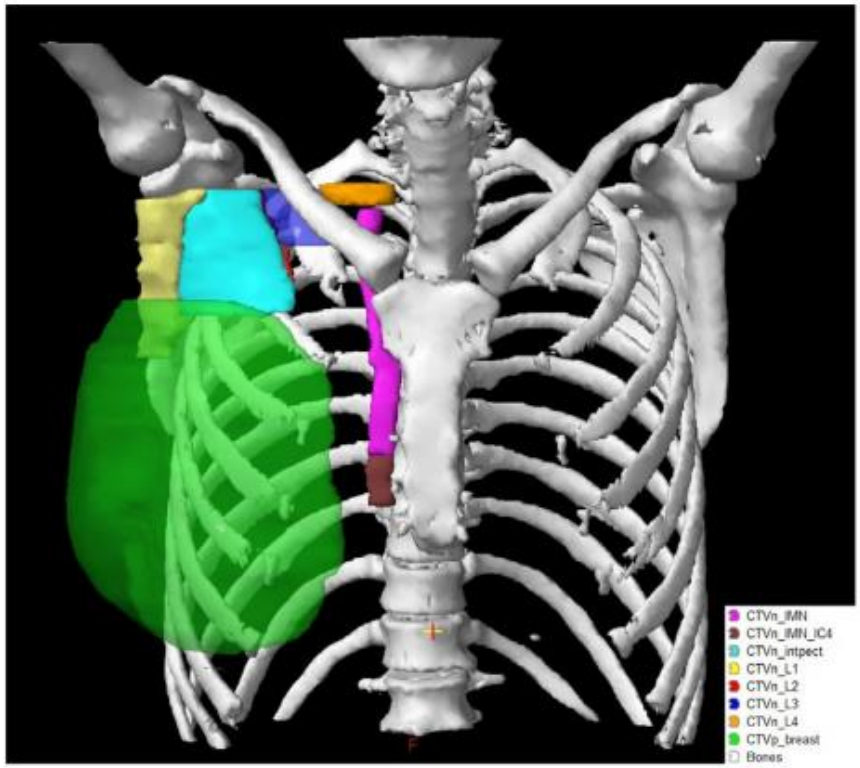
Stråleterapi efter NACT

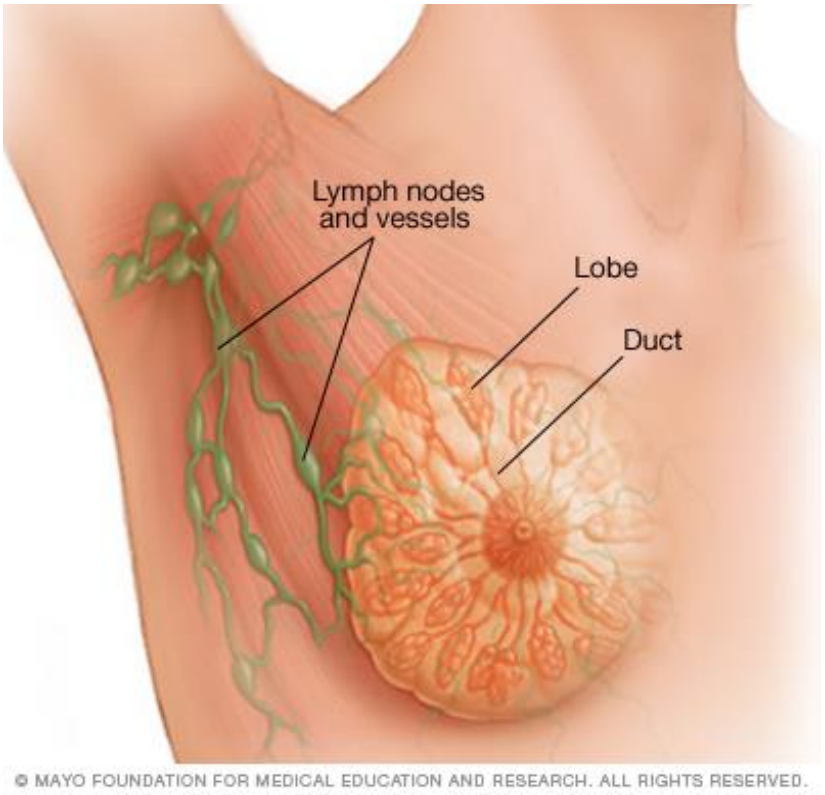


Troels Bechmann

Overlæge, Ph.d.
Onkologisk Afdeling
Vejle Sygehus

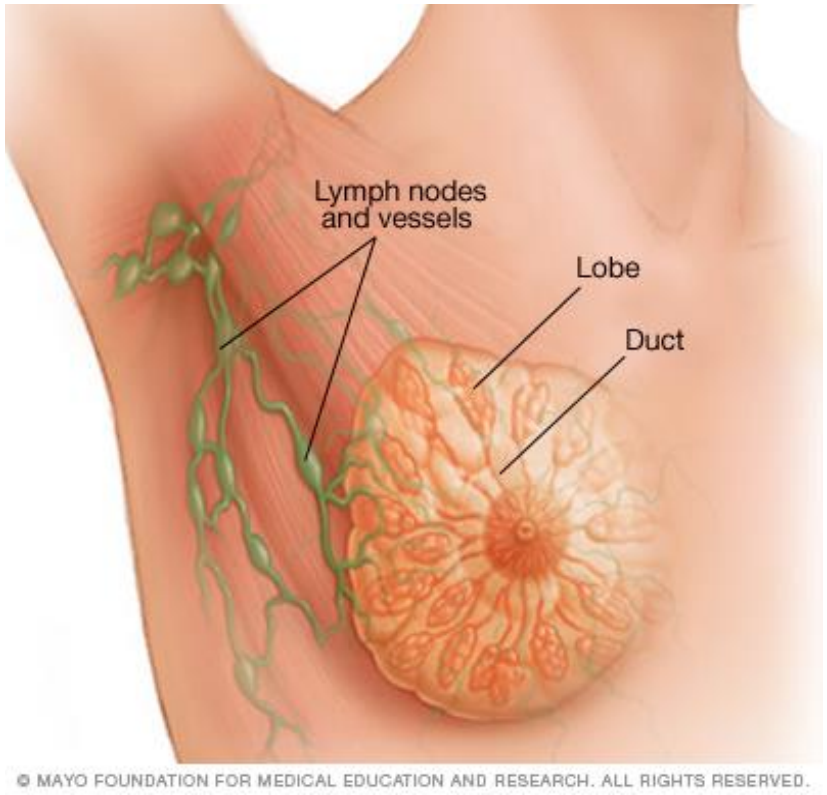
Stråleterapi efter NACT

- Udredning
- Teknik
- pCR
- Non-pCR
- Nye studier



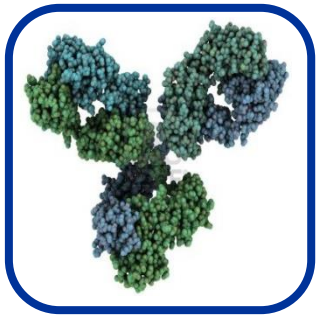
Stråleterapi efter NACT

- **Udredning**
- Teknik
- pCR
- Non-pCR
- Nye studier



NACT forløb 2019

Staging



HER2 target

Radiotherapy

Endocrine

Chemotherapy

Surgery

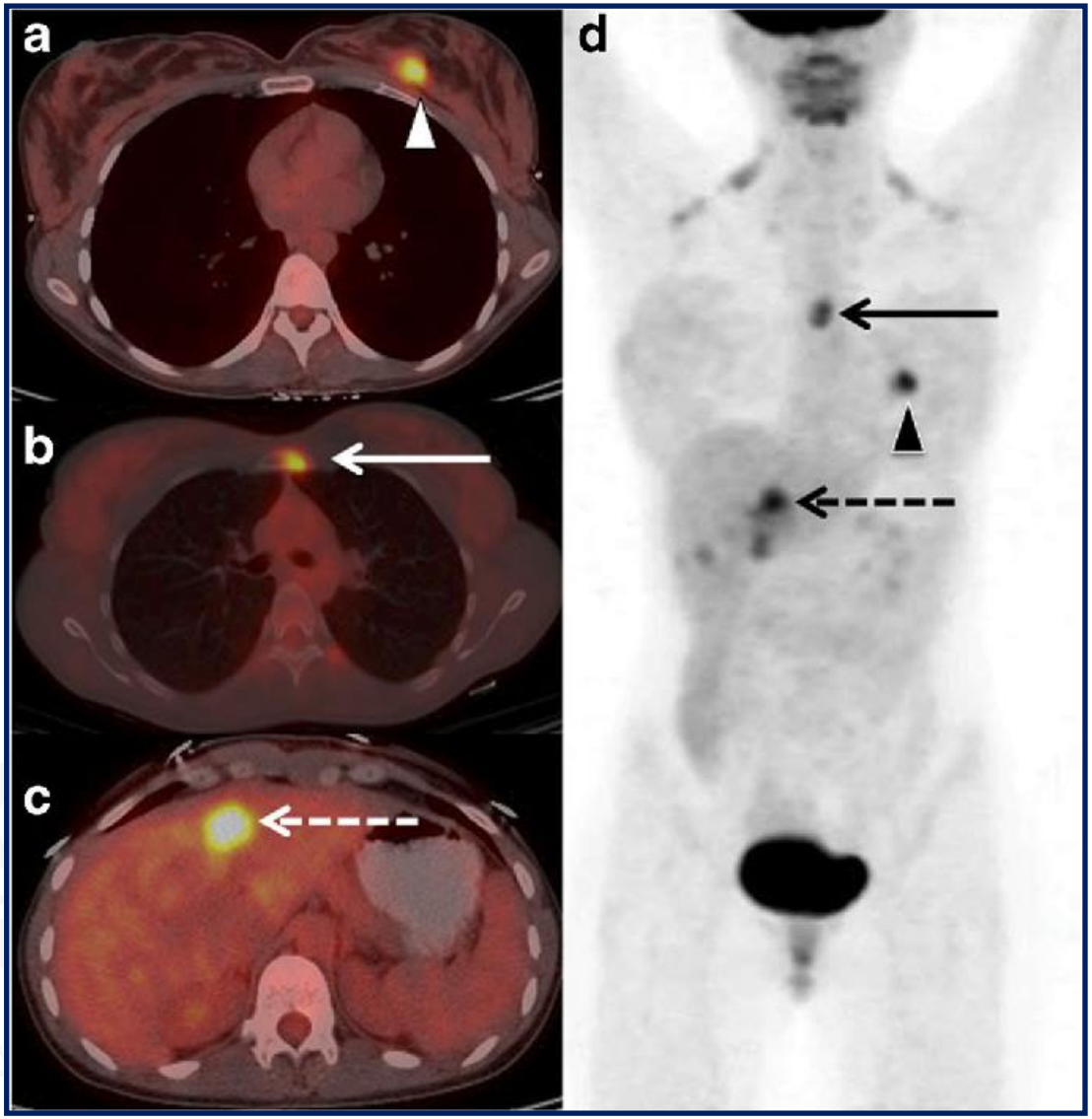
Chemotherapy

Udredning

Før NACT

Efter NACT

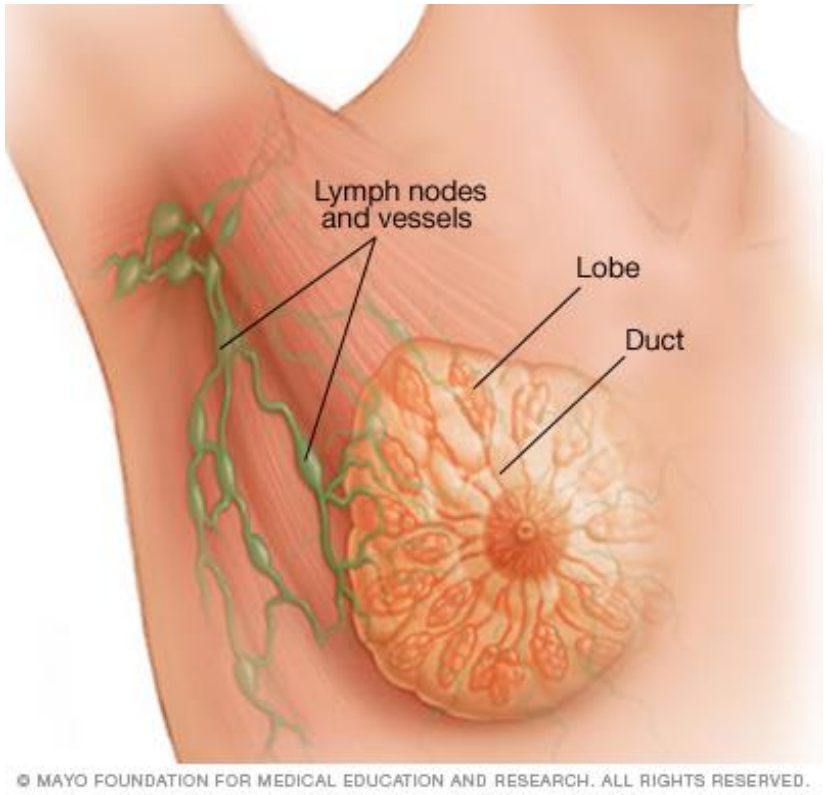
Venligst udlånt af Birgitte Offersen



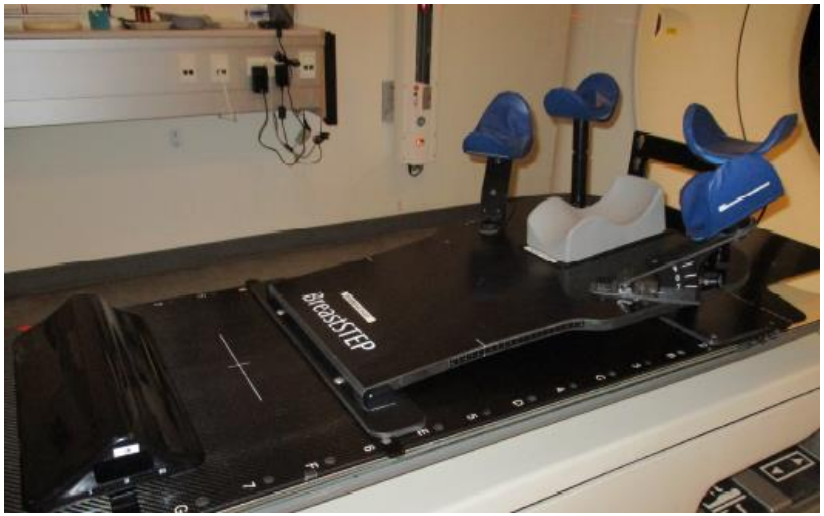
Paydary et al. Mol Imaging Biol 2019

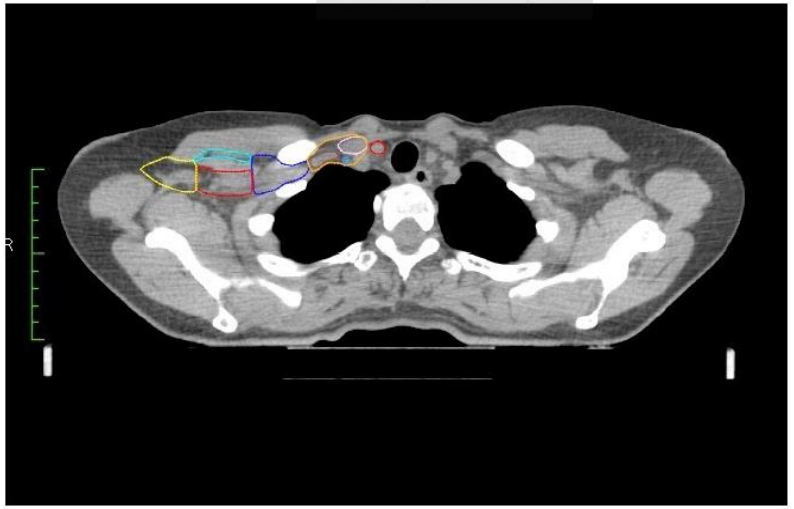
Stråleterapi efter NACT

- Udredning
- Teknik
- pCR
- Non-pCR
- Nye studier

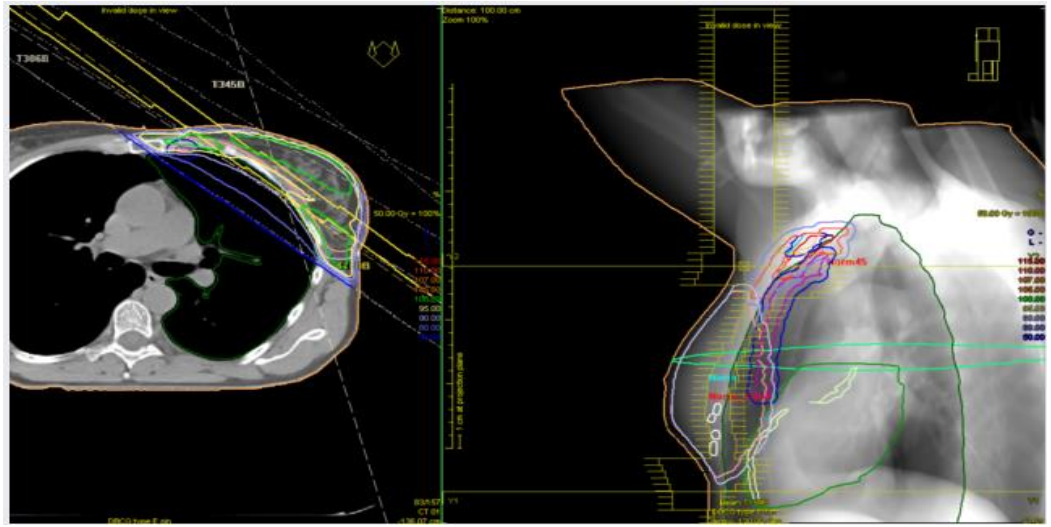


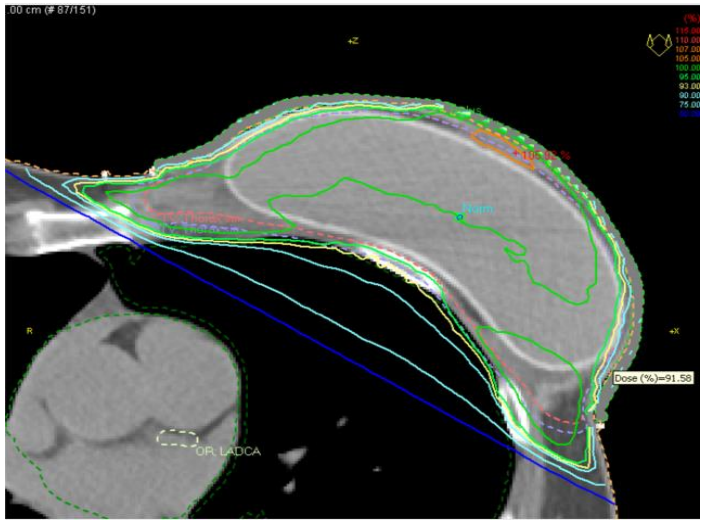
Planlægning af strålebehandling

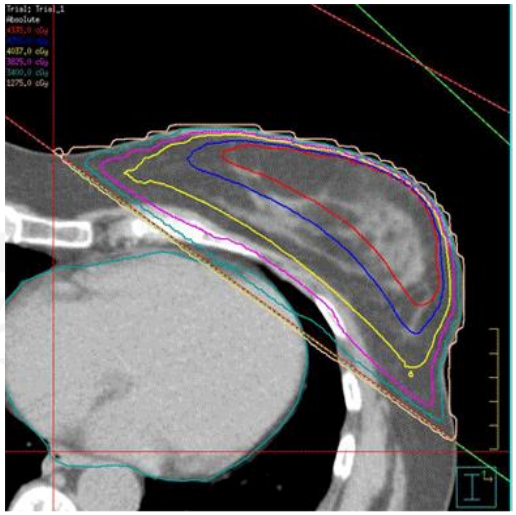


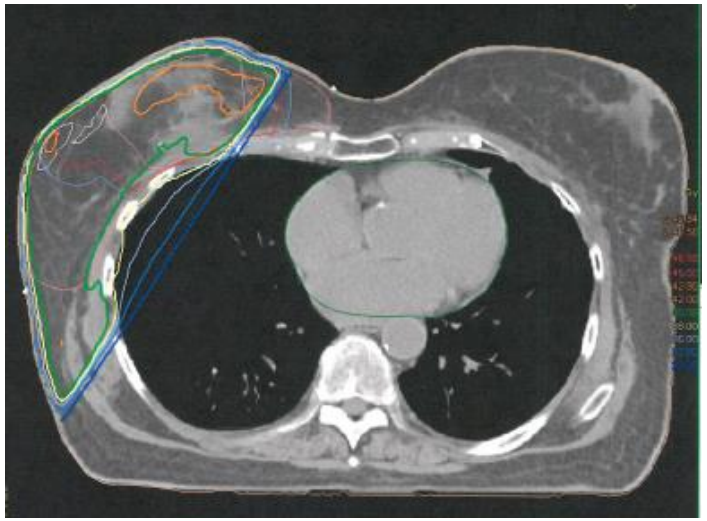


Planlægning af strålebehandling









Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis

Patricia Cortazar, Lijun Zhang, Michael Untch, Keyur Mehta, Joseph P Costantino, Norman Wolmark, Hervé Bonnefoi, David Cameron, Luca Gianni, Pinuccia Valagussa, Sandra M Swain, Tatiana Prowell, Sibylle Loibl, D Lawrence Wickerham, Jan Bogaerts, Jose Baselga, Charles Perou, Gideon Blumenthal, Jens Blohmer, Eleftherios P Mamounas, Jonas Bergh, Vladimir Semiglazov, Robert Justice, Holger Eidtmann, Soonmyung Paik, Martine Piccart, Rajeshwari Sridhara, Peter A Fasching, Leen Slaets, Shenghui Tang, Bernd Gerber, Charles E Geyer Jr, Richard Pazdur, Nina Ditsch, Priya Rastogi, Wolfgang Eiermann, Gunter von Minckwitz

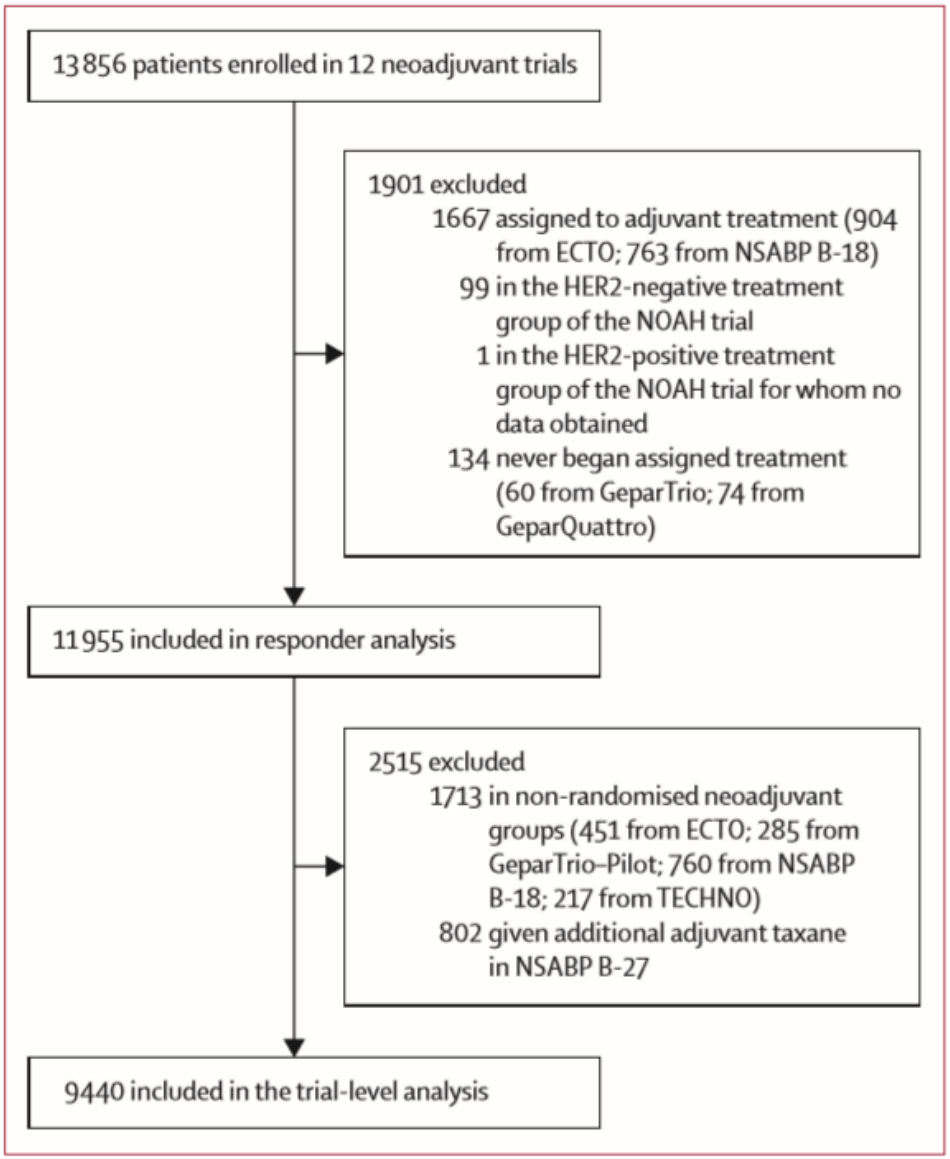
1) Etablerer associationen mellem patologisk komplet respons (pCR) og event free survival (EFS) og overall survival (OS)

2) Etablerer definition på pCR, der bedst korrelerer med langtids outcome

3) Identificerer subtyper hvor pCR korrelerer med langtids outcome

4) Udforsker om øget pCR i behandlingsgrupperne predikterer øget EFS og OS

Cortazar et al. Lancet 2014



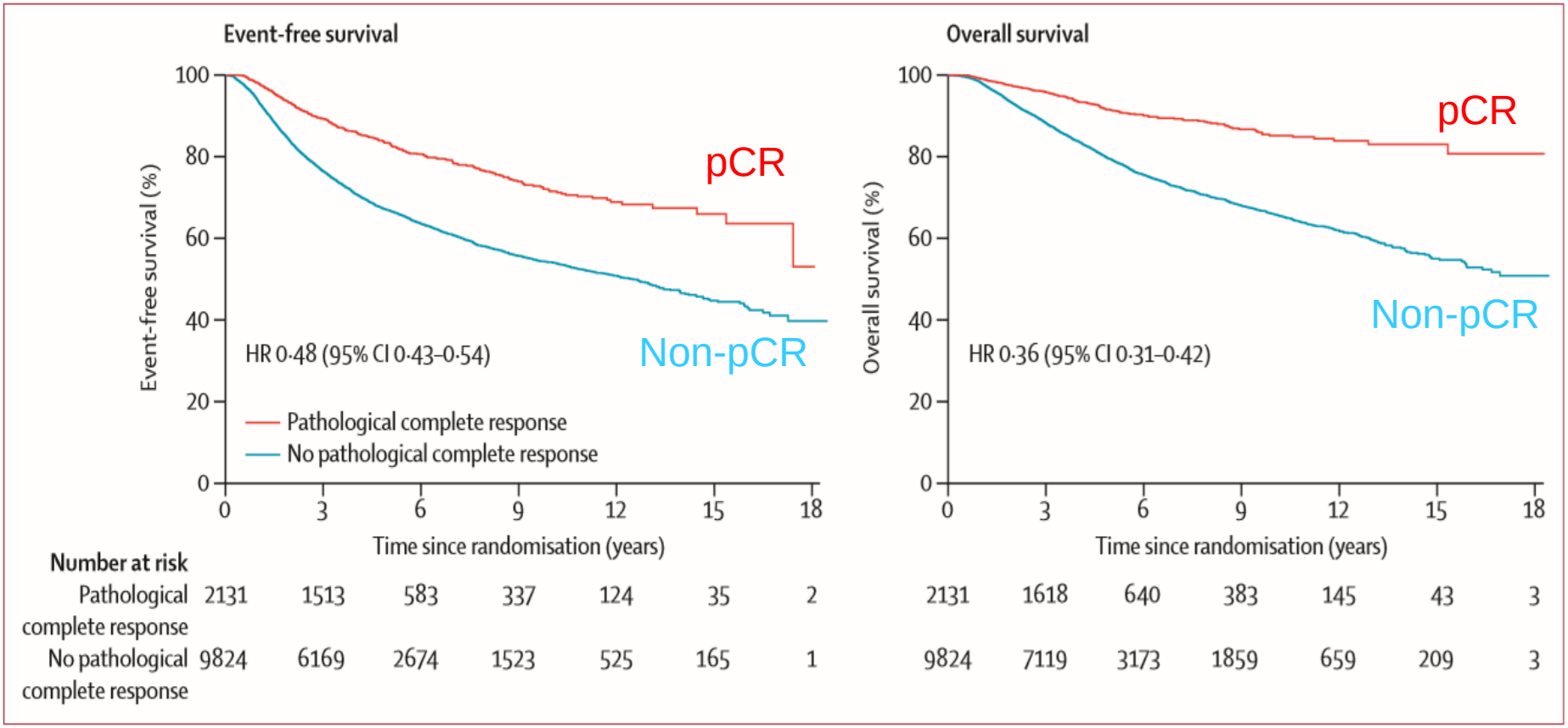
Neoadjuverende studier :
≥200 patients
≥3 års median follow up
Data på pCR, EFS og OS

Søgning: 1990-2011
11/12 studier er RCT
Trastuzumab i 3 studier

Median alder 49 år
61% T2
4% T4d (inflammatorisk)
46% cN+ (lymfeknude positiv)
30% receptor neg
17% HER2 pos

Median follow-up 5.4 år

Association mellem pCR og EFS / OS



Number at risk							
Pathological complete response	2131	1513	583	337	124	35	2
No pathological complete response	9824	6169	2674	1523	525	165	1

	2131	1618	640	383	145	43	3
	9824	7119	3173	1859	659	209	3

Figure 2: **Associations between pathological complete response and event-free survival and overall survival**
ypT0/is ypN0 definition of pathological complete response (ie, absence of invasive cancer in the breast and axillary nodes, irrespective of ductal carcinoma in situ). HR=hazard ratio.

Association mellem definition af pCR og EFS / OS

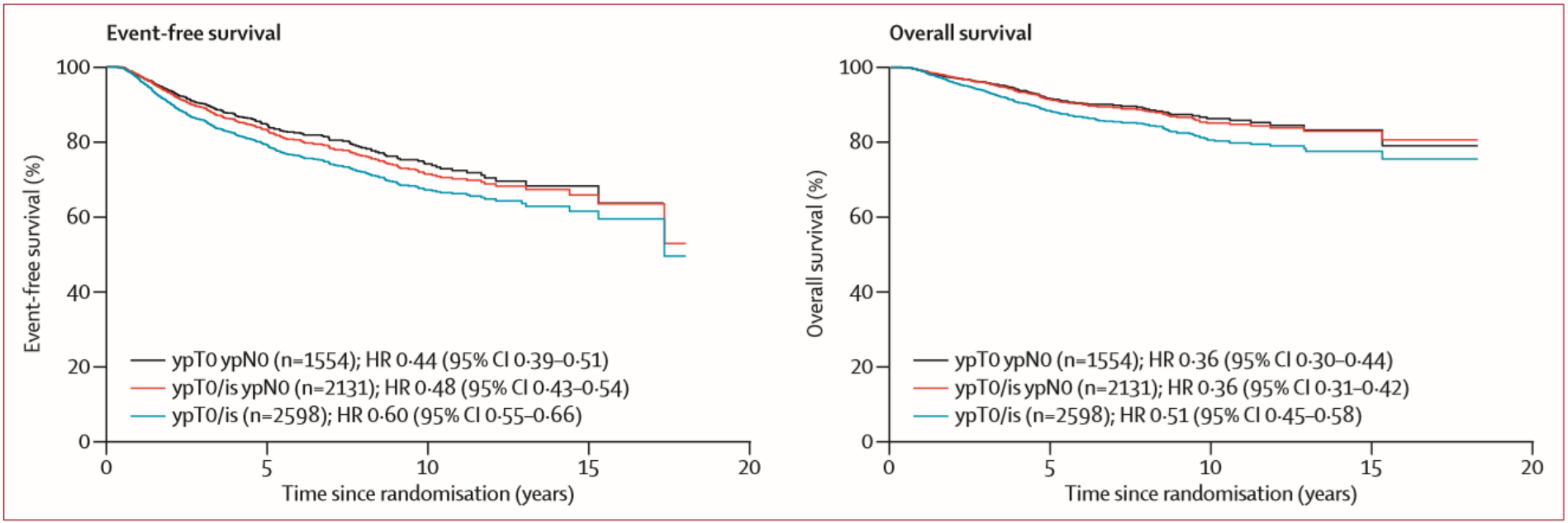
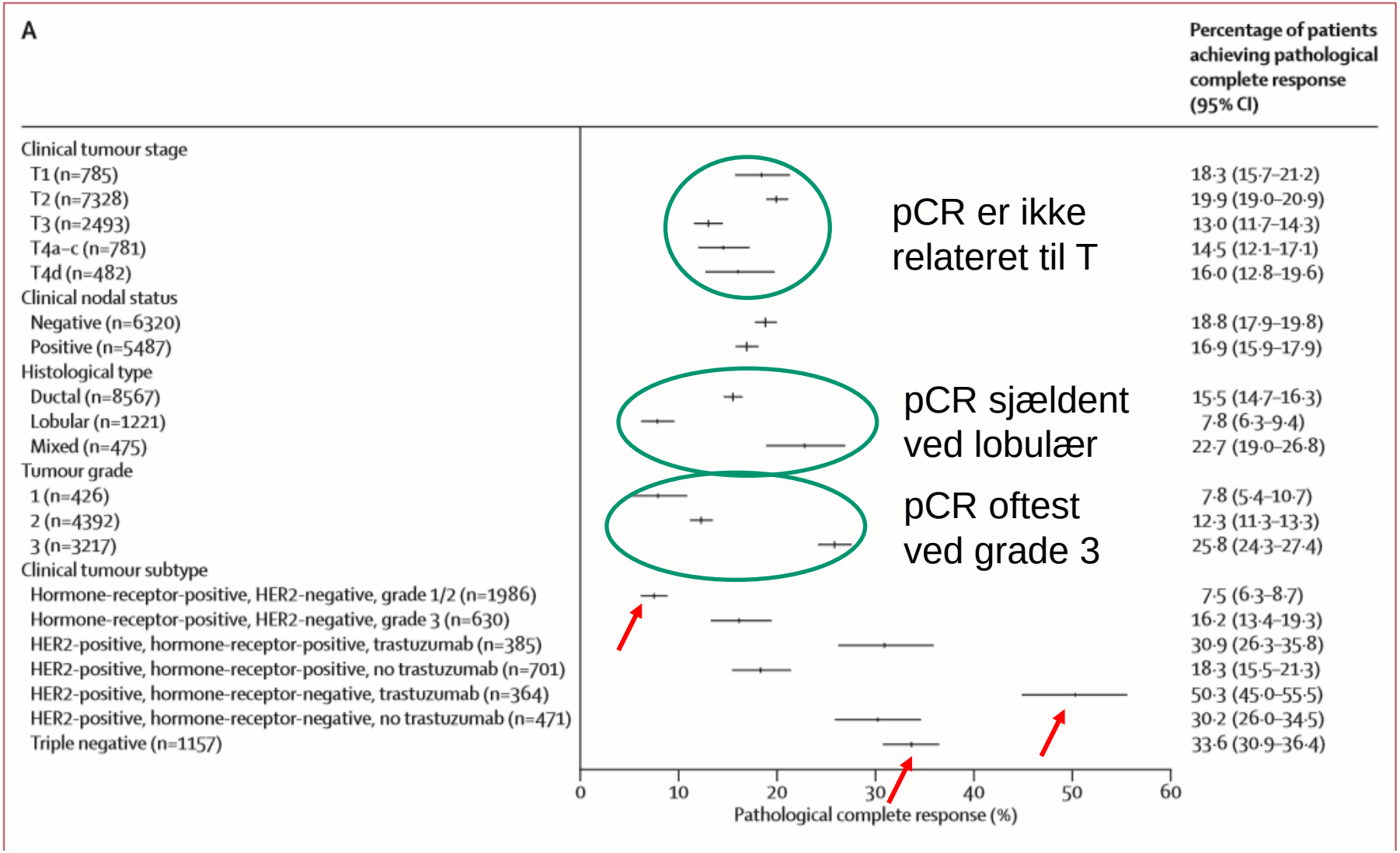
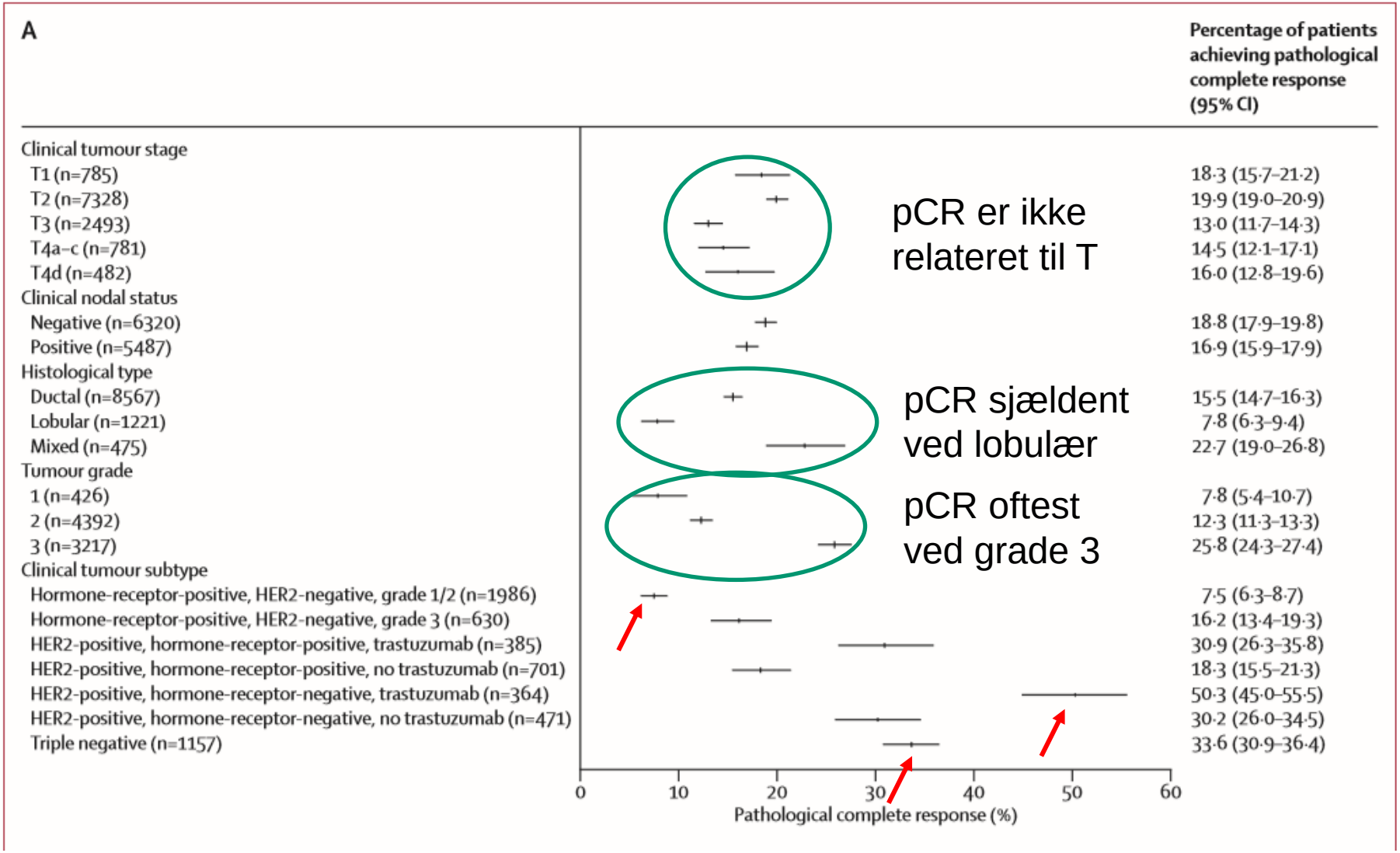


Figure 3: **Associations between three definitions of pathological complete response and event-free survival and overall survival**
We compared event-free survival and overall survival between patients who did and did not achieve a pathological complete response according to one of three definitions. Patients who did not achieve a pathological complete response are not shown. Number of patients who achieved a pathological complete response is listed for each pathological complete response definition. Patients could achieve pathological complete response according to more than one definition. ypT0 ypN0=absence of invasive cancer and in-situ cancer in the breast and axillary nodes. ypT0/is ypN0=absence of invasive cancer in the breast and axillary nodes, irrespective of ductal carcinoma in situ. ypT0/is=absence of invasive cancer in the breast, irrespective of ductal carcinoma in situ or nodal involvement. HR=hazard ratio.

pCR (ypT0/is ypN0) i subgrupper



pCR (ypT0/is ypN0) i subgrupper



Lokoregional strålebehandling efter NACT (LABC)

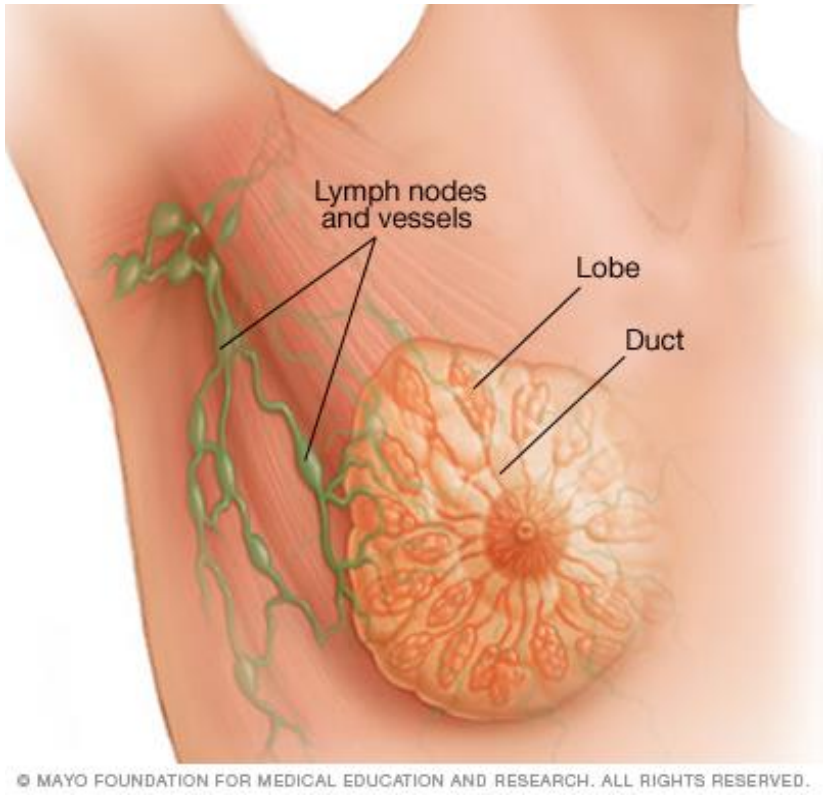
NACT: Neoadjuvant Chemotherapy: Primær operabel sygdom: T2 (2,0 cm < tumor <= 5.0 cm), N0-N1, invasivt c. mammae af non-lobulær type.

LABC: Locally Advanced Breast Cancer: Primær inoperabel lokoregional fremskreden sygdom (stadium III): T3-4 og/eller N2-3 og M0

- **Lumpektomi** (uanset patologisk responsgrad) anbefales postoperativ strålebehandling til alle patienter uanset alder. Der gives strålebehandling mod såvel bryst som lymfeknuder ved metastase i aksillen **inkl. mikrometastase og ITC** samt ved negativ SN, men med tegn på tidligere metastase.
- **Mastektomi** anbefales postoperativ strålebehandling til alle patienter med tumor > 5 cm og/eller metastase i aksillen **inkl. mikrometastase og ITC** samt ved negativ SN (efter NACT), men med tegn på tidligere metastase.
- Udstrækningen af target tilpasses sygdomsstadie (N-stadie) og omfanget af det kirurgiske indgreb (SN, +/- aksildissektion) samt patologisk responsevaluering i lymfeknuder (ved negativ SN og ingen aksildissektion, men patologisk påvist tegn på tidligere metastase gives regional strålebehandling inkl. aksil level 1).

Stråleterapi efter NACT

- Udredning
- Teknik
- pCR
- Non-pCR
- Nye studier



Adjuverende Strålebehandling

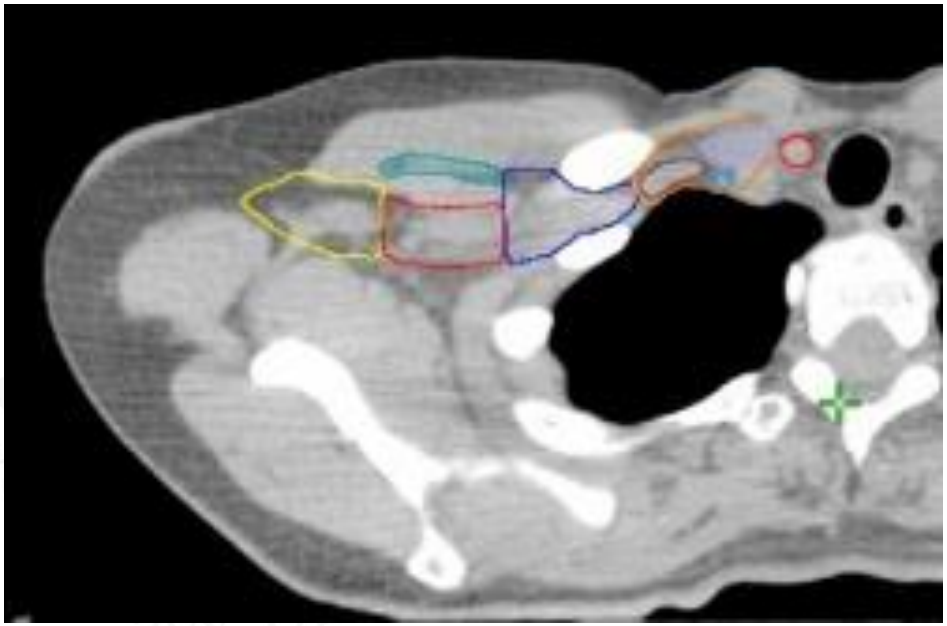
Mastektomerede / lumpektomerede patienter:

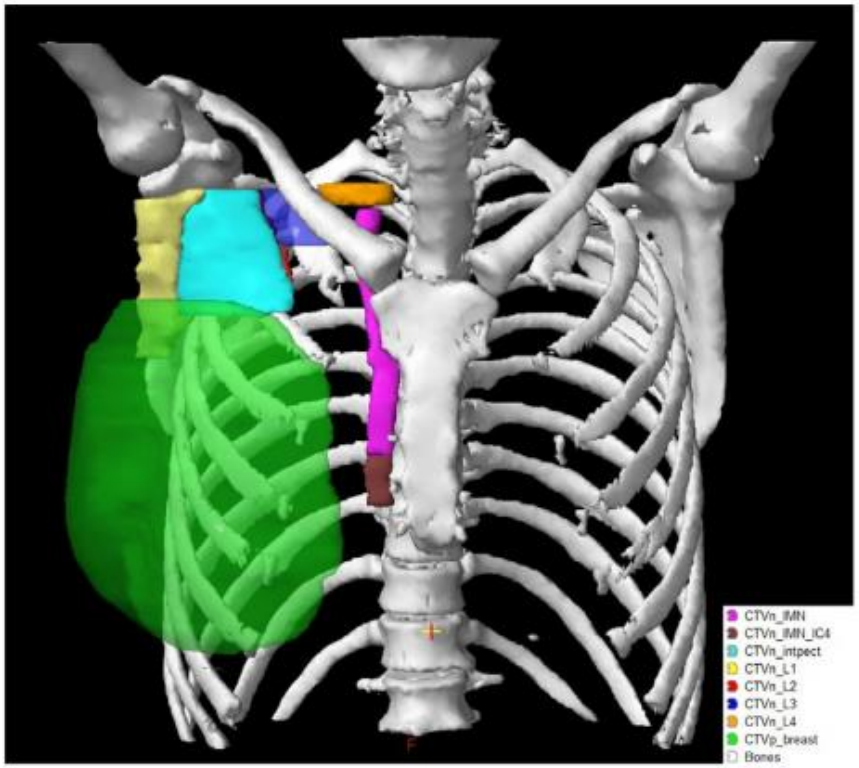
Type A, D: Regio / residuale mamma, lymfeknude level I, II, III, IV, interpectoral, IMN

Type B, E: Regio / residuale mamma, lymfeknude level II, III, IV, interpectoral, IMN IC:1-4

Type C, F: Regio / residuale mamma

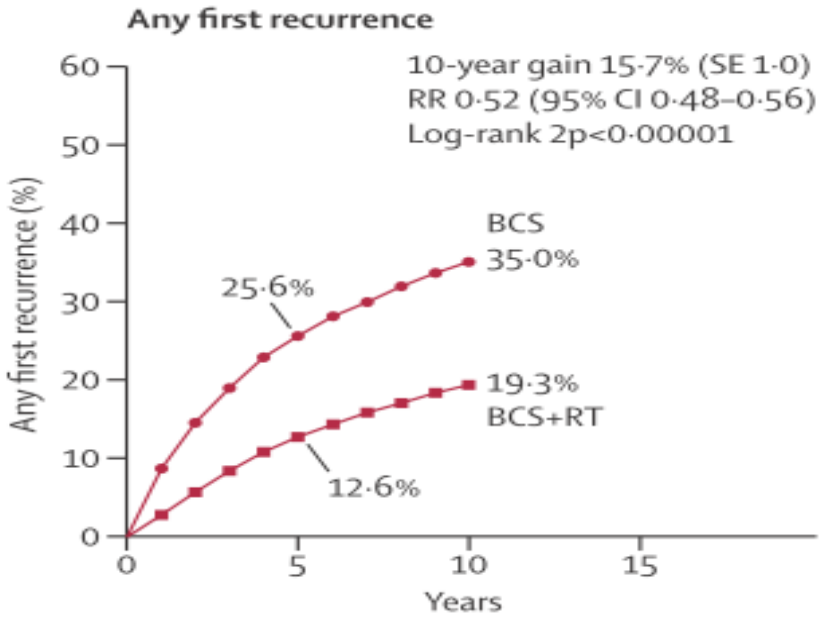
Type G: Delbryst (PBI ≥ 60 år, T1N0M0*)

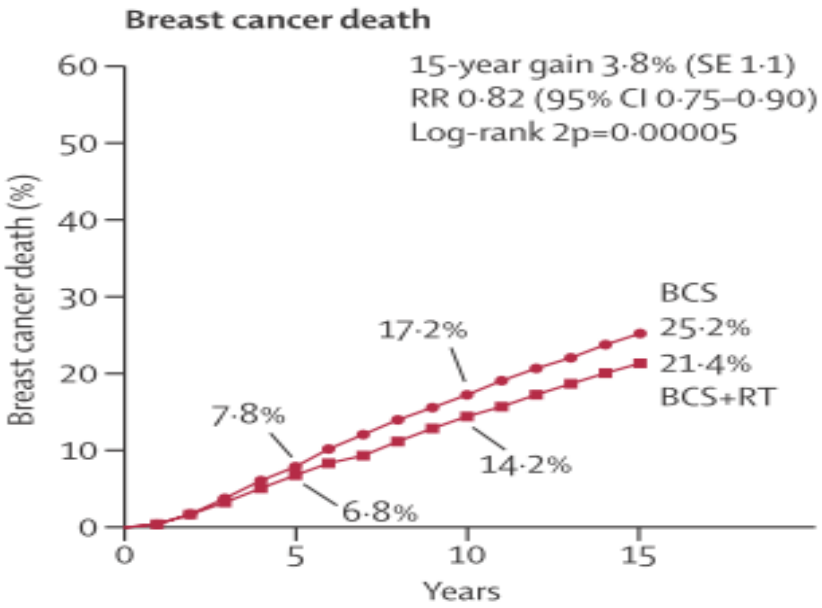




Adjuverende Strålebehandling

- Lumpektomi
- 50 Gy/ 25 F node positiv
  40 Gy/ 15 F node negativ F/G

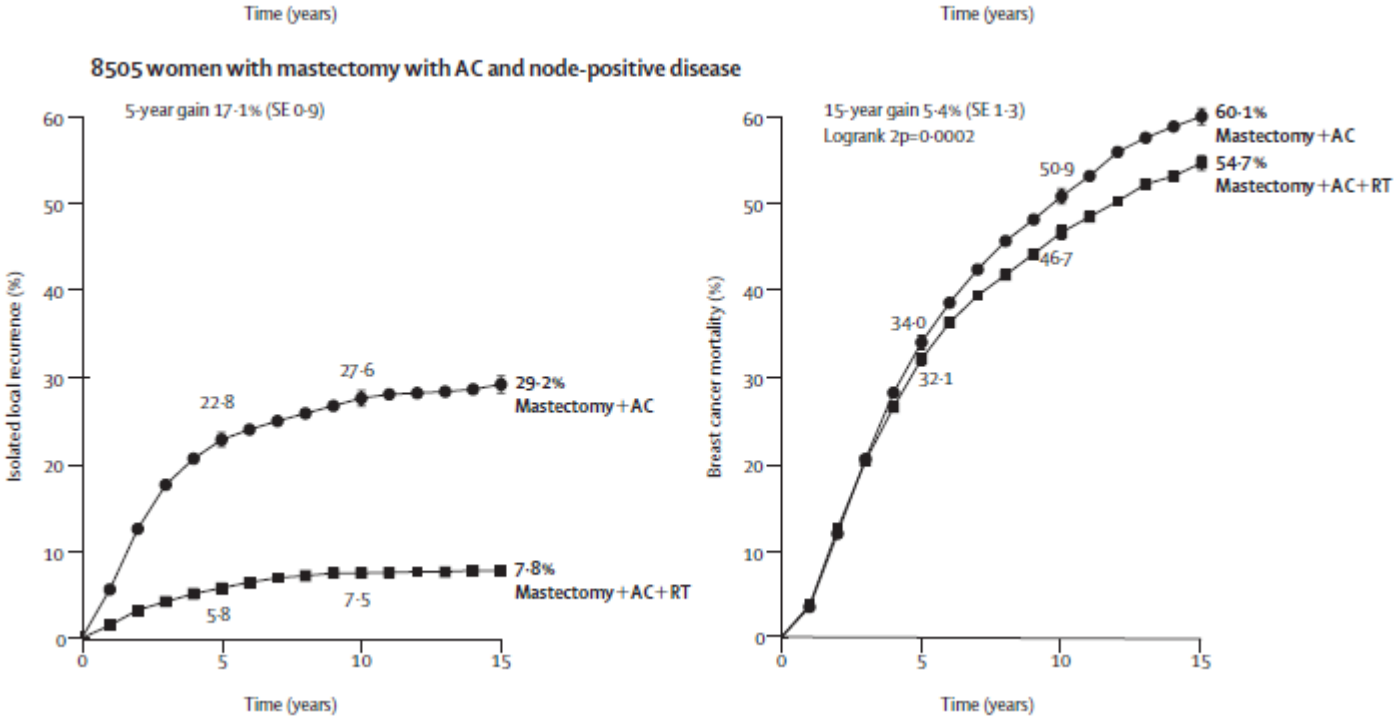




EBCTCG Lancet 2011 (10.800 kvinder)

Adjuverende Strålebehandling

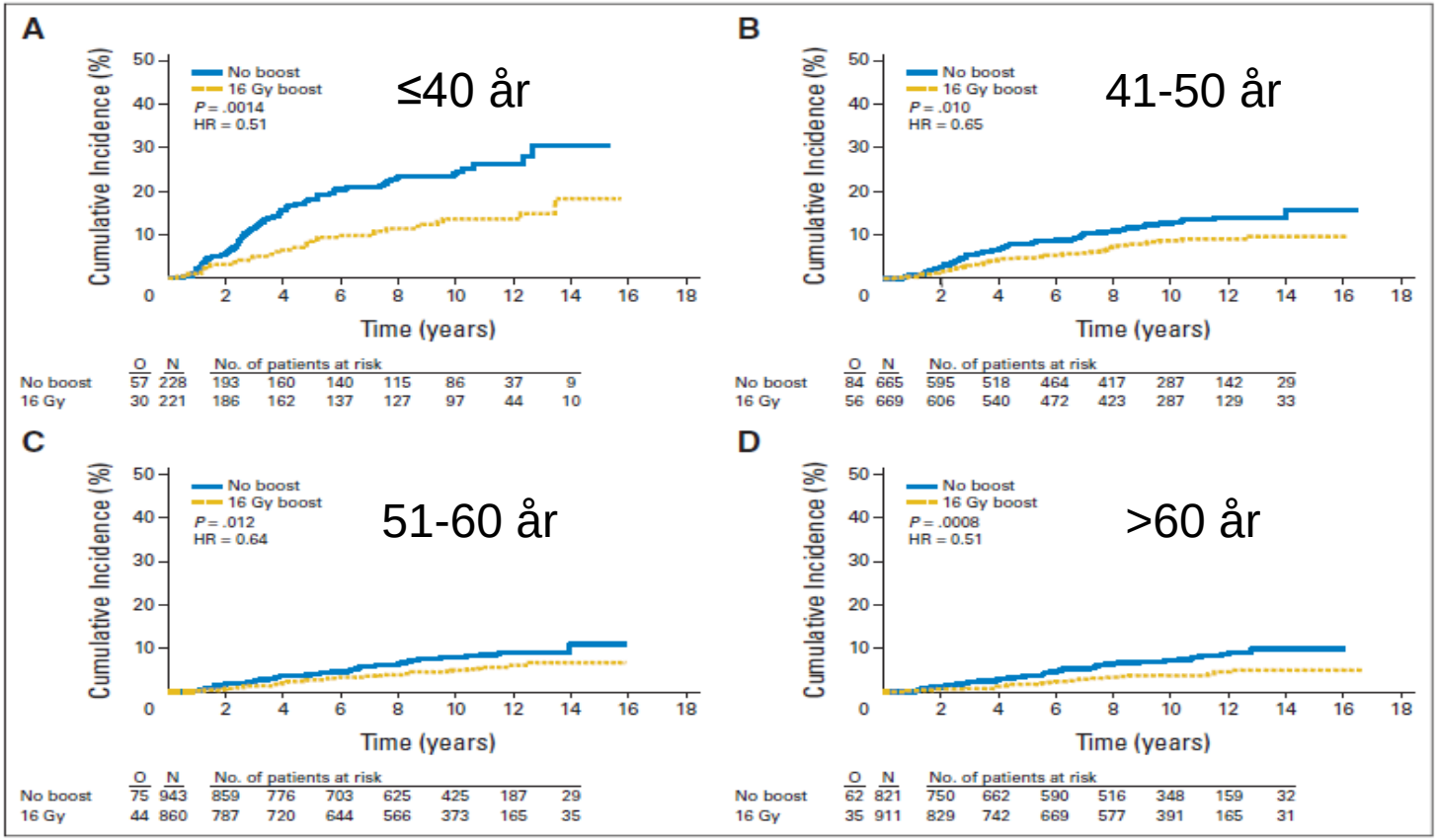
- Mastektomi 50 Gy/25 ved
  Tumor > 50 mm, Lymfeknude
  positiv, uradikal operation



EBCTCG Lancet 2005

Boost

- Boost 10Gy/5 < 50år
  Boost 16Gy/8 ≤ 40år

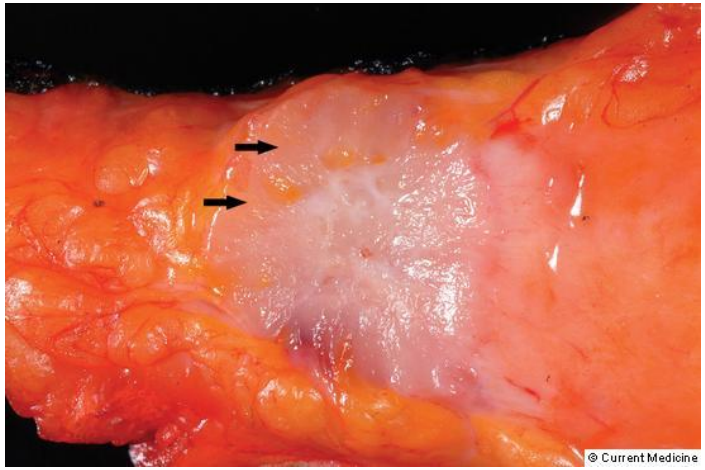


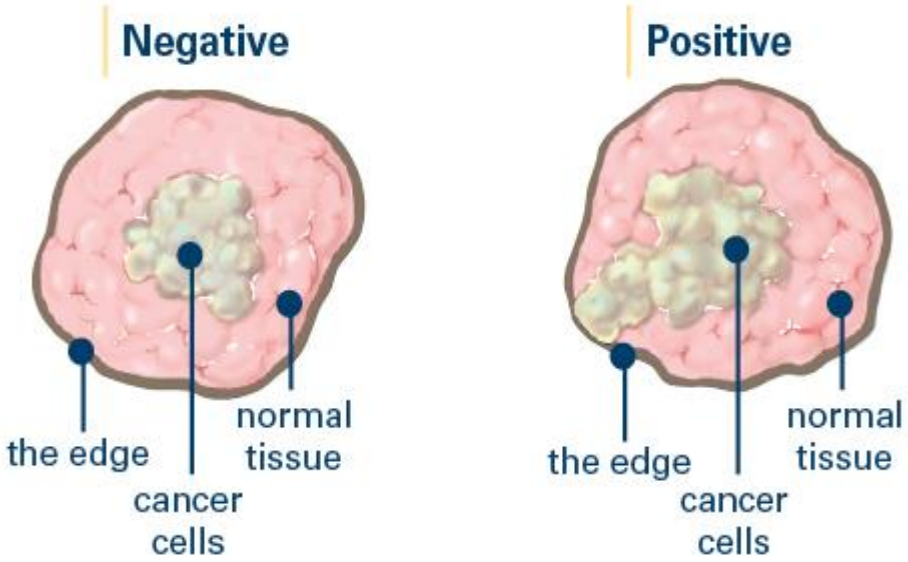
Bartelink et al. JCO 2007

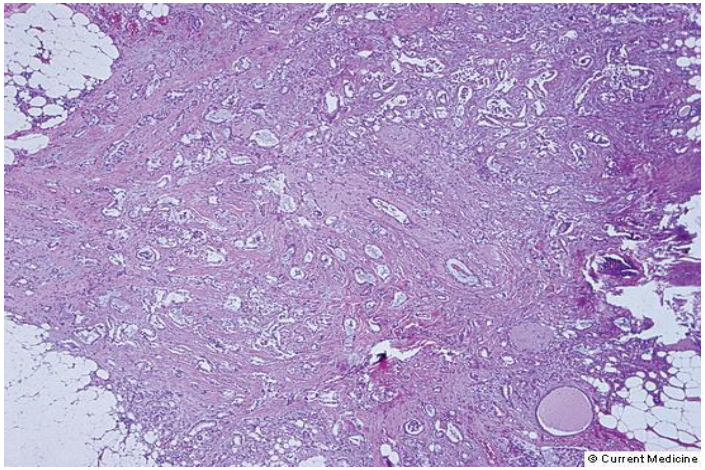
Boost – Not on Ink

Not on Ink

Boost hvis margin < 2 mm







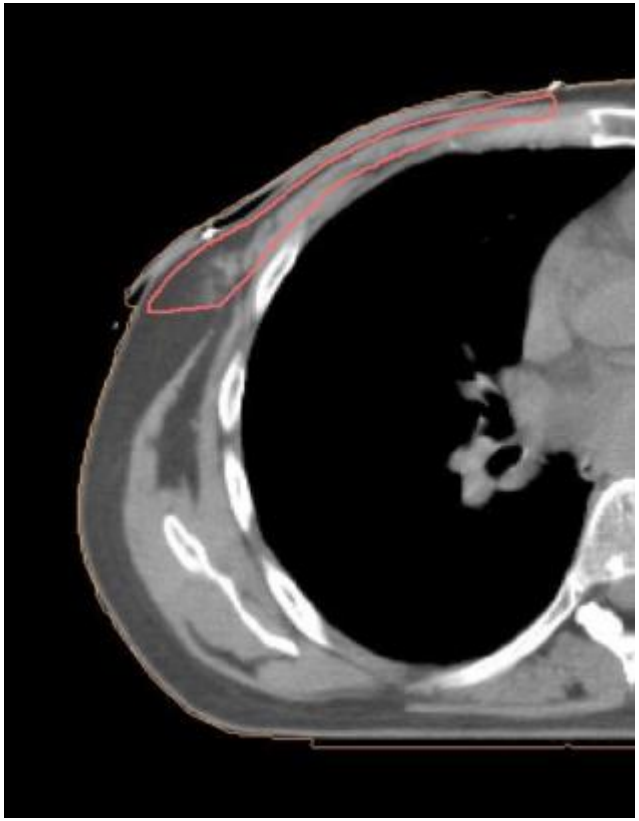
Anvendelsens af bolus

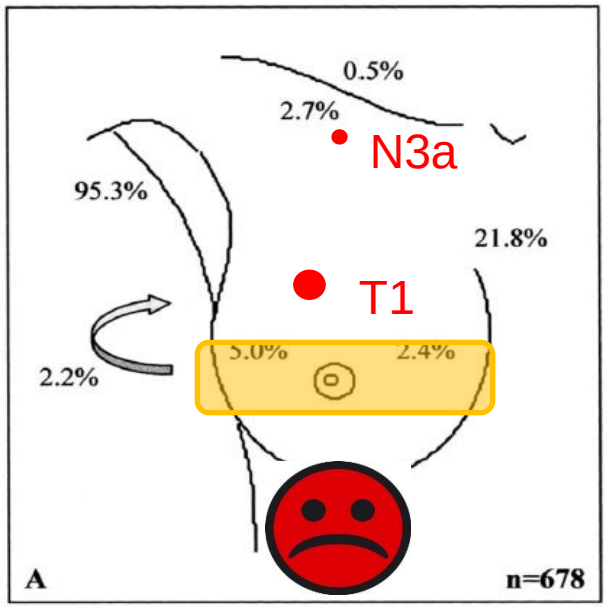
REFERAT: Ordinært møde i DBCG 's Radioterapiudvalg
22.06.17 - Onkologisk afdeling, Vejle Sygehus

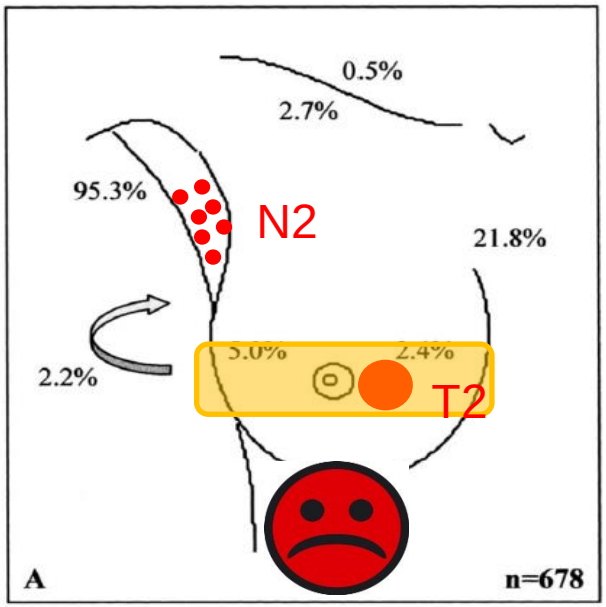
Bolus i regio mammaria:
Det besluttes at ophøre med rutinemæssig anvendelse af bolus til ptt der modtager postoperativ strålebehandling efter **T1-2** sygdom (tumorstr. ≤ 50 mm);

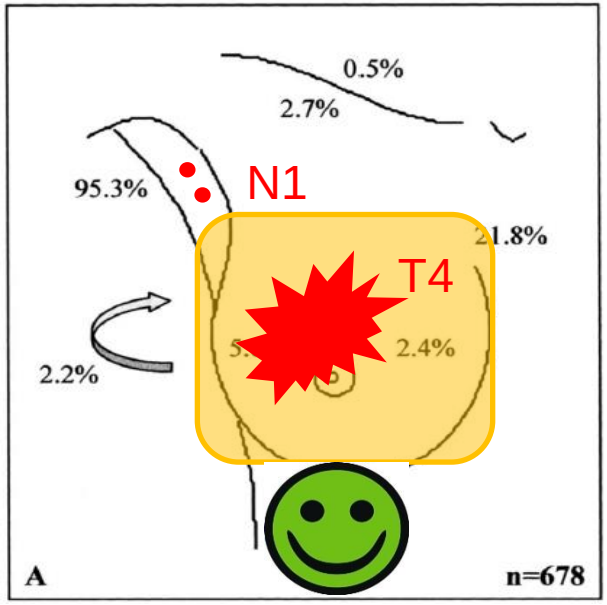
Ptt med **T3** sygdom anbefales bolus omkring cikatricen (+/- 3 cm i kranio-kaudal retning) uanset N status.

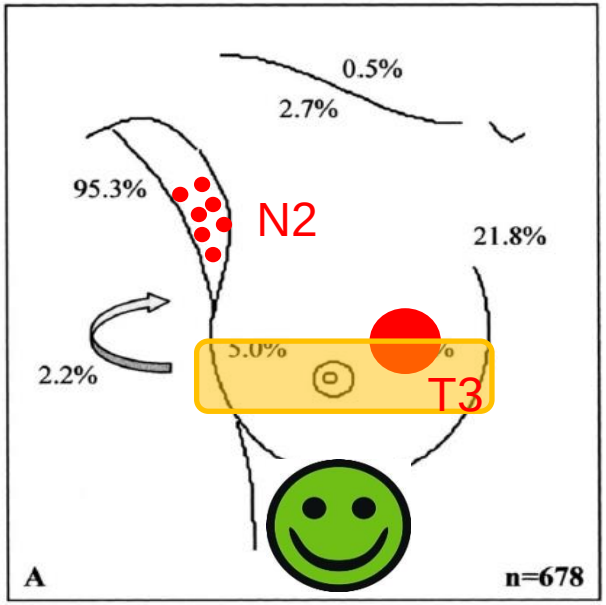
Ptt med **T4d** sygdom (mastitis carcinomatosa) anvendes evt. bolus over hele regio mammaria.



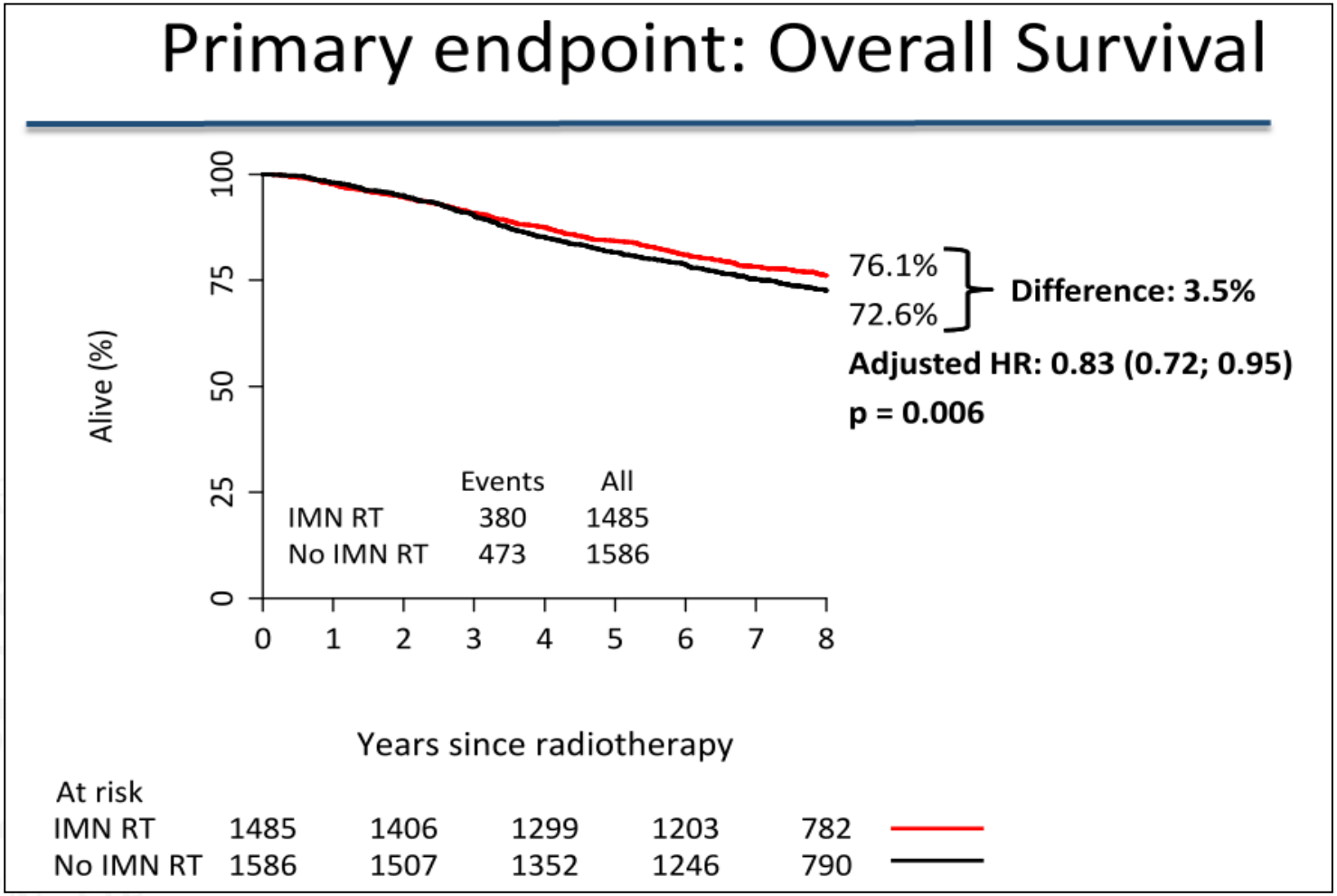

0.5%
2.7%
N3a
95.3%
21.8%
T1
2.2%
A
n=678


0.5%
2.7%
95.3%
N2
21.8%
2.2%
T2
A
n=678


0.5%
2.7%
95.3%
N1
21.8%
T4
2.2%
2.4%
A
n=678


0.5%
2.7%
95.3%
N2
21.8%
2.2%
T3
A
n=678

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



Thorsen et al. 2015

Analysis of subgroups defined by tumor location (lateral vs medial/central) and number of macrometastatic axillary nodes (1-3 nodes vs ≥4 nodes)

Subgroup	IMNI Patients	IMNI Events	No IMNI Patients	No IMNI Events	HR (95% CI)	8-year survival rate (%) IMNI	8-year survival rate (%) No IMNI
Lateral 1–3 nodes	511	91	564	91	1.13 (0.84 to 1.51)	82.9	85.7
Medial/central 1–3 nodes	353	67	382	88	0.80 (0.58 to 1.10)	83.2	78.8
Lateral ≥ 4 nodes	392	137	384	170	0.71 (0.57 to 0.89)	68.0	58.3
Medial/central ≥ 4 nodes	224	86	259	131	0.81 (0.61 to 1.06)	61.9	53.8
All patients	1,480	381	1,589	480	0.82 (0.72 to 0.94)	75.9	72.2
Test for heterogeneity, $P = .10$							

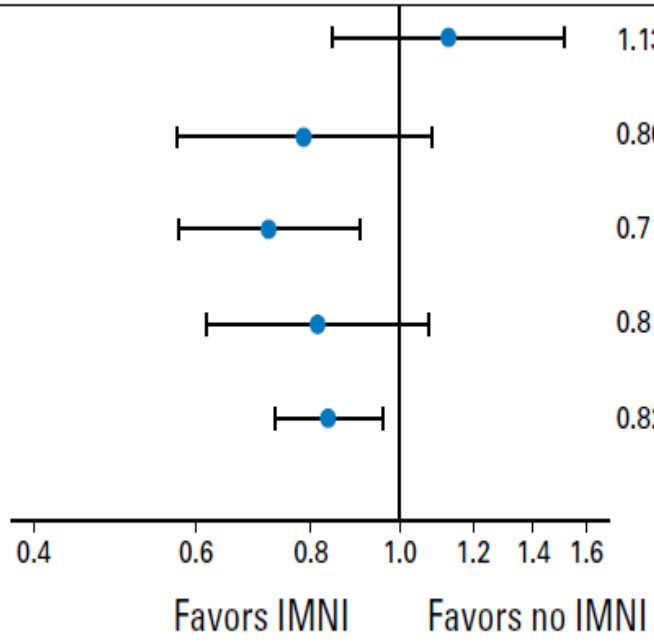


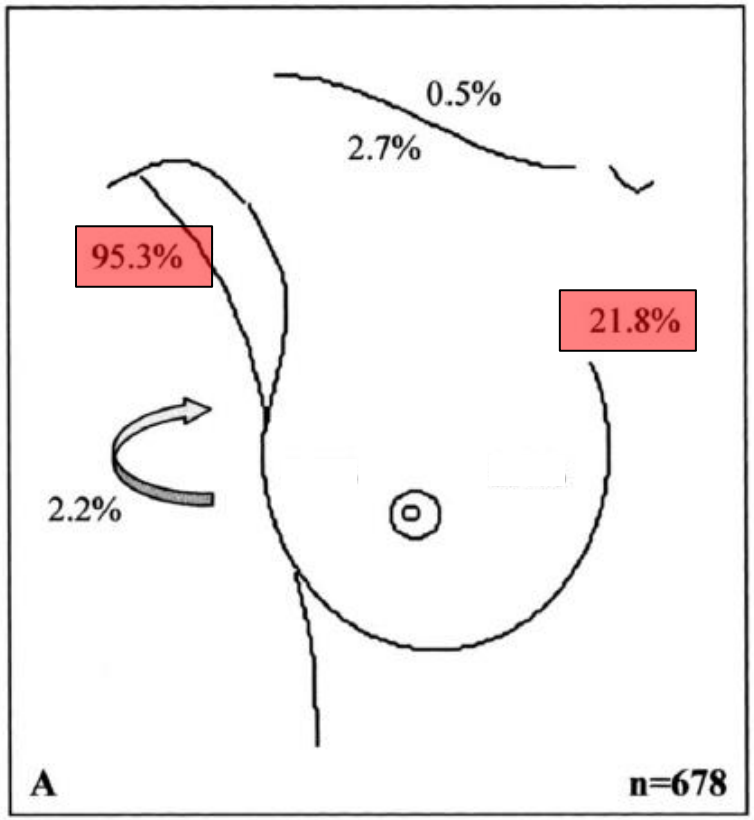
Fig 4. Overall survival rates and corresponding hazard ratios (HR) with versus without internal mammary node irradiation (IMNI) within subgroups defined by tumor location and the number of axillary nodes involved.

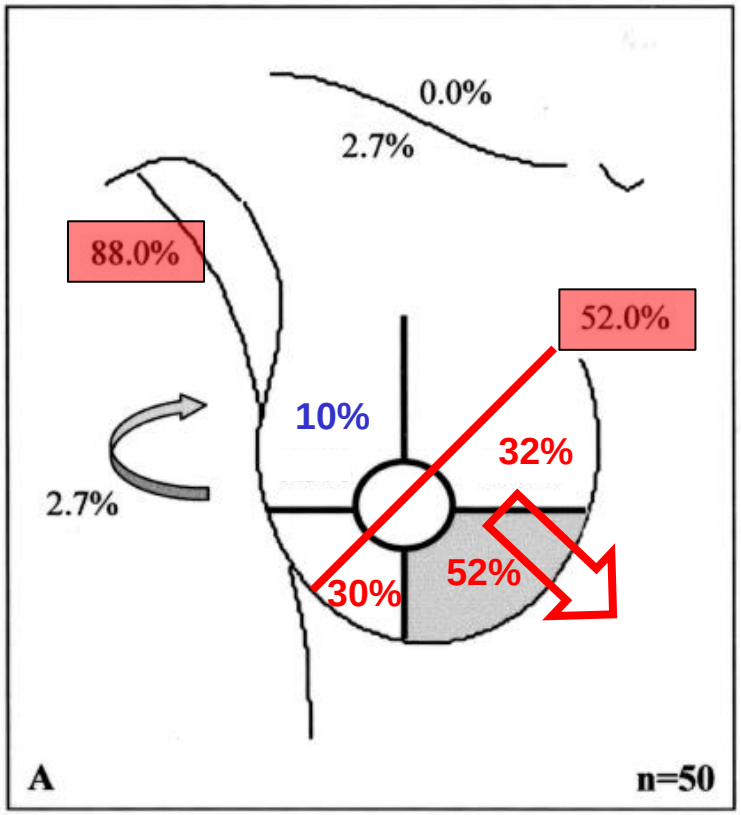
Thorsen et al. 2015

Fra DBCG retningslinje til lokal instruks

Fra folketingslov til bekendtgørelse

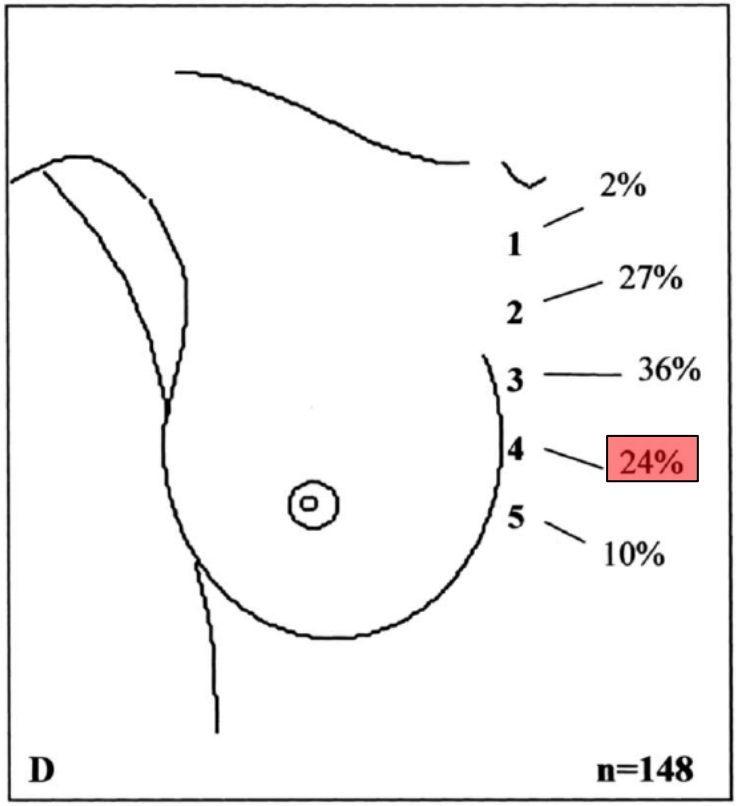
Lymfeknude drænage

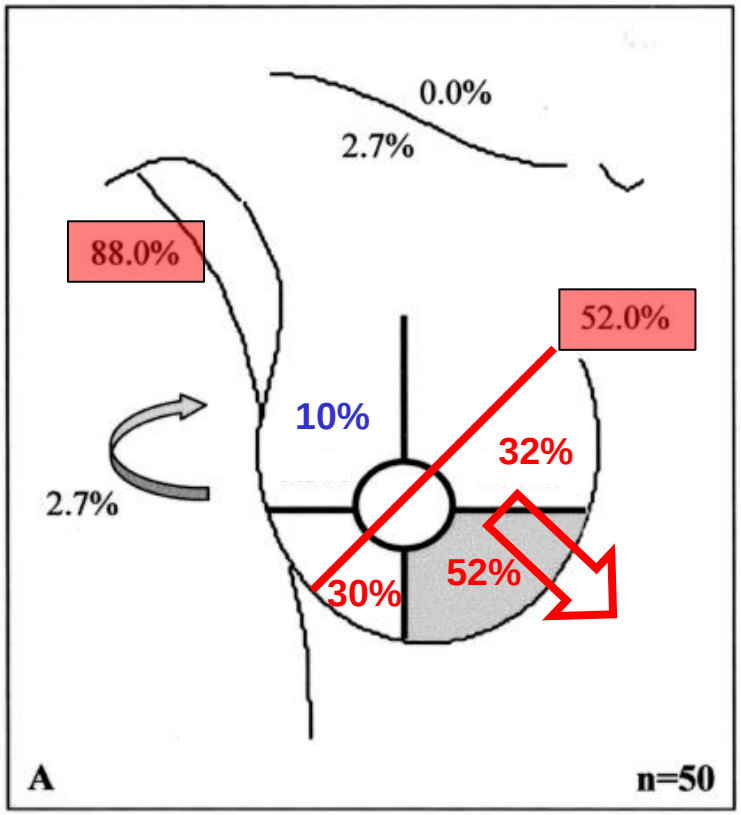




Estourgie et al. Annals of Surgery, February 2004

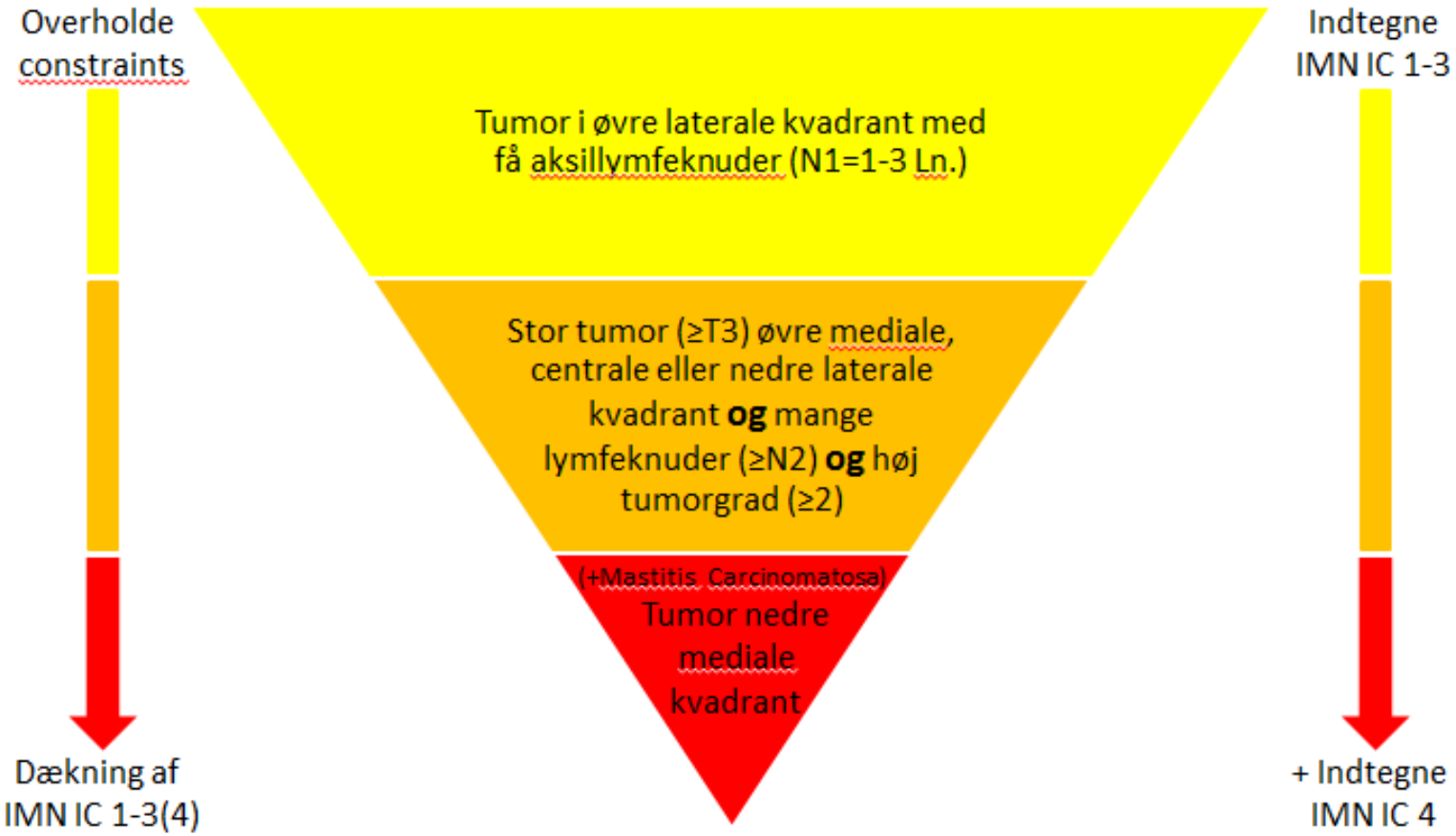
Lymfeknude drænage





Estourgie et al. Annals of Surgery, February 2004

Prioritering af IMN og medinddragelse af IMN IC4



Med i overvejelserne om dækning af IMN IC 1-3(4) medtages også comorbiditet og rygerstatus!
Gul = IC4 medtages aldrig, Orange = IC4 medtages i udvalgte tilfælde, Rød = IC4 bør medtages

Stråleterapi efter NACT ved pCR ?

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The Role of Postmastectomy Radiation Therapy in Patients with Breast Cancer Responding to Neoadjuvant Chemotherapy

Jose G. Bazan, MD MS and **Julia R. White, MD**
Department of Radiation Oncology, The Ohio State University

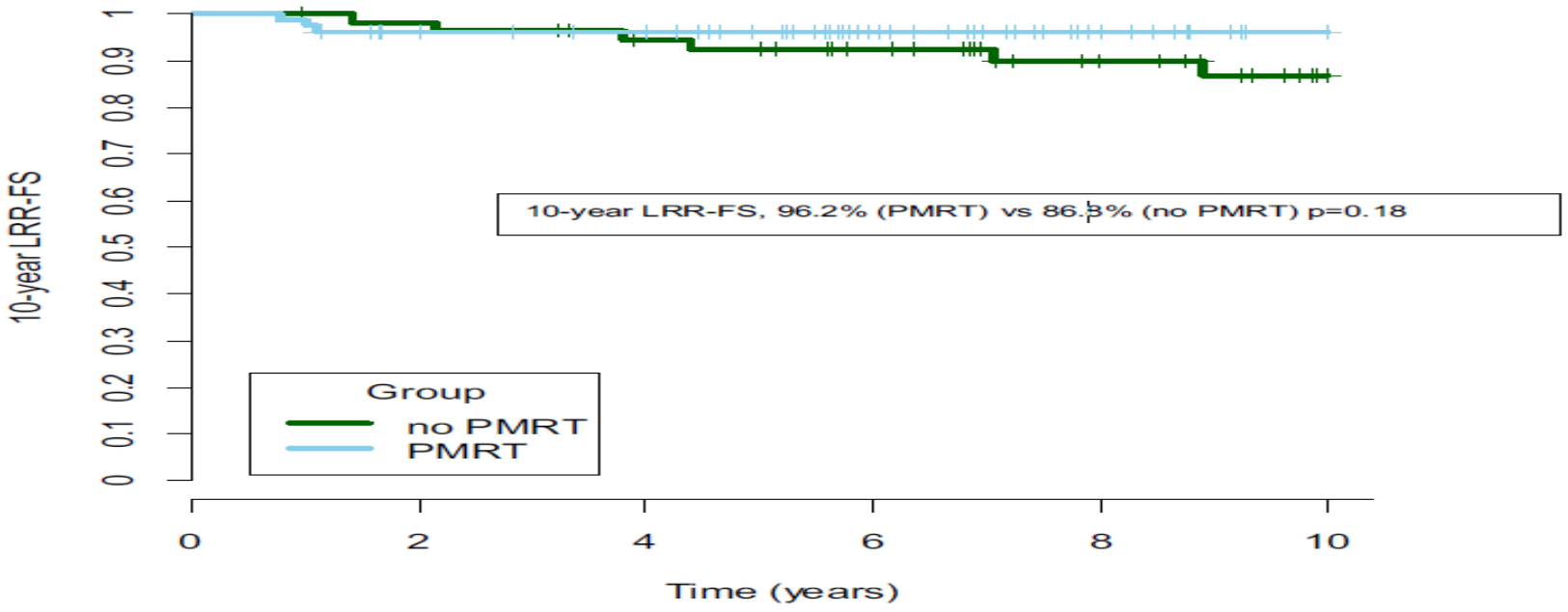
ELSEVIER
Int. J. Radiation Oncology Biol. Phys., Vol. 82, No. 1, pp. e1–e7, 2012

0360-3016/$ - see front matter
doi:10.1016/j.ijrobp.2010.12.054

CLINICAL INVESTIGATION **Breast Cancer**

RADIOTHERAPY FOR STAGE II AND STAGE III BREAST CANCER PATIENTS WITH NEGATIVE LYMPH NODES AFTER PREOPERATIVE CHEMOTHERAPY AND MASTECTOMY

Kaplan Meier estimates of 10-year LRR-FS



No. at Risk						
No PMRT	56	55	50	43	32	21
PMRT	78	70	67	46	29	19

Fig. 1. Locoregional recurrence-free survival (LRR-FS) according to receipt of postmastectomy radiotherapy (PMRT).

1990-2004: 78 pt. + PMRT, 56 pt. - PMRT

Scodan et al 2012

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Clinical Investigation: Breast Cancer

The Role of Postmastectomy Radiation Therapy After Neoadjuvant Chemotherapy in Clinical Stage II-III Breast Cancer Patients With pNO: A Multicenter, Retrospective Study (KROG 12-05)

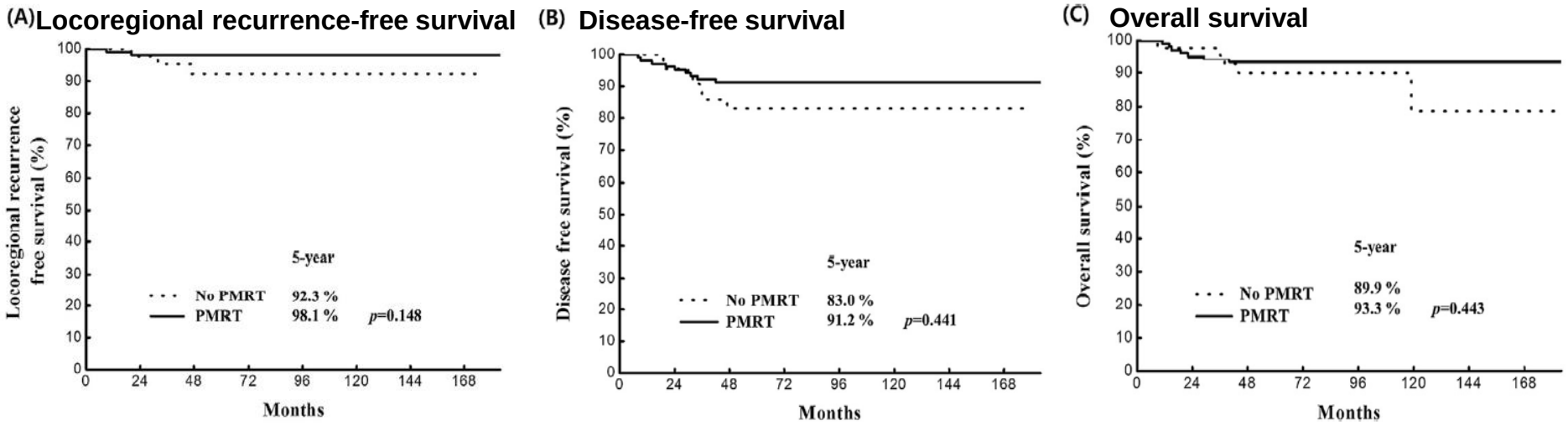
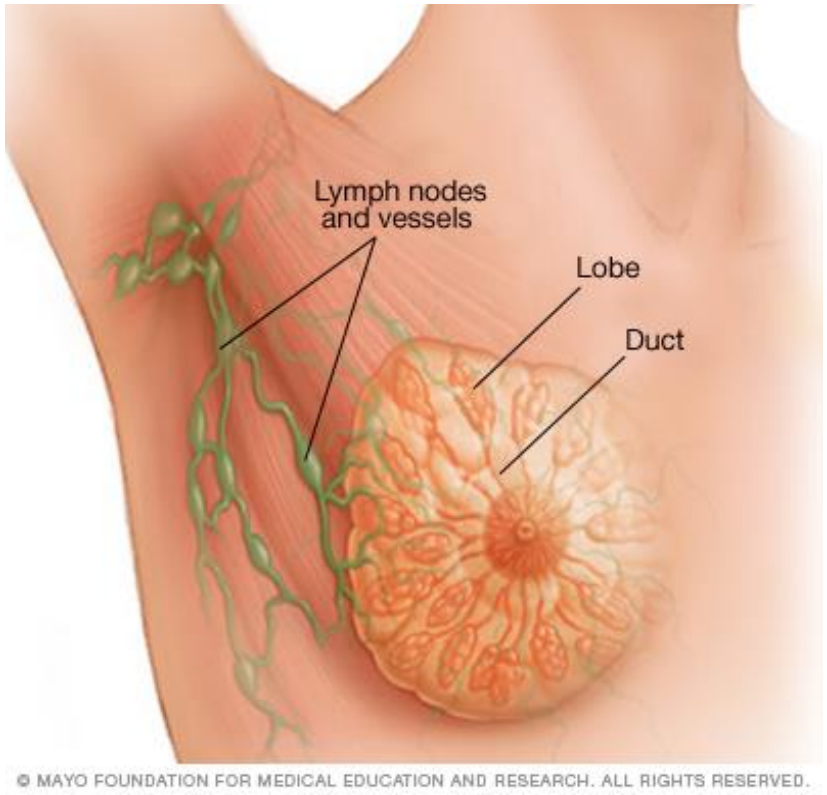


Fig.1. Kaplan-Meier survival curve according to receipt of postmastectomy radiation therapy (PMRT) 1998-2009: 105 pt. + PMRT, 46 pt. - PMRT

Shim et al. 2013

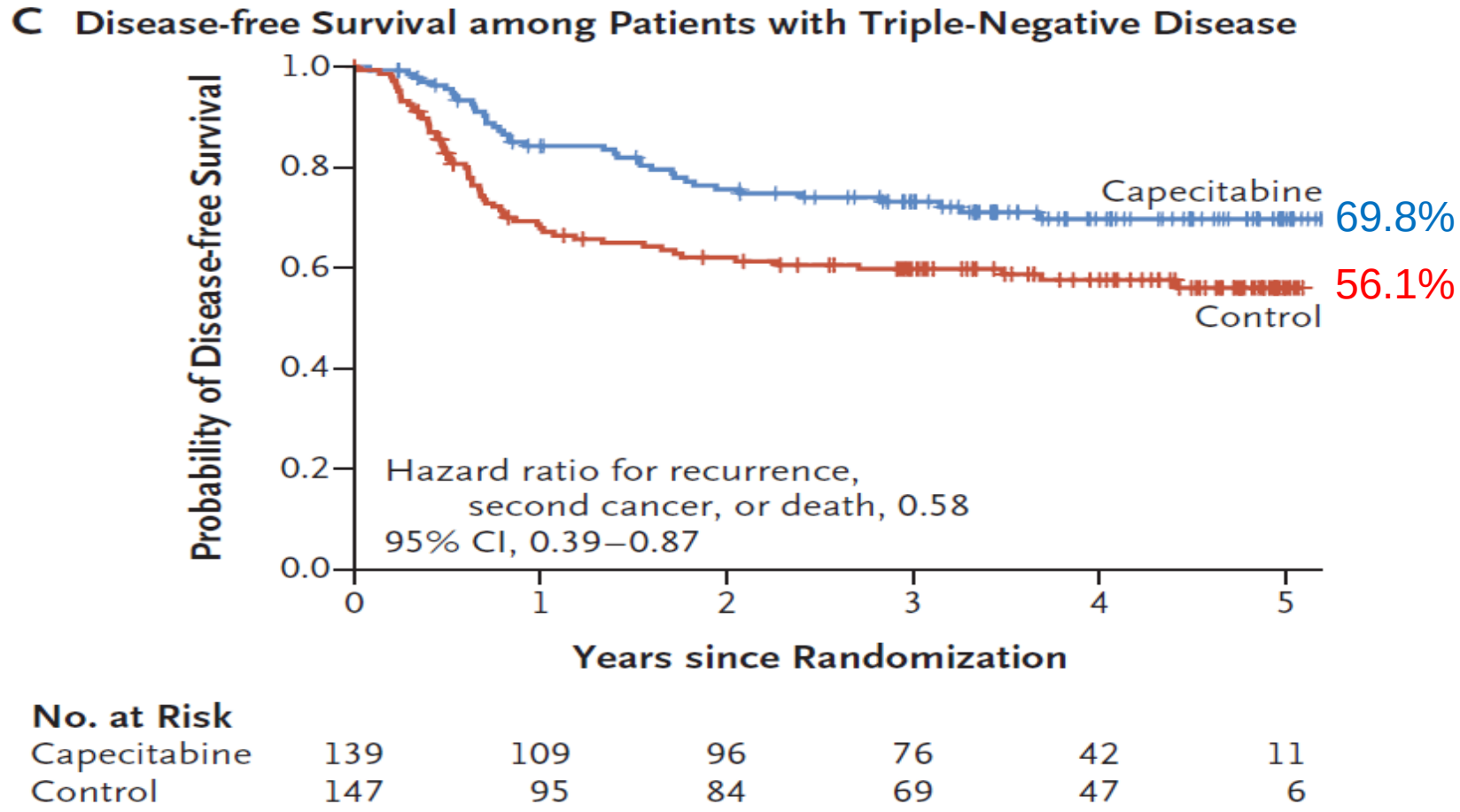
Stråleterapi efter NACT

- Udredning
- Teknik
- pCR
- **Non-pCR**
- Nye studier



Create X

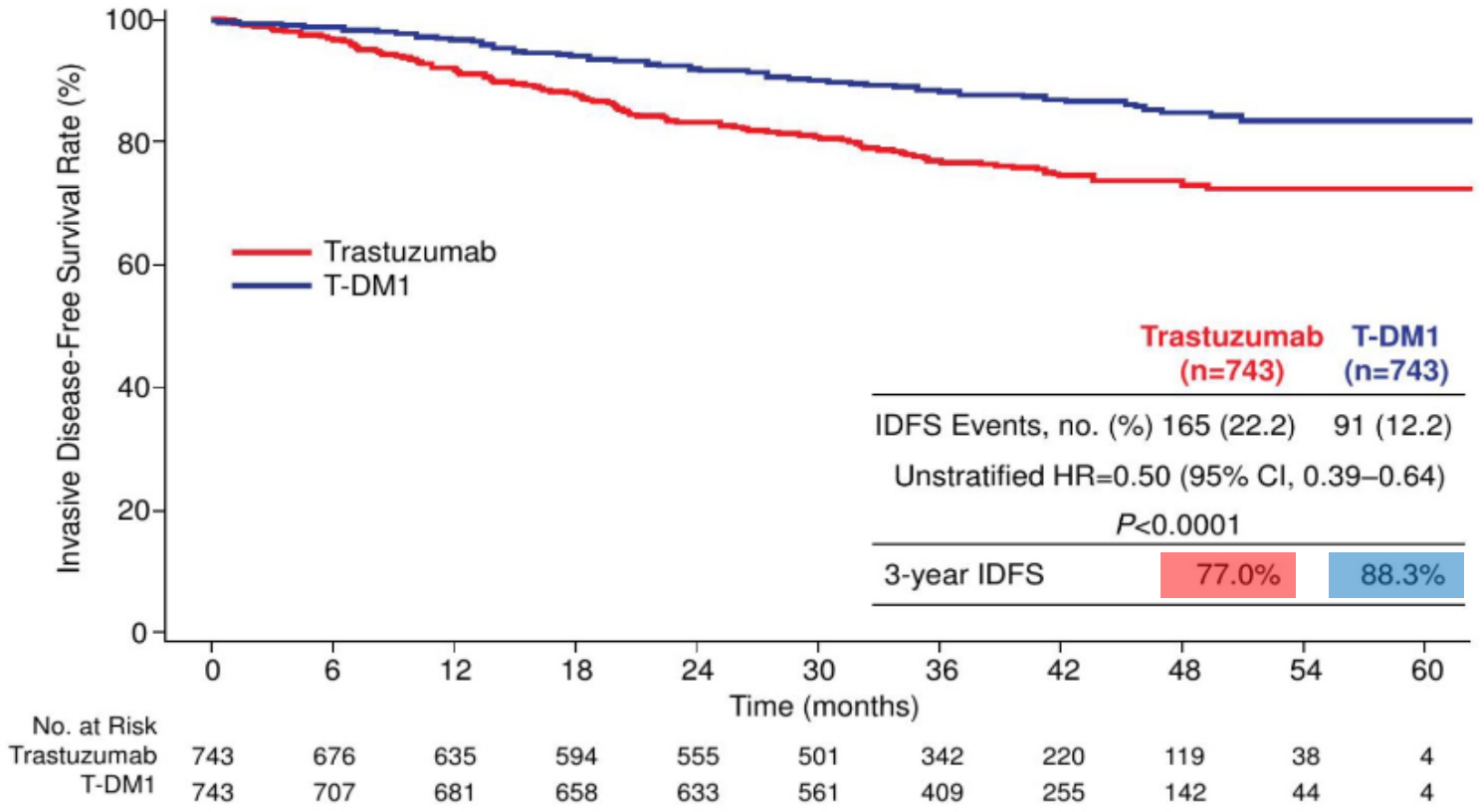
Adjuvant Capecitabine for Breast Cancer after Preoperative Chemotherapy



Masuda et al. NEJM 2017

KATHERINE Study

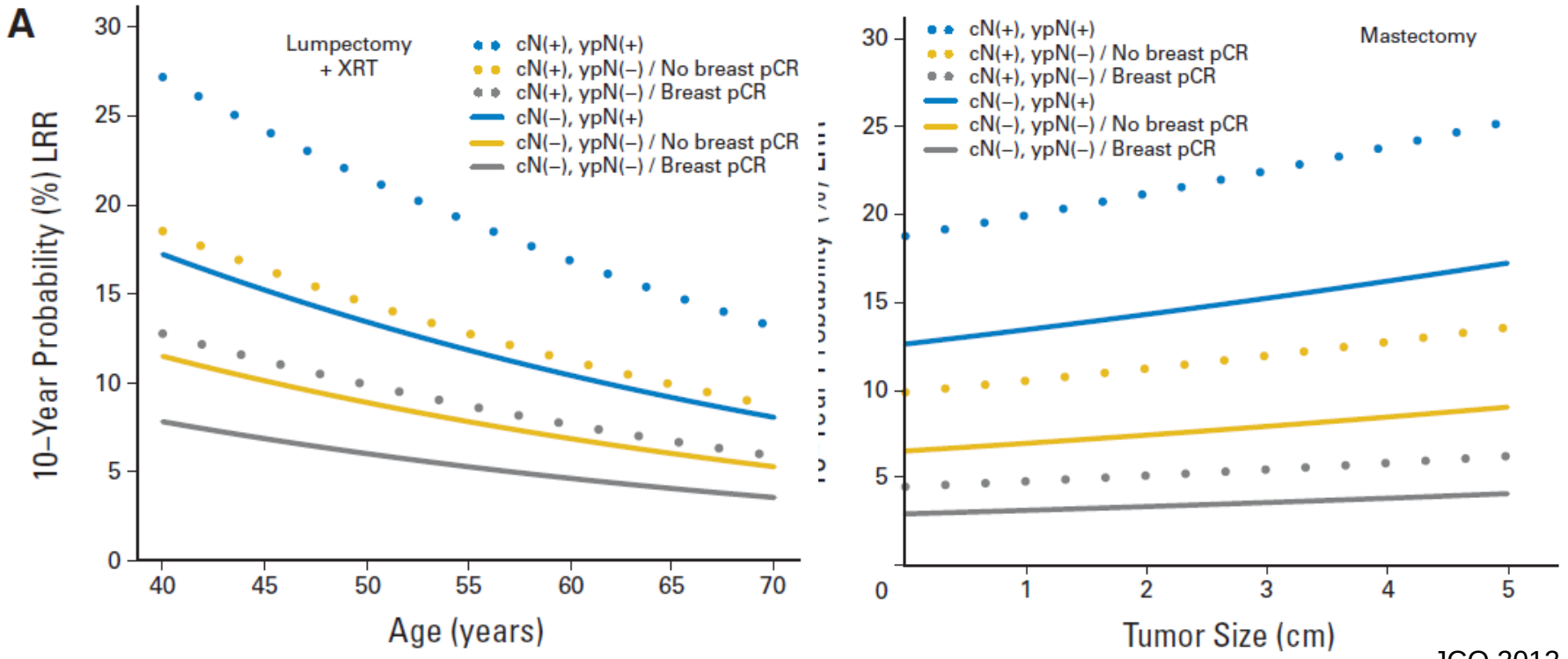
HER2-positive early breast cancer with residual invasive disease after completion of neoadjuvant therapy



von Minckwitz et al. NEJM 2019

Predictors of Locoregional Recurrence After Neoadjuvant Chemotherapy: Results From Combined Analysis of National Surgical Adjuvant Breast and Bowel Project B-18 and B-27

Eleftherios P. Mamounas, Stewart J. Anderson, James J. Dignam, Harry D. Bear, Thomas B. Julian, Charles E. Geyer Jr, Alphonse Taghian, D. Lawrence Wickerham, and Norman Wolmark

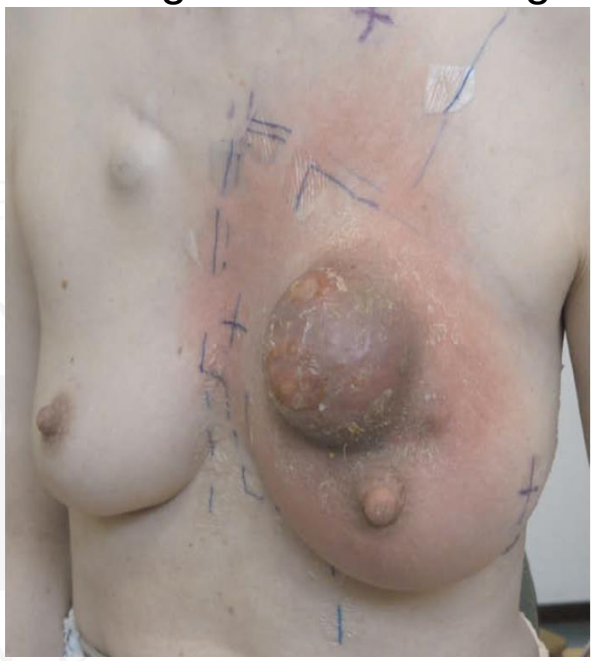


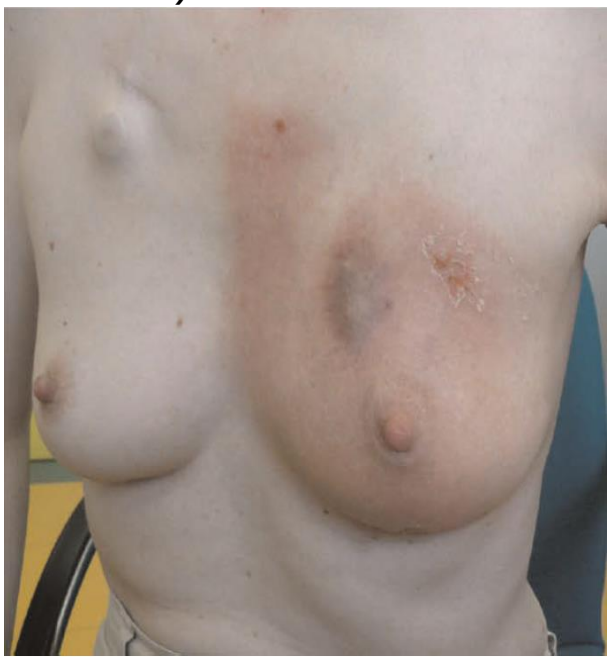
JCO 2012

Hvis patienten ikke er operabel efter neoadj. kemoterapi?
(inoperable og fortsat ingen tegn på systemisk disseminering)

DBCG strategi: 50 Gy / 25 fr. mod bryst og regionale lymfeknuder, sekventiel boost mod tumor samt boost mod patologiske lymfeknuder der ikke fjernes ved operationen (boost ofte 16 Gy / 8 fr.). +/- Bolus
Evt. konkommittant Cyclophosphamide 850 mg / m2 uge 0, 4 and 8

Timing af kirurgien efter RT: 6 uger (ingen evidens)





Chargari C et al, Radiother Oncol 2008

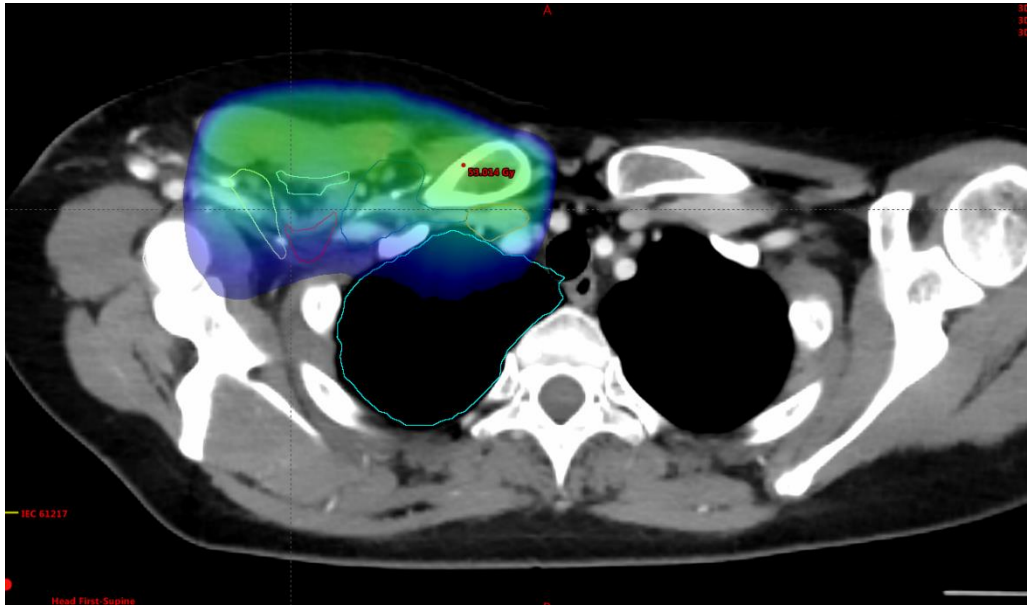
Hvis patienten ikke er operabel efter neoadj. kemoterapi?
(inoperable og fortsat ingen tegn på systemisk disseminering)

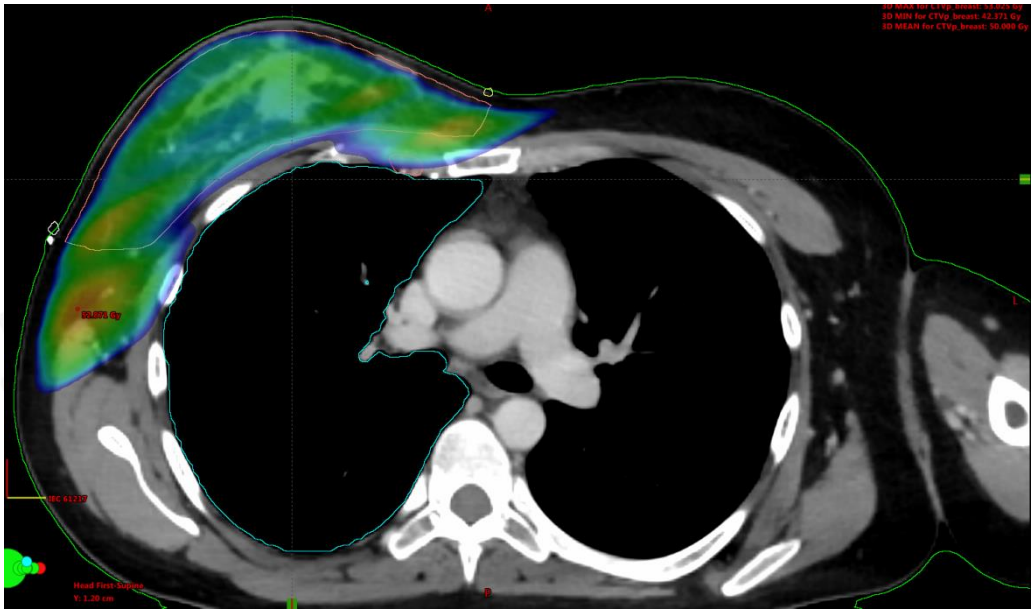
Initial MR mammo:
70 x 60 x 50 mm

MR NC i brystet
Let regres ln.

MR 64 x 54 x 43 mm,
Let regres ln.

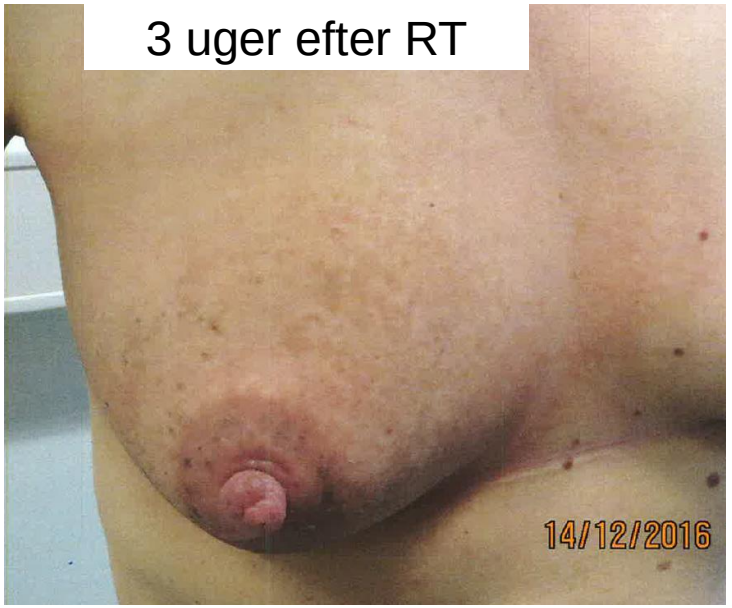
Case venligst udlånt af Birgitte Offersen





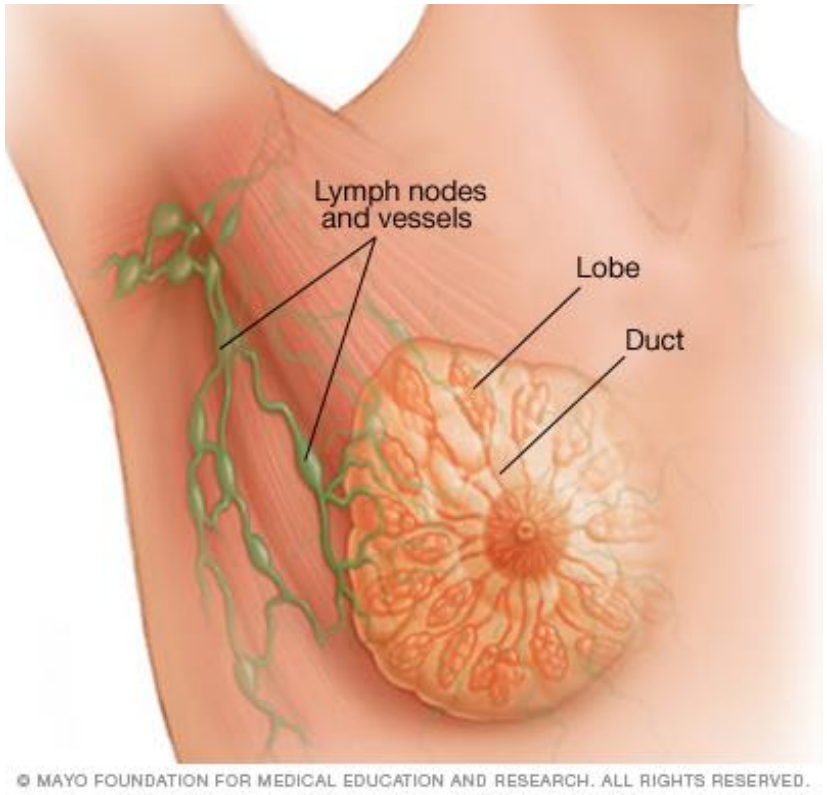
Efter 15 fraktioner

3 uger efter RT

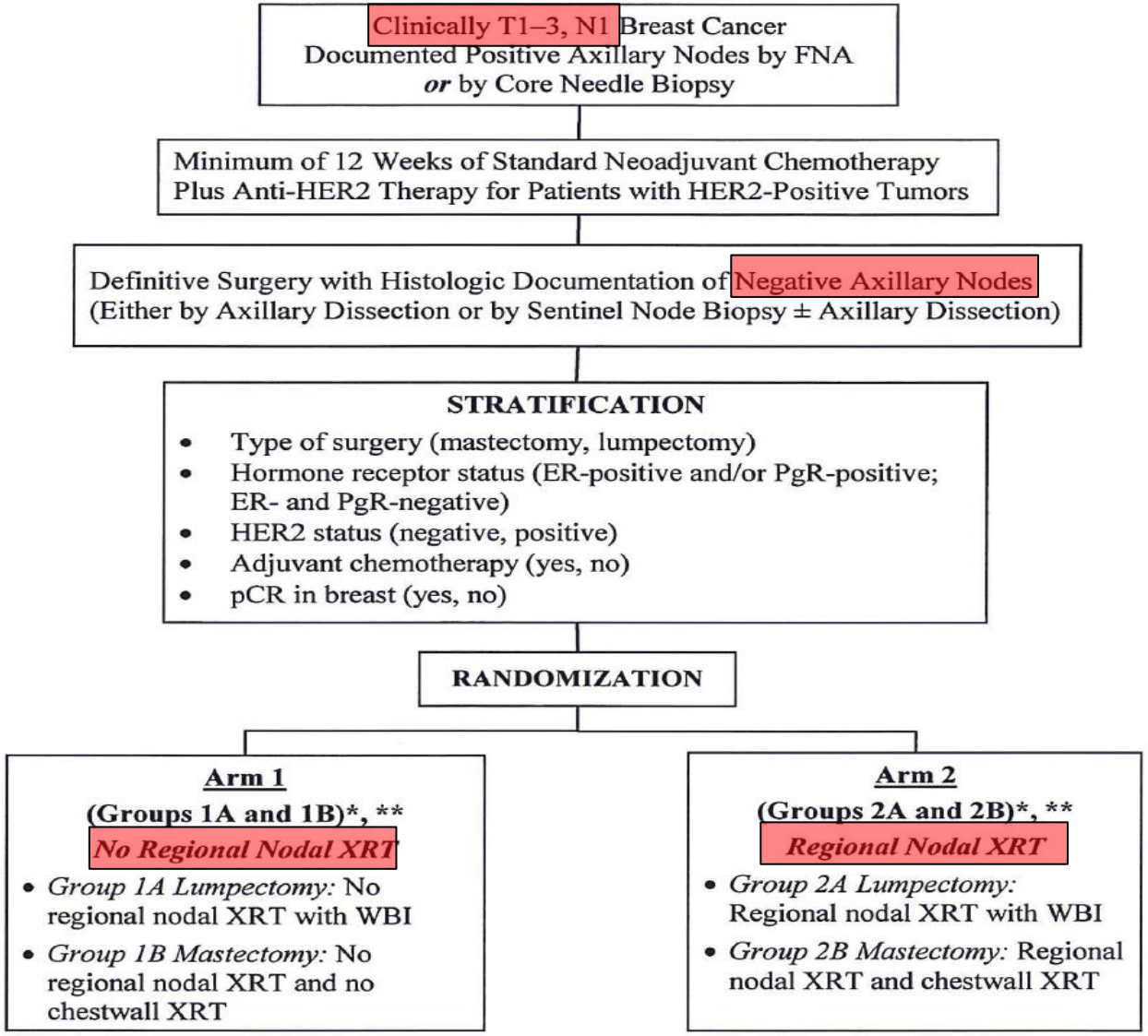


Stråleterapi efter NACT

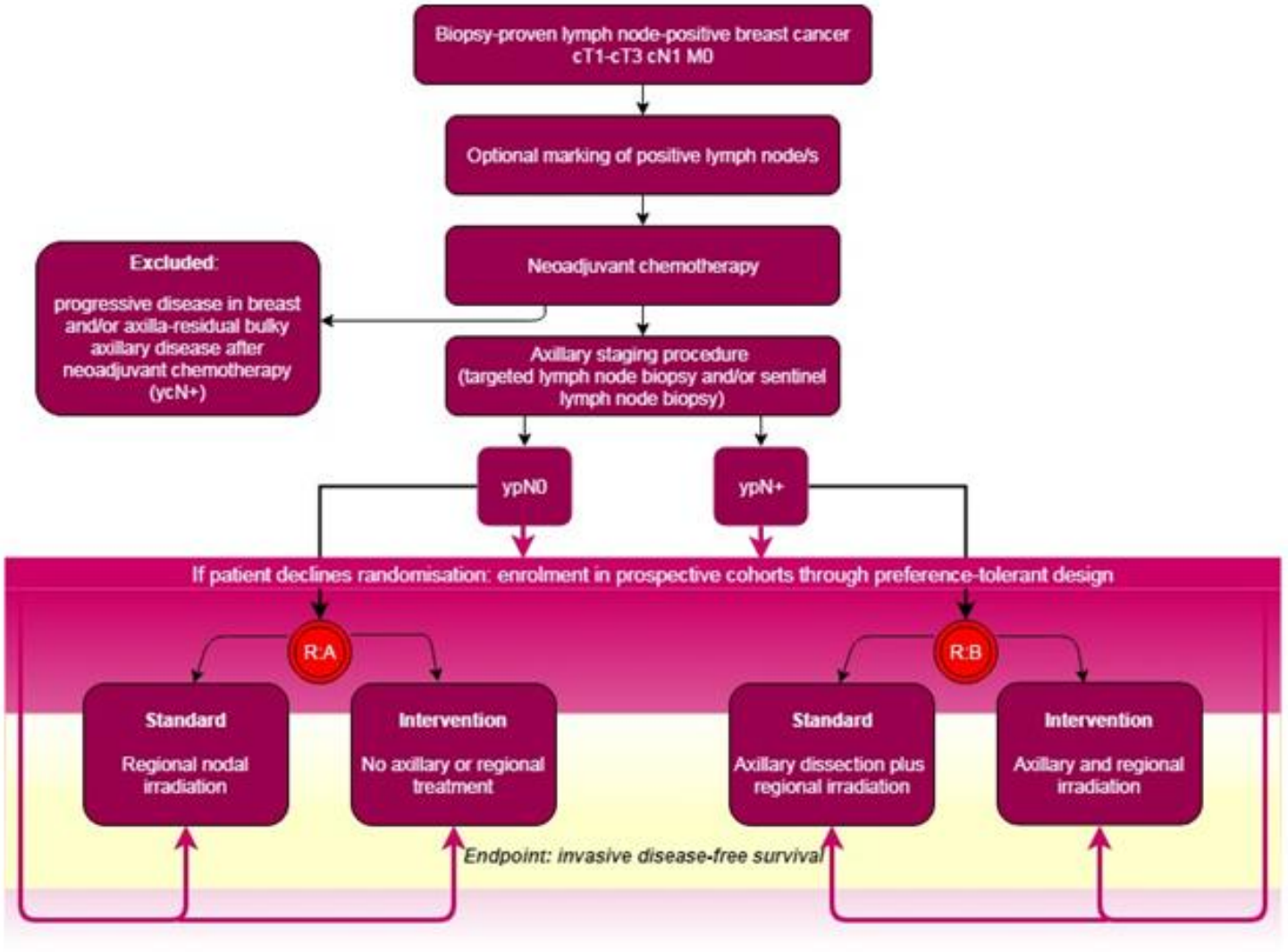
- Udredning
- Teknik
- pCR
- Non-pCR
- Nye studier



NSABP B-51/RTOG 1304 Schema



EUBREAST-2 INDAX TRIAL



Poleszczuk et al. Breast Cancer Research (2017) 19:75
DOI 10.1186/s13058-017-0870-1

Breast Cancer Research

RESEARCH ARTICLE Open Access

Neoadjuvant radiotherapy of early-stage breast cancer and long-term disease-free survival

Jan Poleszczuk[1,7*], Kimberly Luddy[2], Lu Chen[3], Jae K. Lee[3], Louis B. Harrison[4], Brian J. Czerniecki[5], Hatem Soliman[6] and Heiko Enderling[1,4*]

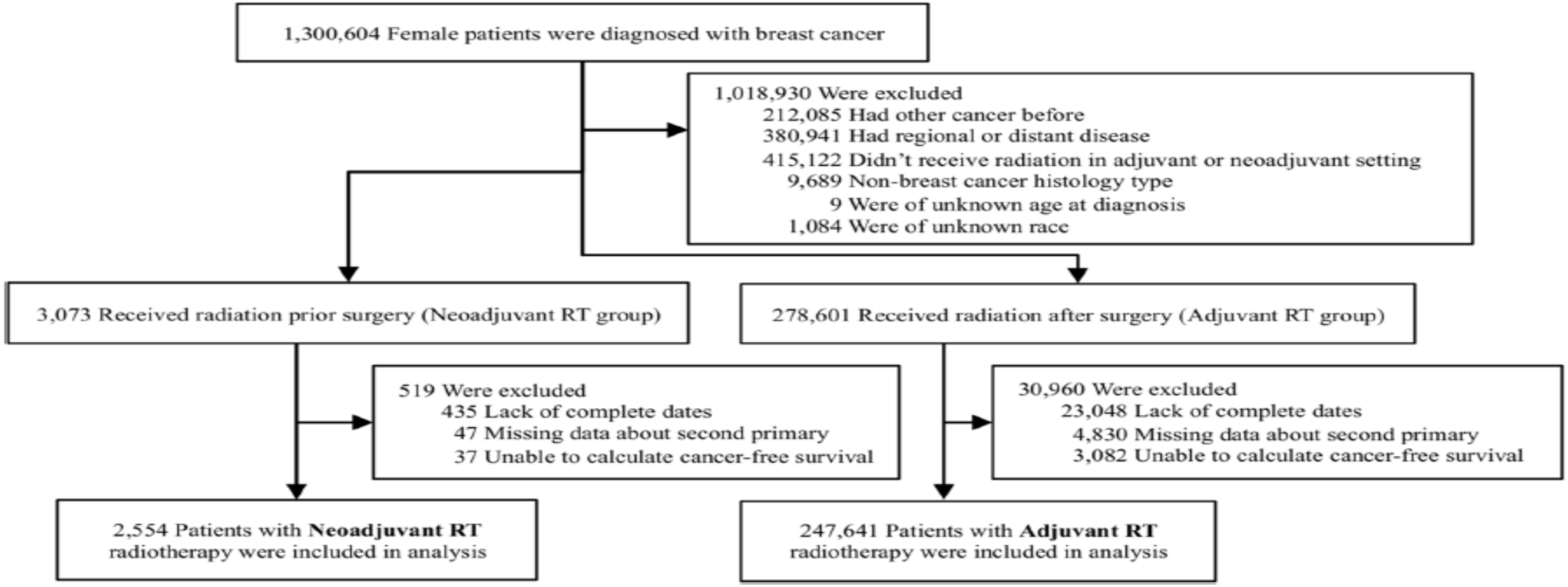
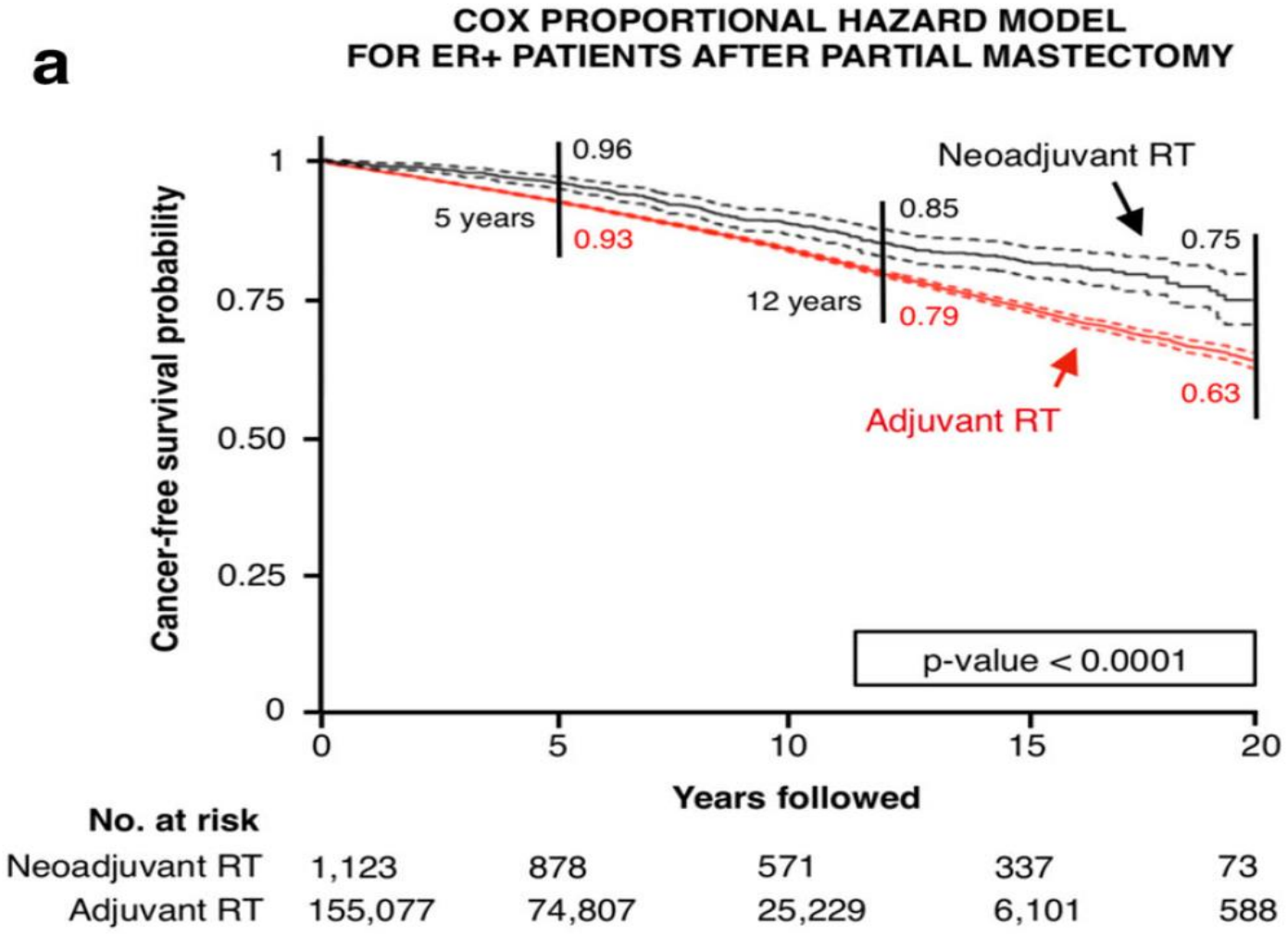


Fig. 1 Study enrollment. Of 1,300,604 female breast cancer records present in the Surveillance, Epidemiology, and End Results database, 2554 patients who had radiotherapy (RT) before surgery (neoadjuvant RT) and 247,641 patients who had RT after surgery (adjuvant RT) were included in the analysis

a


COX PROPORTIONAL HAZARD MODEL
FOR ER+ PATIENTS AFTER PARTIAL MASTECTOMY
Cancer-free survival probability
1
0.75
0.50
0.25
0
0.96
5 years
0.93
0.85
12 years
0.79
0.75
0.63
Neoadjuvant RT
Adjuvant RT
p-value < 0.0001
0
5
10
15
20
Years followed
No. at risk
Neoadjuvant RT 1,123 878 571 337 73
Adjuvant RT 155,077 74,807 25,229 6,101 588

International Journal of Radiation Oncology biology • physics
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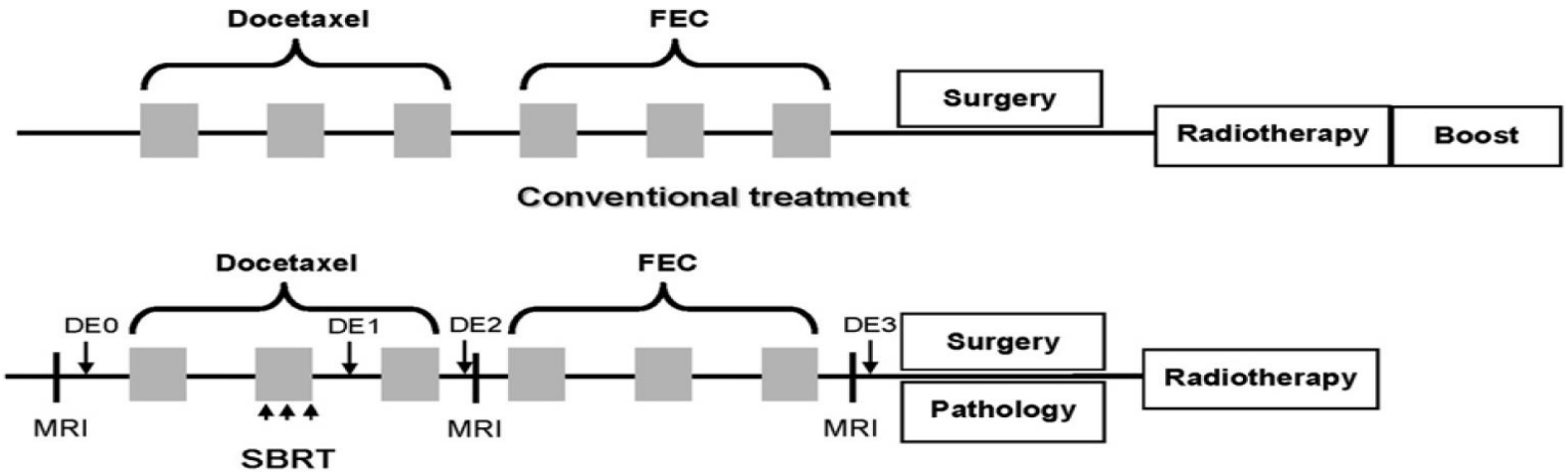
Clinical Investigation: Breast Cancer

Phase 1 Clinical Trial of Stereotactic Body Radiation Therapy Concomitant With Neoadjuvant Chemotherapy for Breast Cancer

Pierre-Yves Bondiau, MD, PhD,* Adel Courdi, MD,* Phillipe Bahadoran, MD, PhD,† Emmanuel Chamorey, PharmD, PhD,* Catherine Queille-Roussel, MD,‡ Michel Lallement, MD,* Isabelle Birtwisle-Peyrottes, MD,* Claire Chapellier, MD,* Sandrine Pacquelet-Cheli, PhD,* and Jean-Marc Ferrero, MD*

**Department of Radiotherapy, Centre Antoine Lacassagne, †Department of Dermatology, University Hospital of Nice, and ‡Centre de Pharmacologie Clinique Appliquée à la Dermatologie, Nice, France*



NACT + SBRT ?

Radiotherapy and Oncology 126 (2018) 177–180

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Phase II trial

Radical radiation therapy for oligometastatic breast cancer: Results of a prospective phase II trial

Marco Trovo [a,*], Carlo Furlan [a], Jerry Polesel [b], Francesco Fiorica [c], Stefano Arcangeli [d], Niccolò Giaj-Levra [e], Filippo Alongi [e], Alessandro Del Conte [f], Loredana Militello [f], Elena Muraro [g], Debora Martorelli [g], Simon Spazzapan [e,f], Massimiliano Berretta [f]

54 Patients with 92 metastatic lesions. Two-year LC and OS were 97% and 95%,

Tak for opmærksomheden!