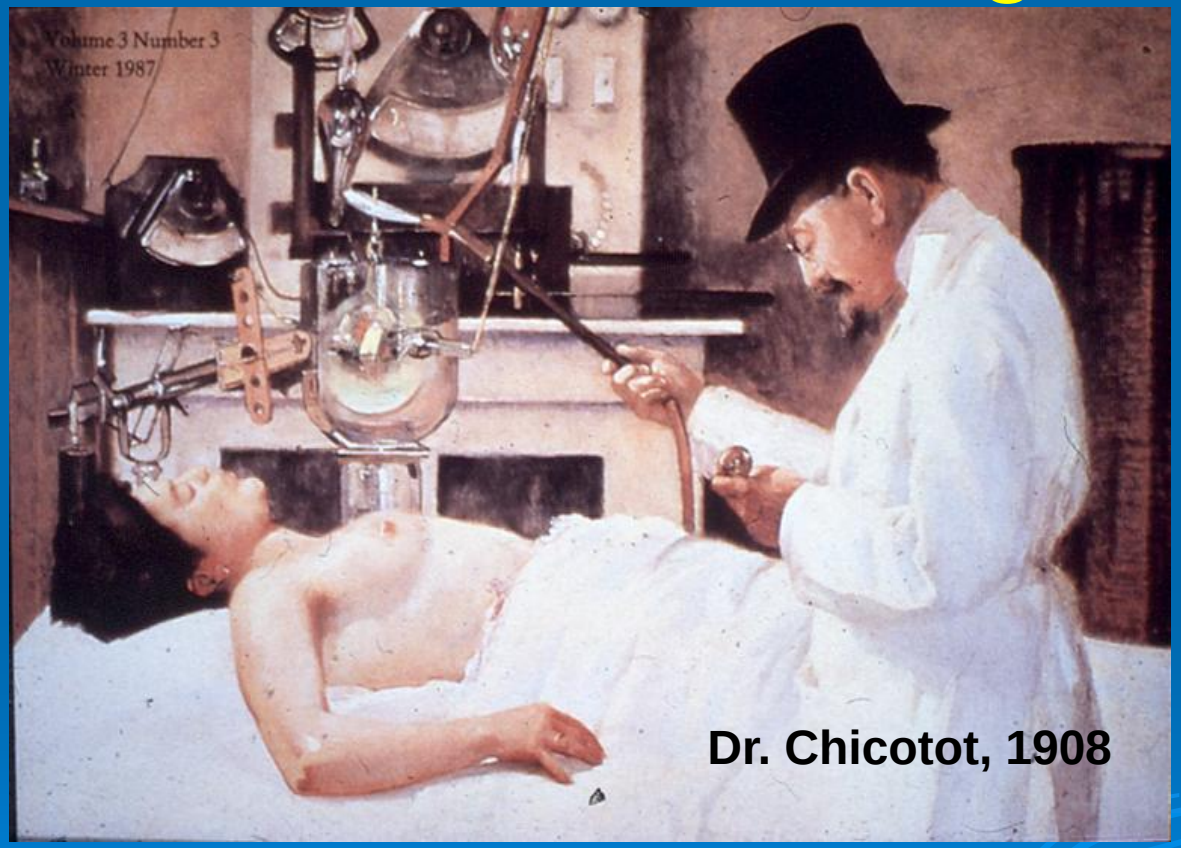
Danish Breast Cancer Group, DBCG

Radiotherapy of early breast cancer, status on the Skagen Trial



Dr. Chicotot, 1908

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Aarhus University Hospital

Danish Breast Cancer Group, DBCG

Moderately hypofractionated adjuvant radiotherapy of early breast carcinoma

CIRRO protocol IP030209
Hypofractionated *versus* standard fractionated whole breast irradiation to lymph-node negative breast cancer patients: a randomized phase II study *(DBCG HYPO)*

CIRRO protocol IP030109
Partial *versus* whole breast irradiation to women ≥ 60 years operated with breast conservation for low risk breast cancer: a randomized phase II study *(DBCG PBI)*

CIRRO protocol IP030315
Hypofractionated *versus* standard fractionated loco-regional radiotherapy of early node-positive breast cancer: a randomized phase II study *(DBCG HYPO II, Skagen Trial 1)*

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Randomization DBCG HYPO

stratification: institution, breast size 600 ml, systemic therapy and boost

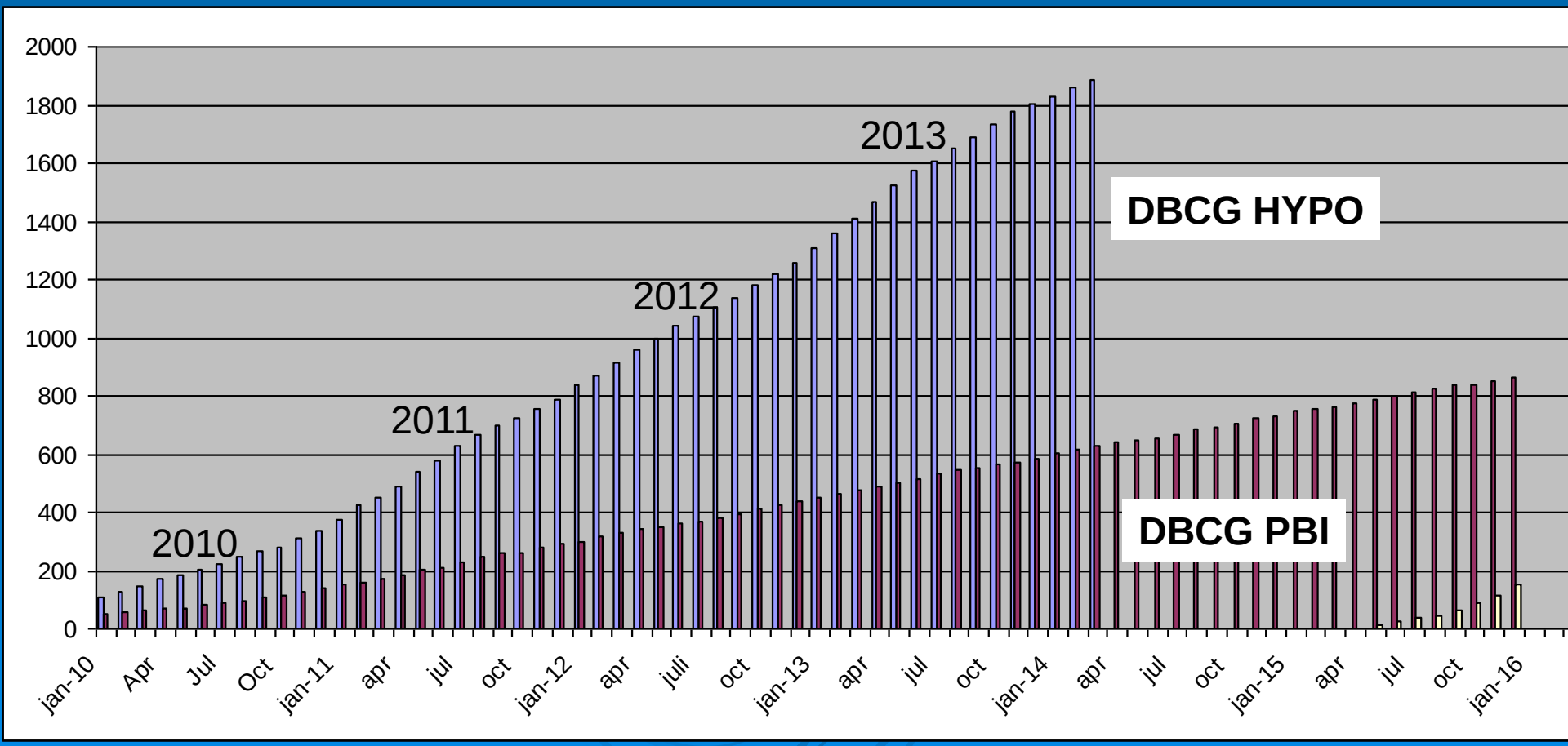
Woman >40 years
c. mammae
pT1-2, pN0(mi+),
ER/PgR +/-,
Grade I, II, III,
HER2 +/-,
Carc. in situ

50 Gy / 25 fractions

40 Gy / 15 fractions

Start May 2009
End Mar 2014

Primary endpoint:
≥ grade 2 breast induration after 3 years
Secondary endpoints:
Specialist and patient evaluated cosmesis.
Genetic risk profile for late morbidity.
Recurrence and localisation of recurrence, death and cause of death



Status DBCG HYPO

- Closed Mar 27th, 2014 with 1883 patients
- Data on morbidity, QA of RT, nationwide dose plan bank, effect of respiratory gating
- Substudies are planned
- Ph.d.project on genetic risk profile for late RT related morbidity
- Change of DBCG guideline as of Mar 27
- LBA submittes til ESTRO 35

CIRRO

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DBCG HYPO II, The Skagen Trial 1

- 75% of all Danish adjuvant RT treatments are residual breast RT only. The majority of these are now based on 40 Gy/15 fr
- 25% of our pts are candidates for loco-regional RT, which in most countries are provided as 50 Gy / 25 fr
- The UK and Holland have started loco-reg RT based on 40 Gy / 15 fr
- In Holland they provide boost as SIB (simultaneous integrated boost) as standard

CIRRO

AIM

- Assure a systematic and quality-controlled introduction of moderately hypofractionated loco-regional breast RT based on 40 Gy/15 fr in Denmark
- Introduce simultaneous integrated boost

Danish Breast Cancer Group, DBCG

Randomization

stratification: institution, surgical type, systemic therapy

Woman ≥18 years
c. mammae
pT1-3, pN1-3,
ER/PgR +/-,
Grade I, II, III,
HER2 +/-,
Primary syst therapy,
breast implant, connective tissue disease accepted

50 Gy / 25 fractions

40 Gy / 15 fractions

If she is a boost candidate, the boost will be provided as a SIB shortening the overall treatment time with 5 days

CIRRO

Endpoints

- Primary: arm lymphedema
- Secondary: DBCG morbididy as previously used incl photos, PROM, ROM, use of sleeve, recurrence (where and when)

This will take place before RT, then yearly 1-5 and 10

Statistics

- Null hypothesis: hypofractionated RT does not increase the risk of lympedema 3 yr after RT compared to normofractionated RT
- Lymphedema is ≥10% increased arm circumference 15 cm above / 10 cm below olecranon
- Cross-sectional study in Aarhus, 2007-12, 277 pts (ALND, taxane, reg RT 50 Gy) showed 10% with lymphedema median 3 yr FU
- We expect 10% risk of lymphedema, accept a 5% increase, 80% power, 1-sided test, 5% sign level, 5% yearly drop out rate, 3 yr accrual and 3 yr follow up
- Thus we need 131 events or 1012 patients with 3 yr follow up
- Accrual continues until 131 events/1012 pts are followed for 3 yr
- Thus potential for >2000 pts included

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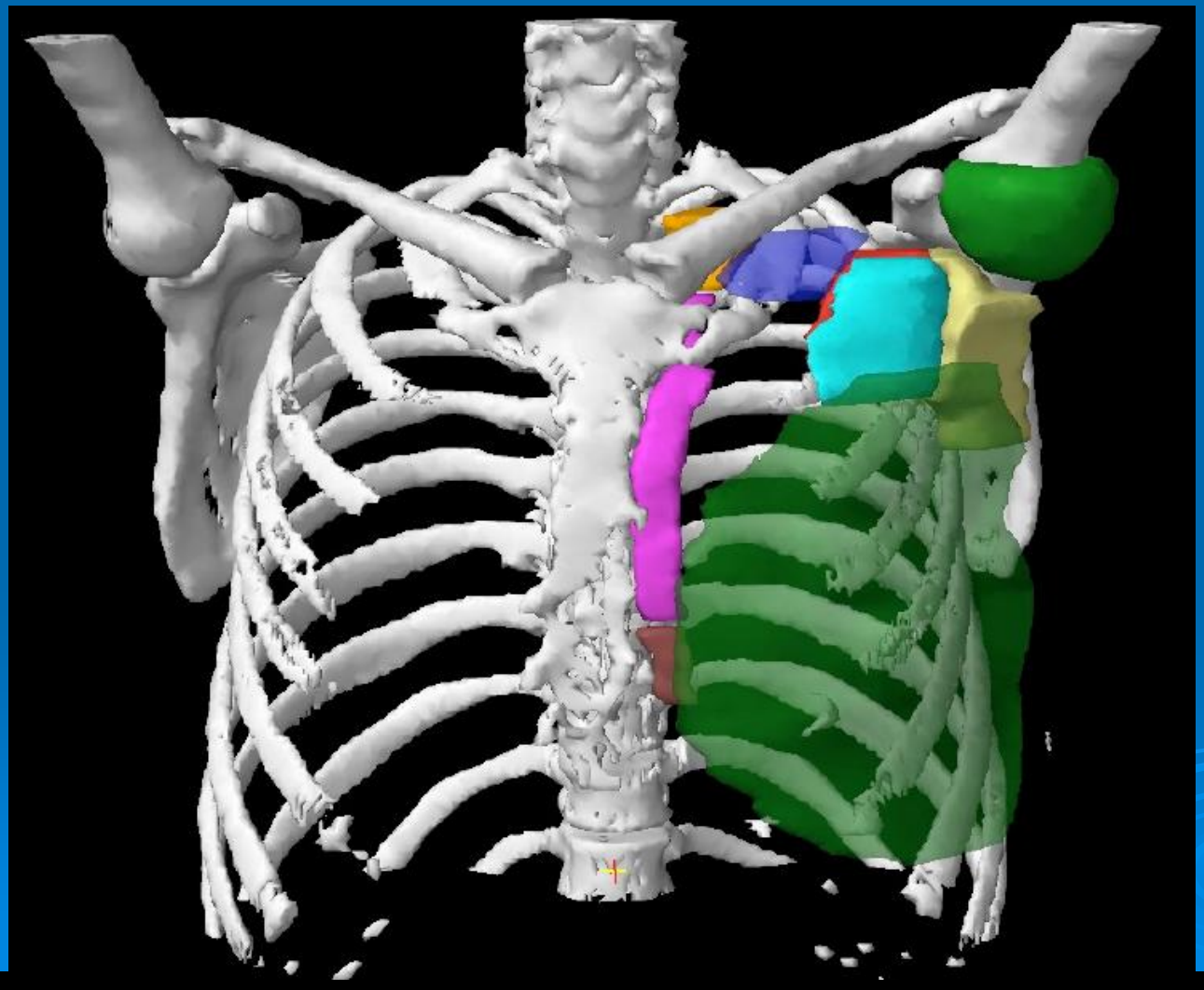
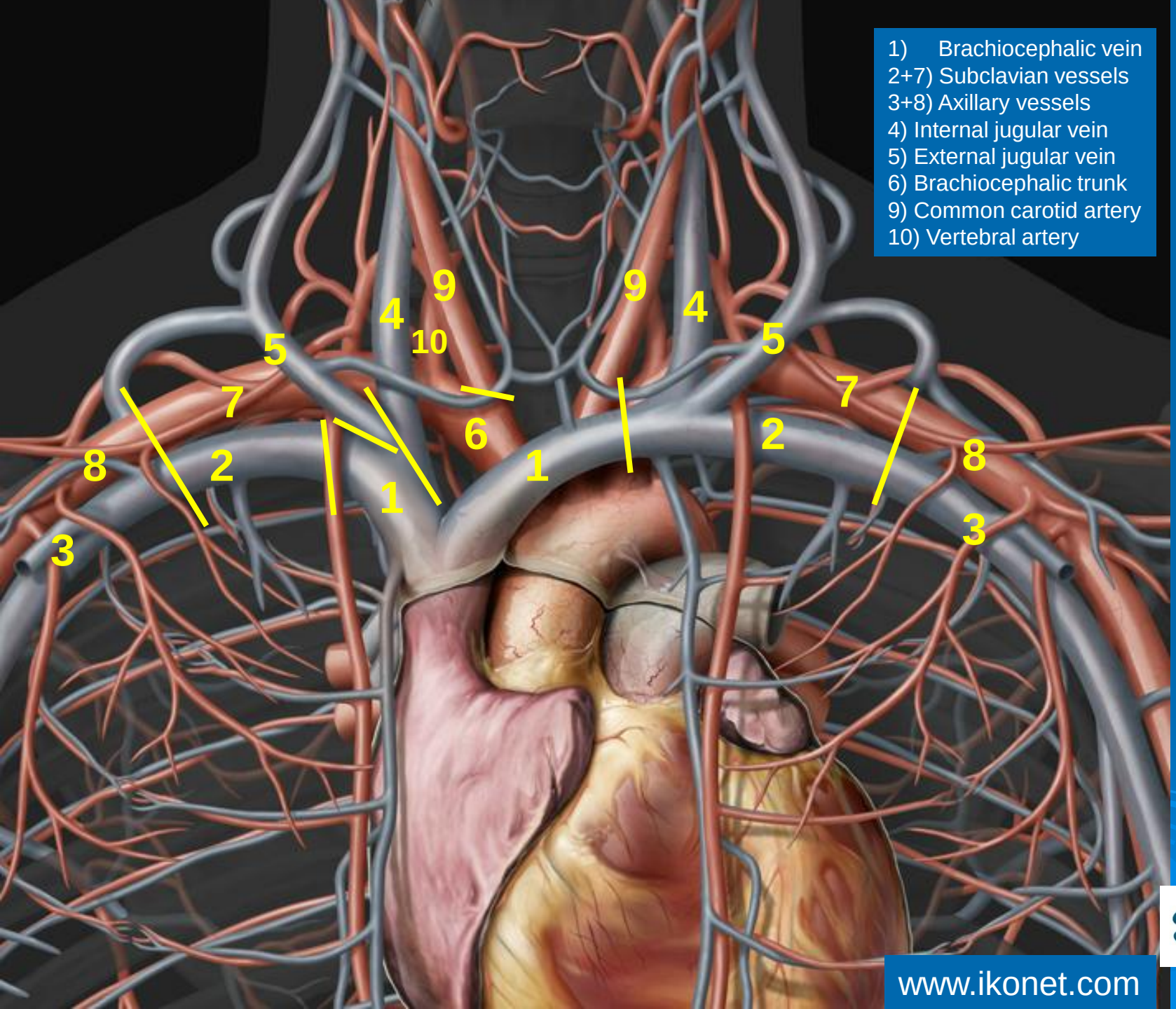
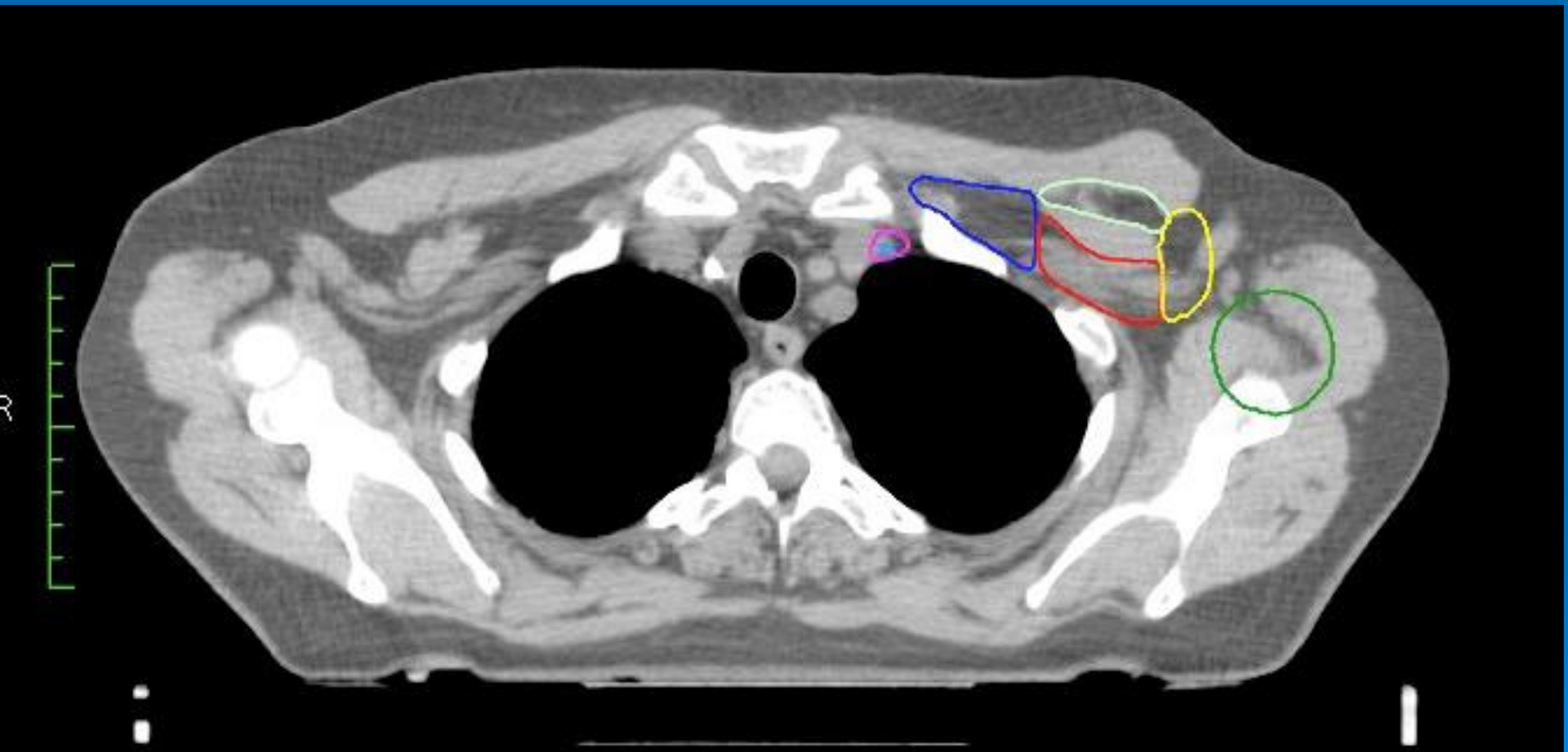
DBCG HYPO II
The Skagen Trial 1



Offersen BV, Boersma L, Kirkove C et al, Radiother & Oncol 2015



ESTRO delineation consensus



Offersen et al, Radiother & Oncol 2015

SIB

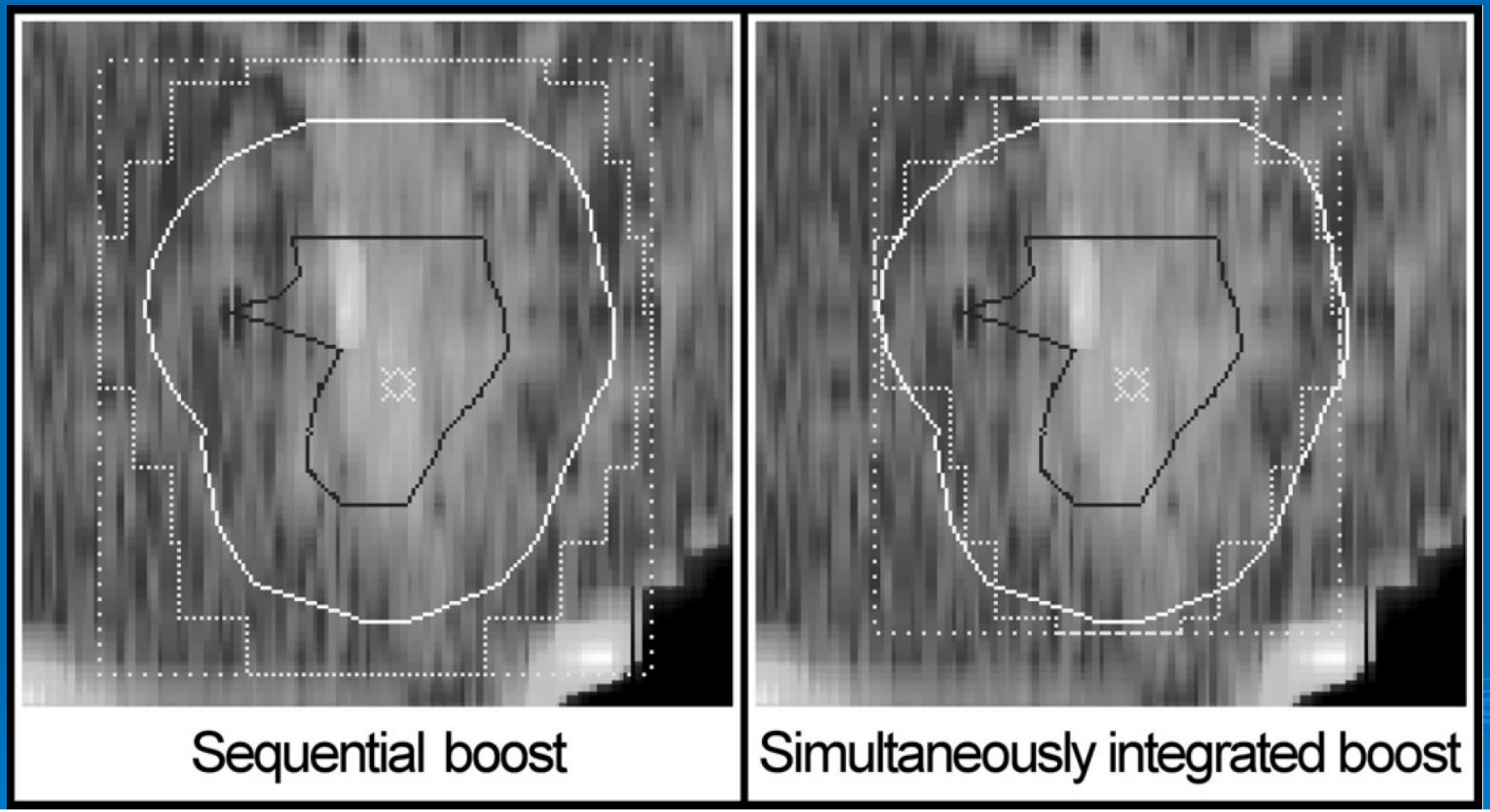
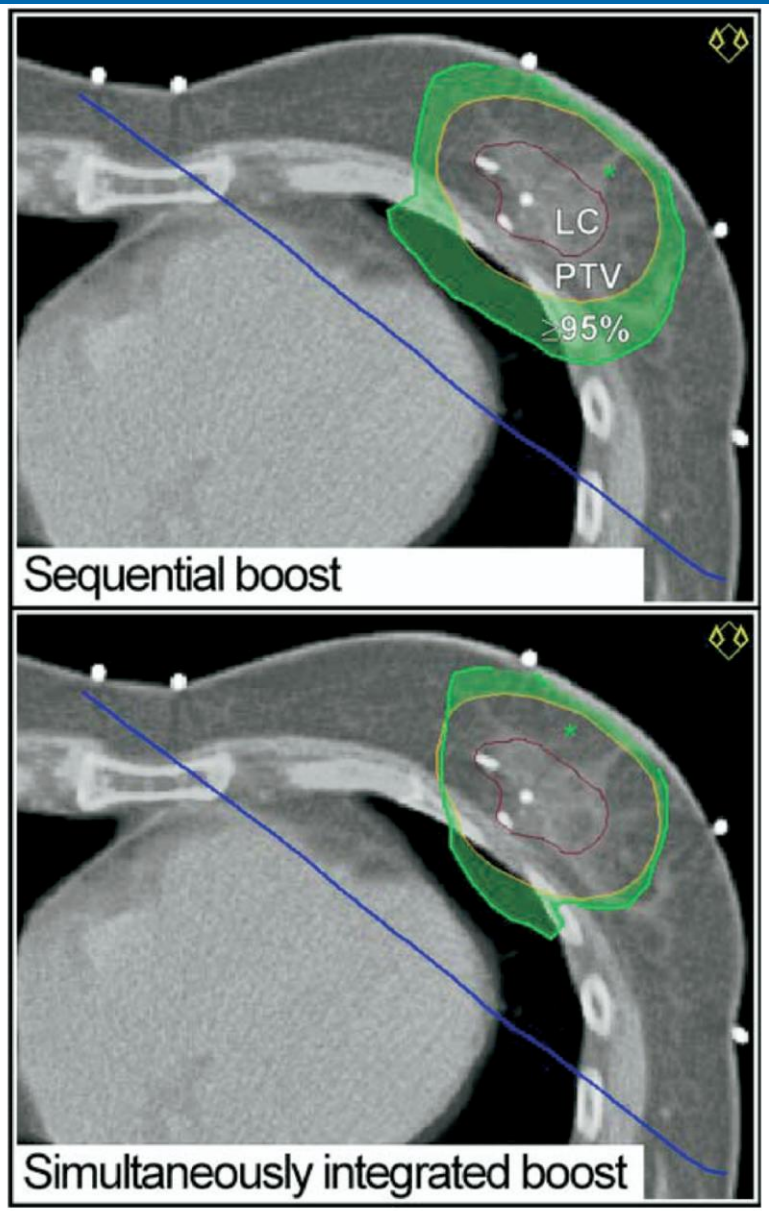


Fig. 1. Reconstructed radiograph from boost beam's-eye-view with sequentially planned and simultaneously integrated boost. With simultaneously integrated boost technique, multileaf collimator shielding (short dotted lines) can be applied without use of margins around boost planning target volume (white solid line), resulting in substantial reduction of excess volumes irradiated.

van der Laan et al, IJROBP 68: 1018-1023, 2007

SIB



Using a simultaneous integrated boost (SIB) a substantial amount of dose can be spared to the rest of the breast

van der Laan et al, IJROBP 68: 1018-1023, 2007

BED(2 Gy)-based doses for SIB

Randomisation arm	Standard boost	SIB / non-SIB breast / fr
50 Gy / 25 fr	16 Gy / 8 fr	63 Gy / 51.52 Gy / 28 fr
50 Gy / 25 fr	10 Gy / 5 fr	57 Gy / 50 Gy / 25 fr
40 Gy / 15 fr	16 Gy / 8 fr	52.2 Gy / 42.3 Gy / 18 fr
40 Gy / 15 fr	10 Gy / 5 fr	45.75 Gy / 40 Gy / 15 fr

Participating centres Skagen Trial

-and Australien
Sydney, Cairns

Current status on accrual Jan 1th, 2016

Aarhus	88
Rigshospitalet	24
Odense	7
Vejle	2
Stavanger	19
Tromsø	2
St.Luc	10
Dresden 1	2
Dresden 2	1
Total	155

Current status

- Online system for storage of photos
- Online system for collection of DICOM files
- 6 months visit from Milan to do QA on dose plans

- Finally finisihed the DBCG online system ☺
  - Kæmpe tak til alle på DBCG´s kontor for stor hjælp!

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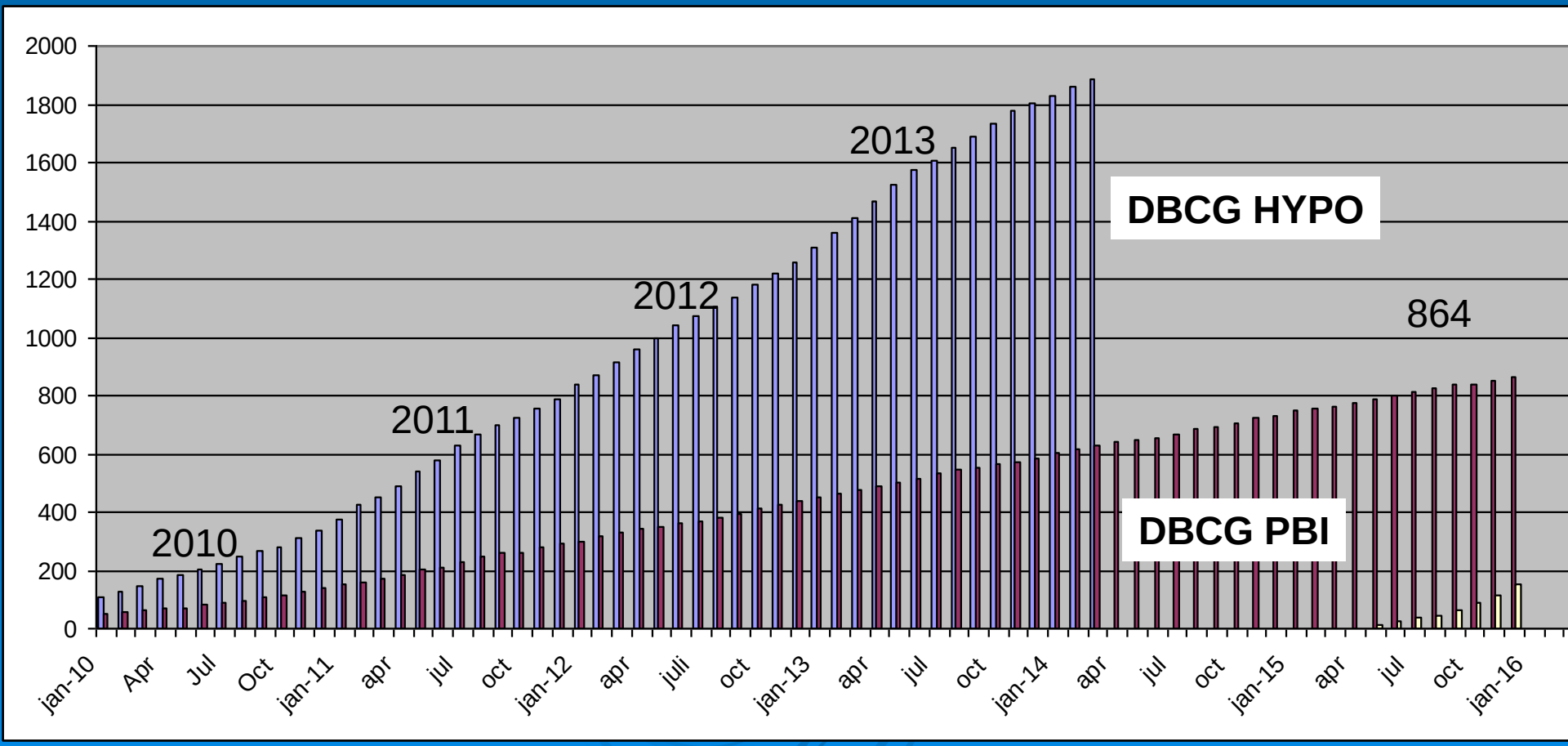
DBCG PBI

Presentation at EBCC Mar 2016



Thanks