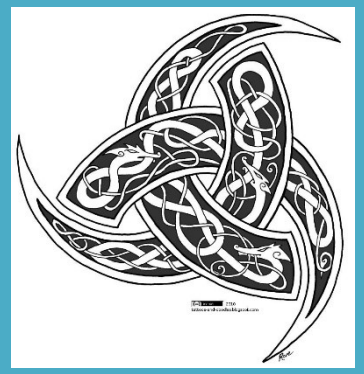
Status for nationale/nordiske forsøg

Medicinsk behandling Ann Knoop	Strålebehandling Birgitte Offersen	Kirurgi Tove Tvedskov
DBCG 07 READ	DBCG IMN2	Senomac
Nordic Trip Trial	DBCG 2009 Hypo	DBCG RT Recon
Master	DBCG 2009 PBI	Melody
CryoPac	DBCG 2015 Skagen	Targit
	DBCG 2018 Natural	
	DBCG 2020 Proton	

Flash talks

DBCG MU UDVALGET



Nordic Trip/NBG-19-01, a translational randomized phase III study exploring the effect of the addition of capecitabine to carboplatinum based chemotherapy in early "triple negative" breast cancer.

Basal-like/ER÷,HER2÷

”Lav”-risiko

T1, cN0

Mammografi +UL

Adjuvant

EC x 4, evt DD->Paclitaxel x 4

Præoperativ systemisk behandling bør altid anbefales til patienter med ER-negativ HER2-normal brystkræft med tumorer > 20 mm og/eller N1 da evt. residual sygdom vil have betydning for den forsatte behandling

T2, N0-1 (0-3 pos.)

T3-4 eller N2-3 (4+ pos.)

Mammografi + UL + MR

Mammografi+Ul+MR+PET-CT

Neoadjuvant

DDEC x 4 -> Paclitaxel + carboplatin x 4 + immunterapi (2023)

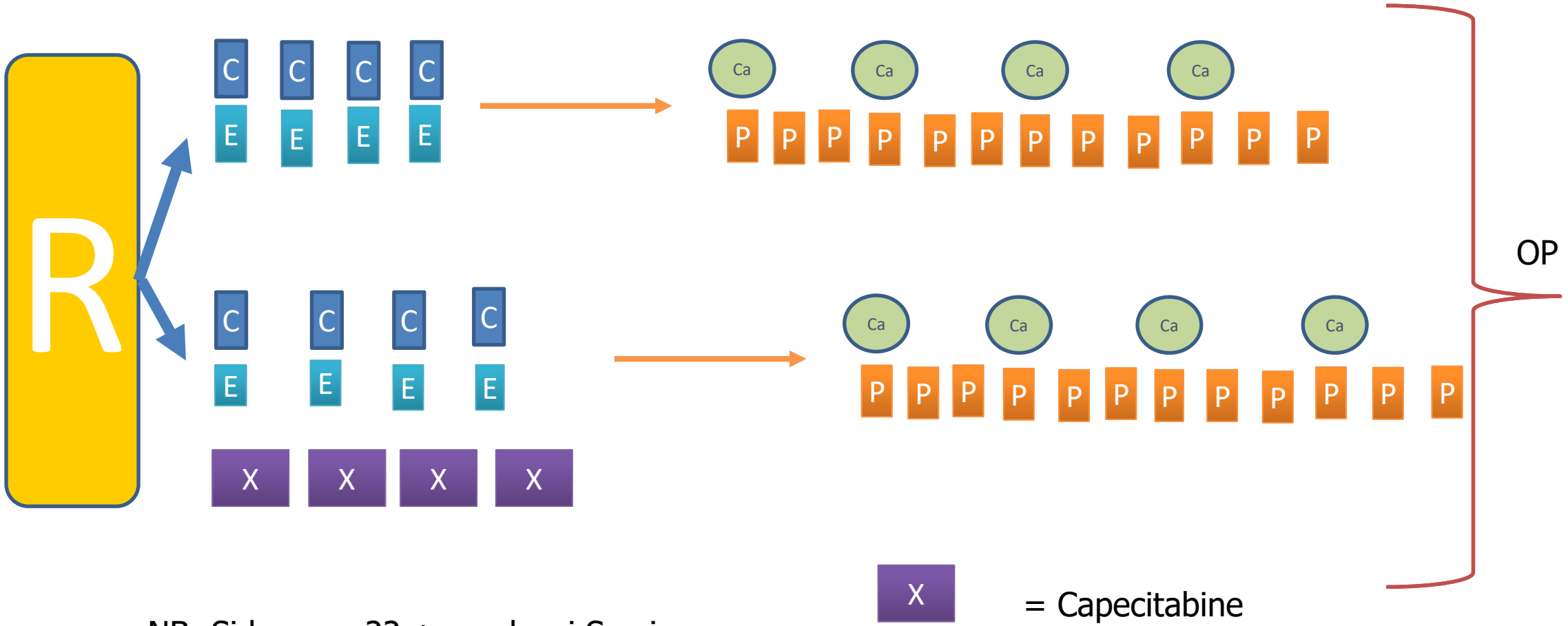
Residual tumor

Capecitabine ELLER immunterapi

pCR

opfølgning

Design



NB: Siden nov 22 + pembro i Sverige

Patientantal og studieforløb

Aim of the study: to evaluate the pCR rate in patients with TNBC receiving preoperative Platinum based Chemotherapy +/- Capecitabine.

- Første patient blev inkluderet januar 2020
- Sidste patient forventes opereret juni 2025
- **Behandlingsvarighed:** 20-23 uger
- **Follow-up:** 10 år
- **Sikkerhedsdata** efter 60 patienter – Q1 2025

- **pCR data** – Q4 2025

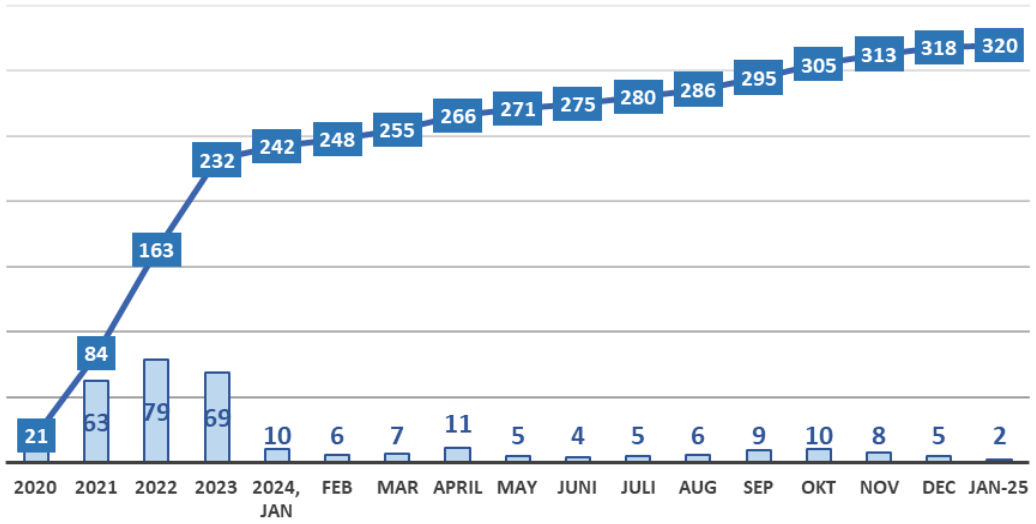
NordicTrip

NBG-19-01; SWEBCG 19-01
A Translational Randomized phase III study

Collaborators

Representatives from:
SABO/SweBCG Sweden, PI Niklas Loman
DBCG Denmark, PI Bent Ejlertsen

Totalt 320 av 325 patienter inkluderats. Vi mangler **6 patienter** då en patient som är felinkluderad kommer att exkluderas.



Study status – included patient per site in Denmark

Principal Investigator	Site	Subjects randomised Dec 2024	Subjects randomised Jan2025	Total subject randomised
Dr Brix Tange	Rigshospitalet København	1		35
Dr Peschardt	Hillerød	-		4
Dr Glavicic	Næstved	-	1	14
Dr Hugger Jacobsen	Sønderborg	1		7
Dr Lone Volmer	Vejle	-		2
Dr Lone Volmer	Esbjerg	-		0
Dr Sopie Yammeni	Aalborg	-		2
Total		**2**	**1**	**64**

Study status – included patient per site in Sweden

Principal Investigator	Site	Subjects randomised Dec 2024	Subjects randomised Jan2025	Total subject randomised
Dr Loman	Malmö	2	-	64
Dr Linderholm	Göteborg	-	-	29
Dr Lindman	Uppsala	-	-	31
Dr Valachis	Örebro	-	-	9
Dr Kraska	Växjö	-	-	13
Dr Wennstig	Sundsvall	-	-	14
Dr Andersson	Umeå	-	-	7
Dr Spång Rosén	Jönköping	-	-	14
Dr Einbeigi	Borås	-	-	11
Dr Wendt	Södersjukhuset i Stockholm	1	1	25
Dr Bachmeier	Karlstad	-	-	5
Dr Bergqvist	St Göran Capio i Stockholm	-	-	8
Dr Nilsson	Västerås	-	-	12
Dr Ilke Cikman	Gävle	-	-	0
Dr Norberg	Kristianstad	-	-	14
Total		**3**	**1**	**256**

The trip team

Bidrag fra DBCG

Randomisering & database
- Maj-Britt Jensen og Michael Jespersen
- DBCG er vært for databasen
- Kirurgi-, patologi-, og onkologidata overføres

Monitoring
- Ann Raaberg, DBCG

Vævsbiobank
- Anne-Vibeke Lænkholm
- Roskilde er forsøgets centrale patologiafd.

Genomisk Medicin på RH varetager forsøgsblodprøver på danske patienter

Study team i Lund
- Niklas Loman, PI og sponsor
- Åke Borg, genomisk lab., Lund
- Heidi Grill Magnusson
- Lina Zander

Laboratoriet I Göteborg
- Barbro Linderholm
- ctDNA lab. i Göteborg

DANISH BREAST CANCER GROUP

MASTER
D B C G

Early breast cancer statin trial
the master trial

A randomized, multicenter, double-blind, placebo-controlled comparison of standard (neo)adjuvant therapy plus placebo versus standard (neo)adjuvant therapy plus atorvastatin in patients with early breast cancer

MAmmary cancer **ST**atin **ER** positive trial

Novo Nordisk Foundation

DANISH BREAST CANCER GROUP

STATINS and BC-progn

BIG 1-98 Study – Pt. der blev behandlet med kolesterol-sænkende medicin, havde en lavere risiko for recidiv

Cholesterol, Cholesterol-Lowering Medication Use, and Breast Cancer Outcome in the BIG 1-98 Study
S Borgquist et al. J Clin Oncol . 2017 Apr 10;35(11):1179-1188.

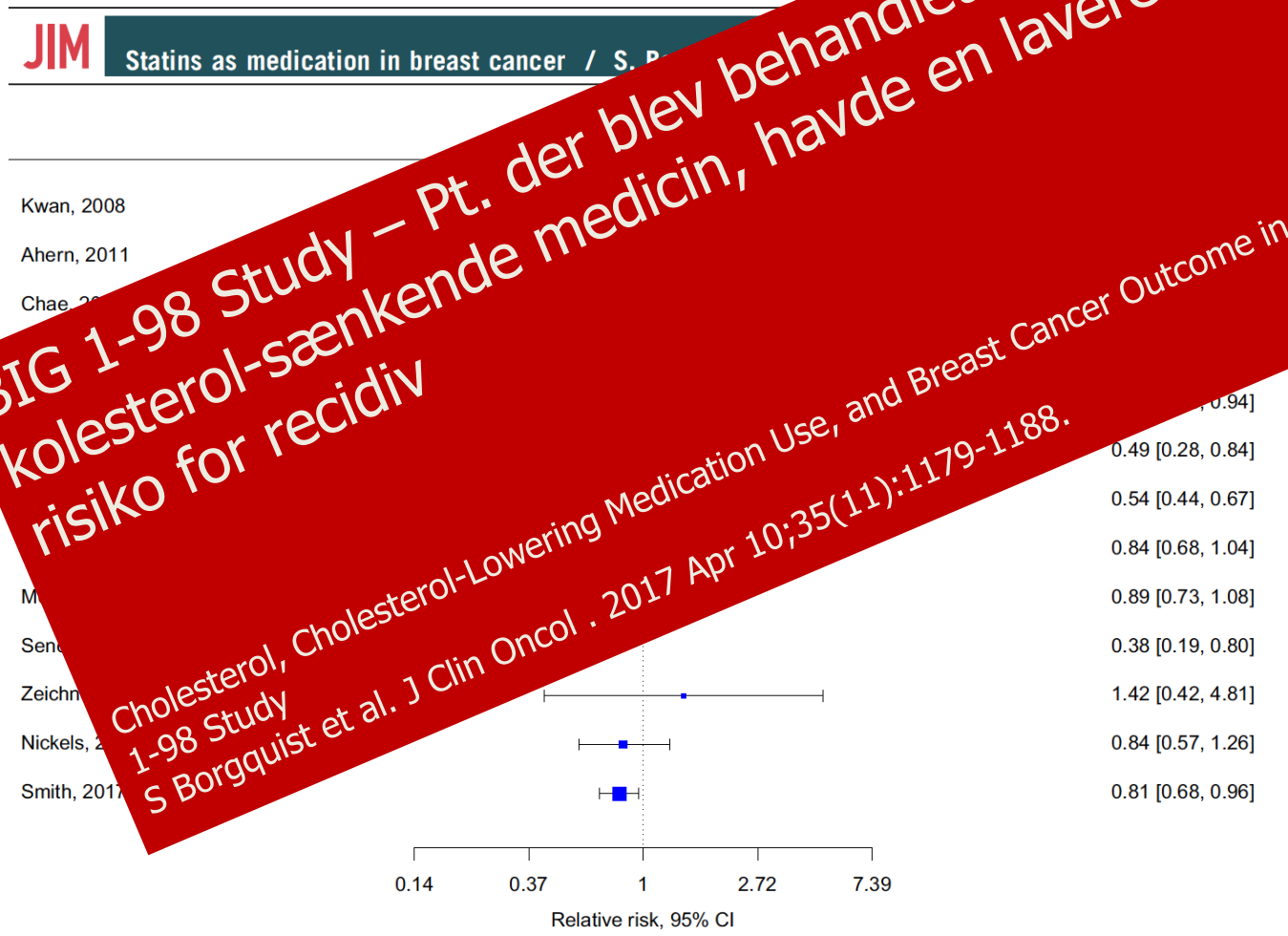


Fig. 2 *The prognostic value of statin treatment in the adjuvant breast cancer setting illustrated by a forest plot of the currently reported studies.*

MASTER trial

- **PRIMARY OBJECTIVE:**
- To compare invasive disease-free survival (IDFS) in patients randomized to standard (neo)adjuvant therapy plus placebo or standard (neo)adjuvant therapy plus atorvastatin

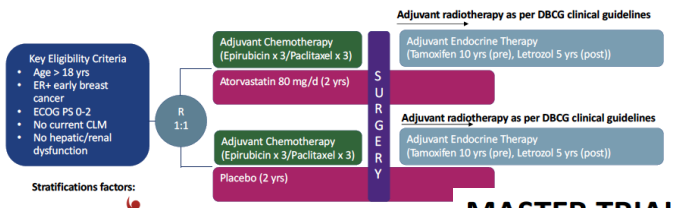
- **SECONDARY OBJECTIVES:**
- - To compare overall survival (OS), recurrence-free interval (RFI), distant recurrence-free interval (DRFI) including associations with first site of recurrence, cardiac death-free interval, and overall safety in the two treatment arms.
- - To investigate morbidity endpoints
- - To address translational endpoints

MASTER trial design

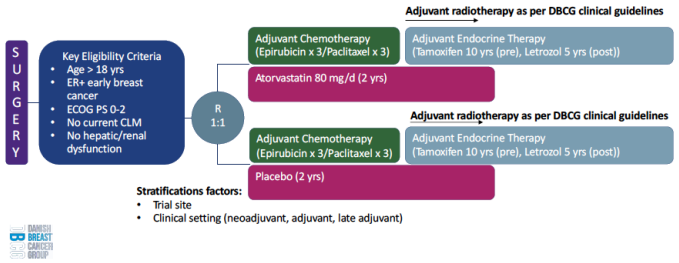
Patients eligible for MASTER –
any clinical setting:

Participation in observational cohort:
1. **CRF**
2. **PRO**
3. **Blood samples**

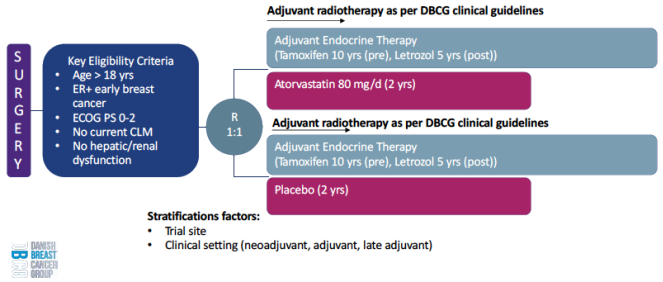
MASTER TRIAL DESIGN, NEOADJUVANT



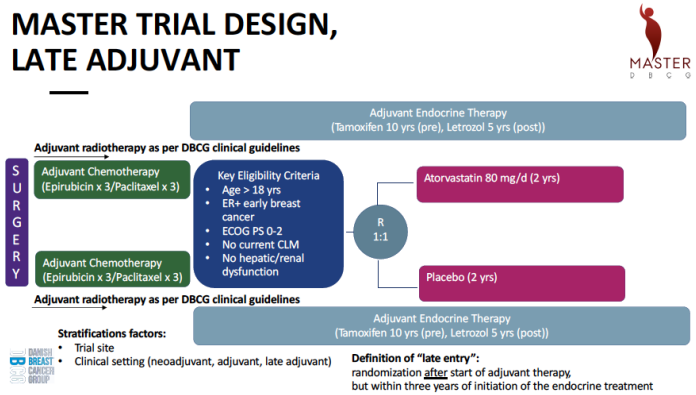
MASTER TRIAL DESIGN, EARLY ADJUVANT



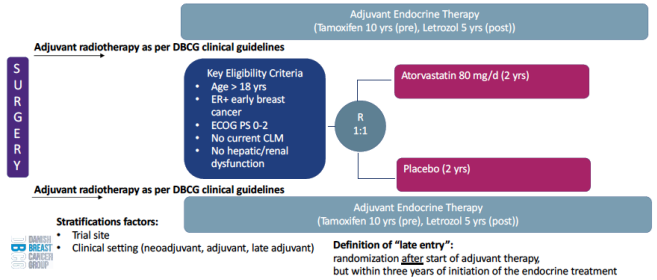
MASTER TRIAL DESIGN, EARLY ADJUVANT, ET ONLY



MASTER TRIAL DESIGN, LATE ADJUVANT



MASTER TRIAL DESIGN, LATE ADJUVANT, ET ONLY



Status

- Der er pr. 1. november 2024 randomiseret 999 patienter i studiet.
- Da vi inkluderede den første patient 14. januar 2021, var det med en formodning om, at vi efter 4 år ville være nået i mål med 3360 patienter – men…
- Inklusionen stopper d. 14. januar 2025.
- Pt der er i forsøg foresætter behandling – og der er en forventning om, at data kan bruges – ex. i en kommende metaanalyse

CryoPac

Effects of Cryotherapy on Objective and Subjective Symptoms of Taxane-Induced Neuropathy in Patients with Early Breast Cancer.

A Randomized Prospective Controlled Trial.

The incidence of CIPN with paclitaxel and docetaxel is dose dependent and occurs with higher cumulative dose and higher dose per cycle.

The incidence of taxane-associated chemotherapy-induced peripheral neuropathy ranges from **11% to 64% for docetaxel** and **57% to 83% for paclitaxel**, which in 2–33% is severe.

A patient-reported outcome study found that **CIPN numbness persisted in 67%–80%** of patients for one year following the completion of paclitaxel therapy .

CryoPac

Effects of Cryotherapy on Objective and Subjective Symptoms of Taxane-Induced Neuropathy in Patients with Early Breast Cancer.

A Randomized Prospective Controlled Trial

Methods

- Patients with early-stage breast cancer scheduled for docetaxel or paclitaxel were recruited between January 2021 and July 2023 at four oncology departments in Denmark (RH, NOH, AUH & Sønderborg).
- Primary endpoint: incidence of CIPN at End of Treatment; CIPN was assessed using the Total Neuropathy Score (TNS). A TNS score ≥ 2 was considered an event.
- Secondary end points: level of experienced peripheral neuropathy, patient-reported outcomes, and Quantitative sensory testing.

Results from EoT evaluation

- 268 patients were randomized, of which 51 dropped out, leaving 217 participants for the EoT analysis.
  - 123 receiving cryotherapy and 94 in the usual care group.
  - NOH: N=50, RH: N=79, AUH: N=78, Sønderborg: N=10.

CryoPac

Results from EoT evaluation, continued…

- Primary end-point: There was no significant difference in CIPN assessed with TNS between the cryotherapy and usual care group at EOT (p = 1.0).
- QST revealed reduced tactile disturbance development by monofilament test (p=0.006) in the cryotherapy arm.
- The analyses of PRO-data showed that
  - Patients in the cryotherapy group experienced reduced tingling in hands, reduced numbness in hand and feet and less trouble manipulating small objects compared with the usual care group.
  - QoL did not differ between the study arms.

Conclusions and Future perspectives

- Cryotherapy did not reduce the incidence of CIPN with taxane treatment at end of treatment.
- Cryotherapy led to patients reporting significantly fewer sensory symptoms.
- Cryotherapy reduced the negative impact on the tactile sensitivity.
- The benefits of cryotherapy regarding sensory symptoms will be further investigated as long-term follow-up are planned - Results from 1 year follow-up are expected in the spring of 2025.

Flash talks

DBCG RT Udvalget

Birgitte V. Offersen
Dept. of Experimental Clinical Oncology,
Aarhus University Hospital,
Denmark

N=1880 ptt
Inklusion 2009-2014
Data klar til 10 års analyse nu

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

Journal of Clinical Oncology 2020

CIRRO **DBCG** Danish Breast Cancer Group

N=880 ptt
Inklusion 2009-2016
Data klar til 10 års analyse nu

Partial Breast Irradiation Versus Whole Breast Irradiation for Early Breast Cancer Patients in a Randomized Phase III Trial: The Danish Breast Cancer Group Partial Breast Irradiation Trial

Birgitte V. Offersen, MD, PhD[1,2]; Jan Alsner, MSc, PhD[1]; Hanne M. Nielsen, MD, PhD[2]; Erik H. Jakobsen, MD[3]; Mette H. Nielsen, MD, PhD[4]; Lars Stenbygaard, MD[5]; Anders N. Pedersen, MD, PhD[6]; Mette S. Thomsen, MSc, PhD[7]; Esben Yates, MSc[7]; Martin Berg, MSc[8]; Ebbe L. Lorenzen, MSc, PhD[4]; Ingelise Jensen, MSc[9]; Mirjana Josipovic, MSc, PhD[6]; Maj-Britt Jensen, MSc[10]; and Jens Overgaard, MD, DMSc[1]; on behalf of the Danish Breast Cancer Group Radiotherapy Committee

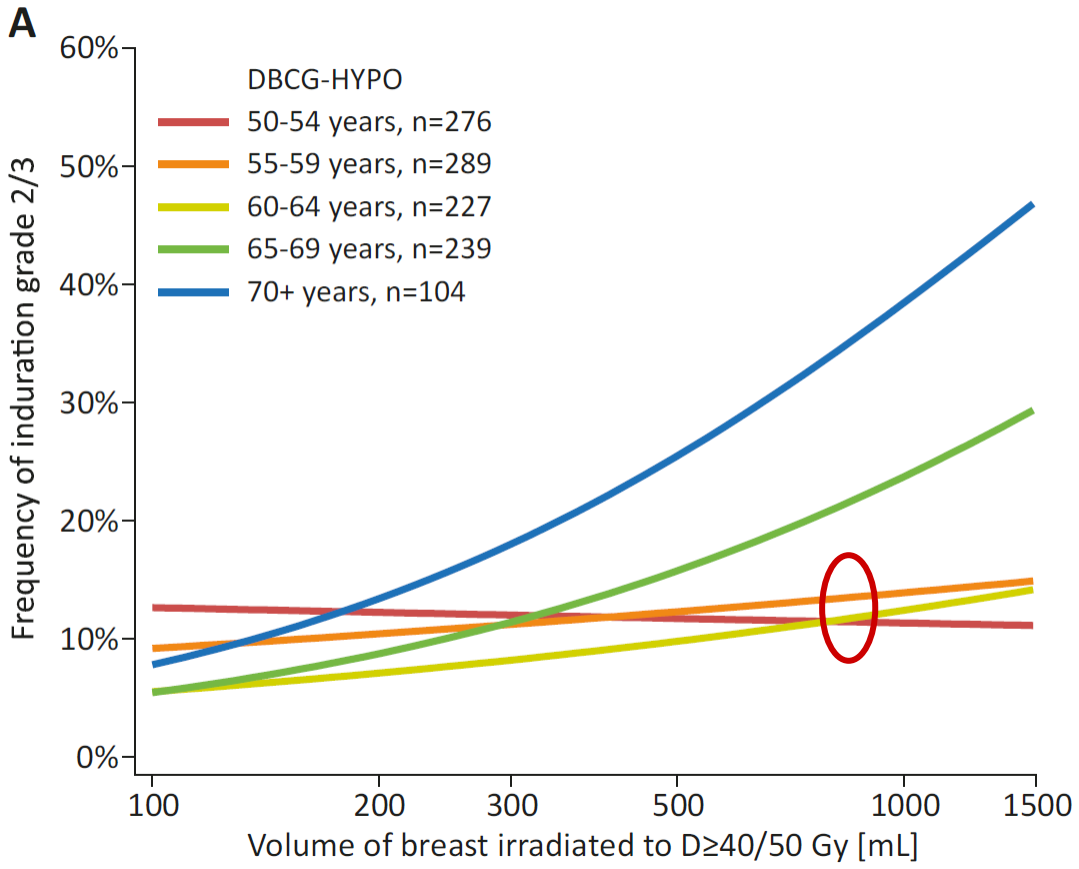
Journal of Clinical Oncology 2022

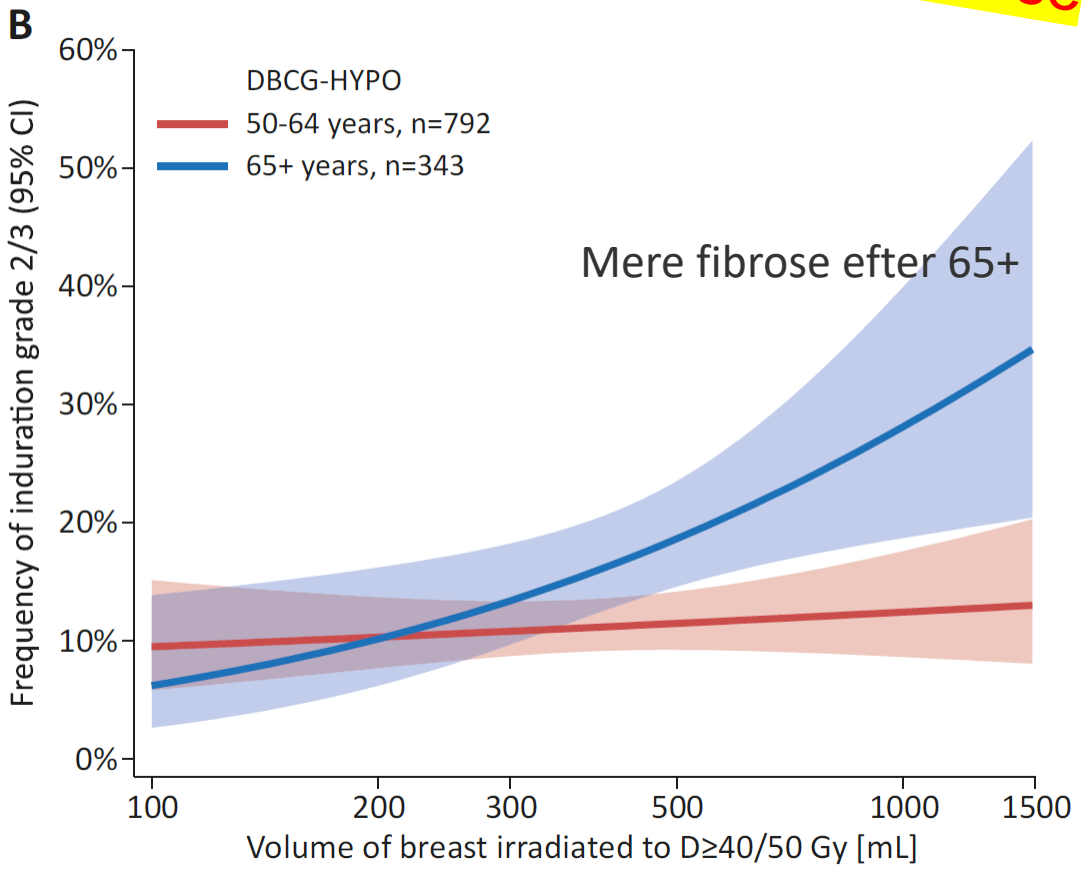
CIRRO DBCG Danish Breast Cancer Group

Breast induration and irradiated volume in the DBCG HYPO trial: The impact of age, smoking, and boost

Mette S. Thomsen[1*], Jan Alsner[2], Christina M. Lutz[1], Martin Berg[3], Ingelise Jensen[4], Ebbe L. Lorenzen[5,6], Hanne M. Nielsen[7], Erik H. Jakobsen[8], Lars Stenbygaard[9], Mette H. Nielsen[10], Maj-Britt Jensen[11], Jens Overgaard[2], Birgitte V. Offersen[2,7] on behalf of the DBCG RT Committee

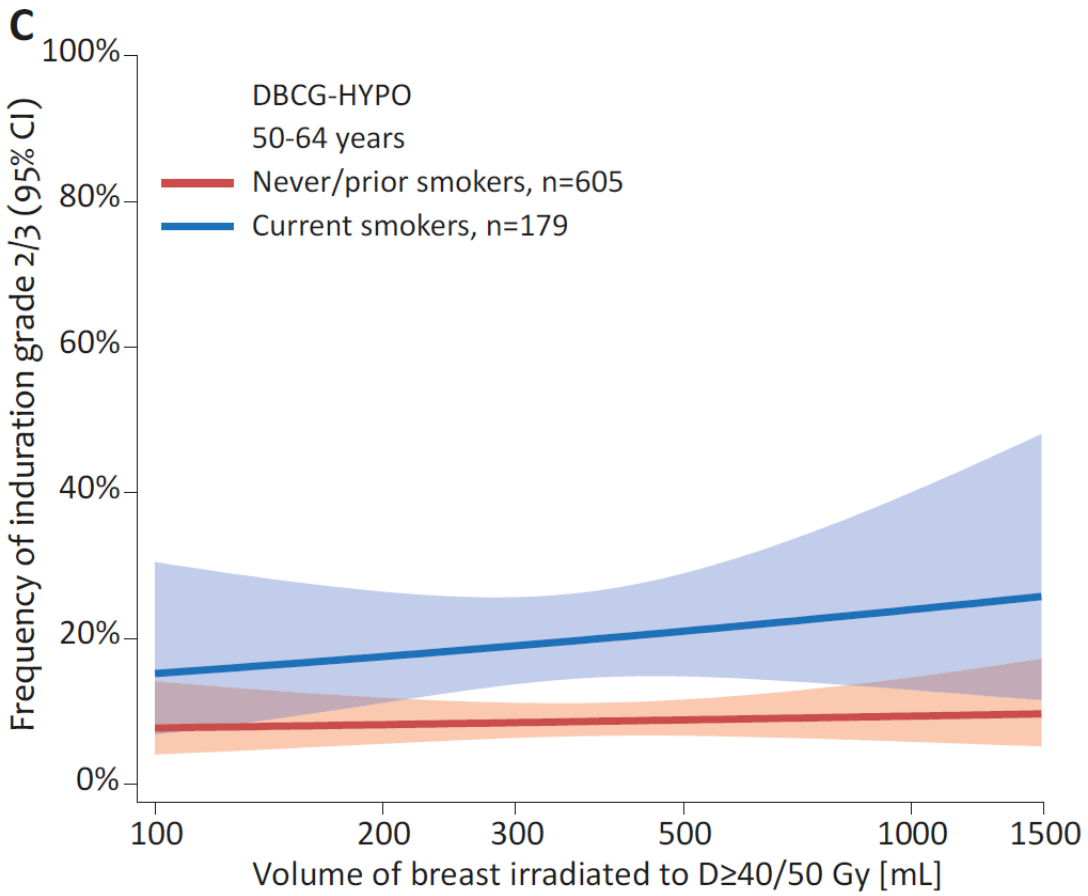
Hypotese udviklet i DBCG PBI
Valideret i DBCG HYPO →
Vil blive lærebogsmateriale
alder, volumen, tobak og fibrose

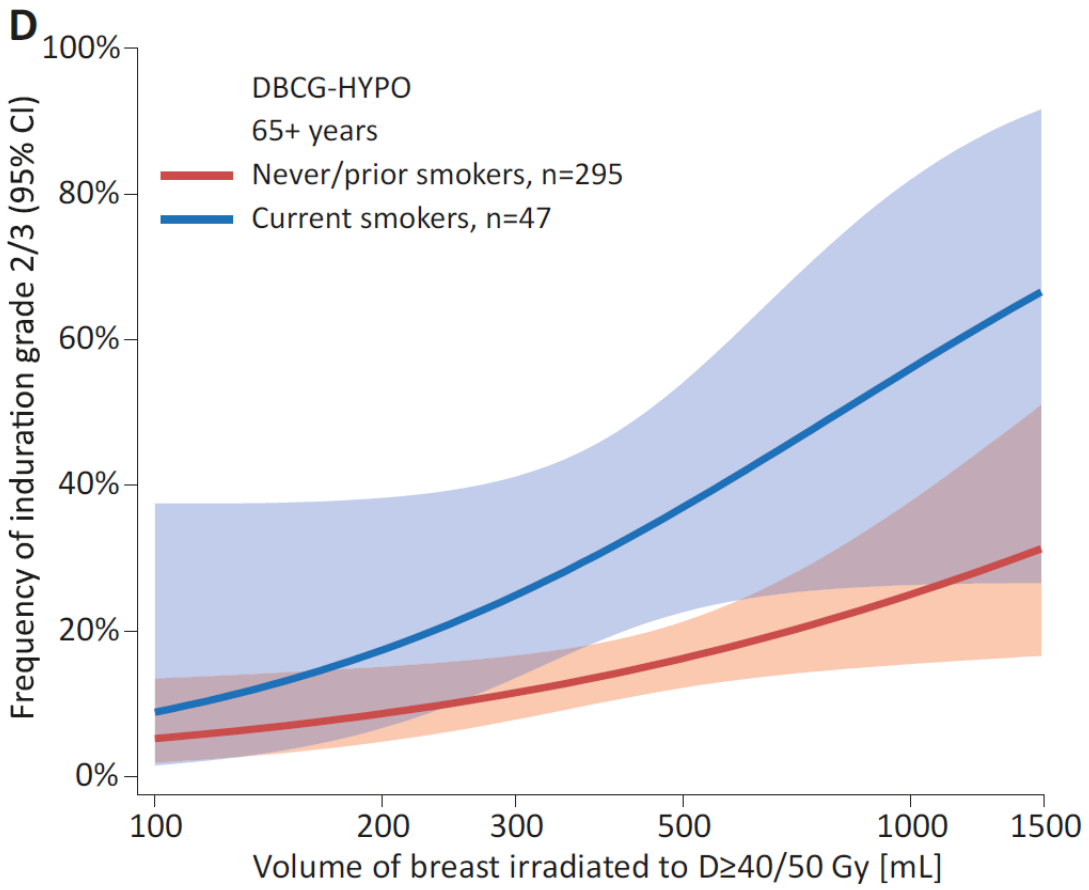




Radiother & Oncol, 2024

Dose-response relation to fibrosis for smokers





TOBAK FORDOBLER FIBROSERISIKO

Projekter på disse trials

10-års opgørelser
Blodprøver taget årligt på knap 1000 ptt → de vil blive brugt nu
DCCL-PRO spørgerammen sendt ud til 10 års overlevere i DBCG HYPO og PBI trials

ESTRO 2022

The DBCG Skagen trial 1: A phase III randomised trial of hypo- vs standard fractionated RT in 2946 node-positive breast cancer patients

Birgitte V Offersen, Jan Alsner, Hanne M Nielsen, Troels Bechmann, Mette H Nielsen, Ingvil Mjaaland, Claus Kamby, Carine Kirkove, Tamaz Lörincz, Sami Al-Rawi, Egil B Støre, Andreas Schreiber, Mechthild Krause, Unn-Miriam Kasti, Louise W Matthiessen, Piotr Kedzierawski, Tanja Marinko, Marjaana Luukkaa, Tanja Skyttä, Maj-Britt Jensen, Jens Overgaard *on behalf of the DBCG RT Committee*

Analyse af kliniske data og RT QA submittes snart

Tæt samarbejde med HYPO G01 trial gruppen

CIRRO *DBCG Danish Breast Cancer Group*

DBCG RT Natural trial

DBCG RT NATURAL
≥60 years
pT1N0
Luminal A (IHC) Grade 1-2 Non-lobular
ER≥10% HER2 neg
≥2mm
(ET) + PBI vs (ET)
5-yr LRR 1% expected 4% accepted
926
Denmark Offersen
Accrual open

R → PBI 40 Gy/15 fr

R → No PBI

Primary endpoint: 5 yr local recurrence

N=820 ptt

Inklusion sat på pause 17. nov 2023

Skal diskuteres i dag

CIRRO *DBCG Danish Breast Cancer Group*

The DBCG Proton Trial

Studiet inkluderer ptt nu

Patients with early high-risk breast cancer with indication for loco-regional RT

Patients with early breast cancer with indication for RT

Photon treatment plan for loco-regional RT shows ≥ 4 Gy MHD and/ or V17/20lung≥ 37%

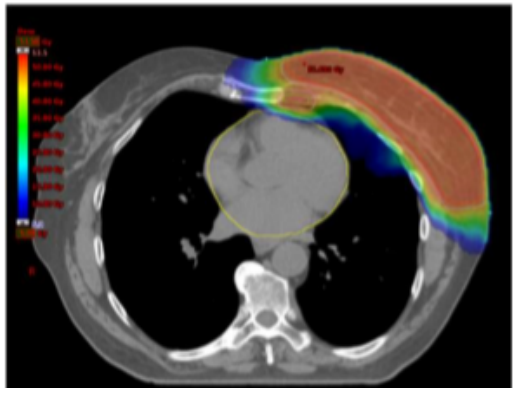
If bilateral, the sum of dose from both sides is calculated

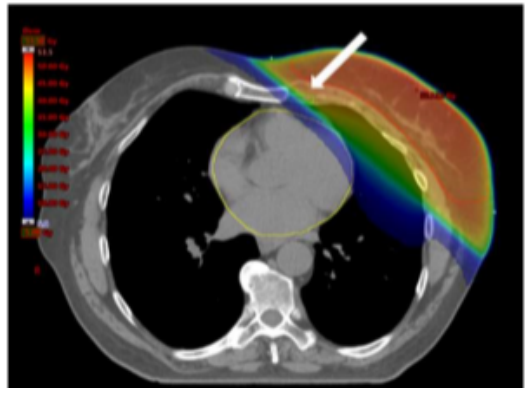
Patient is informed about high heart/lung dose and offered participation in randomized trial

Strata: Institution & selection heart vs lung criteria

Proton loco-regional RT

Photon loco-regional RT





DCCC Radiotherapy

DCPT

Randomisering Proton, Status pr. 01.01.2025

	2020	2021	2022	2023	2024	I alt
Rigshospitalet		1	3	6	9	19
Herlev	-	5	14	15	10	44
Næstved	-	1	11	15	15	42
Odense	-	4	3	5	6	18
Vejle	-	6	14	11	13	44
Aarhus	17	36	32	32	48	165
Aalborg	-	-	1	5	9	15
I alt DK	17	53	78	89	110	**347**

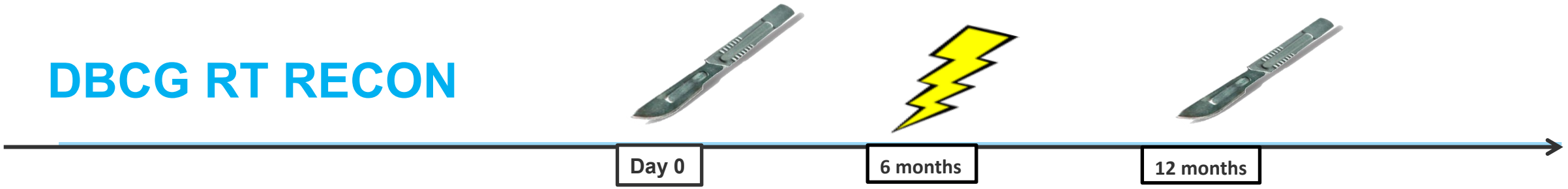
3 PhD studerende i gang med data fra studiet, incl forhold omkring inklusion, udvælgelse af patienter og kvalitetssikring af strålebehandlingen

Status for Kirurgiske forsøg

DBCG's repræsentantskabsmøde

16/1-2025

DBCG RT RECON



The Randomized study

Patients planned for mastectomy, PMRT and reconstruction eligable for the DBCG RT Recon trial

Randomizasion

Arm A:
Skin sparing mastectomy and axillary surgery
Reconstruction with implant or expander and mesh or matrix

PMRT

Final reconstruction with any reconstructive procedure - autolog or implant based

Follow-up for 10 years

Arm B
Total mastectomy and axillary surgery

PMRT

Final reconstruction with any reconstructive procedure - autolog or implant based

Follow-up for 10 years

The Prospective study

Patients planned for mastectomy, PMRT and reconstruction eligable for the DBCG RT Recon trial

Rand asion

Arm A:
Skin sparing mastectomy and axillary surgery
Reconstruction with implant or expander and mesh or matrix

PMRT

Final reconstruction with any reconstructive procedure - autolog or implant based

Follow-up for 10 years

Total ma my and axil gery

PMRT

Final reconstruction with any reconstructive procedure - autolog or implant based

Follow-up for 10 years

Status for inklusion:

- Inklusion start 1. jan 2020 som randomiseret studie
- Ændret til prospektivt studie i nov 2023
- Inkluderede: 91 patienter (RH, GEH, HEH, AUH, Vejle)
- Planlagt PhD studie v. res læge Julie Tastesen ultimo 2025
    - 50.000 kr fra Pink Tribute
    - 500.000 kr fra Gangstedfonden
    - 1.191.650 kr fra Sundhedsstyrelsens pulje for eksperimentel kræftkirurgisk behandling

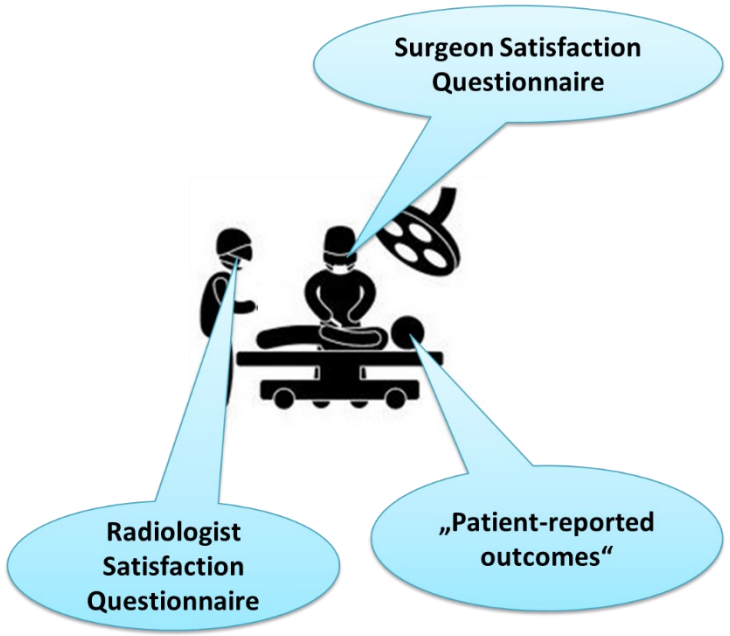
DBCG DANISH BREAST CANCER GROUP

MEthods for LOcalization of Different types of breast lesions (EUBREAST 4)

Study Lead
EUBREAST / iBRA-NET
(Intergroup Study)

Study design
Prospective non-interventional multicenter cohort study (IIT)

Primary outcomes
- Intended target lesion removal
- Negative margin at first surgery



Secondary outcomes
- Second surgery
- Secondary mastectomy
- Resection Ratio
- Duration of surgery
- Marker dislocation
- Marker placement failure
- Localization failure
- “Lost markers”
- Volume and weight of resected tissue
- Learning curve
- MRI artifacts
- Complication rates

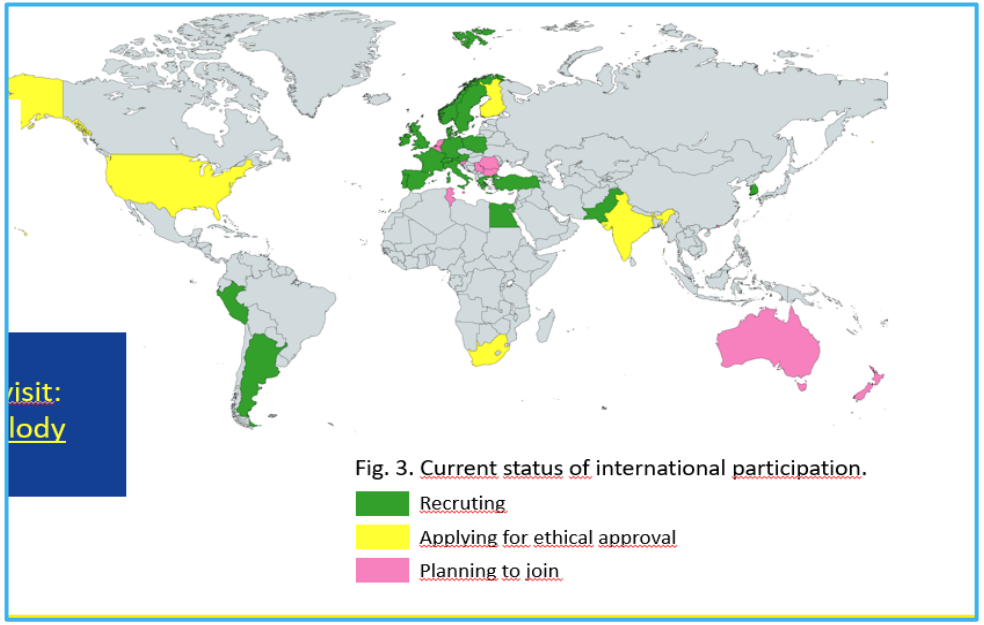
http://eubreast.org/melody

MEthods for LOcalization of Different types of breast lesions (EUBREAST 4)

Target accrual: 7,416 patients

Enrollment begin: January 2023

Current status (Nov 2024):
155 open study sites in 20 countries (3,056 patients)



Danske centre ultimo 2024:

Gentofte hospital: start inklussion nov 2023: **315** pt (top recruiting center)

Esbjerg Sygehus: start inklussion 15/11-24: **15** pt

Sjællands Universitetshospital Roskilde: Søger tilladelser

MEthods for LOcalization of Different types of breast lesions (EUBREAST 4)

Juni 2024

Current enrollment per cohort

Localization method	Patient number
Wire	406
Intraoperative ultrasound	255
Magseed	44
Sirius Pintuition	36
Savi Scout	34
LOCalizer	32
Radioactive seed	208
ROLL	16
Carbon suspension	7

DCCL senfølge app: Kører i RegionMidt og skal opstartes i Ålborg, økonomien bag den videre implementering skal afklares

SENOMAC: Fortsat opfølgning mhp OS

TARGIT studiet om intraoperativ strålebehandling: i alt ca. 839 patienter, 2013 – 19, opgørelse af resultaterne pågår

DBCG DANISH BREAST CANCER GROUP