DANI SRPSKE MEDICINSKE DIJASPORE 2012,
Srbija, Oktobar 4-6, 2012

Preoperativna i intraoperativna dijagnostika u hirurškoj patologiji dojke

Tibor Tot, Švedska

Practical approach: preop

- **The need for neoadjuvant therapy**
- **Type of surgical intervention:**

  the breast
- **Type of surgical intervention:**

  the axilla

Practical approach: patient history

- Woman or man ?
- Young or elderly ?
- Previous breast pathology
- Recurrence ? Ipsilateral or contralateral ?
- Detection mode ?
- Localization within the breast ?
- Palpable ? Discharge ? Skin lesions ?
- Axilla ?

Practical approach: patient history

- Detection mode:
  - screening
  - outside screening
  - interval cancer
  - follow-up

The aim of preoperative diagnosis

- The get a **minimum** of sufficient material
- To motivate **proper** therapeutic interventions
- To **not harm** the patient

Primum non nocere !

Seeding of tumour cells following breast biopsy

- Loughran CF and Keeling CP, BJR 2011, 84:869-74, review 10 papers, 3643 patients

- There is histological evidence of seeding of tumor cells from primary neoplastic sites to adjacent breast tissue following biopsy.
- The incidence is declining with prolonged time between needling and surgery.

Seeding of tumour cells following breast biopsy

- Loughran CF and Keeling CP, BJR 2011, 84:869-74, review 10 papers, 3643 patients

- Needling procedure may cause hematogeneous dissemination of breast cells

Seeding of tumour cells following breast biopsy

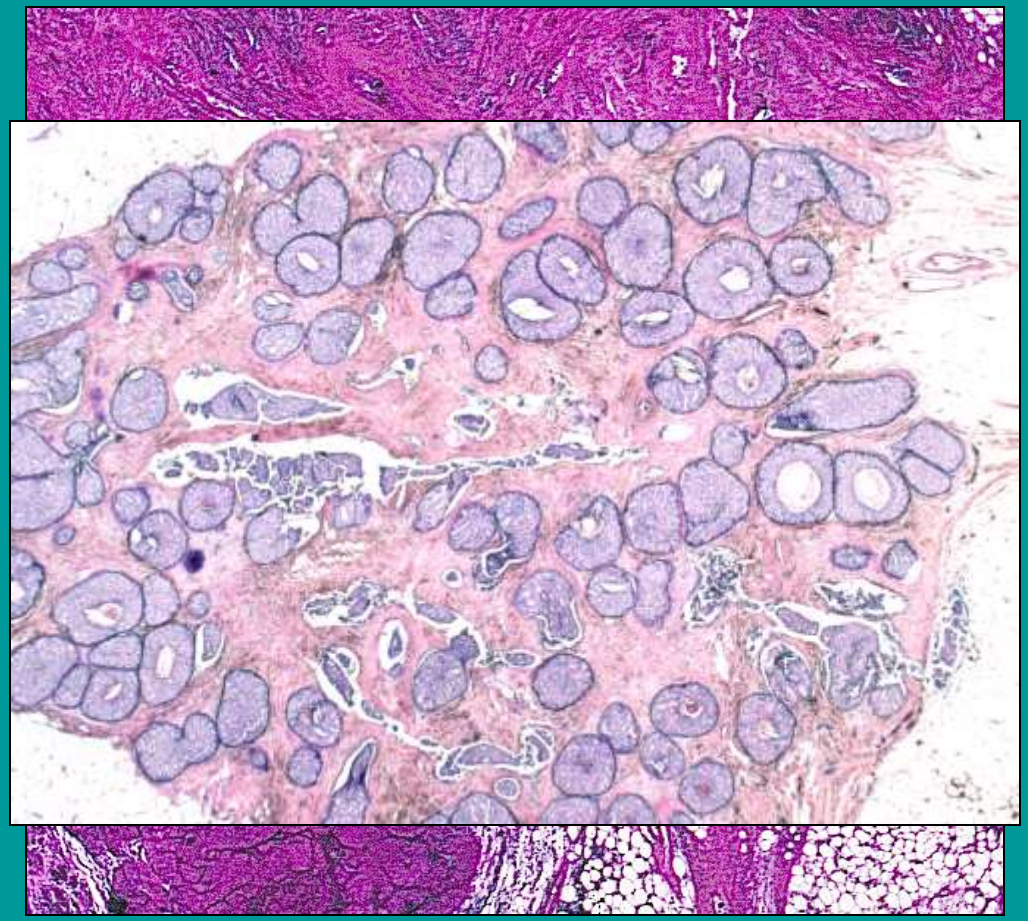
- Loughran CF and Keeling CP, BJR 2011, 84:869-74, review 10 papers, 3643 patients

- Clinical recurrence at the site of needle biopsy is uncommon and the relationship between biopsy and later recurrence is difficult to confirm.

Seeding of tumour cells following breast biopsy

- Loughran CF and Keeling CP, BJR 2011, 84:869-74, review 10 papers, 3643 patients

- There is some evidence to suggest that cell seeding may be reduced when vacuum biopsy devices are deployed.



Needling artifacts in >80% of cases

Angulated ”empty” spaces in >60%

Needle track in >20%

Pseudotumor

Epithelial displacement in <10%

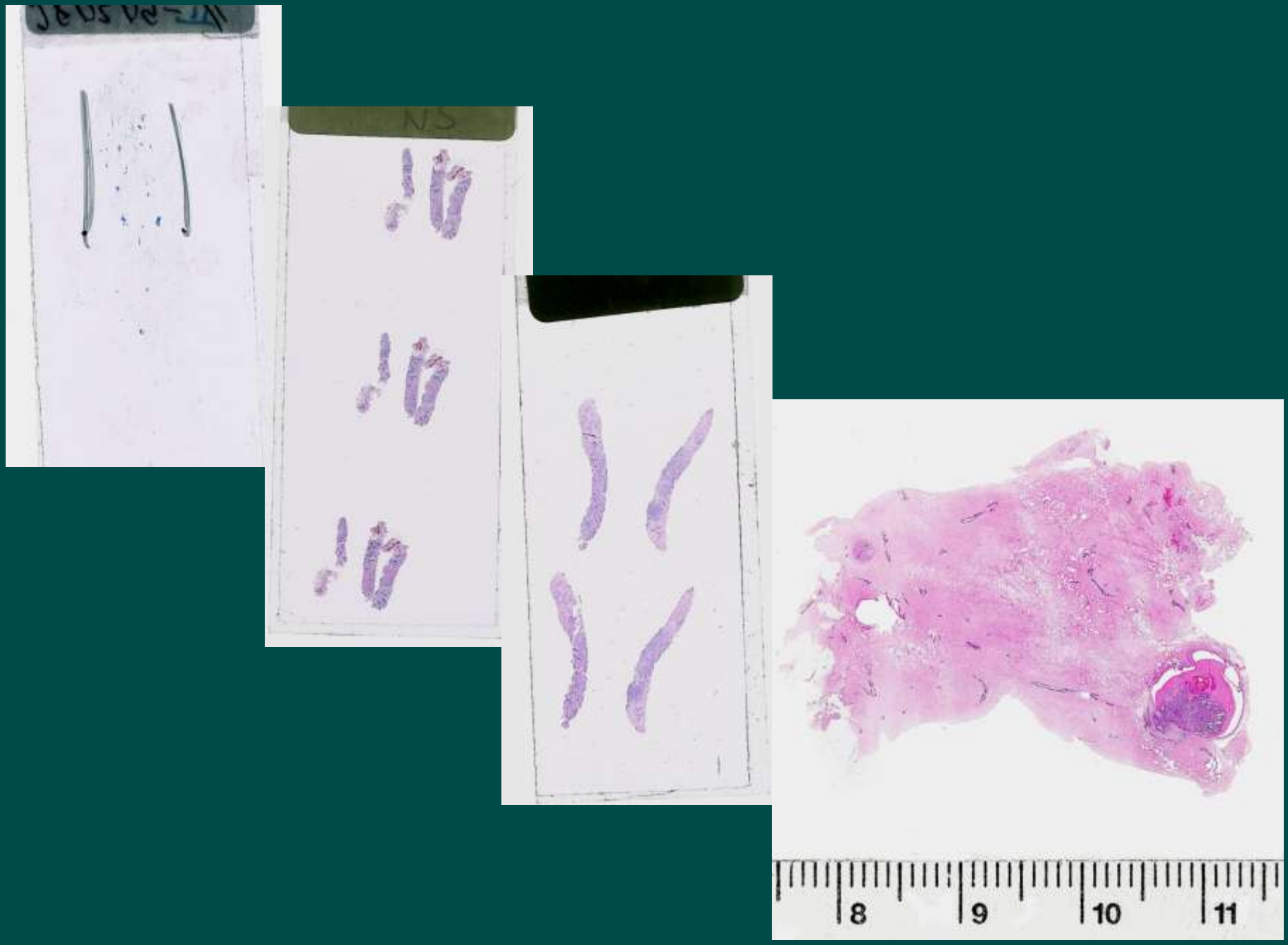
The preoperative needle biopsies are necessary but not totally free of risk.

Use the thinest effective needle !!!

Limit the number of biopsier/case !!

Thinest effective !

FNAB	26, 21 g
Needle biopsy	18 g
Core	14 g
Vacuum	11 g


8
9
10
11

Individual planning

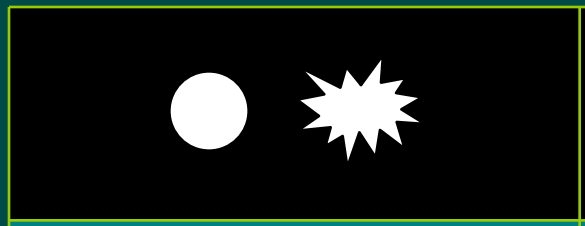
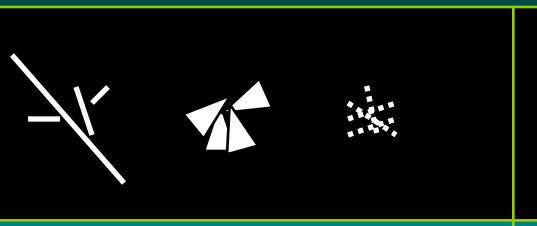
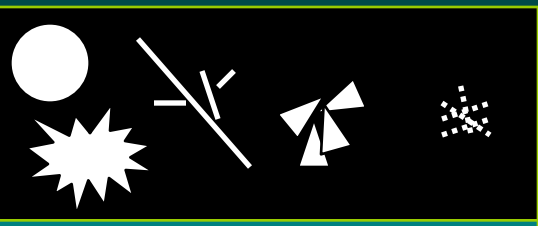
Preoperative diagnosis: planning

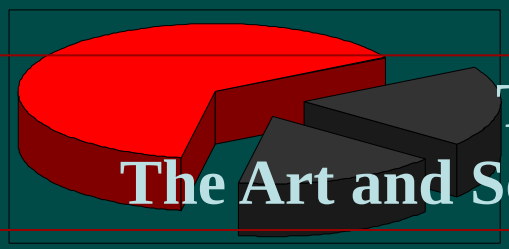
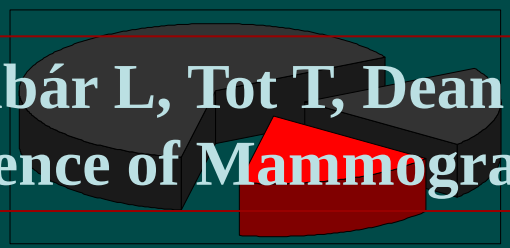
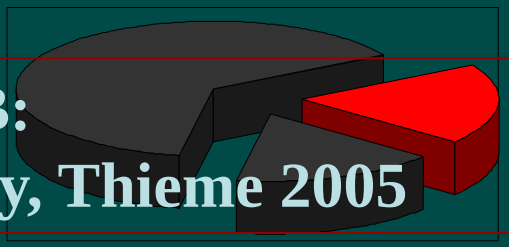
- Mammografic – pathologic correlation
- The experience with different biopsy modalities (advantages and disadvantages)
- The clinical situation and the radiologic image

Preoperative diagnosis: planning

- Mammografic – pathologic correlation
- The experience with different biopsy modalities (advantages and disadvantages)
- The clinical situation and the radiologic image

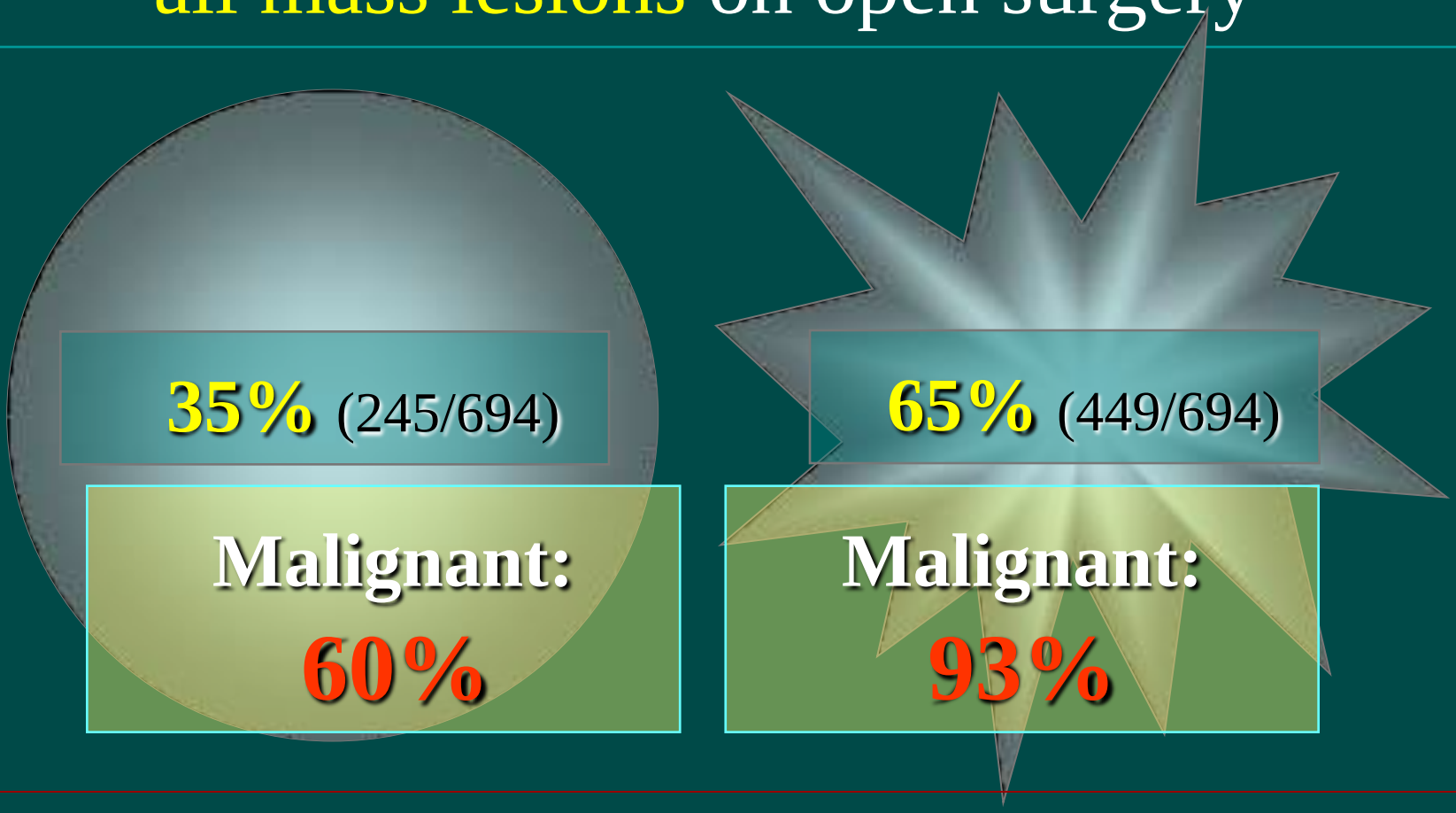
Mammographic appearance of histologically malignant lesions

Mass only	Calcifications only	Combined
		
64% (552/866)	**19%** (166/866)	**17%** (148/866)

Tabár L, Tot T, Dean PB:
The Art and Science of Mammography, Thieme 2005

Mammographic appearance of all mass lesions on open surgery



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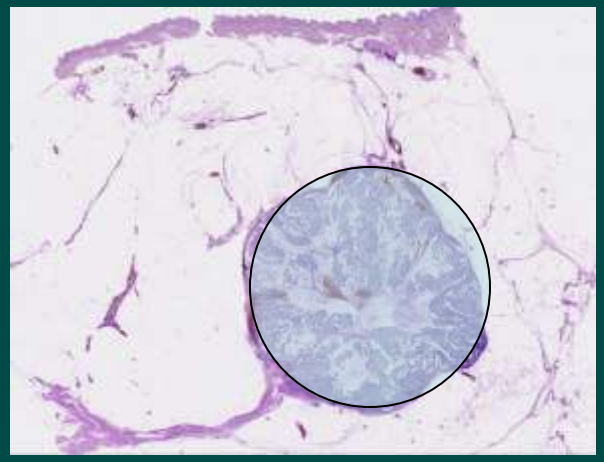
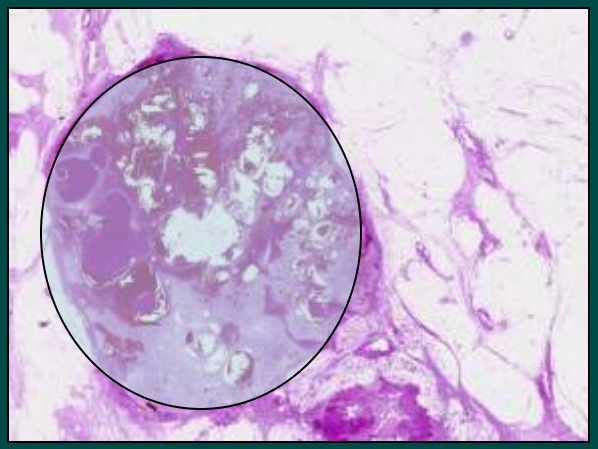
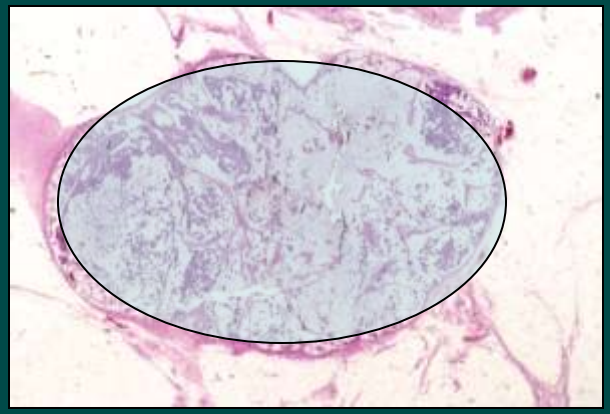
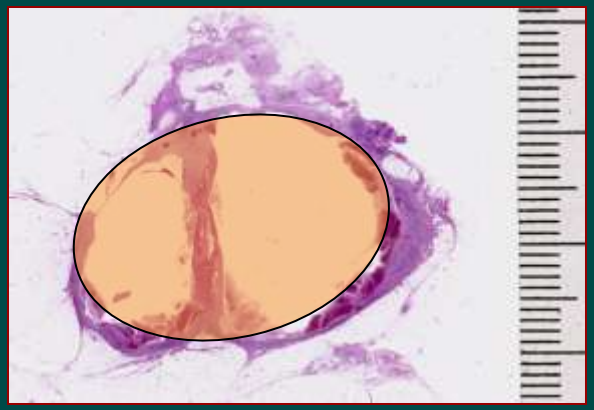
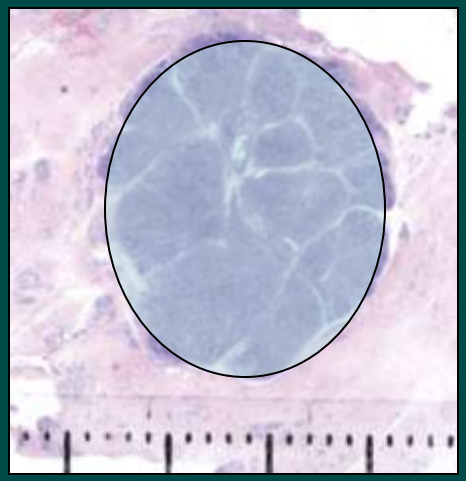
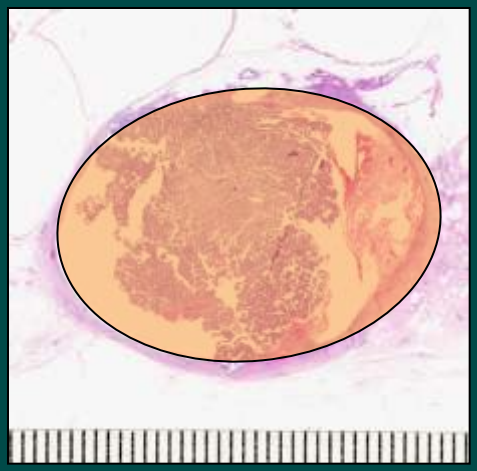


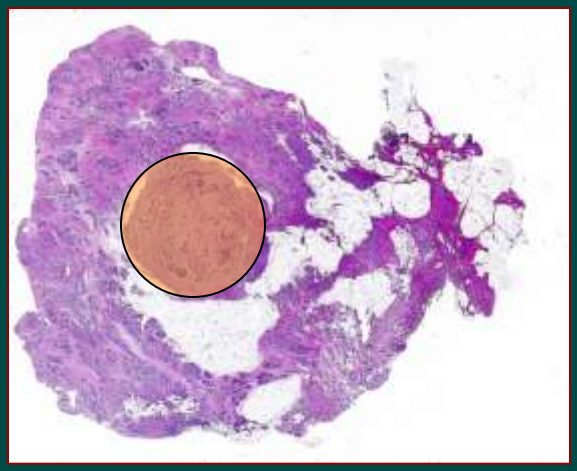




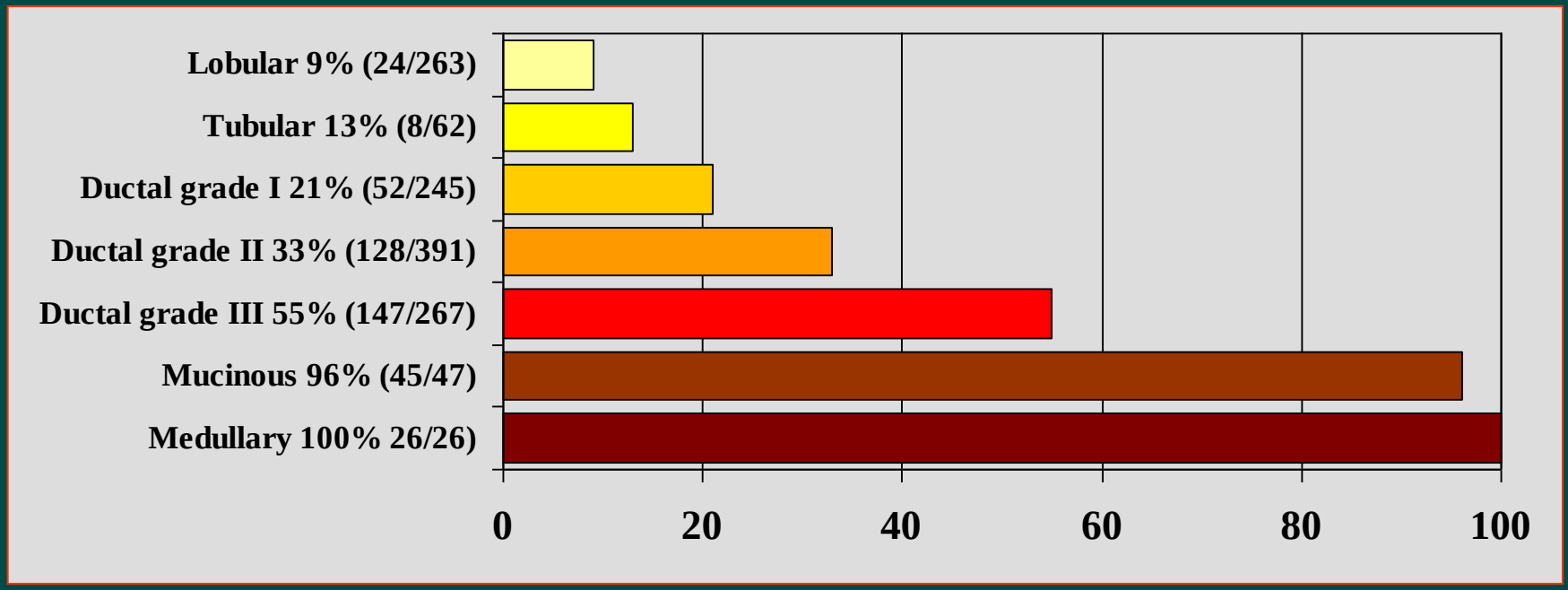






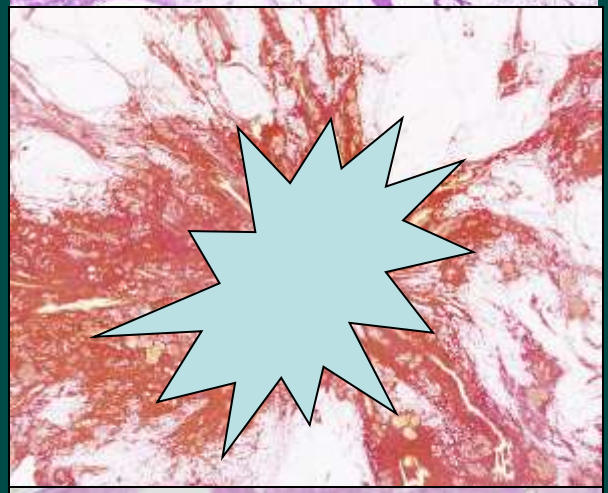


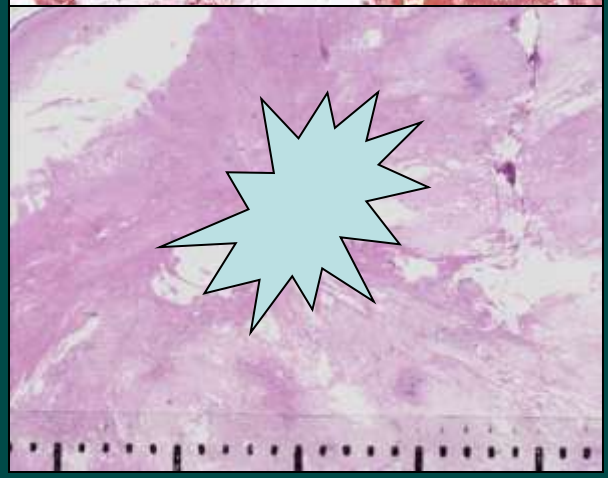
Proportion of circular lesions by histologic tumor type and grade in 1301 invasive carcinomas, Falun 1996-2003



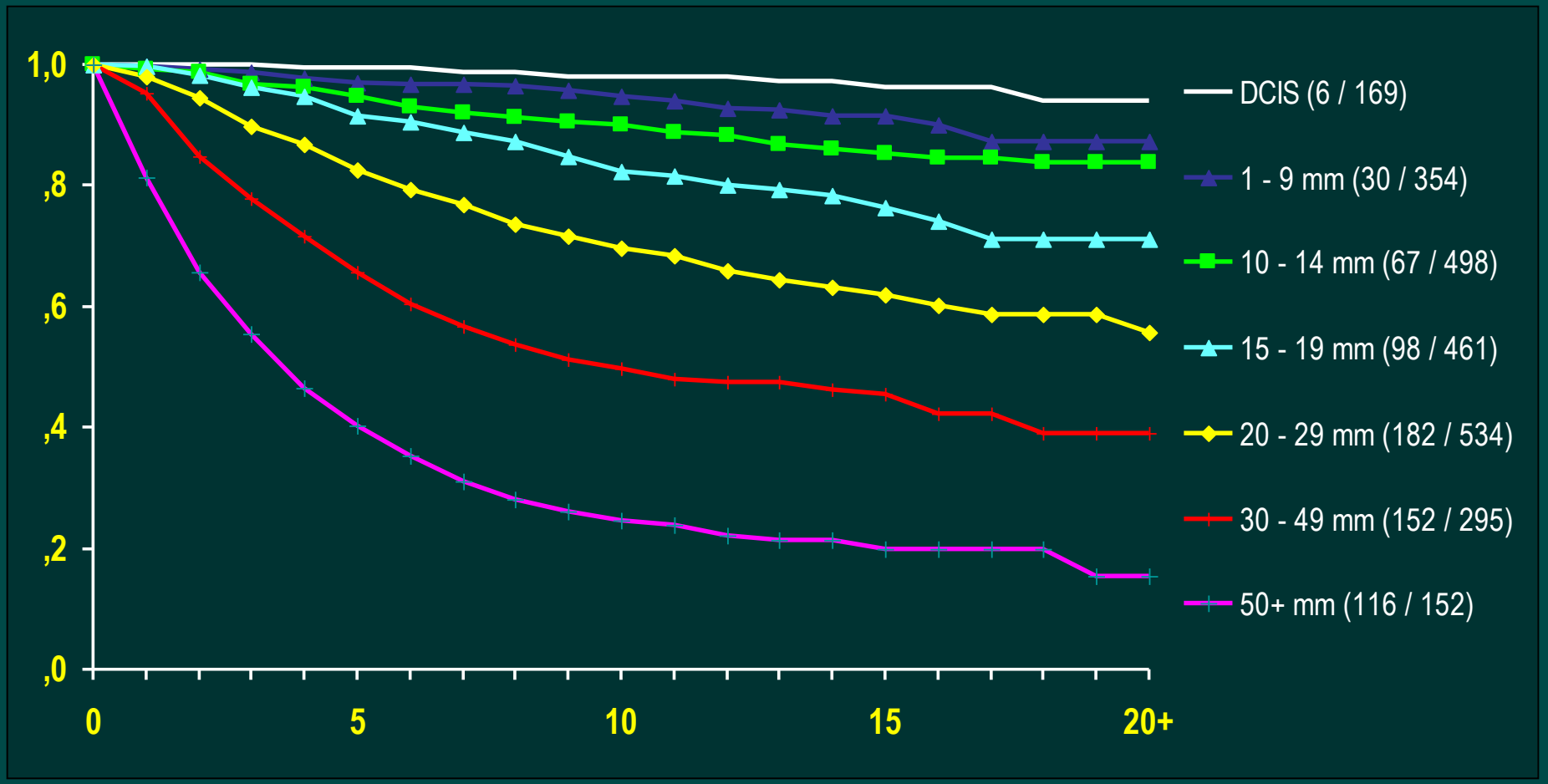
Tot T. The Subgross Morphology of normal and Pathologically Altered Breast Tissue. In Suri, Rangayyan eds. Recent Advances in Breast Imaging, Mammography and Computer – Aided diagosis of Breast Cancer.

Spie Press, Washington, USA, 2006, 1-49



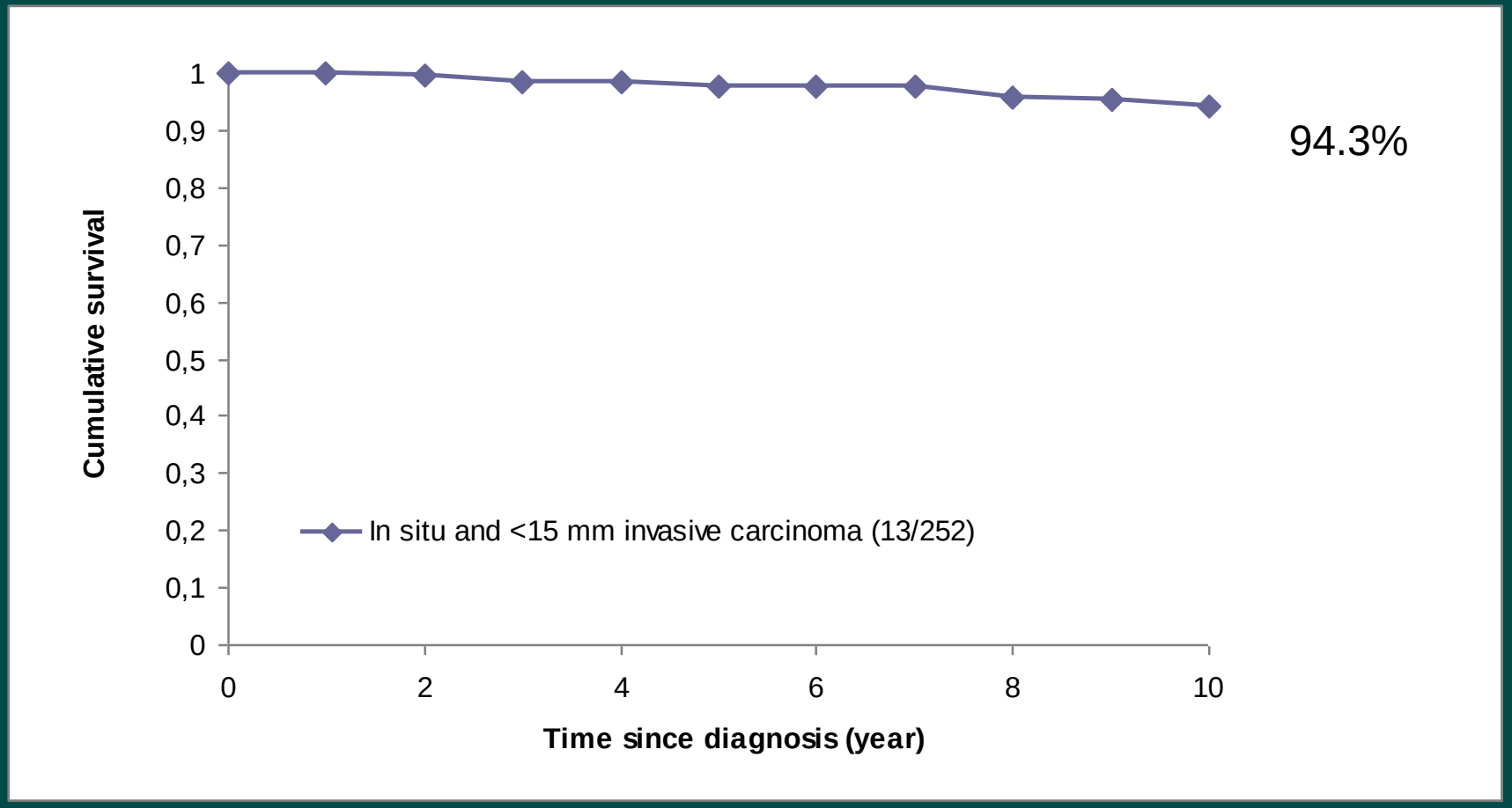


Cumulative survival of women 40-74 years with invasive breast cancer by tumor size



Courtesy of Professor László Tabár

Cumulative survival in early (in situ and <15 mm invasive) breast carcinomas, Falun, 1996-1998



Up to 12 years follow-up, 8.34 at average, SD+/- 3.47 years

Kahán Z, Tot T. Breast Cancer, a Heterogeneous Disease Entity. The Very Early Stage Springer 2011.

Molecular characteristics of early vs more advanced invasive breast carcinomas

	Early BC < 15 mm	Advanced BC >= 15 mm	Total	P-value
Basal-like	**5.9%** (12/203)	**15.1%** (48/317)	11.5% (60/520)	**= 0.0035**
ER negative*	**12.3%** (42/342)	**18.2%** (93/510)	15.8% (135/852)	= 0.0238
Tripple negative	**6.4%** (22/341)	**10.5%** (53/507)	8.8% (75/848)	= 0.0193
Her-2 positive	**8.9%** (31/347)	**13.3%** (68/511)	11.5% (99/858)	= 0.0917
Grade 3	**12.9%** (46/355)	**29,5%** (151/511)	22.0% (197/866)	**< 0.0005**
Total	41.5% (362/873)	58,5% (511/873)	100% (873/873)	

Kahán Zs., Tot T., eds. Breast Cancer, a Heterogeneous Disease Entity: The Very Early Stage. Springer 2011

Tumor phenotype by radiological tumor shape and histological size, Falun 2005-2009

Size mm	G3	ER -	Triple -	Her2 +	Basal
1-14	5% (10/185)	5% (10/185)	2% (3/185)	4% (7/185)	1% (2/185)
15+	20% (44/219)	9% (19/219)	5% (12/219)	7% (16/219)	5% (10/219)
1-14	22% (22/101)	16% (16/101)	13% (13/101)	7% (7/101)	7% (7/101)
15+	38% (83/217)	26% (57/217)	19% (42/217)	8% (18/217)	13% (28/2127)
Total	22% (159/722)	14% (102/722)	10% (70/722)	7% (48/722)	7% (47/722)

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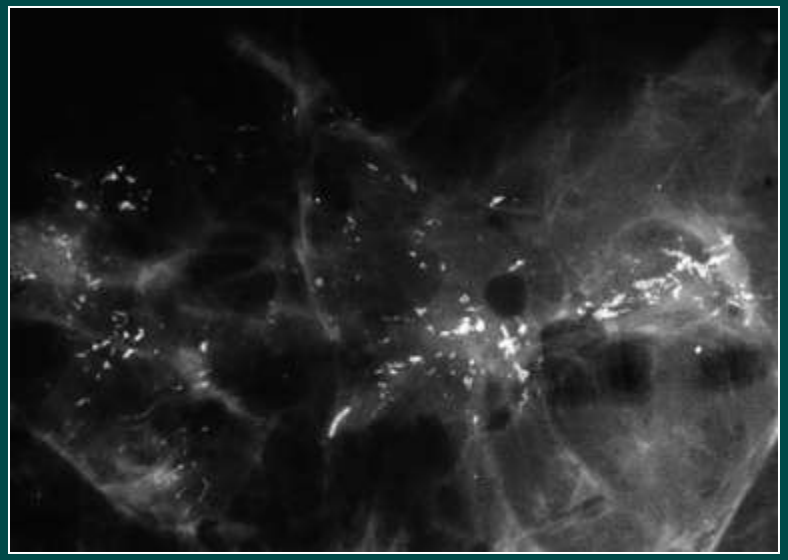
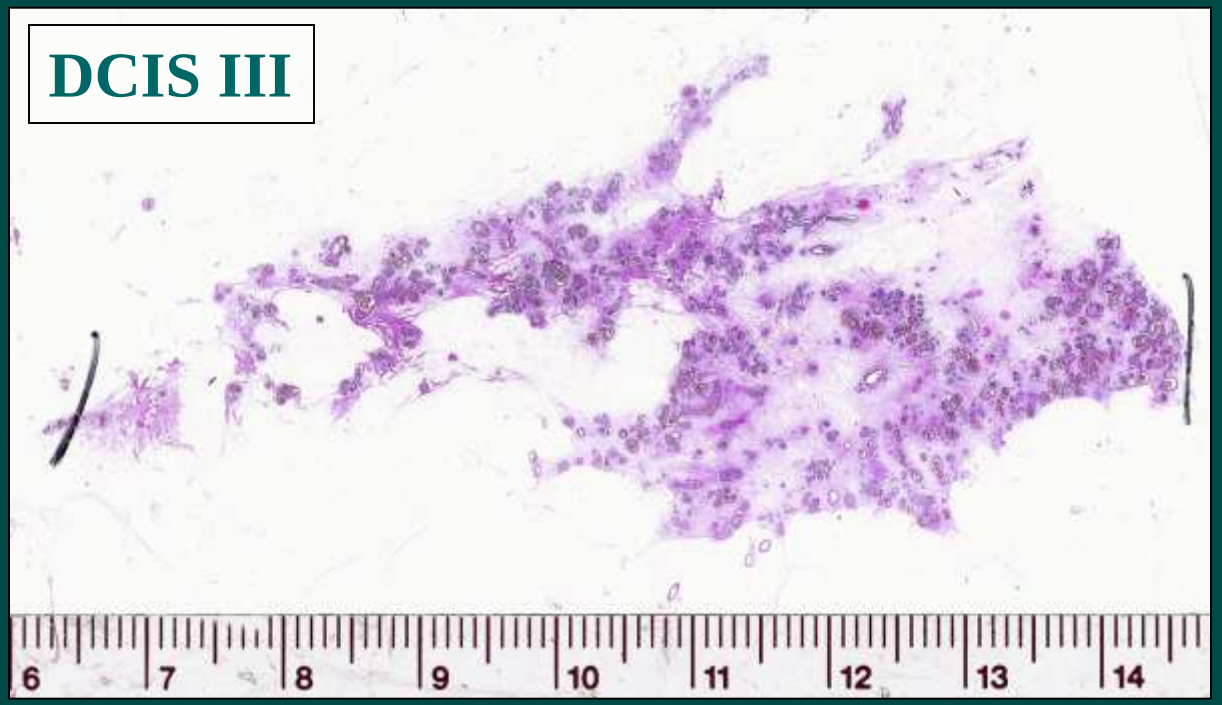
Total	22% (159/722)	14% (102/722)	10% (70/722)	7% (48/722)	7% (47/722)

Mammographic appearance of all calcification cases sent to open surgery

Casting type	Cushed stones type	Powdery
		
19% (51/264)	**45%** (119/264)	**36%** (94/264)
Malignancy rate **94%**	Malignancy rate **63%**	Malignancy rate **50%**




DCIS III
6
7
8
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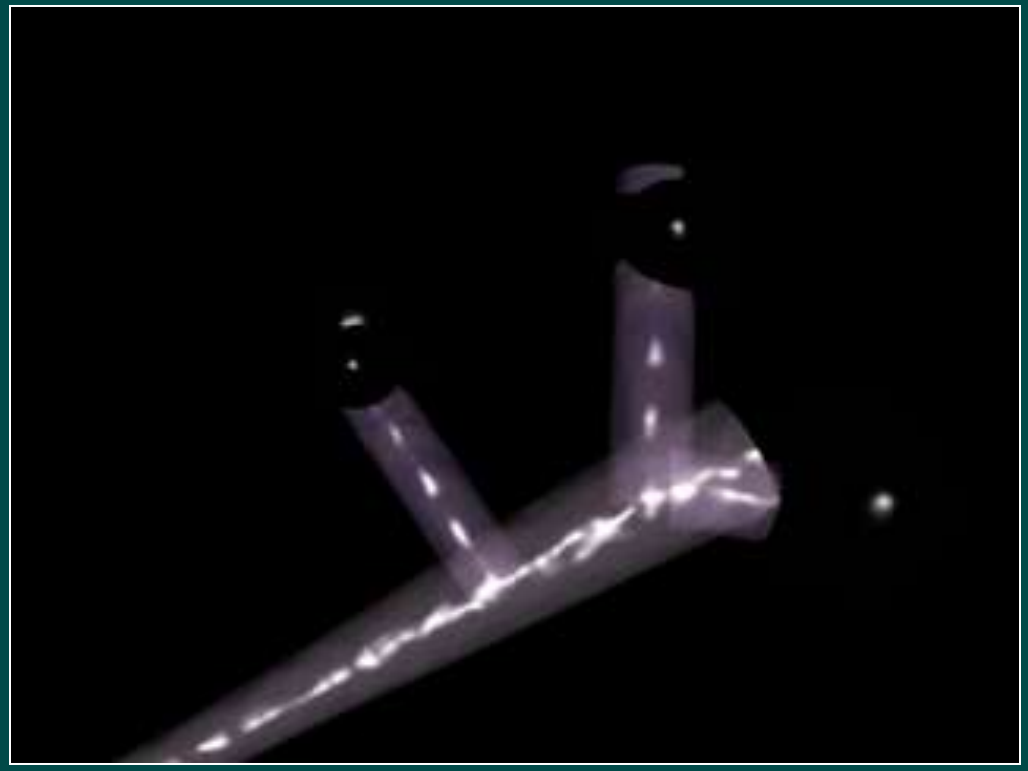
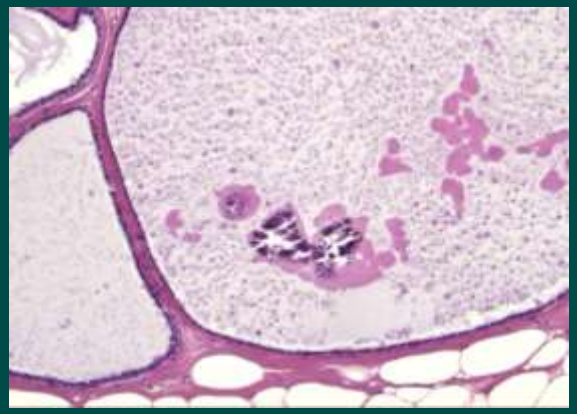
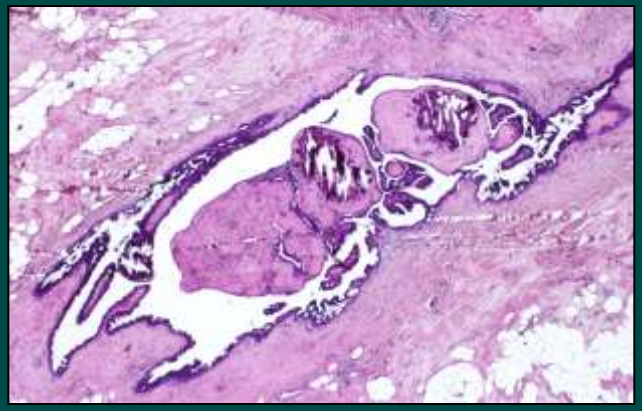
13
14

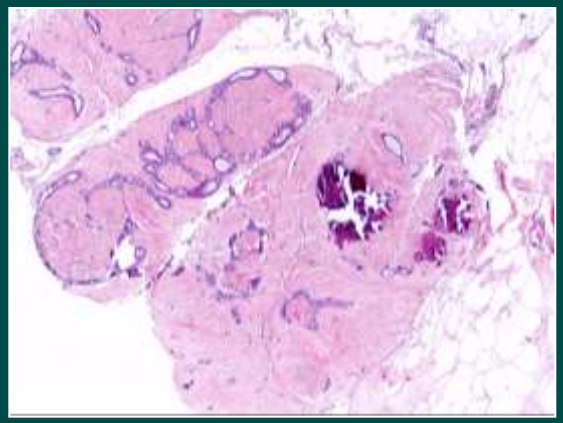


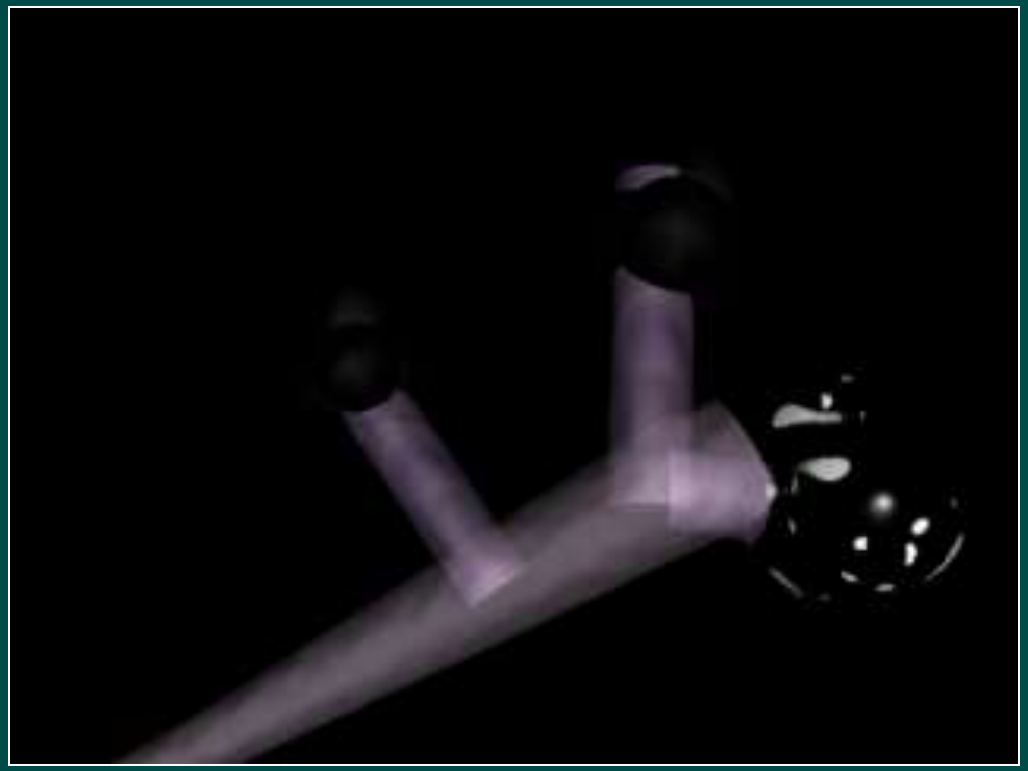
Malignancy rate 94%

DCIS II

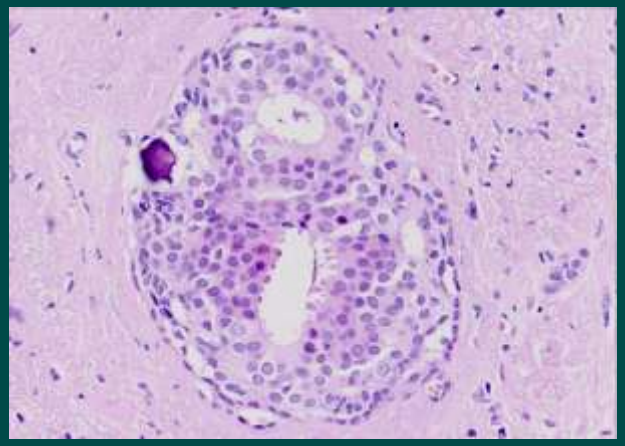


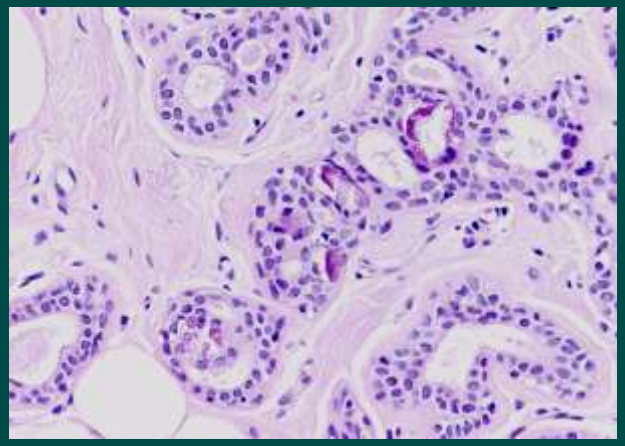




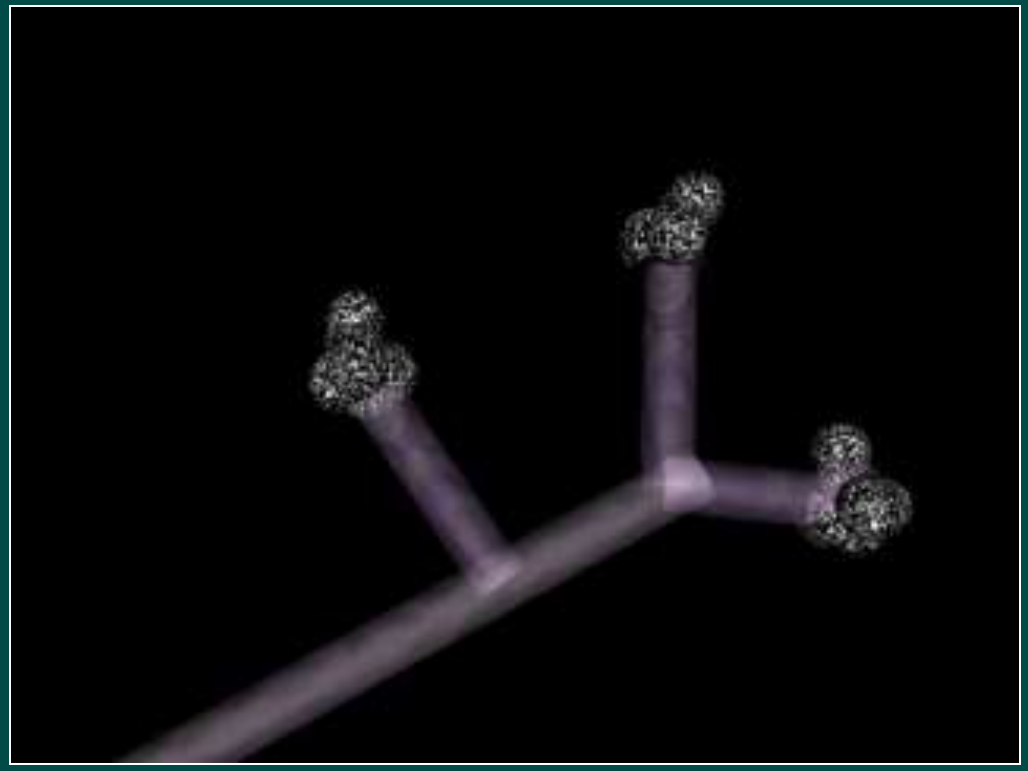


Malignancy rate 63%

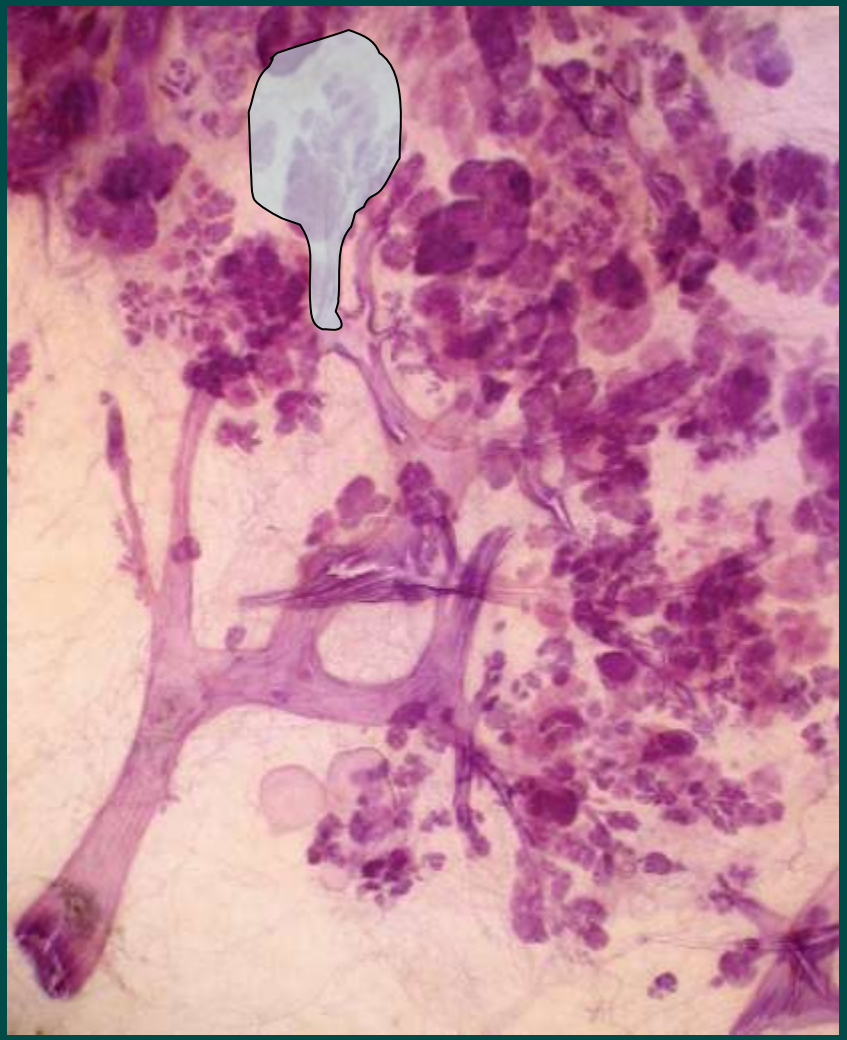


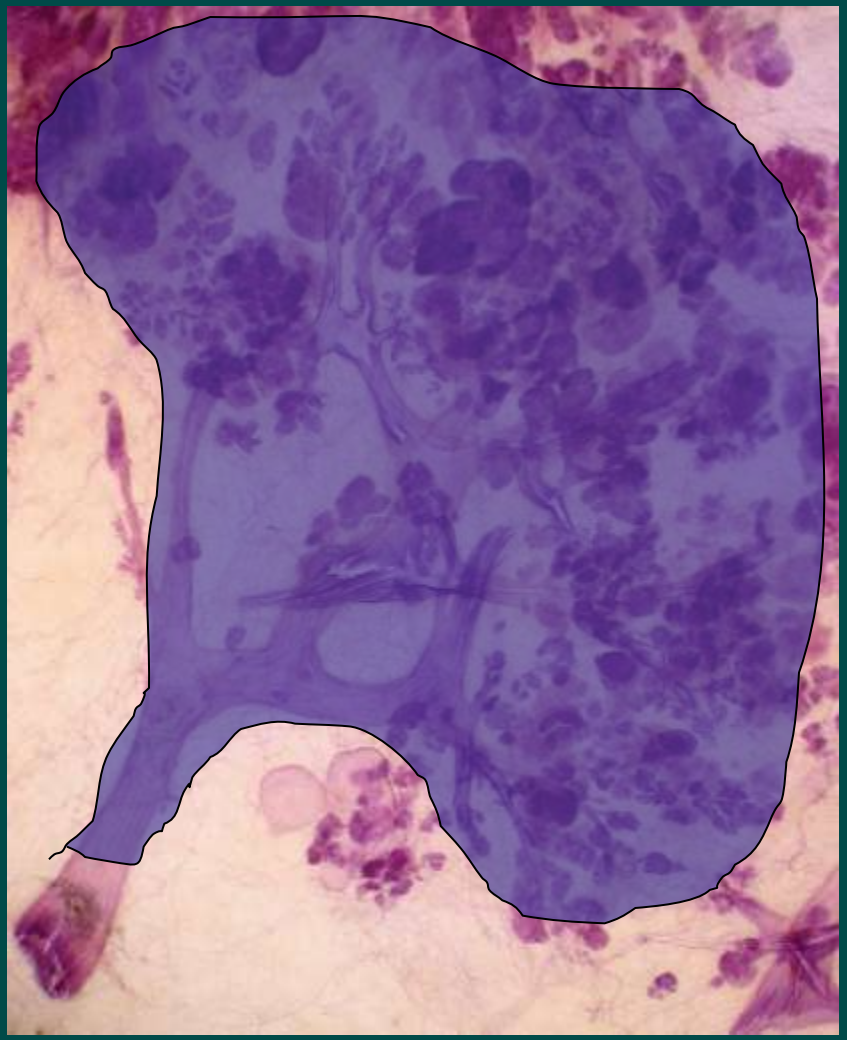


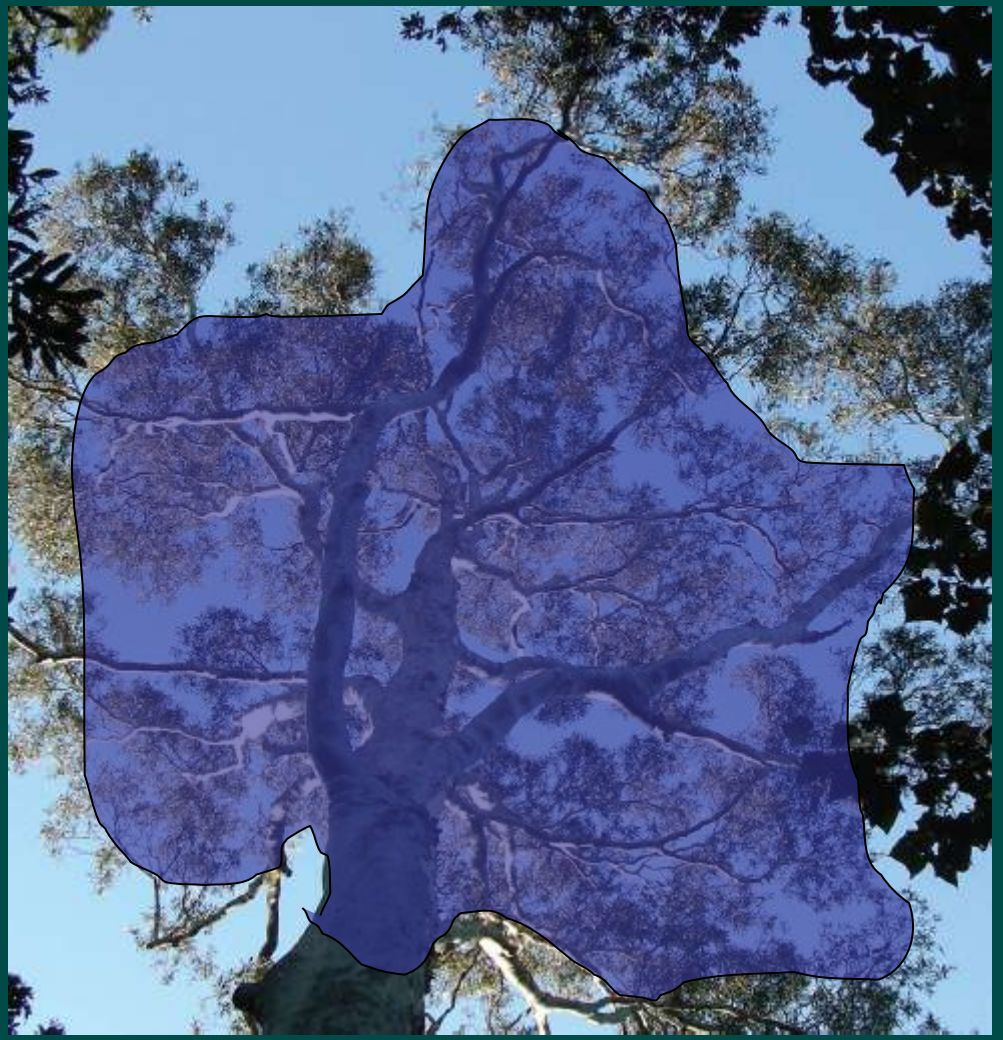
DCIS I

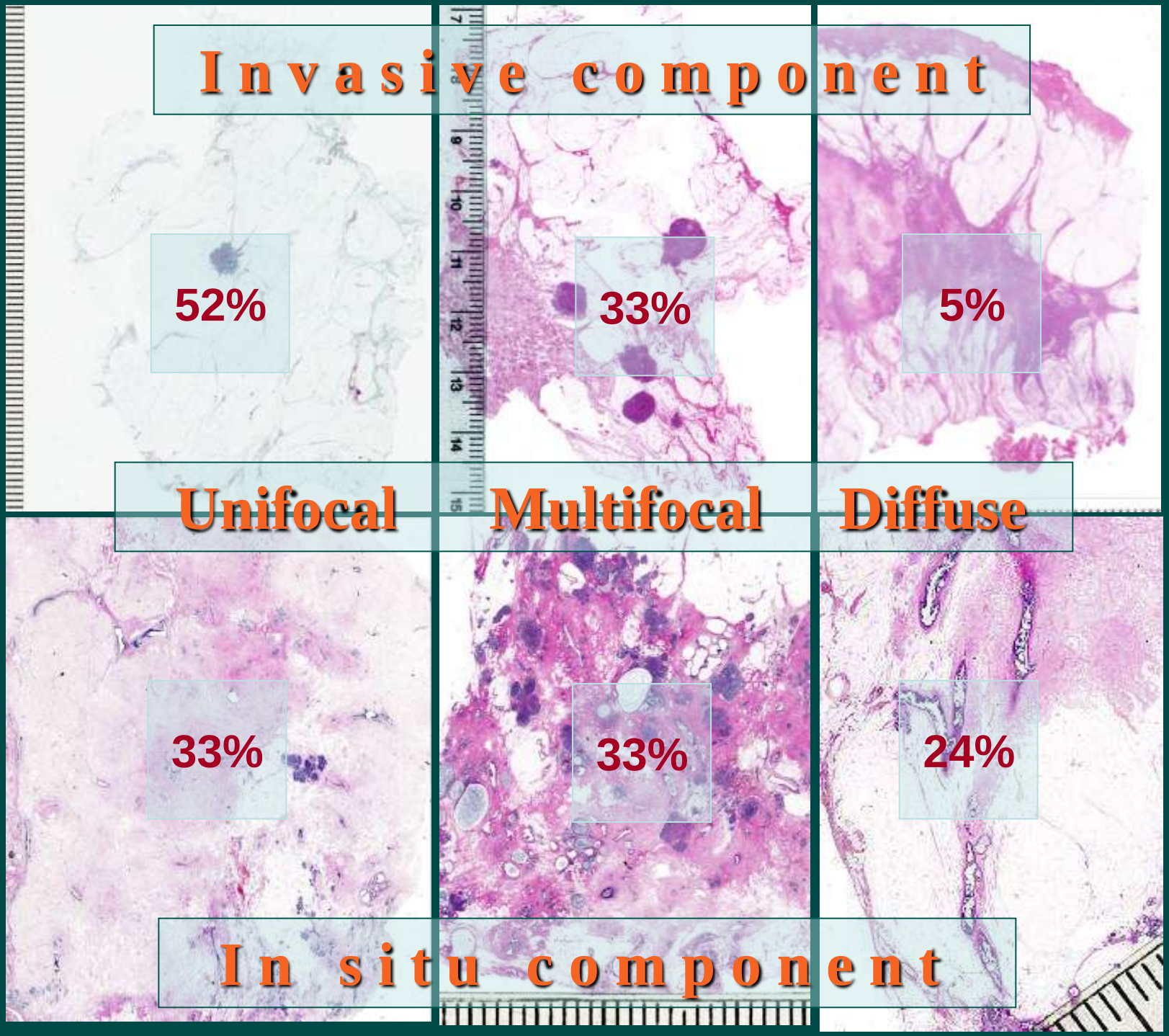


Malignancy rate 50%

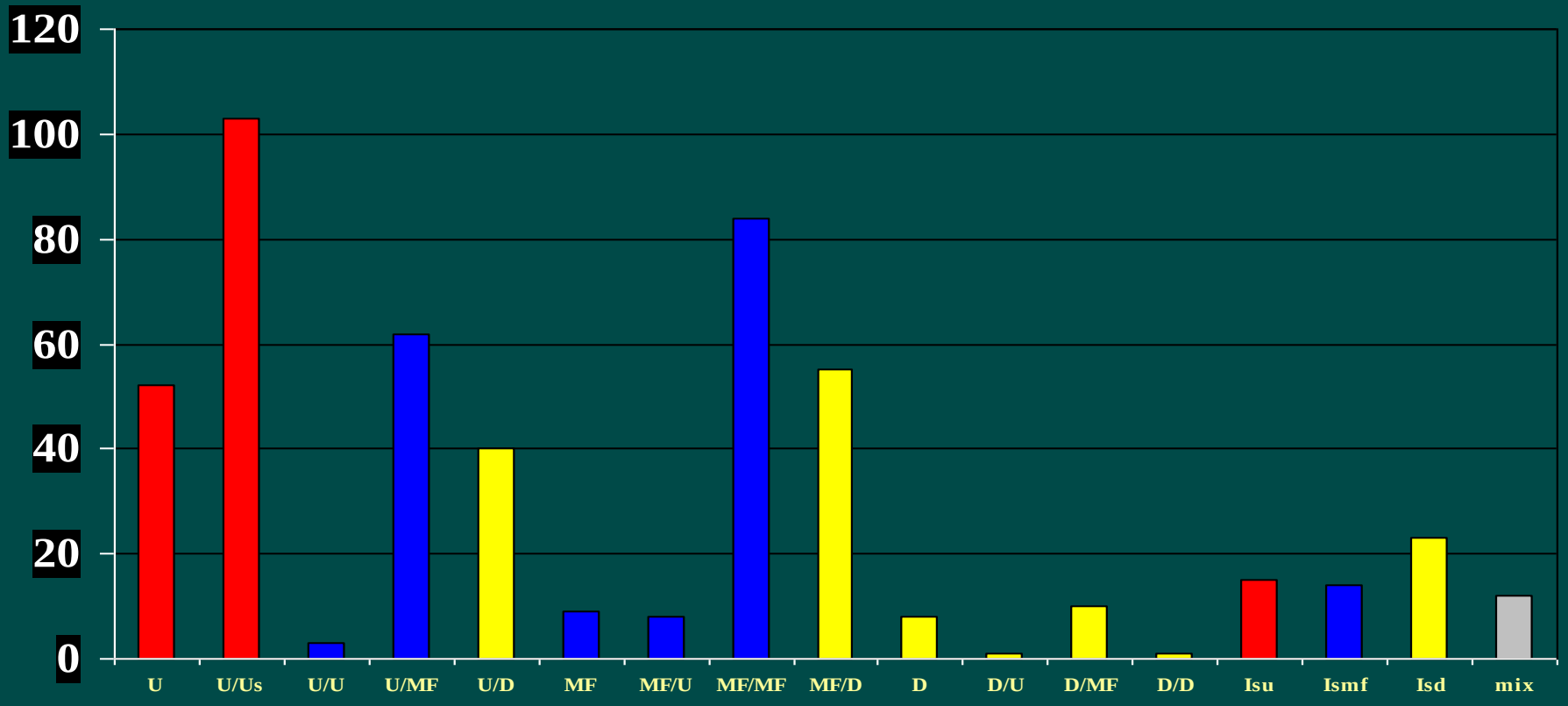






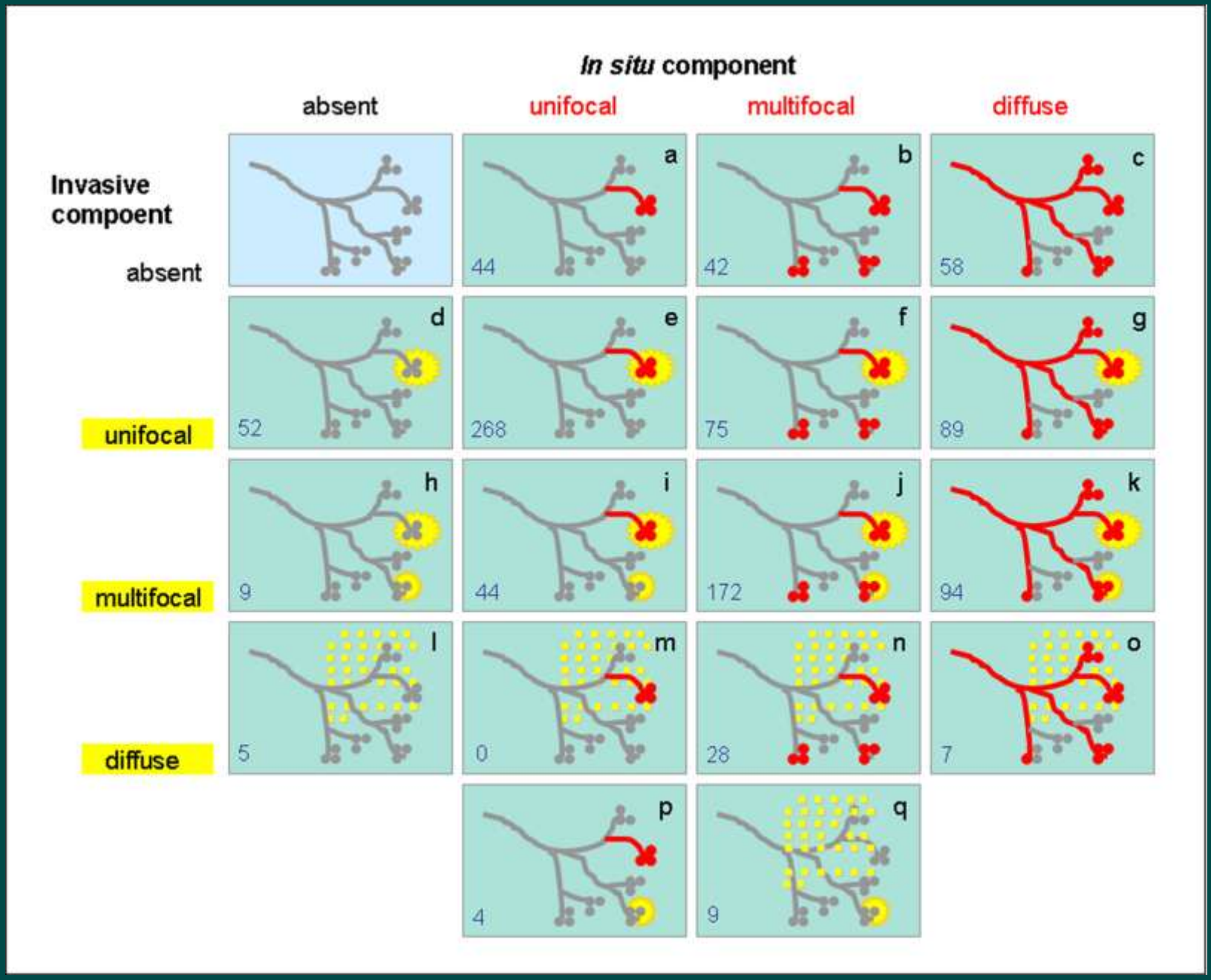

Invasive component
52%
33%
5%
10%
Unifocal
Multifocal
Diffuse
33%
33%
24%
10%
In situ component

500 breast carcinomas by combined lesion distribution, Falun 2005 - 2007

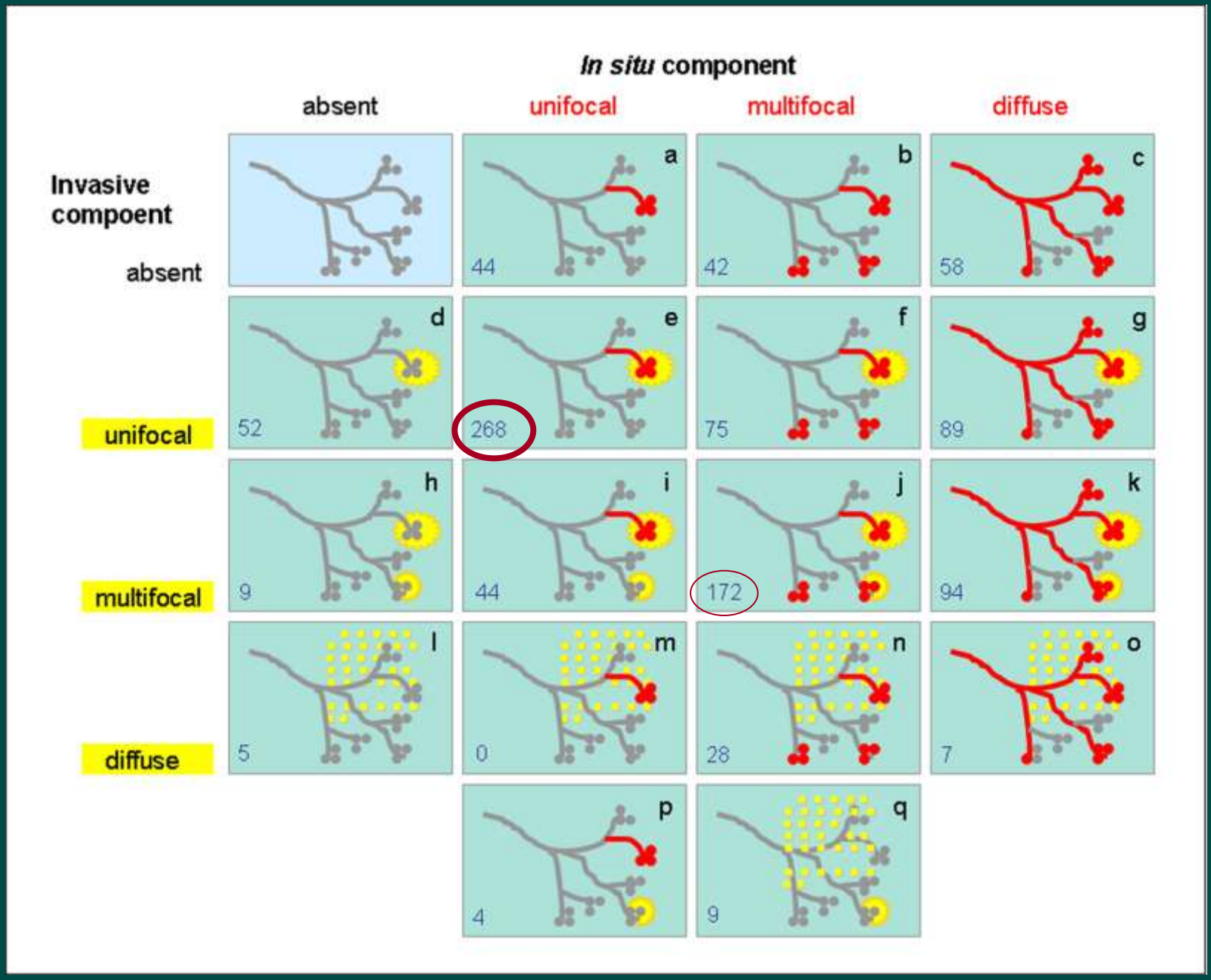


Distribution of the lesions in 500 consecutive breast cancer cases documented on large-format histological sections

Tot T. Cancer 110:2551-60, 2007



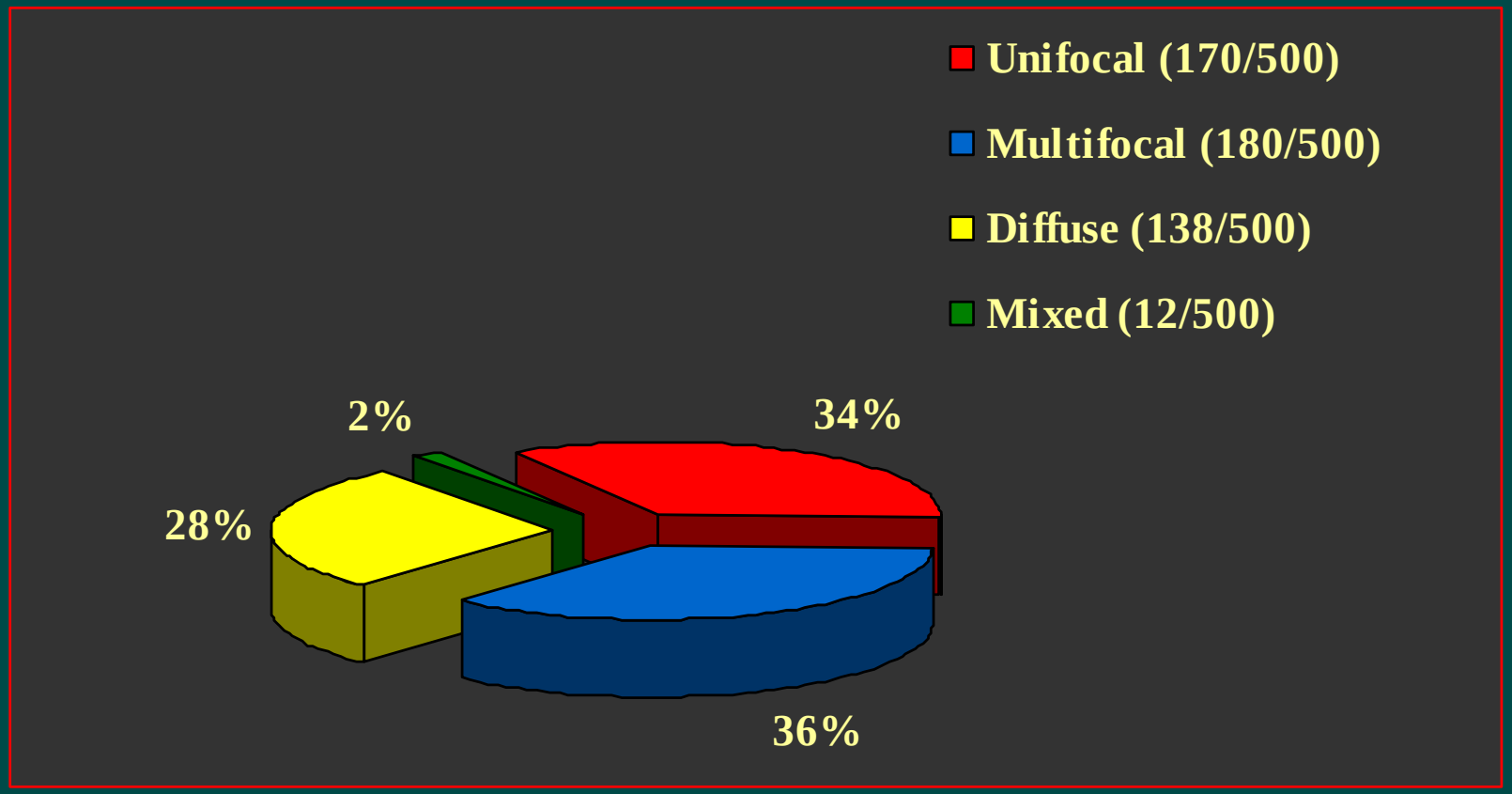
Tot T, Int J Breast Cancer, in press



Tot T, Int J Breast Cancer, in press

Combined lesion distribution

Tumor component				
In situ	Invasive			
	None	Unifocal	Multifocal	Diffuse
None	-	Unifocal	Multifocal	Diffuse
Unifocal	Unifocal	Unifocal	Multifocal	Diffuse
Multifocal	Multifocal	Multifocal	Multifocal	Diffuse
Diffuse	Diffuse	Diffuse	Diffuse	Diffuse



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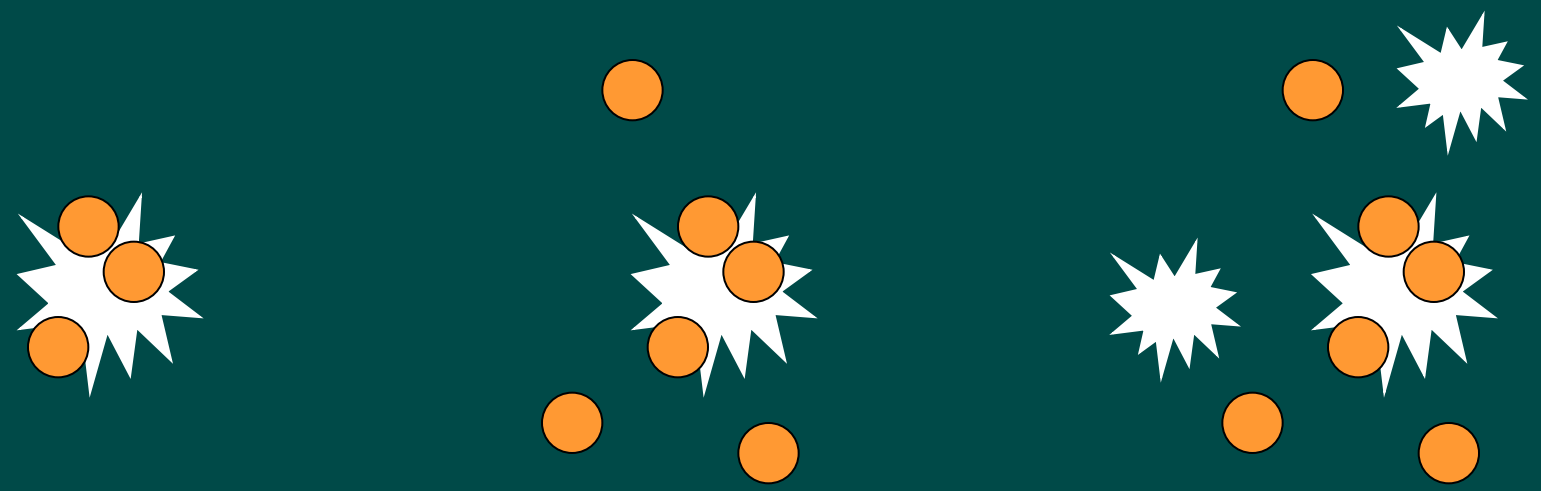


33%,
unifocal

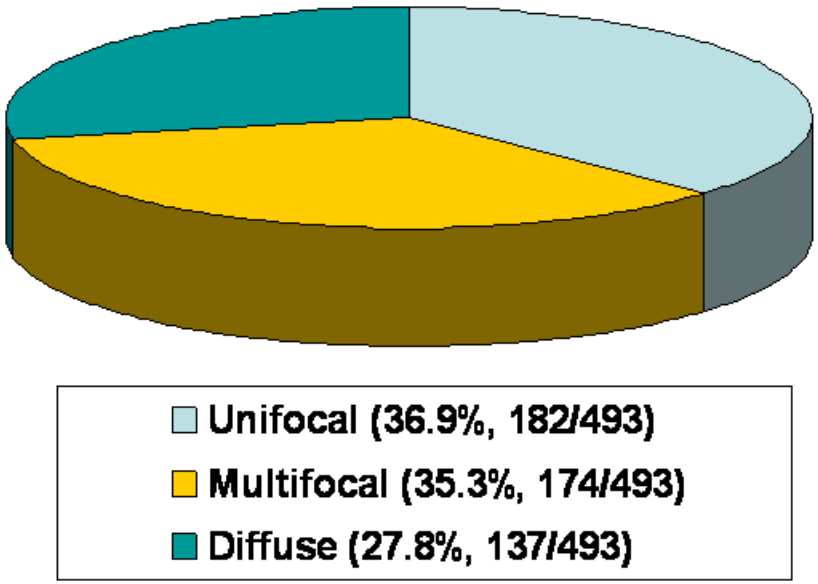
33%,
Multifocal in situ

33%,
Multifocal invasive

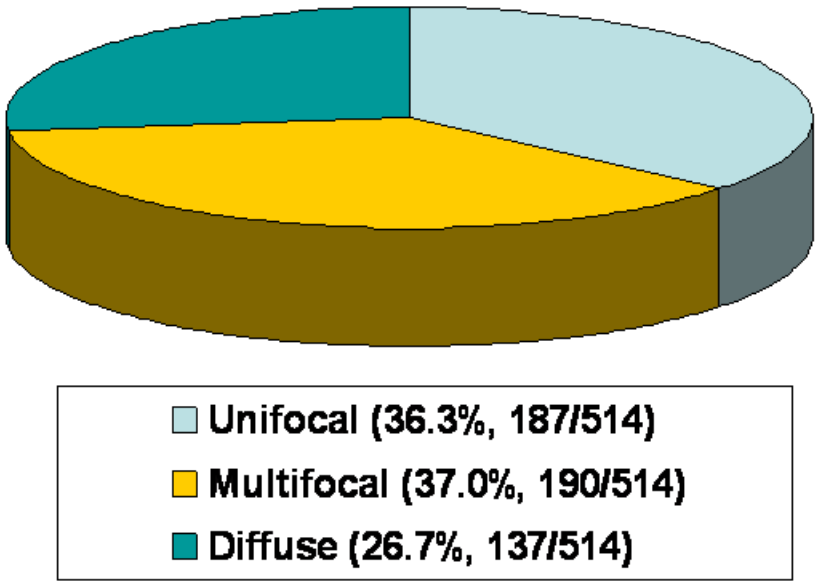
Diffuse invasive 5%

Combined (in situ + invasive) distribution of the lesions in early vs advanced invasive carcinomas, 1007 consecutive cases, Dalarna, 2005-2009

1-14 mm

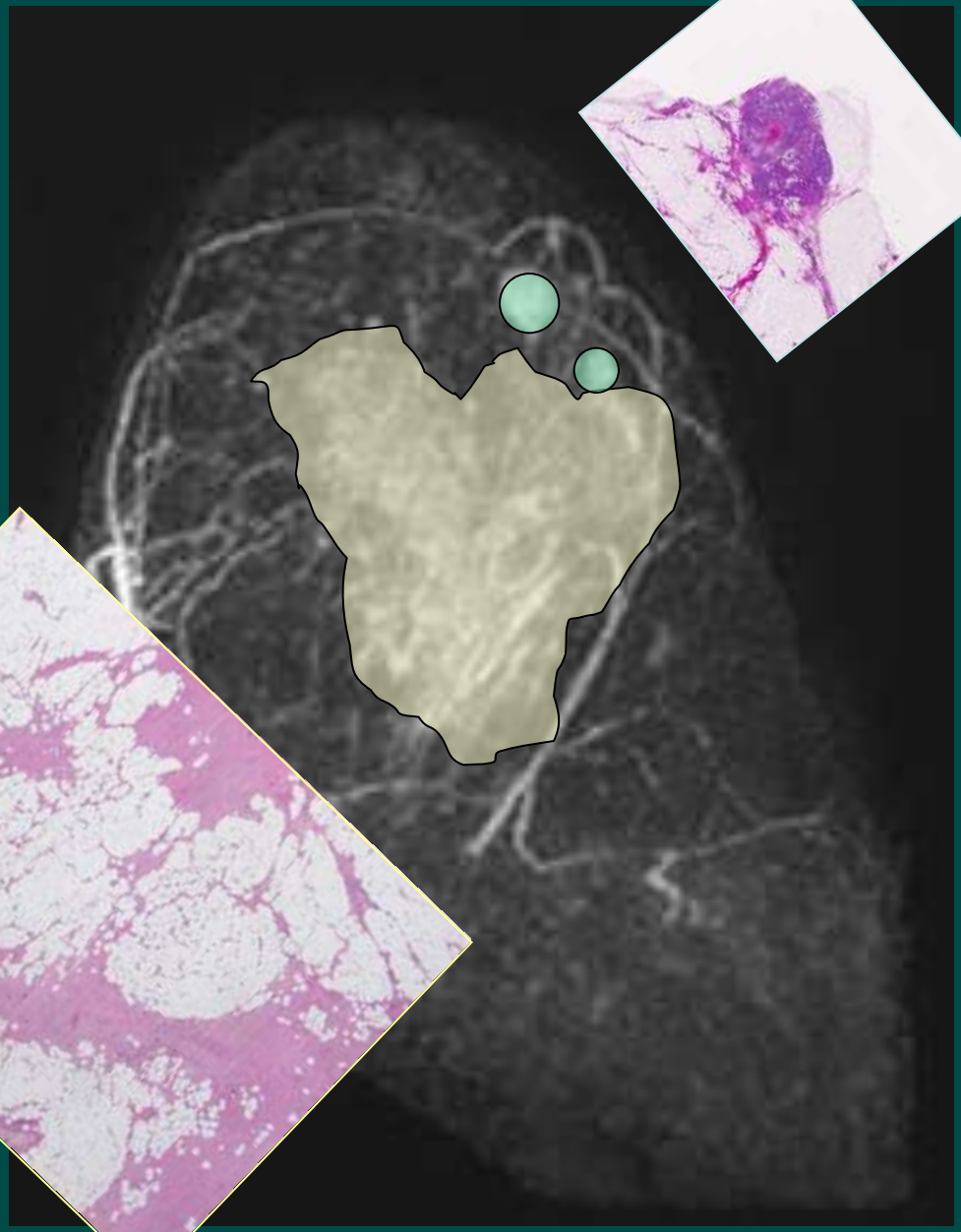


15+ mm

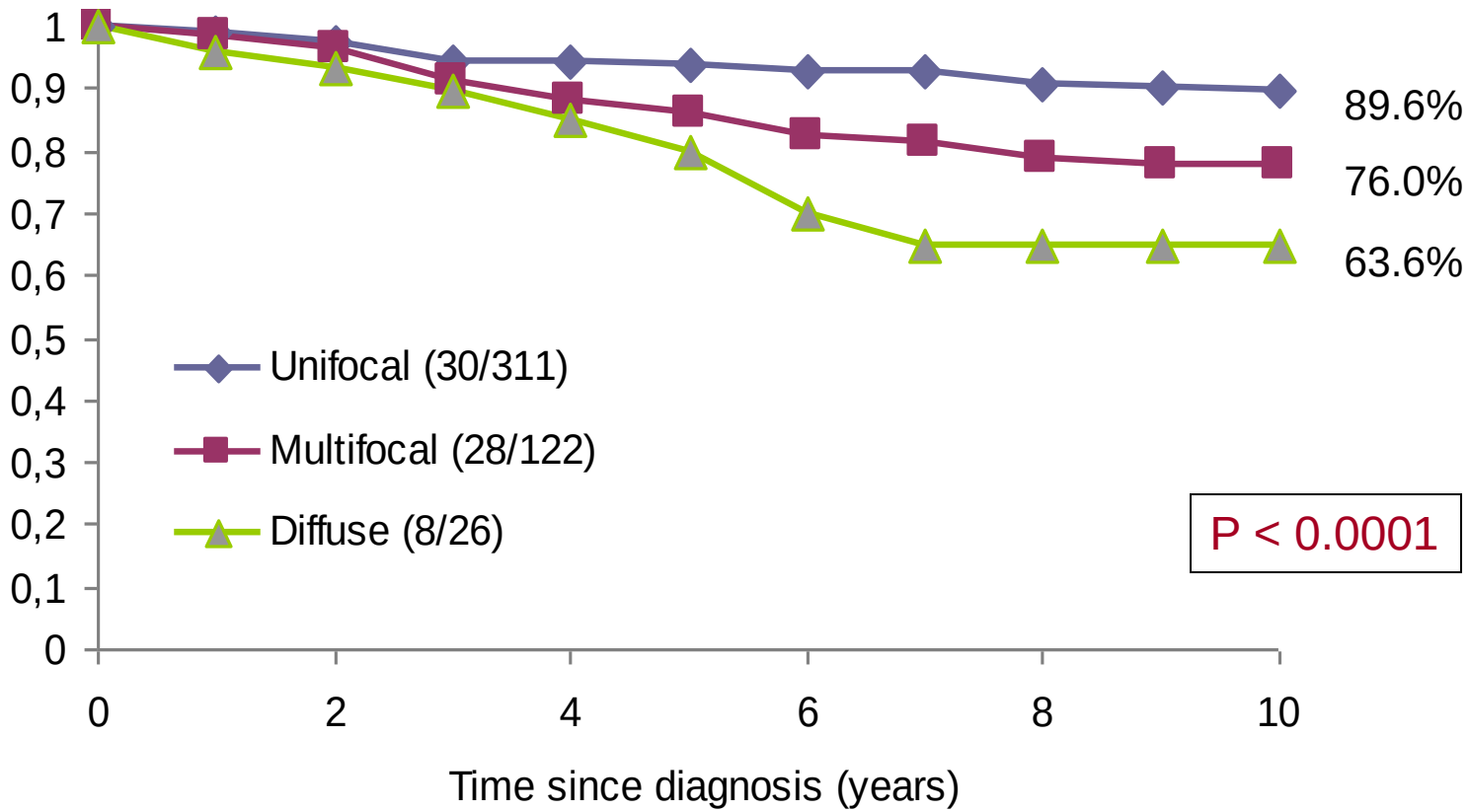


Tot T. Large-format histology, a prerequisite for adequate assessment of early breast carcinomas. In Kahán, Tot, eds. Breast Cancer, a Heterogeneous Disease Entity: The Very Early Stage. Springer 2011.


nattfoto.nu

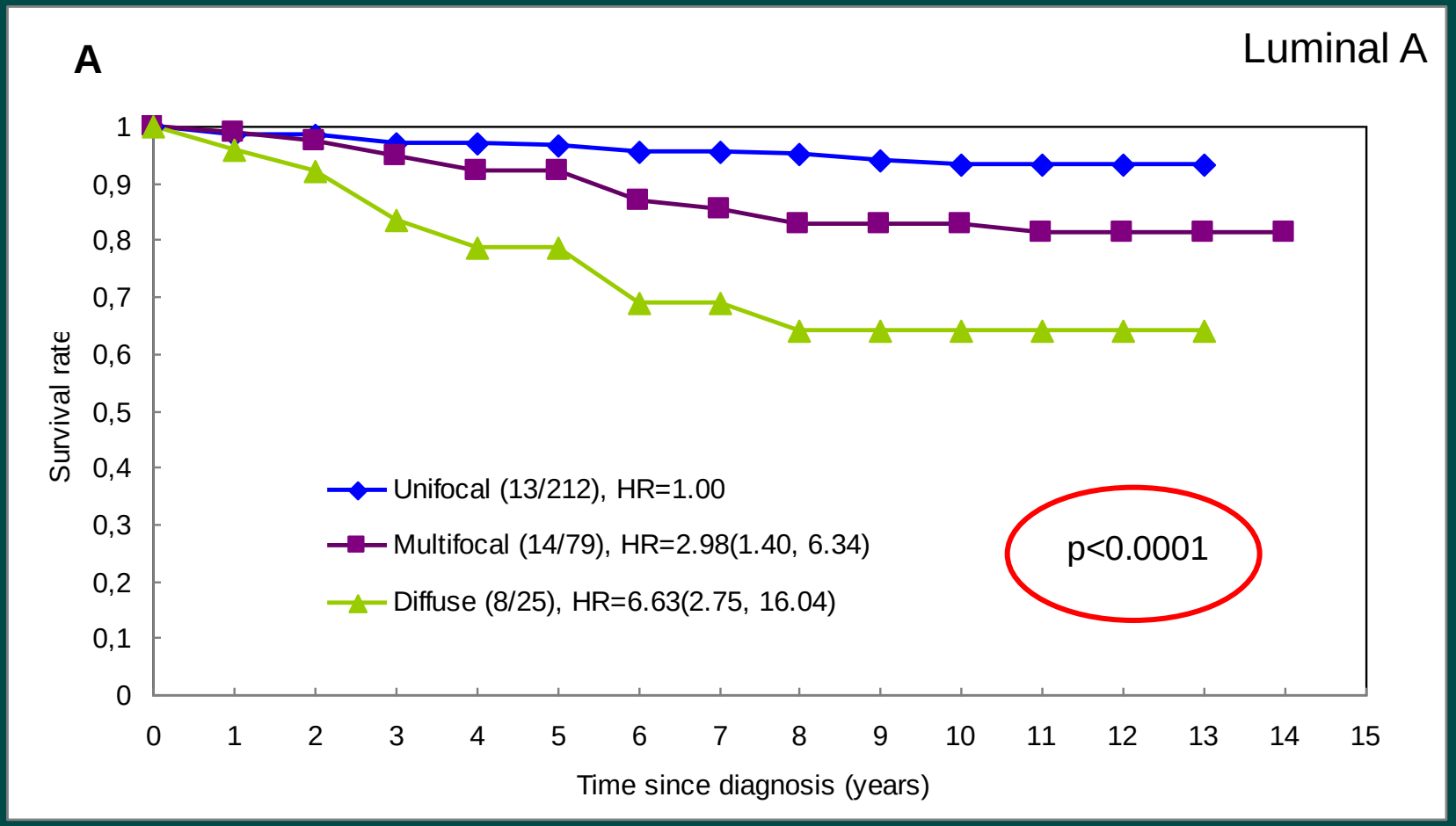


Cumulative survival in 499 invasive breast carcinoma cases by distribution of the invasive component, Falun, 1996-1998



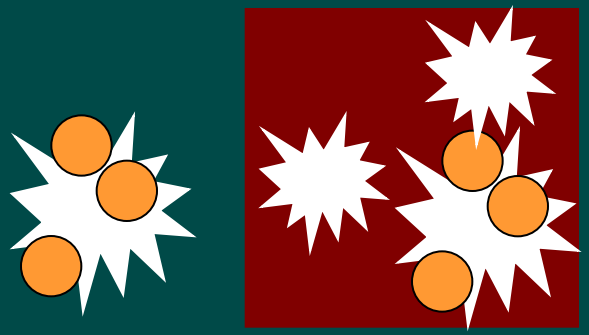
Distribution unknown in 40 cases

Tot et al. Breast cancer multifocality, disease extent, and survival.Hum Path 2011

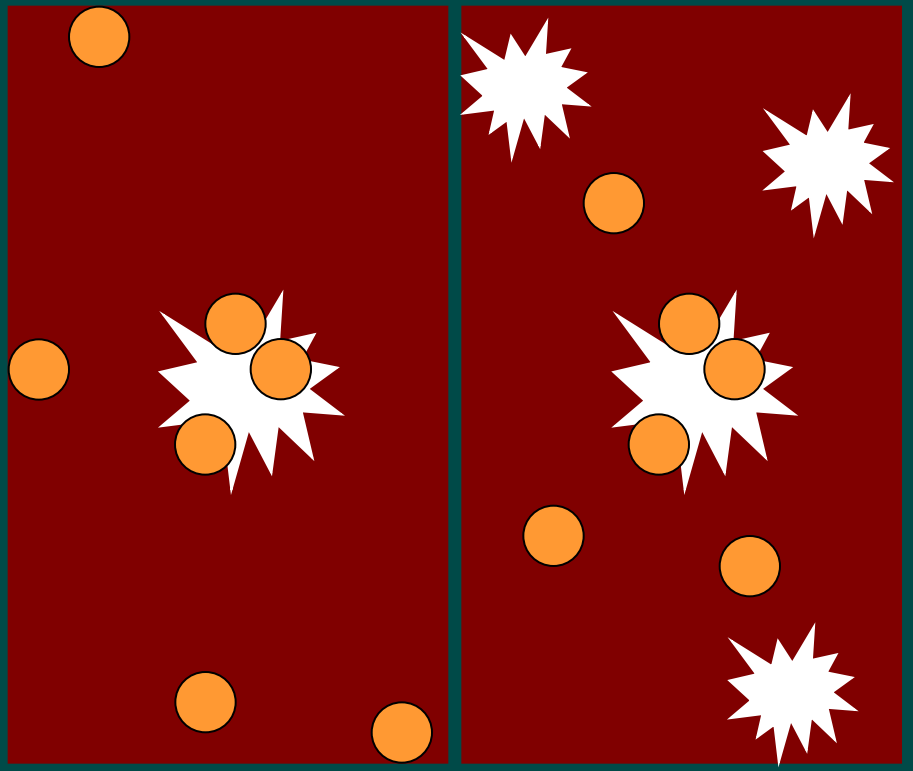


Cumulative disease-specific survival in 444 consecutive invasive breast carcinoma cases by subgross lesion distribution and molecular phenotypes in **A)** 316 luminal A cancers

Pekár G et al Cancer, in press



55%
Unifocal eller multifocal,
limited extent

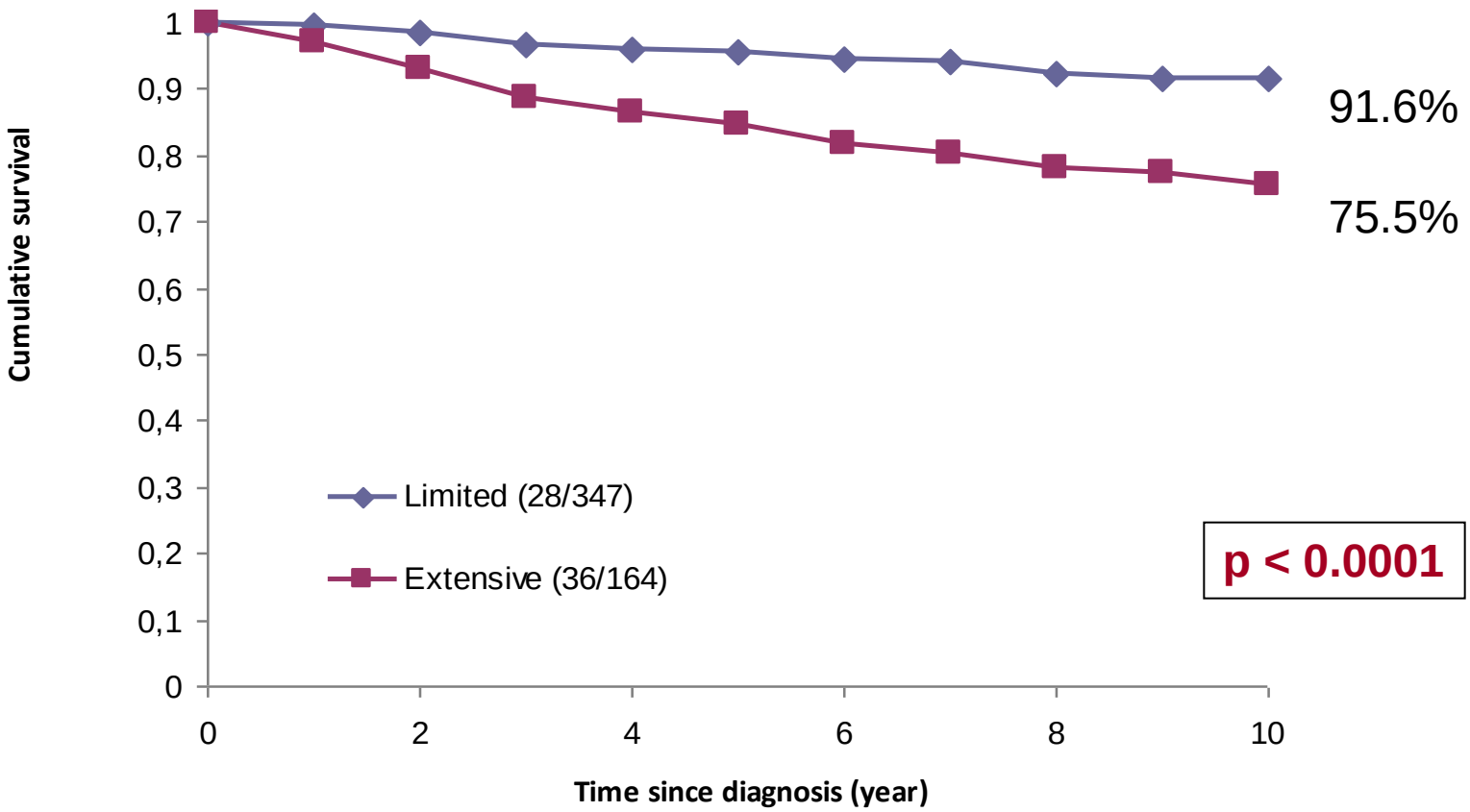


45%
M u l t i f o c a l, d i f f u s e
extensive

	Extensive tumors >= 4 cm	Non-extensive tumors <4cm	Total	Relative risk	Significance level
Mastectomy	7.3% (9/124)	9.3% (8/86)	8.1% (17/210)	RR=0.7802 (CI: 0.3135-1.9429)	P=0.5937
Breast Conserving Surgery	20.5% (9/44)	7.4% (20/269)	8.9% (29/313)	**RR=2.7511** (CI:1.3401-5.6478)	P=0.0058
Sum	10.7% (18/168)	7.9% (28/355)	8.6% (46/523)	RR=1.3584 (CI: 0.7736-2.3852)	P=0.2862
Relative risk	**RR=2.8182** (CI: 1.1955-6.6435)	RR=1.2512 (CI: 0.5717-2.7380)	RR==0.8737 (CI:0.4928-1.5490)		
Significance level	P=0.0179	P=0.5749	P=0.6440		

Ipsilateral local recurrence rates by disease extent and type of surgery: extensive tumor defined as those occupying an area 4 cm or larger in greatest dimension. Falun, 1996-98, 10-year follow-up results.
Tot T. Int J Breast Cancer 2011

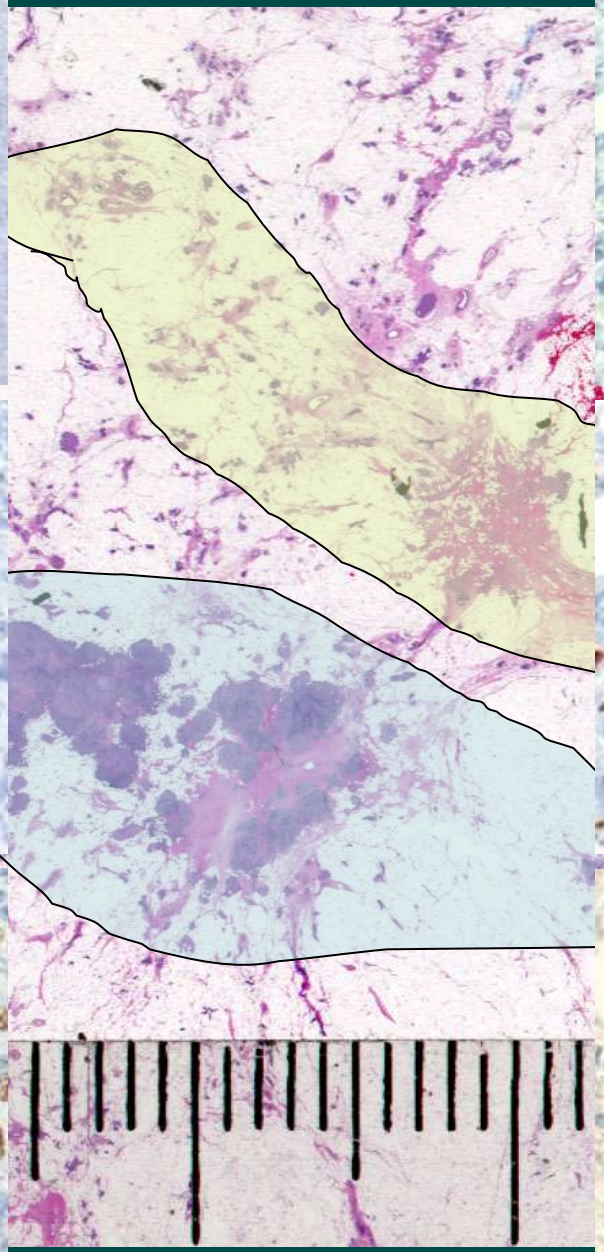
Cumulative survival in a consecutive series of 574 newly diagnosed breast cancer cases by the extent of the disease, Falun 1996-1998

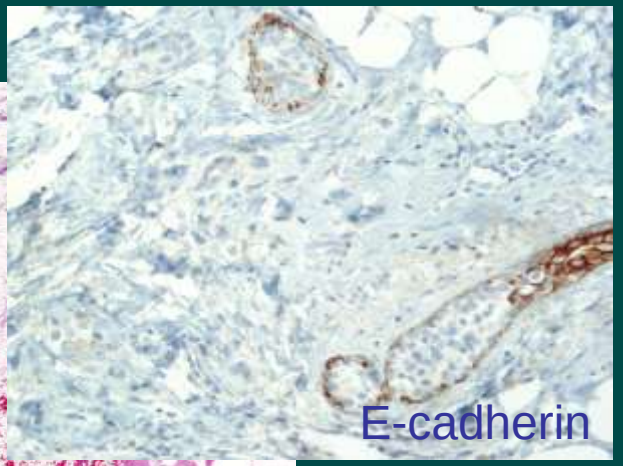


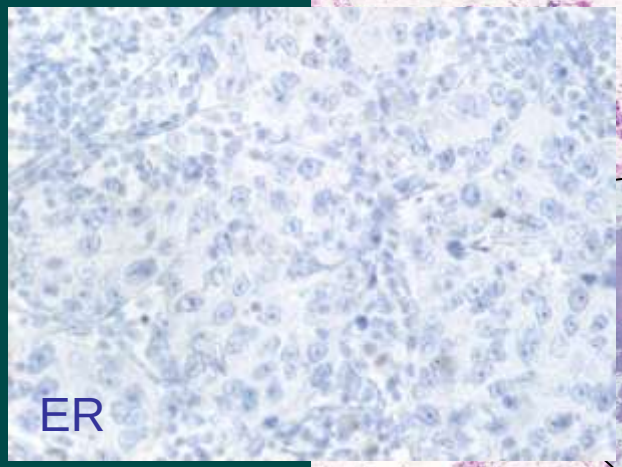
Extensive = extent >= 40mm, limited extent < 40 mm, unknown in 63 cases

Tot T et al: Breast cancer multifocality, disease extent, and survival. Human Pathology 2011:42,1761-9


E-cadherin




E-cadherin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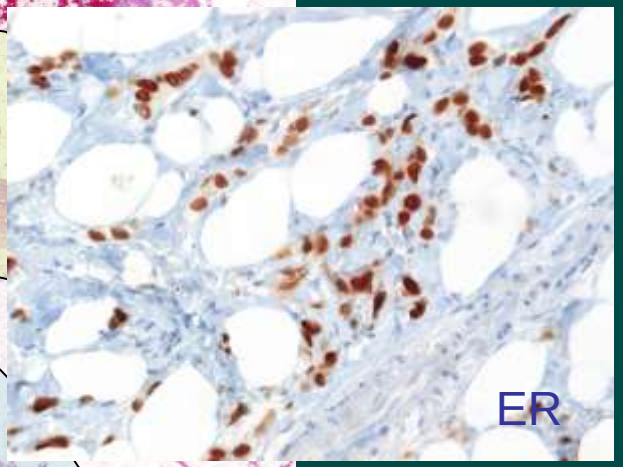
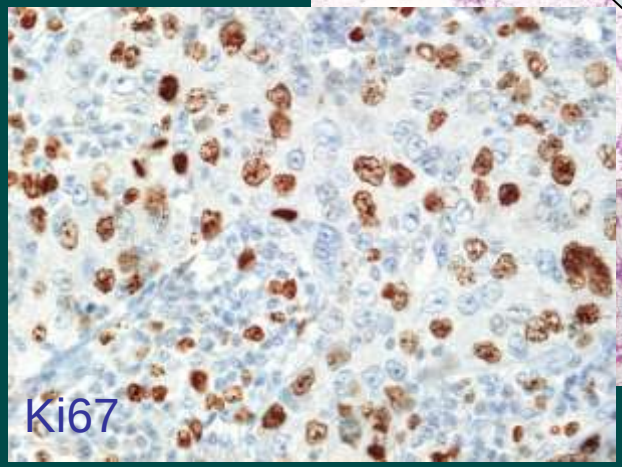
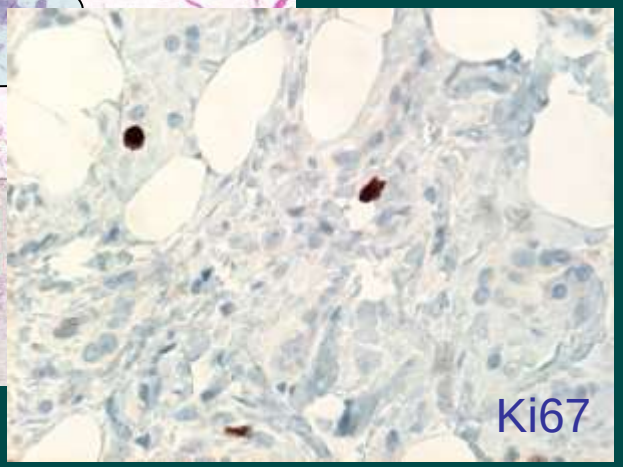

ER


Ki67


Ki67

When describing malignant lesions in the breast, the following morphologic parameters should be listed (independent of the used imaging method):

- **the distribution of the lesions (as unifocal, multifocal or diffuse) separately for invasive and in situ lesions,**
- **the extent of the disease (representing the whole area including all the invasive, in situ and intravascular malignant structures),**
- **the size of the tumor corresponding to the largest diameter of the lagest individual invasive tumor focus,**
- **evidence for intratumoral or intertumoral heterogeneity.**

It is far not sufficient
to preoperatively verify malignancy;

lesion distribution,
disease extent,
localization,
tumor size,
tumor stage

should also be assessed
for adequate therapeutic decision

There are no indications for frozen section on breast tissue in modern breast pathology!

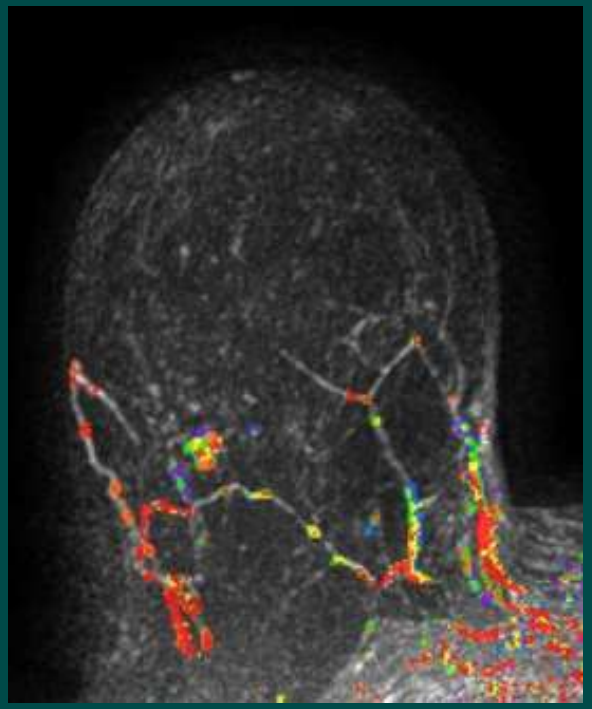
Preoperative conference

Radiological – pathological correlation

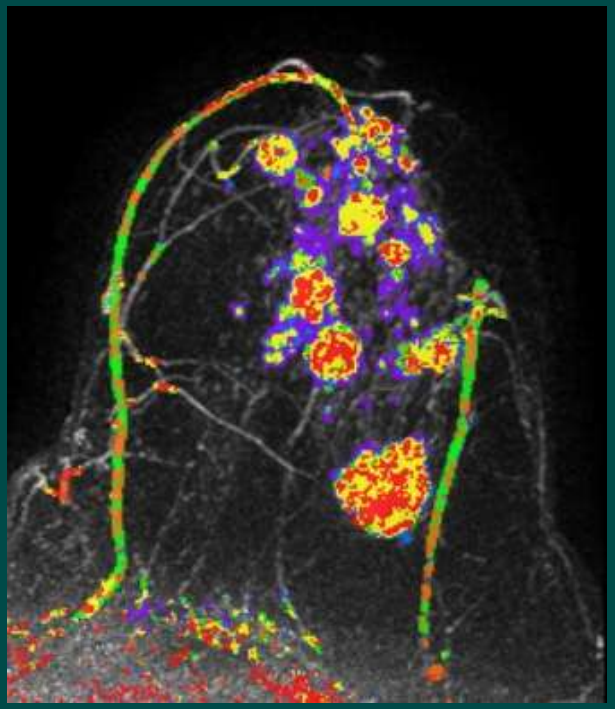
Preoperative interdisciplinary consensus diagnosis

- Benign or malignant (suspicious)
- In situ or invasive
- Tumor size
- Unifocal, multifocal or diffuse
- Extensive or of limited extent
- Position within the breast

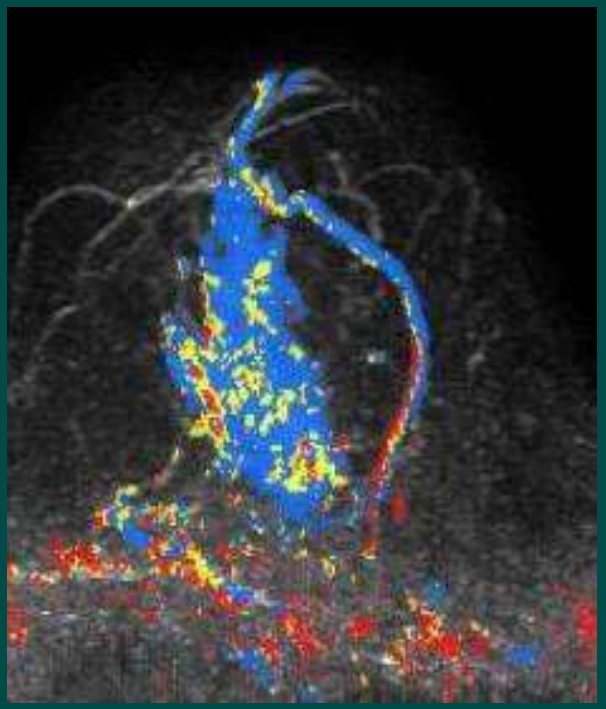
Lobular invasive, high-grade invasive,
associated high - grade in situ component



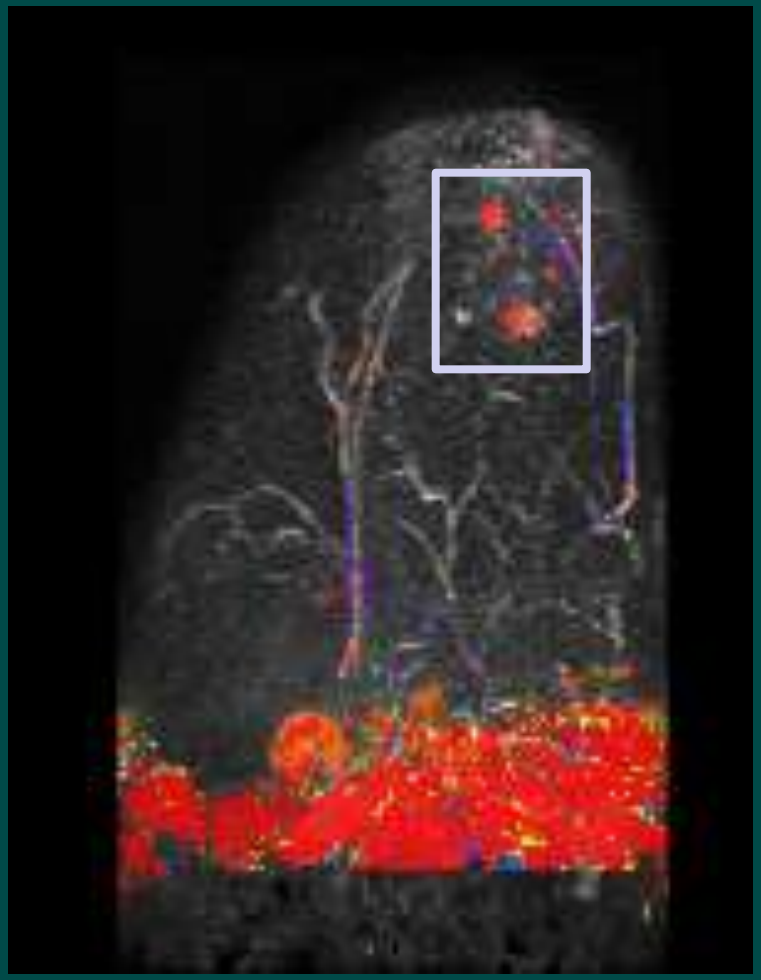
Unifocal



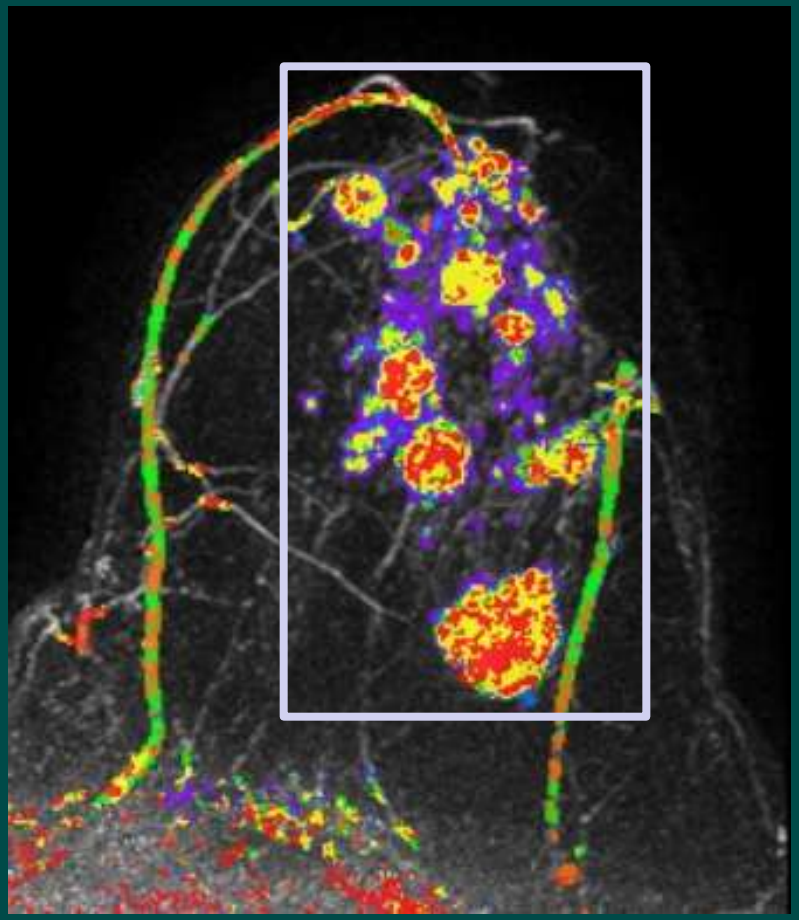
Multifocal



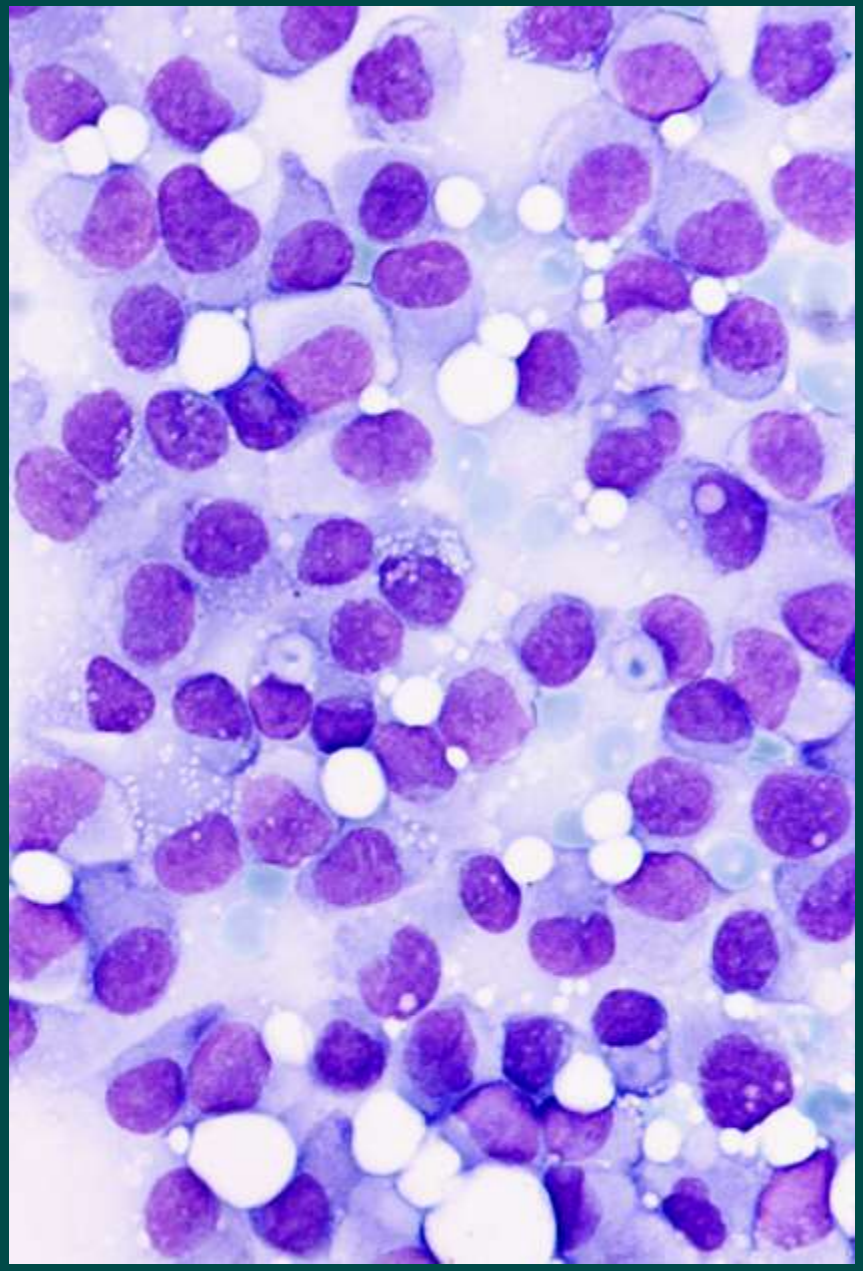
Diffuse

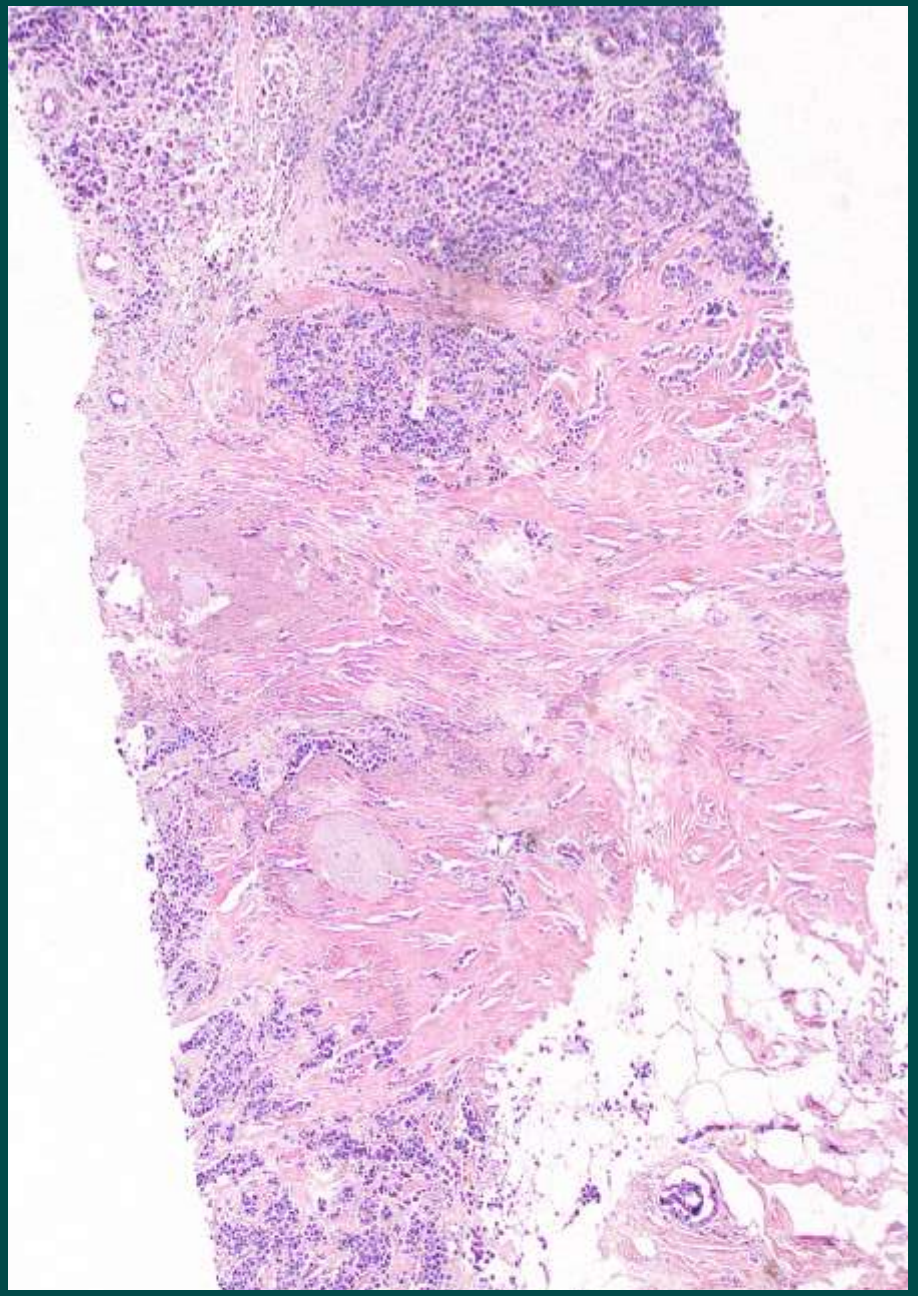


Limited extent < 4 cm



Extensive >= 4cm





Preoperative diagnosis: planning

- Mammografic – pathologic correlation
- The experience with different biopsy modalities (advantages and disadvantages)
- The clinical situation and the radiologic image

FNAB - categories

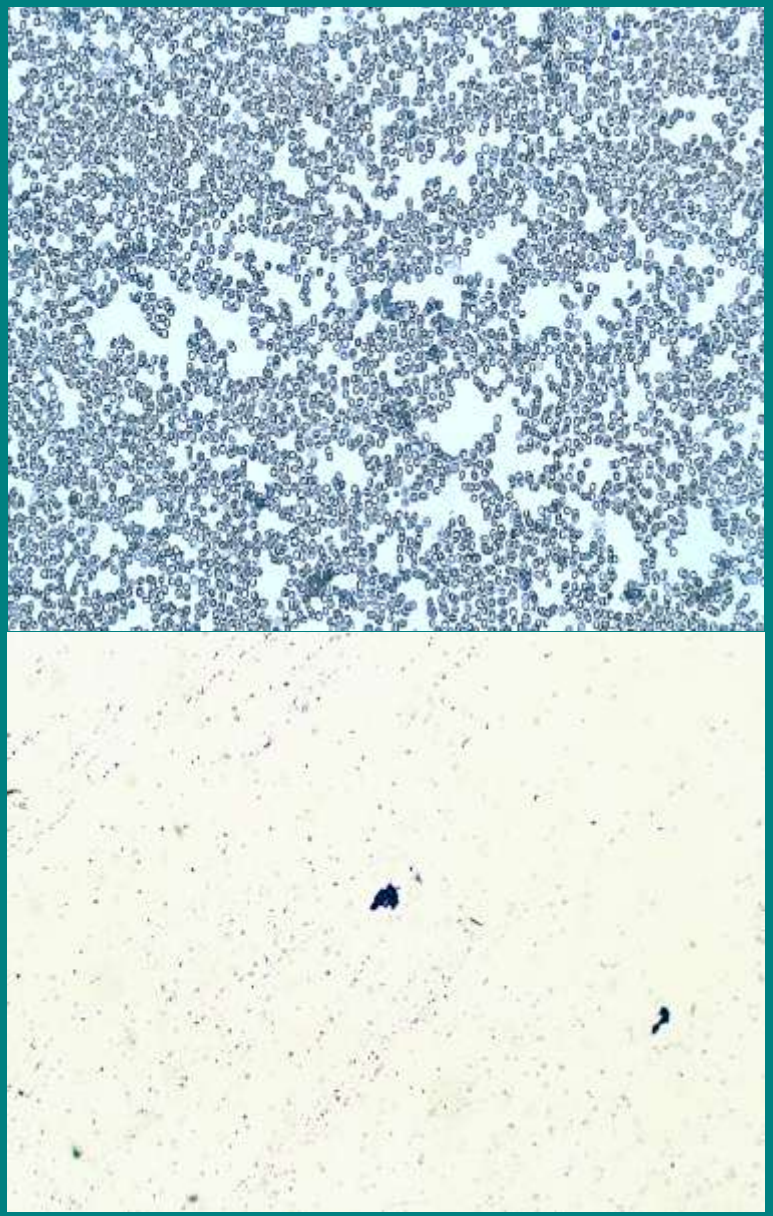
- 1. unsatisfactory
- 2. benign
- 3. atypia. probably benign
- 4. suspicious for malignancy
- 5. malignant

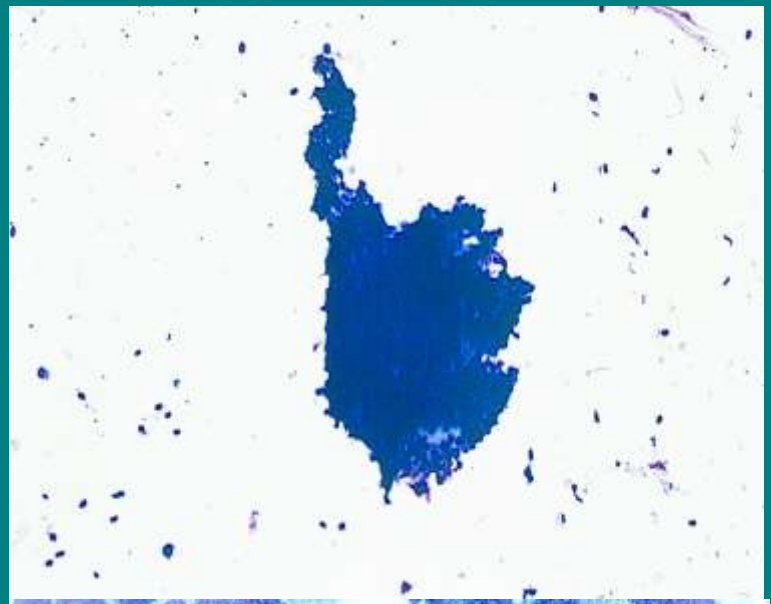
European guidelines...

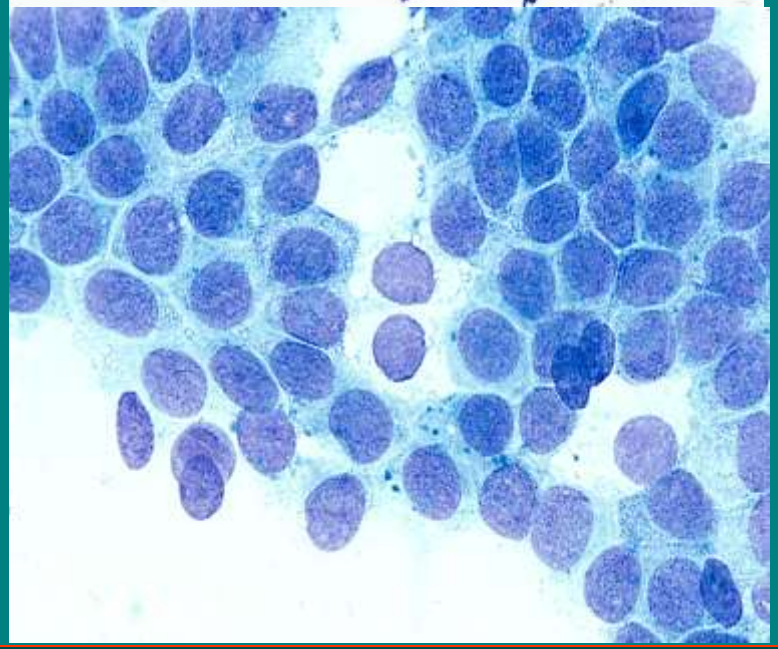
- I not performed
- II insufficient material
- III benign
- IV suspicious
- V malignant

”unsatisfactory benign suspicious.”

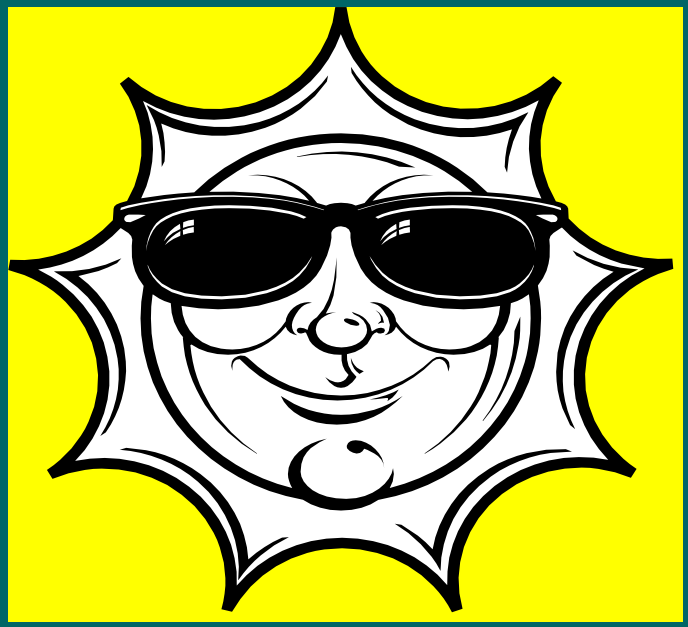
II insufficient material

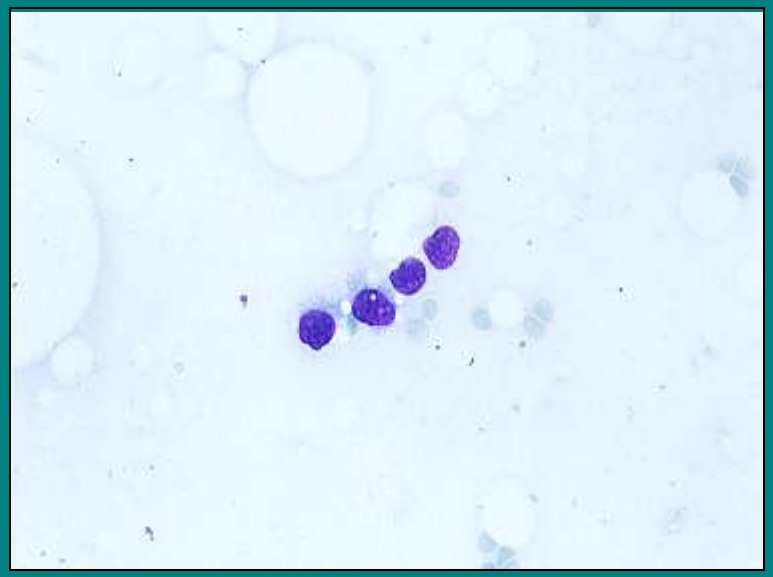


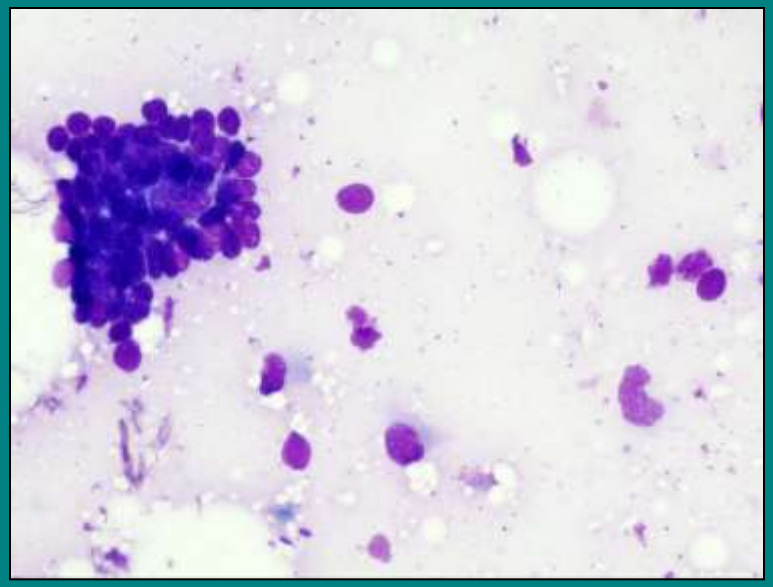




III benign

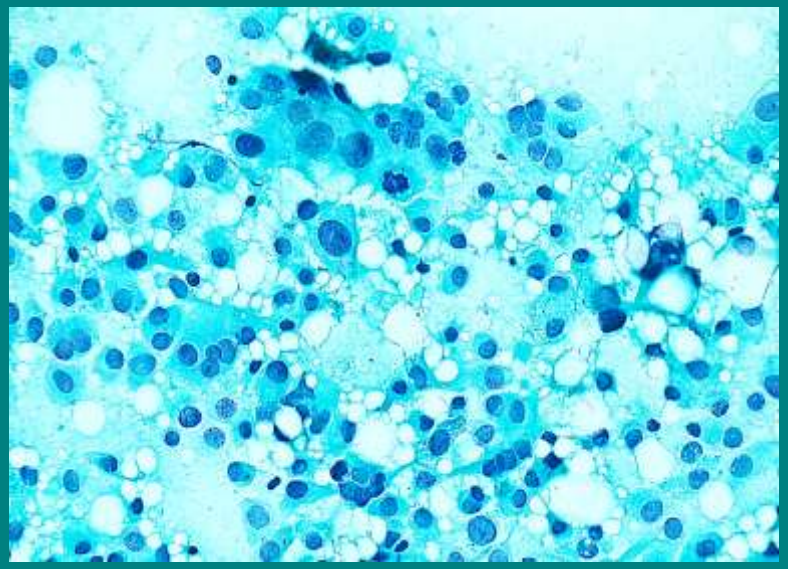


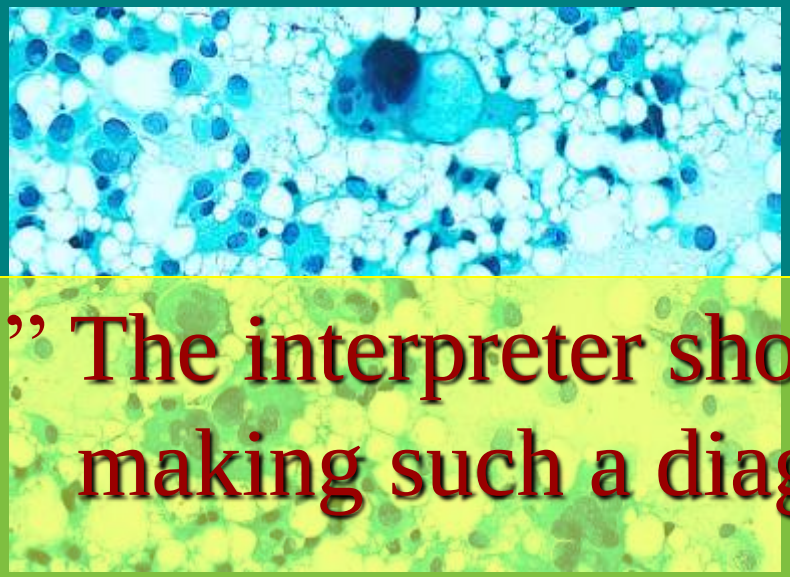




IV suspicious

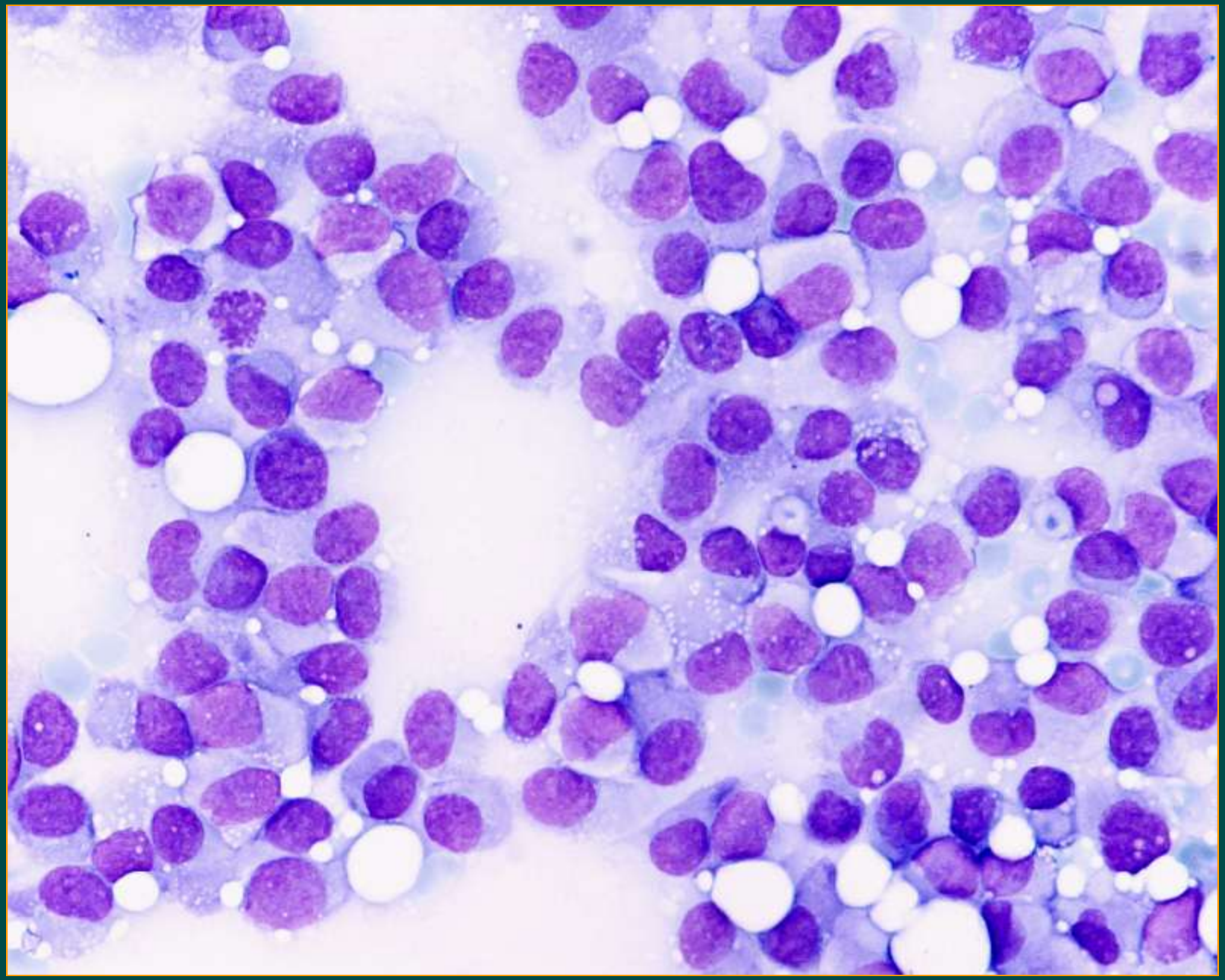
V malignant





” The interpreter should feel at ease in making such a diagnosis”

J Sloane

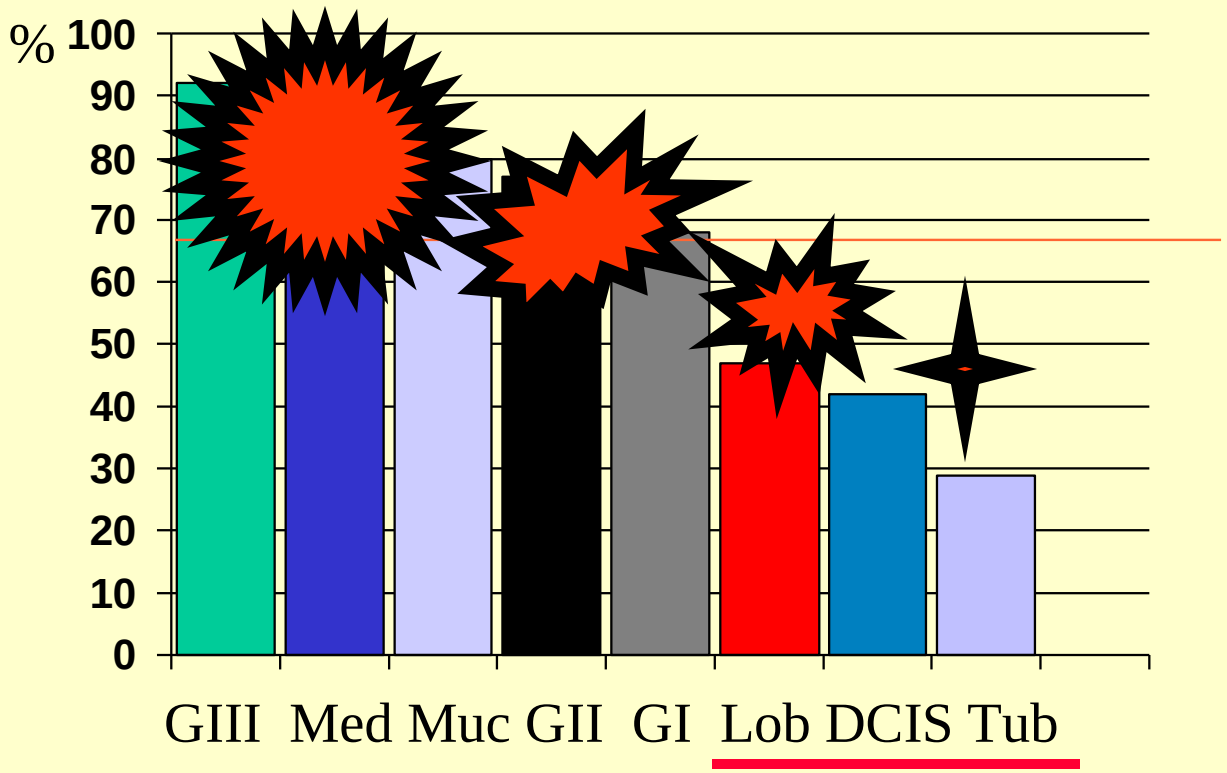


Cytological criteria

	Benign	Malignant
cellularity	-	+
myoepithelium	+	-
cochesiveness	+	-
atypia	-	+

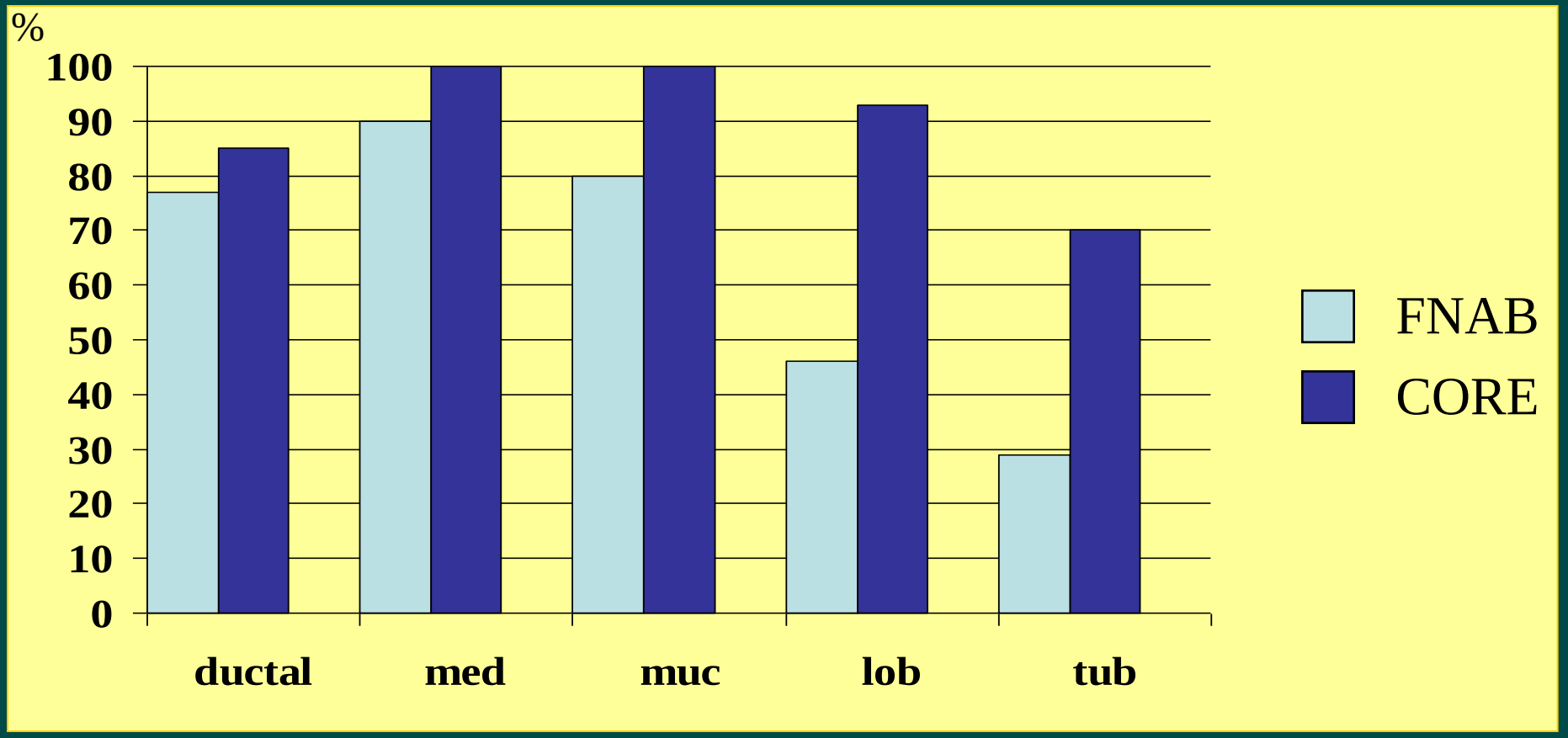
False positive rate = 0

Diagnostic accuracy of FNAB in 240 breast cancers

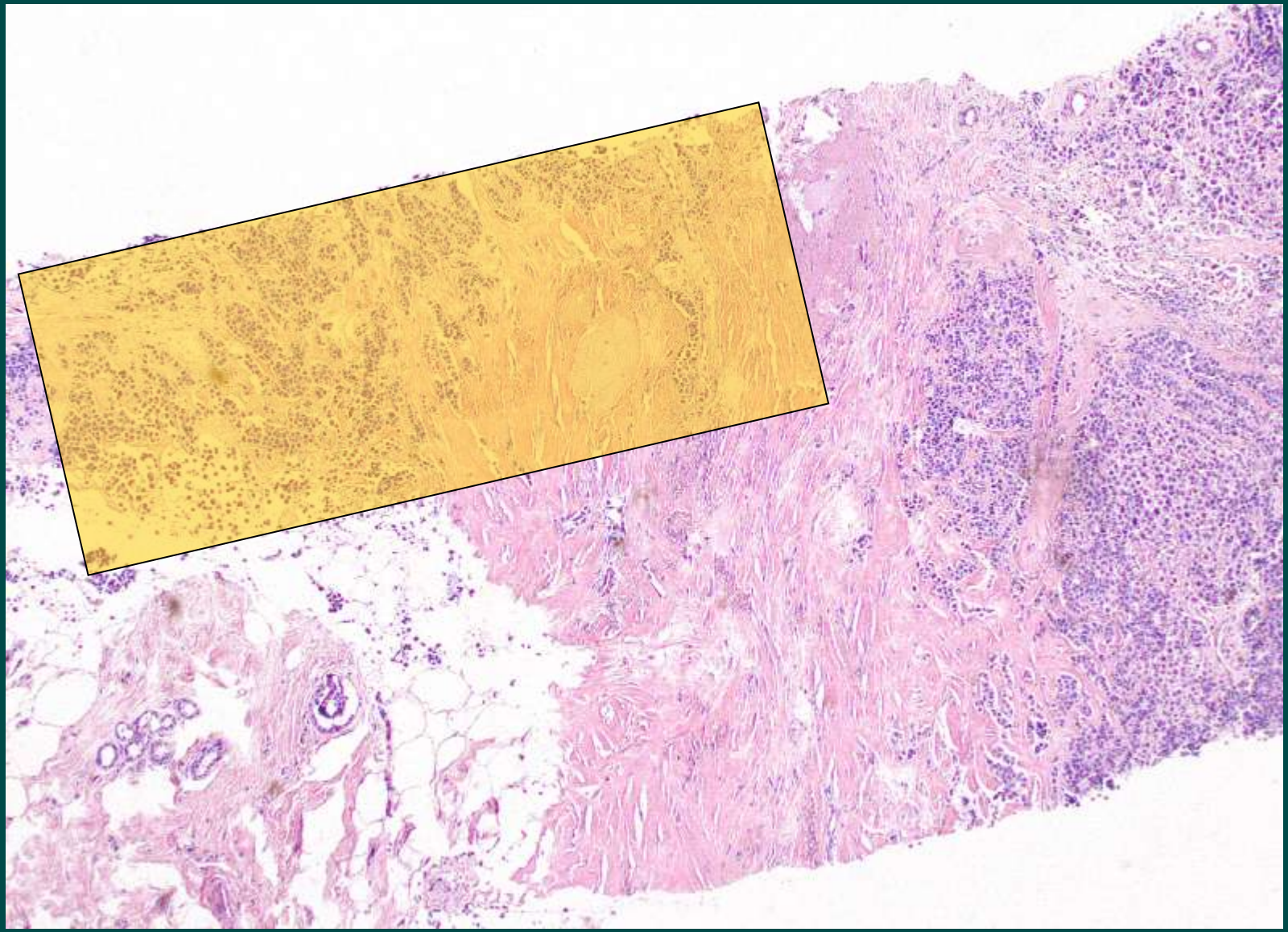


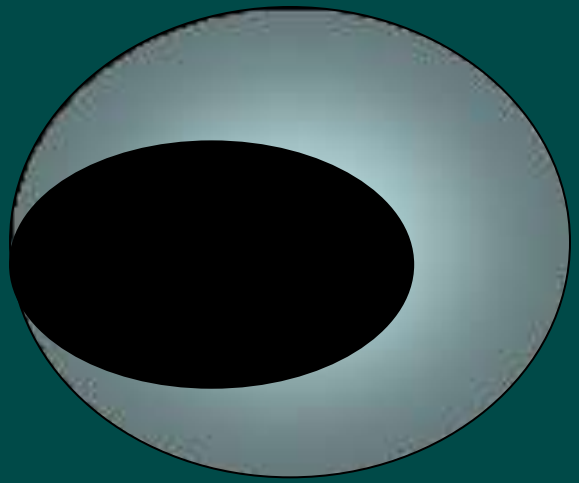
Tot, Tabár, Gere: The role of core needle biopsy of breast lesions when fine needle biopsy is inconclusive Acta Cytol 1999;43(4)

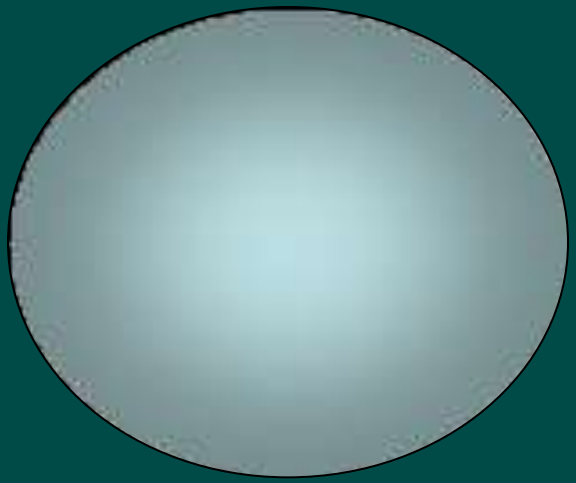
FNAB : CORE
accuracy/tumor type

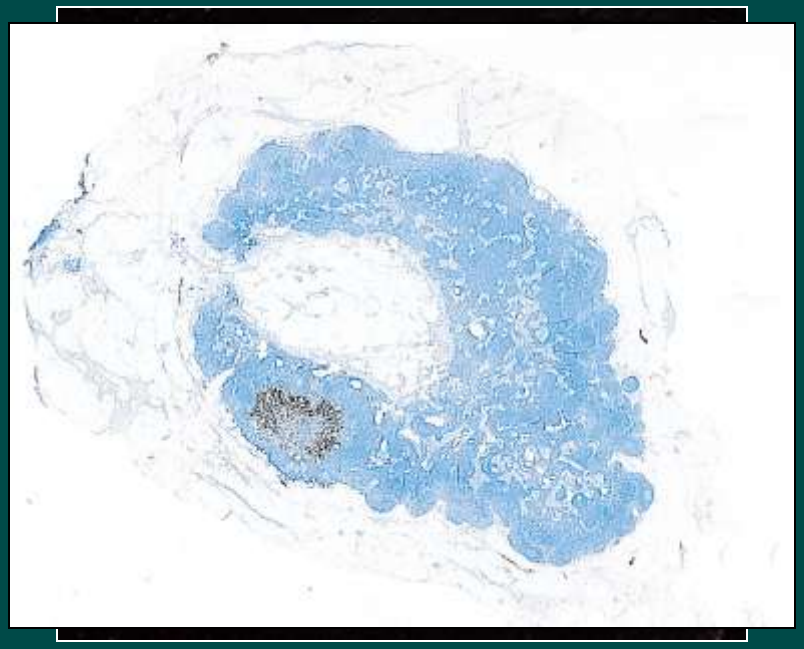


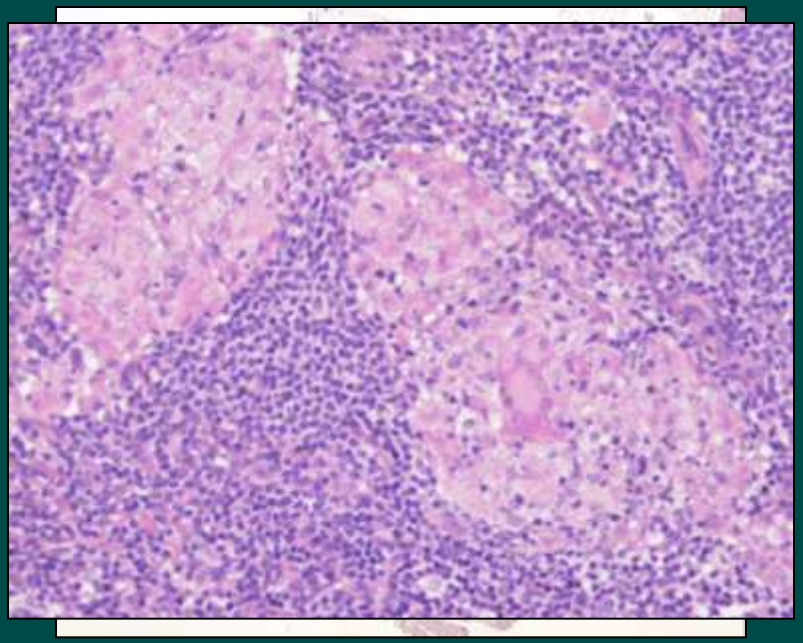
Tot, Tabár, Gere: The role of core needle biopsy of breast lesions when fine needle biopsy is inconclusive Acta Cytol 1999;43(4)

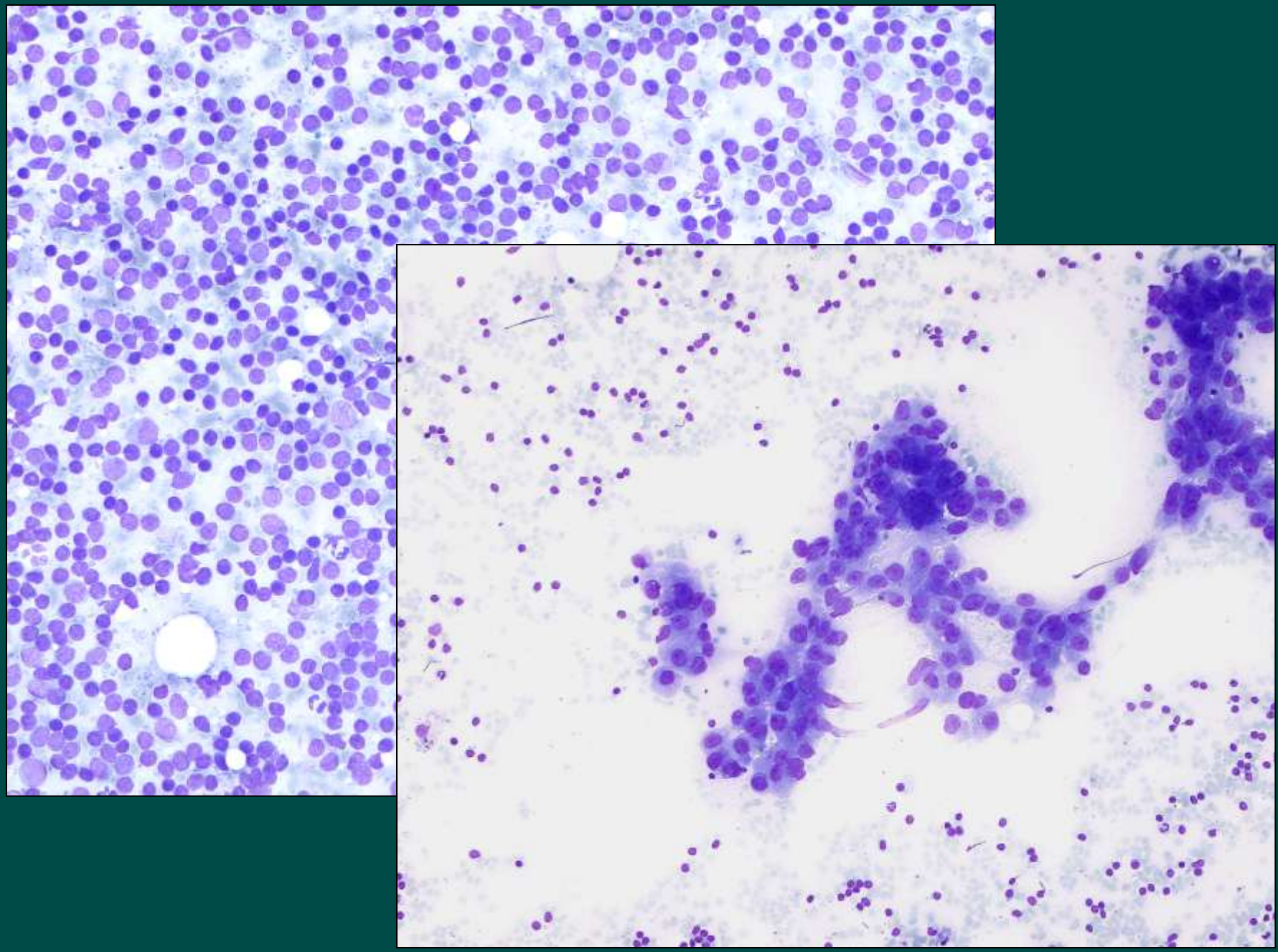












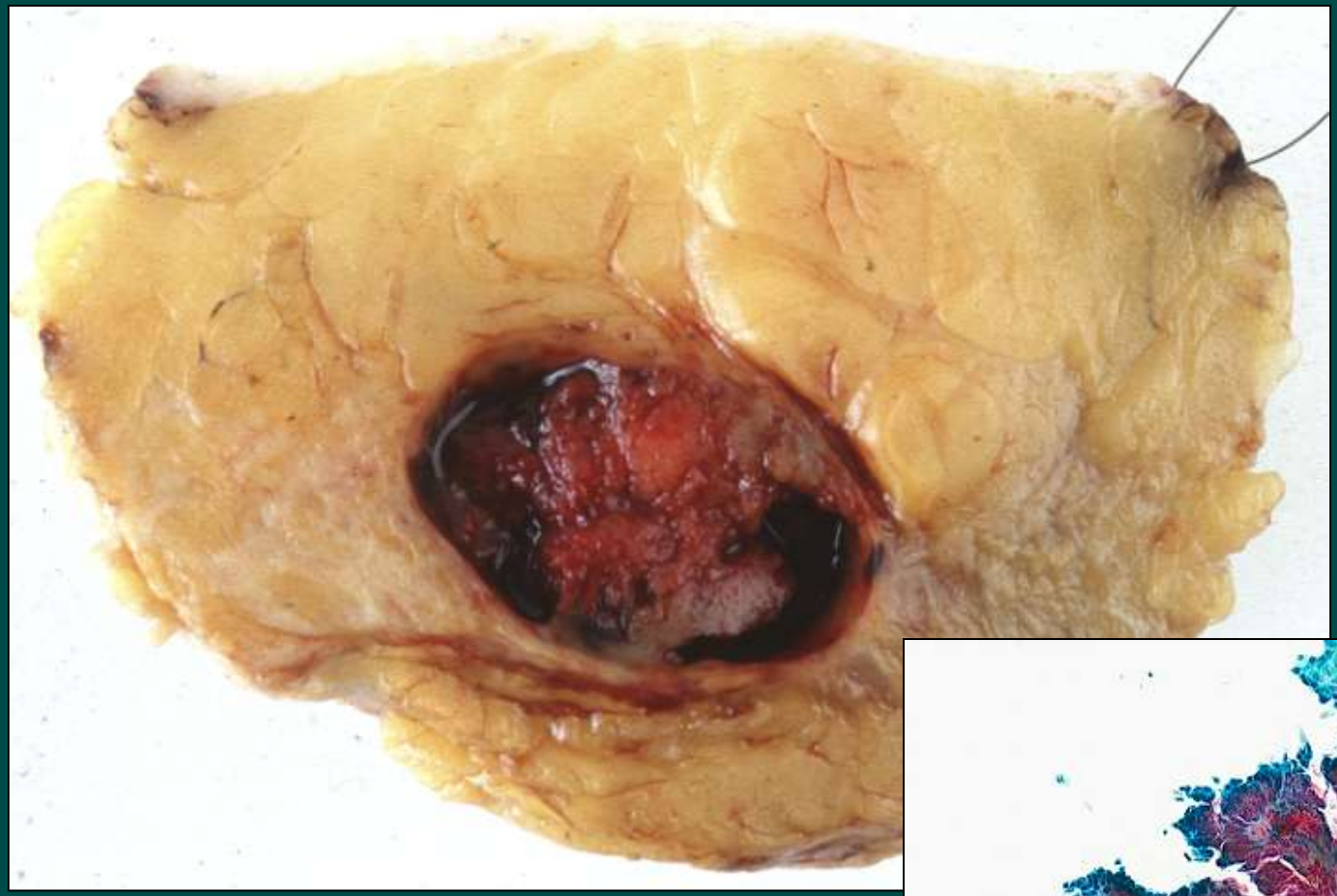
False positive rate = 0

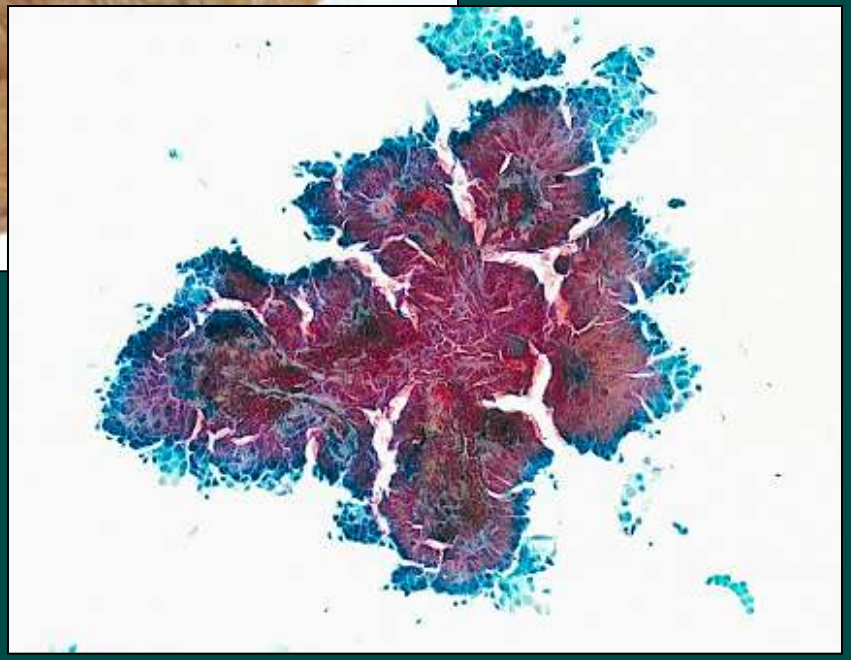
Sapino A et al. Ultrasonographically-guided fine-needle aspiration of axillary lymph nodes: role in breast cancer management.
Br J Cancer 88(5):702-6, 2003

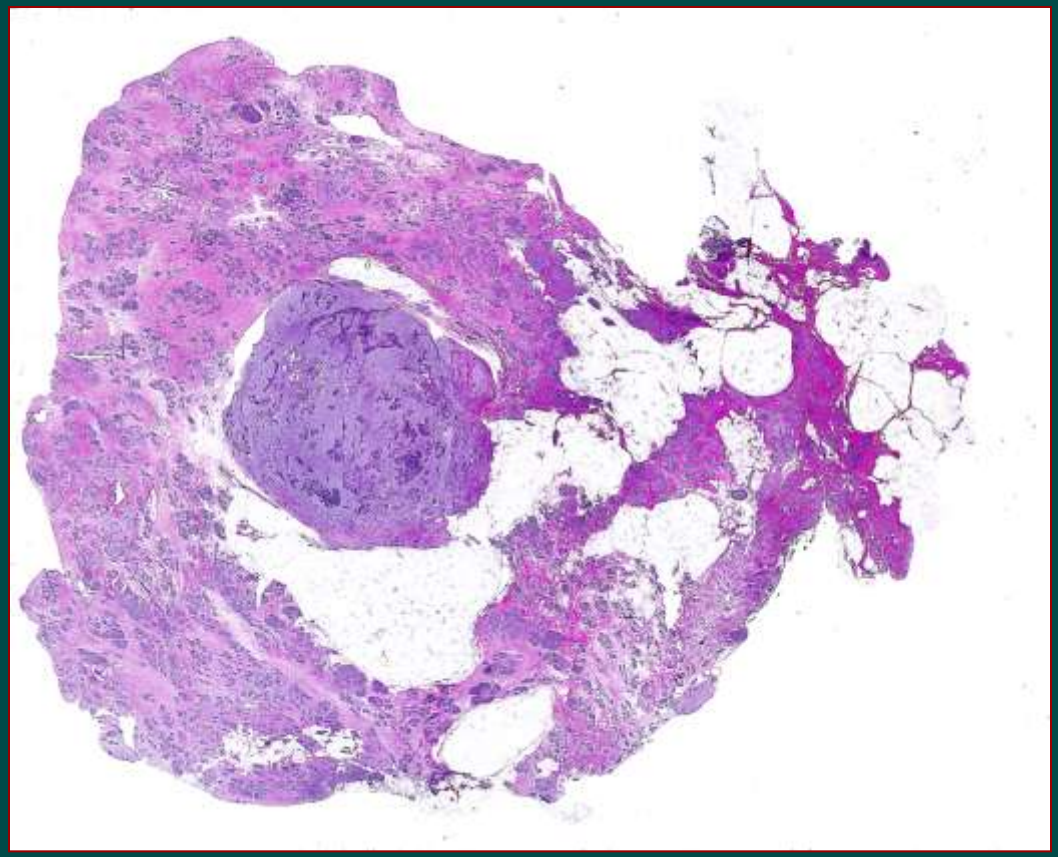
2 / 3

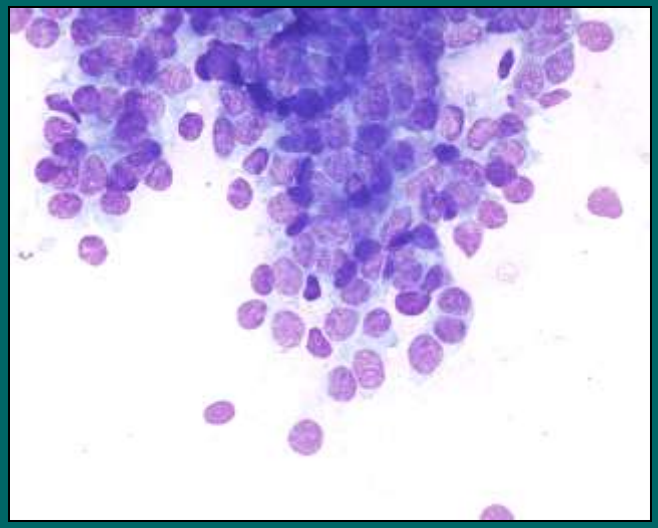
	CNB	FNAB	P value
Inadequacy rate	6.9%	17.7%	<0.001
Inadequacy rate for malignant lesion	0.9%	4.5%	<0.001
Absolute sensitivity	93.1%	74.1%	<0.001
Complete sensitivity	97.4%	93.8%	=0.001
Absolute diagnostic accuracy	84.5%	71.9%	<0.001
False negativity	1.7%	1.7%	
Specificity	88.3%	95.4%	<0.001
Complete diagnostic accuracy	93.2%	95.4%	<0.008

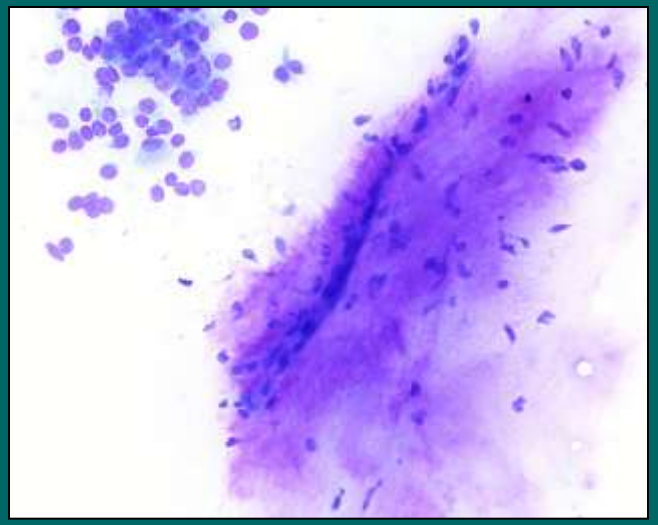
Brancato B, Croetti E, Bianchi S et al. Accuracy of needle biopsy of breast lesions visible on ultrasound: Audit of fine needle versus core needlöe biopsy in **3233 consecutive samplings** with ascertained outcomes. Breast 21:449-454, 2012

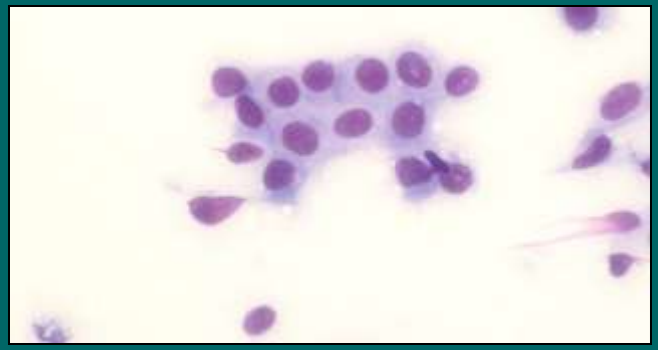




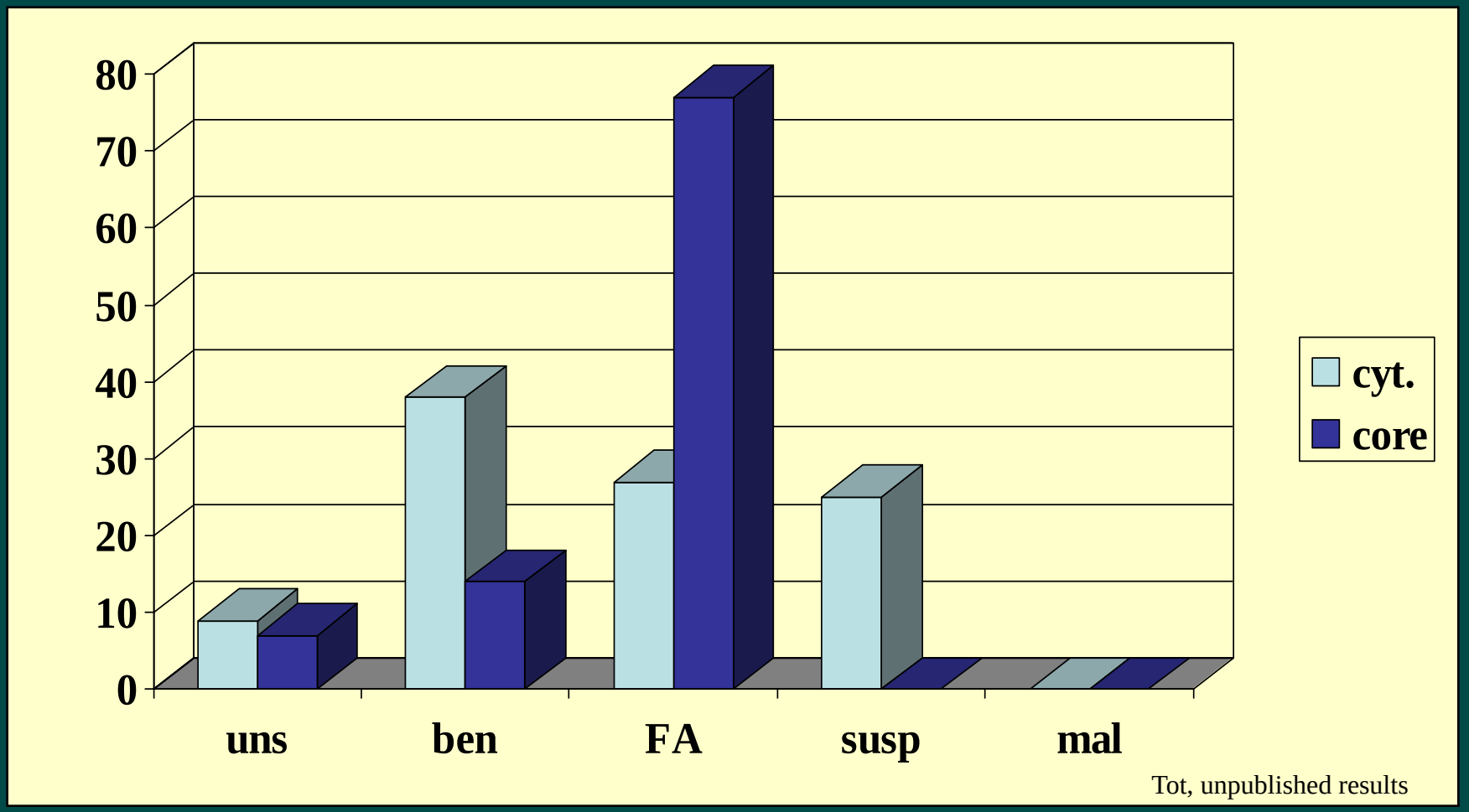




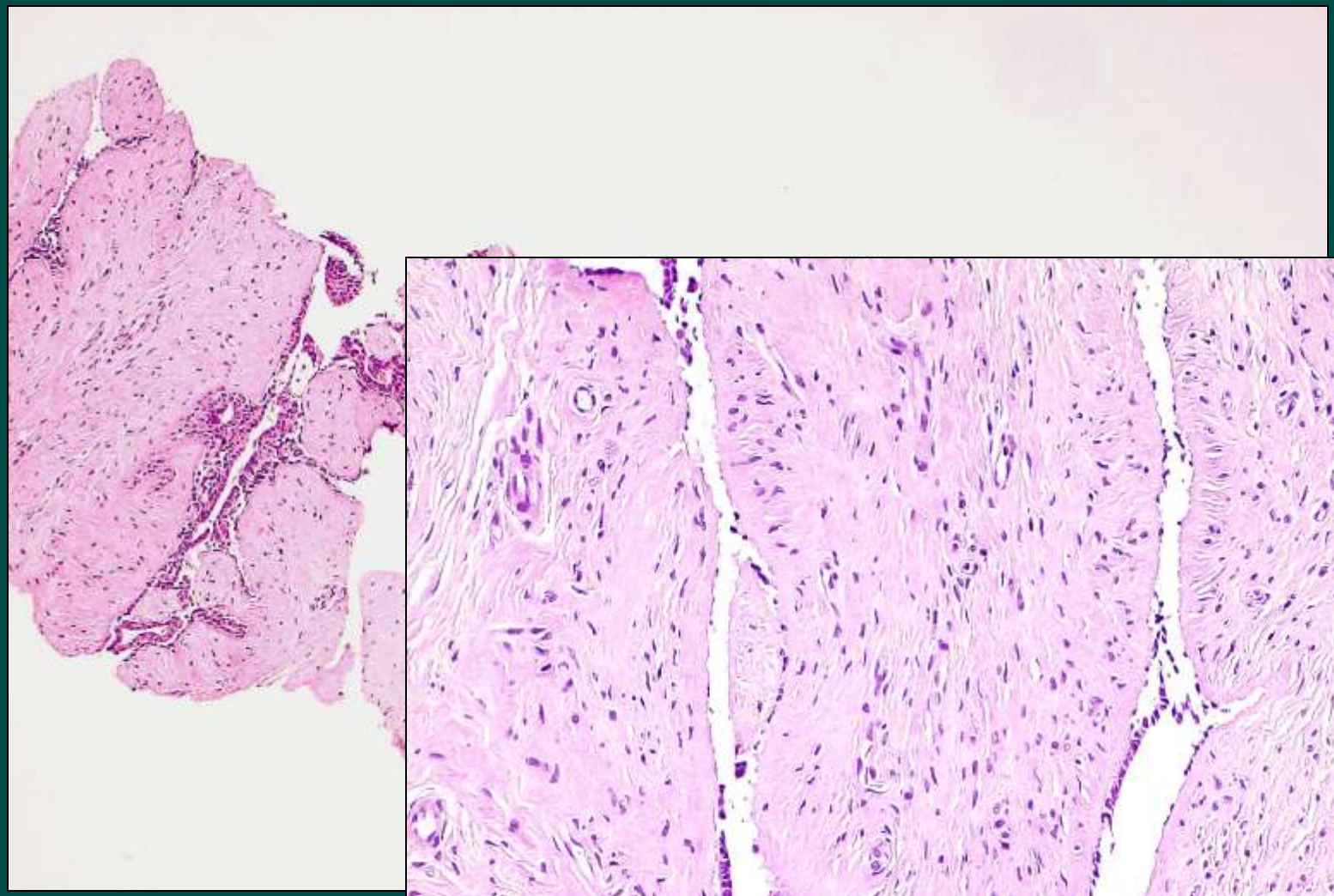




Preoperative diagnosis in 141 cases of fibroadenoma



Tot, unpublished results



False positivity = 0

Malignant FNAB

=

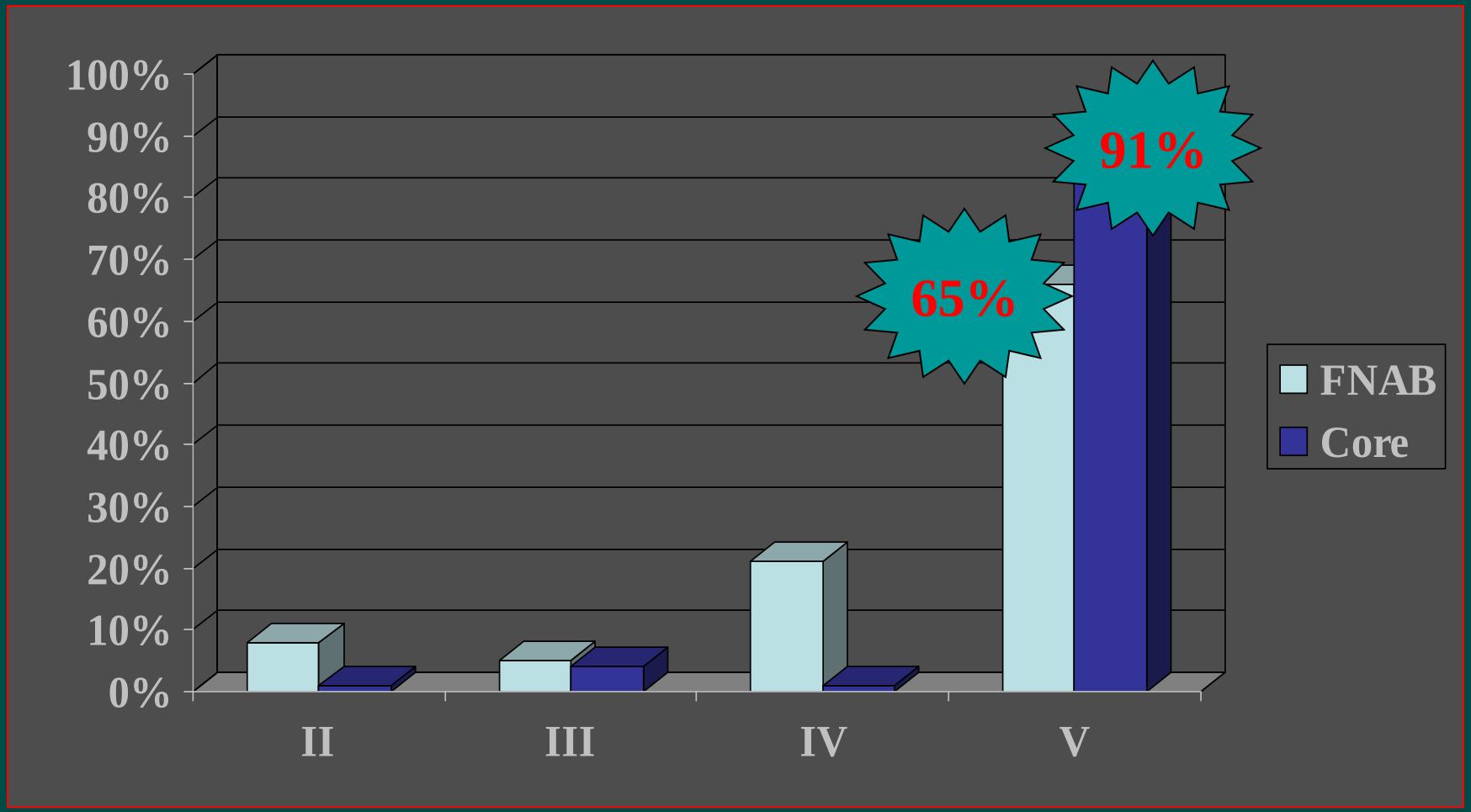
malignant

Non - malignant FNAB

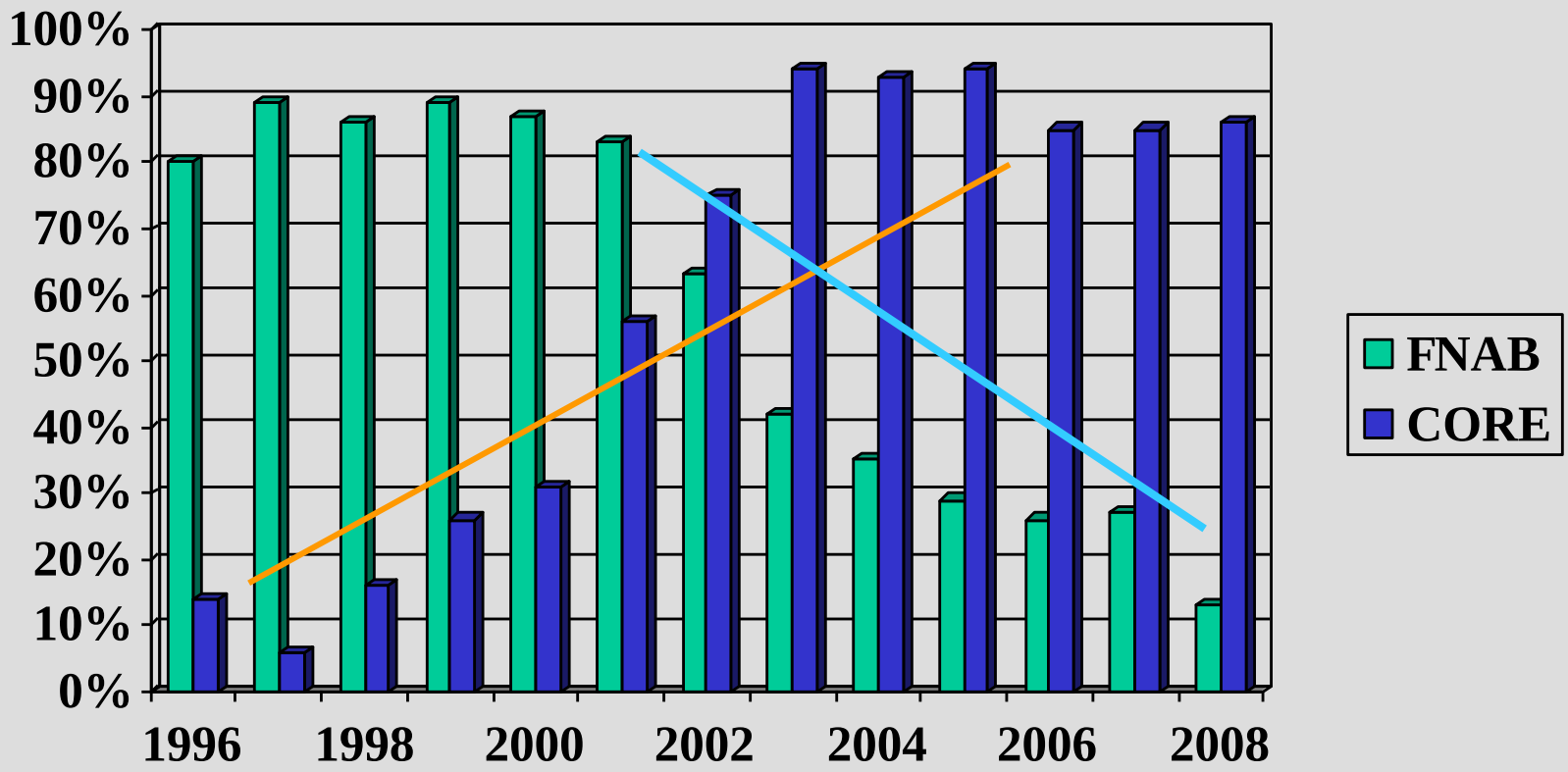
=

anything

Diagnostic accuracy of FNAB and Core biopsy, Falun 1996-2003

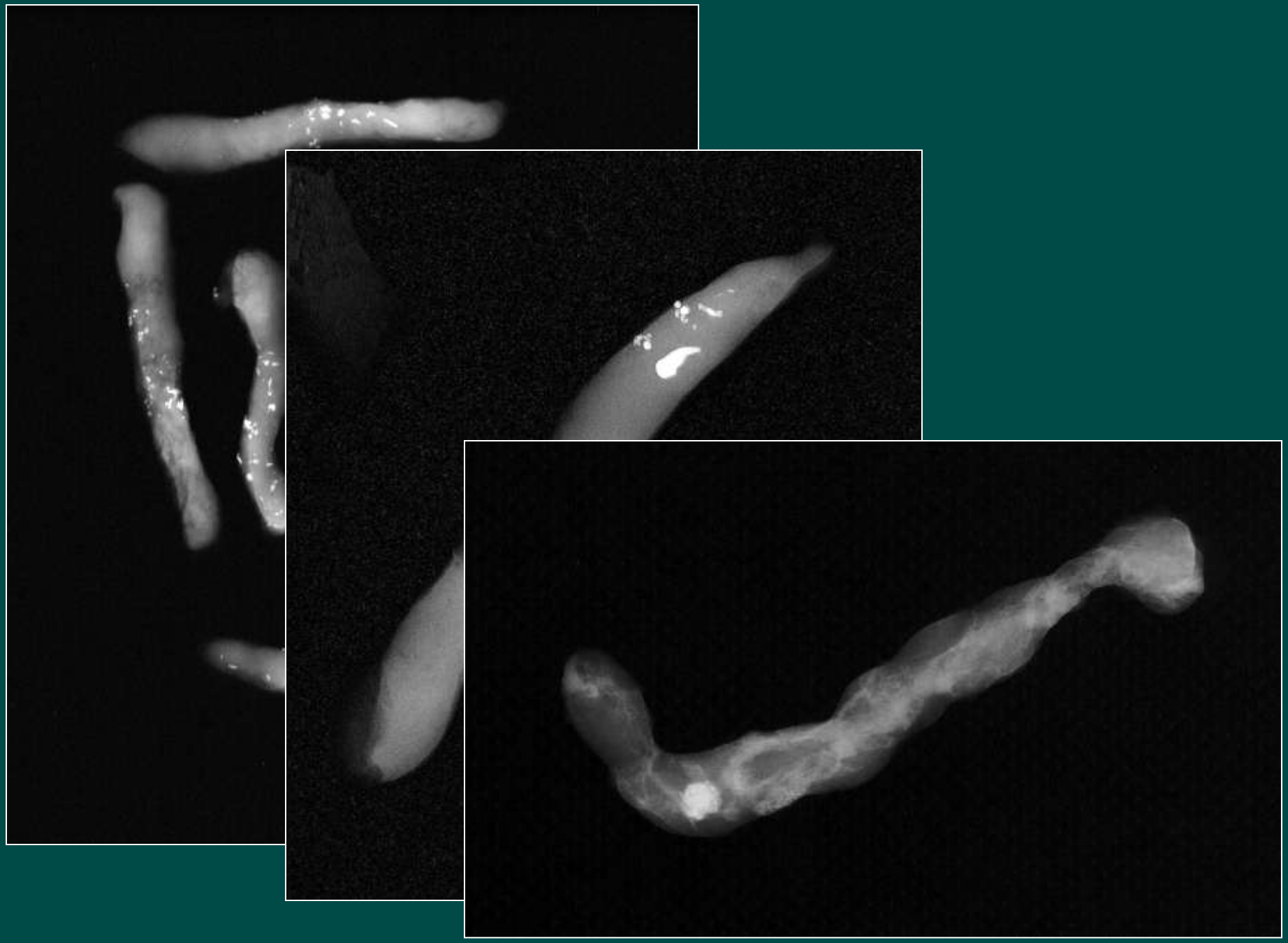


FNAB and CORE biopsy in 2500 breast carcinoma cases (Falun, 1996-2008)



Vacuum biopsy

- 3-4 mm thick cores
- May include in toto an enlarged TDLU
- May include a transsection of a distended duct
- May represent an alternative to open surgical intervention in some cases



INTACT biopsy


0
1
2

Choose the best sample capture size

The ***Intact*** Breast Lesion Excision System (***Intact*** BLES) offers four sizes of capture basket. All four sizes deploy from the same 6 mm diameter wand.

Specimen actual size:				
Specimen diameter:	10mm	12mm	15mm	20mm
Specimen weight:	.8g	1.1g	2.1g	3g

Compared with VACNB, ***Intact*** BLES removes less total tissue for a given diameter

Remove the entire area of interest without taking excess normal breast tissue.

Specimen actual size:			
Method/diameter:	***Intact*** BLES: 12 mm	VACNB 8 gauge	VACNB 11 gauge
Specimen weight:	1.1g	2.5g	2.25g

Preoperative diagnosis: planning

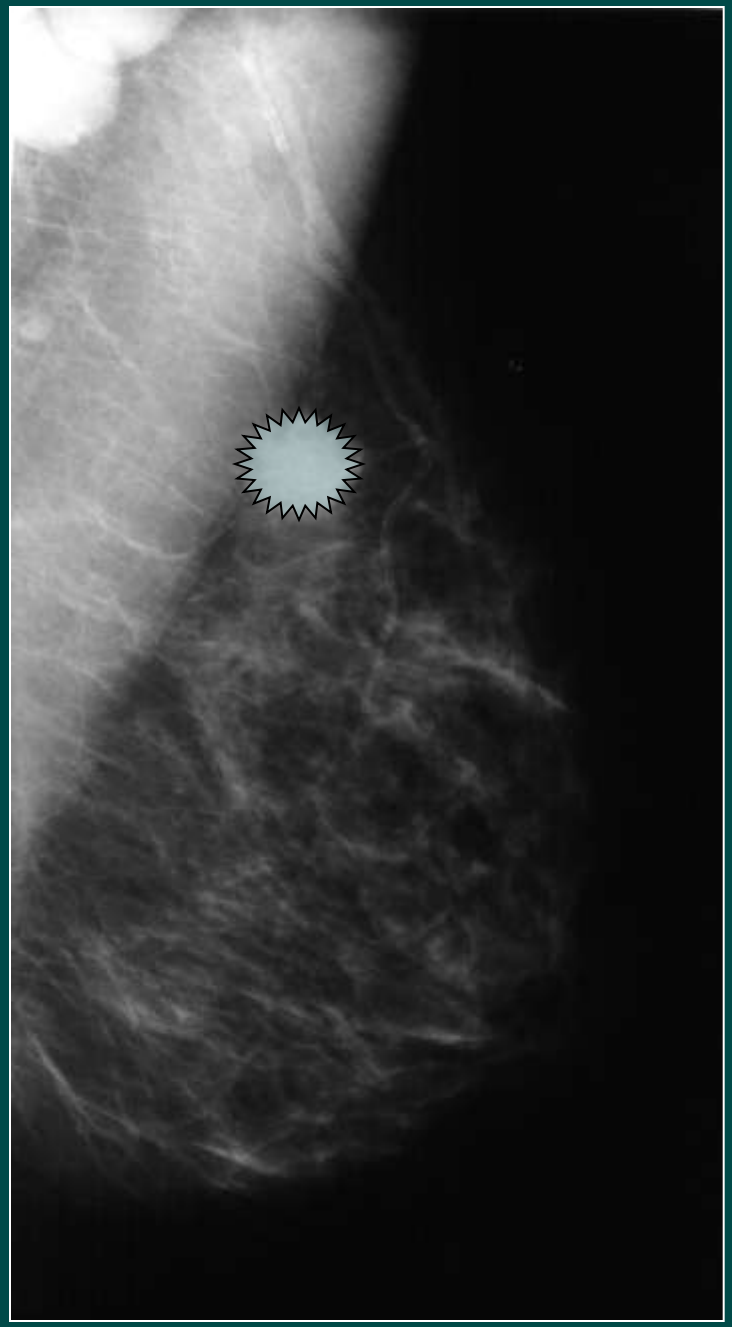
- Mammografic – pathologic correlation
- The experience with different biopsy modalities (advantages and disadvantages)
- The clinical situation and the radiologic image

What I am supposed to do ??

- To prove malignancy
- To prove invasion
- To prove benign character
  - cystic
  - solid
- To role out malignancy

What I am supposed to do ??

- To prove malignancy FNAB/CORE
- To prove invasion CORE
- To prove benign character
  - cystic FNAB
  - solid CORE
- To role out malignancy ……

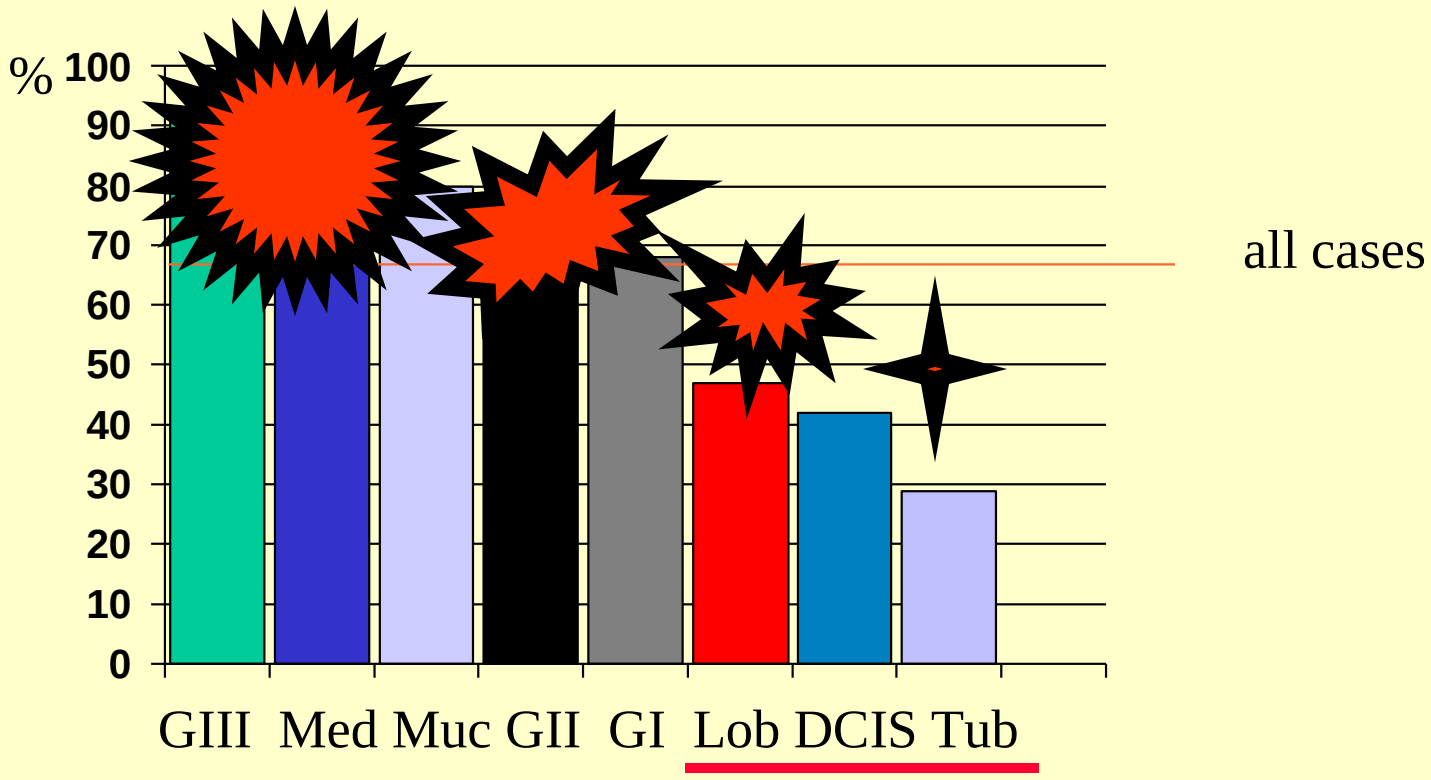


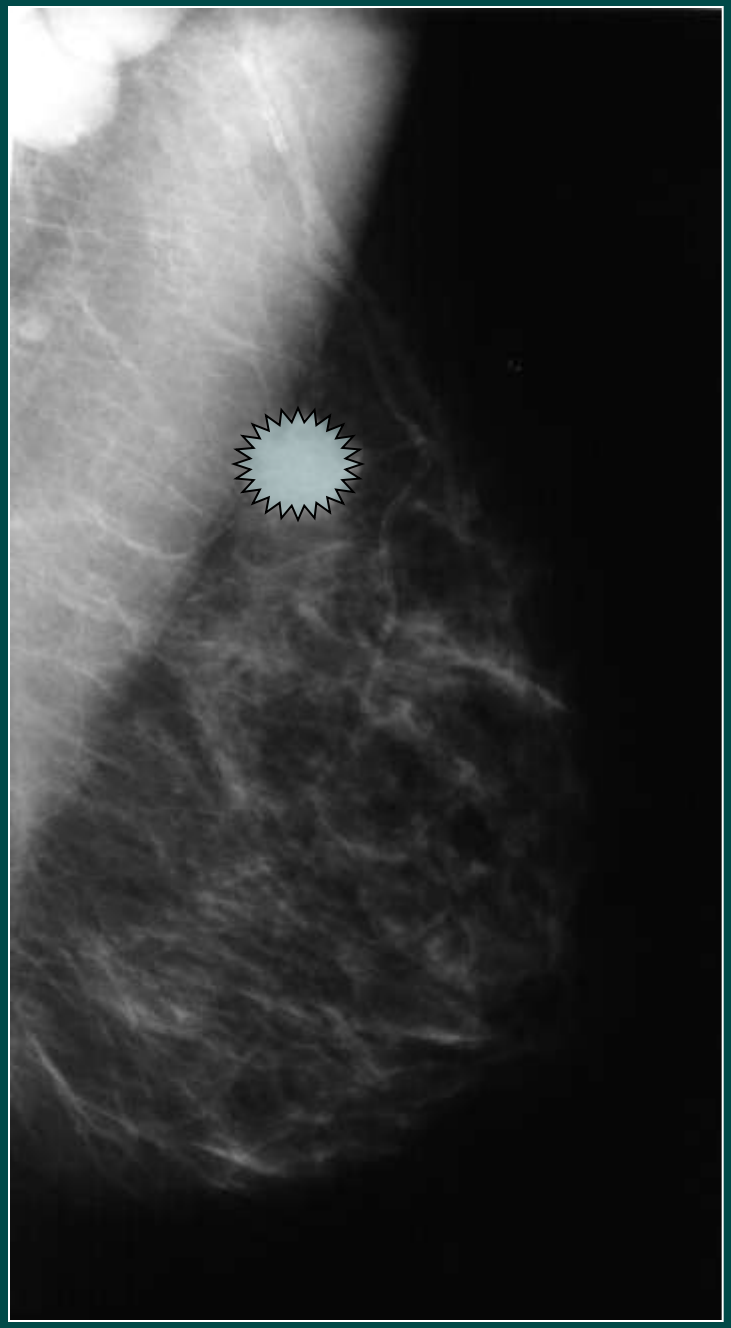
What is the purpose ?

Prove malignancy !

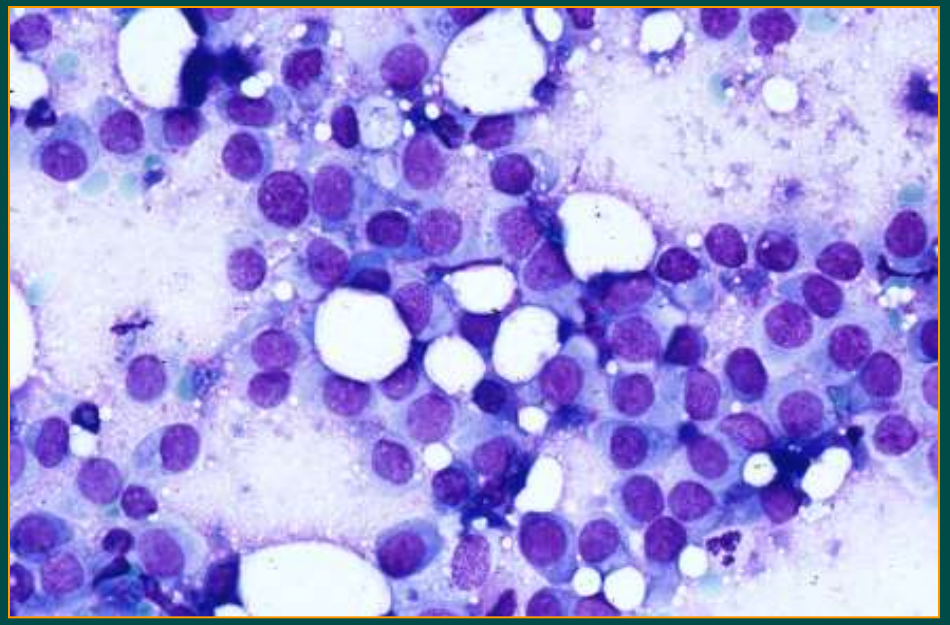
Thinest effective !

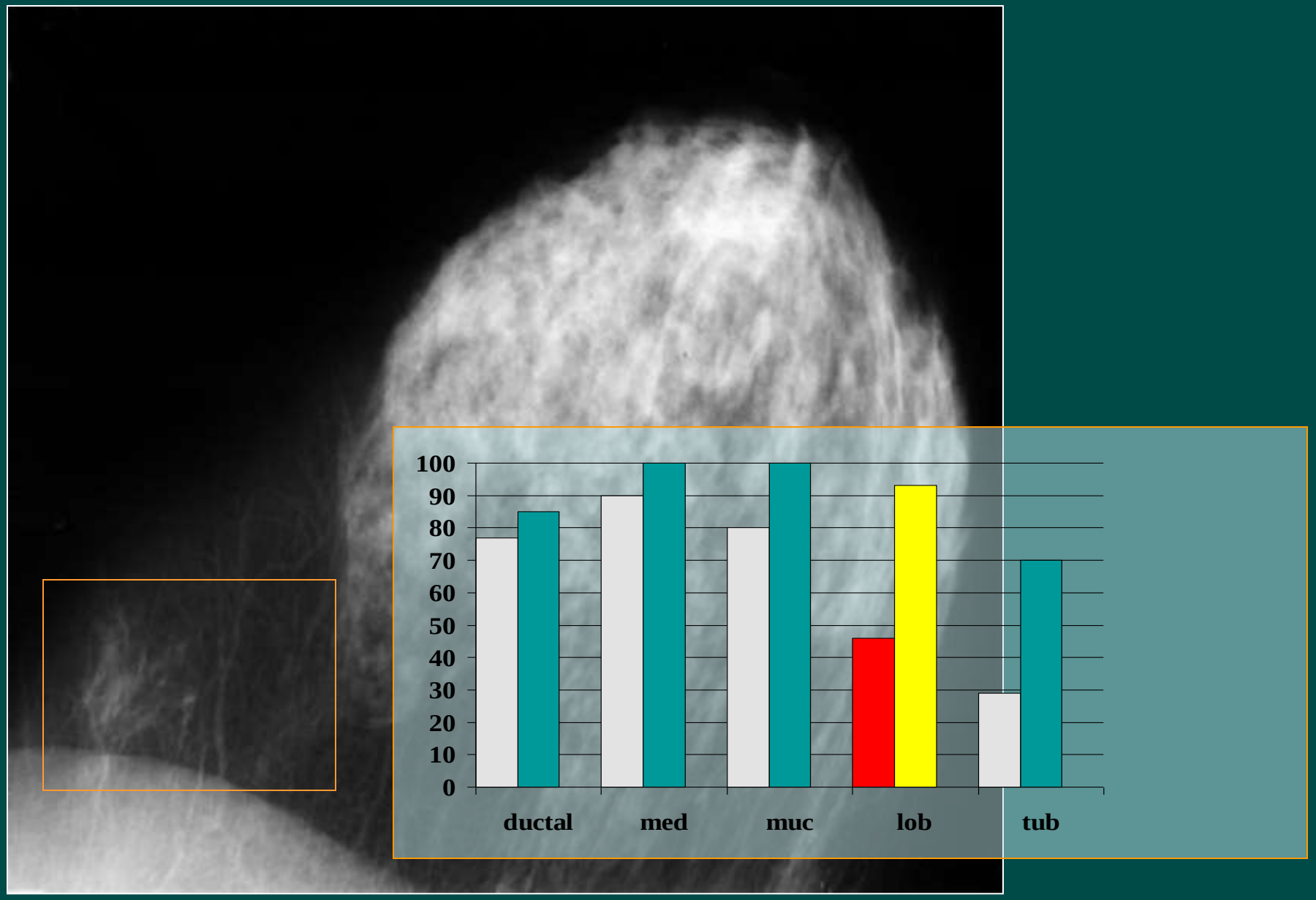
Diagnostic accuracy of FNAB in 240 breast cancers





FNAB

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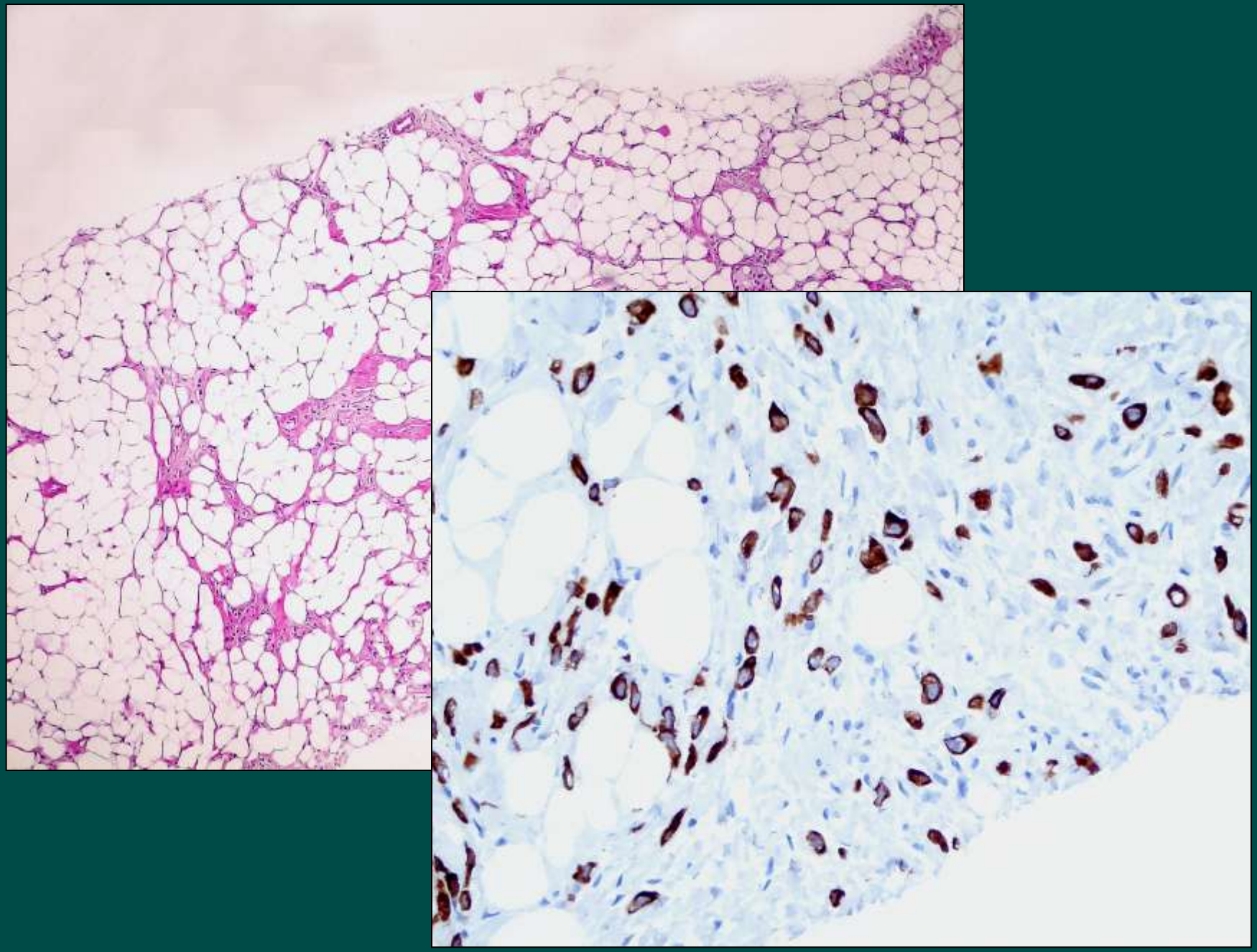


Preoperative diagnosis

- The aim is to categorize the case as
  - Operable vs non-operable
  - Early vs advanced
  - Extensive vs non-extensive

Intra-operative diagnosis

- Margin assessment
- Sentinel lymph node procedure

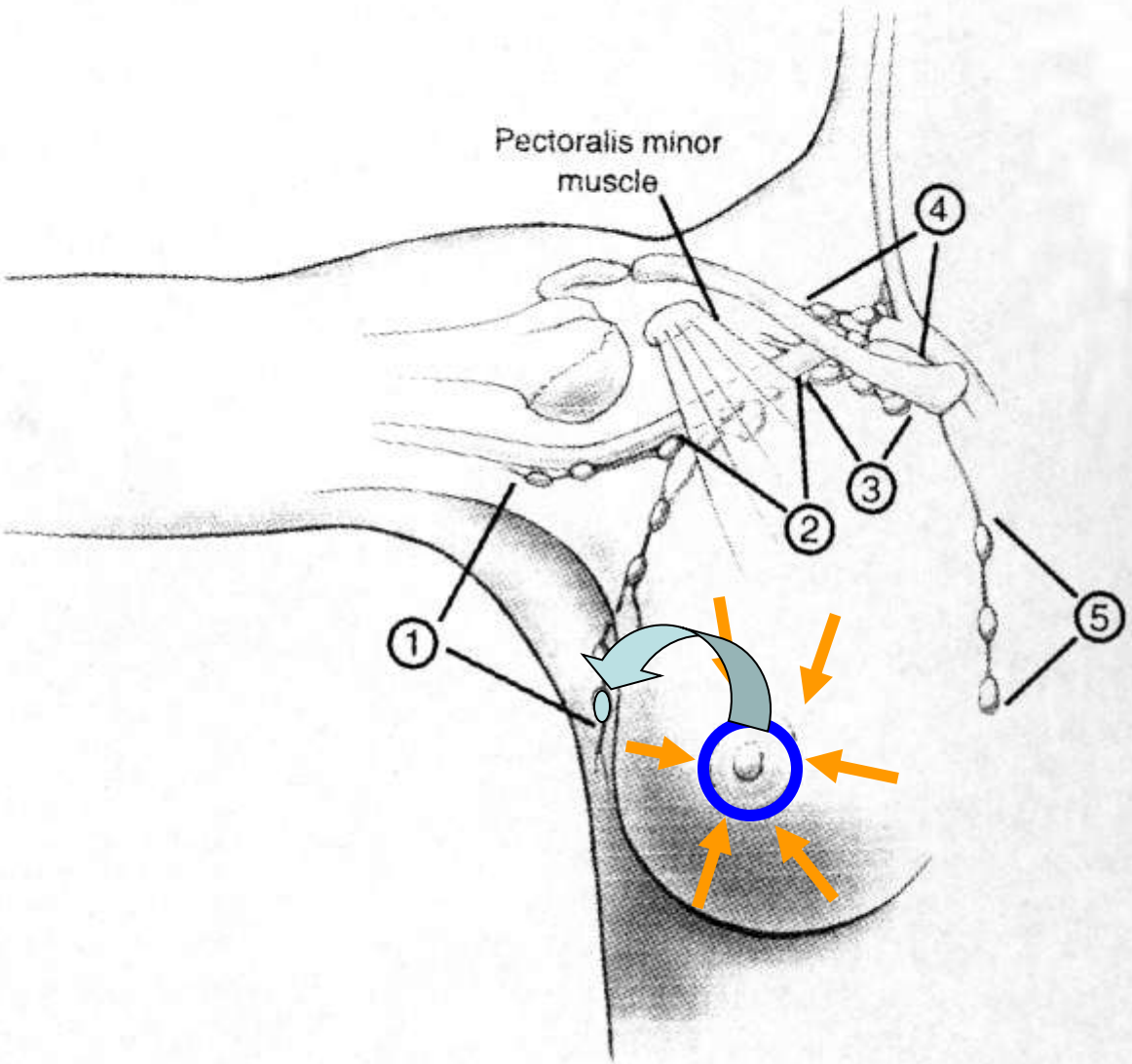


Fig. 25.1. Schematic diagram of the breast and regional lymph nodes. ① Low axillary, Level I; ② Mid-axillary, Level II; ③ High axillary, apical, Level III; ④ Supraclavicular; ⑤ Internal mammary nodes.

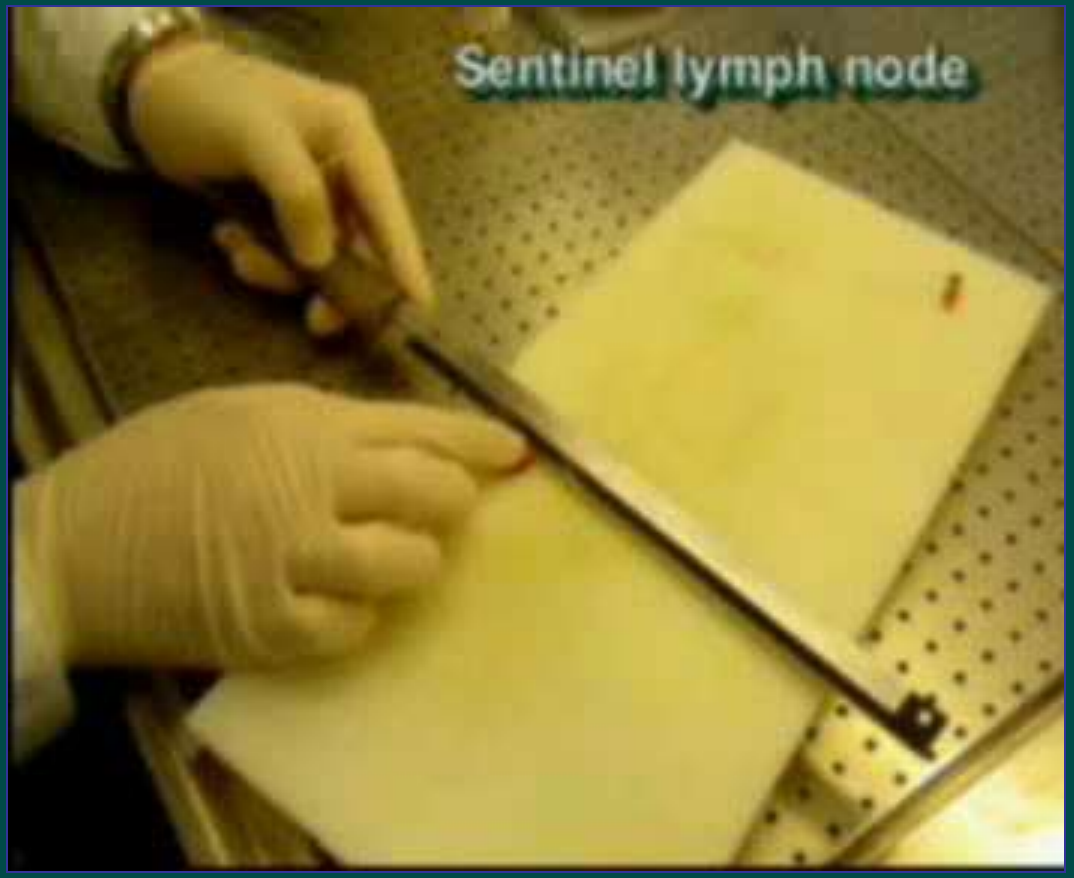
Sentinel node

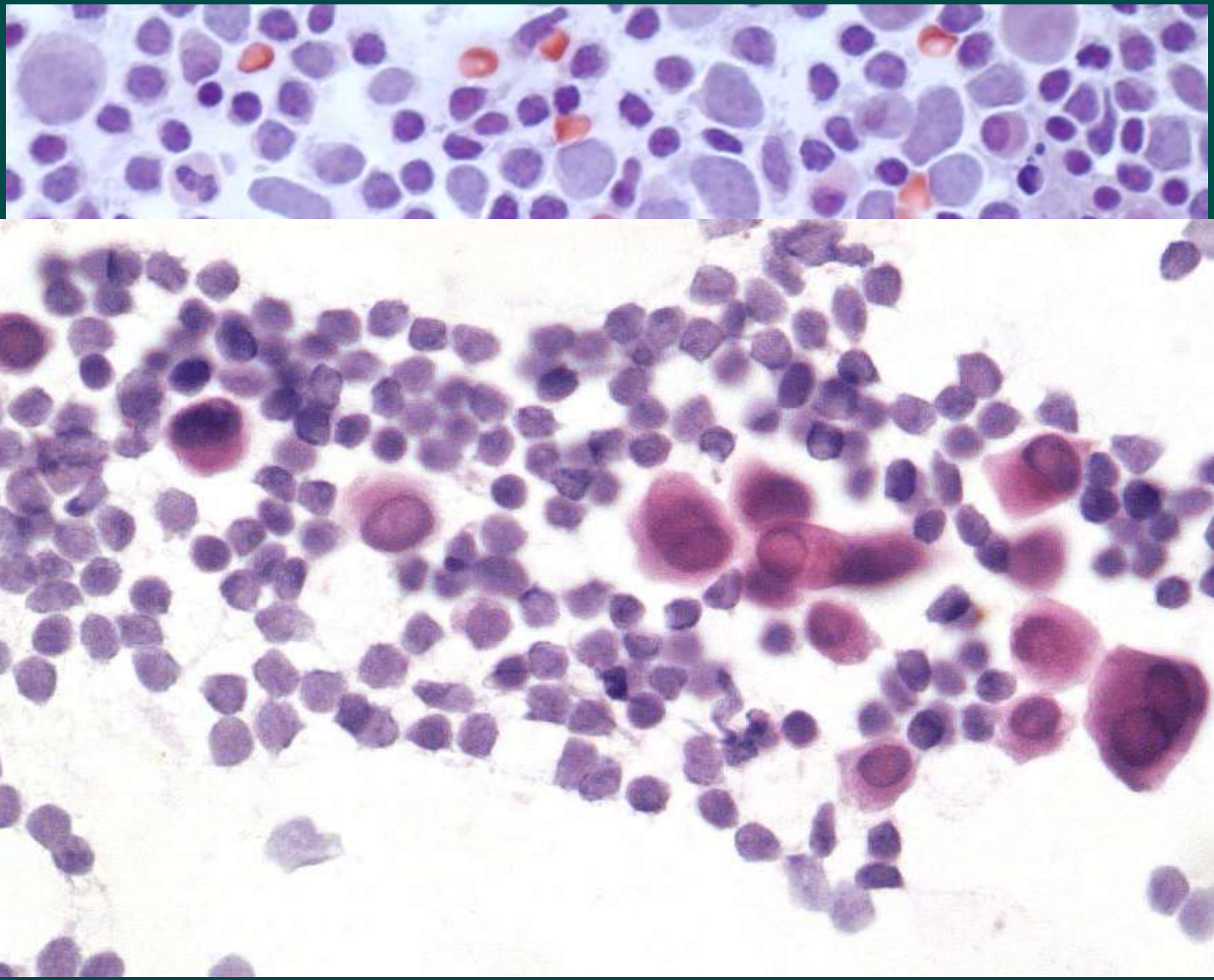
Turner et al. 1997. : 103 patient
with metastasis - free sentinel node

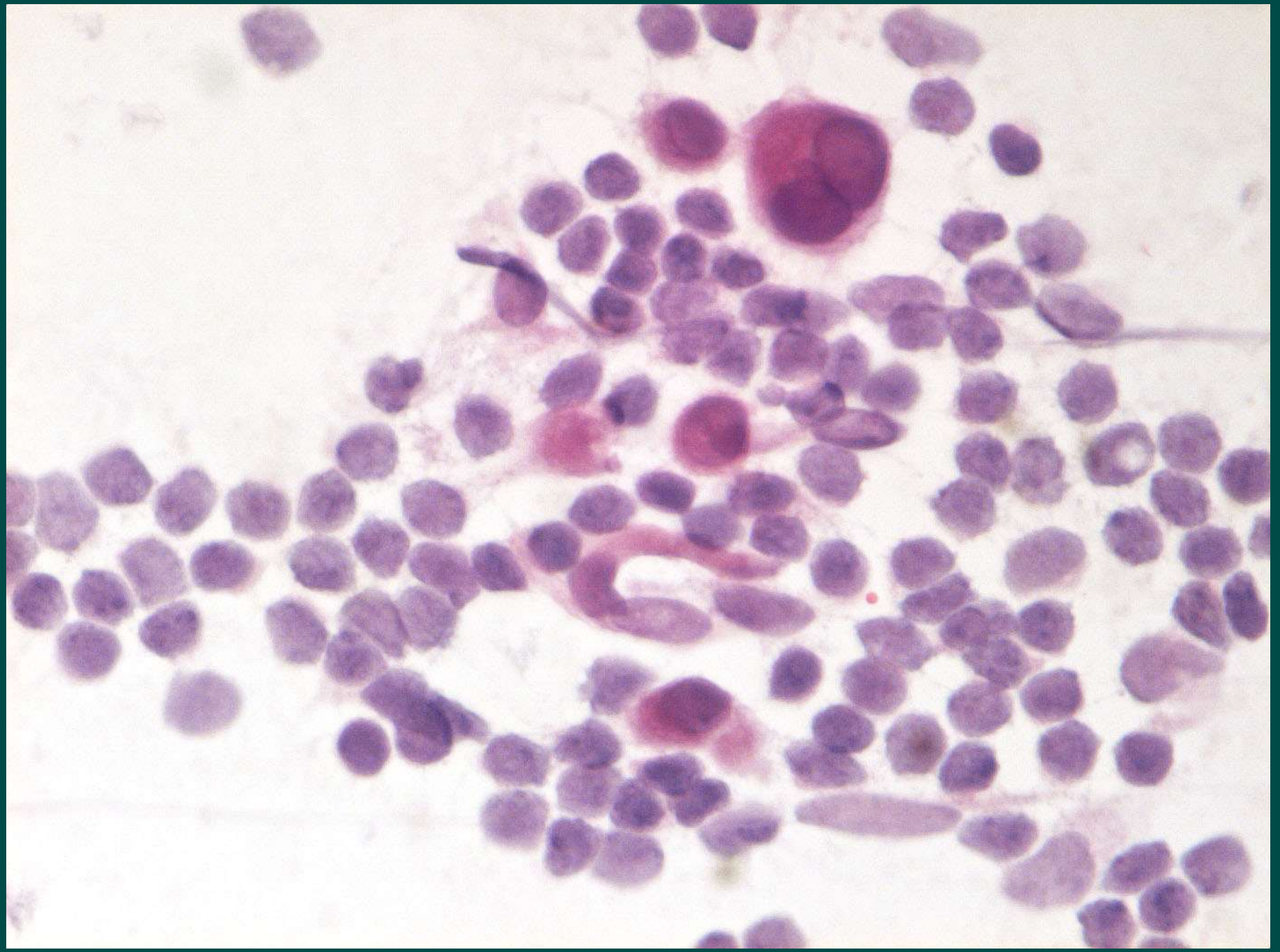
immunhistology detected metastasis in 14,3 %

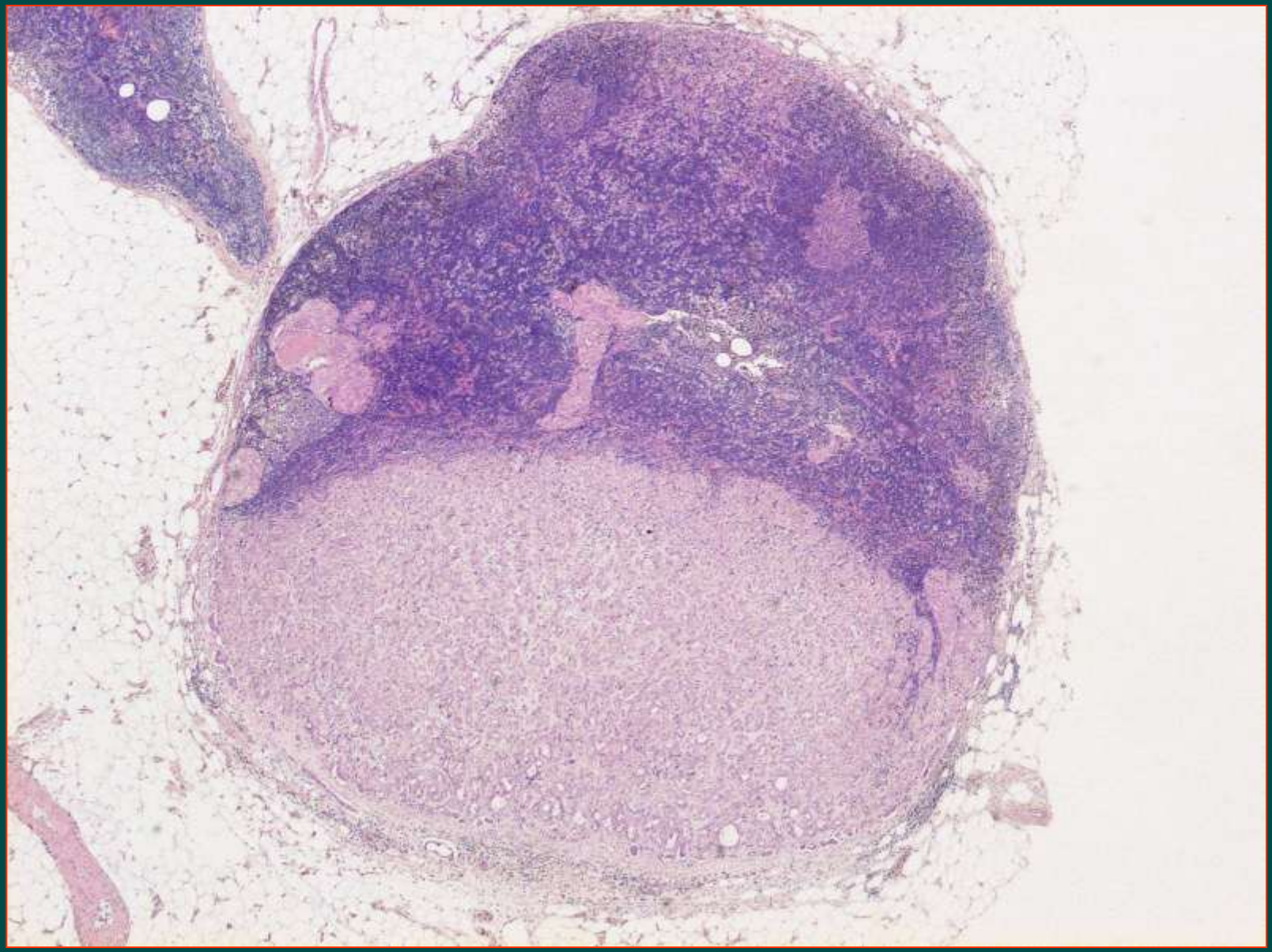
non-sentinel node of the same series 1/1087
contained micrometastasis

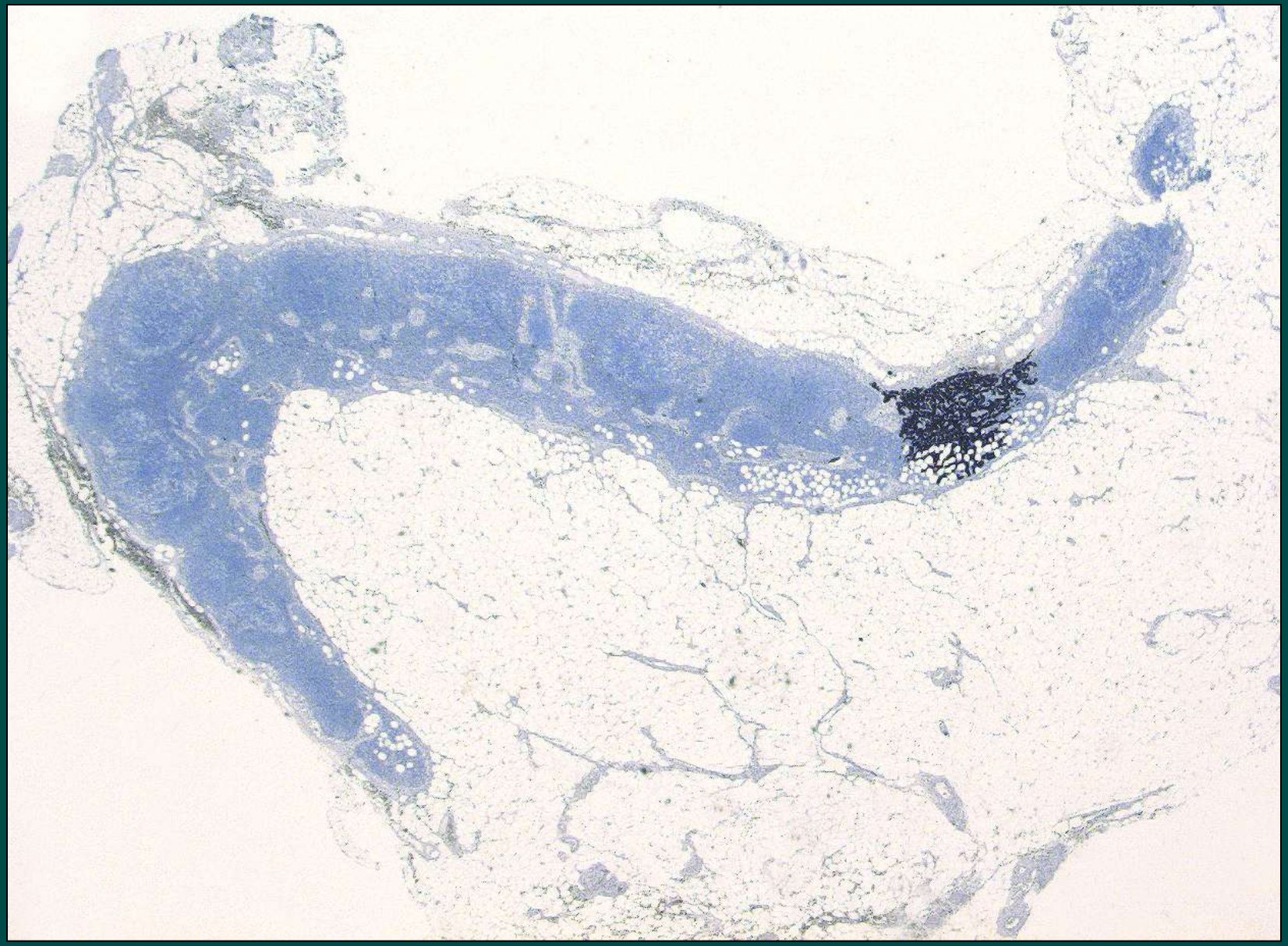
Guliano, Kelemen Cancer 1998. aug. 1.

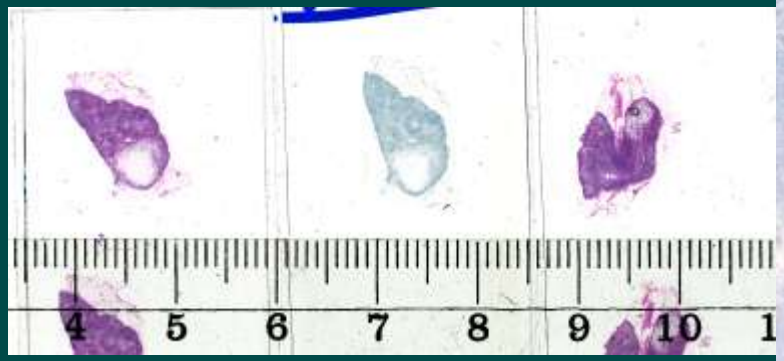

Sentinel lymph node







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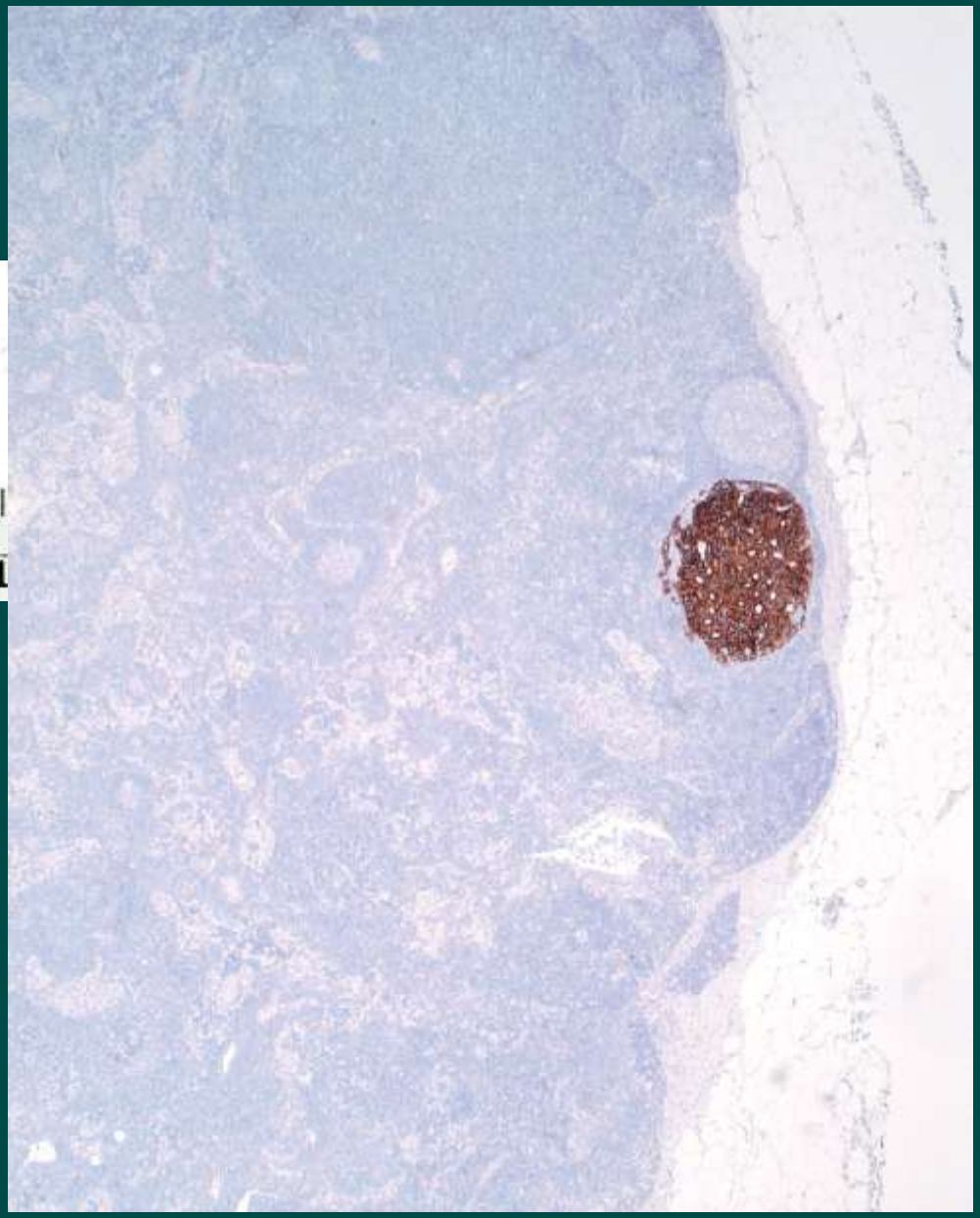

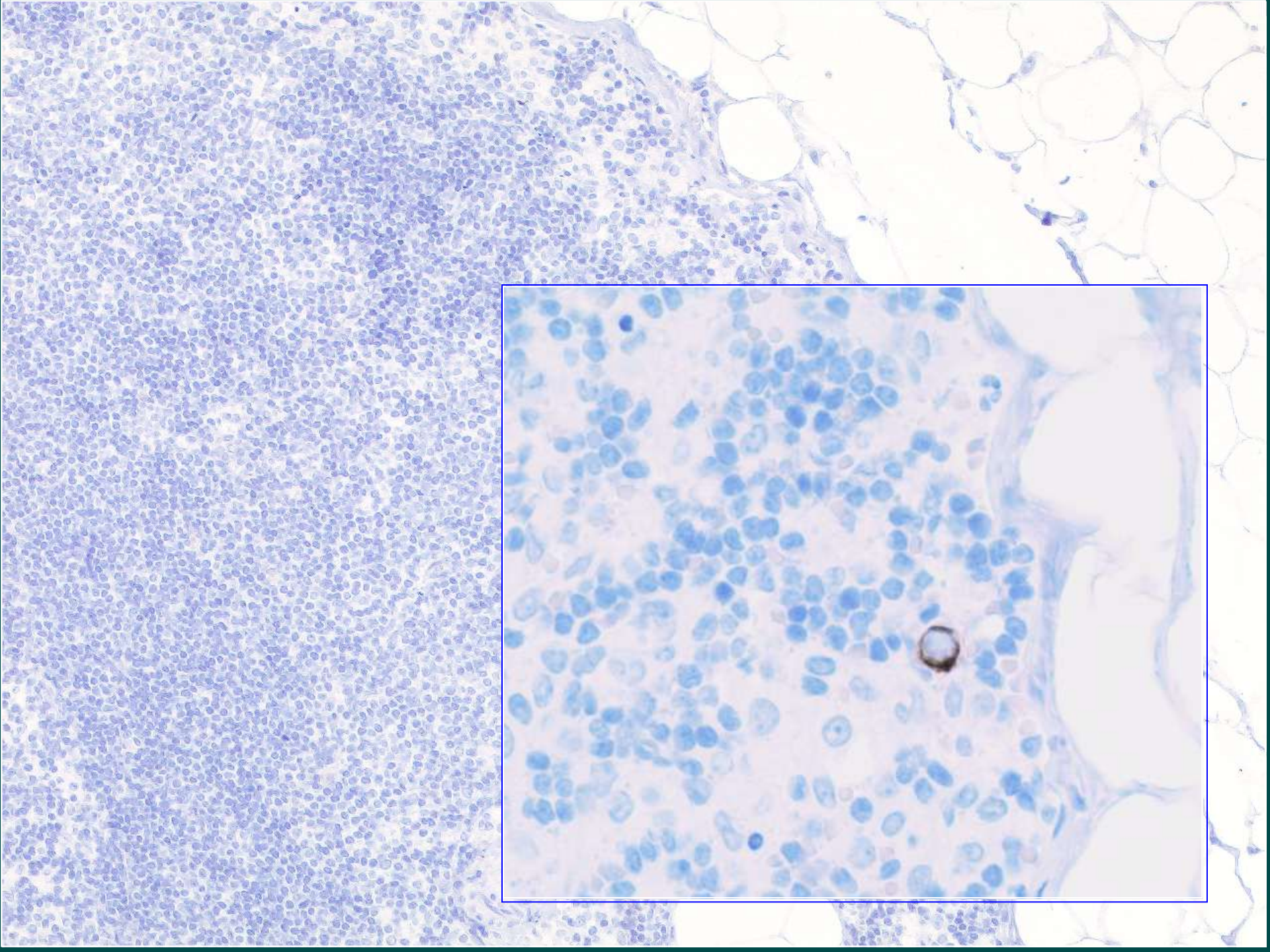

Rapportera:

Metastas > 2,0 mm

Micrometastas > 0,2 mm eller fler än 200 tumörceller i ett histologiskt snitt

Isolerade tumörceller, ITC (Submikrometastas):

<= 0,2 mm eller färr än 200 tumörceller I ett histologiskt snitt

Reaktiv lymfkörtel: utan påvisade tumörceller

	Tumor size	Mastectomy	LVI	LNM	ILC	n
U*	16.3 mm (9,4941)	**33%** (49+3/158)	**18%** (28/158)	**28%** (44/158)	**4%** (6/158)	158
U invasive MF in situ	14.0 mm (7,3696)	**35%** (15+7/62)	**19%** (12/62)	**11%** (7/62)	**10%** (6/62)	62
U invasive D in situ	14.0 mm (9,5018)	**43%** (8+9/40)	**28%** (11/40)	**30%** (12/40)	**3%** (1/40)	40
MF invasive	20.2 mm (11,3253)	**66%** (51+16/101)	**42%** (42/101)	**48%** (48/101)	**25%** (25/101)	101
MF invasive D in situ	16.5 mm (9,5371)	**76%** (29+13/55)	**53%** (29/55)	**42%** (23/55)	**5%** (3/55)	55
D invasive	n.a.	**85%** (14+3/20)	**10%** (2/20)	**60%** (12/20)	**65%** (13/20)	20
Unclassified	n.a.	**17%** (2/12)	n.a.	**33%** (4/12)	**8%** (1/12)	12
All invasives	16.7 mm (9,8998)	**49%** (219/448)	**28%** (124/448)	**33%** (150/448)	**12%** (55/448)	448
P-value	0.8266	< 0.0001	< 0.0001	< 0.0001	< 0.0001	

Tot T. Cancer 110:2551-60, 2007

	Unifocal	Multifocal	Diffuse	Comparison of proportions MF vs U	Comparison of proportions D vs U
Proportion of cases with SN	80.4% (442/550)	51.1% (182/356)	42.9% (18/42)	P<0.0001 (22.6 – 35.2)	P<0.0001 (20.4 – 52.5)
Negative SN	79.9% (353/442)	60.4% (110/182)	55.6% (10/18)	P<0.0001 (11.8 – 28.3)	P=0.0310 (0.8 – 49.1)
ITC	5.0% (22/442)	6.6% (12/182)	5.6% (1/18)	P=0.4253 (-2.1 – 7.1)	P=0.7192 (-5.3 – 23)
Micrometastasis	5.4% (24/442)	9.9% (18/182)	5.6% (1/18)	P=0.0331 (0.3 – 10.6)	P=0.7192 (-5.3 – 23)
Macrometastasis	9.7% (43/442)	23.1% (42/182)	33.3% (6/18)	P<0.0001 (6.3 – 20.3)	P=0.0073 (2.9 – 48.8)
False negative SN	1.1% (5/442)	3.3% (6/182)	11.1% (2/18)	P=0.9015 (-8.1 – 12.7)	P=0.7236 (-7.8 – 30.5)
Radiologically abnormal nodes	11.6% (64/550)	27.2% (97/356)	35.7% (15/42)	P<0.0001 (9.5 - 20.6)	P<0.0001 (9.5 – 40.5)
Complete axillary intervention	26.4% (145/550)	67.7% (241/356)	73.8% (31/42)	P<0.0001 (35.6 - 48)	P<0.0001 (31.7 – 60.8)

Tot T.Axillary lymph node status in unifocal, multifocal, and diffuse breast carcinomas: **Differences are related to macrometastatic disease**. Ann Surg Oncol, 2012

Tu size (mm)	Unifocal tumors			Multifocal tumors			Relative risk of macrometastatic diasese (P-value, 95% CI)
	Macro-metastasis	Micro-metastasis	Isoletad cells	Macro-metastasis	Micro-metastasis	Isoletad cells	
1-9	7.8% (9/115)	1.7% (2/115)	4.7% (7/115)	16.0% (8/50)	8.0% (4/50)	2% (1/50)	2.0444 (P=0.1164, 0.8373-4.9917)
10 -14	14.7% (22/150)	4.0% (6/150)	2.7% (4/150)	36.0% (27/75)	4.0% (3/75)	1.3% (1/75)	2.4545 (P=0.0003, 1.5038-4.0065)
15 -19	23.9% (33/138)	3.6% (5/138)	6.5% (9/138)	46.6% (34/73)	5.5% (4/73)	6.8% (5/73)	1.9477 (P=0.0007, 1.3241-2.865)
20 – 29	26.7% (28/105)	9.5% (10/105)	3.8% (4/105)	59.8% (64/107)	5.6% (6/107)	3.7% (4/107)	2.2430 (P<0.0001, 1.5756-3.1931)
30 – 39	48.5% (16/33)	15.2% (5/33)	0.0% (0/33)	78.1% (25/32)	3.1% (1/32)	6.3% (2/32)	1.6113 (P=0.0184, 1.0838-2.3957)
40+	44.4% (4/9)	0.0% (0/9)	11.1% (1/9)	73.7% (14/19)	0.0% (0/19)	0.0% (0/19)	1.6579 (P=0.2030, 0.7613-3.6105)
Total	20.4% (112/550)	5.1% (28/550)	4.5% (25/550)	48.3% (172/356)	5.1% (18/356)	3.7% (13/356)	2.3726 (P<0.0001, 1.9481-2.8896)

Tot T.Axillary lymph node status in unifocal, multifocal, and diffuse breast carcinomas: **Differences are related to macrometastatic disease**. Ann Surg Oncol, 2012

	Unifocal	Multifocal	Diffuse	Total	RR multifocal vs unifocal	RR diffuse vs unifocal
Grade 1	**9.7%/**18.2% (15/28/154)	**19.2**%/32.8% (11/19/58)	**50.0**%/50.0% (1/1/2)	**12.6**%/22.4% (27/48/214)	**1.9471** (P=0.0685, 0.9506-3.9885)	**5.1333** (P=0.0288, 1.1839-22.2582)
Grade 2	**21.3**%/31.7% (57/85/268)	**48.8**%/55.5% (102/116/209)	**59.5**%/69.0% (22/24/37)	**35.2**%/43.4% (181/223/514)	**2.2946** (P<0.0001, 1.7535-3.0028)	**2.7956** (P<0.0001, 1.9663-3.9749)
Grade 3	**31.0**%/40.5% (39/51/126)	**66.3**%/76.4% (59/68/89)	**100.0**%/100.0% (3/3/3)	**46.3**%/56.0% (101/122/218)	**2.1417** (P<0.0001, 1.5867-2.8909)	**2.8133** (P<0.0001, 1.7904-4.4205)
Total	**20.3**%/29.9% (111/164/548)	**48.3**%/57.0% (172/203/356)	**62.0**%/66.7% (26/28/42)	**32.7**%/41.8% (309/395/946)	**2.3853** (P<0.0001, 1.9571-2.9071)	**3.0562** (P<0.0001, 2.2877-4.0829)

Tot T.Axillary lymph node status in unifocal, multifocal, and diffuse breast carcinomas: **Differences are related to macrometastatic disease**. Ann Surg Oncol, 2012

It is far not sufficient
to preoperatively verify malignancy;

lesion distribution,
disease extent,
localization,
tumor size,
tumor stage

should also be assessed
for adequate therapeutic decision

There are no indications for frozen section on breast tissue in modern breast pathology!

Tack !