



# Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer



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Guidelines Breast  
Version 2009.1.0

## Pathology



FORSCHEN  
LEHREN  
HEILEN

# Pathology

- **Version 2004:  
Sinn**
- **Version 2005–2008:  
Kreipe / Sinn**
- **Version 2009:  
Sinn / Kreipe / Costa**

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# Handling and Reporting of Core Needle Biopsies

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➤ <b>Routine workup in step sections (14G: 3 sections / 11G, 8G: 6–8 sections)</b>	<b>5</b>	<b>D</b>	<b>++</b>
➤ <b>Correlation with imaging (density, calcifications), use of B-Classification</b>	<b>5</b>	<b>D</b>	<b>++</b>
➤ <b>Frozen section diagnosis on core biopsies</b>	<b>5</b>	<b>D</b>	<b>--</b>
➤ <b>Routine evaluation of ER/PgR and HER-2 status</b>	<b>3b</b>	<b>C</b>	<b>+</b>
➤ <b>Turn-around time &lt; 24 h</b>	<b>5</b>	<b>D</b>	<b>++</b>
➤ <b>Cytology (cysts, nipple-aspiration, or FNC)</b>	<b>5</b>	<b>D</b>	<b>-</b>
➤ <b>Optimal fixation time 6–48 h</b>	<b>5</b>	<b>D</b>	<b>++</b>
➤ <b>Standard fixation and processing</b>	<b>5</b>	<b>D</b>	<b>++</b>
➤ <b>Participation in QA-programs</b>	<b>5</b>	<b>D</b>	<b>+</b>

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# Indications for Frozen Sections

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- |  |    |   |    |
|--|----|---|----|
| ➤ <b>Sentinel node biopsy for invasive cancer</b>  |    |   |    |
| - for macroscopically suspicious node              | 2b | B | ++ |
| - if unsuspecting node                             | 5  | D | +  |
| ➤ <b>Closest margin of resection</b>               |    |   |    |
| - if macroscopically < 1 cm                        | 5  | D | +  |
| - if macroscopically > 1 cm                        | 5  | D | -  |
| ➤ <b>Lesions ≥ 1 cm, without core biopsy</b>       | 5  | D | +  |
| ➤ <b>Non-palpable lesions or lesions &lt; 1 cm</b> | 5  | D | -- |

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# General Recommendations for Specimen Handling

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➤ <b>Adherence to sampling protocols and guidelines for accurate evaluation of tumor size and margins.</b>	<b>5</b>	<b>D</b>	<b>++</b>
➤ <b>Consideration of clinical imaging results (e.g. calcifications, multifocality) and topography</b>	<b>5</b>	<b>D</b>	<b>++</b>
➤ <b>Specimen radiography for non-palpable lesions and microcalcifications</b>	<b>5</b>	<b>D</b>	<b>+</b>
➤ <b>Minimum fixation time 6–48 h to minimize shrinking artefacts and allow determination of angioinvasion</b>	<b>5</b>	<b>D</b>	<b>+</b>
➤ <b>Tissue banking to be performed by the pathologist</b>	<b>5</b>	<b>D</b>	<b>+</b>

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# Workup of Breast-Conserving Specimens

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LoE / GR

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- |   |   |          |          |           |
|---|---|----------|----------|-----------|
| ➤ | <b>Slicing perpendicular to the longitudinal axis (or perpendicular to the nipple-peripheral axis in case of spherical specimens)</b> | <b>5</b> | <b>D</b> | <b>++</b> |
| ➤ | <b>Systematic sampling, at least 1 tissue block every 1 cm</b>  | <b>5</b> | <b>D</b> | <b>++</b> |
| ➤ | <b>Inking of resection margins. Sampling of resection margins in all dimensions.</b>  | <b>5</b> | <b>D</b> | <b>++</b> |
| ➤ | <b>Documentation after slicing using specimen radiography, photodocumentation or diagram.</b>   | <b>5</b> | <b>D</b> | <b>+</b>  |

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# Workup of Mastectomy Specimens

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- |   |  |
|---|--|
| <ul style="list-style-type: none"> <li>➤ <b>Margins always to be sampled</b> <ul style="list-style-type: none"> <li>- Skin close to tumor, at least 2 directions</li> <li>- Deep margin</li> <li>- Other margins, if close (&lt; 1 cm)</li> </ul> </li> </ul> | <p><b>5</b>    <b>D</b>    <b>++</b></p> |
| <ul style="list-style-type: none"> <li>➤ <b>Attention to soft tissue margins in skin sparing mastectomy</b></li> </ul>  | <p><b>5</b>    <b>D</b>    <b>++</b></p> |
| <ul style="list-style-type: none"> <li>➤ <b>Routine sampling of uninvolved quadrants, skin above tumor, and retroareolar region</b></li> </ul>  | <p><b>5</b>    <b>D</b>    <b>++</b></p> |
| <ul style="list-style-type: none"> <li>➤ <b>More extensive sampling in prophylactic mastectomies (BRCA-1 pos. patients)</b></li> </ul>  | <p><b>5</b>    <b>D</b>    <b>++</b></p> |

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# Reporting of Invasive Carcinoma

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- **Tumor type (WHO). Grade (UICC). Size (invasive and total extent). pT classification (UICC).** 5    D    ++
- **Margins, macro- and histologically. Distance and topography of closest margins. R-Classification according to TNM.** 5    D    ++
- **EIC (if present). Multifocality (if present). Lymphovascular invasion (present or not).** 5    D    ++
- **No. of axillary nodes removed. No. and size of lymph node metastases. Perinodal invasion. pN classification (UICC).** 5    D    ++
- **ER, PgR, HER-2 status**

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# Evaluation after Neoadjuvant Chemotherapy

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➤ <b>Identification of tumor bed, otherwise ypTX</b>	<b>4</b>	<b>D</b>	<b>++</b>
➤ <b>Reporting of tumor size as total extent of invasive carcinoma</b>	<b>4</b>	<b>D</b>	<b>++</b>
➤ <b>Reporting of tumor regression according to Miller-Payne (2003), Symmans (2007) or Sinn (1994)</b>	<b>4</b>	<b>D</b>	<b>+</b>
➤ <b>pCR is absence of invasive Ca. and absence of Lymphangiosis ca. or LN metastases (without consideration of DCIS)</b>	<b>4</b>	<b>D</b>	<b>+</b>
➤ <b>Use of IHC to identify tumor rests</b>	<b>4</b>	<b>D</b>	<b>+/-</b>

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- **NSABP B-18:** pCR / pPR / NR
- **Chevallier:** Grade of regression, 1–4
- **Sataloff:** Cellularity (Tu + Lnn), 1–4
- **Miller-Payne:** Cellularität, Score 0–5
- **Symmans:** 6 parameter (Tu + Lnn)
- **Sinn:** Grade of regression, Score 0–4

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# ER, PgR Testing

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- |  | Oxford | AGO |
|--|--------|-----|
| ➤ Immunohistochemical detection on paraffin embedded tissue            | 1a     | ++  |
| ➤ Reporting percentage and intensity of pos. tumor nuclei              | 1a     | ++  |
| ➤ Allred Score (0–8; pos. if $\geq 3$ )                                | 4      | +   |
| ➤ Remmele Score (0–12; pos. if $\geq 3$ )                              | 4      | +   |
| ➤ Re-evaluation on excision specimen if triple-negative on core biopsy | 5      | +   |
| ➤ Use of internal and external quality control schemes                 | 5      | ++  |

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# HER-2 Testing

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<ul style="list-style-type: none"> <li>➤ <b>Reporting of immunohistochemistry</b> <ul style="list-style-type: none"> <li>- if strong membrane staining of <math>\geq 30\%</math> invasive cells: 3+</li> <li>- if <math>&lt;30\%</math> strong staining or <math>&gt; 10\%</math> moderate but circular membrane staining: 2+; FISH required</li> </ul> </li> </ul>	<b>1a</b>	<b>A</b>	<b>++</b>
<ul style="list-style-type: none"> <li>➤ <b>Reporting of single-color FISH</b> <ul style="list-style-type: none"> <li>- positive if signal count <math>\geq 6</math> signals/nucleus</li> <li>- negative if signal count <math>\leq 4</math> signals/nucleus</li> </ul> </li> </ul>	<b>3a</b>	<b>C</b>	<b>++</b>
<ul style="list-style-type: none"> <li>➤ <b>Reporting of dual-color FISH</b> <ul style="list-style-type: none"> <li>- positive if signal ratio <math>\geq 2,2</math> (HER-2 vs. centr. 17)</li> <li>- negative ff signal ratio <math>\leq 1,8</math></li> </ul> </li> </ul>	<b>3a</b>	<b>C</b>	<b>++</b>
<ul style="list-style-type: none"> <li>➤ <b>Equivocal FISH results require additional testing</b></li> </ul>	<b>3a</b>	<b>C</b>	<b>++</b>
<ul style="list-style-type: none"> <li>➤ <b>CISH/SISH instead of FISH</b></li> </ul>	<b>4</b>	<b>C</b>	<b>+/-</b>
<ul style="list-style-type: none"> <li>➤ <b>Use of internal and external quality control schemes</b></li> </ul>	<b>5</b>	<b>D</b>	<b>++</b>

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➤ Full workup using step sections of ≥ 500 µm on paraffin embedded tissue	5	D	++
➤ Cytokeratin immunohistochemistry			
- when suspicious, to detect micromet.	2b	B	++
- as a routine procedure	5	D	+/-
➤ Frozen section (invasive Ca.)			
- on suspicious node	2b	B	++
- on non-suspicious node	2b	B	+
➤ Imprint cytology instead or in addition of frozen section	3b	C	+/-
➤ RT-PCR for epithelial genes	4	D	-
- OSNA	3b	B	-

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