Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Guidelines Breast
Version 2024.1D

In Zusammenarbeit mit:

AWOgyn

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FORSCHEN
LEHREN
HEILEN

Operative Therapie des Mammakarzinoms unter onkologischen Aspekten

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in der DGGG e.V.
sowie
in der DKG e.V.

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FORSCHEN
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- **Versionen 2002–2023:**
  Banys-Paluchowski / Bauerfeind / Blohmer / Böhme / Brunnert / Costa / Ditsch / Fallenberg / Fersis / Friedrich / Gerber / Hanf / Janni / Junkermann / Kaufmann / Kühn / Kümmel / Möbus/ Nitz / Rezai / Simon / Solomayer / Thomssen / Thill / Untch / Wöckel

- **Version 2024:**
  Rody / Schütz

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: ++

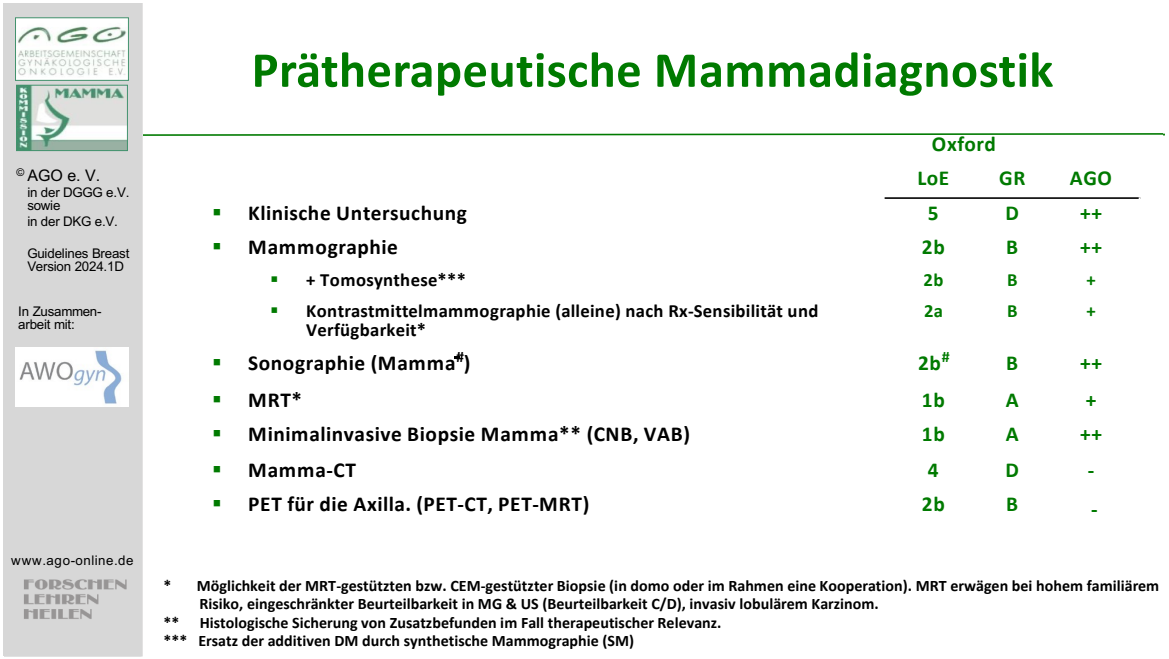
Operative Therapieentscheidungen sollten im Kontext eines multimodalen Therapiekonzeptes getroffen werden, insbesondere sollte der Verzicht auf diagnostische Maßnahmen (z. B. SLNE) im Rahmen einer präoperativen, interdisziplinären Tumorkonferenz beschlossen werden.

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
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;3(12):e2030072. doi: 10.1001/jamanetworkopen.2020.30072. PMID: 33315115; PMCID: PMC7737088.
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



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.
3. 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. 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.
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)).
18. Eisen, A., G. G. Fletcher, S. Fienberg, et al (2023). "Breast Magnetic Resonance Imaging for Preoperative Evaluation of Breast Cancer: A Systematic Review and Meta-Analysis." Can Assoc Radiol J: 8465371231184769.

Reviews CEM:

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, et al. Contrast-enhanced mammography: past, present, and future. Clin Imaging. 2021;69:269-79.
6. Lobbes MBI, Heuts EM, Moossdorff M, van Nijnatten TJA. Contrast enhanced mammography (CEM) versus magnetic resonance imaging (MRI) for staging of breast cancer: The pro CEM perspective. (1872-7727 (Electronic)).
7. 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.
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.
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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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multicentric study. Acta Radiol. 2020;61(10):1335-42.

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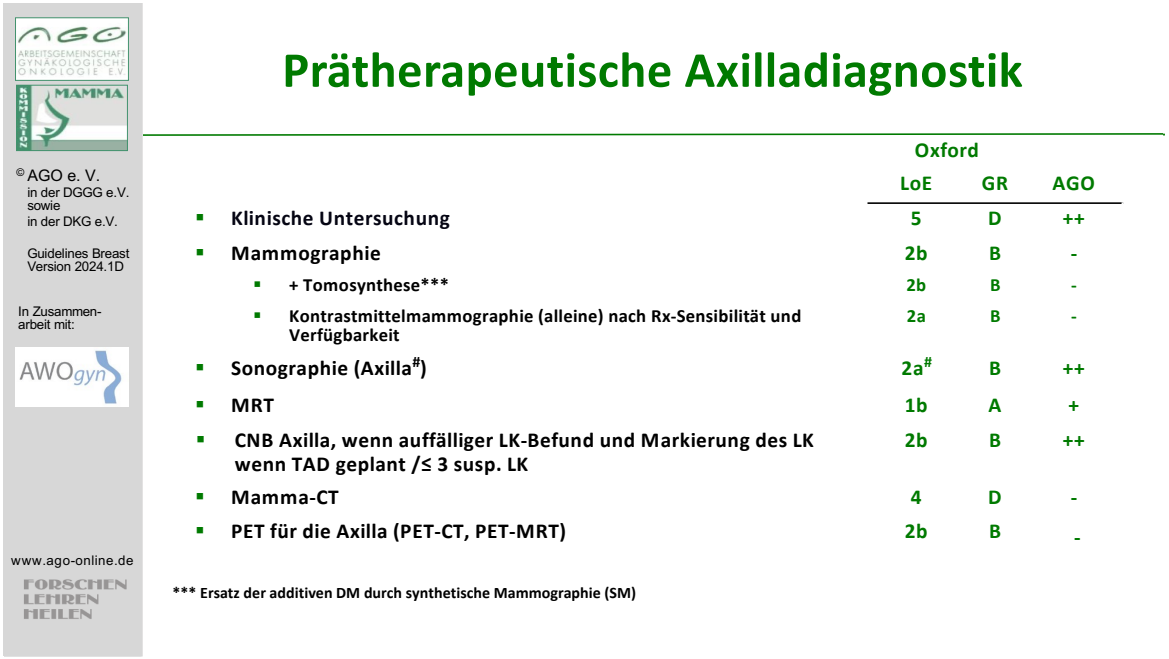
12. Sumkin JH, Berg WA, Carter GJ, et al. Diagnostic Performance of MRI, Molecular Breast Imaging, and Contrast-enhanced Mammography in Women with Newly Diagnosed Breast Cancer. Radiology. 2019;293(3):531-40.
13. Sung JS, Lebron L, Keating D, et al. Performance of Dual-Energy Contrast-enhanced Digital 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.

Brust-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.



Prätherapeutische Axilladiagnostik

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

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

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.

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Brust-CT:

1. Uhlig, J. A.-O., A. Uhlig, L. Biggemann, U. Fischer, J. Lotz and S. Wienbeck "Diagnostic accuracy of cone-beam breast computed

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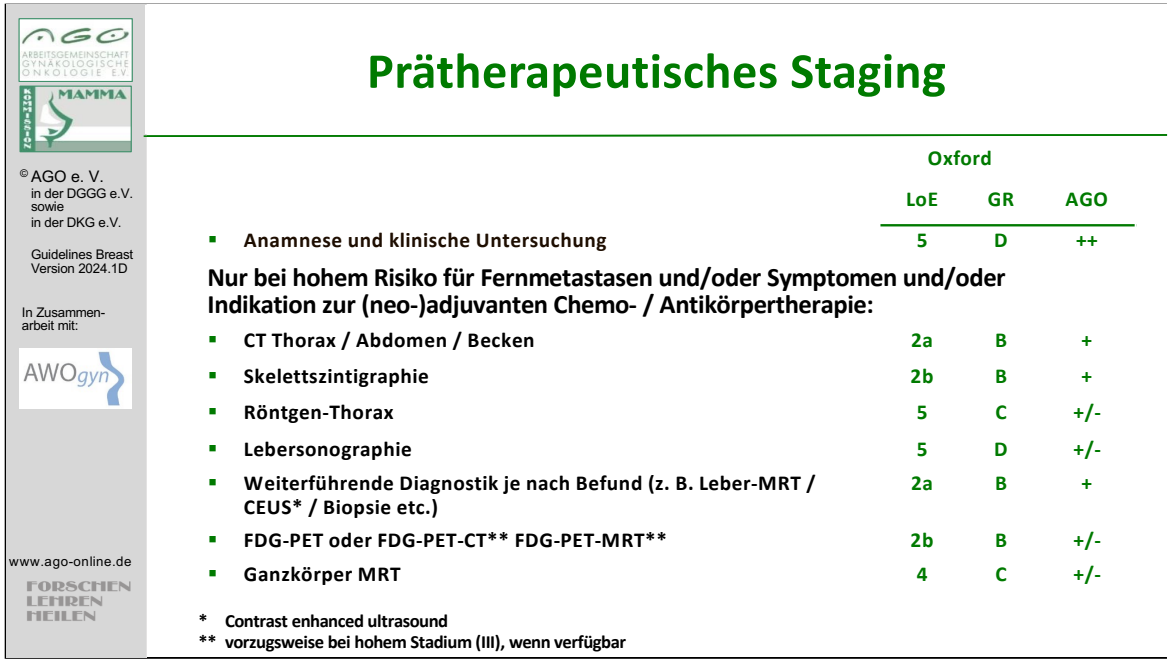
Conventional Imaging, MRI and 18F-FDG PET/MRI for N and M Staging in Patients with Newly Diagnosed Breast Cancer. Morawitz J, Bruckmann NM, Jannusch K, Dietzel F, Milosevic A, Bittner AK, Hoffmann O, Mohrmann S, Ruckhäberle E, Häberle L, Fendler WP, Herrmann K, Giesel FL, Antoch G, Umutlu L, Kowall B, Stang A, Kirchner J.Cancers (Basel). 2023 Jul 17;15(14):3646. doi: 10.3390/cancers15143646.PMID: 37509307 Free PMC article.



Prätherapeutisches Staging

	Oxford LoE	Oxford 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 / Becken	2a	B	+
▪ Skelettszintigraphie	2b	B	+
▪ Röntgen-Thorax	5	C	+/-
▪ Lebersonographie	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**	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.
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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

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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

<u>Statement: lumpectomy – mastectomy</u>

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Guidelines Breast
Version 2024.1D

In Zusammenarbeit mit:

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FORSCHEN
LEHREN
HEILEN

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

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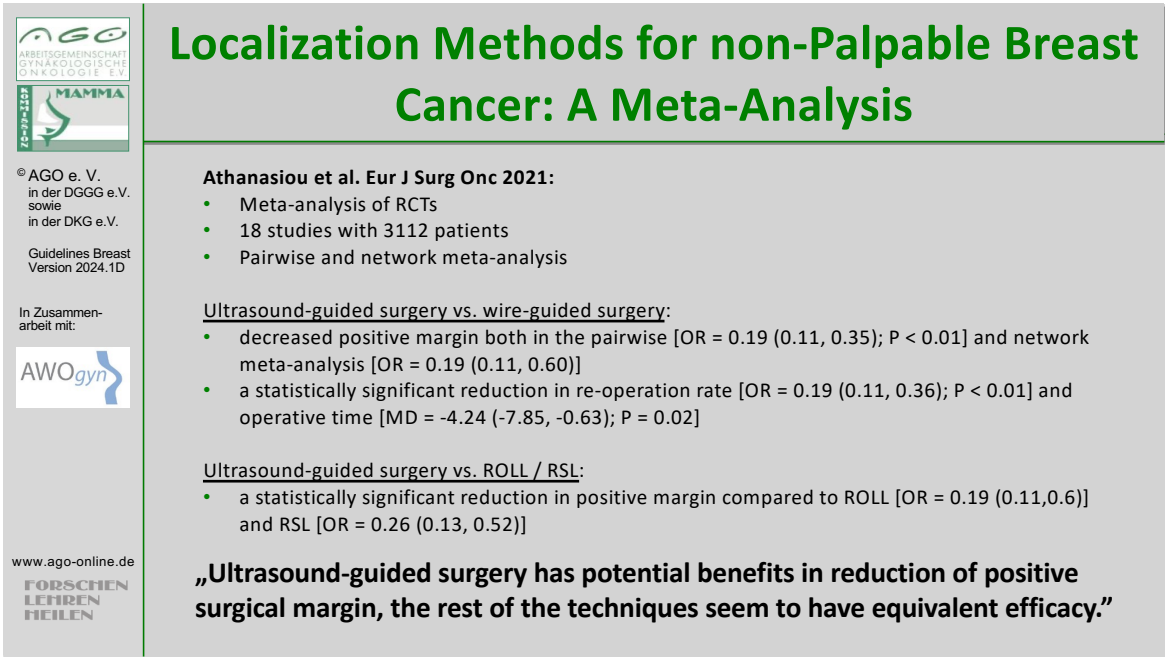
ROLL: for RCTs see meta-analyses above



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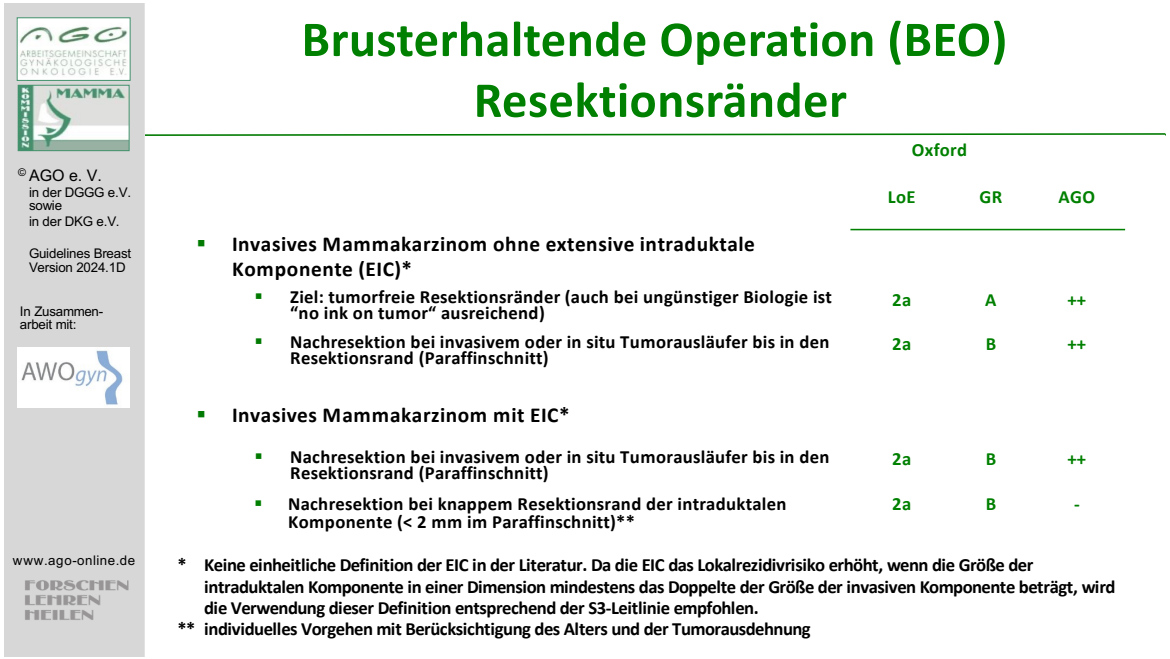

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Extensive intraductal component:

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 Schnittrandbeurteilung (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
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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. Indian J Cancer 55:361-365. 10.4103/ijc.IJC_2_18

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.
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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.
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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-Vroegindeweij 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, Odrazka 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
▪ **Multifokalität / Multizentrizität (Voraussetzung: R0-Resektion aller Herde)**	2b	B	+
▪ **Histologisch befallene Resektionsränder trotz wiederholter Nachresektion**	2b	B	--
▪ **Inflammatorisches Mammakarzinom**	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.
6. Boughey JC, Rosenkranz KM, Ballman KV et al., Impact of breast conservation therapy on local recurrence in patients with multiple ipsilateral breast cancer - results from ACOSOG Z11102 (Alliance). SABCS 2022, GS4-01

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

	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)	2b	B	--
▪ cN0 pN1 (sn) (T1/2, < 3 SN+*, BEO + RT + adäquate Systemtherapie)	1b	A	-
▪ cN0 pN1 (sn) und Mastektomie (keine Radiotherapie der Thoraxwand)	1b	B	+**
▪ cN0 pN1 (sn) und Mastektomie (T1/2, < 3 SN+, Radiotherapie der Thoraxwand)	5	D	+/-**
▪ ALND indiziert, aber nicht möglich			
▪ Radiatio analog AMAROS-Studie (evaluiert für cN0 pN1sn)	1b	B	+

* ACOSOG Z0011 Studie ohne klare Definition eines extrakapsulären Wachstums
** Studienteilnahme empfohlen

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 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, Zurrida 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.
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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 2018268(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) LoE 1b B AGO +*

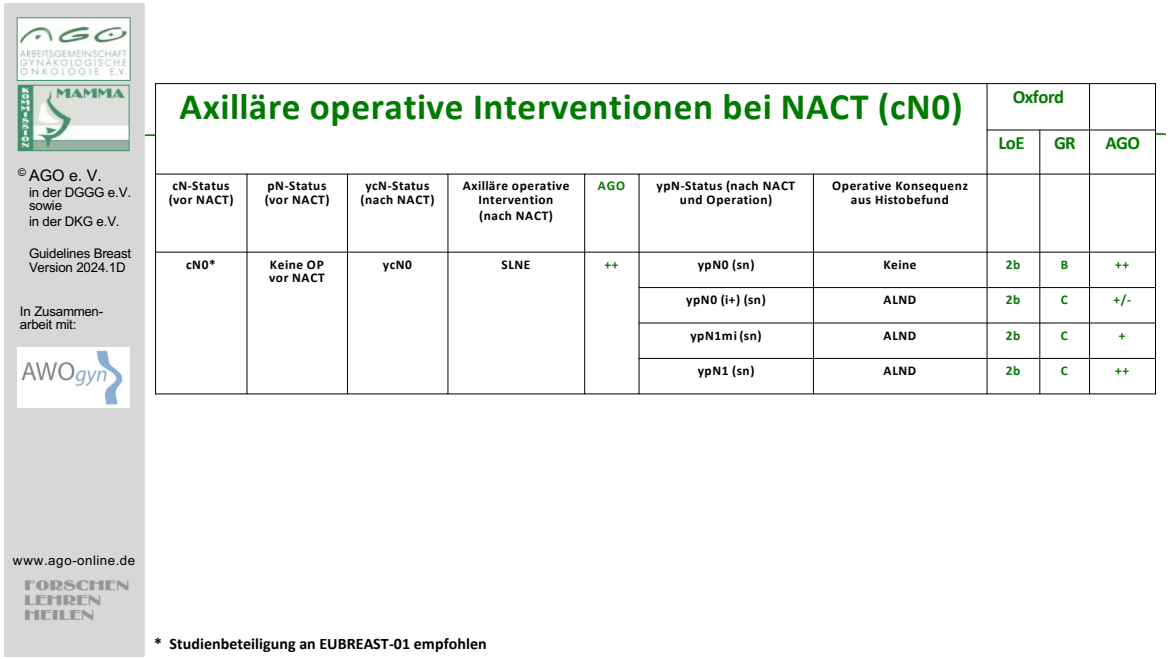
1. Cody HS 3rd1. Extending ACOSOG Z0011 to Encompass Mastectomy: What Happens Without RT? Ann Surg Oncol. 2017 Mar;24(3):621-623.

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.

ACOSOG Z0011 ohne klare Definition des extrakapsulären Wachstums: A, Giuliano: persönliche Kommunikation 04. Januar 2023



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Guidelines Breast
Version 2024.1D

In Zusammenarbeit mit:

AWOgyn

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FORSCHEN
LEHREN
HEILEN

Axilläre operative Interventionen bei NACT (cN0)

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	Oxford LoE	Oxford GR	AGO
cN0*	Keine OP vor NACT	ycN0	SLNE	++	ypN0 (sn)	Keine	2b	B	++
					ypN0 (i+) (sn)	ALND	2b	C	+/-
					ypN1mi (sn)	ALND	2b	C	+
					ypN1 (sn)	ALND	2b	C	++

* Studienbeteiligung an EUBREAST-01 empfohlen

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
2. Reimer TS, Nekljudova V, Loibl, S et al. Restricted axillary staging in clinically and sonographically node-negative early invasive breast cancer (c/i t1-2) in the context of breast concerving therapy: First results following commencement of the intergroup-sentinel-mamma (insema) trial. Geburtsh Frauenheilk 2017, 77, 149-157
3. Gion M, Pérez-García JM, Llombart-Cussac A et al. Surrogate endpoints for early-stage breast cancer: a review of the state of the art, controversies, and future prospects. Ther Adv Med Oncol 2021, 13:17588359211059587.
4. Chiec L, Shah AN. Risk-based Approaches for Optimizing Treatment in HER2-Positive Early Stage Breast Cancer. Semin Oncol 2020, 47:249-258.
5. Cortazar P, Geyer CE Jr. Pathological complete response in neoadjuvant treatment of breast cancer. Ann Surg Oncol 2015, 22, 1441-1446.
6. 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 ten randomised trials. Lancet Oncol 2018, 19, 27-39.
7. Cirier J, Body G, Jourdan ML et al. Impact of pathological complete response to neoadjuvant chemotherapy in invasive breast cancer according to molecular subtype. Gynecologie, obstetrique, fertilite & senologie 2017, 45, 535-544.
8. Gustavo Werutsky G, Untch M, Hanusch C, Fasching PA, Blohmer JU, Seiler S, Denkert C, Tesch H, Jackisch C, Gerber B et al.

Locoregional recurrence risk after neoadjuvant chemotherapy: A pooled analysis of nine prospective neoadjuvant breast cancer trials. Eur J Cancer 2020, 130, 92-101.
9. Kuehn T, Bauerfeind I, Fehm T et al. Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (sentina): A prospective, multicentre cohort study. Lancet Oncol 2013, 14, 609-618.
10. Boughey JC, Suman VJ, Mittendorf EA et al. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: The acosog z1071 (alliance) clinical trial. Jama 2013, 310, 1455-1461.
11. Carter S, Neuman H, Mamounas EP et al. Debating the optimal approach to nodal management after pathologic complete response to neoadjuvant chemotherapy in patients with breast cancer. American Society of Clinical Oncology educational book. American Society of Clinical Oncology. Annual Meeting 2019, 39, 42-48.
12. Simons JM, van Nijnatten TJA, van der Pol CC et al. Diagnostic accuracy of different surgical procedures for axillary staging after neoadjuvant systemic therapy in node-positive breast cancer: A systematic review and meta-analysis. Ann Surg 2019, 269, 432-442.
13. Tee, S.R.; Devane, L.A.; Evoy, D.; et al. E.W. Meta-analysis of sentinel lymph node biopsy after neoadjuvant chemotherapy in patients with initial biopsy-proven node-positive breast cancer. Br J Surg 2018, 105, 1541-1552.
14. Schneeweiss A, Mobus V, Tesch H et al. Intense dose-dense epirubicin, paclitaxel, cyclophosphamide versus weekly paclitaxel, liposomal doxorubicin (plus carboplatin in triple-negative breast cancer) for neoadjuvant treatment of high-risk early breast cancer (geparocto-gbg 84): A randomised phase iii trial. Eur J Cancer 2019, 106, 181-192.
15. Barron AU, Hoskin TL, Day CN et al. Association of low nodal positivity rate among patients with erbb2-positive or triple-negative breast cancer and breast pathologic complete response to neoadjuvant chemotherapy. JAMA surgery 2018.
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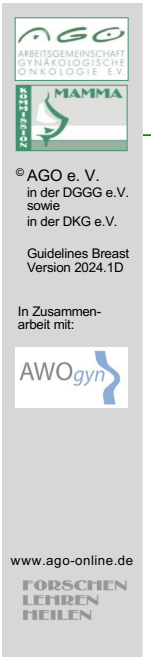
Statement: SLNE after NACT

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.



Axilläre operative Interventionen bei NACT (cN+)

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	Oxford LoE	Oxford GR	AGO
cN+*	pN+CNB	ycN0	ALND	+	ypN0 / ypN+	Keine	2b	B	++
			TAD	+	ypN0	Keine	2b	B	+
					ypN0 (i+)	ALND	2b	B	+/-
					ypN+ inkl. ypN1mi	ALND	2b	B	+
			SLNE	+/-	ypN0	Keine	2b	B	+/-
					ypN0 (i+)	ALND	2b	B	+/-
					ypN+ inkl. ypN1mi	ALND	2b	B	+
			TLNE	+/-	ypN0	keine	2b	B	+/-
					ypN0 (i+)	ALND	3b	B	+/-
					ypN+ inkl. ypN1mi	ALND	3b	B	+
		ycN+**	ALND	++	ypN0 / ypN+	Keine	2b	B	++

*** Studienbeteiligung an AXSANA empfohlen; **Cave: In 30,3% falsch-positive Befunde, ggf. CNB**

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Statement: SLNE after NACT

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involving 3,398 patients. Am J Surg. 2016 Nov;212(5):969-981.

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. Geburtsh Frauenheilk 2022, online

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
▪ Stanzbioptische 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	5	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

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Statement: TLNE alone:

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Sentinel-Lymphknoten-Exzision (SLNE)
Indikationen I

Guidelines Breast
Version 2024.1D

In Zusammenarbeit mit:

AWOgyn

www.ago-online.de

FORSCHEN
LEHREN
HEILEN

	Oxford		
	LoE	GR	AGO
▪ Klinisch / sonographisch neg. Axilla (cN0)	1b	A	++
▪ cT 1–2	2b	A	++
Verzicht auf SLNE analog SOUND-Studie	1b	B	+
▪ cT 3–4c	3b	B	+
▪ Multifokales / multizentrisches Mammakarzinom	2b	B	+
▪ DCIS			
▪ Mastektomie	3b	B	+
▪ BET	3b	B	-
▪ DCIS beim Mann	5	D	+/-
▪ Mammakarzinom des Mannes	2b	B	+
▪ Verzicht auf axilläre Intervention bei der älteren Patientin (≥ 70 J., Co-Morbiditäten, pT1, HR+)	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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experience of the European institute of oncology on 854 patients in 10 years. Ann Surg. 2008 Feb;247(2):315-9
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<u>Statement: preoperative FNA / CNB (core needle biopsy) of suspicious lymph nodes</u>

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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Statement: Multifocal / multicentric MaCa

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Statement: DCIS

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Statement: Male

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

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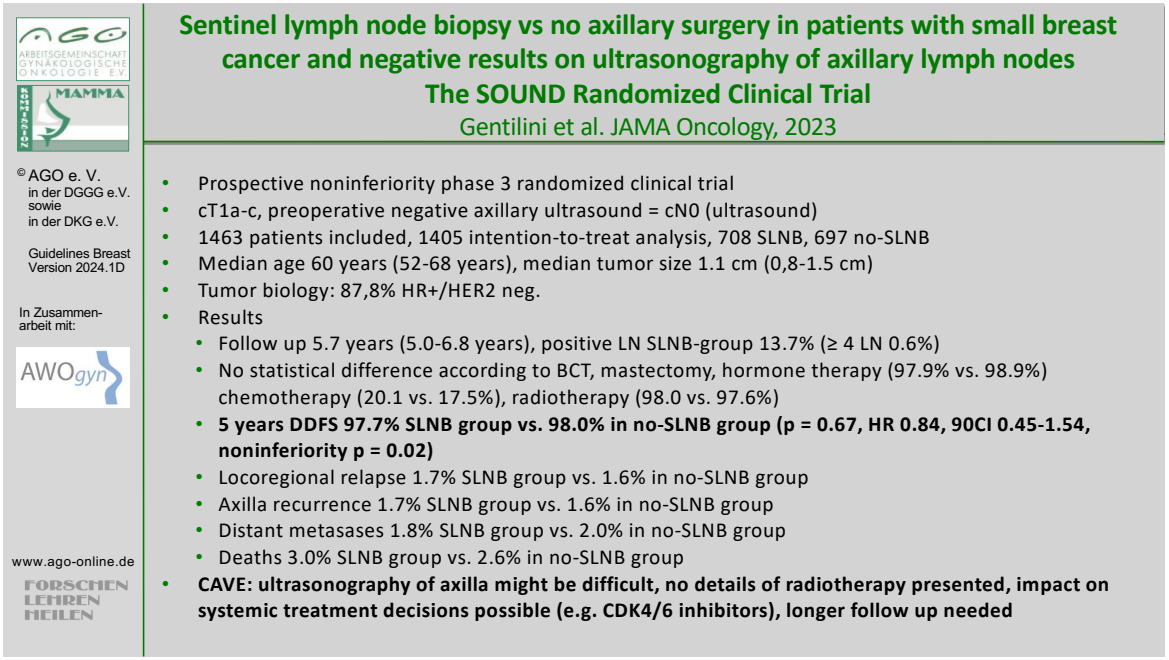

1. Gentilini, Botteri, Sangalli et al., Sentinel Lymph Node Biopsy vs No Axillary Surgery in Patients With Small Breast Cancer and Negative Results on Ultrasonography of Axillary Lymph Nodes: The SOUND Randomized Clinical Trial, JAMA Oncol. 2023 Nov 1;9(11):1557-1564

Sentinel-Lymphknoten-Exzision (SLNE)
Indikationen II

	Oxford		
	LoE	GR	AGO
▪ Während Schwangerschaft oder Stillzeit (nur ^{99m}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.
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Statement: prophylactic mastectomy

1. Dupont et al. The role of sentinel lymph node biopsy in women undergoing prophylactic mastectomy. Am J Surg 2000 Oct;180(4):274-7
2. Soran A et al.: Is routine sentinel lymph node biopsy indicated in women undergoing contralateral prophylactic mastectomy? Magee-Womens Hospital experience. Ann Surg Oncol 2007 Feb;14(2):646-51.
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
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4. Ruano R, Ramos M, Garcia-Talavera JR: Staging the axilla with selective sentinel node biopsy in patients with previous excision of non-palpable and palpable breast cancer. Eur J Nucl Med Mol Imaging. 2008 Jul;35(7):1299-304.

Statement: Ipsilateral breast recurrence after prior BCS and prior SLNB

1. Mattia Intra M,Triro G, Viale G: Second Biopsy of Axillary Sentinel Lymph Node for Reappearing Breast Cancer After Previous Sentinel Lymph Node Biopsy. Ann Surg Oncol. 2005;12(11):895-9
2. Intra et al. Second axillary sentinel node biopsy for ipsilateral breast tumour recurrence. Br J Surg 2007 Oct;94(10):1216-9
3. Schrenk P et al. Lymphatic mapping in patients with primary or recurrent breast cancer following previous axillary surgery. Eur J Surg Oncol. 2008 Aug;34(8):851-6.
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2008;29:565-567
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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. Breast Cancer Res Treat. 2020 Feb;180(1):207-217.
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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 mammaplasty 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

	Oxford		
	LoE	GR	AGO
▪ ^{99m}Tc Kolloid	1a	A	++
▪ Präoperative Lymphszintigraphie (diagnostischer Zugewinn limitiert, aber gesetzlich vorgeschrieben)*	1b	A	+
▪ Patentblau	1a	A	+/-
▪ Indocyaningrün (ICG)°	2a	B	+
▪ SPIO#	2a	B	+
▪ Methylenblau	2a	B	+/-

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

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.
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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.
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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
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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.
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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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8. Yang S, Xiang HY, Xin Let 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: Methylen blue / patent blue and anaphylactic reactions:

1. Perenyei 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.
6. Kedrzycki MS, Leiloglou M, Ashrafian H et al. Meta-analysis Comparing Fluorescence Imaging with Radioisotope and Blue Dye-Guided Sentinel Node Identification for Breast Cancer Surgery. Ann Surg Oncol. 2021 Jul;28(7):3738-3748.

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 ^{99}. Ann Surg Oncol. 2021;28(6):3232-3240. doi: 10.1245/s10434-020-09280-1
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4. 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.
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.
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7. Vidya R, Khosla M, Laws S et al. Axillary sentinel lymph node identification using superparamagnetic iron oxideversus 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.

Operatives Vorgehen im Rahmen der neoadjuvanten Therapie

Guidelines Breast
Version 2024.1D

In Zusammenarbeit mit:

AWOgyn

www.ago-online.de

FORSCHEN
LEHREN
HEILEN

	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.

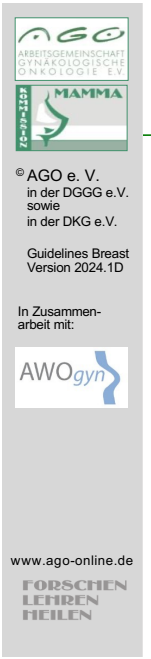
Statement: operation and : tumor resection in new margins

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



Beginn adjuvanter Therapiemaßnahmen nach primärer Operation

	Oxford		
	LoE	GR	AGO
▪ **Zeitnaher Beginn der Systemtherapie und adjuvanten Radiotherapie (RT) nach OP**	1b	A	++
▪ **Beginn der Chemo- ± AK-Therapie nach OP baldmöglichst, vor Radiotherapie**	1b	A	++
▪ **Wenn keine Chemo- ± 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 RT	2b	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, Marczewska 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.
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Statement start of radiation after surgery

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