Barcelona February 23, 2018

Screening with Tomosynthesis and Synthesized 2D:

The Norway experience

Professor dr.med. emeritus Per Skaane

Oslo University Hospital Ullevaal
Breast Imaging Center
Oslo / Norway
PERSKA@ous-hf.no

50 min

ClinicalTrials.gov

Tomosynthesis in the Oslo Breast Cancer Screening Program (DBT)

The study was closed December 2012

ClinicalTrials.gov Identifier: NCT01248546

- **Enrollment (one screening round): 25,547 / 34,742**
- ***Study Start Date:*** ***November 22, 2010***
- ***Completion Date:*** ***December 19, 2012***

(Final data collection date for primary outcome measure)

Oslo Tomosynthesis Screening Trial:

- **Part of the Norwegian Breast Cancer Screening Program**
- **Age group 50-69 years**
- **Two-view (CC and MLO) mammography**
- **Independent double reading with consensus (arbitration)**
- **5-point rating scale (1=normal/benign; 2-5=positive score)**
- **On-line reporting directly into the database of the Norwegian Cancer Registry**

Disclosure: Oslo Tomosynthesis Screening Trial
Equipment and support for additional reading provided by Hologic, Inc.

Oslo Mammography Screening

Mammography Screening Unit Aker

2 Hologic Dimensions

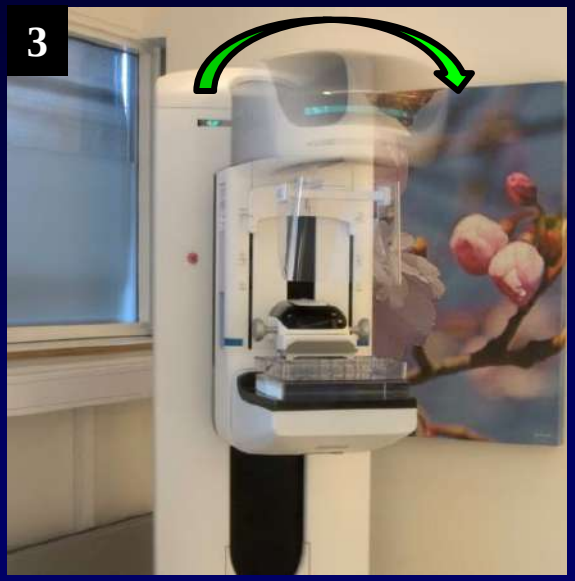
Ullevaal Hospital Breast Imaging Center: Batch reading and assessment

Hologic Dimensions w/ tomo-guided biopsy

Oslo Breast Cancer Screening: 2-view Tomosynthesis with C-View

Virtual Private Network – VPN (Closed User Group Network)

Oslo Mammography Screening Unit, Aker hospital: Hologic Selenia Dimensions



Scan (sweep) angle 15 gr.:
4 seconds

* Scan angle: 15 grade (arc)
* Projections: 15 low dose
* Tube motion: Continuous
* Scan time: 4 sec. (exposure)
* Tube movement (1-5): 8 sec.

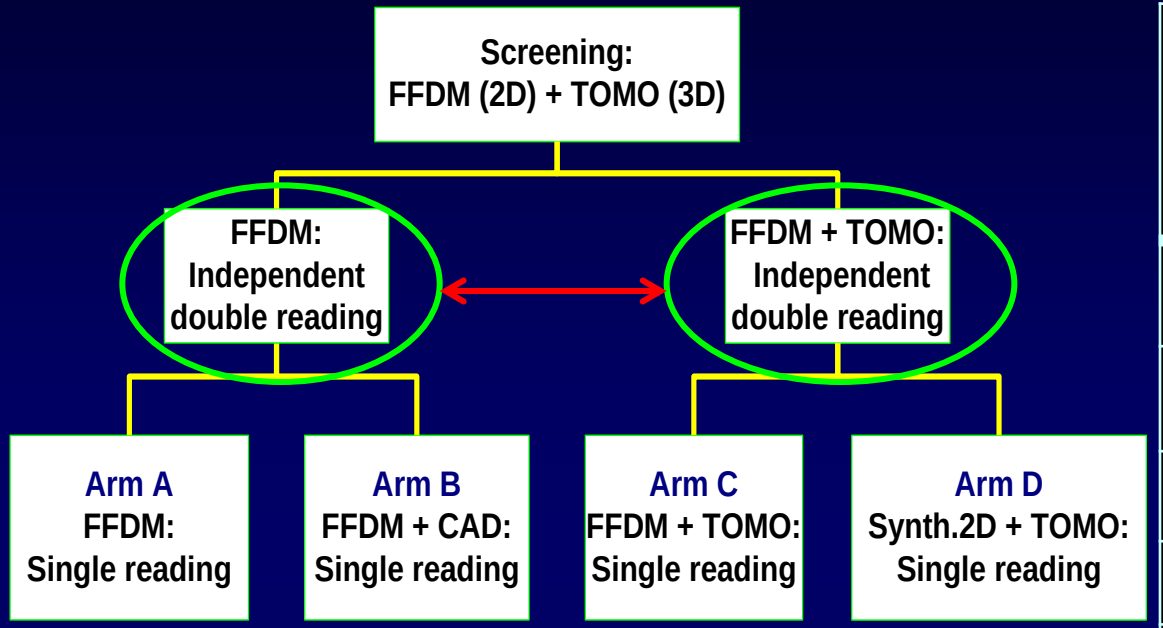
Examination time one woman: 5 minutes (2-view DBT+synth2D)
Women examined / hour: n = 10 (scheduled exams / hour: n = 12)

Digital Breast Tomosynthesis (DBT) screening: Norway 2015

A) From February 2014 ongoing:
Prospective study within the NBCSP comparing
2-view DBT+C-view
(Oslo County)
vs.
2-view conventional FFDM
(Buskerud County and Vestfold County as geographical controls)
(to be published soon in Radiology)

B) From 2015 ongoing:
Prospective study comparing FFDM vs. 2D+DBT
(Bergen/Hordaland County)

Oslo Tomosynthesis Screening Trial (OTST) : Preliminary results



SDC: Mammographic feature	Double reading A+B Pos	C+D Pos	Diff.
Circum. mass	9	9	0
Spicul. mass	33	42	9
Distortion	9	20	11
Asymm. dens	4	5	1
Microcalc's	28	29	1
Calc+dens.	7	14	7
Total	90	119	29

SDC: Screening-detected cancer

Eur Radiol
DOI 10.1007/s00330-013-2820-3

BREAST

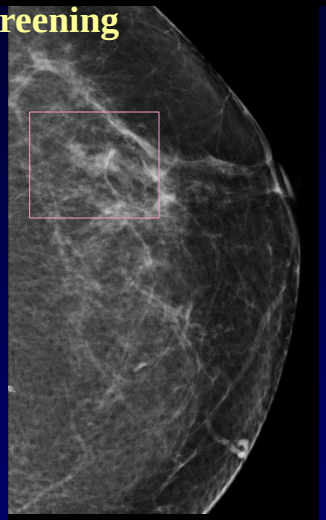
Prospective trial comparing full-field digital mammography (FFDM) versus combined FFDM and tomosynthesis in a population-based screening programme using independent double reading with arbitration

Per Skaane · Andriy I. Bandos · Randi Gullien · Ellen B. Eben · Ulrika Ekseth · Unni Haakenaasen · Mina Izadi · Ingvild N. Jebsen · Gunnar Jahr · Mona Krager · Solveig Hofvind

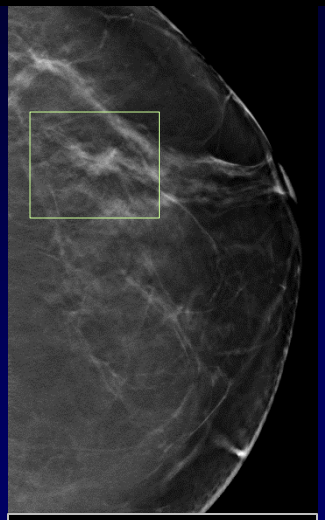
Skaane P et al.:
Eur Radiol 2013;23:2061-2071

Cancer detection: rel. increase (2D+TOMO) vs. (2D): 32%

Subtle preclinical cancers: A challenge in DBT screening

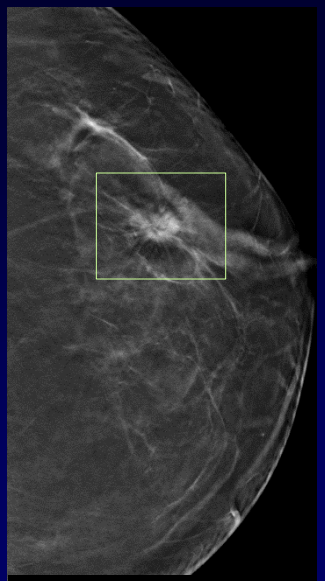


FFDM Lcc 11.01.2011

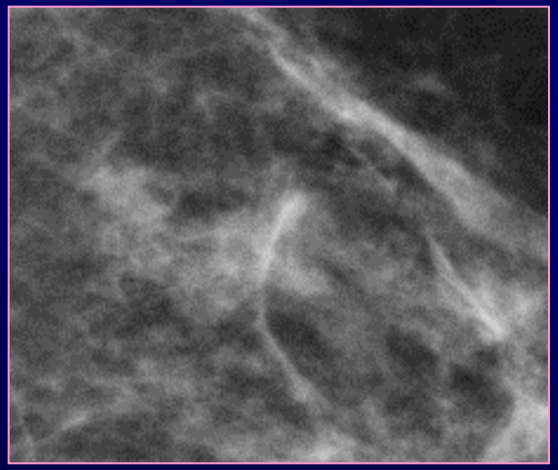


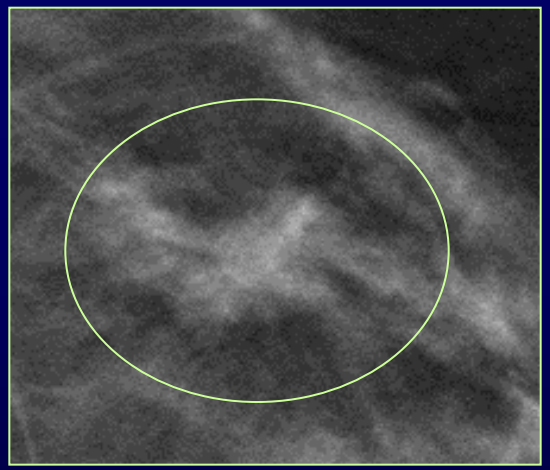
DBT Lcc 11.01.2011

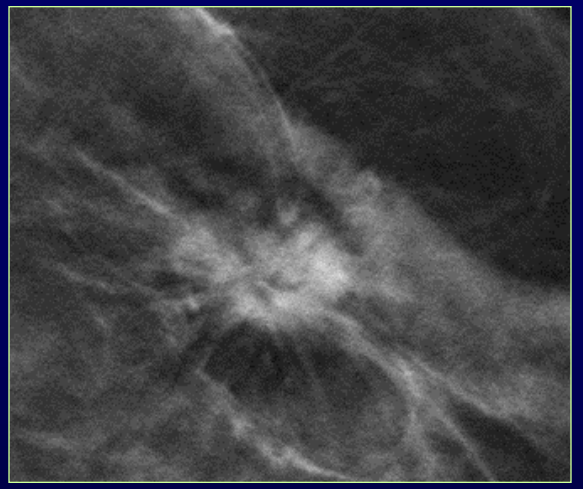
2 years



DBT Lcc 12.01.2013







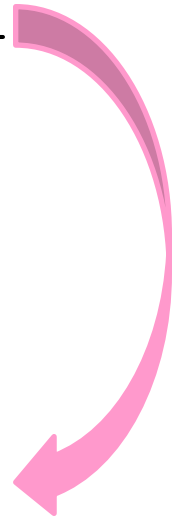
Reader (Arm)	A	B	C	D
Score 11.01.2011	1	1	3	1
Reading time (sec)	84	61	209	116
Recalled for assessment: FN work-up (faulty assessment !)				

Histology 02.2013:
Invasive ductal carcinoma (IDC)
G2, 14 mm, N1 (+ DCIS G3 18 mm)

Oslo Tomosynthesis Screening Trial (OTST) : Final results *

Screen-detected cancer (SDC) diagnosed in arm C and/or arm D but missed at 2D only («Tomo-only cancer») n = 55 : Concordant and discordant interpretations stratified on mammographic findings

Mammographic findings	Concordant n	%	Discordant n	%	Total n	%
Circumscribed mass	1		0		1	
Spiculated mass *	13		14		27	
Architectural distortion *	8		7		15	
Asymmetric density	1		1		2	
Calcifications (mc's) **	0		2		2	
Density + microcalcifications **	2		6		8	
Total	25	45%	30	55%	55	100%
* Spiculated mass + arch. distortion	21	50%	21	50%	42	76%
** Calcifications (with/without density)	2	20%	8	80%	10	18%



* Skaane P et al.: Breast Cancer Res Treat 2018; doi

Objectives

- Why do we need syn2D
- What is synthetic mammograms (syn2D)
- Syn2D and diagnostic performance:
  - Circumscribed masses
  - Spiculated masses
  - Distortions
  - Microcalcifications
- Conclusion of DBT-screening using syn2D

Screening with Tomosynthesis and Synthesized 2D: The Norway experience

Objectives

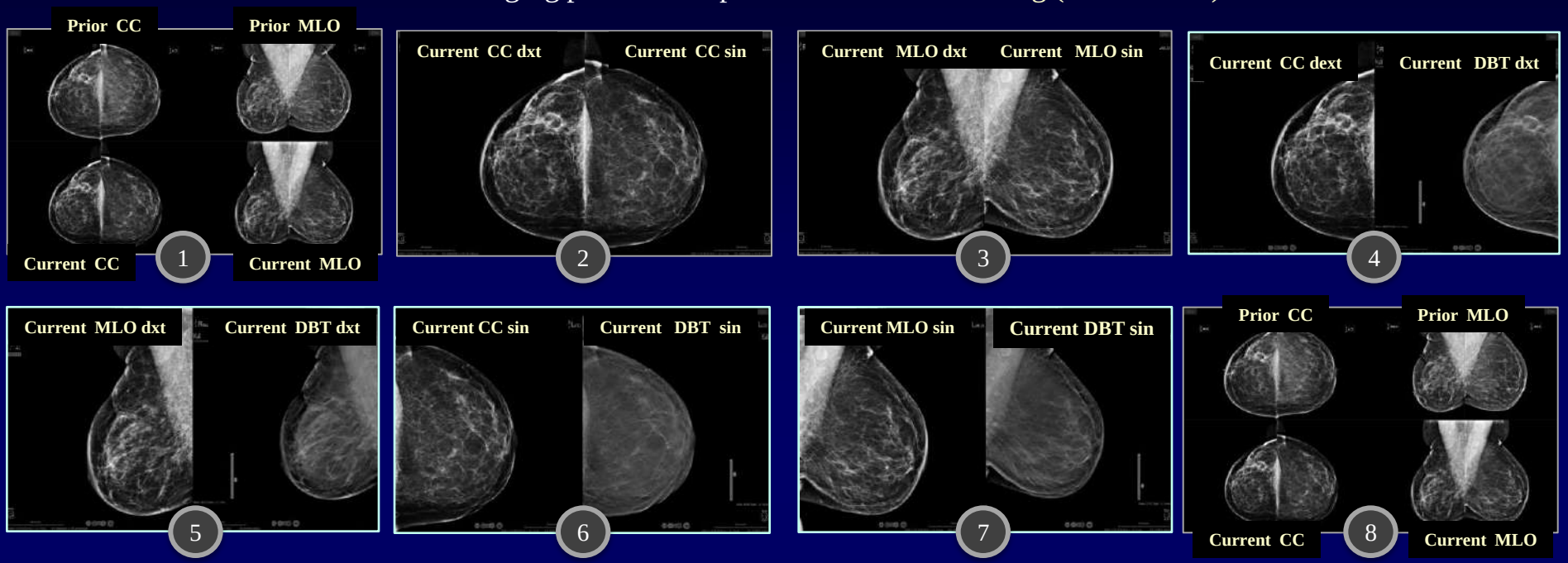
- What is ”synthetic” mammograms (”syn2D”)
- **Why do we need syn2D ?**

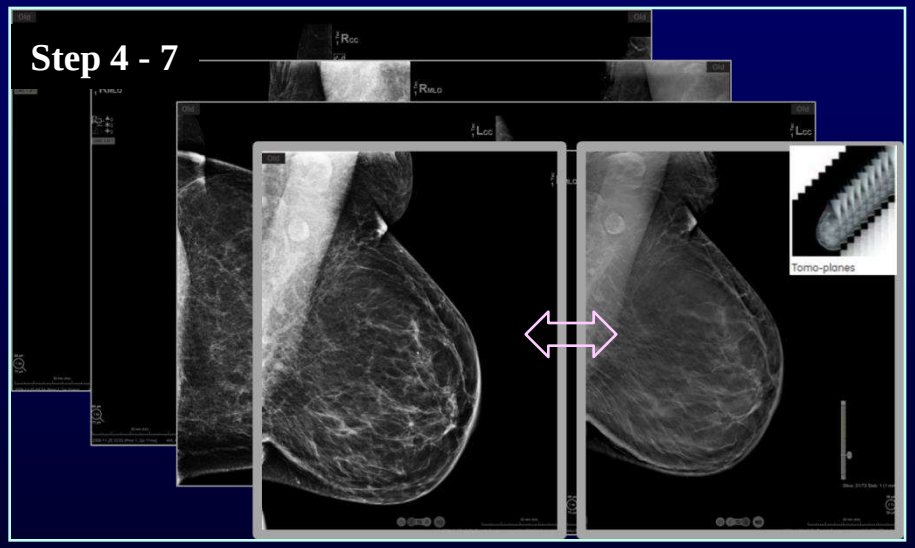
  For 2 important reasons:

  1. **Comparison**
     - **with prior mammograms**
     - **right-left breast**
     - **2D with DBT**
  2. **Higher performance (cancer detection) when DBT is combined with 2D and when using two-view DBT: Replacement for FFDM in combined 2D+DBT mode (radiation dose reduction!)**
- Syn2D and diagnostic performance

DBT – challenges: Detection of small subtle cancers

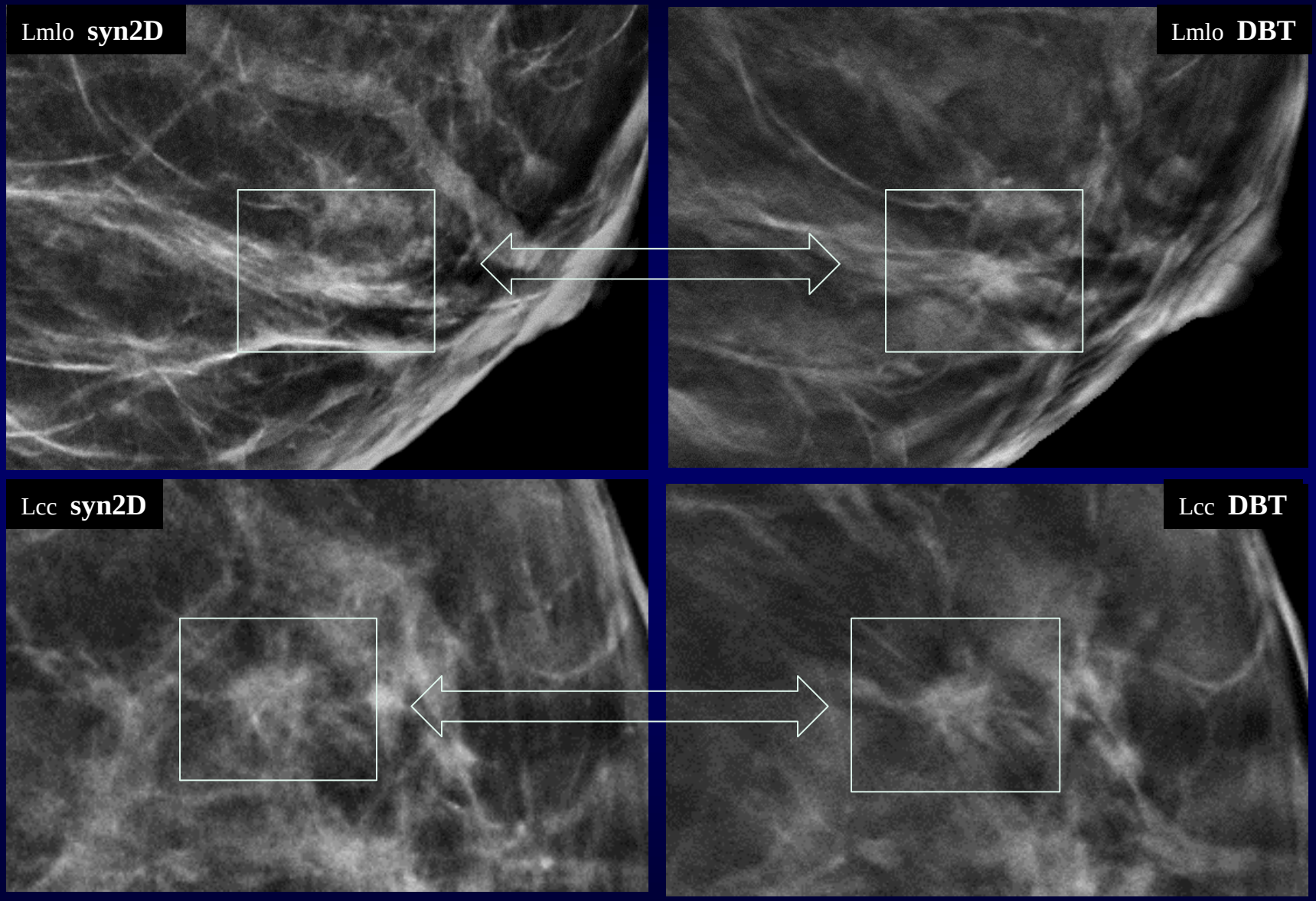
OTST: Hanging protocol step 1 – 8 for batch reading (2D + DBT)





Step 4 – 7:
(2D on left and 3D scrolling on right monitor):
Looking for
- (Fine) microcalcifications
- Subtle spiculated masses
- Distortion

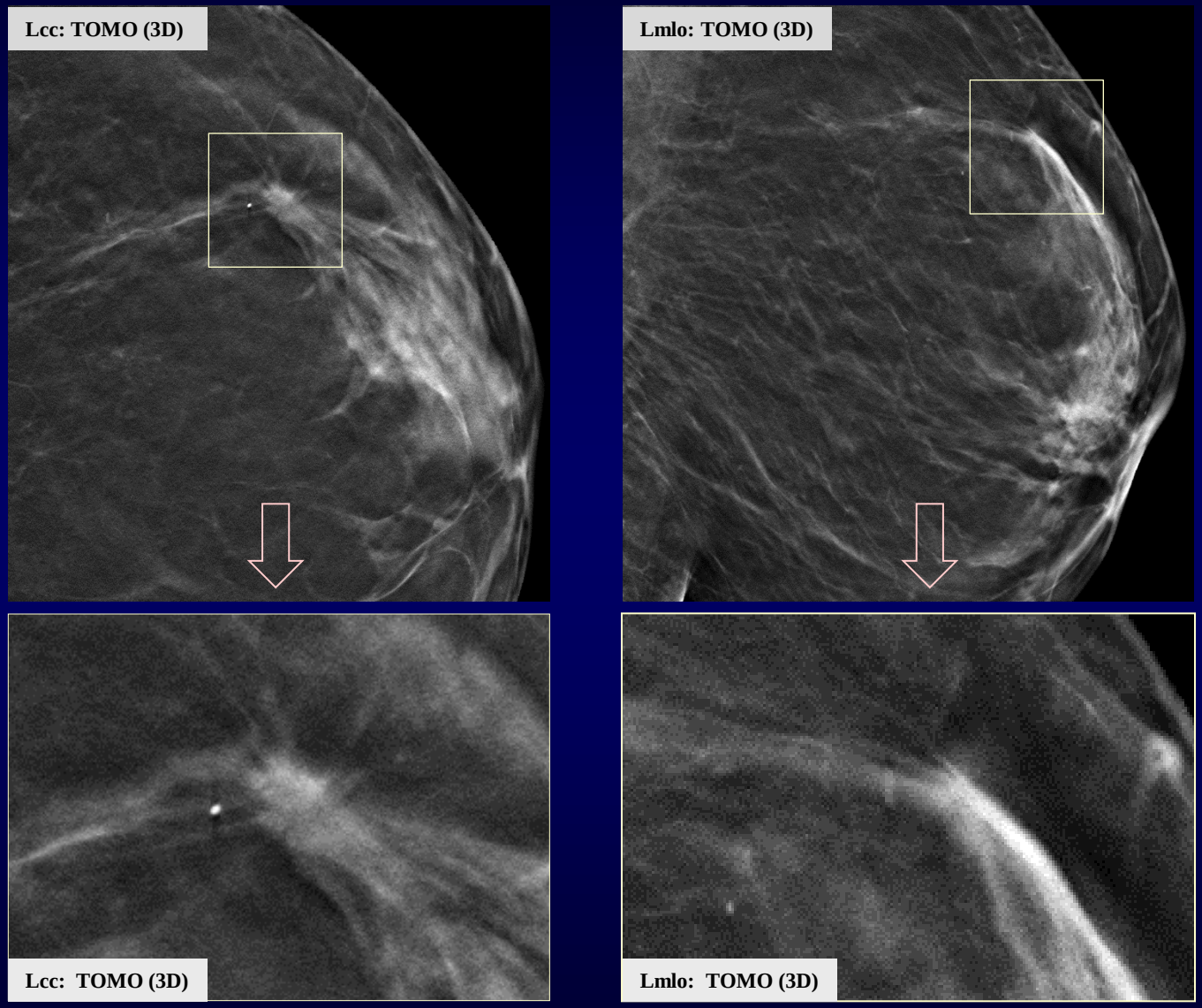
Cancer visibility: 2D vs. Tomosynthesis



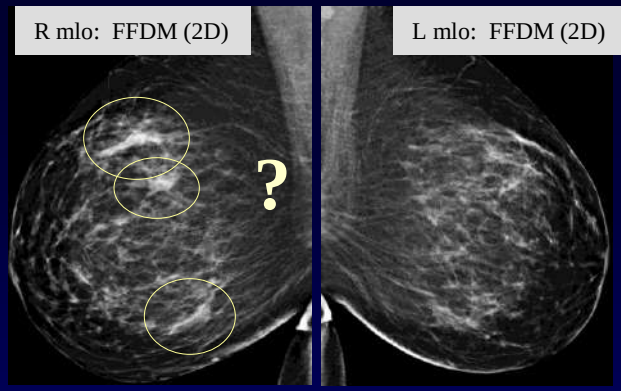
Histology: **Tubular carcinoma** (screening 2014)

DBT – challenges: One- vs. two-view DBT

Cancer obvious on CC but could easily be overlooked on MLO!

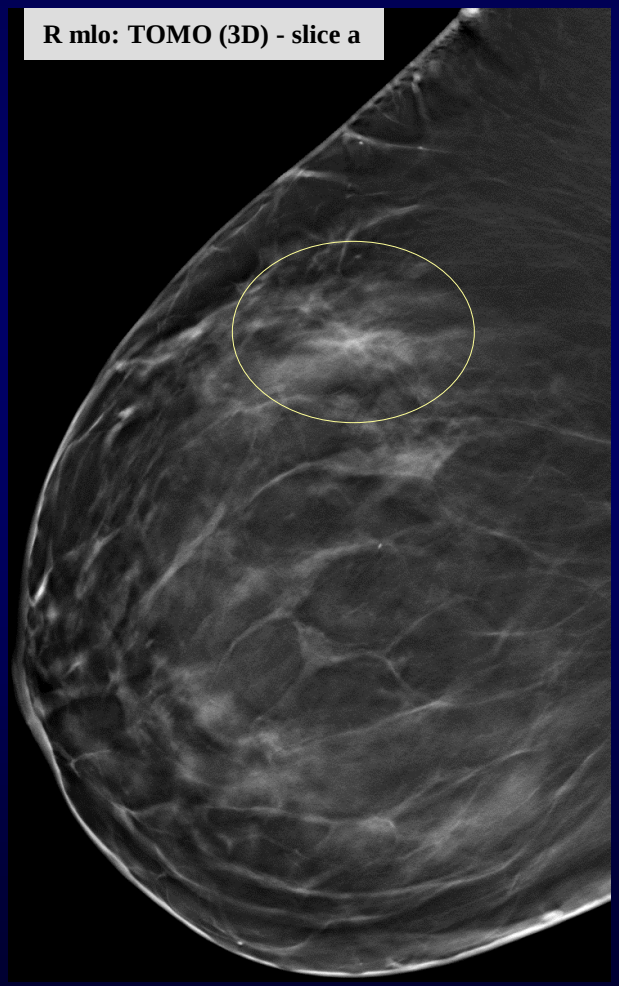


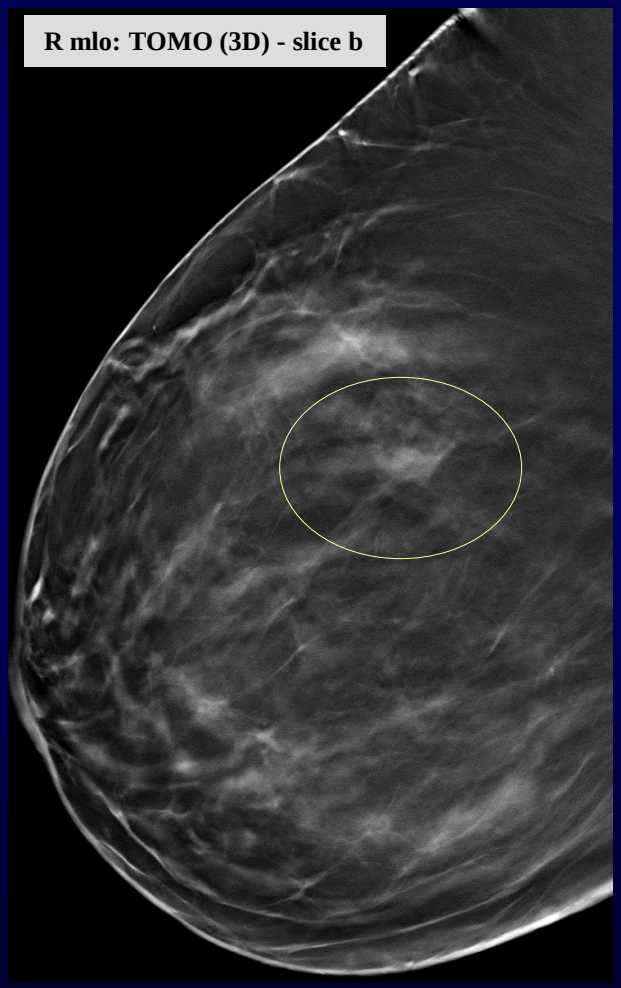
Histology: Invasive ductal carcinoma (IDC) grade 1, 6 mm

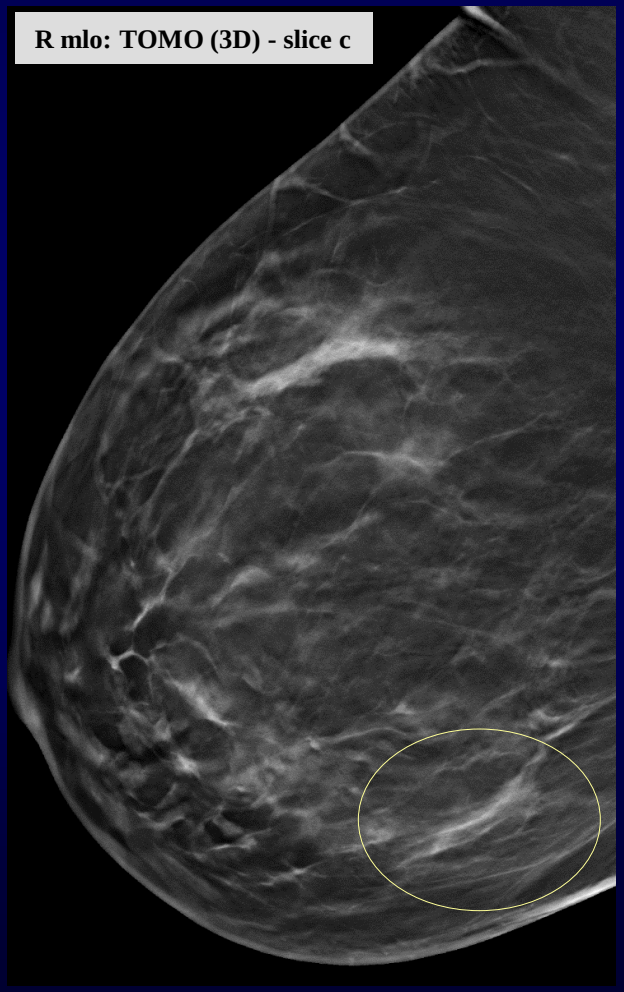


a)

Do you see a cancer in the right breast ?
or
Do you see three asymmetric densities ?

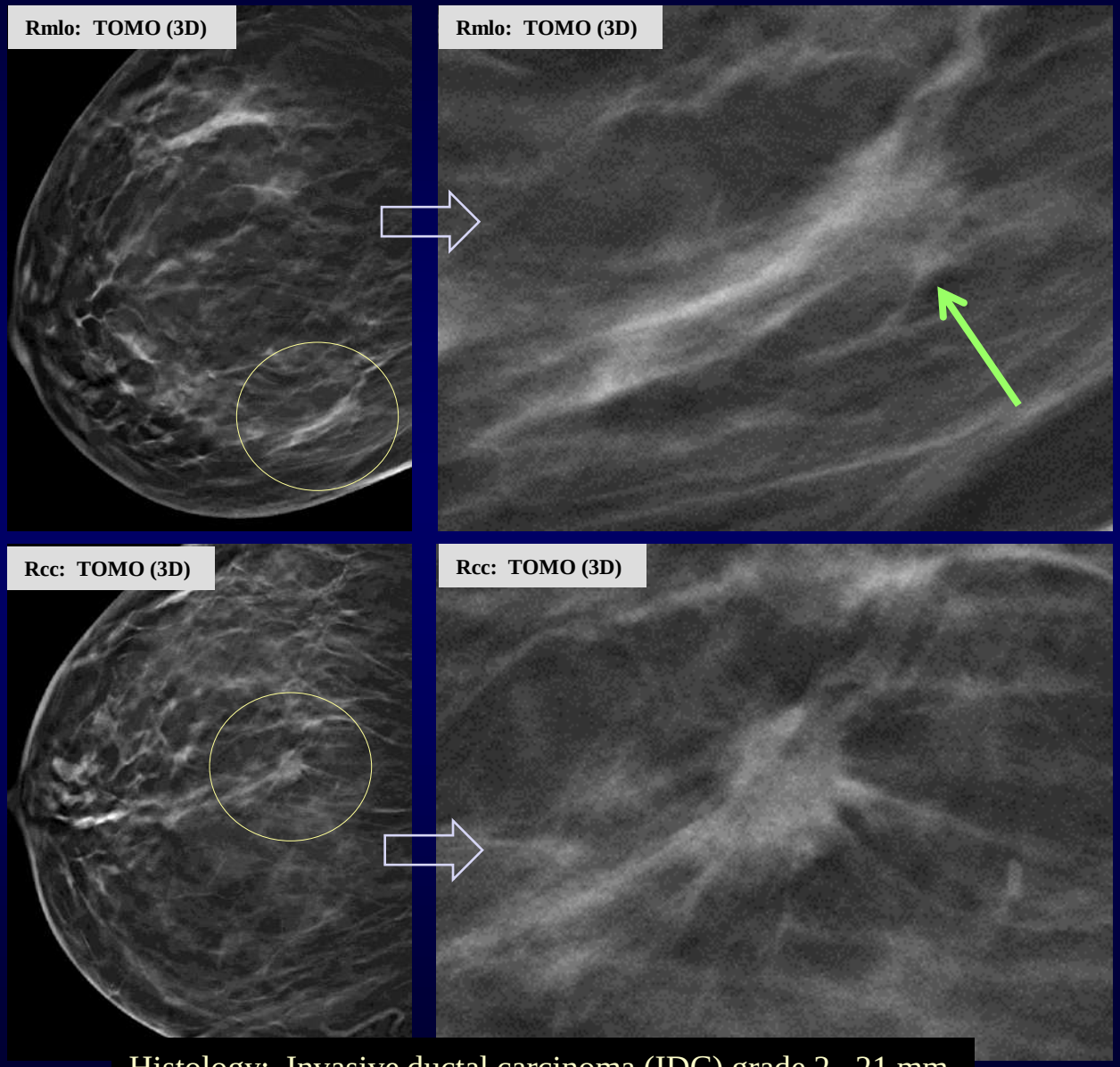






b)

- **DBT mlo**: Very subtle fine spiculations (easily missed!)
- **DBT cc**: Cancer is easily identified on this projection!



Histology: Invasive ductal carcinoma (IDC) grade 2, 21 mm

DBT – challenges: One- vs. two-view DBT, radiation dose, and synthetic 2D

Images to be included:

- One view TOMO (mlo) only?
- One view TOMO + one view 2D?
- One view TOMO + two view 2D?
- Two view TOMO only?
- Two view TOMO + one view 2D?
- Two view TOMO + two view 2D?

Why do we need 2D (+ TOMO):

- 2D maximize mc detection?
  (TOMO: ”Thin-slice-effect”)
- Comparison with prior exams
- Comparison right-left breast
- Externals may request current 2D

Experience from clinical studies :

Two view 2D (FFDM: MLO + CC) plus two view TOMO (MLO + CC) seems to offer highest clinical performance .

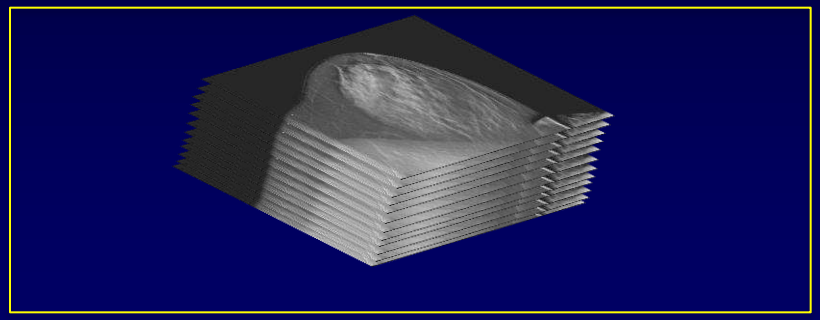
However: This means a double radiation dose !

⇩

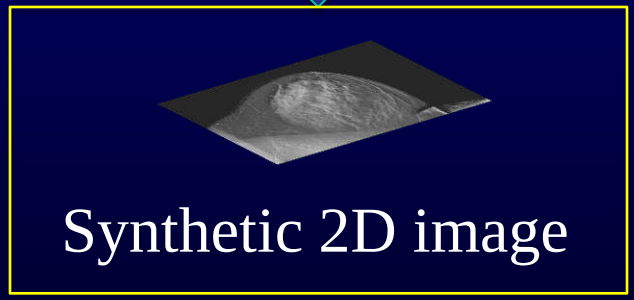
Synthetic 2D may substitute for FFDM images (when combined with tomosynthesis) without additional radiation dose !!

Synthetic 2D generation:

Tomosynthesis reconstructed slices



Synthesized Projection



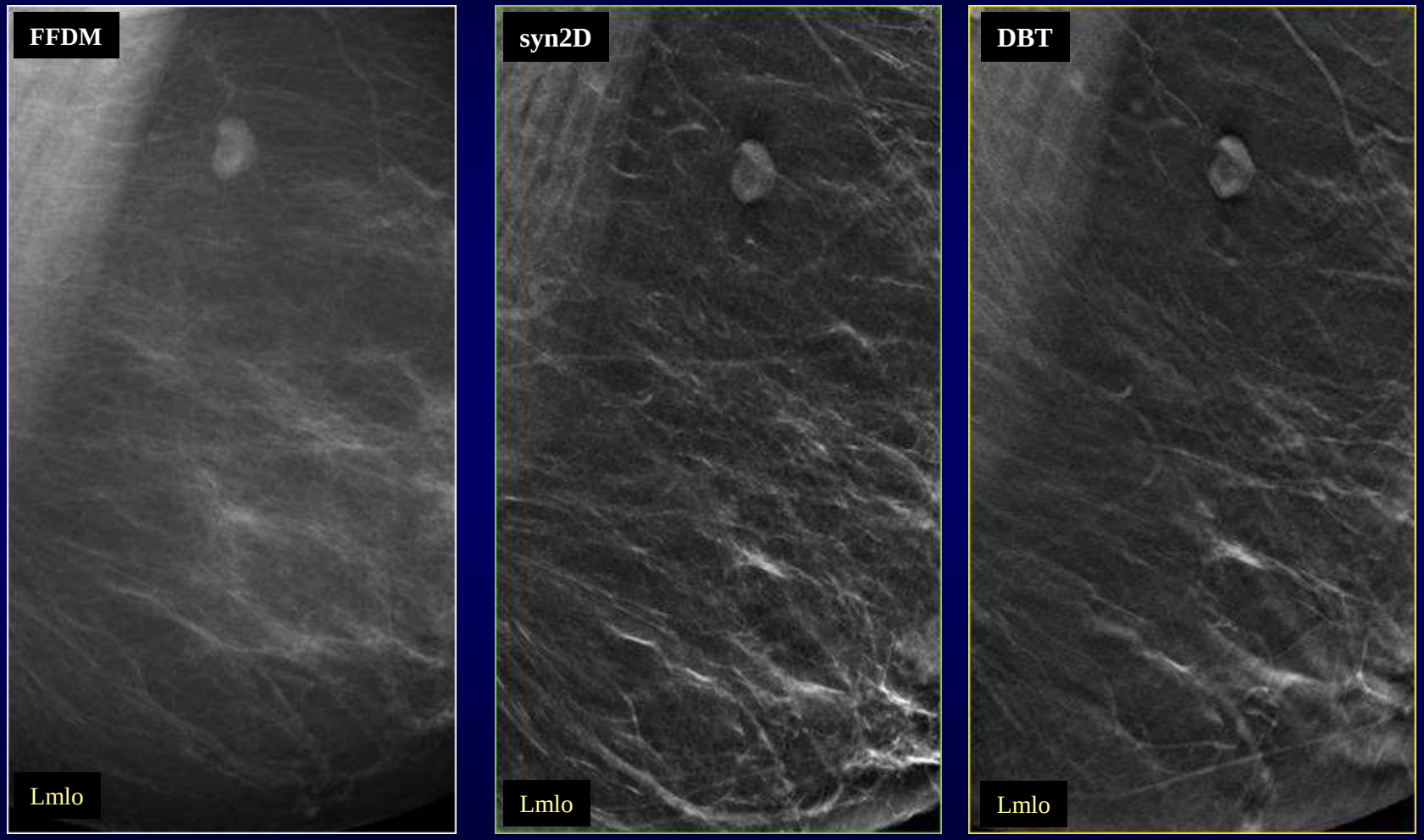
Synthetic 2D image (called C-View by Hologic) shows a roadmap of the important features from tomosynthesis slices

Objectives

- What is ”synthetic” mammograms (”syn2D”)
- Why do we need syn2D
- Syn2D and diagnostic performance:
  - Circumscribed masses
  - Spiculated masses
  - Distortions
  - Microcalcifications
- Syn2D in screening setting
- Conclusion

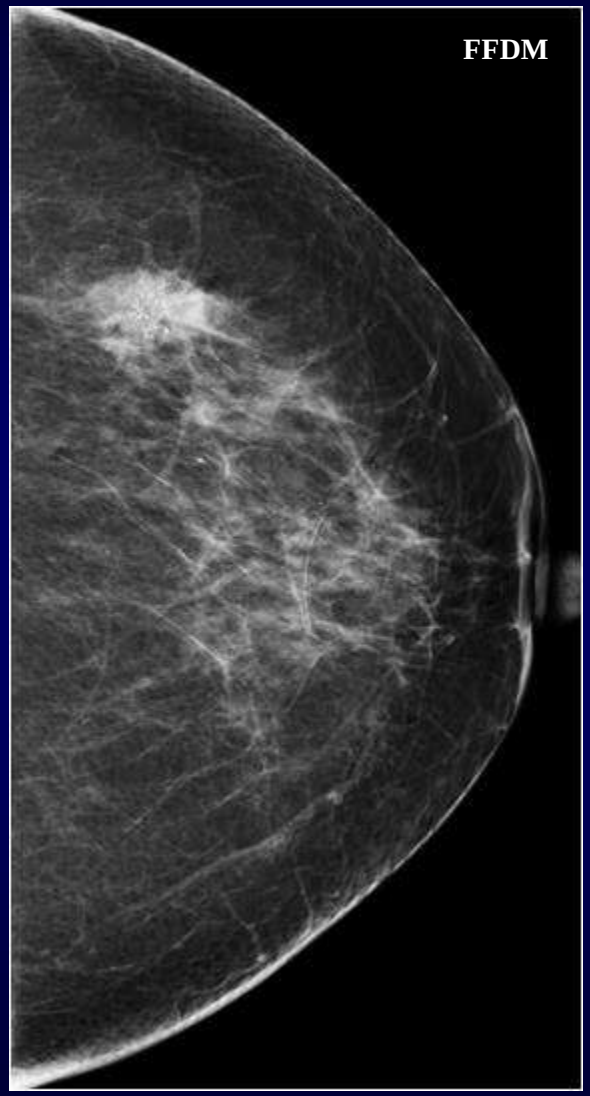
Circumscribed masses:

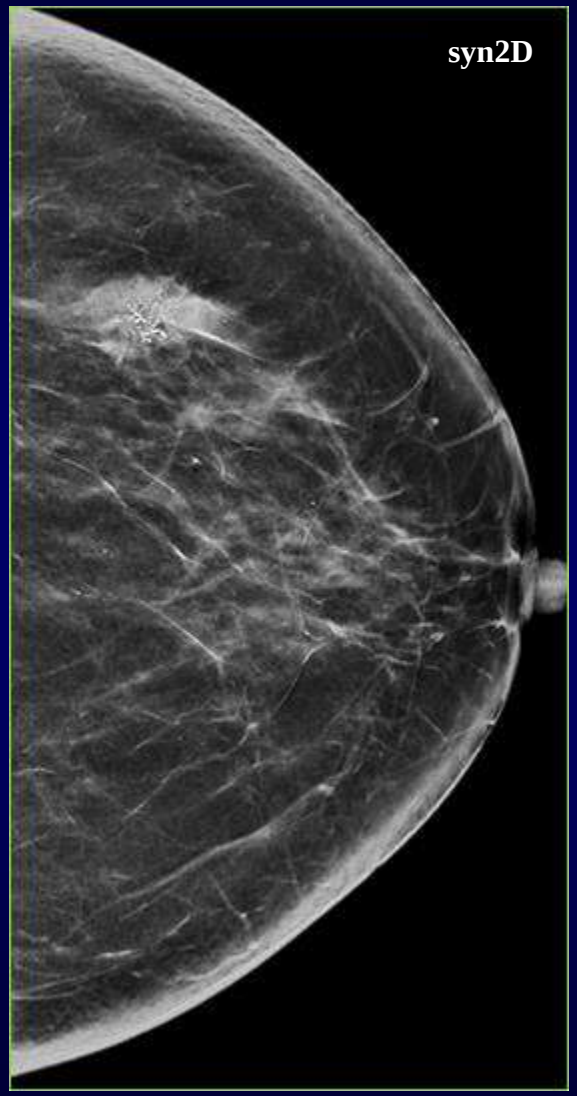
Intra-mammary lymph node

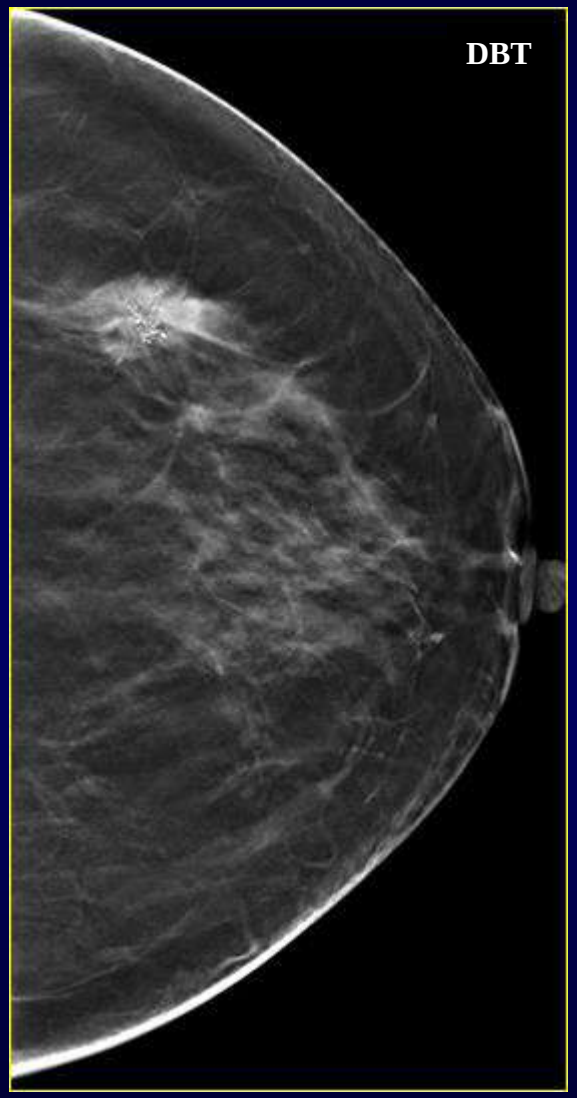


Spiculated masses:

Do we see the same on synthetic 2D as on conventional FFDM and tomosynthesis (3D) ?

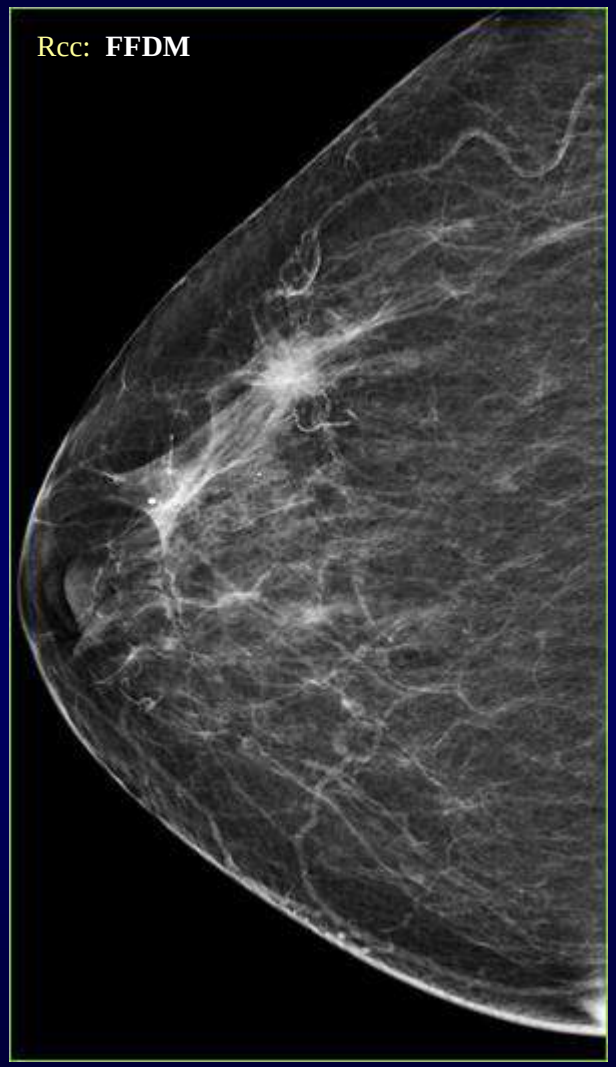


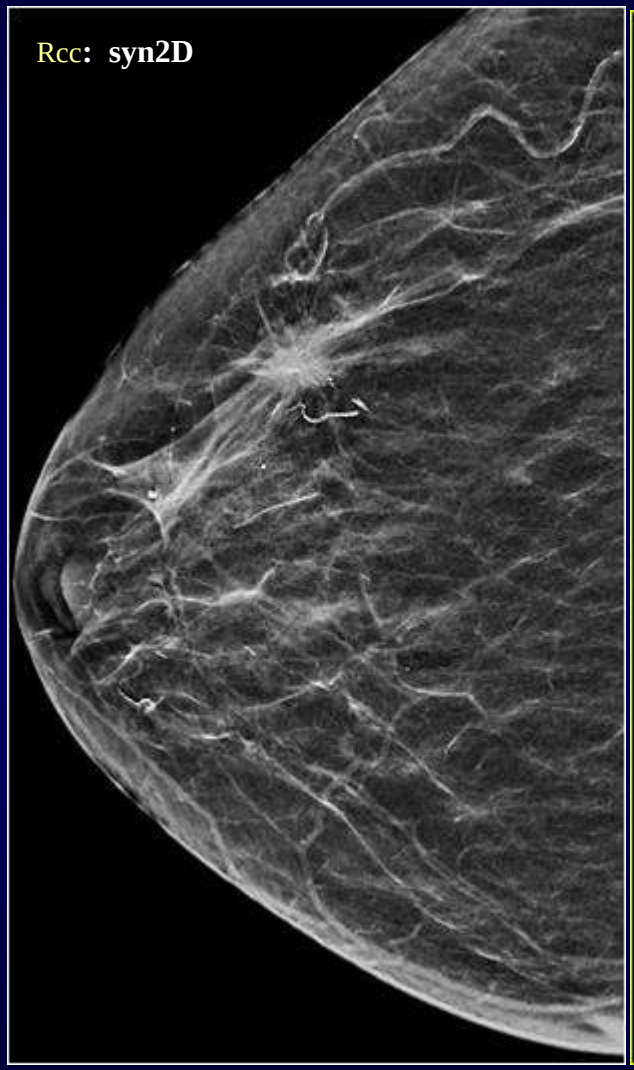




Do we see the same on C-view as on conventional 2D FFDM and tomosynthesis (3D) ?

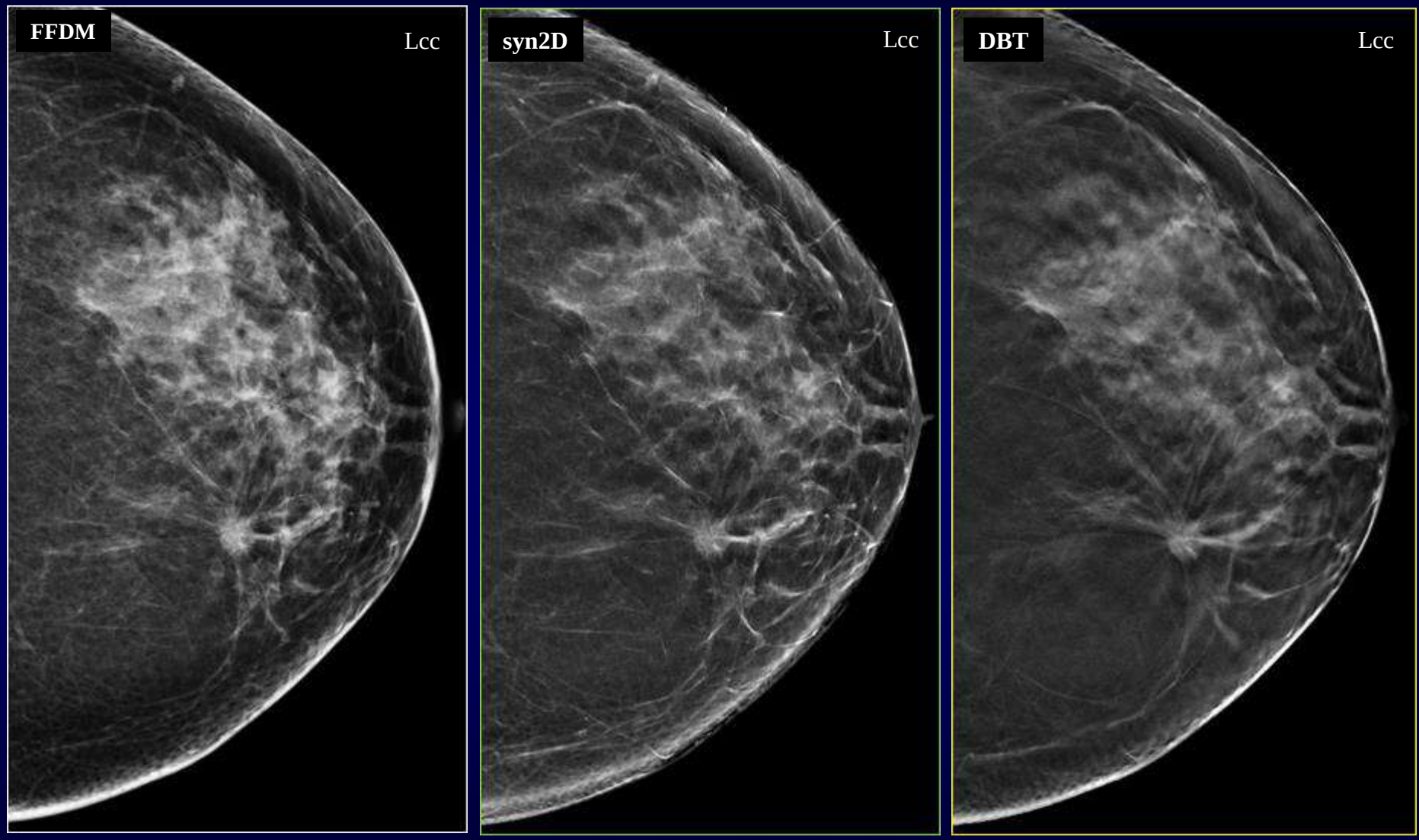
Oslo Tomosynthesis Screening Trial





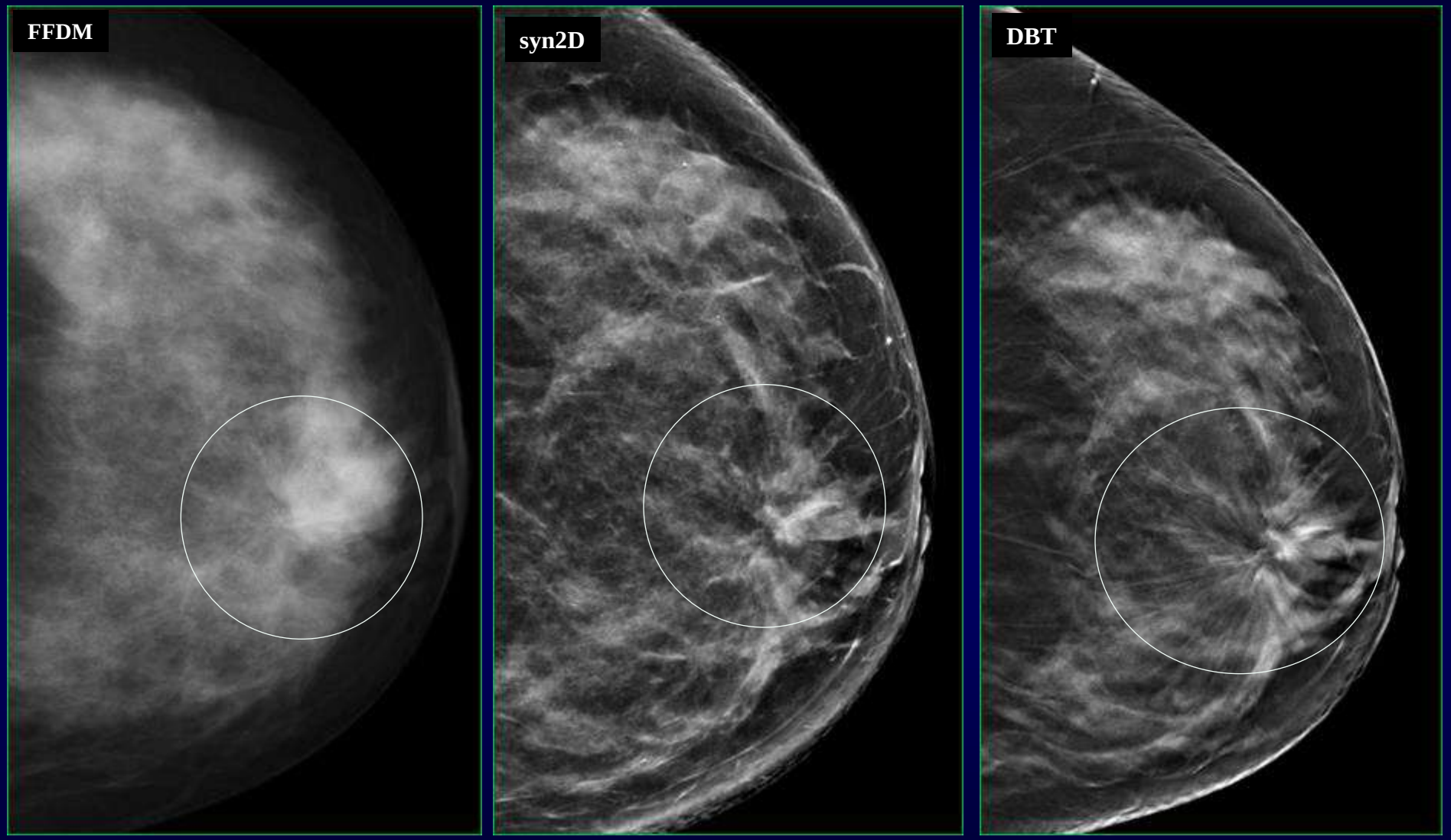
Histology: Tubular carcinoma 13 mm

Synthetic 2D image ⇩



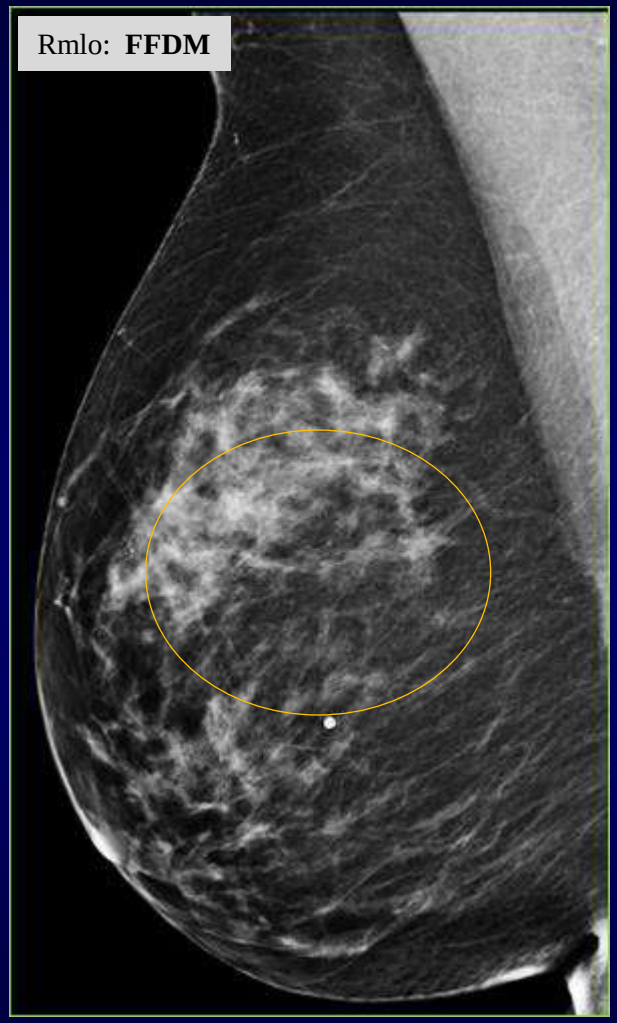
Invasive ductal carcinoma 9 mm

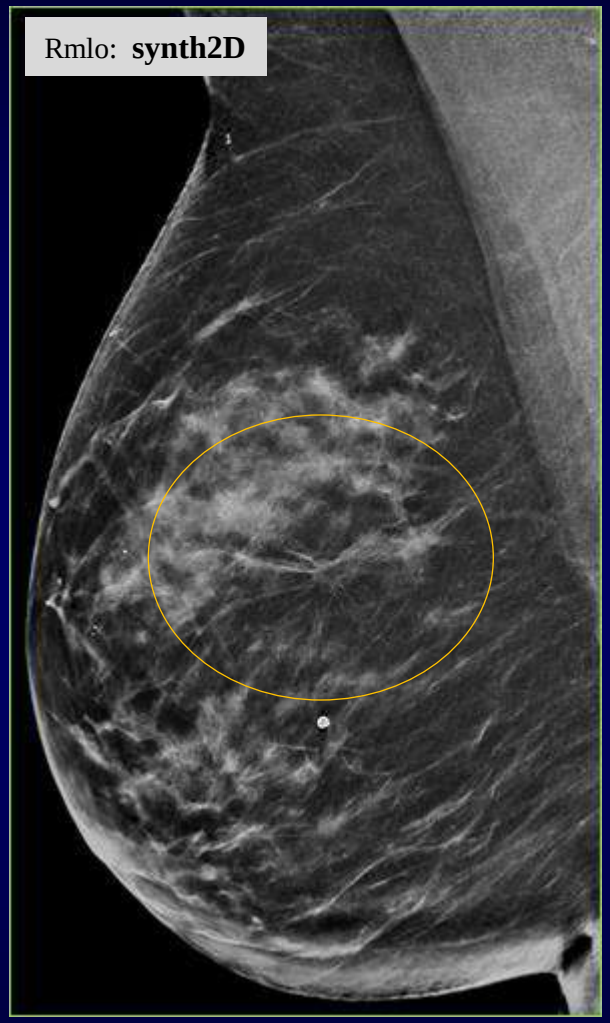
Distortion:

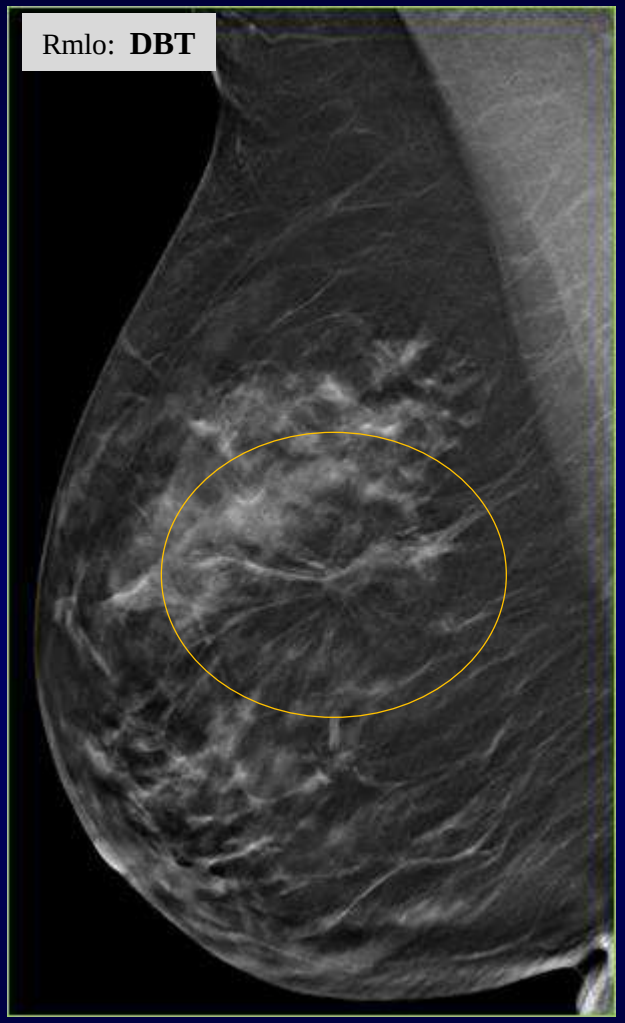


Invasive ductal carcinoma (IDC) gr. 1, 24 mm

Invasive lobular carcinoma (ILC) G1, 12 mm (+ DCIS G3)

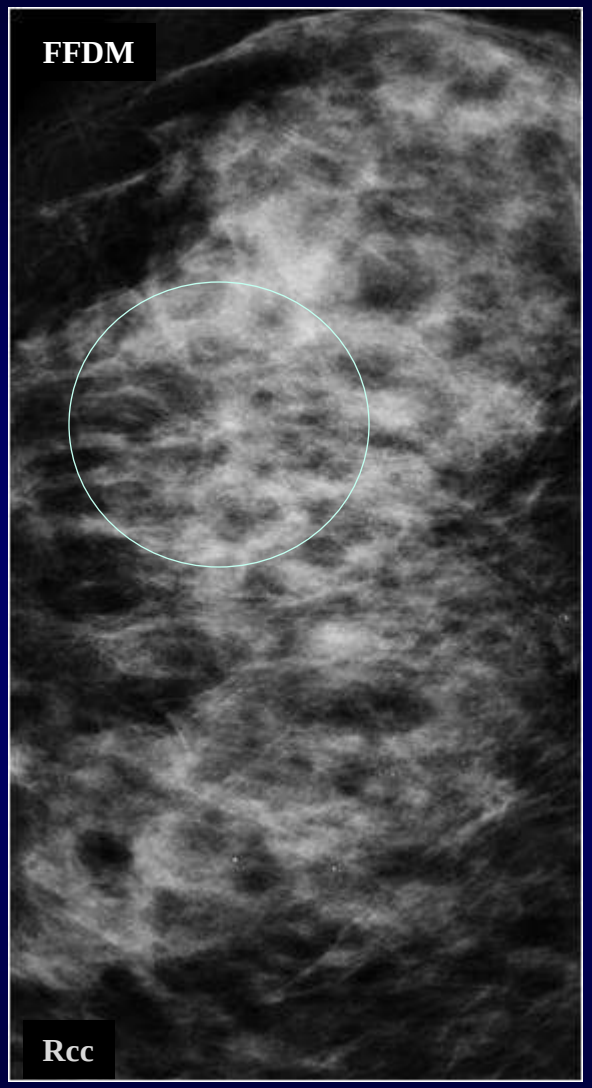


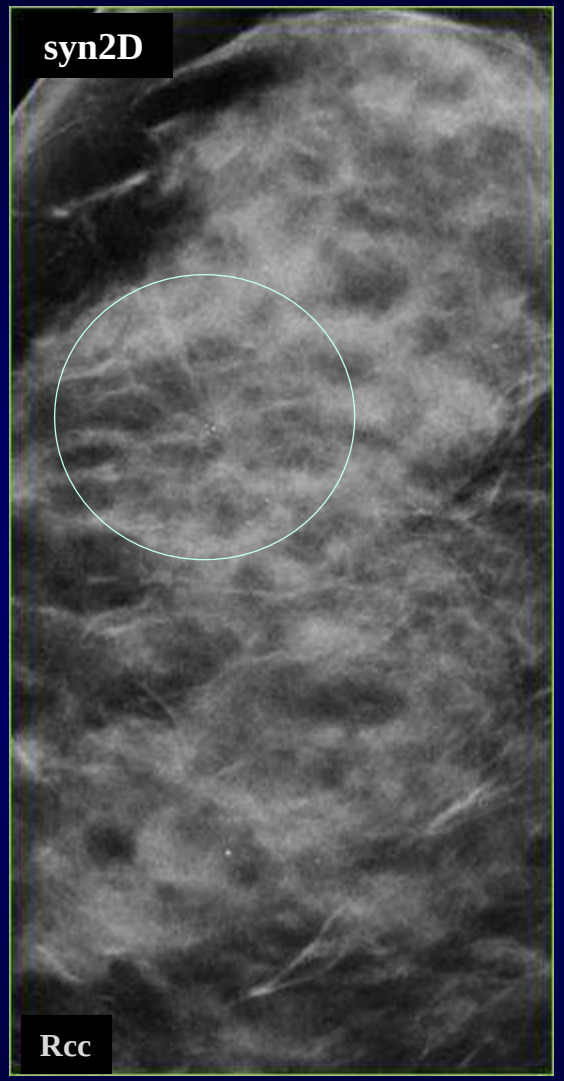


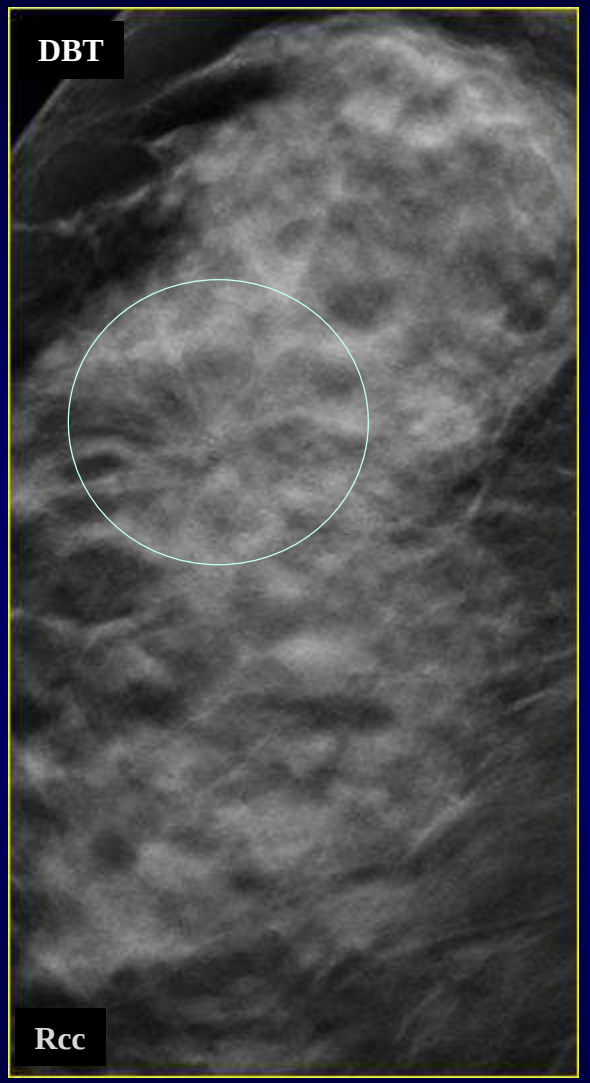


Reader (Arm)	A	B	C	D
Score (NBCSP)	1	1	3	4

Histology: Invasive lobular carcinoma (ILC) , G1 , 14 mm



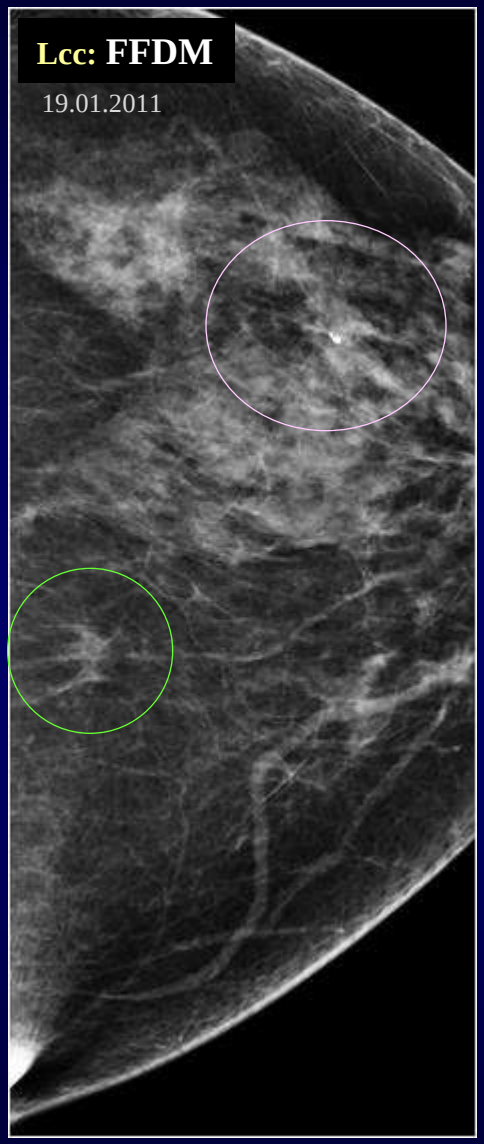


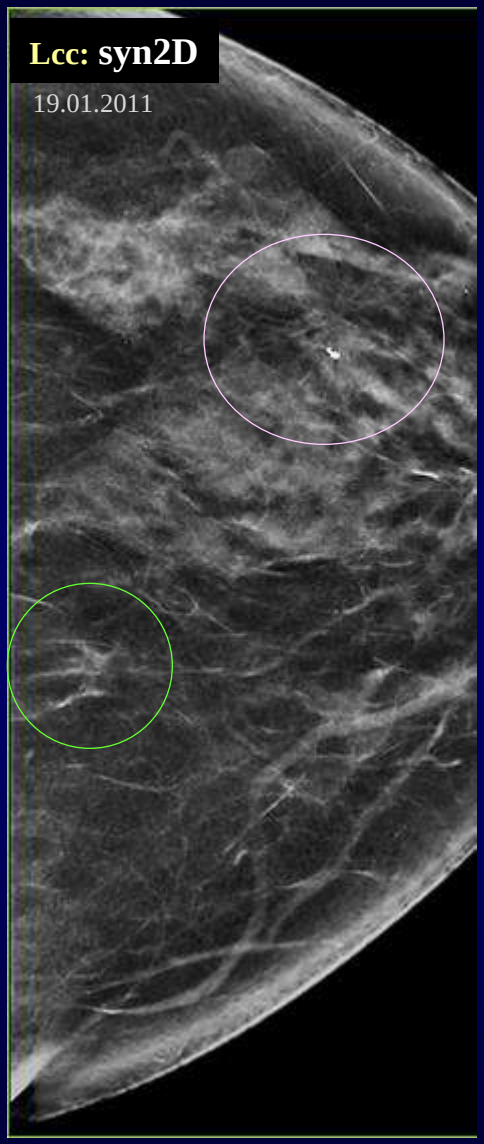


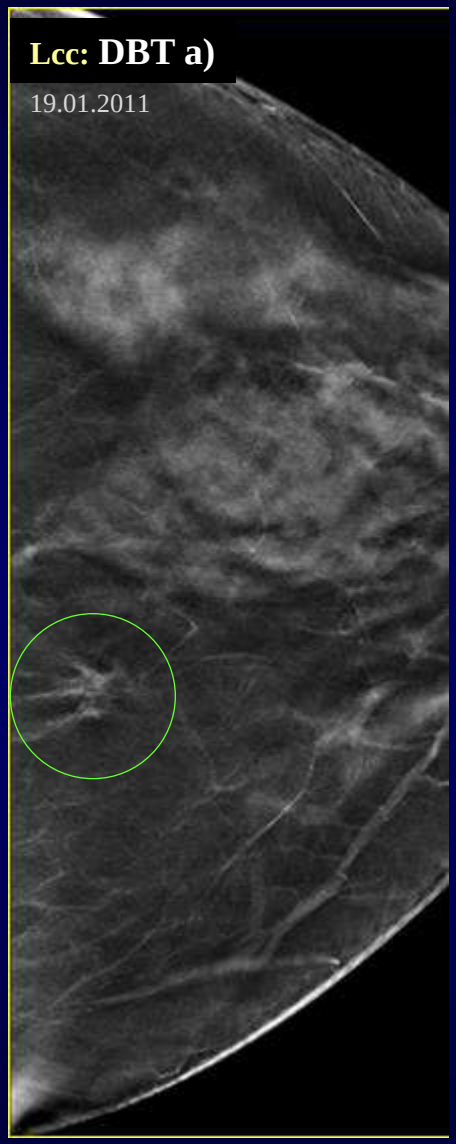
Reader (arm)	A	B	C	D
Score (NBCSP)	1	1	1	3

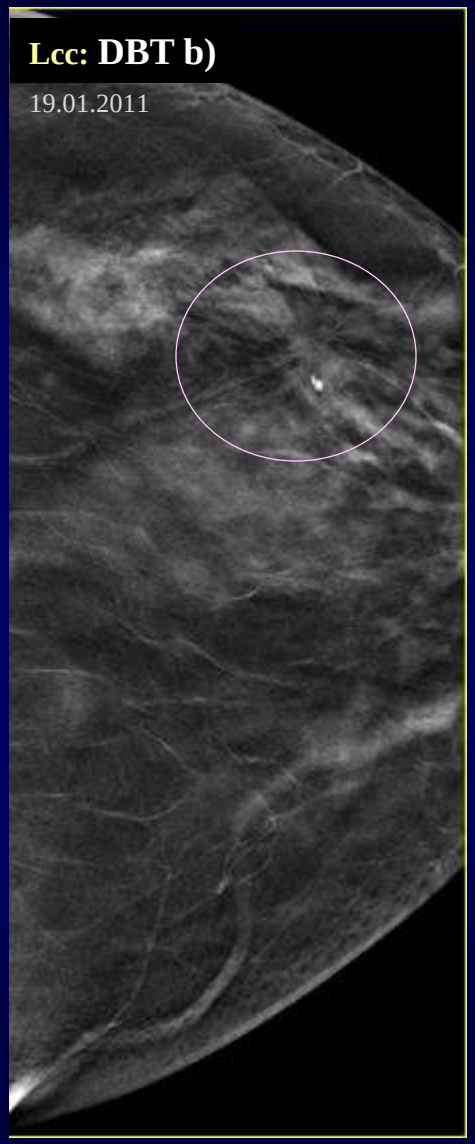
OTST

Synthetic 2D ⇩



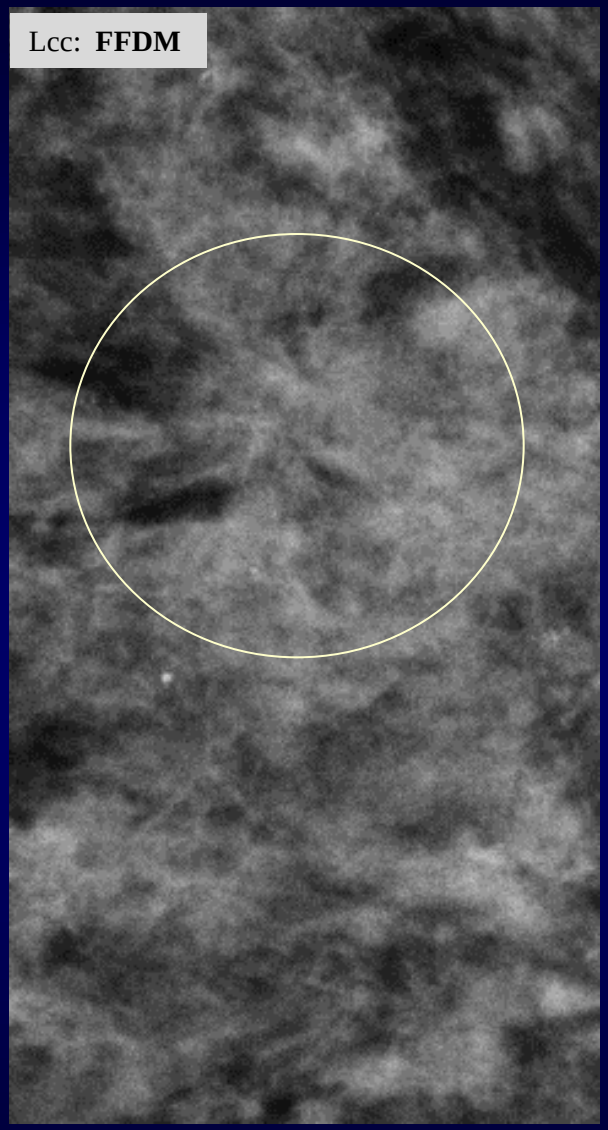


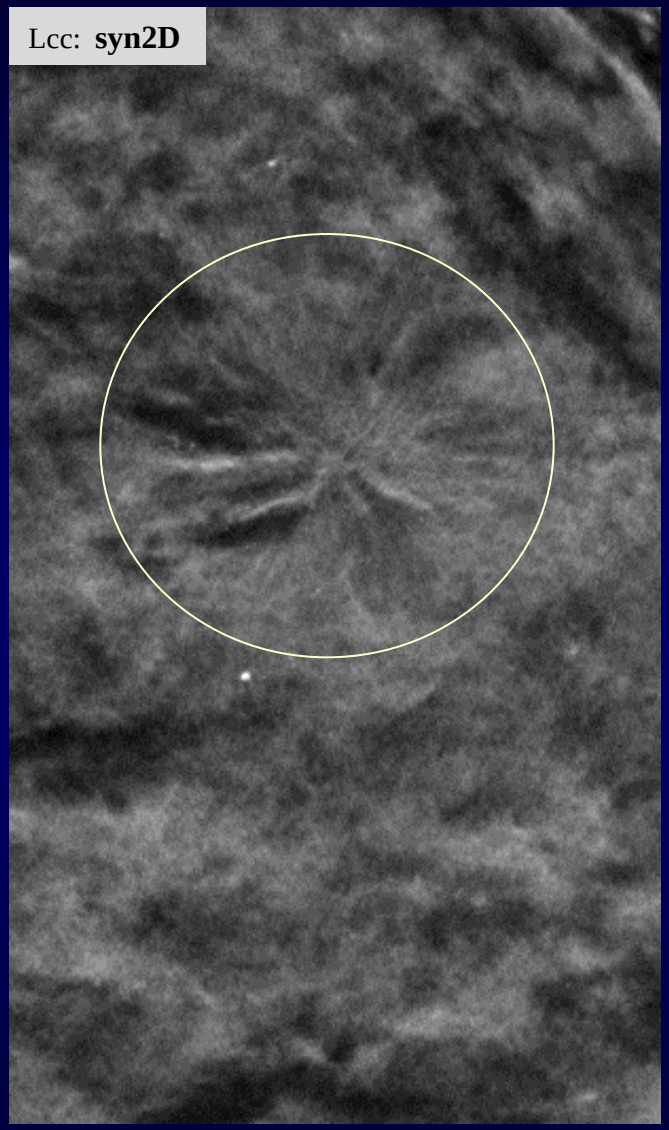


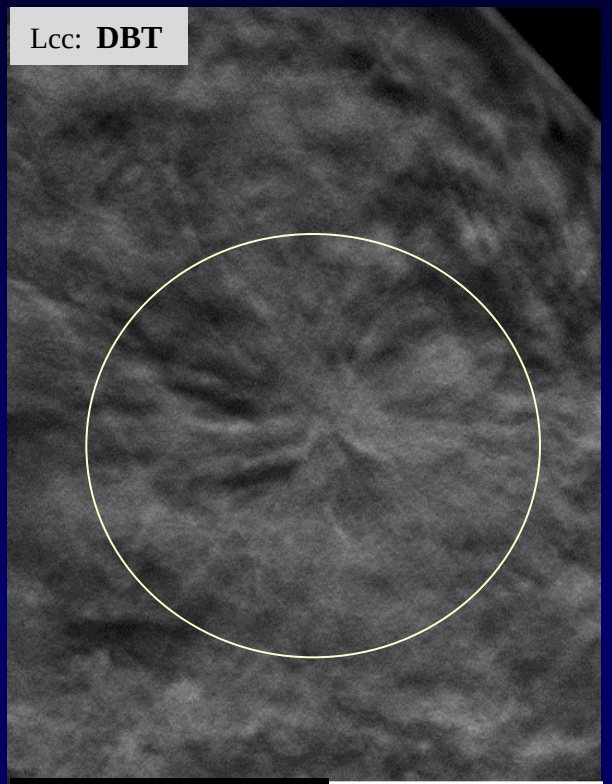


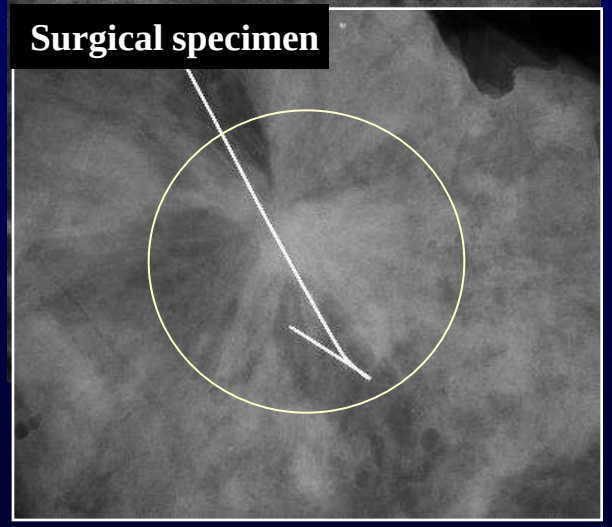
2 cancers: ILC gr. 2, 8 mm (medial) + tubular carcinoma 8 mm (lateral)

OTST: Invasive ductal carcinoma (IDC) G1, 10 mm



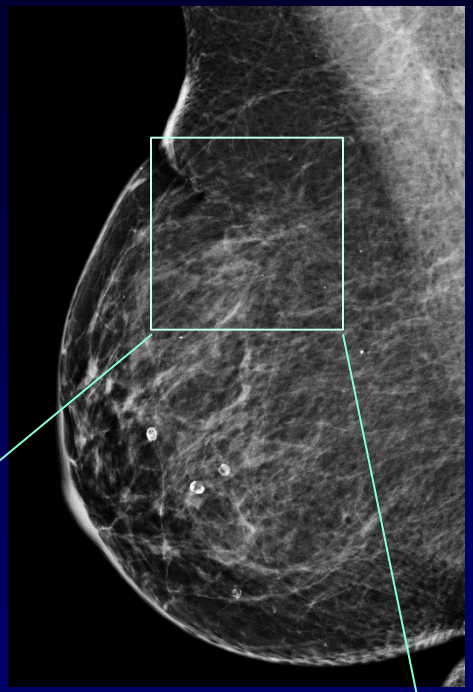


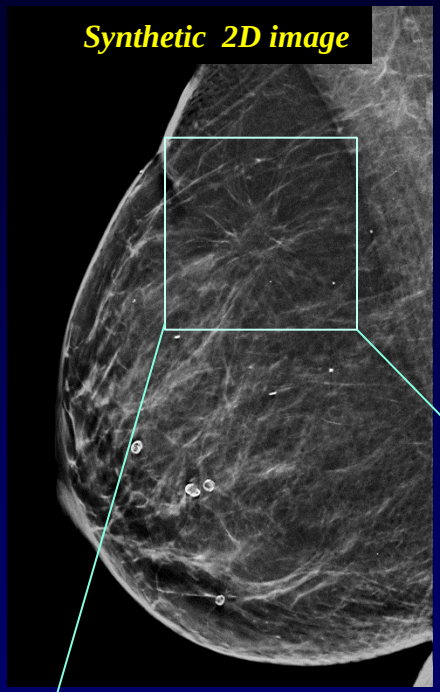


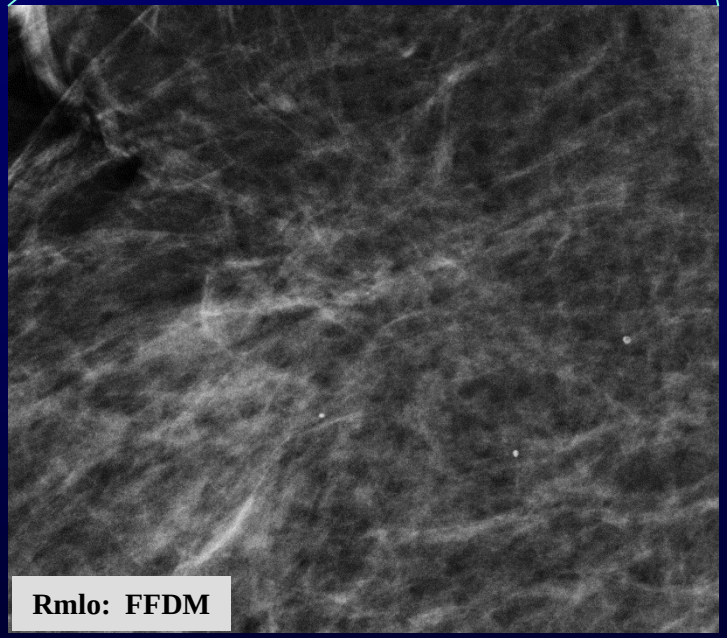


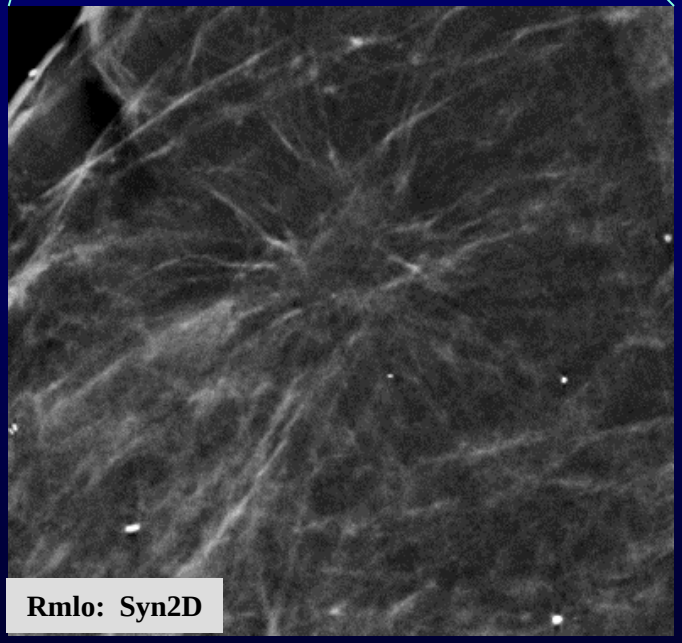
Reader (Arm)	A	B	C	D
Score (NBCSP)	1	3	5	5

FFDM vs. syn2D:
Scarring tissue
(previous BCT)



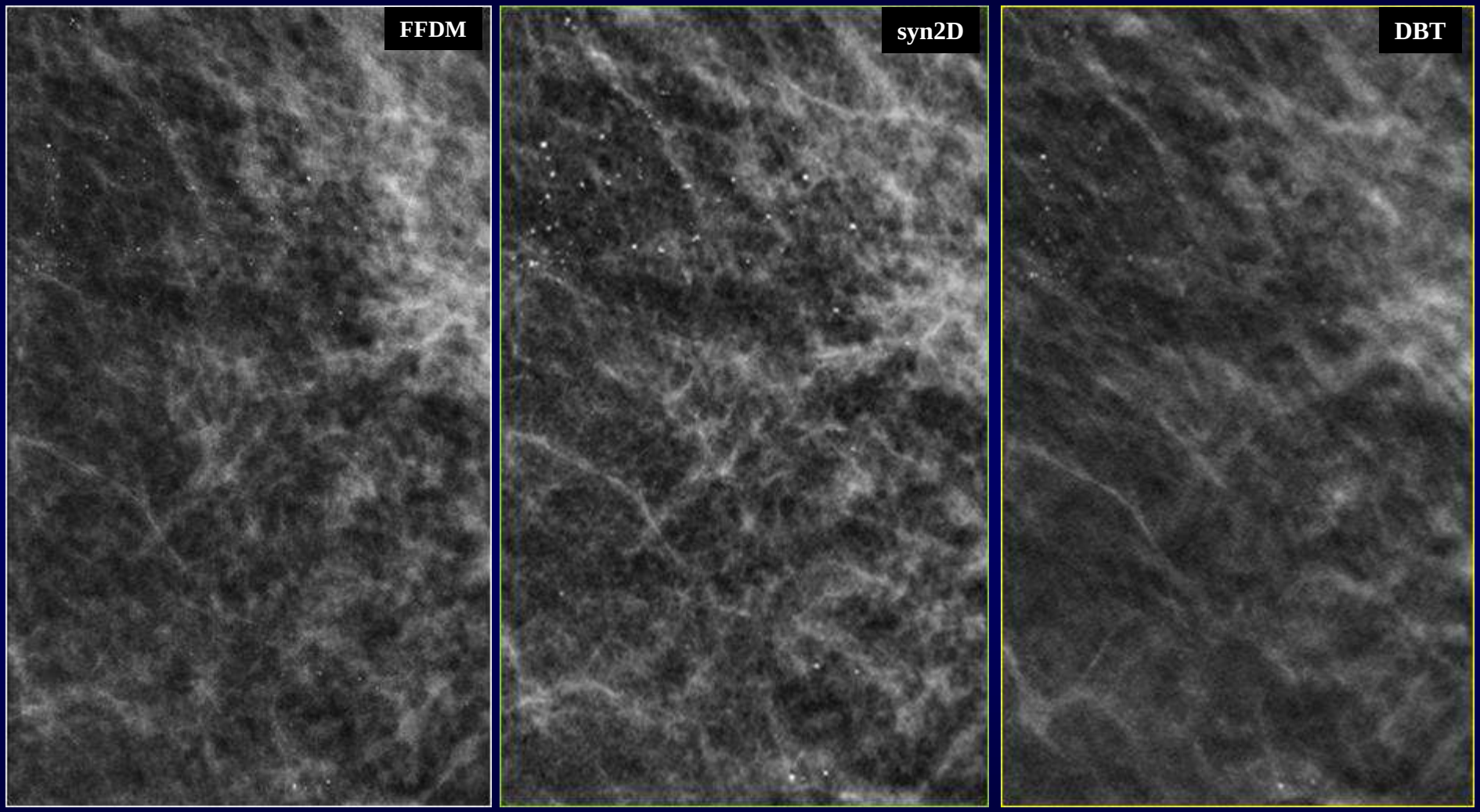






Microcalcifications:

Synthetic 2D image

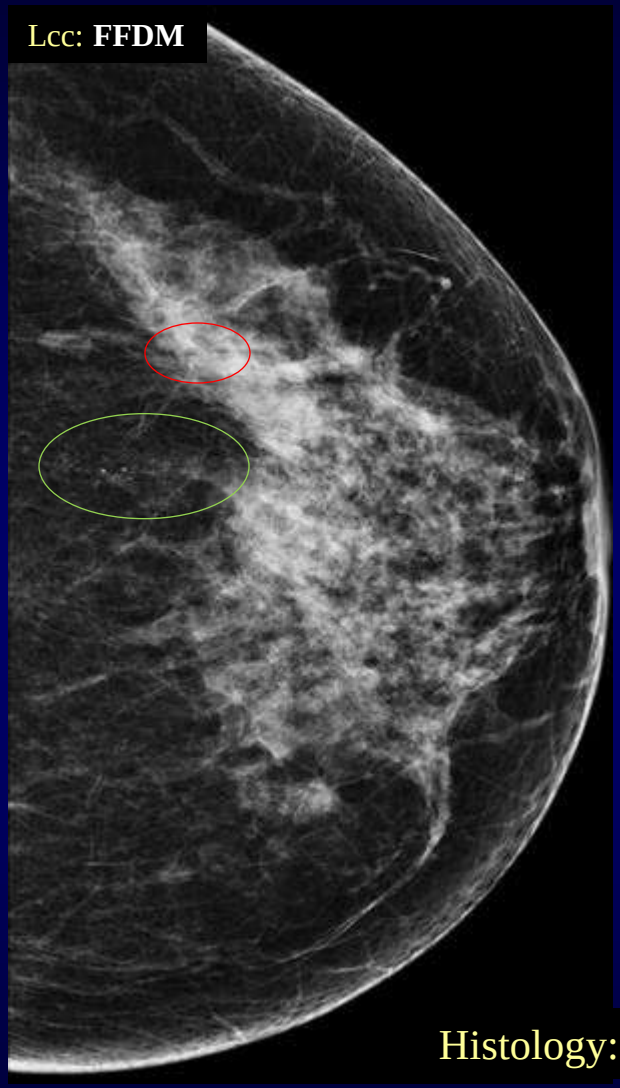


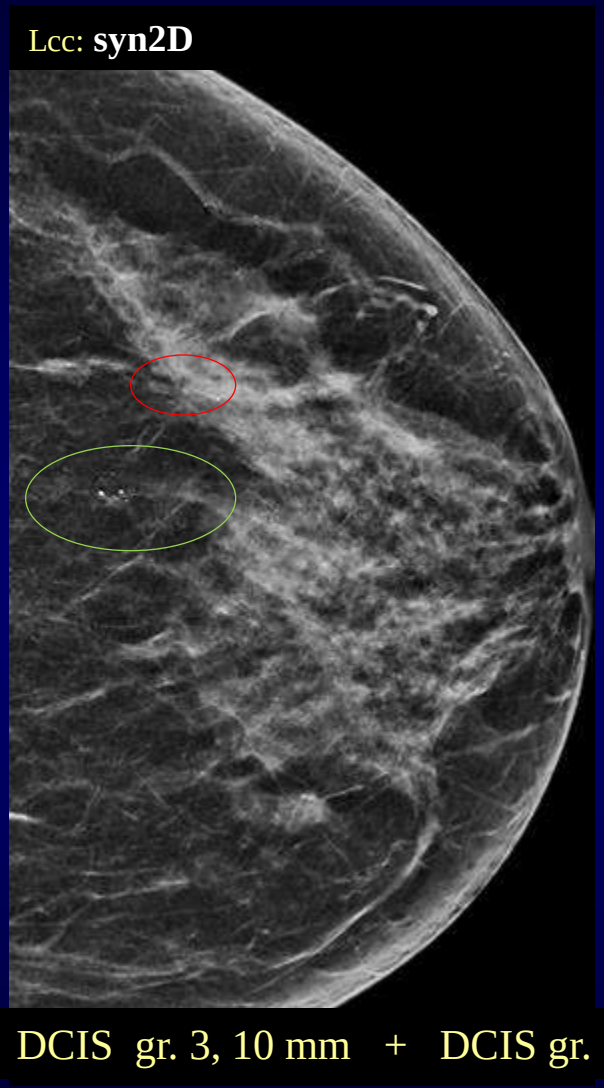
Synthetic 2D (C-view): Highlighting

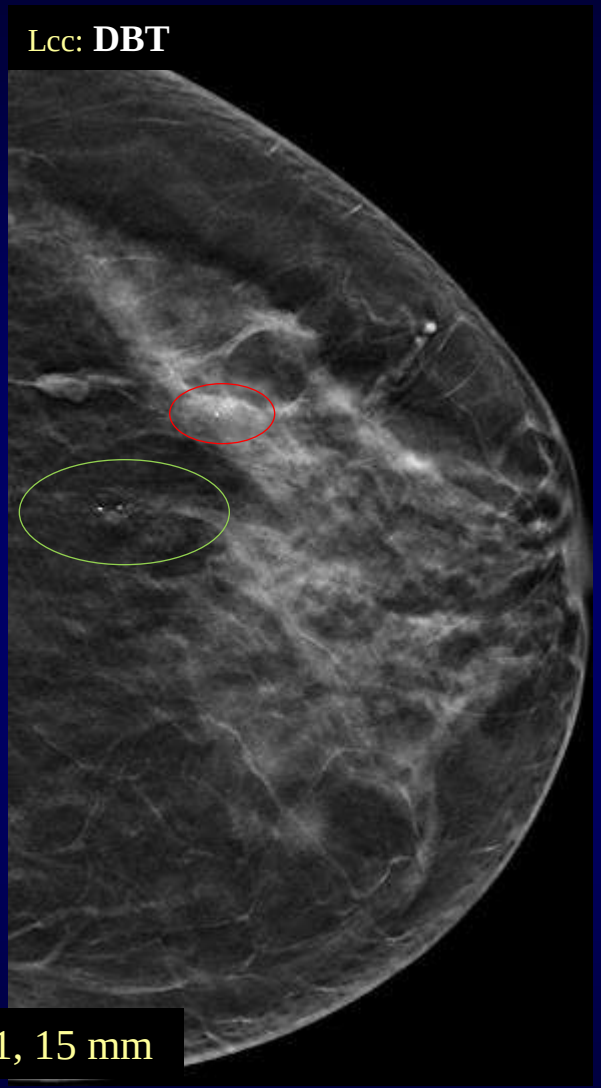
Tomo: ”Thin-slice-effect”

a)

Oslo Tomosynthesis Screening Trial





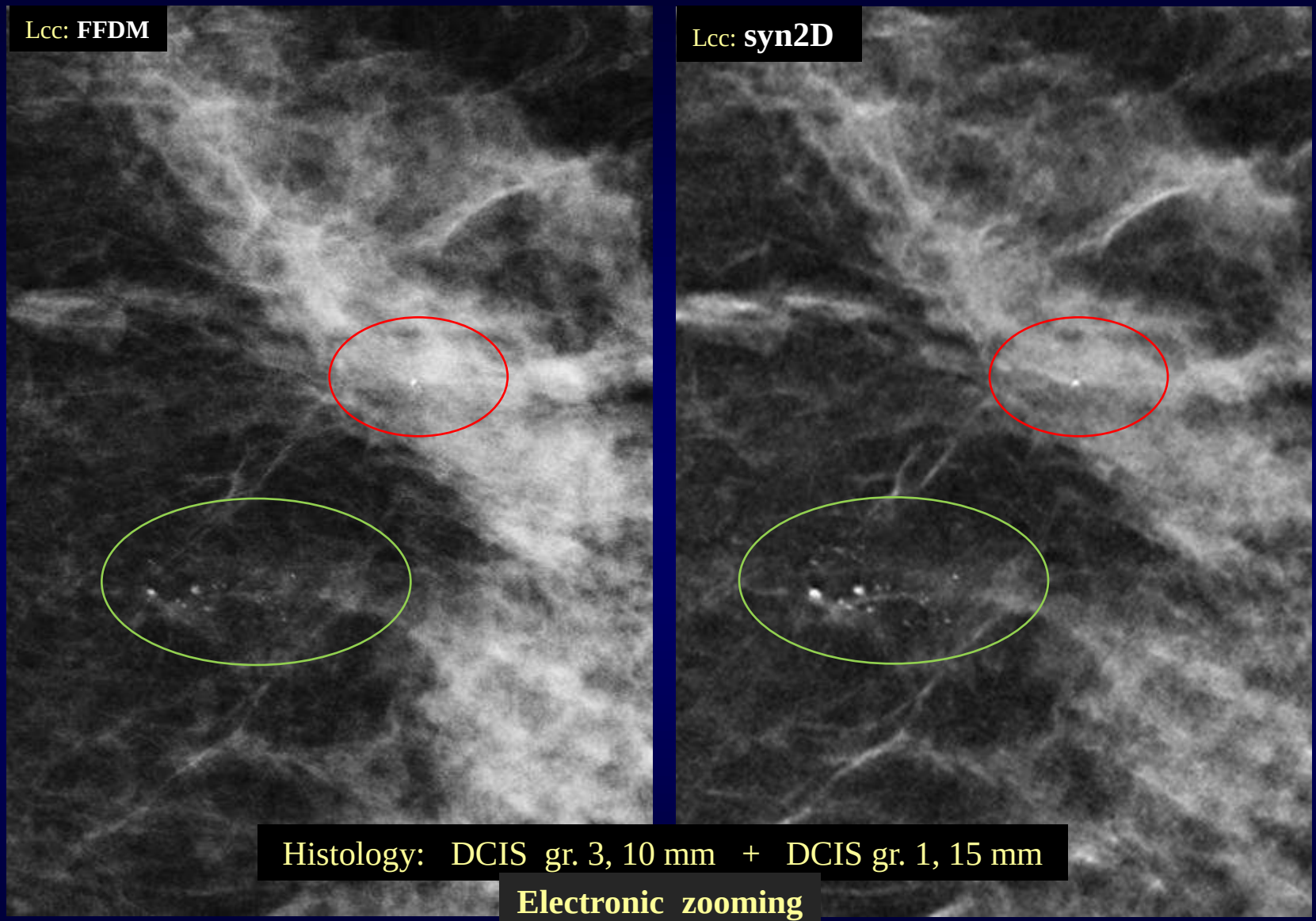


Histology: DCIS gr. 3, 10 mm + DCIS gr. 1, 15 mm

Reader (arm)	A	B	C	D
Score (mc's)	3	4	2	1

Oslo Tomosynthesis Screening Trial

a1)



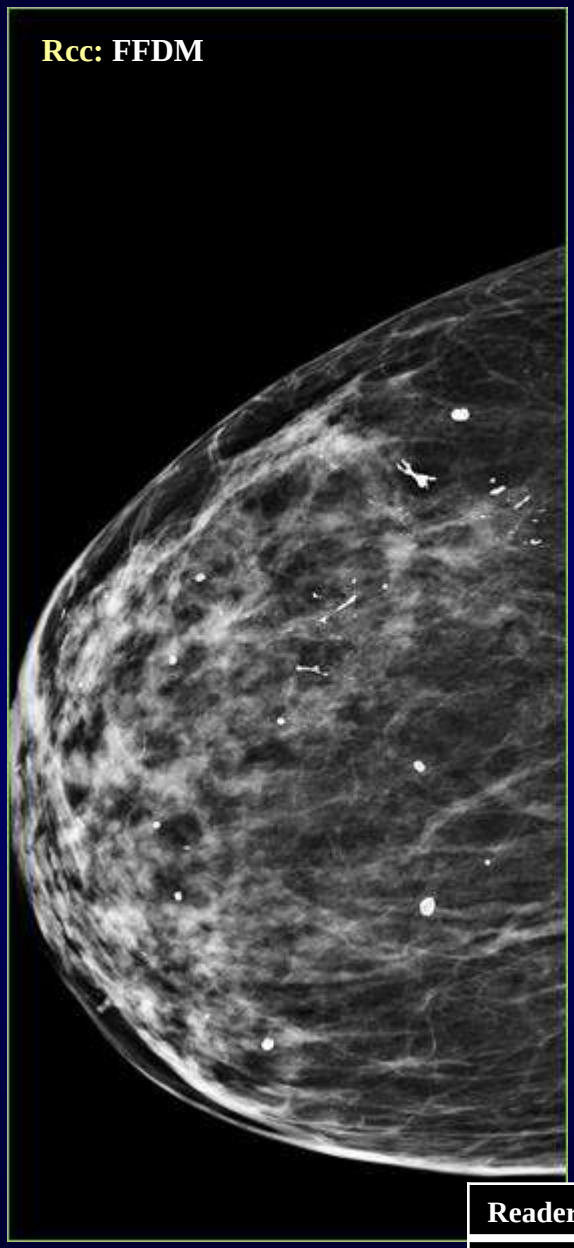
Histology: DCIS gr. 3, 10 mm + DCIS gr. 1, 15 mm

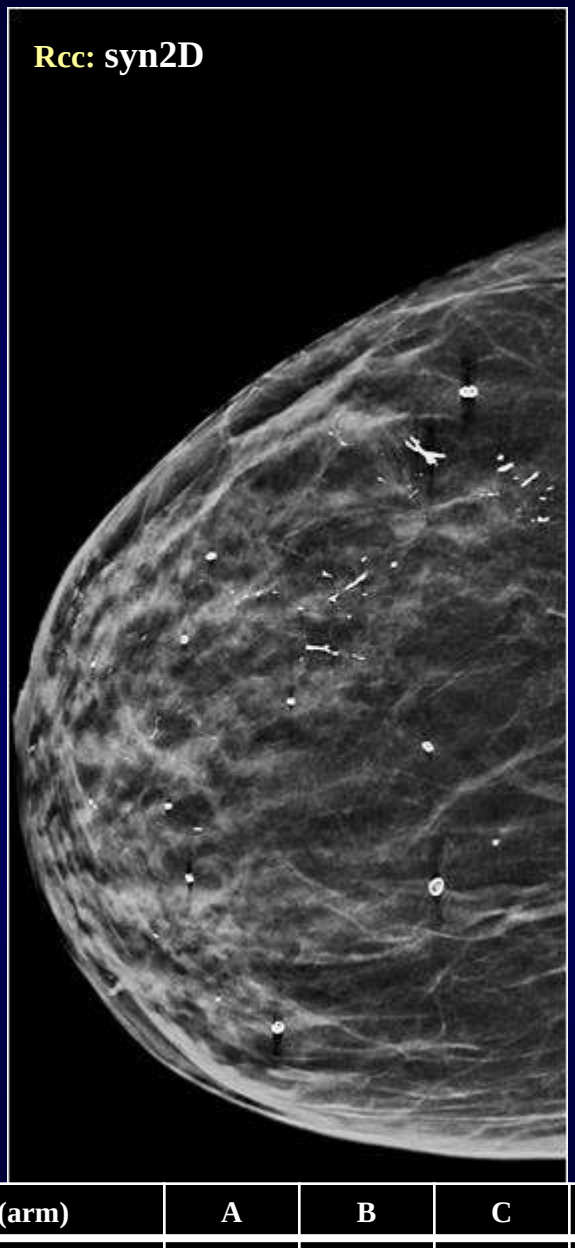
Electronic zooming

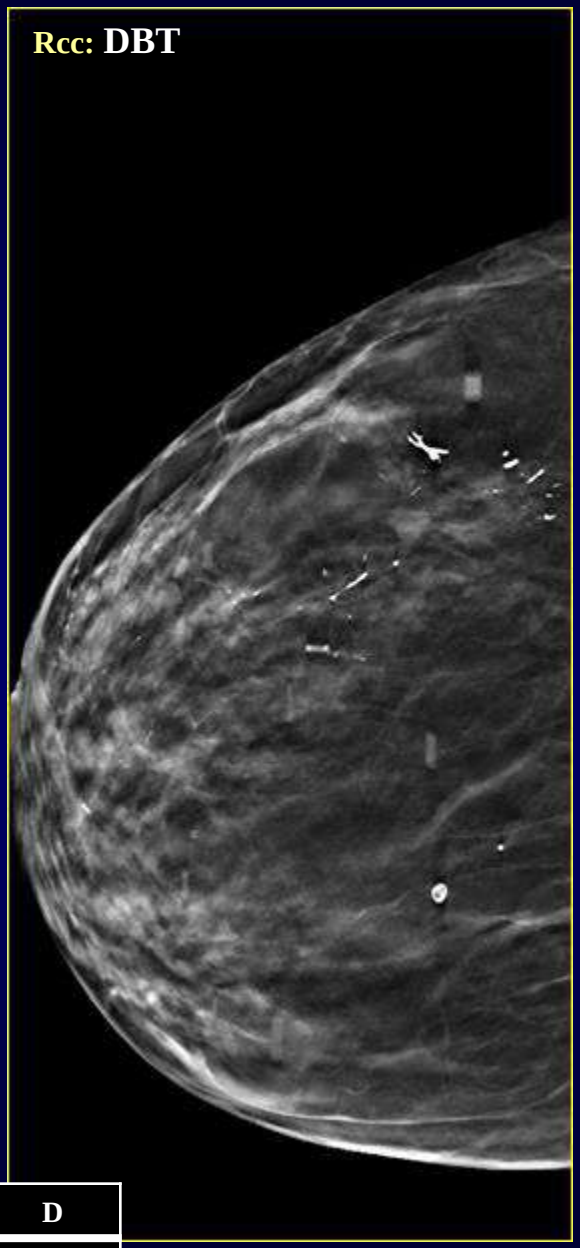
Reader (arm)	A	B	C	D
Score (mc's)	3	4	2	1

Oslo Tomosynthesis Screening Trial: **DCIS gr. 3 + IDC**

a)



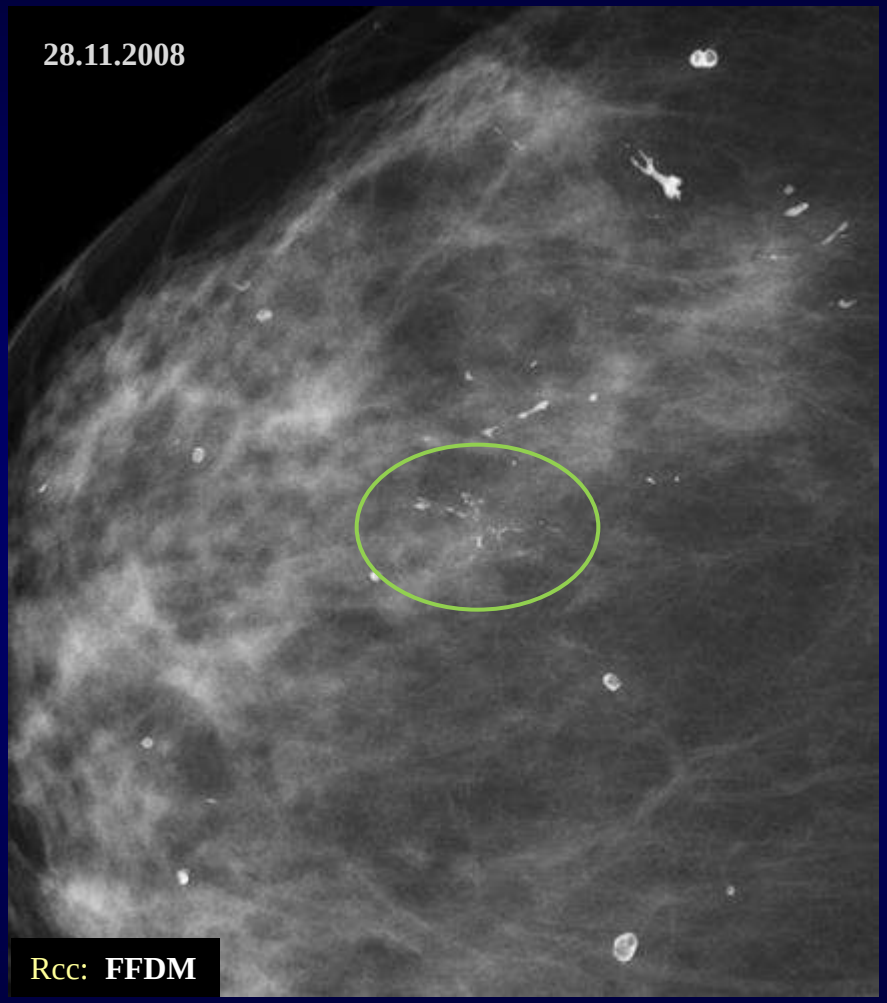


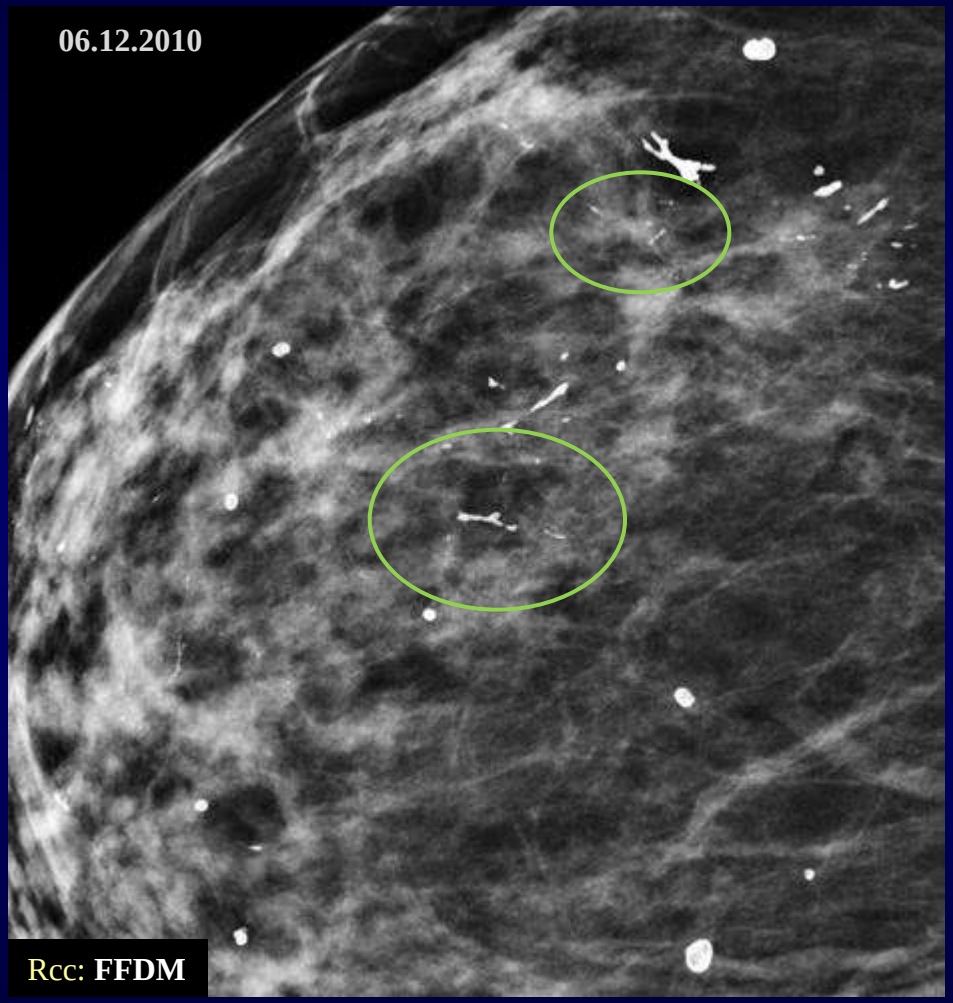


Reader (arm)	A	B	C	D
Score	1	1	1	4

b)

Disappearance of calcifications: ⇨ Development of invasive cancer !!
(note also development of casting-type calcification)

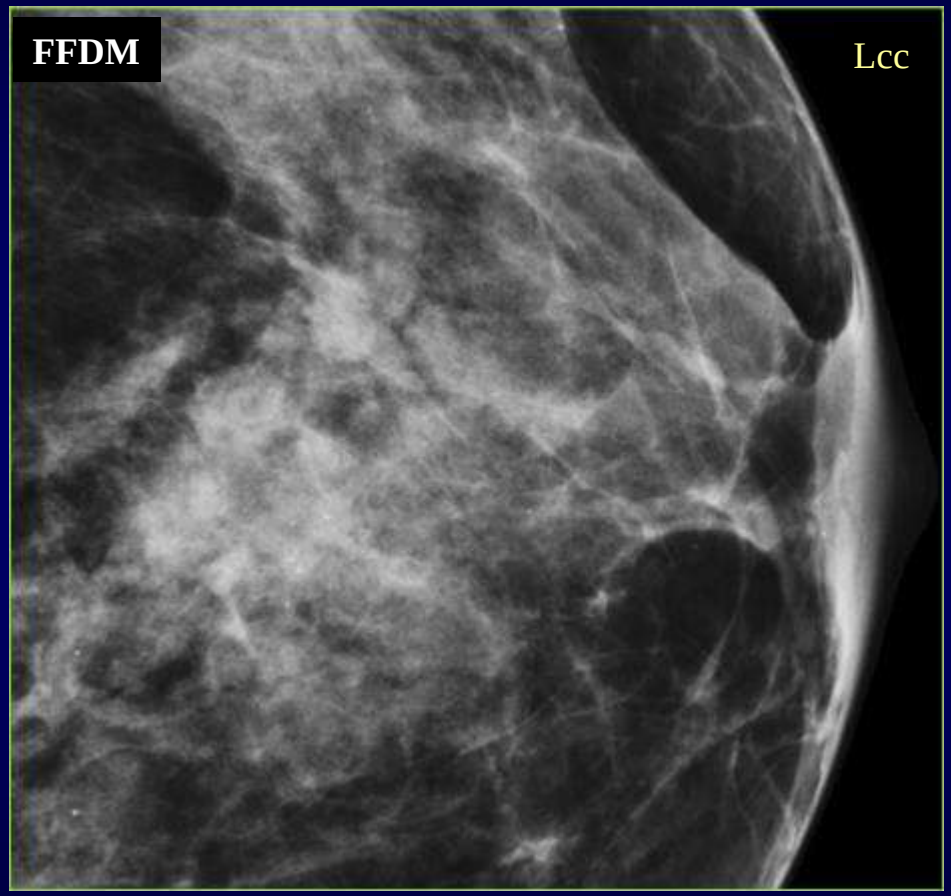


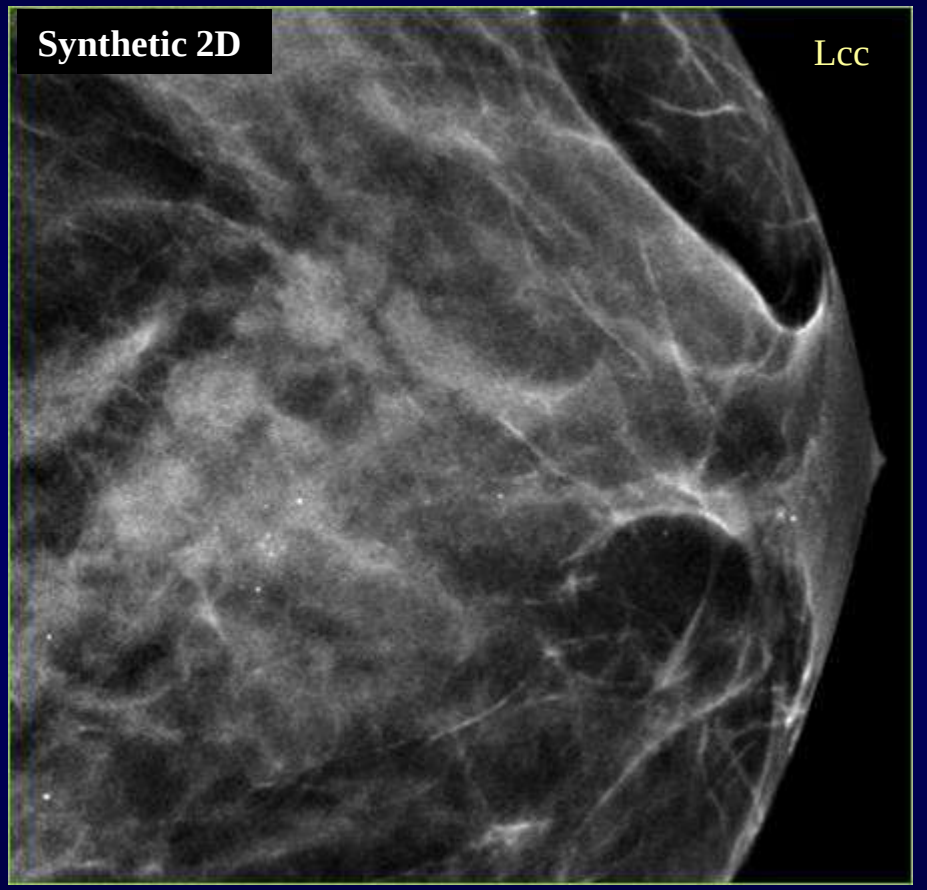


Histology: DCIS gr. 3 + IDC

Oslo Tomosynthesis Screening Trial (OTST)

a)



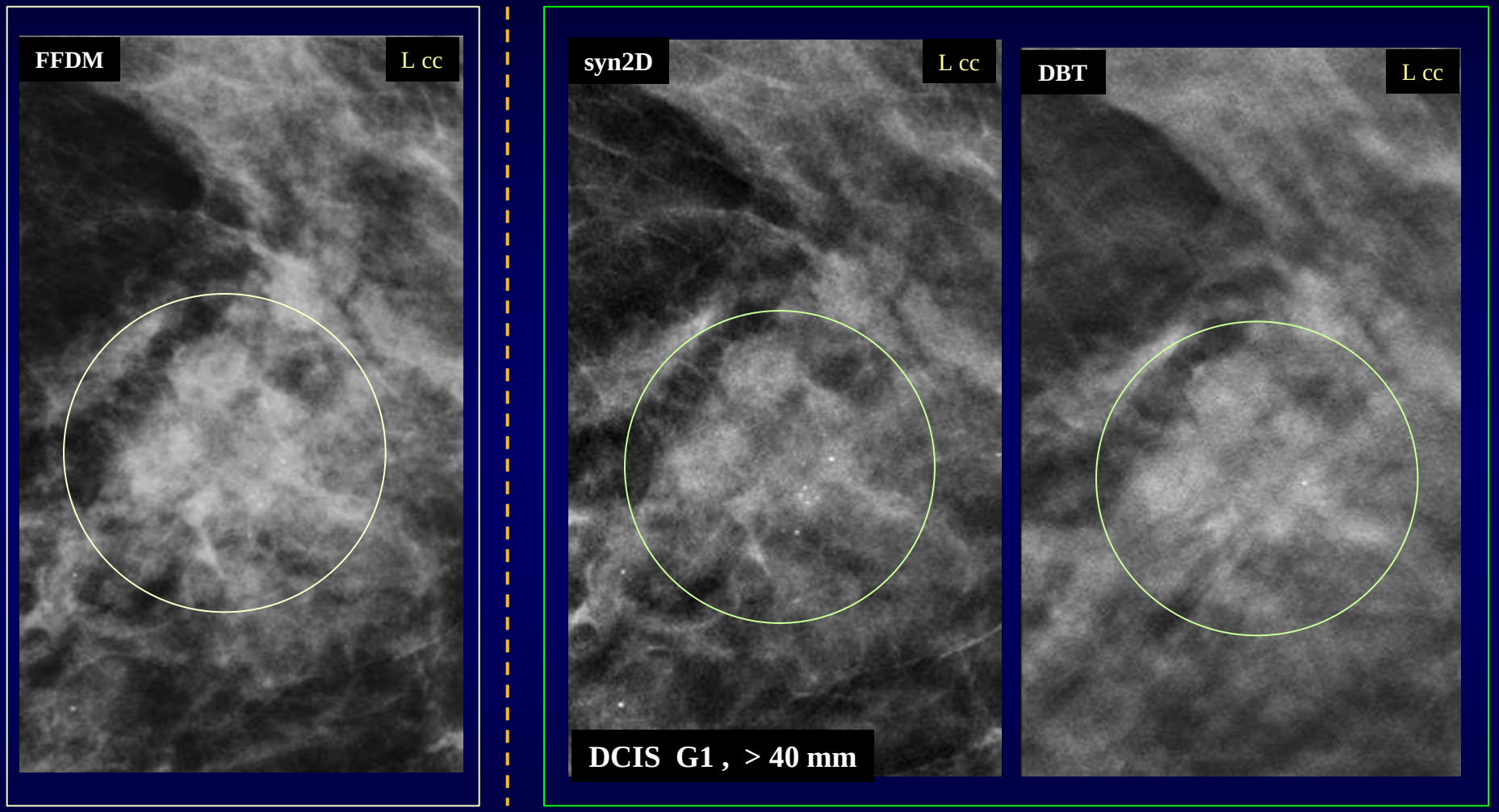


DCIS grade 1 , > 40 mm

DBT – challenges: Microcalcifications FFDM vs. syn2D vs. DBT

b)

Digital Breast Tomosynthesis (DBT) with reconstructed syn2D: Comparable radiation dose with conventional FFDM

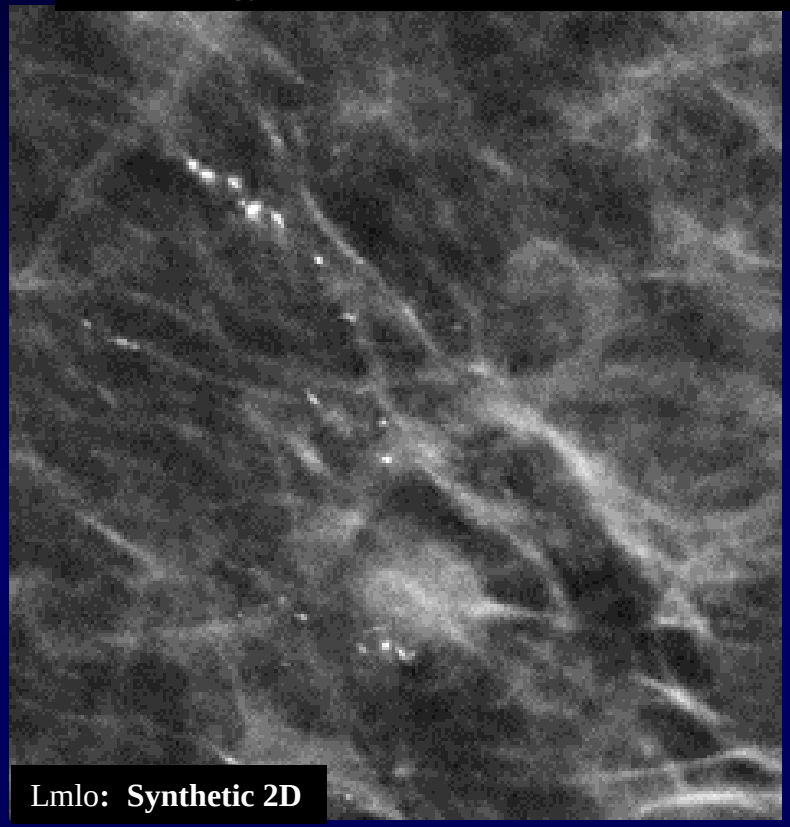


Conventional FFDM ⟺ Synthetic 2D + Tomosynthesis

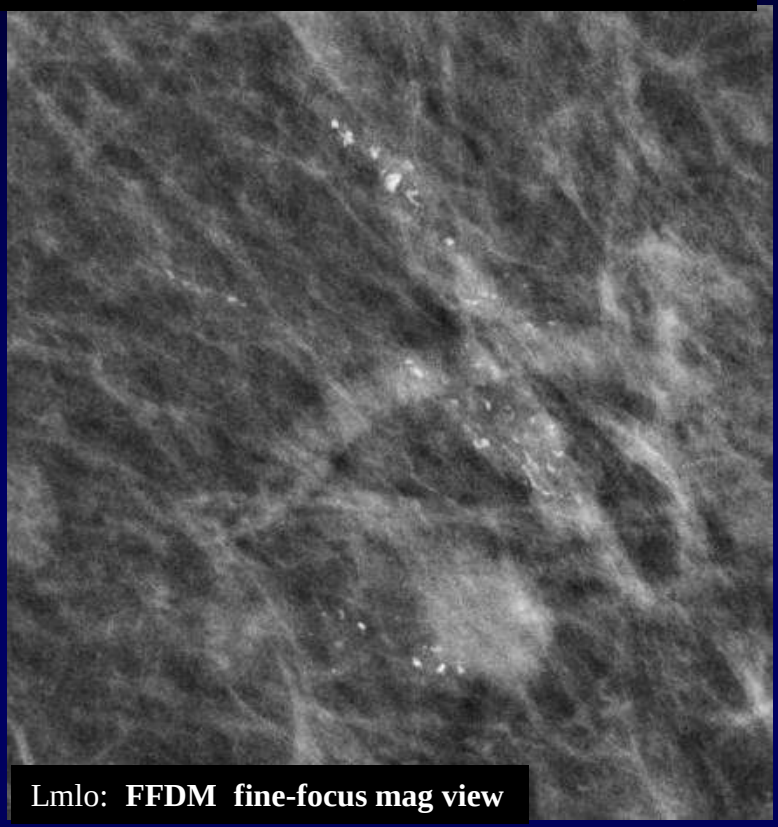
Comparable radiation dose !

Microcalcifications: Synthetic 2D and 3D vs FFDM mag-view

Histology: DCIS 30 mm, G3 (+ two small foci of microinvasive cancer + fibroadenoma)



Lmlo: **Synthetic 2D**



Lmlo: **FFDM fine-focus mag view**

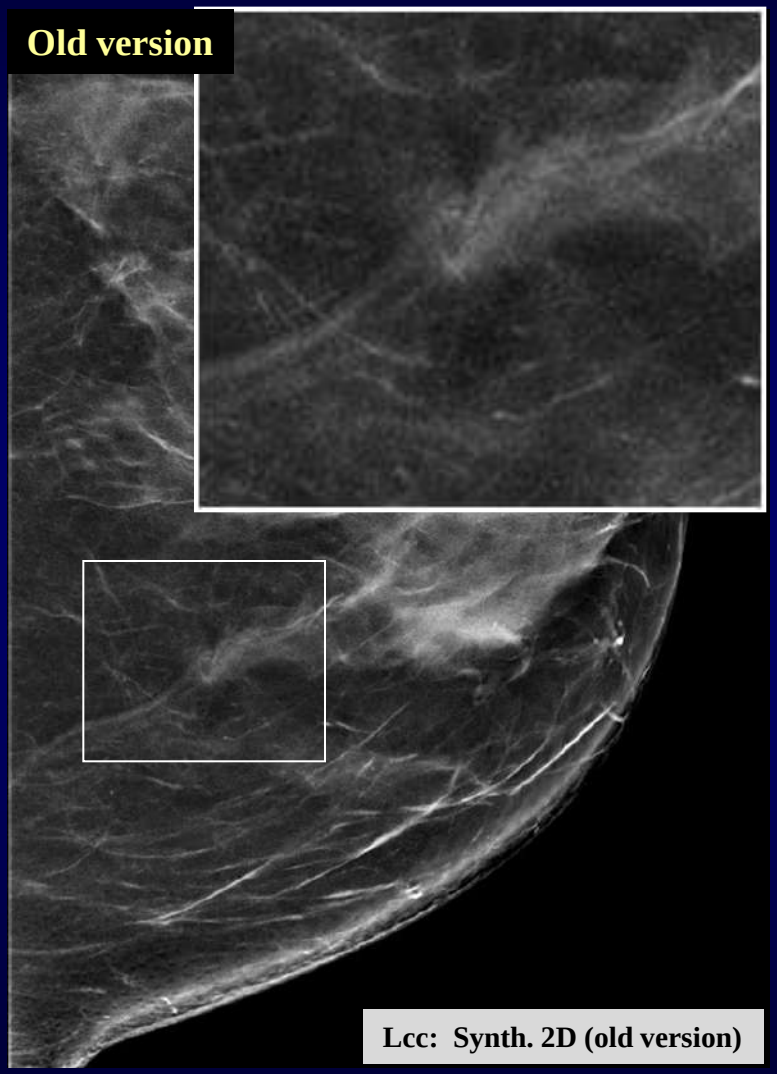
Screening with DBT and synthetic 2D images: Microcalcifications

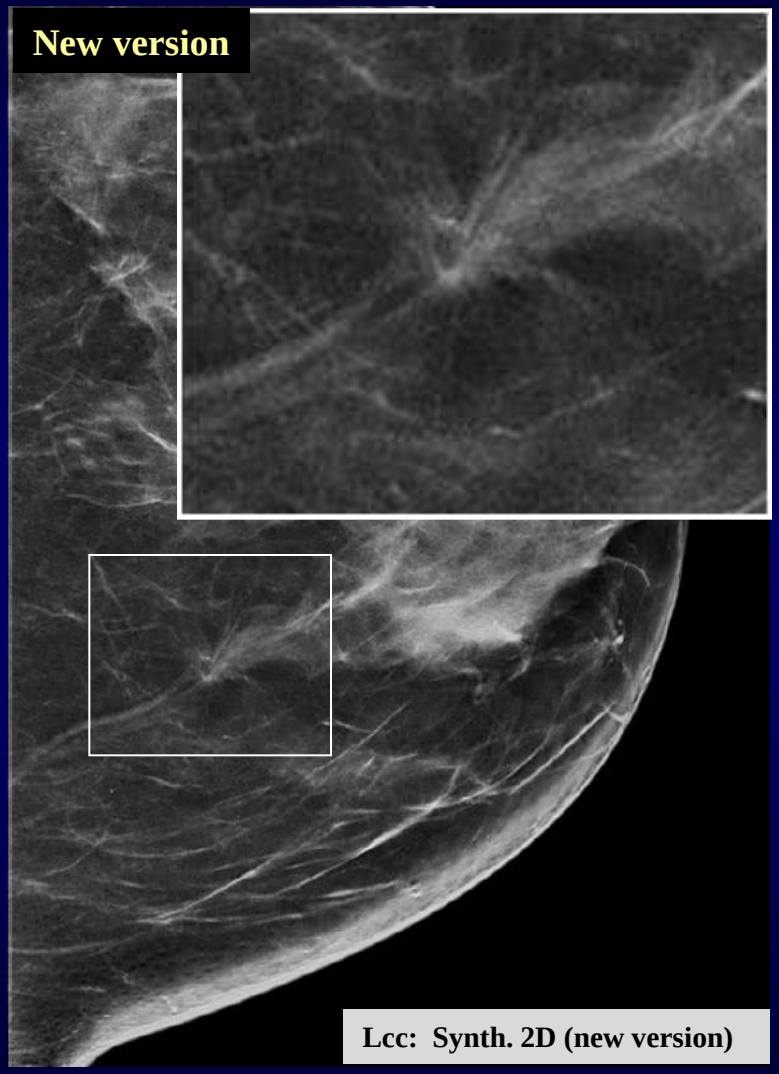
- Definitely suspicious: Recall for biopsy (VAB)
- Indeterminate benign-malignant: Recall for suppl. mag-views
- Definitely benign: Dismiss; back to screening

Indeterminate mc cluster (i.e., to biopsy or not):
Still indication for fine-focus magnification views !

Summary of syn2D in screening setting

On-going improvements of synthetic 2D images !





Oslo Tomosynthesis Screening Trial (OTST): Invasive ductal carcinoma (IDC), 8 mm

Breast cancer screening: Tomosynthesis pros and cons

- A) **DBT – pros:**
  - Increased specificity (reduced recall rate)
  - Increased cancer visibility / conspicuity (increased sensitivity; i.e., cancer detection rate)
- B) **DBT – cons («challenges»):**
  - One- vs. two-view DBT, radiation dose, and synthetic 2D
  - Microcalcifications: syn2D and DBT vs. FFDM
  - The (very) dense breast
  - Lesions seen only on DBT («tomo-only lesions»)
  - Increased work-load / interpretation time
  - ⇨ Overdiagnosis («length-time bias»)
  - Cost-effectiveness

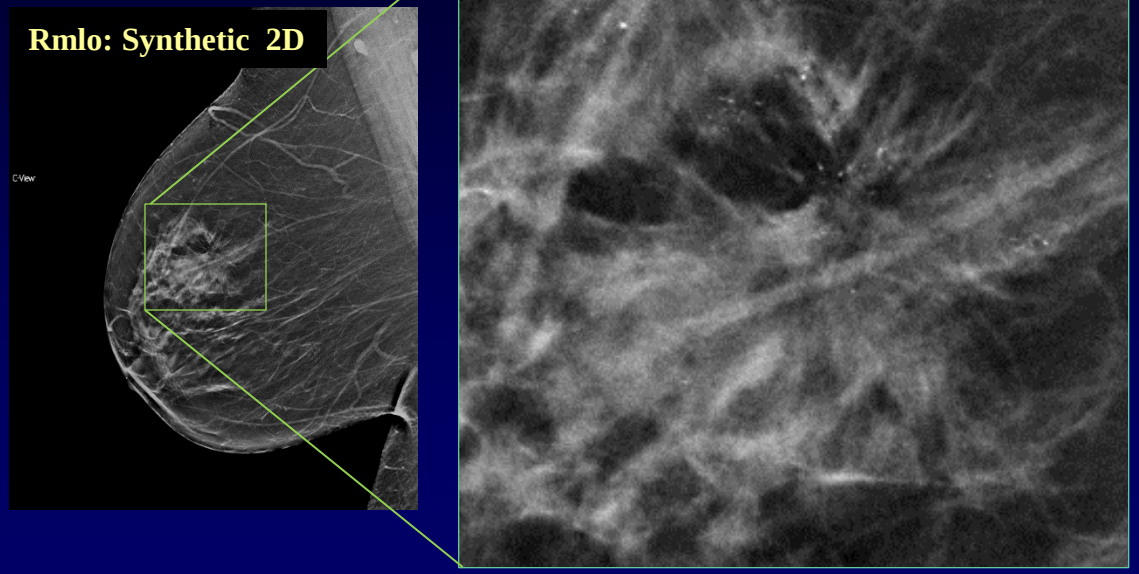
DBT: Potential for «overdiagnosis» !?

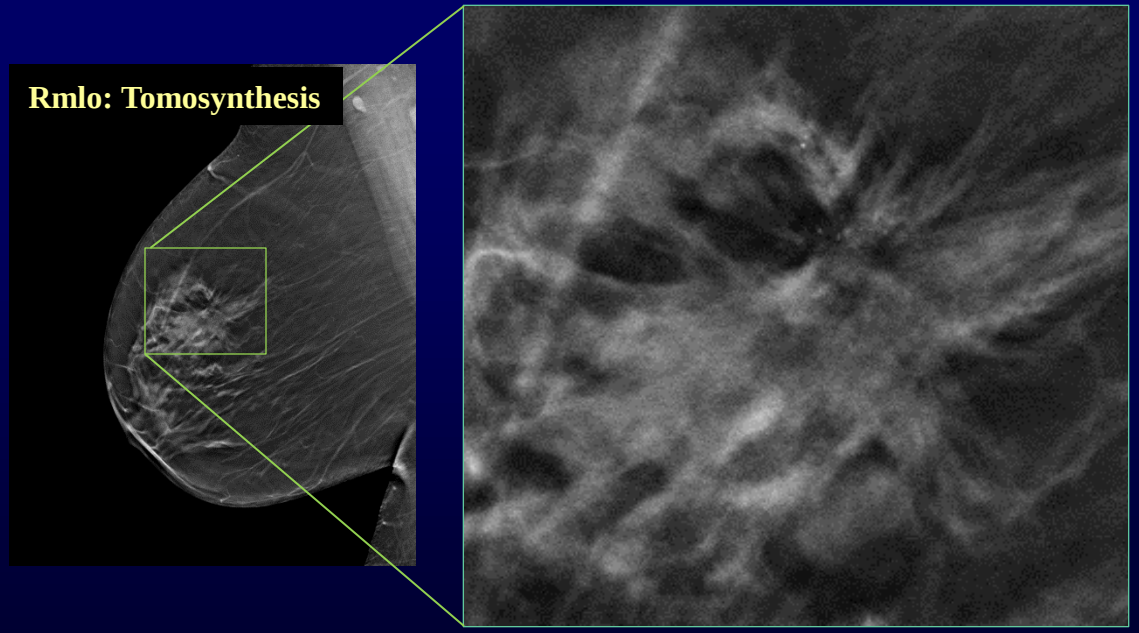
a)

2014

Oslo Breast Cancer Screening
(DBT + syn2D)

Reader (Arm)	A	B
Score (NBCSP)	**5**	**5**

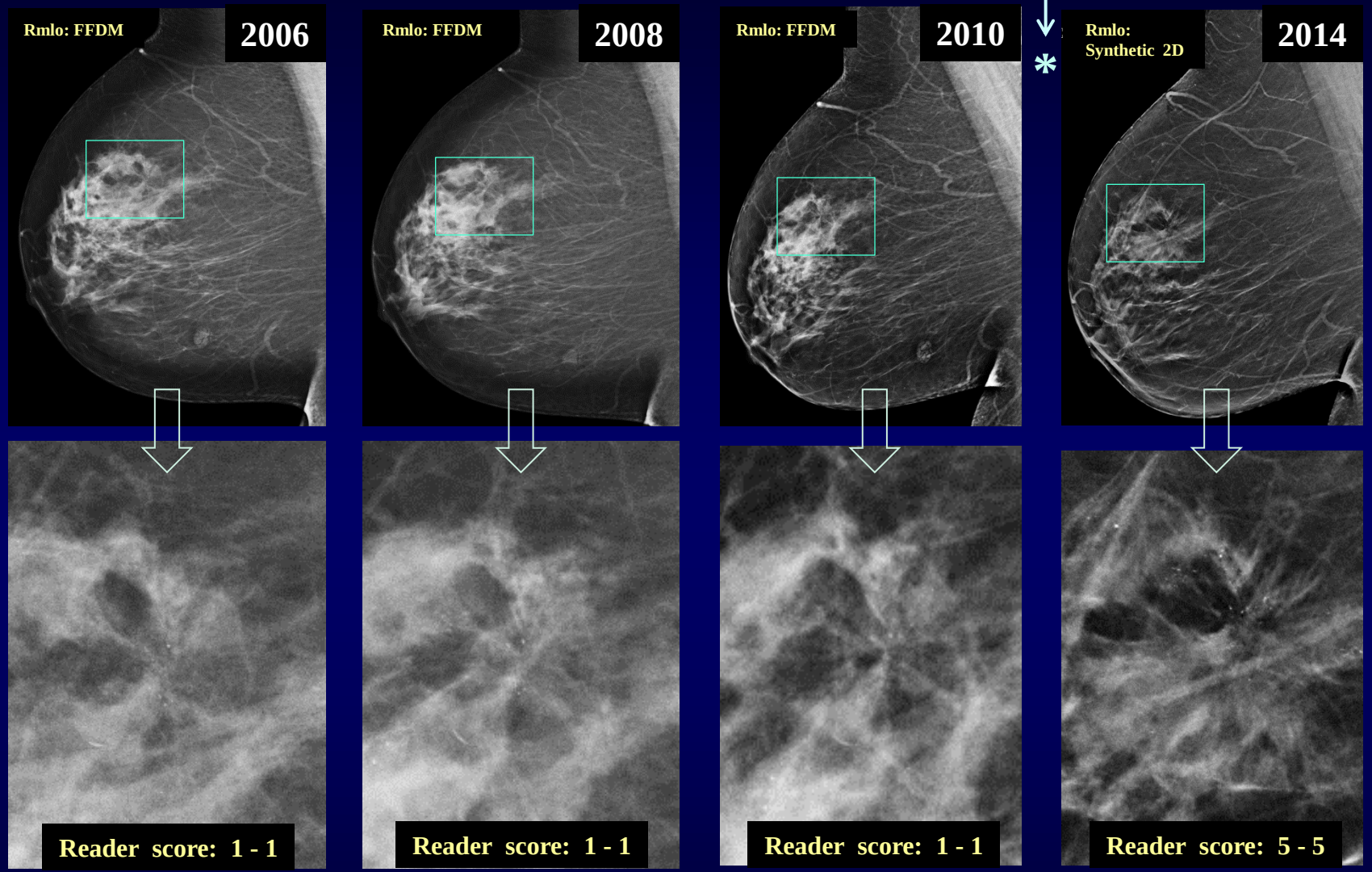




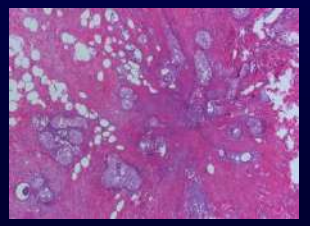
Radial scar +
DCIS grade 1

DBT: Potential for «overdiagnosis» - «prevalent tomo-round» !!

b)



Screening-detected cancer 2014: 62 year woman
Histology: Radial scar + DCIS G1



Objectives

- What is ”synthetic” mammograms (”syn2D”)
- Why do we need syn2D
- Syn2D and diagnostic performance:
  - Circumscribed masses
  - Spiculated masses
  - Distortions
  - Microcalcifications
- **Conclusion: DBT incl. syn2D in screening**

Studies comparing 2D (FFDM) versus 2D+3D (DBT) in mammography screening

Retrospective US studies comparing FFDM (2D) and 2D+3D (DBT)	Recall: %	Relative
Yale Uni, New Haven, CT Haas BM: Radiology 2013	12.0% 8.4%	↓ - 30% (sign)
TOPS, Houston, TX Rose SL: AJR 2013	8.7% 5.5%	↓ - 37% (sign)
US Comm. Practice, MD-VA Greenberg JS: AJR 2014	16.2% 13.6%	↓ - 16% (sign)
E. Wende Breast Care, NY Destounis S: J Clin Imag Sci 2014	11.5% 4.2%	↓ - 63% (sign)
Pennsylvania Uni, Philadelphia, PA McCarthy AM: JNCI 2014	10.4% 8.8%	↓ - 15% (sign)
Yale Uni, New Haven, CT Durand MA: Radiology 2015	12.3% 7.8%	↓ - 37% (sign)
Brown Uni, Providence, R! Lourenco AP: Radiology 2015	9.3% 6.4%	↓ - 31% (sign)
US multicenter study (13 centers) Friedewald SM: JAMA 2014	10.7% 9.1%	↓ - 16% (sign)
Beth Israel, Harvard, Boston, MA Sharpe RE: Radiology 2016	7.5% 6.1%	↓ - 19% (sign)
Pennsylvania Uni, Philadelphia, PA McDonald ES: AJR 2015	9.1% 7.8%	↓ -14% (sign)

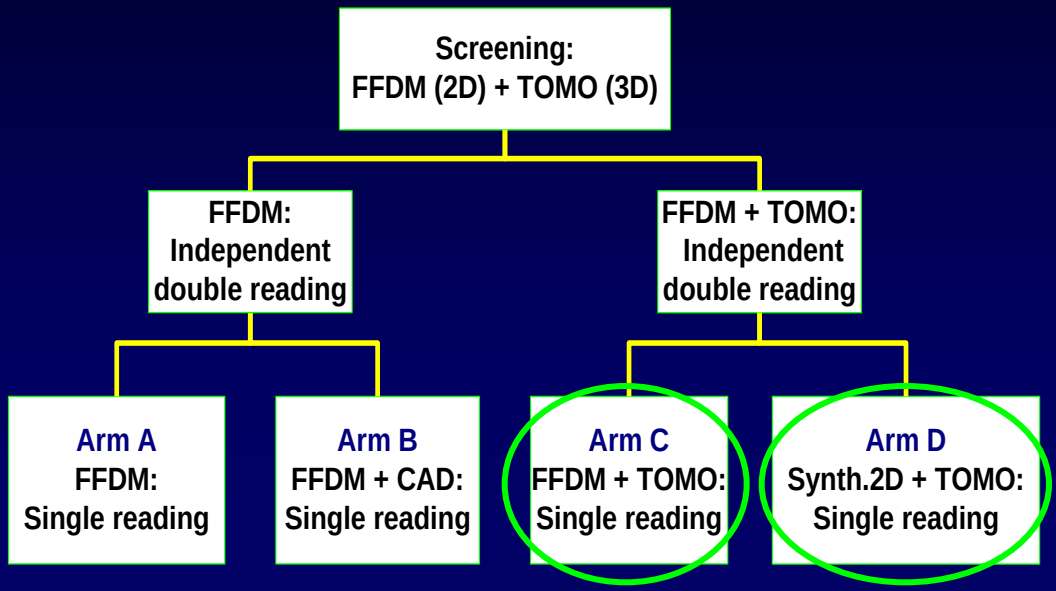
Significant ↓↑ (in favour of 2D+DBT)

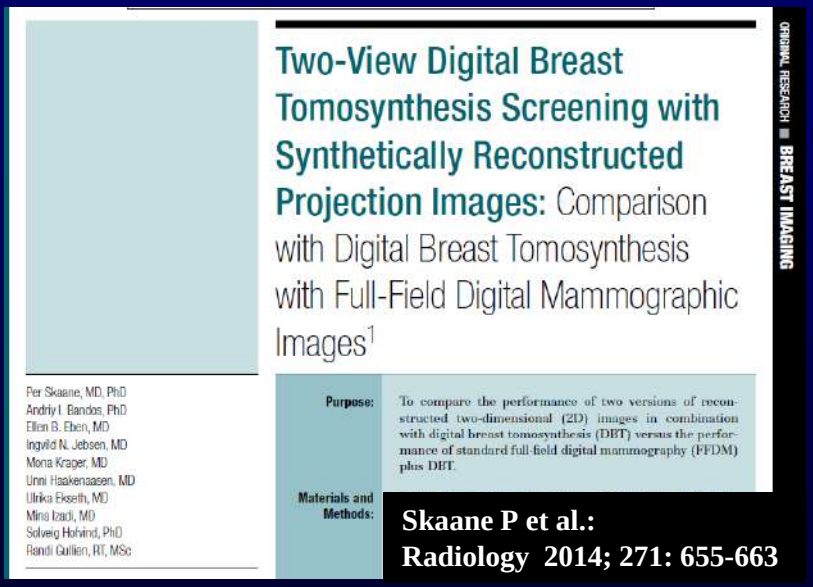
Prospective European trials comparing FFDM (2D) and 2D+3D (DBT)

Study	Cancer detection (n / 1,000)	Rel. increase ca. detect
STORM (Italy) 1)	5.3 vs. 8.1: + 2.8/1000	↑ 53 %
OSLO (OTST) 2)	6.1 vs. 8.0: + 1.9/1000	↑ 27 %
Malmø (MBTST) 3)	6.3 vs. 8.9: + 2.6/1000	↑ 43 %
Cordoba (Spain) 4)	5.7 vs. 4.7: + 1.0/1000	↑ 17 %
US multicenter Study 5)	4.2 vs. 5.4: + 1.2/1000	↑ 29%

1) Screening with Tomo OR standard Mammography; Final results. Ciatto S: Lancet Oncol 2013;14:583-9
2) Oslo Tomosynthesis Screening Trial); Interim analysis. Skaane P: Radiology 2013;267:47
3) Malmø Breast Tomosynthesis Screening Trial); Interim analysis. Lång K: Eur Radiol 2015
4) Cordoba Screening Study; Romero Martin S: Eur Radiol 2018
5) US multicenter study (13 centers); Final report. Friedewald SM: JAMA 2014;311:2499

Oslo Tomosynthesis Screening Trial:
Preliminar results comparing FFDM+DBT (arm C) vs. syn2D+DBT (arm D)




ORIGINAL RESEARCH ■ BREAST IMAGING

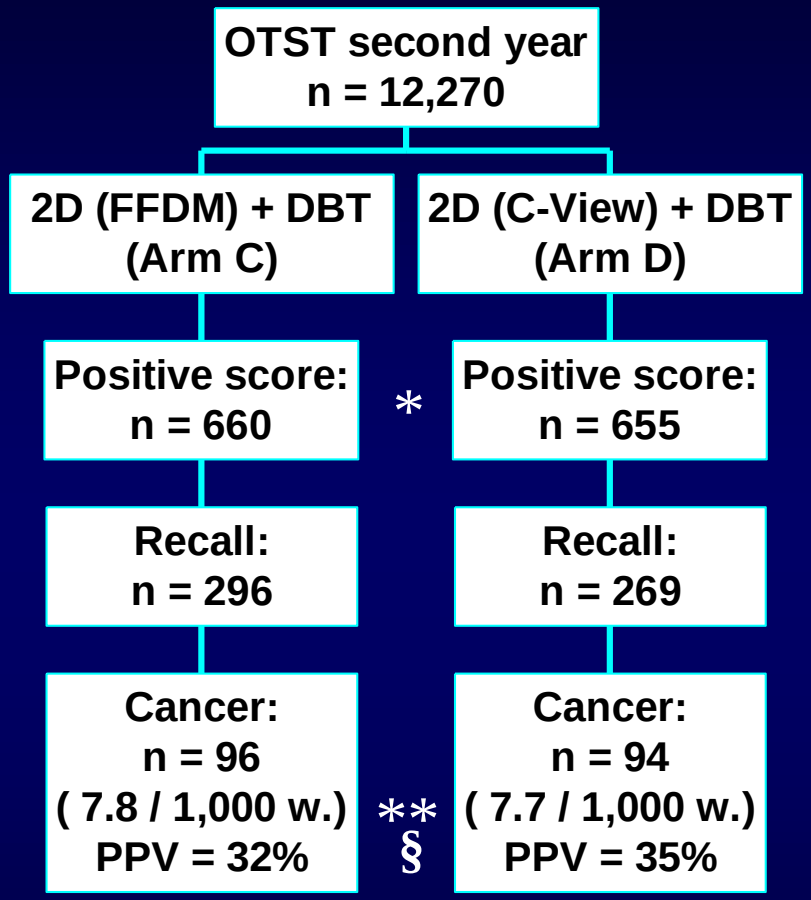
Two-View Digital Breast Tomosynthesis Screening with Synthetically Reconstructed Projection Images: Comparison with Digital Breast Tomosynthesis with Full-Field Digital Mammographic Images[1]

Per Skaane, MD, PhD
Andriy I. Bandos, PhD
Ellen B. Eben, MD
Ingvild N. Jebsen, MD
Mona Krager, MD
Unni Haakenaasen, MD
Ulrika Ekseth, MD
Mina Izadi, MD
Solveig Hofvind, PhD
Randi Gullien, RT, MSc

Purpose: To compare the performance of two versions of reconstructed two-dimensional (2D) images in combination with digital breast tomosynthesis (DBT) versus the performance of standard full-field digital mammography (FFDM) plus DBT.

Materials and Methods:

Skaane P et al.:
Radiology 2014; 271: 655-663



*** Positive score p = 0.85 (n.s.)**

**** Ca. detection p = 0.89 (n.s.)**

§ PPV p = 0.47 (n.s.)

i.e., no significant difference

Screening studies comparing FFDM+DBT vs. syn2D+DBT

Study	Study Design	Population (n)	Recall (%)	p-value (sign.)	Cancer § detection	p-value (sign.)
OTST 1)	Prospective; screening	FFDM: 12,270 syn 2D: 12,270	4.6* 4.5*	n.s.	7.8 7.7	n.s.
STORM-2 2)	Prospective; screening	FFDM: 9,672 syn 2D: 9,672	4.0* 4.5*	↑ p<0.05	8.5 8.8	n.s.
Cordoba 3)	Prospective; screening	FFDM: 16,067 syn 2D: 16,067	2.8** 2.9**	n.s.	5.0** 5.4**	n.s.
Uni Penn, PA 4)	Retrospective; screening	FFDM: 15,571 syn 2D: 5,366	8.8 7.1	↓ p<0.01	5.4 5.0	n.s
Baltimore , MD 5)	Retrospective; screening	FFDM: 7,845 syn 2D: 14,776	7.6 7.1	↓ p=0.04	5.3 5.6	n.s.
Newark, DE 6)	Retrospective; screening	FFDM: 30,561 syn 2D: 16,173	5.8 4.3	↓ p<0.01	6.4 6.1	n.s.
TOMMY trial 7)	Retrospective; experimental	FFDM: 7,060 syn 2D: 7,060	70%*** 72%***	n.s.	89%*** 88%***	n.s.

§: Cancer/1000 exam *: False positive score **: Single reading s2D+FFDM+DBT vs s2D+DBT
***: Sensitivity and specificity

1) Skaane P et al.: Radiology 2014
2) Bernardi D et al.: Lancet Oncol 2016
3) Romero Martin S : Eur Radiol 2018
4) Zuckermann SP: Radiology 2017
5) Ambinder EB: Acad Radiol 2018
6) Aujero MP et al.: Radiology 2017
7) Gilbert FJ et al.: Radiology 2015

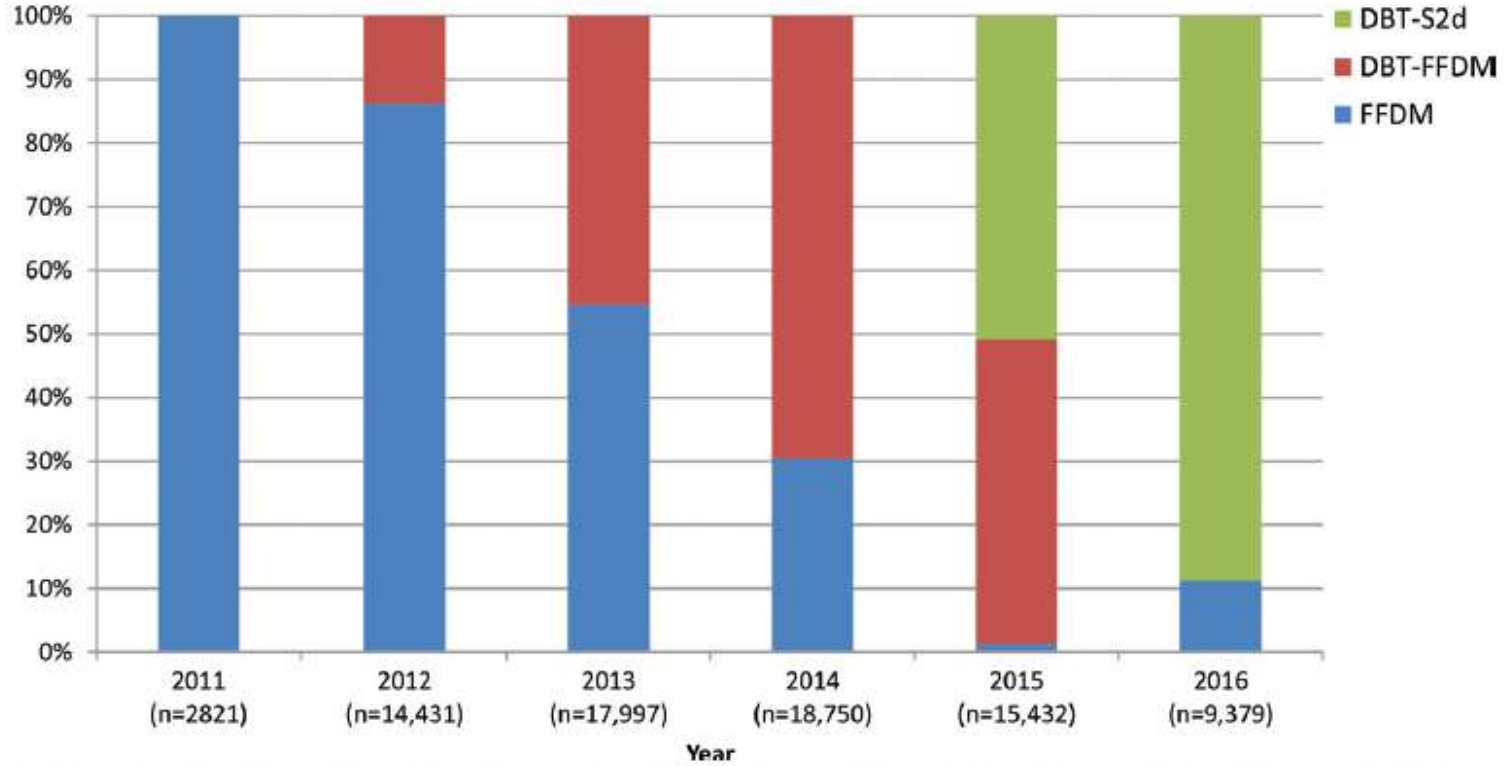
Significant:
- ↓ favour of syn2D+DBT
- ↑ disfavour of syn2D

Clinical Performance of Synthesized Two-dimensional Mammography Combined with Tomosynthesis in a Large Screening Population[1]

Radiology 2017

Mirelle P. Aujero, MD
Sara C. Gavenonis, MD
Ron Benjamin, DO
Zugui Zhang, PhD
Jacqueline S. Holt, MD, FACR

Purpose: To compare the clinical performance of synthesized two-dimensional (s2D) mammography combined with digital breast tomosynthesis (DBT) with that of full-field digital mammography (FFDM) alone and FFDM combined with DBT in a large community-based screening population by analyzing recall rate, positive predictive value, and cancer detection rate.



Graph shows percentage of screening breast examinations of each modality per year included in the study period. Note gradual decrease in percentage of FFDM studies from 2011 to 2015 and corresponding increase in percentage of DBT studies. Sample size (*n*) refers to number of breast examinations.

3D Imaging May Revolutionize Cancer Screening


Radiology

A New Era in Mammography Screening[1]

Daniel B. Kopans, MD

Contrary to criticism by those who ... but only a few of us used CT in breast

Tomosynthesis systems installed in U.S.A.

……so what are we waiting for in Europe ?