New paradigms in regional nodal irradiation – breast cancer

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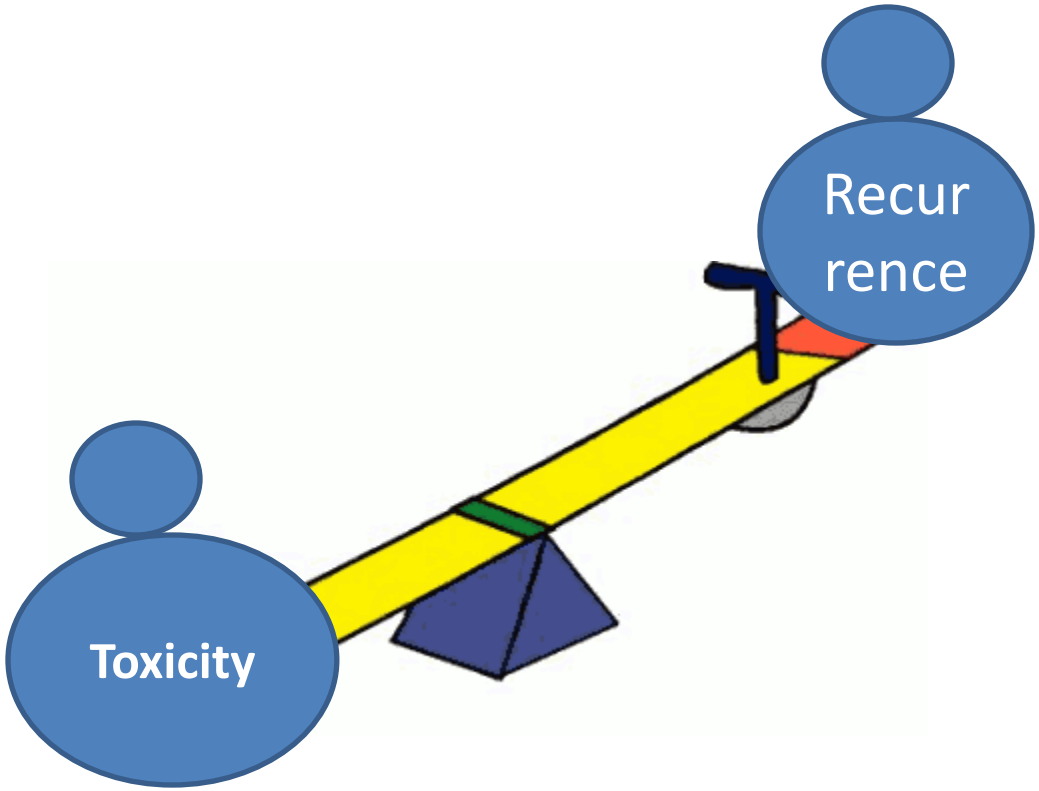
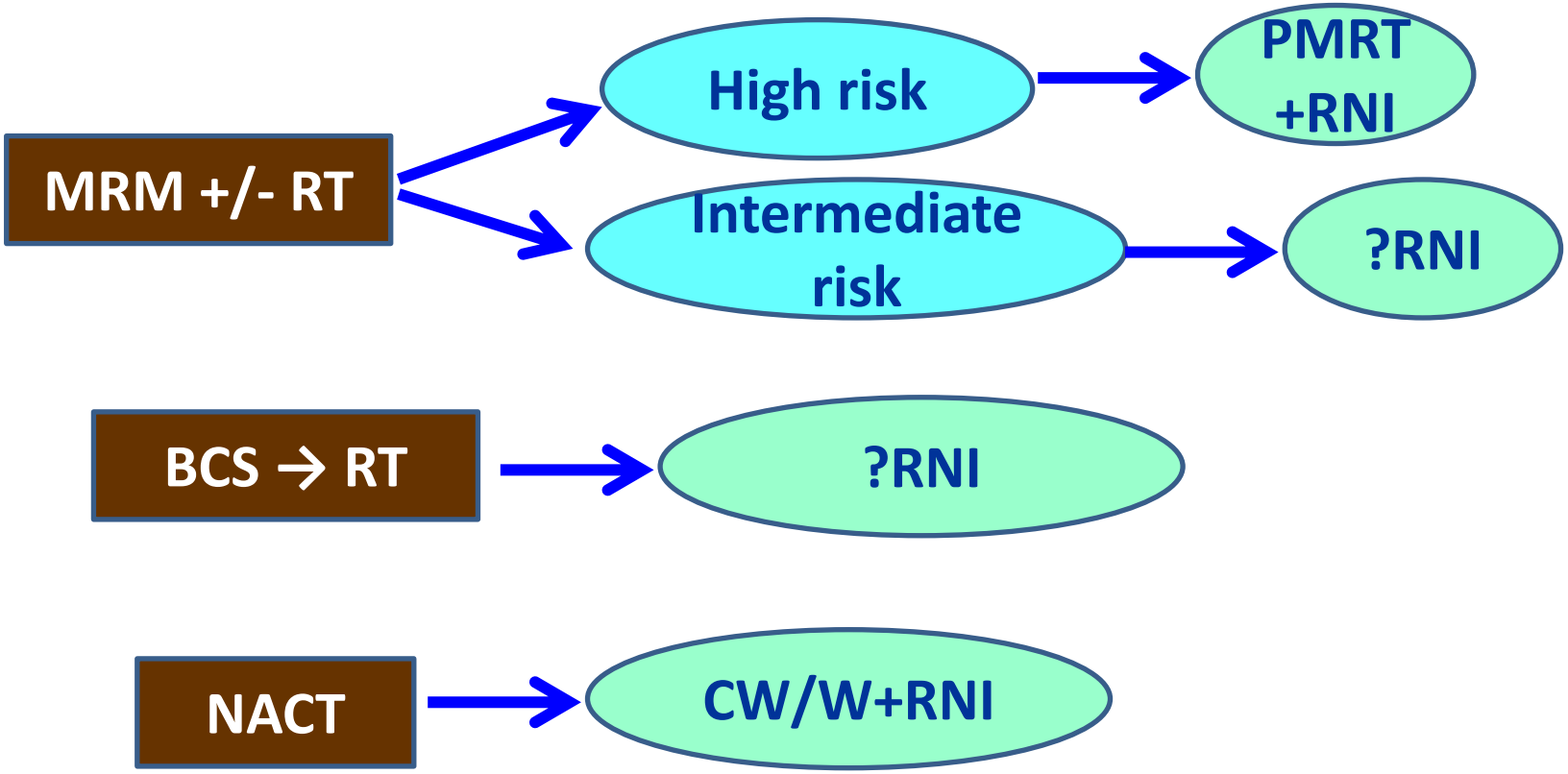
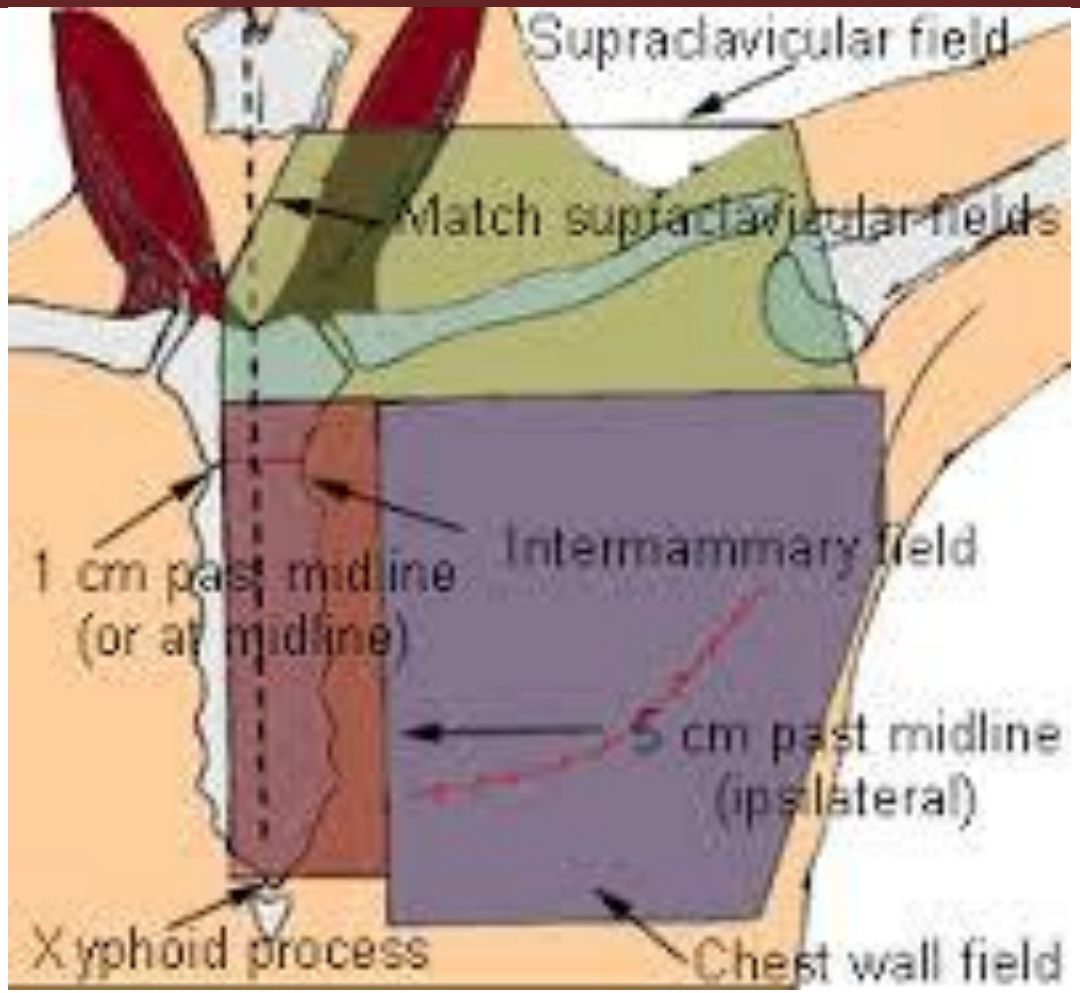
Breast cancers- Regional Radiotherapy



Aspects to be touched upon



Breast radiotherapy planning



2 case scenario
- Post mastectomy
- Post BCS

- RNI integral

Aim of Regional nodal irradiation

- To eradicate micro/macroscopic disease within the lymph nodes
- To reduce the risk of loco-regional recurrences and distant metastasis & confer survival benefit
- Goals to be set balancing the potential toxicity

Regional radiotherapy – untill recently

Axilla – if axillary dissection omitted/ incomplete
Concern – limb edema/Br plexus

SCF - > 4 Level 1 evidence; 1-3 insufficent

IMC- debatable; Concern heart

High risk breast cancer

- 5 cm tumors
- 4 or more Axillary Lymph node positive

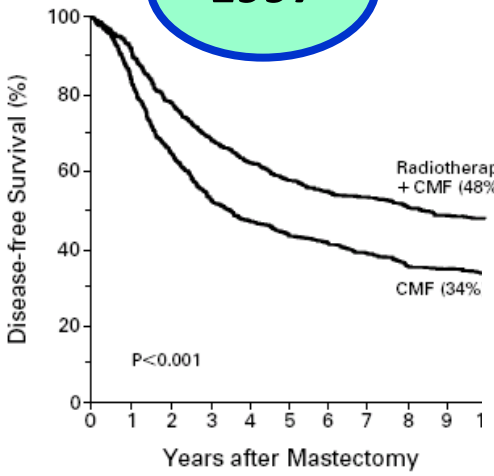
Modified radical mastectomy – gold standard

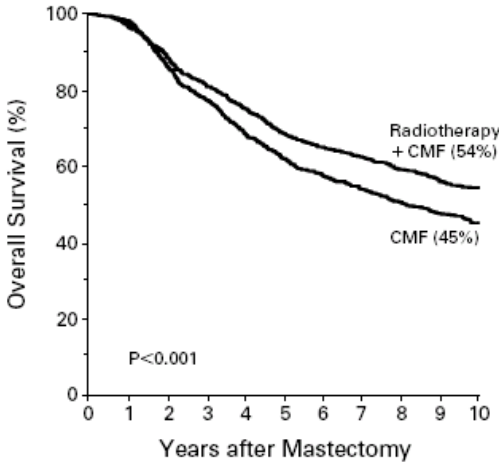
1997

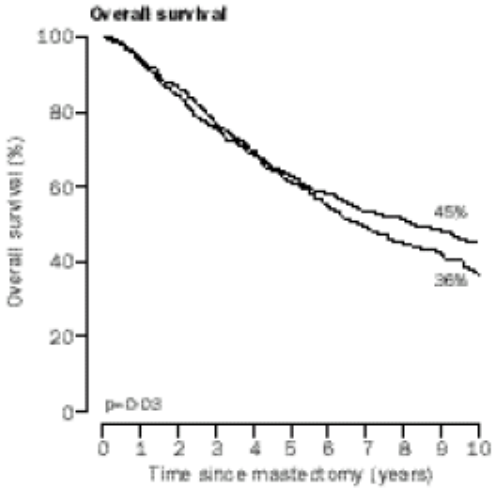
Overgaard et al. NEJM 1997 337:949

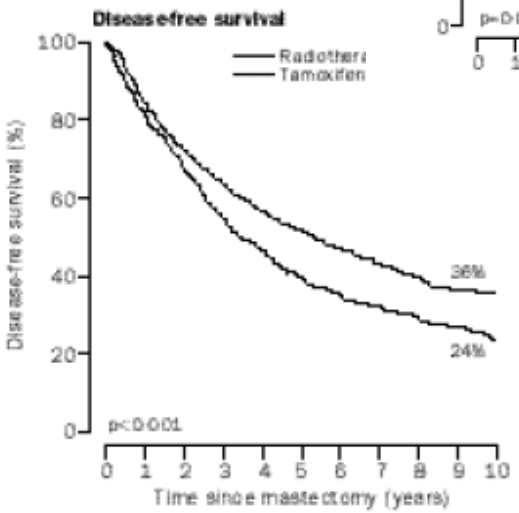
Ragaz et al. NEJM 1997 337:956

Overgaard et al. 1999, 353:1641







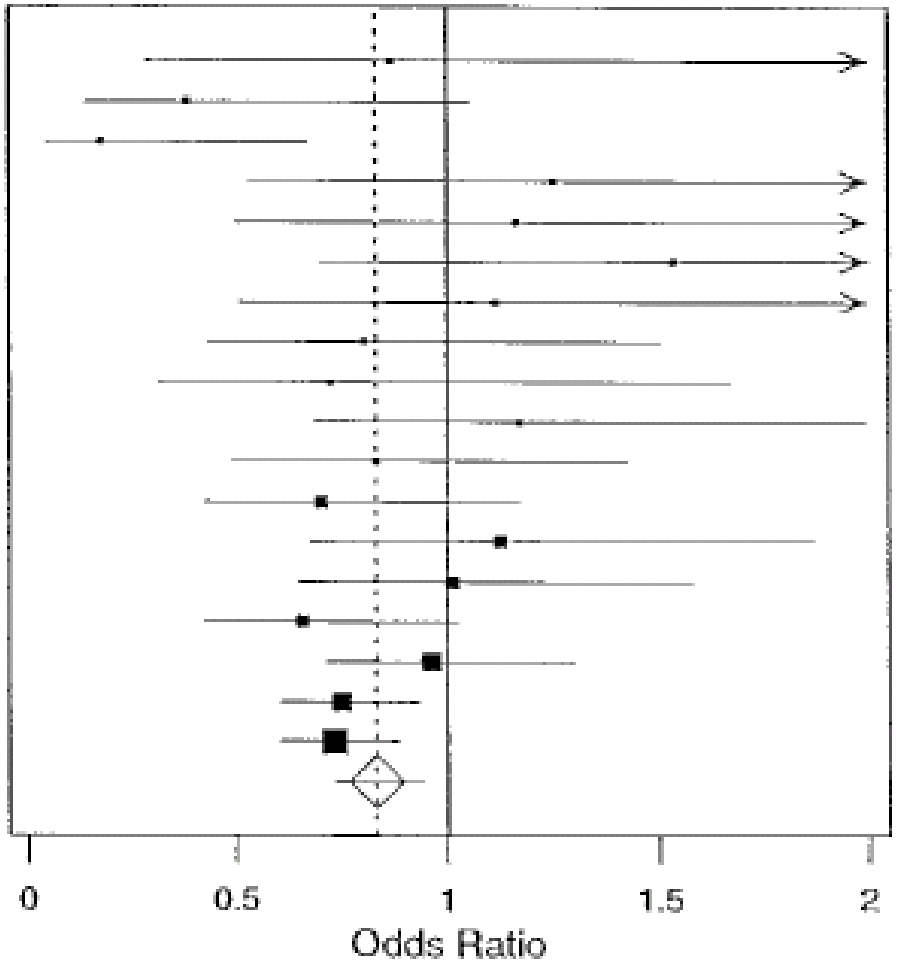


PMRT – Improved DFS and OS

Does Locoregional Radiation Therapy Improve Survival in Breast Cancer? A Meta-Analysis

Study	N	OR	95% CI
DeBoer	50	0.87	0.28, 2.65
Foroglou	71	0.38	0.14, 1.05
Klefstrom	79	0.17	0.04, 0.67
Tramprisch	88	1.25	0.53, 2.95
Blomqvist	99	1.16	0.50, 2.70
Hayat	112	1.53	0.70, 3.37
Gervasio	112	1.11	0.51, 2.43
Muss	159	0.81	0.43, 1.50
Schmoor	199	0.72	0.32, 1.67
Griem	218	1.17	0.68, 1.99
McArdle	219	0.83	0.49, 1.43
Velez-Garcia	239	0.70	0.42, 1.17
Martinez	241	1.12	0.67, 1.87
Olson	312	1.01	0.65, 1.58
Ragaz	318	0.66	0.42, 1.02
Tennvall-Nittby	768	0.96	0.71, 1.30
Overgaard(TAM)	1375	0.75	0.61, 0.93
Overgaard(CMF)	1708	0.73	0.61, 0.89

Random Effects OR = 0.83 95% CI = 0.74, 0.94



Survival

Whole breast RT

- **7 prospective randomized trials** have shown no significant difference between
- BCS+RT vs. Mastectomy in Early Breast cancer
  - **No difference in terms of LR/DM**
    - Survival (26.3 vs 24.1% death rate)

Post BCS RT :– RT to whole breast and LN± Boost to tumor bed

Post BCS	End point	Outcome
With RT	Ipsilateral recurrence	1/3
	Any recurrence	1/2

Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10 801 women in 17 randomised trials

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

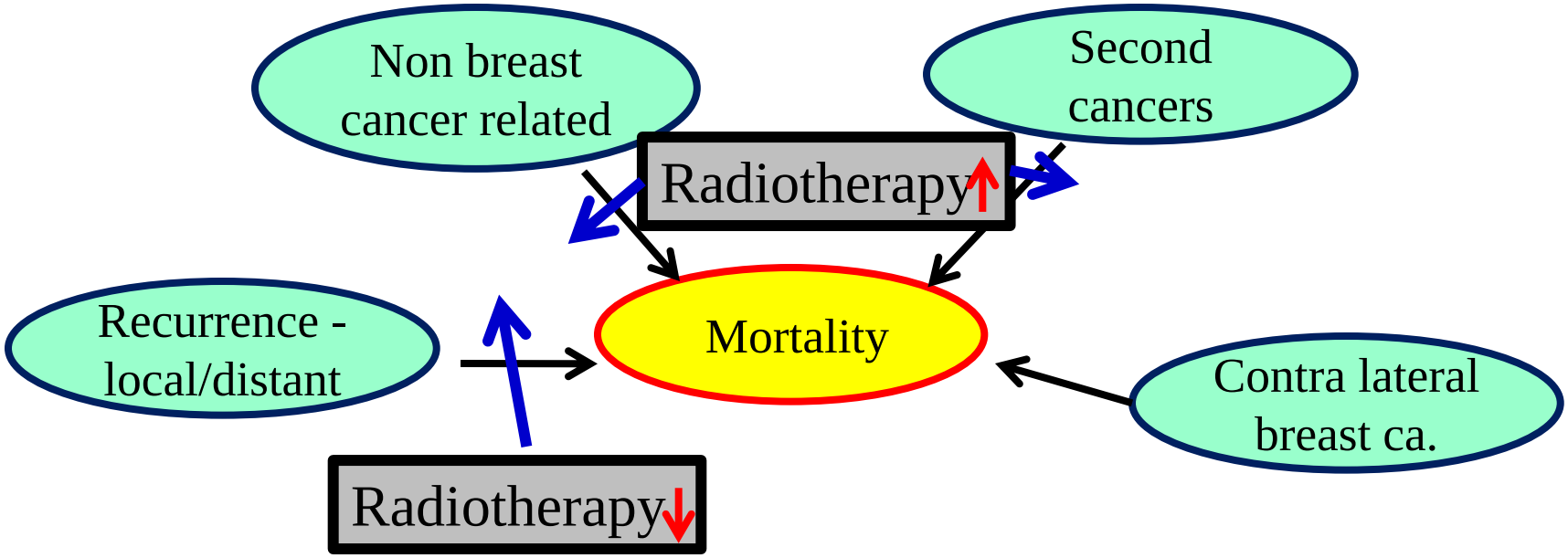
	Any rec at 10yrs	Br ca mortality↓ at 5yrs	pN0 rec ↓ 10 yrs	P N+ rec ↓ at 10 yrs	Br ca. mortality ↓ 15yrs
RT	19%	21%	16%	43%	43%
No RT	35%	25%	31%	64%	51%
P value	s	s	s	s	s

4 rec (any) avoided at 10 yrs → 1 breast cancer death at 15yrs.

RT – reduces recurrence by ½ and prevents breast cancer death by 1/6

EBCTCG, Lancet 2011

A new paradigm



RT kills tumor foci – prevents local & distant rec

Substantial decrease in rec; modest decrease in death

A paradigm shift is due to….

Adjuvant Systemic therapy
Chemotherapy
Hormones
Targeted therapy

Cardiac toxicity
Brachial plexus
Lymph edema
Second cancers
Contralateral breast rec

Screen detected

Intermediate risk breast cancer

High risk node negative pT3N0M0/ pT2N0M0 – grade 3/ ER negative/ LVI+

Low risk node positive disease (1-3LN+)

The genesis of 3 trials

- SCF LN – life time risk > 5%
- IMN – Axillary LN (-) - <10%
- IMN – Axillary LN(+)- > 30%

- Older overviews – No survival benefit
- Detriment - Cardiac toxicity

Cuzick et al, Recent Results Ca Res 1988,111;108-29

Better RT techniques

EORTC & MA20 trials

- Research question - Whether more extensive lymphatic radiation treatment benefited patients with higher-risk lymph node-negative, or lower risk lymph node-positive disease.
- Regional nodal irradiation (RNI) to the level III axillary, supraclavicular and upper internal mammary lymph nodes
- End points disease free survival and distant metastasis free survival as well as overall survival advantage.

EORTC22922-NCIC MA20-French trial

	Incl	Design	n	BCS	Med FU	OS	DFS	DDFS	BCM	
EORTC '96-'04	Central / med LN+/-	RNI No RNI	4004	75%	10.9	82% 80%	72% 69%	78% 75%	14% 13%	OS ns
MA20 00-07	LN+ LN-(H)	RNI No RNI	1832	100%	9.5	83% 82%	82% 77%			OS ns
French	pN+ C/M N+/-	IMN No IMN	1334	-	11.3	63% 59%				IM N x

Issue of1-3 LN - MA 20 & EORTC 22922

Enrollment characteristics	NCIC MA.20	EORTC 22922
Accrual time period	2000–2007	1996–2004
Number of patients	1832	4004
% Breast conserving surgery	100%	76.1%
RNI targets	IMC + SCV + Level III axilla	IMC + medial SCV
Median age (years)	53–54	54
% Tumor size ≥ 2 cm, RNI vs. Control	50.1% vs. 54.7%	60.2% vs. 60.1%
% ALN(+), RNI vs. Control		
0 ALN positive	9.6% vs. 9.7%	44.4% vs. 44.5%
1–3 ALN positive	84.9% vs. 85.1%	42.9% vs. 43.3%
>3 ALN positive	5.5% vs. 5.1%	12.2% vs. 12.2%
% Chemotherapy, RNI vs. Control	90.7% vs. 90.5%	54.6% vs. 55.1%
% Endocrine therapy, RNI vs. Control	75.7% vs. 76%	59.2% vs. 60%
Results		
Median follow up (years)	9.5	10.9
10-yr OS, RNI vs. Control	82.8% vs. 81.8% ($P = 0.38$)	82.3% vs. 80.7% ($P = 0.06$)
10-yr DFS, RNI vs. Control	**82%** vs. **77%**	**72.1%** vs. **69.1%**
10-yr Distant DFS, RNI vs. Control	**86.3%** vs. **82.4%**	**78%** vs. **75%**
10-yr Breast cancer mortality	10.3% vs. 12.3%	**12.5%** vs. **14.4%**
Toxicities, RNI vs. Control		
Grade 2 acute pneumonitis	**1.2%** vs. **0.2%**	NA
Pulmonary fibrosis	NA	**4.4%** vs. **1.7%**
Cardiac	0.9% vs. 0.4%	5.6% vs. 6.5%
Lymphedema	**8.4% vs. 4.5%**	12% vs. 10.5%

Inference from EORTC & MA20 trials

- Neither showed survival benefit. EORTC – nearly significant!
- MA20 – HR(-) benefits with RNI
- **Exact impact of IMN & SCF can't be ascertained**
- **Risk – benefit for patient selection**

Meta analysis – Budach et al

Budach *et al. Radiation Oncology* (2015) 10:258
DOI 10.1186/s13014-015-0568-4

Radiation Oncology

RESEARCH Open Access

Adjuvant radiation therapy of regional lymph nodes in breast cancer - a meta-analysis of randomized trials- an update

Wilfried Budach[1*], Edwin Bölke[1], Kai Kammers[2], Peter Arne Gerber[3], Carolin Nestle-Krämling[4] and Christiane Matuschek[1]

RNI – Improved DFS, DMFS, and OS

Meta analysis – Budach et al

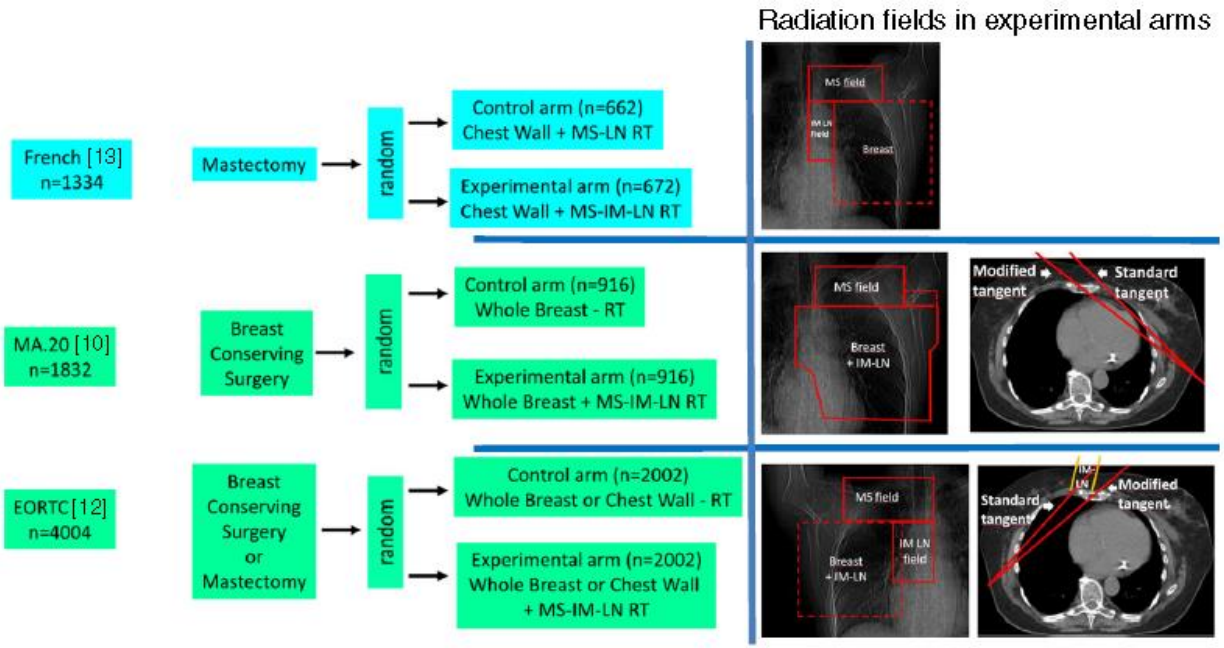
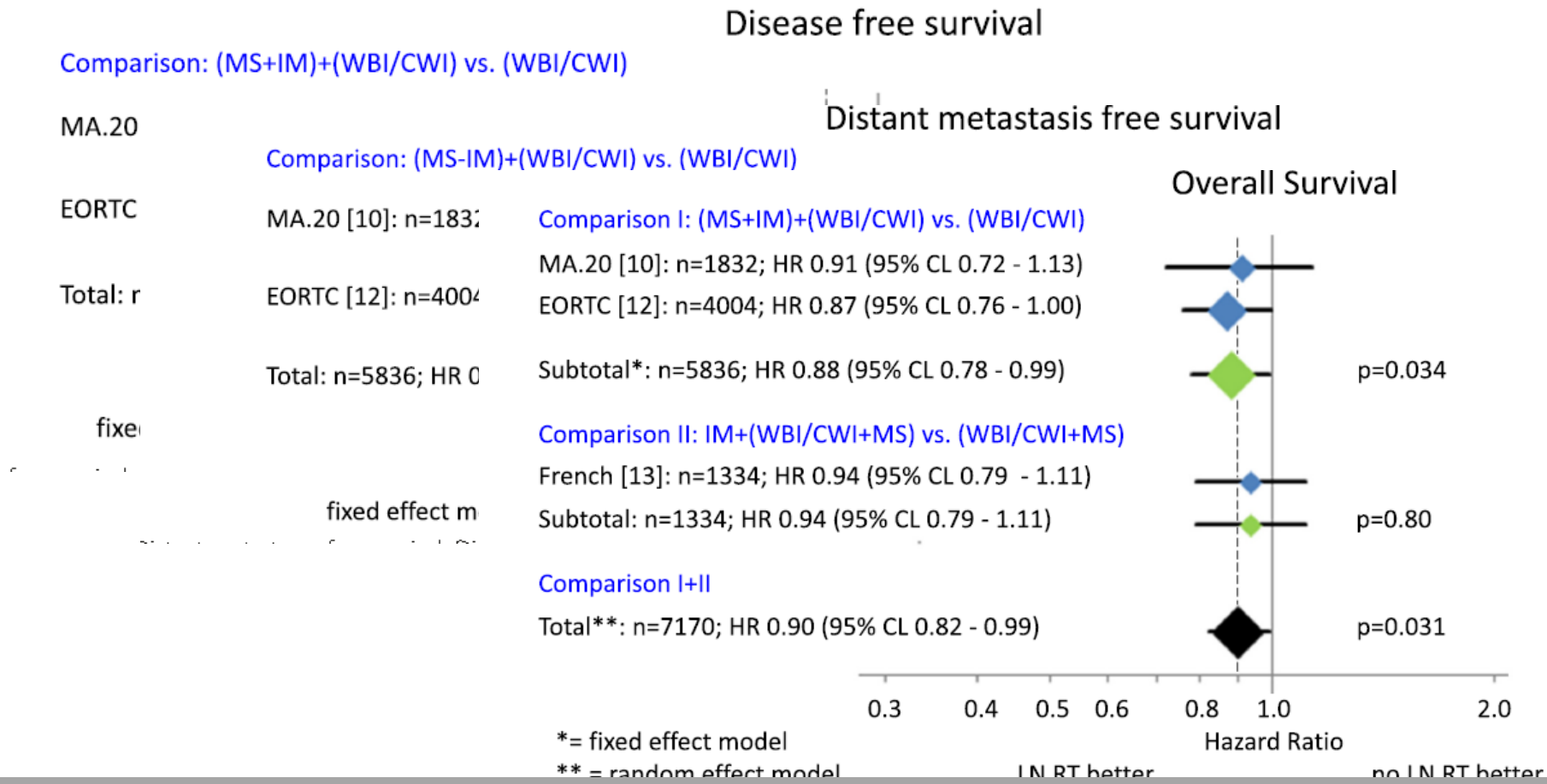


Fig. 1 Trial designs. Random = randomization. RT = RT. MS LN RT = RT of medial supraclavicular LN. MS IM RT = RT of medial supraclavicular and internal mammary LN.

Preliminary results show addition of both IMN and SCF improve DFS and OS

With IMN – concern heart

Meta analysis – Budach et al



St Gallen 2019 consensus guidelines

The panel clearly agreed that irradiation should be applied to regional nodes in all patients with ≥4 positive nodes (94%), but in cases of 1–3 positive nodes, a majority (56%) indicated that RNI should only be administered if the present features are poor (e.g., TNBC, residual disease after PST), while 29% felt that RNI should be indicated for all patients with 1–3 positive nodes.

Original Article

Predicting loco-regional recurrence risk in T1, T2 breast cancer with 1–3 positive axillary nodes postmastectomy: Development of a predictive nomogram

Wadasadawala T, Kannan S[1], Gudi S, Rishi A, Budrukkar A, Parmar V[2], Shet T[3], Desai S[3], Gupta S[4], Badwe R[2], Sarin R

Departments of Radiation Oncology, [1]Medical Statistics, [2]Surgical Oncology, [3]Pathology and [4]Medical Oncology, Tata Memorial Centre, Mumbai, Maharashtra, India

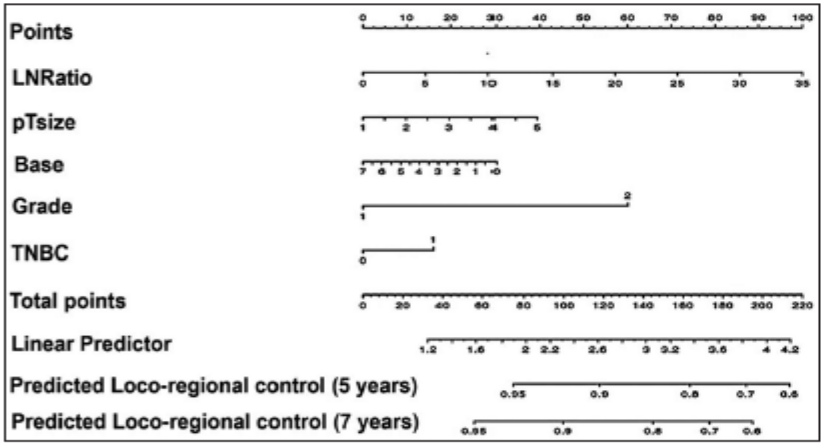


Figure 1: Nomogram showing predicted risk of loco-regional recurrence at 5 and 7 years. LNRatio – Lymphnode ratio = number of lymph nodes positive/number of lymph nodes dissected; pTsize – Pathologic tumor size in centimeters; Base – Distance of base from tumor in millimeter; Grade – Grade grouping scored as 1 if Grade I or Grade II and scored as 2 if Grade III; TNBC – Triple negative breast cancer scored as 0 if non-TNBC and 1 if TNBC; OS prob – Overall survival probability. As an example if patient with tumor size of 5 cm (40 points), 7 mm from base (0 points), Grade III tumor (60 points), lymph node ratio of 5 (score 15) and non-TNBC receptor status (0 points) will have total points of 115 and predicted LRC is between 90% and 95%. TNBC = Triple negative breast cancer; LRC = Loco-regional control

Table 3: Multivariate analysis for loco-regional control

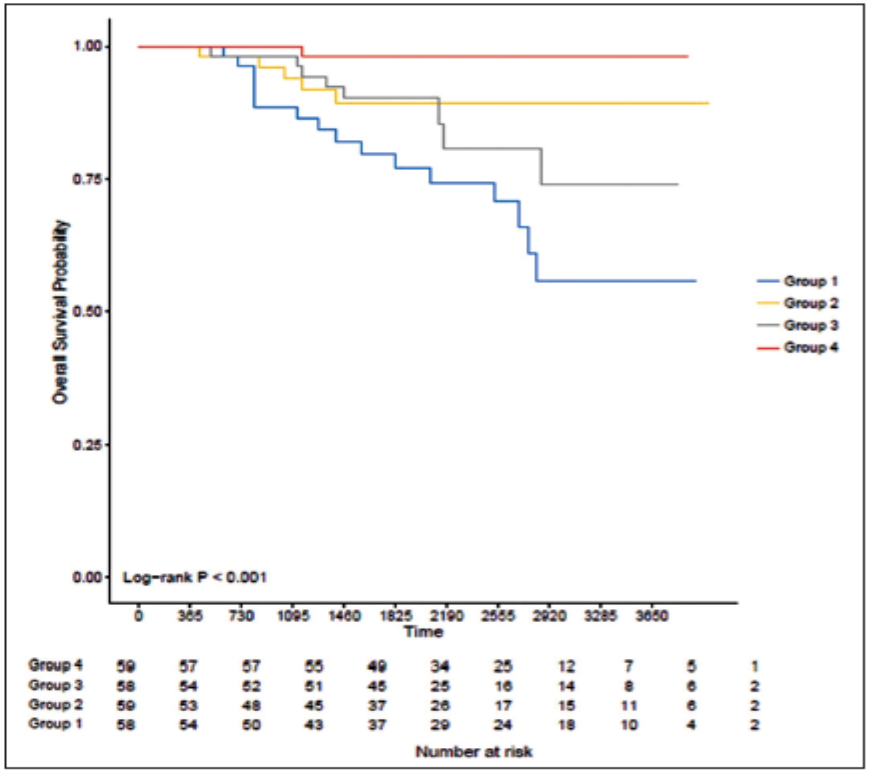


Figure 2: Kaplan–Meier curves for the four groups derived for predictive nomogram. The difference in the survival among these groups was statistically significant as estimated by log rank test

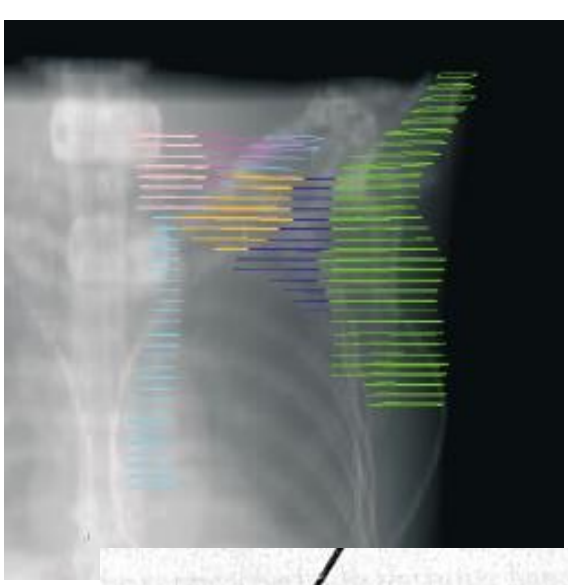
Summary

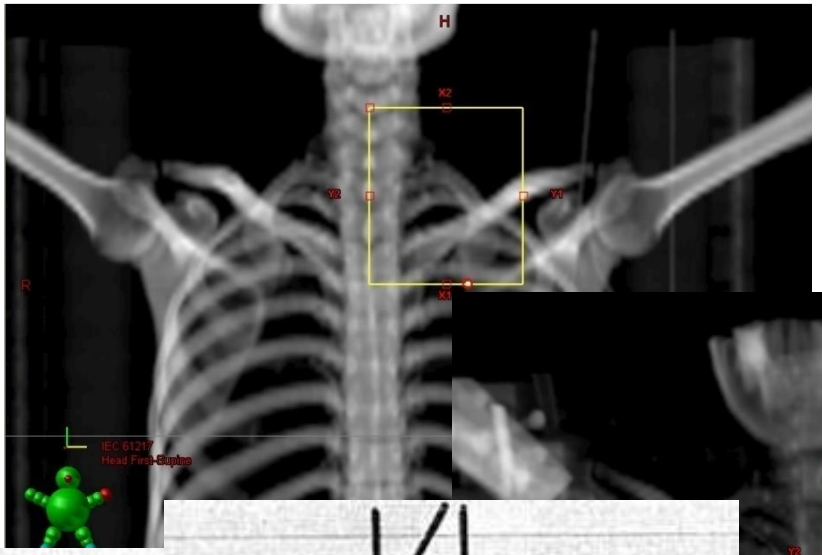
- Modest benefit – DFS, DMFS, OS
- pN+ benefit
- No difference between N1-3 and N≥ 4
- pN0 central & medial quadrant tumors

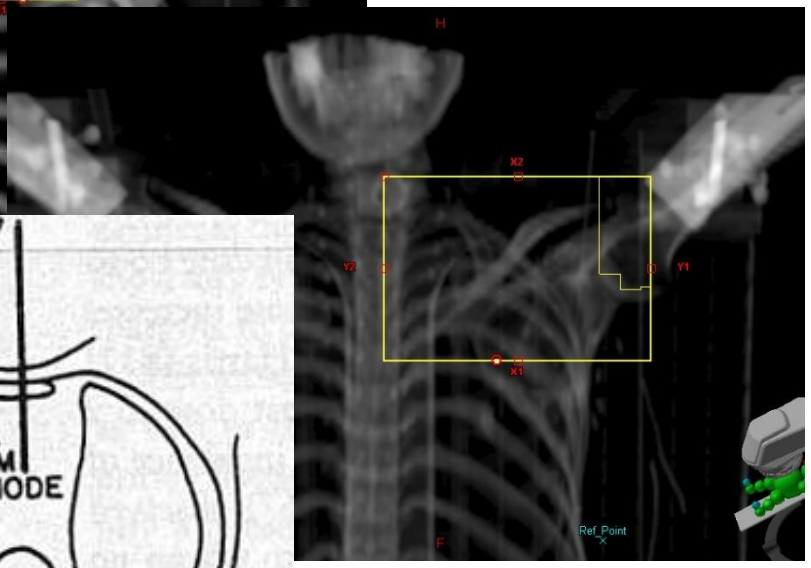
Supra clavicular LN + Axillary LN

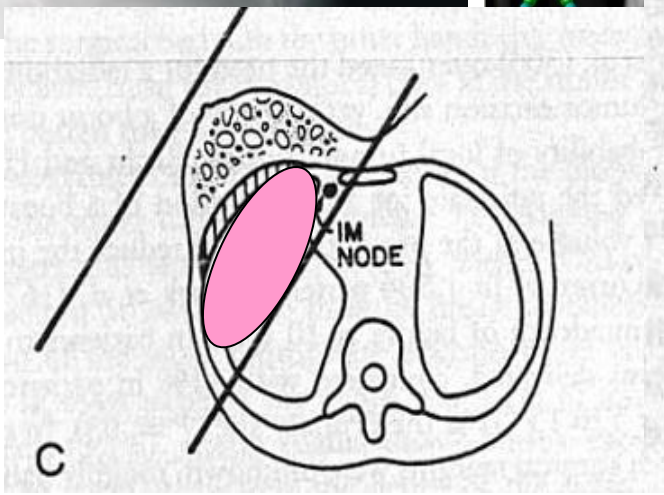
Internal mammary LN

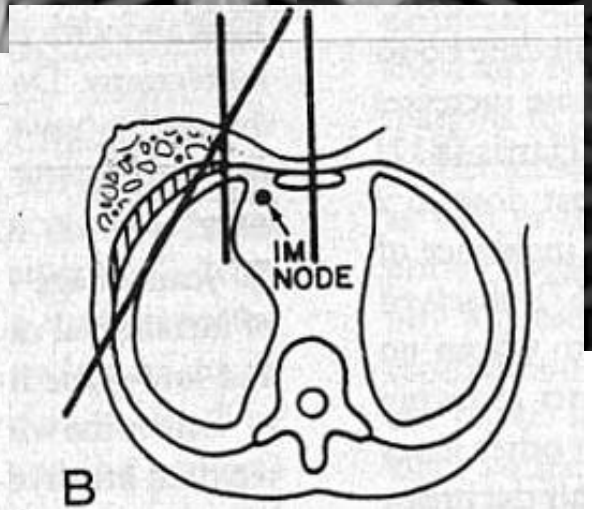
Regional RT portals











Internal Mammary LN RT – an eternal debate until recently

International Journal of Radiation Oncology biology • physics

www.redjournal.org

Clinical Investigation: Breast Cancer

Ten-Year Survival Results of a Randomized Trial of Irradiation of Internal Mammary Nodes After Mastectomy

Christophe Hennequin, MD, PhD,* Nadine Bossard, MD, PhD,†

- 3% benefit in OS (59% to 62%)
- over estimated IMN involvement – overestimated survival diff
- Subgroup – Central/Medial tumors –benefit
- "Cannot recommend IMN RT for or against"

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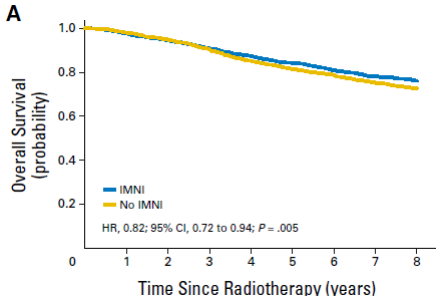
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT



DBCG-IMN: A Population-Based Cohort Study on the Effect of Internal Mammary Node Irradiation in Early Node-Positive Breast Cancer

Lise Bech Jellesmark Thorsen, Birgitte Vrou Offersen, Hella Danø, Martin Berg, Ingelise Jensen, Anders Navrsted Pedersen, Sune Jürg Zimmermann, Hans-Jürgen Brodersen, Marie Overgaard, and Jens Overgaard

- Right sided – IMN RT
- Left sided –No IMN RT

	OS at 8 yrs	BC Mortality
IMN RT	76%	21%
No IMN RT	72%	23%

Subset analysis – Only subset that doesn't benefit with IMN RT– lateral lesions with 1-3 LN nodes

Small benefit. IHD deaths similar. Cardiac morbidity?

Points of debate- 1. Added toxicity of IMN RT in left sided lesions not determined

2. OS benefit with IMN RT right side when excess cardiac deaths left side.

There is mounting evidence towards the use of IMN RT

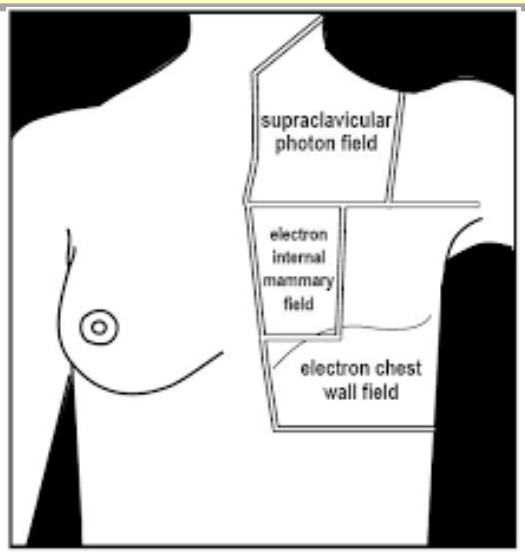
The NEW ENGLAND JOURNAL of MEDICINE

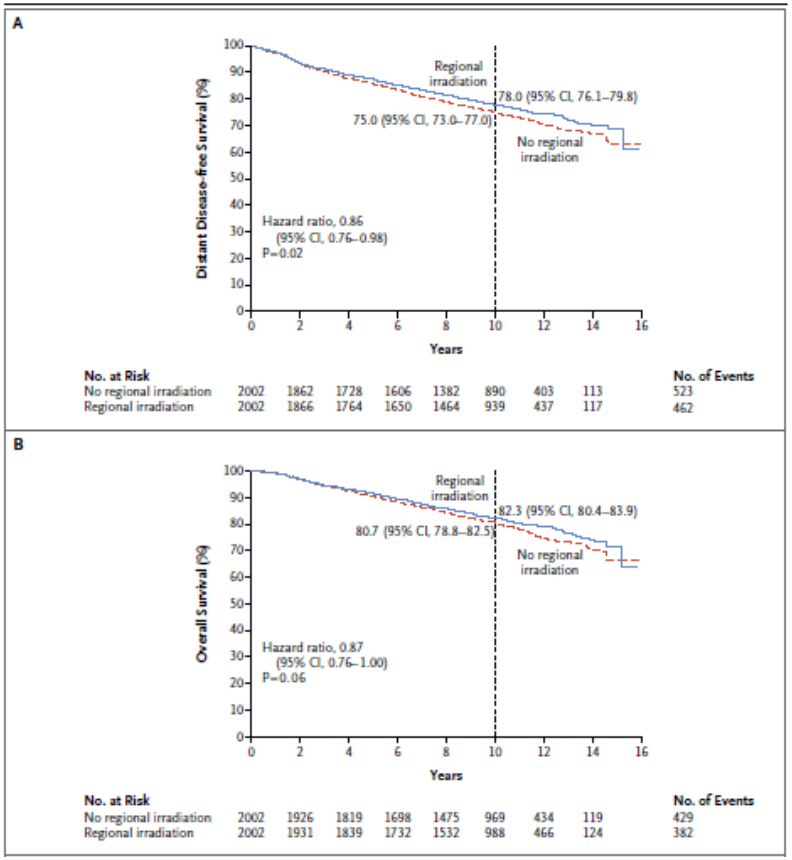
ORIGINAL ARTICLE

Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer

P.M. Poortmans, S. Collette, C. Kirkove, E. Van Limbergen, V. Budach, H. Struikmans, L. Collette, A. Fourquet, P. Maingon, M. Valli, K. De Winter, S. Marnitz, I. Barillot, L. Scandolaro, E. Vonk, C. Rodenhuis, H. Marsiglia, N. Weidner, G. van Tienhoven, C. Glanzmann, A. Kuten, R. Arriagada, H. Bartelink, and W. Van den Bogaert, for the EORTC Radiation Oncology and Breast Cancer Groups*

- EBC- Central/Inner quad lesions with +ve axilla
- Role in LOBC/LABC
- Cardiac issue - unresolved





CONCLUSIONS

In patients with early-stage breast cancer, irradiation of the regional nodes had a marginal effect on overall survival. Disease-free survival and distant disease-free survival were improved, and breast-cancer mortality was reduced. (Funded by Fonds Cancer; ClinicalTrials.gov number, NCT00002851.)

There is limited experience of IMN RT with Hypofr RT & its consequences on heart

IMC RT- where do we stand?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer

P.M. Poortmans, S. Collette, C. Kirkove, E. Van Limbergen, V. Budach, H. Struikmans, L. Collette, A. Fourquet, P. Maingon, M. Valli, K. De Winter, S. Marnitz, I. Barillot, L. Scandolaro, E. Vonk, C. Rodenhuis, H. Marsiglia, N. Weidner, G. van Tienhoven, C. Glanzmann, A. Kuten, R. Arriagada, H. Bartelink, and W. Van den Bogaert, for the EORTC Radiation Oncology and Breast Cancer Groups*

End point – OS DFS & DDFS benefit	Exact role of IMN RT - unclear	Debatable – cardiac !

EORTC trial. NEJM, 2015;373:317-27

To conclude

- RNI beneficial
- Every 4 recurrences avoided – 1 death prevented
- Distinction of 1-3 LN artificial
- Cardiac risk

Are we ready to give IMN RT routinely to our patients?

Axillary Surgery and implications for RNI

- Sentinel LN surgery → Stage migration (newer techniques – occult micrometastasis 10-50%) – Will Rogers phenomenon

Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial

Mila Donker, Geertjan van Tienhoven, Marieke E Straver, Philip Meijnen, Cornelis J H van de Velde, Robert E Mansel, Luigi Cataliotti, A Helen Westenberg, Jean H G Klinkenbijl, Lorenzo Orzalesi, Willem H Bouma, Huub C J van der Mijle, Grard A P Nieuwenhuijzen, Sanne C Veltkamp, Leen Slaets, Nicole J Duez, Peter W de Graaf, Thijs van Dalen, Andreas Marinelli, Herman Rijna, Marko Snoj, Nigel J Bundred, Jos W S Merkus, Yazid Belkacemi, Patrick Petignat, Dominic A X Schinagl, Corneel Coens, Carlo G M Messina, Jan Bogaerts, Emiel J T Rutgers

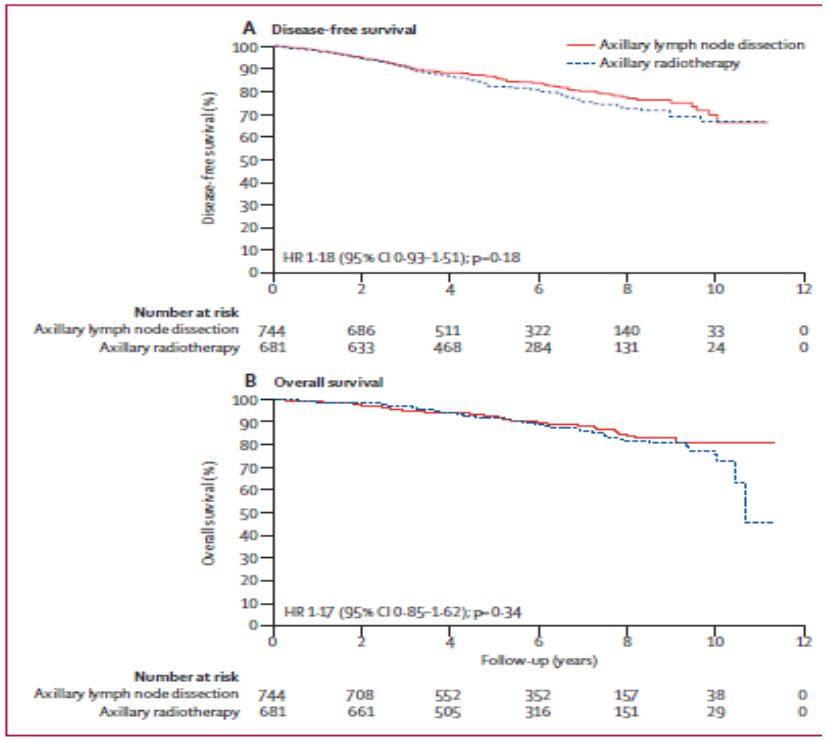


Figure 2: **Disease-free survival and overall survival**
HR=hazard ratio.

Amaros trial

•Underpowered results to show non-inferiority

• RNI an alternative to ALND –potential treatment option in early stage, node-positive breast cancer treated with SLN dissection alone.

• ↓ rates of lymphedema

• Comparable 5-year DFS and OS.

Interpretation Axillary lymph node dissection and axillary radiotherapy after a positive sentinel node provide excellent and comparable axillary control for patients with T1–2 primary breast cancer and no palpable lymphadenopathy. Axillary radiotherapy results in significantly less morbidity.

Donker et al, Lancet Oncology, 2014

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)*

	n	LRR	OR	BCM
LN0	700	↓	↓	↓
LN1-3	1314	↓	↓	↓
LN≥4	1772	↓	↓	↓

N 1-3 (Int risk) even with syst th – abs gains smaller BUT proportional gains large due to effective RT

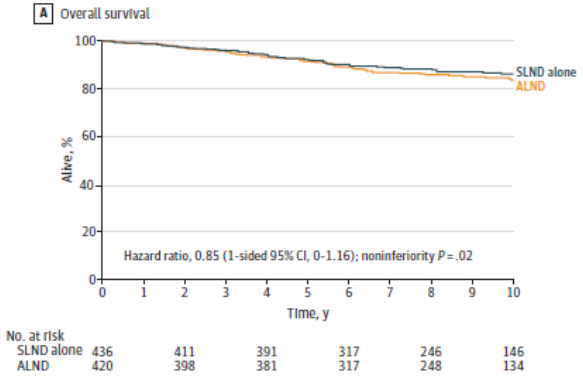
EBCTCG, Lancet,2014

JAMA | Original Investigation

Effect of Axillary Dissection vs No Axillary Dissection on 10-Year Overall Survival Among Women With Invasive Breast Cancer and Sentinel Node Metastasis
The ACOSOG Z0011 (Alliance) Randomized Clinical Trial

Armando E. Giuliano, MD; Karla V. Ballman, PhD; Linda McCall, MS; Peter D. Beitsch, MD; Meghan B. Brennan, RN, ONP, PhD; Pond R. Kelemen, MD; David W. Ollila, MD; Nora M. Hansen, MD; Pat W. Whitworth, MD; Peter W. Blumencranz, MD; A. Marilyn Leitch, MD; Sukamal Saha, MD; Kelly K. Hunt, MD; Monica Morrow, M

Figure 2. Overall and Disease-Free Survival in the ACOSOG Z0011 (Alliance) Trial

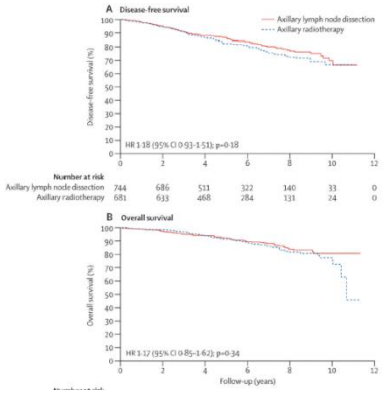


CONCLUSIONS AND RELEVANCE Among women with T1 or T2 invasive primary breast cancer, no palpable axillary adenopathy, and 1 or 2 sentinel lymph nodes containing metastases, 10-year overall survival for patients treated with sentinel lymph node dissection alone was noninferior to overall survival for those treated with axillary lymph node dissection. These findings do not support routine use of axillary lymph node dissection in this patient population based on 10-year outcomes.

Node positive disease - Axillary Sx or RT?

Lancet Oncol. 2014 November ; 15(12): 1303–1310. doi:10.1016/S1470-2045(14)70460-7.

Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS):a randomised, multicentre, open-label, phase 3 non-inferiority trial



- cN0 disease – SNLB
- Positive axilla needs to be addresed
- Axillary dissection – Gold standard
- Lymphedema & shoulder movement
- Factors – size, grade, VI, ECE

Axillary RT – comparable results; less morbidity

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)*

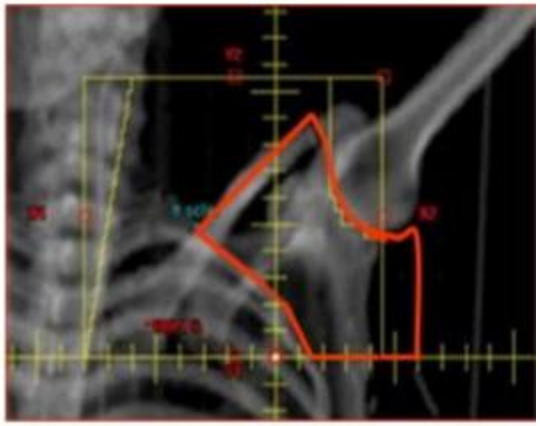
. For 1314 women with axillary dissection and one to three positive nodes, radiotherapy reduced locoregional recurrence (2p<0·00001), overall recurrence (RR 0·68, 95% CI 0·57–0·82, 2p=0·00006), and breast cancer mortality (RR 0·80, 95% CI 0·67–0·95, 2p=0·01). 1133 of these 1314 women were in trials in which systemic therapy (cyclophosphamide, methotrexate, and fluorouracil, or tamoxifen) was given in both trial groups and, for them, radiotherapy again reduced locoregional recurrence (2p<0·00001), overall recurrence (RR 0·67, 95% CI 0·55–0·82, 2p=0·00009), and breast cancer mortality (RR 0·78, 95% CI 0·64–0·94, 2p=0·01).

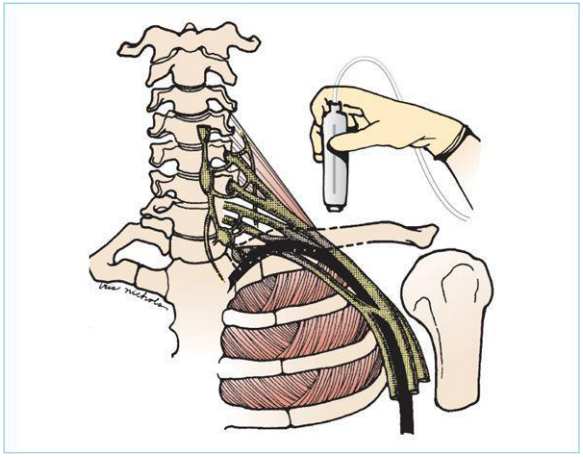
Interpretation After mastectomy and axillary dissection, radiotherapy reduced both recurrence and breast cancer mortality in the women with one to three positive lymph nodes in these trials even when systemic therapy was given. For today's women, who in many countries are at lower risk of recurrence, absolute gains might be smaller but proportional gains might be larger because of more effective radiotherapy.

Reasons

- Use of endocrine therapy
- High tangents
- Level III in SCF LN

What if Axilla needs to be addressed?





- Unaddressed axilla/ incompletely dissected axilla
- Ontario practice advocates normofractionated RT to axilla in “heavy nodal burden”
- Type of surgery and chemotherapy
- Brachial plexus & lung toxicity

In India where the need for axillary RT may be more – issue unresolved

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Chronic Diseases and Translational Medicine 3 (2017) 41–50

www.keaipublishing.com/en/journals/cdtm/

www.cdatm.org

Meta Analysis

Can axillary radiotherapy replace axillary dissection for patients with positive sentinel nodes? A systematic review and meta-analysis

Min Zhao [a], Wei-Guang Liu [a], Lei Zhang, Zi-Ning Jin, Zhan Li, Cheng Liu, Dong-Bao Li, Ying Ma, Jing-Wen Zhang, Feng Jin, Bo Chen*

Department of Breast Surgery, The First Hospital of China Medical University, Shenyang, Liaoning 110001, China

administration of adjuvant systemic therapy.

Conclusions: ART is not inferior to cALND in the patients with clinically node-negative breast cancer who had a positive sentinel lymph node. Information obtained by using cALND after SLNB may have no major impact on the administration of adjuvant systemic therapy.

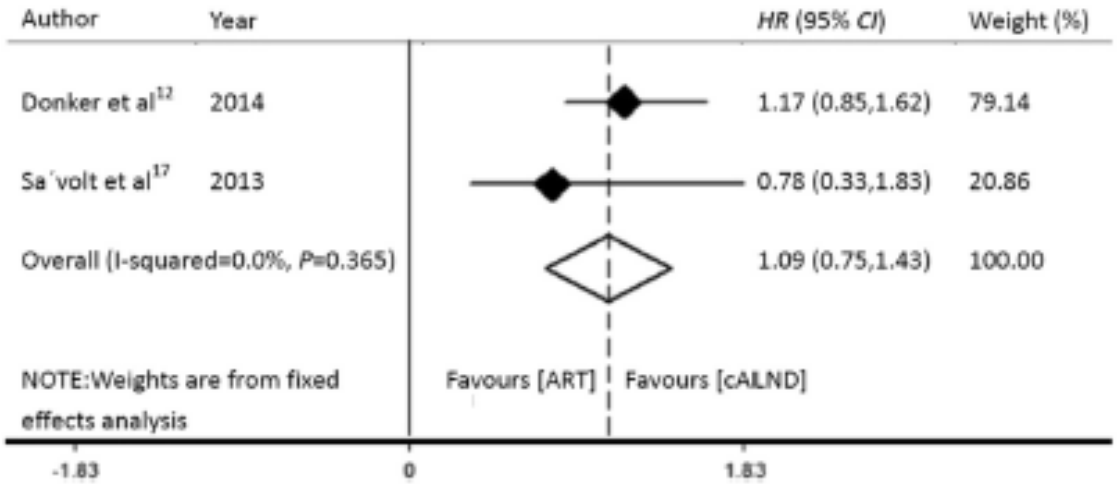

Fig. 2. Forest plot showing the pooled effect of overall survival with ART compared to that with cALND for the patients with SLN-positive breast cancer. *HR*: hazard ratio; *CI*: confidence interval; ART: axillary radiotherapy; cALND: completion axillary lymph node dissection.

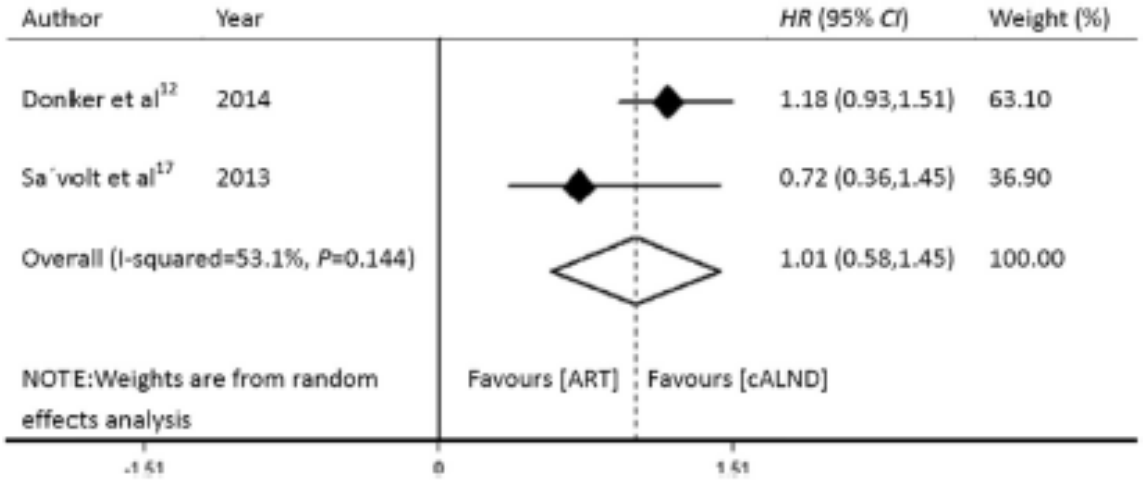

Fig. 3. Forest plot showing the pooled effect of disease-free survival with ART compared to that with cALND for the patients with SLN-positive breast cancer. *HR*: hazard ratio; *CI*: confidence interval; ART: axillary radiotherapy; cALND: completion axillary lymph node dissection.

Hypo fractionation – another dimension to RNI

Radiotherapy and Oncology 110 (2014) 39–44

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Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Review

Hypofractionated regional nodal irradiation for breast cancer: Examining the data and potential for future studies

Shahed N. Badiyan [a], Chirag Shah [b], Douglas Arthur [c], Atif J. Khan [d], Gary Freedman [e], Matthew M. Poppe [f], Frank A. Vicini [g,*]

- Hypofractionated RT – safe & efficacious
- Long term data – limited
- Addition of RNI always adds to toxicity irrespective of fr
- Impact of systemic therapy to Hypo fr RT to be studied

St Gallen 2019 consensus guidelines

The panel indicated that hypofractionated breast irradiation can be used for most patients as a care standard (52% for all patients, 19% following breast conservation only, and 21% abstention). With respect to radiotherapy on the breast and on regional lymph nodes (LNs), hypofractionated radiotherapy did not find a clear consensus (36% for most patients, age >50 years 30%, and 30% abstention).

Concerns regarding Brachial plexopathy

- <1%
- START – FU 9.9yrs – Insufficient
- May manifest up to 30yrs; At least 25% incidence beyond 10yrs. *Budach et al Breast care, 2015*.

Acta Oncologica, 2006; 45: 280–284

ORIGINAL ARTICLE

Radiation-induced brachial plexopathy and hypofractionated regimens in adjuvant irradiation of patients with breast cancer–a review

JACEK GAŁECKI[1], JOANNA HICER-GRZENKOWICZ[1], MAŁGORZATA GRUDZIEŃ-KOWALSKA[1], TERESA MICHALSKA[2] & WOJCIECH ZAŁUCKI[1]

[1]*Department of Radiotherapy, Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, W. K. Roentgen 5, 02–781 Warsaw, Poland and* [2]*Neurological Clinic, Second Department, Academy of Medicine, Warsaw, Poland*

regimens increase the risk of damage to the brachial plexus. A review of the published literature shows that the use of doses per fraction in the range from 2.2 Gy to 4.58 Gy with the total doses between 43.5 Gy and 60 Gy causes a significant risk of brachial plexus injury which ranged from 1.7% up to 73%. The risk of radiation induced brachial plexopathy was smaller than 1% using regimens with doses per fraction between 2.2 and 2.5 Gy with the total doses between 34 and 40 Gy. Surgical manipulations in the axilla and chemotherapy have to be taken into account as additional factors which may increase the risk of brachial plexopathy.

RNI – post NACT

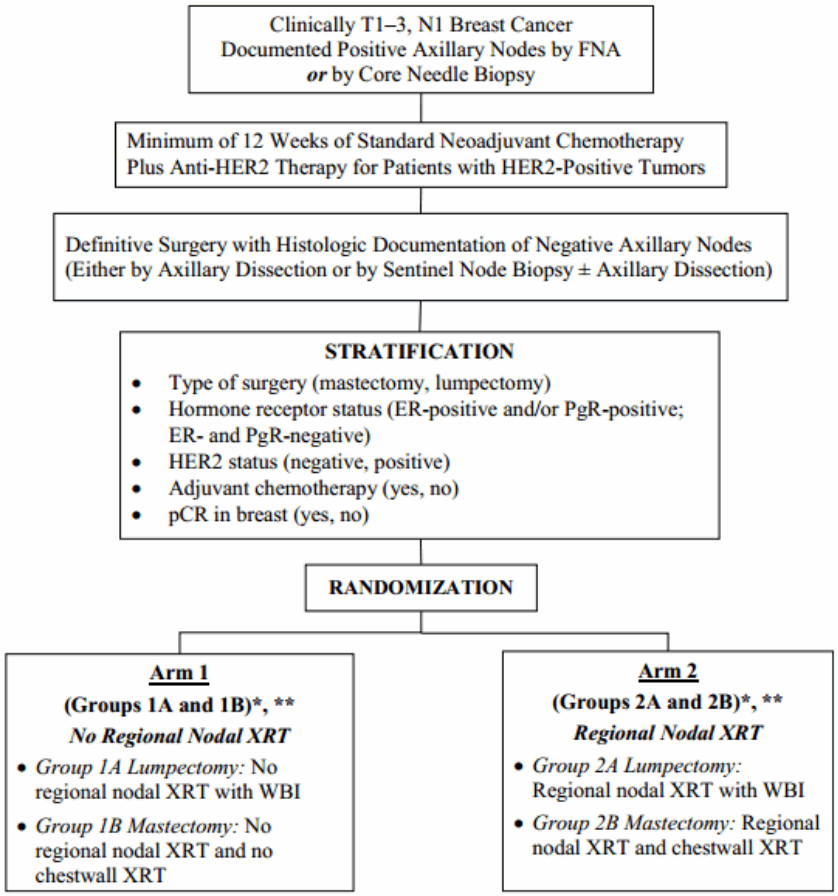
Accurately staged Pre NACT stag
Post NACT pathological stage

Un ambiguous role –
Advanced tumor pre NACT
All residual LN positive disease

Grey area –
Moderate burden disease; pCR
ypN0 – Clinical trials

Post NACT

NSABP – B 51



St Gallen 2019 consensus guidelines

RNI was also decided on as a standard by 44% of the panelists for patients with cN1 → PST situations when post-PST SLNB has retrieved a negative SN, while 23% felt that RNI should only be indicated if risk factors are present, and 17% did not think RNI should be a standard in such situations.

PMRT – ASCO/ASTRO/SSO guidelines

Clinical Question 1

Is PMRT indicated in patients With T1-2 tumors with one to three positive axillary lymph nodes who undergo ALND?

↓LRF, ↓ Any Rec, ↓ BCM

Clinical Question 2

Is PMRT indicated in patients with T1-2 tumors and a positive SNB who do not undergo completion ALND?

SLNB +; ALND not done – risk adaptive

Clinical Question 3

Is PMRT indicated in patients with clinical stage I c cancers who have received NAST?

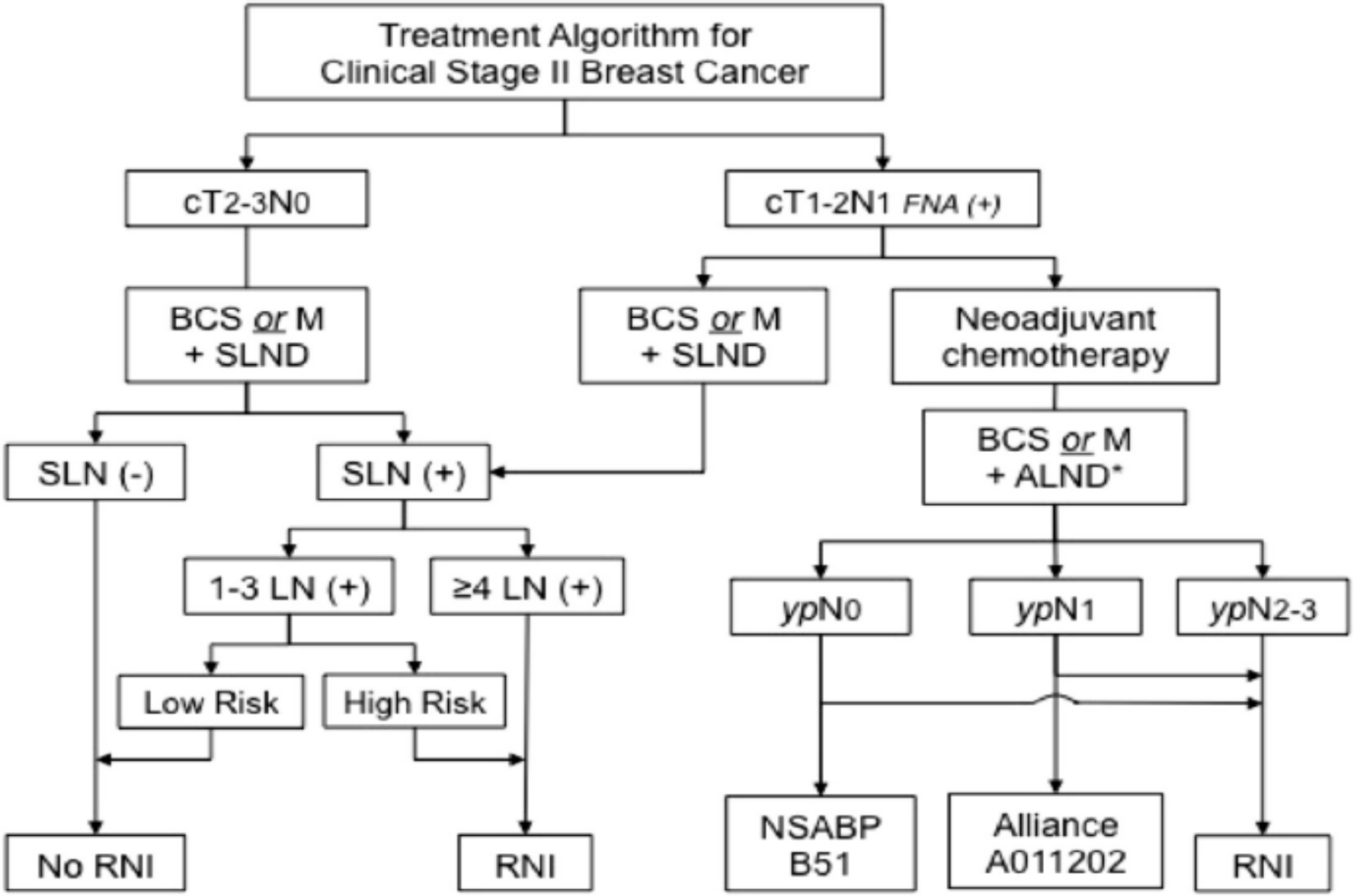
Post NACT – pCR Insuff evidence for PMRT

Clinical Question 4

Should RNI include both the IMNs and supraclavicular-axillary apical nodes when PMRT is used in patients with T1-2 tumors with one to three positive axillary nodes?

Most will need both RT

Recht et al, Ann Surg Oncol; 2017:24. 38-51



Low Risk: Favorable histology, ER(+) HER2(-), low Oncotype Dx score, micrometastatic disease.
High Risk: Triple negative, high Oncotype DX score, large nodal deposits, lymphovascular invasion, gross extracapsular extension

Moreno et al, The Breast 2017

50 years ago and now…..

Understanding of biology & pathology

Early diagnosis

Surgery, RT, Systemic th

Understanding of late toxicity

	50	Now
Measuring the benefit of RT	Rec	n "any first event (LRR or DM)"
Breast-conserving therapy (BCT)	Hig	of care with survival and LRR rates similar to ny
Post-mastectomy RT	The	roves survival in appropriate patients
Fractionation	1.8-	s just as effective and safe in BCT shortening to 3-4 wk
Adjuvant systemic therapy	Not	nd serendipitously makes RT more effective and ortant
Delivery of RT	• C • R	nergy linear accelerators simulation modulation for much greater dose eity imaging as needed for greater accuracy eath hold to reduce cardiac dose
Cardiac toxicity	High cardiac doses and no knowledge of the problem	Cardiac doses are minimized by the use of heart blocks, prone technique, and deep inspiration breath hold techniques

Thank you