94.Deutscher Rontgenkongress
Hamburg 01.06.2013
Workshop ”Mammadiagnostik II – Ueberdiagnosen im Mammographiescreening”

Wie geht man in Skandinavien mit dem Thema Ueberdiagnosen um ?

Prof.dr.med. Per Skaane

**Department of Radiology, Oslo University Hospital Ullevaal,
University of Oslo, Oslo
Norway**

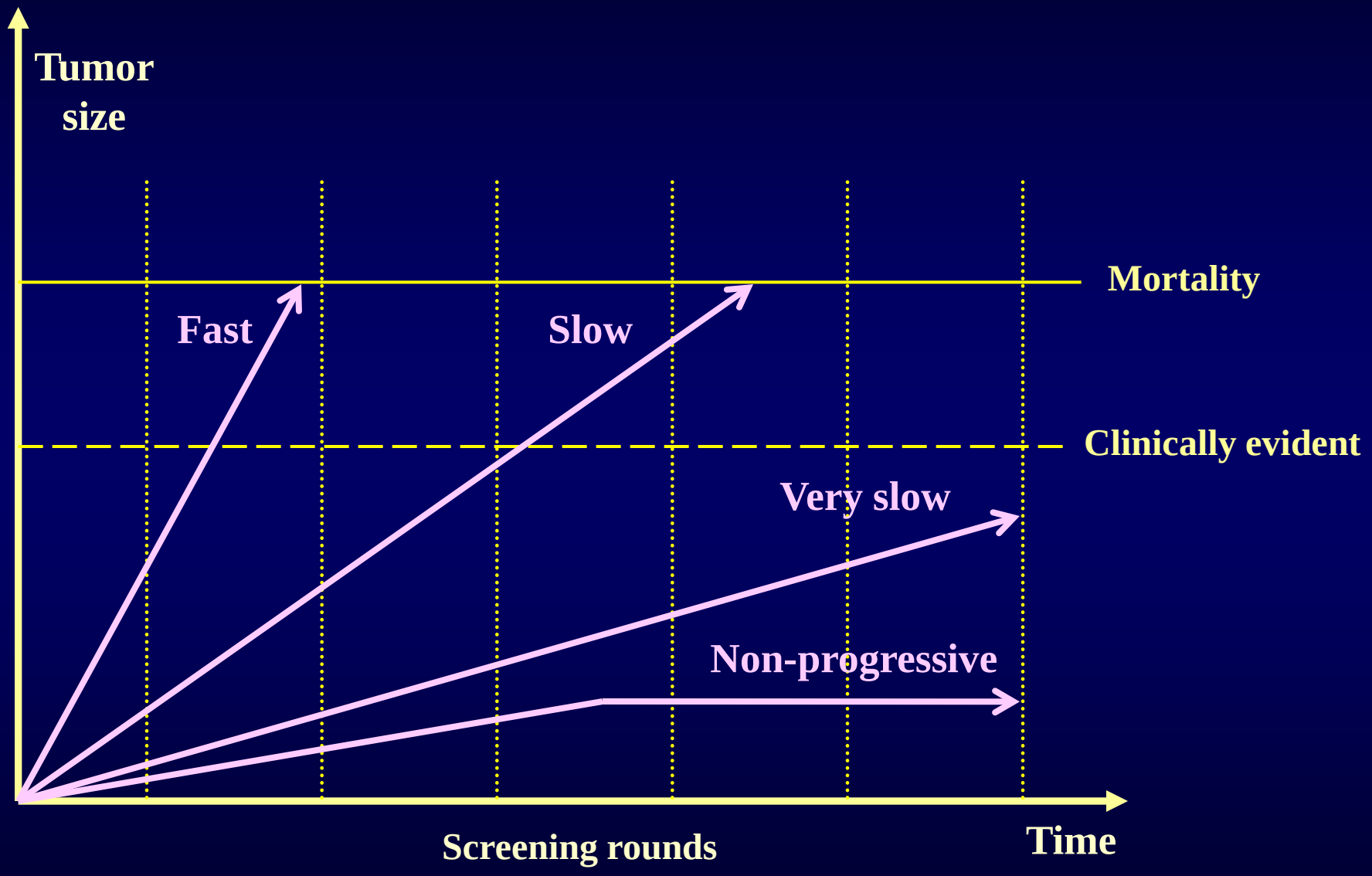
PERSKA@ous-hf.no

30 min.

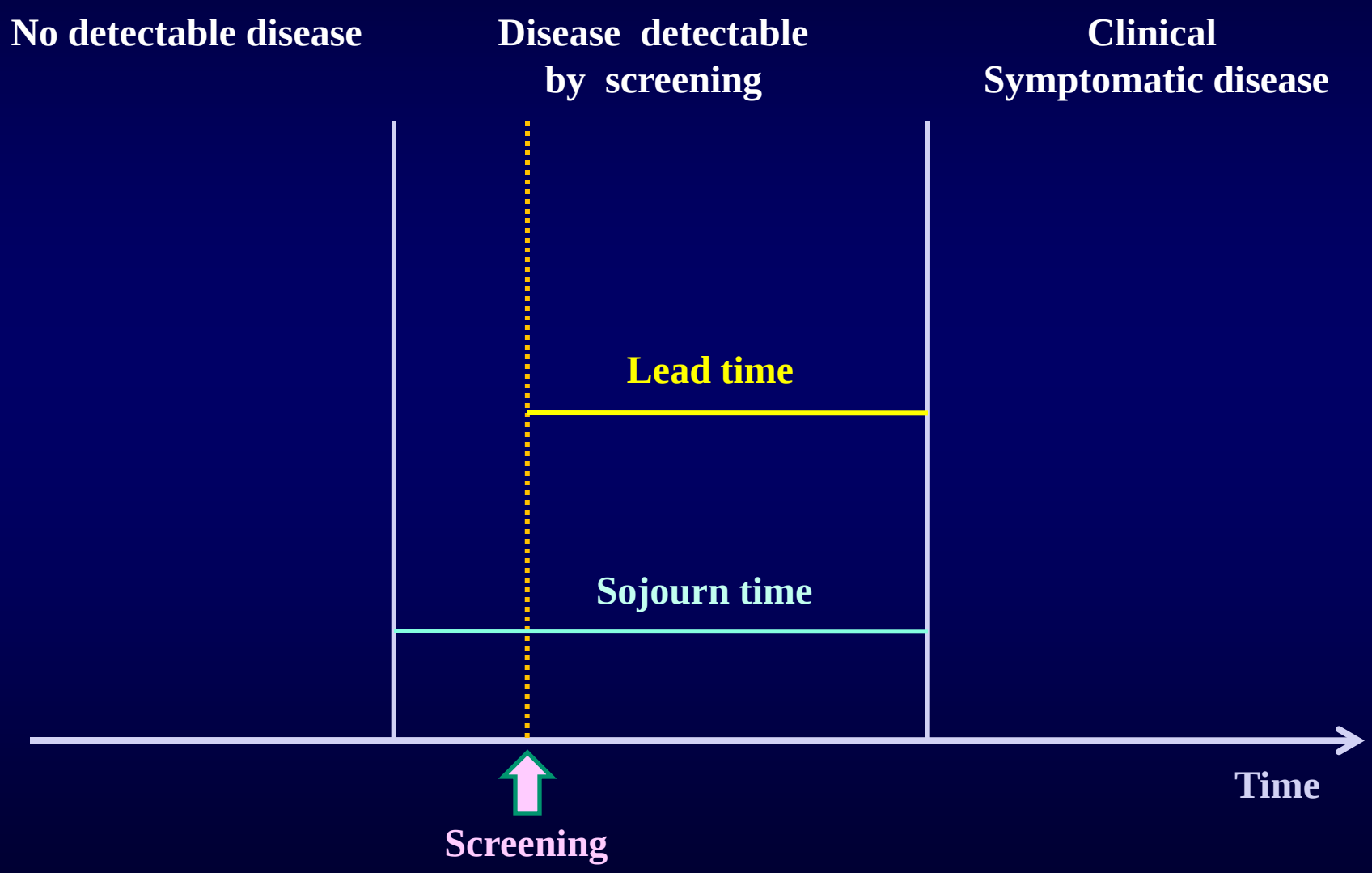
Adverse effects of screening mammography

- **Mammographic examination**
  - Discomfort (painful)
  - Radiation dose
- **Overdiagnosis** (⇨ overtreatment)
- **False positives** (⇨ unnecessary recalls)
- **False negatives** (⇨ interval cancers)

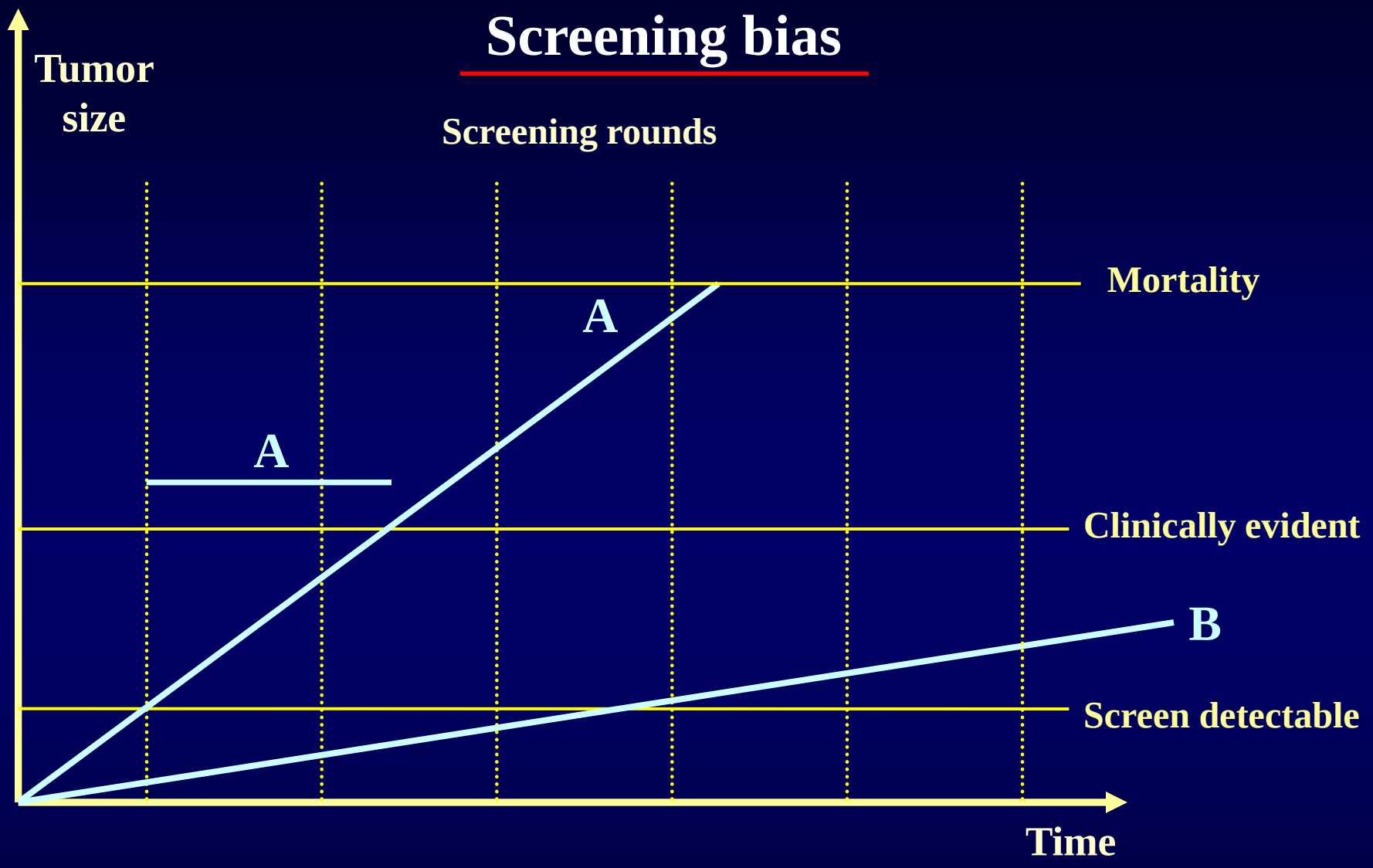
Growth rates of breast cancers



Natural history of breast cancer and screening



Screening bias



- **A) Lead-time bias:** Earlier detection but no impact on date of death
- **B) Length-time bias:** Indolent tumors more likely to be detected

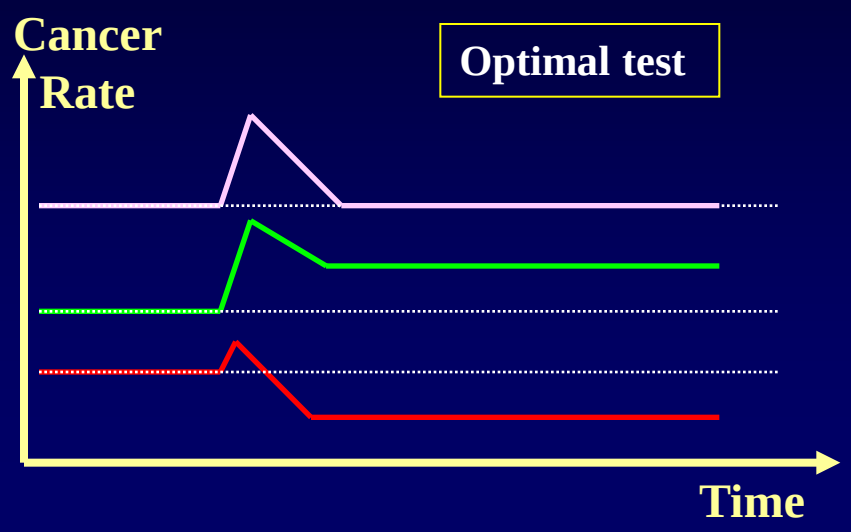
  Overdiagnosis: Extreme form of length-time bias

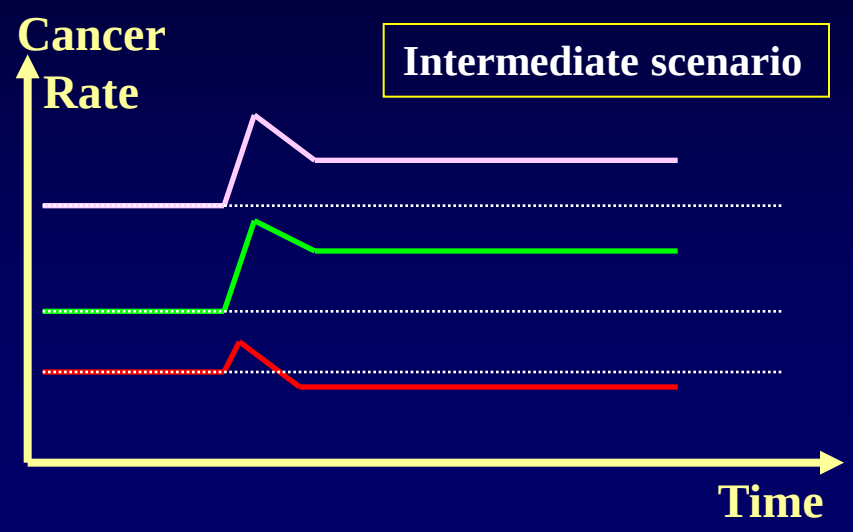
Overdiagnosis

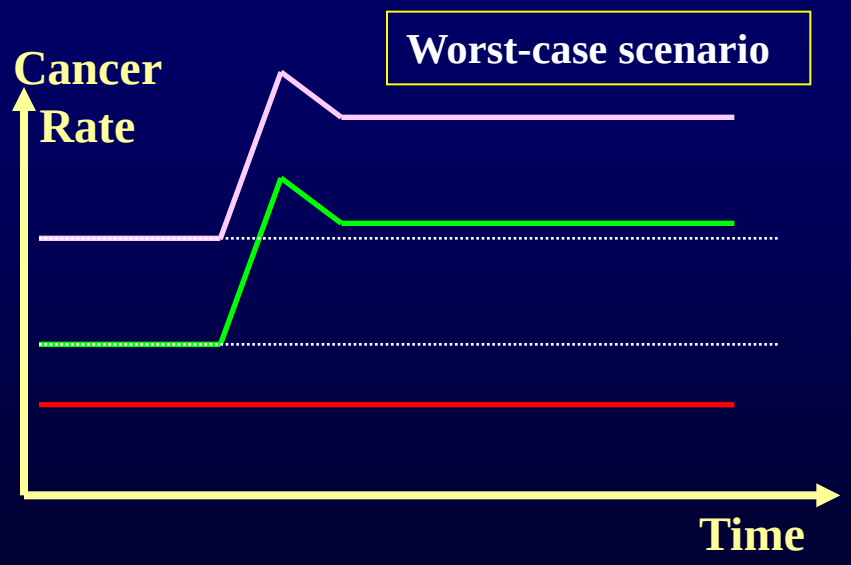
Overdiagnosis* **in mammographic screening is the diagnosis of (small grade 1) invasive cancers or DCIS that, in the absence of screening, would not have presented clinically during the woman's lifetime**

*** Overdiagnosis: An extreme form of length bias !**

Hypothetical screening scenarios







Overall invasive cancers

Localized cancers*

Regional cancers

* Node negative, no skin or chest wall involvement

Esserman L: JAMA 2009;302:1685-1692 (modified)

Overdiagnosis

likely to be driven by:

- The radiologist's fear of missing a cancer, and the fear of litigation
- Technological developments:
  - Digital mammography (FFDM)
  - Computer aided detection (CAD)
  - Improved biopsy techniques (VAB)
  - Tomosynthesis (DBT)

Studies comparing SFM and FFDM in breast cancer screening:

DCIS detection rate and proportion of DCIS in FFDM*

Study	Examinations (n) SFM	Examinations (n) FFDM	DCIS detection Rate (%) SFM	DCIS detection Rate (%) FFDM	DCIS detection Difference (p-value)	Proportion DCIS (FFDM) n	Proportion DCIS (FFDM) %
Oslo II	16,985	6,944	0.12	0.16	n.s.	11 / 41	27
DMIST a)	42,760	42,760	0.12	0.14	n.s.	61 / 184	33
Florence b)	14,385	14,385	0.12	0.26	p < 0.01	38 / 104	28
Vestfold c)	324,763	18,239	0.11	0.21	p< 0.01	38 / 140	27
INBSP*	153,619	35,204	0.09	0.13	p = 0.07	46 / 221	21
DSPP* d)	311,082	56,518	0.08	0.13	p < 0.01	74 / 56	23

* Studies with no specification of DCIS or a small number of DCIS excluded

a) Cancers diagnosed within 455 days after imaging

b) Cancers presenting as clustered microcalcifications

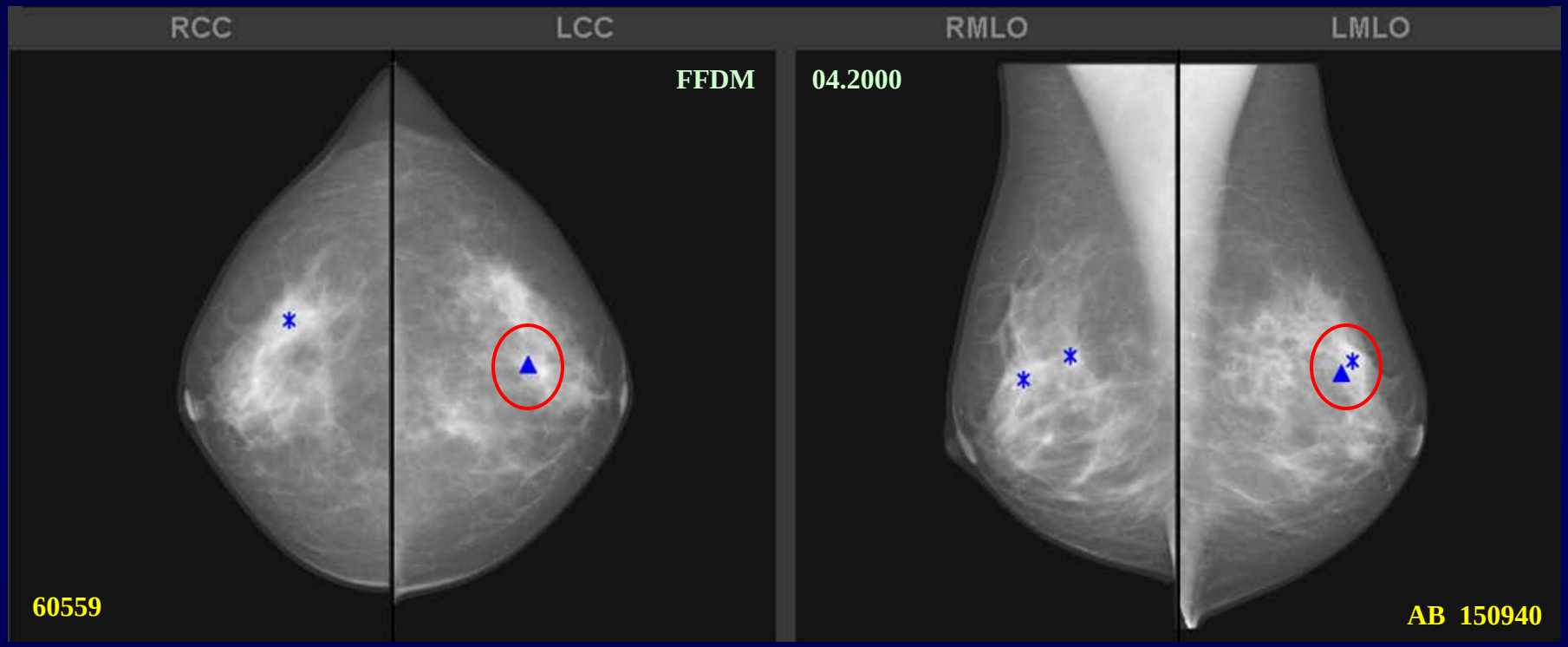
c) Prevalent screening rounds; SFM is mean value of merged data from 18 counties

d) CAD used for FFDM only

*) INBSP: Irish National Breast Screening Program

*) DSPP: Digital Screening Project Preventicon

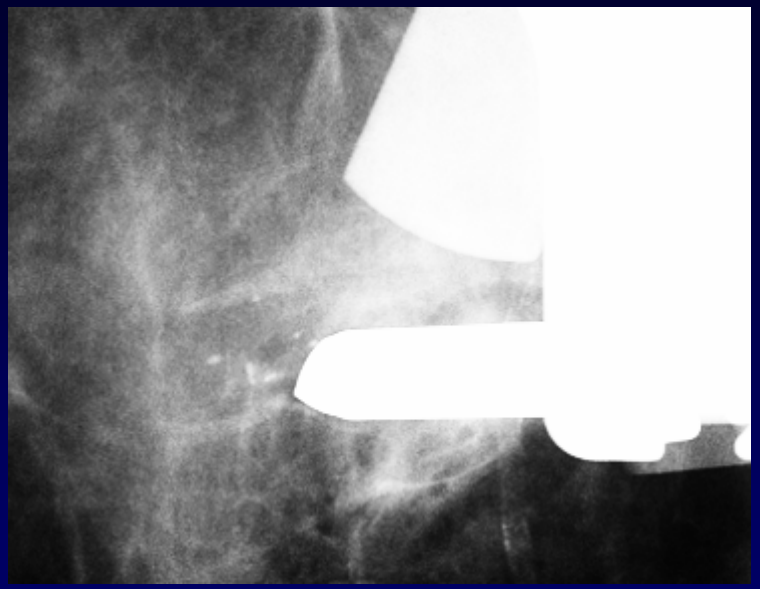
Oslo I Study FFDM: Independent double-reading 1 - 1

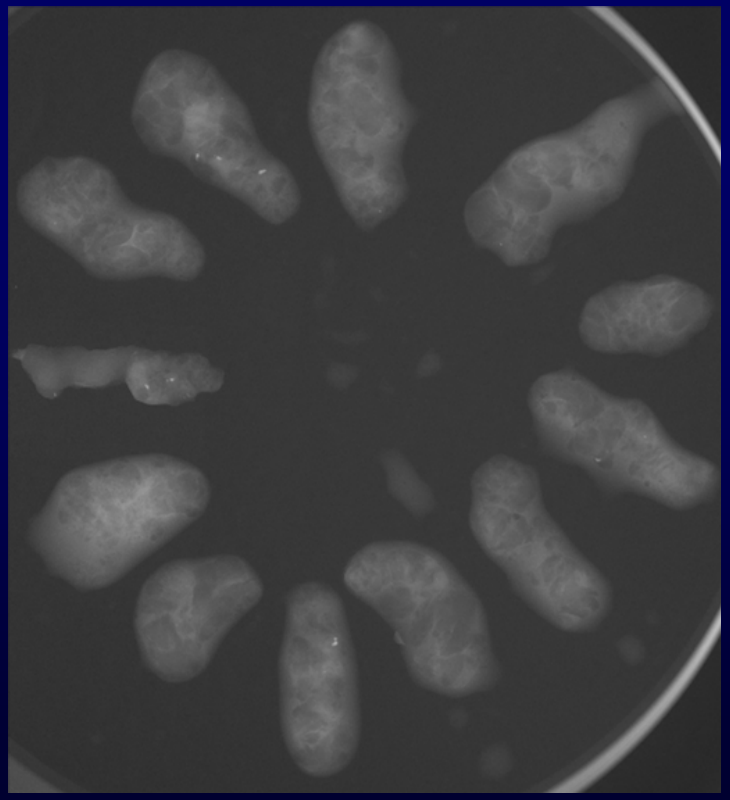


Cancer in subsequent round:
IDC and DCIS Grade 3

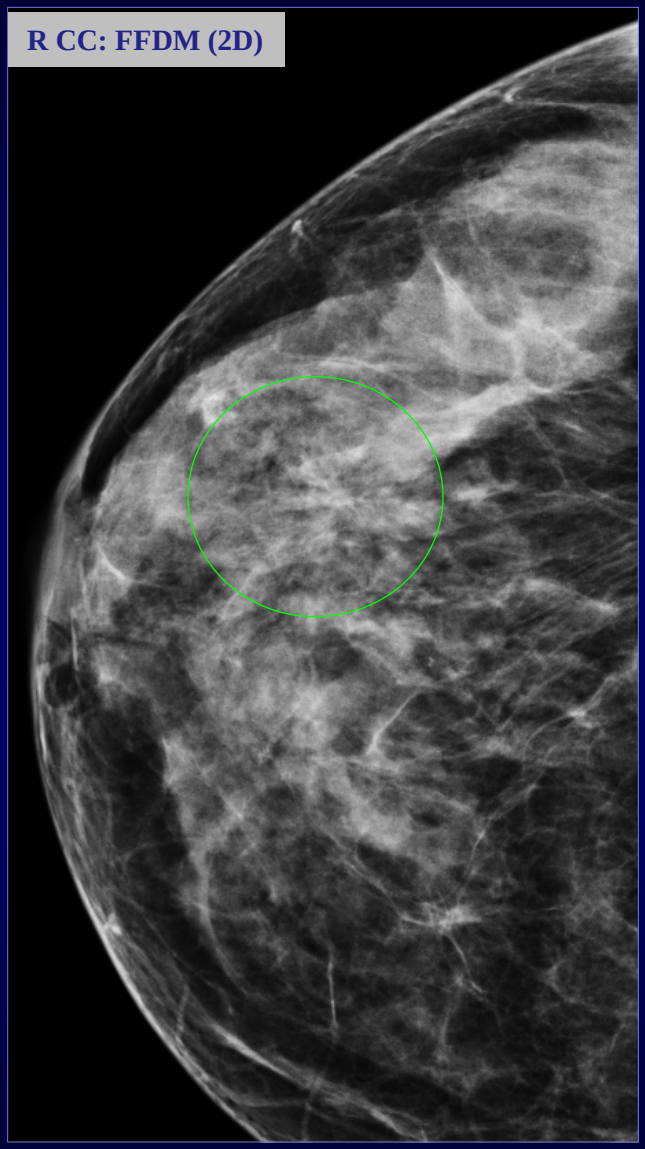
Improved biopsy techniques: Vacuum Assisted Biopsy (VAB)

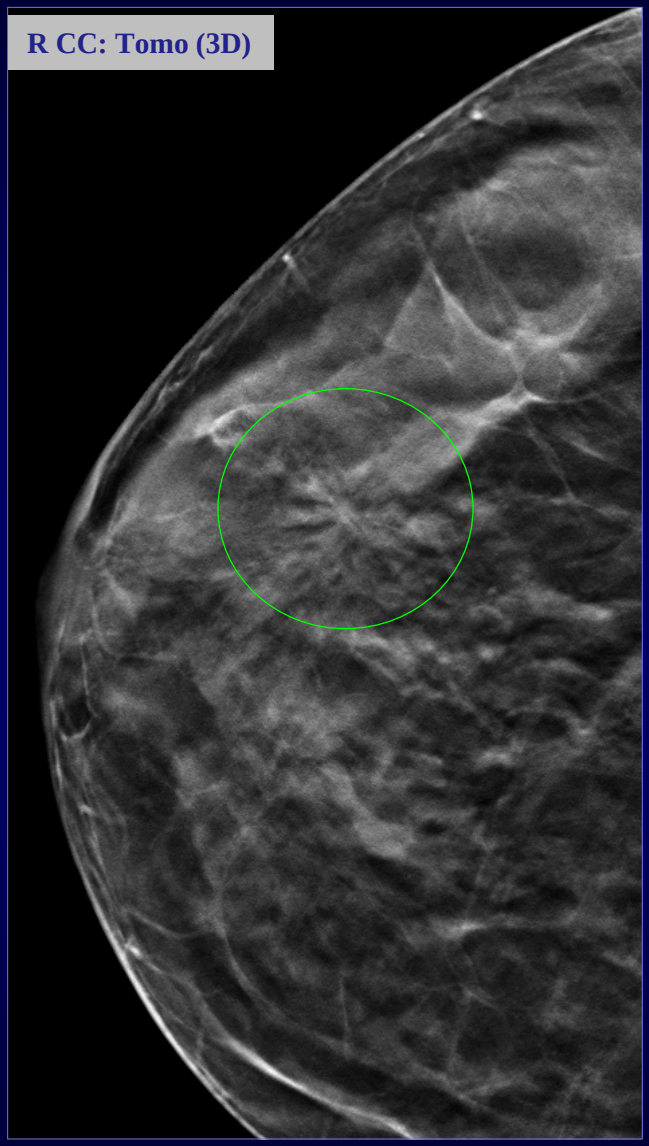
Histology: DCIS grade 3, 10 mm





Oslo Tomosynthesis Screening Trial: Radial scar (+ fibrocystic changes)

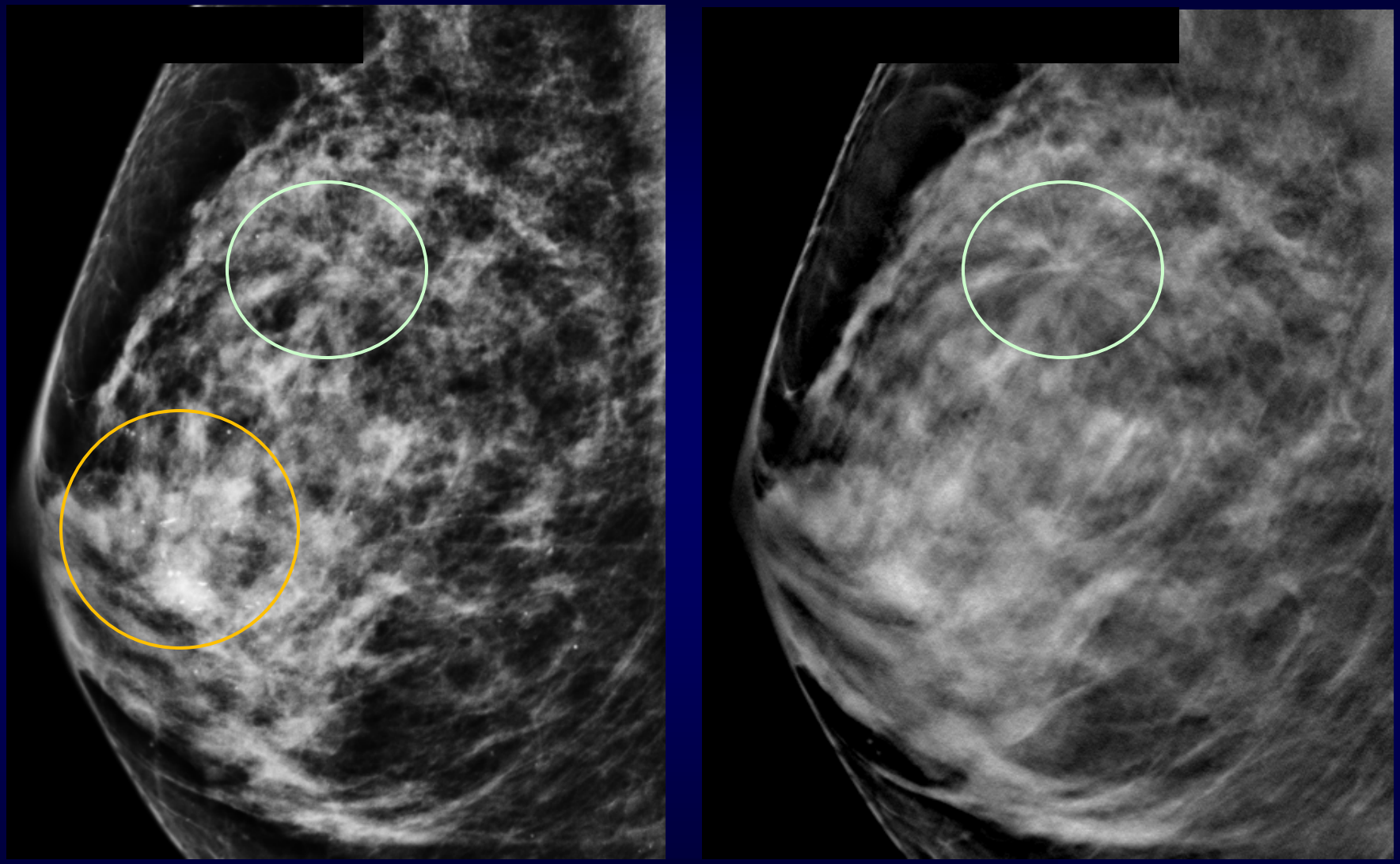




Radiologist	A	B	C	D
Score (NBCSP)	1	1	4	4

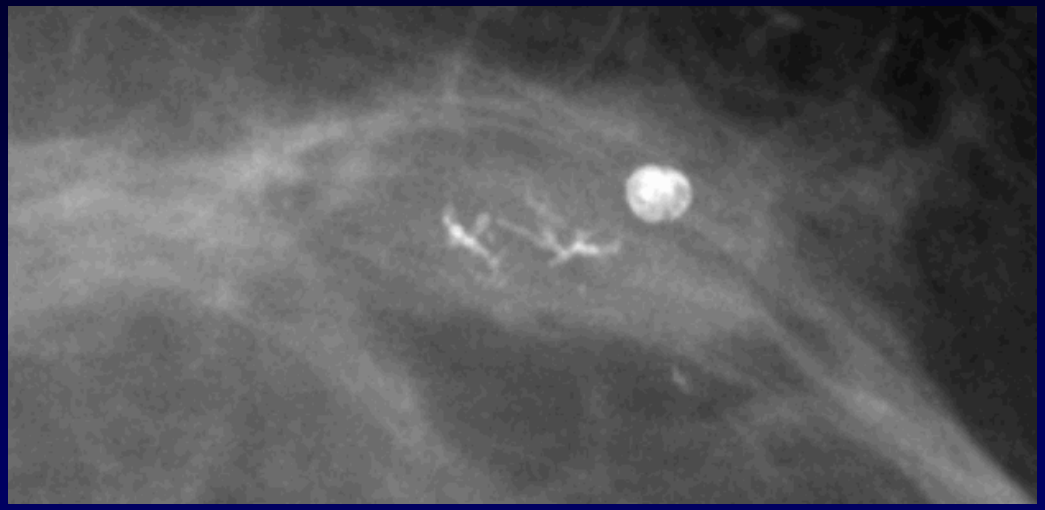
101012HJE150354

Tomosynthesis: Potential for increased sensitivity

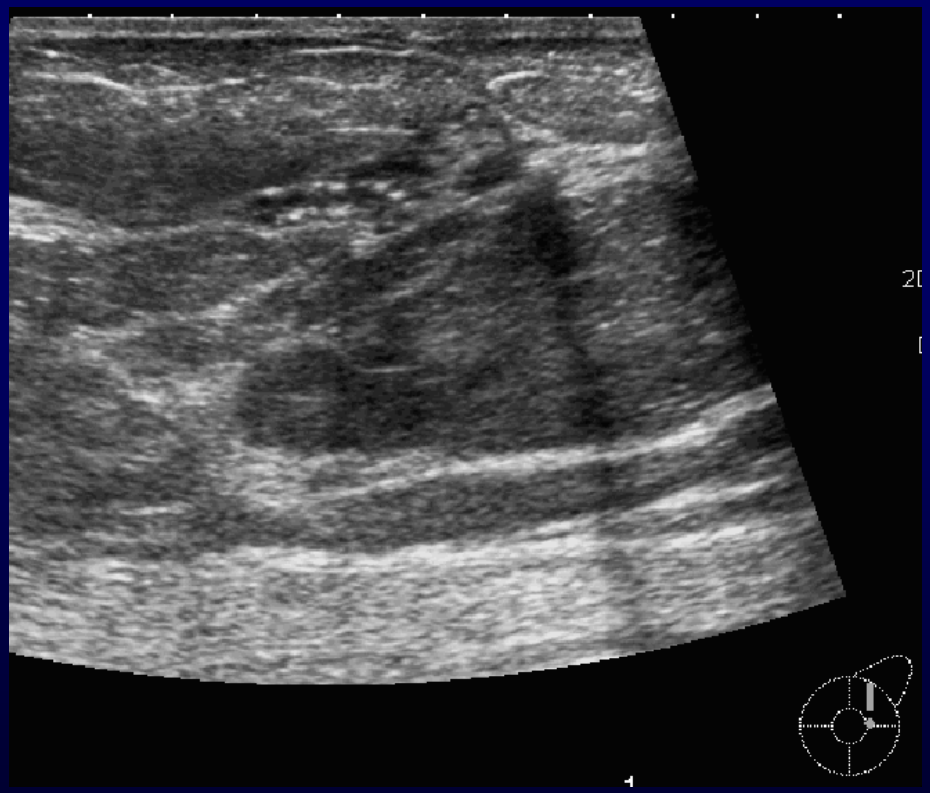


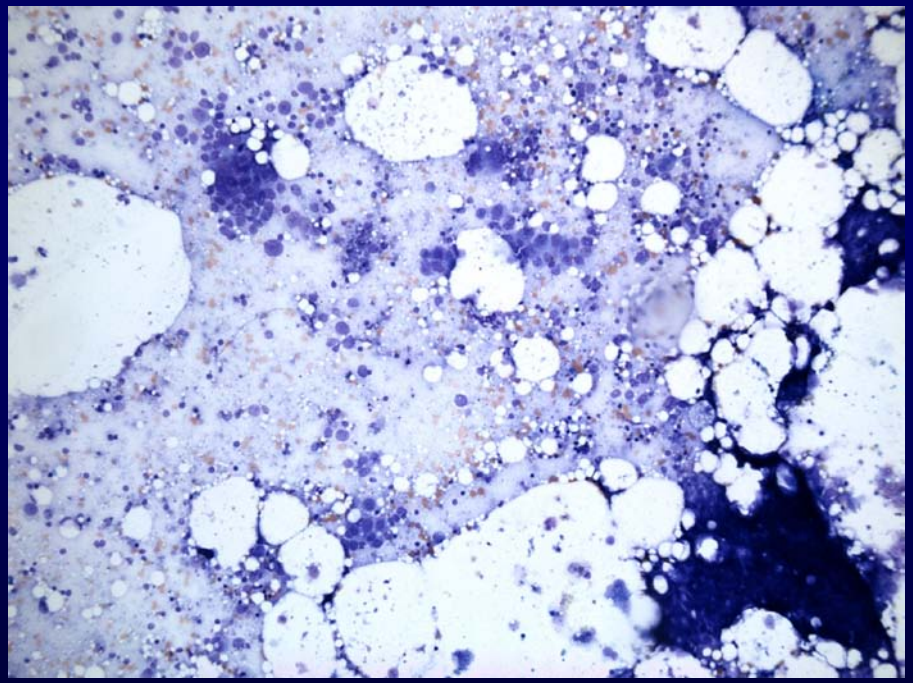
Invasive lobular carcinoma (ILC) : 2 mm, gr. 1
(+ LCIS 20 mm and ALH / LCIS)

H,LAB 210948



Microcalcifications:
The great challenge !





US - guided FNAC:
DCIS high grade (G3)

Theory of linear progression

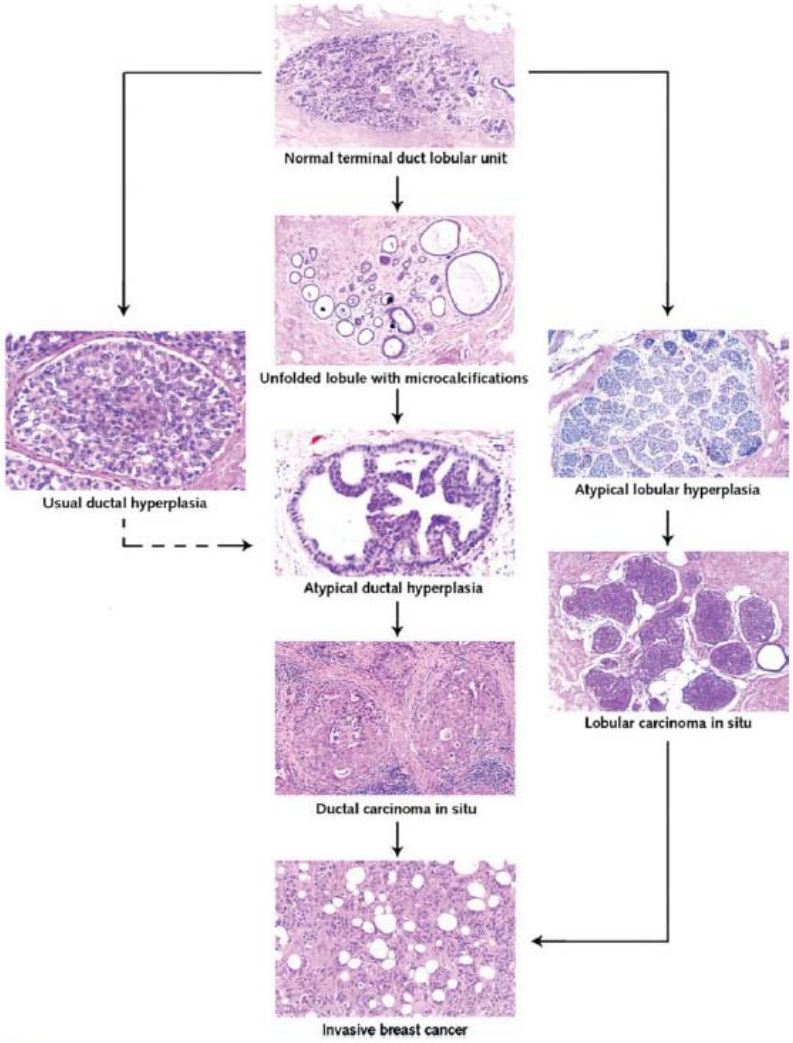


FIGURE 1. Theory of linear progression. Proposed histologic evolution of breast cancer. Reprinted by permission from Macmillan Publishers Ltd: Arpino G, Laucirica R, Elledge RM. Premalignant and in situ breast disease: biology and clinical implications. *Ann Intern Med.* 2005;143:446–457 (©2005).[36]

Theory of parallel disease

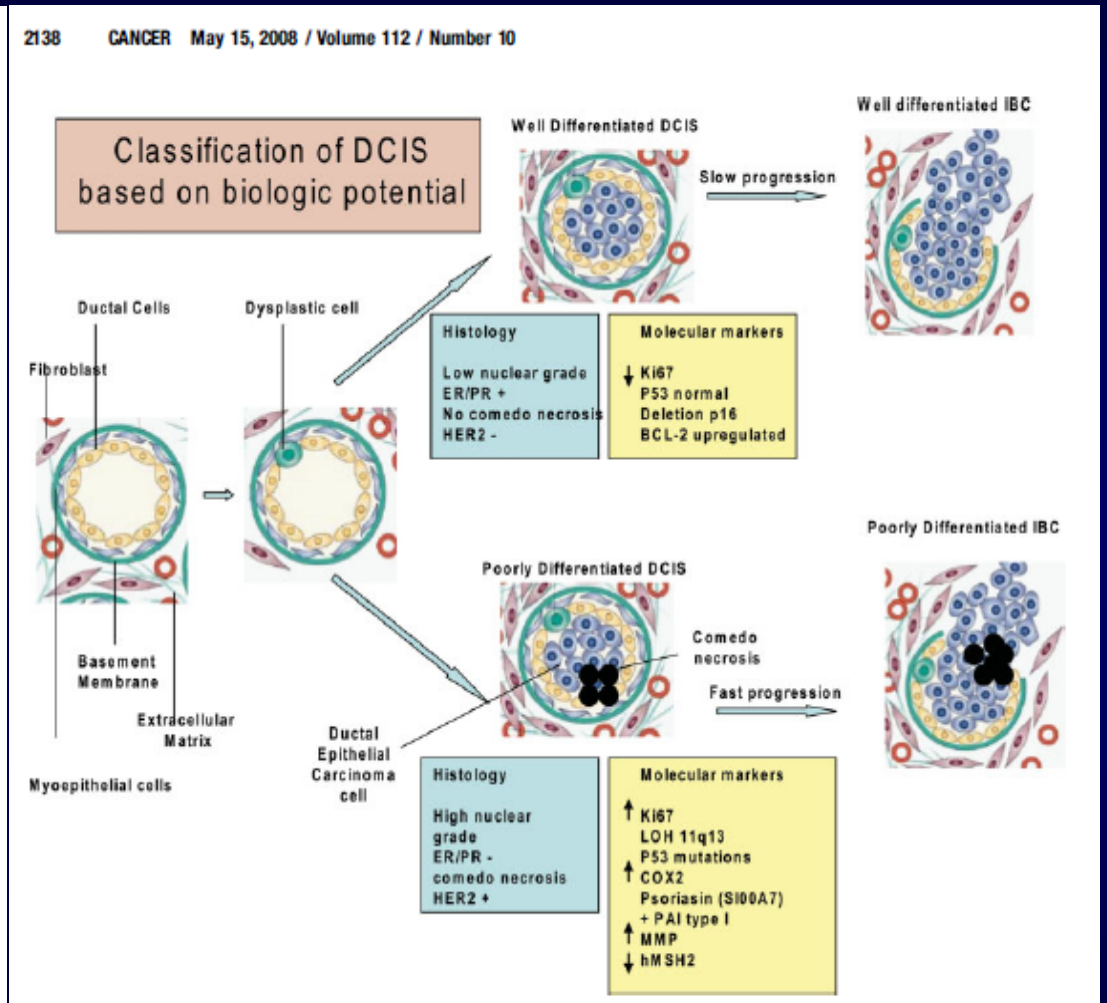


FIGURE 2. Classification of ductal carcinoma in situ based on biologic potential to progress to invasive breast cancer. DCIS indicates ductal carcinoma in situ; IBC, invasive breast cancer; ER+, estrogen receptor positive; PR+, progesterone receptor positive; ER−, ER negative; PR−, PR negative; LOH, loss of heterozygosity; COX2, cyclooxygenase-2; PAI type I; plasminogen activator inhibitor type 1; MMP, matrix metalloproteinase; hMSH2, human mutL homolog 2.

Arpino G: Ann Intern Med 2005;143:446

Wiechmann L: Cancer 2008;112:2130

Diagnosis of DCIS

BI-RADS – Mammography: Microcalcifications*

Morphologic descriptors

1. Typically benign
2. Suspicious (intermediate concern)
   - Amorphous (indistinct) calcifications
   - Coarse heterogeneous calcifications
3. Higher probability of malignancy
   - Fine pleomorphic calcifications
   - Fine linear / fine linear branching

Distribution descriptors

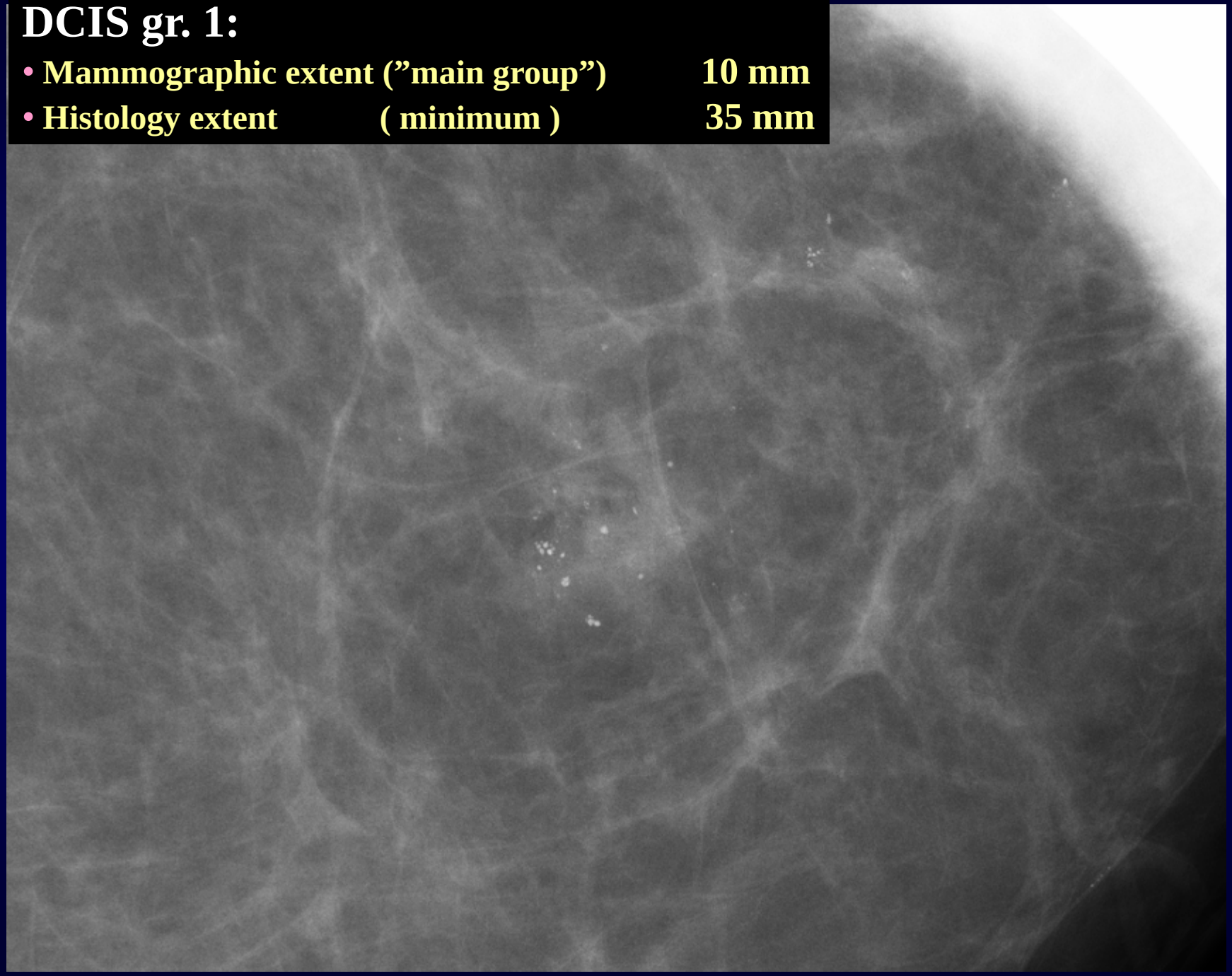
Stability descriptors**

* American College of Radiology: Breast Imaging Reporting and Data System

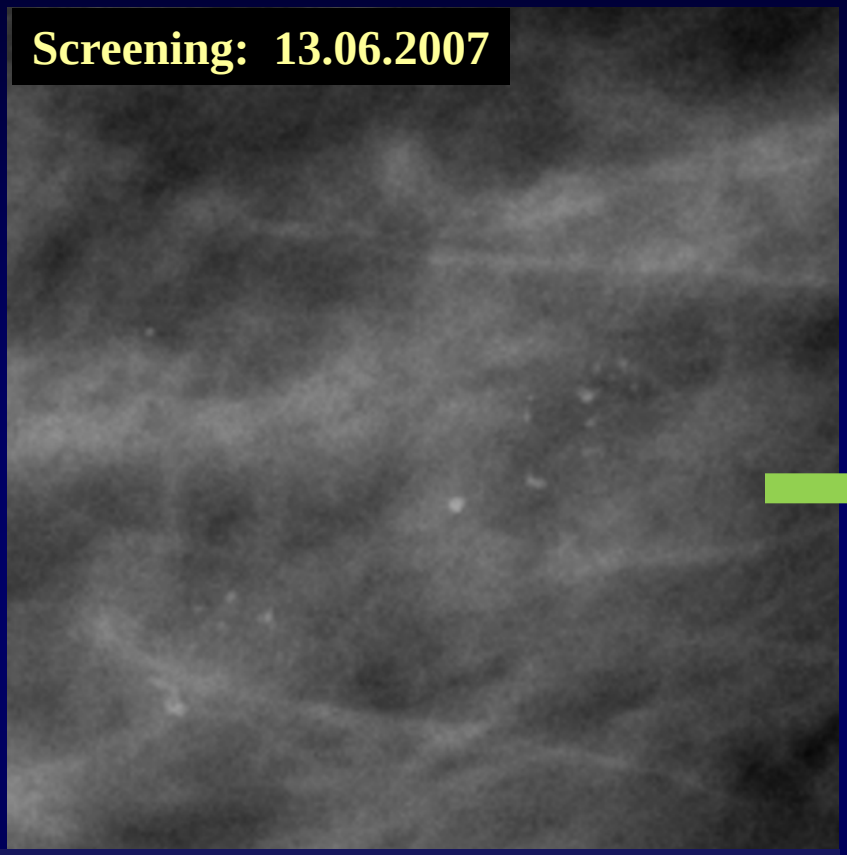
** not officially included in the BI-RADS lexicon

DCIS gr. 1:

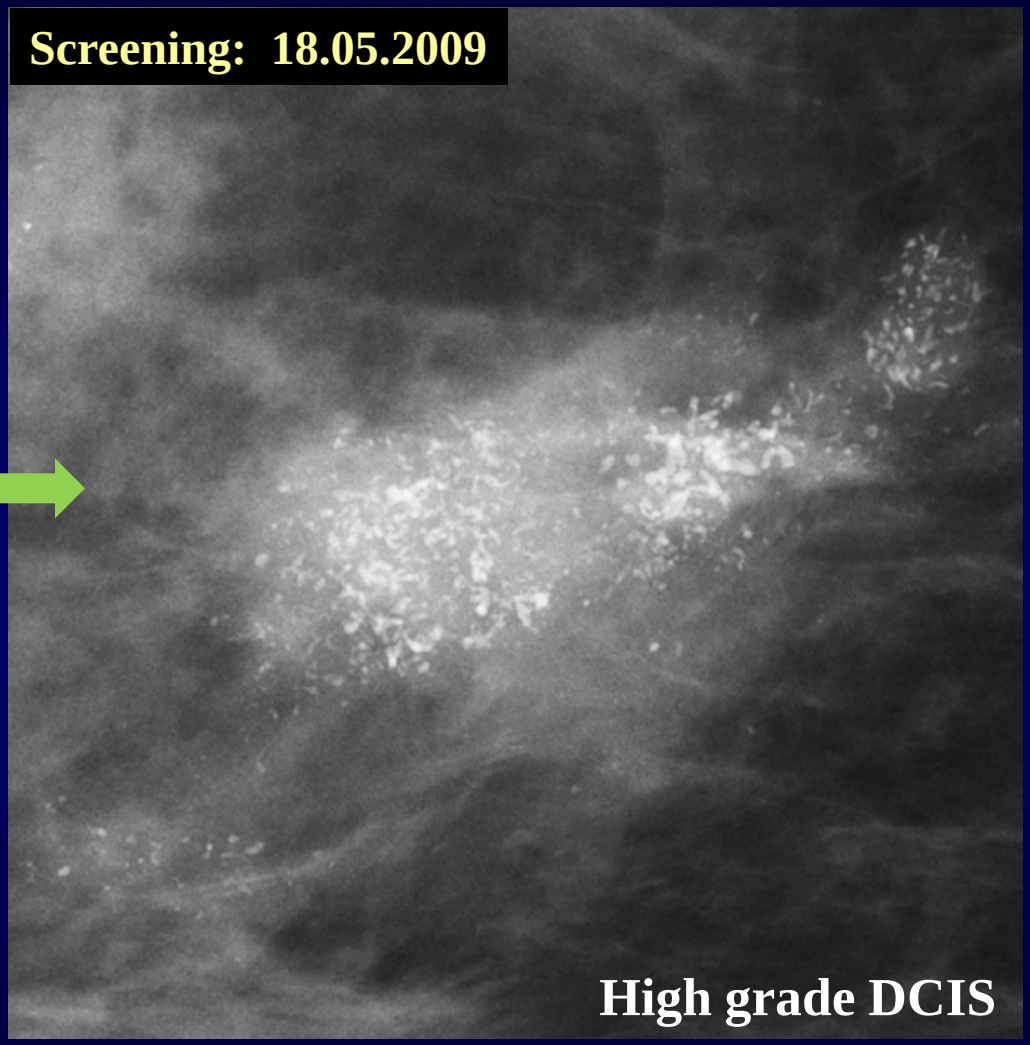
- Mammographic extent (”main group”) 10 mm
- Histology extent (minimum) 35 mm



B) Interpretation error:



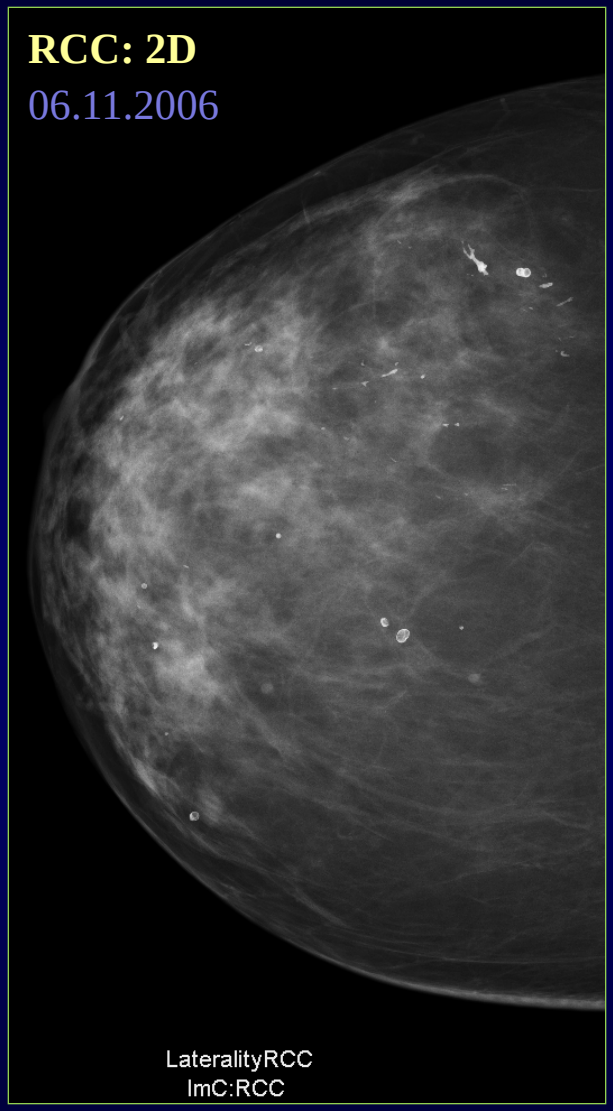
Amorphous and indistinct/heterogeneous calcifications:
Linear distribution elevates suspicion of any morphology !!

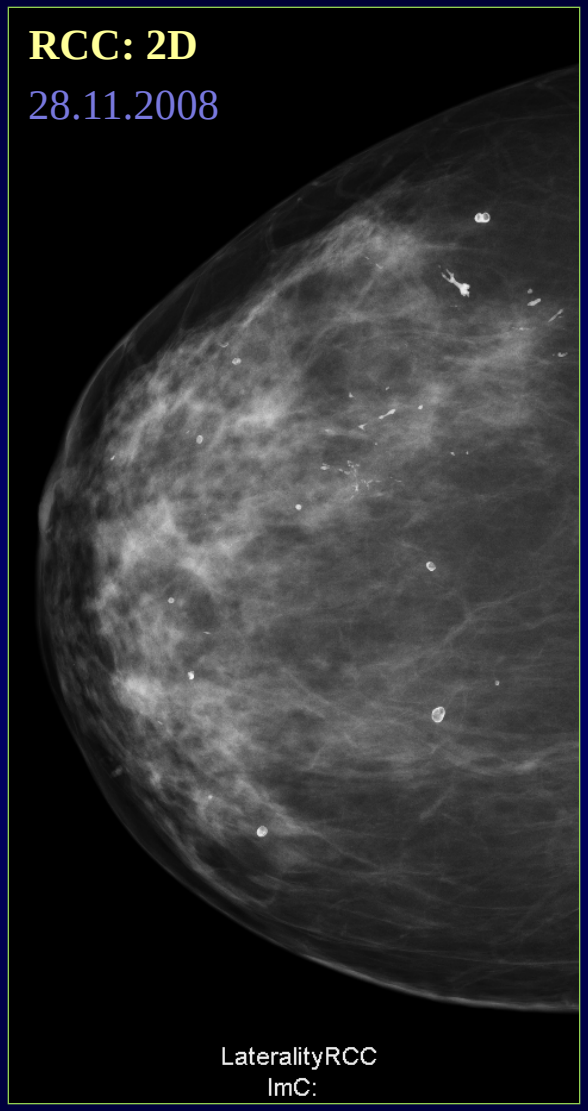


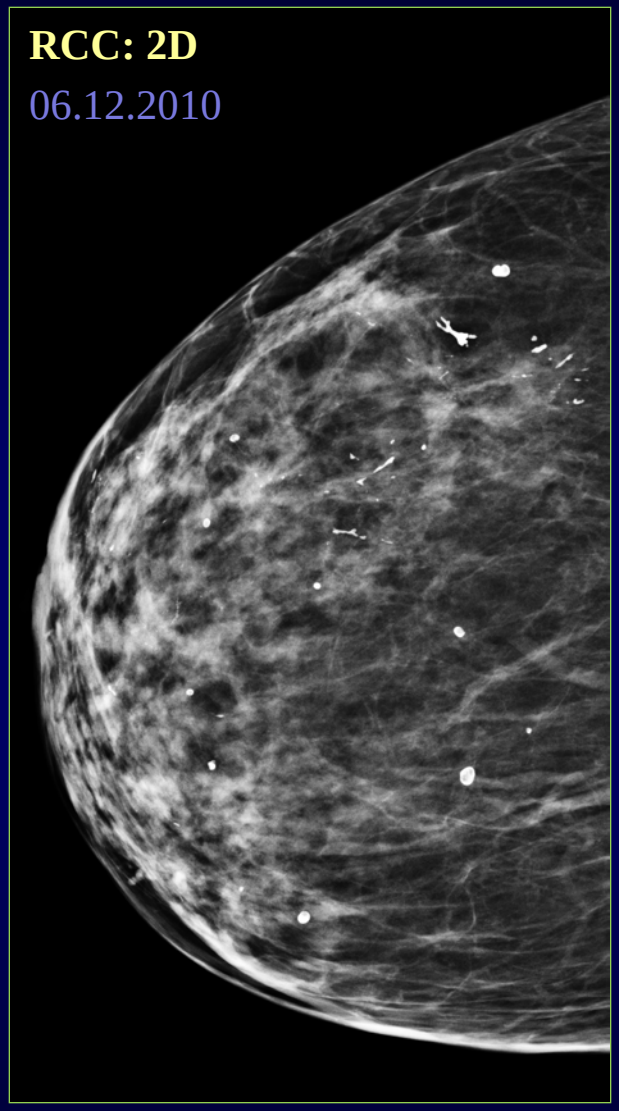
Histology (mastectomy): DCIS gr. 3; extent 50 mm (with comedo-necroses and multiple foci of microinvasive cancer less than 1 mm)

Interpretation error:

a)







Oslo Tomosynthesis Screening Trial

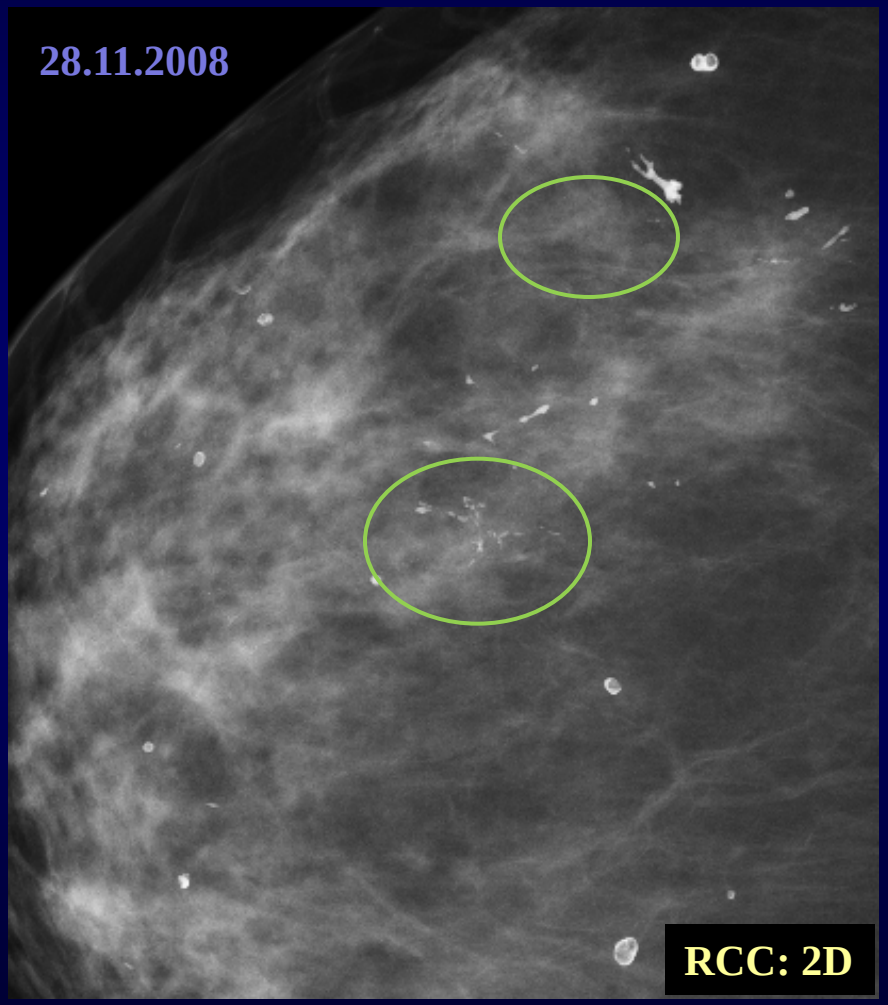
Radiologist	A	B	C	D
Score (2010)	1	1	1	4

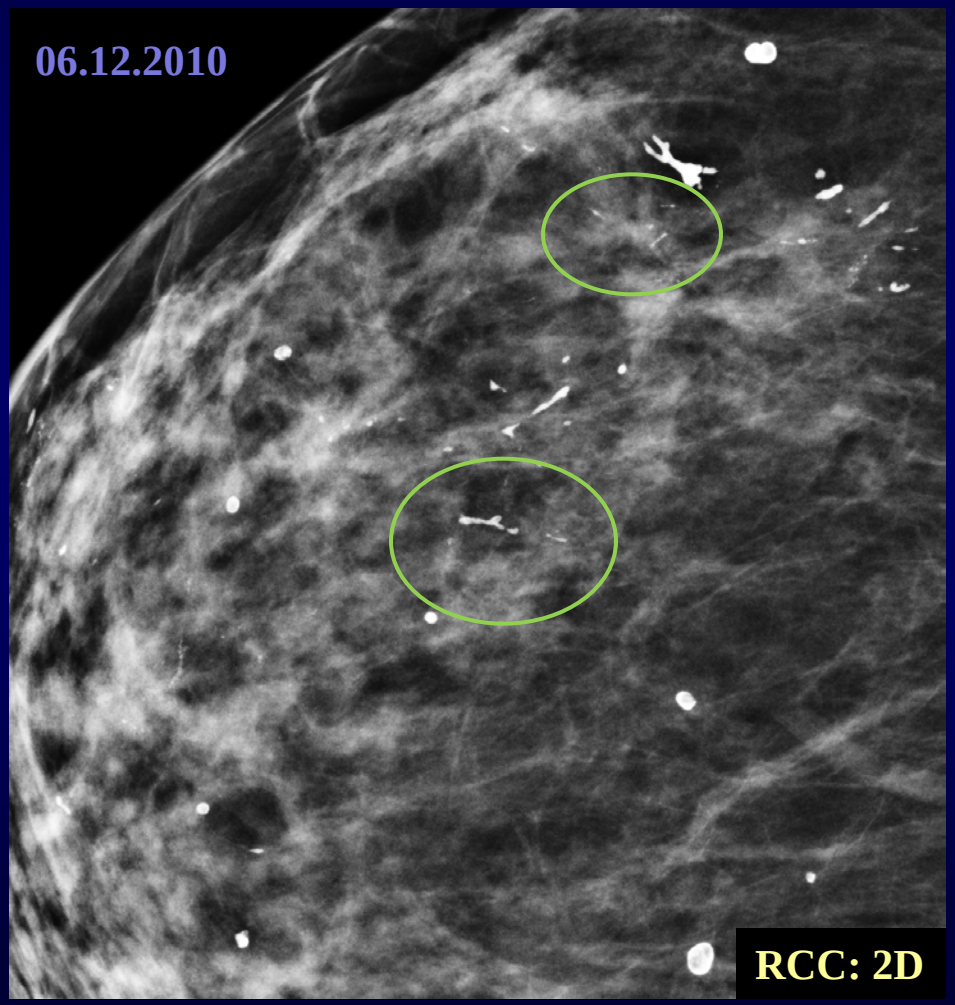
061210ES031245

Interpretation error:

b)

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





Histology: DCIS gr. 3 + IDC

Relationship between the histological size and the mammographic calcification morphology of DCIS according to histological grade*

Grade	Size (mm)	Casting no.	Casting (%)	Granular no.	Granular (%)	Punctate no.	Punctate (%)	Total no.
High	< 10	253	(50)	203	(40)	55	(11)	511
	10-20	223	(59)	120	(31)	38	(10)	381
	21-30	87	(76)	20	(18)	7	(6)	114
	> 30	94	(77)	22	(18)	6	(5)	122
	Total	657	(58)	365	(32)	106	(9)	1128
Intermed	Total	182	(37)	208	(43)	95	(20)	485
Low	< 10	22	(22)	55	(54)	24	(24)	101
	10-20	11	(26)	20	(48)	11	(26)	42
	21-30	6	(43)	6	(43)	2	(14)	14
	> 30	6	(46)	6	(46)	1	(8)	13
	Total	45	(26)	87	(51)	38	(22)	170

* Evans A et al.: The Sloane project (a large, multicentre audit of screen-detected DCIS in the UK). Clin Radiol 2010;65:181-184 (modified)

DCIS and overdiagnosis:

How many of the DCIS diagnosed at screening would be expected to progress to invasive cancer if left untreated ?

- **DCIS would have progressed:**
  Major benefit of screening !
- **DCIS would not have progressed:**
  Overdiagnosis (overtreatment) !

Estimated rate per 100,000 of non-progressive DCIS ($DCIS_0$) at prevalence screen and first subsequent screen, under the six-state Markov model *

Study	Prevalence screen $DCIS_0$ / DCIS	Subsequent screen $DCIS_0$ / DCIS
Swedish Two-County		
40-49 y.	19 %	3 %
50-59 y.	23 %	4 %
60-69 y.	46 %	6 %
UK	39 %	21 %
Netherland	41 %	4 %
South Australia	46 %	7 %
New York	42 %	6 %
Overall	37 %	4 %

* Yen MF, Tabar L, Vitak B, et al.: Eur J Cancer 2003; 39: 1746-1754

Incidence of Ductal Carcinoma *in situ* in the period before, during and after implementation of a population-based screening program

Sørum R[1], Hofvind S[1,2], Skaane P[3] and Haldorsen T[1]

[1]The Cancer Registry of Norway, Department of screening-based research, Oslo, Norway, [2]Oslo University College, Faculty of Health Sciences, Oslo, Norway , [3]Ullevaal University Hospital, Department of Radiology, University of Oslo, Oslo, Norway

Poster EBCC7

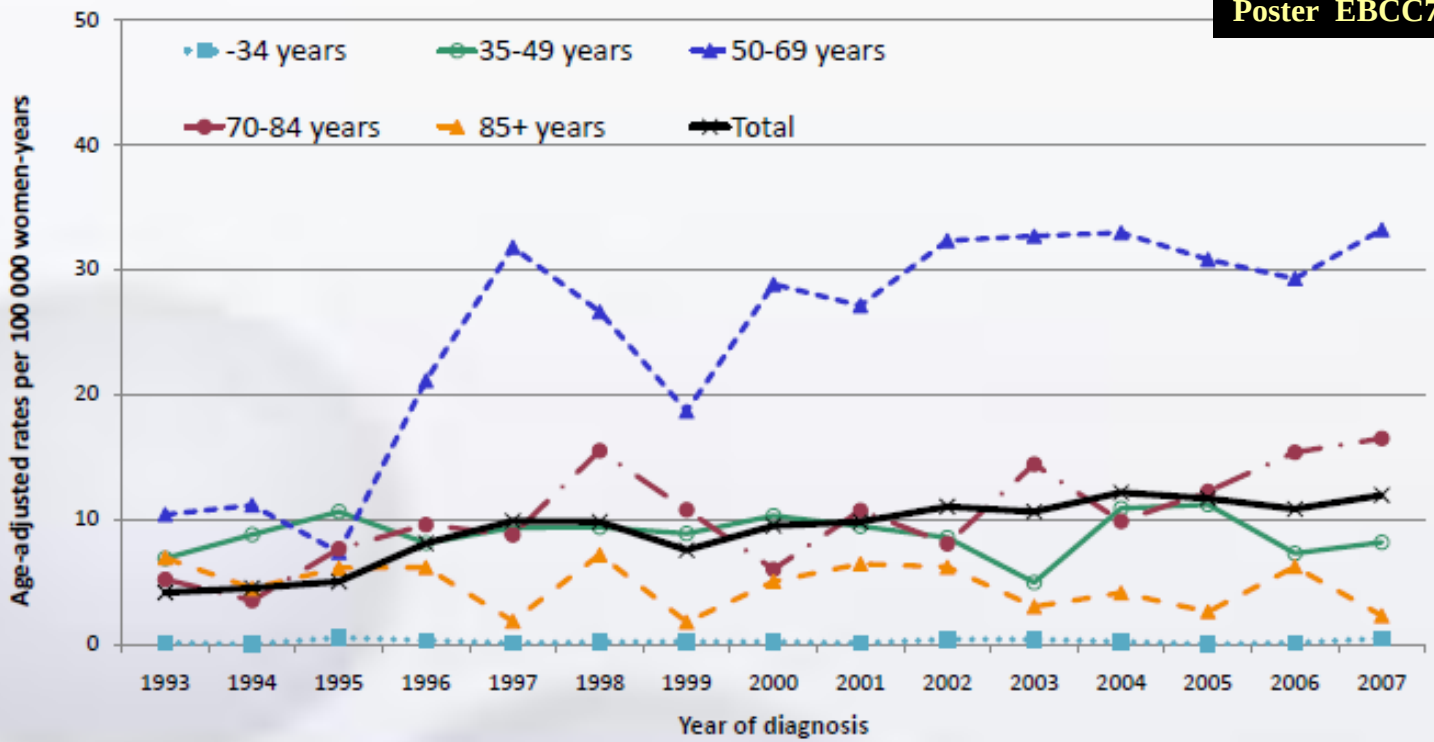
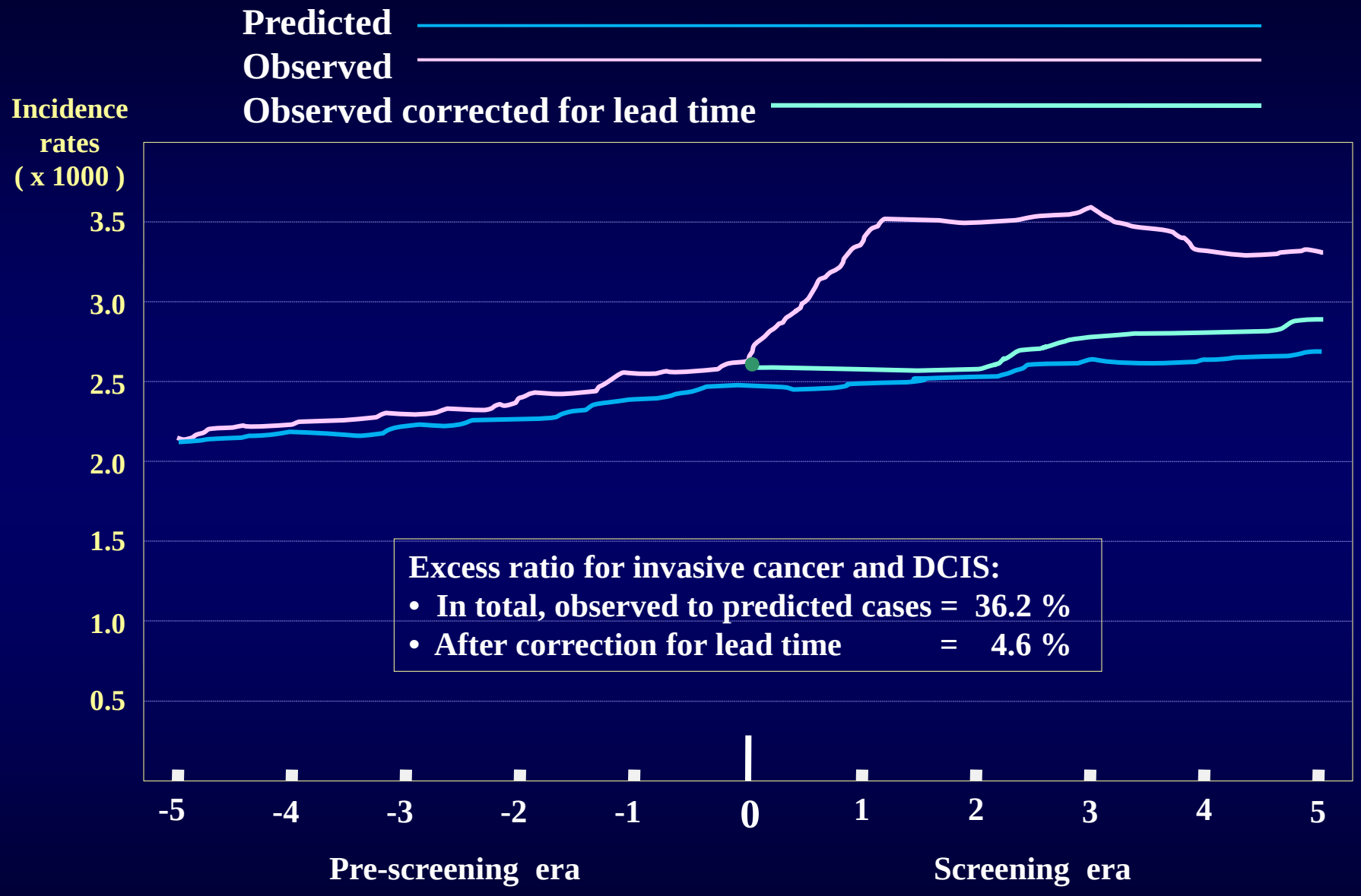


***Figure 1**: Age-adjusted incidence of primary pure DCIS in Norway, 1993-2007*

Women aged 50-74 years: Breast cancer incidence rates



Modified: Paci E et al: Estimate of overdiagnosis of breast cancer due to mammography after adjustment for lead time. A service screening study in Italy. Breast Cancer Research 2006

Gøtzsche PC:
Mammography Screening.Truth, lies and controversy

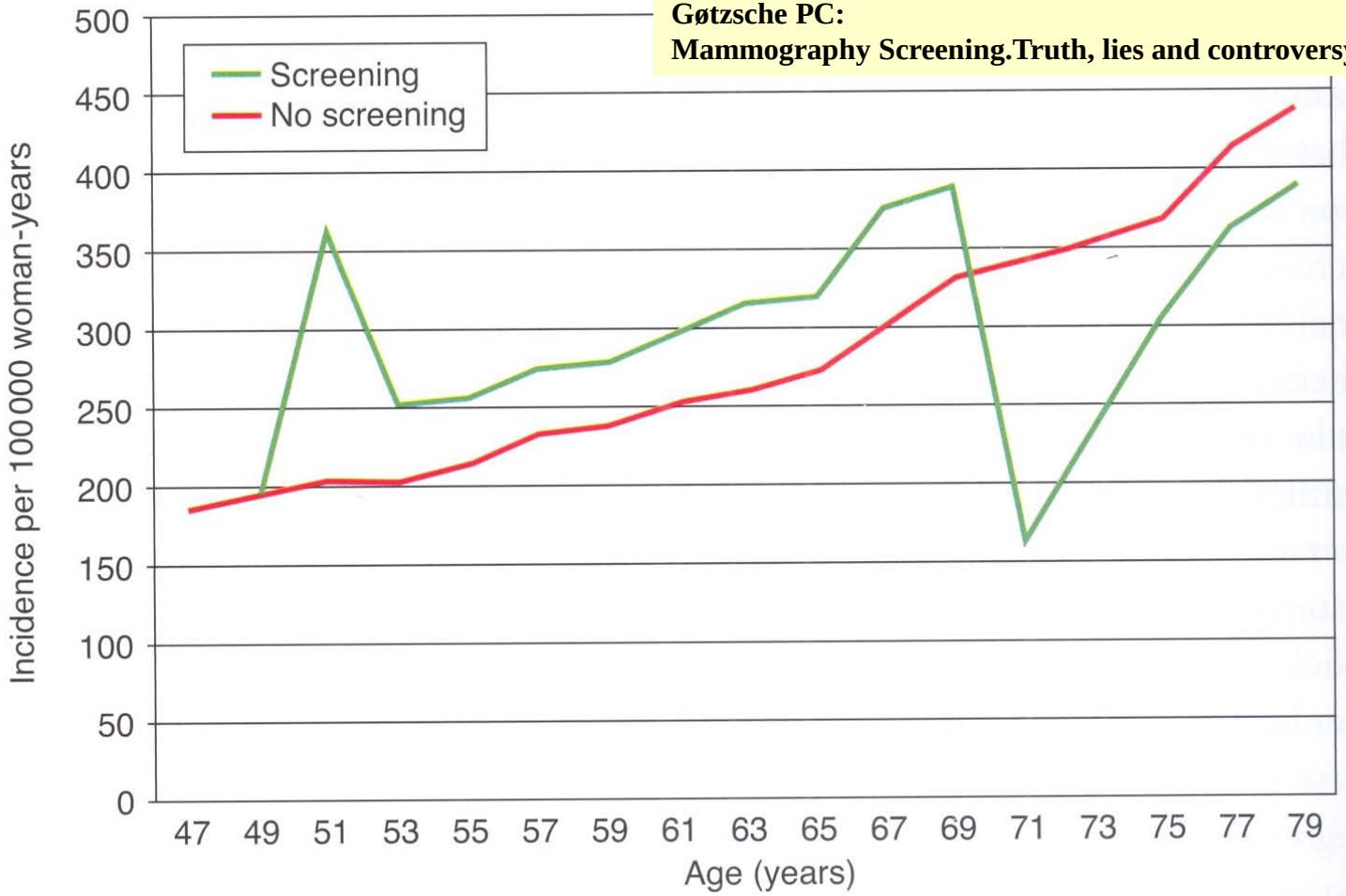
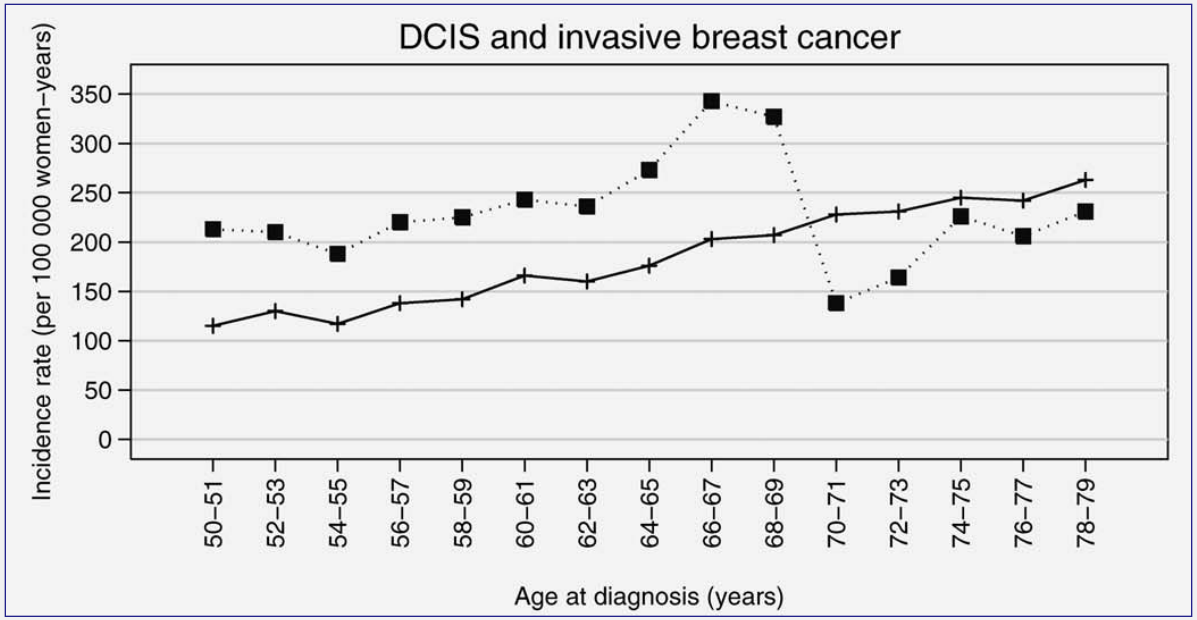
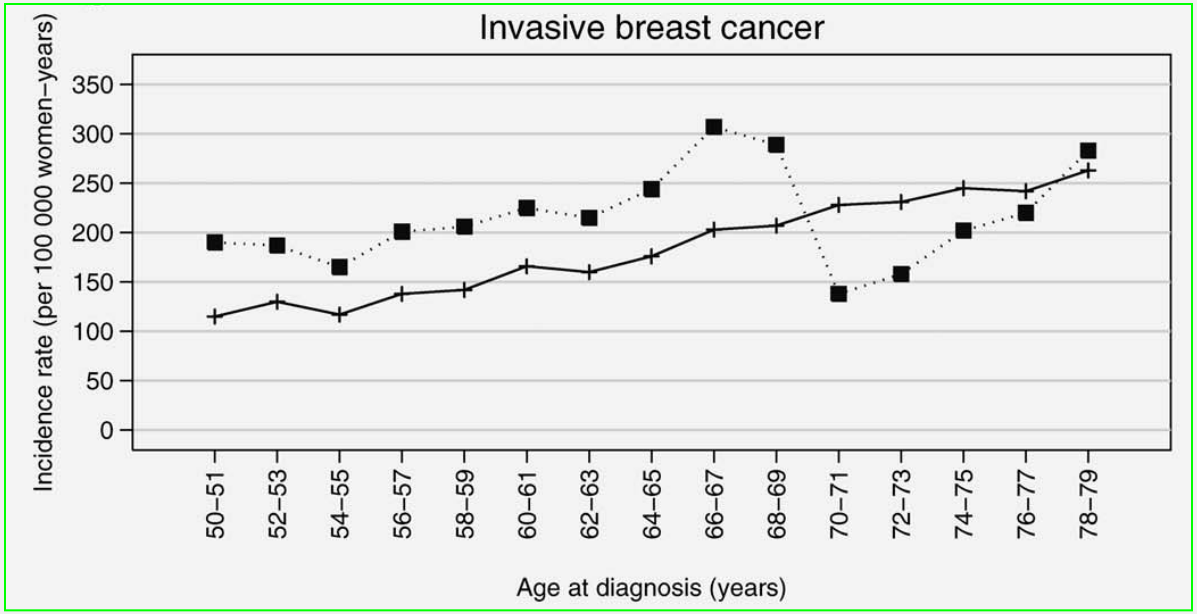


FIGURE 16.5 Expected breast cancer incidence with screening (green line) and without screening (red line). Wishful thinking, as the huge drop in elderly women has never been observed in practice (redrawn)

Boer R et al.: Extra incidence caused by mammographic screening. Lancet 1994;343:979





Overdiagnosis among women attending a population-based mammography screening program

Falk RS, Hofvind S, Skaane P, Haldorsen T: Int.J.Cancer 2013;133:705-713

Annals of Internal Medicine | ORIGINAL RESEARCH

Overdiagnosis of Invasive Breast Cancer Due to Mammography Screening: Results From the Norwegian Screening Program

Mette Kalager, MD; Hans-Olov Adami, MD, PhD; Michael Bretthauer, MD, PhD; and Rulla M. Tamimi, ScD

Background: Precise quantification of overdiagnosis of breast cancer (defined as the percentage of cases of cancer that would not have become clinically apparent in a woman's lifetime without screening) due to mammography screening has been hampered by lack of valid comparison groups that identify incidence trends attributable to screening versus those due to temporal trends in incidence.

Objective: To estimate the percentage of overdiagnosis of breast cancer attributable to mammography screening.

Design: Comparison of invasive breast cancer incidence with and without screening.

Setting: A nationwide mammography screening program in Norway (inviting women aged 50 to 69 years), gradually implemented from 1996 to 2005.

Participants: The Norwegian female population.

Measurements: Concomitant incidence of invasive breast cancer from 1996 to 2005 in counties where the screening program was implemented compared with that in counties where the program was not yet implemented. To adjust for changes in temporal trends in breast cancer incidence, incidence rates during the preceding decade were also examined. The percentage of overdiagnosis was calculated by accounting for the expected decrease in incidence following cessation of screening after age 69 years (approach 1) and by comparing incidence in the current screening group with incidence among women 2 and 5 years older in the historical screening groups, accounting for average lead time (approach 2).

Results: A total of 39 888 patients with invasive breast cancer were included, 7793 of whom were diagnosed after the screening program started. The estimated rate of overdiagnosis attributable to the program was 18% to 25% ($P < 0.001$) for approach 1 and 15% to 20% ($P < 0.001$) for approach 2. Thus, 15% to 25% of cases of cancer are overdiagnosed, translating to 6 to 10 women overdiagnosed for every 2500 women invited.

Limitation: The study was registry-based.

Conclusion: Mammography screening entails a substantial amount of overdiagnosis.

Primary Funding Source: Norwegian Research Council and Frontier Science.

Ann Intern Med. 2012;156:491-499. www.annals.org
For author affiliations, see end of text.

Original Research: **Overdiagnosis of Invasive Breast Cancer Due to Mammography Screening: Results From the Norwegian Screening Program**
Ann Intern Med 2012; 156:491–499.

Annals of Internal Medicine

Established in 1927 by the American College of Physicians

7 August 2012, Vol 157, No. 3>

Letters | 7 August 2012

Overdiagnosis of Invasive Breast Cancer due to Mammography Screening

Per-Henrik Zahl, DrMedSci

[+] Article and Author Information

Ann Intern Med. 7 August 2012;157(3):220-221

TO THE EDITOR:

Kalager and colleagues (1) reported a 15% to 25% overdiagnosis rate of invasive cancer in the Norwegian Breast Cancer Screening Program. In 2004, my coworkers and I reported (2) that screening led to a 51% increase in breast cancer cases that could not be explained by earlier diagnosis and called this increase overdiagnosis. We updated our study in 2012 (3) and reported the same high level of overdiagnosis. Our updated study had longer follow-up and included 11 631 breast cancer cases diagnosed after screening started, whereas Kalager and colleagues' analysis included only 3862 cases. The difference in estimates of overdiagnosis between our study and theirs, however, is not explained by data per se but by the methods for adjusting for underlying incidence increase and lead time.

Overdiagnosis of Invasive Breast Cancer Due to Mammography Screening: Results From the Norwegian Screening Program Ann Intern Med 2012; 156:491-499:

Letters to the Editor

a)

"Overdiagnosis in Norway"

Karsten J. Jørgensen, MD
The Nordic Cochrane Centre

"We have estimted 37% overdiagnosis of invasive breast cancer in Norway, and 52% when including ductal carcinoma in situ (1)"

"Error in numbers"

Ragnhild S. Falk, Statistician; Per Skaane; Solveig Hofvind
Cancer Registry of Norway

"We are concerned about the numbers that are reported. According to Results approx. 500,000 women have been invited while the correct number is 592,155….The number 4,204,064 (Table 1) is different from what can be found in Statistics Norway (4,518,003). This discrepancy of almost 314,000 person-years is also found in a previous paper by some of the authors (3)."

Overdiagnosis of Invasive Breast Cancer Due to Mammography Screening: Results From the Norwegian Screening Program Ann Intern Med 2012; 156:491-499:

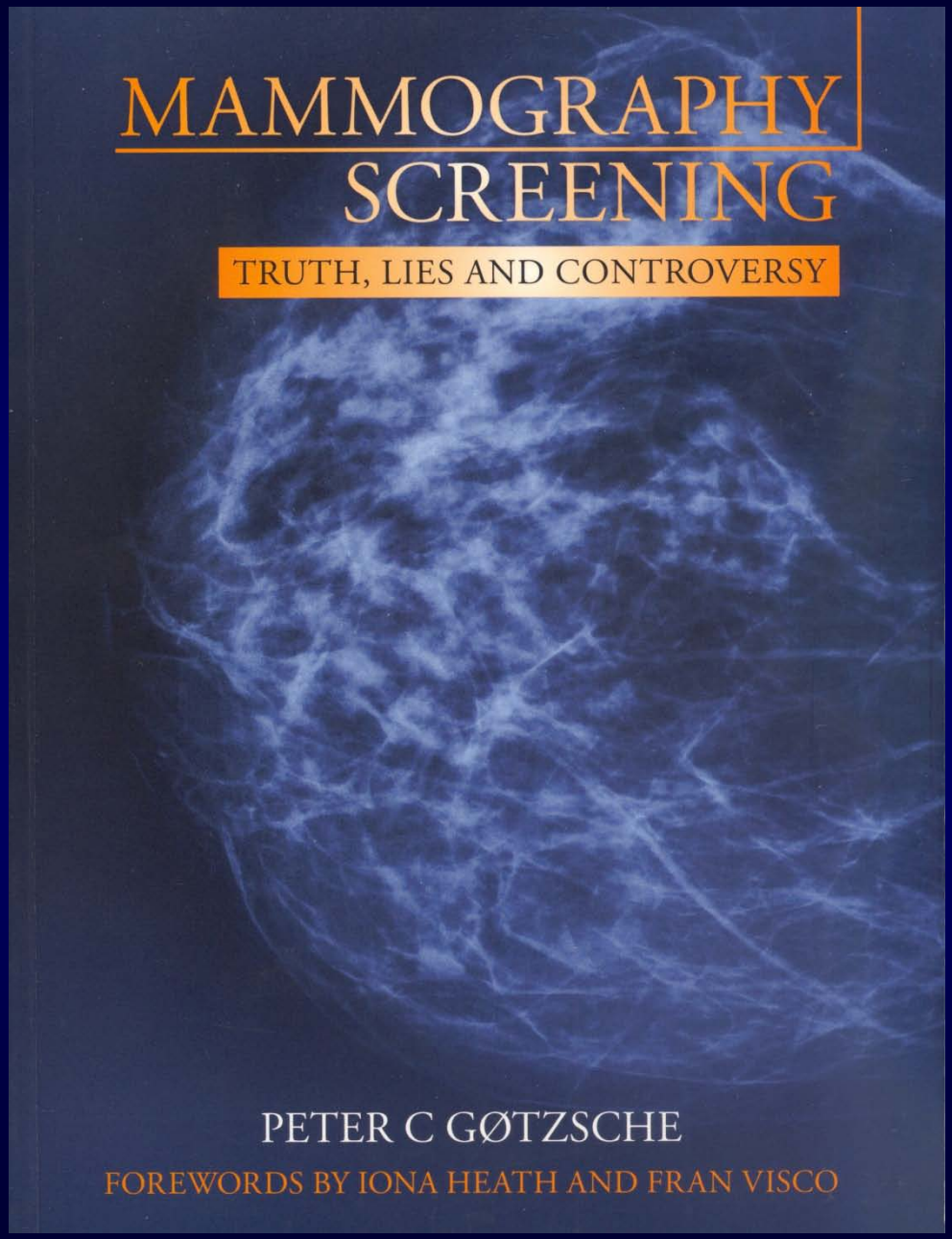
Letters to the Editor

b)

”The rate of overdiagnosis is overestimated”

Tor Haldorsen, Researcher; Steinar Tretli, Giske Ursin
Cancer Registry of Norway

”The estimation of overdiagnosis assumes that the ”Current screening group” contains observations during (50-69 years) and after screening (70-79 years). However, this is not the case. Only 37% of person-years 70-79 years are among women after ended invitation to screening. The rest of person-years are mostly from unscreened cohorts (born 1926 and before). The authors therefore underestimated the incidence deficit after screening. Their exclusion of data from the ”first screening round” in each region does not exclude all prevalent cancers. The inclusion of data on prevalent cancers will lead to an overestimation of the excess incidence in the subsequent period.
We conclude that the rate of overdiagnosis is overestimated in Kalager et al (1)”.


MAMMOGRAPHY SCREENING
TRUTH, LIES AND CONTROVERSY
PETER C GØTZSCHE
FOREWORDS BY IONA HEATH AND FRAN VISCO

Overdiagnostisering ved mammografiscreening

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Sammendrag

Bakgrunn. Erfaringer fra mammografi-screening i Norge og Sverige indikerer at mammografiscreening medfører påvisning av svulster som ikke ville ha gitt symptomer, dvs. en overdiagnosti-

Overdiagnosis in mammography screening.

Per-Henrik Zahl, Jan Mæhlen

Background. In Norway and Sweden, the introduction of mammography screening programmes has been associated with about a 50 % increase in breast cancer incidence for the screened age groups and almost stable incidence in higher age groups. This suggests that mammography screening results in a substantial degree of overdiagnosis

EJSO (2004) 30, 711-712

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the Journal of Cancer Surgery
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EDITORIAL

Overdiagnosis of breast cancer in screening

The recent paper by Zahl et al.[1] has again raised doubts about the supposed benefits of breast screening as a public health policy. Theoretically, the introduction of breast screening in risk population should (and does) detect more cancers specifically because of the lead and length time bias, which make the evaluation of a screening programme so difficult. A consequence of these factors is overdiagnosis of breast cancer which is defined as the detection of low malignancy lesions that would otherwise have not been detected in a patients lifetime.

The recent reported rates of 'overdiagnosis' of breast cancer in Norway (54%) and Sweden (45%) appear to be higher than those expected[2] or reported previously[3] in clinical trials. However, another recent study of increases in incidence of

The detractors of breast screening point out that many of these tumours would never become symptomatic, and although it has been shown in several studies that breast cancer specific mortality has decreased in countries which have implemented a national screening programme,[11-13] overall mortality has in general not followed this trend.[14] Many would argue that overall mortality should not be the benchmark for the evaluation of a breast screening programme because of the increasingly important effect of other-cause mortality with increasing age.[12] However, whilst it is true that the introduction of breast screening programmes in various countries has coincided with better surgery and with the introduction of effective adjuvant treatment for breast cancer, the reductions in mortality from breast cancer are not

Er 50 % overdiagnostisering ved mammografiscreening akseptabelt?

klusjoner (6). Kvinner er i ti år blitt systematisk feilinformert om nytte- og skadeeffekter av mammografiscreening. Ledende brystkreftmiljøer i Norge lar dette bare skure og gå.

Per-Henrik Zahl
Nasjonalt folkehelseinstitutt

Jan Mæhlen
Ullevål universitetessykehus

Zahl PH al.:
Tidsskr Nor Lægeforen 2007;127:207-8

HELSE: Hvis å være føre var betyr å påføre sykdom, smerte, angst og lidelse på kvinner og familier, da er jeg imot.

Legg ned mammografiprogrammet

KRONIKK

Nils August Andresen
Redaktør i Minerva

MED NY TEKNOLOGI kan vi behandle stadig flere for stadig mer. At dette koster stadig mer

OMSTRIDT: Er screeningprogrammet mot brystkreft effektivt eller unødvendig? Foto: Lise Åserud /Scanpix

Screening funker

Berit Damtjernhaug
Overlege og leder av Mammografiprogr.

SCREENING: I en replikk i Dagbladet 7. juni henviste jeg til at samleanalyser av studier på mammografiscreening har vist 20-25 % redusert brystkreftdødelighet hos kvinner som inviteres til screening. Etter at en Tromsø-studie i forbindelse med evalueringen av Mammografiprogrammet har vist 11 % dødelighetsreduksjon, som ikke er signifikant, repliserer professor og overlege Michael Bretthauer i Dagbladet 26. juni: «Det finnes altså nå to uavhengige studier som viser at mammografiscreening ikke har noe særlig effekt. Til tross for dette henviser Mammografiprogrammets leder til eldre utenlandske studier…». Den andre studien Bretthauer sikter til, ble publisert av hans kone og kollega Mette Kalager i New England Journal of Medicine i 2010 og viste heller ingen signifikant dødelighetsreduksjon (10 %).

EN KUNNE BLI fristet til å tro at jeg med vilje har holdt tilbake disse norske resultatene, men det finnes en enkel forklaring: Evaluering av populasjonsbaserte screeningprogrammers effekt på dødelighet er komplisert og krever at man har tilgang til detaljerte screeningdata på hver enkelt kvinne. Ingen av de to studiene Bretthauer referer til kvalifiserer i så måte. Erfaringer fra andre land viser at effekten blir underestimert dersom man ikke har slike data på individnivå. Man må altså vite hvem som ble invitert, når de ble invitert og hvem som faktisk deltok. Kalagers studie fra 2010 har i tillegg vært kritisert for å ha for kort oppfølgingstid etter diagnose. Da blir resultatene nærmest ubrukelige til en evaluering. Tromsø-miljøet nevner selv som en alvorlig begrensning at de ikke har hatt tilgang til opplysninger om kvinnen har møtt på sin invitasjon. De anser at kombinasjonen av mangelfulle individdata og utbredt mammografivirksomhet før programmet startet, fører til at de finner en lavere dødelighetsreduksjon enn det som er reelt.

DET ER ET stortingsvedtak på at vi skal ha mammografiscreening i Norge. Regjeringen har satt i gang en forskningsbasert evaluering av programmet. Når de endelige resultatene fra evalueringen foreligger, og disse blir sammenholdt med en nær forestående samlestudie på europeiske mammografiscreeningprogram, vil det være klart både for helsemyndigheter og politikere hva som er fordelen ved regelmessig mammografiscreening. Dette er ikke sagt fordi Kreftregisteret, som Bretthauer nevner «har en egeninteresse i screening», men fordi vi ser hvilken effekt programmet har hatt, blant annet på reduksjon i langtkommen brystkreft. Kreftregisteret har selvsagt ingen interesse av å være ansvarlig for screeningprogram som ikke fungerer, enten det gjelder brystkreft eller andre krefttyper.

Mammografiprogrammet best uten mammografi?

Michael Bretthauer
Professor Universitetet i Oslo
Overlege Rikshospitalet

BRYSTKREFT: «Legg ned mammografiprogrammet!», skrev Nils August Andresen i Dagbladet 30. mai. Dette står i sterk motsetning til hjemmesidene til si at den er reell (såkalt statistisk signifikans). Nedgangen ligger langt under de 30 prosent som Stortinget forventet da programmet startet i 1996.

Resultatene av studien er for øvrig akkurat like som i en annen stor studie, som i 2010 ble publisert i det mest anerkjente medisinske tidsskriftet New England Journal of Medicine og som viste en nedgang på ti pro-

HELSE: Hvis å være føre var betyr å påføre sykdom, smerte, angst og lidelse på kvinner og familier, da er jeg imot.

Legg ned mammografiprogrammet

grammet ikke hjelper, er det nemlig slik, sies det, at mange kvinner allerede gikk til mammografiscreening før programmet begynte. Derfor kunne man ikke finne en nedgang etter at programmet ble innført. Man snur resultatene på hodet og sier at mammografiprogrammet «egentlig» virker, selv om tallene sier det motsatte.

April 2012

MAMMOGRAFI-SJOKKET:

1900 FIKK FEIL KREFTDIAGNOSE

SIDE 6

VG

Nr. 93
Tirsdag
3. april
2012
Uke 14
Kr. 13,00

NORGES MEST LESTE AVIS!

MØTTE VG I CHILE:

OPPDATERT 10-DAGE

Nytt norsk mammografi-sjokk:

1900 SKADET – 47 REDDET

DEPARTEMENTET: KAN VURDERE Å AVSLUTTE PROGRAMMET

– FORVENTER OKONOMISTYRA

ORIGINAL ARTICLE

Absolute numbers of lives saved and overdiagnosis in breast cancer screening, from a randomized trial and from the Breast Screening Programme in England

Stephen W Duffy, Laszlo Tabar, Anne Helene Olsen, Bedrich Vitak, Prue C Allgood, Tony H H Chen, Amy M F Yen and Robert A Smith

J Med Screen 2010;**17**:25–30
DOI: 10.1258/jms.2009.009094

Conclusions:

”The benefit of mammographic screening in terms of lives saved is greater in absolute terms than the harm in terms of overdiagnosis.

Between 2 and 2.5 lives are saved for every overdiagnosed case.”

BMJ

BMJ 2013;346:f1064 doi: 10.1136/bmj.f1064 (Published 26 February 2013)

RESEARCH

Overdiagnosis in screening mammography in Denmark: population based cohort study

OPEN ACCESS

Sisse Helle Njor *statistician*[1], Anne Helene Olsen *statistician*[2], Mogens Blichert-Toft *professor emeritus*[3], Walter Schwartz *chief physician*[4], Ilse Vejborg *chief physician*[5], Elsebeth Lynge *professor*[1]

[1]Department of Public Health, University of Copenhagen, Østre Farimagsgade 5, DK 1014 Copenhagen K, Denmark; [2]Institute of Community Medicine, University of Tromsø, Tromsø, Norway; [3]Danish Breast Cancer Cooperative Group, 2100 Copenhagen Ø, Denmark; [4]Mammography Screening Clinic, University Hospital Odense, 5000 Odense, Denmark; [5]Diagnostic Centre, University Hospital Copenhagen, Blegdamsvej, 2100 Copenhagen Ø, Denmark

Conclusions On the basis of combined data from the two screening programmes, this study indicated that overdiagnosis most likely amounted to 2.3% (95% confidence interval –3% to 8%) in targeted women. Among participants, it was most likely 1-5%. At least eight years after the end of screening were needed to compensate for the excess incidence during screening.

Overdiagnosis in breast cancer screening

Author	Publ.	Study	Journal	Overdiagnosis
Paci E	2004	Florence	J Med Screen	< 5 %
Zahl PH*	2004	Norway Sweden	BMJ	54% 45%
Duffy SW	2005	Two-county Gothenburg	Breast Cancer Research	1 %
de Koning	2006	Netherlands	Breast Cancer Research	3 %
Zackrisson S	2006	Malmø	BMJ	10 %
Olsen AH	2006	Copenhagen	Breast Journal	5 %
Gøtzsche PC	2006	Overview	Cochrane Library	30 %

Paci E et al.: J Med Screen 2004; 11: 23-27
Zahl PH et al.. BMJ 2004; 328: 921-924 - * 66% (Tidsskr Nor Laegeforen 2004; 124: 2238)
Duffy SW et al: Breast Cancer Research 2005; 7: 258-265
de Koning et al.: Breast Cancer Research 2006; 8: 202
Zackrisson S et al.: BMJ 2006; 332: 689-691
Olsen AH et al.: Breast Journal 2006; 12: 338-342
Gøtzsche PC et al.: Cochrane Database of Systematic Reviews 2006, Issue 4.

ORIGINAL ARTICLE

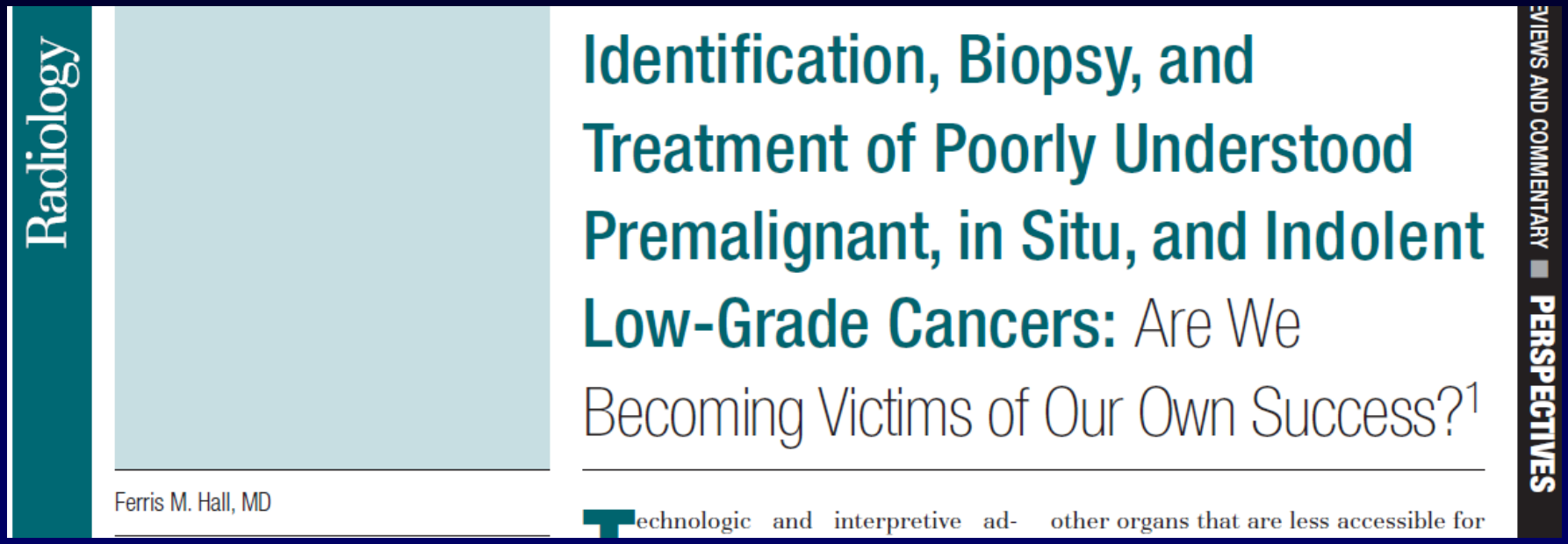
Overdiagnosis in mammographic screening for breast cancer in Europe: a literature review

Donella Puliti, Stephen W Duffy, Guido Miccinesi, Harry de Koning, Elsebeth Lynge, Marco Zappa, Eugenio Paci and the EUROSCREEN Working Group (members listed at the end of the paper)

J Med Screen 2012;**19 Suppl 1**:42–56
DOI: 10.1258/jms.2012.012082

Results There were 13 primary studies reporting 16 estimates of overdiagnosis in seven European countries (the Netherlands, Italy, Norway, Sweden, Denmark, UK and Spain). Unadjusted estimates ranged from 0% to 54%. Reported estimates adjusted for breast cancer risk and lead time were 2.8% in the Netherlands, 4.6% and 1.0% in Italy, 7.0% in Denmark and 10% and 3.3% in England and Wales.

Conclusions The most plausible estimates of overdiagnosis range from 1% to 10%. Substantially higher estimates of overdiagnosis reported in the literature are due to the lack of adjustment for breast cancer risk and/or lead time.



Radiology

Identification, Biopsy, and Treatment of Poorly Understood Premalignant, in Situ, and Indolent Low-Grade Cancers: Are We Becoming Victims of Our Own Success?[1]

Ferris M. Hall, MD

Technologic and interpretive ad- other organs that are less accessible for

EVIEWS AND COMMENTARY ■ PERSPECTIVES

”Imagers are increasingly detecting and performing percutaneous biopsies on borderline, preinvasive, or low grade cancers that were heretofore rarely identified and that may never progress to meaningful disease.”

”As regards screening mammography, my area of expertise, I believe that, particularly in the United States, the problem lies less with the examination itself than with the interpretations and recommendations these examinations engender: specifically, the obsession of some radiologists with low-suspicion micro-calcifications and of some pathologists with epithelial atypia.”

Evaluation of the Norwegian Breast Cancer Screening Program (NBCSP):

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 23, 2010 VOL. 363 NO. 13

Effect of Screening Mammography on Breast-Cancer Mortality in Norway

Mette Kalager, M.D., Marvin Zelen, Ph.D., Frøydis Langmark, M.D., and Hans-Olov Adami, M.D., Ph.D.

Kalager M et al. NEJM 2010:

- Aggregated data
- Short follow-up

Mortality reduction: 10%

Original Article

Breast Cancer Mortality in Participants of the Norwegian Breast Cancer Screening Program

Solveig Hofvind, PhD[1,2]; Giske Ursin, MD, PhD[3,4,5]; Steinar Tretli, PhD[1,6]; Sofie Sebuødegård, BSc[1]; and Bjørn Møller, PhD[7]

BACKGROUND: The Norwegian Breast Cancer Screening Program started in 1996. To the authors' knowledge, this is the first report using individual-based data on invitation and participation to analyze breast cancer mortality among screened and nonscreened women in the program. **METHODS:** Information on dates of invitation, attendance, breast cancer diagnosis, emigration, death, and cause of death was linked by using unique 11-digit personal identification numbers assigned all inhabitants of Norway at birth or immigration. In total, 699,628 women ages 50 to 69 years without prior a diagnosis of breast cancer were invited to the program from 1996 to 2009 and were followed for breast cancer through 2009 and death through 2010. Incidence-based breast cancer mortality rate ratios (MRRs) were compared between the screened and nonscreened cohorts using a Poisson regression model. The MRRs were adjusted for calendar period, attained age, years since inclusion in the cohorts, and self-selection bias. **RESULTS:** The crude breast cancer mortality rate was 20.7 per 100,000 women-years for the screened cohort compared with 39.7 per 100,000 women-years for the nonscreened cohort, resulting in an MRR of 0.52 (95% confidence interval, 0.47-0.59). The mortality reduction associated with attendance in the program was 43% (MRR, 0.57; 95% confidence interval, 0.51-0.64) after adjusting for calendar period, attained age, years after inclusion in the cohort, and self-selection bias. **CONCLUSIONS:** After 15 years of follow-up, a 43% reduction in mortality was observed among women who attended the national mammographic screening program in Norway. *Cancer* 2013;000:000-000.

Hofvind S et al. Cancer 2013:

- Individual data
- Long-term follow-up

Mortality reduction: 43%

Norges største avis

Aftenposten

Torsdag
30. mai 2013
Uke 22 Nr. 140
154. årgang
Kr 30

NYHETER • DEL 1 • SIDE 6-7

- Mammografi reddet livet mitt

En studie anslår at mammografi-screening redder 100 liv i året. Laila Kværner fikk avdekket en aggressiv svulst.

ØKONOMIMAGASINET • SIDE 6-9

Kjærligheten har sin pris

Veteranbiler, isskulpturer og fyrverkeri. Norske brylluper er blitt milliardindustri. Mange kjemper om en bit av kaken.

Laila Kværner (54) fikk påvist en aggressiv svulst. – For meg var det livreddende å ta mammografi, sier hun.

– Mammografi redder 100 liv hvert år

KREFT-SCREENING

TINE DOMMERUD

En norsk studie med data fra 70 000 kvinner slår fast at det er helsegevinst ved å undersøke brystene med mammografi.

Laila Kværner er mor til to store gutter og informasjonsmedarbeider ved Follo folkehøyskole.

Som alle andre norske kvinner fikk hun invitasjon til screening da hun fylte 50 år, men takket nei til fordi det var for langt å reise.

Da hun på ny fikk invitasjon til screeningprogrammet, bestemte hun seg for å dra, fordi undersøkelsen ble gjort ved Ski sykehus, ikke langt unna.

Operert bort

På undersøkelsen ble det oppdaget at Laila Kværner, som da var 52 år, hadde en kul i brystet.

– Den satt så dypt inne at jeg ikke hadde kjent til den uansett hvor mye jeg selv hadde kjent etter, forteller Kværner.

Deretter gikk det på skinner. Hun ble raskt innkalt til en ny mammografi ved Ahus, hun tok ultralyd og biopsi, og kulen ble operert bort. Den var ondartet og Laila Kværner hadde spredning til 8 av 17 lymfeknuter under venstre arm.

– Uten mammografi hadde

Fakta

Mammografi-programmet

- Alle kvinner i alderen 50–69 år inviteres hvert annet år til deltagelse i Mammografiprogrammet.
- Ca 75 % velger å delta.
- Det er satt som et hovedmål for Mammografiprogrammet at det skal oppnå en 30 % reduksjon av dødelighet av brystkreft for kvinner som inviteres til screening

Skal evalueres

- Mammografiprogrammet skal evalueres.
- Evalueringen var opprinnelig planlagt sluttført i 2010.
- Det er blitt betydelig forsinket på grunn av vedtak i Datatilsynet og Personvernnemnda om at informasjon om kvinner med negativt mammogram ikke kunne brukes til forskningsformål før kvinnene hadde gitt informert samtykke til det.
- Forhold knyttet til bruk av data fra kvinner med negativt mammogram er nå klargjort og nødvendige tillatelser er innhentet.
- Det er antatt at alle evalueringsprosjektene vil bli sluttført i løpet av 2014.
- Evalueringens formål er å undersøke om målsetningene ved Mammografiprogrammet nås.

ble sammenlignet med dødeligheten blant dem som ikke deltok.

Brystkreftdødeligheten var nær halvert blant deltagerne.

Aggressiv

Reduksjonen i dødelighet er større enn tidligere norske studier har vist, men er helt på linje med resultater fra nyere internasjonale publiseringer, sier Solveig Hofvind

Laila Kværner er klar over at screeningsprosjektet evalueres. Hun håper det fortsetter.

– For meg var det livreddende å få tatt mammografi. Etter at mine venninner så at screeningen avdekket kreft, har flere av dem også tatt mammografi, sier hun.

– Kan svulsten din ha vært der i to år?

Nei, den var så aggressiv. Men hadde jeg ikke tatt mammografi gang nummer to hadde det nok gått galt.

Det er uenighet om screeningprogrammet, og kritikere mener at friske kvinner blir overbehandlet.

Solveig Hofvind avviser dette, og sier at friske kvinner ikke behandles.

– Det er kun kvinner som har fått påvist kreftceller ved nåleprøve (biopsi) som blir behandlet i Norge. I noen få tilfeller vil ikke svulsten utvikle seg slik at kvinnene dør av noen annet før kreftsykdommen tar livet av dem. Fordi vi ikke har nok kunnskap om hvilke svulster dette er, tilbys alle kvinner som har fått di-

Editorial

Controversies in mammography screening: let us not ignore science in this never-ending debate

Acta Radiologica 2011; **52**: 1061–1063.

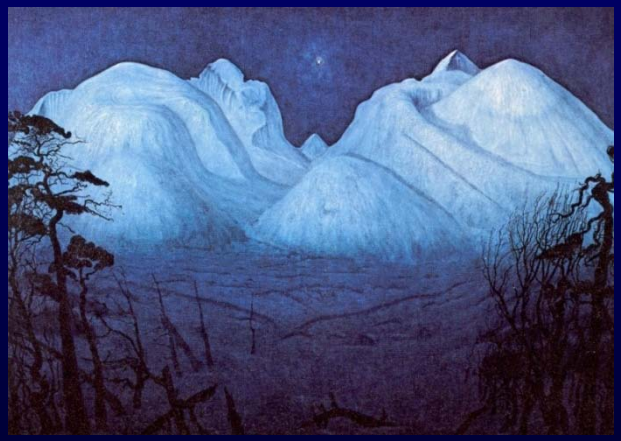
Per Skaane

Department of Radiology, Section Mammography, Oslo University Hospital, Ullevaal, University of Oslo, Norway
Email: PERSKA@ous-hf.no

of early detection of breast cancer. Opponents of screening from the Scandinavian countries have published studies against screening based on cancer registry information with several potential confounding bias, and further studies should critically investigate these results. Perhaps we should be happy about this ongoing discussion and never-ending debate since it will, without doubt, continuously improve our understanding of breast cancer screening to the benefit of the women. However, a most regrettable consequence of wrong damaging headlines in the newspapers is that many women may choose not to attend life-saving screening programs – or mammography at all.

Attendance rate in the Norwegian Breast Cancer Screening Program NBCSP: All counties 2005 - 2012

2005	2006	2007	2008	2009	2010	2011	2012
76%	77%	75%	75%	75%	74%	75%	75%



Harald Sohlberg (1869-1935):
Winter night in Rondane (Norway) (1914)

Vielen Dank fur Ihre Zeit und Aufmerksamkeit !

PERSKA@ous-hf.no