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Guidelines Breast
Version 2021.1D

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FORSCHEN
LEHREN
HEILEN

Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Operative Therapie des Mammakarzinoms unter onkologischen Aspekten



Operative Therapie des Mammakarzinoms unter onkologischen Aspekten

- **Versionen 2002–2020:**
Bauerfeind / Blohmer / Böhme / Brunnert / Costa / Fersis / Gerber / Hanf / Janni / Junkermann / Kaufmann / Kühn / Kümmel / Möbus/ Nitz / Rezai / Simon / Solomayer / Thomssen / Thill / Thomssen / Untch / Wöckel
- **Version 2021:**
Ditsch / Fallenberg / Friedrich

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. Download Jan 19, 2020.

Cochrane library:

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

Pubmed 2008 - 2020, ASCO 2003 – 2020, SABCS 2003 – 2020, Cochrane data base (n.d.)

Operative Therapie des Mammakarzinoms unter onkologischen Aspekten

AGO: ++

Die operative Therapie ist einer von mehreren Teilschritten bei der Behandlung des Mammakarzinoms. Für jeden Brustoperateur ist eine umfangreiche diagnostische und onkologische Expertise erforderlich.

AGO: +

Vermeidung von erheblichen Therapieverzögerungen

Delay of surgical therapy:

1. Hanna TP, King WD, Thibodeau S et al: Mortality due to cancer treatment delay: systematic review and meta-analysis. BMJ371:m4087
2. Cone EB, Marchese M, Paciotti M, et al: Assessment of Time-to-Treatment Initiation and Survival in a Cohort of Patients With Common Cancers. JAMA Netw Open. 2020 Dec 1;3(12):e2030072. doi: 10.1001/jamanetworkopen.2020.30072. PMID: 33315115; PMCID: PMC7737088.

Surgeon:

1. Dixon JM, Grewar J, Twelves D, et al: Factors affecting the number of sentinel lymph nodes removed in patients having surgery for breast cancer. Breast Cancer Res Treat 184:335-343, 2020

Prätherapeutische Mamma- und Axilladiagnostik

	Oxford		
	LoE	GR	AGO
■ Klinische Untersuchung	5	D	++
■ Mammographie	2b	B	++
■ Tomosynthese***	2b	B	+
■ Kontrastmittel-mammographie	2a	B	+
■ Sonographie (Mamma und Axilla)	2b	B	++
■ MRT*	1b	B	+
■ Minimalinvasive Biopsie Mamma** (CNB, VAB)	1b	A	++
■ Axilla CNB, wenn auffälliger LK-Befund	2b	B	++
■ Mamma-CT	5	D	-

* Möglichkeit der MRT-gestützten Biopsie (in domo oder im Rahmen einer Kooperation). MRT erwägen bei hohem familiärem Risiko, eingeschränkter Beurteilbarkeit in MG & US (Beurteilbarkeit C/D), invasiv lobulärem Karzinom. Keine Reduktion der Nachresektionsrate.

** Histologische Sicherung von Zusatzbefunden im Fall therapeutischer Relevanz.

*** Ersatz der DM durch synthetische Mammographie (SM)

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.

US-Axilla +FNA/CNB

1. 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
2. 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]
3. 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.
4. Evans A, Trimboli RM, Athanasiou A et al. Breast ultrasound: recommendations for information to women and referring physicians by the European Society of Breast Imaging. *European of Breast Imaging (EUSOBI)* , with language review by Europa Donna–The

European Breast Cancer Coalition. Insights Imaging. 2018 Aug;9(4):449-461. doi: 10.1007/s13244-018-0636-z. Epub 2018 Aug 9.

Biopsie

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.

MRT

1. Mann RM, Loo CE, Wobbes 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. Debald 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 Surg2015;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, Lobbes MB, et al. 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. Lobbes 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
16. Achim Wöckel, Jasmin Festl, Tanja Stüber, et al: Interdisciplinary Screening, Diagnosis, Therapy and Follow-up of Breast Cancer. Guideline of the DGGG and the DKG (S3-Level, AWMF Registry Number 032/045OL, December 2017) – Part 1 with Recommendations for the Screening, Diagnosis and Therapy of Breast Cancer. *Geburtshilfe Frauenheilkd*. 2018 Oct; 78(10): 927–948.

Reviews CESM:

1. Dromain, C., N. Vietti-Violi, and J.Y. Meuwly, Angiomammography: A review of current evidences. *Diagn Interv Imaging*, 2019.
2. Patel, B.K., M.B.I. Lobbes, and J. Lewin, Contrast Enhanced Spectral Mammography: A Review. *Semin Ultrasound CT MR*, 2018. 39(1): p. 70-79.
3. Tagliafico, A.S., et al., Diagnostic performance of contrast-enhanced spectral mammography: Systematic review and meta-analysis. *Breast*, 2016. 28: p. 13-9.
4. Zhu, X., et al., Diagnostic Value of Contrast-Enhanced Spectral Mammography for Screening Breast Cancer: Systematic Review and Meta-analysis. *Clin Breast Cancer*, 2018. 18(5): p. e985-e995.
5. Sogani J, Mango VL, Keating D, Sung JS, Jochelson MS. Contrast-enhanced mammography: past, present, and future. *Clin Imaging*. 2021;69:269-79.

CESM Originalarbeiten:

1. Luczynska, E., et al., Comparison of the Mammography, Contrast-Enhanced Spectral Mammography and Ultrasonography in a Group of 116 patients. *Anticancer Res*, 2016. 36(8): p. 4359-66.
2. Fallenberg, E.M., et al., Contrast-enhanced spectral mammography: Does mammography provide additional clinical benefits or can some radiation exposure be avoided? *Breast Cancer Res Treat*, 2014. 146(2): p. 371-81.
3. Tennant, S.L., et al., Contrast-enhanced spectral mammography improves diagnostic accuracy in the symptomatic setting. *Clin Radiol*, 2016. 71(11): p. 1148-55.
4. Fallenberg, E.M., et al., Contrast-enhanced spectral mammography vs. mammography and MRI - clinical performance in a multi-reader evaluation. *Eur Radiol*, 2017. 27(7): p. 2752-2764.
5. Jochelson, M.S., et al., Comparison of screening CEDM and MRI for women at increased risk for breast cancer: A pilot study. *Eur J Radiol*, 2017. 97: p. 37-43.
6. Kim, E.Y., et al., Diagnostic Value of Contrast-Enhanced Digital Mammography versus Contrast-Enhanced Magnetic Resonance Imaging for the Preoperative Evaluation of Breast Cancer. *Journal of breast cancer*, 2018. 21(4): p. 453-462.
7. Patel, B.K., et al., Value Added of Preoperative Contrast-Enhanced Digital Mammography in Patients With Invasive Lobular Carcinoma of the Breast. *Clin Breast Cancer*, 2018. 18(6): p. e1339-e1345.
8. Gluskin J, Rossi Saccarelli C, Avendano D, Marino MA, Bitencourt AGV, Pilewskie M, et al. Contrast-Enhanced Mammography for Screening Women after Breast Conserving Surgery. *Cancers (Basel)*. 2020;12(12).
9. Sogani J, Mango VL, Keating D, Sung JS, Jochelson MS. Contrast-enhanced mammography: past, present, and future. *Clin Imaging*. 2021;69:269-79.
10. González-Huebra I, Malmierca P, Elizalde A, Etxano J, Vejborg I, Uhlenbrock D, et al. The accuracy of titanium contrast-enhanced mammography: a retrospective multicentric study. *Acta Radiol*. 2020;61(10):1335-42.
11. Åhsberg K, Gardfjell A, Nimeus E, Rasmussen R, Behmer C, Zackrisson S, et al. Added value of contrast-enhanced mammography (CEM) in staging of malignant breast lesions-a feasibility study. *World journal of surgical oncology*. 2020;18(1):100.
12. Sumkin JH, Berg WA, Carter GJ, Bandos AI, Chough DM, Ganott MA, et al. Diagnostic Performance of MRI, Molecular Breast Imaging, and Contrast-enhanced Mammography in Women with Newly Diagnosed Breast Cancer. *Radiology*. 2019;293(3):531-40.
13. Sung JS, Lebron L, Keating D, D'Alessio D, Comstock CE, Lee CH, et al. Performance of Dual-Energy Contrast-enhanced Digital

Mammography for Screening Women at Increased Risk of Breast Cancer. Radiology. 2019;293(1):81-8.

14. Schünemann HJ, Lerda D, Quinn C, Follmann M, Alonso-Coello P, Rossi PG, et al. Breast Cancer Screening and Diagnosis: A Synopsis of the European Breast Guidelines. Annals of Internal Medicine. 2020;172(1):46-56.

Prätherapeutisches Staging

	Oxford		
	LoE	GR	AGO
▪ Anamnese und klinische Untersuchung	5	D	++
Nur bei hohem Risiko für Fernmetastasen und / oder Symptomen und / oder Indikation zur (neo-)adjuvanten Chemo-/Antikörpertherapie:			
▪ CT Thorax/Abdomen	2a	B	+
▪ Skelettszintigraphie	2b	B	+
▪ RÖ-Thorax	5	C	+/-
▪ Leberzonographie	5	D	+/-
▪ Weiterführende Diagnostik je nach Befund (z.B. Leber-MRT/CEUS*/Biopsie etc.)	2a	B	+
▪ FDG-PET oder FDG-PET-CT**	2b	B	+/-
▪ Ganzkörper MRT	4	C	+/-

* Contrast enhanced ultrasound **vorzugsweise bei hohem Stadium (III), wenn verfügbar

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. ¹⁸F-FDG 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. 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.
17. Ulaner GA, Castillo R, Goldman DA, et al. ¹⁸F-FDG-PET/CT for systemic staging of newly diagnosed triple-negative breast cancer. *Eur J Nucl Med Mol Imaging* 2016; 43:1937–1944
18. Ulaner GA, Castillo R, Wills J, Gönen M, Goldman DA. ¹⁸F-FDG-PET/CT for systemic staging of patients with newly diagnosed ER-positive and HER2-positive breast cancer. *Eur J Nucl Med Mol Imaging* 2017
19. Groheux D, Giacchetti S, Espié M, et al. The yield of ¹⁸F-FDG PET/CT in patients with clinical stage IIA, IIB, or IIIA breast cancer: a prospective study. *J Nucl Med* 2011; 52:1526–1534
20. Groheux D, Hindié E, Delord M, et al. Prognostic impact of ¹⁸F-FDG-PET-CT findings in clinical stage III and IIB breast cancer. *J Natl Cancer Inst* 2012; 104:1879–1887
21. Ulaner GA. PET/CT for Patients With Breast Cancer: Where Is the Clinical Impact? *AJR American journal of roentgenology*. 2019;213(2):254-65.
22. Reddy Akepati NK, Abubakar ZA, Bikkina P.. Role of ¹⁸F-Fluorodeoxyglucose Positron-Emission Tomography/Computed Tomography Scan in Primary Staging of Breast Cancer Compared to Conventional Staging.. *Indian J Nucl Med*.; 2018.
23. Krammer J, Schnitzer A, Kaiser CG, Buesing KA, Sperk E, Brade J, Wasgindt S, Suetterlin M, Schoenberg SO, Sutton EJ, Wasser K.. (18) F-FDG PET/CT for initial staging in breast cancer patients - Is there a relevant impact on treatment planning compared to

conventional staging modalities?. Eur Radiol. ; 2015.

24. Ng SP, David S, Alamgeer M, Ganju V.. Impact of Pretreatment Combined (18)F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography Staging on Radiation Therapy Treatment Decisions in Locally Advanced Breast Cancer.. Int J Radiat Oncol Biol Phys.; 2015.
25. Goorts, B., Vöö, S., van Nijnatten, T.J.A. et al. Hybrid ^{18}F –FDG PET/MRI might improve locoregional staging of breast cancer patients prior to neoadjuvant chemotherapy. Eur J Nucl Med Mol Imaging 44, 1796–1805 (2017). <https://doi.org/10.1007/s00259-017-3745-x>
26. <https://healthcare-quality.jrc.ec.europa.eu/european-breast-cancer-guidelines/staging-breast-cancer>

Stellenwert der operativen Optionen

	Oxford	
	LoE	GR
■ Die Überlebensraten nach BET (Tumorektomie + RT) und MRM sind äquivalent	1a	A
■ Die Lokalrezidivraten nach „skin sparing mastectomy“ (SSM) und MRM sind äquivalent	2b	B
■ Die Erhaltung des Mamillen-Areola-Komplexes (MAK) ist bei R0-Resektion onkologisch sicher	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.

3. Slavin SA, Schnitt SJ, Duda RB et al. Skin-sparing mastectomy and immediate reconstruction: oncologic risks and aesthetic results in patients with early-stage breast cancer. *Plast Reconstr Surg* 1998; 102:49-62.
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.
6. 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
7. 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.
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 literatur. *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.

Brusterhaltende Operation (BEO) Nicht-palpable Läsionen

	Oxford		
	LoE	GR	AGO
▪ Bildgebend gestützte Drahtmarkierung	2b	B	++
▪ Intraoperative sonographische Lokalisation ohne Draht-Markierung*	2b	B	+
▪ Andere Markierungsarten (Radionuklidmarkierung, Radar-Reflexion, Magnetic Seeds**, RFID)	2a	B	+/-

*Die Läsion muss von demselben Untersucher prä- und intraoperativ in der Gesamtausdehnung sicher dargestellt werden können.
 Voraussetzung: Adäquate Geräteausstattung und Ausbildung des Operateurs
 **nicht geeignet bei MRT-Verlaufsbeurteilung unter NACT

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.

Intraoperative ultrasound-guided:

1. Colakovic N, Zdradovic D, Zladko S, et al. Intraoperative ultrasound in breast cancer surgery - from localization of non-palpable tumors to objectively measurable excision. World Journal of Surgical Oncology 2018; 16: 184

Statement: Radioguided ..

1. van der Ploeg IM, Hobbelenk 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.
2. Ahmed M, van Hemelrijck M, Douek M. Systematic review of radioguided versus wire-guided localization in the treatment of non-

- palpable breast cancers. Breast Cancer Res Treat. 2013 Jul;140(2):241-52
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.
 4. Cheang E, Ha R, Thornton CM, Mango VL. Innovations in image-guided preoperative breast lesion localization. Br J Radiol. 2018 May;91(1085):20170740.
 5. Kapoor MM, Patel MM, Scoggins ME. The Wire and Beyond: Recent Advances in Breast Imaging Preoperative Needle Localization. Radiographics. 2019 Nov-Dec;39(7):1886-1906
 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.
 7. Simons J, v Nijnatten JA, Koppert LB, et al: Radioactive Iodine Seed placement in the Axilla with Sentinel lymph node biopsy after neoadjuvant chemotherapy in breast cancer: Results of the prospective multicenter RISAS trial. SABCS 2020, GS1-10
 8. Kasem I and Mokbel K: Savi Scout Radar-Localization of non-palpable breast lesions: systematic review and pooled analysis of 842 cases.

Statement: Magseed

1. Gera R, Tayeh S, et al: Evolving Role of Magseed in wireless localization of breast lesions: systematic review and pooled analysis of 1.559 procedures. Anticancer Res 40: 1809-1815, 2020

Statement: Intraoperative ultrasound.

1. 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.
2. Pan H, Wu N, Ding H, et al. Intraoperative Ultrasound Guidance Is Associated with Clear Lumpectomy Margins for Breast Cancer: A Systematic Review and Meta-Analysis. PLOS One 2013;8(9), e74028
3. Eggemann H, Ignatov T, Beni A, et al. Ultrasonography-guided breast-conserving surgery is superior to palpation-guided surgery for palpable breast cancer. Clin Breast Cancer. 2014 Feb;14(1):40-5.
4. Karanlik H, Ozgur I, Sahin D et al: Intraoperative ultrasound reduces the need for re-excision in breast-conserving surgery. World J

Surg Oncol. 2015 Nov 24;13:321.

5. Karadeniz Cakmak G, Emre AU, Tascilar O, et al: Surgeon performed continuous intraoperative ultrasound guidance decreases re-excisions and mastectomy rates in breast cancer. Breast. 2017 Jun;33:23-28
6. Hu X, Si Li, Yi Jiang et al: Intraoperative ultrasound-guided lumpectomy versus wire-guided excision for nonpalpable breast cancer. J Int Med Res 48 (1):1-12, 2020
7. Hoffmann J, Marx M, Hengstmann A, et al:Ultrasound-Assisted Tumor Surgery in Breast Cancer - A Prospective, Randomized, Single-Center Study (MAC 001); Ultraschall Med. 2019 Jun;40(3):326-332. doi: 10.1055/a-0637-1725. Epub 2018 Jul 5.

Brusterhaltende Operation (BEO)

Vorgehensweise, Technische Aspekte

	Oxford		
	LoE	GR	AGO
▪ Tumorfreie Resektionsränder (auch bei ungünstiger Biologie ist "no ink on tumor" ausreichend)	2a	A	++
▪ Sekundäre Nachresektion bei invasivem Tumorausläufer bis in den Resektionsrand (Paraffinschnitt)	3b	C	+
▪ Stereotaktische Befundentfernung als alleinige Therapie	4	D	--
▪ Intraop. Sonographie zur Reduktion der Nachresektionsrate	2a	B	+
▪ Intraop. Schnitttrandbeurteilung (mit Margin Probe®)	1b	A	+/-
▪ Präparateradiographie oder -sonographie	2b	B	++

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, Hobbelenk 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.
2. Ahmed M, van Hemelrijck M, Douek M. Systematic review of radioguided versus wire-guided localization in the treatment of non-palpable breast cancers. Breast Cancer Res Treat. 2013 Jul;140(2):241-52
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.
4. Cheang E, Ha R, Thornton CM, Mango VL. Innovations in image-guided preoperative breast lesion localization. Br J Radiol. 2018 May;91(1085):20170740.
 5. Kapoor MM, Patel MM, Scoggins ME. The Wire and Beyond: Recent Advances in Breast Imaging Preoperative Needle Localization. Radiographics. 2019 Nov-Dec;39(7):1886-1906
 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 ≥ 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 ...

1. Cendán JC et al., Accuracy of Intraoperative Frozen-Section Analysis of Breast Cancer Lumpectomy-Bed Margins. J Am Coll Surg 2005;201:194–198.
2. Cabioglu N, Hunt, Sahin et al: Role for Intraoperative Margin Assessment in Patients Undergoing Breast-Conserving Ann Surg Oncol. 2007 Apr;14(4):1458-71.
3. Ciccarelli G, Di Virgilio MR, Menna S. Radiography of the surgical specimen in early stage breast lesions: diagnostic reliability in the analysis of the resection margins. Radiol Med (Torino). 2007 Apr;112(3):366-76.

4. Houssami N, Macaskill P, Marinovich ML, et al. Metaanalysis of the impact of surgical margins on local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy. *Eur J Cancer*. 2010 Dec;46(18):3219-32.
5. Harness JK, Giuliano AE, Pockaj BA, et al: a status report from the Annual Meeting of the American Society of Breast Surgeons. *Ann Surg Oncol*. 2014 Oct;21(10):3192-7.
6. Houssami N, Macaskill P, Marinovich ML, et al. The association of surgical margins and local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy: a meta-analysis. *Ann Surg Oncol*. 2014 Mar;21(3):717-30
7. Buchholz TA, Somerfield MR, Griggs JJ, et al. Margins for breast-conserving surgery with whole-breast irradiation in stage I and II invasive breast cancer: American Society of Clinical Oncology endorsement of the Society of Surgical Oncology/American Society for Radiation Oncology consensus guideline. *J Clin Oncol*. 2014 May 10;32(14):1502-6.

Statement: tumor free margins in intrinsic subtypes

1. Sioshansi S, Ehdaivand S, Cramer C, et al. Triple negative breast cancer is associated with an increased risk of residual invasive carcinoma after lumpectomy. *Cancer*. 2012 Aug 15;118(16):3893-8
2. Gangi A, Chung A, Mirocha J et al. Breast-conserving therapy for triple-negative breast cancer. *JAMA Surg*. 2014 Mar;149(3):252-8
3. Vaz-Luis I, Ottesen RA, Hughes ME, et al. Outcomes by tumor subtype and treatment pattern in women with small, node-negative breast cancer: a multi-institutional study. *J Clin Oncol*. 2014 Jul 10;32(20):2142-50.
4. Pilewski M, Ho A, Orell E, et al. Effect of margin width on local recurrence in triple-negative breast cancer patients treated with breast conserving therapy. *Ann Surg Oncol*. 2014 Apr;21(4):1209-14.

Statement: ... re-excision ...

1. Kitchen PR, Cawson JN, Moore SE: Margins and outcome of screen-detected breast cancer with extensive in situ component. *ANZ J Surg*. 2006 Jul;76(7):591-5
2. Schouten van der Velden AP, Van de Vrande SL, Boetes C: Residual disease after re-excision for tumor-positive surgical margins in both ductal carcinoma in situ and invasive carcinoma of the breast: The effect of time. *J Surg Oncol*. 2007 Dec 1;96(7):569-74
3. McIntosh A, Freedman G, Eisenberg D: Recurrence rates and analysis of close or positive margins in patients treated without re-

excision before radiation for breast cancer. Am J Clin Oncol. 2007 Apr;30(2):146-51.

4. Kurniawan ED, Wong MH, Windle I: Predictors of surgical margin status in breast-conserving surgery within a breast screening program. Ann Surg Oncol. 2008 Sep;15(9):2542-9.

Statement: stereotactic excision alone ...

1. Jackman RJ, Birdwell RL, Ikeda DM: Atypical ductal hyperplasia: can some lesions be defined as probably benign after stereotactic 11-gauge vacuum-assisted biopsy, eliminating the recommendation for surgical excision? Radiology. 2002 Aug;224(2):548-54
2. Jacobs TW, Connolly JL, Schnitt SJ: Nonmalignant lesions in breast core needle biopsies: to excise or not to excise? Am J Surg Pathol. 2002 Sep;26(9):1095-110
3. Plantade R, Hammou JC, Fighiera M: Underestimation of breast carcinoma with 11-gauge stereotactically guided directional vacuum-assisted biopsy. J Radiol. 2004 Apr;85(4 Pt 1):391-401
4. Jeevan R, Cromwell DA, Trivella M, et al. Reoperation rates after breast conserving surgery for breast cancer among women in England: retrospective study of hospital episode statistics. BMJ. 2012 Jul 12;345:e4505. doi: 10.1136/bmj.e4505.

Statement: Intraoperative ultrasound..

1. 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.
2. Pan H, Wu N, Ding H, et al. Intraoperative Ultrasound Guidance Is Associated with Clear Lumpectomy Margins for Breast Cancer: A Systematic Review and Meta-Analysis. PLOS One 2013;8(9), e74028
3. Eggemann H, Ignatov T, Beni A, et al. Ultrasonography-guided breast-conserving surgery is superior to palpation-guided surgery for palpable breast cancer. Clin Breast Cancer. 2014 Feb;14(1):40-5.
4. Karanlik H, Ozgur I, Sahin D et al: Intraoperative ultrasound reduces the need for re-excision in breast-conserving surgery. World J Surg Oncol. 2015 Nov 24;13:321.
5. Karadeniz Cakmak G, Emre AU, Tascilar O, et al: Surgeon performed continuous intraoperative ultrasound guidance decreases re-excisions and mastectomy rates in breast cancer. Breast. 2017 Jun;33:23-28

6. Colakovic N, Zdradovic D, Zladko S, et al. Intraoperative ultrasound in breast cancer surgery - from localization of non-palpable tumors to objectively measurable excision. World Journal of Surgical Oncology 2018; 16: 184
7. Hu X, Si Li, Yi Jiang et al: Intraoperative ultrasound-guided lumpectomy versus wire-guided excision for nonpalpable breast cancer. J Int Med Res 48 (1):1-12, 2020
8. Hoffmann J, Marx M, Hengstmann A, et al:Ultrasound-Assisted Tumor Surgery in Breast Cancer - A Prospective, Randomized, Single-Center Study (MAC 001); Ultraschall Med. 2019 Jun;40(3):326-332. doi: 10.1055/a-0637-1725. Epub 2018 Jul 5.

Statement: Margine probe

1. Freya Schnabel, Susan K. Boolbol, Mark Gittleman, et al: A Randomized Prospective Study of Lumpectomy Margin Assessment with Use of MarginProbe in Patients with Nonpalpable Breast Malignancies Ann Surg Oncol (2014) 21:1589–1595
2. Gola S, Doyle-Lindrud S.: The MarginProbe® System: An Innovative Approach to Reduce the Incidence of Positive Margins Found After Lumpectomy. Clin J Oncol Nurs. 2016 Dec 1;20(6):598-599

Brusterhaltende Operation (BEO) ohne neoadjuvante Therapie

	Oxford		
	LoE	GR	AGO
▪ Multizentrität (MF/MZ) (Voraussetzung: R0-Resektion aller Herde)	2b	B	+
▪ Histologisch befallene Resektionsränder trotz wiederholter Nachresektion	2b	B	--
▪ Inflammatorisches MaCa	2b	B	--

OP nach neoadjuvanter Chemotherapie siehe Kap. „Neoadjuvante Chemotherapie“

Statement: Multicentricity

1. Wolters R, Wöckel A, Janni W. et al; BRENDA Study Group. Comparing the outcome between multicentric and multifocal breast cancer: what is the impact on survival, and is there a role for guideline-adherent adjuvant therapy? A retrospective multicenter cohort study of 8,935 patients. Breast Cancer Res Treat. 2013 Dec;142(3):579-90.
2. Tan MP, Sitoh NY, Sim AS. Breast conservation treatment for multifocal and multicentric breast cancers in women with small-volume breast tissue. ANZ J Surg. 2014 Dec 5. doi: 10.1111/ans.12942.
3. Winters ZE, Horsnell J, Elvers KT et al. Systematic review of the impact of breast-conserving surgery on cancer outcomes of multiple ipsilateral breast cancers. BJS Open. 2018 May 22;2(4):162-174.
4. Masannat YA, Agrawal A, Maraqa L et al. Multifocal and multicentric breast cancer, is it time to think again? Ann R Coll Surg Engl. 2020 Jan;102(1):62-66.
5. Neri A, Marrelli D, Megha T et al. Clinical significance of multifocal and multicentric breast cancers and choice of surgical treatment: a retrospective study on a series of 1158 cases. BMC Surg. 2015 Jan 14;15:1.

Statement: positive microscopic margins

1. Houssami N, Macaskill P, Marinovich ML, et al. The association of surgical margins and local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy: a meta-analysis. Ann Surg Oncol. 2014 Mar;21(3):717-30.

2. Marinovich ML, Azizi L, Macaskill P, et al: The Association of Surgical Margins and Local Recurrence in Women with Ductal Carcinoma In Situ Treated with Breast-Conserving Therapy: A Meta-Analysis. *Ann Surg Oncol*. 2016 Nov;23(12):3811-3821

Statement: Inflammatory Carcinoma

1. Coleman CN, Wallner PE, Abrams JS. Inflammatory breast issue. *J Natl Cancer Inst*. 2003 Aug 20;95(16):1182-3.
2. Kell MR, Morrow M. Surgical aspects of inflammatory breast cancer. *Breast Dis*. 2005-2006;22:67-7
3. Woodward WA, Buchholz TA. The role of locoregional therapy in inflammatory breast cancer. *Semin Oncol*. 2008 Feb;35(1):78-86
4. Bristol IJ, Woodward WA, Strom EA. Locoregional treatment outcomes after multimodality management of inflammatory breast cancer. *Int J Radiat Oncol Biol Phys*. 2008 Oct 1;72(2):474-84.
5. Singletary SE. Surgical management of inflammatory breast cancer. *Semin Oncol*. 2008 Feb;35(1):72-7
6. van Uden DJ, van Laarhoven HW, Westenberg AH et al. Inflammatory breast cancer: An overview. *Crit Rev Oncol Hematol*. 2014 Oct 16. pii: S1040-8428(14)00154-1. doi: 10.1016/j.critrevonc.2014.09.003. [Epub ahead of print]
7. Matro JM, Li T, Cristofanilli M, Hughes ME, et al. Inflammatory breast cancer management in the national comprehensive cancer network: the disease, recurrence pattern, and outcome. *Clin Breast Cancer*. 2015 Feb;15(1):1-7.
8. Mamouch F, Berrada N, Aoullay Z et al. Inflammatory Breast Cancer: A Literature Review. *World J Surg*;9(5-6):129-135

Statement: general

1. Marret H, Perrotin F, Bognoux P. Histologic multifocality is predictive of skin recurrences after conserving treatment of stage I and II breast cancers. *Breast Cancer Res Treat*. 2001 Jul;68(1):1-8.
2. Cho LC, Senzer N, Peters GN. Conservative surgery and radiation therapy for macroscopically multiple ipsilateral invasive breast cancers. *Am J Surg*. 2002 Jun;183(6):650-4.
3. Okumura S, Mitsumori M, Yamauchi C. Feasibility of breast-conserving therapy for macroscopically multiple ipsilateral breast cancer. *Int J Radiat Oncol Biol Phys*. 2004 May 1;59(1):146-51.
4. Oh JL, Dryden MJ, Woodward WA. Locoregional control of clinically diagnosed multifocal or multicentric breast cancer after neoadjuvant chemotherapy and locoregional therapy. *J Clin Oncol*. 2006 Nov 1;24(31):4971-5
5. Meijnen P, Bartelink H. Multifocal ductal carcinoma in situ of the breast: a contraindication for breast-conserving treatment? *J Clin Oncol*. 2007 Dec 10;25(35):5548-9.
6. Chen H, Wu K, Wang M, et al: Standard mastectomy should not be the only recommended breast surgical treatment for non-metastatic inflammatory breast cancer: A large population-based study in the Surveillance, Epidemiology, and End Results database

18. Breast. 2017 Oct;35:48-54.

Primäre Axilläre Lymphknotendisektion (ALND) I

	Oxford		
	LoE	GR	AGO
▪ Endpunkt: Überleben (bei adäquater, multimodaler Therapie)	3	D	-
▪ Endpunkt: Staging	3	A	-
▪ Endpunkt: Lokoregionale Tumorkontrolle	2a	A	+/-
▪ pN+ (präoperativ histologisch gesichert) ohne neoadjuvante Systemtherapie	2a	B	+
▪ cN0 pN0 (sn)(i+)	1b	A	--
▪ cN0 pN1 (sn) (mi)	2b	B	--
▪ cN0 pN1 (sn) (cT1/2, <3SN+, BEO + RT + adäquate Systemtherapie)	1b	A	-
▪ cN0 pN1 (sn) und Mastektomie (keine Radiotherapie der Thoraxwand)	1b	B	+*
▪ cN0 pN1 (sn) und Mastektomie (T1/2, <3SN+) Strahlentherapie der Thoraxwand	5	D	+/-*
▪ ALND indiziert, aber nicht möglich			
▪ Radiatio analog AMAROS-Studie (evaluiert für cN0 pN1sn)	1b	B	+
* Studienteilnahme empfohlen			

Statements: Axillary lymph node dissection I

Statement: Axillary lymph node dissection

1. Kuehn T, Bembenek A, Decker T. A concept for the clinical implementation of sentinel lymph node biopsy in patients with breast carcinoma with special regard to quality assurance. Cancer. 2005 Feb 1;103(3):451-61
2. Rudenstam CM, Zahrieh D, Forbes JF: Randomized trial comparing axillary clearance versus no axillary clearance in older patients with breast cancer: first results of International Breast Cancer Study Group Trial 10-93. J Clin Oncol 24(3): 337-344, 2006.
3. Van la Parra: The value of sentinel lymph node biopsy in ductal carcinoma in situ (DCIS) and DCIS with microinvasion of the breast. Eur J Surg Oncol. 2008 Jun;34(6):631-5
4. D'Angelo-Donovan DD, Dickson-Witmer D, Petrelli NJ. Sentinel lymph node biopsy in breast cancer: A history and current clinical recommendations. Surg Oncol. 2012 Jan 9.
5. 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.
6. Gerber B, Heintze K, Stubert J, et al. Axillary lymph node dissection in early-stage invasive breast cancer: is it still standard today?

Breast Cancer Res Treat. 2011 Aug;128(3):613-24. Epub 2011 Apr 27. Review.

7. Lyman GH, Temin S, Edge SB, et al; American Society of Clinical Oncology Clinical Practice. Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. Clin Oncol. 2014 May 1;32(13):1365-83
8. Lyman GH, Somerfield MR, Bosserman CD et al. Sentinel Lymph Node Biopsy for Patients with Early Stage Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. DOI :10.1200/JCO.2016.71.
9. Bromham N, Schmidt-Hansen M, Astin M, et al. Axillary treatment for operable primary breast cancer. Cochrane Database Syst Rev. 2017 Jan 4;1:CD004561.

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 –

1. Rutgers EJ. Sentinel node biopsy: interpretation and management of patients with immunohistochemistry-positive sentinel nodes and those with micrometastases. J Clin Oncol. 2008 Feb 10;26(5):698-702.
2. Li Y, Zhang H, Zhang W, et al: A competing risk analysis model to determine the prognostic value of isolated tumor cells in axillary lymph nodes for T1N0M0 breast cancer patients based on the surveillance, epidemiology, and end results database. Frontiers in Oncology 10:572316, 2020

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

1. Mamtani A, Patil S, Stempel M, et al. Axillary Micrometastases and Isolated Tumor Cells Are Not an Indication for Post-mastectomy Radiotherapy in Stage 1 and 2 Breast Cancer. *Ann Surg Oncol*. 2017 Aug;24(8):2182-2188.
2. Cserni G, Gregori D, Merletti F: Meta-analysis of non-sentinel node metastases associated with micrometastatic sentinel nodes in breast cancer. *Br J Surg* 91(10): 1245-1252, 2004.
3. Rutgers EJ. Sentinel node biopsy: interpretation and management of patients with immunohistochemistry-positive sentinel nodes and those with micrometastases. *J Clin Oncol*. 2008 Feb 10;26(5):698-702
4. Galimberti V, Cole BF, Zurrada S, et al. International Breast Cancer Study Group Trial 23-01 investigators. Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial. *Lancet Oncol*. 2013 Apr;14(4):297-305.

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.
2. Hennings A, Köpke M, Feisst M et al. Which patients with sentinel-positive breast cancer after breast conservation still receive completion axillary node dissection in routine clinical practice. *Breast Cancer Res Treat* 2018 <https://doi.org/10.1007/s10549-018-5009-2>
3. Morrow M, Jagsi R, Mclead MC et al. Surgeons Attitudes toward the Omission of Axillary Dissection in Early Breast Cancer. *JAMA Oncol* 2018;4(11):1511-16
4. Poodt IGM, Spronk PER, Vugts G et al. Trends on Axillary Surgery in Nondistant Metastatic Breast Cancer Treated Between 2011 and 2015: A Dutch Population based Study in The ACOSOC Z0011 and AMAROS Era. *Ann Surg Oncol* 2018;26(6):1084-1090.
5. Jagsi R, Chadha M, Moni J, et al. Radiation field design in the ACOSOG Z0011 (Alliance) Trial. *J Clin Oncol*. 2014 Nov 10;32(32):3600-6.

6. Jung J, Han W, Lee ES et al. Retrospectively validating the results of the ACOSOG Z0011 trial in a large Asian Z0011-eligible cohort. Breast Cancer Res Treat. 2019 May;175(1):203-215
7. Barrio AV, Downs-Canner S, Edelweiss M et al. Microscopic Extracapsular Extension in Sentinel Lymph Nodes Does Not Mandate Axillary Dissection in Z0011-Eligible Patients. Ann Surg Oncol. 2019 Dec 9.

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 +

1. Donker M, van Tienhoven G, Straver ME, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. Lancet Oncol. 2014 Nov;15(12):1303-10.
2. Euhus DM. Management of the clinically positive axilla. Breast J. 2020 Jan;26(1):35-38.

Axilläre operative Interventionen bei NACT						Oxford		
						LoE	GR	AGO
SLNE nach NACT						2b	B	++
SLNE vor NACT						2b	B	-
cN-Status (vor NACT)	pN-Status (vor NACT)	cN-Status (nach NACT)	Axilläre operative Intervention (nach NACT)	pN-Status (nach NACT und Operation)	Operative Konsequenz aus Histobefund			
cN0	---	ycN0	SLNE alleine	ypN0 (sn)	---	2b	B	++***
				ypN0 (i+)	ALND	2b	C	+ (+/- bei i+)
				ypN1 _{inc} (sn)	Keine **	5	D	+/-
				ypN1 (sn)	ALND	2b	C	++
					Keine**	5	D	+/-
cN+	pN _{CNS}	ycN0	SLNE alleine* TAD (TLNE + SLNE)* ALND*	ypN0 ypN0 ypN0	---	2b 2b 2b	B B B	+/-*** +*** +***
			SLNE alleine* TAD (TLNE + SLNE)*	ypN+ inkl. ypN0 (i+)	ALND	2b	B	+ (+/- bei i+)
			ALND	ypN+	---	2b	B	++
			keine	n.d.	keine**	5	D	-
cN+	pN _{CNS}	ycN+	ALND	ypN+ inkl. ypN0 (i+)	---	2b	B	++
			Keine	n.d.	keine**	5	D	-

*Studienbeteiligung an Axsana empfohlen; ** s. Empfehlungen Kapitel Strahlentherapie; alleinige Radiatio bei ypN1(sn), ypN+ nicht empfohlen ;
*** Empfehlungsgrad bezieht sich auf Staging bei cN0 und cN+ ypN0

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

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.
2. Tuttle TM, Shamliyan T, Virnig BA, et al. The impact of sentinel lymph node biopsy and magnetic resonance imaging on important outcomes among patients with ductal carcinoma in situ. *J Natl Cancer Inst Monogr*. 2010;2010(41):117-20. Review.
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TAD (+SLNE) after PST, if pN1 (CNB prior to PST and ycN0

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ypN0 (i+)

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Verbesserung der Falsch-Negativ-Rate des operativen Stagings bei pN_{CNB}^{+} vor NACT und $ycN0$ nach NACT

- Entfernung von > 2 SLNs (SLNE, kein ungezieltes axilläres Sampling!)
- Kombinierte Tracermethode
- IHC zur Detektion von ITC oder Mikrometastasen
- Markierung von positiven LK vor NACT
- Targeted Axillary Dissection (TAD = TLNE + SLNE)
- Alleinige TLNE

* Teilnahme an Studien empfohlen

	Oxford		
	LoE	GR	AGO
	2a	B	+
	2a	B	+/-
	2b	B	+
	2b	B	+*
	2b	B	+*
	2b	B	+/-*

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FORSCHEN
LEHREN
HEILEN

Verminderung der individuellen Versagerrate für die SLNE bei pN1 ypN0

- **Prädiktive Faktoren für eine Konversion von pN1 (vor NACT) nach ypN0_{sn/TAD} (nach NACT)**
 - Junges Alter
 - Intrinsischer Subtyp (ER neg, HER 2 pos)
 - Grade 3
 - N1 (vs N2)
 - pCR (Brust)

Kantor et al. Ann Surg Oncol 2018

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Sentinel-Lymphknoten-Exzision (SLNE) Indikationen I

- **Klinisch / sonographisch neg. Axilla (cN0)**
 - Zusätzliche CNB bei cN1 um eine SLNE zu ermöglichen
- **cT 1–2**
- **cT 3–4c**
- **Multifokales / multizentrisches MaCa**
- **DCIS**
 - Mastektomie
 - BET
 - DCIS beim Mann
- **MaCa des Mannes**
- **Bei der älteren Patientin**

Oxford		
LoE	GR	AGO
1b	A	++
2a	B	+
2b	A	++
3b	B	+
2b	B	+
3b	B	+
3b	B	-
5	D	+/-
2b	B	+
3b	B	+

Statement: SLNE

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

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Statement: Multifocal / multicentric MaCa

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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-Lymphknoten-Exzision (SLNE) Indikationen II

- Während Schwangerschaft oder Stillzeit
(nur ^{99m}Tc-Kolloid, keine Markierung mit Patentblau)
- Nach vorausgegangener Tumorektomie
- Nach vorausgegangener „großer“ Brust-Operation
(z.B. Reduktionsplastik)
- Ipsilaterales intramammäres Rezidiv nach
vorheriger BET und SNLE
- SLNE entlang der A. mammaria interna
- Nach Axilla-Voroperation
- Prophylaktische bilaterale / kontralaterale Mastektomie
- Inflammatorisches MaCa

Oxford		
LoE	GR	AGO
3	C	++
2b	B	+
3b	C	+/-
4	D	-
2b	B	-
3b	B	+/-
3b	B	--
3b	C	-

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
2. Bergkvist L. Resolving the controversies surrounding lymphatic mapping in breast cancer. Future Oncol. 2008 Oct;4(5):681-8.
3. Classe JM, Loussouarn D, Campion L, et al. Validation of axillary sentinel lymph node detection in the staging of early lobular invasive breast carcinoma: a prospective study. Cancer. (2004); 100(5):935-41.
4. Han SN, Amant F, Cardonick EH, et al. International Network on Cancer, Infertility and Pregnancy: Axillary staging for breast cancer during pregnancy: feasibility and safety of sentinel lymph node biopsy. Breast Cancer Res Treat. 2017 Dec 12. doi: 10.1007/s10549-017-4611-z. [Epub ahead of print]

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.
3. Wouters MW, van Geel AN, Menke-Pluijmers M: Should internal mammary chain (IMC) sentinel node biopsy be performed? Outcome in 90 consecutive non-biopsied patients with a positive IMC scintigraphy. Breast. 2008 Apr;17(2):152-8.

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.
3. Boughey JC et al.: Decision analysis to assess the efficacy of routine sentinel lymphadenectomy in patients undergoing prophylactic mastectomy. Cancer 2007 Dec 1;110(11):2542-50

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, Tiro 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.
4. Palit G, Jacquemyn ML, Tjalma W. Sentinel node biopsy for ipsilateral breast cancer recurrence: a review. Eur J Gynecol Oncol

2008;29:565-567

5. Intra M, Viale G, Vila J, et al. Second Axillary Sentinel Lymph Node Biopsy for Breast Tumor Recurrence: Experience of the European Institute of Oncology. *Ann Surg Oncol*. 2014 Dec 17.
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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.
2. Singletary SE. Surgical management of inflammatory breast cancer. *Semin Oncol*. 2008 Feb;35(1):72-7
3. van Uden DJ, van Laarhoven HW, Westenberg AH, et al. Inflammatory breast cancer: An overview. *Crit Rev Oncol Hematol*. 2014 Oct 16. pii: S1040-8428(14)00154-1. doi: 10.1016/j.critrevonc.2014.09.003. [Epub ahead of print]
4. Matro JM, Li T, Cristofanilli M, Hughes ME, et al. Inflammatory breast cancer management in the national comprehensive cancer network: the disease, recurrence pattern, and outcome. *Clin Breast Cancer*. 2015 Feb;15(1):1-7.

Statement: Others

1. Schwartz GF, Giuliano AE, Veronesi U; Consensus Conference Committee. Proceedings of the consensus conference on the role of sentinel lymph node biopsy in carcinoma of the breast, April 19-22, 2001, Philadelphia, Pennsylvania. *Cancer* 2002;94:2542-51
2. Kuehn T, Bembenek A, Decker T. A concept for the clinical implementation of sentinel lymph node biopsy in patients with breast carcinoma with special regard to quality assurance. *Cancer*. 2005 Feb 1;103(3):451-61
3. Golshan M et al. Sentinel lymph node biopsy for occult breast cancer detected during breast reduction surgery. *Am Surg* 2006 May;72(5):397-400
4. Schrenk et al. Symmetrization reduction mammoplasty combined with sentinel node biopsy in patients operated for contralateral breast cancer. *J Surg Oncol* 2006 Jul 1;94(1):9-15.
5. Lyman GH, Temin S, Edge SB, et al. American Society of Clinical Oncology Clinical Practice. Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. *Clin Oncol*. 2014 May 1;32(13):1365-83.

6. 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.

Sentinel-Lymphknoten-Exzision (SLNE) Markierung

- ^{99m}Tc Kolloid
- Präoperative Lymphszintigraphie (diagnostischer
Zugewinn limitiert, aber gesetzlich vorgeschrieben)*
- Patentblau
- Methylenblau
- Indocyaningrün (ICG)
- SPIO[#]

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

- * Qualitätssicherung Nuklearmedizin
[#] 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.
2. Ditsch N, Rubio IT, Gasparri ML, de Boniface J, Kuehn T. Breast and axillary surgery in malignant breast disease: a review focused on literature of 2018 and 2019. *Curr Opin Obstet Gynecol*. 2020;32(1):91–99.
3. Krag DN, Anderson SJ, Julian TB, et al. National Surgical Adjuvant Breast and Bowel Project Technical outcomes of sentinel-lymph-node resection and conventional axillary-lymph-node dissection in patients with clinically node-negative breast cancer: results from the NSABP B-32 randomised phase III trial. *Lancet Oncol*. 2007 Oct;8(10):881-8.
4. Rodier JF, Velten M, Wilt M, et al. Prospective multicentric randomized study comparing periareolar and peritumoral injection of radiotracer and blue dye for the detection of sentinel lymph node in breast sparing procedures: FRANSENODE trial. *J Clin Oncol*. 2007 Aug 20;25(24):3664-
5. Bines S, Kopkash K, Ali A, Fogg L, et al. The use of radioisotope combined with isosulfan Blue dye is not superior to radioisotope alone for the identification of sentinel lymph nodes in patients with breast cancer. *Surgery*. 2008 Oct;144(4):606-9; discussion 609-10.
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9. Ang CH, Tan MY, Teo C, et al. Blue dye is sufficient for sentinel lymph node biopsy in breast cancer. *Br J Surg*. 2014 Mar;101(4):383-9; discussion 389.
10. Ahmed M, Purushotham AD, Horgan K, et al. Meta-analysis of superficial versus deep injection of radioactive tracer and blue dye for lymphatic mapping and detection of sentinel lymph nodes in breast cancer. *Br J Surg*. 2015 Feb;102(3):169-81.

Statement Magnetic Seeds/Tracer:

Thompson W, Argáez C. Ottawa (ON):

Magnetic Localization System for Sentinel Lymph Node Biopsy: A Review of the Diagnostic Accuracy, Cost-Effectiveness, and Guidelines. Canadian Agency for Drugs and Technologies in Health; 2020 Feb 26.

Statement: pre-operative lymphoscintigraphy

1. Sherko Kummel, Johannes Holtschmidt, Bernd Gerber, et al.: Randomized surgical multicenter trial to evaluate the usefulness of lymphoscintigraphy (LSG) prior to sentinel node biopsy (SLNB) in early breast cancer: SenSzi (GBG80) trial. *Journal of Clinical Oncology* 35, no. 15_suppl (May 2017) 555-555.

Statement: methylene blue

1. Varghese P, Mostafa A, Abdel-Rahman AT, et al. Methylene blue dye versus combined dye-radioactive tracer technique for sentinel lymph node localisation in early breast cancer. *Eur J Surg Oncol*. 2007 Mar;33(2):147-52.
2. Soni M, Saha S, Korant A, et al. A prospective trial comparing 1% lymphazurin vs 1% methylene blue in sentinel lymph node mapping of gastrointestinal tumors. *Ann Surg Oncol*. 2009 Aug;16(8):2224-30.
3. Kang SS, Han BK, Ko EY, et al. Methylene blue dye-related changes in the breast after sentinel lymph node localization. *J Ultrasound Med*. 2011;30(12):1711-21.
4. Kaklamanos IG, Birbas K, Syrigos K, et al. Prospective comparison of peritumoral and subareolar injection of blue dye alone, for

identification of sentinel lymph nodes in patients with early stage breast cancer. J Surg Oncol. 2011 Jul 1;104(1):37-40.

5. Fattahi AS, Tavassoli A, Rohbakhshfar O, et al. Can methylene blue dye be used as an alternative to patent blue dye to find the sentinel lymph node in breast cancer surgery? J Res Med Sci. 2014 Oct;19(10):918-22.

Statement: ICG

1. Mok CW, Tan SM, Zheng Q, Shi L. Network meta-analysis of novel and conventional sentinel lymph node biopsy techniques in breast cancer. BJS Open. 2019 Mar 25;3(4):445-452.
2. Sugie T, Ikeda T, Kawaguchi A, Shimizu A, Toi M. Sentinel lymph node biopsy using indocyanine green fluorescence in early-stage breast cancer: a meta-analysis. Int J Clin Oncol. 2017 Feb;22(1):11-17.
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Statement: SPIO

1. Rubio IT, Diaz-Botero S, Esgueva A, et al. The superparamagnetic iron oxide is equivalent to the Tc99 radiotracer method for identifying the sentinel lymph node in breast cancer. Eur J Surg Oncol. 2015 Jan;41(1):46-51
2. Thill M, Kurylcio A, Welter R, et al. The Central-European SentiMag study: sentinel lymph node biopsy with superparamagnetic iron oxide (SPIO) vs. Radioisotope. Breast. 2014 Apr;23(2):175-9.
3. Douek M, Klaase J, Monypenny I, et al. SentiMAG Trialists Group. Sentinel node biopsy using a magnetic tracer versus standard technique: the SentiMAG Multicentre Trial. Ann Surg Oncol. 2014 Apr;21(4):1237-45.
4. Thompson W, Argáez C. Magnetic Localization System for Sentinel Lymph Node Biopsy: A Review of the Diagnostic Accuracy, Cost-Effectiveness, and Guidelines [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2020 Feb 26.

Statement: General

1. Ahmed M, Purushotham AD, Douek M. Novel techniques for sentinel lymph node biopsy in breast cancer: a systematic review. Lancet Oncol. 2014 Jul;15(8):e351-62.

Statement: Comparisons

1. Jung SY, Kim SK, Kim SW, et al. Comparison of sentinel lymph node biopsy guided by the multimodal method of indocyanine green fluorescence, radioisotope, and blue dye versus the radioisotope method in breast cancer: a randomized controlled trial. *Ann Surg Oncol*. 2014 Apr;21(4):1254-9.
2. Sugie T, Sawada T, Tagaya N, et al. Comparison of the indocyanine green fluorescence and blue dye methods in detection of sentinel lymph nodes in early-stage breast cancer. *Ann Surg Oncol*. 2013 Jul;20(7):2213-8. doi: 10.1245/s10434-013-2890-0. Epub 2013 Feb 21.

Operatives Vorgehen im Rahmen der neoadjuvanten Therapie

	Oxford		
	LoE	GR	AGO
▪ Frühzeitige Markierung des Tumors mit exakter topographischer Dokumentation	5	D	++
▪ Resektion des Tumors / repräsentative Exzision des posttherapeutischen, markierten Tumorareals	2b	C	++
▪ Exzision in neuen Tumorgrenzen	2b	C	++
▪ Freie Resektionsränder	2a	B	++

OP nach neoadjuvanter Chemotherapie
 siehe Kap. „Neoadjuvante Chemotherapie“

Statement: clip marking

1. Kuerer HM, Singletary SE, Buzdar AU, et al. Surgical conservation planning after neoadjuvant chemotherapy for stage II and operable stage III breast carcinoma. Am J Surg. 2001 Dec;182(6):601-8.
2. Thomassin-Naggara I, Lalonde L, David J, et al. A plea for the biopsy marker: how, why and why not clipping after breast biopsy? Breast Cancer Res Treat. 2012 Apr;132(3):881-93.

Statement: operation and : tumor resection in new margins

1. Mauri D, Pavlidis N, Ioannidis JP. Neoadjuvant versus adjuvant systemic treatment in breast cancer: a meta-analysis. J Natl Cancer Inst. 2005 Feb 2;97(3):188-94.
2. Berruti A, Generali D, Kaufmann M, et al. International expert consensus on primary systemic therapy in the management of early breast cancer: highlights of the Fourth Symposium on Primary Systemic Therapy in the Management of Operable Breast Cancer, Cremona, Italy (2010). J Natl Cancer Inst Monogr. 2011;2011(43):147-51.
3. Kümmel S, Holtschmidt J, Loibl S. Surgical treatment of primary breast cancer in the neoadjuvant setting. Br J Surg. 2014 Jul;101(8):912-24.
4. Ataseven B, Lederer B, Blohmer JU, et al. Impact of Multifocal or Multicentric Disease on Surgery and Locoregional, Distant and Overall Survival of 6,134 Breast Cancer Patients Treated With Neoadjuvant Chemotherapy. Ann Surg Oncol. 2014 Oct 9. [Epub ahead

of print]

5. Early Breast Cancer Trialists Collaborative Group. Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: a metaanalysis of individual patient data from ten randomised trials. *Lancet Oncol* 2018;19(1):27-39

Statement: tumor free margins ...

1. Cendán JC et al., Accuracy of Intraoperative Frozen-Section Analysis of Breast Cancer Lumpectomy-Bed Margins. *J Am Coll Surg* 2005;201:194–198.
2. Cabioglu N, Hunt, Sahin et al: Role for Intraoperative Margin Assessment in Patients Undergoing Breast-Conserving Ann Surg Oncol. 2007 Apr;14(4):1458-71.
3. Ciccarelli G, Di Virgilio MR, Menna S. Radiography of the surgical specimen in early stage breast lesions: diagnostic reliability in the analysis of the resection margins. *Radiol Med (Torino)*. 2007 Apr;112(3):366-76.
4. Houssami N, Macaskill P, Marinovich ML, et al. Metaanalysis of the impact of surgical margins on local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy. *Eur J Cancer*. 2010 Dec;46(18):3219-32.
5. Harness JK, Giuliano AE, Pockaj BA, et al. Margins: a status report from the Annual Meeting of the American Society of Breast Surgeons. *Ann Surg Oncol*. 2014 Oct;21(10):3192-7.
6. Houssami N, Macaskill P, Marinovich ML, et al. The association of surgical margins and local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy: a meta-analysis. *Ann Surg Oncol*. 2014 Mar;21(3):717-30
7. Buchholz TA, Somerfield MR, Griggs JJ et al. Margins for breast-conserving surgery with whole-breast irradiation in stage I and II invasive breast cancer: American Society of Clinical Oncology endorsement of the Society of Surgical Oncology/American Society for Radiation Oncology consensus guideline. *J Clin Oncol*. 2014 May 10;32(14):1502-6.
8. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from randomised trials. (published online Dec 11.)*Lancet Oncol*. 2017; [http://dx.doi.org/10.1016/S1470-2045\(17\)30777-5](http://dx.doi.org/10.1016/S1470-2045(17)30777-5)

Beginn adjuvanter Therapiemaßnahmen bei primärer Operation

	Oxford		
	LoE	GR	AGO
▪ Zeitnahe Anschluss systemischer Therapie und adjuvanter Radiotherapie (RT) nach OP	1b	A	++
▪ Beginn der Chemo- \pm AK-Therapie nach OP baldmöglichst, vor Radiotherapie	1b	A	++
▪ Wenn keine Chemo- \pm Antikörpertherapie:			
▪ Beginn der adjuvanten RT innerhalb von 6–8 Wochen nach OP	2b	B	++
▪ Beginn der endokrinen Therapie nach OP baldmöglichst	5	D	++
▪ Endokrine Therapie gleichzeitig mit Radiotherapie	3b	C	+

Statement: Timing of radiation and chemotherapy

1. Piroth MD, Pinkawa M, Gagel B et al. Sequencing chemotherapy and radiotherapy in locoregional advanced breast cancer patients after mastectomy - a retrospective analysis. BMC Cancer. 2008 Apr 23;8:114.
2. Tsoutsou PG, Koukourakis MI, Azria D, Belkacémi Y. et al. Optimal timing for adjuvant radiation therapy in breast cancer: a comprehensive review and perspectives. Crit Rev Oncol Hematol. 2009;71(2):102-16.
3. Balduzzi A, Leonardi MC, Cardillo A, et al. Timing of adjuvant systemic therapy and radiotherapy after breast-conserving surgery and mastectomy. Cancer Treat Rev. 2010;36(6):443-50.
4. Karlsson P, Cole BF, Colleoni M, et al; International Breast Cancer Study Group; Timing of radiotherapy and outcome in patients receiving adjuvant endocrine therapy. Int J Radiat Oncol Biol Phys. 2011;80(2):398-402.

Statement: Tamoxifen concurrent with chemotherapy

1. Adamowicz K, Marczevska M, Jassem J. Combining systemic therapies with radiation in breast cancer. Cancer Treat Rev. 2009 Aug;35(5):409-16
2. Harris EE, Christensen VJ, Hwang WT, et al. Impact of concurrent versus sequential tamoxifen with radiation therapy in early-stage breast cancer patients undergoing breast conservation treatment. J Clin Oncol. 2005 Jan 1;23(1):11-6.
3. Pierce LJ, Hutchins LF, Green SR et al. Sequencing of tamoxifen and radiotherapy after breast-conserving surgery in early-stage breast

cancer. J Clin Oncol. 2005 Jan 1;23(1):24-9.

Statement A1 concurrent with radiotherapy

1. Azria D, Belkacemi Y, Romieu G, et al. Concurrent or sequential adjuvant letrozole and radiotherapy after conservative surgery for early-stage breast cancer (CO-HO-RT): a phase 2 randomised trial. Lancet Oncol 2010;11(3):258-65
2. Chargari C, Castro-Pena P, Toledano I, et al. Concurrent use of aromatase inhibitors and hypofractionated radiation therapy. World J Radiol. 2012;4(7):318-23.
3. Ishitobi M, Shiba M, Nakayama T, et al. Treatment sequence of aromatase inhibitors and radiotherapy and long-term outcomes of breast cancer patients. Anticancer Res. 2014;34(8):4311-4.