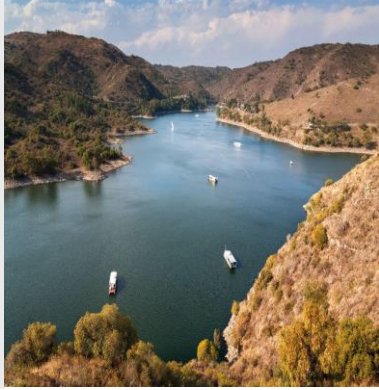
FUNDACION MARIE CURIE
Córdoba - Argentina

Congreso sobre Avances Integrados en Oncología, Radiocirugía y Física Médica: Innovación y Precisión en el tratamiento del cáncer



Indicación de irradiación ganglionar en pacientes N0

Philip Poortmans, MD, PhD

Iridium Netwerk & Antwerp University, Antwerpen (B)

Former President

Conflict of interest

Affidea – medical advisor

MSD - consultant

And I worry about the future…


STOP
WARS

RNI after upfront surgery for N0-disease

- Introduction – a word about history
- Evidence – from the past
- More recent data
- What to wait for
- Take home messages

RNI for N0-disease: *Introduction – a word about history*

Who of you would advise/give RNI to N0-patients?

- Never
- In ≤25% of N0 cases
- In 25-75% of N0 cases
- In ≥75% of N0 cases

RNI for N0-disease: *Introduction – a word about history*

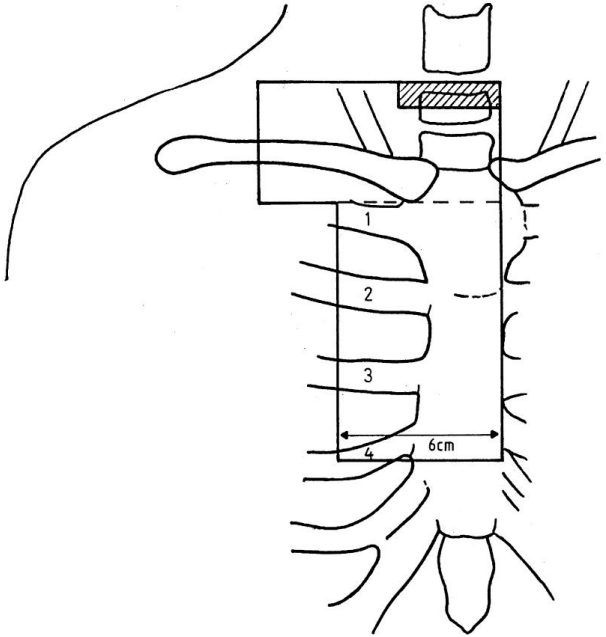
What we learned during my residency training:

- RT improves locoregional control
- Systemic T *(preMP=CMF*6; postMP=tam20mg)* delays recurrences
- Survival is about stage
- All breast cancer is equal
- Introduction BST – always (in Europe) + WBI & boost (BT)
- PMRT for all N+ and central/medial located N0
- Field-based RT

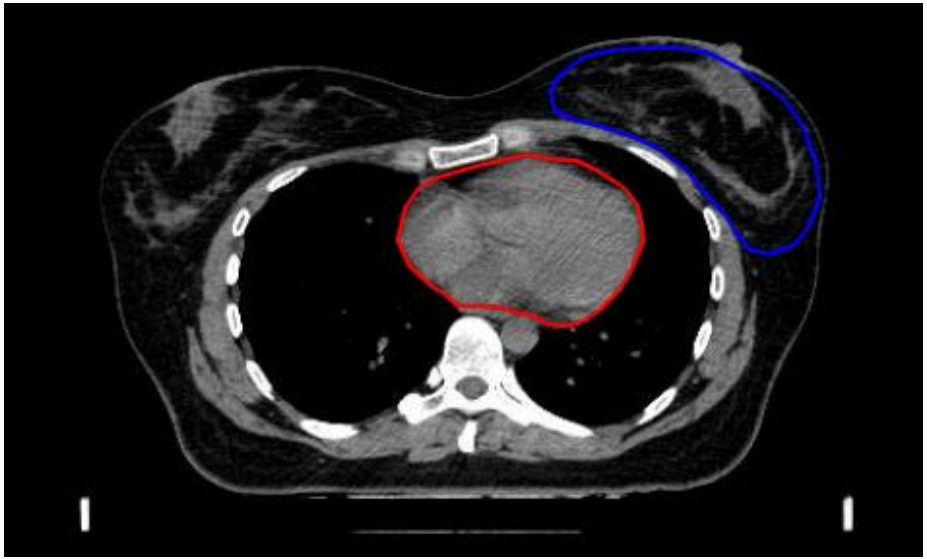
RNI for N0-disease: *Introduction – a word about history*

So what we actually **thought that we** did:

With RNI



Without RNI



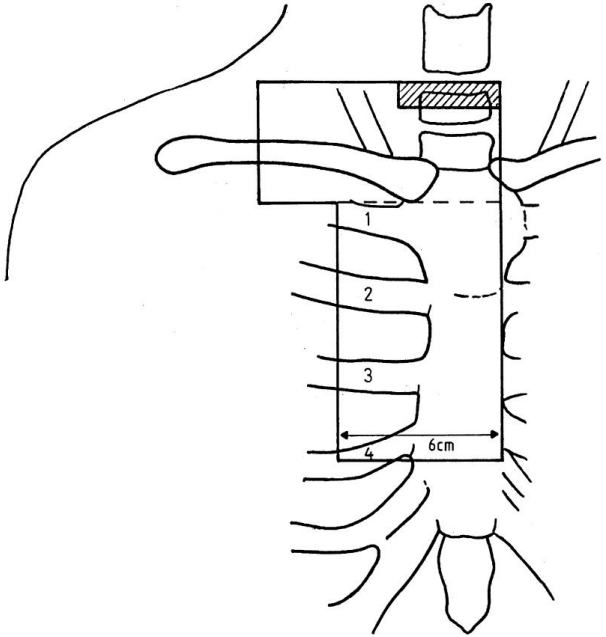
Lievens Y, et al. Radiother Oncol 2001;60:257-65.

Falcon contouring WS

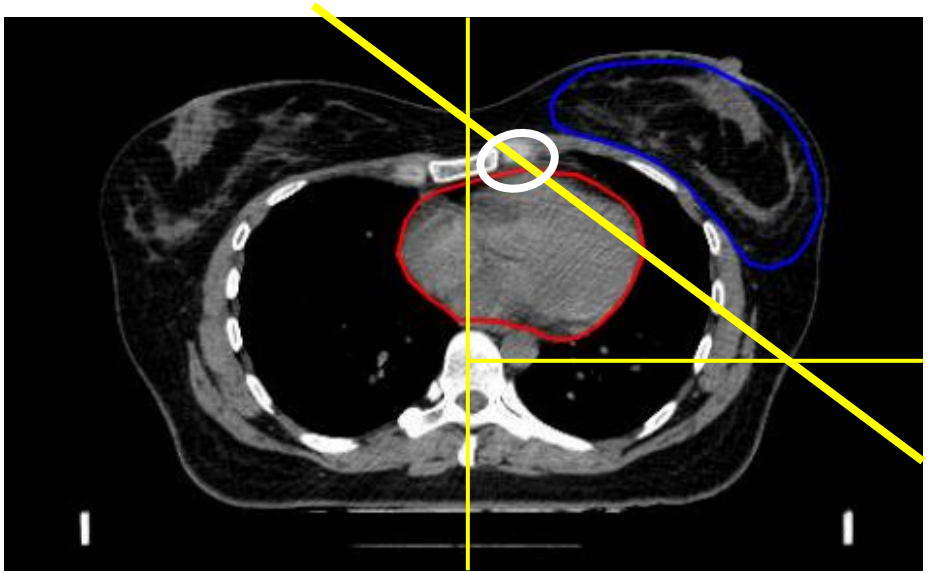
RNI for N0-disease: *Introduction – a word about history*

So what we actually ~~thought that we~~ did:

With RNI



Without RNI



Lievens Y, et al. Radiother Oncol 2001;60:257-65.

Falcon contouring WS

RNI for N0-disease: *Introduction – a word about history*

So what we actually ~~thought that we~~ did:

With RNI Without RNI

Table 6. Summary of the dose at the internal mammary lymph node chain for both treatment arms

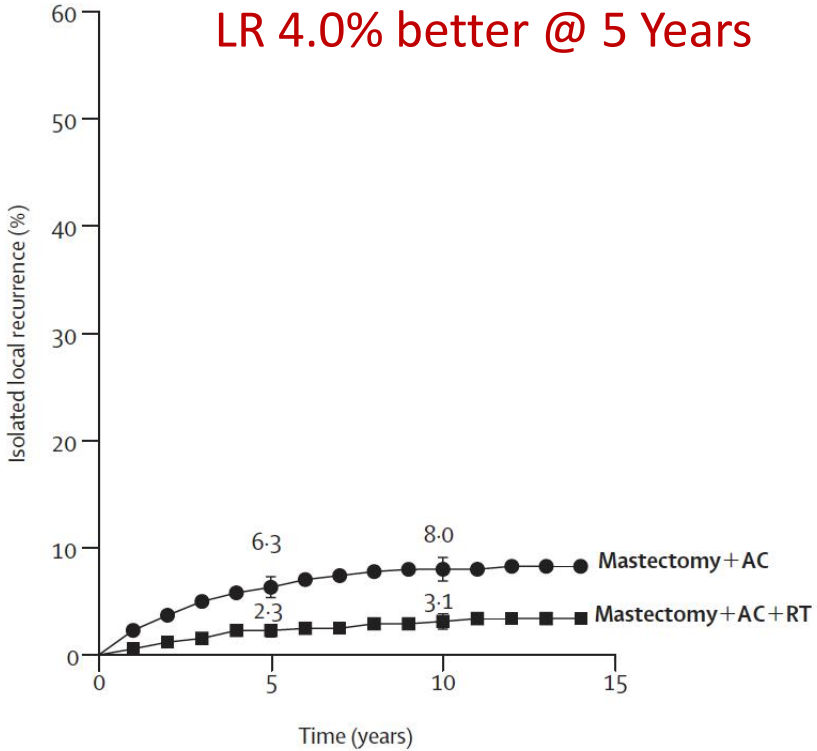
% of prescribed dose:	<50%	50–84%	≥85%
Arm 1 = without RNI	90	6	4
Arm 2 = with RNI	5	16	79

Poortmans P, et al. IJROBP 2001;49:1399–408.

RNI for N0-disease: *Introduction – a word about history*

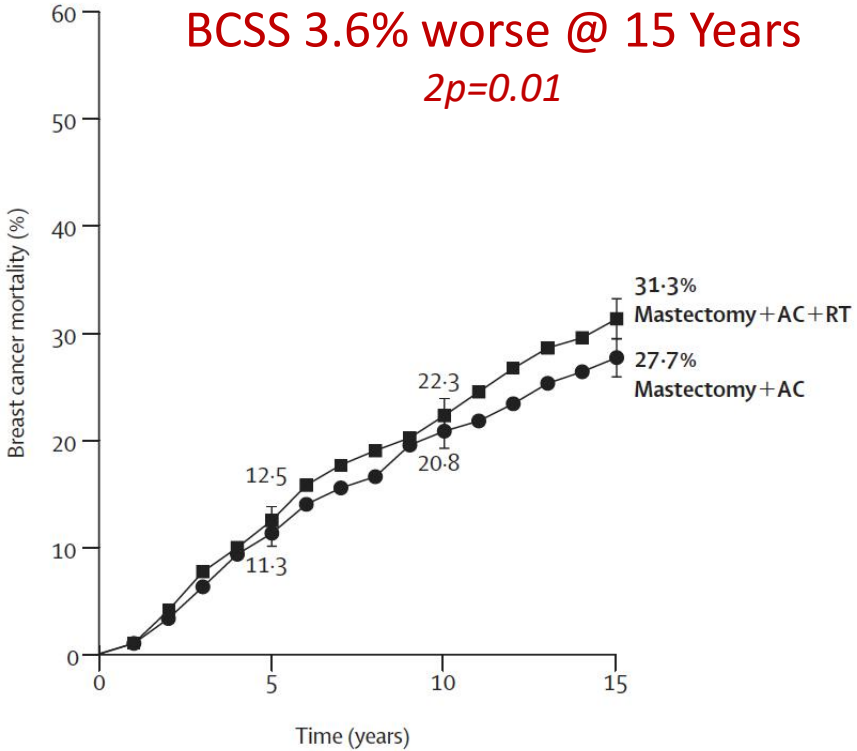
1428 women with node-negative disease after mastectomy with axillary clearance

LR 4.0% better @ 5 Years



BCSS 3.6% worse @ 15 Years

2p=0.01



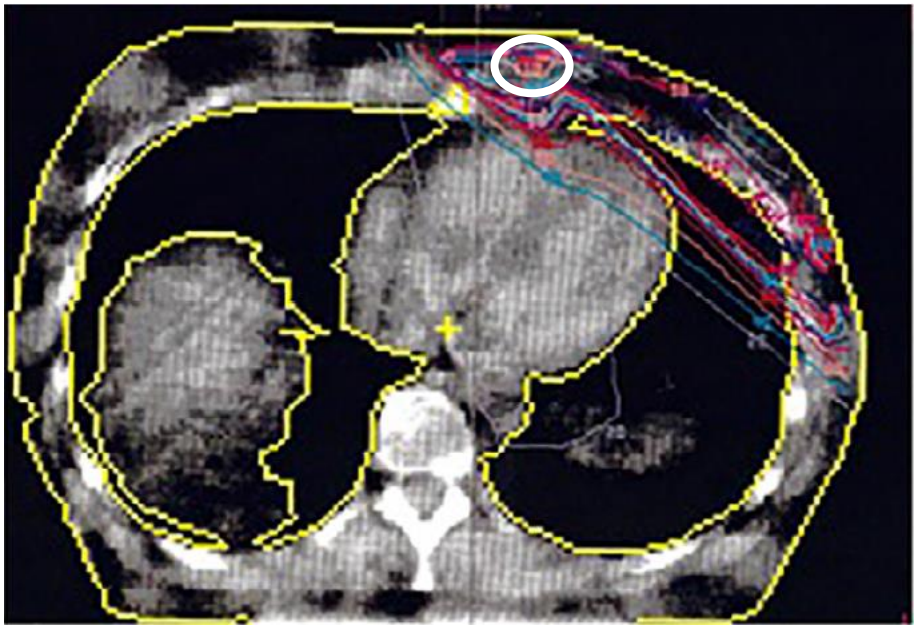
EBCTCG. Lancet 2005; 366: 2087–106.

AC = axillary clearance

RNI for N0-disease: *Introduction – a word about history*

But what was the real reason to abandon IMN-RT … or to develop new techniques?

BVI-technique 1995: from up to ≥185% hotspot to ≤135%



Kaidar-Person O, et al. Radiother Oncol. 2022;172:99–110.

RNI after upfront surgery for N0-disease

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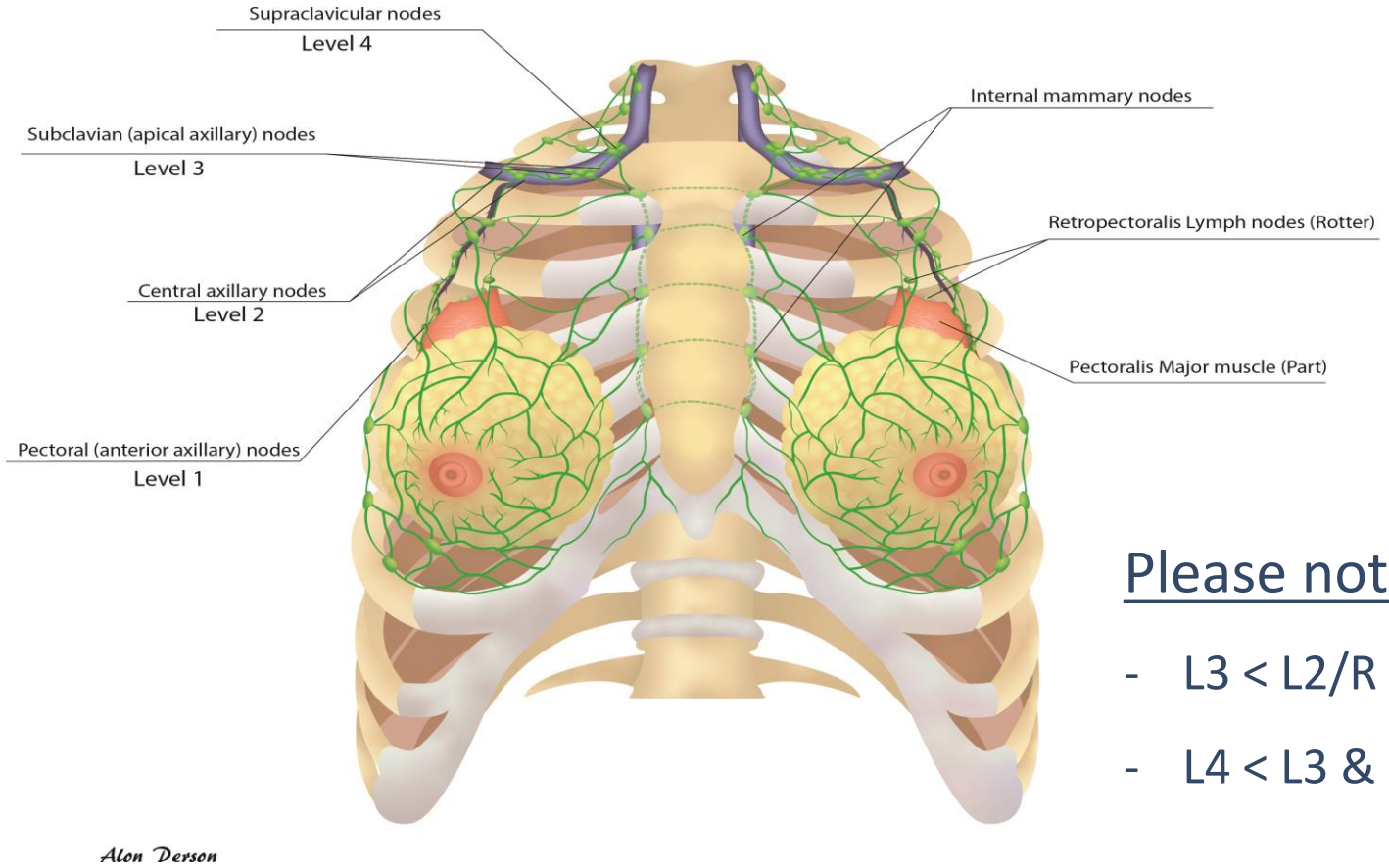
RNI for N0-disease: *Evidence – from the past*

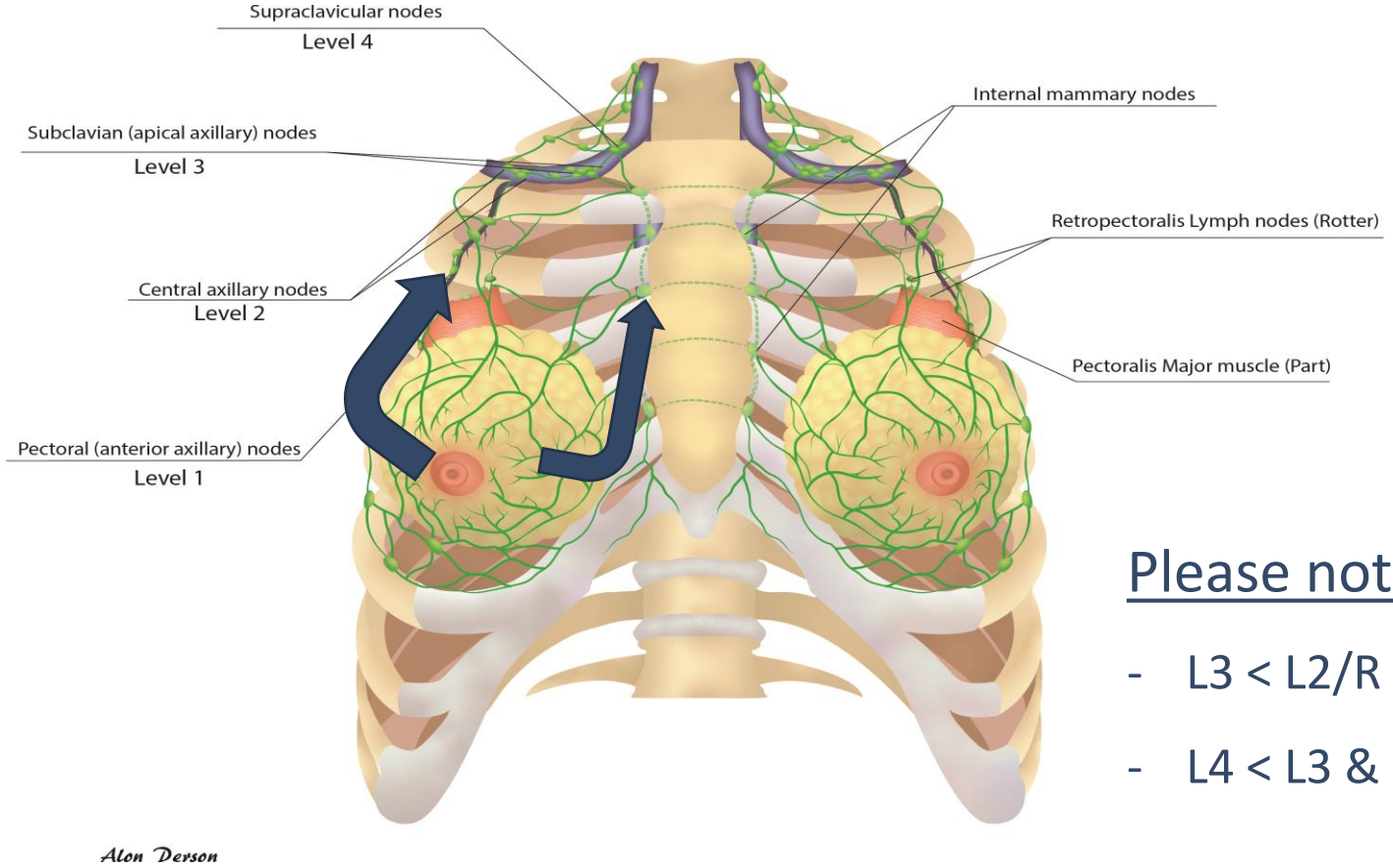


Please note:

- L3 < L2/R & IMC
- L4 < L3 & IMC

Kaidar-Person O, et al. R&O 2019;137:159–166.

RNI for N0-disease: *Evidence – from the past*



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Kaidar-Person O, et al. R&O 2019;137:159–166.

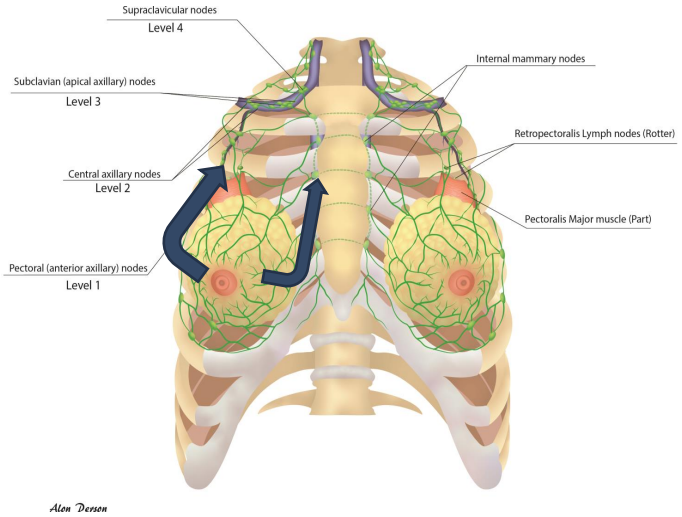
RNI for N0-disease: *Evidence – from the past*

The frequency of internal mammary chain (IMC) drainage as a function of primary tumour location (P=0.017)

Tumour quadrant	Number of Patients (%)	Rate of drainage to IMC (%)
Upper outer	128 (46)	14.1
Upper inner	30 (11)	16.7
Lower outer	19 (7)	31.6
Lower inner	14 (5)	42.9
Central	88 (31)	28.4

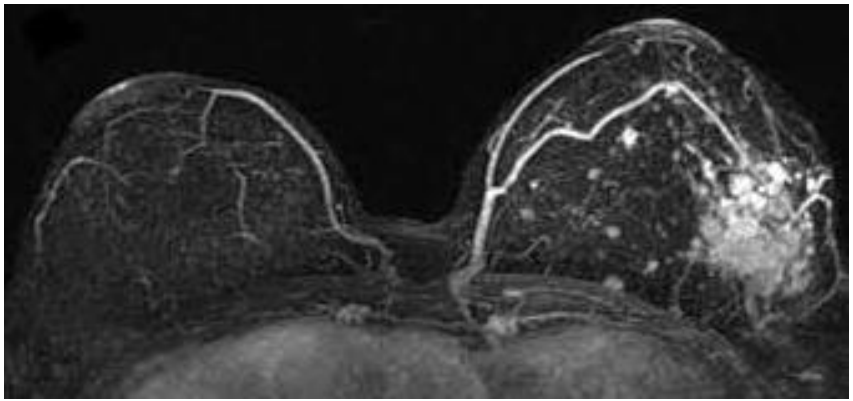
Shahar KH, et al. Cancer 2005;103:1323-9.

RNI for N0-disease: *Evidence – from the past*



Other factors influencing drainage:

- Deep lymphatic plexus more ➔ IMC
- Site of injection for SLNB: IT > periT >> subareolar/subdermal ➔ IMC



https://breast-cancer.ca/mrifacts/

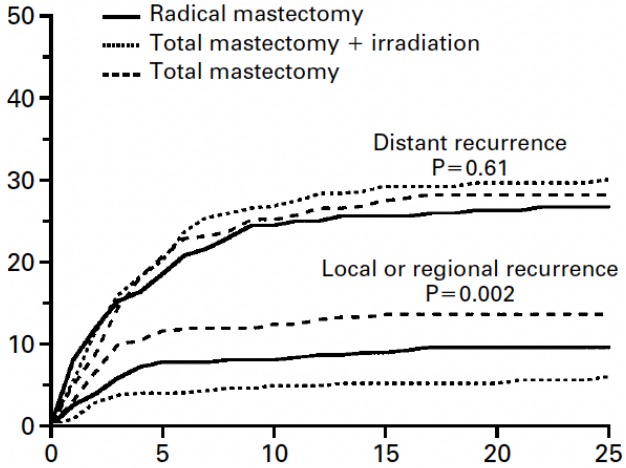
Kaidar-Person O, et al. R&O 2019;137:159–166.

RNI for N0-disease: *Evidence – from the past*

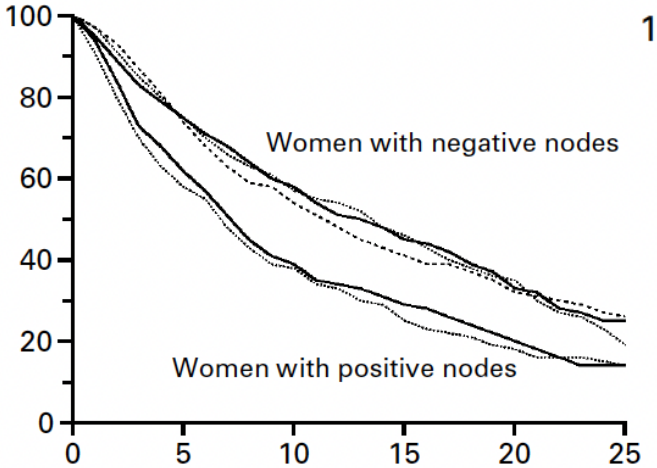
NSABP B-04 (1971-74): n=1079 cN0: radical mast. vs total mast. + PMRT vs total mast.

Total mastectomy = without ALND; radical mast. = 40% pN+; total mast. = 18.6% RR (not considered as such)

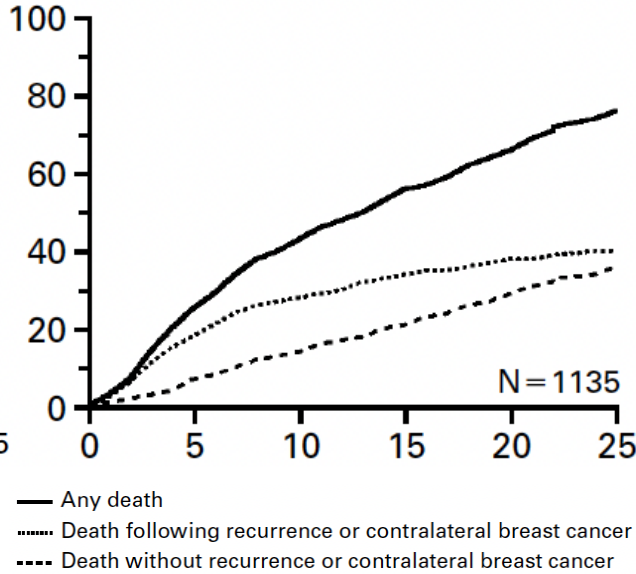
LR – RR – DM



Overall survival



Causes of death



Fisher B, et al. N Engl J Med. 2002;347:567-575.

RNI for N0-disease: *Evidence – from the past*

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Total mastectomy = without ALND; radical mast. = 40% pN+; total mast. = 18.6% RR (not considered as such)

TM alone: 21% of patients without any nodes removed developed an axillary recurrence
12% in patients who had “incidentally” 1 to 5 nodes removed
none in those with ≥6 “incidentally” removed

RM: nodal recurrences exclusively occurred if ≥4 involved nodes

Fisher B, et al. N Engl J Med. 2002;347:567-575.

RNI for N0-disease: *Evidence – from the past*

Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer

N = 1778 / 4004 are pN0

Internal mammary and medial supraclavicular lymph node chain irradiation in stage I–III breast cancer (EORTC 22922/10925): 15-year results of a randomised, phase 3 trial

Poortmans P, et al. N Engl J Med 2015;373:317-27.

Poortmans P, et al. Lancet Oncol. 2020;21:1602-10.

RNI for N0-disease: *Evidence – from the past*

Comprehensive regional LN irradiation – pulled together

Radiotherapy to Regional Nodes in Early Breast Cancer:

An Individual Patient Data Meta-Analysis of

14,324 Women in 16 Trials.

N = 2188 are pN0 ➔ 81% < EORTC trial

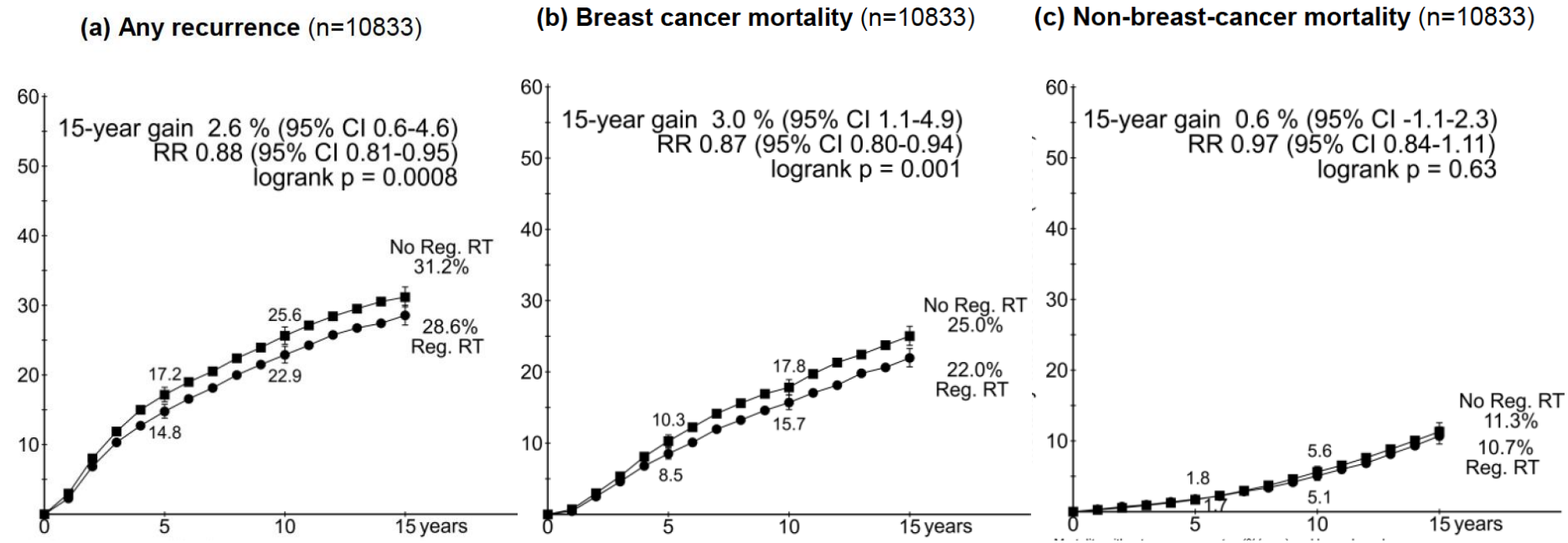
Early Breast Cancer Trialists' Collaborative Group* (EBCTCG)

Dodwell D, et al. Lancet. 2023;402:1991-2003.

RNI for N0-disease: *Evidence – from the past*

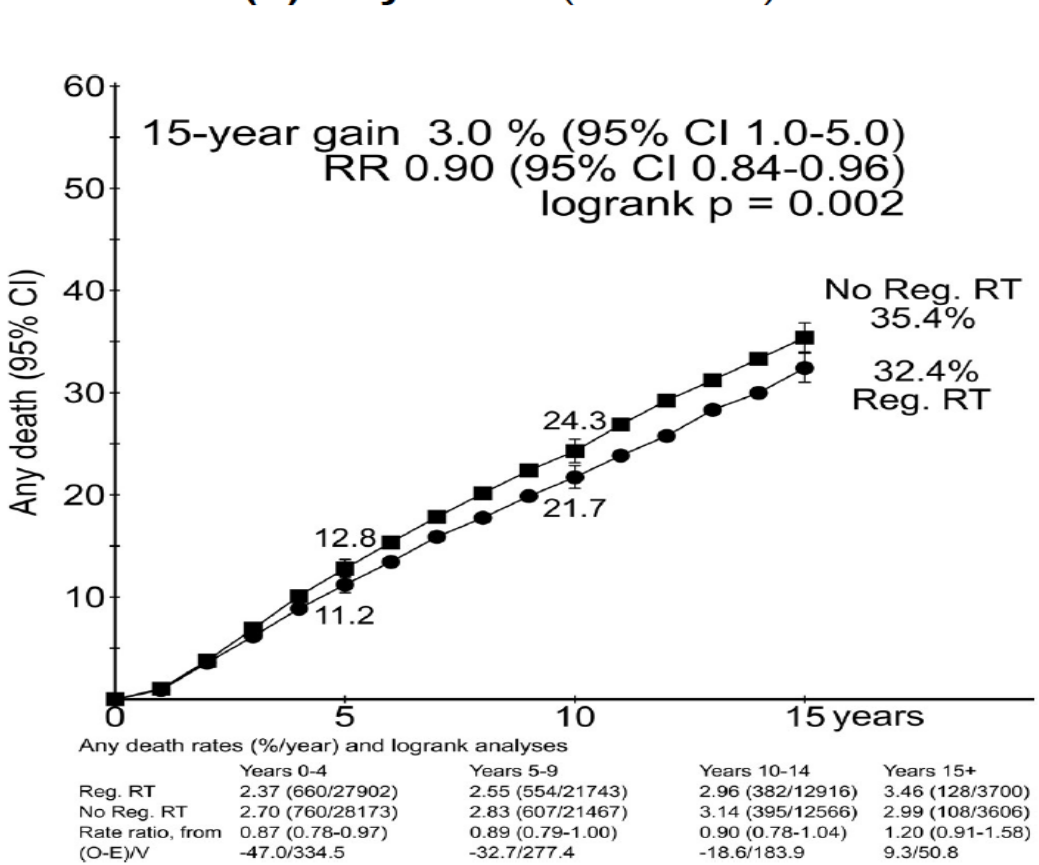
Comprehensive regional LN irradiation – pulled together

New trials, starting after 1989, only *(n = 12167)*



Dodwell D, et al. Lancet. 2023;402:1991-2003.

RNI for N0-disease: *Evidence – from the past*



Any death rates (%/year) and logrank analyses

	Years 0-4	Years 5-9	Years 10-14	Years 15+
Reg. RT	2.37 (660/27902)	2.55 (554/21743)	2.96 (382/12916)	3.46 (128/3700)
No Reg. RT	2.70 (760/28173)	2.83 (607/21467)	3.14 (395/12566)	2.99 (108/3606)
Rate ratio, from	0.87 (0.78-0.97)	0.89 (0.79-1.00)	0.90 (0.78-1.04)	1.20 (0.91-1.58)
(O-E)/V	-47.0/334.5	-32.7/277.4	-18.6/183.9	9.3/50.8

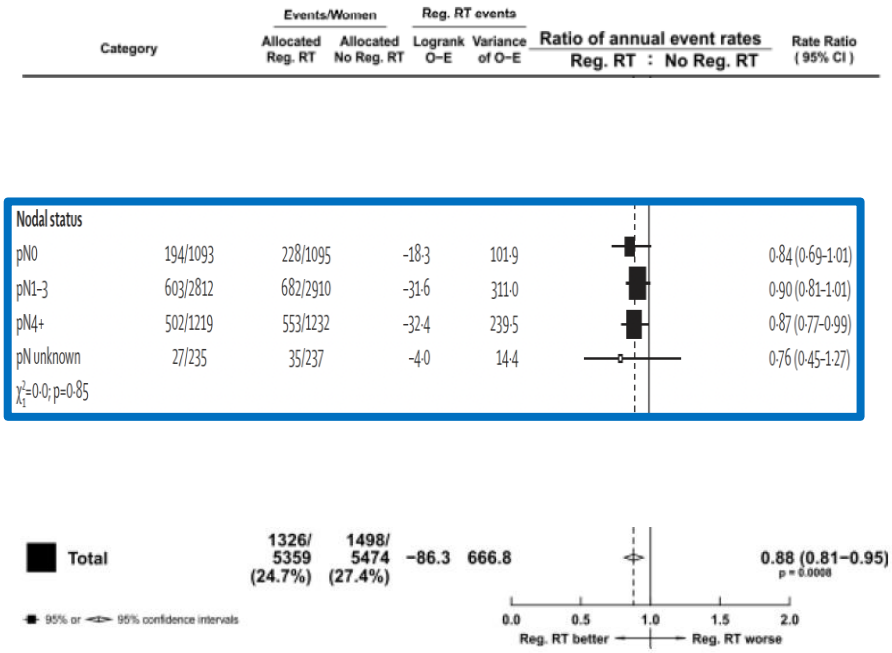
Dodwell D, et al. Lancet. 2023;402:1991-2003.

RNI for N0-disease: *Evidence – from the past*

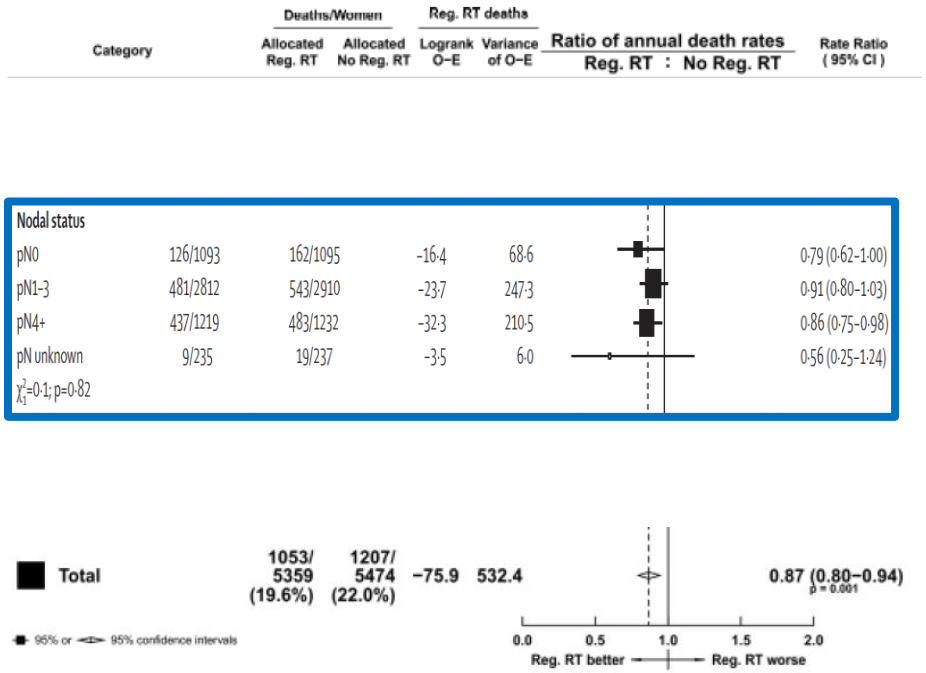
Comprehensive regional LN irradiation – pulled together

Trials starting after 1989 only

(a) Any recurrence



(b) Breast cancer mortality



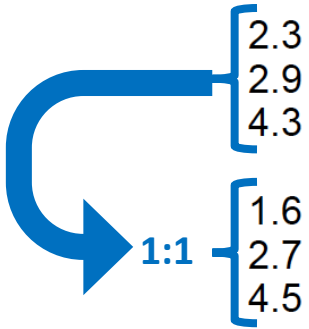
Dodwell D, et al. Lancet. 2023;402:1991-2003.

RNI for N0-disease: *Evidence – from the past*

Comprehensive regional LN irradiation – pulled together

Trials starting after 1989 only

Outcome	Nodal status	15-year risk		
		Regional RT (%)	No Regional RT (%)	Gain from regional RT (%)
Any recurrence	pN0	19.0	21.3	2.3
	pN1-3	25.6	28.5	2.9
	pN4+	46.8	51.1	4.3
Breast cancer mortality	pN0	10.9	12.5	1.6
	pN1-3	20.3	23.0	2.7
	pN4+	40.5	45.0	4.5



Dodwell D, et al. Lancet. 2023;402:1991-2003.

RNI after upfront surgery for N0-disease

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RNI for N0-disease: *More recent data*

Post-Mastectomy Radiation Therapy in Human Epidermal Growth Factor Receptor 2 Positive Breast Cancer Patients: Analysis of the HERA Trial

International Journal of Radiation Oncology biology • physics

www.redjournal.org

Joseph Abi Jaoude, MD,* Evandro de Azambuja, MD,† Maha Makki, MS,‡ Hani Tamim, PhD,§ Arafat Tfayli, MD,§,‖ Fady Geara, MD, PhD,¶ Martine Piccart, MD, PhD,† Philip Poortmans, MD,# and Youssef H. Zeidan, MD, PhD¶

With PMRT in:

98/488 = 20%

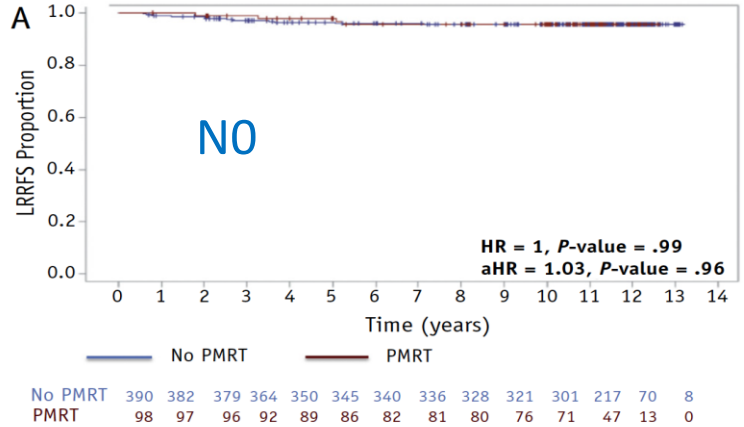
250/517 = 48%

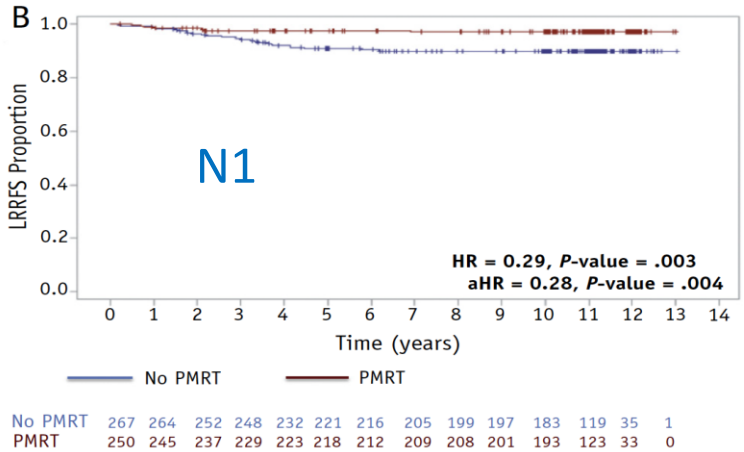
592/628 = 94%

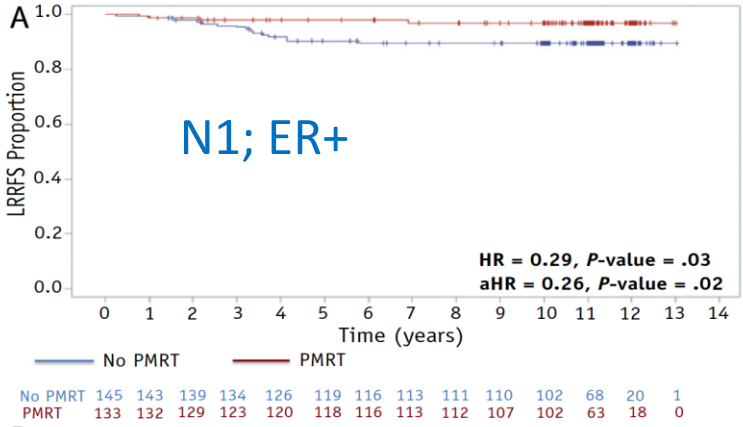
	PMRT (n = 940)	No PMRT (n = 693)	*P* value
Nodal status, no. (%)			
N0	98 (10.4)	390 (56.3)	<.0001
1-3 positive lymph nodes	250 (26.6)	267 (38.5)	
≥4 positive lymph nodes	592 (63.0)	36 (5.2)	

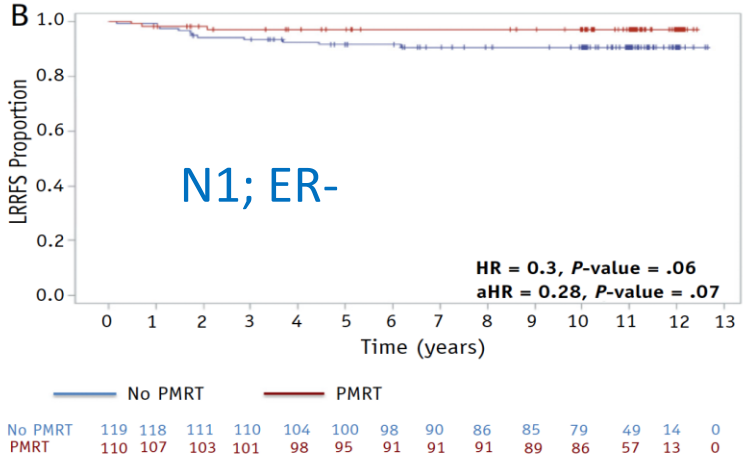
Abi Jaoude J, et al. IJROBP 2020;106:503-10.

RNI for N0-disease: *More recent data*









Abi Jaoude J, et al. IJROBP 2020;106:503-10.

RNI for N0-disease: *More recent data*

Ann Surg Oncol
https://doi.org/10.1245/s10434-021-10511-2

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BREAST ONCOLOGY

Post-mastectomy Radiation Therapy in Triple-Negative Breast Cancer Patients: Analysis of the BEATRICE Trial

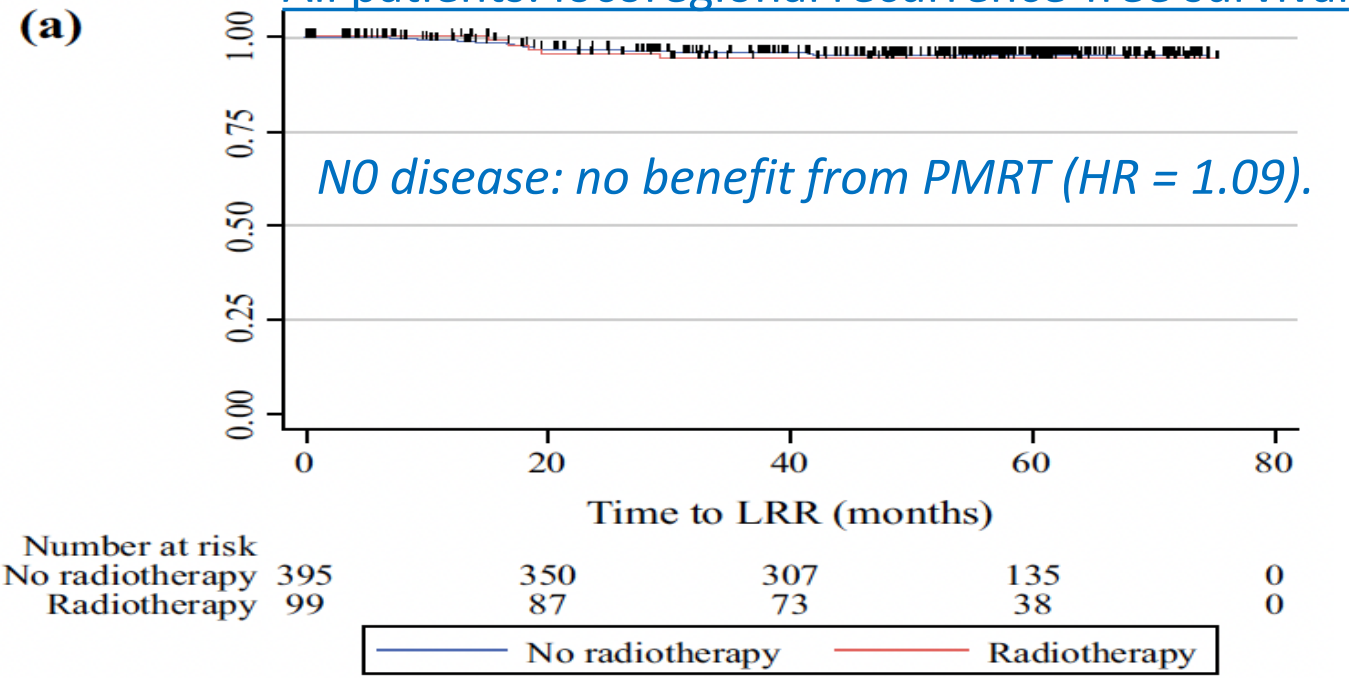
Majd Kayali, MD[1], Joseph Abi Jaoude, MD[1], Mohammed Mohammed, MD[1], Joanne Khabsa, MPH[3], Arafat Tfayli, MD[4], Philip Poortmans, MD, PhD[5,6], and Youssef H. Zeidan, MD, PhD[1,2]

	PMRT (n = 359)	No PMRT (n = 581)	p-Value
Nodal status, no. (%)			With PMRT in: < ***0.0001***
0 positive lymph nodes	99 (27.58)	395 (67.99)	99/494 = 20%
1–3 positive lymph nodes	119 (33.15)	156 (26.85)	119/274 = 43%
≥ 4 positive lymph nodes	141 (39.28)	30 (5.16)	141/171 = 82%

Kayali M, et al. Ann Surg Oncol. 2022;29:460-466.

RNI for N0-disease: *More recent data*

All patients: locoregional recurrence-free survival



N0 disease: no benefit from PMRT (HR = 1.09).

Kayali M, et al. Ann Surg Oncol. 2022;29:460-466.

RNI for N0-disease: *More recent data*

Interaction between systemic and locoregional treatments

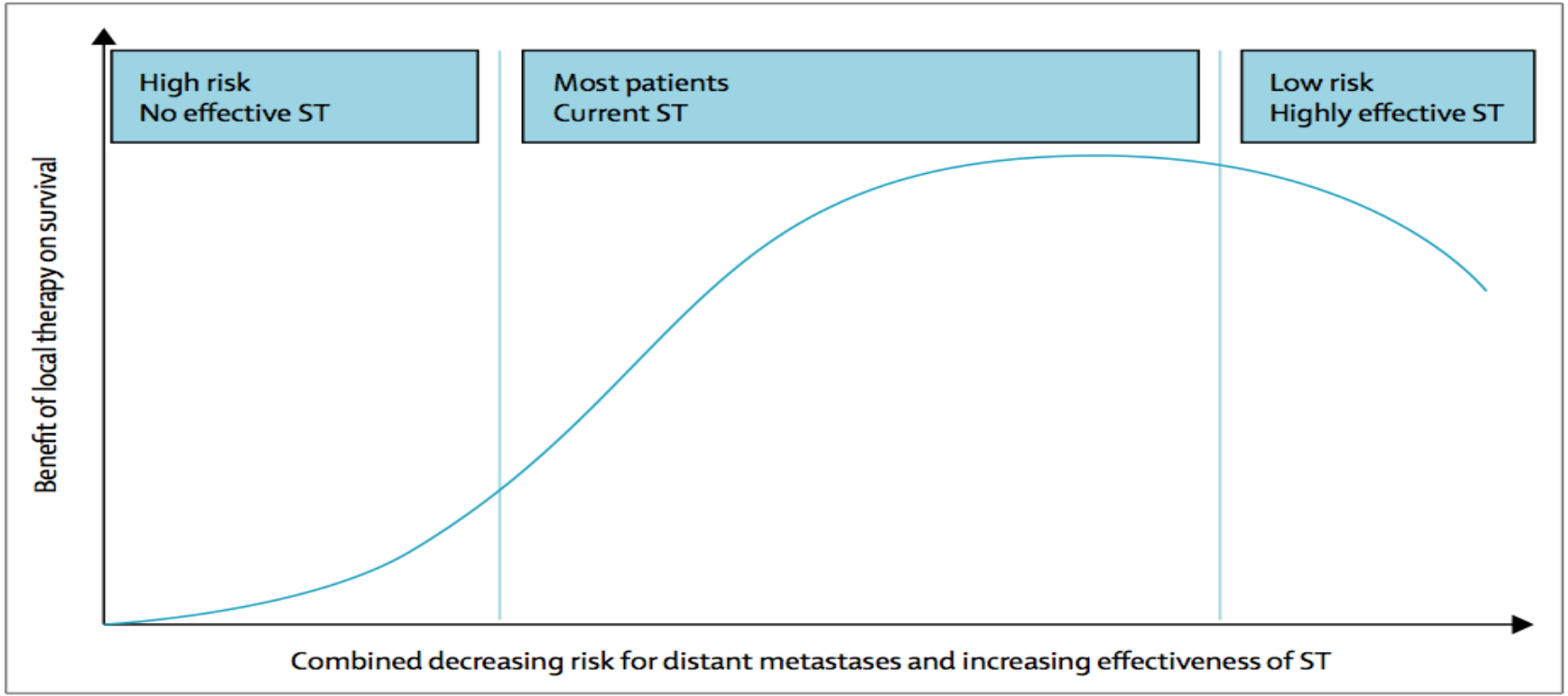


***Figure*: Combined hypothetical benefit of local tumour control on survival with increasing effectiveness of systemic therapy (ST) and decreasing risk of distant metastases of the primary tumour**

Poortmans P. Lancet. 2014 Jun 21;383(9935):2104-6.

RNI for N0-disease: *More recent data*

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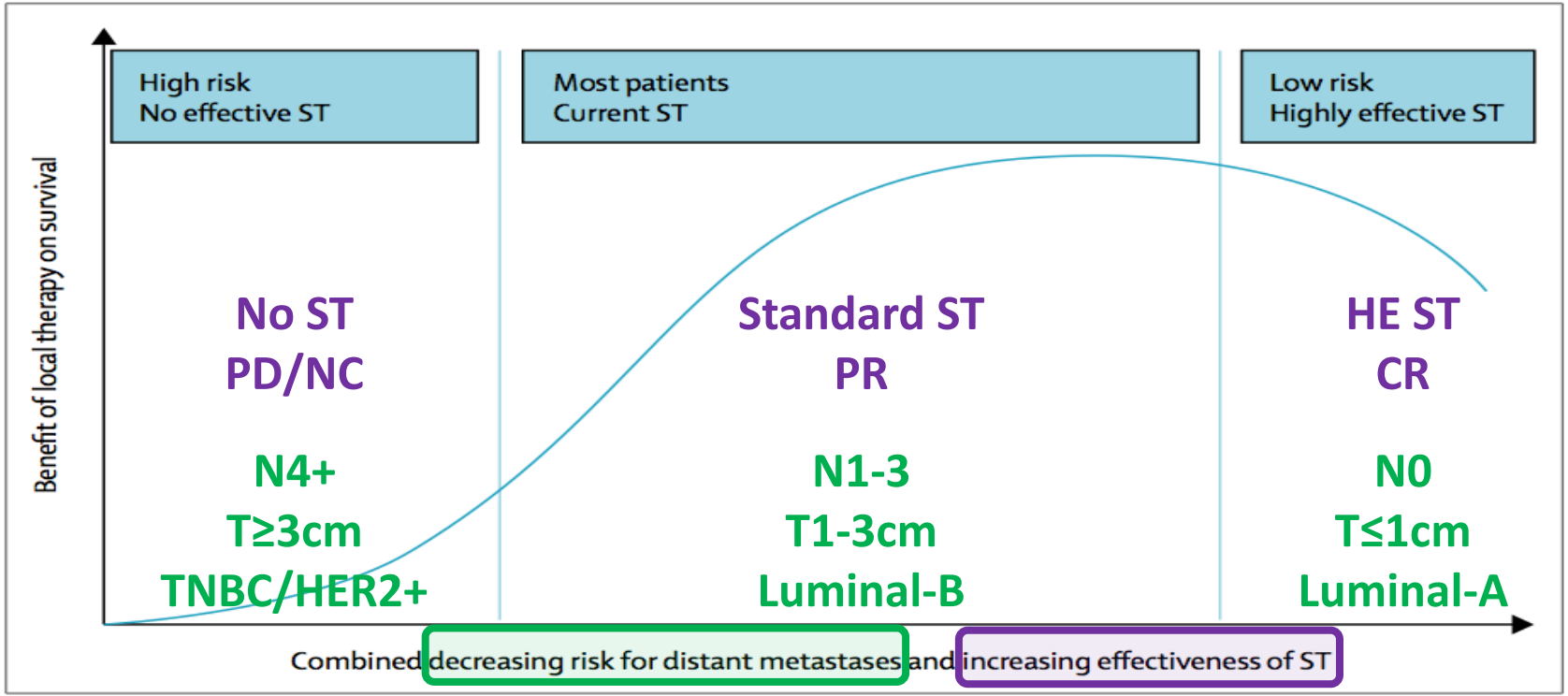

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RNI for N0-disease: *What to wait for*

Table S6. Data available in trials beginning before the year 2009 comparing radiotherapy versus no radiotherapy to the regional nodes

Characteristic		61H B-03	64E Oslo	69A H'berg	72A WSSA	73C Mayo	73E Milan	74Q P'mont	78B Toron.-Ed.	89* T'pere	91V Lyon	95L IOSG	96T EORTC	00B MA-20	03! DBCG	07H IAEA	08# KROG
Nodal status	pN0	0	355	75	0	0	0	13	0	195	309	0	1778	177	0	38	0
	pN1-3	0	142	0	0	112	43	128	27	34	631	0	1725	1558	1818	283	304
	pN4+	0	44	0	0	129	13	0	22	6	392	0	498	97	1271	148	431
	pN unknown	748	1	68	217	0	0	19	1	27	2	435	3	0	0	7	0

Dodwell D, et al. Lancet. 2023;402:1991-2003.

RNI for N0-disease: *What to wait for*

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	pN unknown	748	1	68	217	0	0	19	1	27	2	435	3	0	0	7	0

Planned analysis using the data of the (data on file!) 20-years analysis ➔ focussing on the pN0 patients

Dodwell D, et al. Lancet. 2023;402:1991-2003.

RNI for N0-disease: *What to wait for*

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	pN unknown	748	1	68	217	0	0	19	1	27	2	435	3	0	0	7	0

DBCG IMN-1 & IMN-2 studies: included ~ 300-400

T3N0 patients ➔ will be analysed separately

Personal communication Birgitte Offersen

Dodwell D, et al. Lancet. 2023;402:1991-2003.

RNI for N0-disease: *What to wait for*

XXth century

ONE SIZE
FITS ALL

http://ithare.com/cpp-guidelines-made-to-measure-s-one-size-fits-all/

RNI for N0-disease: *What to wait for*

Lancet Oncol 2016
Published Online
December 16, 2016
http://dx.doi.org/10.1016/
S1470-2045(16)30660-X

Comment

*Philip Poortmans, Orit Kaidar-Person, Paul Span

Radiation oncology enters the era of individualised medicine

Lancet Oncol 2020
Published Online
August 4, 2021
https://doi.org/10.1016/
S1470-2045(21)00411-3

Comment

*Orit Kaidar-Person, Philip Poortmans, Roberto Salgado

Genomic-adjusted radiation dose to personalise radiotherapy

CrossMark

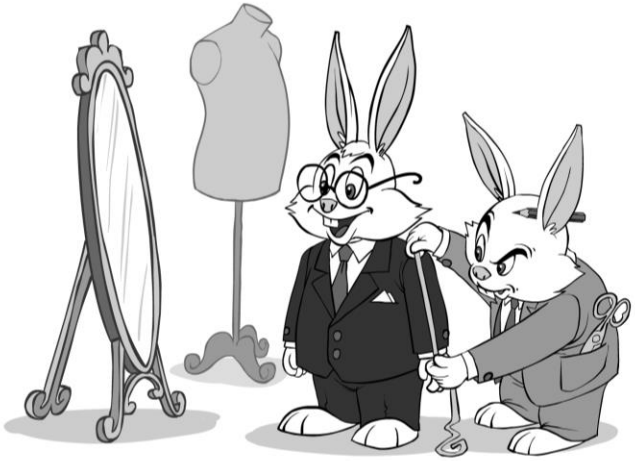
Poortmans P, et al. TLO 2017;18:159-60.

RNI for N0-disease: *What to wait for*

XXth century

ONE SIZE
FITS ALL

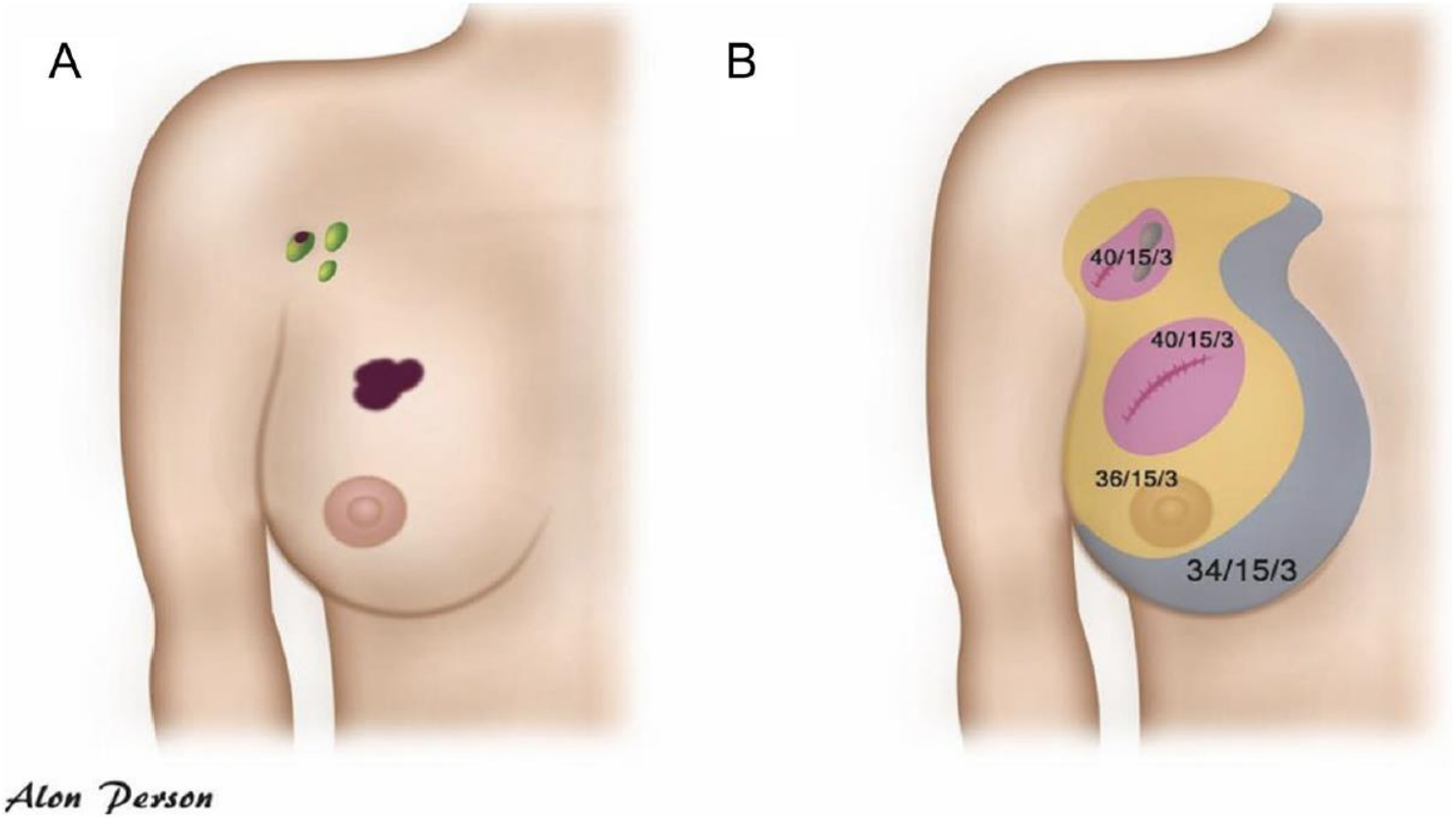
XXIst century



MADE TO
MEASURE

http://ithare.com/cpp-guidelines-made-to-measure-s-one-size-fits-all/

RNI for N0-disease: *What to wait for*



Kaidar-Person O, et al. La radiologia medica 2024;129:315-327.

RNI after upfront surgery for N0-disease

- Introduction – a word about history
- Evidence – from the past
- More recent data
- What to wait for
- Take home messages

RNI for N0-disease: *Take home messages*

The Breast 31 (2017) 295–302

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

Over-irradiation

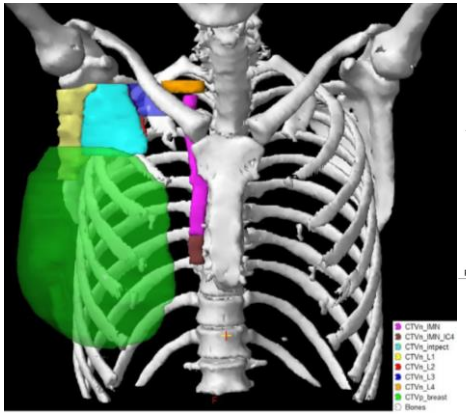
Philip M.P. Poortmans [a, *], Meritxell Arenas [b], Lorenzo Livi [c]

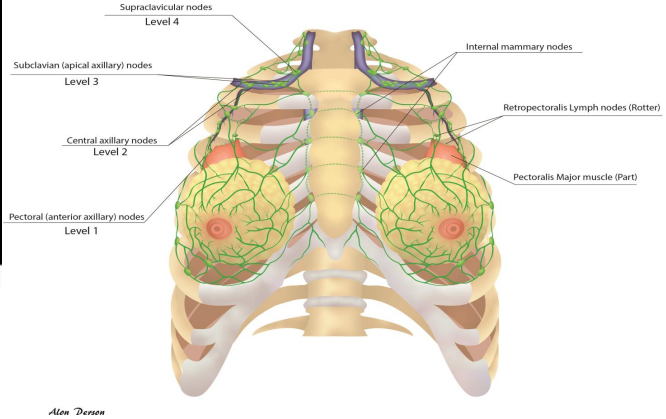
Poortmans P, et al. Breast. 2017;31:295-302.

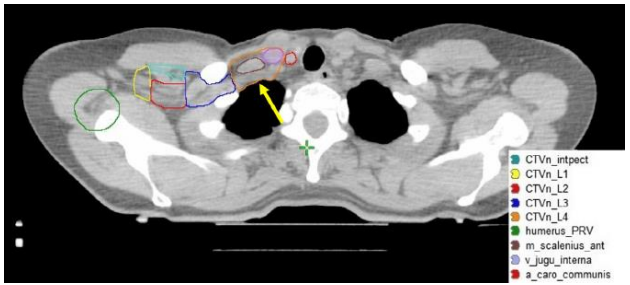
RNI for N0-disease: *Take home messages*

Transition 20th ➔ 21st century

- *Number of target volumes*
- *Size of target volumes*
- *Dose*
- *Number of fractions*







Offersen BV, et al. Radiother Oncol 2015;114:3-10 & 2016;118:205-8. Kaidar-Person O, et al. R&O 2019;137:159–166.

RNI for N0-disease: *Take home messages*

- ✓ *Elective nodal irradiation improves DFS for N0 patients in the presence of risk factors and/or in case of central/medial location.*
- ✓ *Absolute benefit depends on the absolute recurrence risks in combination with the effectiveness of systemic therapy.*
- ✓ *The side effects of RT delivered with contemporary techniques are very limited.*

RNI for N0-disease: *Take home messages*

Interaction between systemic and locoregional treatments

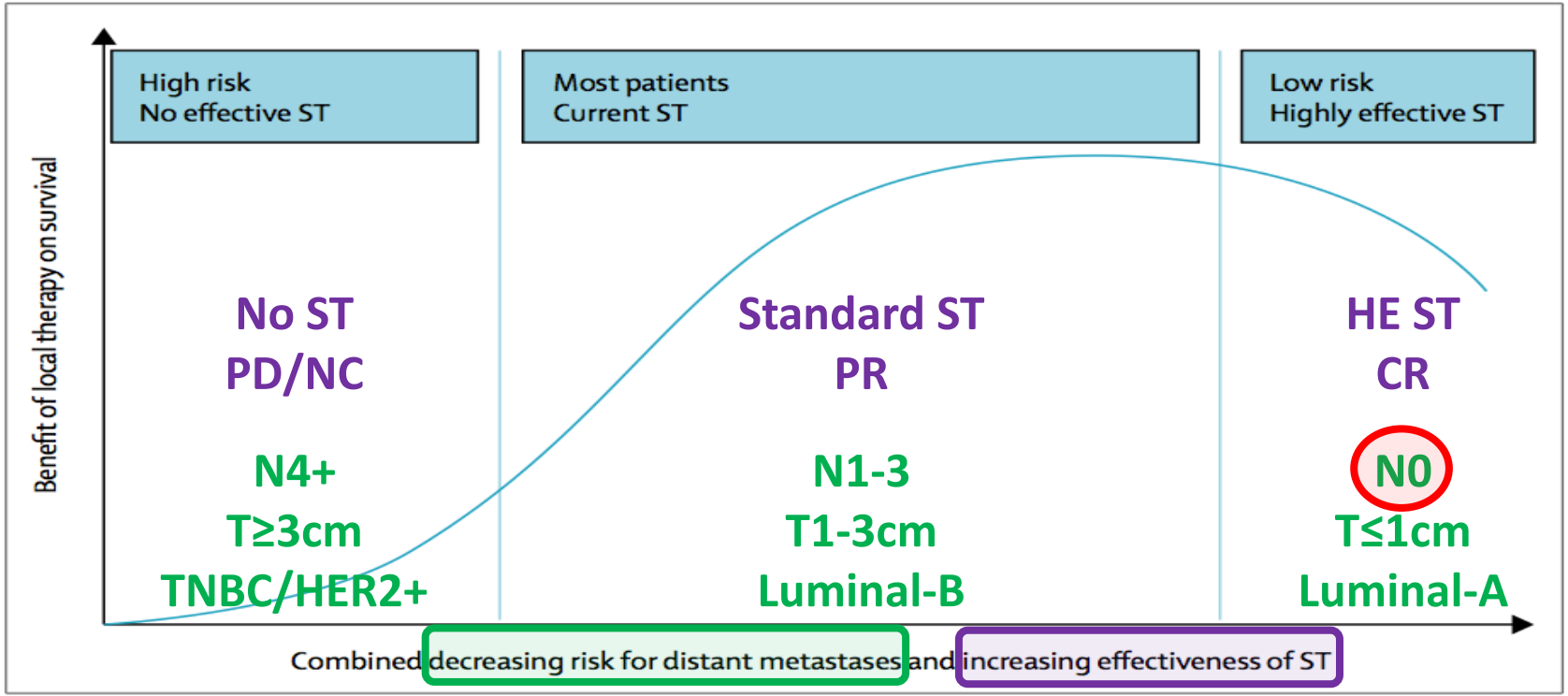
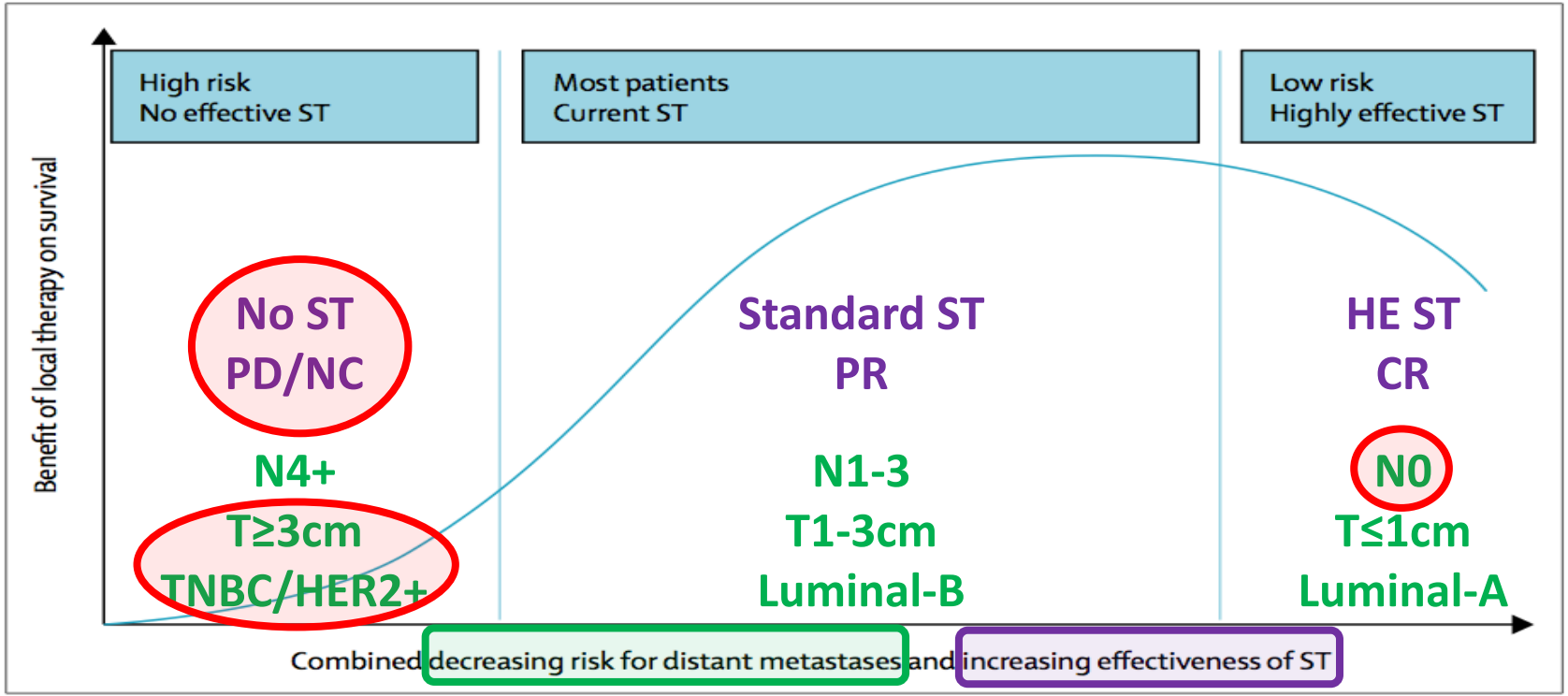


***Figure*: Combined hypothetical benefit of local tumour control on survival with increasing effectiveness of systemic therapy (ST) and decreasing risk of distant metastases of the primary tumour**

Poortmans P. Lancet. 2014 Jun 21;383(9935):2104-6.

RNI for N0-disease: *Take home messages*

Interaction between systemic and locoregional treatments



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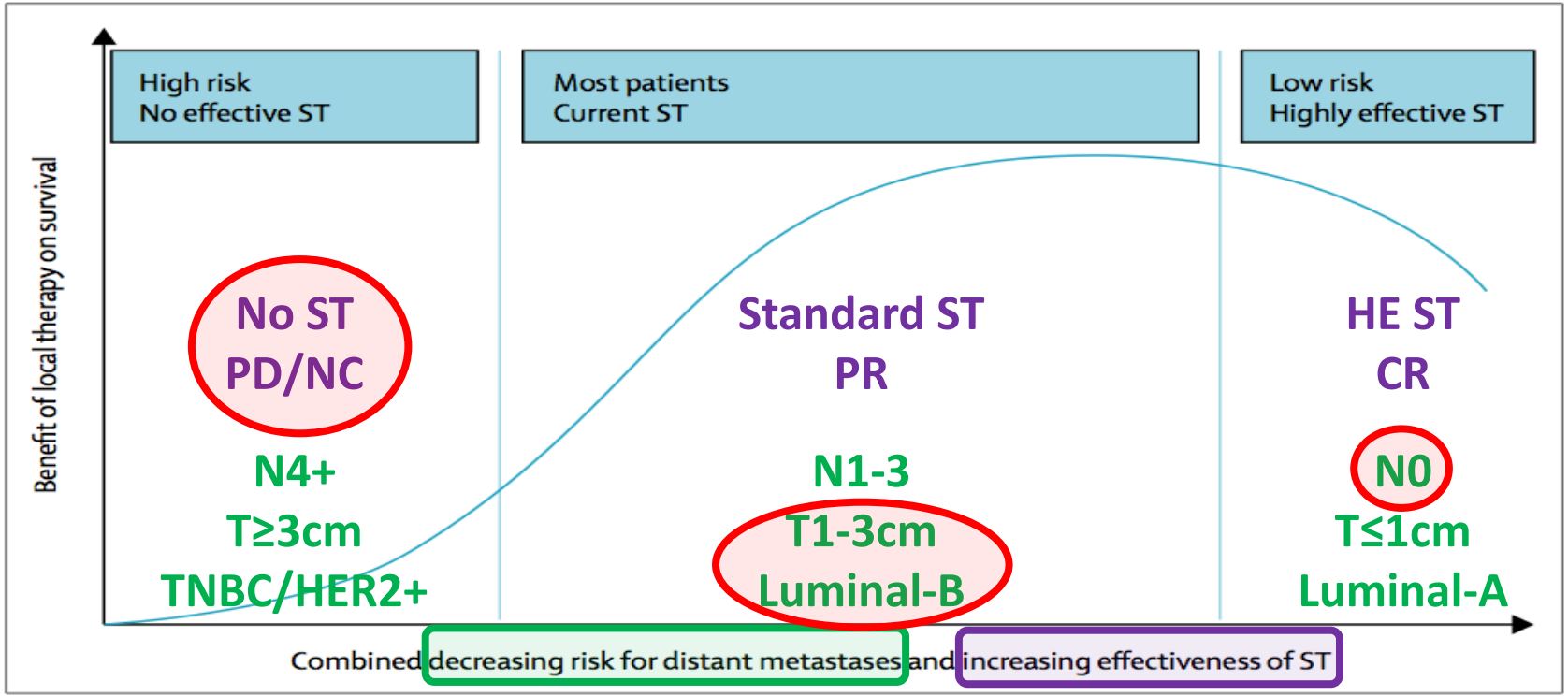

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RNI for N0-disease: *Take home messages*

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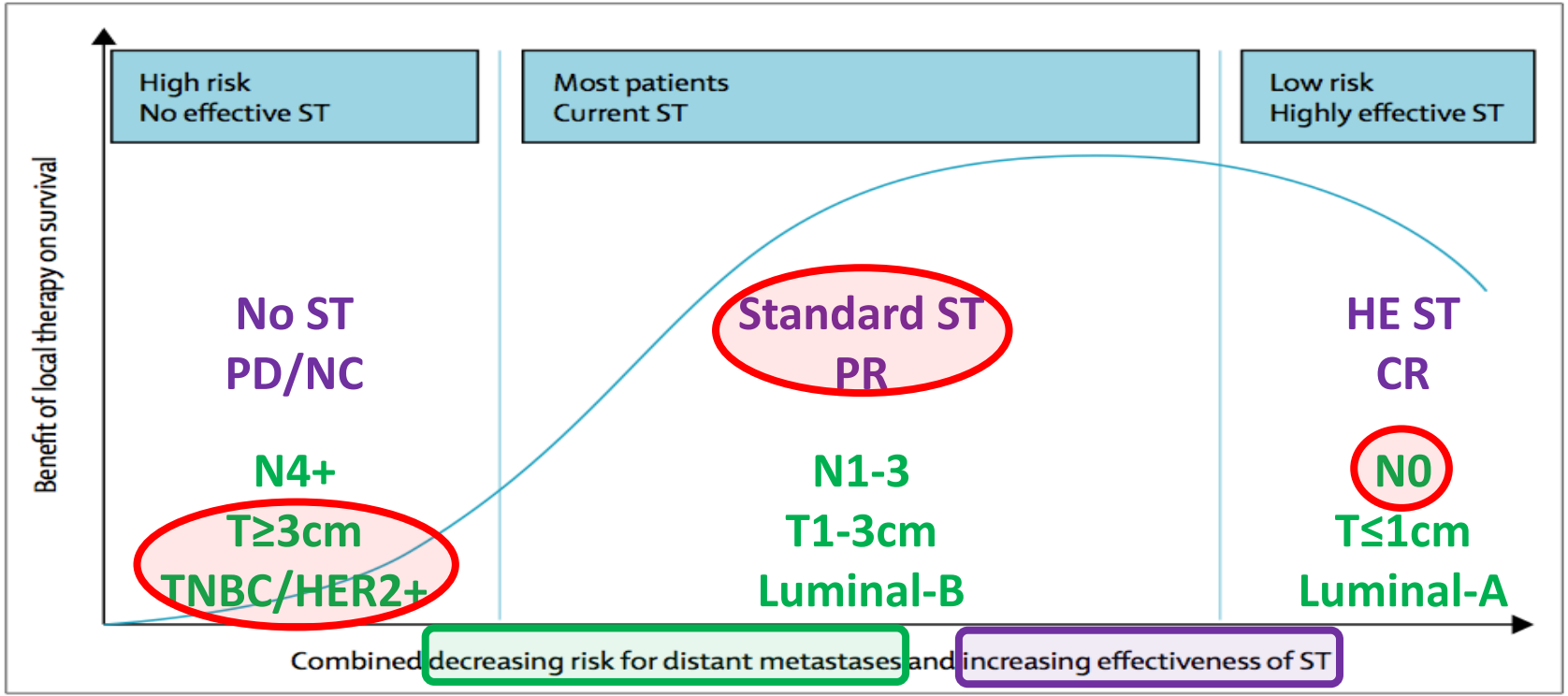

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RNI for N0-disease: *Take home messages*

What would you do for:

- Pre-MP woman, aged 43

- TNBC cT2G3N0M0, 3 cm upper-lower quadrant

- PST with good clinical response

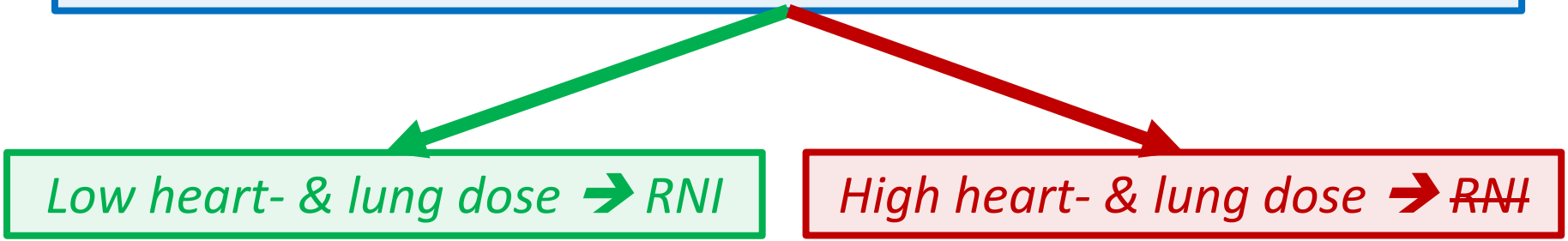
- Lumpectomy and SLNB: ypT1aN0 – zone of fibrotic response of 2.8cm (R0)

RNI for N0-disease: *Take home messages*

What would you do for:

- Pre-MP woman, aged 43
- TNBC cT2G3N0M0, 3 cm upper-lower quadrant
- PST with good clinical response
- Lumpectomy and SLNB: ypT1aN0 – zone of fibrotic response of 2.8cm (R0)

Why not: WBI + treatment planning for IM and axilla levels 3-4?



RNI for N0-disease: *Acknowledgements*

Too many to list…

… risking forgetting people…

Orit Kaidar-Person · Icro Meattini · Philip Poortmans *Editors*

Breast Cancer Radiation Therapy

A Practical Guide for Technical Applications

The book provides, in a comprehensive yet concise way, essential information to improve the knowledge and skills of all healthcare providers involved in the treatment of patients with breast cancer. The content does not focus on general information that is widely available via different sources, but on technical aspects – "hands-on" daily practices and principles of radiation oncology that are not included in other books. Drawing on information taught in courses at e.g. the ESTRO School, as well as the authors' broad clinical experience, the respective contributions reflect and share the expertise of leading experts in breast cancer radiation therapy, supported by sound data and evidence. Each chapter includes a short introduction summarizing the evidence in the literature and "pearls" (a short bullet-point summary), and is enriched by tables, figures and illustrations to provide a concise, easy-to-follow and appealing overview.

The book, containing also useful electronic supplementary material, will be of interest to a wide range of readers, including radiation oncologists, radiation technicians, medical physicists, and others involved in breast cancer care.

ISBN 978-3-030-91169-0

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Kaidar-Person · Meattini · Poortmans *Eds.*

Breast Cancer Radiation Therapy

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A Practical Guide for Technical Applications

Orit Kaidar-Person
Icro Meattini
Philip Poortmans
Editors

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