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# Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

## Operative Therapie des Mammakarzinoms unter onkologischen Aspekten

# Operative Therapie des Mammakarzinoms unter onkologischen Aspekten

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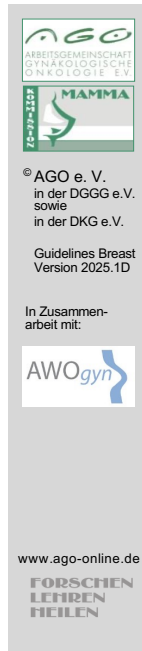
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## ■ Versionen 2002-2024:

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## ■ Version 2025:

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## 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

### AGO: ++

Operative Therapieentscheidungen sollten im Kontext eines multimodalen Therapiekonzeptes getroffen und im Rahmen einer präoperativen, interdisziplinären Tumorkonferenz beschlossen werden.

### 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
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3. Wiener, Hanlon, Schumacher et al., Reexamining Time From Breast Cancer Diagnosis to Primary Breast Surgery, JAMA Surg, 2023 May 1;158(5):485-492

### 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

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## Prätherapeutische Mammadiagnostik (nach histologischer Sicherung der Indexläsion)

	Oxford		
	LoE	GR	AGO
▪ Klinische Untersuchung	5	D	++
▪ Sonographie (Mamma)	2b	B	++
▪ Mammographie (wenn noch nicht vorliegend)	2b	B	++
▪ MRT*	1b	A	+
▪ Kontrastmittelmammographie (alleine) nach Verfügbarkeit und Strahlensensibilität der Brust (Alter)*	2a	B	+
▪ Tomosynthese + SM**	2b	B	+
▪ Mamma-CT	4	D	-
▪ Minimalinvasive Biopsie weiterer Mammabefunde (CNB, VAB)	1b	A	++
▪ Markierung des Tumors, wenn neoadjuvante Therapie geplant	1c	A	++

\* Möglichkeit der MRT-gestützten bzw. CEM-gestützter 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, und ggf. vor neoadjuvanter Therapie.

\*\* Reduktion der Strahlenexposition durch DBT mit synthetischer Mammographie (SM) statt zusätzlicher DM.

### DM, DBT, US, MRI

1. Neeter LMFH, Nelemans PJ, Raat HPJ et al. Contrast-enhanced mammography versus conventional imaging in women recalled from breast cancer screening (RACER trial): a multicentre, open-label, randomised controlled clinical trial. *Lancet Reg Health Eur.* 2024 Jul 3;44:100987.
2. Cozzi A, Schiaffino S, Fanizza M et al. Contrast-enhanced mammography for the assessment of screening recalls: a two-centre study. *Eur Radiol.* 2022 Nov;32(11):7388-7399.
3. Hadadi I, Rae W, Clarke J et al. Diagnostic Performance of Adjunctive Imaging Modalities Compared to Mammography Alone in Women with Non-Dense and Dense Breasts: A Systematic Review and Meta-Analysis. *Clin Breast Cancer.* 2021 Aug;21(4):278-291.
4. Mattar A, Antonini M, Amorim A. PROMRIINE (PRE-operative Magnetic Resonance Imaging is INEffective) Study: A Systematic Review and Meta-analysis of the Impact of Magnetic Resonance Imaging on Surgical Decisions and Clinical Outcomes in Women with Breast Cancer. *Ann Surg Oncol.* 2024 Nov;31(12):8021-8029.
5. Aroney S, Lloyd T, Birch S et al. Preoperative breast MR imaging influences surgical management in patients with invasive lobular carcinoma. *J Med Imaging Radiat Oncol.* 2024 Sep;68(6):680-686.
6. Willen LPA, Spiekerman van Weezenburg MA, Bruijsten AA et al. The Role of Magnetic Resonance Imaging in the Preoperative Staging and Treatment of Invasive Lobular Carcinoma. *Clin Breast Cancer.* 2024 Jun;24(4):e266-e272.
7. Cozzi A, Di Leo G, Houssami N et al. Preoperative breast MRI positively impacts surgical outcomes of needle biopsy-diagnosed

- pure DCIS: a patient-matched analysis from the MIPA study. *Eur Radiol.* 2024 Jun;34(6):3970-3980. doi: 10.1007/s00330-023-10409-5. Epub 2023 Nov 24. PMID: 37999727; PMCID: PMC11166778.
8. Schiaffino S, Cozzi A, Clauser P et al.; European Society of Breast Imaging (EUSOBI). Current use and future perspectives of contrast-enhanced mammography (CEM): a survey by the European Society of Breast Imaging (EUSOBI). *Eur Radiol.* 2024 Aug;34(8):5439-5450.
  9. Terzoni A, Basile P, Gambaro AC et al. Locoregional staging of breast cancer: contrast-enhanced mammography versus breast magnetic resonance imaging. *Radiol Med.* 2024 Apr;129(4):558-565.
  10. 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.
  11. 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.
  12. Schünemann HJ, Lerda D, Quinn C, et al. Breast Cancer Screening and Diagnosis: A Synopsis of the European Breast Guidelines. *Annals of Internal Medicine.* 2020;172(1):46-56.

#### US+FNA/CNB

1. 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.

#### 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, 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. 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 Surg*2015;192(8)883-893
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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
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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.
17. Panico CA-O, Ferrara F, Woitek R, D'Angelo AA-O, Di Paola VA-OX, Bufi E, et al. Staging Breast Cancer with MRI, the T. A Key Role in the Neoadjuvant Setting. LID - 10.3390/cancers14235786 [doi] LID - 5786. (2072-6694 (Print)).
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#### Reviews CEM:

1. Chung WS, Tang YC, Cheung YC. Contrast-Enhanced Mammography: A Literature Review of Clinical Uses for Cancer Diagnosis and Surgical Oncology. Cancers (Basel). 2024 Dec 12;16(24):4143.
2. Dromain, C., N. Vietti-Violi, and J.Y. Meuwly, Angiomammography: A review of current evidences. Diagn Interv Imaging, 2019.
3. 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.
4. Tagliafico, A.S., et al., Diagnostic performance of contrast-enhanced spectral mammography: Systematic review and meta-analysis. Breast, 2016. 28: p. 13-9.
5. 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.
6. Sogani J, Mango VL, Keating D, et al. Contrast-enhanced mammography: past, present, and future. Clin Imaging. 2021;69:269-79.
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8. The performance of contrast-enhanced mammography and breast MRI in local preoperative staging of invasive lobular breast cancer. Lobbes MBI, et al. Eur J Radiol. 2023. PMID: 37201248

#### CEM 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.

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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, et al. Contrast-Enhanced Mammography for Screening Women after Breast Conserving Surgery. *Cancers (Basel)*. 2020;12(12).
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10. González-Huebra I, Malmierca P, Elizalde A, 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, 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, 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, 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. Preoperative staging by multimodal imaging in newly diagnosed breast cancer: Diagnostic performance of contrast-enhanced spectral mammography compared to conventional mammography, ultrasound, and MRI. Daniaux M, Gruber L, De Zordo T, Geiger-Gritsch S, Amort B, Santner W, Egle D, Baltzer PAT. *Eur J Radiol*. 2023 Jun;163:110838. doi: 10.1016/j.ejrad.2023.110838. Epub 2023 Apr 15. PMID: 37080064 Free article.

15. The PROCEM study protocol: Added value of preoperative contrast-enhanced mammography in staging of malignant breast lesions - a prospective randomized multicenter study. Åhsberg K, Gardfjell A, Nimeus E, Ryden L, Zackrisson S. BMC Cancer. 2021 Oct 18;21(1):1115. doi: 10.1186/s12885-021-08832-2. PMID: 34663236 Free PMC article. Clinical Trial

#### Mamma-CT:

1. Uhlig, J. A.-O., A. Uhlig, L. Biggemann, U. Fischer, J. Lotz and S. Wienbeck "Diagnostic accuracy of cone-beam breast computed tomography: a systematic review and diagnostic meta-analysis." (1432-1084 (Electronic)).
2. Zhu, Y., A. M. O'Connell, Y. Ma, A. Liu, H. Li, Y. Zhang, X. Zhang and Z. Ye (2022). Dedicated breast CT: state of the art-Part II. Clinical application and future outlook. Eur Radiol. Germany. 32: 2286-2300.



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## Prätherapeutische Axilladiagnostik

	Oxford		
	LoE	GR	AGO
▪ <b>Klinische Untersuchung</b>	5	D	++
▪ <b>Sonographie</b>	2a	B	++
▪ <b>CNB Axilla, wenn auffälliger LK-Befund und Markierung des LK wenn TAD geplant / ≤ 3 susp. LK*</b>	2b	B	++
▪ <b>MRT</b>	1b	A	+
▪ <b>Mammographie (DM)</b>	2b	B	-
▪ <b>Tomosynthese (DBT)</b>	2b	B	-
▪ <b>Kontrastmittelmammographie (CEM, alleine)</b>	2a	B	-
▪ <b>PET für die Axilla (PET-CT, PET-MRT)</b>	2b	B	-
▪ <b>Mamma-CT</b>	4	D	-

\* Studienteilnahme empfohlen (AXSANA / EuBreast 3 – Studie)

### 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.

### CEUS for Sentinel

#### Diagnosis of malignant lymph node infiltration

1. Niu Z, Gao Y, Xiao M et al. Contrast-enhanced lymphatic US can improve the preoperative diagnostic performance for sentinel lymph nodes in early breast cancer. Eur Radiol. 2023 Mar;33(3):1593-1602.

2. Liu X, Wang M, Wang Q et al. Diagnostic value of contrast-enhanced ultrasound for sentinel lymph node metastasis in breast cancer: an updated meta-analysis. *Breast Cancer Res Treat.* 2023 Nov;202(2):221-231.
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4. Nielsen Moody A, Cox K, Haigh I et al. Does Contrast Enhanced Ultrasound (CEUS) of Normal/Benign Axillary Lymph Nodes in Patients with Breast Cancer Identify Significant Axillary Nodal Burden? *Eur J Radiol.* 2020 Nov;132:109311.
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#### Identification and tagging of the SLN (e.g carbon nanoparticle or wire guided)

1. Luo Y, Chen J, Feng L et al. Study on Sentinel Lymph Node and Its Lymphatic Drainage Pattern of Breast Cancer by Contrast-Enhanced Ultrasound. *J Ultrasound Med.* 2022 Nov;41(11):2727-2737.
2. Huang D, Cao W, Luo Y et al. Can preoperative percutaneous injection of ultrasound contrast agent locate sentinel lymph nodes of breast cancer? *Front Oncol.* 2024 Nov 25;14:1471443.
3. Omoto K, Futsuhara K, Watanabe T. Sentinel lymph node identification using contrast-enhanced ultrasound in breast cancer: review of the literature. *J Med Ultrason (2001).* 2024 Oct;51(4):581-585. Erratum in: *J Med Ultrason (2001).* 2024 Oct;51(4):693 (The Erratum announces copyright change).
4. Nielsen Moody A, Bull J, Culpan AM et al. Preoperative sentinel lymph node identification, biopsy and localisation using contrast enhanced ultrasound (CEUS) in patients with breast cancer: a systematic review and meta-analysis. *Clin Radiol.* 2017 Nov;72(11):959-971.
5. 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.
6. Goyal A. New Technologies for Sentinel Lymph Node Detection. *Breast Care (Basel).* 2018 Oct;13(5):349-353.

#### MRT

1. Panico C, Ferrara F, Woitek R et al. Staging Breast Cancer with MRI, the T. A Key Role in the Neoadjuvant Setting. *Cancers (Basel).* 2022 Nov 24;14(23):5786.
2. 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)

3. 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.
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6. 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.
7. 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
8. 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.



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## Prätherapeutisches Staging

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

\* Contrast-enhanced ultrasound.  
\*\* Vorzugsweise bei hohem Stadium (III), wenn verfügbar.

### Statement: history and physical examination

1. GCP

### Statement: high metastatic potential / symptoms

1. Gerke O, Naghavi-Behzad M, Nygaard ST et al.. Diagnosing Bone Metastases in Breast Cancer: A Systematic Review and Network Meta-Analysis on Diagnostic Test Accuracy Studies of 2-[<sup>18</sup>F]FDG-PET/CT, <sup>18</sup>F-NaF-PET/CT, MRI, Contrast-Enhanced CT, and Bone Scintigraphy. Semin Nucl Med. 2025 Jan;55(1):137-151.
2. Rutgers, EJ et al: Quality control in the locoregional treatment of breast cancer (2001) EJC 37: 447-453
3. 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
4. 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.
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7. 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.
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## Stellenwert der operativen Optionen

	Oxford	
	LoE	GR
▪ Die Überlebensraten nach BET (Tumorektomie + RT) sind denen nach MRM mindestens 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

### Statement: lumpectomy – mastectomy

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## Brusterhaltende Operation (BEO)

### Markierungsoptionen nicht-palpabler Läsionen

	Oxford		
	LoE	GR	AGO
▪ Drahtmarkierung	1a	A	++
▪ Intraoperative sonographische Lokalisation ohne Drahtmarkierung*	1a	A	++
▪ Andere Markierungsarten:**			
Radar-Reflexion	2b	B	+/-
Magnetische Marker***	2b	B	+/-
Paramagnetische Marker***			
MagSeed® (im Vergleich zur Drahtmarkierung)***	1b	A	+
Radiofrequenz-Marker (RFID) ***	2b	B	+/-
Radionuklidmarkierung (ROLL)	1a	A	+/-
Radioaktive Seeds****	1a	A	+/-

\* Die Läsion muss von demselben Untersucher prä- und intraoperativ sonographisch in der Gesamtausdehnung sicher dargestellt werden können. Voraussetzung: Adäquate Geräteausstattung und Ausbildung des Operateurs.

\*\* gemäß Zulassung

\*\*\* nicht geeignet bei MRT-Verlaufsbeurteilung unter NACT

\*\*\*\* in Deutschland nicht zugelassen

#### Meta-analyses of different techniques:

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#### Meta-analysis intraoperative ultrasound vs. wire-guided localization:

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2. Pan H, Wu N, Ding H, et al. (2013) Intraoperative ultrasound guidance is associated with clear lumpectomy margins for breast cancer: a systematic review and meta-analysis. PLoS One 8:e74028. 10.1371/journal.pone.0074028
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RCTs intraoperative ultrasound vs. wire-guided localization:

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#### Magnetic seeds:

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#### Radar reflector markers:

1. Kasem I, Mokbel K. Savi Scout® Radar Localisation of Non-palpable Breast Lesions: Systematic Review and Pooled Analysis of 842 Cases. Anticancer Res. 2020 Jul;40(7):3633-3643. doi: 10.21873/anticancer.14352.
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Radiofrequency-based markers (RFID): cohort studies (no RCTs available):

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Radioactive seeds (for RCTs see meta-analyses above):

1. Schermers B, van Riet YE, Schipper RJ et al. Nationwide registry study on trends in localization techniques and reoperation rates in non-palpable ductal carcinoma in situ and invasive breast cancer. Br J Surg. 2021 Oct 13;znab339. doi: 10.1093/bjs/znab339.

ROLL:

for RCTs see meta-analyses above



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## Localization Methods for non-Palpable Breast Cancer: A Meta-Analysis

### Athanasίου et al. Eur J Surg Onc 2021:

- Meta-analysis of RCTs
- 18 studies with 3112 patients
- Pairwise and network meta-analysis

### Ultrasound-guided surgery vs. wire-guided surgery:

- decreased positive margin both in the pairwise [OR = 0.19 (0.11, 0.35);  $p < 0.01$ ] and network meta-analysis [OR = 0.19 (0.11, 0.60)]
- a statistically significant reduction in re-operation rate [OR = 0.19 (0.11, 0.36);  $p < 0.01$ ] and operative time [MD = -4.24 (-7.85, -0.63);  $p = 0.02$ ]

### Ultrasound-guided surgery vs. ROLL / RSL:

- a statistically significant reduction in positive margin compared to ROLL [OR = 0.19 (0.11, 0.6)] and RSL [OR = 0.26 (0.13, 0.52)]

**„Ultrasound-guided surgery has potential benefits in reduction of positive surgical margin, the rest of the techniques seem to have equivalent efficacy.”**

1. Athanasίου C, Mallidis E, Tuffaha H. Comparative effectiveness of different localization techniques for non-palpable breast cancer. A systematic review and network meta-analysis. Eur J Surg Oncol. 2021 Oct 11;S0748-7983(21)00751-4. doi: 10.1016/j.ejso.2021.10.001.

## Brusterhaltende Operation (BEO) Resektionsränder

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li> <b>Invasives Mammakarzinom ohne extensive intraduktale Komponente (EIC)*</b> <ul style="list-style-type: none"> <li>Ziel: tumorfreie Resektionsränder (auch bei ungünstiger Biologie ist "no ink on tumor" ausreichend)</li> <li>Nachresektion bei invasivem oder in situ Tumorausläufer bis in den Resektionsrand (Paraffinschnitt)</li> </ul> </li> </ul>	2a	A	++
<ul style="list-style-type: none"> <li> <b>Invasives Mammakarzinom mit EIC*</b> <ul style="list-style-type: none"> <li>Nachresektion bei invasivem oder in situ Tumorausläufer bis in den Resektionsrand (Paraffinschnitt)</li> <li>Nachresektion bei knappem Resektionsrand der intraduktalen Komponente (&lt; 2 mm im Paraffinschnitt)**</li> </ul> </li> </ul>	2a	B	++
	2a	B	-

\* Keine einheitliche Definition der EIC in der Literatur. Da die EIC das Lokalrezidivrisiko erhöht, wenn die Größe der intraduktalen Komponente in einer Dimension mindestens das Doppelte der Größe der invasiven Komponente beträgt, wird die Verwendung dieser Definition entsprechend der S3-Leitlinie empfohlen.  
 \*\* Individuelles Vorgehen mit Berücksichtigung des Alters und der Tumorausdehnung.

### Invasive cancer – margins:

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- 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.
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#### Invasive cancer with intraductal component - margins:

1. Morrow M, Van Zee KJ, Solin LJ et al. Society of Surgical Oncology-American Society for Radiation Oncology-American Society of Clinical Oncology Consensus Guideline on Margins for Breast-Conserving Surgery With Whole-Breast Irradiation in Ductal Carcinoma In Situ. J Clin Oncol. 2016 Nov 20;34(33):4040-4046. doi: 10.1200/JCO.2016.68.3573.
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. doi: 10.1245/s10434-016-5446-2.

#### 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. Hennigs A, Fuchs V, Sinn HP et al. Do Patients After Reexcision Due to Involved or Close Margins Have the Same Risk of Local Recurrence as Those After One-Step Breast-Conserving Surgery? Ann Surg Oncol. 2016 Jun;23(6):1831-7. doi: 10.1245/s10434-015-5067-1
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6. 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.
7. Tamburelli F, Maggiorotto F, Marchio C, et al. (2020) Reoperation rate after breast conserving surgery as quality indicator in breast cancer treatment: A reappraisal. *Breast* 53:181-188. 10.1016/j.breast.2020.07.008

Extensive intraductal component:

1. Sinn HP, Anton HW, Magener A et al. Extensive and predominant in situ component in breast carcinoma: their influence on treatment results after breast-conserving therapy. *Eur J Cancer*, 1998. 34(5): p. 646- 53.
2. S3-Guideline Early Detection, Diagnosis, Treatment and Follow-up Care of Breast Cancer (Version 4.4, June 2021)
3. Ha SM, Cha JH, Shin HJ et al. Mammography, US, and MRI to Assess Outcomes of Invasive Breast Cancer with Extensive Intraductal Component: A Matched Cohort Study. *Radiology*. 2019 Aug;292(2):299-308. doi: 10.1148/radiol.2019182762.

## Brusterhaltende Operation (BEO)

### Vorgehensweise, Technische Aspekte

	Oxford		
	LoE	GR	AGO
▪ Präparateradiographie und / oder -sonographie bei nicht-palpablen Befunden und / oder tumorassoziiertem Mikrokalk*	2b	B	++
▪ Intraoperative Sonographie zur Erhöhung der R0-Resektionsrate bei nicht-palpablen Befunden	1a	A	+
▪ Intraoperative Sonographie zur Erhöhung der R0-Resektionsrate bei palpablen Befunden (geringeres Resektionsvolumen)	1b	B	+
▪ Intraoperative Clipmarkierung des Tumorbetts bei Indikation für Boost- oder Teilbrustbestrahlung	2b	B	+
▪ Intraoperative Schnitttrandbeurteilung (mit Margin Probe®)	1b	A	+/-
▪ Stereotaktische Befundentfernung als alleinige Therapie	4	D	--

\* obligat auch bei Verwendung von sondengestützten Detektionssystemen (magnetische Seeds, Radar-Reflexion, RFID, radioaktive Seeds, ROLL)

#### 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.

#### Intraoperative ultrasound: Meta-analyses:

1. Athanasiou C, Mallidis E, Tuffaha H. Comparative effectiveness of different localization techniques for non-palpable breast cancer. A systematic review and network meta-analysis. *Eur J Surg Oncol*. 2021 Oct 11;S0748-7983(21)00751-4. doi: 10.1016/j.ejso.2021.10.001.

2. 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.
3. 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
4. Banys-Paluchowski M, Rubio IT, Karadeniz Cakmak G et al. Intraoperative ultrasound-guided excision of non-palpable and palpable breast cancer: systematic review and meta-analysis. in press 2022

Intraoperative ultrasound: RCTs in non-palpable breast cancer:

1. 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
2. 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.
3. Rahusen FD, Bremers AJ, Fabry HF, et al. (2002) Ultrasound-guided lumpectomy of nonpalpable breast cancer versus wire-guided resection: a randomized clinical trial. *Ann Surg Oncol* 9:994-998. 10.1007/BF02574518

Intraoperative ultrasound: RCTs in palpable breast cancer:

1. Volders JH, Haloua MH, Krekel NM et al. (2017) Intraoperative ultrasound guidance in breast-conserving surgery shows superiority in oncological outcome, long-term cosmetic and patient-reported outcomes: Final outcomes of a randomized controlled trial (COBALT). *Eur J Surg Oncol* 43:649-657. 10.1016/j.ejso.2016.11.004
2. Volders JH, Negenborn VL, Haloua MH, et al. (2018) Breast-specific factors determine cosmetic outcome and patient satisfaction after breast-conserving therapy: Results from the randomized COBALT study. *J Surg Oncol* 117:1001-1008. 10.1002/jso.25012
3. Krishna KL, Srinath BS, Santosh D, Velusamy S, Divyamala KP, Sariya Mohammadi J, Kurpad V, Kulkarni S, Yaji P, Goud S, Dhanireddy S, Ram J (2020) A comparative study of perioperative techniques to attain negative margins and spare healthy breast tissue in breast conserving surgery. *Breast Dis* 39:127-135. 10.3233/BD-200443
4. Vispute T, Suhani, Seenu V, et al. (2018) Comparison of resection margins and cosmetic outcome following intraoperative ultrasound-guided excision versus conventional palpation-guided breast conservation surgery in breast cancer: A randomized controlled trial.

Margin 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. Geha RC, Taback B, Cadena L et al. A Single institution's randomized double-armed prospective study of lumpectomy margins with adjunctive use of the MarginProbe in nonpalpable breast cancers. *Breast J.* 2020 Nov;26(11):2157-2162. doi: 10.1111/tbj.14004.
3. Allweis TM, Kaufman Z, Lelcuk S et al. A prospective, randomized, controlled, multicenter study of a real-time, intraoperative probe for positive margin detection in breast-conserving surgery. *Am J Surg.* 2008 Oct;196(4):483-9. doi: 10.1016/j.amjsurg.2008.06.024.
4. Thill M, Dittmer C, Baumann K, Friedrichs K, Blohmer JU. MarginProbe®--final results of the German post-market study in breast conserving surgery of ductal carcinoma in situ. *Breast.* 2014 Feb;23(1):94-6.

Specimen radiography/Specimen ultrasound:

1. Versteegden DPA, Keizer LGG, Schlooz-Vries MS et al. Performance characteristics of specimen radiography for margin assessment for ductal carcinoma in situ: a systematic review. *Breast Cancer Res Treat.* 2017 Dec;166(3):669-679. doi: 10.1007/s10549-017-4475-2
2. St John ER, Al-Khudairi R, Ashrafian H et al. Diagnostic Accuracy of Intraoperative Techniques for Margin Assessment in Breast Cancer Surgery: A Meta-analysis. *Ann Surg* 2017 Feb;265(2):300-310. doi: 10.1097/SLA.0000000000001897.
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. 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.
5. Singletary: Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. *Am J Surg.* 2002 Nov;184(5):383-93.
6. Funk A, Heil J, Harcos A et al. Efficacy of intraoperative specimen radiography as margin assessment tool in breast conserving

surgery. *Breast Cancer Res Treat.* 2020 Jan;179(2):425-433. doi: 10.1007/s10549-019-05476-6.

Intraoperative clip marking of the tumor bed:

1. van Mourik AM, Elkhuizen PHM, Minkema D et al.; Dutch Young Boost Study Group; Corine van Vliet-Vroegindeweyj  
Multiinstitutional study on target volume delineation variation in breast radiotherapy in the presence of guidelines. *Radiother Oncol* 2010 Mar;94(3):286-91.
2. Hlavka A, Vanasek J, Odrázka K et al. Tumor bed radiotherapy in women following breast conserving surgery for breast cancer-safety margin with/without image guidance. *Oncol Lett.* 2018 Apr;15(4):6009-6014.
3. Goldberg H, Prosnitz RG, Olson JA, Marks LB. Definition of postlumpectomy\_tumor\_bed\_for\_radiotherapy boost field planning: CT versus surgical\_clips. *Int J Radiat Oncol Biol Phys.* 2005 Sep 1;63(1):209-13.
4. Koch CA, Corey G, Liu ZA et al. Partial Breast Irradiation and Surgical Clip Usage for Tumor Bed Delineation After Breast-Conserving Surgery in Canada: A Radiation Oncology Perspective. *Adv Radiat Oncol.* 2021 Apr 20;6(4):100701. doi: 10.1016/j.adro.2021.100701. eCollection 2021 Jul-Aug. PMID: 34409206
5. Ebner F, de Gregorio N, Rempen A, To clip or not to clip the breast tumor bed? A retrospective look at the geographic miss index and normal tissue index of 110 patients with breast cancer. *J Turk Ger Gynecol Assoc.* 2017 Jun 1;18(2):67-71.

## Brusterhaltende Operation (BEO) ohne neoadjuvante Therapie

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li>▪ <b>Multifokalität / Multizentrität (Voraussetzung: R0-Resektion aller Herde)</b></li> </ul>	2b	B	+
<ul style="list-style-type: none"> <li>▪ <b>Histologisch befallene Resektionsränder trotz wiederholter Nachresektion</b></li> </ul>	2b	B	--
<ul style="list-style-type: none"> <li>▪ <b>Inflammatorisches Mammakarzinom</b></li> </ul>	2b	B	--

### 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.
6. Boughey JC, Rosenkranz KM, Ballman KV et al. Local recurrence after breast-conserving therapy in patients with multiple ipsilateral breast cancer: Results from ACOSOG Z11102 (Alliance). J Clin Oncol 2023; 41: 3184-3193.

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*. 2015 Feb;93(2):116-26.
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, Bougnoux 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.

## Axilläre Lymphknotendissektion (ALND) ohne neoadjuvante Chemotherapie

Empfehlung zur ALND:	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)	2a	B	+
▪ cN0 pN0 (i+) (sn)	1b	A	--
▪ cN0 pN1mi (sn)	1b	A	--
▪ cN0 pN1 (sn) (T1-3, < 3 SN+, BEO + RT + adäquate Systemtherapie)	1b	A	-
▪ cN0 pN1 (sn) und Mastektomie (T1-2, < 3 SN+, keine Radiotherapie der Thoraxwand)	2b	B	+/-
▪ cN0 pN1 (sn) und Mastektomie (T1-3, < 3 SN+, Radiotherapie der Thoraxwand + LAG)	1b	B	-

### Statement: Axillary lymph node dissection

1. Brackstone M, Baldassarre FG, Perera FE et al. Management of the Axilla in Early-Stage Breast Cancer: Ontario Health (Cancer Care Ontario) and ASCO Guideline. J Clin Oncol. 2021 Sep 20;39(27):3056-3082. doi: 10.1200/JCO.21.00934
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. 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.
4. 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
5. 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.
6. 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

7. 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.
8. 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.

#### pN+ (pre-surgery) without neoadjuvant systemic therapy

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

#### cN0 pN0(sn)(i+)

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 pN1mi

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 pN1 (sn) ( cT1/2 , < 3 SN +, BCS + tangential radiation field, adequate systemic therapy)

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, Mcleod 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. 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)




1. Cody HS 3rd. Extending ACOSOG Z0011 to Encompass Mastectomy: What Happens Without RT? Ann Surg Oncol. 2017 Mar;24(3):621-623.
2. Tinterri C, Canavese G, Gatzemeier W, et al. Sentinel lymph node biopsy versus axillary lymph node dissection in breast cancer patients undergoing mastectomy with one to two metastatic sentinel lymph nodes: Sub-analysis of the SINODAR-ONE multicenter randomized clinical trial and reopening of enrolment. Br J Surg 2023; 110: 1143-1152.
3. Alamoodi M, Patani N, Mokbel K, et al. Reevaluating axillary lymph node dissection in total mastectomy for low axillary burden breast cancer: Insights from a meta-analysis including SINODAR-ONE trial. Cancers 2024; 16: 742

cN0 pN1(sn) and mastectomy with PMRT + RNI

1. de Boniface J, Filtenborg Tvedskov T, Ryden L, et al. Omitting axillary dissection in breast cancer with sentinel-node metastases. N Engl J Med 2024; 390: 1163-1175.

ALND indicated, but not feasible – Radiotherapy according to AMAROS-trial (validated for cN0 pN1sn)

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.


  
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							LoE	GR	AGO
cN-Status (vor NACT)	pN-Status (vor NACT)	ycN-Status (nach NACT)	Axilläre operative Intervention (nach NACT)	AGO	ypN-Status (nach NACT und Operation)	Operative Konsequenz aus Histobefund			
cN0	Keine OP vor NACT	ycN0	SLNE	++	ypN0 (sn)	Keine	2b	B	++
					ypN0 (i+) (sn)	ALND	2b	B	-
					ypN1mi (sn)	ALND	2b	C	+/-
					ypN1 (sn)	ALND	2b	C	++

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, 318, 918-926
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chemotherapy for breast cancer. *Ann Surg Oncol* 2018, 25, 1304-1311.

Statement: SLNB after NACT

1. El Hage Chehade H, Headon H, El Tokhy O et al. Is sentinel lymph node biopsy a viable alternative to complete axillary dissection following neoadjuvant chemotherapy in women with node-positive breast cancer at diagnosis? An updated meta-analysis involving 3,398 patients. *Am J Surg.* 2016 Nov;212(5):969-981.
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Axilläre operative Interventionen bei NACT (cN+)							Oxford		
							LoE	GR	AGO
cN-Status (vor NACT)	pN-Status (vor NACT)	ycN-Status (nach NACT)	Axilläre operative Intervention (nach NACT)	AGO	ypN-Status (nach NACT und Operation)	Operative Konsequenz aus Histobefund			
cN+*	pN+cN#	ycN0	ALND	+	ypN0 / ypN+	Keine	2b	B	++
			TAD	+	ypN0	Keine	2b	B	+
					ypN0 (i+)	ALND	2b	B	-
					ypN1mi	ALND	2b	B	+/-
				ypN+	ALND	2b	B	+	
			SLNE	+/-	ypN0	Keine	2b	B	+/-
					ypN0 (i+)	ALND	2b	B	+/-
					ypN+ inkl. ypN1mi	ALND	2b	B	+
			TLNE	+/-	ypN0	ALND	2b	B	+/-
					ypN0 (i+)	ALND	3b	B	+/-
					ypN+ inkl. ypN1mi	ALND	3b	B	+
					ycN+**	ALND	+	ypN0 / ypN+	Keine

\* Studienbeteiligung an AXSANA empfohlen; \*\* Cave: In 21,1 % falsch-positive Befunde, ggf. CNB/TAD

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, 318, 918-926
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Statement: False-positives in ALND after ycN+

1. Hartmann S, Kühn T, Hauptmann M et al., Axillary staging after neoadjuvant chemotherapy for initially node-positive breast carcinoma in Germany: Initial data from the AXSANA trial. *Geburtsh Frauenheilk* 2022; 82: 932-940.

Statement: TLNE alone:

1. Swarnkar PK, Tayeh S, Michell MJ et al., The Evolving Role of Marked Lymph Node Biopsy (MLNB) and Targeted Axillary Dissection (TAD) after Neoadjuvant Chemotherapy (NACT) for Node-Positive Breast Cancer: Systematic Review and Pooled Analysis. *Cancers (Basel)* 2021; 13(7):1539

## Targeted Axillary Dissection (TAD)

### = TLNE + SLNE

	Oxford		
	LoE	GR	AGO
▪ Stanzbiopsische Sicherung der LK-Metastase und Markierung	2b	B	++
▪ Markierung von mehreren Lymphknoten bei mehr als 1 suspekten LK	2b	B	+/-
▪ Evidenz für den Vergleich einzelner Marker (Clip / Coil, Kohle, magnetischer Seed, Radar-Reflexion, Radiofrequenzmarker etc.) nicht ausreichend*	2b	B	
▪ TAD bei 1-3 suspekten LK vor NACT	2b	B	+
▪ TAD bei ≥ 4 suspekten LK vor NACT	5	D	+/-
▪ Vollständige Aufarbeitung aller Lymphknoten am Paraffinschnitt mit Schnittstufen von ≤ 500 µm	5	D	++
▪ Immunhistochemie zum Nachweis von ITC	2b	D	-
▪ ALND bei prä- oder intraoperativ nicht auffindbarem Marker	5	D	+
▪ Weitere Intervention zur Entfernung des nicht auffindbaren Markers (auch nach ALND)	5	D	-
▪ Alleinige TLNE ohne SLNE	2B	B	+/-

\* Studienbeteiligung an AXSANA empfohlen.

1. Kümmel S, Heil J, Rueland A, et al: A prospective multicenter registry study to evaluate the clinical feasibility of targeted axillary dissection (TAD) in node-positive breast cancer patients. *Ann Surg.* 2020 Nov 4. doi: 10.1097/SLA.0000000000004572
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Statement: TLNE alone:

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(TAD) after Neoadjuvant Chemotherapy (NACT) for Node-Positive Breast Cancer: Systematic Review and Pooled Analysis. *Cancers (Basel)* 2021; 13(7):1539

## Sentinel-Lymphknoten-Exzision (SLNE) Indikationen I

	Oxford		
	LoE	GR	AGO
▪ Klinisch / sonographisch neg. Axilla (cN0)	1b	A	++
▪ cT 1-2	1b	A	++
▪ cT 3-4c	3b	B	+
▪ DCIS			
▪ Mastektomie	3b	B	+
▪ BET	3b	B	-
<b>Verzicht auf SLNE:</b>			
▪ postmenopausale Patientin (≥ 50 J., cT1 cN0, BEO + Ganzbrustbestrahlung, HR+/HER2-, G1/G2) analog SOUND/INSEMA	1b	B	+
▪ bei der älteren Patientin (≥ 70 J., cT1/cN0, HR+/HER2-, Mastektomie)	3b	B	+

### Statement: SLNE

1. Brackstone M, Baldassarre FG, Perera FE et al. Management of the Axilla in Early-Stage Breast Cancer: Ontario Health (Cancer Care Ontario) and ASCO Guideline. J Clin Oncol. 2021 Sep 20;39(27):3056-3082. doi: 10.1200/JCO.21.00934. Epub 2021 Jul 19.
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4. 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
5. van der Ploeg IM, Nieweg OE, van Rijk MC Axillary recurrence after a tumour-negative sentinel node biopsy in breast cancer patients: A systematic review and meta-analysis of the literature. Eur J Surg Oncol. 2008 Dec;34(12):1277-84.
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7. 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
8. Intra M, Rotmensz N, Veronesi P. Sentinel node biopsy is not a standard procedure in ductal carcinoma in situ of the breast: the

- experience of the European institute of oncology on 854 patients in 10 years. *Ann Surg*. 2008 Feb;247(2):315-9
9. Classe JM, Bordes V, Campion L: Sentinel Lymph Node Biopsy After Neoadjuvant Chemotherapy for Advanced Breast Cancer: Results of Ganglion Sentinelle et Chimiotherapie Neoadjuvante, a French Prospective Multicentric Study. *J Clin Oncol*. 2008 Dec 29. [Epub ahead of print]
  10. Pugliese MS, Karam AK, Hsu M, et al. Predictors of Completion Axillary Lymph Node Dissection in Patients With Immunohistochemical Metastases to the Sentinel Lymph Node in Breast Cancer. *Ann Surg Oncol*. 2009 Dec 22. [Epub ahead of print]
  11. Lyman GH, Temin S, Edge S 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
  12. 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.
  13. Charalampoudis P, Markopoulos C, Kovacs T.: Controversies and recommendations regarding sentinel lymph node biopsy in primary breast cancer: A comprehensive review of current data. *Eur J Surg Oncol*. 2017 Nov 13. pii: S0748-7983(17)30955-1. doi: 10.1016/j.ejso.2017.10.215. [Epub ahead of print]
  14. Morrow M1, Van Zee KJ, Patil S, et al: Axillary Dissection and Nodal Irradiation Can Be Avoided for Most Node-positive Z0011-eligible Breast Cancers: A Prospective Validation Study of 793 Patients. *Ann Surg*. 2017 Sep;266(3):457-462.
  15. Gentilini OD, Botteri E, Sangalli C et al., Sentinel Lymph Node Biopsy vs No Axillary Surgery in Patients With Small Breast Cancer and Negative Results on Ultrasonography of Axillary Lymph Nodes. The SOUND Randomized Clinical Trial; *JAMA Oncol* 2023;9(11):1557-1564.
  16. Reimer T, Stachs A, Veselinovic K, et al. Axillary Surgery in Breast Cancer - Primary Results of the INSEMA Trial. *N Engl J Med*. 2024 Dec 12. doi: 10.1056/NEJMoa2412063.

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

1. Houssami N, Ciatto S, Turner RM, et al. Preoperative ultrasound-guided needle biopsy of axillary nodes in invasive breast cancer – a metaanalysis. *Ann Surg Oncol* 2011;254:243-251
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patients with suspicious node positive breast cancer. *Breast Cancer*. 2018;25(1):86–93.

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

1. 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.
2. Kotani H, Yoshimura A, Adachi Y, et al. Sentinel lymph node biopsy is not necessary in patients diagnosed with ductal carcinoma in situ of the breast by stereotactic vacuum-assisted biopsy. *Breast Cancer*. 2014 Jul 3. [Epub ahead of print]
3. van Roozendaal LM, Goorts B, Klinkert M, et al. Sentinel lymph node biopsy can be omitted in DCIS patients treated with breast conserving therapy. *Breast Cancer Res Treat*. 2016 Apr;156(3):517-525.
4. Bonev V, De Paz Villanueva CC, et al. Is Sentinel Lymph Node Dissection Necessary in All Patients with Ductal Carcinoma In Situ Undergoing Total Mastectomy? *Am Surg*. 2016 Oct;82(10):982-984.

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.
2. Gentilini O et al. Sentinel Lymph Node Biopsy in Male Patients with Early Breast Cancer. *Oncologist* 2007;12;512-515

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.
2. 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

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.

	SOUND (median follow-up 5.7 years)	INSEMA (median follow-up 6.1 years)
<b>Randomization</b>	SLNB vs no SLNB (1:1)	SLNB vs no SLNB (4:1)
<b>n</b>	1,405 708 SLNB vs 697 no SLNB	4,858 3,896 SLNB vs 962 no SLNB
<b>Population</b>	cT ≤ 2 cm, cN0 (incl. ultrasound), invasive BC, BCT + radiotherapy	cT ≤ 5 cm (90% ≤ 2 cm), cN0 (incl. ultrasound), invasive BC, BCT + WBI
<b>Age</b>	Median (IQR) 60 years (52-68)	Median (IQR) 62 years (53-68)
<b>Intrinsic subtype, Grading, Ki-67 index</b>	HR-pos./HER2-neg. 87.8% G3: 17.9% Ki-67 index ≥ 20%: 36.1%	HR-pos./HER2-neg. 95.2% G3: 3.6% Ki-67 index > 20%: 12.9%
<b>Survival</b>	5y DDFS: 97.7% SLNB vs 98.0% no SLNB HR 0.84 (90% CI: 0.45-1.54)  5y OS 98.2% vs 98.4%	5y iDFS: 91.7% SLNB vs 91.9% no SLNB HR 0.91 (95% CI: 0.73-1.14)  5y OS: 96.9% vs 98.2%
<b>Recurrence</b>	Local 1.0% SLNB vs 0.9% no SLNB Axillary 0.4% vs 0.7%	Local 1.1% SLNB vs 0.8% no SLNB Axillary 0.3% vs 1.0%



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Version 2025.1D

In Zusammen-  
arbeit mit:



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FORSCHEN  
LEHREN  
HEILEN

1. Gentilini, Botteri, Sangalli et al., Sentinel Lymph Node Biopsy vs No Axillary Surgery in Patients With Small Breast Cancer and Negative Results on Ultrasonography of Axillary Lymph Nodes: The SOUND Randomized Clinical Trial, JAMA Oncol. 2023 Nov 1;9(11):1557-1564.
2. Reimer T, Stachs A, Veselinovic K, et al. Axillary Surgery in Breast Cancer - Primary Results of the INSEMA Trial. N Engl J Med. 2024 Dec 12. doi: 10.1056/NEJMoa2412063.

## Sentinel-Lymphknoten-Exzision (SLNE) Indikationen II

	Oxford		
	LoE	GR	AGO
▪ Während Schwangerschaft oder Stillzeit (nur <sup>99m</sup> Tc-Kolloid, keine Markierung mit Patent- oder Methylenblau, keine Daten zu SPIO oder ICG)	3	C	++
▪ Nach vorausgegangener Tumorektomie	2b	B	+
▪ Nach vorausgegangener „großer“ Brust-Operation (z. B. Reduktionsplastik)	3b	C	+/-
▪ Ipsilaterales intramammäres Rezidiv nach vorheriger BET und SLNE	4	D	-
▪ SLNE entlang der A. mammaria interna	2b	B	-
▪ Nach Axilla-Voroperation	3b	B	+/-
▪ Prophylaktische bilaterale / kontralaterale Mastektomie	3b	B	--
▪ Inflammatorisches Mammakarzinom	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. 2018 Apr;168(2):551-557.
5. Liberale V, Tripodi E, Ottino L, Biglia N. Surgery on breast cancer in pregnancy. Transl Cancer Res. 2019 Oct;8(Suppl 5):S493-S502.

### 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, Jacqemyn ML, Tjalma W. Sentinel node biopsy for ipsilateral breast cancer recurrence: a review. Eur J Gynecol Oncol

2008;29:565-567

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7. Folli S, Falco G, Mingozzi M, et al. Repeat sentinel lymph node biopsy in patients with ipsilateral recurrent breast cancer after breast-conserving therapy and negative sentinel lymph node biopsy: a prospective study. *Minerva Chir*. 2016 Apr;71(2):73-9.

#### 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. *Breast Cancer Res Treat*. 2020 Feb;180(1):207-217.
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*. 2015 Feb;93(2):116-26.
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.



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In Zusammen-  
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# Sentinel-Lymphknoten-Exzision (SLNE) Markierung

- <sup>99m</sup>Tc Kolloid
- Präoperative Lymphszintigraphie (diagnostischer Zugewinn limitiert, aber gesetzlich vorgeschrieben)\*
- Patentblau
- Indocyaningrün (ICG)<sup>°</sup>
- SPIO<sup>#</sup>
- Methylenblau

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

- \* Qualitätssicherung Nuklearmedizin
- zur Darstellung des SN in der Axilla nicht zugelassen, Off-Label
- # SPIO: Superparamagnetic Iron Oxide; Cave: eingeschränkte MRT-Sensitivität in der Nachsorge

## Statement radiotracer/blue dye:

1. Shams S, Lippold K, Blohmer JU, et al. A Pilot Study Evaluating the Effects of Magtrace® for Sentinel Node Biopsy in Breast Cancer Patients Regarding Care Process Optimization, Reimbursement, Surgical Time, and Patient Comfort Compared With Standard Technetium99. Ann Surg Oncol. 2021 Jun;28(6):3232-3240. doi: 10.1245/s10434-020-09280
2. 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.
3. Ditsch N, Rubio IT, Gasparri ML, et al. 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.
4. 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.
5. 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-
6. 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.
7. Straver ME, Meijnen P, van Tienhoven G, et al. Sentinel node identification rate and nodal involvement in the EORTC 10981-22023 AMAROS trial. *Ann Surg Oncol*. 2010 Jul;17(7):1854-61.
  8. Pesek S, Ashikaga T, Krag LE, et al. The false-negative rate of sentinel node biopsy in patients with breast cancer: a meta-analysis. *World J Surg* 2012;36(9): 2239-2251
  9. 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
  10. 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.
  11. 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.
  12. Liu HJ, Sun MS, Liu LY et al. The detection rate of methylene blue combined with another tracer in sentinel lymph node biopsy of early-stage breast cancer: a systematic review and network meta-analysis. *Transl Cancer Res*. 2021 Dec;10(12):5222-5237.

#### Statement Magnetic Tracer

1. Shams S, Lippold K, Blohmer JU, et al. A Pilot Study Evaluating the Effects of Magtrace® for Sentinel Node Biopsy in Breast Cancer Patients Regarding Care Process Optimization, Reimbursement, Surgical Time, and Patient Comfort Compared With Standard Technetium99. *Ann Surg Oncol*. 2021 Jun;28(6):3232-3240. doi: 10.1245/s10434-020-09280
2. 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

#### Statement: pre-operative lymphoscintigraphy

1. Kummel S, Holtschmidt J, Gerber B 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.
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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.
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6. Devarakonda S, Thomas SS, Sen S et al. Sentinel Lymph Node Biopsy in Early Breast Cancer Using Methylene Blue Dye Alone: a Safe, Simple, and Cost-Effective Procedure in Resource-Constrained Settings. *Indian J Surg Oncol*. 2021 Mar;12(1):210-217
7. Hermansyah D, Rahayu Y, Azrah A et al. Accuracy of Methylene Blue Test as Single Technique for Sentinel Lymph Node Biopsy in Early Stages Breast Cancer. *Asian Pac J Cancer Prev*. 2021 Sep 1;22(9):2765-2769.
8. Yang S, Xiang HY, Xin L et al. Retrospective analysis of sentinel lymph node biopsy using methylene blue dye for early breast cancer. *Chin Med J (Engl)*. 2021 Jan 11;134(3):318-325

Statement: Methylene blue / patent blue and anaphylactic reactions:

1. Perenyi M, Barber ZE, Gibson J et al. Anaphylactic Reaction Rates to Blue Dyes Used for Sentinel Lymph Node Mapping: Systematic Review and Meta-analysis. *Ann Surg*. 2021 Jun 1;273(6):1087-1093.
2. Liberale V, Tripodi E, Ottino L, Biglia N. Surgery on breast cancer in pregnancy. *Transl Cancer Res*. 2019 Oct;8(Suppl 5):S493-S502.

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, et al. 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.
3. Zhang X, Li Y, Zhou Y, et al. Diagnostic Performance of Indocyanine Green-Guided Sentinel Lymph Node Biopsy in Breast Cancer: A Meta-Analysis. *PLoS One*. 2016 Jun 9;11(6):e0155597.

4. Xiong L, Gazyakan E, Yang W, et al. Indocyanine green fluorescence-guided sentinel node biopsy: a meta-analysis on detection rate and diagnostic performance. *Eur J Surg Oncol.* 2014 Jul;40(7):843-9.
5. Bargon CA, Huibers A, Young-Afat DA et al. Sentinel Lymph Node Mapping in Breast Cancer Patients Through Fluorescent Imaging Using Indocyanine Green: The INFLUENCE Trial. *Ann Surg.* 2022 Nov 1;276(5):913-920.
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#### Statement: SPIO

1. Shams S, Lippold K, Blohmer J et al. A Pilot Study Evaluating the Effects of Magtrace® for Sentinel Node Biopsy in Breast Cancer Patients Regarding Care Process Optimization, Reimbursement, Surgical Time, and Patient Comfort Compared With Standard Technetium <sup>99</sup>. *Ann Surg Oncol.* 2021;28(6):3232-3240. doi: 10.1245/s10434-020-09280-1
2. 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
3. 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.
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5. 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.
6. Rubio IT, Rodriguez-Revuelto R, Espinosa-Bravo M et al. A randomized study comparing different doses of superparamagnetic iron oxide tracer for sentinel lymph node biopsy in breast cancer: The SUNRISE study. *Eur J Surg Oncol.* 2020 Dec;46(12):2195-2201.
7. Vidya R, Khosla M, Laws S et al. Axillary sentinel lymph node identification using superparamagnetic iron oxide versus radioisotope in early stage breast cancer: The UK SentiMag trial (SMART study). *Surgeon.* 2022 May 9:S1479-666X(22)00063-4. doi: 10.1016/j.surge.2022.04.006. Online ahead of print. PMID: 35551871

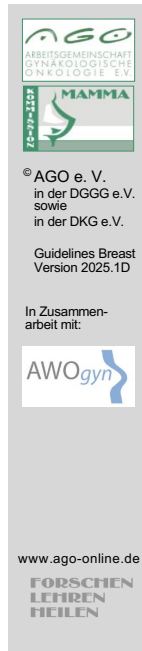
#### Statement: General

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.
2. Mok CW, Tan SM, Zheng Q et al. Network meta-analysis of novel and conventional sentinel lymph node biopsy techniques

in breast cancer. BJS Open. 2019 Mar 25;3(4):445-452.

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.
3. Mok CW, Tan SM, Zheng Q et al. Network meta-analysis of novel and conventional sentinel lymph node biopsy techniques in breast cancer. BJS Open. 2019 Mar 25;3(4):445-452.
4. Liu HJ, Sun MS, Liu LY et al. The detection rate of methylene blue combined with another tracer in sentinel lymph node biopsy of early-stage breast cancer: a systematic review and network meta-analysis. Transl Cancer Res. 2021 Dec;10(12):5222-5237.



## Beginn adjuvanter Therapiemaßnahmen nach primärer Operation

	Oxford		
	LoE	GR	AGO
▪ <b>Zeitnaher Beginn der Systemtherapie und adjuvanten Radiotherapie (RT) nach OP</b>	<b>1b</b>	<b>A</b>	<b>++</b>
▪ <b>Beginn der Chemo- ± AK-Therapie nach OP baldmöglichst, vor Radiotherapie</b>	<b>1b</b>	<b>A</b>	<b>++</b>
▪ <b>Wenn keine Chemo- ± Antikörpertherapie:</b>			
▪ <b>Beginn der adjuvanten RT innerhalb von 6-8 Wochen nach OP</b>	<b>2b</b>	<b>B</b>	<b>++</b>
▪ <b>Beginn der endokrinen Therapie nach OP baldmöglichst</b>	<b>5</b>	<b>D</b>	<b>++</b>
▪ <b>Endokrine Therapie gleichzeitig mit RT</b>	<b>2b</b>	<b>B</b>	<b>+</b>

### 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 AI 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.

Statement start of radiation after surgery

1. Olivotto IA, Lesperance ML, Truong PT et al. Intervals longer than 20 weeks from breast-conserving surgery to radiation therapy are associated with inferior outcome for women with early-stage breast cancer who are not receiving chemotherapy. J Clin Oncol. 2009 Jan 1;27(1):16-23.

## Neoadjuvante systemische Therapie Lokoregionäre Operation (Mamma)

	Oxford		
	LoE	GR	AGO
▪ Prätherapeutische Vorstellung im Tumorboard (z. B. zur Festlegung des OP-Verfahrens)	1a	B	++
▪ 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	++

### Pretherapeutic definition of the definitive surgical procedure

1. EBCTCG. Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials. Lancet Oncol Lancet Oncol. 2018 Jan;19(1):27-39.
2. Bossuyt V, Symmans WF. Standardizing of Pathology in Patients Receiving Neoadjuvant Chemotherapy. Ann Surg Oncol. 2016 Oct;23(10):3153-61.
3. Zdenkowski N et al. A survey of Australian and New Zealand clinical practice with neoadjuvant systemic therapy for breast cancer. Intern Med J. 2016 Jun;46(6):677-83.

### Mark previous tumor region

1. Kaufmann M, et al. Recommendations from an international consensus conference on the current status and future of neoadjuvant systemic therapy in primary breast cancer. Ann Surg Oncol 2012: 19; 1508

### Surgery

1. Kaufmann M, et al. Recommendations from an international consensus conference on the current status and future of neoadjuvant systemic therapy in primary breast cancer. Ann Surg Oncol 2012: 19; 1508

#### Microscopically clear margins

1. Kaufmann M, et al. Recommendations from an international consensus conference on the current status and future of neoadjuvant systemic therapy in primary breast cancer. Ann Surg Oncol 2012; 19; 1508

#### Tumor resection according to imaging result

1. Kaufmann M, et al. Recommendations from an international consensus conference on the current status and future of neoadjuvant systemic therapy in primary breast cancer.. Ann Surg Oncol 2012; 19; 1508

## Neoadjuvante systemische Therapie

### Indikationen für Mastektomie

	Oxford		
	LoE	GR	AGO
▪ <b>Positive Absetzungsränder trotz mehrfacher Nachresektion</b>	<b>3b</b>	<b>C</b>	<b>++</b>
▪ <b>Radiotherapie nicht durchführbar</b>	<b>5</b>	<b>D</b>	<b>++</b>
▪ <b>Bei einer klinisch kompletten Remission</b>			
▪ <b>Inflammatorisches Mammakarzinom (bei pCR)</b>	<b>2b</b>	<b>C</b>	<b>+/-</b>
▪ <b>Multizentrisches Mammakarzinom</b>	<b>2b</b>	<b>C</b>	<b>+/-</b>
▪ <b>cT4a-c Mammakarzinom</b>	<b>2b</b>	<b>B</b>	<b>+/-</b>

#### Positive margins after repeated excisions

1. Kaufmann M, et al. Recommendations from an international consensus conference on the current status and future of neoadjuvant systemic therapy in primary breast cancer. Ann Surg Oncol 2012; 19; 1508
2. Dawood S, et al. International expert panel on inflammatory breast cancer: consensus statement for standardized diagnosis and treatment. Ann Oncol 2011; 22; 515

#### Radiotherapy not feasible

1. Kaufmann M, et al. Recommendations from an international consensus conference on the current status and future of neoadjuvant systemic therapy in primary breast cancer. Ann Surg Oncol 2012; 19; 1508

#### In case of clinical complete response:

##### Inflammatory breast cancer in case of pCR

1. Dawood S, et al. International expert panel on inflammatory breast cancer: consensus statement for standardized diagnosis and treatment. Ann Oncol 2011; 22; 515
2. Brzezinska M, Williams LJ, Thomas J et al.: Outcomes of patients with inflammatory breast cancer treated by breast-conserving surgery. Breast Cancer Res Treat 2016;160(3):387-91.

#### Multicentric lesions

1. Ataseven B, 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 20215;;22(4):1118-1127.

#### cT4a-c breast cancer

1. Ataseven B, 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 20215;;22(4):1118-1127.

## Neoadjuvante systemische Therapie Zeitablauf von Diagnosestellung und Operation und Radiotherapie

	Oxford		
	LoE	GR	AGO
<b>Zeitpunkt der Operation nach NACT</b>			
▪ 4-8 Wochen nach dem letzten Chemotherapiezyklus	2a	B	++
<b>Radiotherapie innerhalb von 2 Monaten nach der Operation</b>	2b	B	++

### Initiation of chemotherapy after histologic diagnosis

1. de Melo Gagliato D, Lei X, Giordano SH, et al. Impact of Delayed Neoadjuvant Systemic Chemotherapy on Overall Survival Among Patients with Breast Cancer. *Oncologist*. 2020;25(9):749-757. doi: 10.1634/theoncologist.2019-0744.
2. Hanna TP, King WD, Thibodeau S, et al. Mortality due to cancer treatment delay: systematic review and meta-analysis. *BMJ* 2020 Nov 4;371:m4087.doi: 10.1136/bmj.m4087

### Time between surgery and last chemotherapy

1. Cullinane C, Shrestha A, Al Maksoud A, et al. Optimal timing of surgery following breast cancer neoadjuvant chemotherapy: A systematic review and meta-analysis. *J Surg Oncol*. 2021 Jul;47(7):1507-1513.
2. Suleman K, Almalik O, Haque E et al. Does the Timing of Surgery after Neoadjuvant Therapy in Breast Cancer Patients Affect the Outcome? *Oncology*. 2020;98(3):168-173.
3. Grubstein A, Rapson Y, Stemmer SM et al. Timing to imaging and surgery after neoadjuvant therapy for breast cancer. *Clin Imaging*. 2020;71:24-28..
4. Sanford RA, Lei X, Barcenas CH et al. Impact of Time from Completion of Neoadjuvant Chemotherapy to Surgery on Survival Outcomes in Breast Cancer Patients. *Ann Surg Oncol* 2016;23(5):1515-21.

Radiotherapy 2 mths after surgery BCS

1. Silva SB, Pereira AAL, Marta GN, et al. Clinical impact of adjuvant radiation therapy delay after neoadjuvant chemotherapy in locally advanced breast cancer. *Breast*. 2018;38:39-44. doi: 10.1016/j.breast.2017.11.012