



World Congress on

Breast Cancer

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Changes in Breast Cancer Reports After Second Opinion

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Second Opinion in Breast Pathology

- Usually requested when a patient is referred from another institution for treatment
- An opportunity to detect diagnostic errors that impact on patient management.

Who's requesting a second opinion in Breast Cancer ?

- Medical Oncologists
- Breast Surgeons
- Patients
- Pathologists

Prognostic Factors in Breast Cancer

- Tumor size
- Tumor grade
- Histological type
- Margins of resection
- Lymphovascular invasion
- Proliferative Index
- Lymph node stage
- Predictive markers
 - Estrogen & progesterone receptors
 - HER2

Breast cancer management team effort



Oncologists



Surgeons



Pathologists

“Castellers in Catalunya, Spain”

Questions for the pathologist when providing a second opinion in breast biopsies

- Is it cancer?
- Is it breast cancer?
- Is it invasive breast cancer?
- Are the margins of resection free of disease?
- Are the predictive markers of response accurate (Hormone Receptors, HER2)?

Special situations

- Patient with previous history of breast cancer presenting with disease in other organs.
- Patient with history of non-breast cancer presenting a breast lesion.
- Tumor presenting in the axilla without a clinically evident breast lesion.

Tumors of the axillary region

- Metastatic tumors to axillary lymph nodes.
- Metastases from occult breast cancer
- Primary tumors of the axilla
 - Breast cancer arising in ectopic breast tissue
 - Primary tumors of skin appendages

Original Investigation

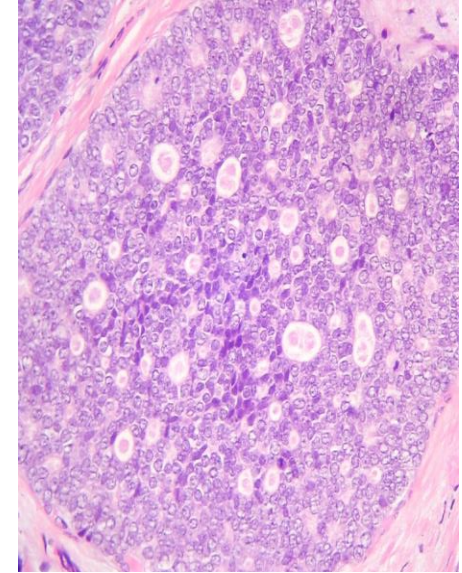
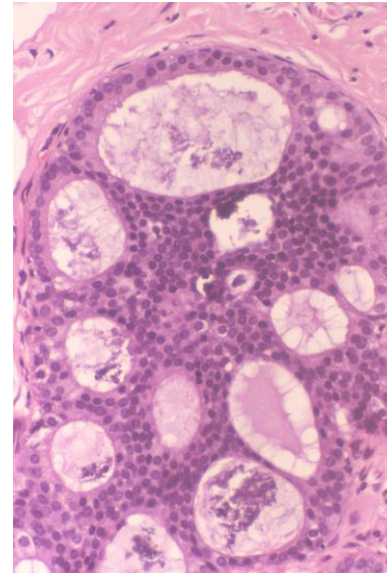
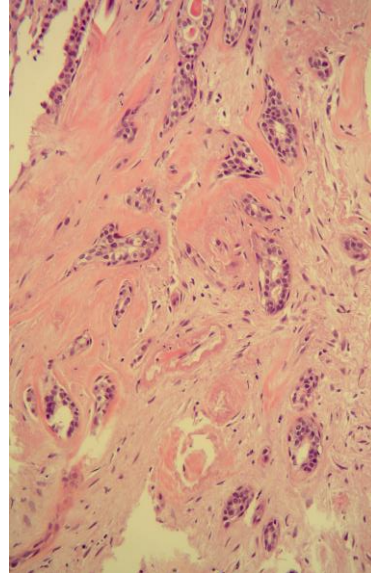
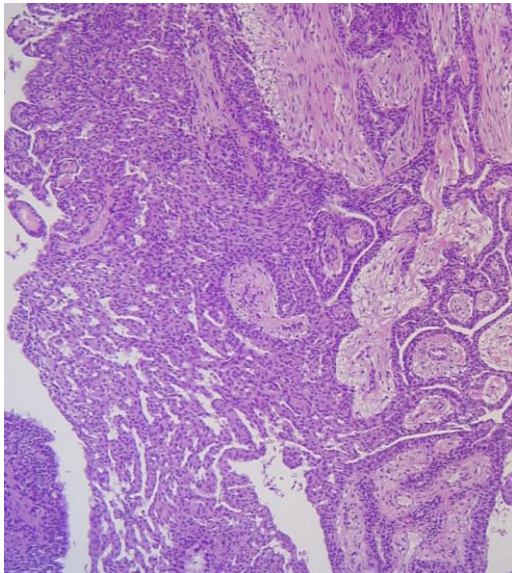
Diagnostic Concordance Among Pathologists Interpreting Breast Biopsy Specimens

JAMA. 2015;313(11):1122-1132. doi:10.1001/jama.2015.1405

Joann G. Elmore, MD, MPH; Gary M. Longton, MS; Patricia A. Carney, PhD; Berta M. Geller, EdD; Tracy Omega, PhD; Anna N. A. Tosteson, ScD; Heidi D. Nelson, MD, MPH; Margaret S. Pepe, PhD; Kimberly H. Allison, MD; Stuart J. Schnitt, MD; Frances P. O'Malley, MB; Donald L. Weaver, MD

Concordance among pathologists in the diagnosis of breast lesions

- Benign lesions without atypia
- Atypical Hyperplasia
- Ductal Carcinoma in situ
- Invasive cancer



Diagnostic concordance among pathologists interpreting breast biopsy specimens

Diagnosis	Concordance rate	Overinterpretation rate	Underinterpretation rate
Benign without atypia	87% (85-89)	13% (11-15)	
Atypia	48% (44-52)	17% (15-21)	35% (31-39)
DCIS	84% (82-86)	3% (2-4)	13% (12-15)
Invasive carcinoma	96% (94-97)		4% (3-6)

Modified after Elmore JG et al. JAMA 2015;313 (11):1122-1132.

Why do pathologists disagree in the diagnosis of breast lesions?

- Different levels of training and experience
- Different levels of interest in breast pathology
- Interpretation of borderline or grey zone cases
- Diagnosis of rare cases
- Special clinical situations
- Technical issues

Classification of second opinion results in breast pathology





- Concordant
- Major discrepancies
 - Potential for significant change in prognosis and/or treatment.
- Minor discrepancies
 - Don't impact significantly in prognosis and/or treatment.

Rate of major discrepancies in breast cancer pathology after review

Author/ year	Number of cases reviewed	Major discrepancies %
Staradub et al. 2002	340	7.8
Newman et al. 2006	149	9
Price et al. 2010	93	11
Kennecke et al. 2012	405	6
Middleton et al. 2014	2718	6.20
Marco et al. 2014	205	16
Romanoff et al. 2014	430	10
Khazai et al. 2015	1970	11.47

Second Opinion in Breast Pathology

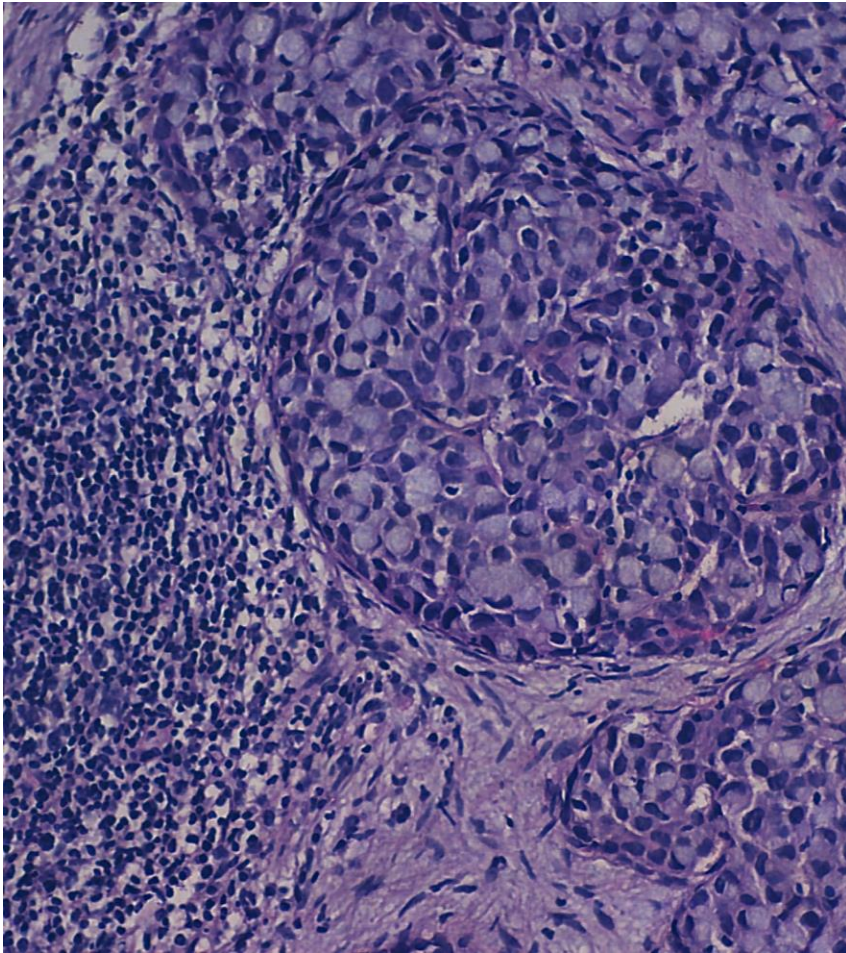
Major Discrepancies

- Changes in Histologic Diagnoses (37.7%)
- Invasive Carcinoma vs DCIS (32 %)
 - Invasive Ca  DCIS
 - DCIS  Invasive Ca
- Hormone Receptors Results (9.4%)
 - ER-  ER+
- HER2 Results (20.7%)
 - HER2+  HER2 -

Second Opinion in Breast Pathology

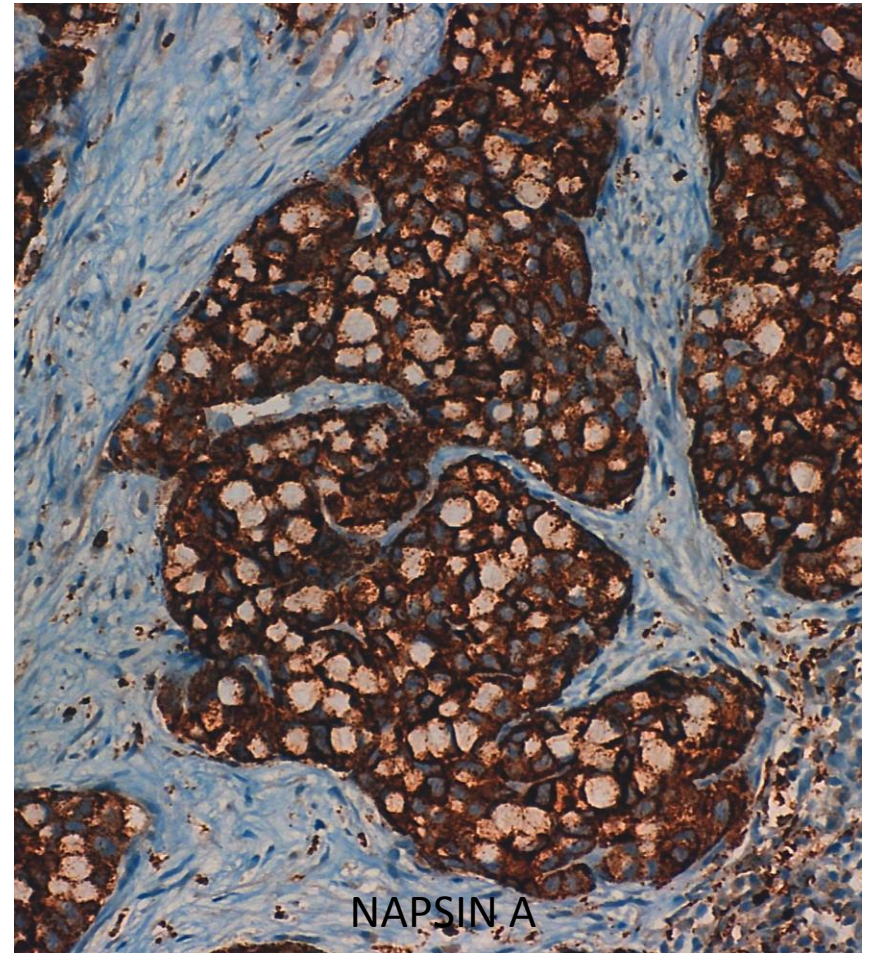
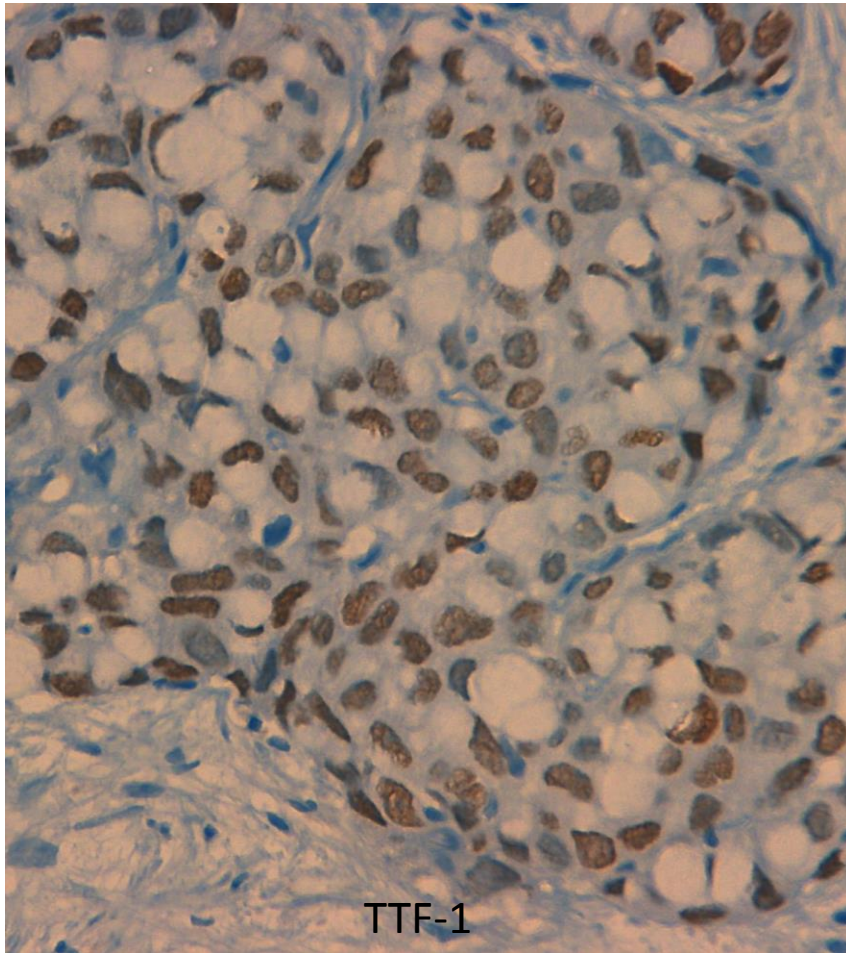
Major Discrepancies in 46 Patients

First Diagnosis	Second Opinion	N
Invasive breast cancer	Benign	4
	Lung cancer in breast, brain and lymph nodes	4
	Cutaneous axillary adnexal carcinoma	2
	Axillary metastasis of melanoma	1
Lung cancer metastasis to lymph node	Breast cancer metastasis to lymph node	1
Lung cancer metastasis to breast	Primary breast cancer, small cell type	1
Fibroadenoma/DCIS/ Lobular neoplasia	Fibroadenoma/Lobular neoplasia	1
Atypical ductal hyperplasia	DCIS high grade	1
Atypical papilloma/DCIS	Papilloma with ductal hyperplasia	1
Changes in histologic type of primary breast tumor (phyllodes tumor, adenoid cystic ca, atypical vascular lesion, fibromatosis)	Spindle cell ca, cribriform ca, angiosarcoma, myofibroblastic sarcoma	4
Invasive carcinoma NST	DCIS	9
	DCIS with microinvasion	2
DCIS with microinvasion	DCIS	2
DCIS	DCIS with invasive carcinoma	4
Estrogen receptor negative	Estrogen receptor positive	4
Estrogen receptor positive	Estrogen receptor negative	1
HER2 positive	HER2 negative	10
HER2 negative	HER2 positive	1



- 30 y-o woman with axillary mass.
- First diagnosis:
 - Consistent with breast cancer metastasis.

Second opinion: Metastatic adenocarcinoma of lung



Immunohistochemistry in the differential diagnosis of lung and breast cancer

	Lung Cancer	Breast Cancer
TTF-1	+	-
Mammaglobin	-	+
p63	+	-
ER	-	+
GATA-3	-	+

Assessment of predictive factors of response in Breast Cancer

- Hormone Receptors:
 - Estrogen Receptors
 - Progesterone Receptors
- HER2
 - Immunohistochemistry
 - In situ hybridization

Assessment of predictive factors of response in Breast Cancer

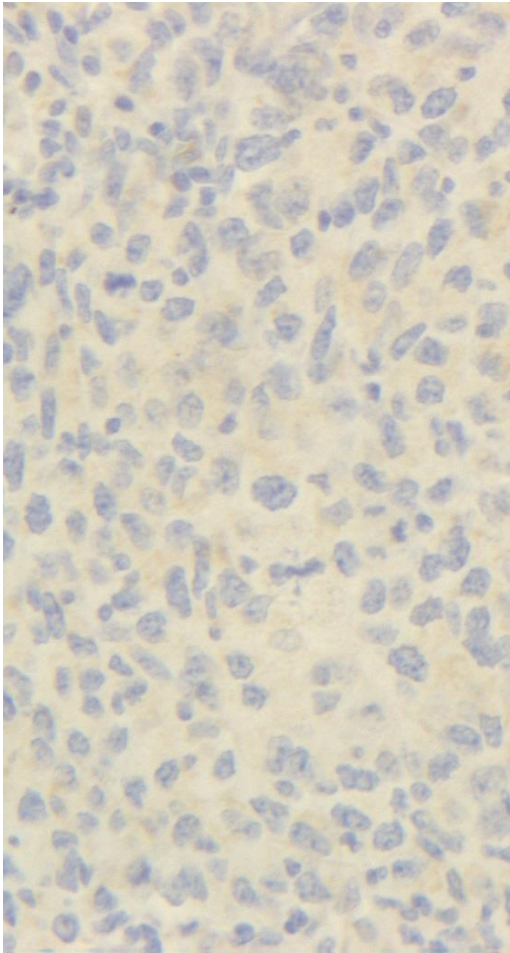
- Technical Issues
 - Fixation
 - Methodology
- Interpretative Issues

Estrogen Receptors

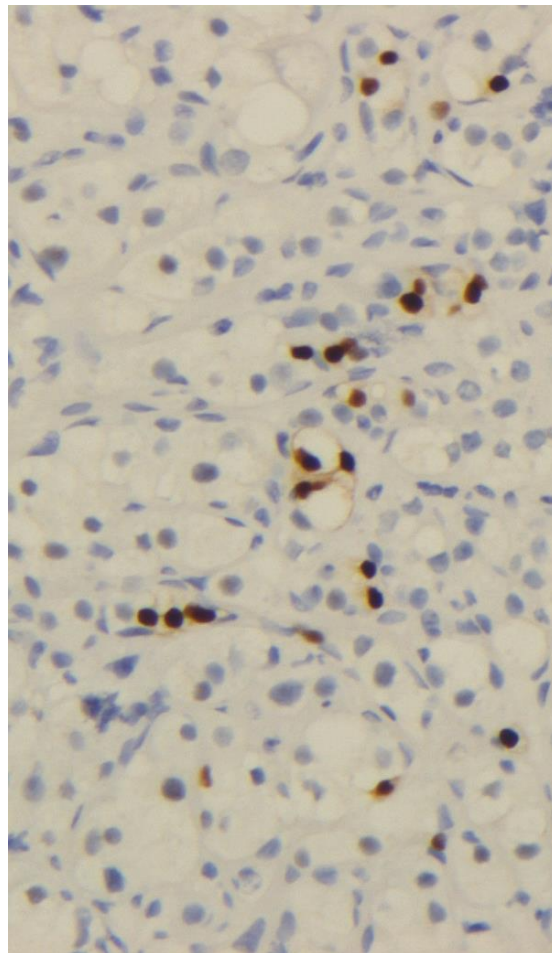
Assessment by Immunohistochemistry

- NIH Consensus 2001
 - “....patients with any extent of hormone receptors in their tumor cells may still benefit from hormonal therapy”
- Dichotomous results
 - 99% of tumors are negative (0%) or positive in 70% or more of cells.
- 1% cutoff for ER positivity
- False negative ER is more problematic

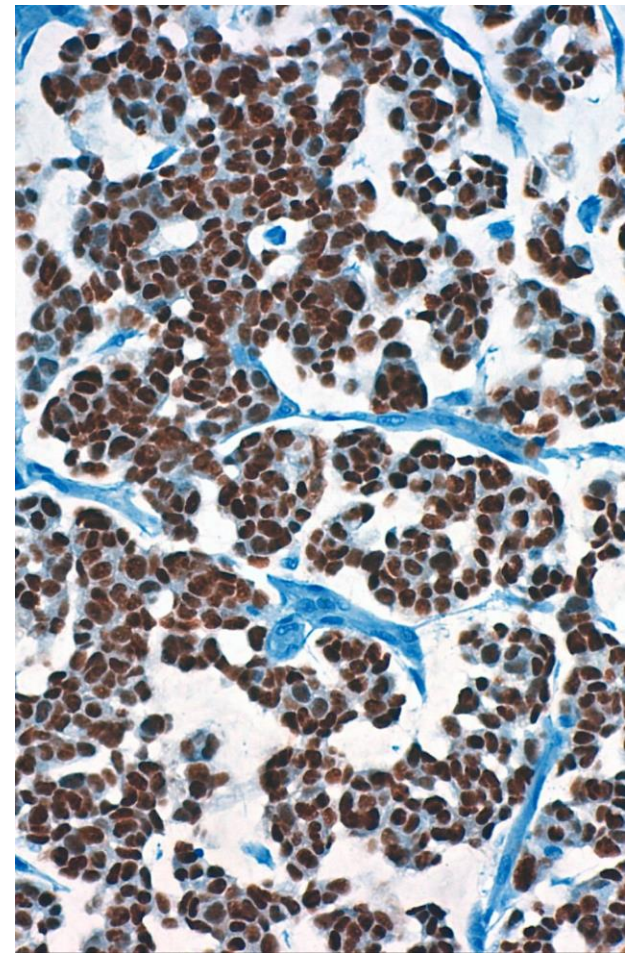
Estrogen Receptor IHC



NEGATIVE



POSITIVE LOW



POSITIVE HIGH

HER2 Assessment ASCO-CAP Guidelines

Published Ahead of Print on October 7, 2013 as 10.1200/JCO.2013.50.9984
The latest version is at <http://jco.ascopubs.org/cgi/doi/10.1200/JCO.2013.50.9984>

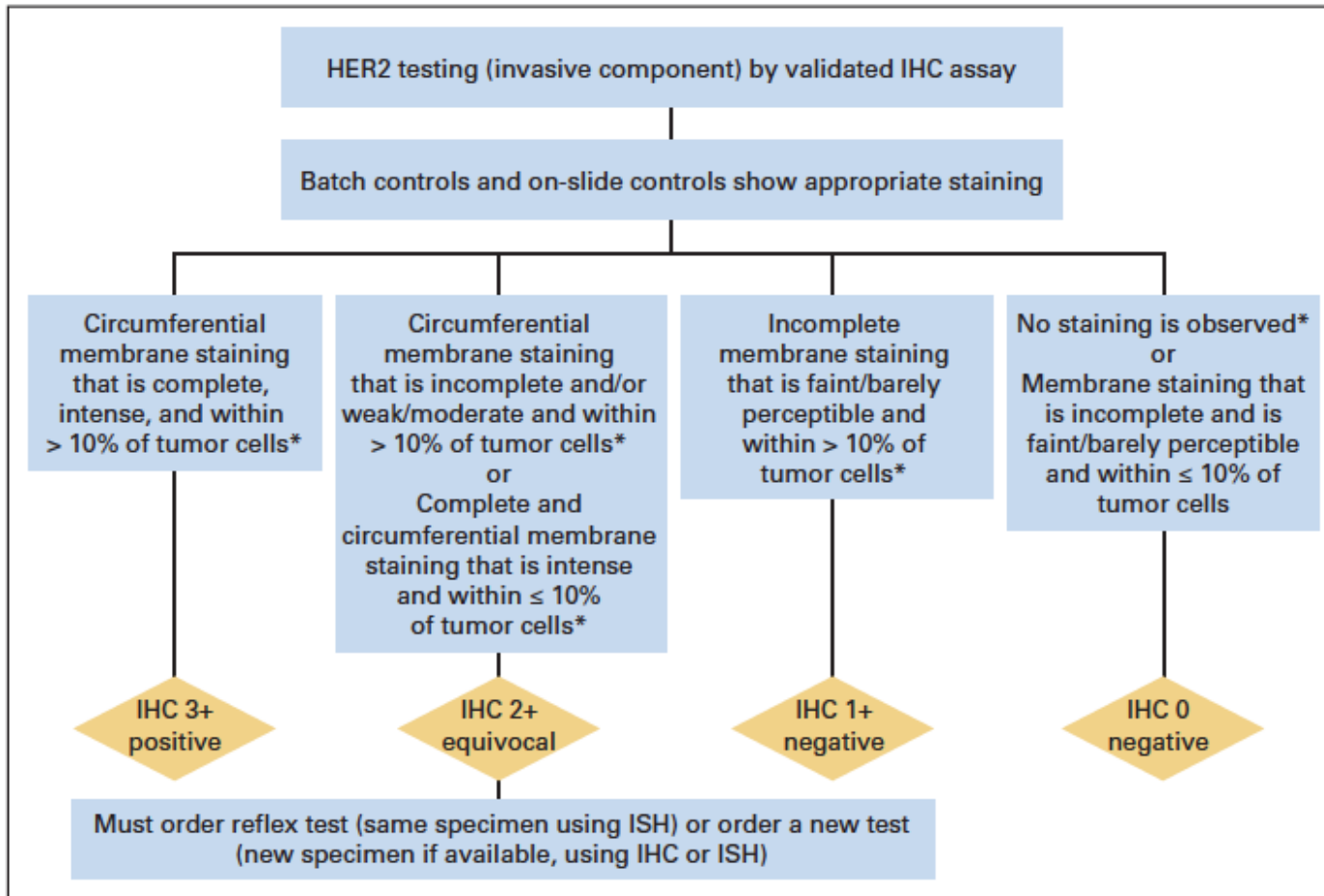
JOURNAL OF CLINICAL ONCOLOGY

A S C O S P E C I A L A R T I C L E

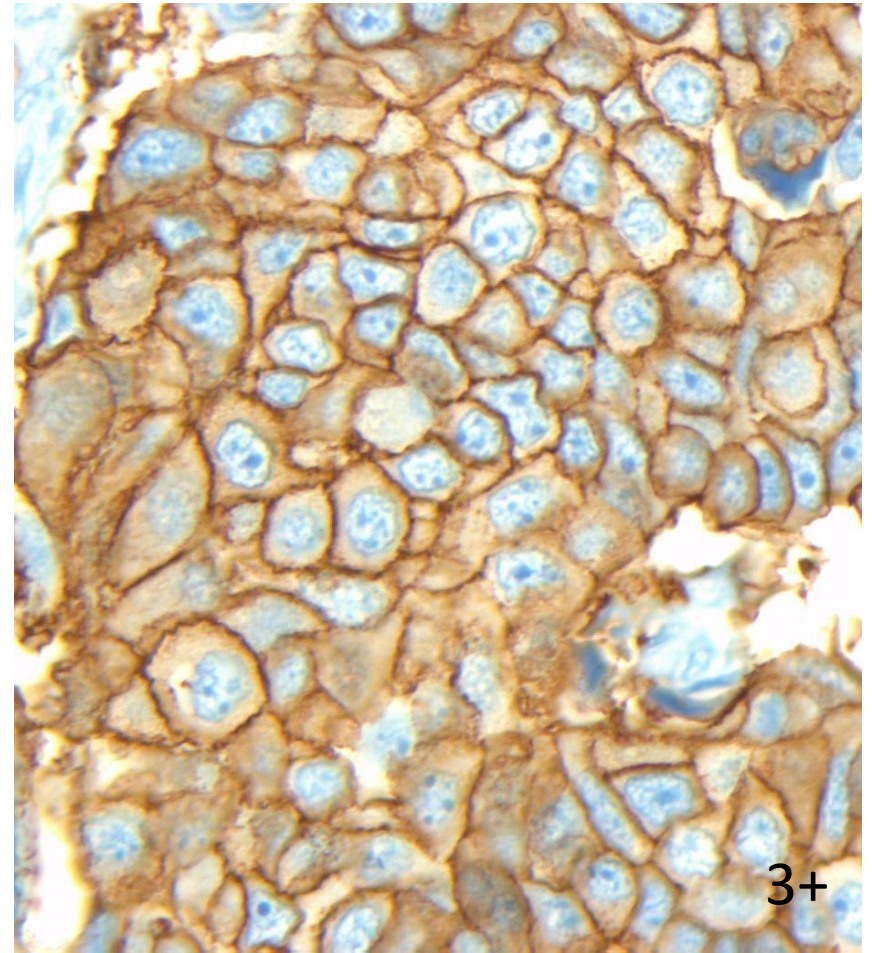
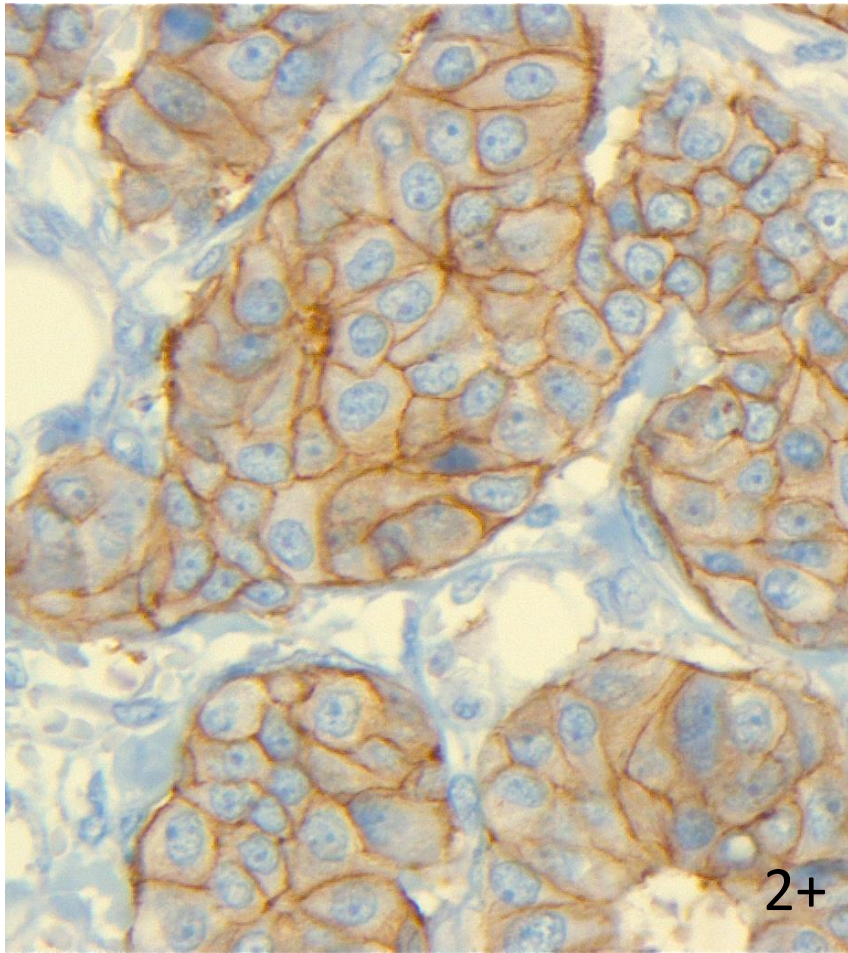
Recommendations for Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Update

Antonio C. Wolff, M. Elizabeth H. Hammond,* David G. Hicks,* Mitch Dowsett,* Lisa M. McShane,*
Kimberly H. Allison, Donald C. Allred, John M.S. Bartlett, Michael Bilous, Patrick Fitzgibbons, Wedad Hanna,
Robert B. Jenkins, Pamela B. Mangu, Soonmyung Paik, Edith A. Perez, Michael F. Press, Patricia A. Spears,
Gail H. Vance, Giuseppe Viale, and Daniel F. Hayes**

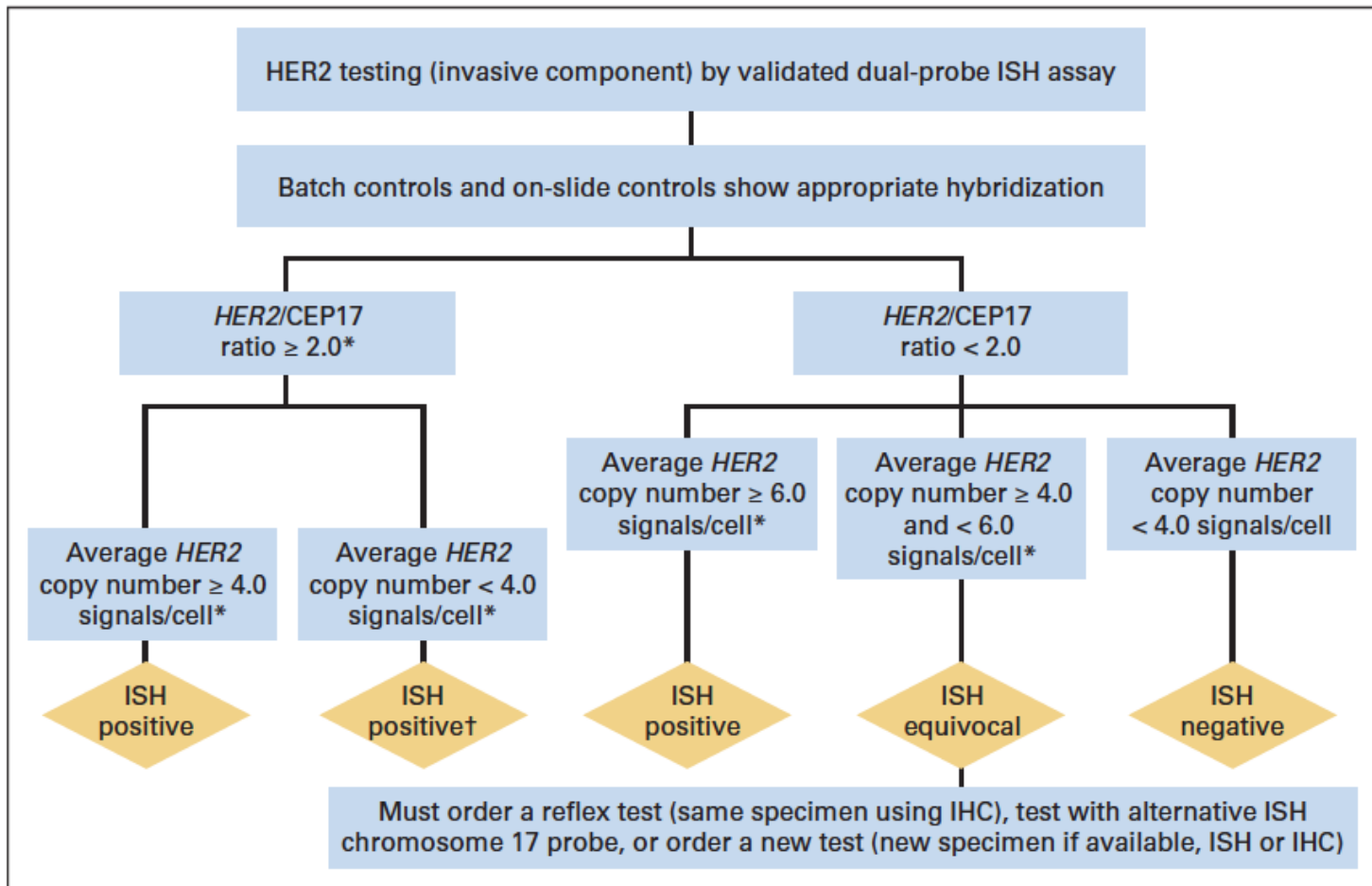
HER2 SCORE IHC



HER2 IHC SCORE

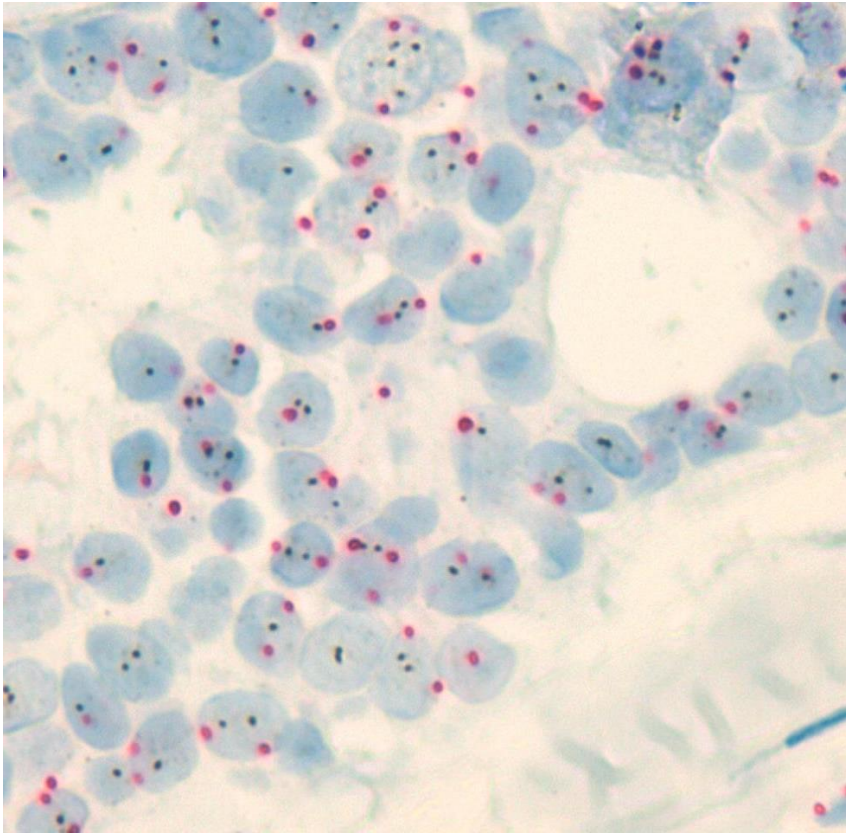


HER2 ISH Assay

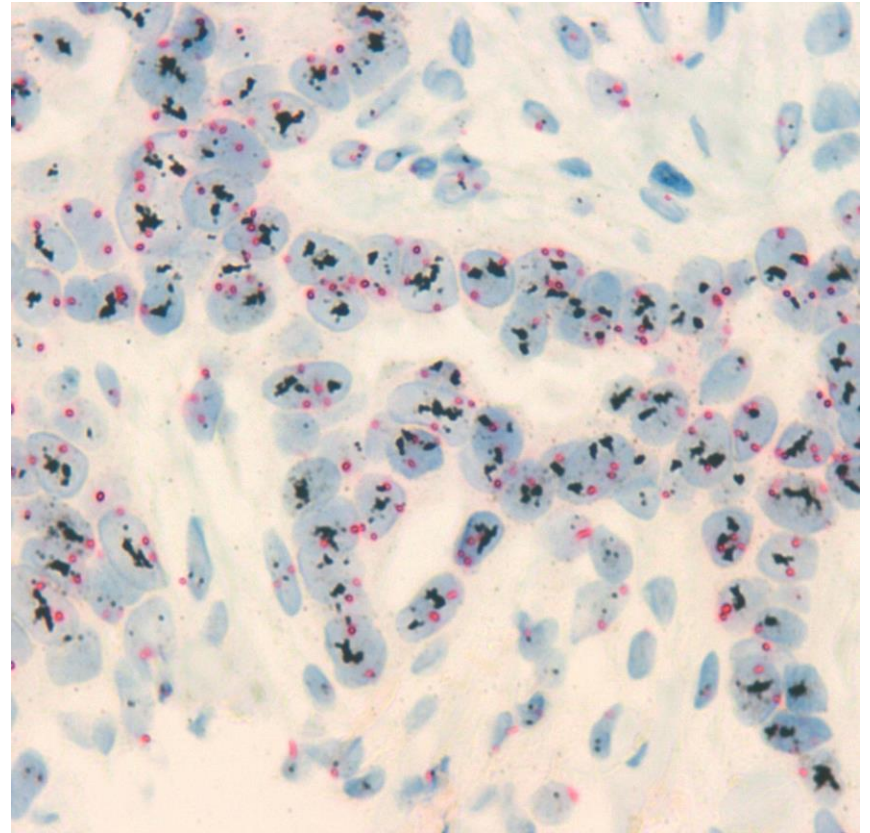


HER2 ISH

Negative. Ratio < 2



Positive. Ratio > 2



CONCLUSIONS

- Major discrepancies in the evaluation of breast cancer reports are often related to the assessment of the degree of invasion of breast carcinoma and the immunohistochemical results of predictive markers, in particular HER2.
- The assessment of axillary lesions and distant metastasis in patients suspected of having breast cancer or with a history of treated breast cancer may reveal non-mammary tumors.

Conclusions

- Significant improvement in the concordance among pathologists in the assessment of breast lesions can be achieved by careful histological study, following standardized criteria, and having complete clinical information.
- Using high quality IHC techniques will improve the evaluation of markers of prognosis and therapeutic response.



Thank you