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# Diagnosis and Treatment of Patients with early and advanced Breast Cancer

## Breast Cancer Surgery Oncological Aspects



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## Breast Cancer Surgery Oncological Aspects

- **Versions 2002–2019:**  
 Bauerfeind / Blohmer / Böhme / Brunnert / Costa / Fersis / Gerber /  
 Hanf / Janni / Junkermann / Kaufmann / Kühn / Kümmel / Möbus / Nitz /  
 Rezai / Simon / Solomayer / Thomssen / Thill / Untch
  
- **Version 2020:**  
 Thomssen / Wöckel

### Screened data bases

Pubmed 1998 – 2019, ASCO 2019, SABCS 2019, ESMO 2019, EBCC 2018, ABC-5 2019, Cochrane data base 1998 - 2019

### Guidelines screened

1. St.Gallen/Vienna 2019: Burstein HJ, Curigliano G, Loibl S et al.; Members of the St. Gallen International Consensus Panel on the Primary Therapy of Early Breast Cancer 2019. Estimating the benefits of therapy for early-stage breast cancer: the St. Gallen International Consensus Guidelines for the primary therapy of early breast cancer 2019. Ann Oncol. 2019 Oct 1;30(10):1541-1557.
2. Balic M, Thomssen C, Würstlein R, Gnant M, Harbeck N. St. Gallen/Vienna 2019: A Brief Summary of the Consensus Discussion on the Optimal Primary Breast Cancer Treatment. Breast Care (Basel). 2019 Apr;14(2):103-110.
3. ABC4: Cardoso F, Senkus E, Costa A et al. 4th ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 4)†. Ann Oncol. 2018 Aug 1;29(8):1634-1657.
4. NCCN 2019: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Breast Cancer. NCCN Evidence Blocks™. Version 3.2019 – September 6, 2019. [https://www.nccn.org/professionals/physician\\_gls/pdf/breast\\_blocks.pdf](https://www.nccn.org/professionals/physician_gls/pdf/breast_blocks.pdf). Download Jan 19, 2020.

Cochrane library:

- <http://onlinelibrary.wiley.com/cochranelibrary/search>

Pubmed 2008 - 2019, ASCO 2003 – 2019, SABCS 2003 – 2019, Cochrane data base (n.d.)



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# Breast Cancer Surgery Oncological Aspects

## AGO: ++

**Surgery is one sub-step out of multiple steps in breast cancer treatment. Thus, both diagnostic and oncological expertise are an essential requirement for every breast surgeon.**

Pre-therapeutic Assessment of Breast and Axilla			
	Oxford		
	LoE	GR	AGO
■ Clinical examination	5	D	++
■ Mammography	2b	B	++
■ + Tomosynthesis (DBT)	3b	B	+
■ + Contrast-enhanced mammography	3a	B	+/-
■ Sonography (breast and axilla)	2b	B	++
■ MRI*	1b	B	+
■ Minimally invasive biopsy**	1b	A	++
■ CNB of axillary lymph nodes if suspicious	2b	B	++
■ Breast-CT	5	D	-

\* MRI-guided vacuum biopsy is mandatory in case of MRI-detected additional lesions. Individual decision for patients at high familiar risk, with dense breast (density 3-4/diagnostic assessability C-D), lobular invasive tumors, suspicion of multilocal disease. No reduction in re-excision rate.  
 \*\*Histopathology of lesions if relevant for treatment



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## Review on additional imaging

1. Ong E. Preoperative imaging for breast conservation surgery-do we need more than conventional imaging for local disease assessment? Gland Surg. 2018 Dec;7(6):554-559.

## Clinical assessment (inspection, palpation)

=

## Mammography

=

## Combined DM + DBT + US + MRI

1. Mariscotti G, Houssami N, Durando M, et al. Accuracy of mammography, digital breast tomosynthesis, ultrasound and MR imaging in preoperative assessment of breast cancer. *Anticancer Res.* 2014 Mar;34(3):1219-25.
2. Campanino PP, Ruggieri C, Regini E, et al. Accuracy of mammography, digital breast tomosynthesis, ultrasound and MR imaging in preoperative assessment of breast cancer. *Anticancer Res.* 2014 Mar;34(3):1219-25.

### Tomosynthesis

1. Thompson W, Argaez C. Digital Breast Tomosynthesis for the Screening and Diagnosis of Breast Cancer: A Review of the Diagnostic Accuracy, Cost-Effectiveness and Guidelines [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2019 Oct 28.

### Contrast-enhanced digital mammography (CEM, CEDM), Contrast-enhanced spectral mammography (CESM)

1. Bicchierai G, Tonelli P, Piacenti A et al. Evaluation of contrast-enhanced digital mammography (CEDM) in the preoperative staging of breast cancer: Large-scale single-center experience. *Breast J.* 2020 Jan 30.
2. Amato F, Bicchierai G, Cirone D, et al. Preoperative loco-regional staging of invasive lobular carcinoma with contrast-enhanced digital mammography (CEDM). *Radiol Med.* 2019 Dec;124(12):1229-1237.
3. Ghaderi KF, Phillips J, Perry H et al. Contrast-enhanced Mammography: Current Applications and Future Directions. *Radiographics.* 2019 Nov-Dec;39(7):1907-1920.
4. Jochelson, MS, Dershaw, DD, Sung, J et al. Bilateral Contrast-enhanced dual-energy digital mammography: Feasibility and comparison with conventional digital mammography and MR imaging in women with known breast carcinoma. *Radiology* 2013; 266:743–751.
5. Fallenberg, EM, Schmitzberger, FF, Amer, H et al. Contrast-enhanced spectral mammography vs. mammography and MRI - clinical performance in a multi-reader evaluation. *Eur Radiol* 2017; 27:2752–2764.

### US-Axilla +FNA/CNB

1. Preda T, McGrath R, Bingham J et al. How much does axillary ultrasound contribute in women undergoing breast-conserving surgery with no palpable axillary nodes? ANZ J Surg. 2020 Jan 20.
2. Diepstraten SC, Sever AR, Buckens CFM, et al. Value of preoperative ultrasound guided lymphnode biopsy for preventing completion axillary lymphnode dissection in breast cancer: a systematic review and meta-analysis. Ann Surg Oncol 2014;21:51-59
3. Evans A, Rauchhaus P, Whelehan P, et al. Does shear wave ultrasound independently predict axillary lymph node metastasis in women with invasive breast cancer? Breast Cancer Res Treat. 2013 Dec 4. [Epub ahead of print]
4. Feng Y, Huang R, He Y, et al. Efficacy of physical examination, ultrasound, and ultrasound combined with fine-needle aspiration for axilla staging of primary breast cancer. Breast Cancer Res Treat. 2015 Feb;149(3):761-5. doi: 10.1007/s10549-015-3280-z. Epub 2015 Feb 10.

#### Biopsy

1. Chan KY, WiseberdFirtell, J, Jois HSR, et al. Localisation techniques for guided surgical excision of non-palpable breast lesions. Cochrane Database of Systematic reviews 2015;vol 12
2. Lourenco AP, Mainiero MB Incorporating imaging into the locoregional management of breast cancer. Semin Radiat Oncol 2016;26(1)
3. Mariscotti G, Houssami N, Durando M, et al. Accuracy of mammography, digital breast tomosynthesis, ultrasound and MR imaging in preoperative assessment of breast cancer. Anticancer Res. 2014 Mar;34(3):1219-25.

#### MRI


1. Mann RM, Loo CE, Wobbles T et al The impact of preoperative MRI on the re-excision rate in invasive lobular carcinoma of the breast. Breast Cancer Res Treat 2010; 119: 415-422
2. Houssami N, Turner R, Morrow M. Preoperative magnetic resonance imaging in breast cancer: meta-analysis of surgical outcomes. Ann Surg. 2013 Feb;257(2):249-55.
3. Debal M, Abramian A, Nemes L, et al. Who may benefit from preoperative MRI? A single-center analysis of 1102 consecutive patients with primary breast cancer. Breast Cancer Res Treat 2015;153(3):531-537

4. Arnaut A, Catley C, Booth CM, et al. Use of preoperative Magnetic Resonance Imaging for breast cancer: A Canadian population-based study. *JAMA Oncol* 2015;1(9):1238-1250
5. Fancellu A, Turner RM, Dixon JM, et al. Metaanalysis of the effect of preoperative MRI on the surgical management of ductal carcinoma in situ. *Brit J Surg* 2015;192(8):883-893
6. Houssami N, Turner R, Macaskill P, et al. An individual person data meta-analysis of preoperative magnetic resonance imaging and breast cancer recurrence. *J Clin Oncol* 2014;32(5):392-401
7. Vos EL, Voogd AC, Verhoef C, et al. Benefits of preoperative MRI in breast cancer surgery studied in a large population-based cancer registry. *Br J Surg* 2015;102(13):1649-1657
8. Lehman CD, Lee JM, DeMartini WS, et al. Screening MRI in women with a personal history of breast cancer. *J Natl Cancer Inst* 2016;108(3)
9. Wang SY, Long JB, Killelea BK, et al. Preoperative breast MRI and contralateral breast cancer occurrence among older women with breast cancer. *J Clin Oncol* 2015;Nov 30, epub ahead of print
10. Riedl CC, Luft N, Clemens B et al. Triple-modality screening trial for familial breast cancer underlines the importance of magnetic resonance imaging and questions the role of mammography and ultrasonography regardless of patient mutation status, age and breast density. *JCO* 2015;33(10):1128-1135
11. El Sharouni M, Postma EL, Menezes GLG et al. High prevalence of MRI-detected contralateral and ipsilateral malignant findings in patients with invasive ductolobular breast cancer: Impact on surgical management. *Clin Breast Cancer*. 2016 Aug;16(4):269-75.
12. Vriens BE, de Vries B, Lobbès MB, van Gastel SM, et al. INTENS Study Group. Ultrasound is at least as good as magnetic resonance imaging in predicting tumour size post-neoadjuvant chemotherapy in breast cancer. *Eur J Cancer*. 2016 Jan;52:67-76.
13. Health Quality Ontario..Magnetic Resonance Imaging as an Adjunct to Mammography for Breast Cancer Screening in Women at Less Than High Risk for Breast Cancer: A Health Technology Assessment. *Ont Health Technol Assess Ser*. 2016; Nov 1;16(20):1-30
14. Lobbès MB, Vriens IJ, van Bommel AC, et al. Breast MRI increases the number of mastectomies for ductal cancers, but decreases them for lobular cancers. *Breast Cancer Res Treat*. 2017;162:353-364.
15. Houssami N, Turner RM, Morrow M. Meta-analysis of pre-operative magnetic resonance imaging (MRI) and surgical treatment for breast cancer. *Breast Cancer Res Treat*. 2017 Sep;165(2):273-283



### Breast-CT (CBCT)

1. Berger N, Marcon M, Frauenfelder T, Boss A. Dedicated Spiral Breast Computed Tomography With a Single Photon-Counting Detector: Initial Results of the First 300 Women. Invest Radiol. 2020 Feb;55(2):68-72.

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	<table> <tr> <th></th><th colspan="3">Oxford</th></tr> <tr> <th></th><th>LoE</th><th>GR</th><th>AGO</th></tr> <tr> <td>History and clinical examination</td><td>5</td><td>D</td><td>++</td></tr> <tr> <td colspan="4">Additional diagnosis for patients with high metastatic potential and/or symptoms (in decision making for chemotherapy and/or anti-HER2-therapy):</td></tr> <tr> <td>CT scan of thorax/abdomen</td><td>2a</td><td>B</td><td>+</td></tr> <tr> <td>Bone scan</td><td>2b</td><td>B</td><td>+</td></tr> <tr> <td>Chest X-ray</td><td>5</td><td>C</td><td>+/-</td></tr> <tr> <td>Liver ultrasound</td><td>5</td><td>D</td><td>+/-</td></tr> <tr> <td>In case of suspicious lesions further diagnosis (e.g. liver-MRI, CEUS*, biopsy etc.)</td><td>2a</td><td>B</td><td>+</td></tr> <tr> <td>FDG-PET or FDG-PET /CT</td><td>3a</td><td>C</td><td>+/-</td></tr> <tr> <td>Whole body MRI</td><td>4</td><td>C</td><td>+/-</td></tr> </table> <p>* Contrast enhanced ultrasound</p>				Oxford				LoE	GR	AGO	History and clinical examination	5	D	++	Additional diagnosis for patients with high metastatic potential and/or symptoms (in decision making for chemotherapy and/or anti-HER2-therapy):				CT scan of thorax/abdomen	2a	B	+	Bone scan	2b	B	+	Chest X-ray	5	C	+/-	Liver ultrasound	5	D	+/-	In case of suspicious lesions further diagnosis (e.g. liver-MRI, CEUS*, biopsy etc.)	2a	B	+	FDG-PET or FDG-PET /CT	3a	C	+/-	Whole body MRI	4	C
	Oxford																																													
	LoE	GR	AGO																																											
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Whole body MRI	4	C	+/-																																											

## Statement: history and physical examination


### 1. GCP

## Statement: high metastatic potential / symptoms

1. Rutgers, EJ et al: Quality control in the locoregional treatment of breast cancer (2001) EJC 37: 447-453
2. Gerber B, Seitz E, Muller H et al: Perioperative screening for metastatic disease is not indicated in patients with primary breast cancer and no clinical signs of tumor spread. Breast Cancer Res Treat 82:29-37; 2003
3. Schneider C, Fehr MK, Steiner RA et al: Frequency and distribution pattern of distant metastases in breast cancer patients at the time of primary presentation Arch Gynecol Obstet. 2003 Nov;269(1):9-12.
4. Isasi CR, Moadel RM, Blaufox MD. A meta-analysis of FDGPET for the evaluation of breast cancer recurrence and metastases. Breast Cancer Res Treat 2005;90(2):105–12.
5. Schmidt GP, Baur-Melnyk A, Haug A, et al.: Comprehensive imaging of tumor recurrence in breast cancer patients using whole-body MRI at 1.5 and 3 T compared to FDG–PET–CT. European Journal of Radiology 2008; 65, 47–58.
6. Shie P, Cardarelli R, Brandon D et al: Meta-analysis: comparison of F-18 Fluorodeoxyglucose-positron emission tomography and bone scintigraphy in the detection of bone metastases in patients with breast cancer. Clin Nucl Med. 2008 Feb;33(2):97-101.
7. Barrett T, Bowden DJ, Greenberg DC et al.: Radiological staging in breast cancer: which asymptomatic patients to image and how.

British Journal of Cancer 2009; 101, 1522 – 1528.

8. Rong J, Wang S, Ding Q, et al. Comparison of 18 FDG PET-CT and bone scintigraphy for detection of bone metastases in breast cancer patients. A meta-analysis. Surg Oncol. 2013 Jun;22(2):86-91
9. Hong S, Li J, Wang S. 18FDG PET-CT for diagnosis of distant metastases in breast cancer patients. A meta-analysis. Surg Oncol. 2013 Jun;22(2):139-43.
10. Gutzeit A, Doert A, Froehlich JM, et al. Comparison of diffusion-weighted whole body MRI and skeletal scintigraphy for the detection of bone metastases in patients with prostate or breast carcinoma. Skeletal Radiol. 2010 Apr;39(4):333-43.
11. Department of Health. Diagnosis, staging and treatment of patients with breast cancer. National Clinical Guideline No. 7. June 2015. ISSN 2009-6259
12. Bychkovsky BL, Lin NU: Imaging in the evaluation and follow-up of early and advanced breast cancer: When, why, and how often? 2017; 31, 318–324.
13. deSouza NM, Liu Y, Chiti A et al.: Strategies and technical challenges for imaging oligometastatic disease: Recommendations from the European Organisation for Research and Treatment of Cancer imaging group. Eur J Cancer. 2018 Jan 10. [Epub ahead of print].
14. NCCN 2019: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Breast Cancer. NCCN Evidence Blocks™. Version 3.2019 – September 6, 2019. [https://www.nccn.org/professionals/physician\\_gls/pdf/breast\\_blocks.pdf](https://www.nccn.org/professionals/physician_gls/pdf/breast_blocks.pdf). Download Jan 19, 2020.
15. Mishima M, Toh U, Iwakuma N, Takenaka M, Furukawa M, Akagi Y. Evaluation of contrast Sonazoid-enhanced ultrasonography for the detection of hepatic metastases in breast cancer. Breast Cancer. 2016 Mar;23(2):231-41
16. Zhang L, Zhang L, Wang H, Chen L, Sui G. Diagnostic performance of contrast-enhanced ultrasound and magnetic resonance imaging for detecting colorectal liver metastases: A systematic review and meta-analysis. Dig Liver Dis. 2019 Sep;51(9):1241-1248.



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# Evidence of Surgical Procedure

	Oxford		AGO
	LoE	GR	
■ Survival rates after lumpectomy + RT are equivalent to those after (modified) radical mastectomy	1a	A	
■ Local recurrence rates after skin sparing mastectomy are equivalent to those after mastectomy	2b	B	
■ Conservation of the NAC (nipple areola complex) is an adequate surgical procedure, if R0 resection is achieved	2b	C	

## Evidence of surgical procedure

### Statement: lumpectomy – mastectomy

1. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer (2002) N Engl J Med 347:1233-1241
2. Veronesi U et al.: Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. NEJM 2002 Oct 17;347(16):1227-32
3. Christiansen P, Carstensen SL, Ejlersen B, et al. Breast conserving surgery versus mastectomy: overall and relative survival-a population based study by the Danish Breast Cancer Cooperative Group (DBCG). Acta Oncol. 2017 Nov 23:1-7.
4. Hamelinck VC, Bastiaannet E, Pieterse AH, et al. prospective comparison of younger and older patients' preferences for breast-conserving surgery versus mastectomy in early breast cancer. J Geriatr Oncol. 2017 Sep 11. pii: S1879-4068(17)30175-3

### Statement: skin sparing mastectomy


1. Carlson GW, Bostwick J, Styblo TM et al. Skin-sparing mastectomy. Oncologic and reconstructive considerations. Ann Surg 1997;

225:570-575.

2. Kroll SS, Schusterman MA, Tadjalli HE et al. Risk of recurrence after treatment of early breast cancer with skin- sparing mastectomy. *Ann Surg Oncol* 1997; 4:193-197.
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4. Simmons RM, Fish SK, Gayle L et al. Local and distant recurrence rates in skin-sparing mastectomies compared with non-skin-sparing mastectomies. *Ann Surg Oncol* 1999; 6:676-681.
5. Rivadeneira D, Simmons RM, Fish SK et al. Skin-sparing mastectomy with immediate breast reconstruction: a critical analysis of local recurrence. *Cancer* 2000; 6:331-335.
6. Foster et al. Skin-sparing mastectomy and immediate breast reconstruction: a prospective cohort study for the treatment of advanced stages of breast carcinoma. *Ann Surg Oncol* 2002 Jun;9(5):462-6
7. Greenway RM, Schlossberg L, Dooley WC. Fifteen-year series of skin-sparing mastectomy for stage 0 to 2 breast cancer. *Am J Surg* 2005; 190:918-922.
8. Howard MA, Polo K, Pusic AL et al. Breast cancer local recurrence after mastectomy and TRAM flap reconstruction: incidence and treatment options. *Plast Reconstr Surg* 2006; 117:1381-1386.
9. Patani N, Devalia H, Anderson A et al. Oncological safety and patient satisfaction with skin-sparing mastectomy and immediate breast reconstruction. *Surg Oncol* 2007; 17:97-105.
10. Paepke S, Schmid R, Fleckner S, et al. Subcutaneous mastectomy with conservation of the nipple-areola skin: broadening the indications *Ann Surg.* 2009;250(2):288-92
11. Gerber et al.: Skin-sparing mastectomy with conservation of the nipple-areola complex and autologous reconstruction is an oncologically safe procedure. *Ann Surg* 2009 Mar;249(3):461-8
12. Lanitis S1, Tekkis PP, Sgourakis G, et al.: Comparison of skin-sparing mastectomy versus non-skin-sparing mastectomy for breast cancer: a meta-analysis of observational studies. *Ann Surg.* 2010 Apr;251(4):632-9.

Statement: Nipple sparing mastectomy

1. Petit JY, Veronesi U, Orecchia R et al. Nipple-sparing mastectomy in association with intra operative radiotherapy (ELIOT): A new type of mastectomy for breast cancer treatment. *Breast Cancer Res Treat* 2006; 96:47-51.
2. Sacchini V, Pinotti JA, Barros AC et al. Nipple-sparing mastectomy for breast cancer and risk reduction: oncologic or technical problem? *J Am Coll Surg* 2006; 203:704-714.
3. Caruso F, Ferrara M, Castiglione G et al. Nipple sparing subcutaneous mastectomy: sixty-six months follow-up. *Eur J Surg Oncol* 2006; 32:937-940.
4. Howard MA, Polo K, Pusic AL et al. Breast cancer local recurrence after mastectomy and TRAM flap reconstruction: incidence and treatment options. *Plast Reconstr Surg* 2006; 117:1381-1386
5. Benediktsson KP, Perbeck L. Survival in breast cancer after nipple-sparing subcutaneous mastectomy and immediate reconstruction with implants: A prospective trial with 13 years median follow-up in 216 patients. *Eur J Surg Oncol* 2008; 34:143-148.
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8. Burdge EC, Yuen J, Hardee M, et al. Nipple skin-sparing mastectomy is feasible for advanced disease. *Ann Surg Oncol*. 2013 Oct;20(10):3294-302.
9. Mellon P, Feron JG, Couturud B et al. The role of nipple sparing mastectomy in breast cancer: a comprehensive review of the literature. *Plast Reconstr. Surg* 2013;131(5):969-84
10. Muller T, Baratte A, Bruant-Rodier C, et al. Oncological safety of nipple-sparing prophylactic mastectomy: A review of the literature on 3716 cases. *Ann Chir Plast Esthet*. 2017 Oct 10 pii: S0294-1260(17)30137-1.

Breast Conservation: Surgical Technical Aspects			
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 <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2020.1</p> <p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p>	<ul style="list-style-type: none"> <li>▪ <b>Non-palpable lesion</b> <ul style="list-style-type: none"> <li>▪ Wire guided localisation</li> <li>▪ Other procedures (Radionuclide guided localisation/RADAR reflection, Magnetic Seeds/RFID etc.)</li> <li>▪ Specimen radiography or ultrasound</li> </ul> </li> <li>▪ <b>Tumor-free margins required</b> (also in unfavorable biology, „no ink on tumor“ is sufficient)</li> <li>▪ <b>Immediate intraoperative re-excision for close margins</b> (specimen radiography or ultrasound and/or intra-operative pathology)</li> <li>▪ <b>Re-excision required for involved margins (paraffin section)</b></li> <li>▪ <b>Therapeutic stereotactic excision alone</b></li> <li>▪ <b>Ultrasound guided surgery to prevent re-excision</b></li> <li>▪ <b>Intraoperative margin evaluation (with Margin Probe®)</b></li> </ul>		
	2b	B	++
	2a	B	+/-
	2b	B	++
	2a	A	++
	1c	B	++
	3b	C	+
	4	D	--
	1a	A	+/-
	1b	A	+/-

#### Statement: Wire guided ..

1. Hanna et al.: The use of stereotactic excisional biopsy in the management of invasive breast cancer. World J Surg. 2005 Nov;29(11):1490-4
2. Köhler J, Krause B, Grunwald S, et al. Ultrasound and mammography guided wire marking of non-palpable breast lesions: analysis of 741 cases. Ultraschall Med. 2007 Jun;28(3):283-90.
3. Ahmed M, Douek M. Intra-operative ultrasound versus wire-guided localization in the surgical management of non-palpable breast cancers: systematic review and meta-analysis. Breast Cancer Res Treat. 2013 Aug;140(3):435-46.

#### Statement: Radioguided ..

1. van der Ploeg IM, Hobbelink M, van den Bosch MA: 'Radioguided occult lesion localisation' (ROLL) for non-palpable breast lesions: a review of the relevant literature. Eur J Surg Oncol. 2008 Jan;34(1):1-5.
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3. Ong JSL, Teh J, Saunders C, Bourke AG, et al: Patient satisfaction with Radioguided Occult Lesion Localisation using iodine-125 seeds ('ROLLIS') versus conventional hookwire localisation. Eur J Surg Oncol. 2017 Dec;43(12):2261-2269.
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6. Srour MK, Kim S, Amersi F et al. Comparison of wire localization, radioactive seed, and Savi scout® radar for management of surgical breast disease. Breast J. 2019 Aug 25.

Statement: specimen radiography

1. Singletary: Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. Am J Surg. 2002 Nov;184(5):383-93.
2. Mazouni C, Rouzier R, Balleyguier C. Specimen radiography as predictor of resection margin status in non-palpable breast lesions. Clin Radiol. 2006 Sep;61(9):789-96.
3. Tan KY et al. Breast specimen ultrasound and mammography in the prediction of tumour-free margins. ANZ J Surg. 2006 Dec;76(12):1064-7.
4. Kunos C, Latson L, Overmoyer B Breast conservation surgery achieving  $\geq 2$  mm tumor-free margins results in decreased local-regional recurrence rate, Breast J. 2006 Jan-Feb;12(1):28-36

Statement: tumor free margins ...

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## Breast Conservation Surgery (BCS)

	Oxford		
	LoE	GR	AGO
▪ <b>Multicentric disease (MF/MZ) (R0-Resection of all lesions)</b>	2b	B	+
▪ <b>Positive microscopic margins after repeated excision</b>	2b	B	--
▪ <b>Inflammatory breast cancer</b>	2b	B	--

**For surgery after neoadjuvant chemotherapy  
see chapter „neoadjuvant chemotherapy“**

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 <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2020.1</p> <p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p>	Primary Axillary Lymph Node Dissection (ALND) I			
	Oxford			
	LoE	GR	AGO	
▪ Endpoint: Survival	3	D	-	
▪ Endpoint Staging	3	A	-	
▪ Endpoint: Locoregional control	2a	A	+/-	
▪ pN+ (pre-surgery) without neoadjuvant systemic therapy	2a	B	+	
▪ cN0 pN0(sn)(i+)	1b	A	--	
▪ cN0 pN1(mi)	2b	B	--	
▪ cN0 pN1(sn) ( cT1/2 , < 3 SN +, BCS + tangential radiation field, adequate systemic therapy)	1b	A	-	
▪ cN0 pN1 (sn) and mastectomy (no chestwall radiotherapy)	1b	B	+*	
▪ cN0 pN1(sn) and mastectomy (T1/2, <3SN+) (chestwall radiotherapy)	5	D	+/-*	
▪ <b>ALND indicated, but not feasible</b>				
▪ Radiotherapy according to AMAROS-trial (validated for cN0 pN1sn)	1b	B	+	

\* Study participation recommended

## Statements: Axillary lymph node dissection I

### Statement: Axillary lymph node dissection

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Endpoint: Survival LoE 3D AGO-

-

Endpoint: Staging LoE3A AGO -

-

Endpoint: Locoregional control LoE 2aA AGO+/-

-

pN+ (pre-surgery) without neoadjuvant systemic therapy LoE 2a B AGO +

1. Euhus DM. Management of the clinically positive axilla. Breast J. 2020 Jan;26(1):35-38.



cN0 pN0(sn)(i+)LoE 1b A AGO –

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cN0 pN1 (mi) LoE 2b B AGO --

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cN0 pN 1(sn) ( cT1/2 , < 3 SN +, BCS + tangential radiation field, adequate systemic therapy) LoE 1b A AGO -

1. Giuliano AE, Ballman KV, McCall L, et al. Effect of Axillary Dissection vs No Axillary Dissection on 10-Year Overall Survival Among Women With Invasive Breast Cancer and Sentinel Node Metastasis: The ACOSOG Z0011 (Alliance) Randomized Clinical Trial. JAMA. 2017 Sep 12;318(10):918-926.
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cN0 pN1 (sn) and mastectomy (no chestwall radiotherapy) LoE 1b B AGO +\*

1. Cody HS 3rd. Extending ACOSOG Z0011 to Encompass Mastectomy: What Happens Without RT? Ann Surg Oncol. 2017 Mar;24(3):621-623.

cN0 pN1(sn) and mastectomy (T1/2, <3SN+) (chestwall radiotherapy) LoE 5 D AGO +/-\*


-

ALND indicated, but not feasible – Radiotherapy according to AMAROS-trial (validated for cN0 pN1sn) LoE 1b B AGO +

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(EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. Lancet Oncol. 2014 Nov;15(12):1303-10.

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 © AGO e. V. in der DGGG e.V. sowie in der DKG e.V.  Guidelines Breast Version 2020.1  www.ago-online.de FORSCHEN LEHREN HEILEN		Axillary Surgery and NACT			Oxford		AGO
					LoE	GR	
SLNE after NACT					2b	B	++
SLNE before NACT					2b	B	+/-
cN-status (before NACT)	pN-status (before NACT)	N-status (after NACT)	Surgical Procedure (after NACT)				
cN0	pN0(sn)	ycN0	None	1a	A		+
cN0	pN+(sn) according to ACOSOG Z0011	ycN0	None	1b	B		+
cN0	pN+(sn) different from ACOSOG Z0011	ycN0	ALND or Axillary RT	2b	B		+
cN0	Not done (no SLNE)	ypN0 (sn)	SLNE only	2b	B		++
		ypN1 <sub>mic</sub> (sn)	ALND Axillary RT	2b 5	C D		+ +/-
		ypN1 (sn)	ALND Axillary RT	2b 5	C D		++ +/-
cN+	pN+ <sub>CNB</sub>	ycN0	SLNE only*	2b	B		+/-
			TAD (TLNE + SLNE)*	2b	B		+
			ALND*	2b	B		+
cN+	pN+ <sub>CNB</sub>	ycN+	ALND	2b	B		++
			Axillary RT	5	D		-

NACT=Neoadjuvant chemotherapy; ALND=Axillary Lymph Node Dissection; SLNE=Sentinel Lymph Node Excision;  
TAD=Targeted Axillary Dissection; TLNE=Targeted Lymph Node Excision; RT=Radiotherapy – \*Trial participation recommended

Complete Axillary lymph node dissection after positive sentinel lymph node may be omitted in certain cases due to lack of benefit in prospectively randomized studies

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Women With Invasive Breast Cancer and Sentinel Node Metastasis: The ACOSOG Z0011 (Alliance) Randomized Clinical Trial. JAMA. 2017 Sep 12;318(10):918-926.

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#### TAD (+SLNE) after PST, if pN1 (CNB prior to PST and ycN0


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## Improvement of the False-Negative Rate of SLNE in Patients with pN+<sub>CNB</sub> before NACT and ycN0 after NACT

	Oxford		
	LoE	GR	AGO
■ Removal of > 2 SLNs (SLNE, no untargeted axillary sampling)	2a	B	+
■ Combined tracer	2a	B	+/-
■ IHC and serial sections to detect ITC or micrometastases	2b	B	+
■ Localization of pos. LN before NACT (clip/coil/tattoo)	2b	B	+*
■ Targeted Axillary Dissection (TAD = TLNE + SLNE)**	2b	B	+*
■ TLNE only	2b	B	+/-*

\* Study participation recommended ;


\*\* TAD =Targeted axillary dissection; TLNE = Targeted lymph node excision; SLNE = Sentinel lymph node excision

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## Reduction of individual failures for SLNB in pN1 ypN0

■ **Predictive factors for axillary remission**  
**pN1 (before NACT) to ypN0<sub>sn/TAD</sub> (after NACT)**


- Young age
- Intrinsic Subtype (ER neg, HER 2 pos)
- Grade 3
- N1 (vs N2)
- pCR (breast)

Kantor et al. Ann Surg Oncol 2018

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Sentinel Lymph Node Excision (SLNE) Indications I			
	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li> <b>Clinically / sonographically negative axilla (cN0)</b> <ul style="list-style-type: none"> <li>Add CNB in cN1 (clinically/sonographically suspicious) in order to enable SLNB</li> </ul> </li> <li>cT 1–2</li> <li>cT 3–4c</li> <li>Multifocal / multicentric lesions</li> <li>DCIS <ul style="list-style-type: none"> <li>Mastectomy</li> <li>BCT</li> <li>DCIS in male</li> </ul> </li> <li>Male breast cancer</li> <li>In elderly patients</li> </ul>	1b	A	++
	2a	B	+
	2b	A	++
	3b	B	+
	2b	B	+
	3b	B	+
	3b	B	-
	5	D	+/-
	2b	B	+
	3b	B	+


  
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### Statement: SLNE

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Results of Ganglion Sentinelle et Chimiotherapie Neoadjuvante, a French Prospective Multicentric Study. *J Clin Oncol*. 2008 Dec 29. [Epub ahead of print]

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Statement: preoperative FNA / CNB (core needle biopsy) of suspicious lymph nodes

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Statement: Multifocal / multicentric MaCa

1. Ferrari A, Dionigi P, Rovera F. Multifocality and multicentricity are not contraindications for sentinel lymph node biopsy in breast

cancer surgery. World J Surg Oncol. 2006 Nov 20;4:79.

#### Statement: DCIS

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#### Statement: Male

1. Boughey JC et al. Comparative analysis of sentinel lymph node operation in male and female breast cancer patients. J Am Coll Surg 2006 Oct;203(4):475-80.
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#### Statement: Elderly


1. Reimer T, Gerber B. Quality-of-life considerations in the treatment of early-stage breast cancer in the elderly. Drugs Aging. 2010 Oct 1;27(10):791-800.
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#### Statement: Lymphedema



1. Miller CL, Specht MC, Skolny MN, et al. Sentinel lymph node biopsy at the time of mastectomy does not increase the risk of lymphedema: implications for prophylactic surgery. *Breast Cancer Res Treat.* 2012 Oct;135(3):781-9.

Sentinel Lymph Node Excision (SNLE) Indications II			
	Oxford		
	LoE	GR	AGO
▪ During pregnancy and / or breast feeding (only <sup>99m</sup> Tc-colloid, no blue dye)	3	C	++
▪ After prior tumor excision	2b	B	+
▪ After prior major breast surgery (e.g. reduction mammoplasty)	3b	C	+/-
▪ Ipsilateral breast recurrence after prior BCS and prior SNLE	4	D	-
▪ SLNE in the mammary internal chain	2b	B	-
▪ After axillary surgery	3b	B	+/-
▪ Prophylactic bilateral / contralateral mastectomy	3b	B	--
▪ Inflammatory breast cancer	3b	C	-


  
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#### Statement: pregnancy

1. Khera SY, Kiluk JV, Hasson DM Pregnancy-associated breast cancer patients can safely undergo lymphatic mapping. Breast J. 2008 May-Jun;14(3):250-4
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#### Statement: internal mammarian

1. Avisar E, Molina MA, Scarlata M: Internal mammary sentinel node biopsy for breast cancer. Am J Surg. 2008 Oct;196(4):490-4.
2. Chen RC, Lin NU, Golshn M: Internal mammary nodes in breast cancer: diagnosis and implications for patient management -- a

systematic review. J Clin Oncol. 2008 Oct 20;26(30):4981-9.

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#### Statement: prophylactic mastectomy

1. Dupont et al. The role of sentinel lymph node biopsy in women undergoing prophylactic mastectomy. Am J Surg 2000 Oct;180(4):274-7
2. Soran A et al.: Is routine sentinel lymph node biopsy indicated in women undergoing contralateral prophylactic mastectomy? Magee-Womens Hospital experience. Ann Surg Oncol 2007 Feb;14(2):646-51.
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#### Statement: After previous tumor excision

1. Celebioglu et al.: Sentinel node biopsy in non-palpable breast cancer and in patients with a previous diagnostic excision. Eur J Surg Oncol 2007 Apr;33(3):276-80.

#### Statement: previous major breast surgery

1. Intra et al. Sentinel lymph node biopsy is feasible even after total mastectomy. J Surg Oncol 2007 Feb 1;95(2):175-9
2. Kaminski A, Amr D, Kimbrell ML: Lymphatic mapping in patients with breast cancer and previous augmentation mammoplasty. Am Surg. 2007 Oct;73(10):981-3
3. Karam A, Stempel M, Cody HS 3rd: Reoperative sentinel lymph node biopsy after previous mastectomy. J Am Coll Surg. 2008;207(4):543-8
4. Ruano R, Ramos M, Garcia-Talavera JR: Staging the axilla with selective sentinel node biopsy in patients with previous excision of non-palpable and palpable breast cancer. Eur J Nucl Med Mol Imaging. 2008 Jul;35(7):1299-304.

Statement: Ipsilateral breast recurrence after prior BCS and prior SLNB


1. Mattia Intra M, Triro G, Viale G: Second Biopsy of Axillary Sentinel Lymph Node for Reappearing Breast Cancer After Previous Sentinel Lymph Node Biopsy. *Ann Surg Oncol*. 2005;12(11):895-9
2. Intra et al. Second axillary sentinel node biopsy for ipsilateral breast tumour recurrence. *Br J Surg* 2007 Oct;94(10):1216-9
3. Schrenk P et al. Lymphatic mapping in patients with primary or recurrent breast cancer following previous axillary surgery. *Eur J Surg Oncol*. 2008 Aug;34(8):851-6.
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Statement: inflammatory breast cancer

1. Fayanju OM, Ren Y, Greenup RA, et al. Extent of axillary surgery in inflammatory breast cancer: a survival analysis of 3500 patients [published online ahead of print, 2020 Jan 20]. *Breast Cancer Res Treat*. 2020;10.1007/s10549-020-05529-1.
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#### Statement: Others

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## Sentinel Lymph Node Excision (SLNE) Marking

Oxford		
LoE	GR	AGO
1a	A	++
1b	A	+
1a	A	+/-
4	D	-
2a	B	+/-
2a	B	+/-

- **<sup>99m</sup>Tc Kolloid**
- **Preoperative lymphoscintigraphy (added information limited, but mandatory by legal regulations)\***
- **Patent blue dye**
- **Methylen blue**
- **Indocyanin green (ICG)**
- **SPIO<sup>#</sup>**

\* In Germany required for quality assurance of nuclear medicine

# SPIO: Superparamagnetic Iron Oxide

### Statement radiotracer/blue dye

1. Lyman GH, Somerfield MR et al. Sentinel Lymph Node Biopsy for Patients With Early-Stage Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2017;35(5):561–564.
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## Procedure after Neoadjuvant Therapy

- Early clip or coil marking of tumor (incl. detailed topographic documentation)
- Surgical removal of tumor/tumor bed
- Microscopically clear margins
- Tumor resection in new margins

For „Surgery after neoadjuvant chemotherapy“  
see chapter „Neoadjuvant chemotherapy“

Oxford		
LoE	GR	AGO
5	D	++
2b	C	++
2	B	++
2	C	+

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## Adjuvant Therapy after Primary Surgery

	Oxford		
	LoE	GR	AGO
▪ <b>Start adjuvant systemic therapy and radiotherapy (RT) as soon as possible (asap) after surgery</b>	<b>1b</b>	<b>A</b>	<b>++</b>
▪ <b>Start of adjuvant chemotherapy +/- HER2 therapy asap after surgery, prior to RT</b>	<b>1b</b>	<b>A</b>	<b>++</b>
▪ <b>Without cytotoxic therapy +/- anti-HER2 therapy:</b>			
▪ <b>Start RT 6–8 weeks after surgery</b>	<b>2b</b>	<b>B</b>	<b>++</b>
▪ <b>Start endocrine therapy after surgery asap</b>	<b>5</b>	<b>D</b>	<b>++</b>
▪ <b>Endocrine therapy concurrent with radiotherapy</b>	<b>3b</b>	<b>C</b>	<b>+</b>

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