Back to the future

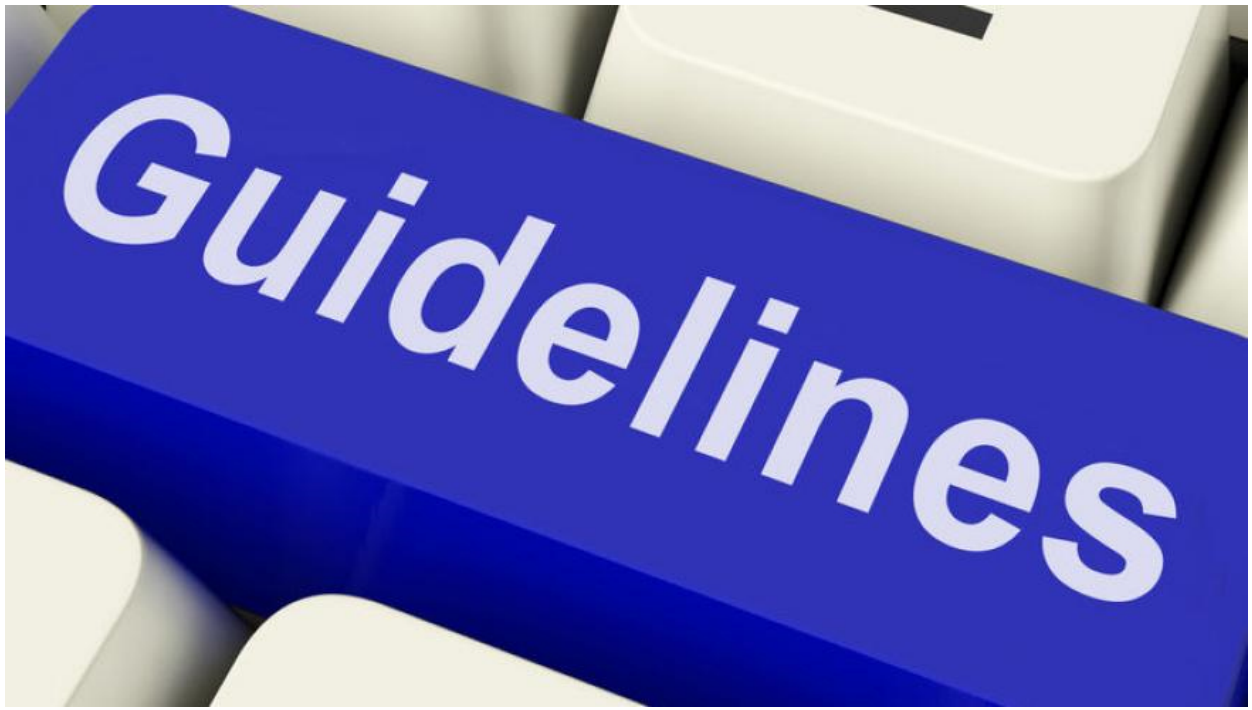
Adaptive management: what have we not to forget?

Birgitte Vrou Offersen
Professor, PhD
Dept Experimental Clinical Oncology
Aarhus University Hospital
Denmark

No conflicts of interest

Take home message 1

Develop guidelines



The Danish Breast Cancer Group Radiotherapy Committee

Guidelines

Contents lists available at ScienceDirect

Radiotherapy and Oncology 2015

journal homepage: www.thegreenjournal.com

ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer

Birgitte V. Offersen [a,*], Liesbeth J. Boersma [b], Carine Kirkove [c], Sandra Hol [d], Marianne C. Aznar [e], Albert Biete Sola [f], Youlia M. Kirova [g], Jean-Philippe Pignol [h], Vincent Remouchamps [i], Karolien Verhoeven [j], Caroline Weltens [j], Meritxell Arenas [k], Dorota Gabrys [l], Neil Kopek [m], Mechthild Krause [n], Dan Lundstedt [o], Tanja Marinko [p], Angel Montero [q], John Yarnold [r], Philip Poortmans [s]

Radiotherapy and Oncology 118 (2016) 205–208

Contents lists available at ScienceDirect

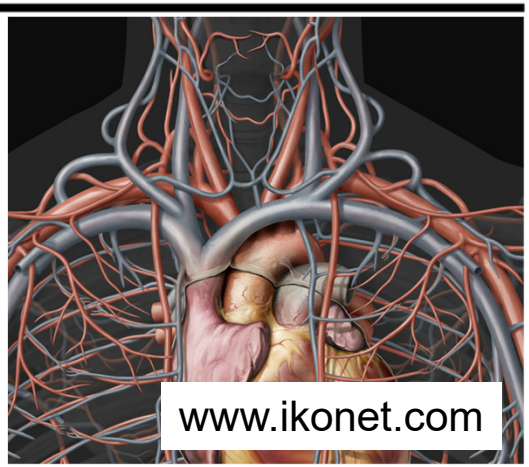
Radiotherapy and Oncology 2016

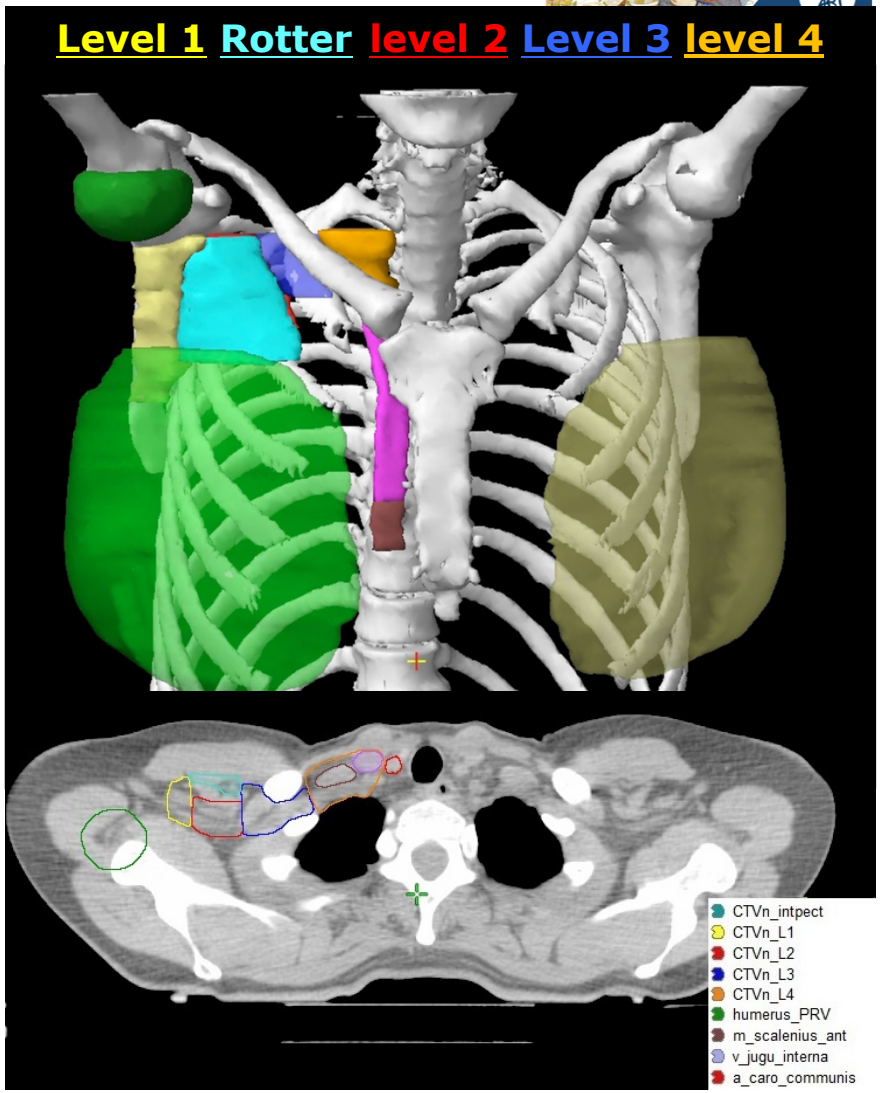
journal homepage: www.thegreenjournal.com

ESTRO breast cancer consensus guidelines

ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer, version 1.1 ☆

Link available on X @BOffersen
1 hour delineation guide for early breast cancer





Take home message 2

Make sure to follow the guidelines

How to initiate adaptive breast cancer RT?

The DBCG RT Nation study

Physics and Imaging in Radiation Oncology 27 (2023) 100485

Contents lists available at ScienceDirect

Physics and Imaging in Radiation Oncology

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

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 Lorenzen [i], Carsten Brink [i], Lise Bech Jellesmark Thorsen [a,c], Birgitte Vrou Offersen [a,b,c], Stine Sofia Korreman [b,c,j,*]

[a] Department of Experimental Clinical Oncology, Aarhus University Hospital, Denmark
[b] Danish Center for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark
[c] Department of Oncology, Aarhus University Hospital, Aarhus, Denmark
[d] Department of Oncology, Vejle Hospital, University Hospital of Southern Denmark, Denmark
[e] Department of Oncology, Zealand University Hospital, Department of Clinical Oncology and Palliative Care, Næstved, Denmark
[f] Department of Oncology, Copenhagen University Hospital - Rigshospitalet, Copenhagen, Denmark
[g] Department of Medical Physics, Aalborg University Hospital, Aalborg, Denmark
[h] Department of Oncology, Copenhagen University Hospital – Herlev and Gentofte, Copenhagen, Denmark
[i] Laboratory of Radiation Physics, Department of Oncology, Odense University Hospital, Odense, Denmark
[j] Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

Data flow for the end-to-end framework

All loco-regional breast cancer RT 2008-2016 across Denmark

Assessed for eligibility
DBCG Database
(n=9861)

Ineligible (total) (n=761)
Non-Danish centre (n=355)
No RT centre (n=406)

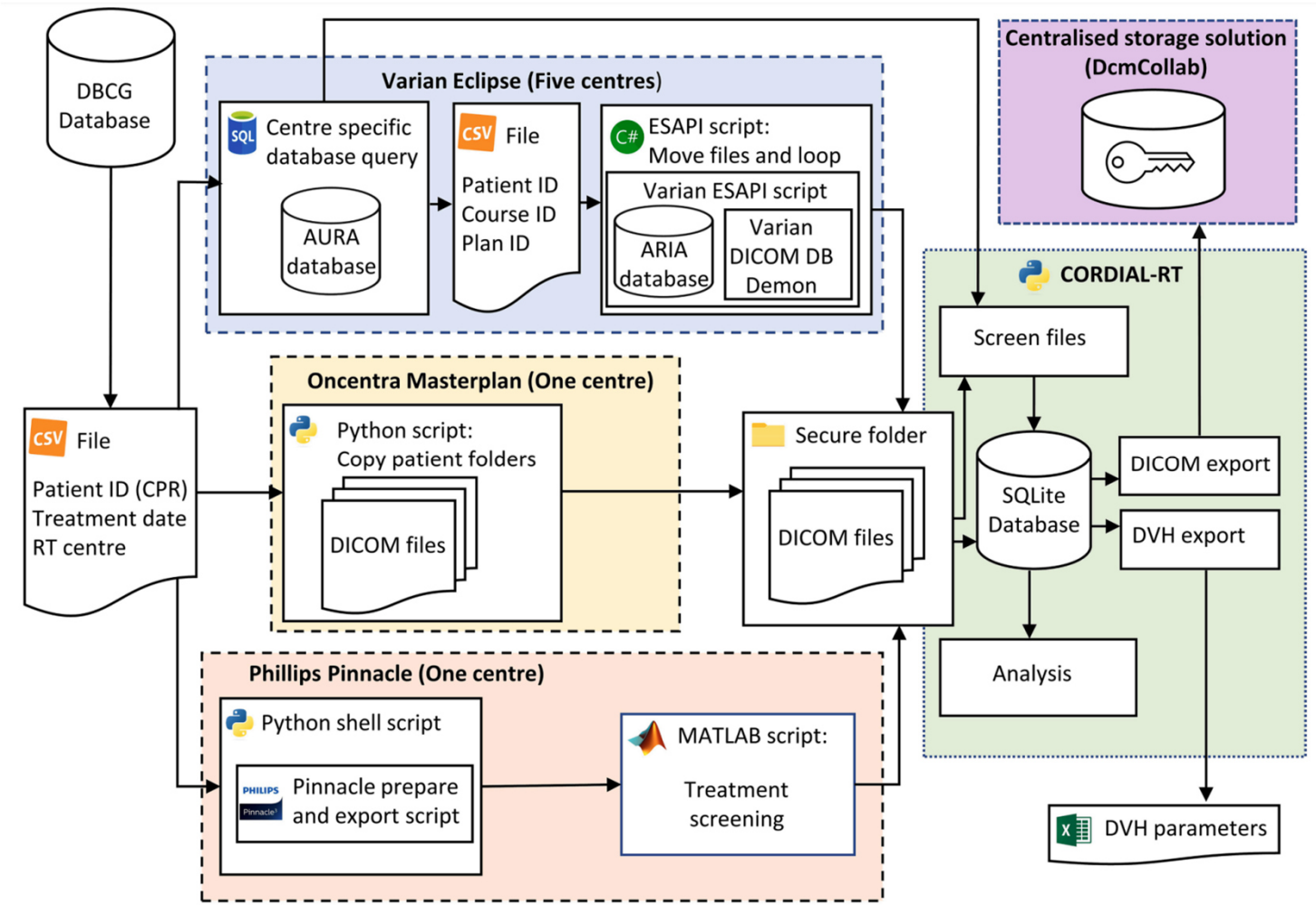
Eligible available for study
(n= 9100)

Missing data (total) (n=1187)
Data export unsuccessful (n=826)
Missing or inconclusive data (n=361)

Excluded (total) (n=465)
Bilateral RT (n=261)
Non breast RT (n=87)
RT cancelled (n=54)
Treatment later than 2017 (n=15)
No lymph nodes delineate (n=48)

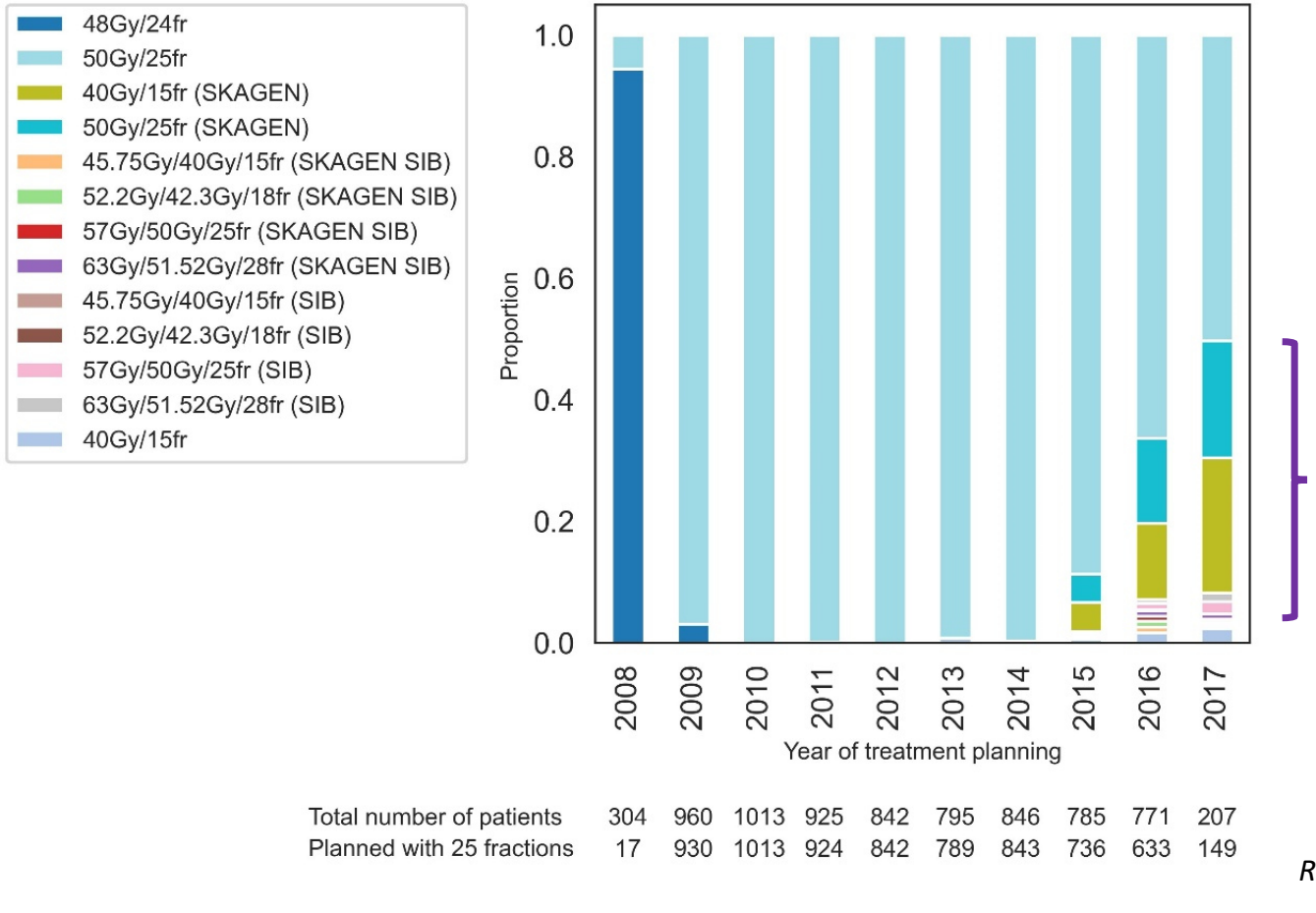
Patients included
(n= 7448)

Non-protocol (n = 7042)
Skagen 1 trial (n = 407)



Change of guideline for fractionation

Jan 1, 2009: 48Gy/24fr → 50Gy/25fr
Spring 2015: The DBCG Skagen trial 1 starts



Randomised patients
DBCG Skagen trial 1

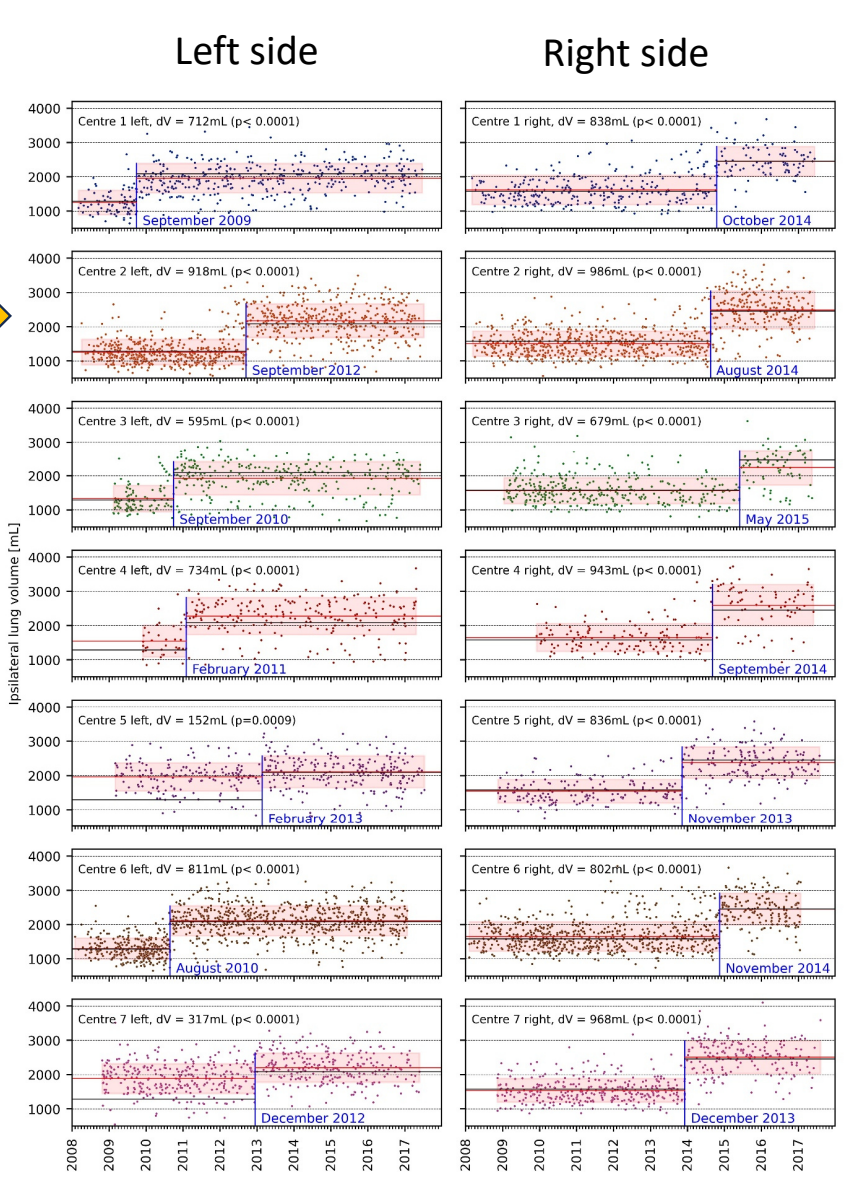
Refsgaard L et al, manuscript in preparation

Guideline for gating

What is the effect of respiratory gating separated by center & laterality?

Aarhus

Centres 5 & 7 started before 2008



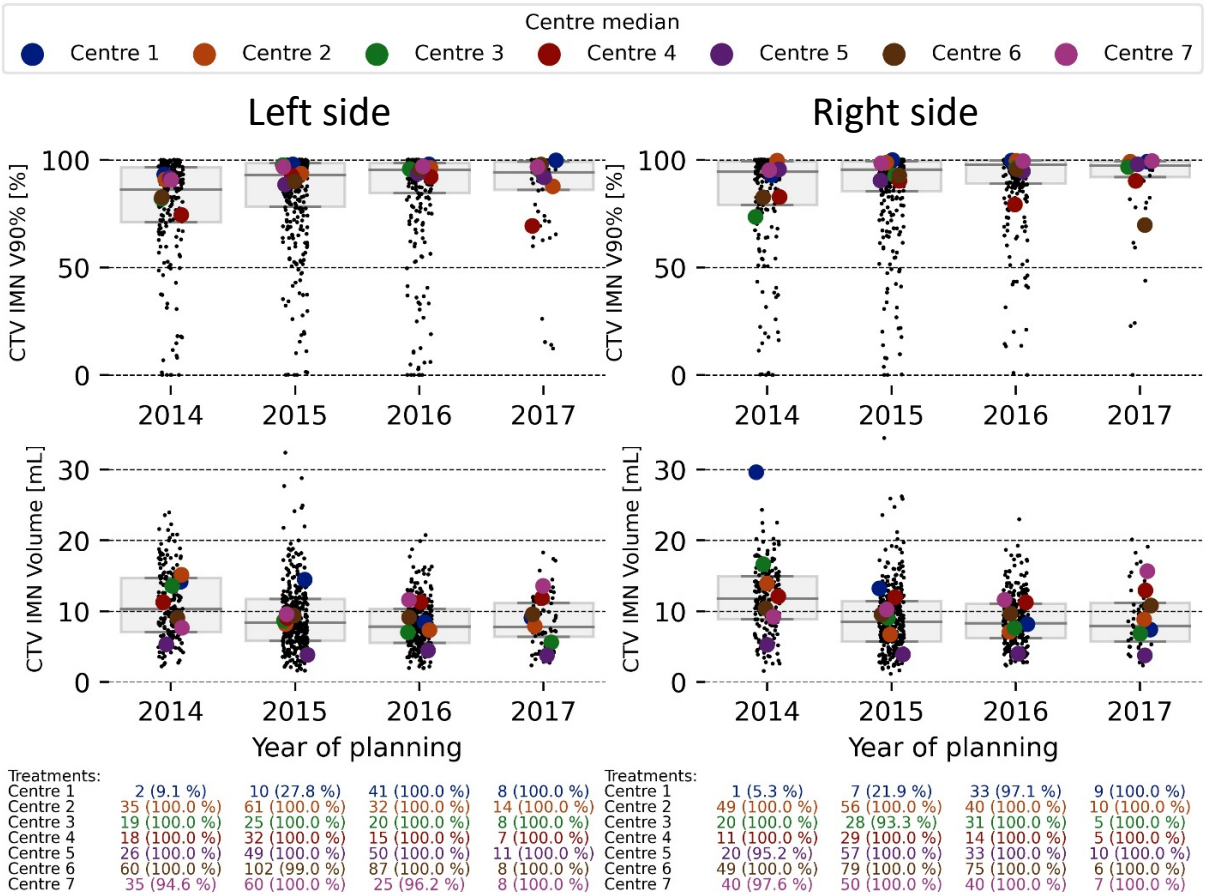
Different timing
- Per center
- Per laterality

Different techniques
- dV
- compliance

Refsgaard L et al, manuscript in preparation

Delineation of the internal mammary nodes

The volume of CTVn_IMN declines from 2015 (ESTRO guideline)
After 2014, higher and less variation in dose to CTVn_IMN



Refsgaard L et al, manuscript in preparation

Take home message 3

Develop future guidelines through clinical trials

Inter-center variations in contouring and planning compromises in the DBCG Skagen trial 1

EL Lorenzen[1], MS Thomsen[2], T Bechmann[3], M Berg[4], MH Nielsen[5], HV Hansen[6], K Boye[6], T Lörincz[7], I Jensen[8], SA Al-Rawi[9], MMB Nielsen[9], LW Matthiessen[10], K Andersen[10], MR Jensen[11], J Overgaard[12], BV Offersen[12]

[1]Odense University Hospital, Laboratory of Radiation Physics, Odense, Denmark; [2]Aarhus University Hospital, Department of Medical Physics, Aarhus, Denmark; [3]Vejle Hospital, Department of Oncology, Vejle, Denmark; [4]Vejle Hospital, Department of Medical Physics, Vejle, Denmark; [5]Odense University Hospital, Department of Oncology, Odense, Denmark; [6]Rigshospitalet, Department of Oncology, Copenhagen, Denmark; [7]Aalborg University Hospital, Department of Oncology, Aalborg, Denmark; [8]Aalborg University Hospital, Department of Medical Physics, Aalborg, Denmark; [9]Zealand University Hospital, Department of Oncology and Palliative Care, Naestved, Denmark; [10]Herlev and Gentofte Hospital, Department of Oncology, Herlev, Denmark; [11]Rigshospitalet, Danish Breast Cancer Cooperative Group Secretariat, Copenhagen, Denmark; [12]Aarhus University Hospital, Department of Experimental Clinical Oncology, Aarhus, Denmark

Presented at ESTRO conference 2022

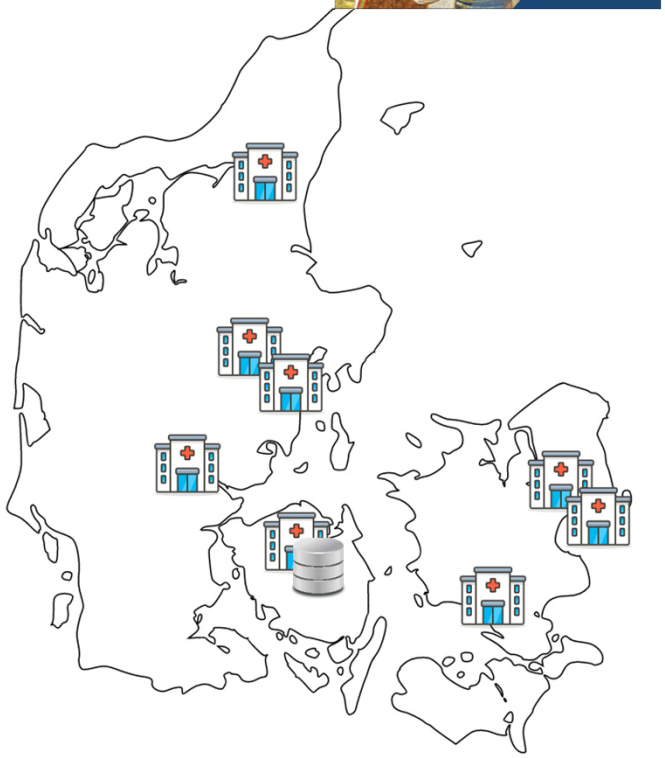
Background

DBCG Skagen trial 1: 40Gy/15fr- vs 50Gy/25fr RT in 2879 pN+ breast cancer patients

DICOM-data from the **seven Danish centers** stored at DCMcollab

Inter-center variation target and OAR:

- Contouring
- Doses



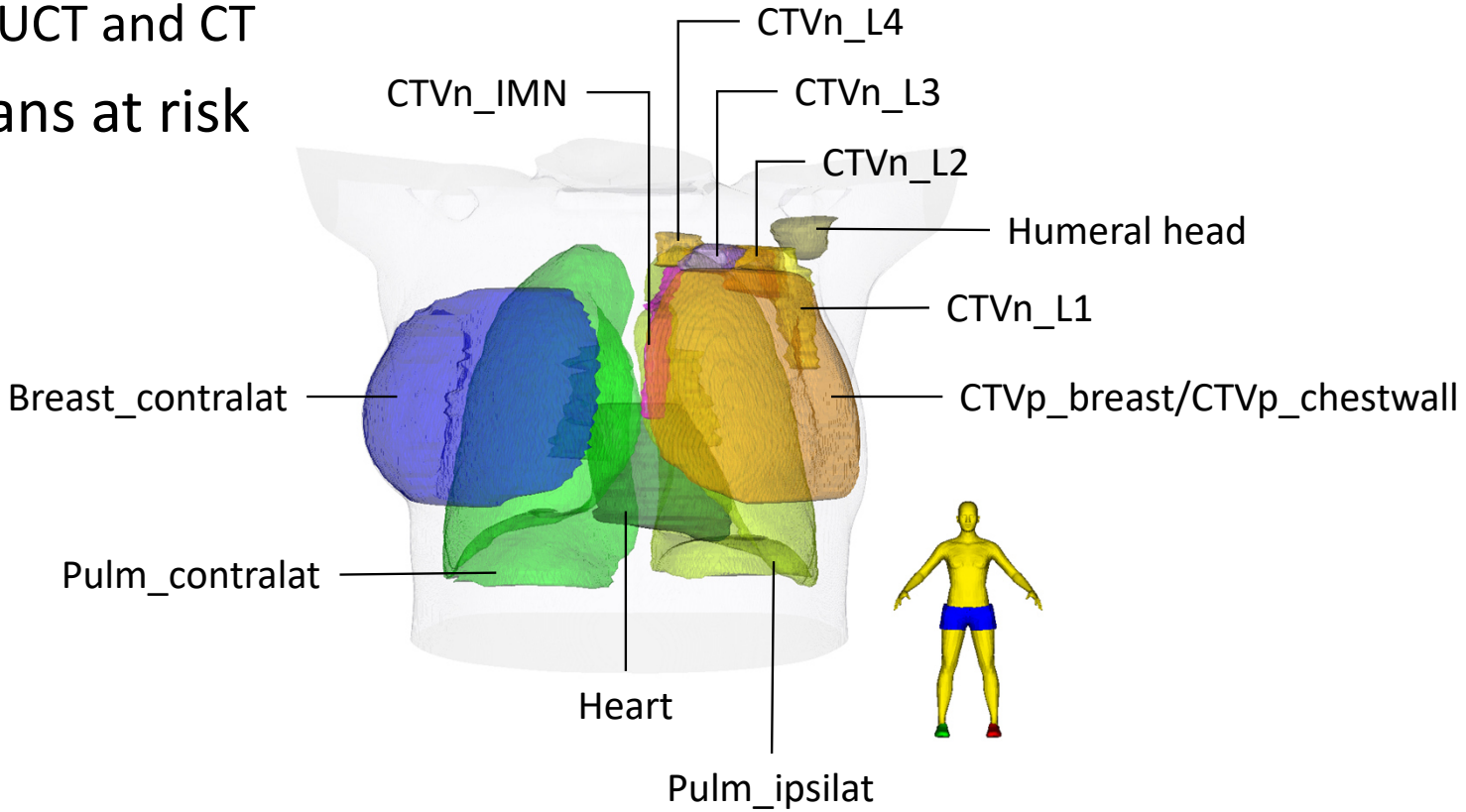
The DICOM Collaboration system

DcmCollab

Presented at ESTRO conference 2022

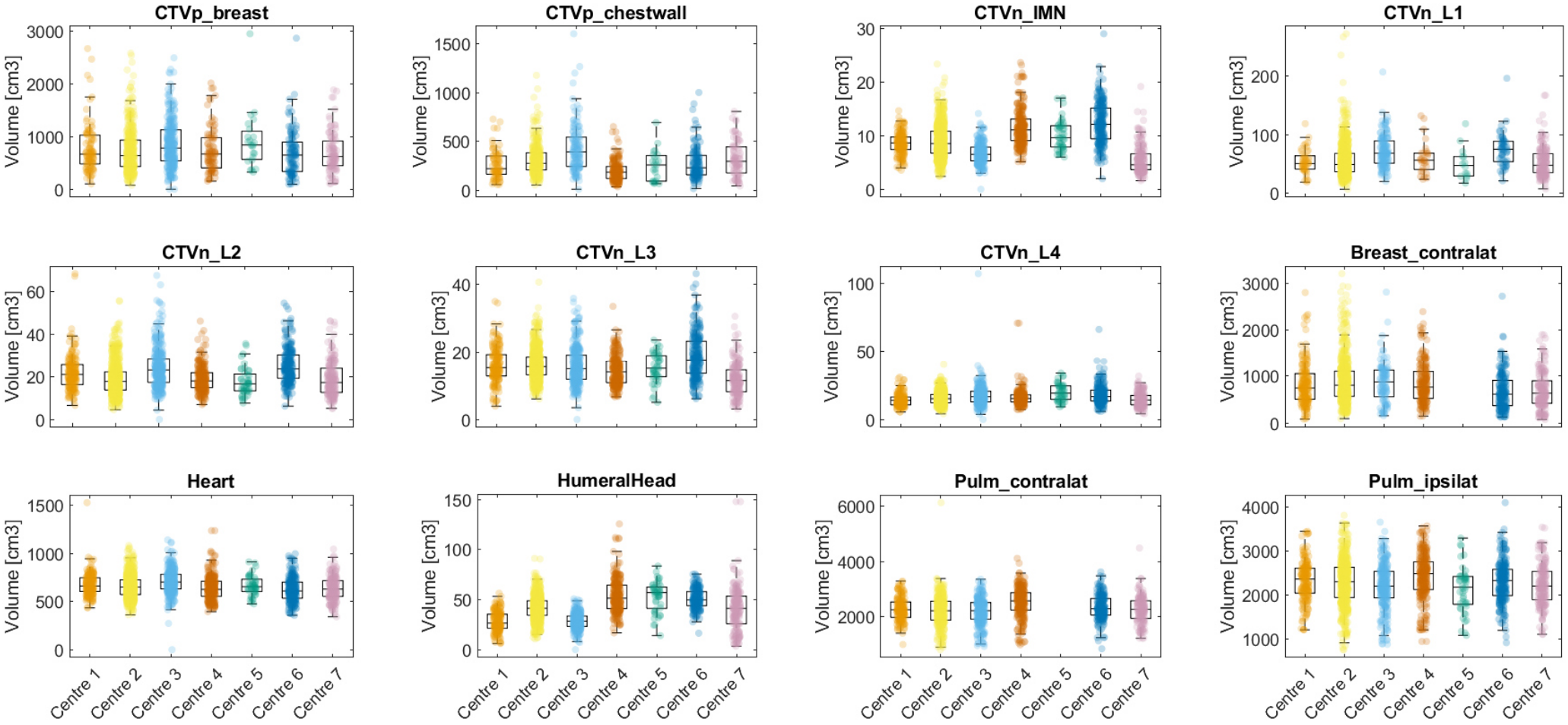
Material

- DICOM data from 1874 patients
  - PLAN, DOSE, STRUCT and CT
- 12 target and organs at risk



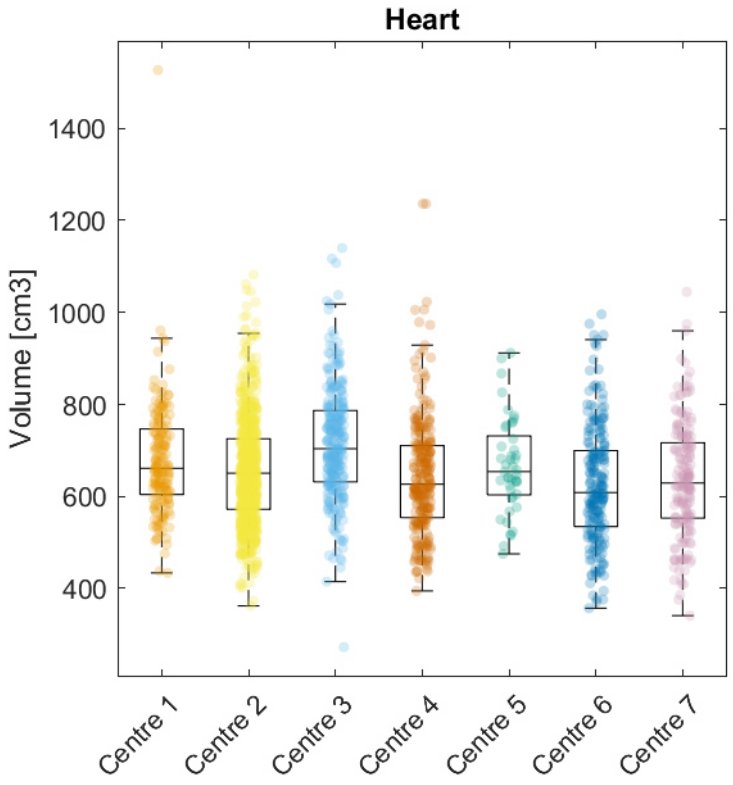
Presented at ESTRO conference 2022

Intra-centre variation in volume – low variation for most



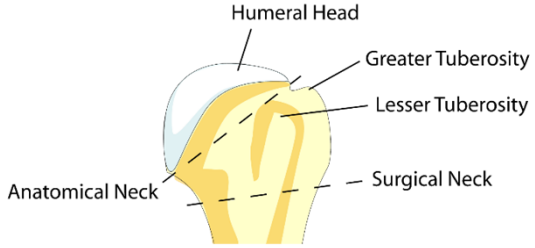
Volume - heart

Guidelines work!

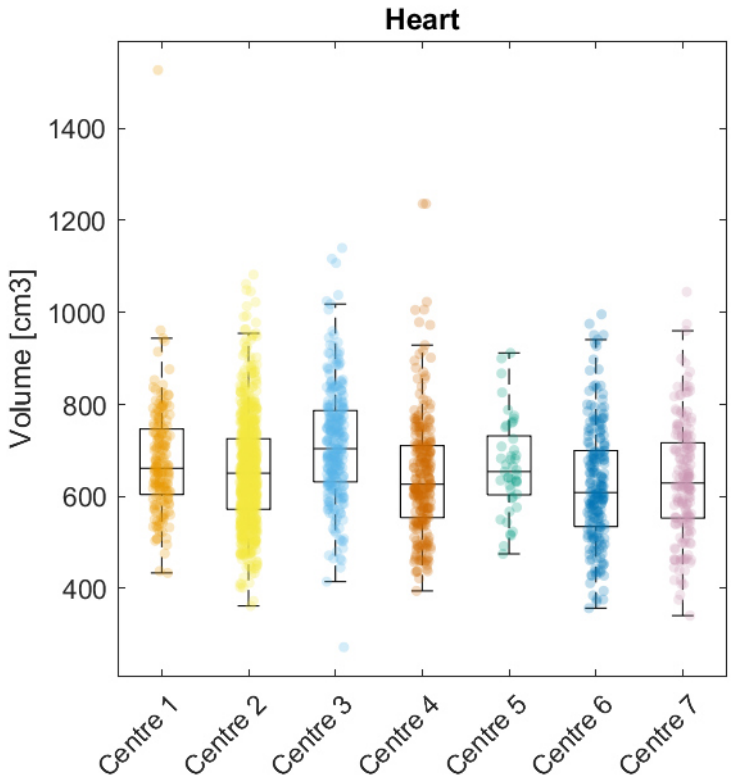


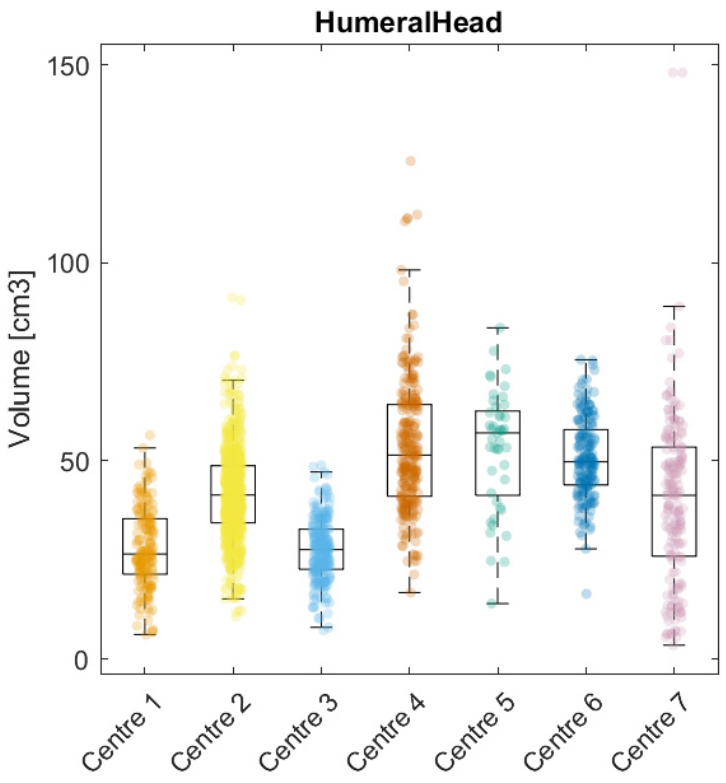
Presented at ESTRO conference 2022

Volume – heart and humeral head



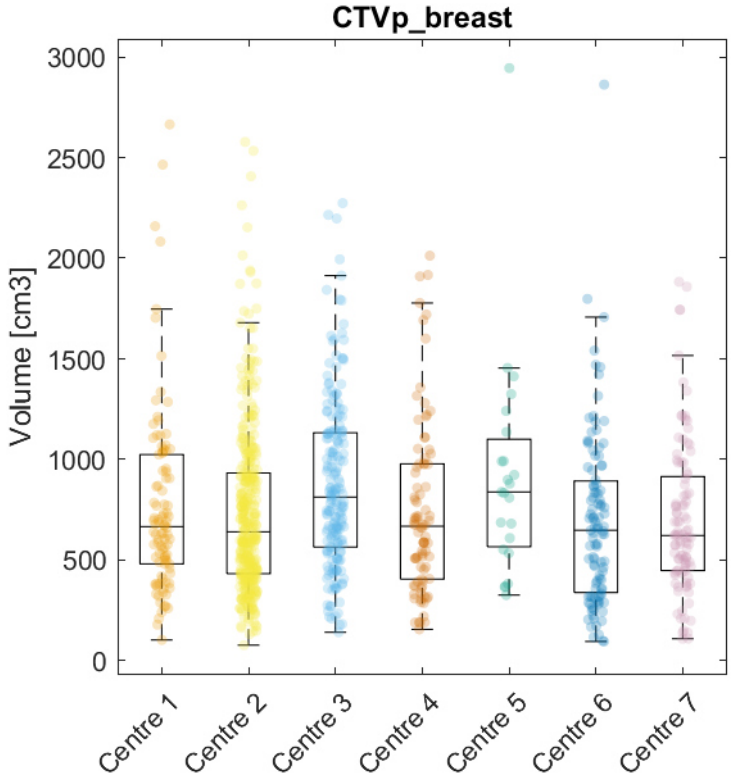
Guidelines works!
… when they exists





Presented at ESTRO conference 2022

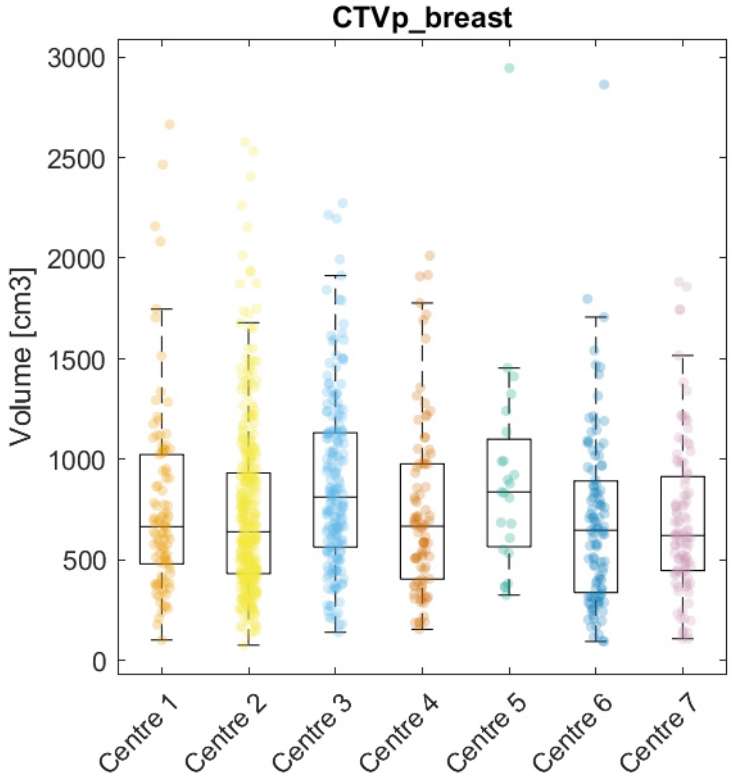
Volume – CTV breast

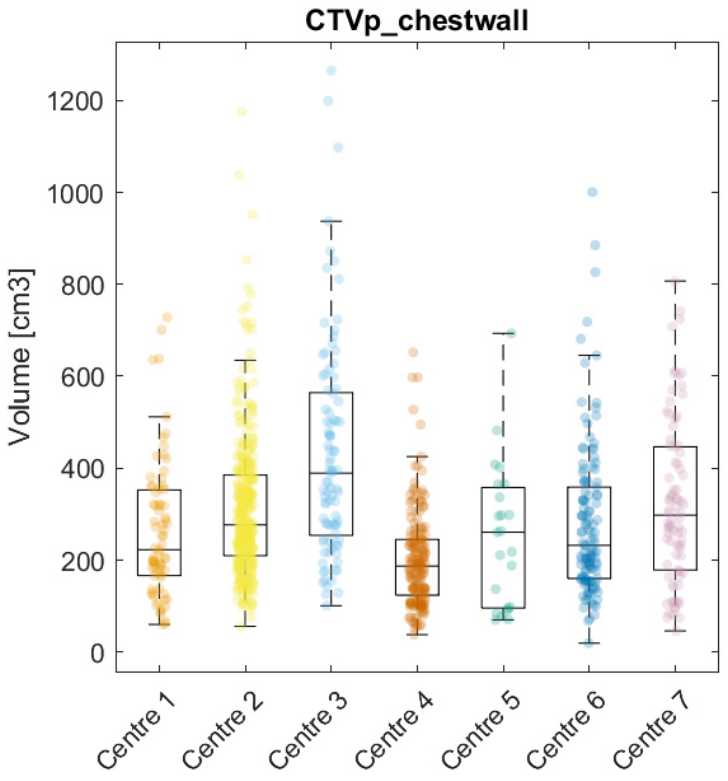


Presented at ESTRO conference 2022

Volume – CTV breast and CTV chest wall

Skin-crop-margin
Delineation differences?
<u>Needs further investigation</u>

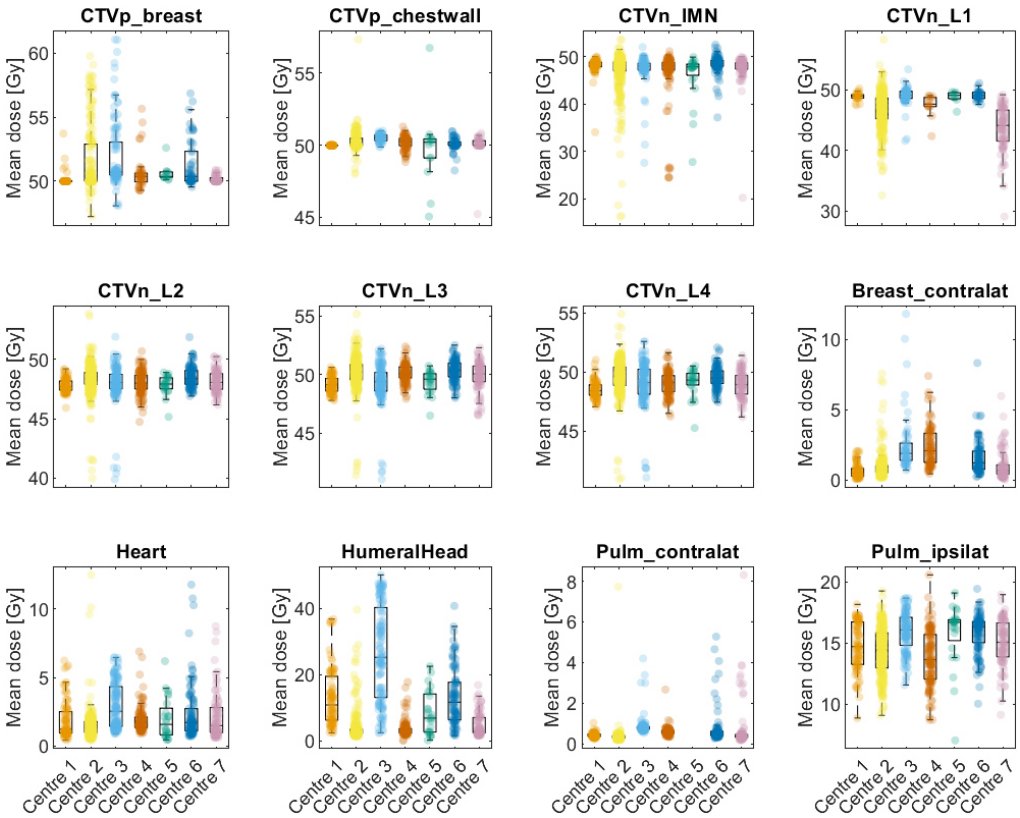




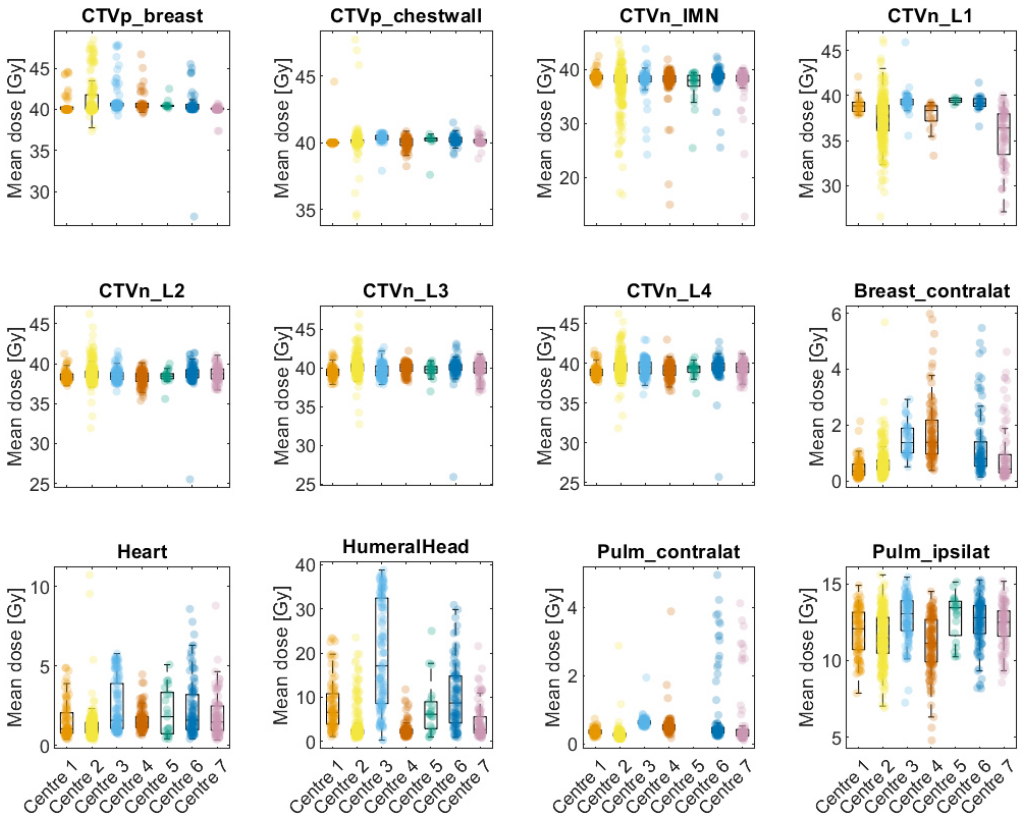
Presented at ESTRO conference 2022

Intra-centre variation in dose – pronounced for several ROI's

Normo-fractionated



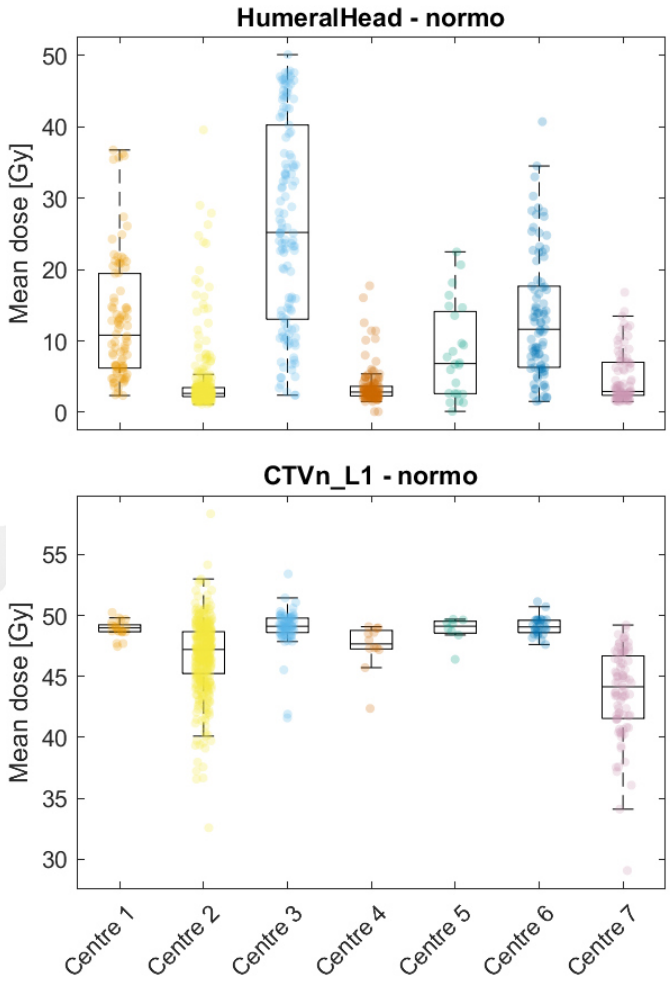
Hypo-fractionated

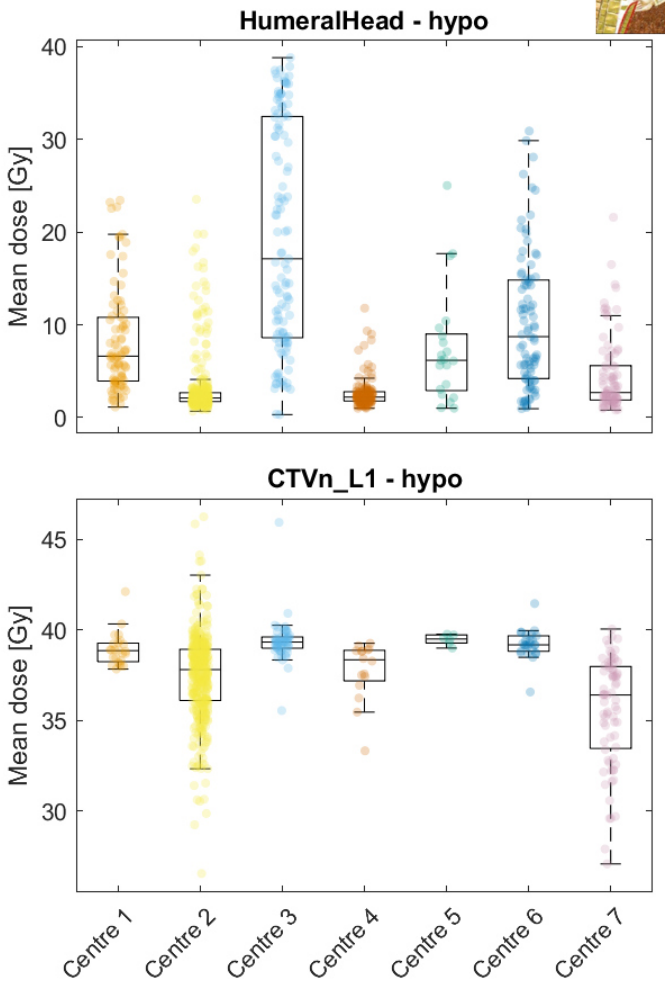


Presented at ESTRO conference 2022

Level 1 - humeral head

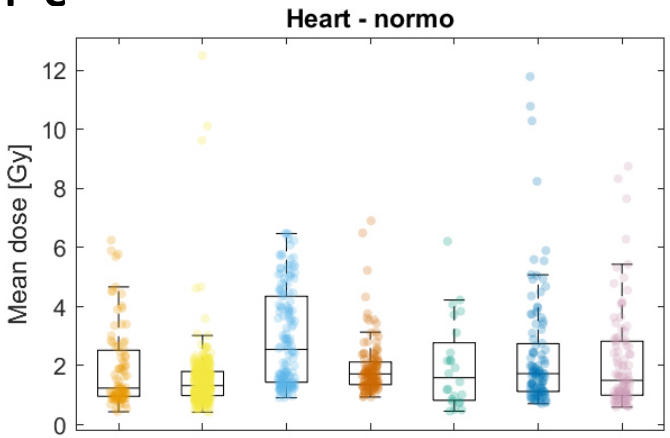
Must be linked to risk of recurrence & arm morbidity

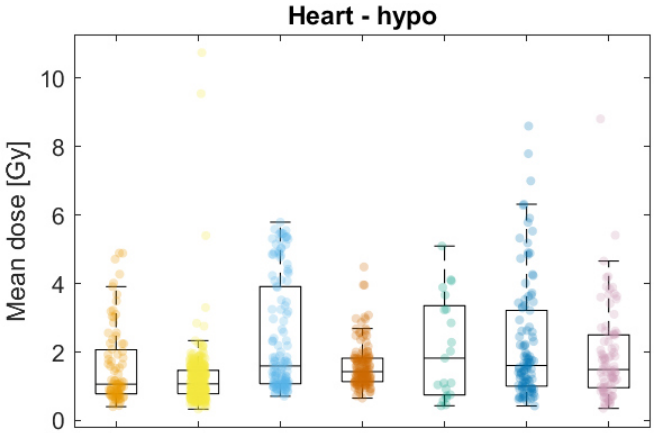


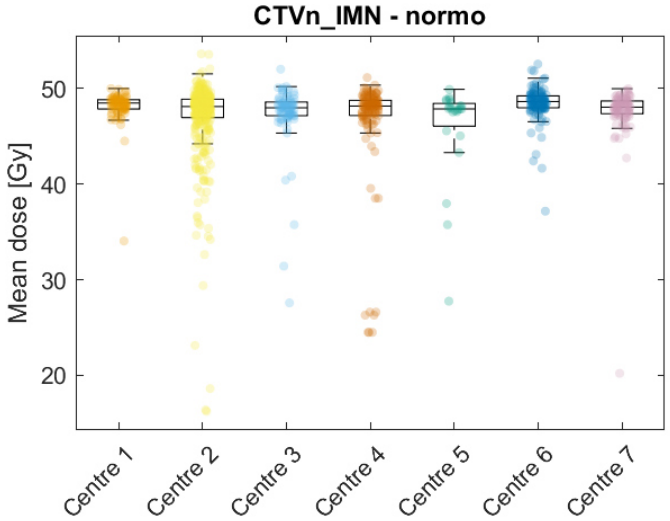


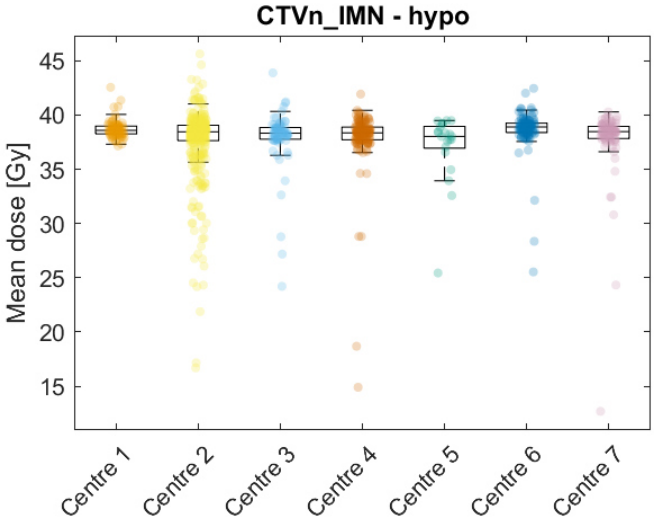
Presented at ESTRO conference 2022

IMN - Heart









Presented at ESTRO conference 2022

Results so far

Intra-centre variation in delineation was limited for most ROI's

Some variation in doses, likely due to different clinical compromises

- Does this translate into different risk of recurrence and morbidity?

- Results from the RT QA of the DBCG Skagen trial 1 & DBCG RT Nation study → evidence based dose constraints for doses to targets and OAR using adaptive RT

Presented at ESTRO conference 2022

Take home message 4:

International collaboration

Take home message 4:

International collaboration

ESTRO

Easy & fast access to current developments in different countries
Possible to use same stratifications, cut-off values etc
Hypotheses from your trial can be validated in another trial

→ Faster access to better treatment for patients

Adaptive management: what have we not to forget?

Big pressure towards new modern techniques (IMRT, VMAT) → but what are the dose constraints for heart, lung, humeral head etc versus doses to targets when combined with modern systemic therapy? → Phase IV studies/clinical trials can help us.

We must continue to develop RT through clinical studies and trials
→ Every patient should be included in minimum one clinical trial

THANKS!