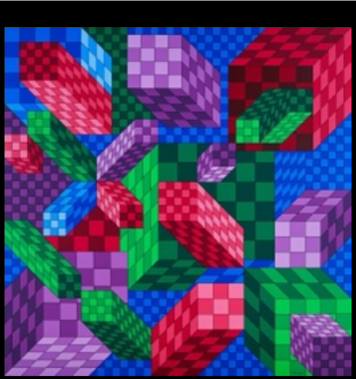
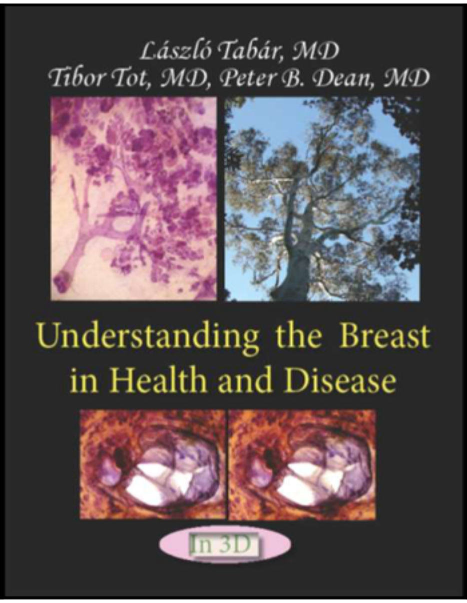
An accolade for Ms. Louise C. Miller's life-time achievement



Louise C. Miller, R.T.(R)(M)(ARRT), CRT(M), FSBI, FNCBC

László Tabár, MD, FACR (Hon)



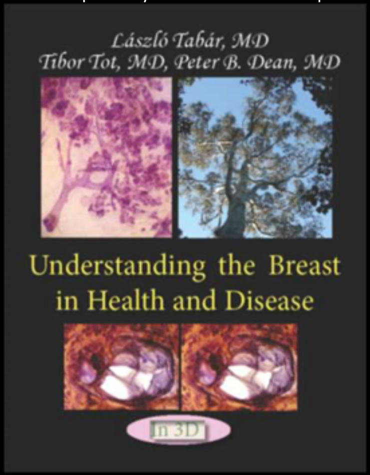
László Tabár, MD
Tibor Tot, MD, Peter B. Dean, MD

Understanding the Breast
in Health and Disease

In 3D

Narrated book: https://www.dropbox.com/scl/fi/fu6d9jl78mjaftewsxbns/PARTS-I-IV-MERGED.mp4.patched.mp4?rlkey=ohw509twformiz52pfh4enf0r&dl=0

ENGLISH



László Tabár, MD
Tibor Tot, MD, Peter B. Dean, MD

Understanding the Breast
in Health and Disease

In 3D

The book page by page: https://www.dropbox.com/scl/fi/alp5pxw3i0pvdxojsburq/Vol-I-High-qual-FINALx.pdf?rlkey=pj3pvif3ldn1pyc7gg2fxo0b1&dl=0

Narrated book in Spanish PARTs I – IV (see next slide)

Dr. László Tabár,
Dr. Tibor Tot, Dr. Peter B. Dean

Bases para entender la mama en
la salud y en la enfermedad

En 3D

The book in Spanish, page by page: https://www.dropbox.com/scl/fi/aldjrsa2tck2co16mymkf/Vol-I-SPANISH.pdf?rlkey=5jb44xbi9215nm8ucl5yvvxqg&dl=0

SPANISH

PART I

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PART II

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PART III

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PART IV

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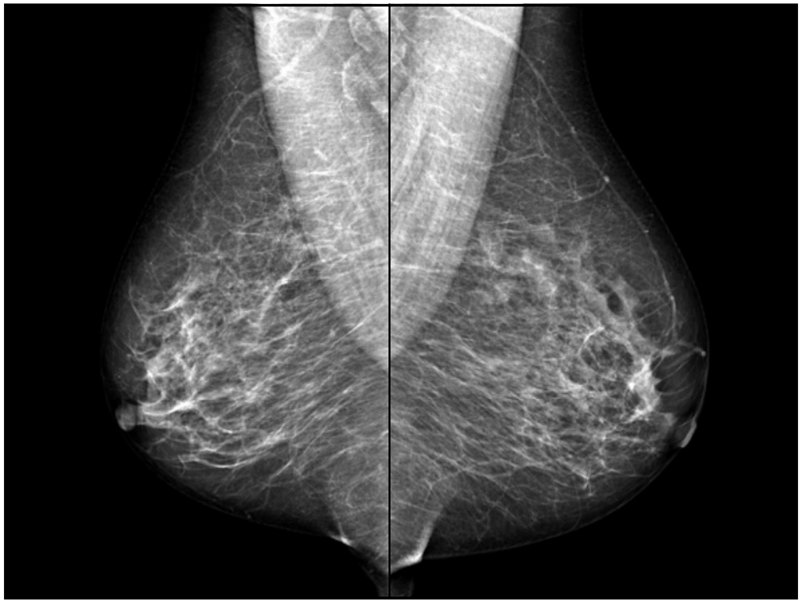
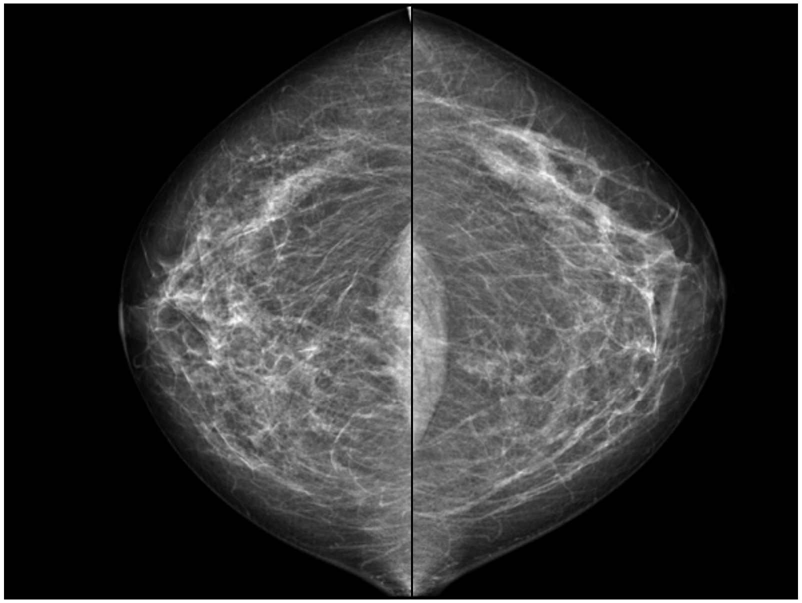
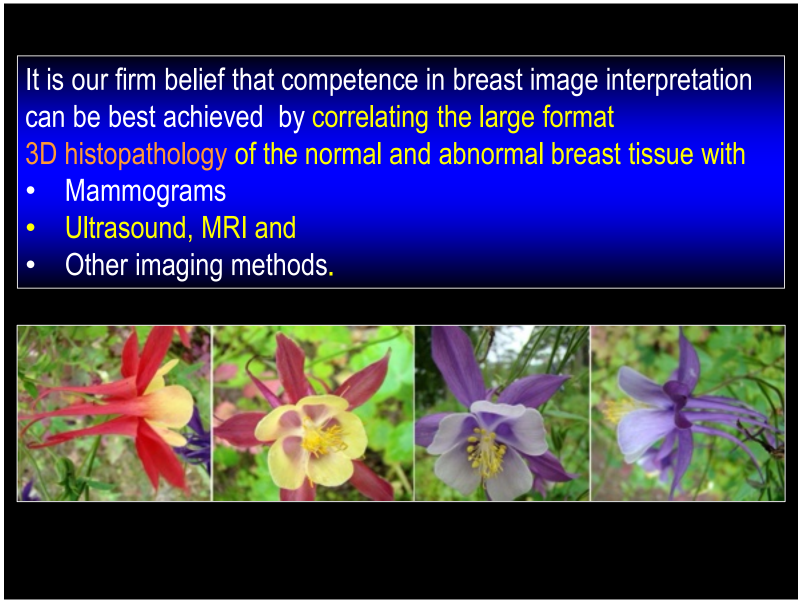
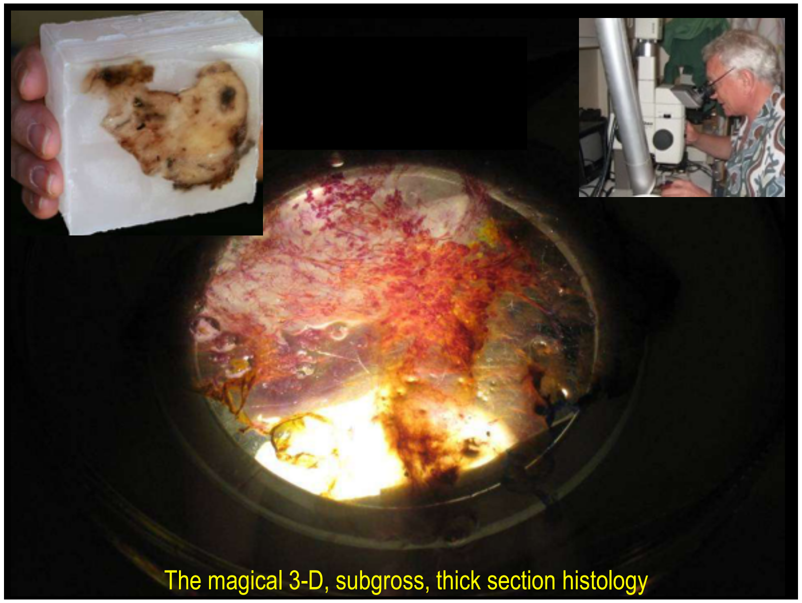




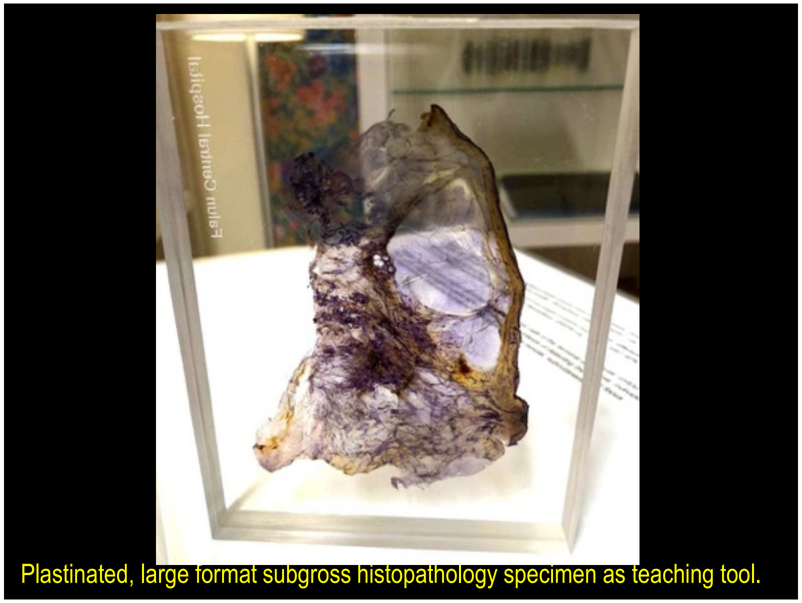


It is our firm belief that competence in breast image interpretation can be best achieved by correlating the large format 3D histopathology of the normal and abnormal breast tissue with

- Mammograms
- Ultrasound, MRI and
- Other imaging methods.



The magical 3-D, subgross, thick section histology



Plastinated, large format subgross histopathology specimen as teaching tool.

The magical 3-D, subgross, thick section histology

13

The magical 3-D, subgross, thick section histology

14

DAB fragmented casting
CASE 04
DAB fragmented casting
CASE 05 slice 01
3D book Vol III-VI
DAB fragmented casting
CASE 05 slice 02
3D book Vol III-VI
DAB fragmented casting
CASE 06

The magical 3-D, subgross, thick section histology

15

The magical 3-D, subgross, thick section histology

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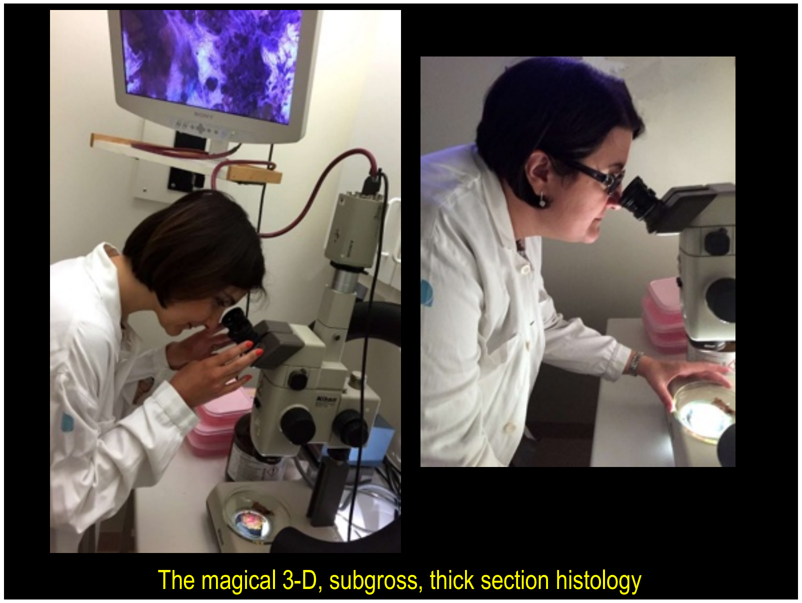


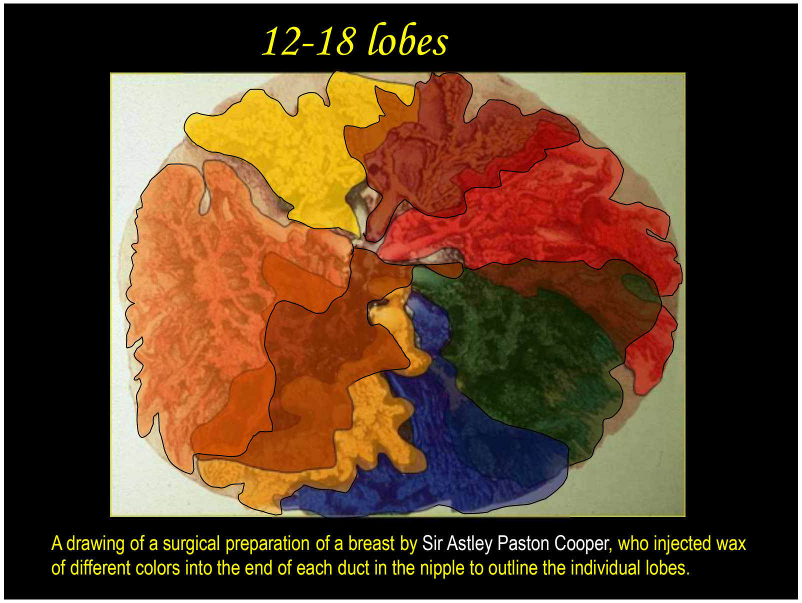
The magical 3-D, subgross, thick section histology

The magical 3-D, subgross, thick section histology

Progress in histologic-mammographic correlation can only be made by examining a histologic specimen of *greater length, width and depth.”*

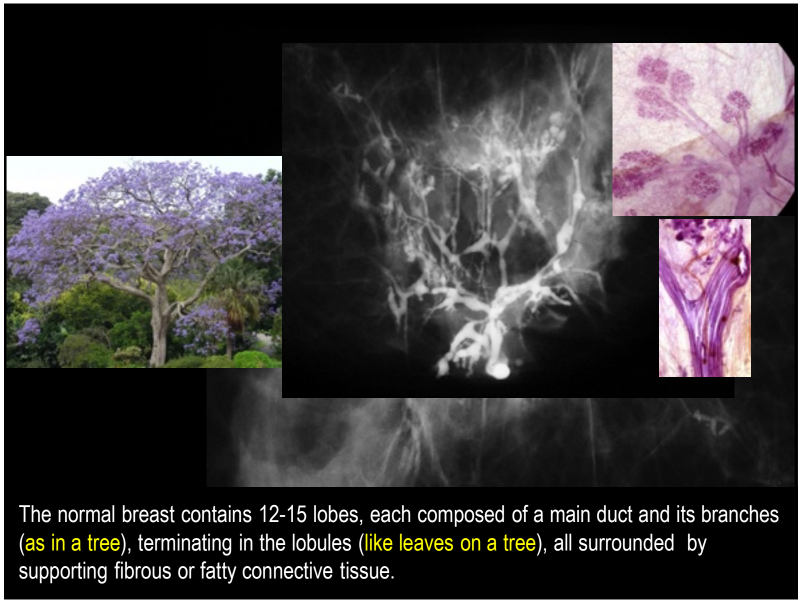
Tot, T, L. Tabar, P.B. Dean

Virchows Arch (2000) 437:338-344.

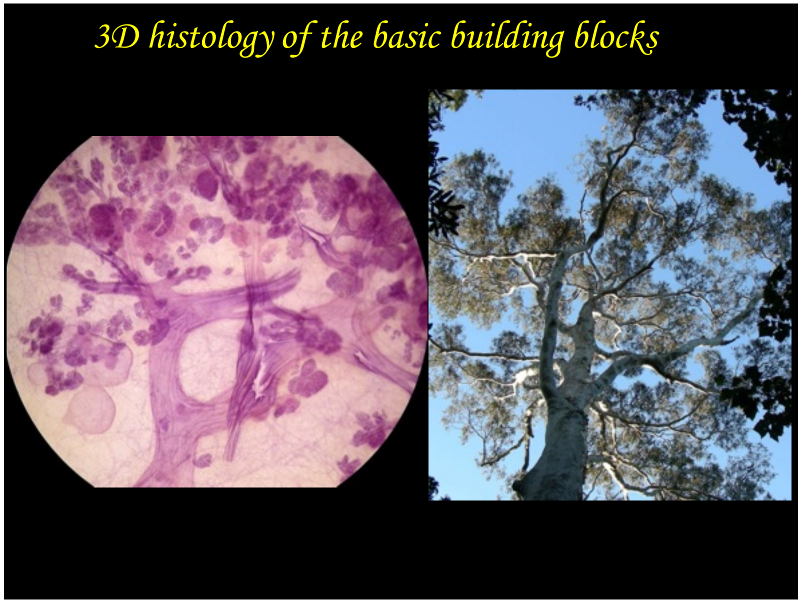


12-18 lobes

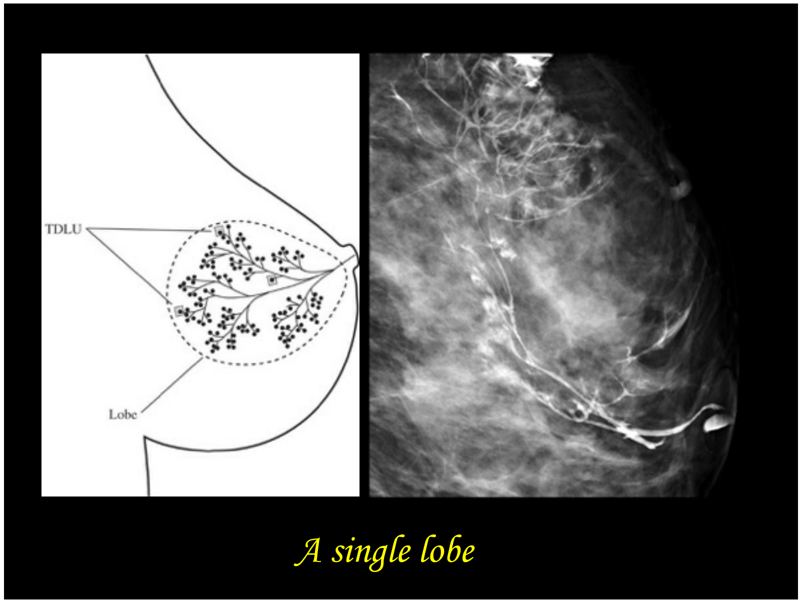
A drawing of a surgical preparation of a breast by Sir Astley Paston Cooper, who injected wax of different colors into the end of each duct in the nipple to outline the individual lobes.



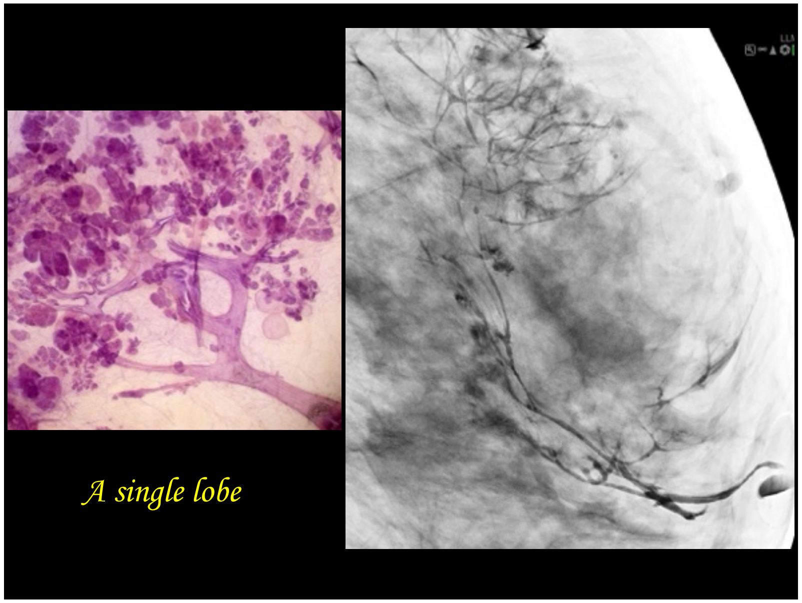
The normal breast contains 12-15 lobes, each composed of a main duct and its branches (as in a tree), terminating in the lobules (like leaves on a tree), all surrounded by supporting fibrous or fatty connective tissue.



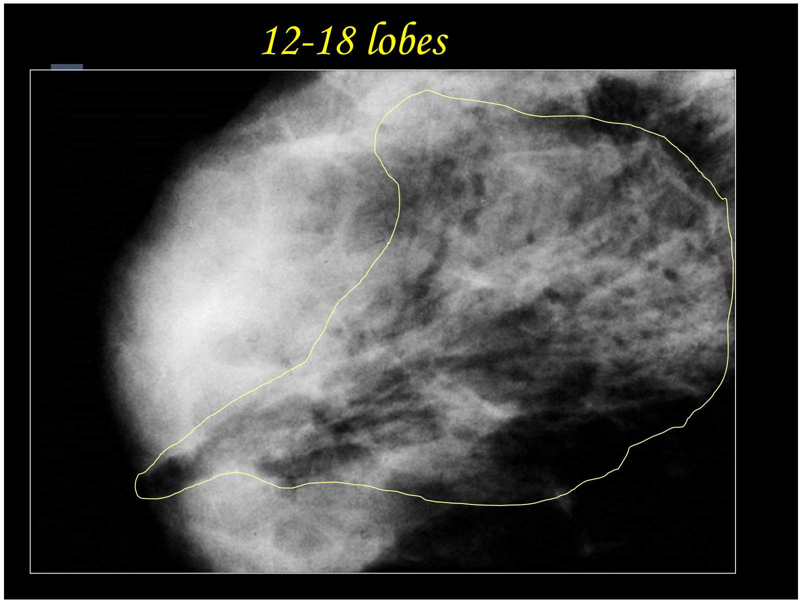
3D histology of the basic building blocks



A single lobe

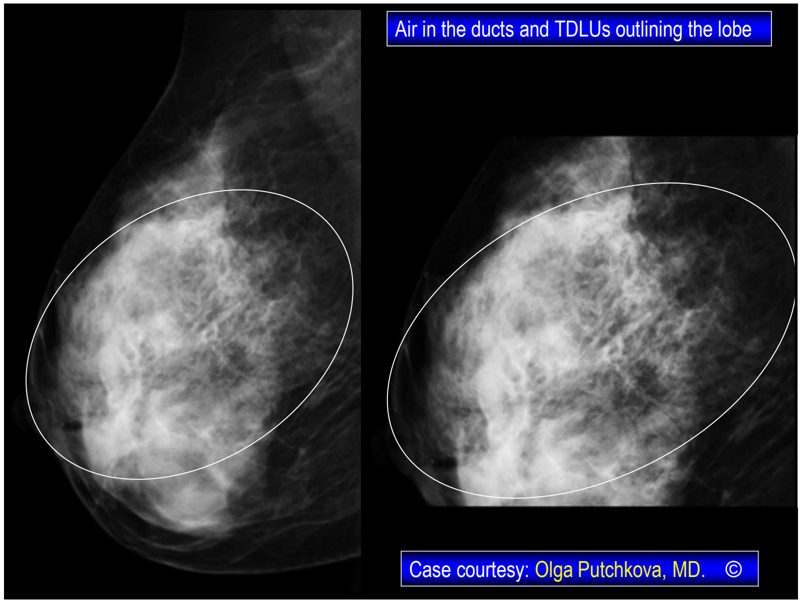


A single lobe



12-18 lobes

25



Air in the ducts and TDLUs outlining the lobe

Case courtesy: Olga Putchkova, MD. ©

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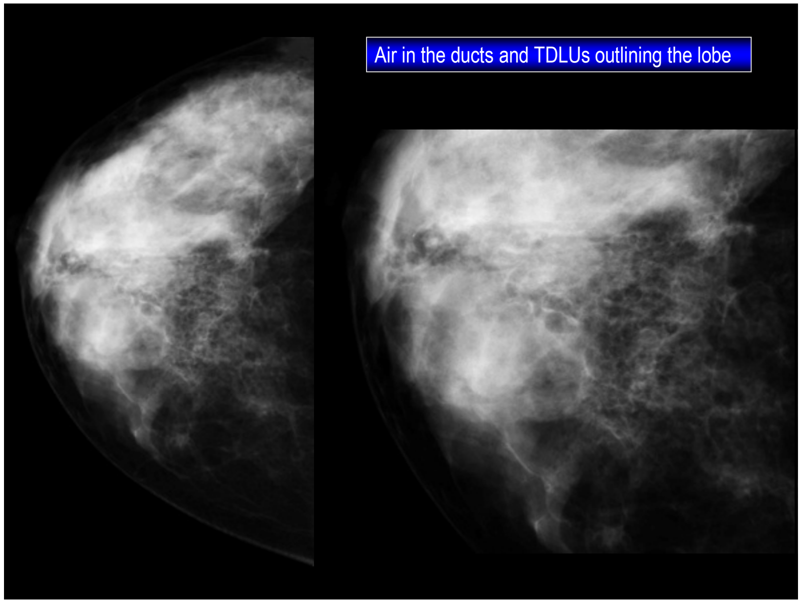
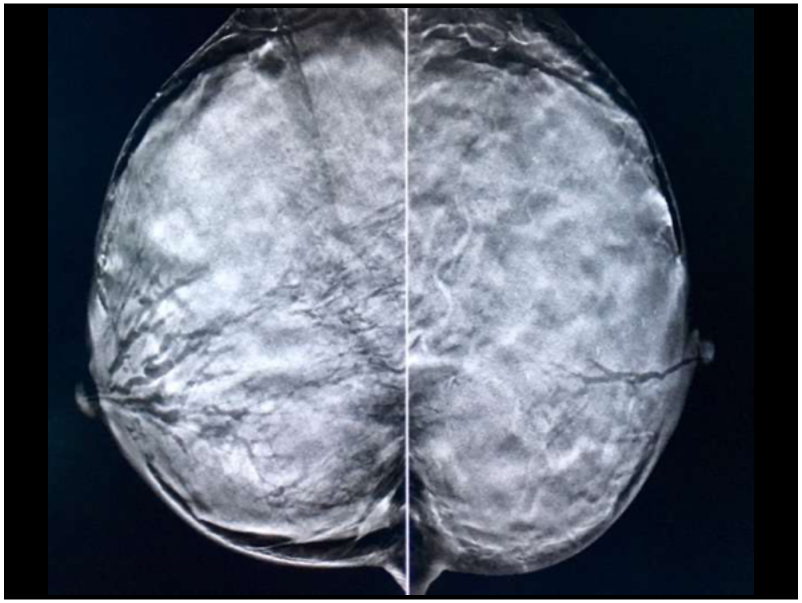


Air in the ducts and TDLUs outlining the lobe

27



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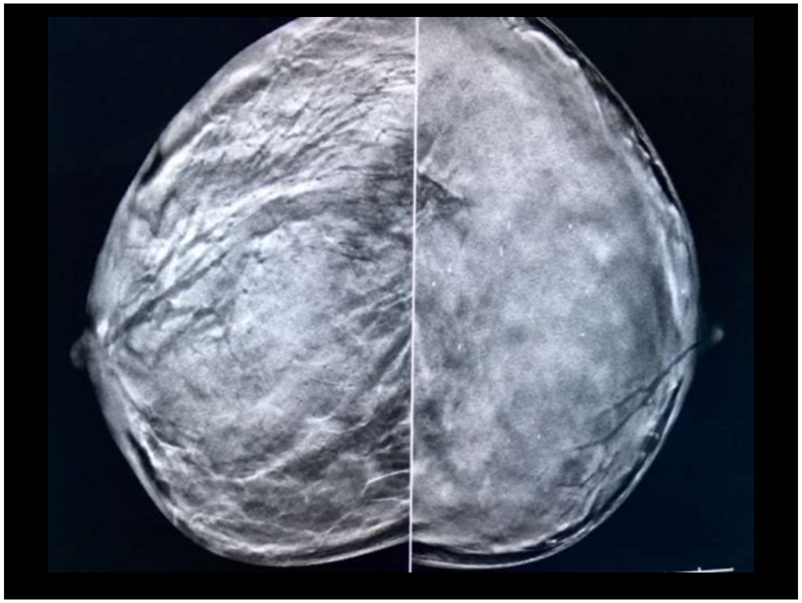

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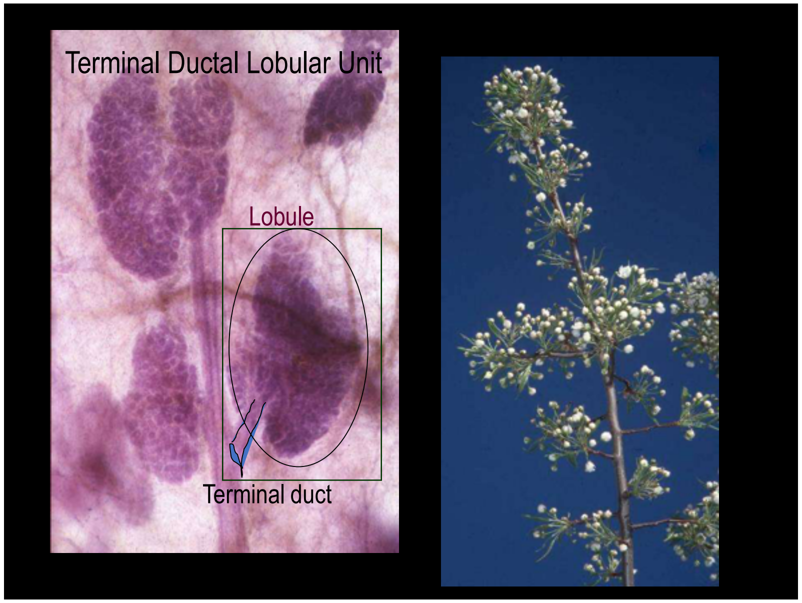
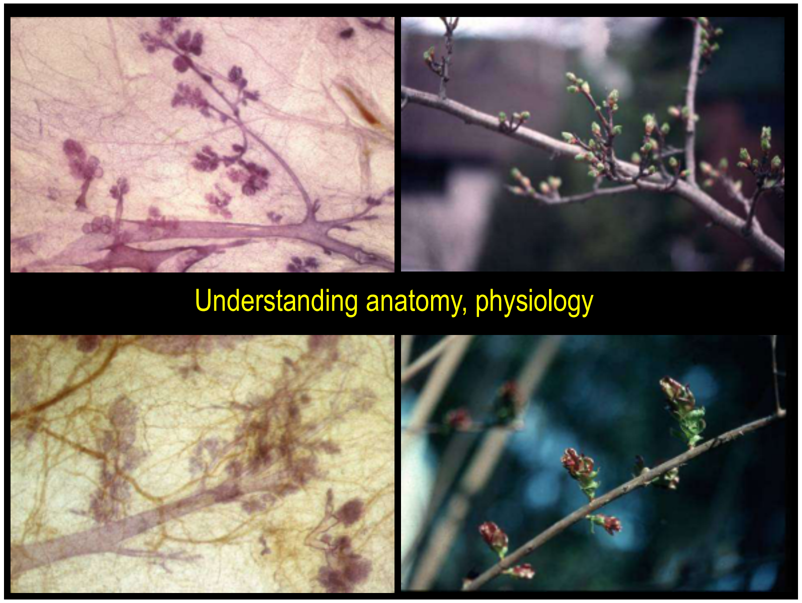


Terminal Ductal Lobular Unit

Lobule
Terminal duct

30



Understanding anatomy, physiology

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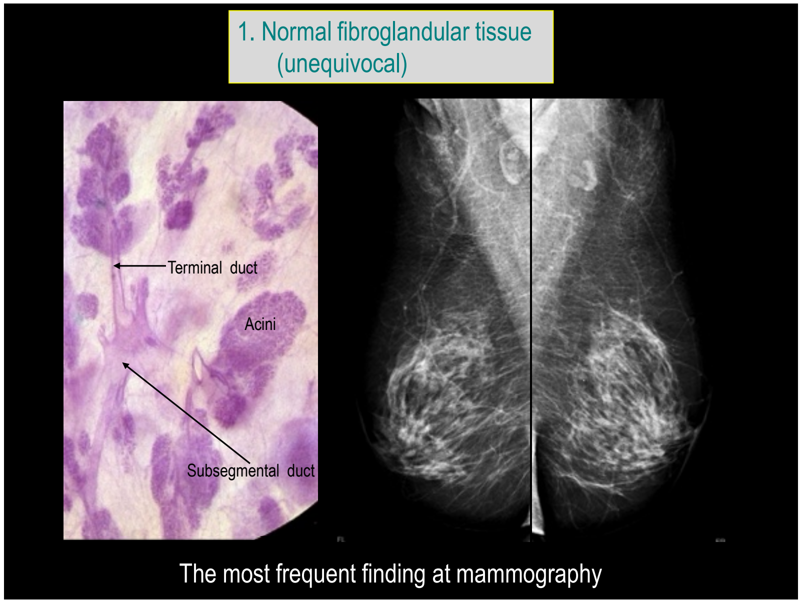
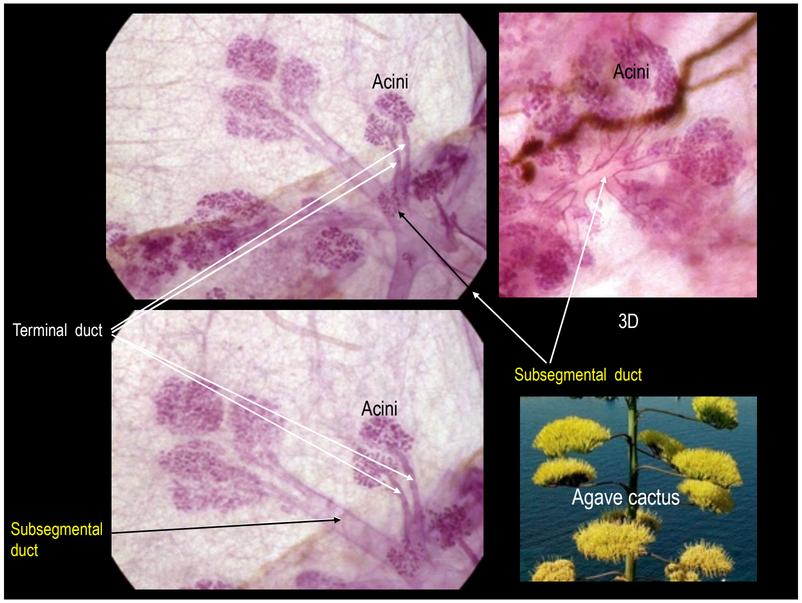


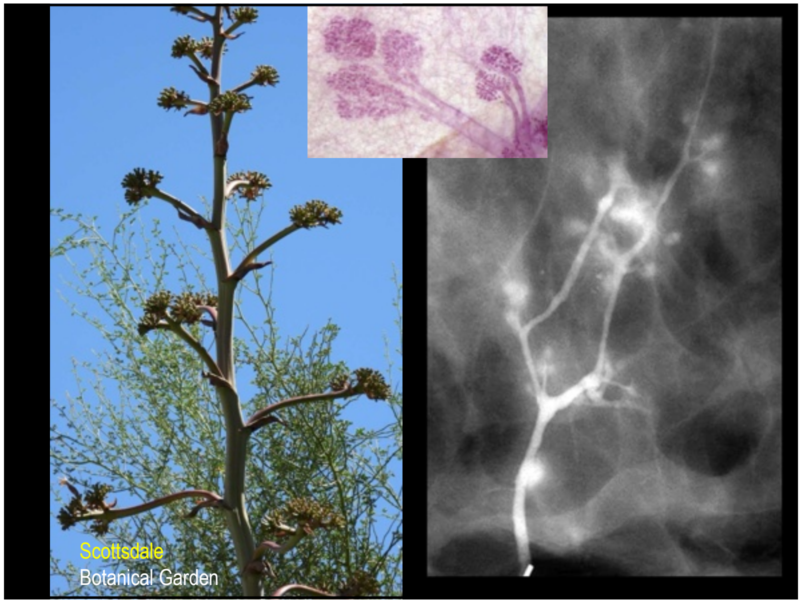
1. Normal fibroglandular tissue
(unequivocal)

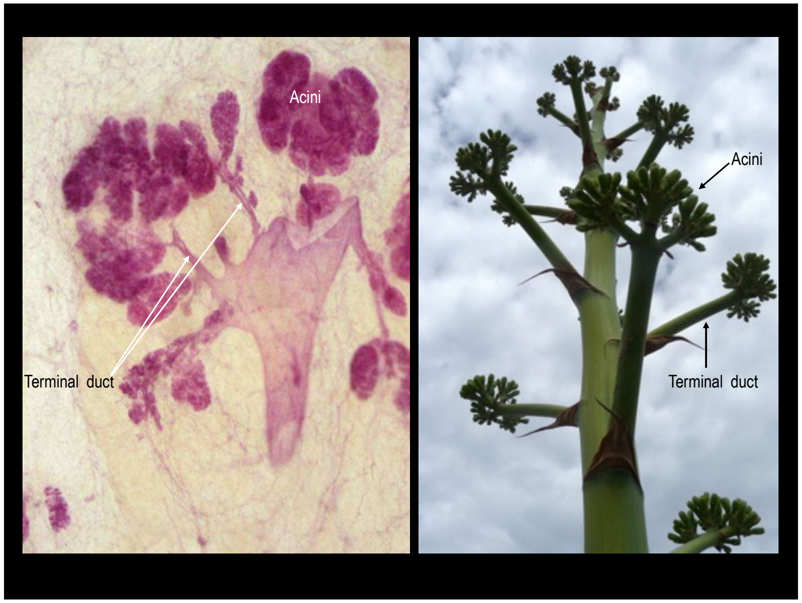
Terminal duct
Acini
Subsegmental duct

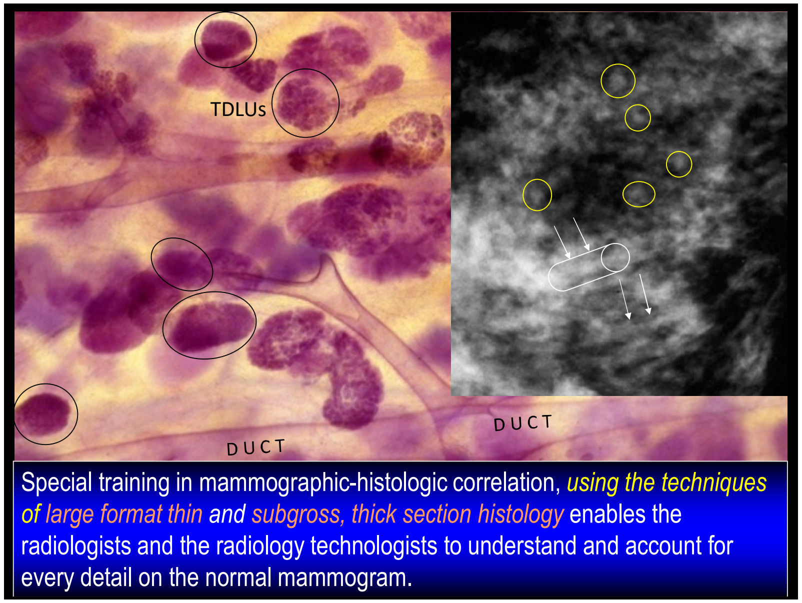
The most frequent finding at mammography

32

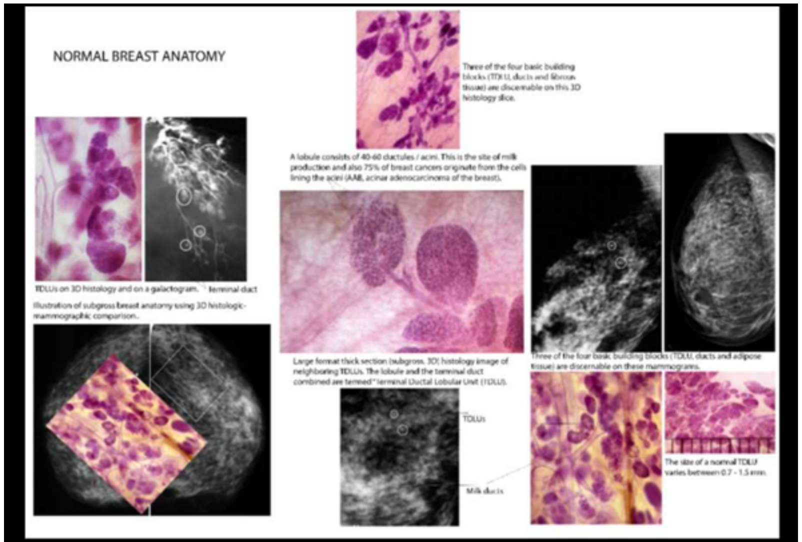

Acini
Acini
Terminal duct
3D
Subsegmental duct
Acini
Agave cactus
Subsegmental duct


Scottsdale
Botanical Garden


Acini
Acini
Terminal duct
Terminal duct


TDLUs
DUCT
DUCT

Special training in mammographic-histologic correlation, *using the techniques of large format thin* and *subgross, thick section histology* enables the radiologists and the radiology technologists to understand and account for every detail on the normal mammogram.



NORMAL BREAST ANATOMY

Three of the four basic building blocks (TDLU, ducts and fibrous tissue) are discernable on this 3D histology slice.

A lobule consists of 40-60 ductules / acini. This is the site of milk production and also 75% of breast cancers originate from the cells lining the acini (AAB, acinar adenocarcinoma of the breast).

TDLUs on 3D histology and on a galactogram. terminal duct

Illustration of subgross breast anatomy using 3D histologic-mammographic comparison..

Large format thick section (subgross, 3D) histology image of neighboring TDLUs. The lobule and the terminal duct combined are termed "Terminal Ductal Lobular Unit (TDLU).

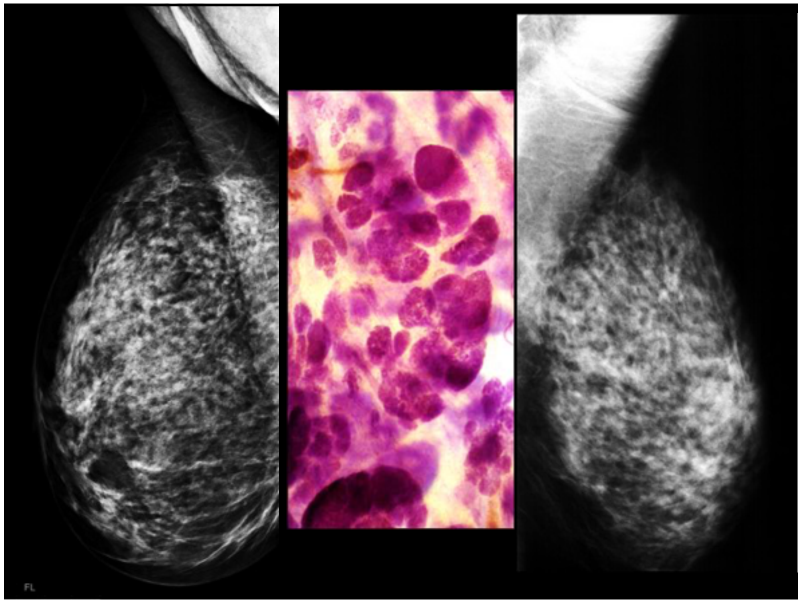
Three of the four basic building blocks (TDLU, ducts and adipose tissue) are discernable on these mammograms.

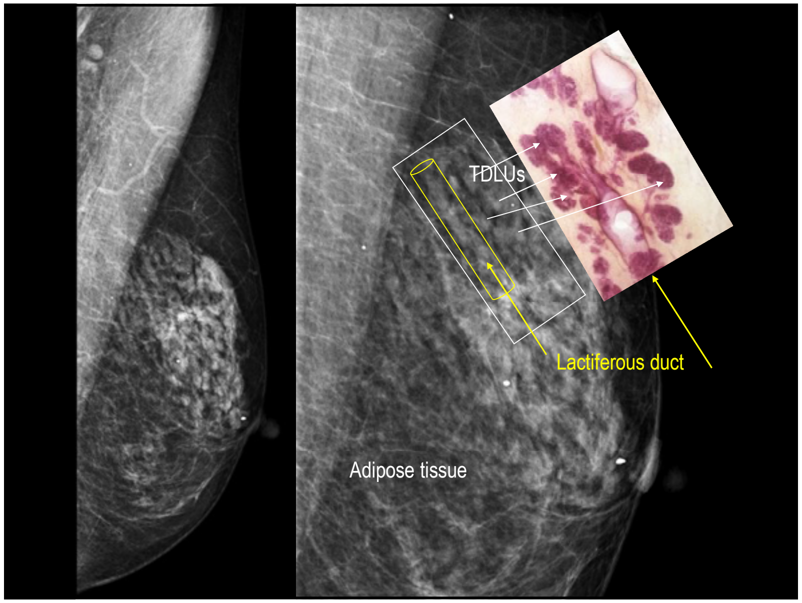
TDLUs

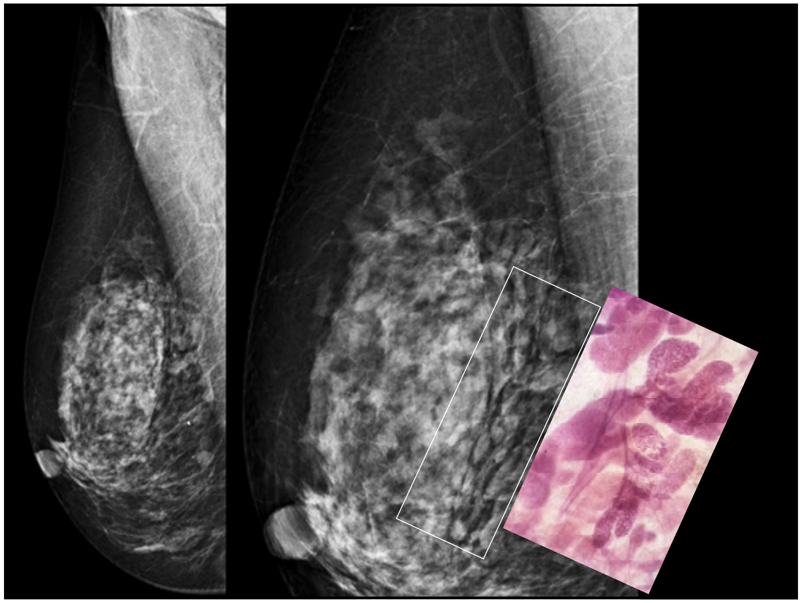
Milk ducts

The size of a normal TDLU varies between 0.7 - 1.5 mm.

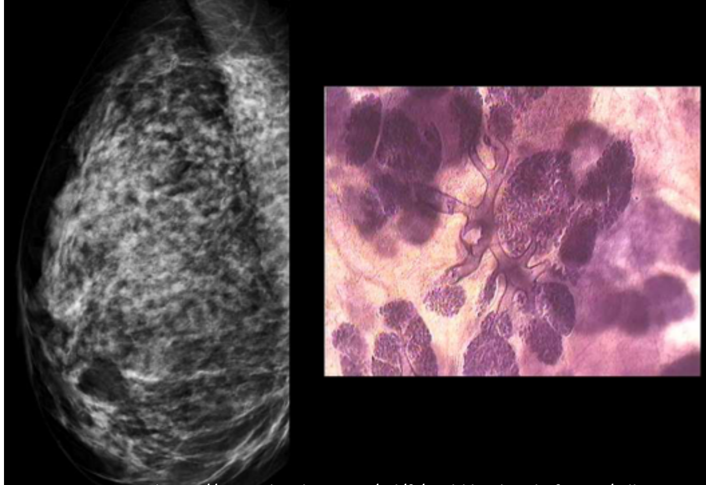
https://www.dropbox.com/scl/fi/kyh1wdjjwvby4wxitq1dn/Case-NORMAL.pdf?rlkey=81uirt1mm6zopqurifz96g353&dl=0







Histopathologic-mammographic correlation



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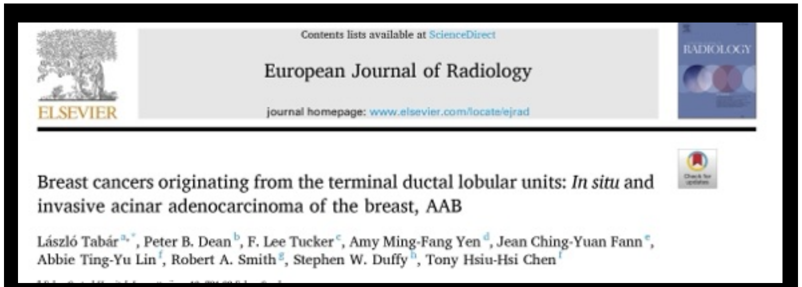

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ELSEVIER
RADIOLOGY

Breast cancers originating from the terminal ductal lobular units: *In situ* and invasive acinar adenocarcinoma of the breast, AAB

László Tabár[a,*], Peter B. Dean[b], F. Lee Tucker[c], Amy Ming-Fang Yen[d], Jean Ching-Yuan Fann[e], Abbie Ting-Yu Lin[f], Robert A. Smith[g], Stephen W. Duffy[h], Tony Hsiu-Hsi Chen[f]

https://www.dropbox.com/scl/fi/epzhqavxd1syjvsjnnnkm/Article-2.pdf?rlkey=xmb5c2iw0mvgsa1he1zgt0brd&dl=0

AI generated video of the article above:

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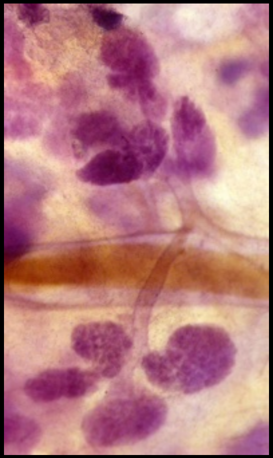
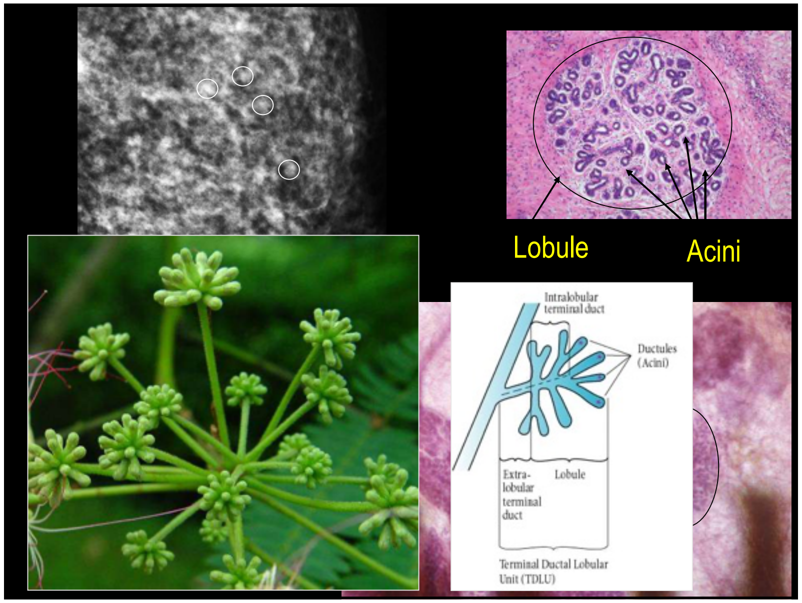


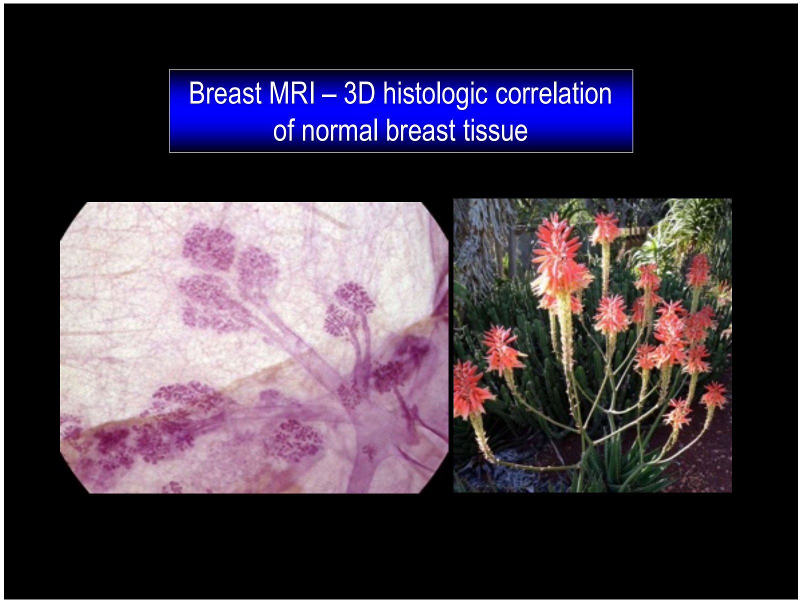
The lobule and the terminal duct, which drains it, form an integrated functional entity, called the

terminal ductal lobular unit (TDLU)

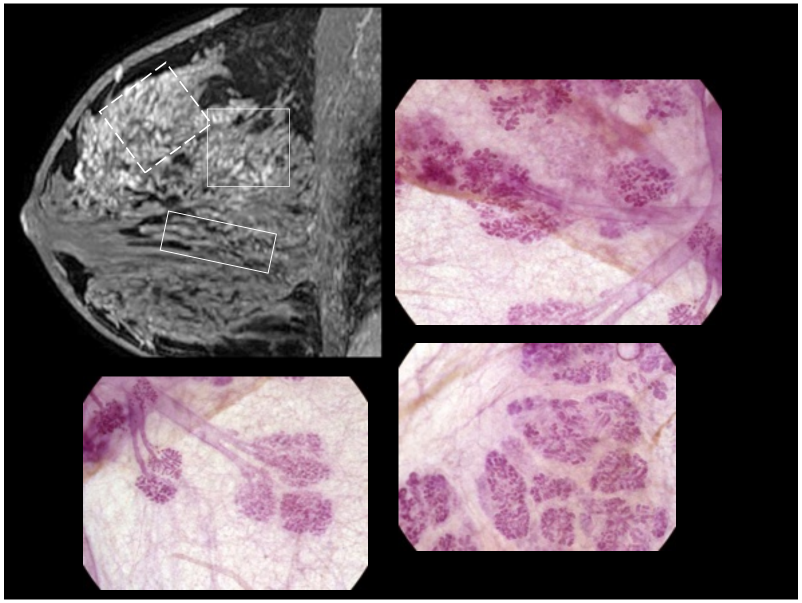
Most benign and malignant breast diseases originate from the TDLU, not from the ducts.

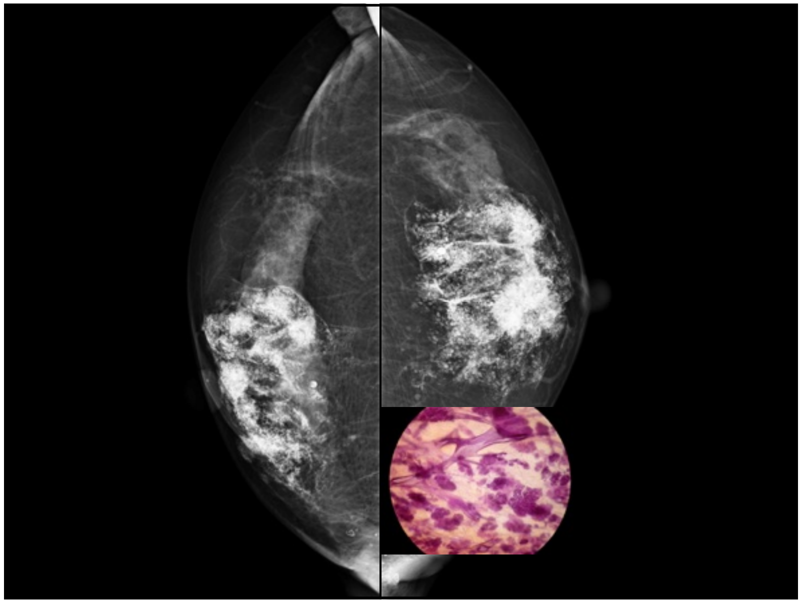


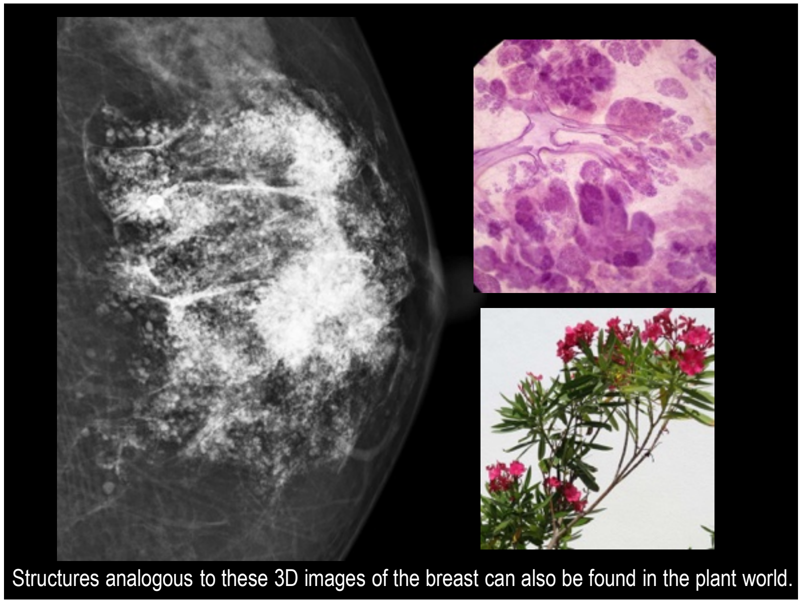
Lobule
Acini
Intralobular terminal duct
Ductules (Acini)
Extra-lobular terminal duct
Lobule
Terminal Ductal Lobular Unit (TDLU)



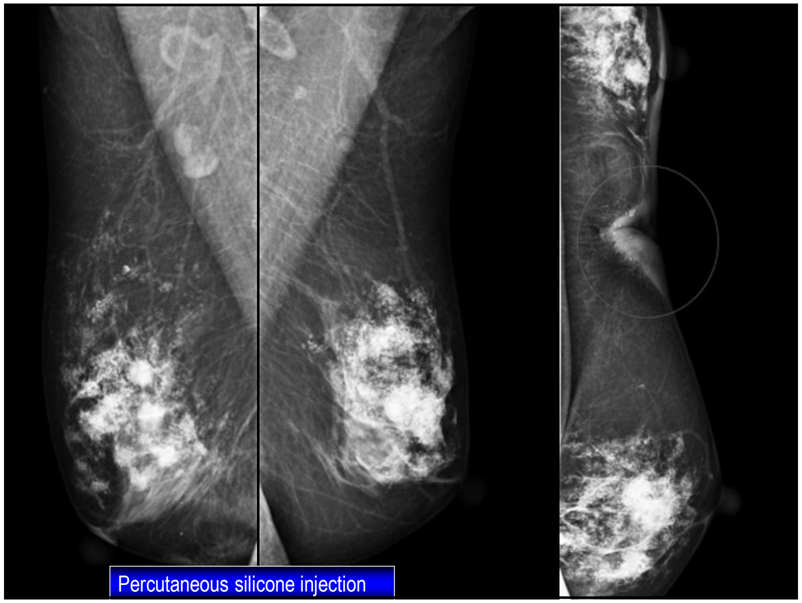
Breast MRI – 3D histologic correlation of normal breast tissue



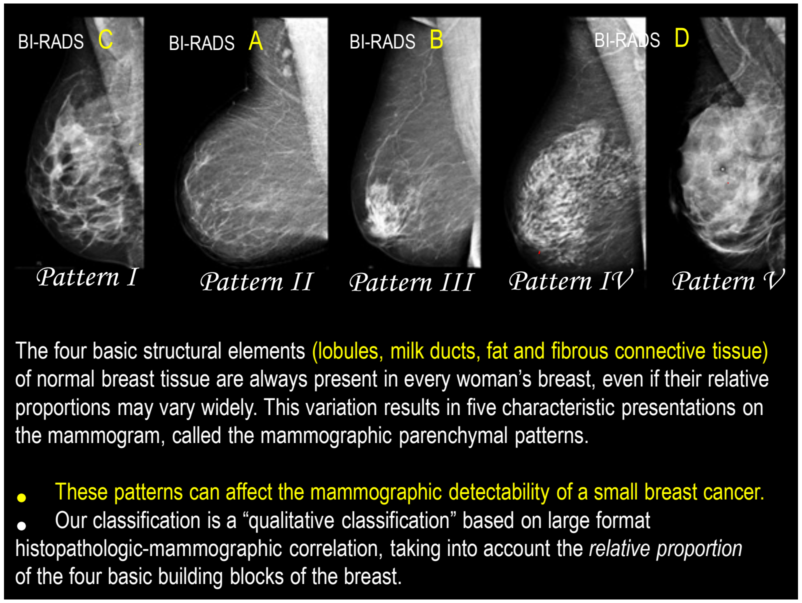




Structures analogous to these 3D images of the breast can also be found in the plant world.



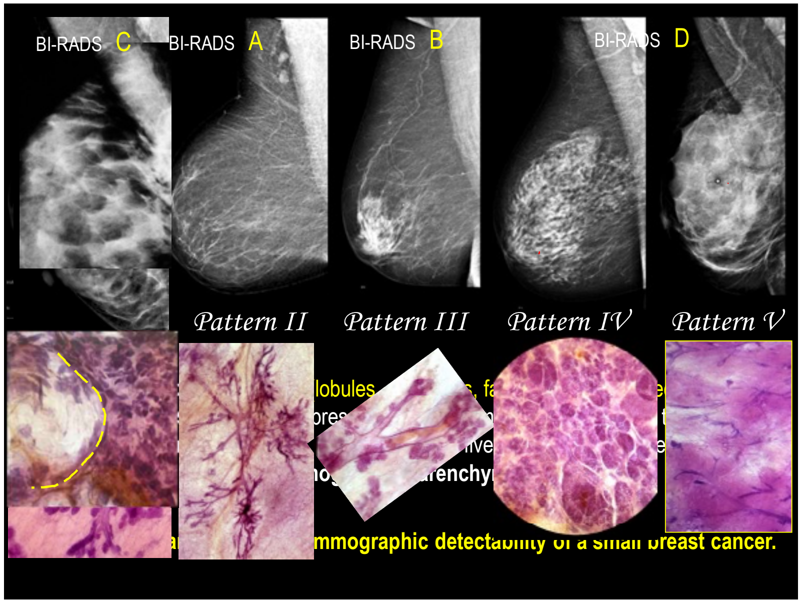
Percutaneous silicone injection



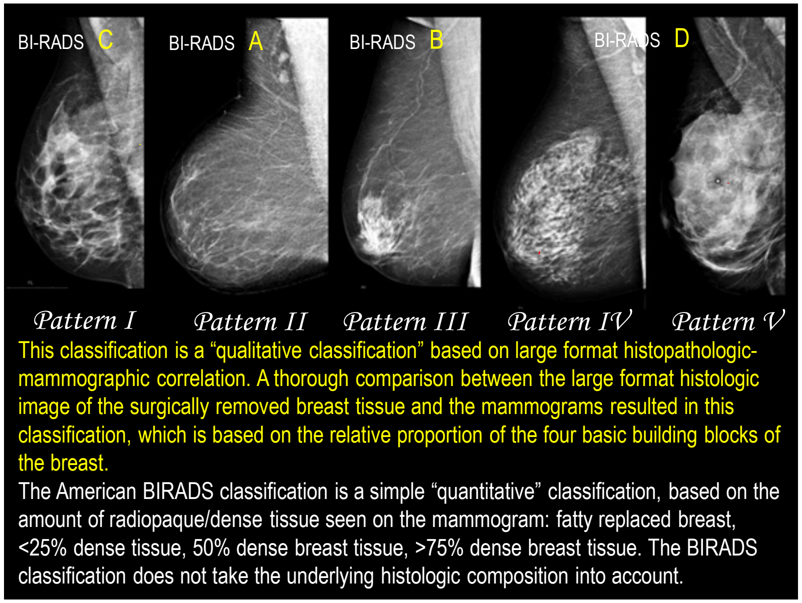
BI-RADS C
BI-RADS A
BI-RADS B
BI-RADS D
Pattern I
Pattern II
Pattern III
Pattern IV
Pattern V

The four basic structural elements (lobules, milk ducts, fat and fibrous connective tissue) of normal breast tissue are always present in every woman's breast, even if their relative proportions may vary widely. This variation results in five characteristic presentations on the mammogram, called the mammographic parenchymal patterns.

- These patterns can affect the mammographic detectability of a small breast cancer.
- Our classification is a "qualitative classification" based on large format histopathologic-mammographic correlation, taking into account the *relative proportion* of the four basic building blocks of the breast.



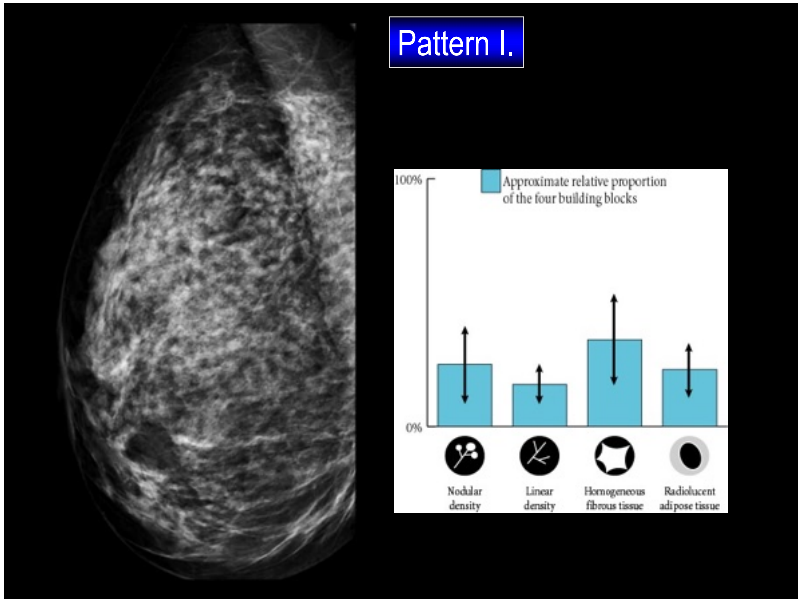
BI-RADS C
BI-RADS A
BI-RADS B
BI-RADS D
Pattern II
Pattern III
Pattern IV
Pattern V
lobules
pres
ive
renchy
mmographic detectability of a small breast cancer.



BI-RADS C
BI-RADS A
BI-RADS B
BI-RADS D
Pattern I
Pattern II
Pattern III
Pattern IV
Pattern V

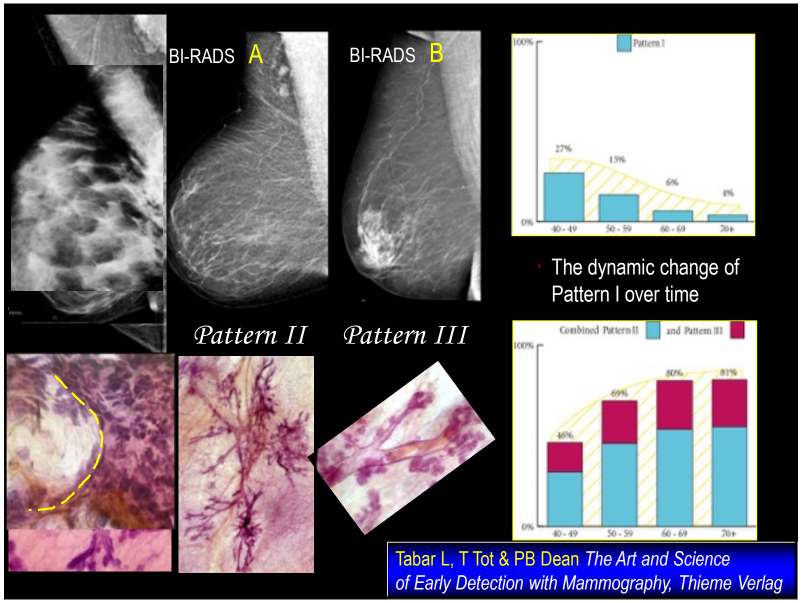
This classification is a "qualitative classification" based on large format histopathologic-mammographic correlation. A thorough comparison between the large format histologic image of the surgically removed breast tissue and the mammograms resulted in this classification, which is based on the relative proportion of the four basic building blocks of the breast.

The American BIRADS classification is a simple "quantitative" classification, based on the amount of radiopaque/dense tissue seen on the mammogram: fatty replaced breast, <25% dense tissue, 50% dense breast tissue, >75% dense breast tissue. The BIRADS classification does not take the underlying histologic composition into account.



Pattern I.

100%
Approximate relative proportion of the four building blocks
0%
Nodular density
Linear density
Homogeneous fibrous tissue
Radiolucent adipose tissue



BI-RADS A

BI-RADS B

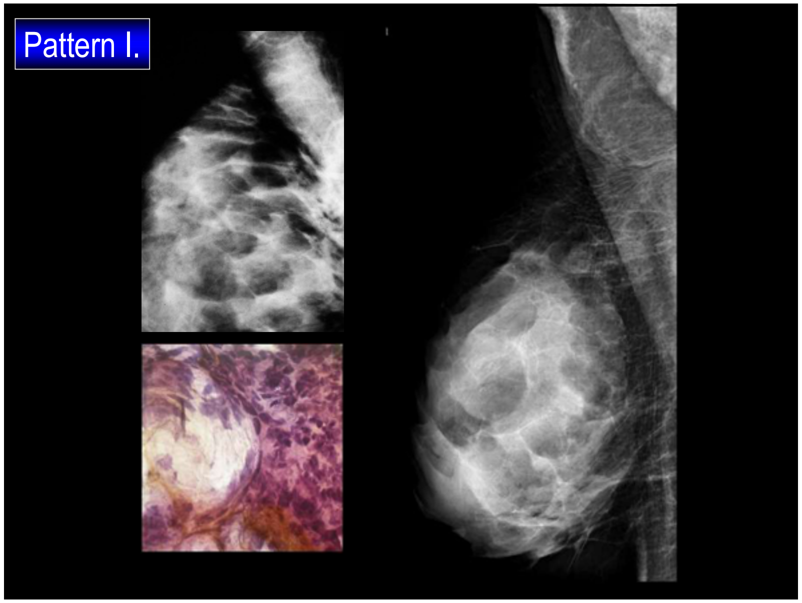
Pattern II

Pattern III

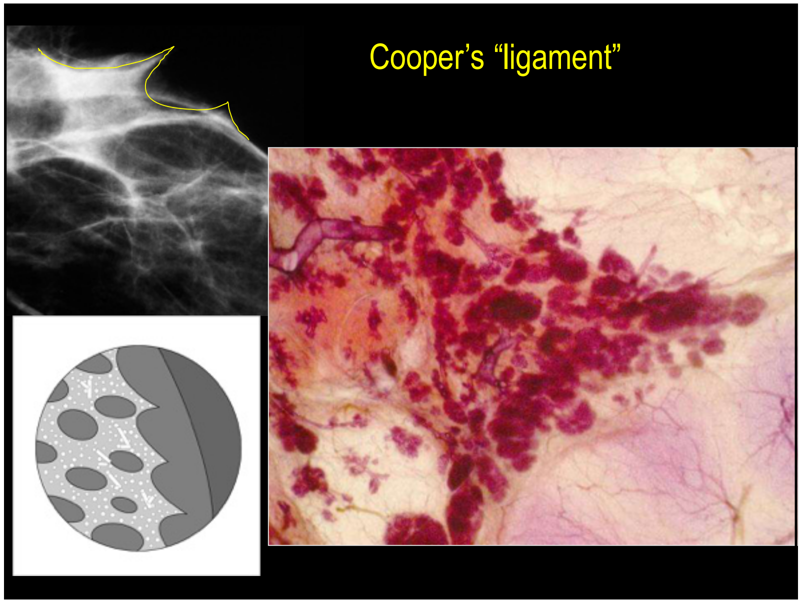
The dynamic change of Pattern I over time

100%
Pattern I
27%
15%
6%
4%
0%
40 - 49
50 - 59
60 - 69
70+
Combined Pattern II
and Pattern III
100%
46%
69%
80%
81%
0%
40 - 49
50 - 59
60 - 69
70+

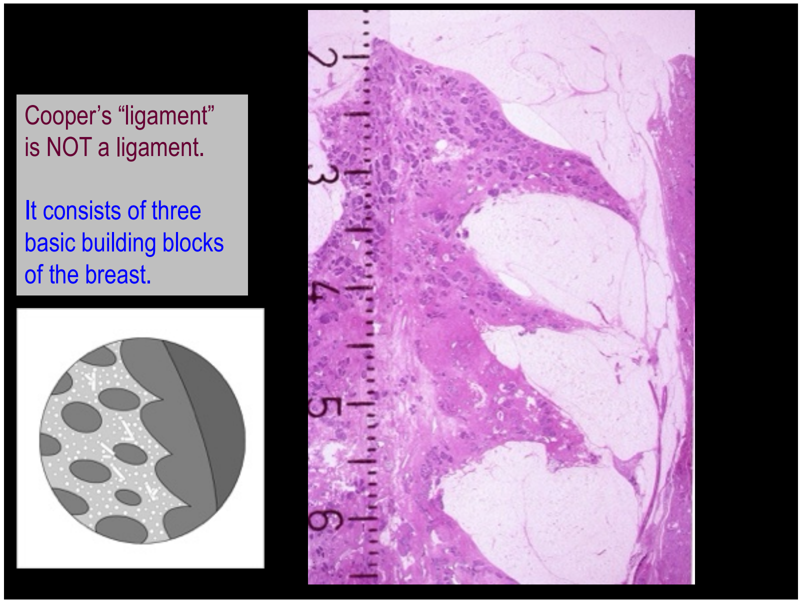
Tabar L, T Tot & PB Dean *The Art and Science of Early Detection with Mammography, Thieme Verlag*



Pattern I.

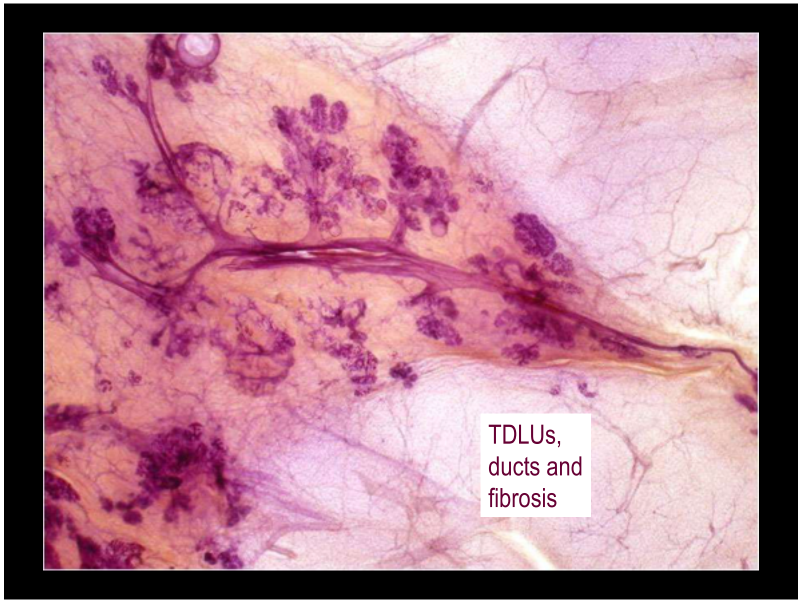


Cooper’s “ligament”

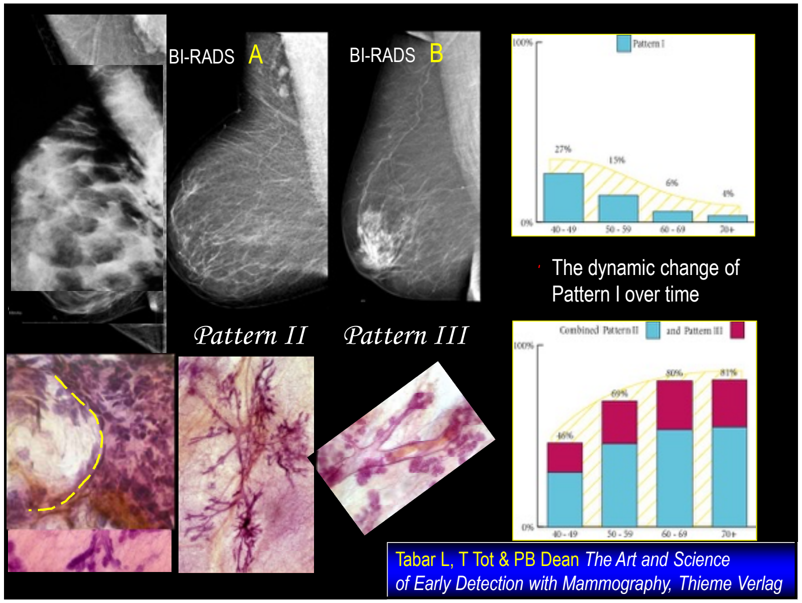


Cooper's "ligament" is NOT a ligament.

It consists of three basic building blocks of the breast.

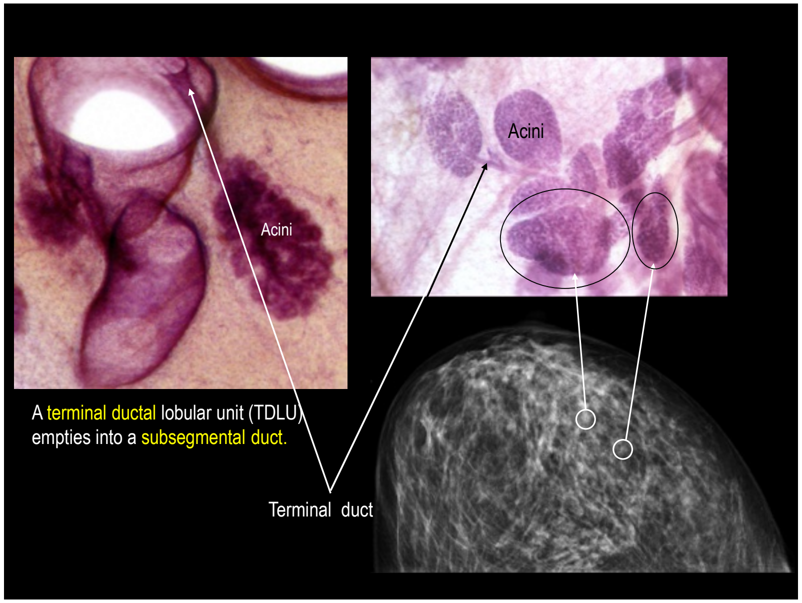


TDLUs, ducts and fibrosis

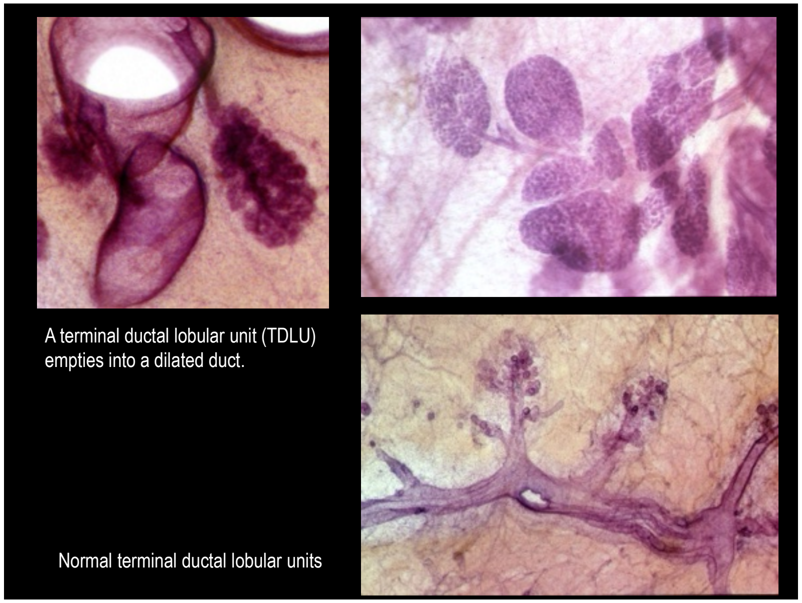

BI-RADS A
BI-RADS B
Pattern II
Pattern III
100%
Pattern I
27%
15%
6%
4%
0%
40 - 49
50 - 59
60 - 69
70+
Combined Pattern II
and Pattern III
100%
46%
69%
80%
81%
0%
40 - 49
50 - 59
60 - 69
70+

- The dynamic change of Pattern I over time

Tabar L, T Tot & PB Dean *The Art and Science of Early Detection with Mammography, Thieme Verlag*


Acini
Acini
Terminal duct

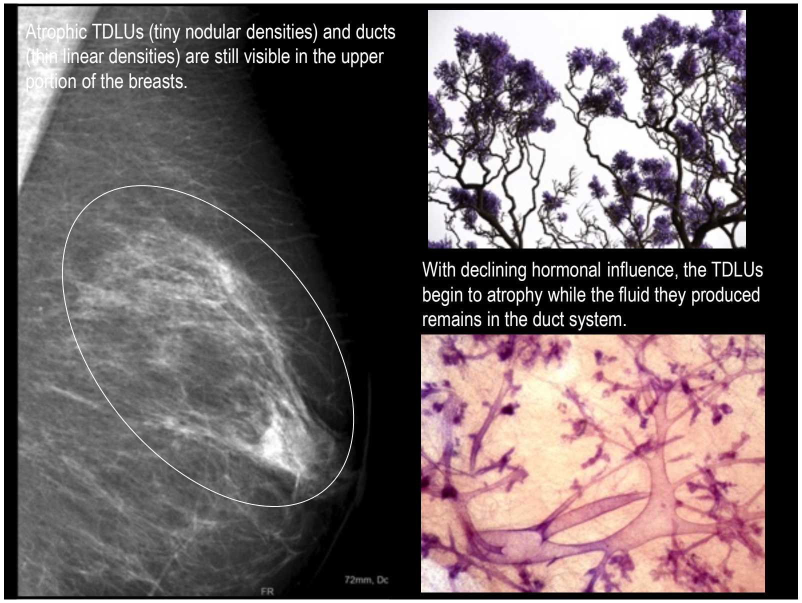
A terminal ductal lobular unit (TDLU) empties into a subsegmental duct.



A terminal ductal lobular unit (TDLU) empties into a dilated duct.

Normal terminal ductal lobular units

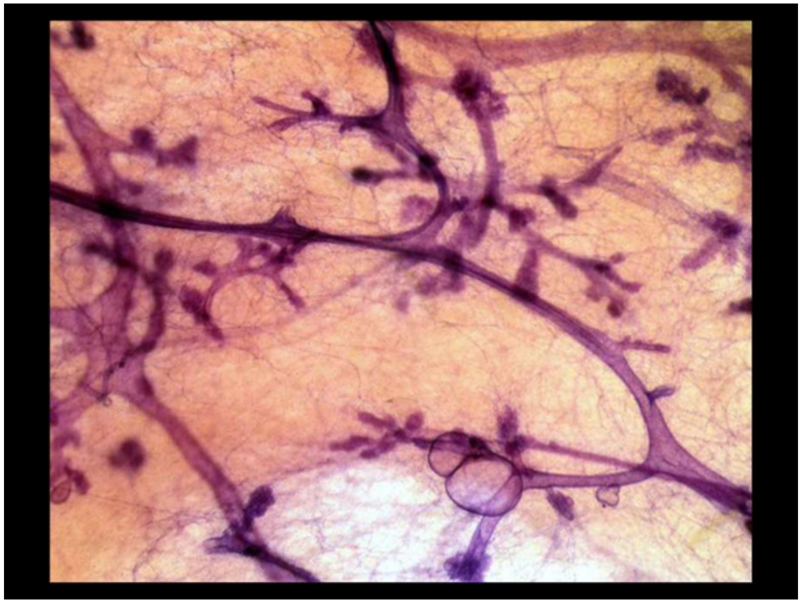
61



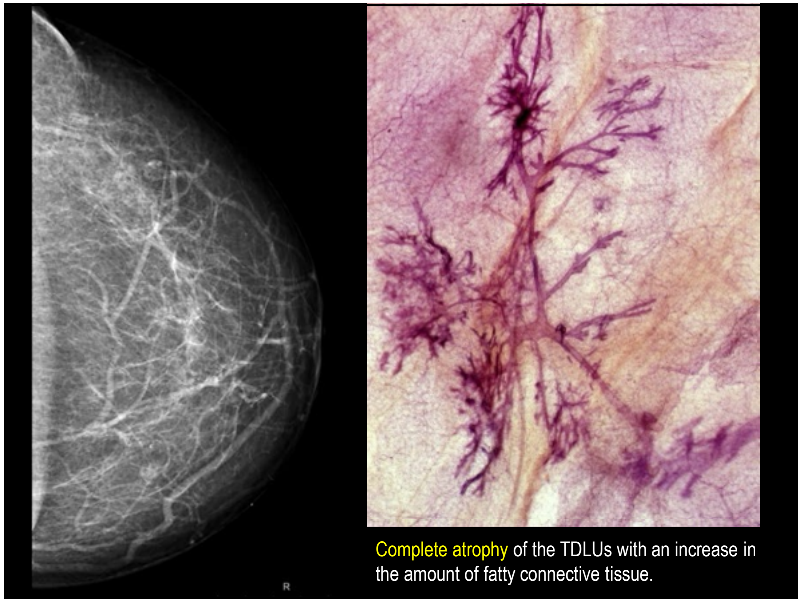
Atrophic TDLUs (tiny nodular densities) and ducts (thin linear densities) are still visible in the upper portion of the breasts.

With declining hormonal influence, the TDLUs begin to atrophy while the fluid they produced remains in the duct system.

62

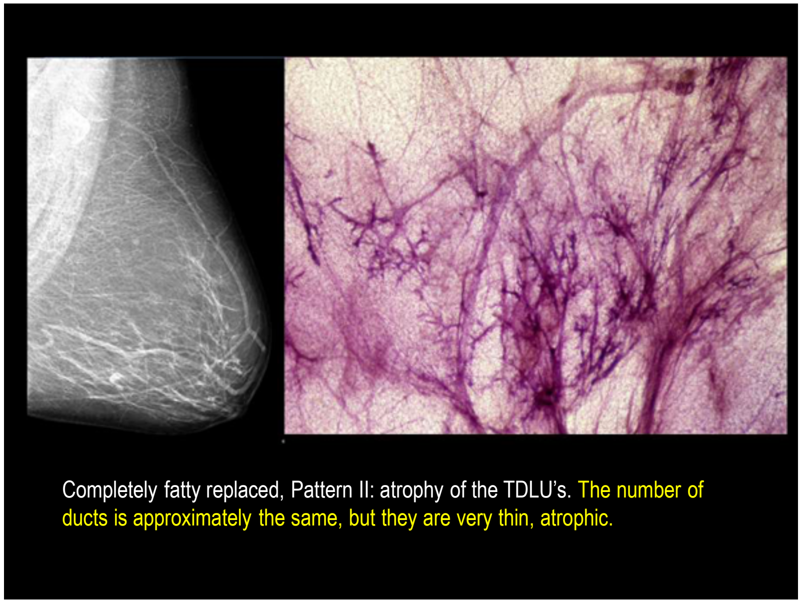


63

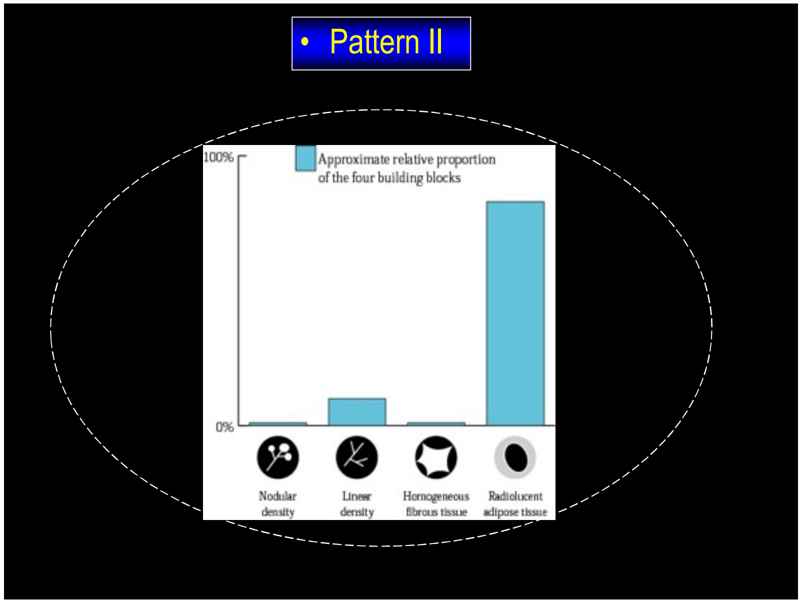


Complete atrophy of the TDLUs with an increase in the amount of fatty connective tissue.

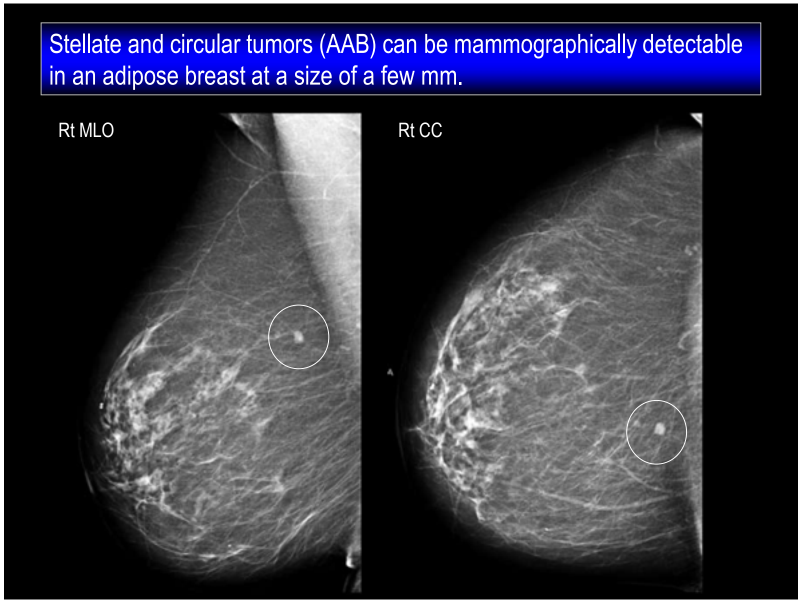
64



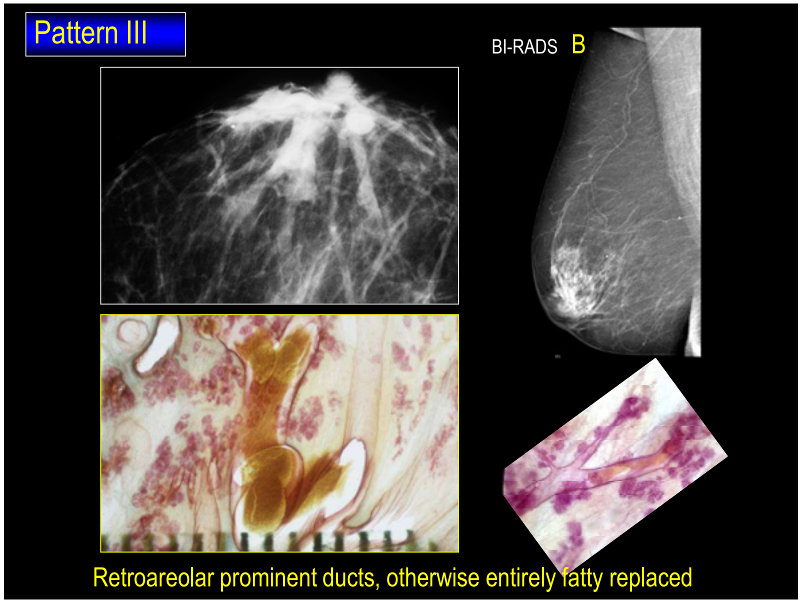
Completely fatty replaced, Pattern II: atrophy of the TDLU's. The number of ducts is approximately the same, but they are very thin, atrophic.



- Pattern II

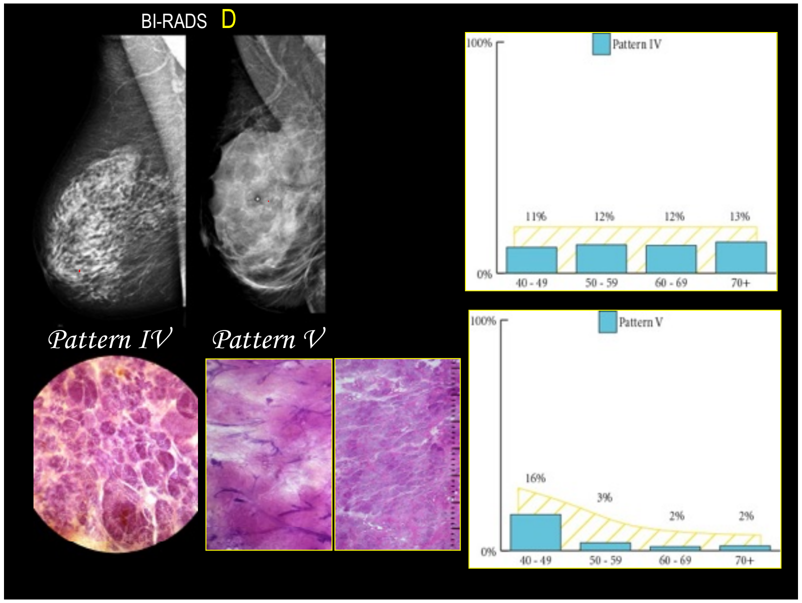


Stellate and circular tumors (AAB) can be mammographically detectable in an adipose breast at a size of a few mm.

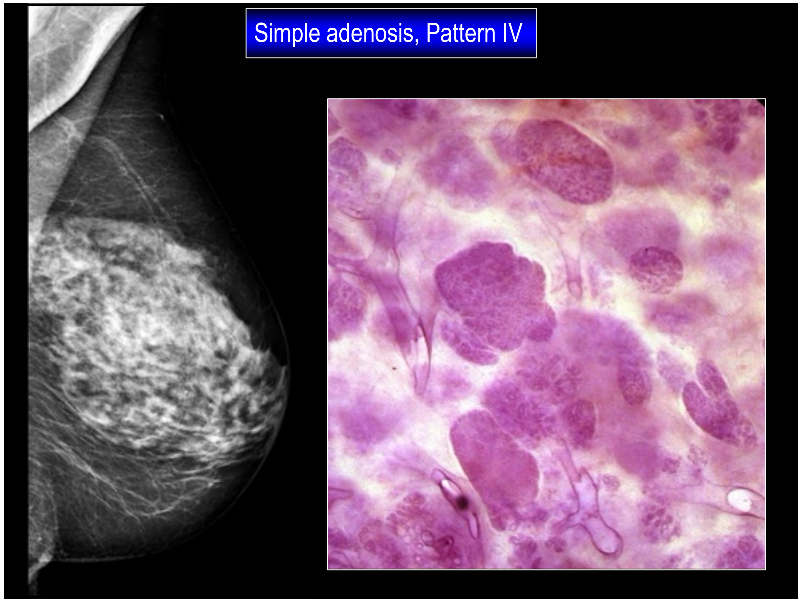


Pattern III

Retroareolar prominent ducts, otherwise entirely fatty replaced

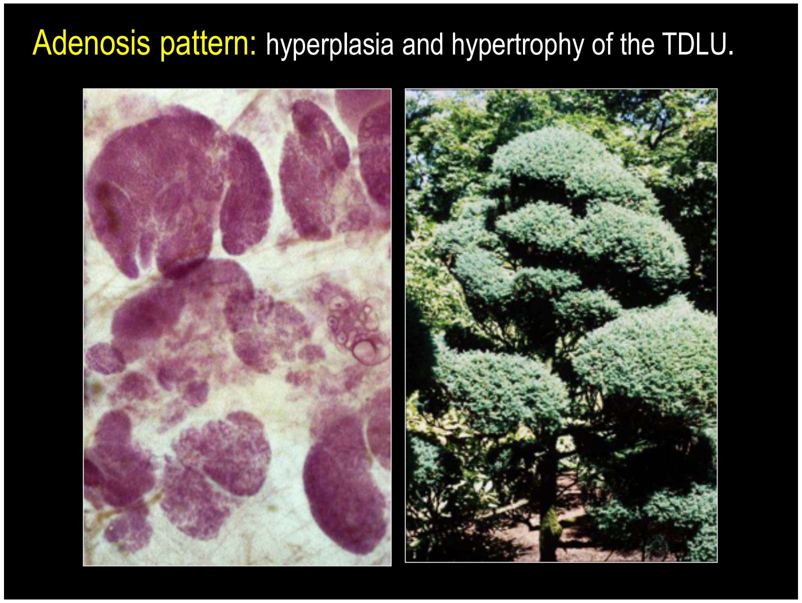

BI-RADS D
Pattern IV
Pattern V
Pattern IV
100%
0%
11%
12%
12%
13%
40 - 49
50 - 59
60 - 69
70+
Pattern V
100%
0%
16%
3%
2%
2%
40 - 49
50 - 59
60 - 69
70+

69



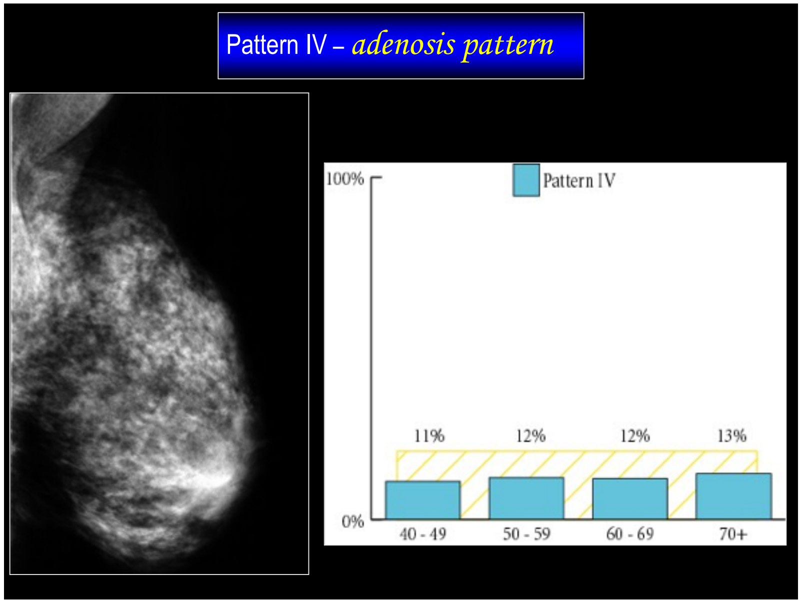
Simple adenosis, Pattern IV

70



Adenosis pattern: hyperplasia and hypertrophy of the TDLU.

71



Pattern IV – *adenosis pattern*

Pattern IV
100%
0%
11%
12%
12%
13%
40 - 49
50 - 59
60 - 69
70+

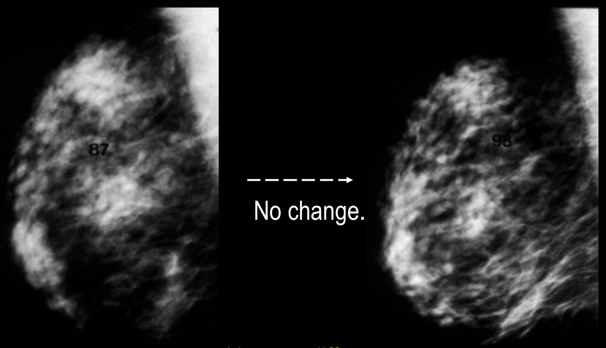
72

Pattern IV does not change over time

Pattern IV.

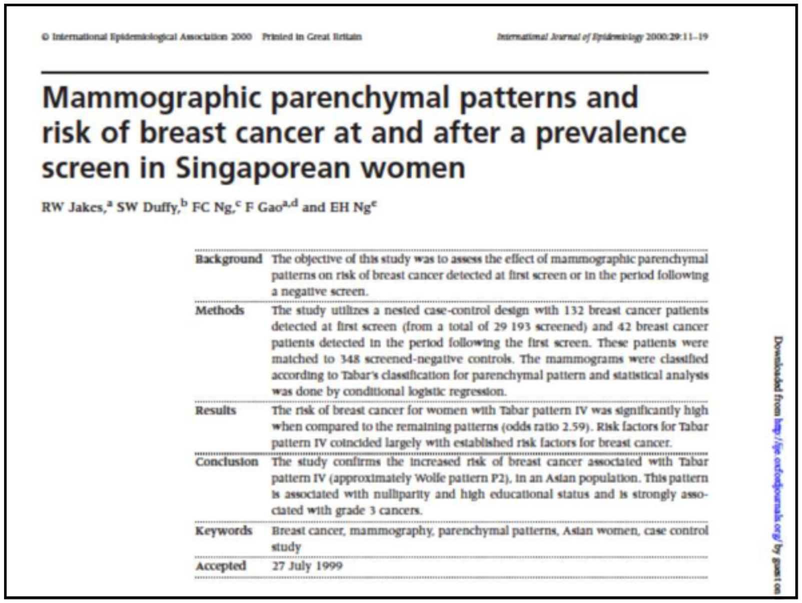
Pattern IV.

Time



No change.

11 years difference



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Mammographic parenchymal patterns and risk of breast cancer at and after a prevalence screen in Singaporean women

RW Jakes,[a] SW Duffy,[b] FC Ng,[c] F Gao[a,d] and EH Ng[e]

Background The objective of this study was to assess the effect of mammographic parenchymal patterns on risk of breast cancer detected at first screen or in the period following a negative screen.

Methods The study utilizes a nested case-control design with 132 breast cancer patients detected at first screen (from a total of 29 193 screened) and 42 breast cancer patients detected in the period following the first screen. These patients were matched to 348 screened-negative controls. The mammograms were classified according to Tabar's classification for parenchymal pattern and statistical analysis was done by conditional logistic regression.

Results The risk of breast cancer for women with Tabar pattern IV was significantly high when compared to the remaining patterns (odds ratio 2.59). Risk factors for Tabar pattern IV coincided largely with established risk factors for breast cancer.

Conclusion The study confirms the increased risk of breast cancer associated with Tabar pattern IV (approximately Wolfe pattern P2), in an Asian population. This pattern is associated with nulliparity and high educational status and is strongly associated with grade 3 cancers.

Keywords Breast cancer, mammography, parenchymal patterns, Asian women, case control study

Accepted 27 July 1999

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Pattern V

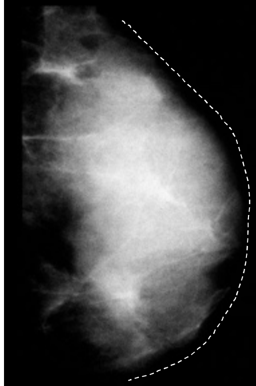
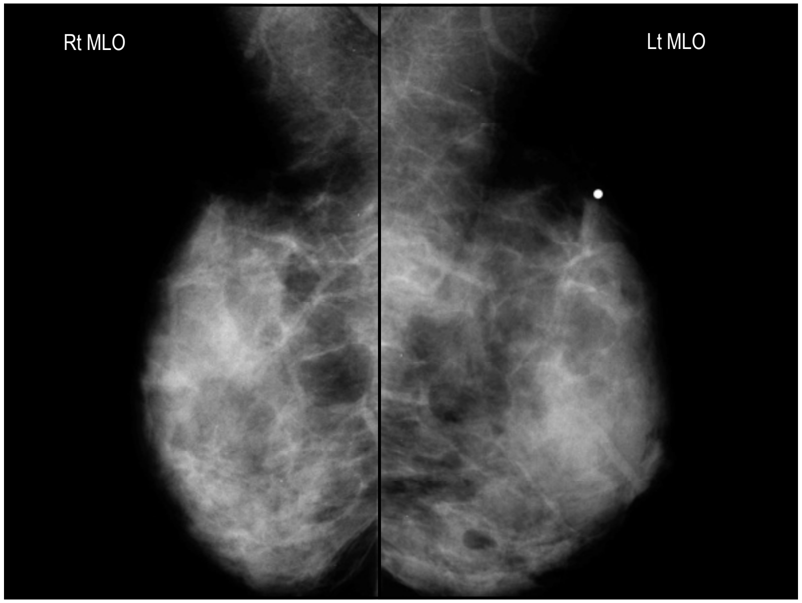
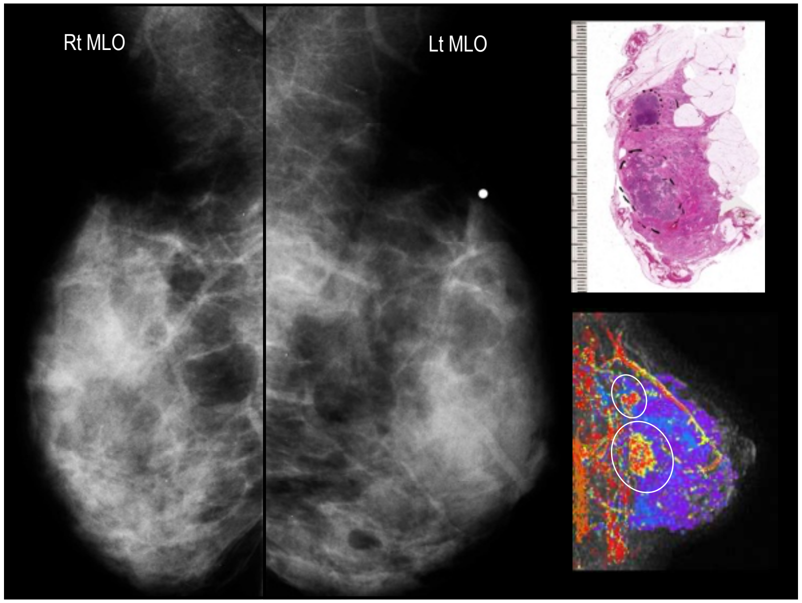
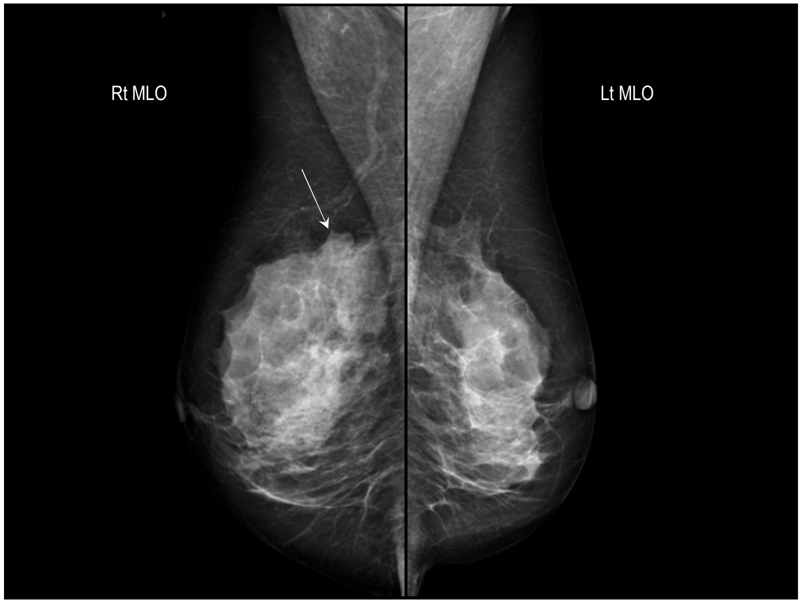


Image courtesy: Hilary Dobson, M.D.

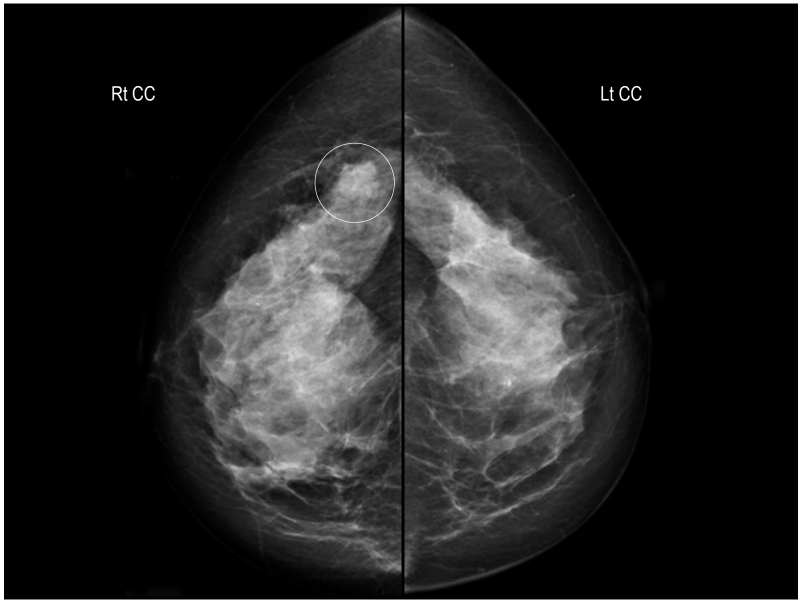



Rt MLO
Lt MLO

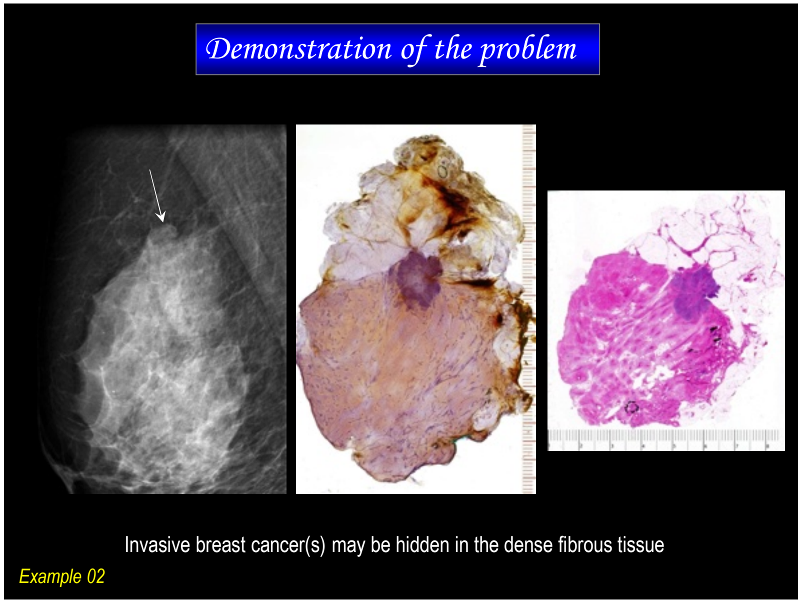
77


Rt MLO
Lt MLO

78



79

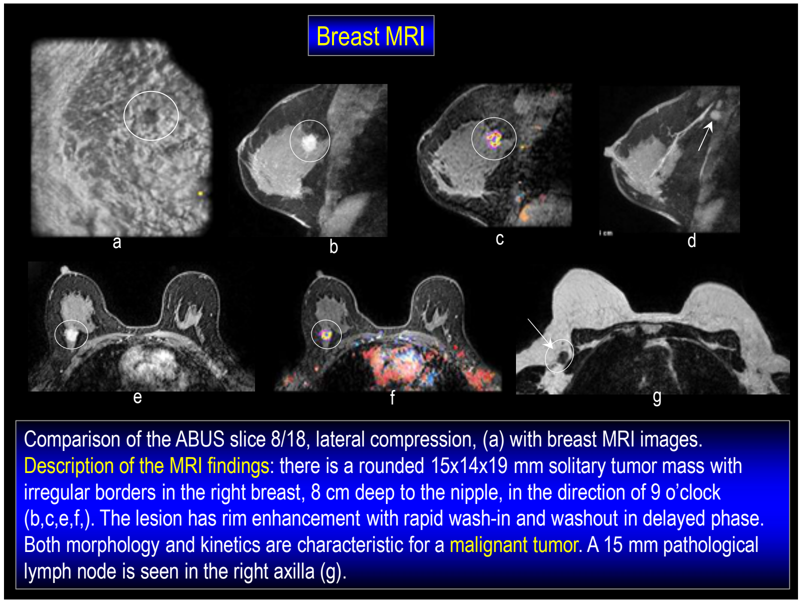


Demonstration of the problem

Invasive breast cancer(s) may be hidden in the dense fibrous tissue

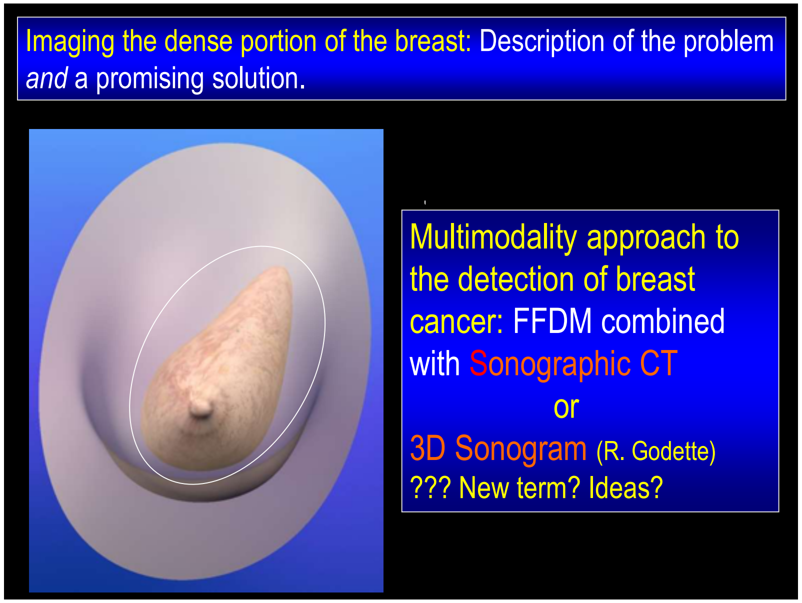
Example 02

80



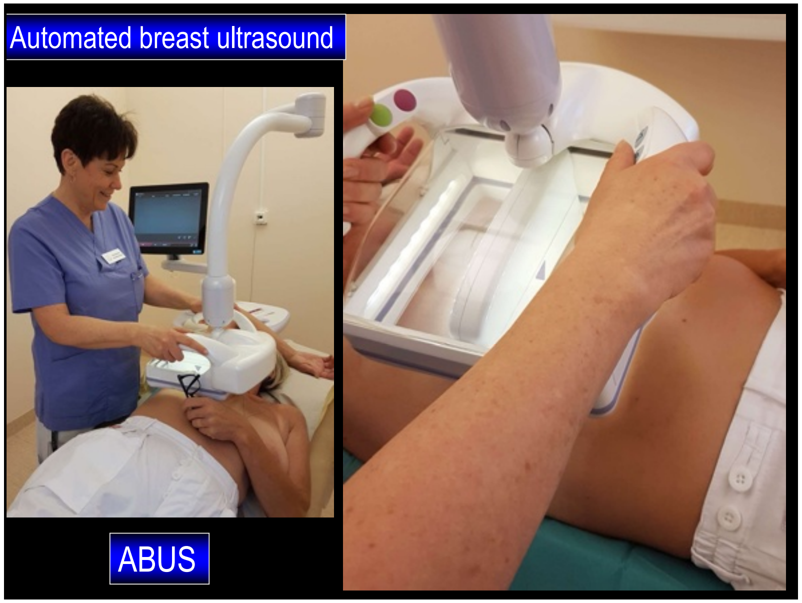
Breast MRI

Comparison of the ABUS slice 8/18, lateral compression, (a) with breast MRI images. Description of the MRI findings: there is a rounded 15x14x19 mm solitary tumor mass with irregular borders in the right breast, 8 cm deep to the nipple, in the direction of 9 o'clock (b,c,e,f,). The lesion has rim enhancement with rapid wash-in and washout in delayed phase. Both morphology and kinetics are characteristic for a malignant tumor. A 15 mm pathological lymph node is seen in the right axilla (g).

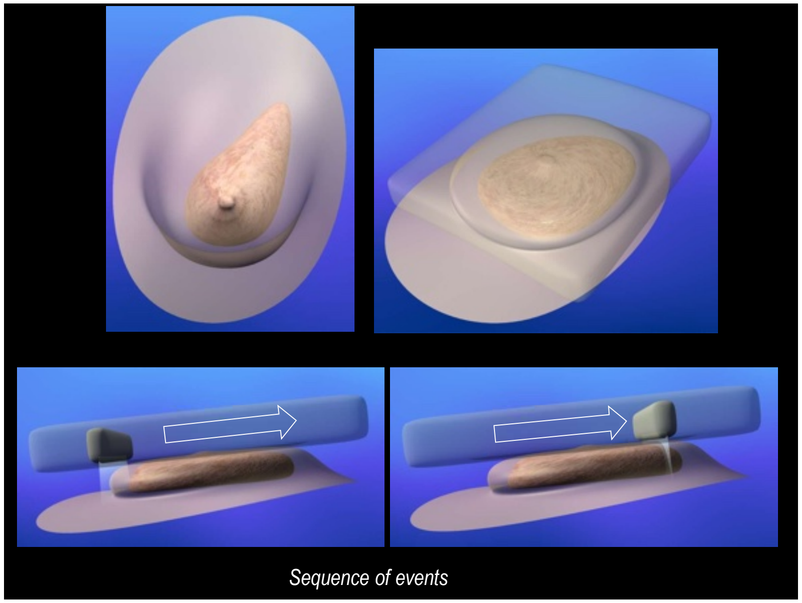


Imaging the dense portion of the breast: Description of the problem *and* a promising solution.

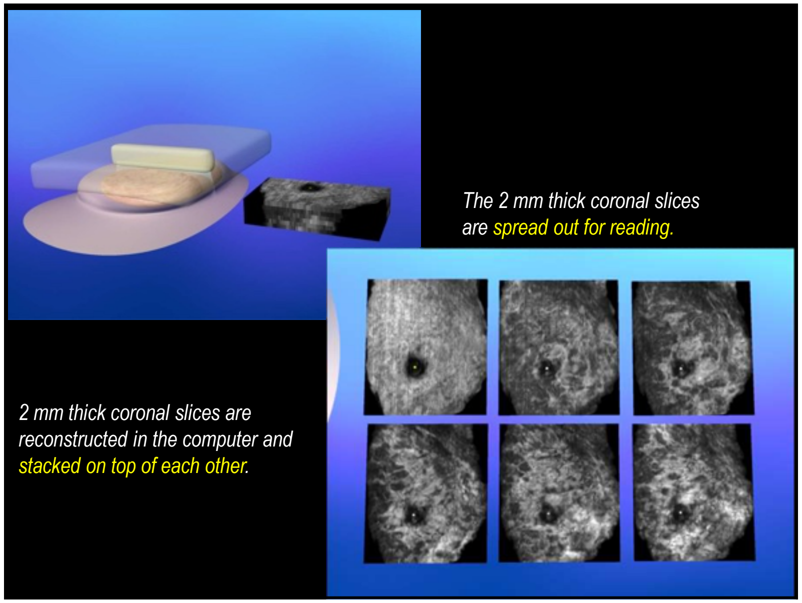
Multimodality approach to the detection of breast cancer: FFDM combined with Sonographic CT
or
3D Sonogram (R. Godette)
??? New term? Ideas?



Automated breast ultrasound



Sequence of events



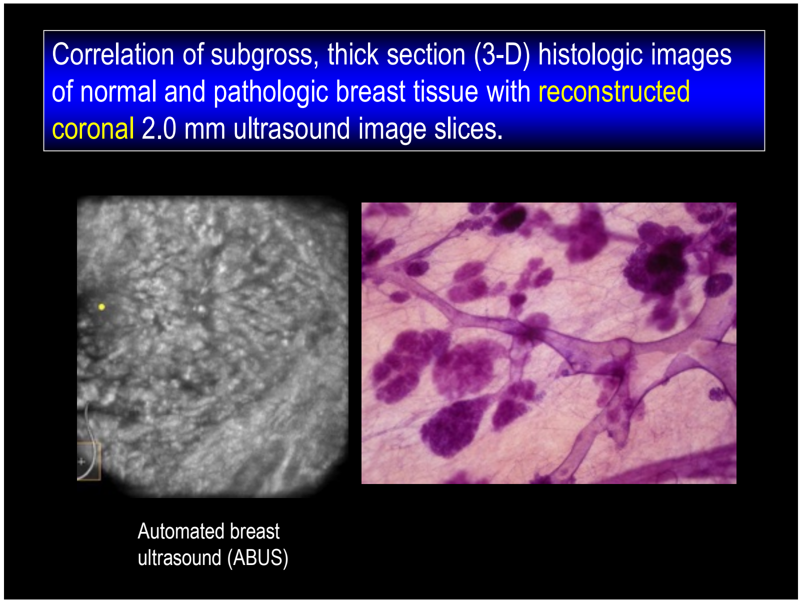
The 2 mm thick coronal slices are spread out for reading.

2 mm thick coronal slices are reconstructed in the computer and stacked on top of each other.

85

86

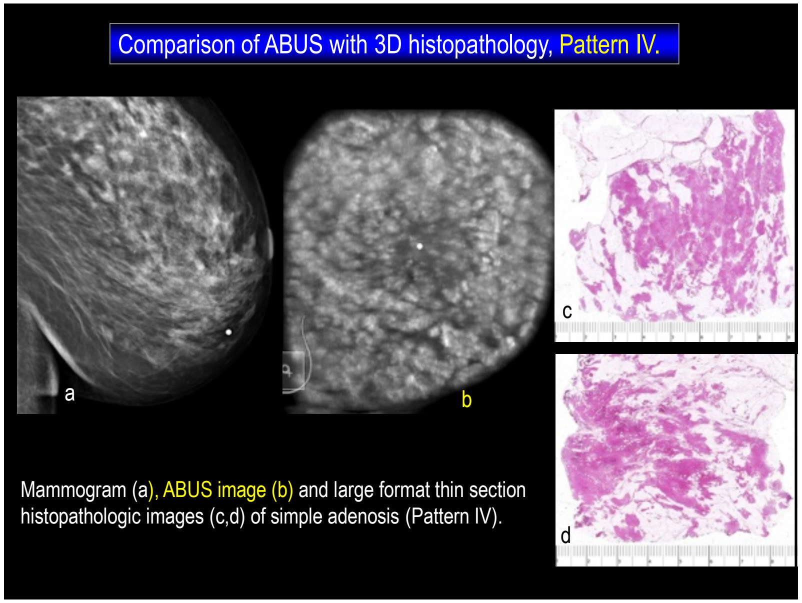
87



Correlation of subgross, thick section (3-D) histologic images of normal and pathologic breast tissue with reconstructed coronal 2.0 mm ultrasound image slices.

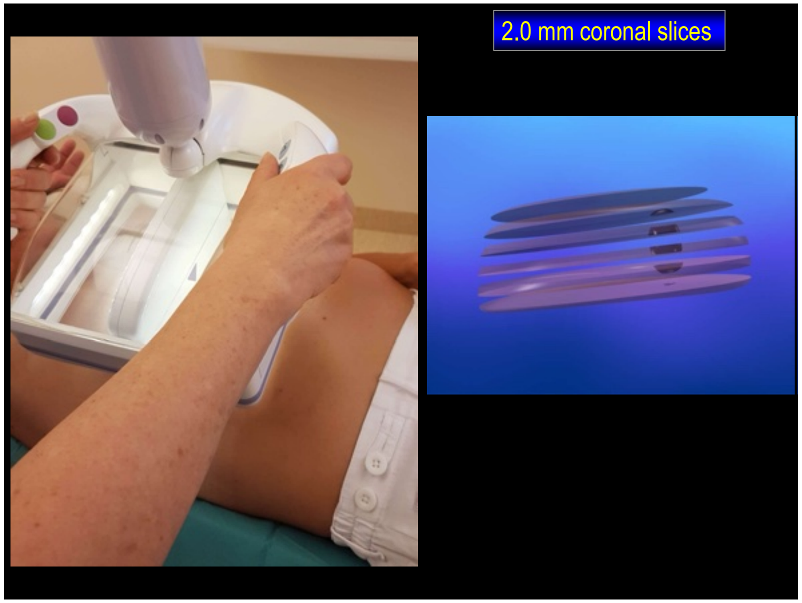
Automated breast ultrasound (ABUS)

88



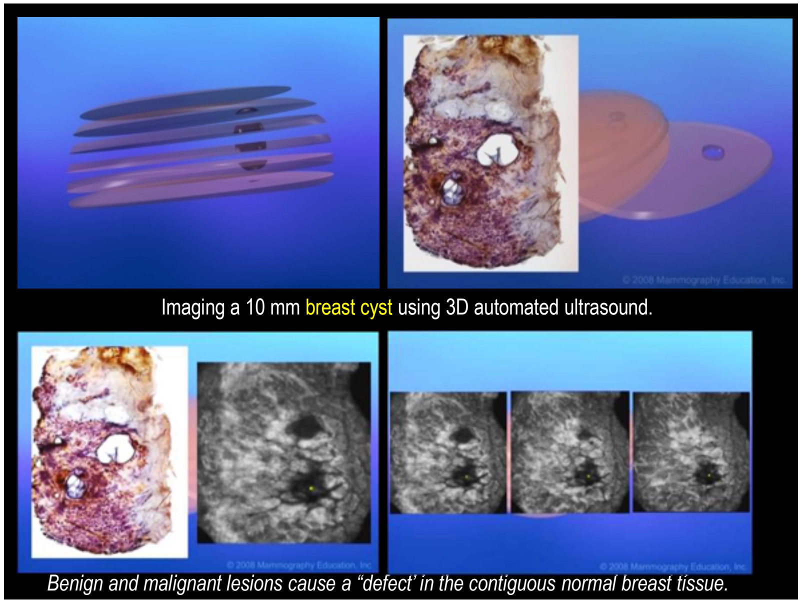
Comparison of ABUS with 3D histopathology, Pattern IV.

Mammogram (a), ABUS image (b) and large format thin section histopathologic images (c,d) of simple adenosis (Pattern IV).



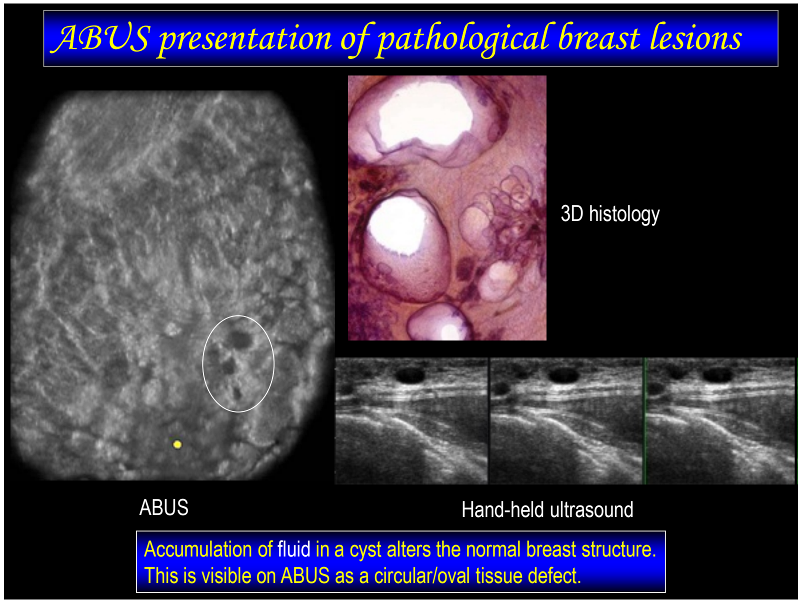
2.0 mm coronal slices

Tut-tut, nästa anhalt är i Dockehus.
Där kliver han snabbt av, vår hungrige mus.


© 2008 Mammography Education, Inc.

Imaging a 10 mm breast cyst using 3D automated ultrasound.

Benign and malignant lesions cause a "defect' in the contiguous normal breast tissue.

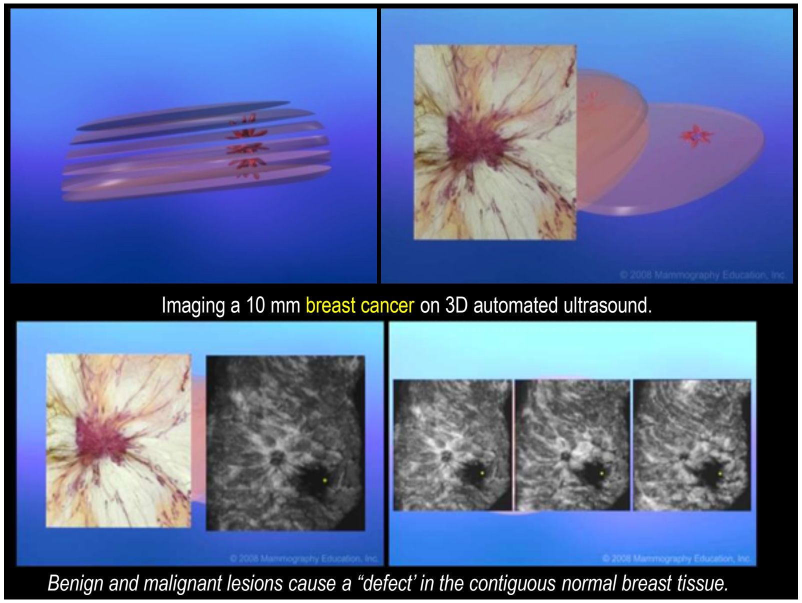


ABUS presentation of pathological breast lesions

3D histology
ABUS
Hand-held ultrasound

Accumulation of fluid in a cyst alters the normal breast structure.
This is visible on ABUS as a circular/oval tissue defect.

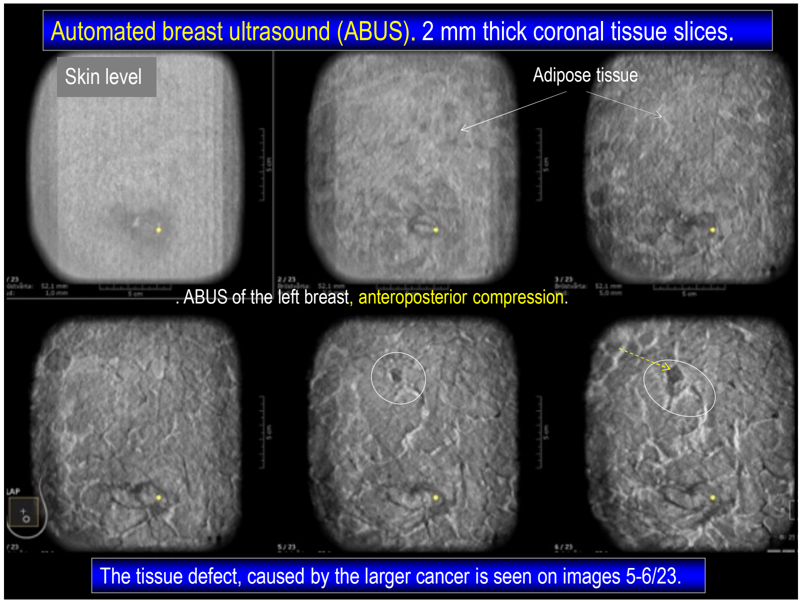
ur tårtan ser ut?
den lille busmusen Knut!
Åh vilket underbart mustårtebo,
hit ska jag flytta, ja det kan du tro!



Imaging a 10 mm breast cancer on 3D automated ultrasound.

© 2008 Mammography Education, Inc.

Benign and malignant lesions cause a "defect" in the contiguous normal breast tissue.

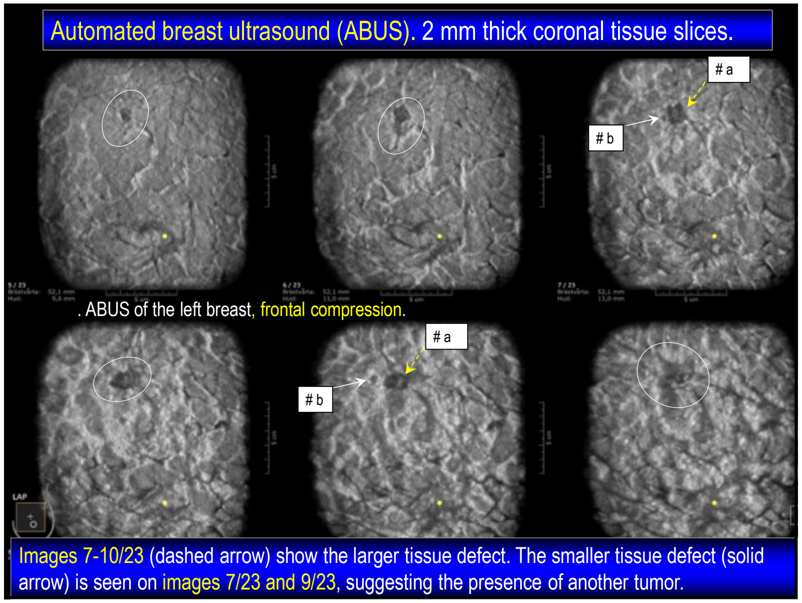


Automated breast ultrasound (ABUS). 2 mm thick coronal tissue slices.

Skin level
Adipose tissue

. ABUS of the left breast, anteroposterior compression.

The tissue defect, caused by the larger cancer is seen on images 5-6/23.

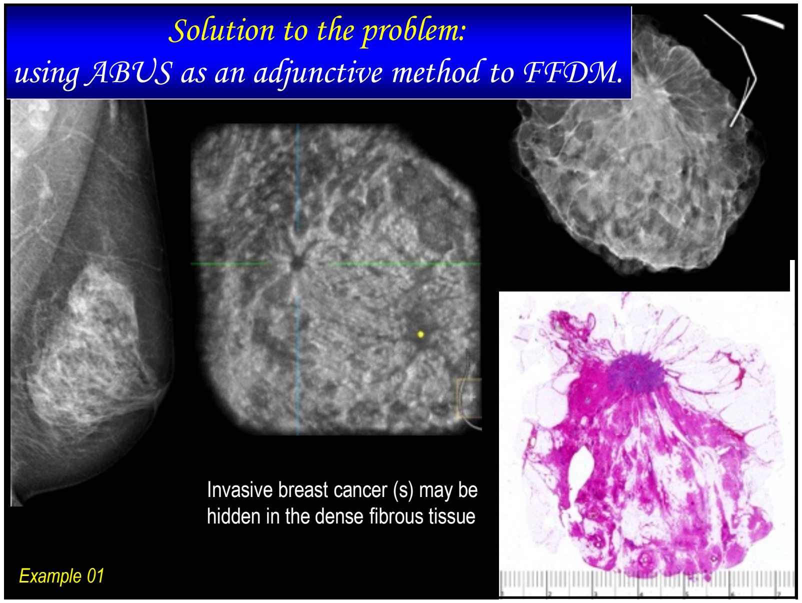


Automated breast ultrasound (ABUS). 2 mm thick coronal tissue slices.

# a
# b
5 / 23
6 / 23
7 / 23
# a
# b

. ABUS of the left breast, frontal compression.

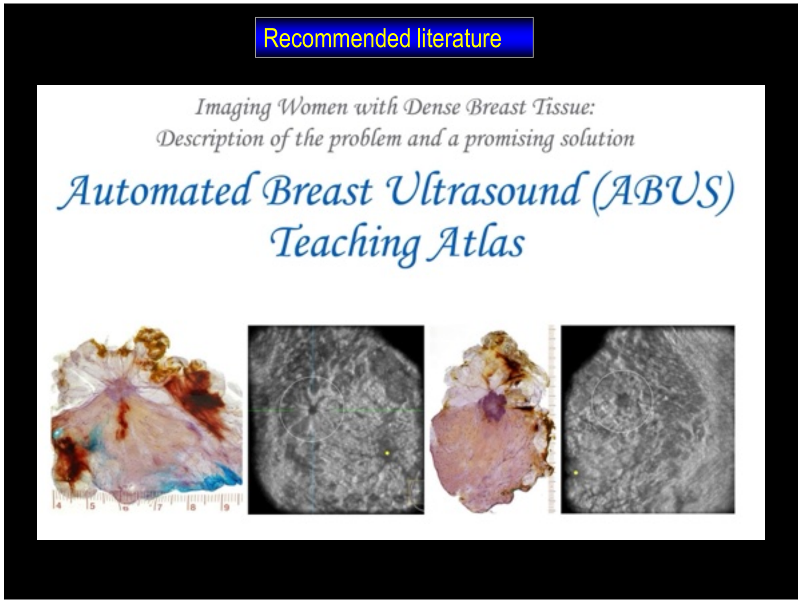
Images 7-10/23 (dashed arrow) show the larger tissue defect. The smaller tissue defect (solid arrow) is seen on images 7/23 and 9/23, suggesting the presence of another tumor.



Solution to the problem: using ABUS as an adjunctive method to FFDM.

Invasive breast cancer (s) may be hidden in the dense fibrous tissue

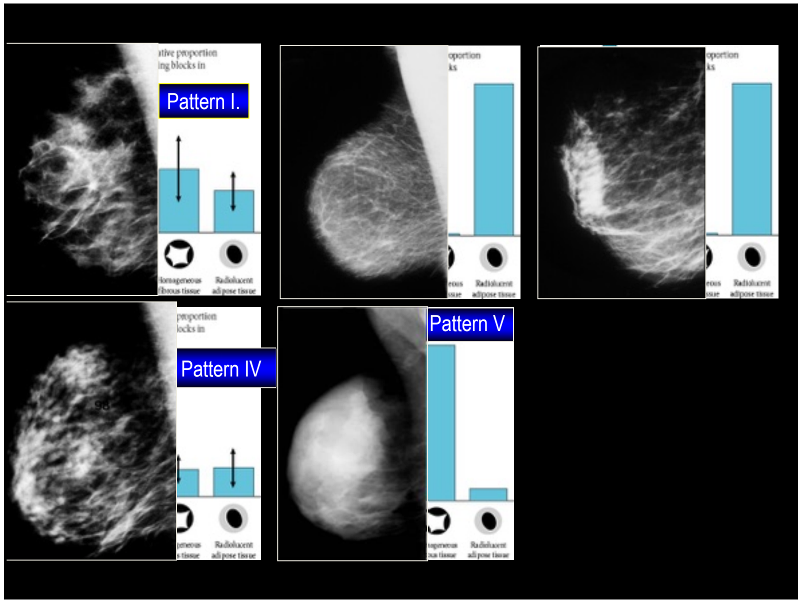
Example 01



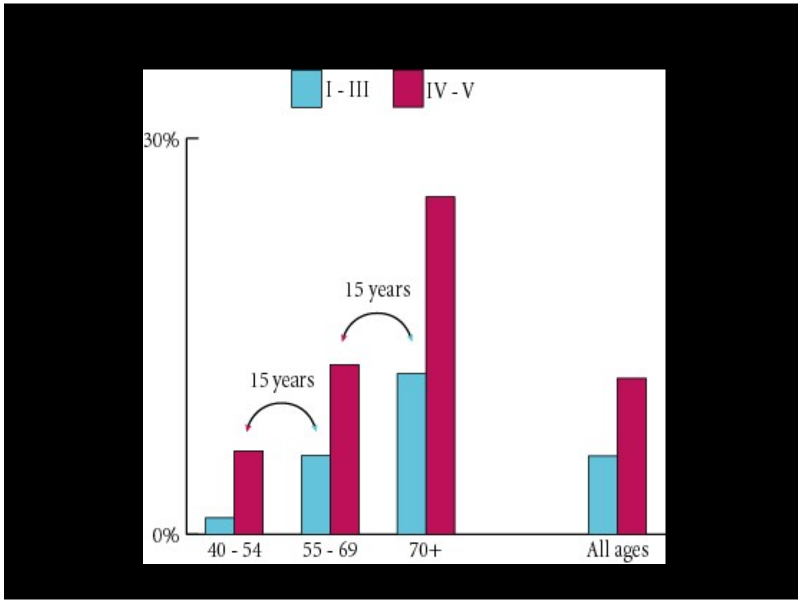
Recommended literature

Imaging Women with Dense Breast Tissue:
Description of the problem and a promising solution

Automated Breast Ultrasound (ABUS)
Teaching Atlas



Pattern I.
Radiolucent adipose tissue
Radiolucent adipose tissue
Radiolucent adipose tissue
Pattern IV
Radiolucent adipose tissue
Pattern V
Radiolucent adipose tissue

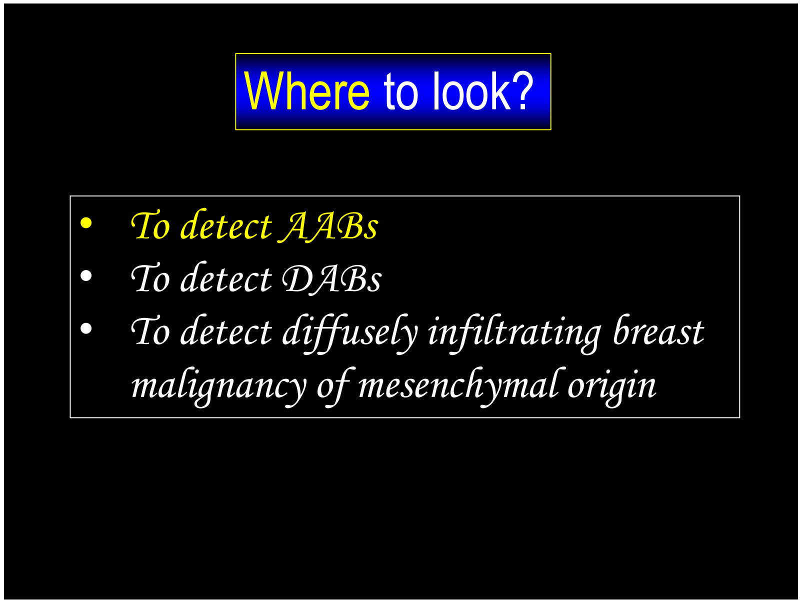


Recommended literature

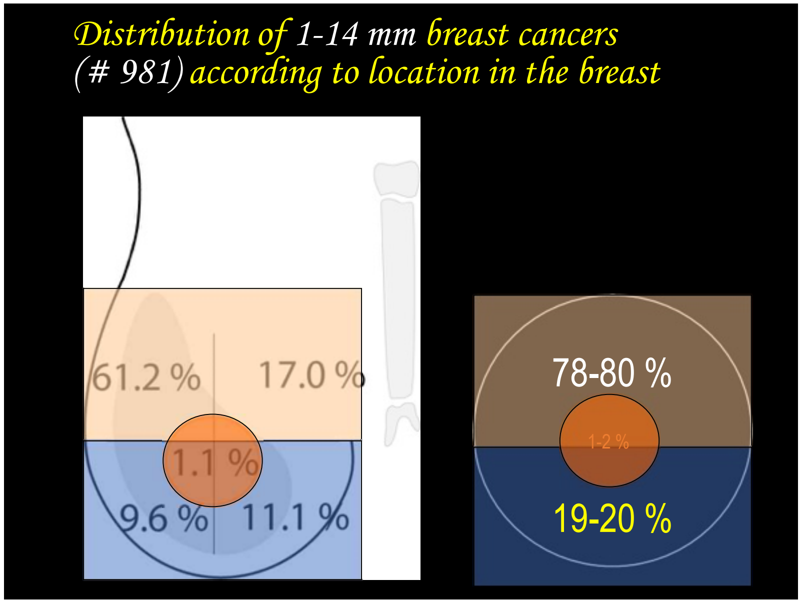
Breast Cancer: The Art and Science of Early Detection with Mammography

www.thieme.com

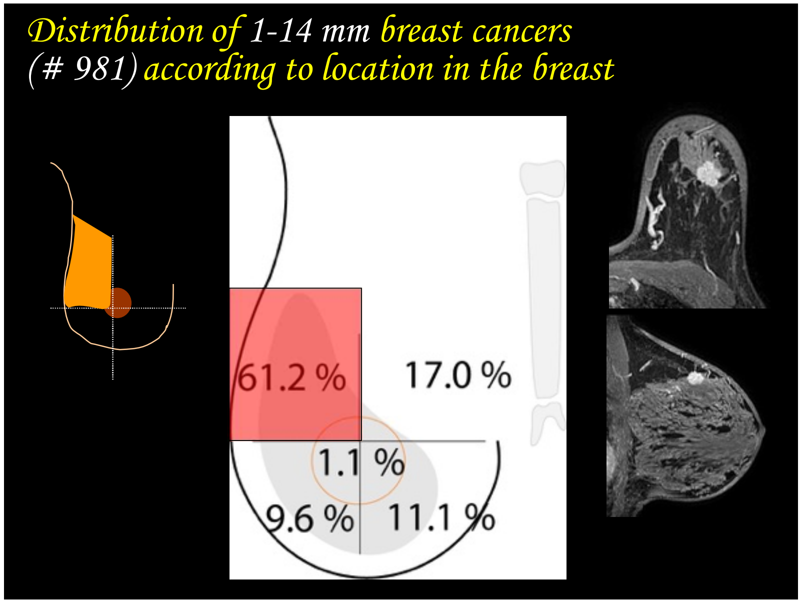
Breast Cancer
The Art and Science of Early Detection with Mammography
László Tabár
Tibor Tot
Peter B. Dean
Perception · Interpretation
Histopathologic Correlation
Thieme


Where to look?

- *To detect AABs*
- *To detect DABs*
- *To detect diffusely infiltrating breast malignancy of mesenchymal origin*

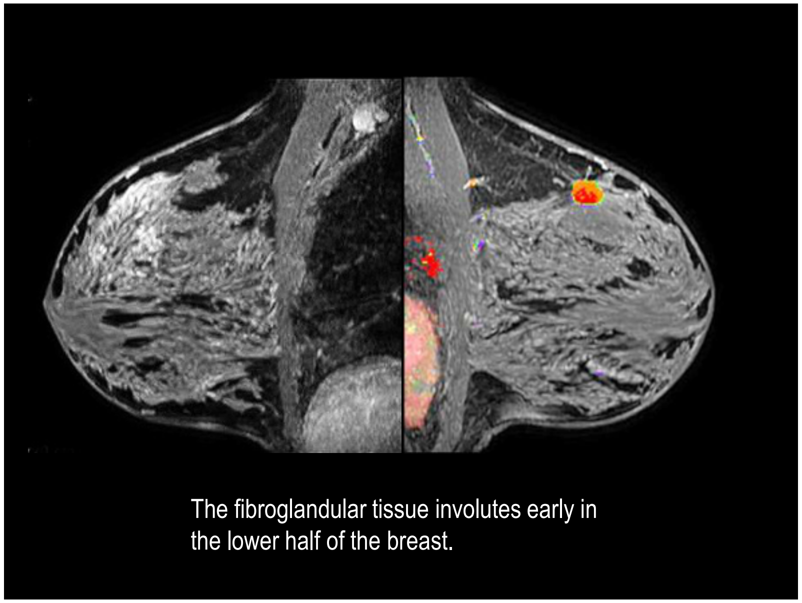

Distribution of 1-14 mm breast cancers (# 981) according to location in the breast

61.2 %
17.0 %
1.1 %
9.6 %
11.1 %
78-80 %
1-2 %
19-20 %

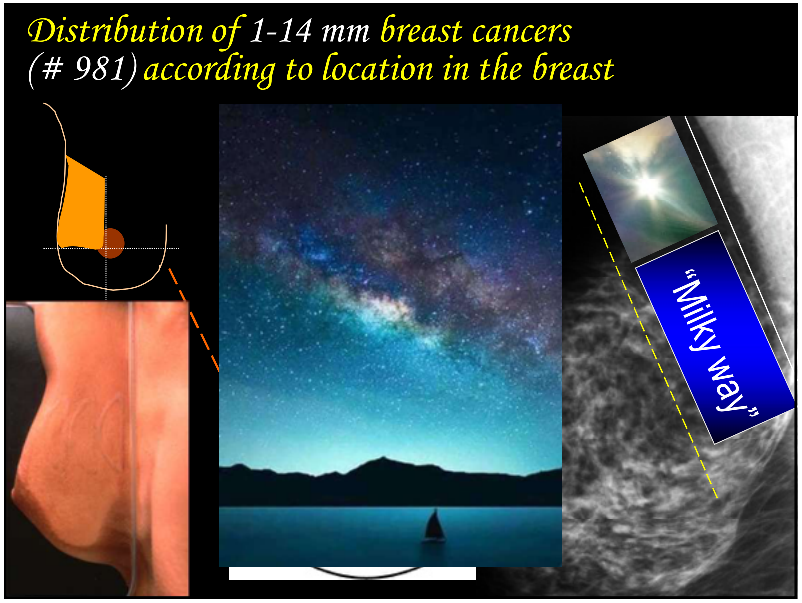


Distribution of 1-14 mm breast cancers (# 981) according to location in the breast

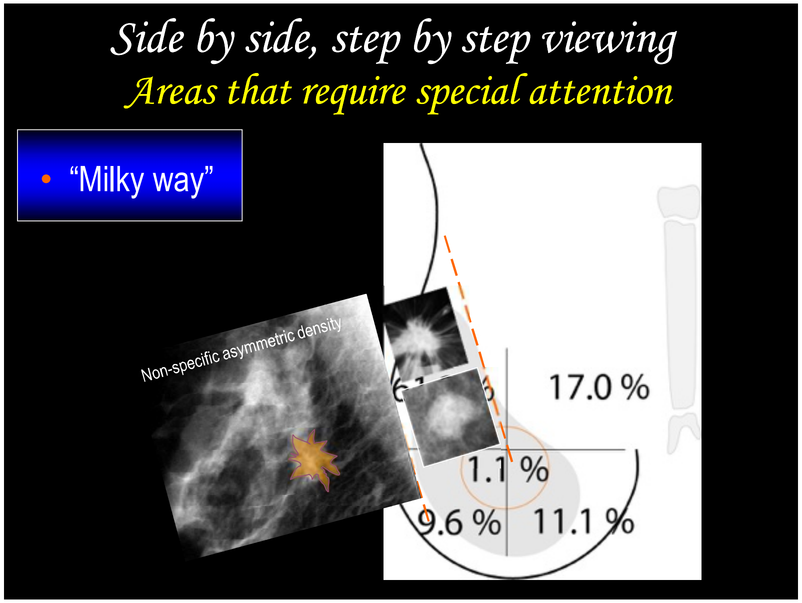
61.2 %
17.0 %
1.1 %
9.6 %
11.1 %



The fibroglandular tissue involutes early in the lower half of the breast.



Distribution of 1-14 mm breast cancers (# 981) according to location in the breast

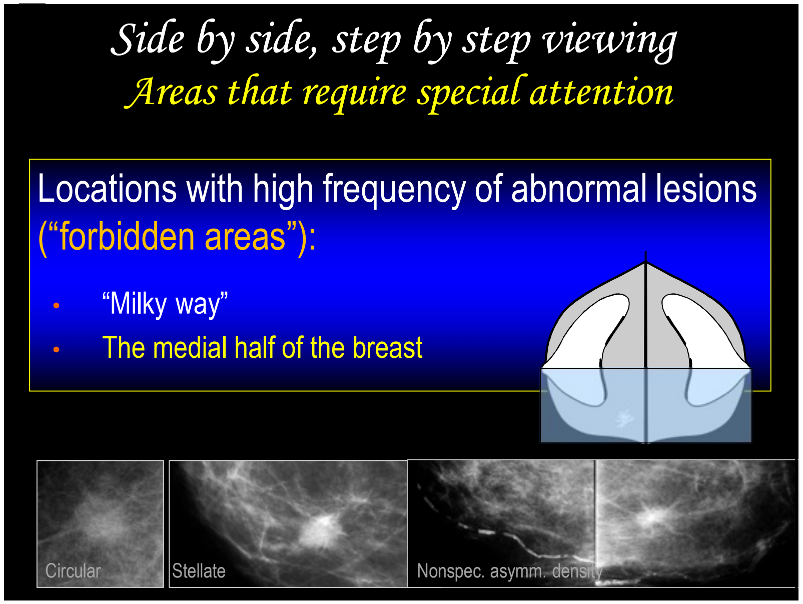


Side by side, step by step viewing

Areas that require special attention

- “Milky way”

Non-specific asymmetric density
17.0 %
1.1 %
9.6 %
11.1 %

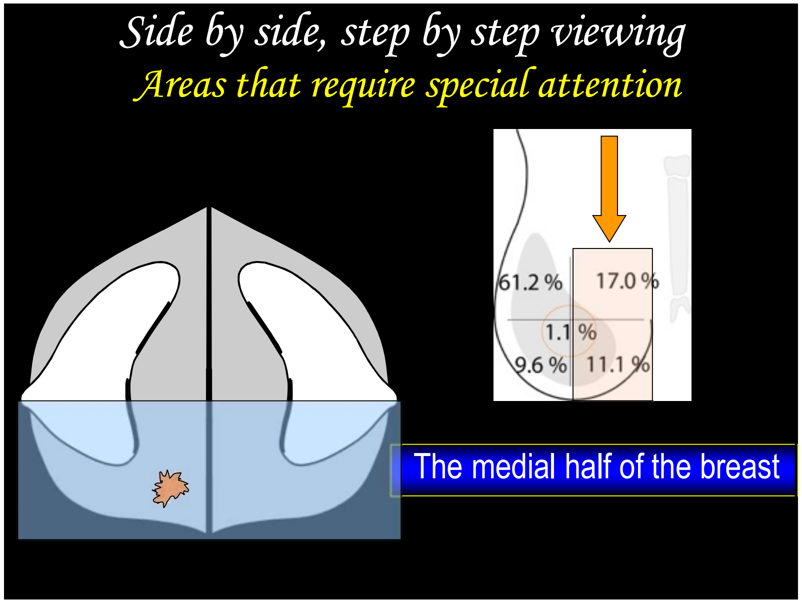


Side by side, step by step viewing

Areas that require special attention

Locations with high frequency of abnormal lesions (“forbidden areas”):

- “Milky way”
- The medial half of the breast



Side by side, step by step viewing

Areas that require special attention

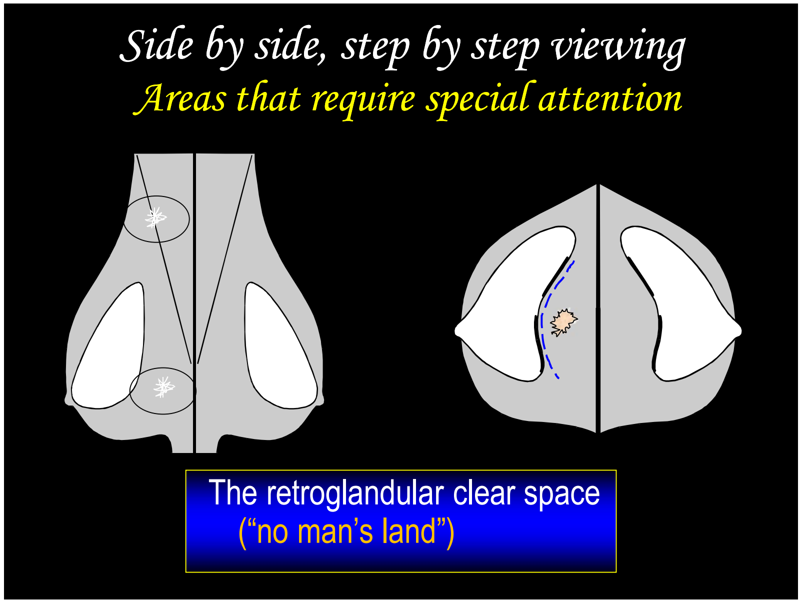
The medial half of the breast

Side by side, step by step viewing

Areas that require special attention

Locations with high frequency of abnormal lesions (“forbidden areas”):

- “Milky way”
- The medial half of the breast
- Retroglandular clear space (“no man’s land”)



Side by side, step by step viewing

Areas that require special attention

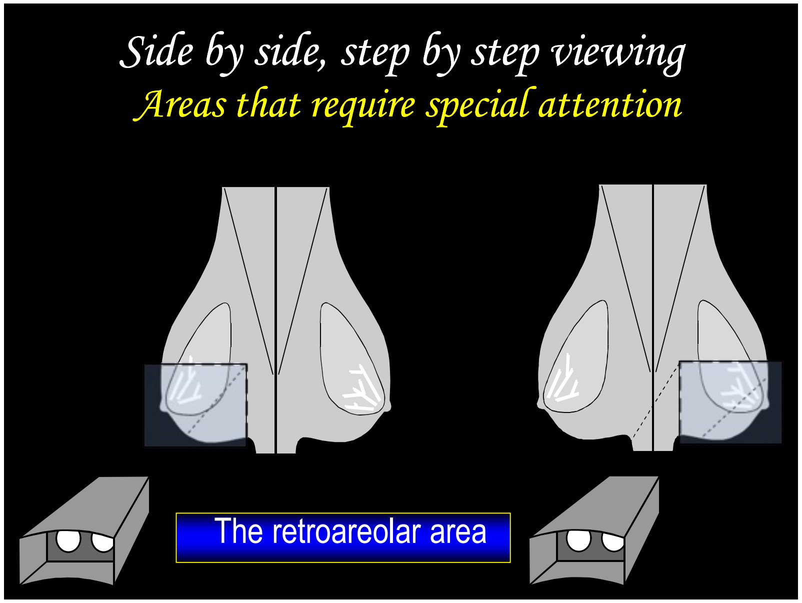
The retroglandular clear space (“no man’s land”)

Side by side, step by step viewing

Areas that require special attention

Locations with high frequency of abnormal lesions (“forbidden areas”):

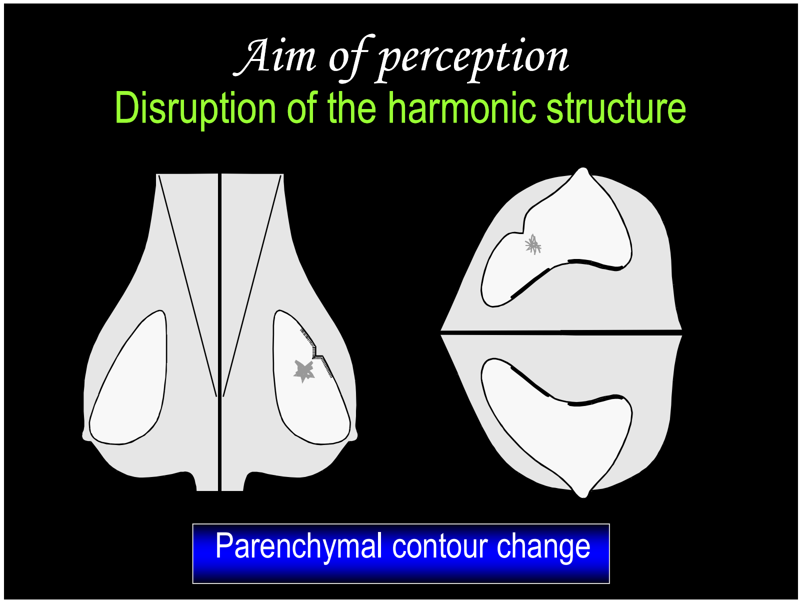
- “Milky way”
- The medial half of the breast
- Retroglandular clear space (“no man’s land”)
- The retroareolar area



Side by side, step by step viewing

Areas that require special attention

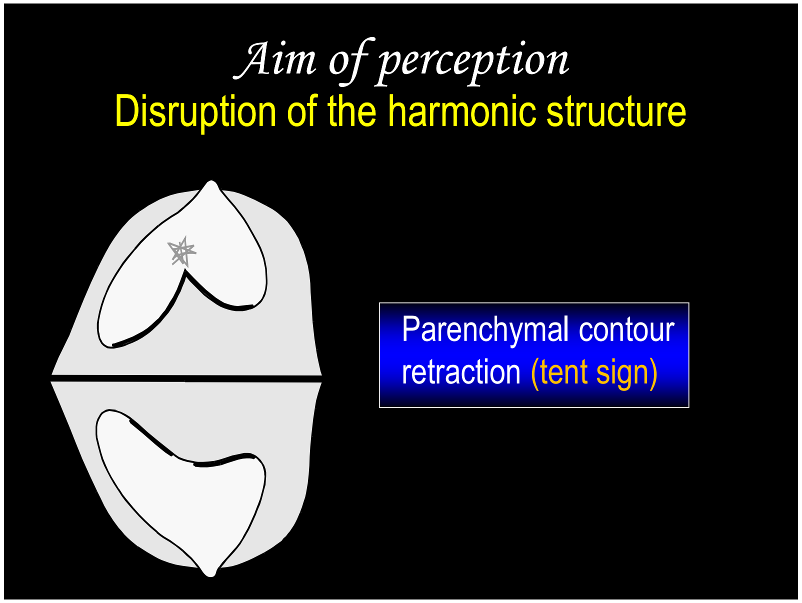
The retroareolar area



Aim of perception

Disruption of the harmonic structure

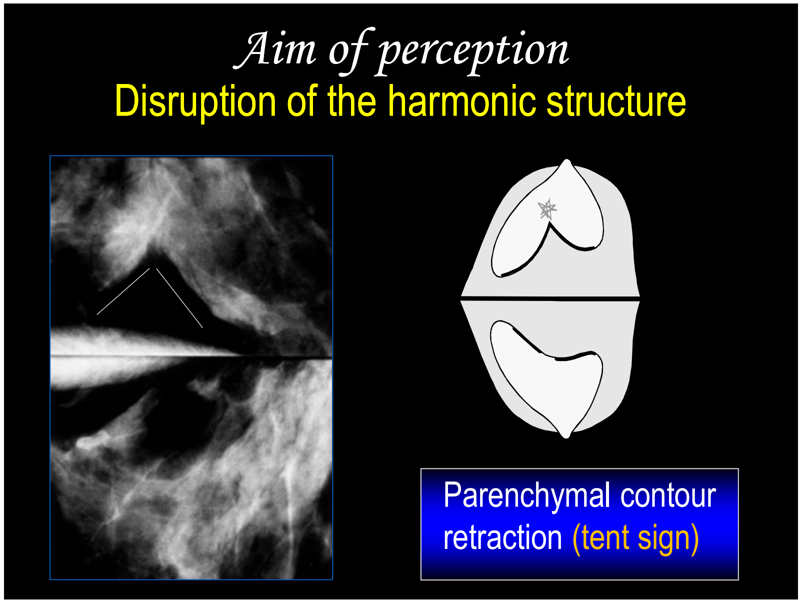
Parenchymal contour change



Aim of perception

Disruption of the harmonic structure

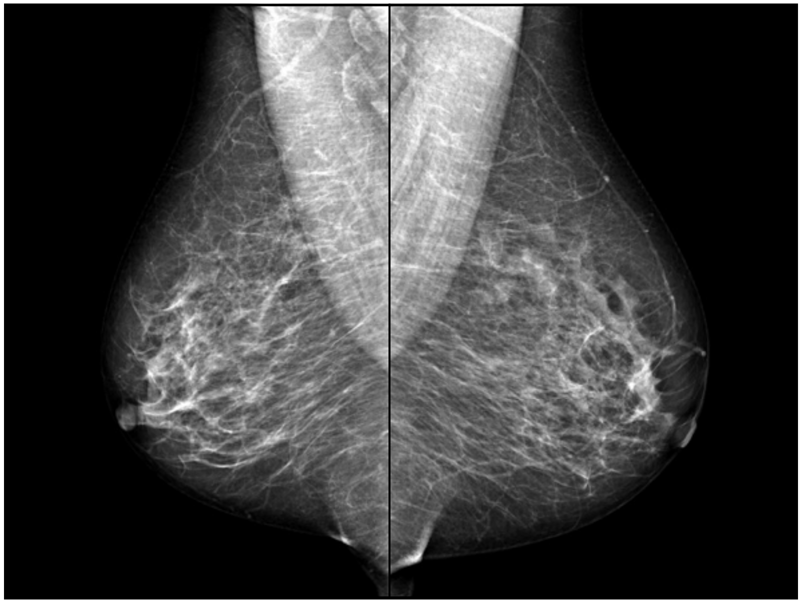
Parenchymal contour retraction (tent sign)

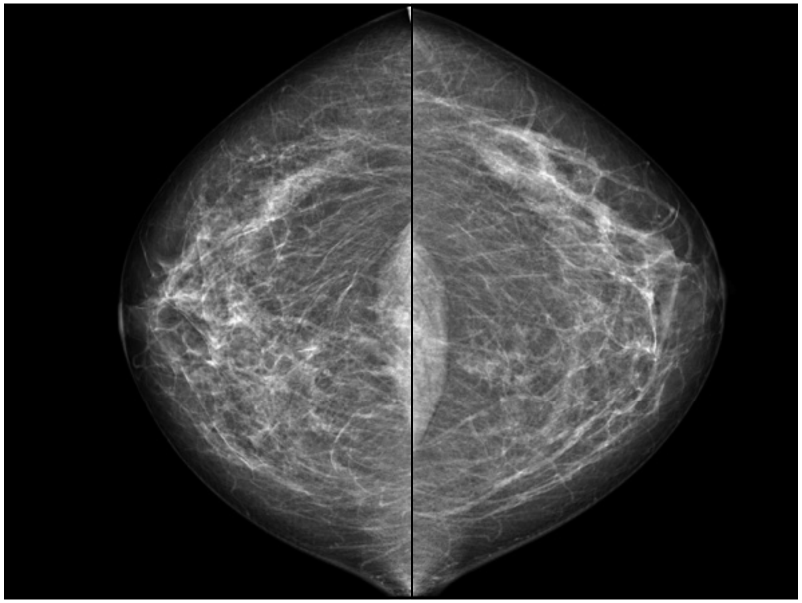


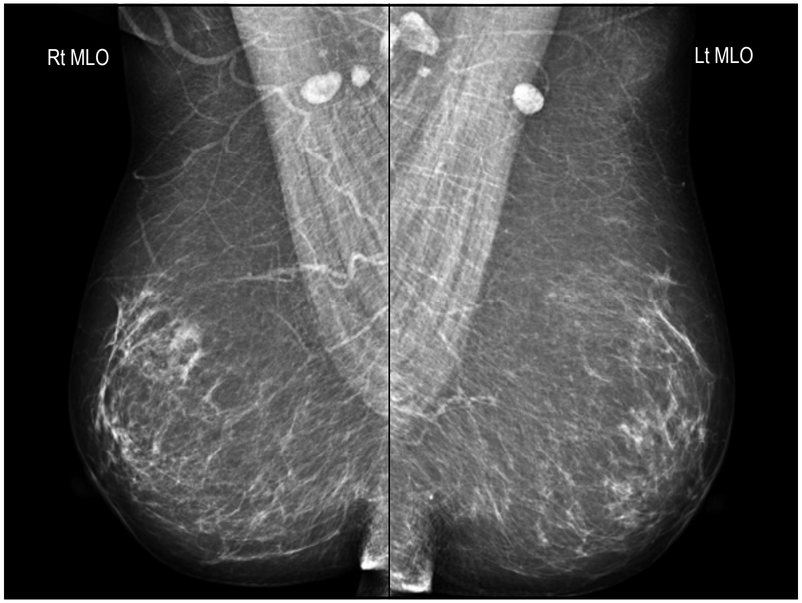
Aim of perception

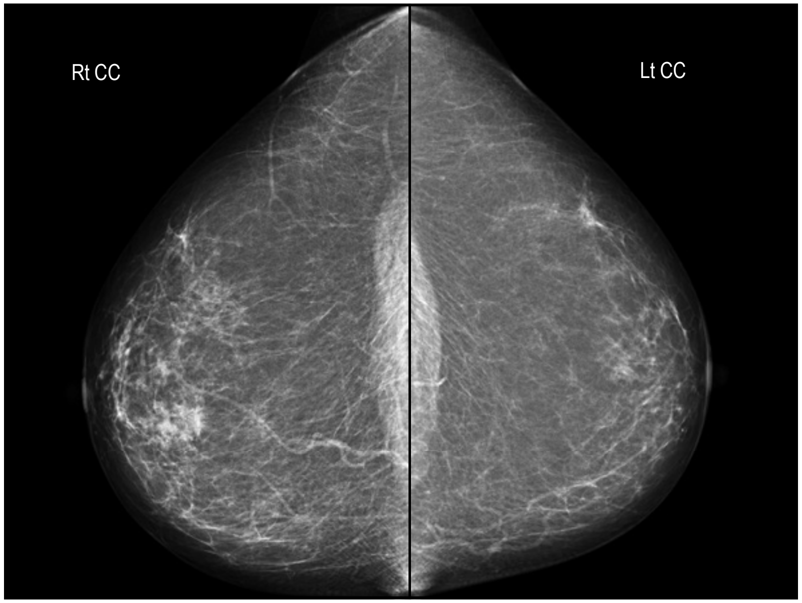
Disruption of the harmonic structure

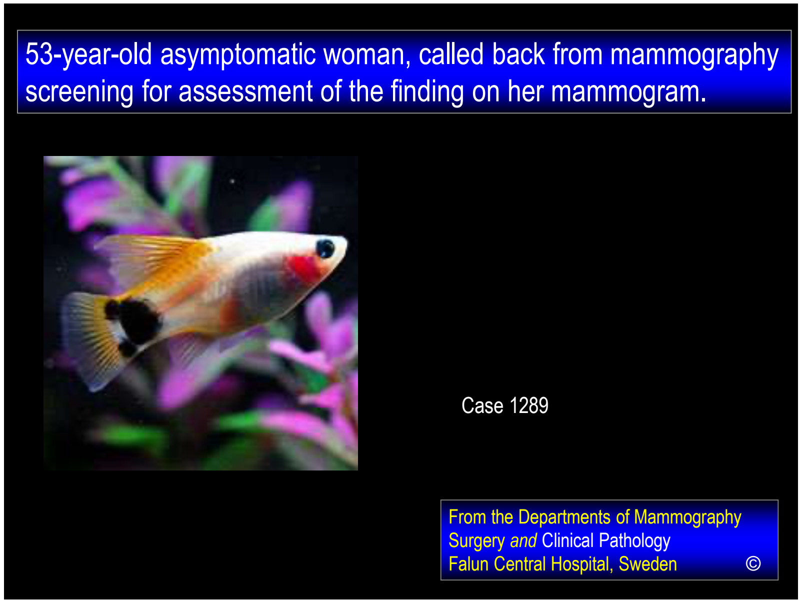
Parenchymal contour retraction (tent sign)





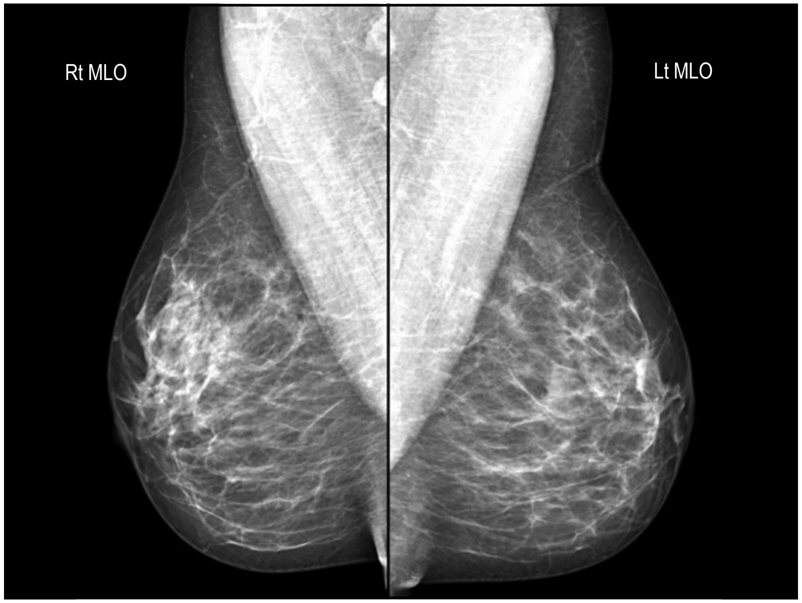


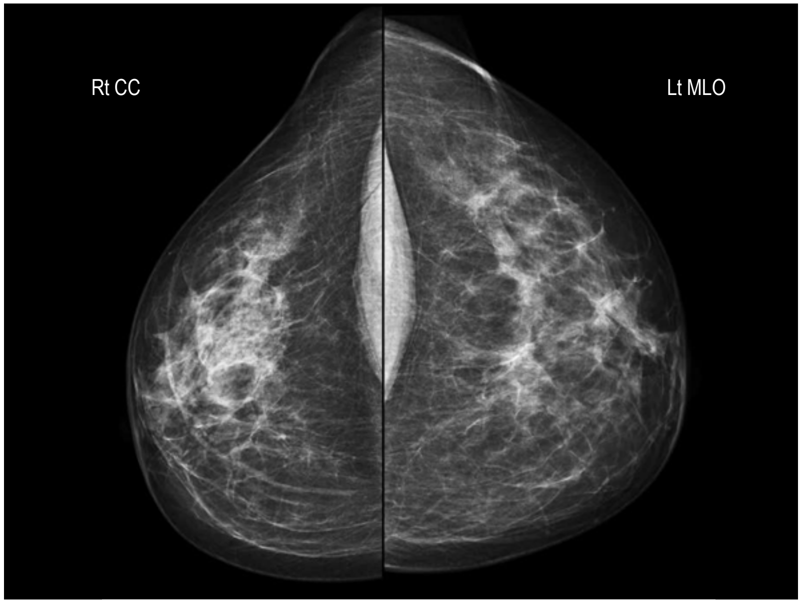


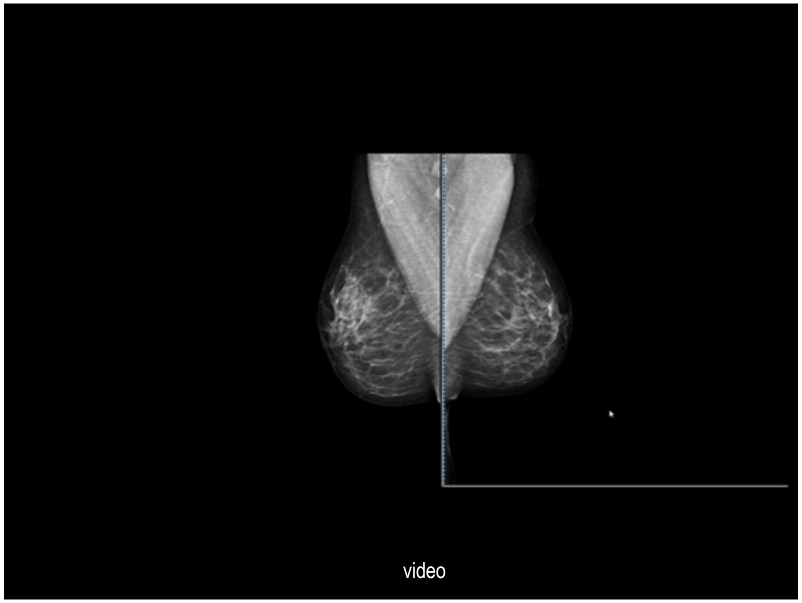

53-year-old asymptomatic woman, called back from mammography screening for assessment of the finding on her mammogram.

Case 1289

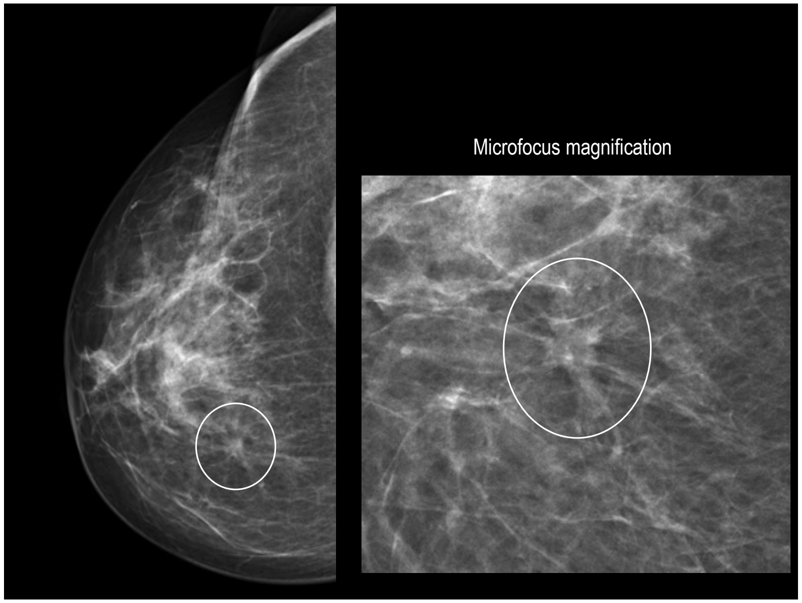
From the Departments of Mammography
Surgery *and* Clinical Pathology
Falun Central Hospital, Sweden ©


Rt MLO
Lt MLO

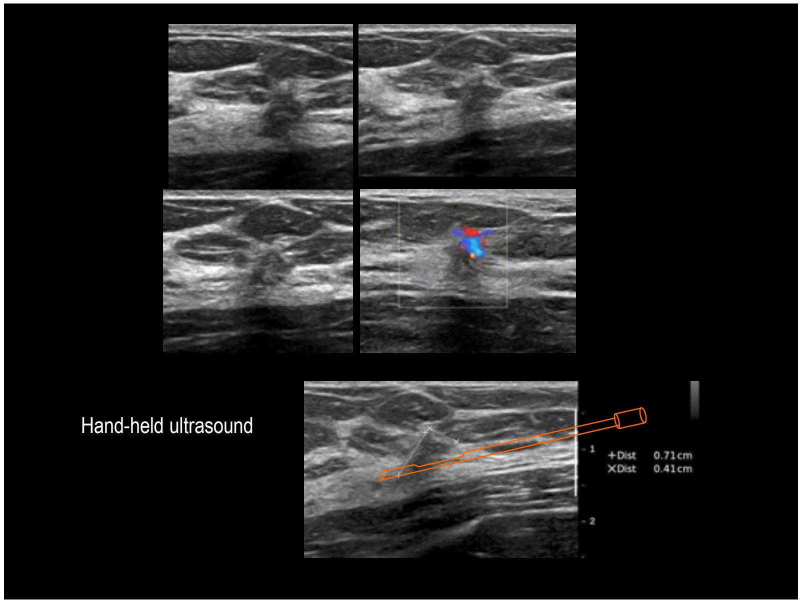



video

125

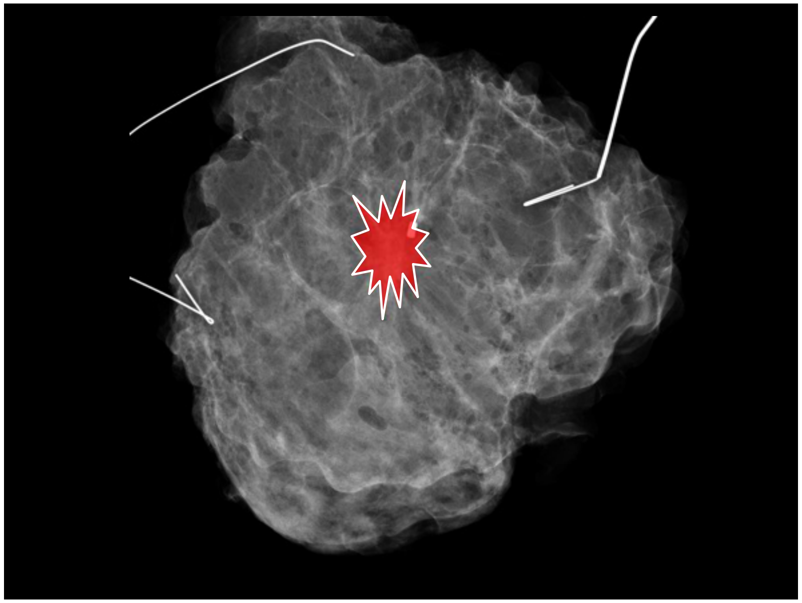

Microfocus magnification

126

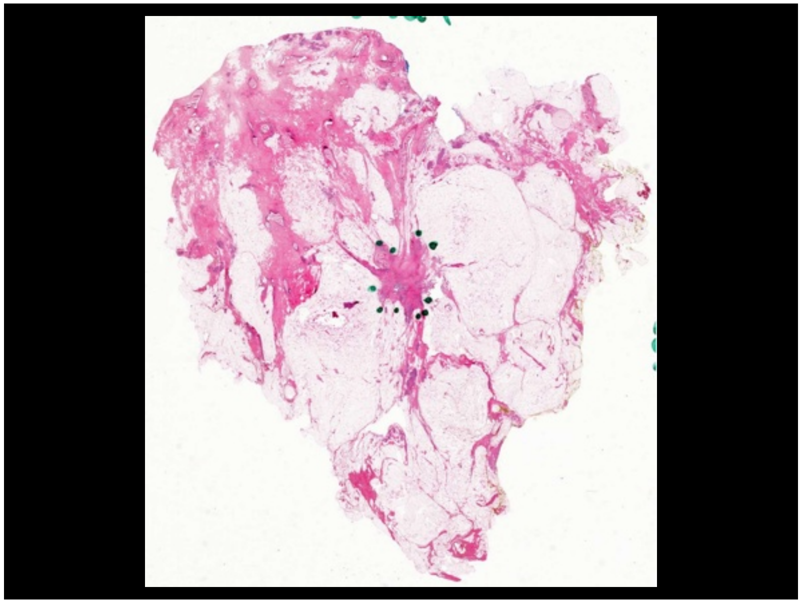

Hand-held ultrasound

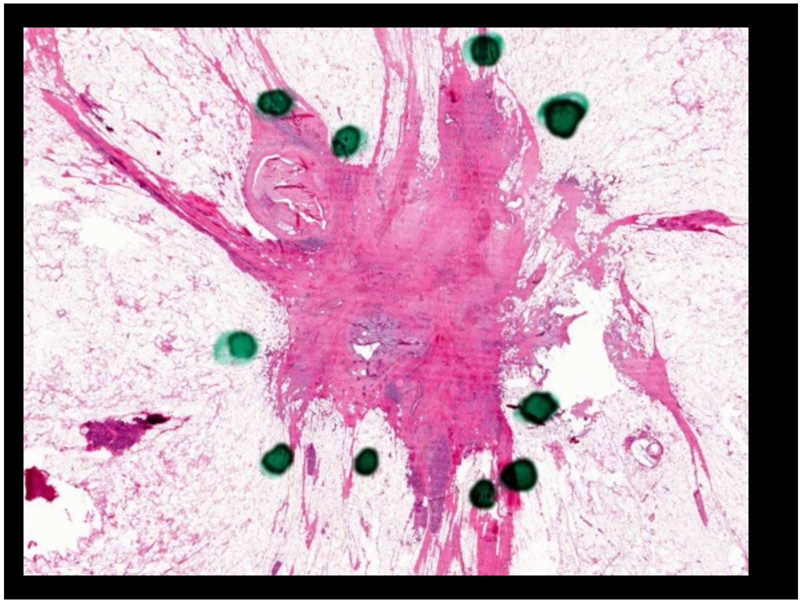
+Dist 0.71cm
×Dist 0.41cm
1
2

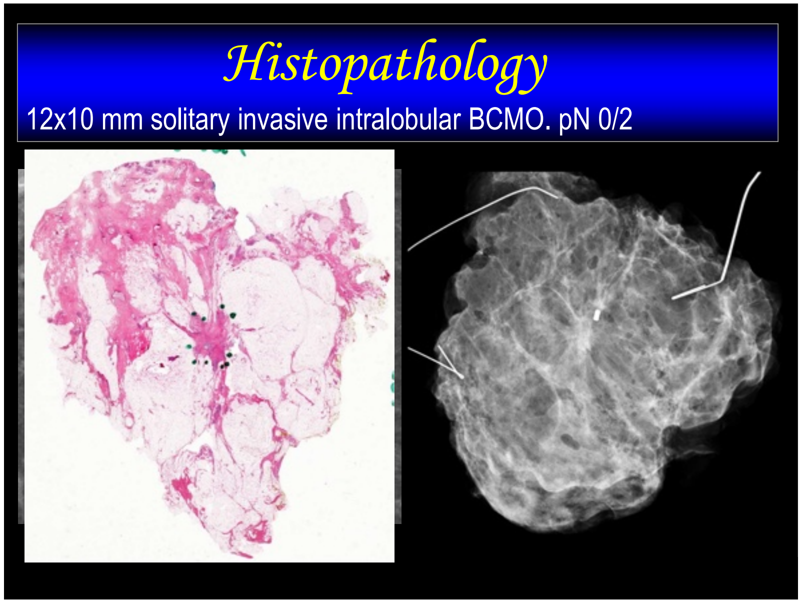
127



128





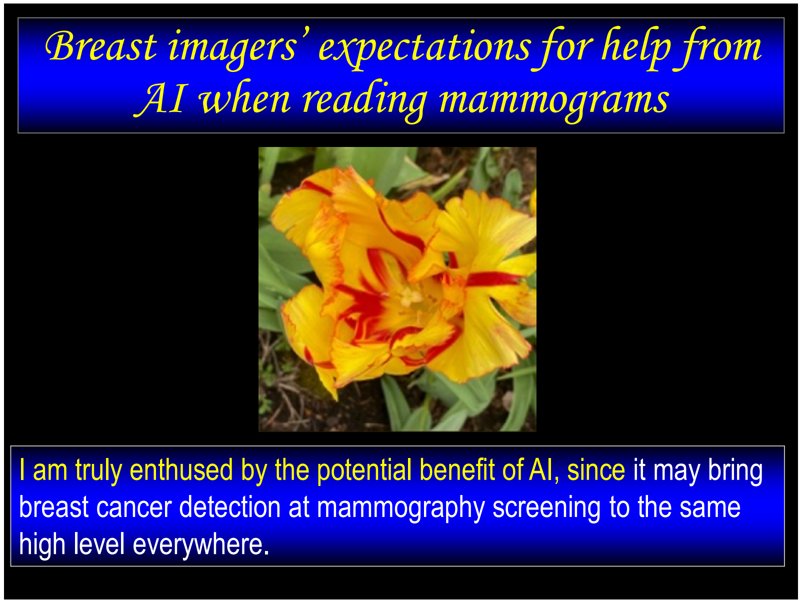


Histopathology

12x10 mm solitary invasive intralobular BCMO. pN 0/2

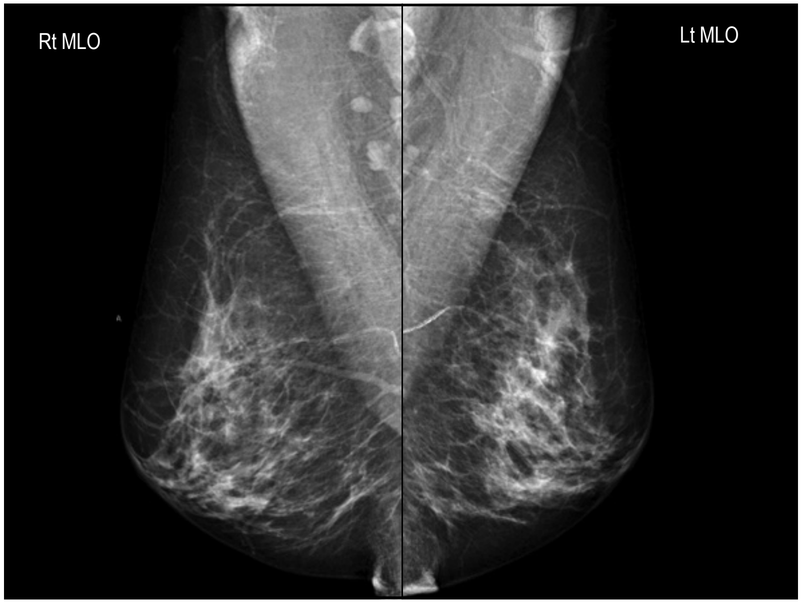
Follow-up

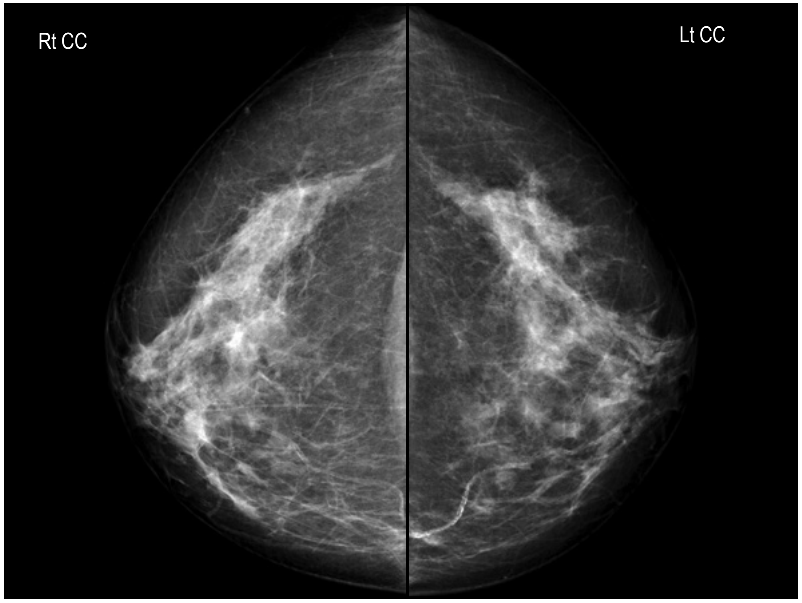
Nine years and seven months after diagnosis and treatment, the patient is well with no signs of recurrence.

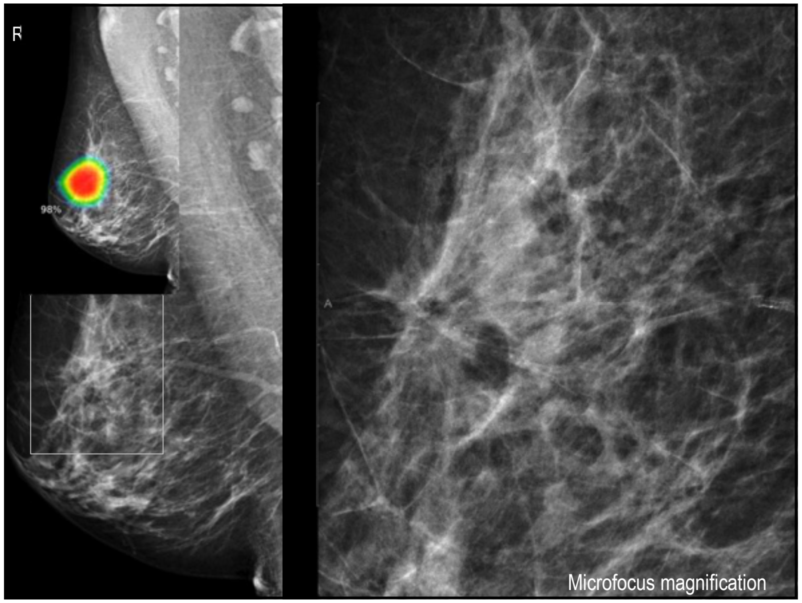


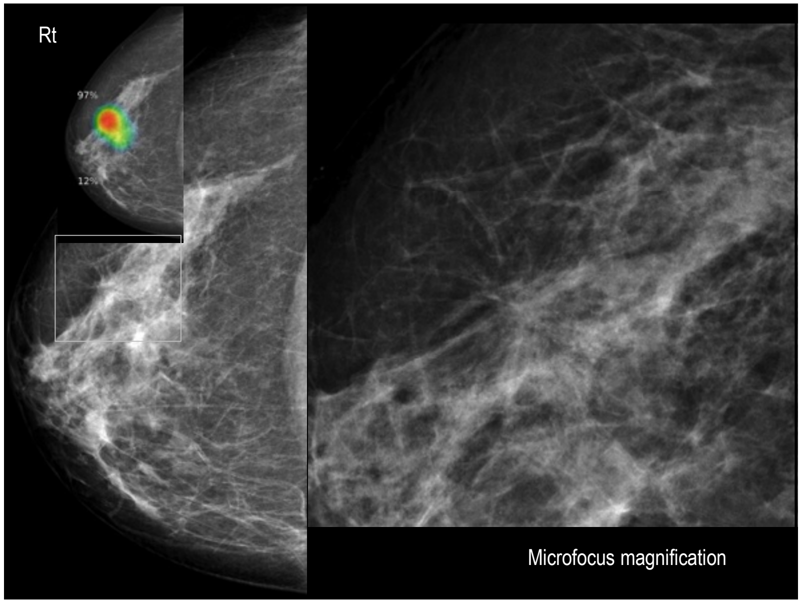
Breast imagers' expectations for help from AI when reading mammograms

I am truly enthused by the potential benefit of AI, since it may bring breast cancer detection at mammography screening to the same high level everywhere.

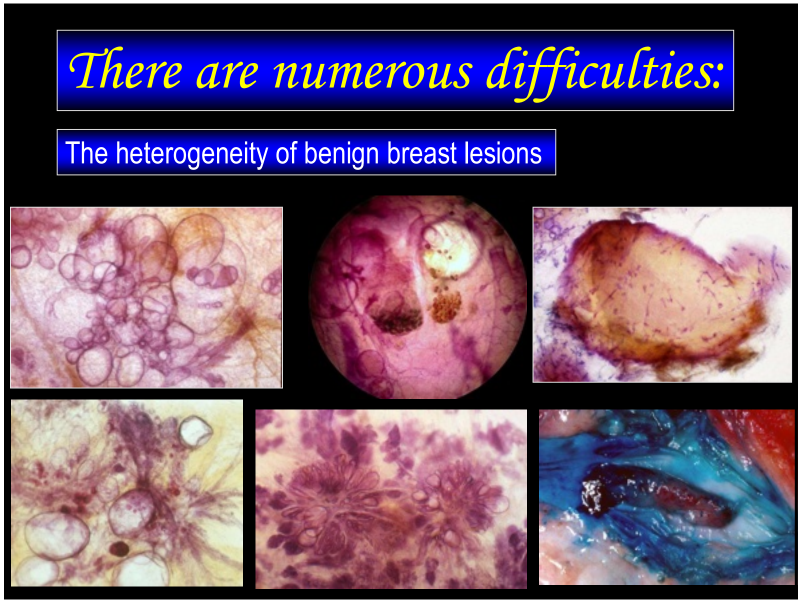

Rt MLO
Lt MLO




R
98%
Microfocus magnification

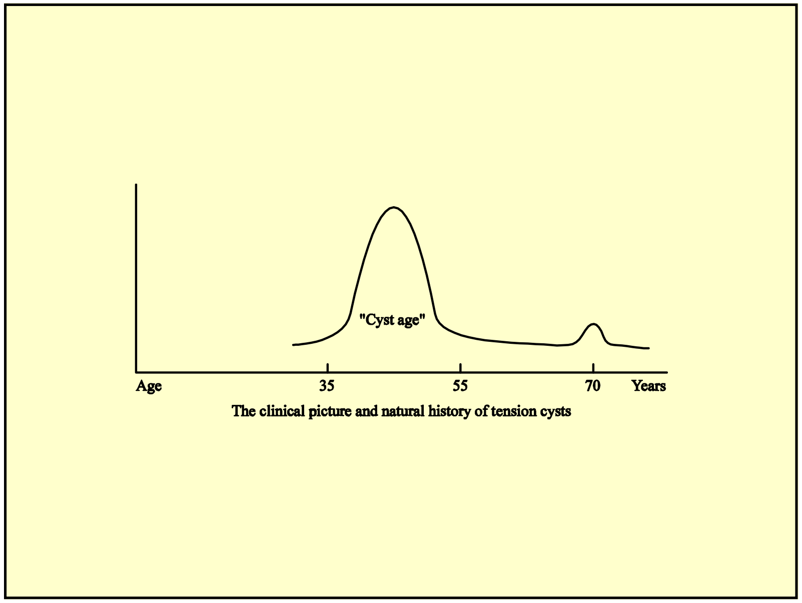


Microfocus magnification

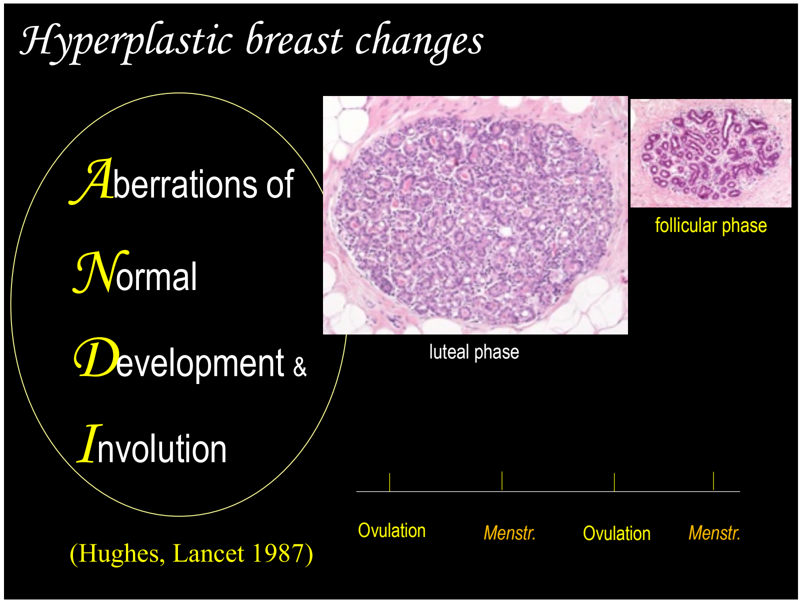


There are numerous difficulties:

The heterogeneity of benign breast lesions



The clinical picture and natural history of tension cysts

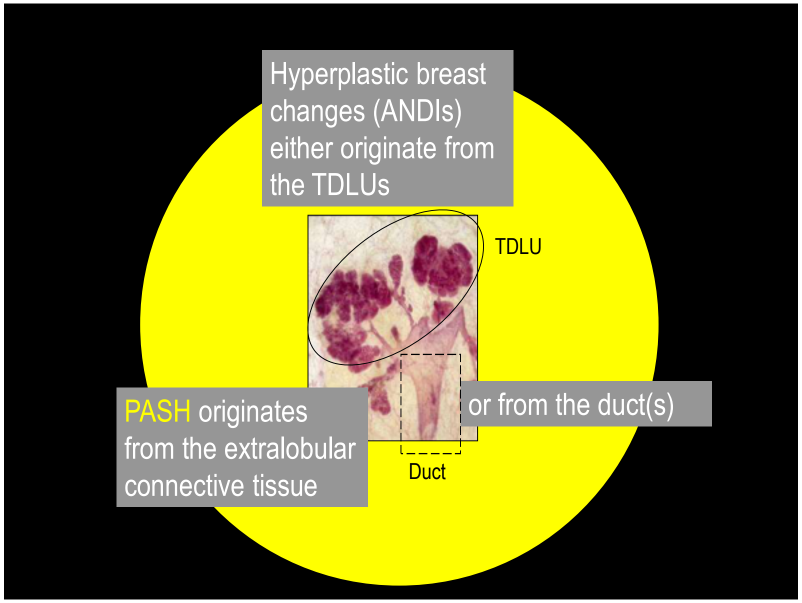


Hyperplastic breast changes

Aberrations of
Normal
Development &
Involution

(Hughes, Lancet 1987)

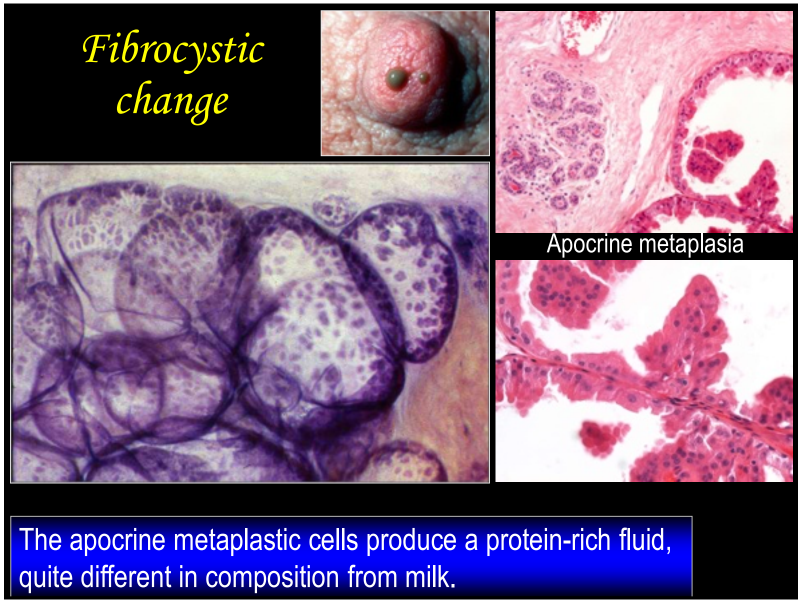
follicular phase
luteal phase
Ovulation
Menstr.
Ovulation
Menstr.



Hyperplastic breast changes (ANDIs) either originate from the TDLUs

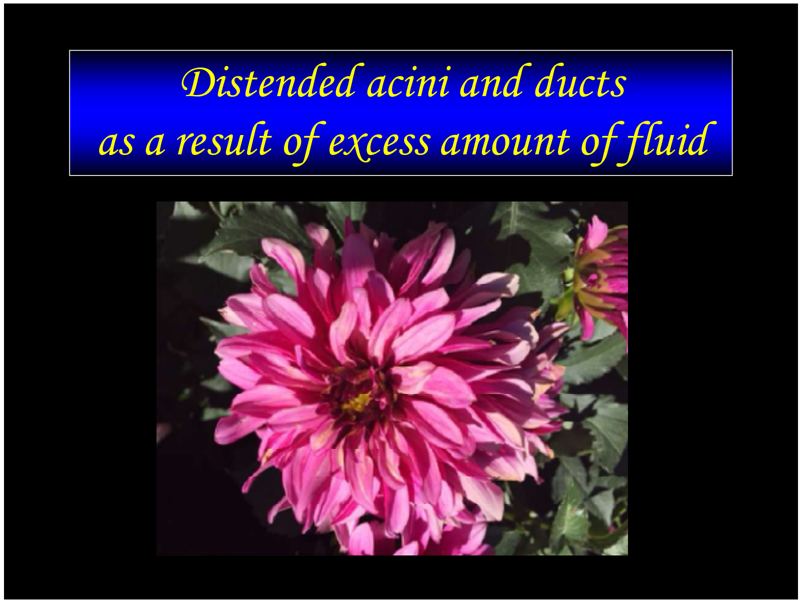
or from the duct(s)

PASH originates from the extralobular connective tissue

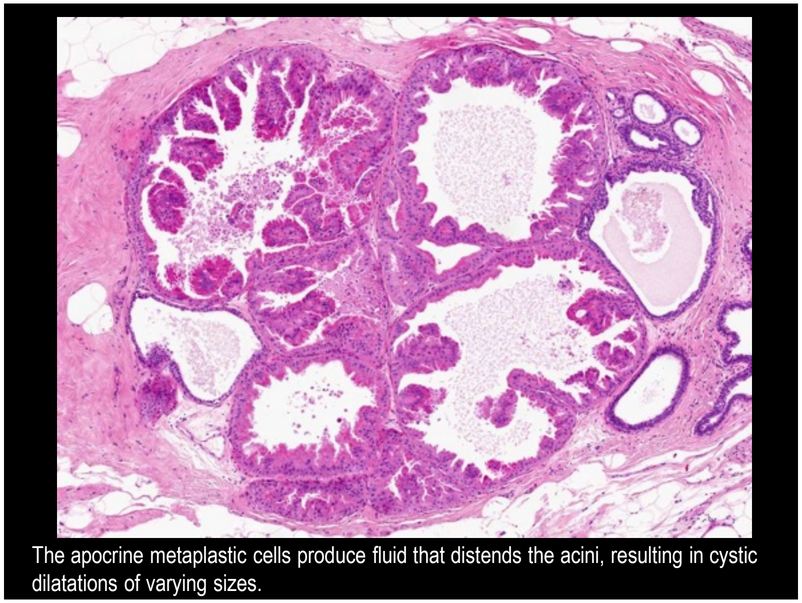


Fibrocystic change

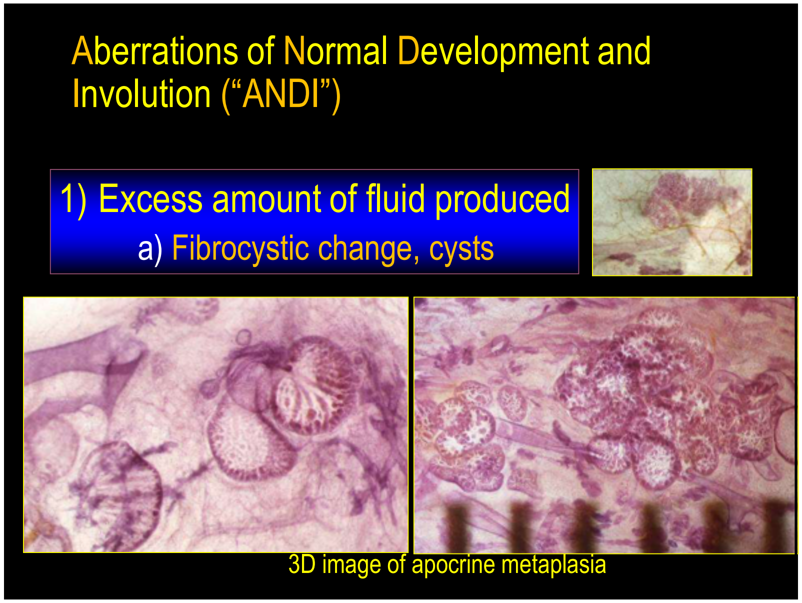
The apocrine metaplastic cells produce a protein-rich fluid, quite different in composition from milk.



Distended acini and ducts as a result of excess amount of fluid



The apocrine metaplastic cells produce fluid that distends the acini, resulting in cystic dilatations of varying sizes.

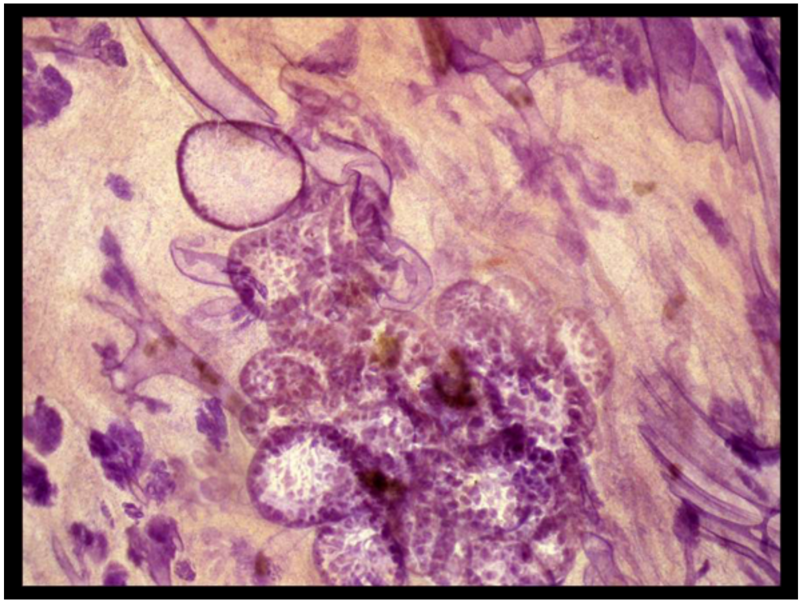


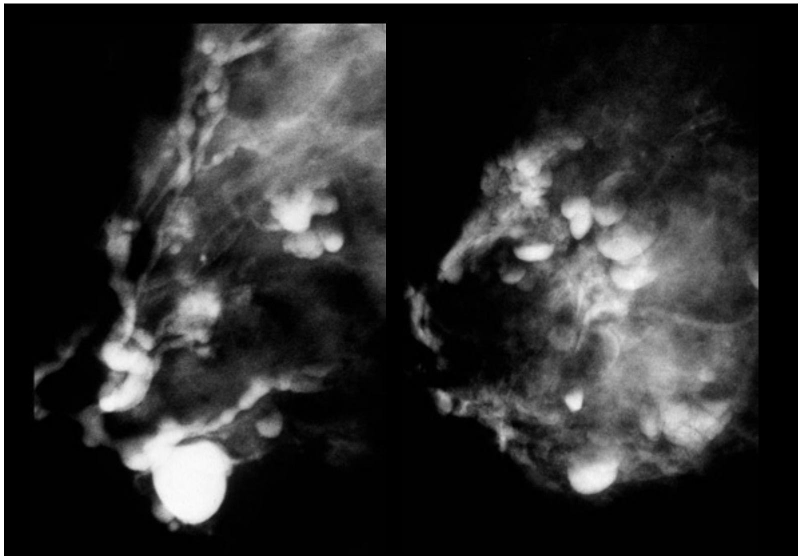
Aberrations of Normal Development and Involution (“ANDI”)

1) Excess amount of fluid produced

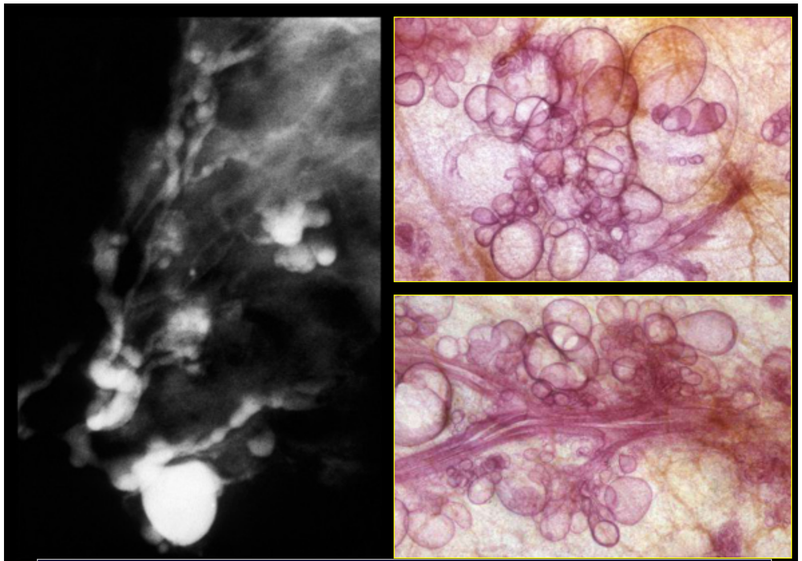
a) Fibrocystic change, cysts

3D image of apocrine metaplasia

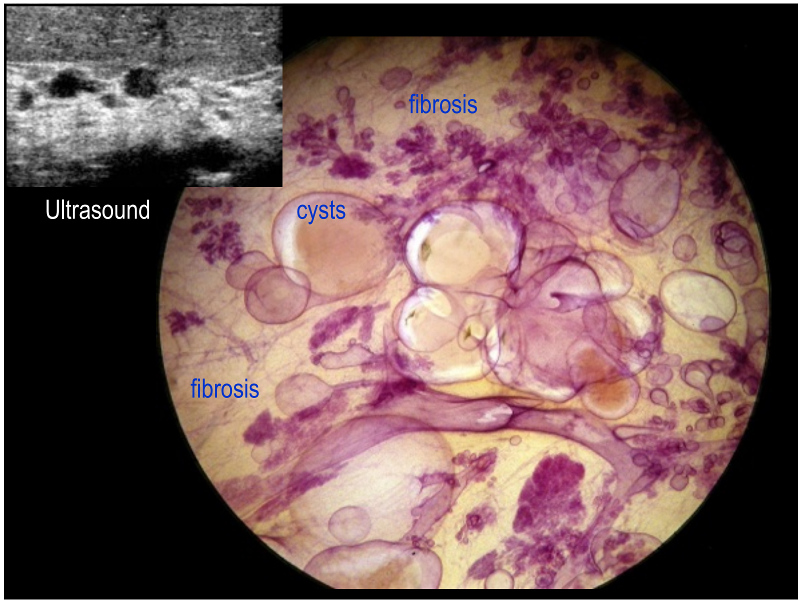


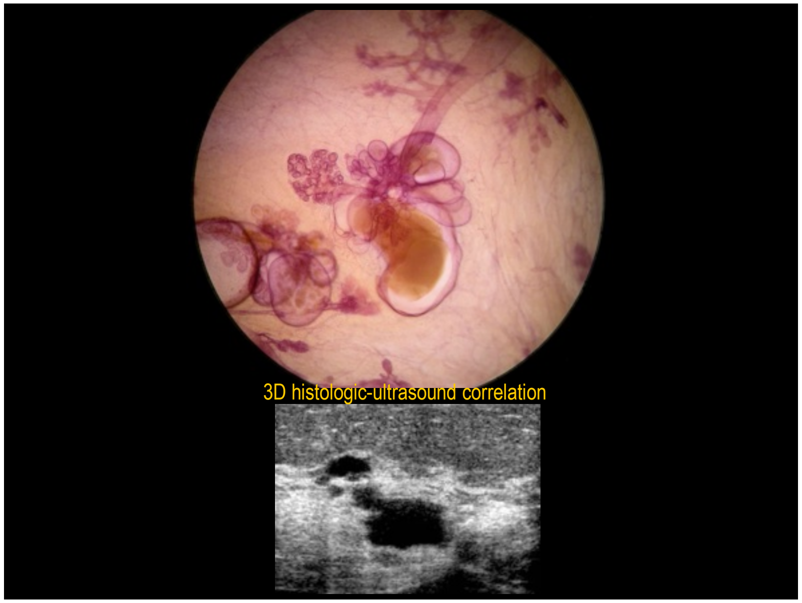


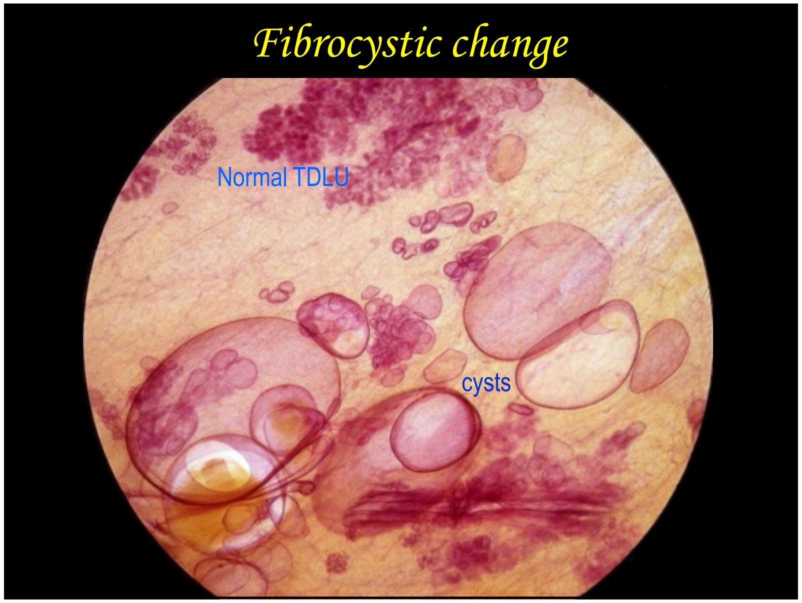
Multiple cysts surrounded by fibrosis



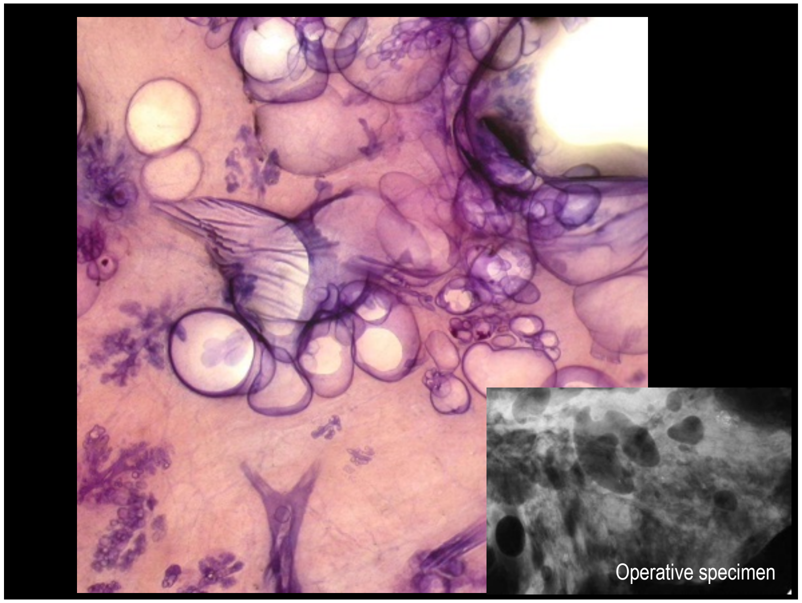
Comparative 3D histologic-galactographic images in fibrocystic change

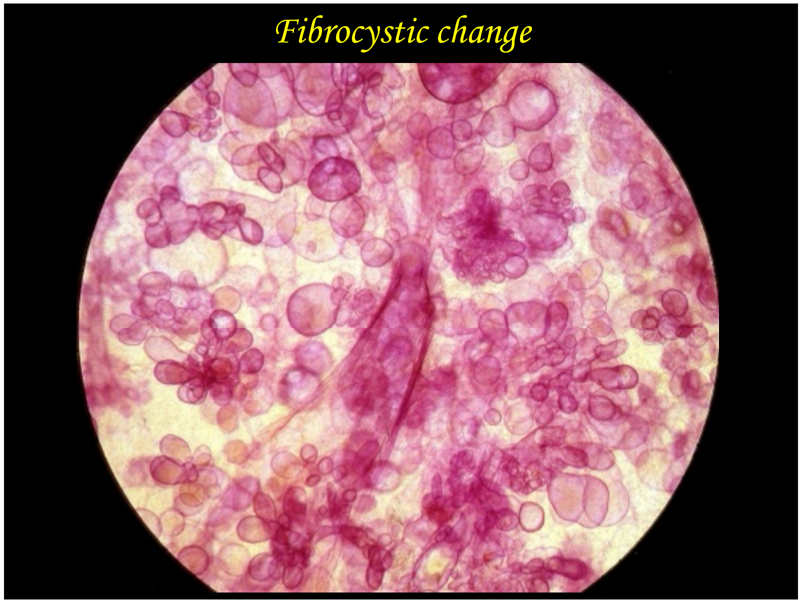

fibrosis
Ultrasound
cysts
fibrosis


3D histologic-ultrasound correlation


Fibrocystic change

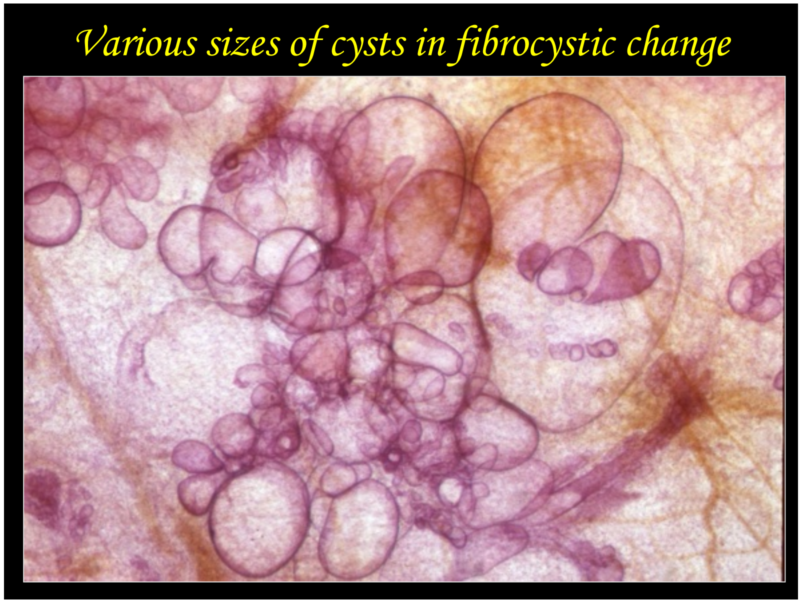
Normal TDLU
cysts


Operative specimen



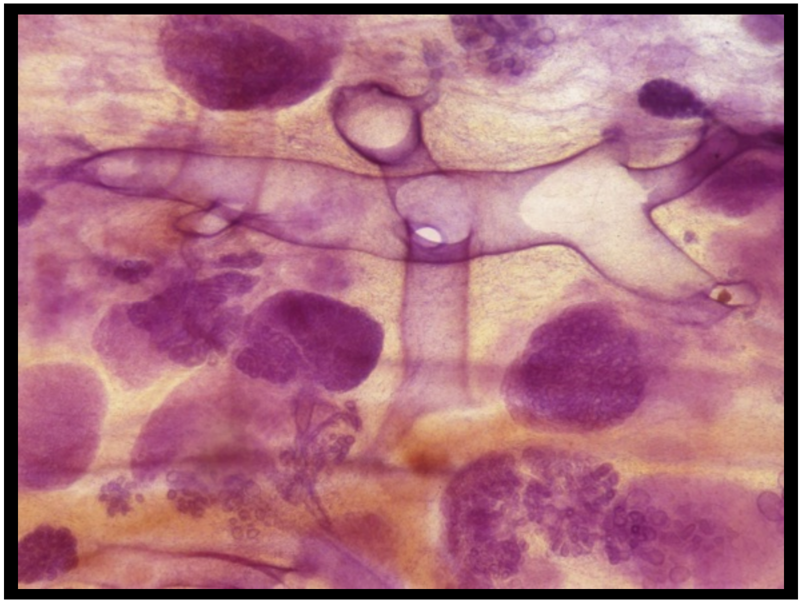
Fibrocystic change

153

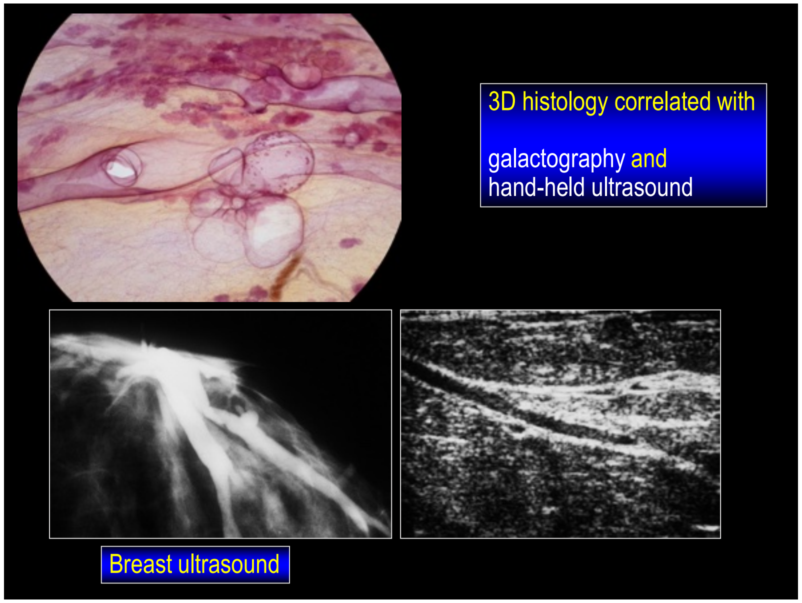


Various sizes of cysts in fibrocystic change

154



155



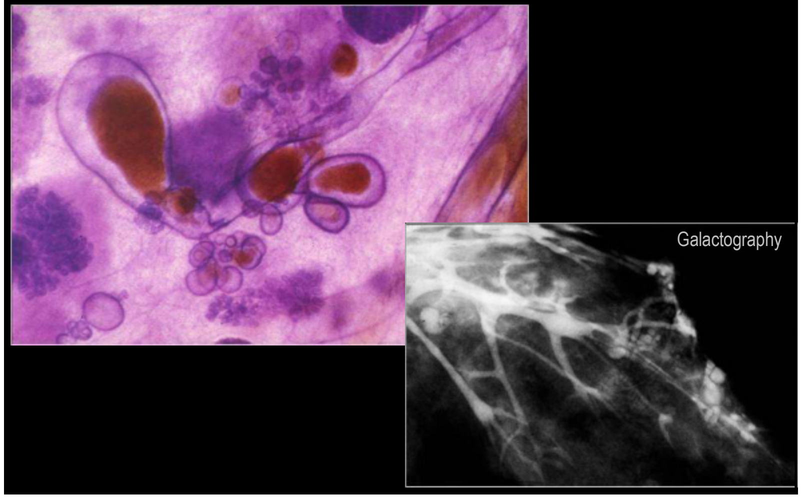
3D histology correlated with

galactography and
hand-held ultrasound

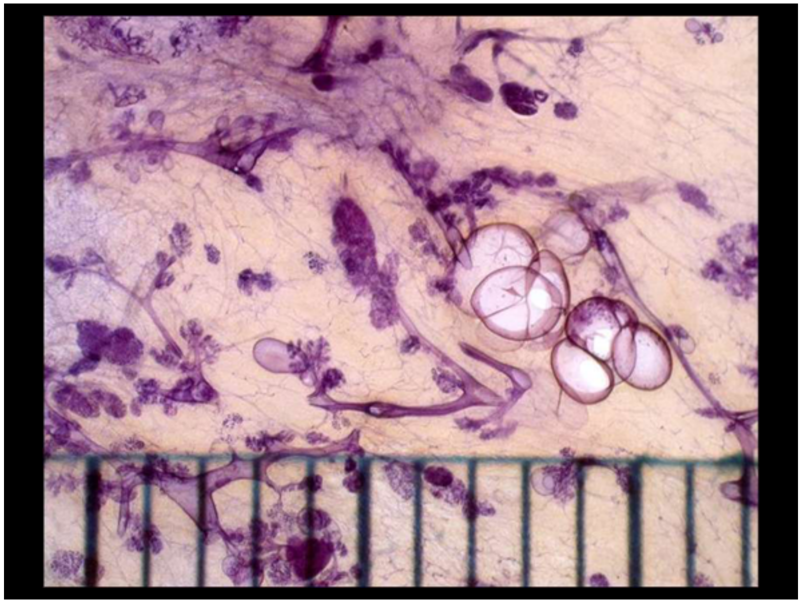
Breast ultrasound

156

Fibrocystic change


Galactography

157



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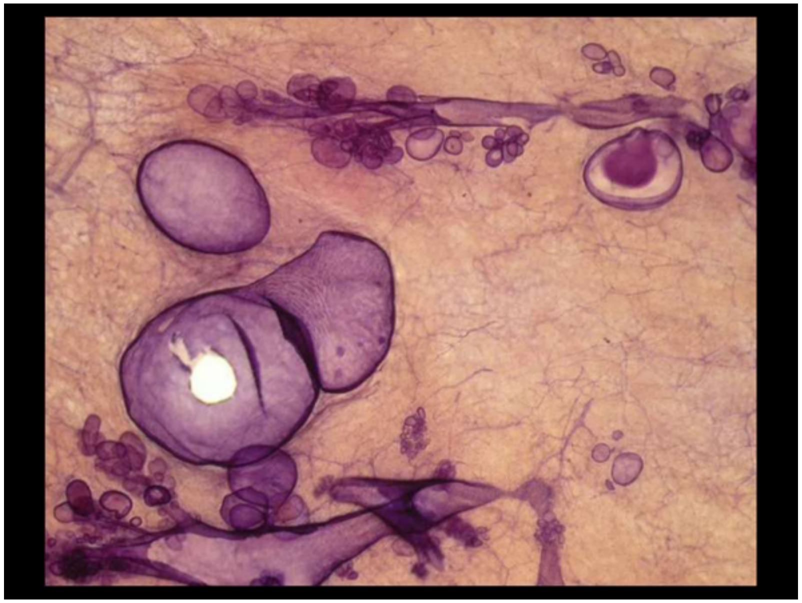

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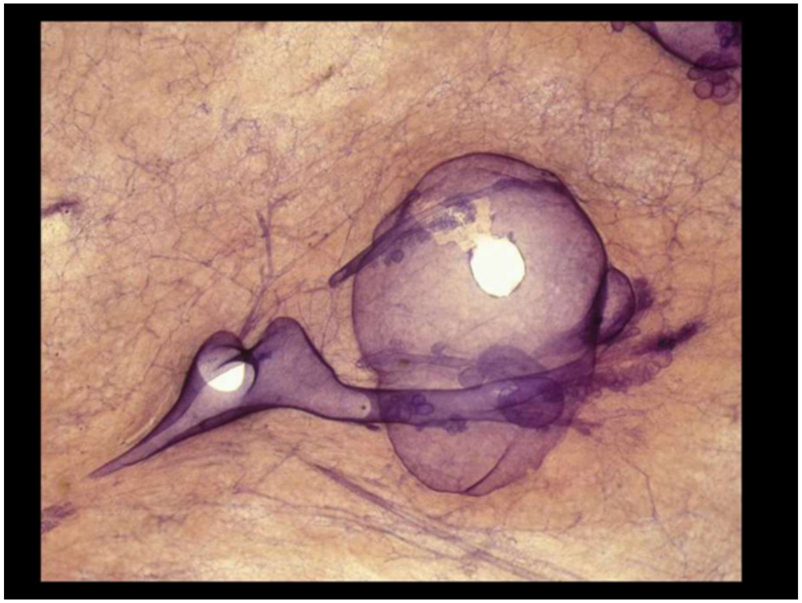

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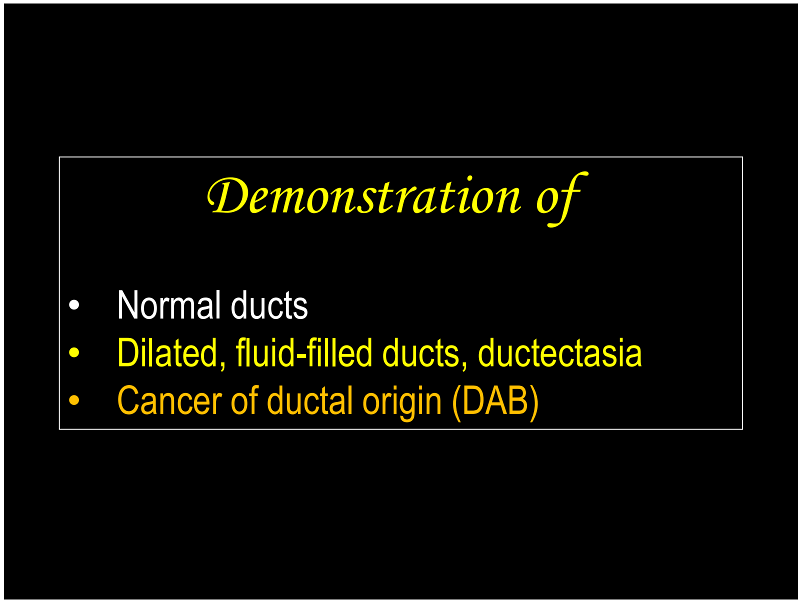
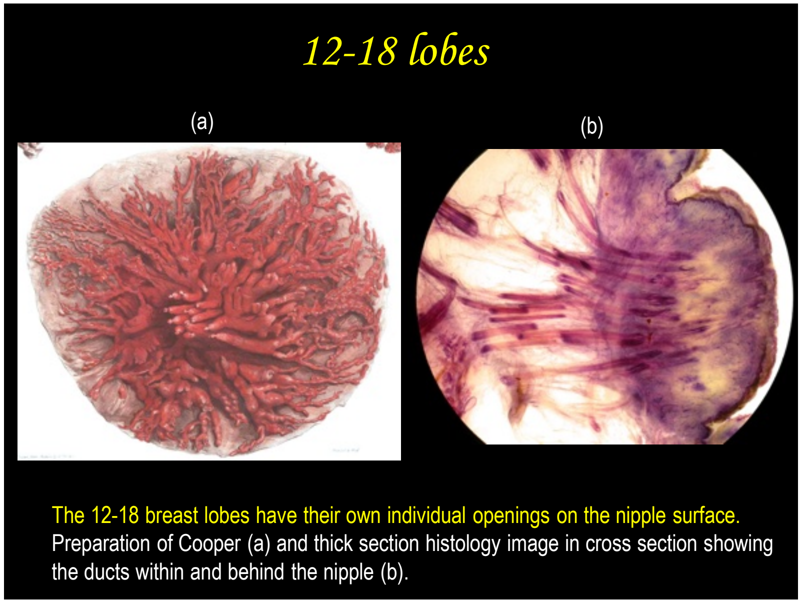


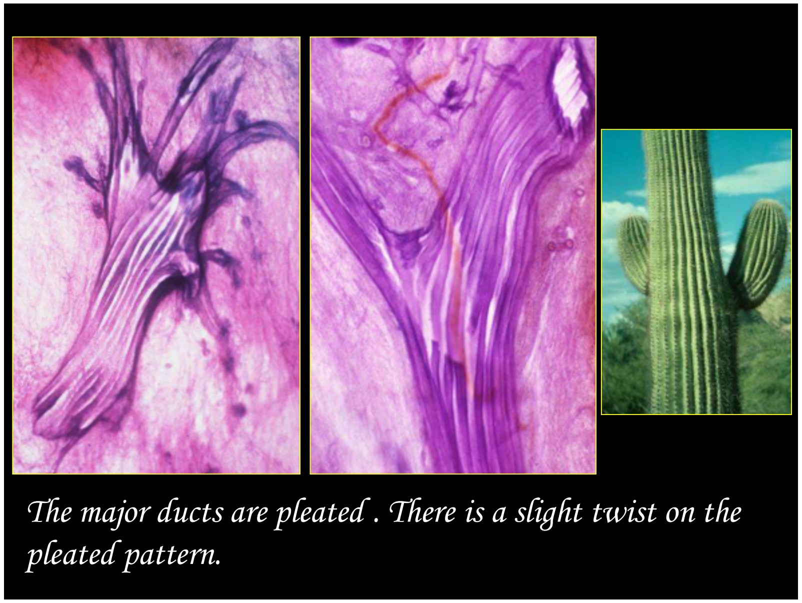
Demonstration of

- Normal ducts
- Dilated, fluid-filled ducts, ductectasia
- Cancer of ductal origin (DAB)

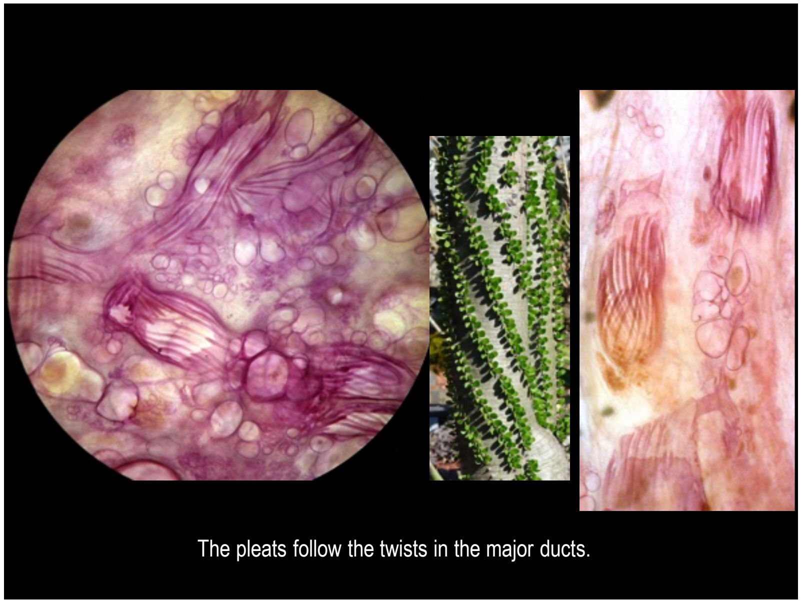


12-18 lobes

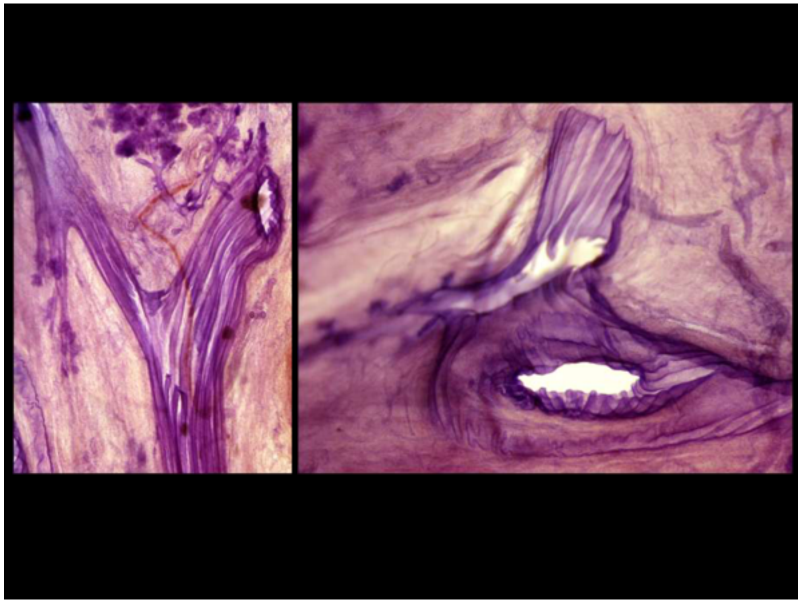
The 12-18 breast lobes have their own individual openings on the nipple surface. Preparation of Cooper (a) and thick section histology image in cross section showing the ducts within and behind the nipple (b).



The major ducts are pleated . There is a slight twist on the pleated pattern.



The pleats follow the twists in the major ducts.



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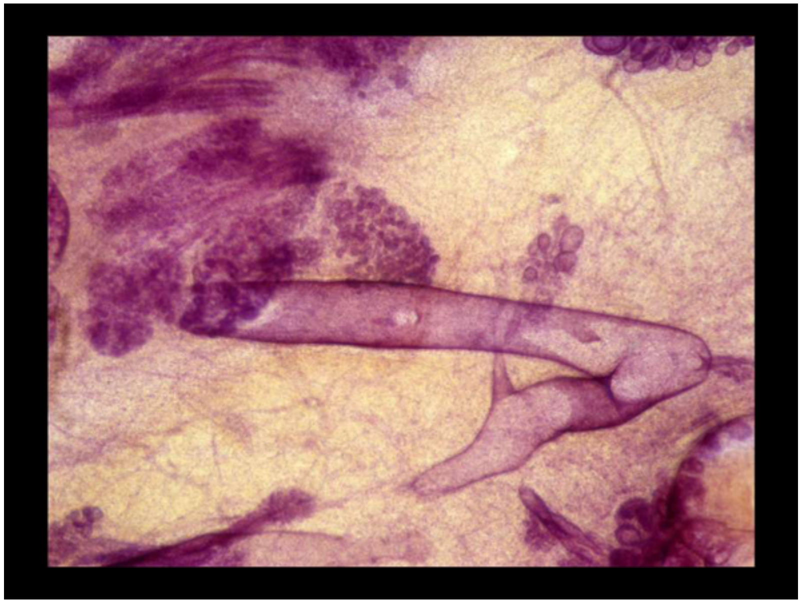
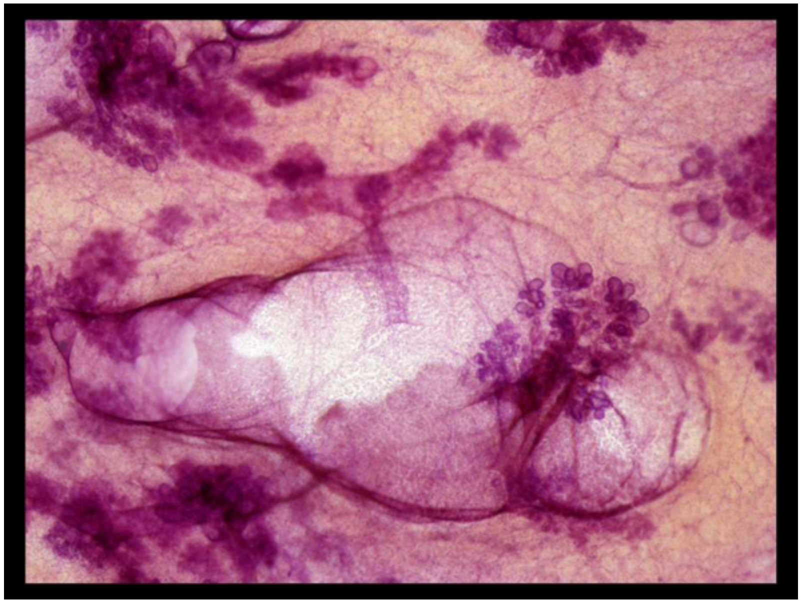


166

167

168



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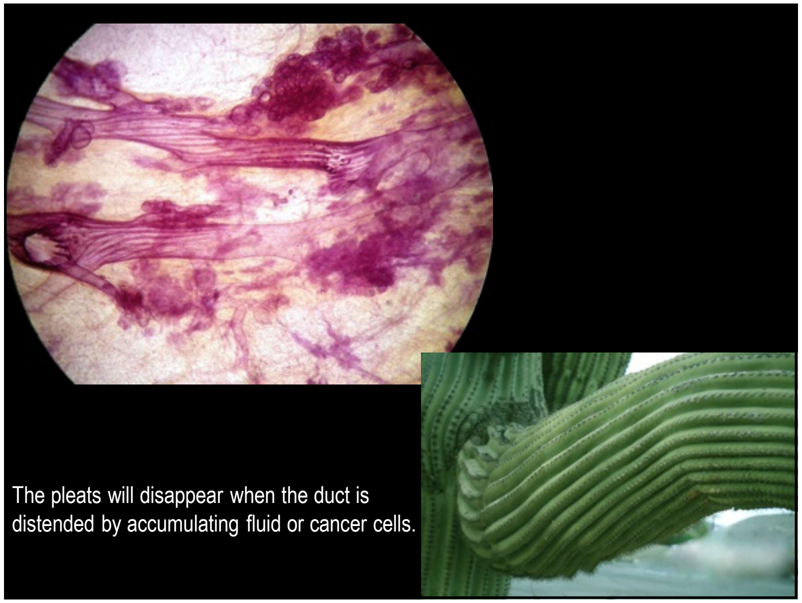
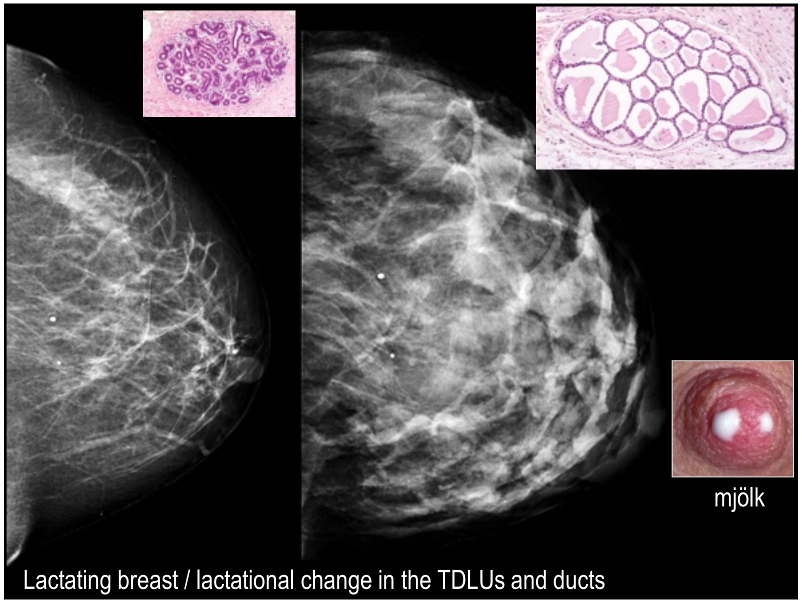


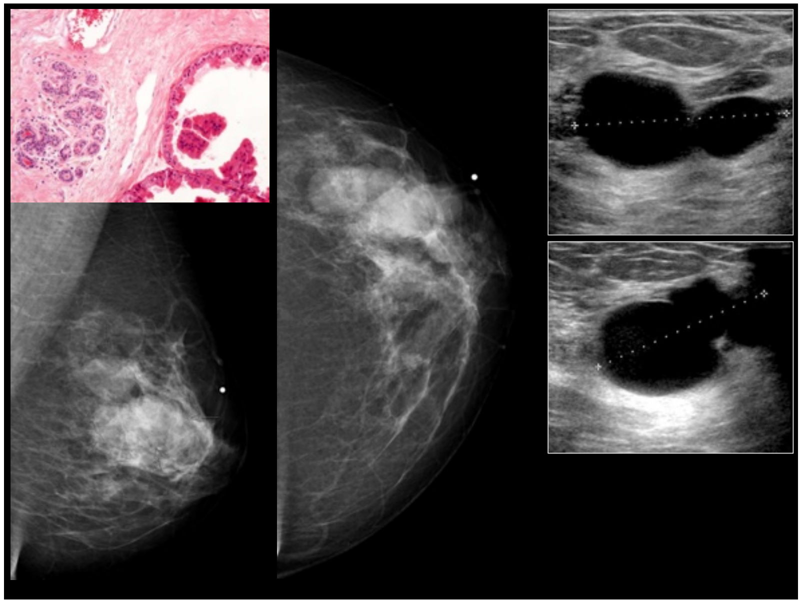
The pleats will disappear when the duct is distended by accumulating fluid or cancer cells.

170



Lactating breast / lactational change in the TDLUs and ducts

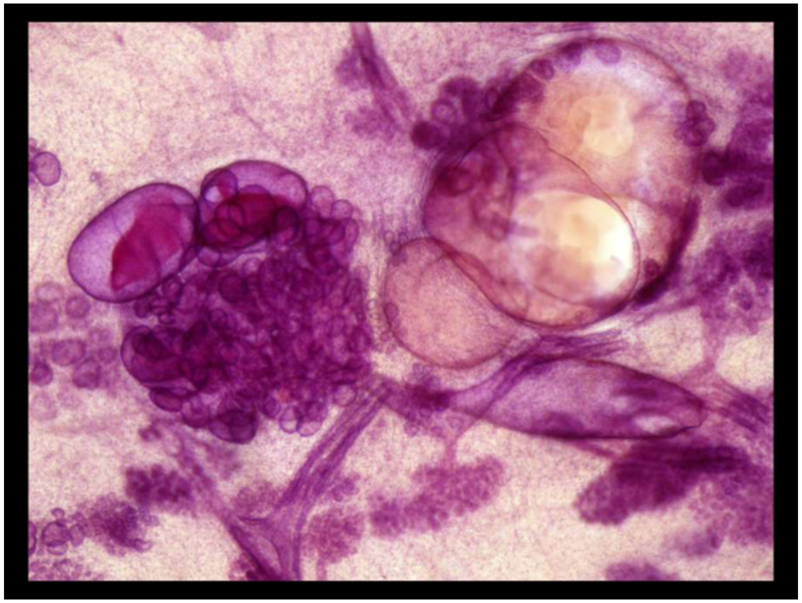
171



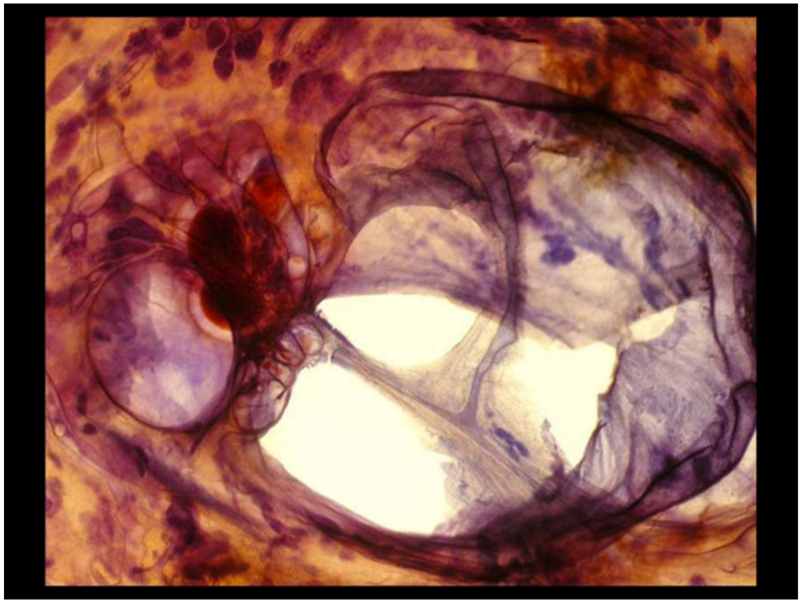
172

Breast cysts

173



174



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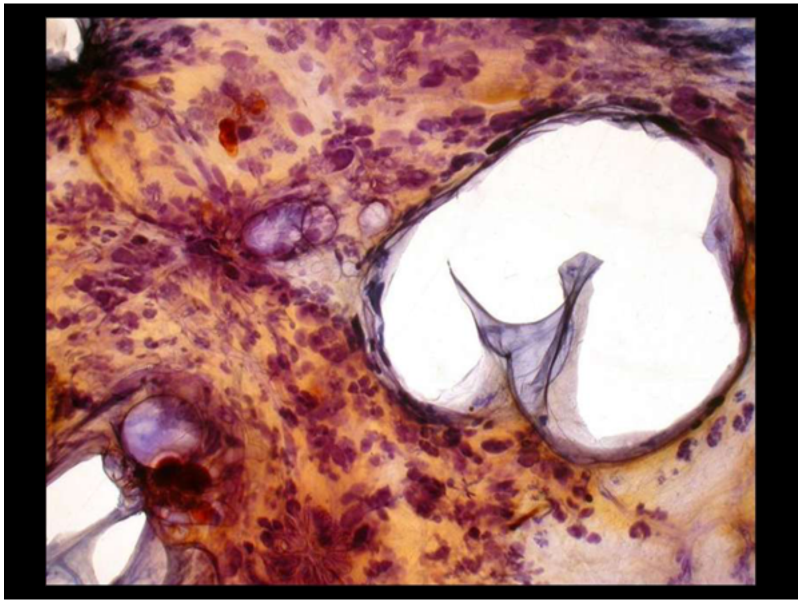

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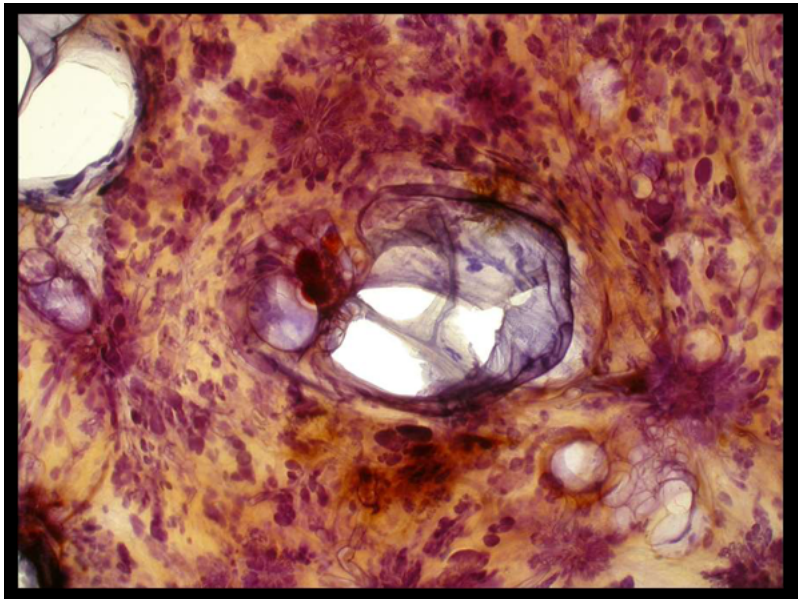

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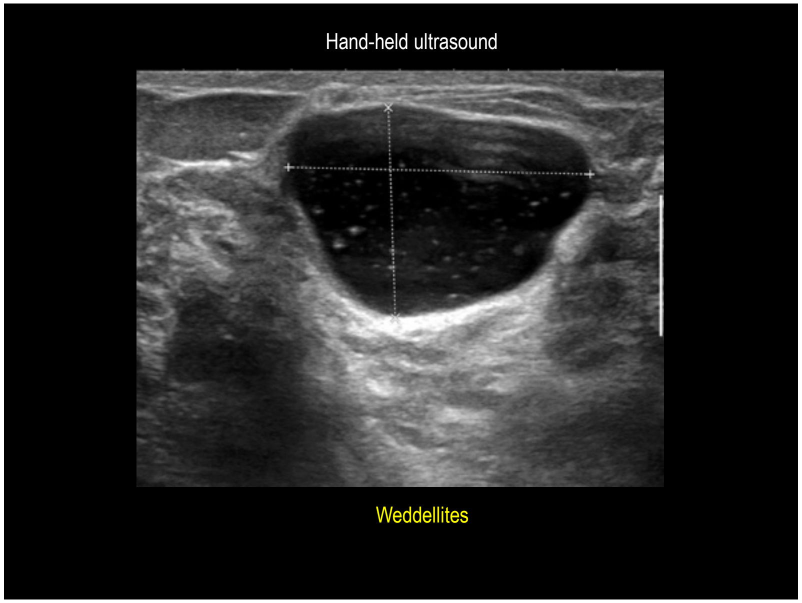
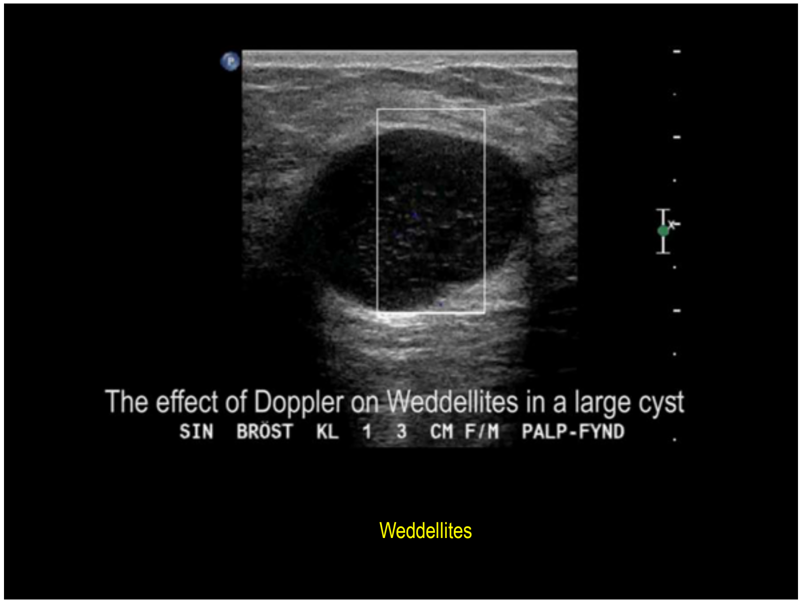


Hand-held ultrasound

Weddellites

178

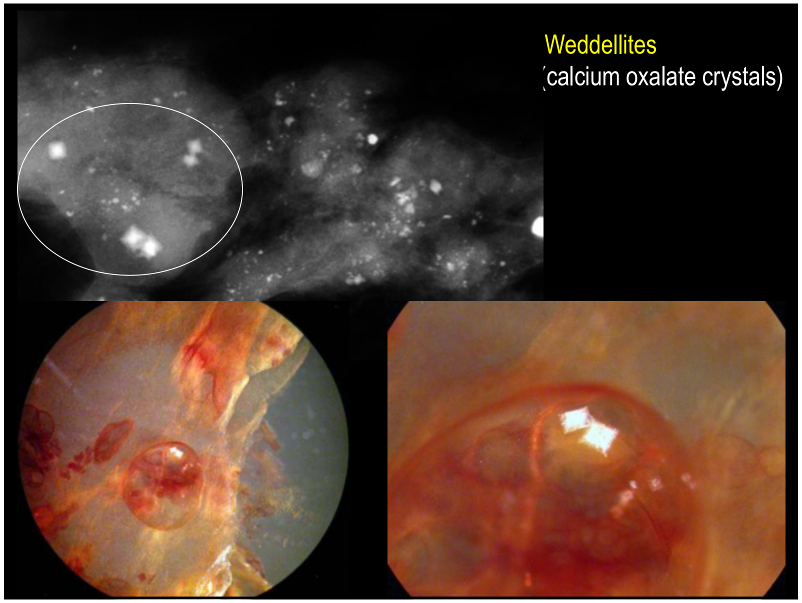


The effect of Doppler on Weddellites in a large cyst

SIN BRÖST KL 1 3 CM F/M PALP-FYND

Weddellites

179

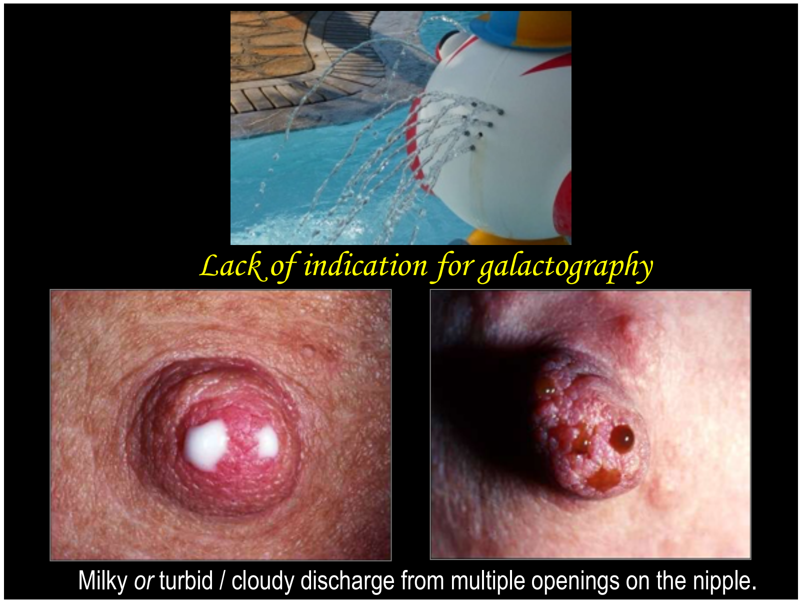


Weddellites
(calcium oxalate crystals)

180

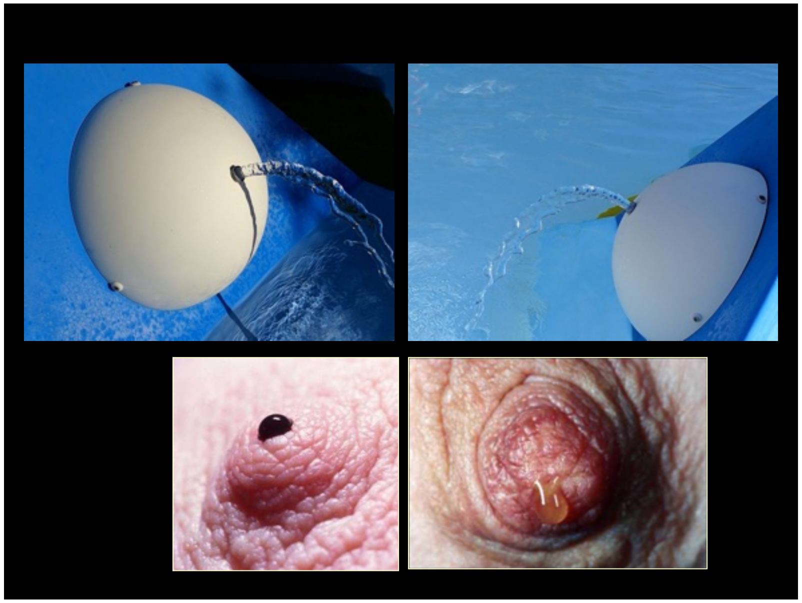
Nipple discharge of the breast.

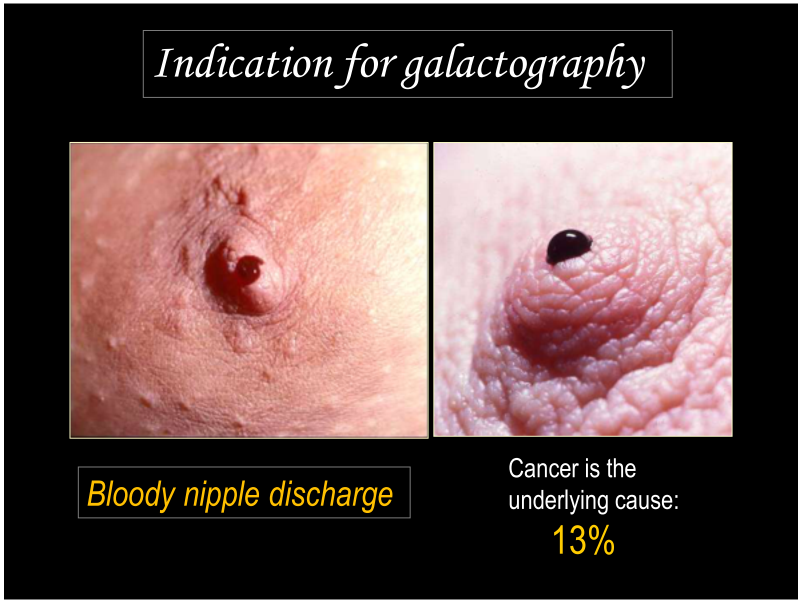
Bologna, Italy



Lack of indication for galactography

Milky *or* turbid / cloudy discharge from multiple openings on the nipple.

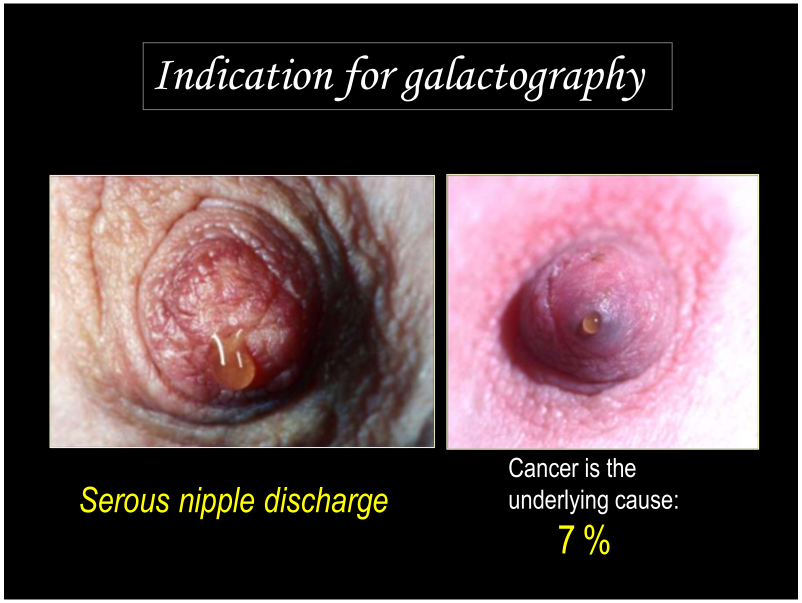




Indication for galactography

Bloody nipple discharge

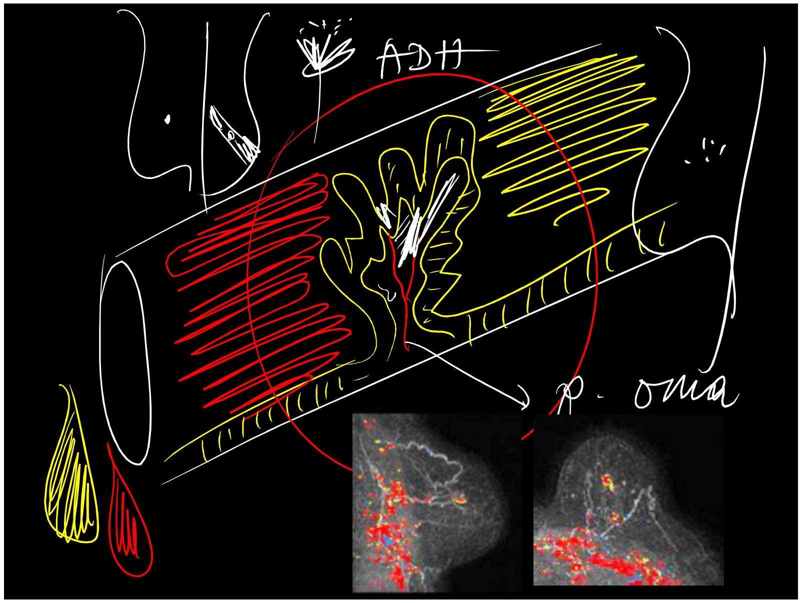
Cancer is the underlying cause: 13%

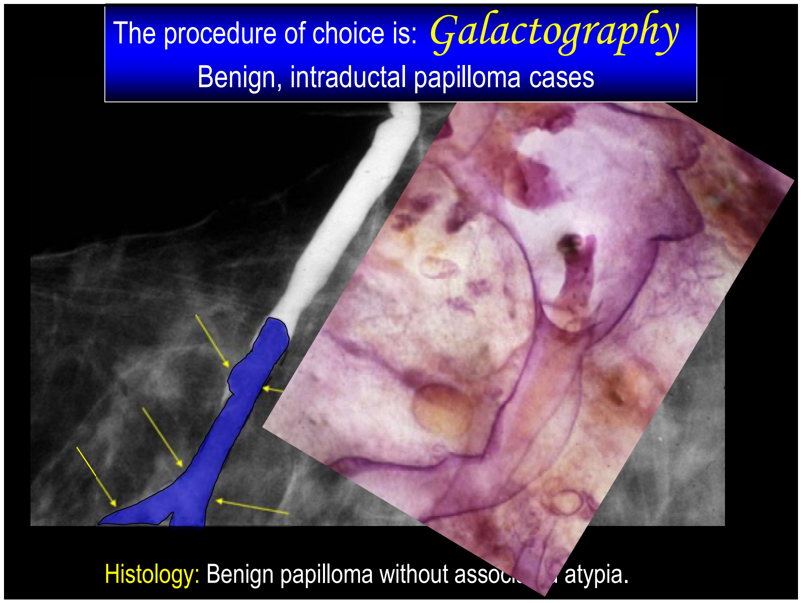


Indication for galactography

Serous nipple discharge

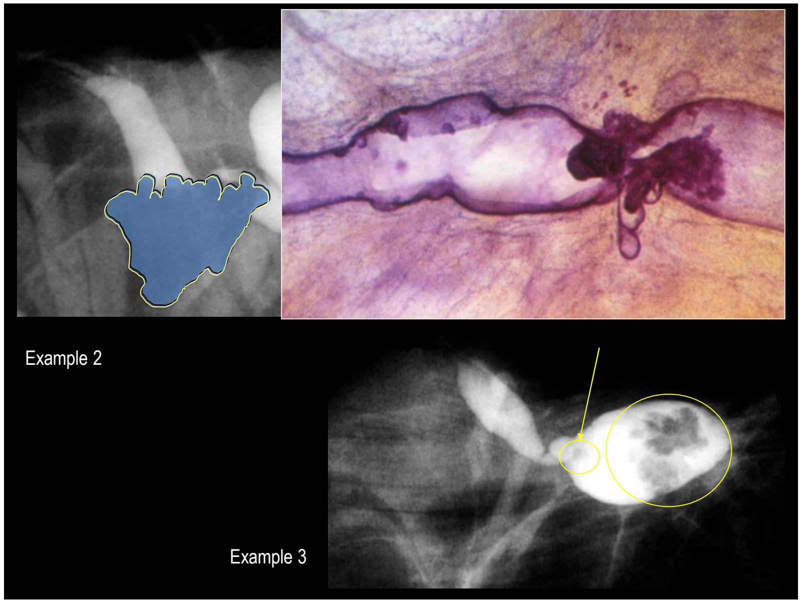
Cancer is the underlying cause:
7 %





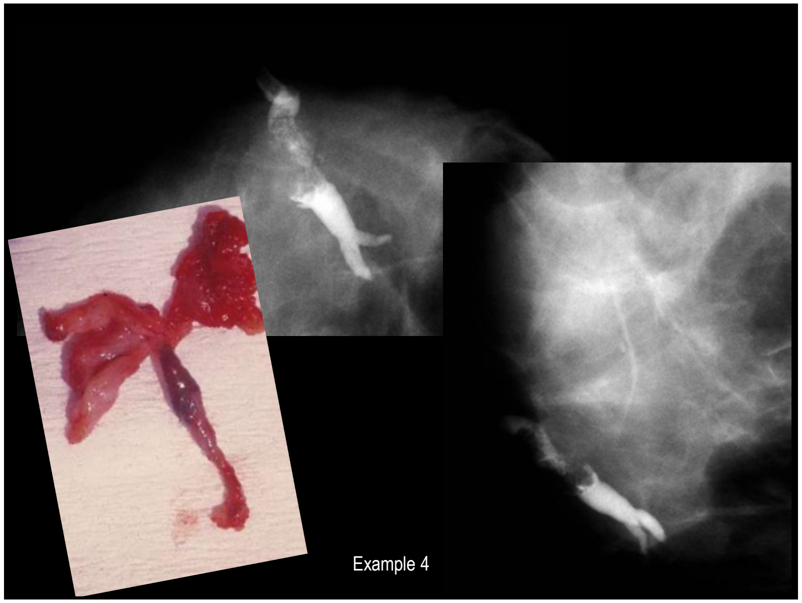
The procedure of choice is: *Galactography*
Benign, intraductal papilloma cases

Histology: Benign papilloma without assoc atypia.

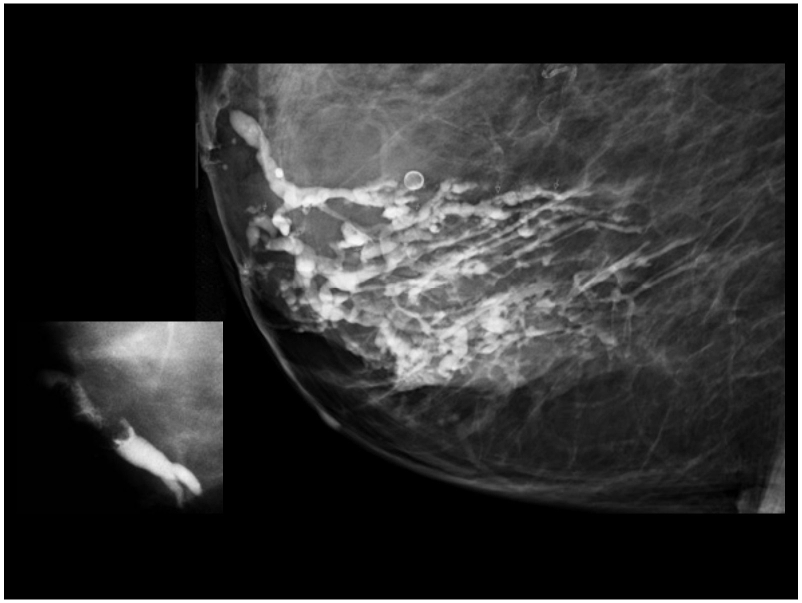


Example 2

Example 3



189



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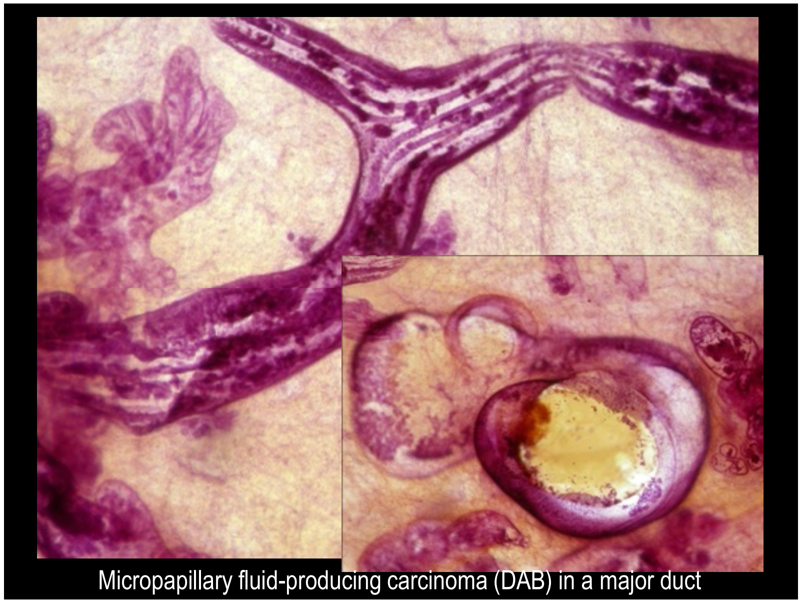
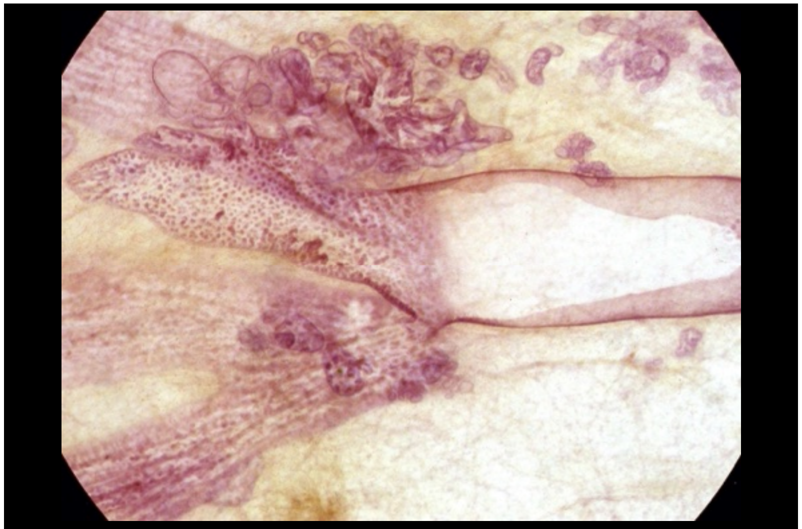


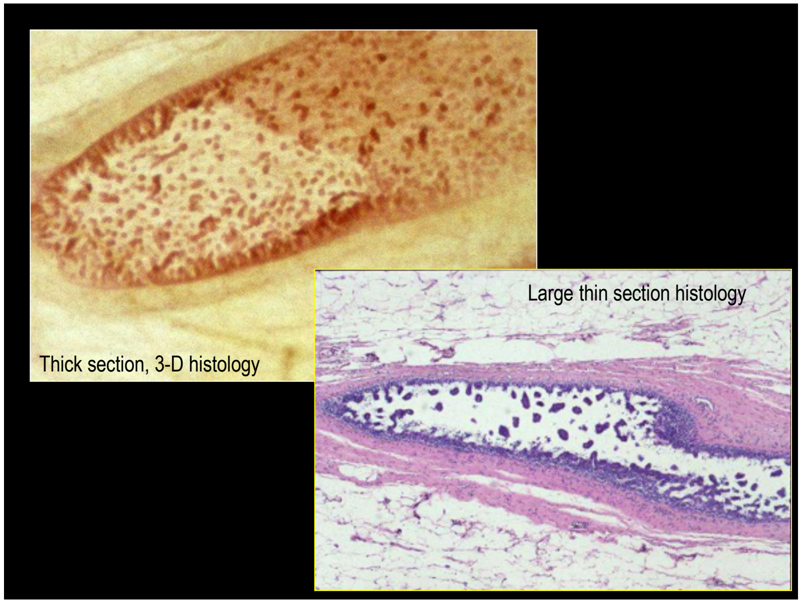
Micropapillary fluid-producing carcinoma (DAB) in a major duct

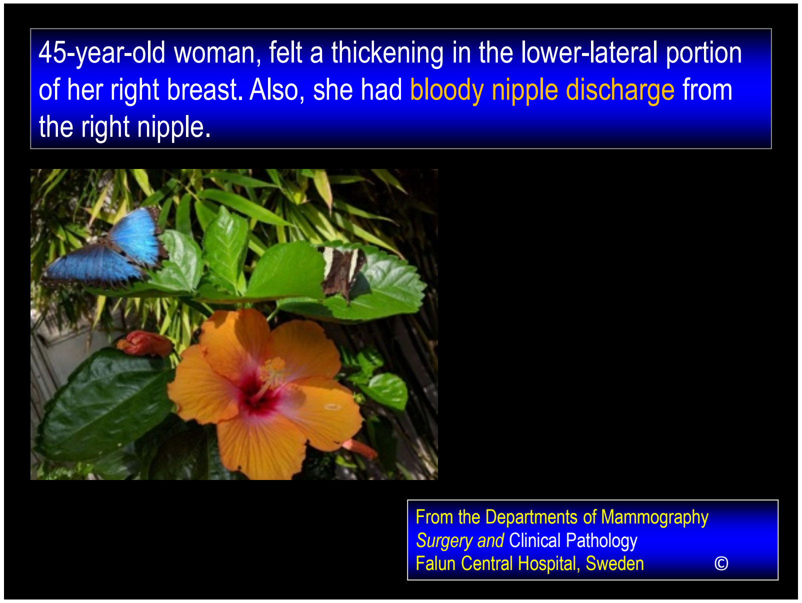
191



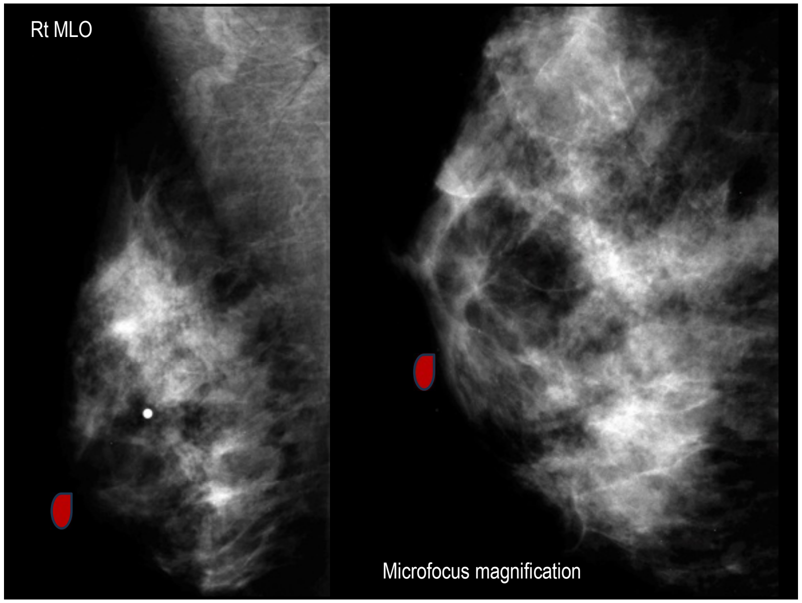
Micropapillary ductal adenocarcinoma (DAB) producing fluid, which distends the duct

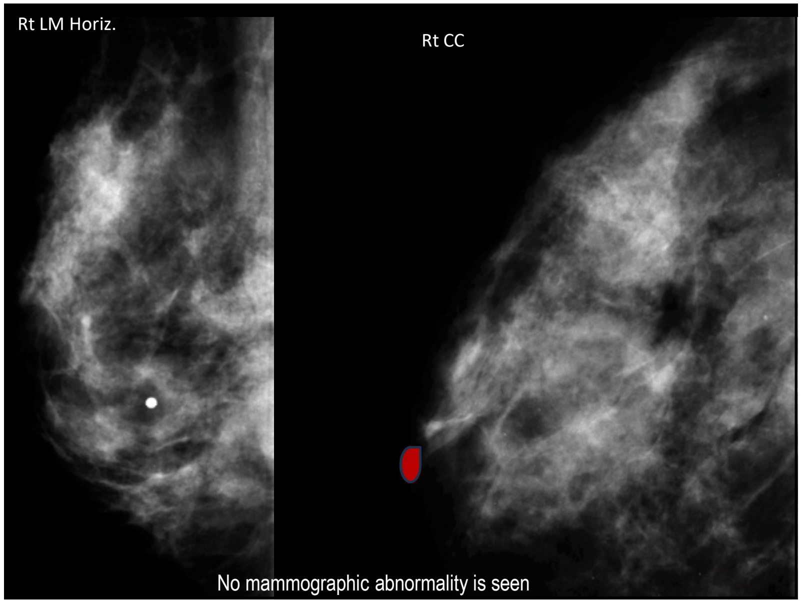
192


Thick section, 3-D histology
Large thin section histology

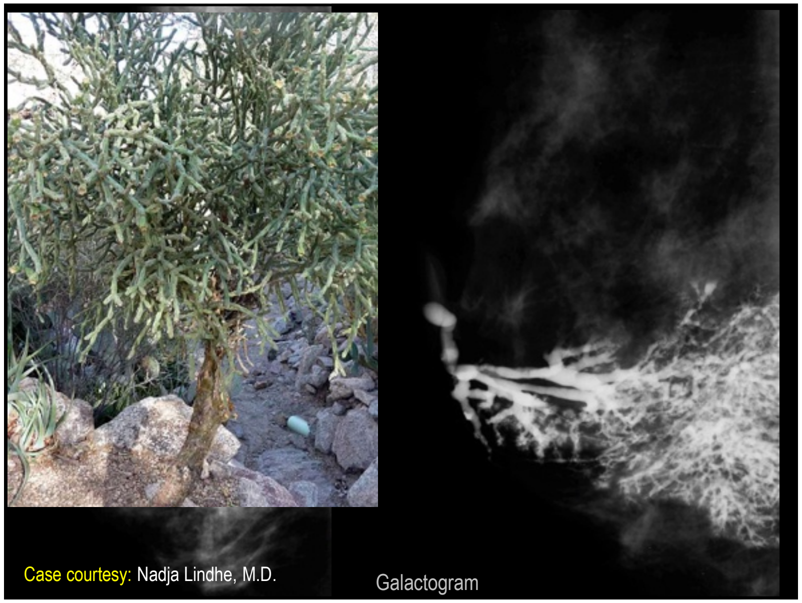

45-year-old woman, felt a thickening in the lower-lateral portion of her right breast. Also, she had bloody nipple discharge from the right nipple.

From the Departments of Mammography
Surgery and Clinical Pathology
Falun Central Hospital, Sweden ©


Rt MLO
Microfocus magnification

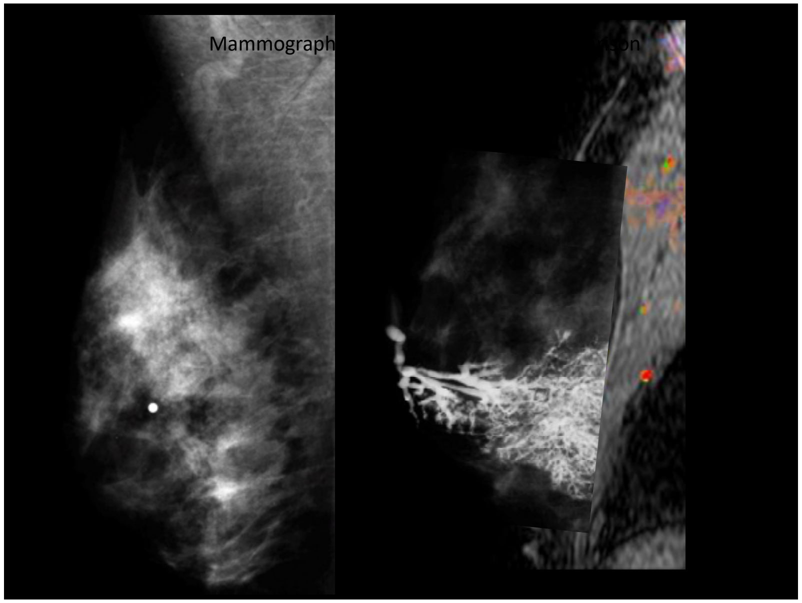

Rt LM Horiz.
Rt CC

No mammographic abnormality is seen

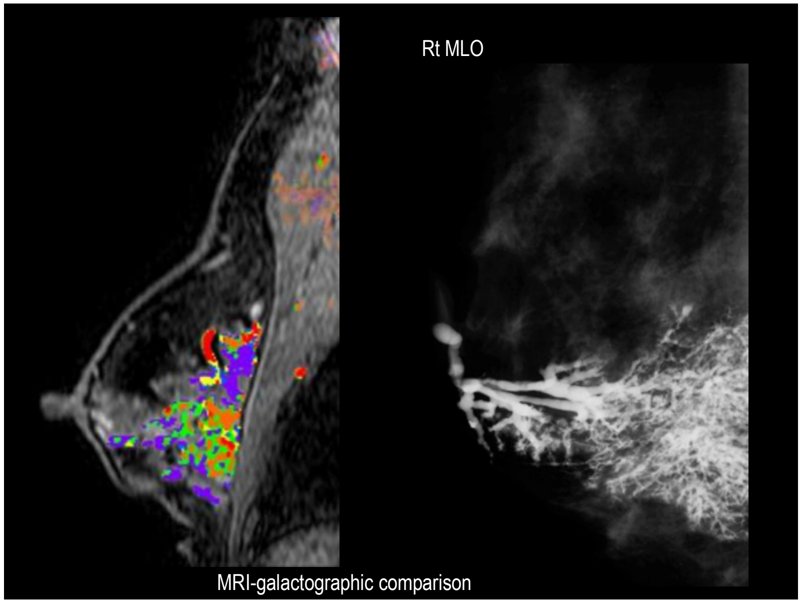

Case courtesy: Nadja Lindhe, M.D.

Galactogram

197

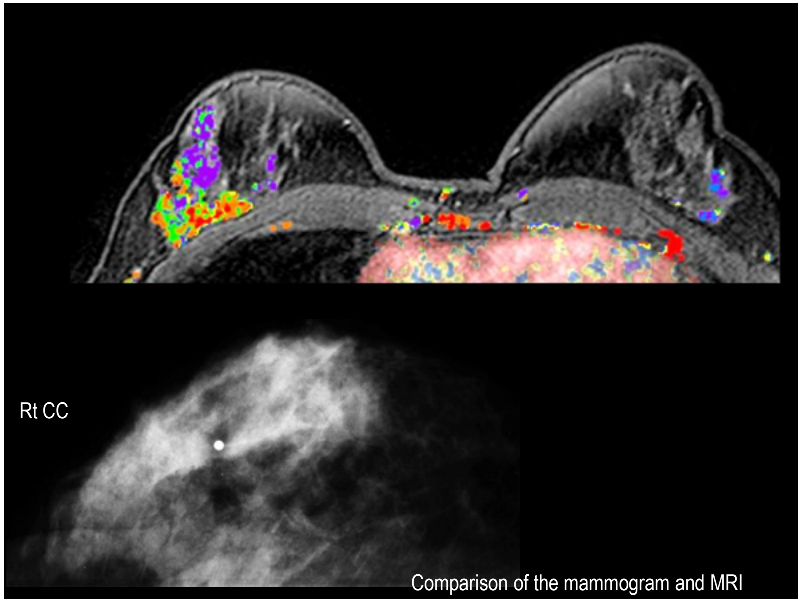

Mammograph

198


Rt MLO

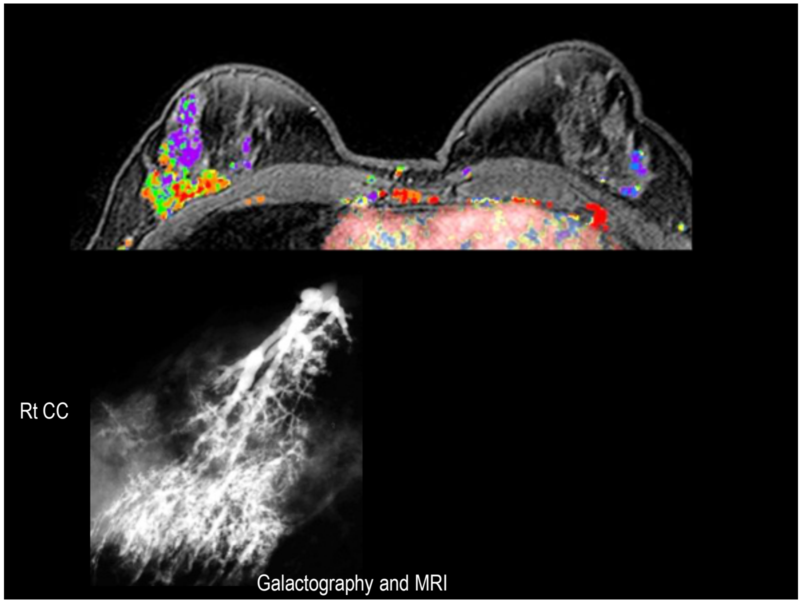
MRI-galactographic comparison

199

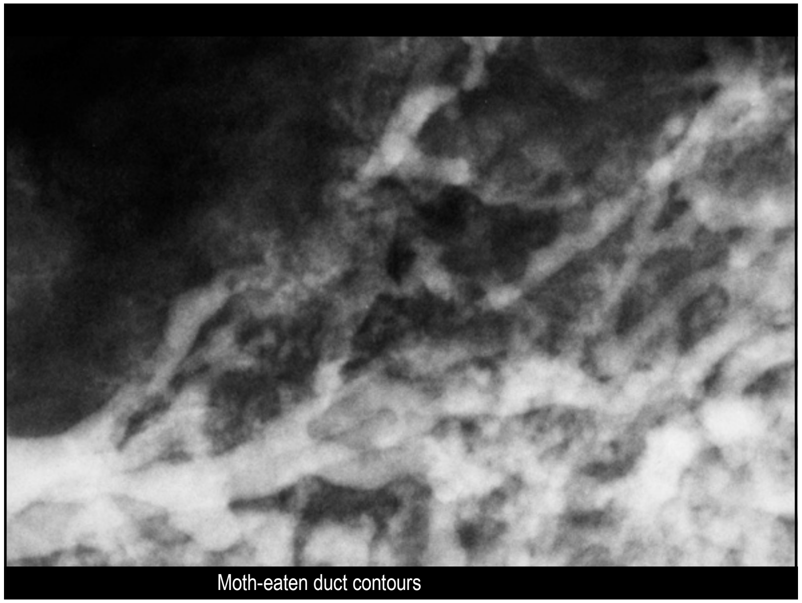

Rt CC

Comparison of the mammogram and MRI

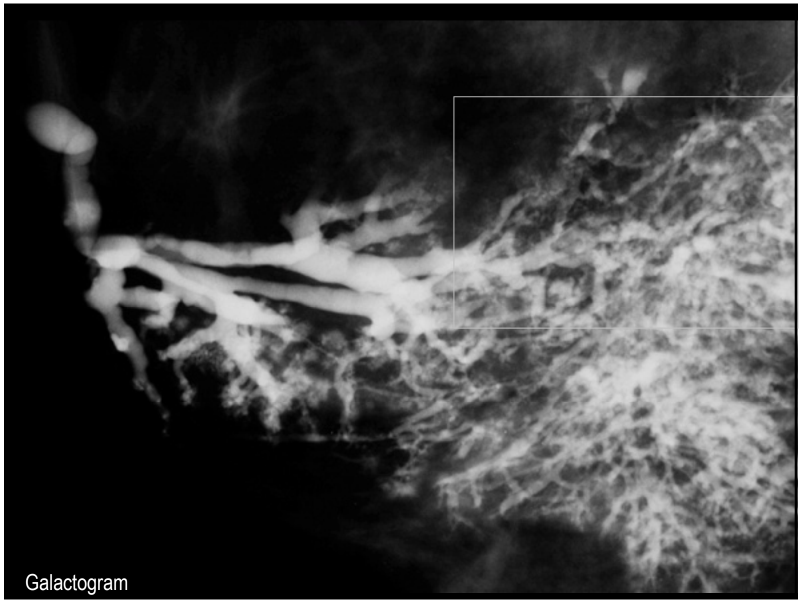
200


Rt CC
Galactography and MRI

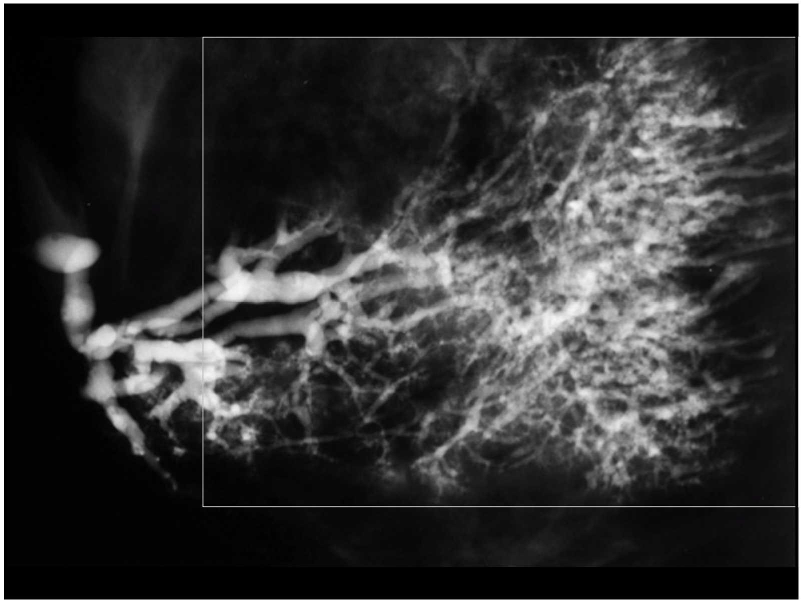
201


Moth-eaten duct contours

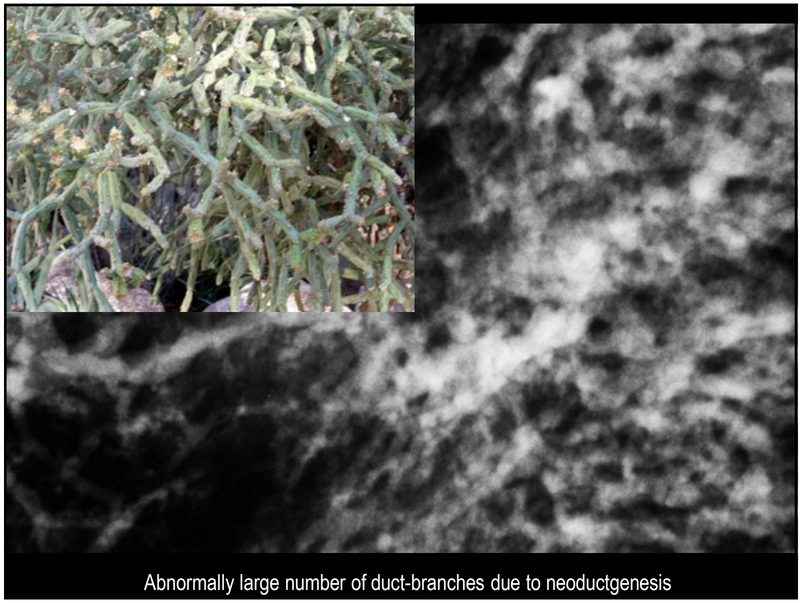
202


Galactogram

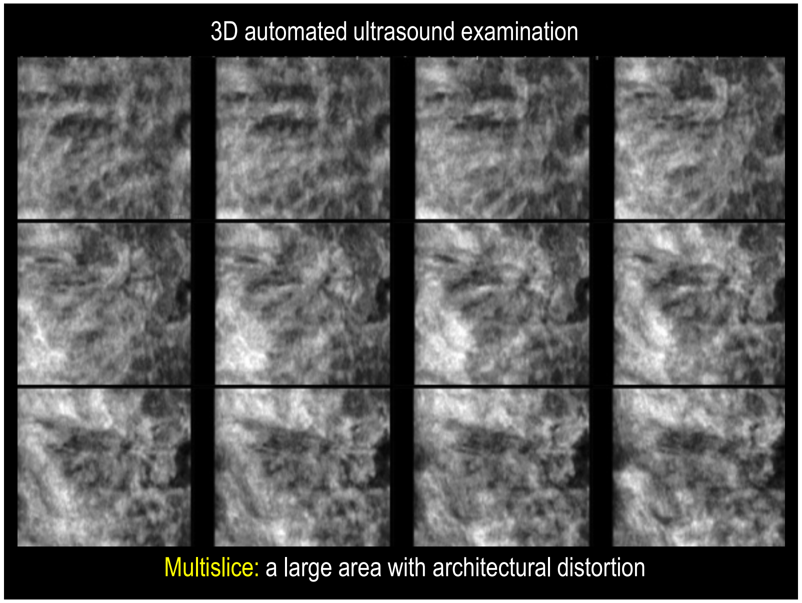
203



204

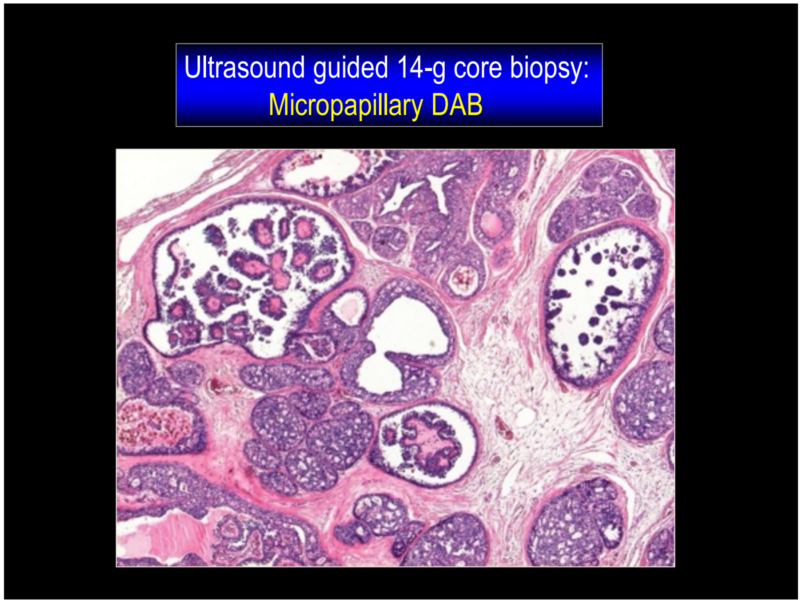


Abnormally large number of duct-branches due to neoductgenesis

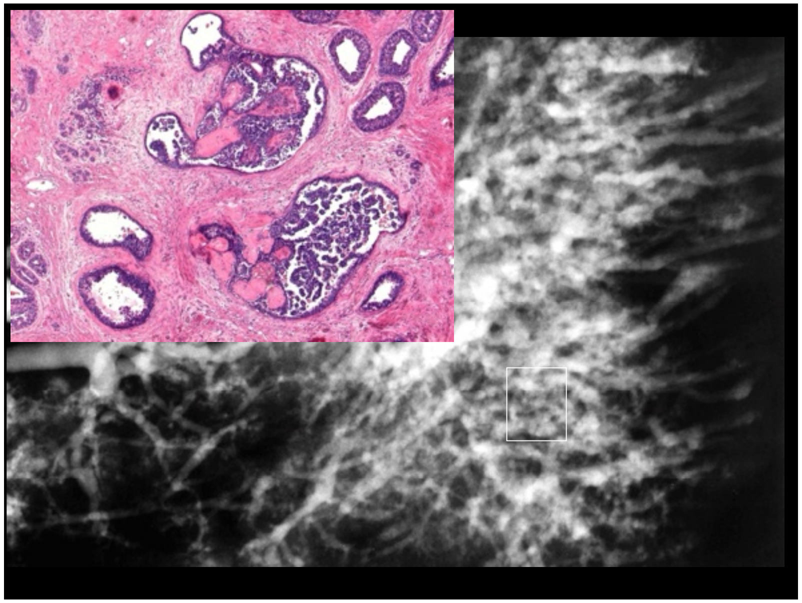


3D automated ultrasound examination

Multislice: a large area with architectural distortion



Ultrasound guided 14-g core biopsy:
Micropapillary DAB



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