

Theranostik til brystkræft

Et præklinisk studie af RM26 målrettet gastrin-releasing peptid receptoren til molekylær scanning og behandling



Christina Baun

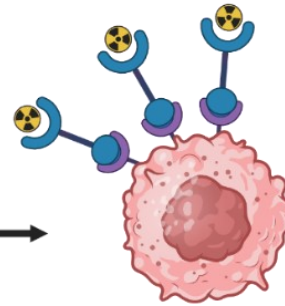
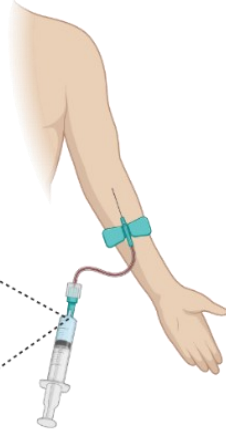
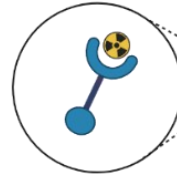
Nuklearmedicinsk Afdeling, Odense Universitets Hospital
Klinisk Institut, Syddansk Universitet, Odense

Therapy + Diagnostics = Theranostics

Injektion af radioaktivt lægemiddel

Målrætte lægemiddel mærket med en radioaktiv isotop (Radioaktivt sporstof)

RM26

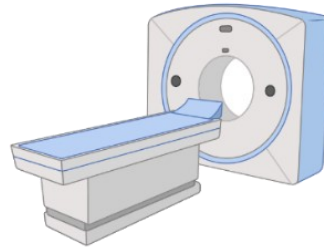


Specifik binding til kræftcellerne

GRPR

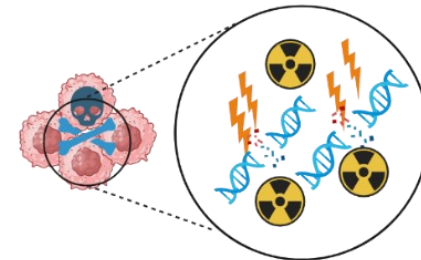
Gastrin-Releasing Peptide Receptor

Scanning 
Diagnostisk isotop

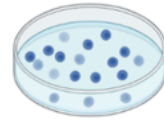


PET scanning, der visualiserer de kræftceller, som lægemidlet har bundet sig til

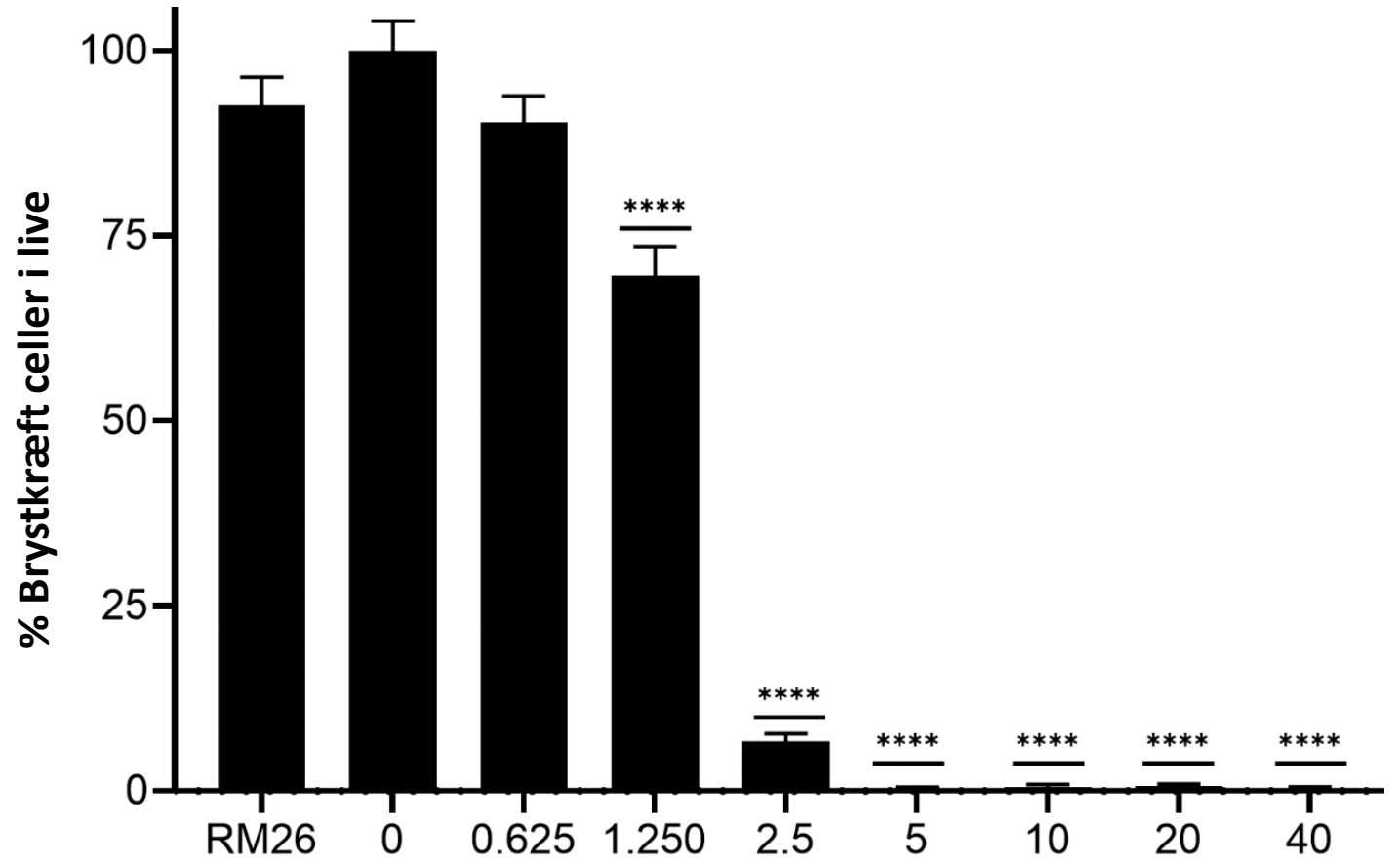
Behandling 
Terapeutisk isotop



Strålingen ødelægger DNA i de ramte kræftceller



Effekt af ^{177}Lu -RM26 terapi i brystkræft celler



^{55}Co -RM26 PET/CT scanning af mus med brystkræft
Koncentration af ^{177}Lu -RM26

****: $p < 0.0001$

Fremtidig klinisk perspektiv

- Relevant for patienter med hormon følsom brystkræft
 - Patient stratificering
- Interesse fra Industrien
- Styrke klinisk translation





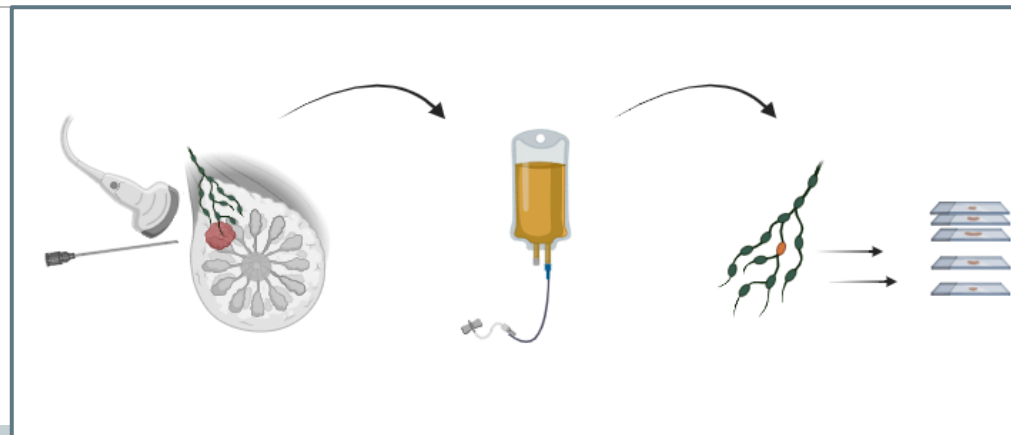
Tak for opmærksomheden

Targeted axillary dissection in breast cancer after neoadjuvant treatment

FREDERIKKE MUNCK, DEP. OF BREAST SURGERY

SUPERVISORS: TOVE TVEDSKOV, NIELS KROMAN

ILSE VEJBORG, CHARLOTTE LANNG



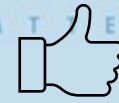
Aim

Compare **marking methods** for targeted axillary dissection to **avoid ALND** because of **non-detection**

In patients with **metastases in the TAD lymph nodes** after NACT, clarify which factors are associated with **metastasis burden** in the **non-TAD lymph nodes**



Methods



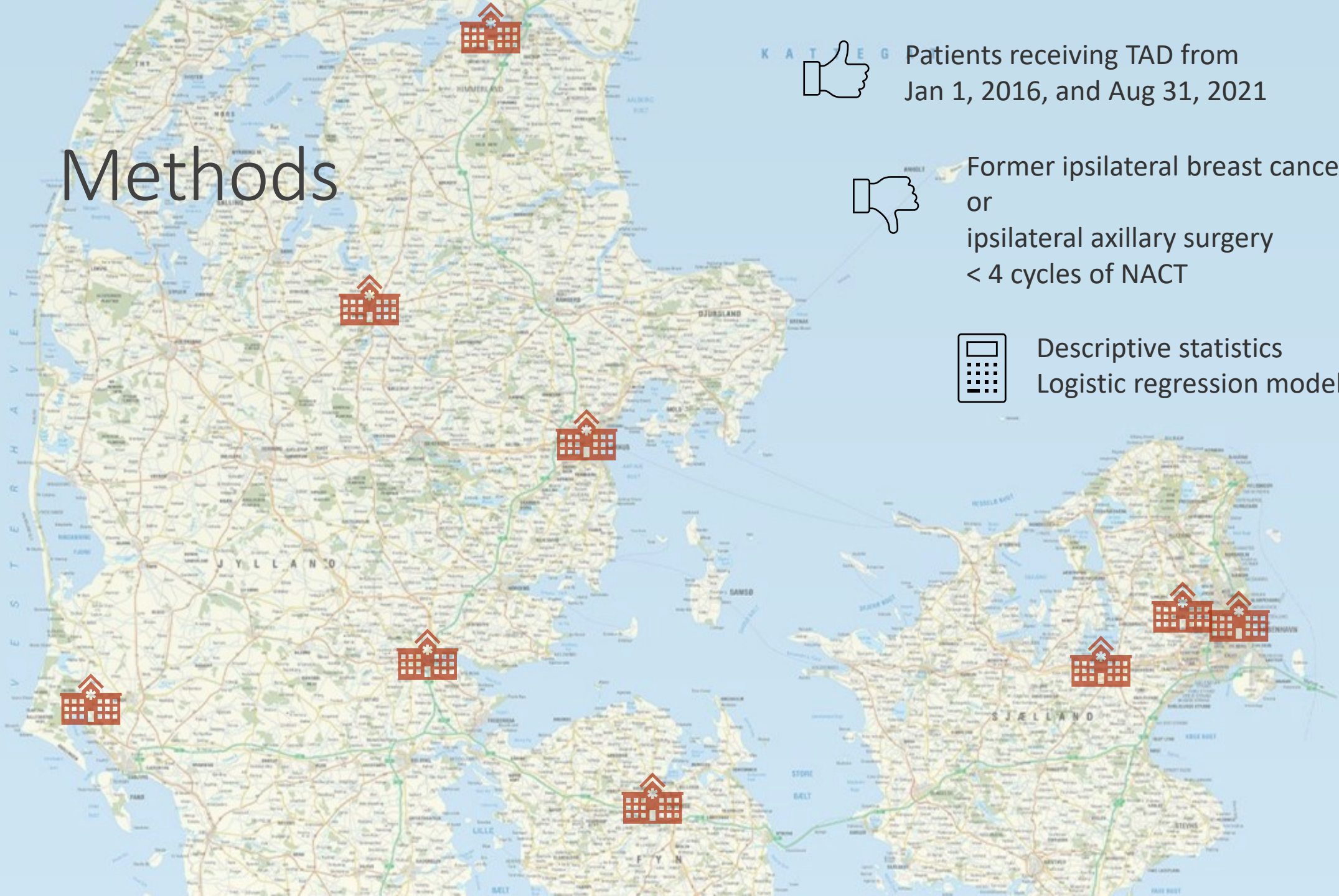
Patients receiving TAD from
Jan 1, 2016, and Aug 31, 2021



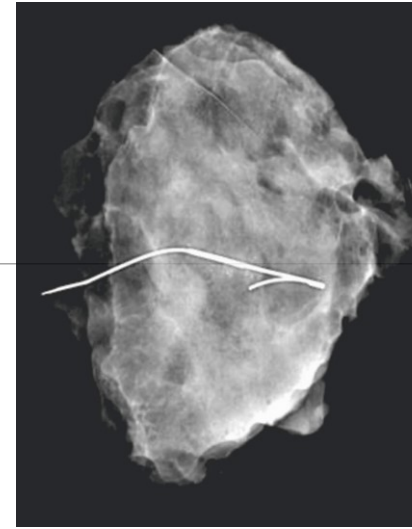
Former ipsilateral breast cancer
or
ipsilateral axillary surgery
< 4 cycles of NACT



Descriptive statistics
Logistic regression models



Comparing of markers

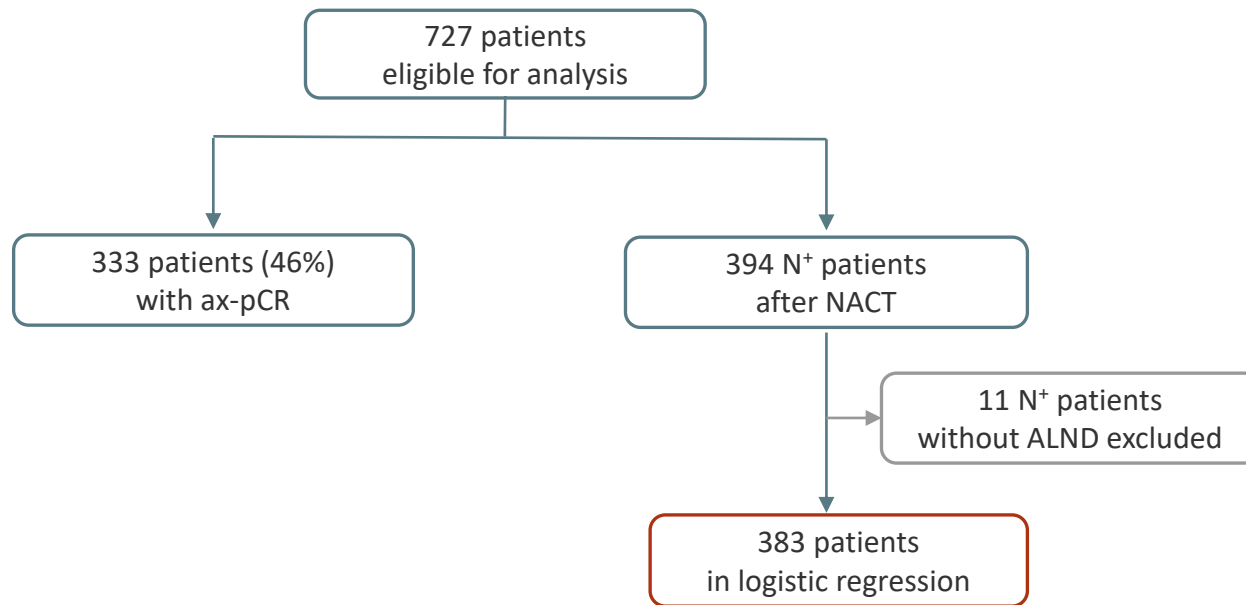


Surgical excision success by TAD marking method	
Marking method	% with successful excision (of attempts)
Clip + ¹²⁵ I seed	96
Clip + WGL	91
Clip + Temporary ink marking on skin	82
¹²⁵ I seed	99

Unsuccessful excision by TAD markers		
Marking method	OR (95% CI)	<i>p</i>
Clip + ¹²⁵ I seed	1.00	<.0001
Clip + WGL	2.48 (0.84-7.35)	
Clip + Temporary ink marking on skin	5.34 (1.62-17.60)	
¹²⁵ I seed	0.18 (0.02-1.59)	



Factors associated with non-TAD lymph node metastases



Factors associated with high non-TAD metastasis burden in breast cancer patients with positive TAD lymph nodes

Variable	Multivariate analysis OR (95% CI)	<i>p</i> ^c
Positive TAD lymph node proportion		<.001
<66.6%	0.34 (0.17-0.62)	
66.6-100%	1.00	
TAD metastasis size		0.02
Isolated tumor cells	0.11 (<.01-0.82)	
Micrometastasis	0.68 (0.21-1.80)	
Macrometastasis	1.00	
In breast at surgery		<.01
Breast pCR	0.07 (<.01-0.56)	
Breast non-pCR	1.00	

The DBCG RT Nation study: Insights from a decade of real-world breast cancer radiotherapy data in Denmark

Lasse Refsgaard, Aarhus University Hospital, Aarhus University

Supervisors: Stine Sofia Korreman, Birgitte Vrou Offeren, Lise Bech Jellesmark Thorsen

The overall aim of this thesis is to establish methodologies for conducting large-scale retrospective studies on real-world data in radiotherapy for breast cancer in Denmark.

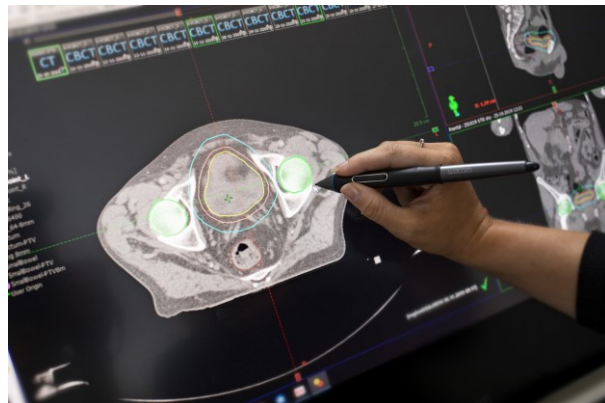


Radiotherapy departments generate a lot of data

CT-scan ->



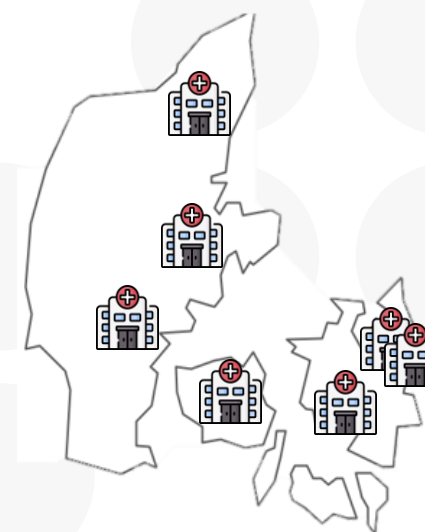
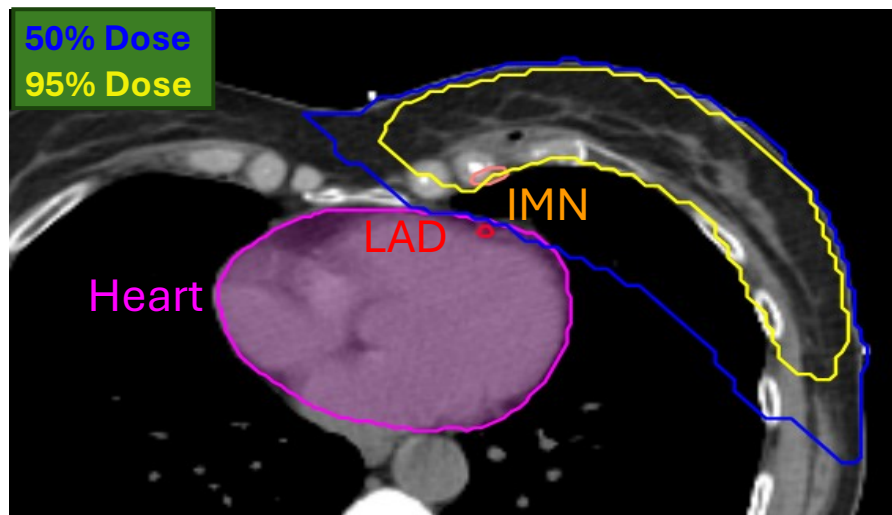
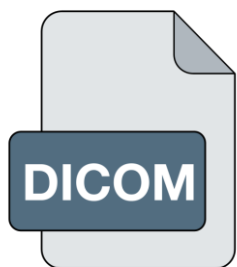
Organ delineation ->



Treatment planning ->



Treatment



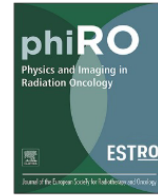
Study 1 and 2 – Data mining and guideline evaluations



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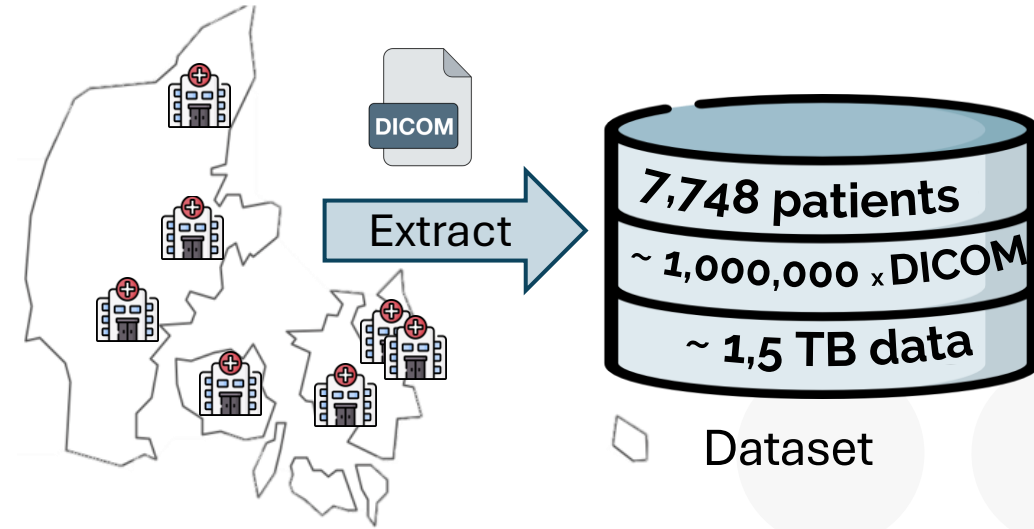
Physics and Imaging in Radiation Oncology

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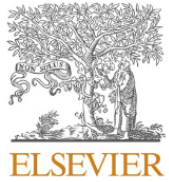


End-to-end framework for automated collection of large multicentre radiotherapy datasets demonstrated in a Danish Breast Cancer Group cohort

Lasse Refsgaard^{a,j}, Emma Riis Skarsø^{b,j}, Thomas Ravkilde^c, Henrik Dahl Nissen^d, Mikael Olsen^e, Kristian Boye^f, Kasper Lind Laursen^g, Susanne Nørring Bekke^h, Ebbe Laugaard Lorenzenⁱ, Carsten Brinkⁱ, Lise Bech Jellesmark Thorsen^{a,c}, Birgitte Vrou Offersen^{a,b,c}, Stine Sofia Korreman^{b,c,j,*}



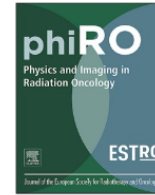
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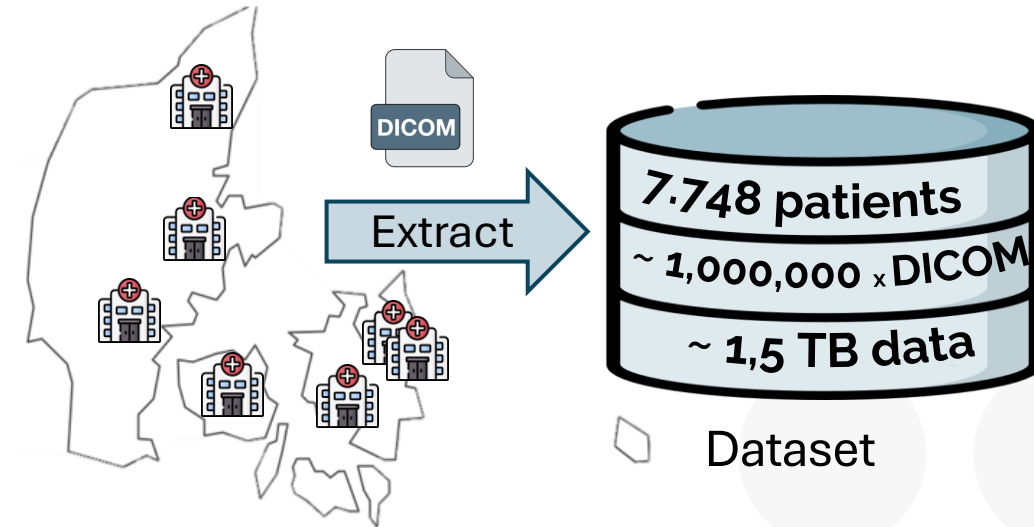
journal homepage: www.thegreenjournal.com



Original Article

Evaluating Danish Breast Cancer Group locoregional radiotherapy guideline adherence in clinical treatment data 2008–2016: The DBCG RT Nation study

Lasse Refsgaard^{a,b,*}, Emma Skarsø Buhl^{b,c}, Esben Yates^d, Else Maae^e, Martin Berg^e, Sami Al-Rawi^f, Abhilasha Saini^f, Maja Vestmø Maraldo^g, Kristian Boye^g, Marie Louise Holm Milo^{h,i}, Ingelise Jensen^h, Louise Wichmann Matthiessen^j, Susanne Nørring Bekke^j, Mette Holck Nielsen^{k,l}, Ebbe Laugaard Lorenzen^k, Lise Bech Jellesmark Thorsen^{a,d}, Stine Sofia Korreman^{b,c}, Birgitte Vrou Offersen^{a,b,c,d}



Guideline changes 2008-2016

- Change in fractionation
- Introduction of respiratory gating
- Irradiation of IMN
- Simultaneously integrated boost
- Delineation of LAD

Study 3 – Use radiotherapy data for outcome prediction



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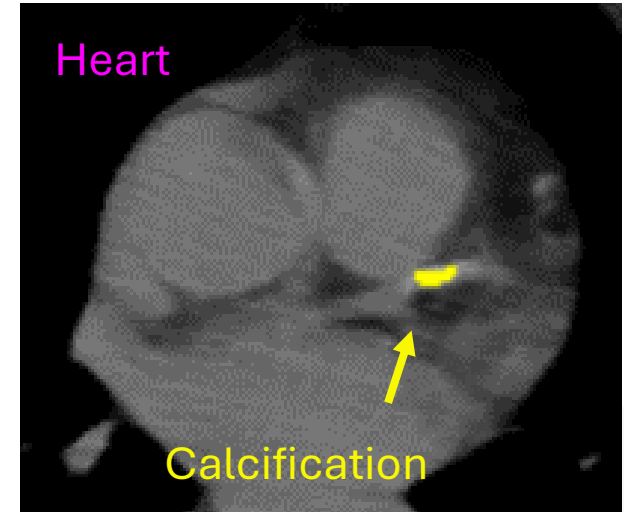
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Original Article

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Study 3 – Use radiotherapy data for outcome prediction



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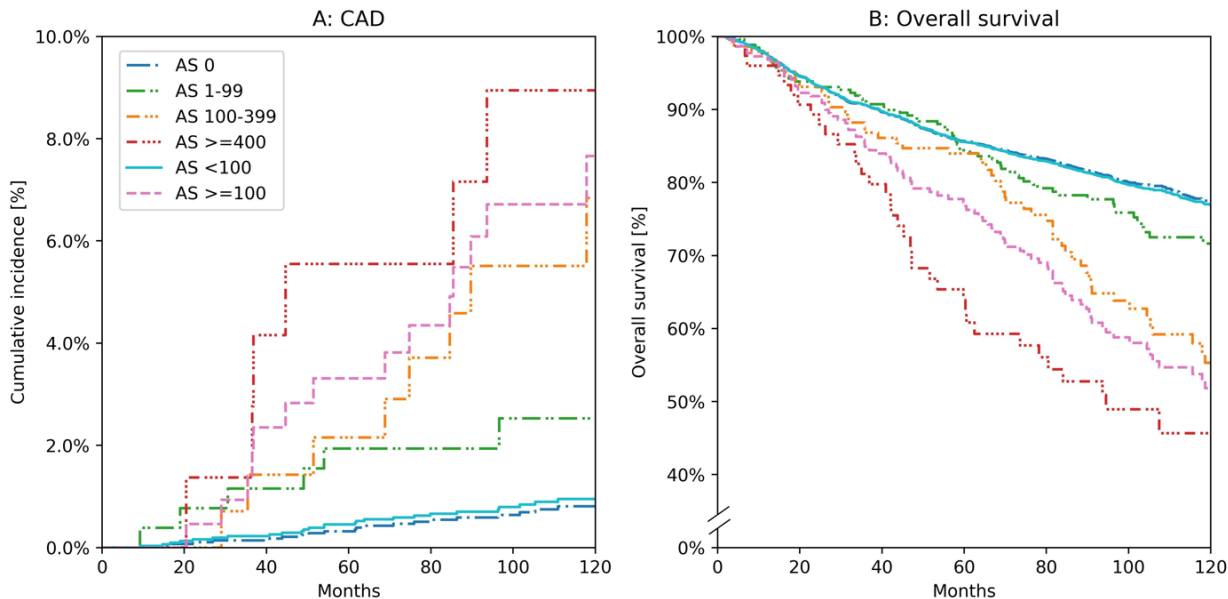
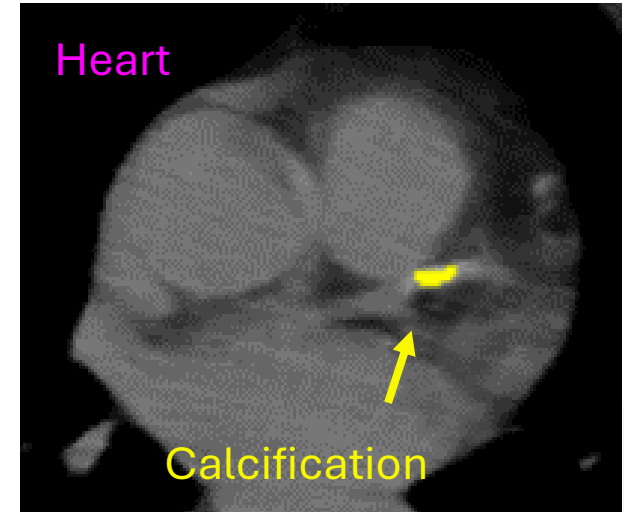
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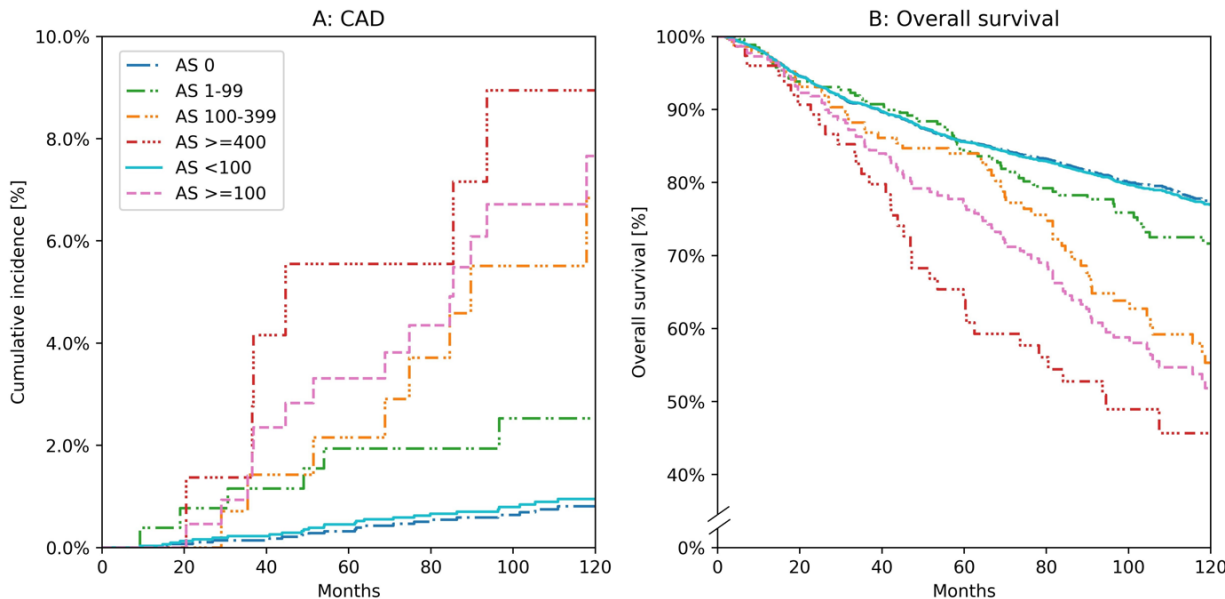
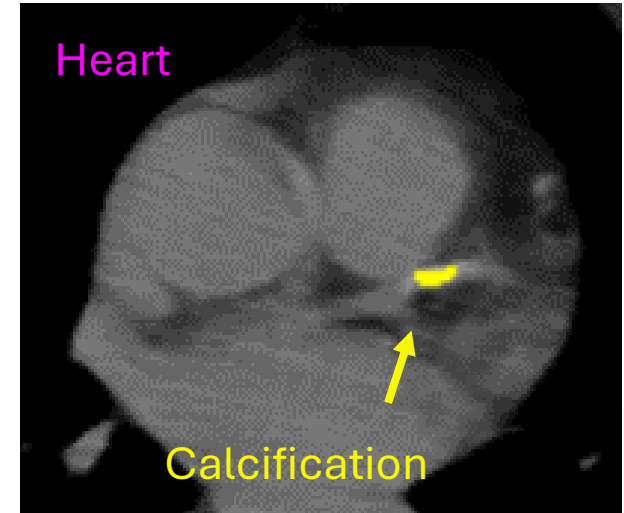
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Model	Covariate	Hazard ratio CAD (95 % confidence intervals)	P value
Model 1	AS \geq 100 [0/1]	23.80 (7.29–77.74)	<0.01
	MHD [Gy]	1.25 (1.01–1.56)	0.04
	MHD * AS \geq 100 [Gy]	0.61 (0.33–1.12)	0.11
Model 2	AS \geq 100 [0/1]	12.43 (6.12–25.24)	<0.01
	LV5Gy [%]	1.03 (0.99–1.06)	0.11
Model 3	LV5Gy * AS \geq 100 [%]	0.95 (0.87–1.03)	0.21
	AS > 100 [0/1]	18.07 (8.00–40.78)	<0.01
	LAD_mean [Gy]	1.04 (1.00–1.09)	0.06
	LAD_mean * AS \geq 100 [Gy]	0.84 (0.70–1.02)	0.07

DBCRT Nation Automation: National consistency in delineations in breast cancer patients



Emma Skarsø Buhl
Aarhus University hospital
Aarhus University

Main supervisor: Stine Sofia Korreman
Co-supervisor: Birgitte Vrou Offersen

The overall aim of this PhD is to investigate the standardization of delineations across the nation by using real-world data from breast cancer patients in Denmark

Development of deep learning models for auto segmentation



ACTA ONCOLOGICA
2023, VOL. 62, NO. 10, 1201–1207
<https://doi.org/10.1080/0284186X.2023.2252582>



ORIGINAL ARTICLE



Development of a national deep learning-based auto-segmentation model for the heart on clinical delineations from the DBCG RT nation cohort

Emma Riis Skarsø^{a,b} , Lasse Refsgaard^{b,c}, Abhilasha Saini^d, Ditte Sloth Møller^{b,e}, Ebbe Laugaard Lorenzen^f , Else Maae^g, Karen Andersen^h, Maja Vestmø Maraldoⁱ, Marie Louise Milo^j, Tine Bisballe Nyeng^e, Birgitte Vrou Offersen^{a,b,c,e} and Stine Sofia Korreman^{a,b,e}



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Data harvesting vs. data farming: A study of the importance of variation vs sample size in deep learning-based auto-segmentation for breast cancer patients

Buhl ES, Maae E, Matthiessen LW, Nielsen MH, Maraldo MV, Moller M, Elleberg S, Al-Rawi SAJ, Offersen BV, Korreman SS.

Published in the ICCR 2024 proceedings and on arXiv,
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Original Article

Development and comprehensive evaluation of a national DBCG consensus-based auto-segmentation model for lymph node levels in breast cancer radiotherapy



Emma Skarsø Buhl^{a,b,*}, Ebbe Laugaard Lorenzen^{c,d}, Lasse Refsgaard^{a,b}, Anders Winther Mølby Nielsen^{b,e}, Annette Torbøl Lund Brixen^f, Else Maae^g, Hanne Spangsberg Holm^g, Joachim Schøler^g, Linh My Hoang Thai^a, Louise Wichmann Matthiessen^f, Maja Vestmø Maraldo^{h,i}, Mathias Maximiliano Nielsen^a, Marianne Besserman Johansen^j, Marie Louise Milo^k, Marie Benzon Mogensen^h, Mette Holck Nielsen^l, Mette Møller^k, Maja Sand^l, Peter Schultz^j, Sami Aziz-Jowad Al-Rawi^m, Saskia Esser-Naumann^m, Sophie Yammeni^k, Stine Elleberg Petersen^a, Birgitte Vrou Offersen^{a,b,e,j}, Stine Sofia Korreman^{a,b,e}

Applying deep learning auto segmentation models



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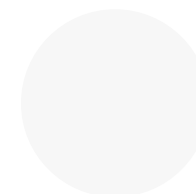
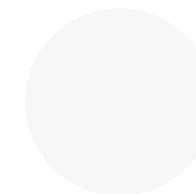
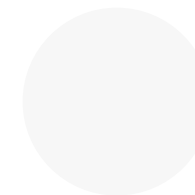
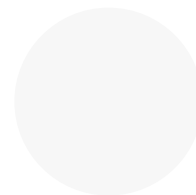
journal homepage: www.sciencedirect.com/journal/physics-and-imaging-in-radiation-oncology



Original Research Article

Geometrical and dosimetrical evaluation of different interpretations of a european consensus delineation guideline for the internal mammary lymph node chain in breast cancer patients

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Applying deep learning auto segmentation models



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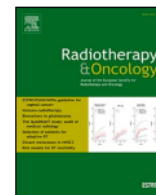


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Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



Original Article

Population based audit of heart radiation doses in 6925 high-risk breast cancer patients from the Danish breast cancer group RT Nation study

Emma Skarsø Buhl^{a,b,*}, Lasse Hindhede Refsgaard^{a,b}, Sami Aziz-Jowad Al-Rawi^c, Karen Andersen^d, Martin Berg^e, Kristian Boye^f, Ingelise Jensen^g, Ebbe Laugaard Lorenzen^{h,i}, Else Maae^e, Maja Vestmø Maraldo^{f,j}, Louise Wichmann Matthiessen^d, Marie Louise Milo^g, Mette Holck Nielsen^l, Abhilasha Saini^c, Esben Yates^k, Birgitte Vrou Offersen^{a,b,k,m}, Stine Sofia Korreman^{a,b,m}



Conclusion and perspectives

- *National delineation differences exist despite of guidelines*
- *The dosimetric consequences vary depending on the structure*
- *Deep learning-based auto-segmentation models has the potential to increase the national delineation consistency.*



DBCGL Nation

A national randomised study of AI assisted target segmentation in breast cancer radiotherapy



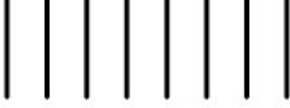
Stine Rauff Søndergaard, M.D., PhD student
Department of Oncology, Lillebaelt Hospital,
University Hospital of Southern Denmark



DBCG

Shared Decision Making with Breast Cancer Patients





Shared Decision Making with Breast Cancer Patients

DBCG



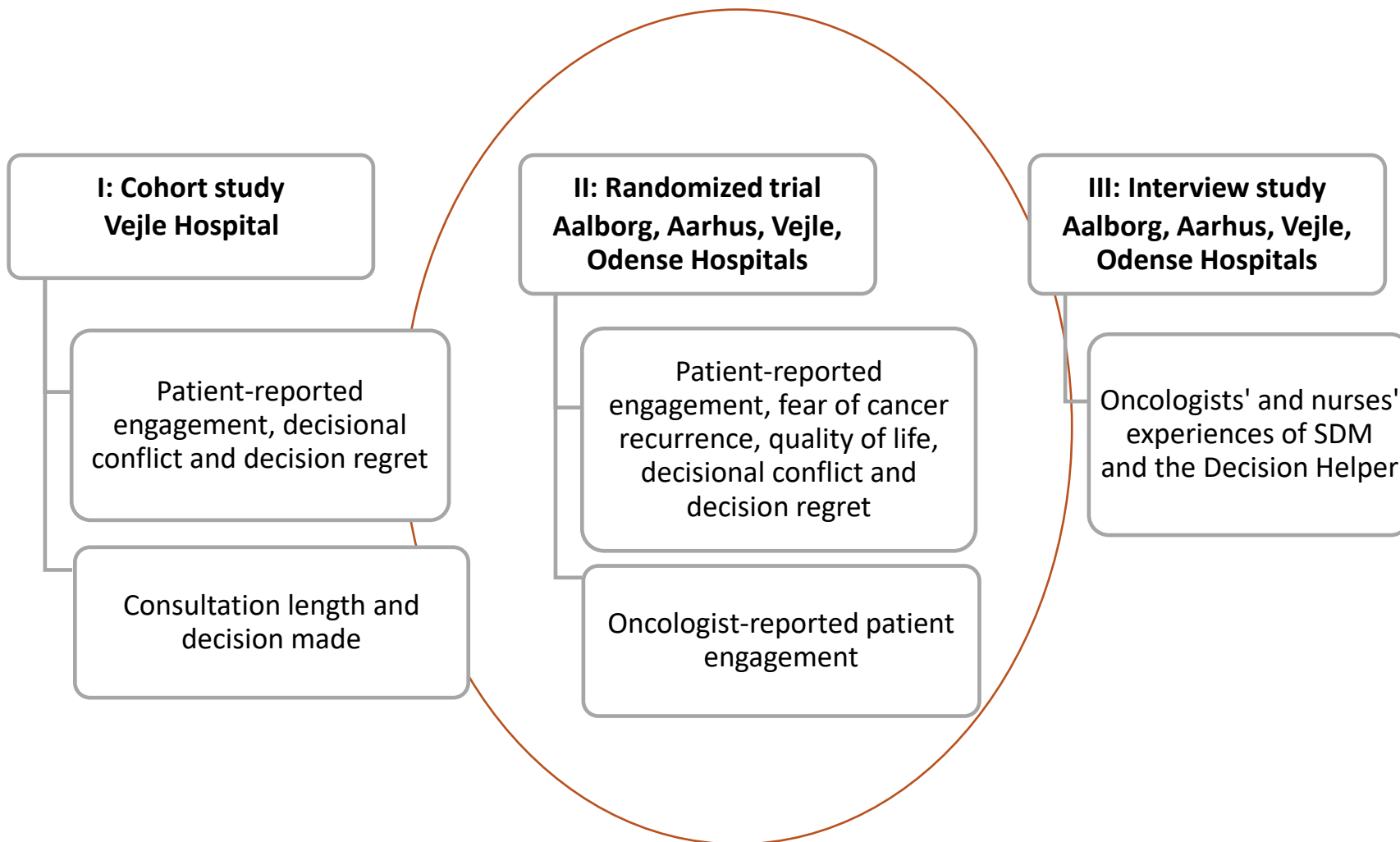

5. SHARED DECISION-MAKING
Participate in shared decision-making with your healthcare team about all aspects of your treatment and care.



Shared Decision Making with Breast Cancer Patients

DBCG





The DBCG RT SDM trial

Hypothesis: SDM supported by a customized Decision Helper will increase patient-reported SDM on adjuvant irradiation after breast-conserving surgery.

Aim: to investigate the effect of SDM supported by a Decision Helper on patient-reported SDM compared to standard.



The DBCG RT SDM trial



SDM-Q-9

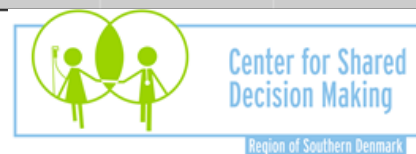
**Primary endpoint:
Patient-reported SDM**

Secondary endpoints:

- Oncologist-reported SDM
- Other measures of SDM
- Fear of recurrence
- Decisional conflict
- Quality of life
- Knowledge of irradiation
- Decision regret after six months

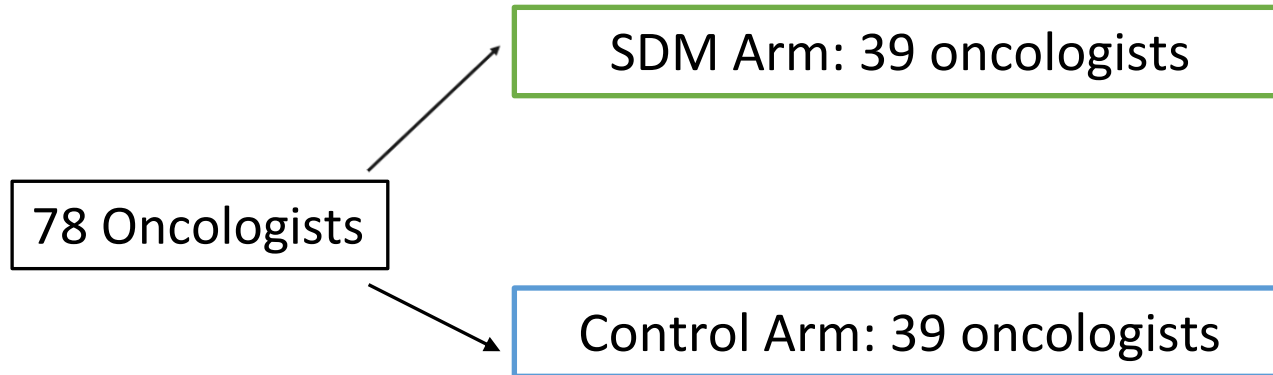


1. My doctor made clear that a decision needs to be made.	completely disagree	strongly disagree	somewhat disagree	somewhat agree	strongly agree	completely agree
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. My doctor wanted to know exactly how I want to be involved in making the decision.	completely disagree	strongly disagree	somewhat disagree	somewhat agree	strongly agree	completely agree
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. There are different options for treating my medical condition.	disagree	somewhat disagree	somewhat agree	strongly agree	completely agree	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
4. I explained the advantages and disadvantages of the treatment options.	disagree	somewhat disagree	somewhat agree	strongly agree	completely agree	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
5. I understand all the information.	disagree	somewhat disagree	somewhat agree	strongly agree	completely agree	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
6. I know which treatment option I prefer.	disagree	somewhat disagree	somewhat agree	strongly agree	completely agree	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
7. I have fully weighed the different treatment options.	disagree	somewhat disagree	somewhat agree	strongly agree	completely agree	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
8. My doctor and I selected a treatment option together.	completely disagree	strongly disagree	somewhat disagree	somewhat agree	strongly agree	completely agree
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. My doctor and I reached an agreement on how to proceed.	completely disagree	strongly disagree	somewhat disagree	somewhat agree	strongly agree	completely agree
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



The DBCG RT SDM trial

DBCG



- Histologically verified breast cancer or ductal carcinoma in situ
- Indication for adjuvant whole-breast radiotherapy (DBCG type F)
- Age \geq 18 years

Setting

The consultation concerning adjuvant whole-breast radiotherapy.

Stratification at department level

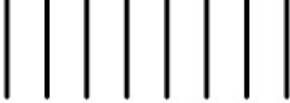


The DBCG RT SDM trial

Table 1: Patient baseline characteristics

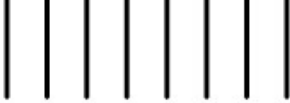
	SDM group	Control group	All
Patients, N	400	274	674
Age, Mean (SD)	59.7 (10)	60 (9.89)	59.86 (10.14)
Site of participation, N (%)			
Site 1	44 (11)	22 (8)	66 (9.8)
Site 2	138 (35)	103 (38)	241 (36)
Site 3	177 (44.3)	110 (40)	287 (43)
Site 4	41 (10.3)	39 (14)	80 (12)

No significant difference in patient social, educational or work-related status.



The DBCG RT SDM trial

Measurement tool	Median (IQR)		p	Ave. marg. effects of SDM (95% CI), p
	SDM	Control		
SDM-Q-9 Scale 0-100	N=376 80 (68.9:94.4)	N=259 71.11 (55.6:82.2)	p<0.0001	9.54 (9.09:9.99), p<0.0001
SDM-Q-9-DOC Scale 0-100	N= 331 93.3 (82.2:100)	N=225 73.3 (60:84.4)	p<0.0001	17.66 (11.70:23.62), p<0.0001
SDMP4 Scale 0-4	N= 376 3 (2:3)	N= 258 2 (1:3)	p<0.0001	0.49 (0.33:0.64), p<0.0001
CollaboRATE Scale 0-9	N=376 8.3 (7.3:9)	N=259 7.5 (6.3:8.3)	p<0.0001	0.63 (0.39:0.871), p<0.0001



The DBCG RT SDM trial



Measurement tool	Median (IQR)		p	Ave. marg. effects of SDM (95% CI), p
	SDM	Control		
Decisional conflict before consultation Scale 0-100	N=327 27.1 (14.6:41.7)	N=216 29.2 (16.7:44.8)	p=0.506	-1.96 (-5.46:1.54), p= 0.272
Decisional conflict after consultation Scale 0-100	N=375 10.9 (0:25)	N=257 15.6 (4.7:26.6)	p=0.006	-2.95 (-5.07:-0.84), p= 0.006
Fear of Cancer Recurrence Scale 0-36	N=374 14 (9:20)	N=255 14 (10:19)	p=0.505	0.281 (-0.84:1.41), p=0.624

The DBCG RT SDM trial

DBC**G**

Fælles beslutningstagning og brug af et beslutningsstøtteværktøj i konsultationen om postoperativ strålebehandling, DBCG type F, vil fremover indgå i national retningslinje.

#DKD2023

#SamarbejdeOmKræft

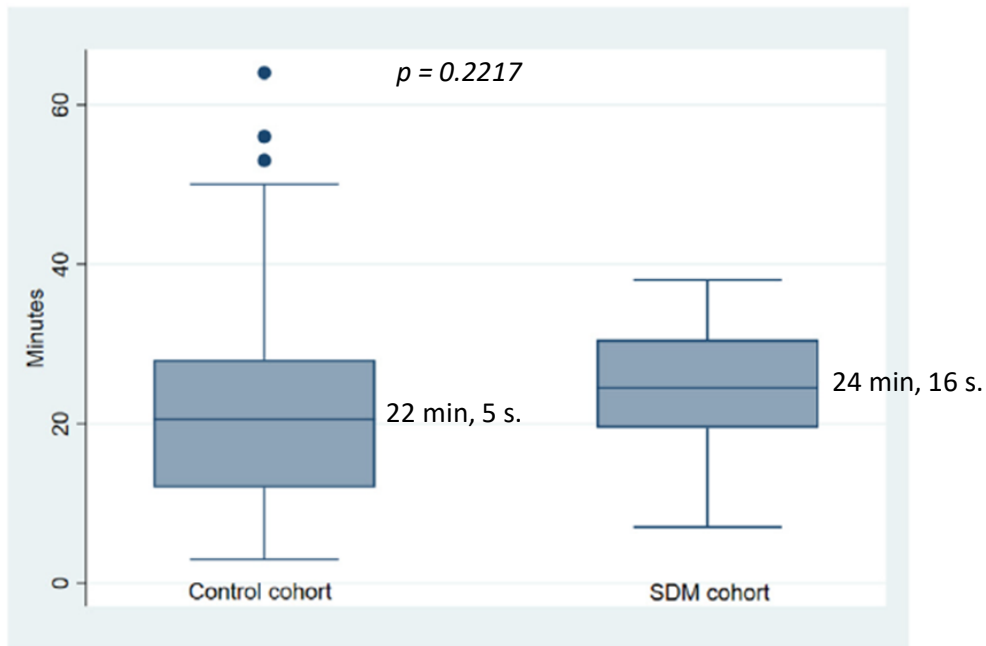
The screenshot shows the website for 'Kræftens Bekæmpelse' (Danish Cancer Society). The main navigation bar includes 'Vælg kræftsygdom', 'Hjælp og viden', 'Forebyg kræft', 'Forskning', 'Nyheder', 'Støt os', and 'Til fagfolk'. The featured article is titled 'Sådan kan patienter inddrages bedre i deres behandling' (How patients can be better involved in their treatment), dated 16-05-2023. The article text states: 'En særlig Beslutningshjælper kan hjælpe læger og patienter med at inddrage patienten i beslutninger om deres behandling. Ny undersøgelse viser gode resultater med at bruge Beslutningshjælperen til at vejlede kvinder, der skal tilbydes strålebehandling mod brystkræft.' Below the text is an image of a decision support tool (SDM) card titled '4 Strålebehandling' (4 Radiation treatment). The card is divided into 'Fordele' (Advantages) and 'Ulemper' (Disadvantages). The 'Fordele' section lists: 'Din egen mening er vigtig', 'Hjælper lægen med at træffe beslutning', and 'Vilker du det?'. The 'Ulemper' section lists: 'Følgeskærm for lægen', 'Ingen behandling i hovedsagen (1-2 måneder)', 'Stråling', 'Smerter', 'Hud', and 'Hvile op længe'. Below the image, a caption reads: 'Beslutningshjælperen består af nogle kort, der viser fordele og ulemper ved en undersøgelse eller behandling, og som kan støtte dialogen mellem patient og sundhedspersonale, når der skal træffes en beslutning.'

ESTRO 2023 | 12-16 May 2023
Vienna, Austria

Hvor lang tid tager det..?

DBCG

The Fast-track Lung Clinic



Breast Cancer Clinic

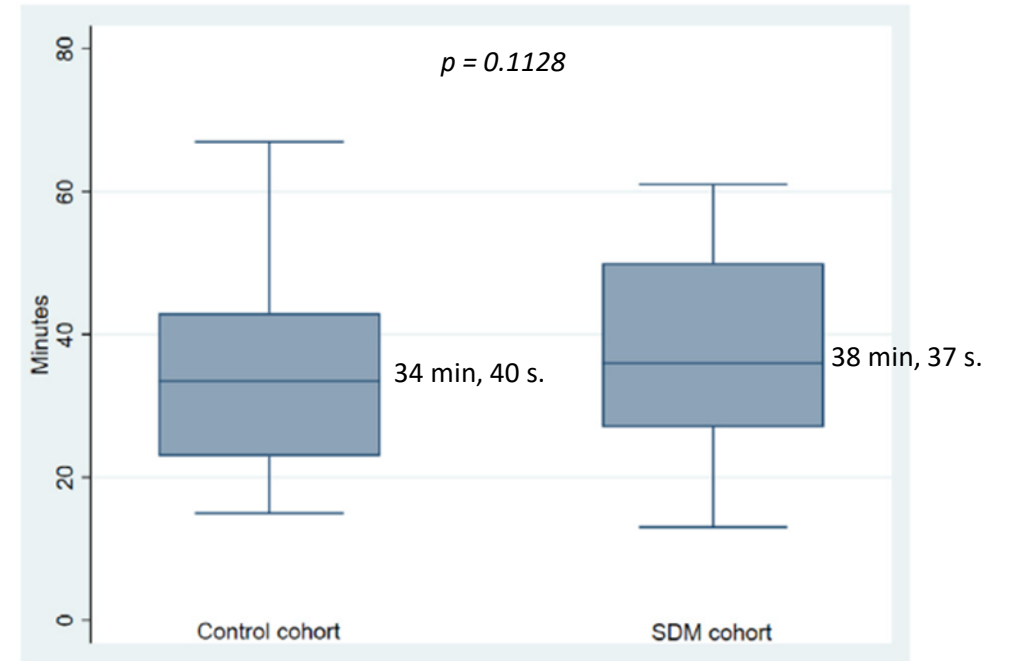


Fig. 2. Consultation length for diagnostic work-up based on a small suspicion of lung cancer in the control cohort (n = 82) and the SDM cohort (n = 52).

Fig. 3. Consultation length for adjuvant treatment after breast cancer in the control cohort (n = 64) and the SDM cohort (n = 49).

Hvordan er det for os læger...?

Læge i DBCG RT SDM: *det [FBT] betyder også at jeg går hjem med mere ro i maven omkring at denne her patient sender jeg igennem noget strålebehandling eller denne her patienten skal netop ikke have strålebehandling for det strider simpelthen imod hvad hun er for en type patient.*

Læge i DBCG RT SDM: *jeg oplever det lidt som sådan en slags, jamen, det er jo faktisk en kulturændring, vi er ved, ved at inddrage vores patienter på en anden måde, fordi, der har været så meget fokus på det i de senere år.*

Læge i DBCG RT SDM: *det kunne da være en drøm, at man havde det på DBCGs hjemmeside for eksempel, gode beslutningsstøtteværktøjer til mammacancer patienter.*

Stine Rauff Søndergaard, M.D., PhD student
Department of Oncology, Lillebaelt Hospital,
University Hospital of Southern Denmark

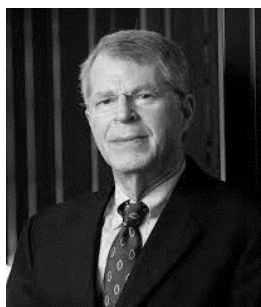


DBCG

Tusind tak

Tak til alle deltagende patienter, læger, sygeplejersker og samarbejdspartnere.

Tak til mine vejledere, DBCG Radioterapiudvalget, Center for Fælles Beslutningstagning og Onkologisk Afdeling, Vejle.



Danish Breast Cancer Group
Radiotherapy Committee





Twenty years of primary metastatic breast cancer

Has survival improved?

Tobias Berg
DBCG, Rigshospitalet

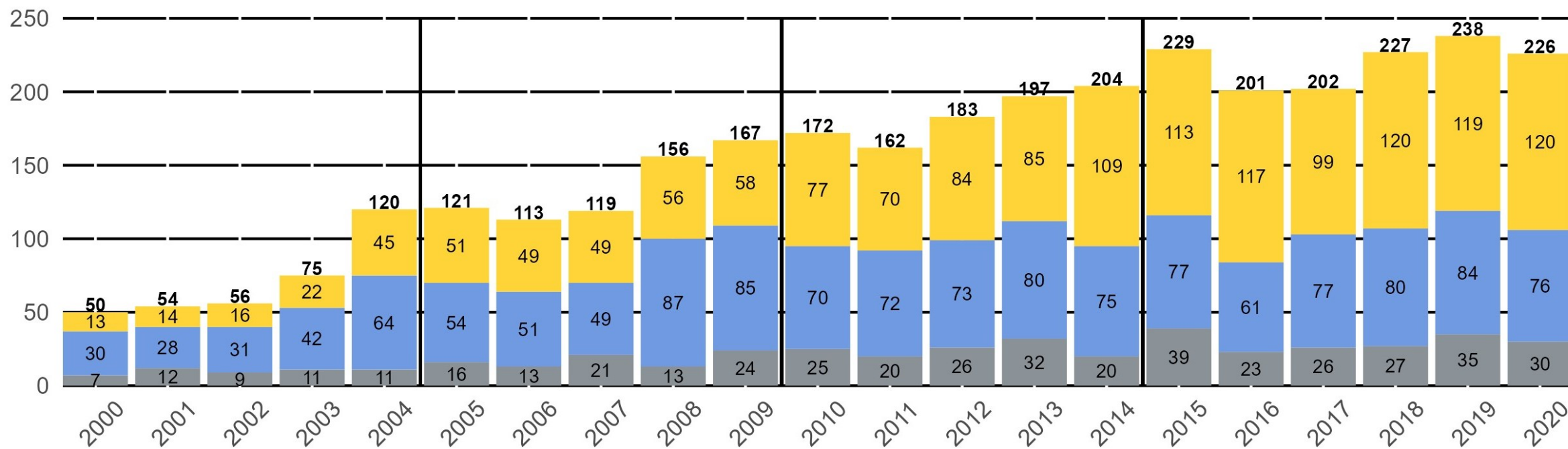
Supervisors: Bent Ejlersen, Ann Knoop, Maj-Britt Jensen and Maria Rossing

All patients in Denmark 2000-2020 with known pMBC



A

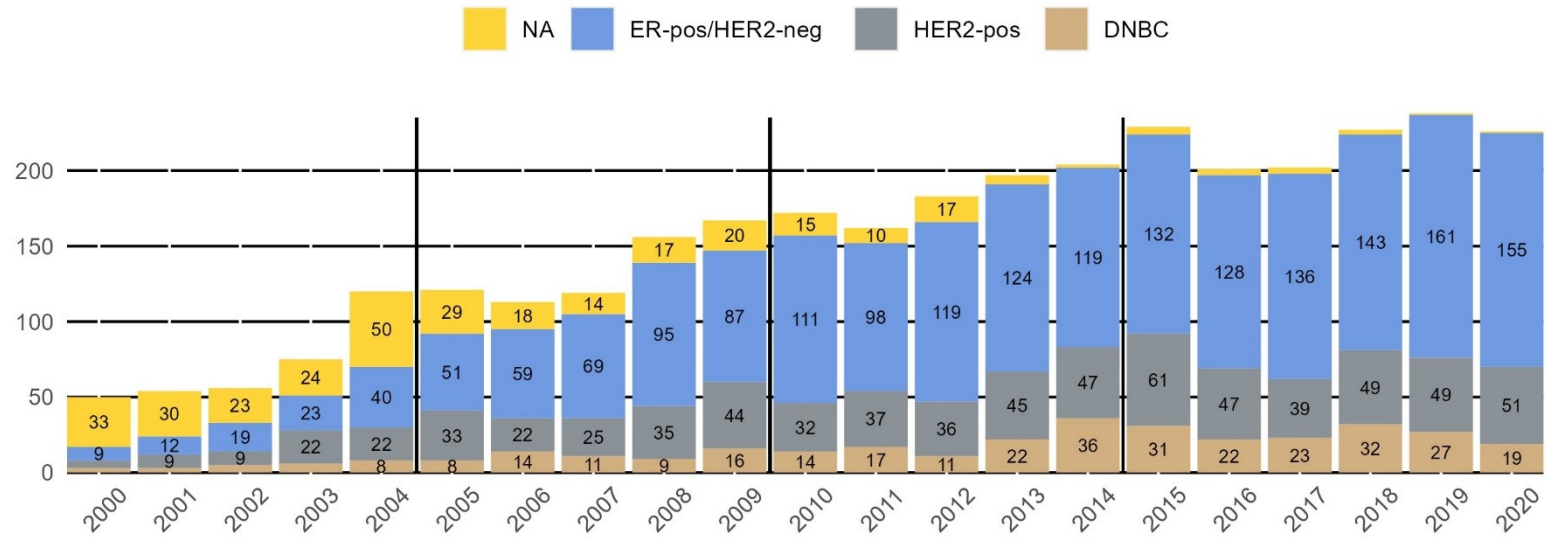
Patients per year



In total 3272 patients from 2000-2020

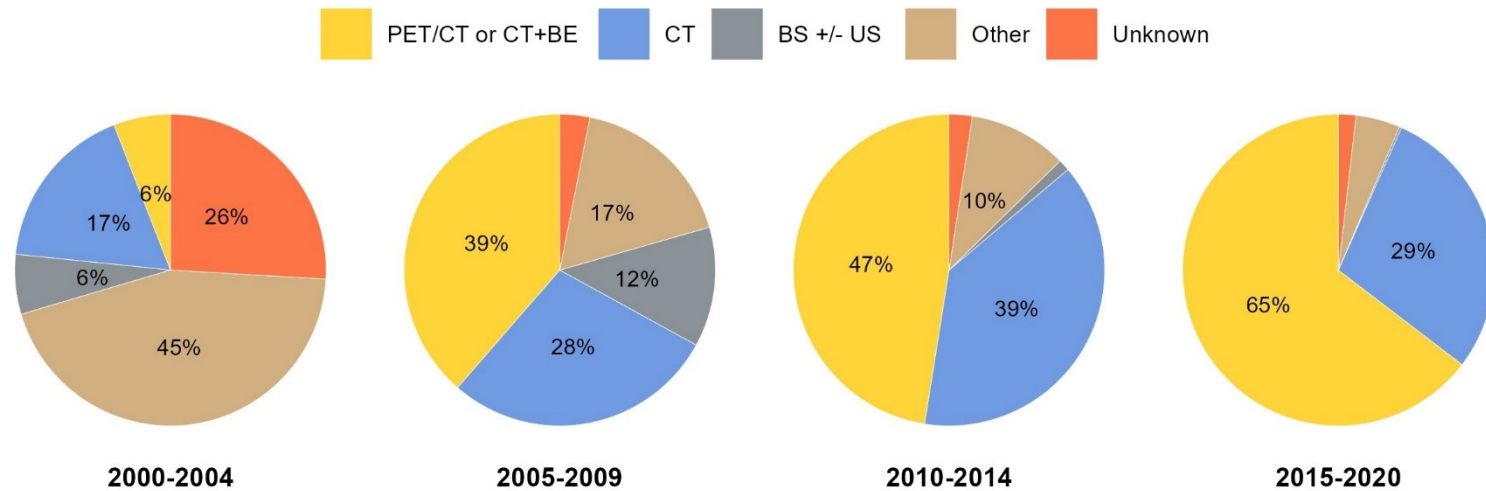
C

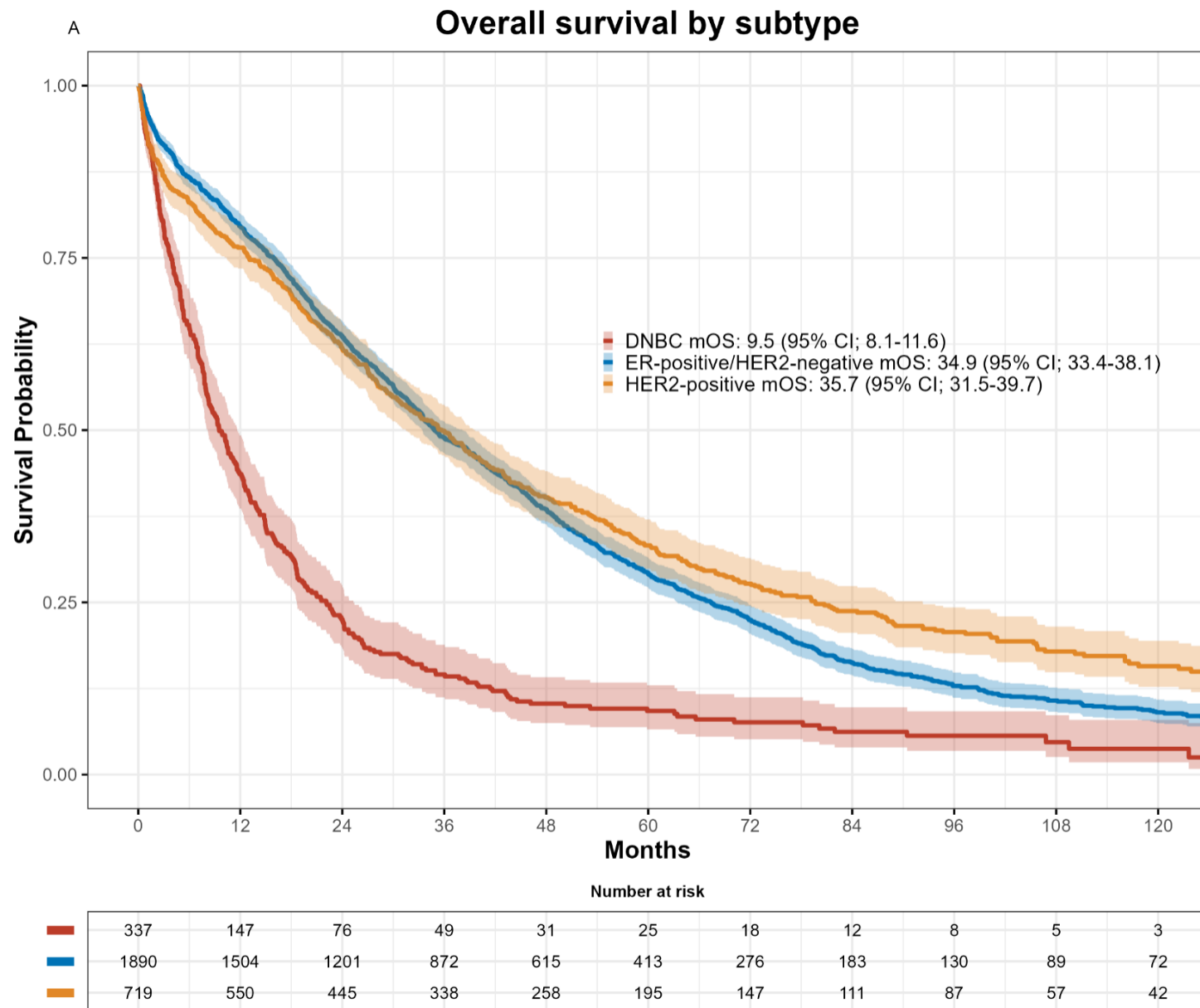
Subtypes per year



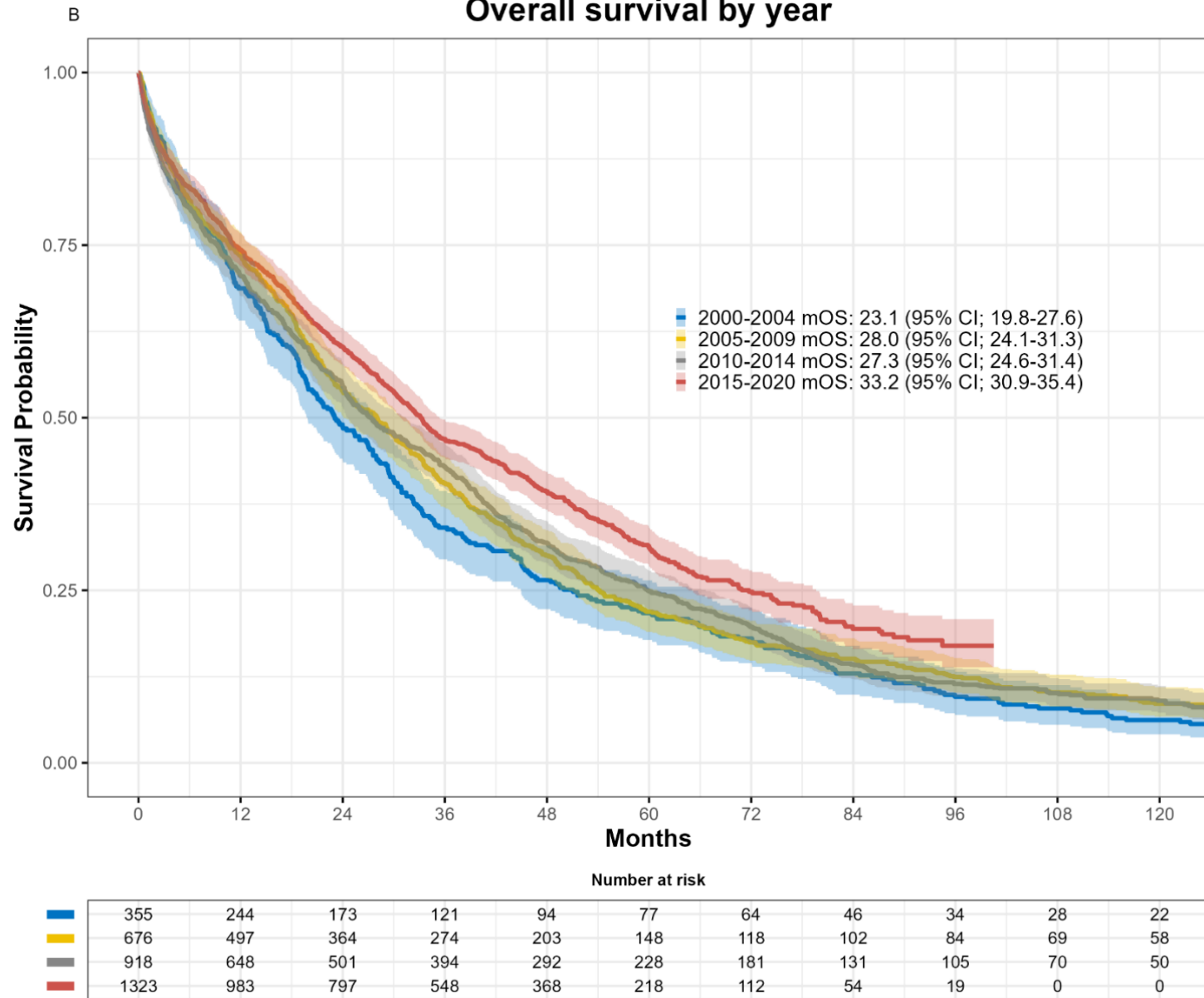
D

Radiological exam by time-period





Overall survival by year



Multivariable analysis

1. Increased risk of death with age
2. Decreased risk with time for luminal and HER2-positive
3. DNBC risk significant the first two years

		Multivariable	
	HR	95% CI	p-value
Age^x	1.10	1.08,1.12	<0.001
Age, time-dependent*	0.98	0.97,0.99	
Year of diagnosis[†]			
ER-pos	0.98	0.96,0.99	<0.001
DNBC	0.99	0.97,1.01	0.48
HER2-pos	0.97	0.96,0.99	0.001
IHC subtype			
ER-pos/HER2-neg		Ref	
DNBC year 0-2	2.72	1.93,3.84	0.001
DNBC year 2+	0.96	0.65,1.42	
HER2-positive	1.00	0.78,1.28	
HER2, time-dependent*	0.83	0.78,0.88	
CCI			
0		Ref	
1-2	1.16	1.06,1.27	<0.001
3	1.50	1.28,1.78	
CCI 3, time-dependent*	0.89	0.81,0.98	
Visceral disease			
No		Ref	
Yes	1.44	1.33,1.56	<0.001
Visceral, time-dependent*	0.83	0.78,0.87	

HR: Hazard ratio, CI: Confidence interval, CCI: Charlson Comorbidity Index, IHC: Immunohistochemistry, ER: estrogen receptor, HER2: human epidermal growth factor receptor 2

^x5-year increments, ^{*}Each year reduces the estimate accordingly. Modelled with a log time-dependency due to lack of proportionality. [†]Hazard per year of diagnosis for each IHC subtype p-values for the overall effect of age, IHC subtype, CCI, and visceral disease



Study II + III

Development and Methodological Validation of a Modified Staging System for de Novo Metastatic Breast Cancer

Molecular subtyping improves breast cancer diagnosis in the Copenhagen Breast Cancer Genomics Study