Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Guidelines Breast
Version 2022.1D

In Zusammenarbeit mit:

AWOgyn

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Operative Therapie des Mammakarzinoms unter onkologischen Aspekten

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In Zusammenarbeit mit:

AWOgyn

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

- **Version 2022:**
  Banys-Paluchowski / Gerber

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FORSCHEN
LEHREN
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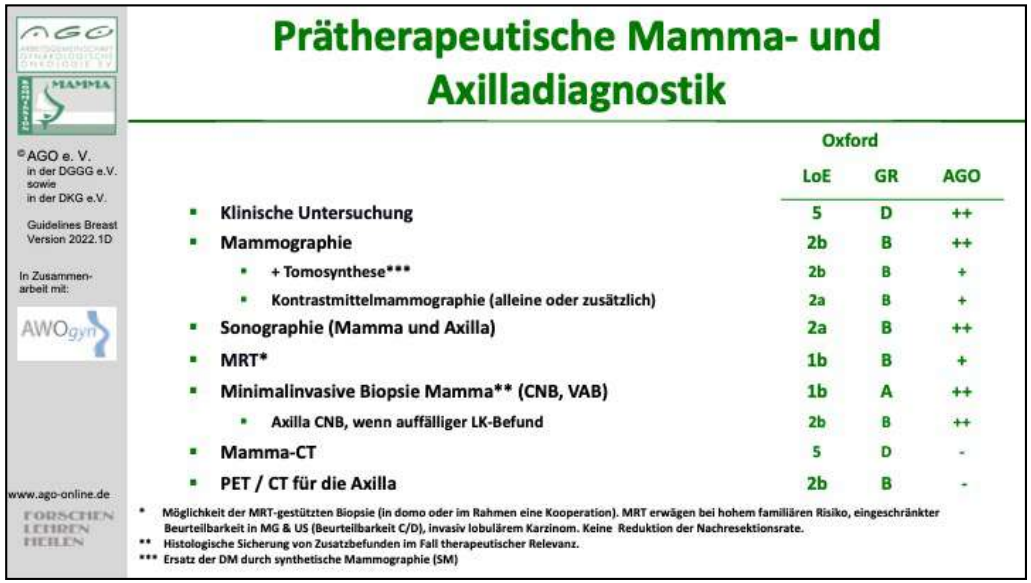
Delay of surgical therapy:

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.

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.
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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.
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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
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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
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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.
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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
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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.

<u>Reviews CESM:</u>

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.

CESM Originalarbeiten:

1. Luczynska, E., et al., Comparison of the Mammography, Contrast-Enhanced Spectral Mammography and Ultrasonography in a Group of 116 patients. Anticancer Res, 2016. 36(8): p. 4359-66.
2. Fallenberg, E.M., et al., Contrast-enhanced spectral mammography: Does mammography provide additional clinical benefits or can some radiation exposure be avoided? Breast Cancer Res Treat, 2014. 146(2): p. 371-81.
3. Tennant, S.L., et al., Contrast-enhanced spectral mammography improves diagnostic accuracy in the symptomatic setting. Clin Radiol, 2016. 71(11): p. 1148-55.
4. Fallenberg, E.M., et al., Contrast-enhanced spectral mammography vs. mammography and MRI - clinical performance in a multi-reader evaluation. Eur Radiol, 2017. 27(7): p. 2752-2764.
5. Jochelson, M.S., et al., Comparison of screening CEDM and MRI for women at increased risk for breast cancer: A pilot study. Eur J Radiol, 2017. 97: p. 37-43.
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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).
9. Sogani J, Mango VL, Keating D, et al. Contrast-enhanced mammography: past, present, and future. Clin Imaging. 2021;69:269-79.
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, Bandos AI, Chough DM, Ganott MA, et al. Diagnostic Performance of MRI, Molecular Breast Imaging, and Contrast-enhanced Mammography in Women with Newly Diagnosed Breast Cancer. Radiology. 2019;293(3):531-40.

13. Sung JS, Lebron L, Keating D, 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.
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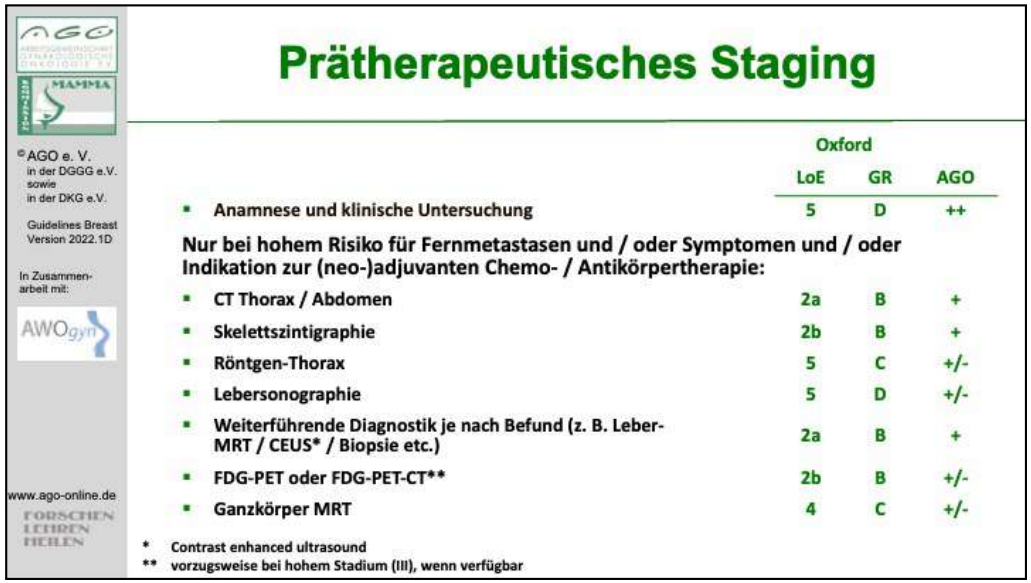
15. Le Boulc'h M, Gilhodes J, Steinmeyer Z, et al. Pretherapeutic Imaging for Axillary Staging in Breast Cancer: A Systematic Review and Meta-Analysis of Ultrasound, MRI and FDG PET. Clin Med. 2021 Apr 6;10(7):1543. doi: 10.3390/jcm10071543.PMID: 33917590 Free PMC article. Review.



Prätherapeutisches Staging

	Oxford LoE	GR	AGO
▪ Anamnese und klinische Untersuchung	5	D	++
Nur bei hohem Risiko für Fernmetastasen und / oder Symptomen und / oder Indikation zur (neo-)adjuvanten Chemo- / Antikörpertherapie:			
▪ CT Thorax / Abdomen	2a	B	+
▪ Skelettszintigraphie	2b	B	+
▪ 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**	2b	B	+/-
▪ Ganzkörper MRT	4	C	+/-

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

Statement: history and physical examination

1. GCP

Statement: high metastatic potential / symptoms

1. Rutgers, EJ et al: Quality control in the locoregional treatment of breast cancer (2001) EJC 37: 447-453
2. Gerber B, Seitz E, Muller H et al: Perioperative screening for metastatic disease is not indicated in patients with primary breast cancer and no clinical signs of tumor spread. Breast Cancer Res Treat 82:29-37; 2003
3. Schneider C, Fehr MK, Steiner RA et al: Frequency and distribution pattern of distant metastases in breast cancer patients at the time of primary presentation Arch Gynecol Obstet. 2003 Nov;269(1):9-12.
4. Isasi CR, Moadel RM, Blaufox MD. A meta-analysis of FDGPET for the evaluation of breast cancer recurrence and metastases. Breast Cancer Res Treat 2005;90(2):105–12.
5. Schmidt GP, Baur-Melnyk A, Haug A, et al.: Comprehensive imaging of tumor recurrence in breast cancer patients using whole-body MRI at 1.5 and 3 T compared to FDG–PET–CT. European Journal of Radiology 2008; 65, 47–58.
6. Shie P, Cardarelli R, Brandon D et al: Meta-analysis: comparison of F-18 Fluorodeoxyglucose-positron emission tomography and bone scintigraphy in the detection of bone metastases in patients with breast cancer. Clin Nucl Med. 2008 Feb;33(2):97-101.
7. Barrett T, Bowden DJ, Greenberg DC et al.: Radiological staging in breast cancer: which asymptomatic patients to image and how. British Journal of Cancer 2009; 101, 1522 – 1528.
8. Rong J, Wang S, Ding Q, et al. Comparison of 18 FDG PET-CT and bone scintigraphy for detection of bone metastases in breast cancer patients. A meta-analysis. Surg Oncol. 2013 Jun;22(2):86-91

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14. NCCN 2019: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Breast Cancer. NCCN Evidence BlocksTM. Version 3.2019 – September 6, 2019. https://www.nccn.org/professionals/physician_gls/pdf/breast_blocks.pdf. Download Jan 19, 2020.
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16. Zhang L, Zhang L, Wang H, et al. Diagnostic performance of contrast-enhanced ultrasound and magnetic resonance imaging for detecting colorectal liver metastases: A systematic review and meta-analysis. Dig Liver Dis. 2019 Sep;51(9):1241-1248.
17. Ulaner GA, Castillo R, Goldman DA, et al. ^{18}F-FDG-PET/CT for systemic staging of newly diagnosed triple-negative breast cancer. Eur J Nucl Med Mol Imaging 2016; 43:1937–1944
18. Ulaner GA, Castillo R, Wills J, et al. ^{18}F-FDG-PET/CT for systemic staging of patients with newly diagnosed ER-positive and HER2-positive breast cancer. Eur J Nucl Med Mol Imaging 2017
19. Groheux D, Giacchetti S, Espié M, et al. The yield of ^{18}F-FDG PET/CT in patients with clinical stage IIA, IIB, or IIIA breast cancer: a prospective study. J Nucl Med 2011; 52:1526–1534
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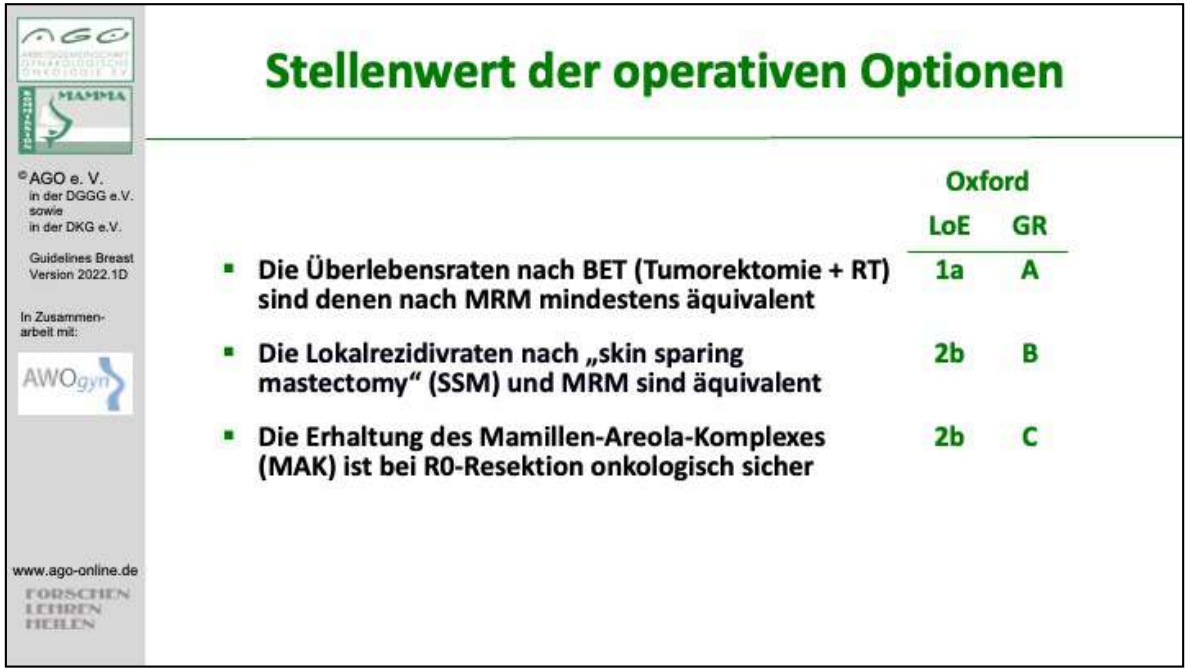
26. https://healthcare-quality.jrc.ec.europa.eu/european-breast-cancer-guidelines/staging-breast-cancer



Statement: lumpectomy – mastectomy

1. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer (2002) N Engl J Med 347:1233-1241
2. Veronesi U, Cascinelli N, Mariani L et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. NEJM 2002 Oct 17;347(16):1227-32
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4. de Boniface J, Szulkin R, Johansson ALV. Survival After Breast Conservation vs Mastectomy Adjusted for Comorbidity and Socioeconomic Status: A Swedish National 6-Year Follow-up of 48 986 Women. JAMA Surg 2021;156(7):628-637. doi: 10.1001/jamasurg.2021.1438
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6. Hofvind S, Holen A, Aas T et al. Women treated with breast conserving surgery do better than those with mastectomy independent of detection mode, prognostic and predictive tumor characteristics. Eur J Surg Oncol. 2015;41(10):1417-22. doi: 10.1016/j.ejso.2015.07.002.

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Statement: skin sparing mastectomy

1. Carlson GW, Bostwick J, Styblo TM et al. Skin-sparing mastectomy. Oncologic and reconstructive considerations. Ann Surg 1997; 225:570-575.
2. Kroll SS, Schusterman MA, Tadjalli HE et al. Risk of recurrence after treatment of early breast cancer with skin- sparing mastectomy Ann Surg Oncol 1997; 4:193-197.
3. Slavin SA, Schnitt SJ, Duda RB et al. Skin-sparing mastectomy and immediate reconstruction: oncologic risks and aesthetic results in patients with early-stage breast cancer. Plast Reconstr Surg 1998; 102:49-62.
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5. Rivadeneira D, Simmons RM, Fish SK et al. Skin-sparing mastectomy with immediate breast reconstruction: a critical analysis of local recurrence. Cancer 2000; 6:331-335.
6. Foster et al. Skin-sparing mastectomy and immediate breast reconstruction: a prospective cohort study for the treatment of advanced stages of breast carcinoma. Ann Surg Oncol 2002 Jun;9(5):462-6
7. Greenway RM, Schlossberg L, Dooley WC. Fifteen-year series of skin-sparing mastectomy for stage 0 to 2 breast cancer. Am J Surg 2005; 190:918-922.
8. Howard MA, Polo K, Pusic AL et al. Breast cancer local recurrence after mastectomy and TRAM flap reconstruction: incidence and treatment options. Plast Reconstr Surg 2006; 117:1381-1386.
9. Patani N, Devalia H, Anderson A et al. Oncological safety and patient satisfaction with skin-sparing mastectomy and immediate breast reconstruction. Surg Oncol 2007; 17:97-105.
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Statement: Nipple sparing mastectomy

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9. Mellon P, Feron JG, Couturud B et al. The role of nipple sparing mastectomy in breast cancer: a comprehensive review of the literatur. Plast Reconstr. Surg 2013;131(5):969-84
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Meta-analyses of different techniques:

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2. Chan BKY, Wiseberg-Firtell JA, Jois RHS et al. Localization techniques for guided surgical excision of non-palpable breast lesions. Cochrane Database Syst Rev. 2015 Dec 31;(12):CD009206. doi: 10.1002/14651858.CD009206.pub2

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

1. Ahmed M, Douek M. Intra-operative ultrasound versus wire-guided localization in the surgical management of non-palpable breast cancers: systematic review and meta-analysis. Breast Cancer Res Treat. 2013 Aug;140(3):435-46.
2. Pan H, Wu N, Ding H, et al. (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
3. 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

RCTs intraoperative ultrasound vs. wire-guided localization:

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
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Intraoperative ultrasound: cohort studies:

1. Layeequr Rahman R, Puckett Y, et al. (2020) A decade of intraoperative ultrasound guided breast conservation for margin negative resection - Radioactive, and magnetic, and Infrared Oh My. Am J Surg 220:1410-1416. 10.1016/j.amjsurg.2020.09.008
2. Haid A, Knauer M, Dunzinger S, et al. (2007) Intra-operative sonography: a valuable aid during breast-conserving surgery for occult breast cancer. Ann Surg Oncol 14:3090-3101. 10.1245/s10434-007-9490-9
3. Ramos M, Diaz JC, Ramos T, et al. (2013) Ultrasound-guided excision combined with intraoperative assessment of gross macroscopic margins decreases the rate of reoperations for non-palpable invasive breast cancer. Breast 22:520-524. 10.1016/j.breast.2012.10.006
4. Arentz C, Baxter K, Boneti C, et al. (2010) Ten-year experience with hematoma-directed ultrasound-guided (HUG) breast lumpectomy. Ann Surg Oncol 17 Suppl 3:378-383. 10.1245/s10434-010-1230-x
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1. Struik GM, Schermers B, Mares I et al. Randomized controlled trial comparing magnetic marker localization (MaMaLoc) with wire-guided localization in the treatment of early-stage breast cancer. Breast J. 2021;27(8):638-650. doi: 10.1111/tbj.14262.

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1. Gera R, Tayeh S, et al: Evolving Role of Magseed in wireless localization of breast lesions: systematic review and pooled analysis of 1.559 procedures. Anticancer Res 40: 1809-1815, 2020
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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/anticanres.14352.
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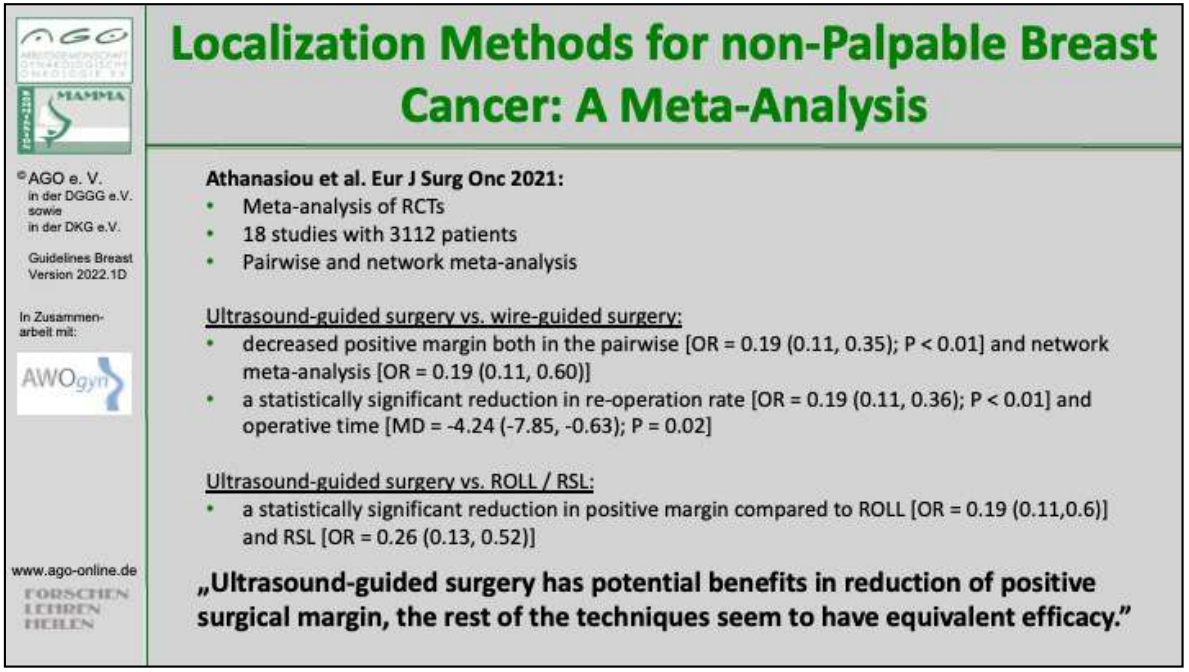
ROLL: for RCTs see meta-analyses above



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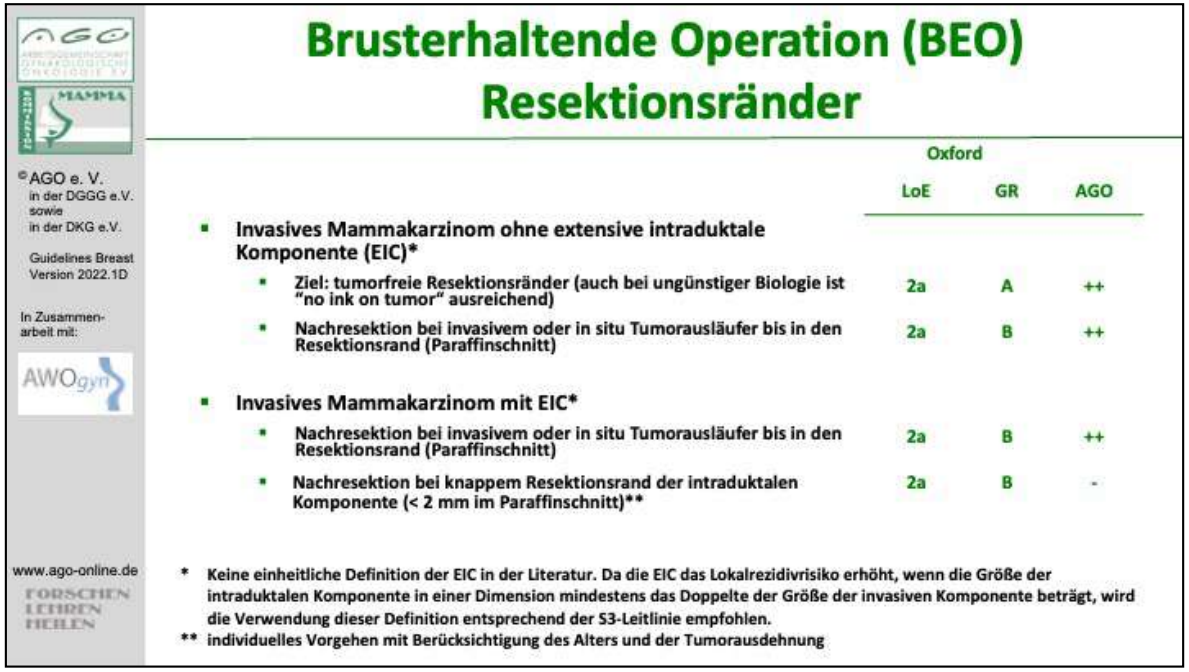

<u>Invasive cancer – margins</u>:

1. Moran MS, Schnitt SJ, Giuliano AE et al. Society of Surgical Oncology-American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. J Clin Oncol. 2014 May 10;32(14):1507-15. doi: 10.1200/JCO.2013.53.3935.
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5. Schnitt SJ, Moran MS, Giuliano AR. Lumpectomy Margins for Invasive Breast Cancer and Ductal Carcinoma in Situ: Current Guideline Recommendations, Their Implications, and Impact. J Clin Oncol. 2020; 38(20):2240-2245. doi: 10.1200/JCO.19.03213.

Invasive cancer with intraductal component - margins:

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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
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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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3. Kitchen PR, Cawson JN, Moore SE: Margins and outcome of screen-detected breast cancer with extensive in situ component. ANZ J Surg. 2006 Jul;76(7):591-5

4. Schouten van der Velden AP, Van de Vrande SL, Boetes C: Residual disease after re-excision for tumor-positive surgical margins in both ductal carcinoma in situ and invasive carcinoma of the breast: The effect of time. J Surg Oncol. 2007 Dec 1;96(7):569-74
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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.
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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.

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
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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.

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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.
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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
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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
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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.

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.

Statement: Multicentricity

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

Statement: positive microscopic margins

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

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

Statement: Inflammatory Carcinoma

1. Coleman CN, Wallner PE, Abrams JS. Inflammatory breast issue. J Natl Cancer Inst. 2003 Aug 20;95(16):1182-3.
2. Kell MR, Morrow M. Surgical aspects of inflammatory breast cancer. Breast Dis. 2005-2006;22:67-7
3. Woodward WA, Buchholz TA. The role of locoregional therapy in inflammatory breast cancer. Semin Oncol. 2008 Feb;35(1):78-86
4. Bristol IJ, Woodward WA, Strom EA, Locoregional treatment outcomes after multimodality management of inflammatory breast cancer. Int J Radiat Oncol Biol Phys. 2008 Oct 1;72(2):474-84.
5. Singletary SE Surgical management of inflammatory breast cancer. Semin Oncol. 2008 Feb;35(1):72-7
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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.
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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.
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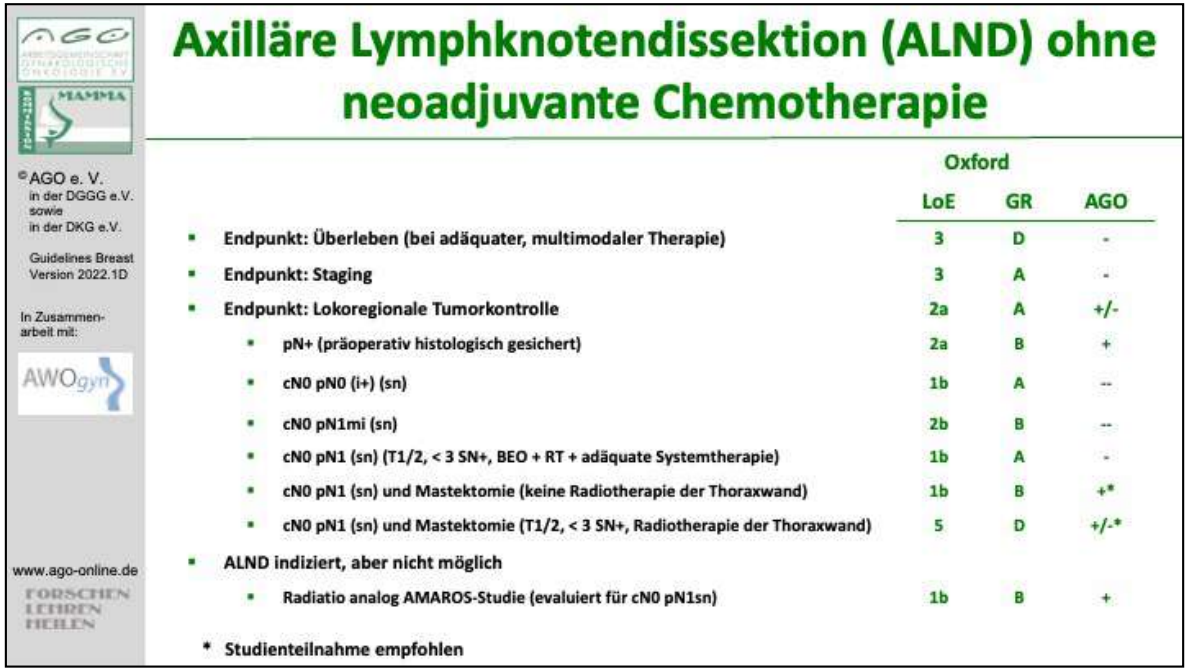

Statement: Axillary lymph node dissection

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
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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

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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.
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
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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 +

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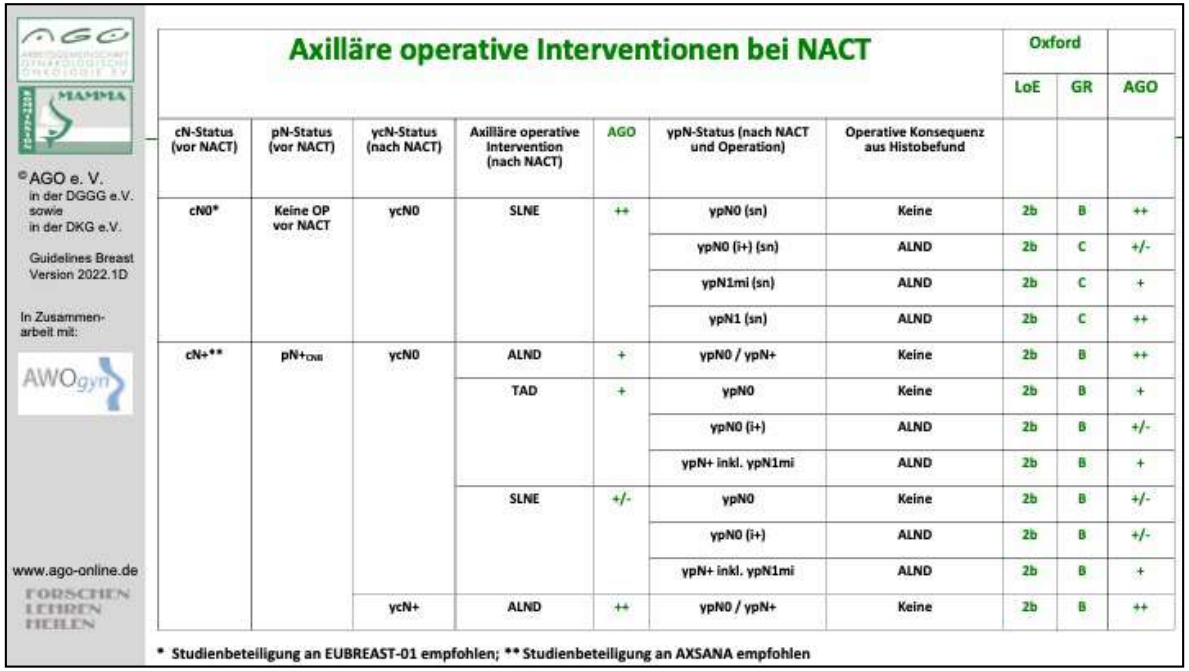

Axilläre operative Interventionen bei NACT

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	++
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	+
		ycN+	ALND	++	ypN0 / ypN+	Keine	2b	B	++

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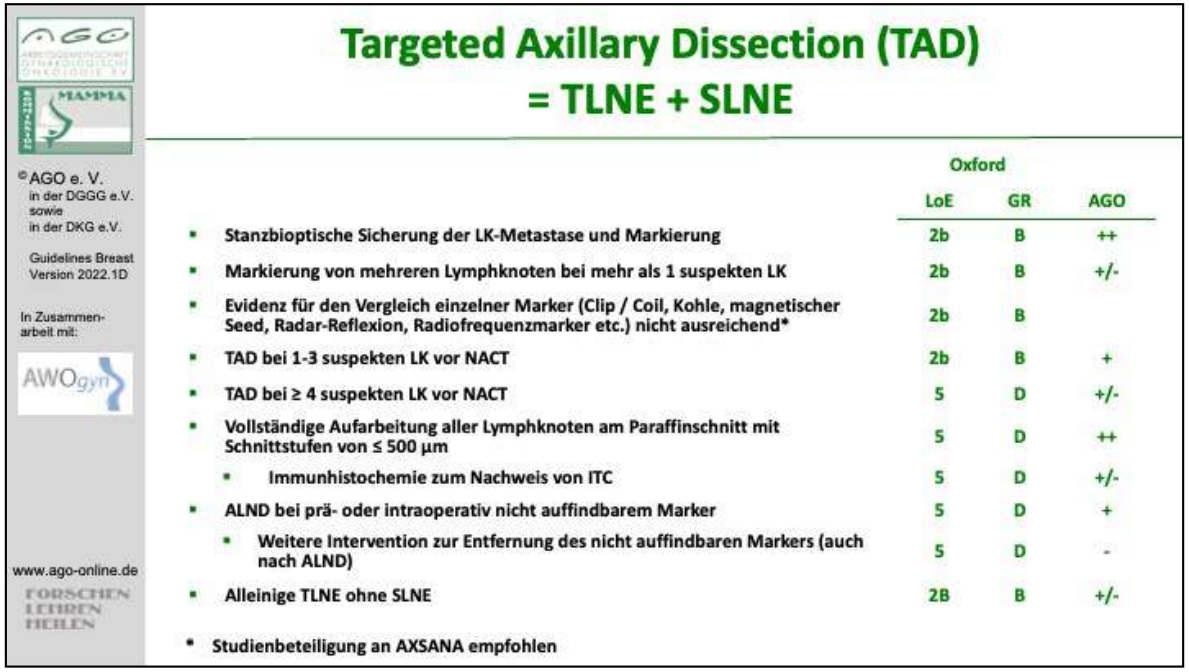

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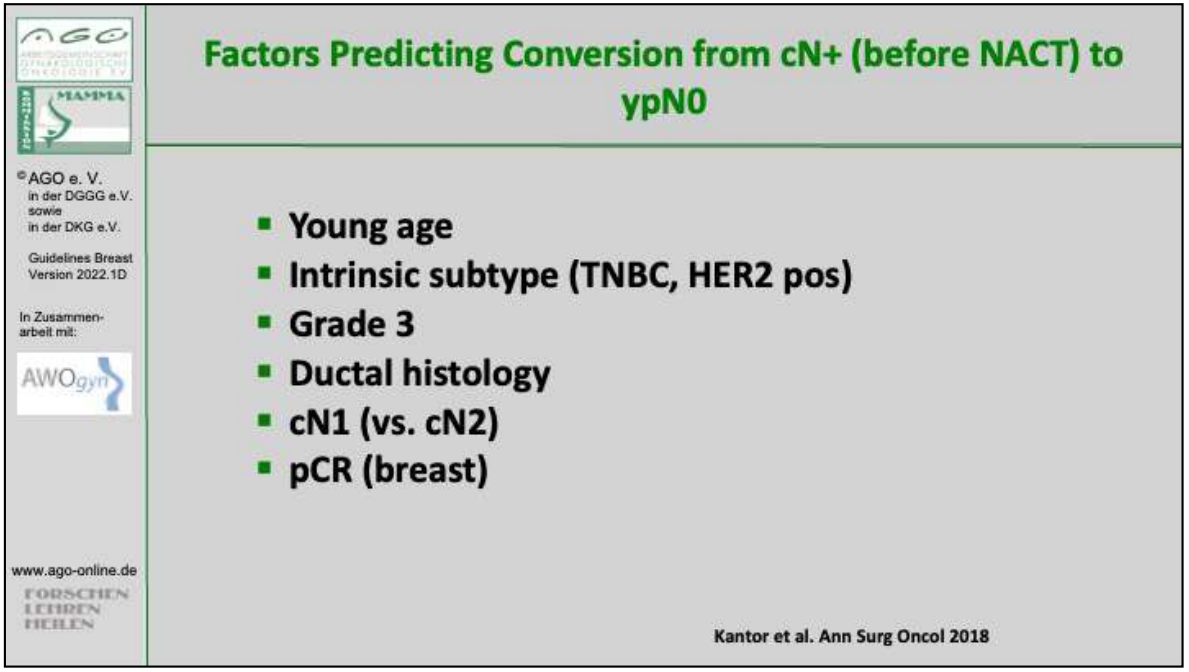

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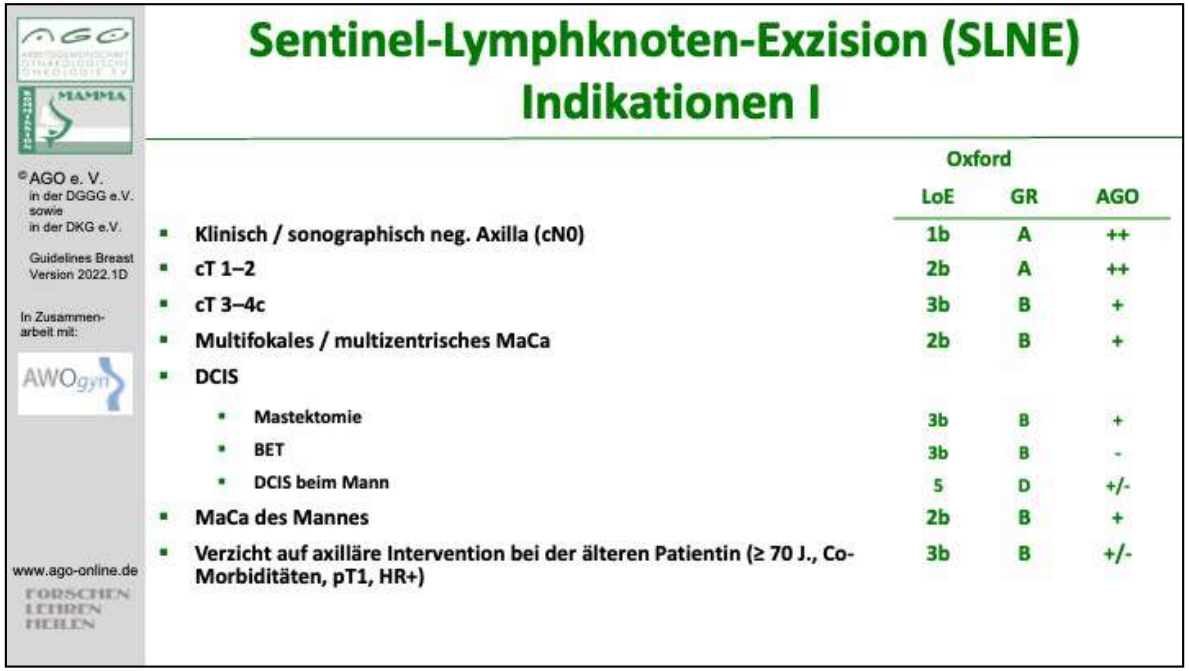

Sentinel-Lymphknoten-Exzision (SLNE)
Indikationen I

	Oxford LoE	Oxford GR	AGO
▪ Klinisch / sonographisch neg. Axilla (cN0)	1b	A	++
▪ cT 1–2	2b	A	++
▪ cT 3–4c	3b	B	+
▪ Multifokales / multizentrisches MaCa	2b	B	+
▪ DCIS			
▪ Mastektomie	3b	B	+
▪ BET	3b	B	-
▪ DCIS beim Mann	5	D	+/-
▪ MaCa des Mannes	2b	B	+
▪ Verzicht auf axilläre Intervention bei der älteren Patientin (≥ 70 J., Co-Morbiditäten, pT1, HR+)	3b	B	+/-

Statement: SLNE

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

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<u>Statement: Multifocal / multicentric MaCa</u>

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Statement: Male

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Statement: Elderly

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Statement: Lymphedema

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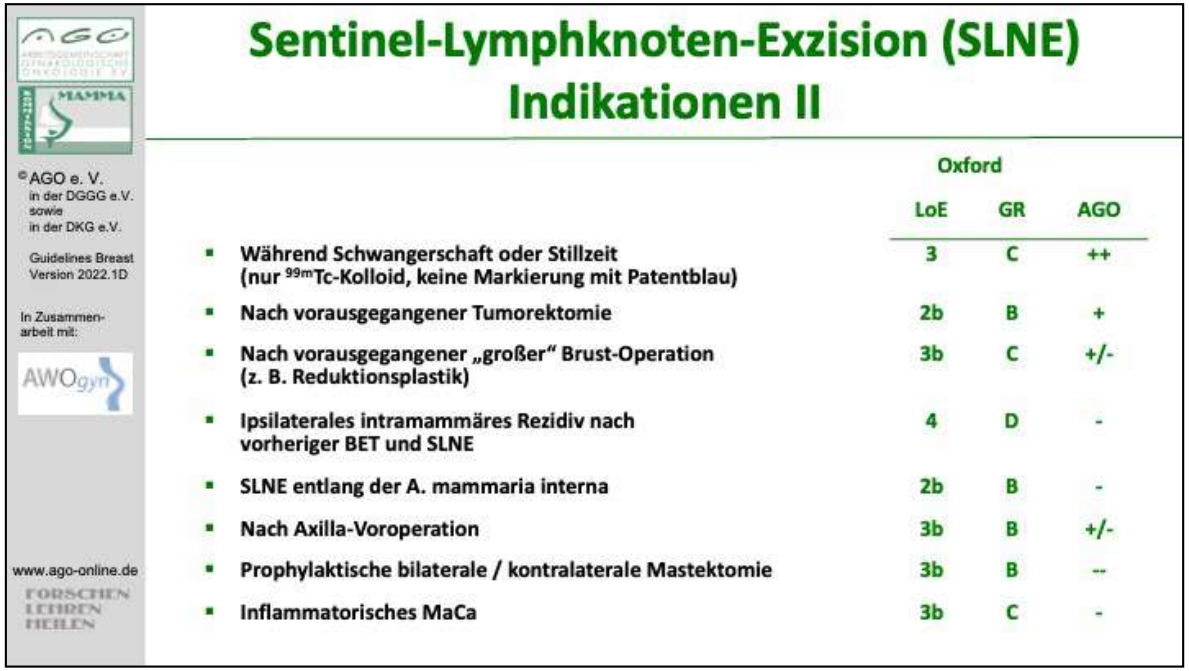

Statement: pregnancy

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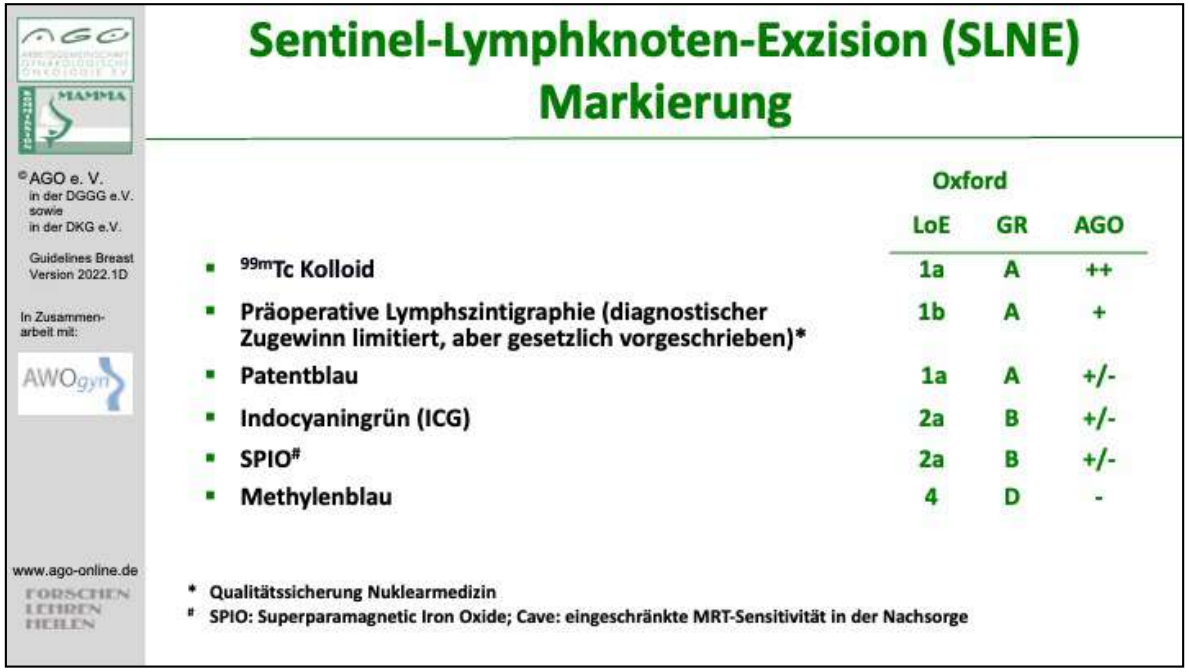

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