and Teresa López-Fernández [10,11,‡]

Correzione fattori di rischio
Modifica stili di vita

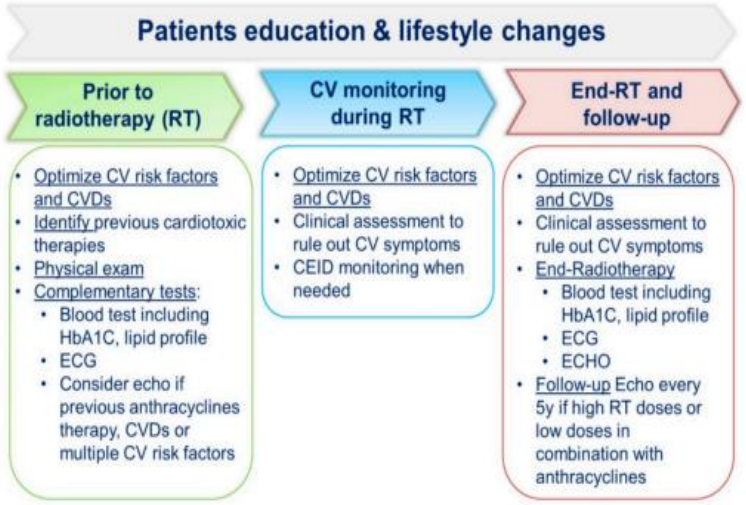


Figure 4. Radiotherapy treatment cardiac-monitoring strategies.

… la tossicità …..

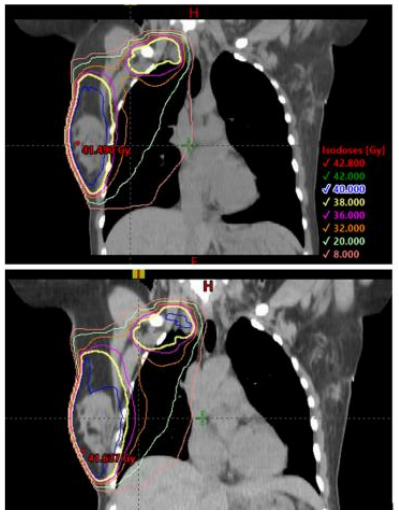
Tecniche volumetriche
Vincoli di dose (V20/17Gy V10Gy e V5Gy)

Journal of Medical Radiation Sciences
Open Access
ORIGINAL ARTICLE

Comprehensive nodal breast VMAT: solving the low-dose wash dilemma using an iterative knowledge-based radiotherapy planning solution

Cameron Stanton, MSc (Res), BMedRadPhys,[1] Linda J. Bell, PhD, B App Sc (MRT), FASMIRT,[1] Andrew Le, M RT,[1] Brooke Griffiths, B MRS RT,[1] Kenny Wu, B MRS RT,[1] Jessica Adams, B MRS RT,[1] Leigh Ambrose, Nat Dip MRT,[1] Denise Andree-Evarts, B MRS RT,[1] Brian Porter, B App Sci (Medical Radiations),[1] Regina Bromley, MSc, BMedPhys (Hons I),[1] Kirsten vanGysen, MBChB, FRANZCR,[1] Marita Morgia, MBBS, FRANZCR,[1] Gillian Lamoury, B Med, FRANZCR,[1] Thomas Eade, MBChB FRANZCR,[1,2] Jeremy T. Booth, BMedPhys (Hon I), PhD, [1,3] & Susan Carroll, MBBS, FRANZCR[1,2]

[1]Radiation Oncology Department, Northern Sydney Cancer Centre, Royal North Shore Hospital, St Leonards, New South Wales, Australia
[2]Northern Clinical School, University of Sydney, St Leonards, New South Wales, Australia
[3]Institute of Medical Physics, School of Physics, University of Sydney, Camperdown, New South Wales, Australia



DIBH

Pandeli et al. Radiation Oncology (2019) 14:223
https://doi.org/10.1186/s13014-019-1430-x

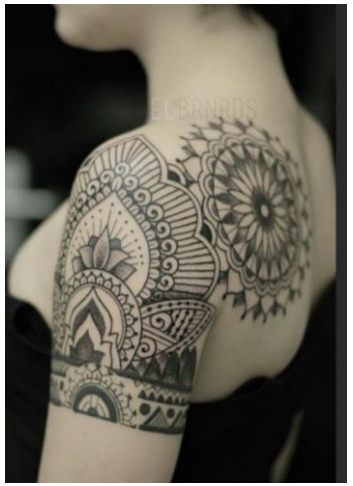
Radiation Oncology

RESEARCH Open Access

Dose reduction to organs at risk with deep-inspiration breath-hold during right breast radiotherapy: a treatment planning study

Chloe Pandeli*, Lloyd M. L. Smyth[1], Steven David[2] and Andrew W. See[1]

… la tossicità …..
Shoulder motion & Lymphedema



Tecniche selettive di LA (sperimentali)
Mobilizzazione adeguata
Controllo del dolore
Identificazione fattori di rischio/normogrammi

Vincoli di dose sulla testa omerale

Screening intensivo della stasi linfatica

2021 Issues - Neoadjuvant RT

Journal of MEDICAL IMAGING and RADIATION ONCOLOGY

Radiation Oncology—Original Article

Neoadjuvant radiotherapy for locally advanced and high-risk breast cancer

Phoebe Chidley, Farshad Foroudi, Mark Tacey, Richard Khor, Janice Yeh, Elaine Bevington, Anthony Hyett, Su Wen Loh, Grace Chew, James McCracken, Derek Neoh, Belinda Yeo, Caroline Baker, Sunil Jassal, Michael Law, Natalie Zantuck, Margaret Cokelek, Mario Guerrieri, Belinda Brown, David Stoney, Michael Ng, Michael Chao ... See fewer authors

First published: 05 April 2021 | https://doi.org/10.1111/1754-9485.13180 | Citations: 1

P Chidley FRANZCR; **F Foroudi** FRANZCR, MPH, DMedSc; **M Tacey** MBiostat, BSc; **R Khor** FRANZCR, DMedSc; **J Yeh** FRANZCR; **E Bevington** FRACS; **A Hyett** FRACS; **SW Loh** FRACS; **G Chew** FRACS, PhD; **J McCracken** FRACP; **D Neoh** FRACS; **B Yeo** BA, FRACP, MD; **C Baker** FRACS; **S Jassal** FRACS; **M Law** FRACS; **N Zantuck** FRACS; **M Cokelek** BSc; **M Guerrieri** FRANZCR; **B Brown** FRACS; **D Stoney** FRACS; **M Ng** FRANZCR; **M Chao** FRANZCR, DMedSc.

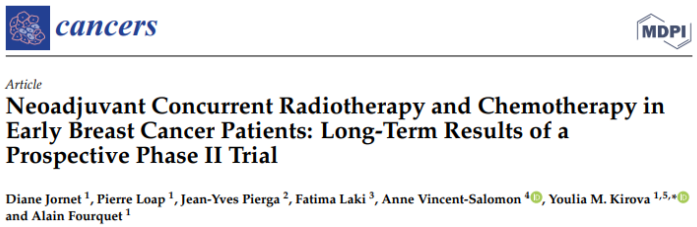
Conflict of interest: There are no conflicts of interest to declare.

153 patients

median 47 years

18/153 Grade 3 acute surgical complications

2021 Issues - Neoadjuvant RT



cancers

MDPI

Article

Neoadjuvant Concurrent Radiotherapy and Chemotherapy in Early Breast Cancer Patients: Long-Term Results of a Prospective Phase II Trial

Diane Jornet [1], Pierre Loap [1], Jean-Yves Pierga [2], Fatima Laki [3], Anne Vincent-Salomon [4], Youlia M. Kirova [1,5,*] and Alain Fourquet [1]

66 patients
Localized, not suitable for BCS
mean age of 49 years

Radiotherapy: Breast 50 Gy/25 Fx + IM and upper axillary nodes 46 Gy/23 Fx

Chemotherapy 5FU iv 24 h infusion 500 mg/m2 , D1 to D5 Vinorelbine IV 25 mg/m2 , D1 and D5 4 cycles, 21 days each

Radiotherapy started concurrently with CT #2

Boost 16 Gy / 8 Fx in no RC

Adj Chemo

2021 Issues - Neoadjuvant RT

Table 1. Patient and tumour characteristics.

Characteristics		*n*	%
Age—years (median [range])	49 (31–65)		
Menopausal			
Yes		24	41
No		35	59
Tumor maximal diameter (Baseline MRI)—mm (median [range])	38 (20–80)		
Clinical stage			
T2N0		26	44
T2N1		17	29
T3N0		9	15
T3N1		7	12
Infiltrating carcinoma			
Ductal		40	68
Lobular		13	22
Other		6	10
Histological grade			
1		12	20
2		29	49
3		18	31
Number of mitoses/10 high power field			
0		4	7
<11		38	64
11–22		4	7
>22		13	22
HER2 over-expression			
Yes		8	14
No		51	86
Ductal carcinoma in situ *component*			
Yes		21	36
No		38	64
Estrogen/progesterone receptors			
ER+/PR unknown		4	7
ER+/PR+		9	15
ER+/PR-		27	46
ER-/PR+		4	7
ER-/PR-		15	25

Median Fup 13 yy
LC 92%

2021 Issues - Hereditary BC

Practical Radiation Oncology® (2020) 10, 235-242

Clinical Practice Guideline

ASTRO Radiation Therapy Summary of the ASCO-ASTRO-SSO Guideline on Management of Hereditary Breast Cancer

Mark G. Trombetta, MD,[a] Anthony Dragun, MD,[b] Nina A. Mayr, MD,[c] and Lori J. Pierce, MD[d,*]

[a]Department of Radiation Oncology, Allegheny Health Network, Pittsburgh, Pennsylvania; [b]Department of Radiation Oncology, MD Anderson-Cooper University Hospital, Camden, New Jersey; [c]Department of Radiation Oncology, University of Washington, Seattle, Washington; and [d]Department of Radiation Oncology, Rogel Cancer Center, University of Michigan, Ann Arbor, Michigan

Received 27 February 2020; accepted 9 April 2020

Patients with newly diagnosed breast cancer **BRCA1/2 mutations may be considered for breast conserving therapy (BCT)**, expecting similar rates of local control of the index cancer as noncarriers.

The significant risk of contralateral breast cancer in these women (especially younger women), coupled with the higher risk of new cancers in the ipsilateral breast, warrant discussion on bilateral mastectomy

There is no evidence of increased toxicity or contralateral breast cancer events from radiation exposure in BRCA1/2 carriers. Patients with mutations in moderate-risk genes should be offered BCT as one choice after appropriate counseling.

2021 Issues - Hereditary BC

Practical Radiation Oncology® (2020) 10, 235-242

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www.practicalradonc.org

Clinical Practice Guideline

ASTRO Radiation Therapy Summary of the ASCO-ASTRO-SSO Guideline on Management of Hereditary Breast Cancer

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[a]*Department of Radiation Oncology, Allegheny Health Network, Pittsburgh, Pennsylvania;* [b]*Department of Radiation Oncology, MD Anderson-Cooper University Hospital, Camden, New Jersey;* [c]*Department of Radiation Oncology, University of Washington, Seattle, Washington; and* [d]*Department of Radiation Oncology, Rogel Cancer Center, University of Michigan, Ann Arbor, Michigan*

Received 27 February 2020; accepted 9 April 2020

Radiation therapy should not be withheld in **ATM carriers** if BCT is planned.

International Journal of Radiation Oncology biology • physics
www.redjournal.org

Clinical Investigations

ATM Variants in Breast Cancer: Implications for Breast Radiation Therapy Treatment Recommendations

Susan G.R. McDuff, MD, PhD,* Jennifer R. Bellon, MD,† Kristen M. Shannon, MS, LCGC,‡ Michele A. Gadd, MD,§ Samantha Dunn, BS,‖ Barry S. Rosenstein, PhD,¶,# and Alice Y. Ho, MD‖

**Duke Cancer Center, Department of Radiation Oncology, Duke Cancer Center, Durham, North Carolina; †Department of Radiation Oncology, Dana-Farber/Brigham and Women's Cancer Center, Boston, Massachusetts; ‡Cancer Center Genetics Program, Massachusetts General Hospital, Boston, Massachusetts; §Department of Surgery, Massachusetts General Hospital, Boston, Massachusetts; ‖Department of Radiation Oncology, Massachusetts General Hospital, Boston, Massachusetts; ¶Department of Radiation Oncology, Icahn School of Medicine at Mount Sinai, New York, New York; and #Department of Genetics & Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, New York*

Received Oct 8, 2020. Accepted for publication Jan 23, 2021.

For patients with germline **TP53 mutations**, mastectomy is advised and radiation therapy is contraindicated except for those with a significant risk of locoregional recurrence

2021 Issues – De-escalation in elderly

Cancer Treatment Reviews 99 (2021) 102254

Contents lists available at ScienceDirect

Cancer Treatment Reviews

journal homepage: www.elsevier.com/locate/ctrv

Systematic or Meta-analysis Studies

De-escalating adjuvant therapies in older patients with lower risk estrogen receptor-positive breast cancer treated with breast-conserving surgery: A systematic review and meta-analysis

Marie-France Savard [a,b,*], Mark Clemons [a,b], Brian Hutton [c], Meshari Jemaan Alzahrani [a], Jean-Michel Caudrelier [d], Lisa Vandermeer [b], Michelle Liu [b], Deanna Saunders [b], Marta Sienkiewicz [b], Carol Stober [b], Katherine Cole [a], Risa Shorr [e], Angel Arnaout [b,f], Lynn Chang [d]

[a] Department of Medicine, Division of Medical Oncology, The Ottawa Hospital and the University of Ottawa, Ottawa, Canada
[b] Cancer Therapeutics Program, Ottawa Hospital Research Institute, Ottawa, Canada
[c] Clinical Epidemiology Program, The Ottawa Hospital Research Institute and University of Ottawa, Ottawa, Canada
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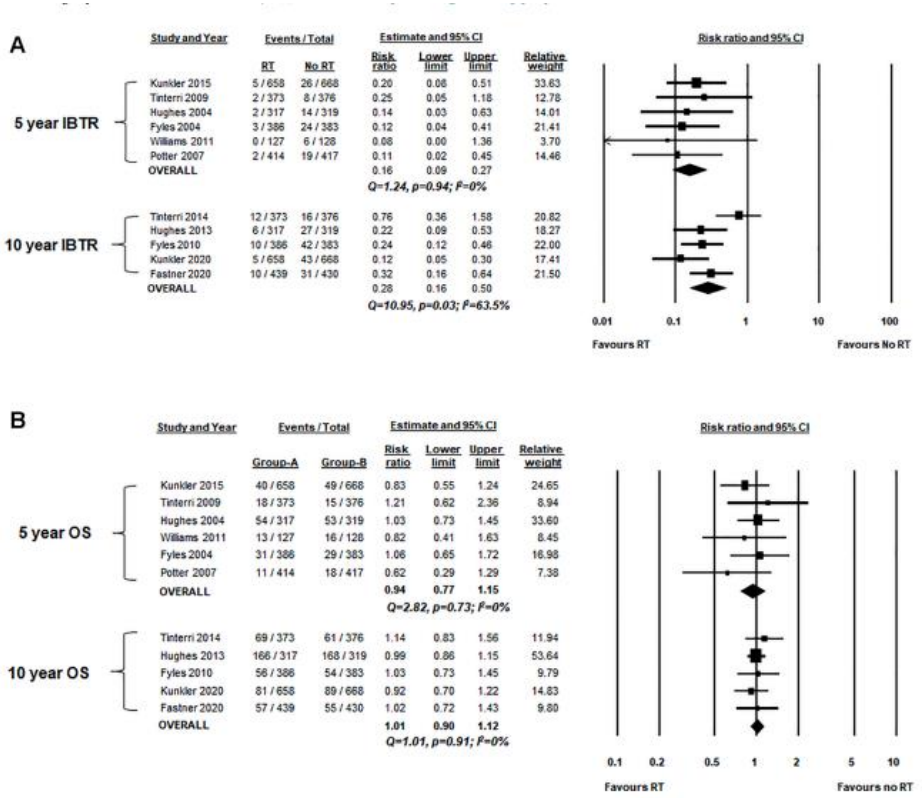
[f] Department of Surgery, Division of General Surgery, The Ottawa Hospital and the University of Ottawa, Ottawa, Canada



Elderly definition

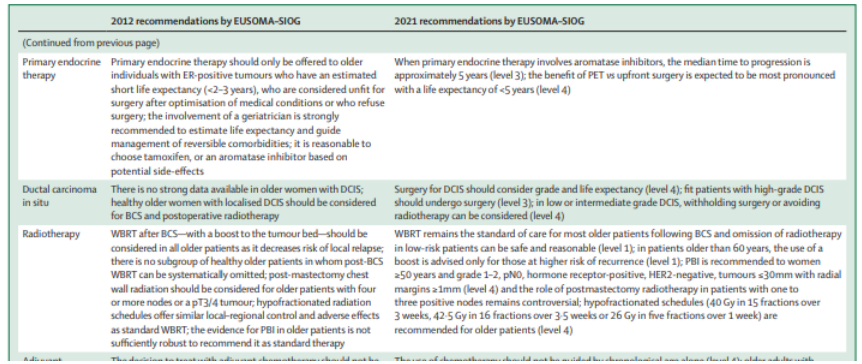
OS is the right end-point?

2021 Issues – De-escalation in elderly

Policy Review

Updated recommendations regarding the management of older patients with breast cancer: a joint paper from the European Society of Breast Cancer Specialists (EUSOMA) and the International Society of Geriatric Oncology (SIOG)

Laura Biganzoli, Nicolò Matteo Luca Battisti, Hans Wildiers, Amelia McCartney, Giuseppe Colloca, Ian H Kunkler, Maria-João Cardoso, Kwok-Leung Cheung, Nienke Aafke de Glas, Rubina M Trimboli, Beatriz Korc-Grodzicki, Enrique Soto-Perez-de-Celis, Antonio Ponti, Janice Tsang, Lorenza Marotti, Karen Benn, Matti S Aapro, Etienne G C Brain



	2012 recommendations by EUSOMA-SIOG	2021 recommendations by EUSOMA-SIOG
(Continued from previous page)		
Primary endocrine therapy	Primary endocrine therapy should only be offered to older individuals with ER-positive tumours who have an estimated short life expectancy (<2–3 years), who are considered unfit for surgery after optimisation of medical conditions or who refuse surgery; the involvement of a geriatrician is strongly recommended to estimate life expectancy and guide management of reversible comorbidities; it is reasonable to choose tamoxifen, or an aromatase inhibitor based on potential side-effects	When primary endocrine therapy involves aromatase inhibitors, the median time to progression is approximately 5 years (level 3); the benefit of PET *vs* upfront surgery is expected to be most pronounced with a life expectancy of <5 years (level 4)
Ductal carcinoma in situ	There is no strong data available in older women with DCIS; healthy older women with localised DCIS should be considered for BCS and postoperative radiotherapy	Surgery for DCIS should consider grade and life expectancy (level 4); fit patients with high-grade DCIS should undergo surgery (level 3); in low or intermediate grade DCIS, withholding surgery or avoiding radiotherapy can be considered (level 4)
Radiotherapy	WBRT after BCS—with a boost to the tumour bed—should be considered in all older patients as it decreases risk of local relapse; there is no subgroup of healthy older patients in whom post-BCS WBRT can be systematically omitted; post-mastectomy chest wall radiation should be considered for older patients with four or more nodes or a pT3/4 tumour; hypofractionated radiation schedules offer similar local-regional control and adverse effects as standard WBRT; the evidence for PBI in older patients is not sufficiently robust to recommend it as standard therapy	WBRT remains the standard of care for most older patients following BCS and omission of radiotherapy in low-risk patients can be safe and reasonable (level 1); in patients older than 60 years, the use of a boost is advised only for those at higher risk of recurrence (level 1); PBI is recommended to women ≥50 years and grade 1–2, pN0, hormone receptor-positive, HER2-negative, tumours ≤30 mm with radial margins ≥1 mm (level 4) and the role of postmastectomy radiotherapy in patients with one to three positive nodes remains controversial; hypofractionated schedules (40 Gy in 15 fractions over 3 weeks, 42·5 Gy in 16 fractions over 3·5 weeks or 26 Gy in five fractions over 1 week) are recommended for older patients (level 4)
Adjuvant	The decision to treat with adjuvant chemotherapy should not be	The use of chemotherapy should not be avoided by chronological age alone (level 4); older adults with

Omissione RT possibile nei casi a basso rischio

The efficacy of adjuvant endocrine therapy is independent of age (level 1); good compliance should be the driving factor for treatment choice and adjusted according to side-effects (level 4); the choice of drug and decisions on its duration should be made in the context of multimorbidities and estimated risk of breast cancer recurrence as side-effects might limit compliance and impact substantially on health domains relevant to older patient

2021 Issues – De-escalation in elderly

Breast Care

Review Article

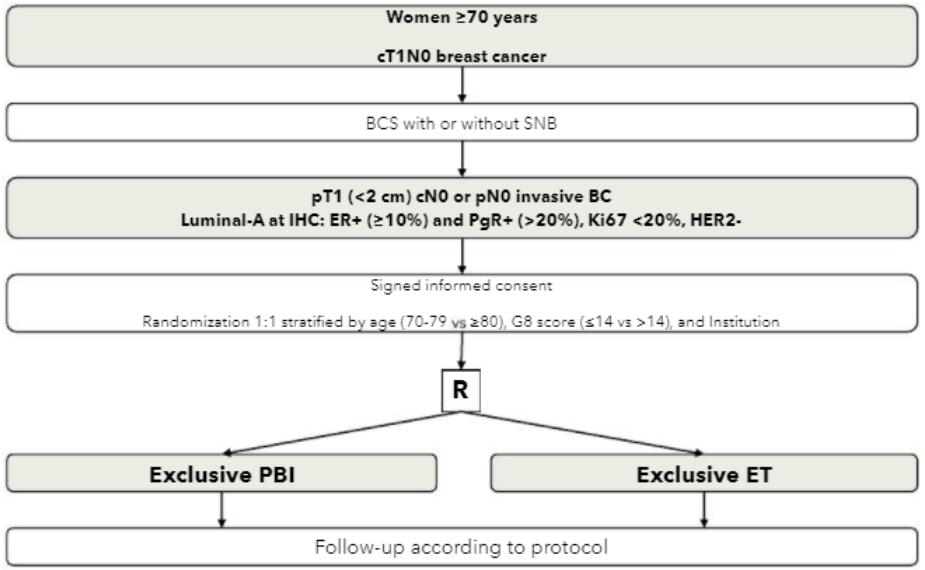
Breast Care 2021;16:135–143
DOI: 10.1159/000516114

Received: March 25, 2021
Accepted: March 25, 2021
Published online: April 7, 2021

St. Gallen/Vienna 2021: A Brief Summary of the Consensus Discussion on Customizing Therapies for Women with Early Breast Cancer

The panel did not endorse omission of radiotherapy after breast conservation in women older than 70 in general (74%), node-positive disease (90%), or tumours >2.5 cm (80%), but was willing to omit radiotherapy in patients with tumours < 2,5 cm, low grade o low genomic score.

EUROPA trial



EUROPA trial. NCT04134533 (v1.3 Nov 2020)

The Future

- Maggiore selezione APBI
- Maggiore diffusione dell’ipofrazionamento FAST Forward
- Ricerca clinica «elderly»
- Combinazioni con immunoterapia/nuovi farmaci

Grazie per l’attenzione!!!!!