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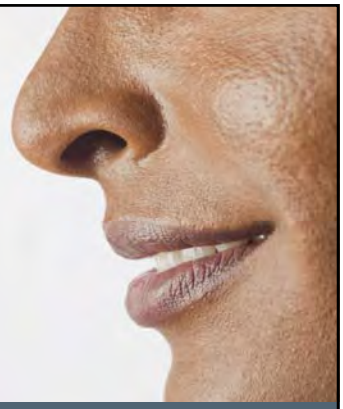

APT 2014, Duisburg, 27.06.2014

Neue Mammografische Verfahren

Thomas Mertelmeier
Siemens AG Healthcare, Erlangen, Germany

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Answers for life.

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Outline

- Breast Tomosynthesis – Image Acquisition and Reconstruction
- Quality Control
- Breast Tomosynthesis - Synthetic Mammogram
- Contrast Enhanced Dual Energy Mammography
- Phase Contrast Mammography
- X-ray/Ultrasound registration

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H CP XP R&D TEC

Outline

- **Breast Tomosynthesis – Image Acquisition and Reconstruction**
- Quality Control
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- X-ray/Ultrasound registration

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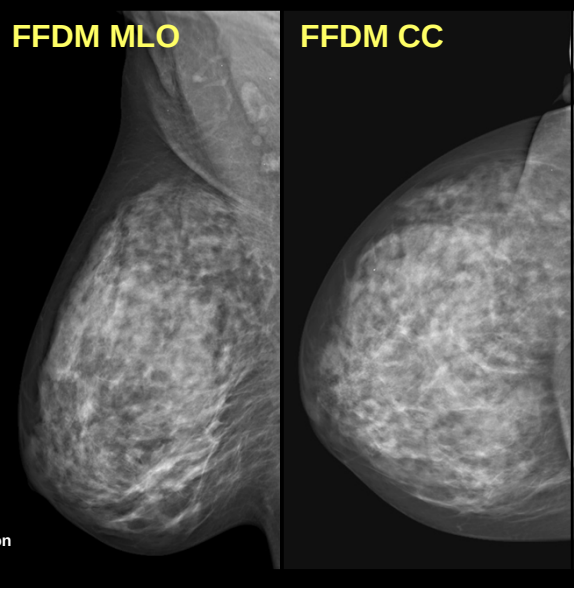
Mammography is not perfect



57-year-old woman
2.8 cm ductal cancer
grade 3

Courtesy of
Malmö University Hospital, Dr. I. Andersson

Mammography is not perfect

SIEMENS

15 - 30% of cancers are missed at screening
Bird 1992, Laming 2000

(Technical problem incl. positioning)
Lesion is not perceived
Feature is misinterpreted

Reasons:

Dense breast tissue – anatomical noise
Small or no attenuation difference – low or no contrast
Tumor growth pattern – diffuse cancer

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Digital Breast Tomosynthesis: Why ?

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- Physical image quality of FFDM is higher than that of SFM, i.e.
  DQE(FFDM) > DQE(SFM) by factor >2

but

- Clinical Studies:
  FFDM similar performance as SFM
  (ACRIN-DMIST:
  E. Pisano, NEJM 353, 1773-1783, 2005)

- Reason:
  Limitation is not quantum or detector noise, but anatomical noise

- Tomosynthesis reduces tissue overlap similar to small specimen imaging

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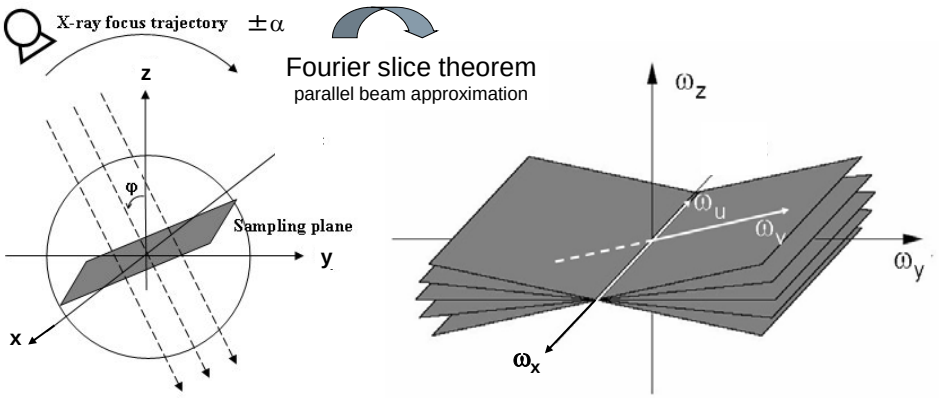
Tomosynthesis Reconstruction

Incomplete Data due to sampling geometry



Spatial domain **frequency domain**

- sampling is incomplete
- sampling is often sparse

➔ approximative inversion only

➔ artifacts

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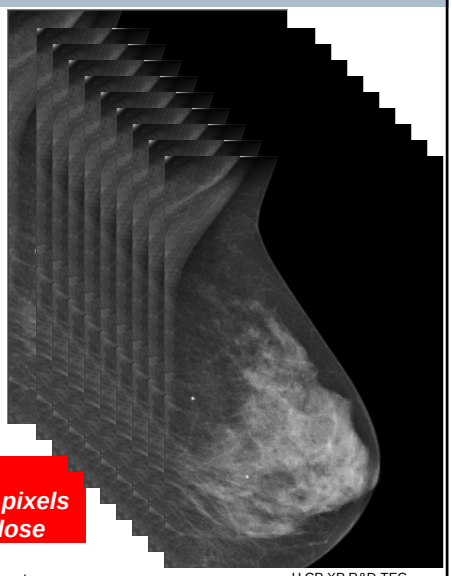
From 2-D to 3-D images

Step 1: Acquisition

25 low dose projections over 50°



Fast aSe detector, 24 x 30 cm, 85µm pixels High DQE at low dose

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From 2-D to 3-D images

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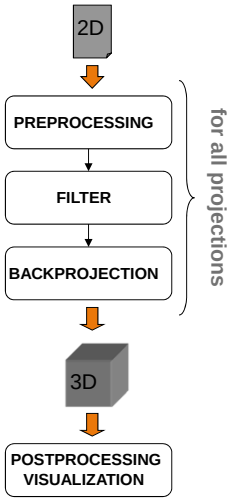
Step 2: Reconstruction by Filtered Backprojection

- pipeline structure
  - pre- & postprocessing
- fast & flexible algorithm
- systematic filter design
  - optimize image quality
  - adjust to the image cha
  - reduction of artifacts
- exact geometry description using projections matrices approach
- Implementation on GPU

Ramp inversion filter
Spectral filter for noise
Slice thickness filter



- J. Orman, T. Mertelmeier, W. Haerer, Lecture Notes in Computer Science **4046**,IWDM 2006, pp175-182, 2006.
- T. Mertelmeier, J. Orman, W. Haerer, M. K. Kumar, Proc. SPIE Proc. **6142**, 61420F-61412 (2006).
- K. Wiesent et al., IEEE TMI, **19**, 391-403, 2000

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Tomosynthesis system design

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It‘s a multiparameter problem

- Angular range
- Number of projections
- X-ray spectrum optimization
- Dose
- Reconstruction method

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Tomosynthesis System Design
Angular range

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Large angular range …

- increases depth resolution (z)
- decreases slice thickness (“in focus“)
- reduces “out-of-plane“ artifacts
- improves contrast of low-frequency objects

but

- decreases field-of-view
  (when using a stationary detector)

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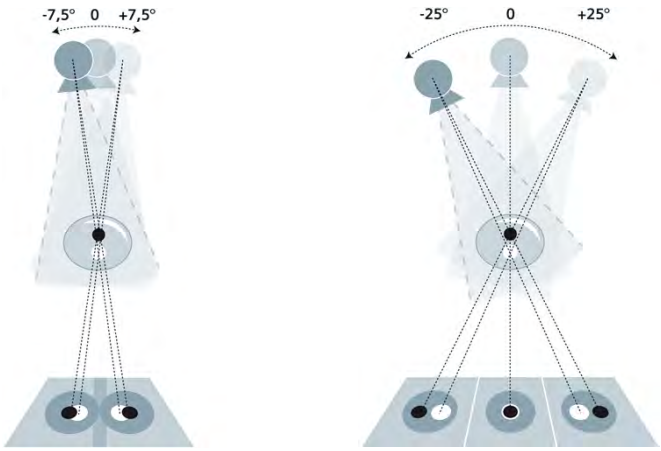
Tomosynthesis: Every degree matters



15°

MAMMOMAT Inspiration
50°

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Tomosynthesis System Design
Number of projections

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More projections …

- decrease streak artifacts (“limited view artifacts“)

but

- reduce signal per projection (at constant total dose), i.e. the detector noise limits the number of projections.
- increases scan duration (at constant frame rate) and therefore, the compression time

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Sponge: No streak artifacts with 25 views

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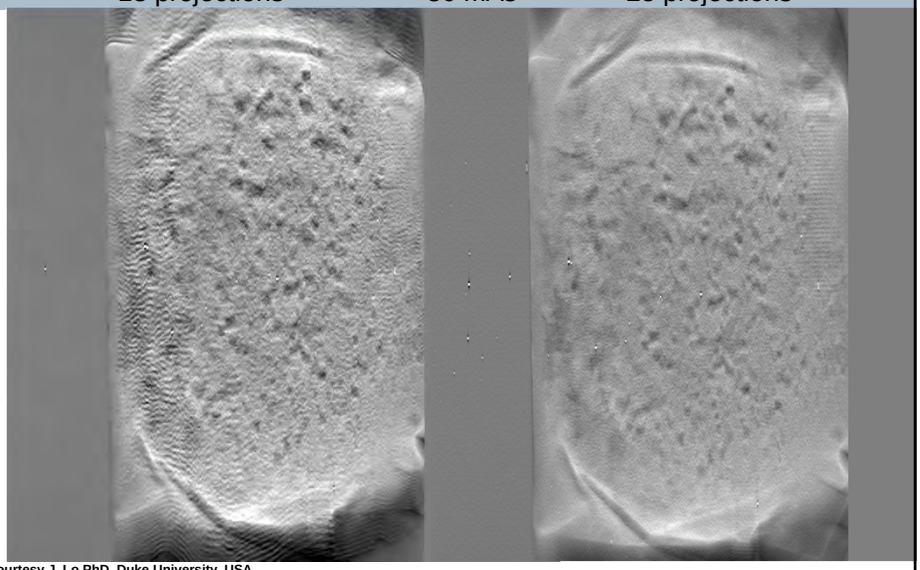
13 projections 80 mAs 25 projections



Courtesy J. Lo PhD, Duke University, USA

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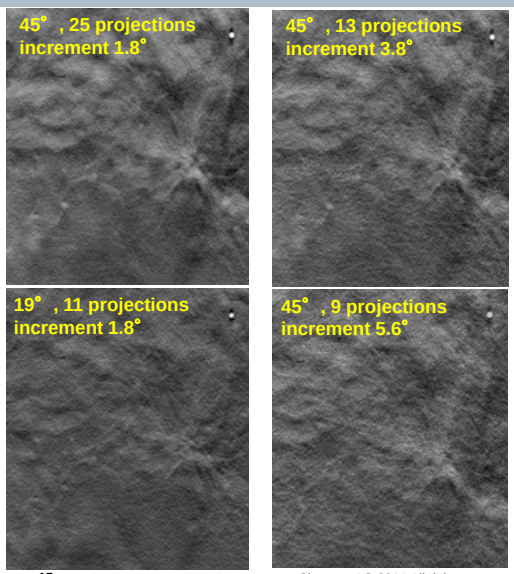
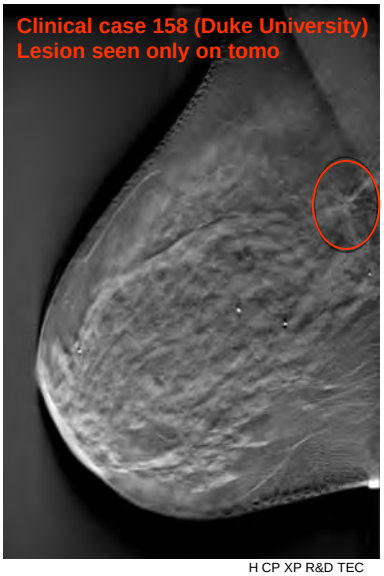
Angular range: contrast | **No. of projections: streak artifacts**





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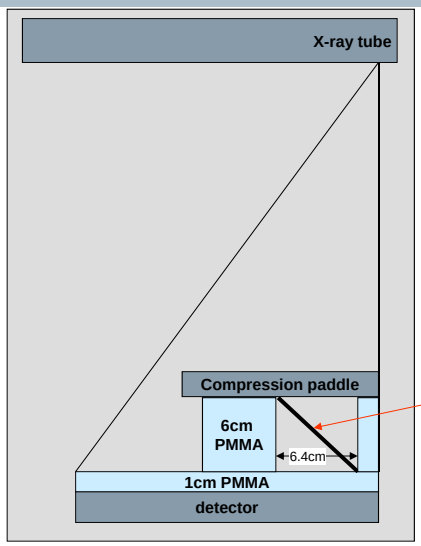
Angular range and slice thickness



Experiment with inclined wire

Reconstructed wire in focus is direct measure for slice thickness

Wire inclined by 43° , oriented perpendicular to scan direction

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Wire phantom and slice thickness

Tomo angle 45° Slice 30 Tomo angle 15°

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Dose of Breast Tomosynthesis

- 1 exposure, dose N_0, additional electronic noise $\boldsymbol{\sigma_e}$

$$SNR_0^2 = \frac{N_0}{1+\frac{\sigma_e^2}{N_0}}$$

- n exposures, dose N_i, $1 \le i \le n$, $N_{tot} = \Sigma N_i$, electr. noise $\boldsymbol{\sigma_e}$

$$SNR_{tot}^2 = \frac{N_{tot}}{1+\frac{n \cdot \sigma_e^2}{N_{tot}}}$$

If $N_{tot} = N_0$ and $\sigma_e^2/N_0 \ll 1$: $SNR_0 \approx SNR_{tot}$

- Literature and experience:
  dose of a tomo scan is in the range of the dose of 1 or 2 mammograms

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Opdose – Automatic exposure control

Opdose®

- Automatically selects the optimum tube voltage (kVp)
- Selects the lowest dose for the individual breast characteristics

Adjusted for tomosynthesis purposes with W/Rh only, for lower dose:

One 2D image: AGD < 1 mGy*

One 3D scan: AGD < 2 mGy*,
configurable between 1 x 2D and 2 x 2D ,
studies ongoing

* Average with W/Rh for a 4.5 cm plexiglas phantom (PMMA; equivalent to 5.3 cm breast);

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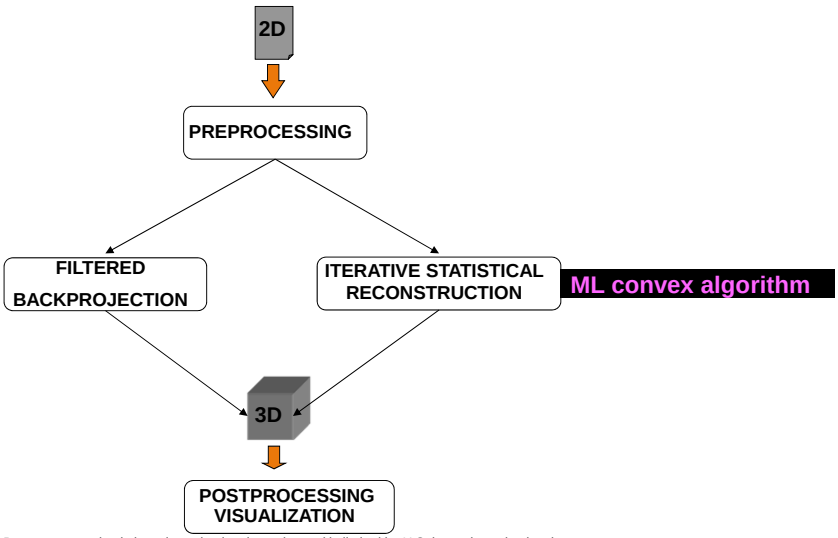
Optimizing reconstruction



Breast tomosynthesis is an investigational practice and is limited by U.S. law to investigational use.
It is not commercially available in the U.S. and its future availability cannot be ensured.

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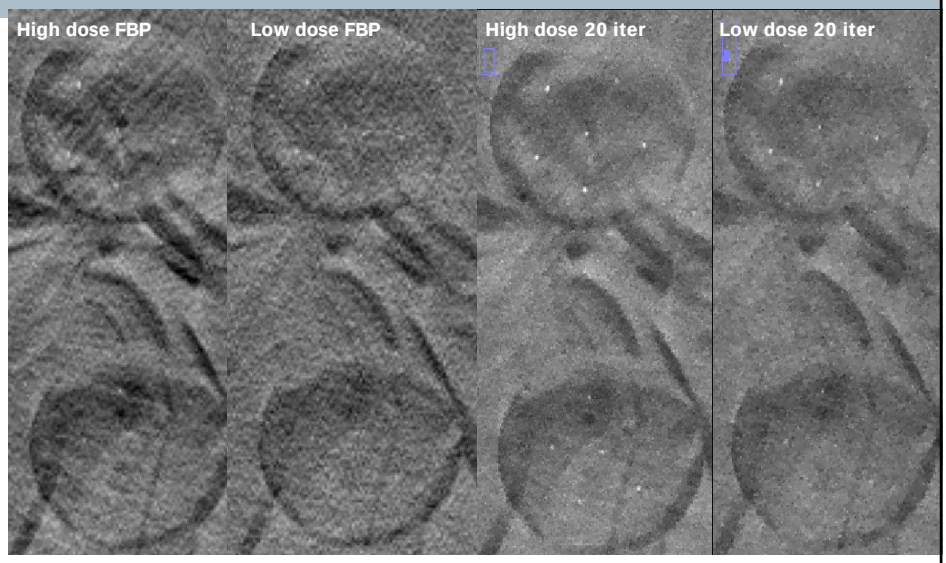
Standard FBP* vs. Iterative ML-convex

CIRS 20 tomo phantom



*Standard FBP = FBP adapted to DBT Low dose: regular FFDM dose; High dose: higher than regular

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Digital Tomosynthesis Acquisition

25 Projections over ≈ 50° and a stationary detector

Good compromise between

- **Dose**
- **Noise**
- **Depth resolution**
- **Acquisition/compression time**
- **Field of view**
- **Computation time**

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A large variety of systems

	Fuji Innovality	GE	Hologic Dimensions	IMS Giotto	Philips Microdose	Siemens MAMMOMAT Inspiration
Status	?	CE	CE/FDA	CE	Prototyp	CE
Tomosynthese-winkel	15°/40°	25°	15°	40°	11°	50°
Anzahl Projektionen	15	9	15	13	21	25
Röhren-bewegung	kontinuierlich	step & shoot	kontinuierlich	step & shoot	kontinuierlich	kontinuierlich
Scandauer/s	4/9	7	4	12	3-10	25
Detektorgröße/cm²	24x 30	24 x 30	24 x 29	24 x 30	mehrere Zeilen-detektoren	24 x 30
Detektorpixel/µm	hexaginal 150/100	100	140	85	50	85
Röntgen-Konverter	a-Se	CsI/a-Si	a-Se	a-Se	Si	a-Se
Anode/Filter	W/Rh	Rh/Rh	W/Al	W/Rh	W/Al	W/Rh

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MAMMOMAT® Inspiration
One platform for all mammography applications

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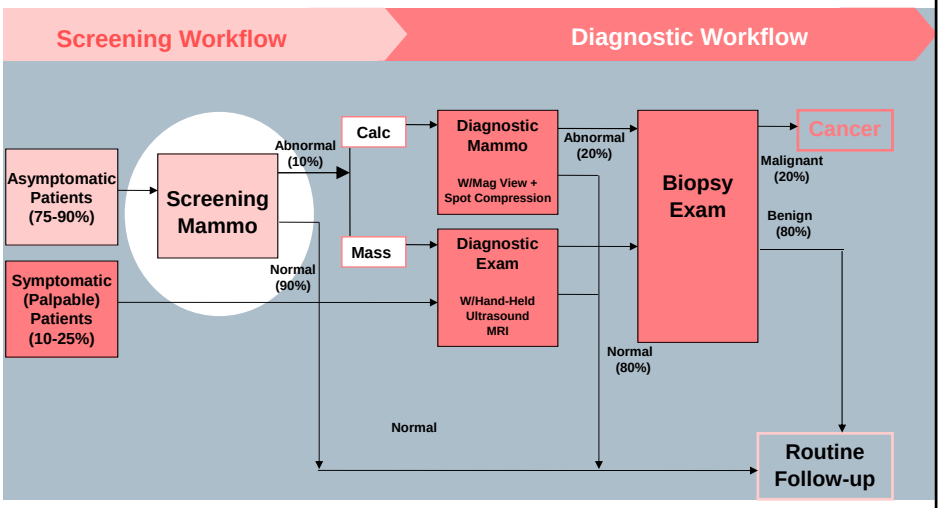
Clinical possibilities



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Clinical Tomo Screening Studies

Authors	device	mode	population	#pts	result
Skaane, Oslo, (2013) Radiology 267,47	Hologic	2-view DBT adjunct to 2D	screening	12 631 interim	Detection rate 0.8% vs 0.61% 27% increase(40% invasive c) FP rate 5.3% vs. 6.1%
Rose, Houston AJR 200, 1401 (2013)	Hologic Sel+DIm	2-view DBT adjunct to 2D	Screening, 2 arms	9499 13856	Det.rate: 0.537% vs 0.404% 33% increase Recall rate 5.5% vs. 8.7% 37% reduction.
Bernardi, Trento, Eur J Cancer. (2014) Feb 27 online	Hologic	2-view DBT adjunct to 2D	screening	7292	TP rate: 87% vs 60%, Improvement of det.rate: 27%, FP rate: 2.2% vs. 2.9%
Zackrisson, Malmö (2014), ECR 2014	Siemens	1-view DBT vs. 2-view FFDM (replacement)	screening	7500 interim	Det. Rate: 0.89% vs 0.63% 43% increase Recall rate: 3.8% vs. 2.6%

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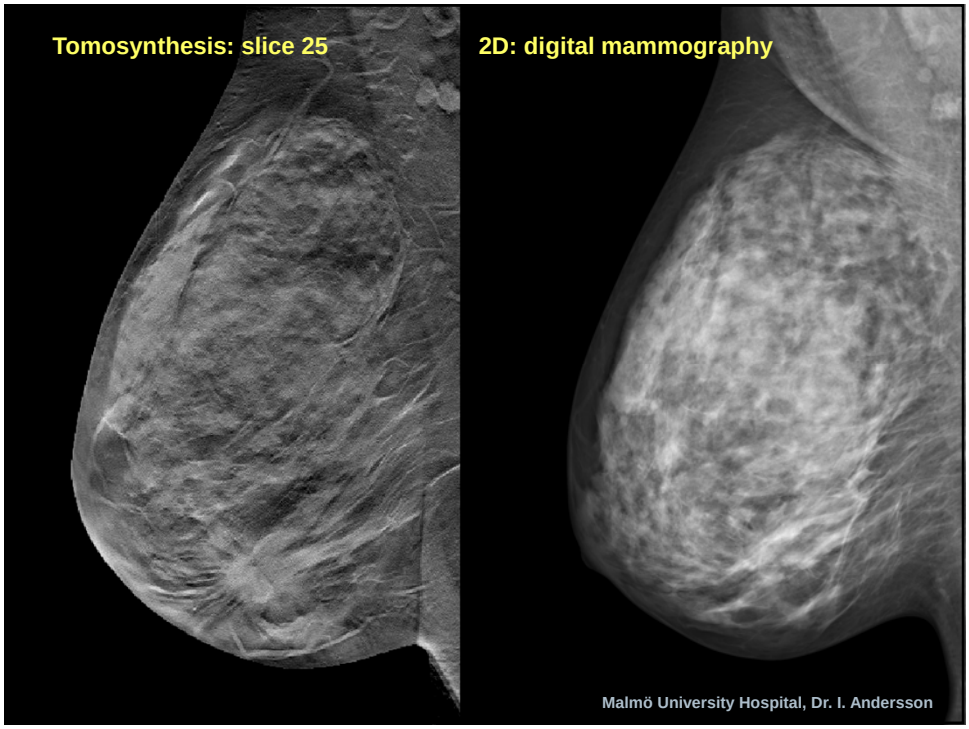

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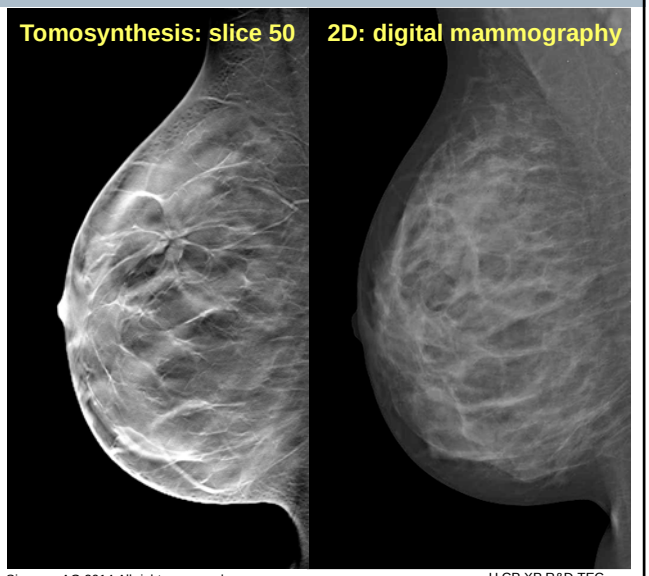
Breast Tomosynthesis human subject 7868



44 year old woman

pathology: 1.8cm ductal invasive carcinoma grade 1

28 kV W/Rh 245mAs

Projection data
Malmö University Hospital
Dr. I. Andersson

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Breast Tomosynthesis Masses

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Tomosynthesis with Inspiration

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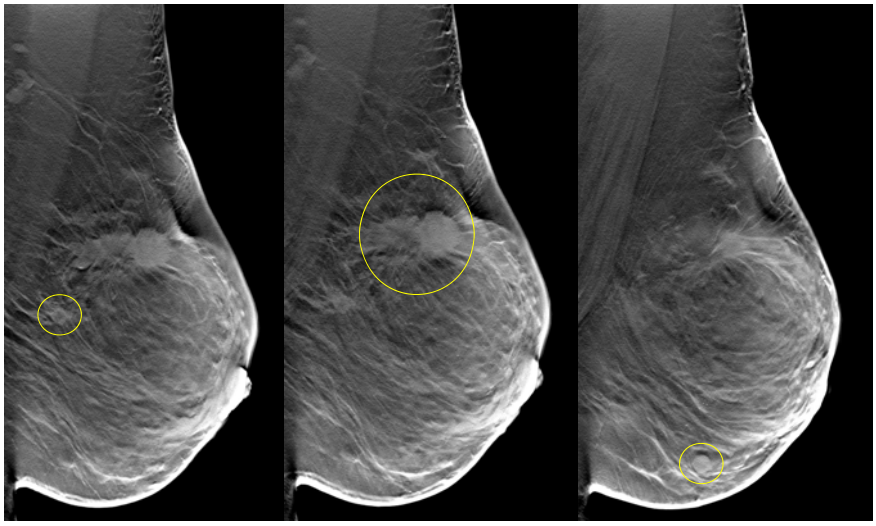
Multifocal cancer

Courtesy Dr. K. Wasser, Univ. Mannheim



slice 24 **slice 27** **slice 37**

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Outline

- Breast Tomosynthesis – Image Acquisition and Reconstruction
- **Quality Control**
- Breast Tomosynthesis - Synthetic Mammogram
- Contrast Enhanced Dual Energy Mammography
- Phase Contrast Mammography
- X-ray/Ultrasound registration

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MAMMOMAT Inspiration Tomosynthesis QC - overview

In Development - before release to production

- Extensive testing to ensure that SW and HW fullfill the specifications

Detector Production

- Production test per detector to ensure that no production problems exist

Final Assembly

- Test of detector together with the rest of the components in the xray beam.

At Installation

- Verification that nothing has been damaged during transport to the customer

Quality Control by the Customer

- Verification on a regular basis that the expected quality still persists

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MAMMOMAT Inspiration
Testing during development I

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In Development – prior to release to production

Defect compensation	■ Verification that the defect compensation algorithms delivers results according to specification also in Tomo mode
Geometric Accuracy	■ Verify that the geometrical accuracy of an object is within tolerances throughout the thickness range of an ACR phantom and an 8-ball phantom
Radiation	■ Radiation field to test the dynamic collimator, tube output, etc…
Phantom (ACR)	■ Although the ACR is not perfect for Tomosynthesis it can be used as a reference test. ■ ACR imaging is done also in different angulations of the swivel arm to ensure that different output due to movement against/ torwards gravity does not have an impact.
Linearity, saturation	■ These parameters are tested in the centre projection of the scan (that can be compared with a low dose 2D image)

33

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MAMMOMAT Inspiration
Testing during development II

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In Development – prior to release to production

Lag and Ghosting	■ Verify that the residual lag between projections and after a scan is acceptable. Also switching between the modes 2D and 3D.
MTF, NPS, and DQE	■ MTF, NPS and DQE is measured in the central projection
Uniformity	■ Verify that the uniformty is within specification in the reconstructed slices at the botton, centre and top slices.
CNR and SNR	■ Verify that the CNR and SNR are acceptable measured in the slice where to contrast is the best.
AEC Stability	■ Verify that the AEC functionality is stable and meets specifications
Average glandular dose	■ Average glandular dose shall be verified that the dose shall be max 2 times the dose of a 2D image. IQ is also verified in the different ranges....
Visual evaluation	■ Evaluation of 100 random clinical cases – re-reconstructed

34

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Tomosynthesis QC manual –
in line with the German radiation protection law RöV

Quality control 45

Introduction 45
Recommended frequency of QC tests 45

Test 1: Glandular dose 46
Test 1 Test Report 47

Test 2: Geometric accuracy 48
Test 2 Test Report 51

Test 3: Radiation field 52
Test 3 Test Report 53

Test 4: Phantom image quality 54
Test 4 Test Report 57

Test 5: Artifact detection 58
Test 5 Test Report 59

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Tomosynthesis QC – permanent update

… by keeping contact and collaborating with

DIN (Germany)	▪ **Member of working groups → S. Schopphoven**
IEC (international)	▪ **Member of MT 31, MT 44**
EUREF	▪ **Contact to Euref team**
AAPM	▪ **Member of SC Tomosynthesis, TG223, 234, 245**

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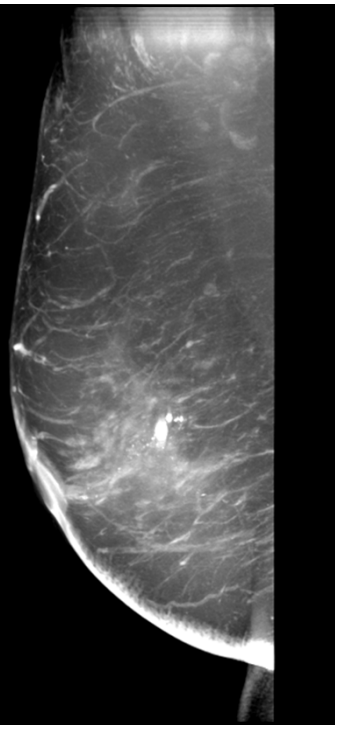
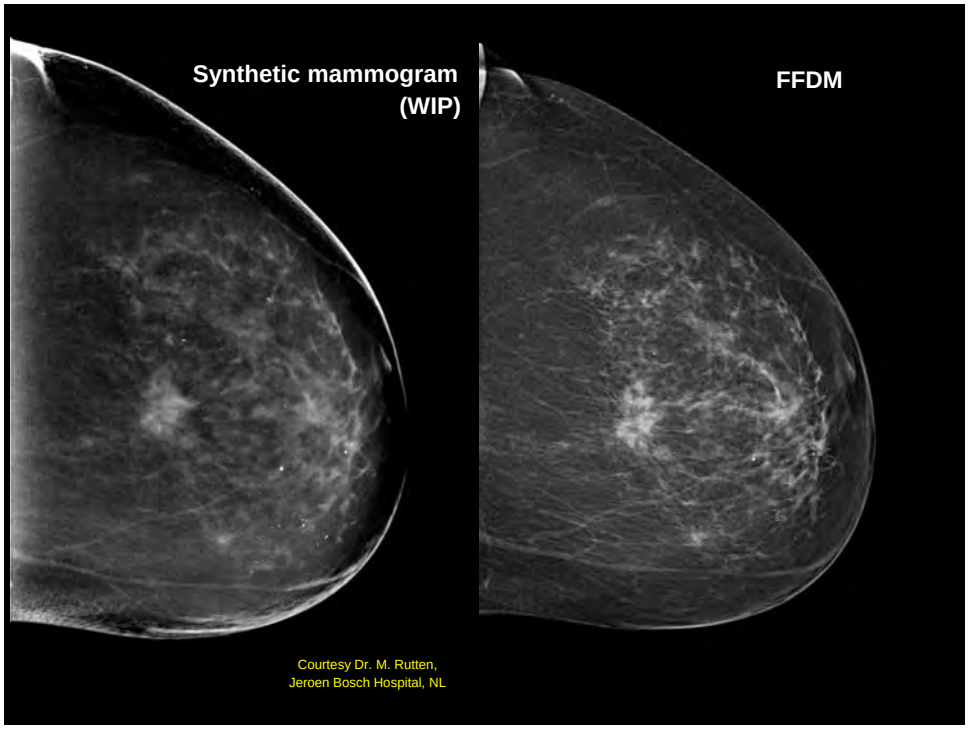
Calc viewer

Maximum Intensity Projection (MIP (WIP))

- **Great for visualizing clusters of calcs**
- **Provide a calcification cluster viewer that allows to view the whole cluster of calcs at the same time from different angles**





Synthesized mammogram has not the same quality as a real FFDM

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DBT+FFDM vs. FFDM

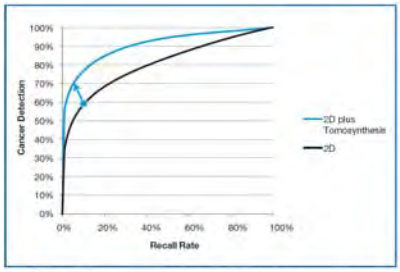

Figure 1. The use of 2D mammography plus tomosynthesis in breast cancer screening is expected to improve cancer detection and decrease recall rates.

DBT+c-view vs. FFDM

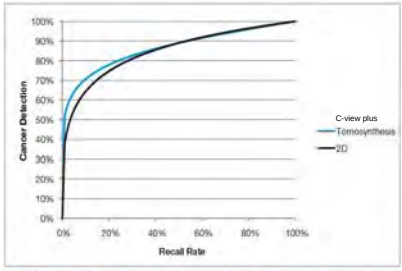

Figure 3. The Hologic ROC analysis showed that the performance of tomo with a synthesized 2D image was superior to 2D mammography alone.

Source: A. Smith, Tomosynthesis: the Use of Breast Tomosynthesis in a Clinical Setting, white paper, 2012

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What is the purpose of a synthesized mammogram

- **Reduce dose of DBT as adjunct**
  (if DBT cannot be used alone)
- **Compare with priors**
  (in transition period prior to the routine use of DBT in screening)
- **Speedup reading workflow**
  - preview
  - calc viewer

but:

- **A synthesized mammogram is not a real FFDM**

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A false-negative case in Tomosynthesis

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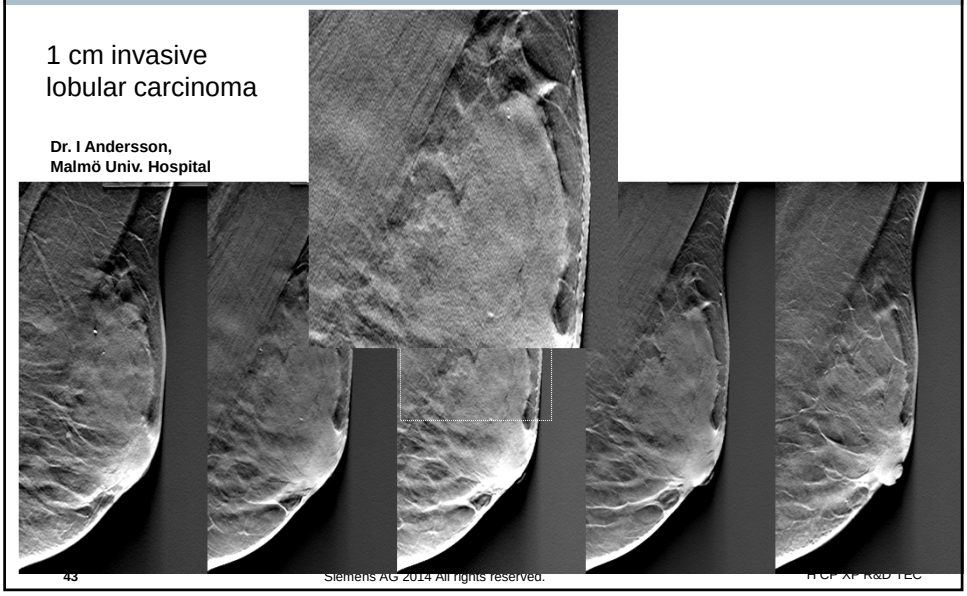
1 cm invasive
lobular carcinoma

Dr. I Andersson,
Malmö Univ. Hospital



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4-D Mammography:
Contrast Enhanced Dual Energy Tomosynthesis

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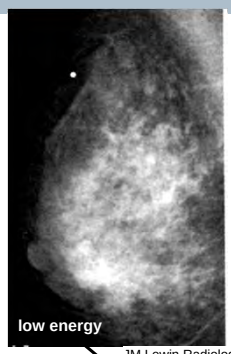
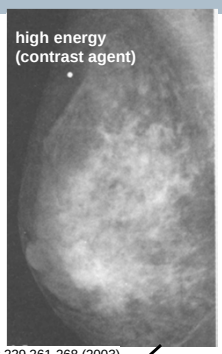
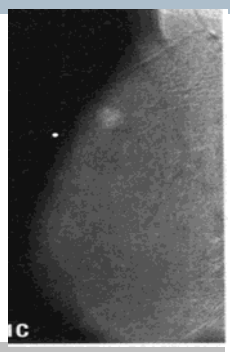




JM Lewin Radiology 229 261-268 (2003)

registration
log
subtraction



Energy subtraction
easy detection
Temporal subtraction
CA dynamics
diagnosis of lesions

Interesting for detection, diagnosis, extent of disease
Poor man's MRI ?
Implementation possible with tomosynthesis

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Contrast Enhanced Mammography

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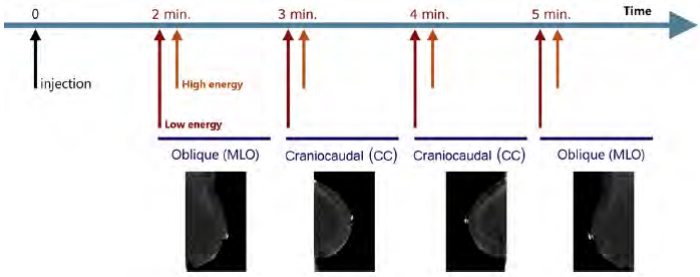
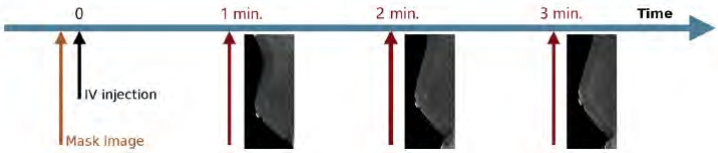
Source: S. Badr et al.: Diagn. Interv. Imaging 2013

Dual energy subtraction for 4-views:



Temporal subtraction at different time steps:



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Dual Energy: Mechanism

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- Dual energy and/or contrast agent
- X-ray beam quality below and/or above the K-edge of iodine (33.1 keV)
- Discrimination of
  - microcalc and tissue → microcal detection
  - glandular and adipose tissue → density computation
  - iodine and tissue → cancer detection and diagnosis
- Vascular neoangiogenesis/neovascularization associated with breast cancer growth with increased vessel permeability
- Iodine is accumulated in carcinomas
- Linear combination (subtraction) of low and high energy images enhances visibility of lesion
- In combination with tomosynthesis, 4D information may be obtained

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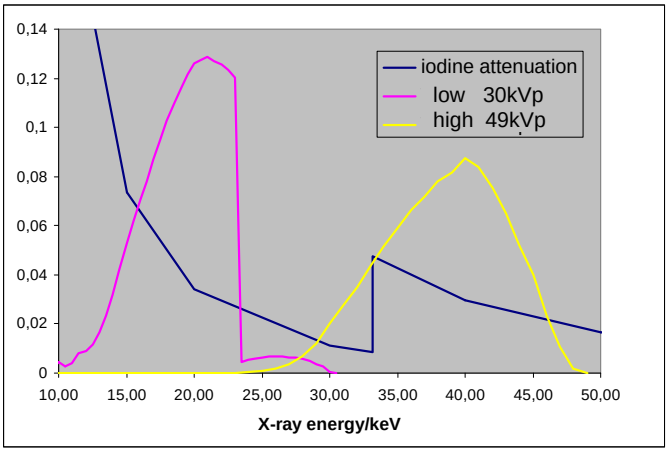
Iodine contrast

- Dual energy
- X-ray beam quality below and above the K-edge of iodine (33.1 keV)



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CEDET: System modifications

What will be changed w.r.t. to the released Inspiration Tomosynthesis?

- Toughen up generator beyond 35 kV up to 49kV
- New additional filters (Cu and other)
- Adapt Mammo Unit SW
- Adapt detector software and tune detector (Se thickness)
- Adapt AWS SW and User interface

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Research status

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Contrast Enhanced Mammography (2D)

- J. Lewin et al. 2001 Colorado:
- R. Jong et al. 2003 Toronto
- F. Diekmann et al., 2003 Berlin
- C. Dromain et al, 2005 France
- C. Dromain et al.: Eur Radiol 2010 Sep 14 DOI 10.1007-s00330-010-1944-y initital clinical results
- …
- S. Badr et al.: Diagn. Interv. Imaging 2013
  Review: Dual-energy contrast-enhanced digital mammography in routine clinical practice in 2013

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Research status

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Contrast Enhanced Dual Energy Tomosynthesis

- A. Maidment/A-K. Carton et al. UPenn 2007, 2010: Tomosynthesis
  BJR 83, 344-350 (2010)
- Schmitzberger et al., Radiology 259, 558-564 (2011)

Siemens related work:

- W. Zhao, Y. Hu, SPIE 2011, 2012, 2013
- E. Samei et al., SPIE 2012
- M. Hörnig, L. Bätz, T. Mertelmeier SPIE 2012

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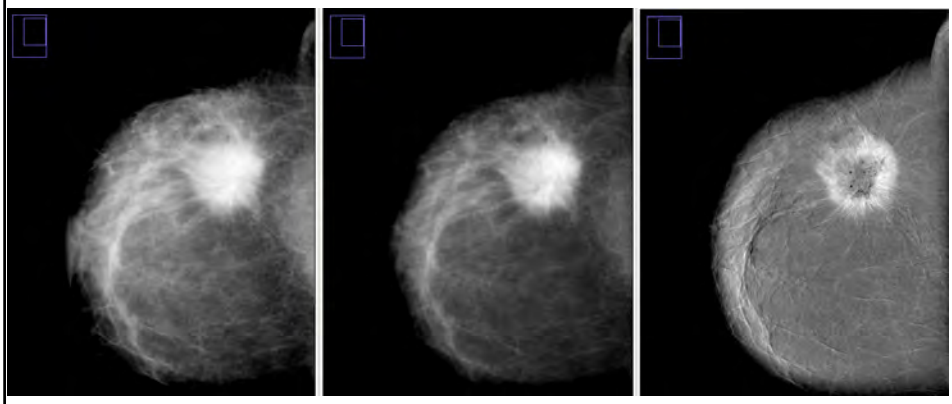
First clinical data
CEDEM – Contrast Enhanced Dual Energy Mammography

Case 2: IDC, 2 ml/kg Iomeron (Bracco, Italy)



LE HE DE subtraction

Courtesy Prof. T. Helbich, Medical University Vienna

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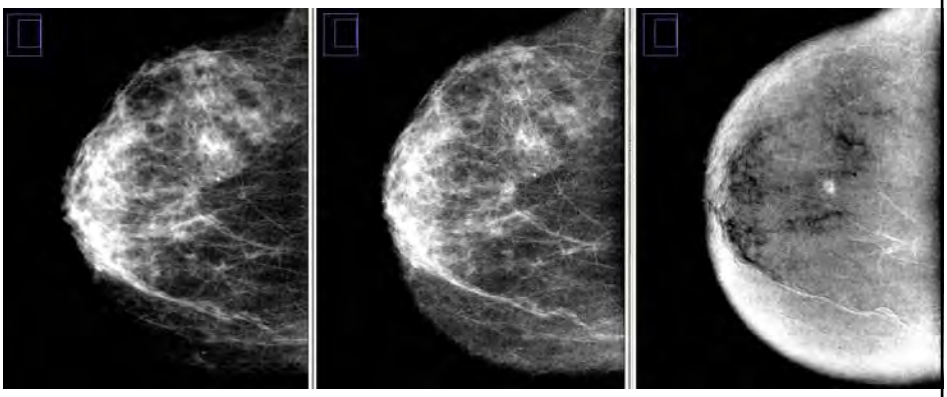
CEDEM First clinical data

Case 6: IDC, 2 ml/kg Iomeron (Bracco, Italy)



LE HE DE subtraction

Courtesy Prof. T. Helbich, Medical University Vienna

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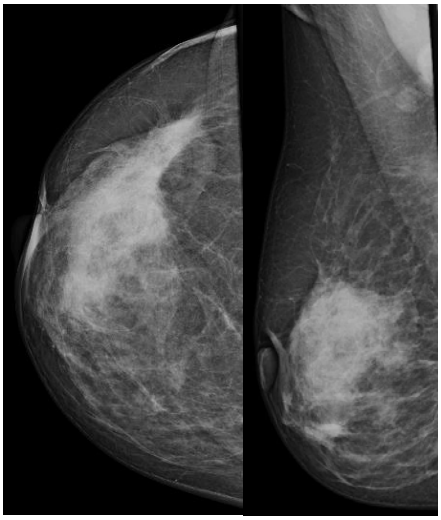
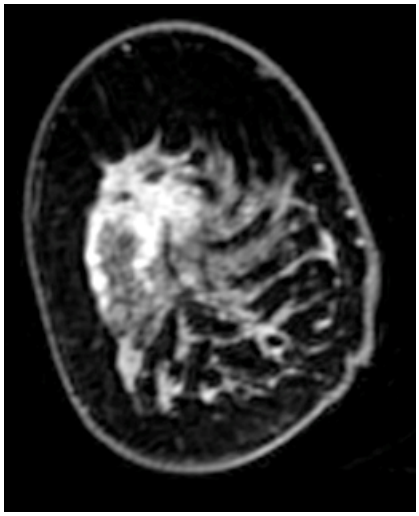
CEDET case 020 – Invasive lobular carcinoma

Courtesy Prof. T. Helbich/Dr. T. Knogler/Univ. Vienna



MG



MRI

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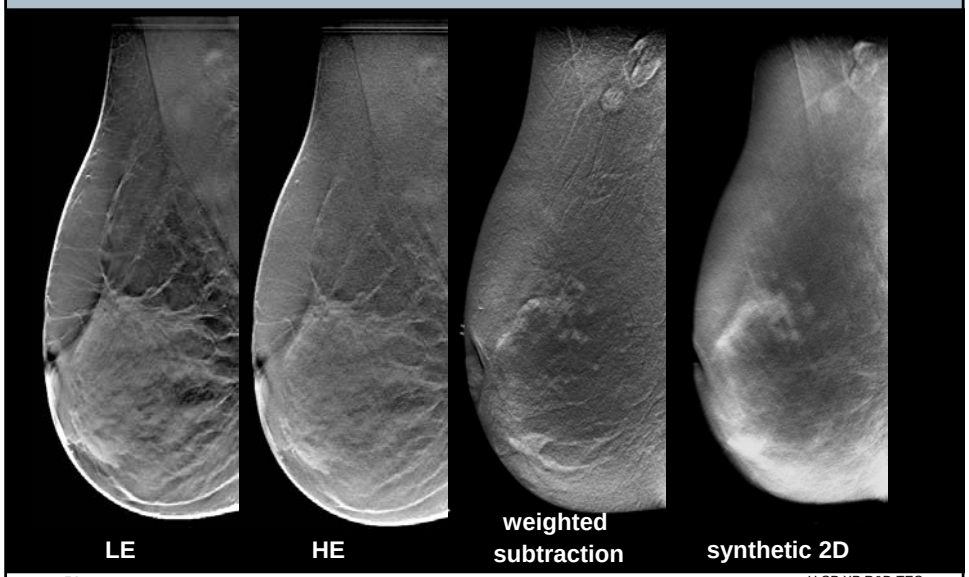
CEDET case 020 – Invasive lobular carcinoma

Courtesy Prof. T. Helbich/Dr. T. Knogler/Univ. Vienna



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Contrast Enhanced Dual Energy Mammo
Potential applications and advantages

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- Better diagnosis of lesions / problem solving
- Detection of occult tumors
  (multifocal, multicentric cancer)
- Staging of disease
- Monitoring of reponse to (neoadjuvant) chemo therapy
- Improved workflow (all imaging in mammo dept.)
- Reduced costs

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Outline

- Breast Tomosynthesis – Image Acquisition and Reconstruction
- Quality Control
- Breast Tomosynthesis - Synthetic Mammogram
- Contrast Enhanced Dual Energy Mammography
- **Phase Contrast Mammography**
- X-ray/Ultrasound registration

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New Information by Phase Contrast Imaging ?

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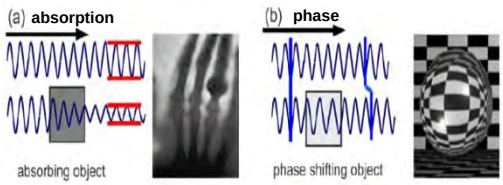
X-ray phase contrast imaging (PCI)

- **probes the refraction index**

  $n = 1 - \delta - i\beta$

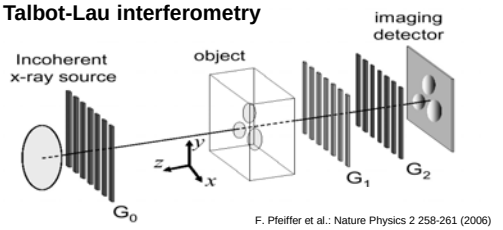
  phase absorption

- **may provide higher contrast and high spatial resolution**
- **may reduce the dose**
- **absorption contrast, phase contrast and dark field in one measurement**



Courtesy: Michael Chabior, Ph.D.-Thesis

Talbot-Lau interferometry



F. Pfeiffer et al.: Nature Physics 2 258-261 (2006)

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Phase Contrast Mammography: Preliminary results

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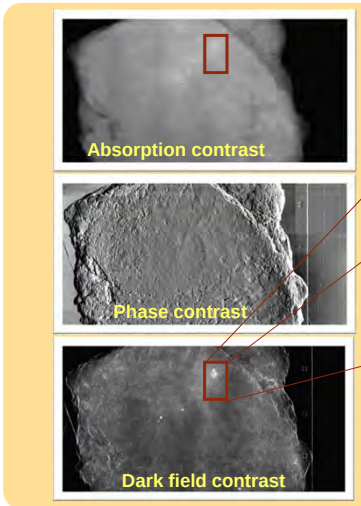
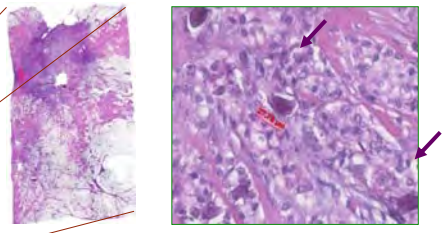
Mastectomy specimen



BMBF-Spitzencluster-Projekt Medical Valley:
- **Gynekologie, Univ. Erlangen**
- **Radiologie, Univ. Erlangen**
- **Physikalisches Institut Univ. Erlangen**
- **Siemens Healthcare**



Histology slice

Signal not visible in absorption imaging can be identified in the histology sllice as microcalc cluster

Clear indication for granular subpixel structures

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Outline

- Breast Tomosynthesis – Image Acquisition and Reconstruction
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- Contrast Enhanced Dual Energy Mammography
- Phase Contrast Mammography
- **X-ray/Ultrasound registration**

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Imaging Patients with Dense Breast Tissue

Mammographic sensitivity for breast cancer declines significantly with increasing breast density.

Ultrasound can detect additional cancers

Kolb: Radiology 225, 165-175 (2002):
31 cancer detected in 13,547 women only by Ultrasound

Berg et al: ACRIN 6666 trial JAMA 299 No. 18, May 14 (2008):
11.8 cancers in 1000 subjects found by combining US and MG compared to 7.6 for MG alone,
(2637 women with high risk and dense breasts)

But increase of false positive rate (from 4.4% to 10.4%)

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Registration of tomosynthesis and ultrasound

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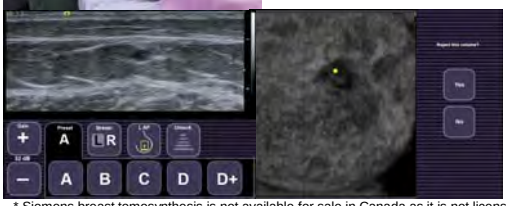
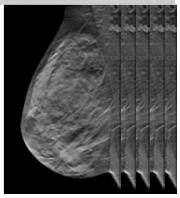
- ABVS:
  3-D automated US
- Screening of young and dense breasts

- Breast tomosynthesis





* Siemens breast tomosynthesis is not available for sale in Canada as it is not licensed in accordance with Canadian Law

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Registration of lesions in 3-D Ultrasound and Tomo

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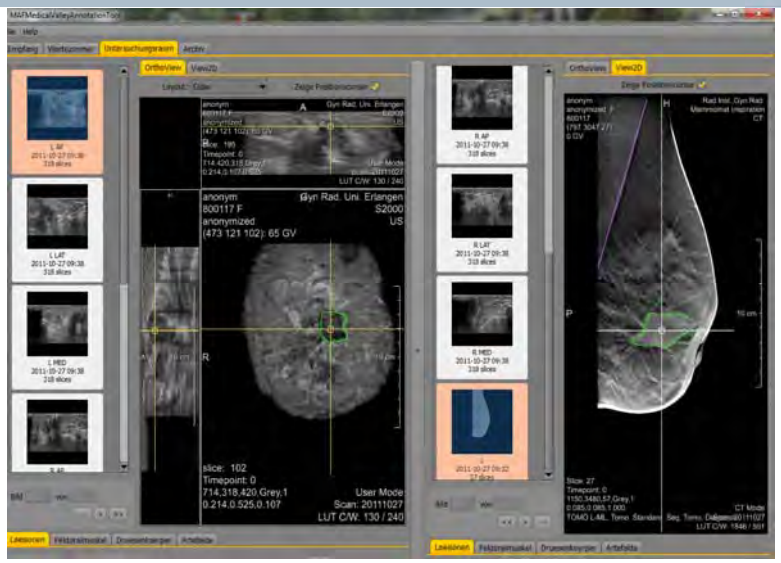
Fraunhofer MEVIS



Work In Progress

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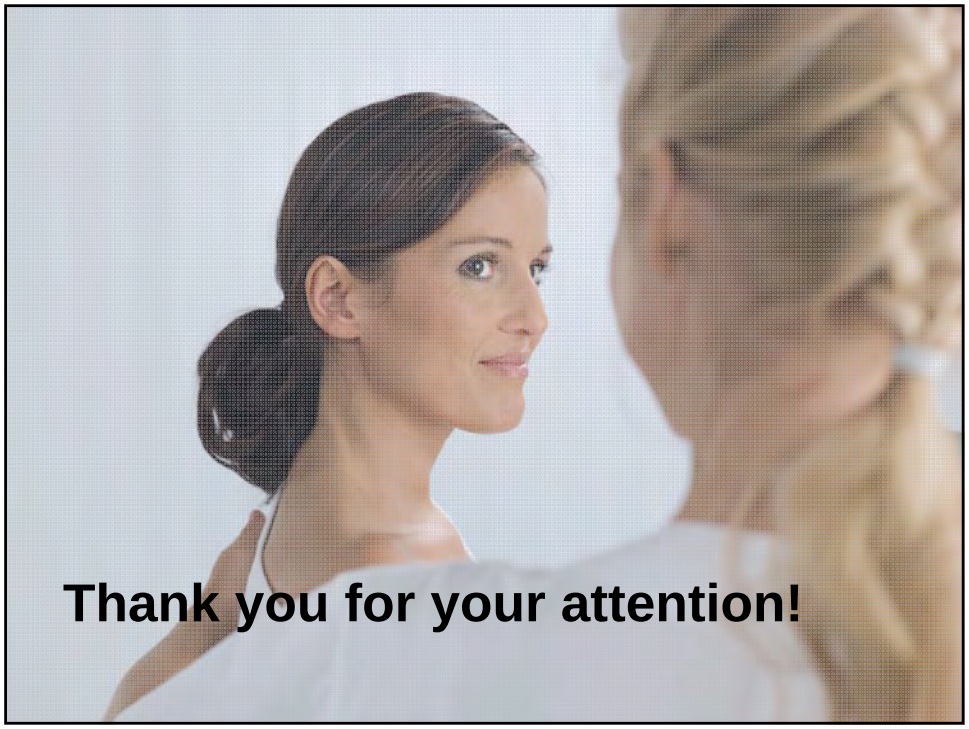
Conclusion

- Tomosynthesis will replace mammography
  - for diagnosis and screening
- We need new QC methods and precedures for BT
- A synthetic mammogram will speed up the reading workflow
- Contrast-Enhanced Dual Energy Mammography may become an additional diagnostic workup method
  - perhaps as alternative to MRI
- Phase contrast imaging is still in the phase of feasibility studies for large objects
- X-ray and ultrasound provide complementary information and should be combined

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