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Guidelines Breast
Version 2021.1E

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FORSCHEN
LEHREN
HEILEN

Diagnosis and Treatment of Patients with early and advanced Breast Cancer

Breast Cancer Surgery
Oncological Aspects

Screened data bases

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

Guidelines screened

1. St.Gallen/Vienna 2019: Burstein HJ, Curigliano G, Loibl S et al.; Members of the St. Gallen International Consensus Panel on the Primary Therapy of Early Breast Cancer 2019. Estimating the benefits of therapy for early-stage breast cancer: the St. Gallen International Consensus Guidelines for the primary therapy of early breast cancer 2019. Ann Oncol. 2019 Oct 1;30(10):1541-1557.
2. Balic M, Thomssen C, Würstlein R, Gnant M, Harbeck N. St. Gallen/Vienna 2019: A Brief Summary of the Consensus Discussion on the Optimal Primary Breast Cancer Treatment. Breast Care (Basel). 2019 Apr;14(2):103-110.
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Cochrane library:

http://onlinelibrary.wiley.com/cochranelibrary/search
Pubmed 2008 - 2020, ASCO 2003 – 2020, SABCS 2003 – 2020, Cochrane data base (n.d.)

Breast Cancer Surgery
Oncological Aspects

AGO: ++

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

AGO: +

Avoidance of a significant delay in cancer treatment

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
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Surgeon:

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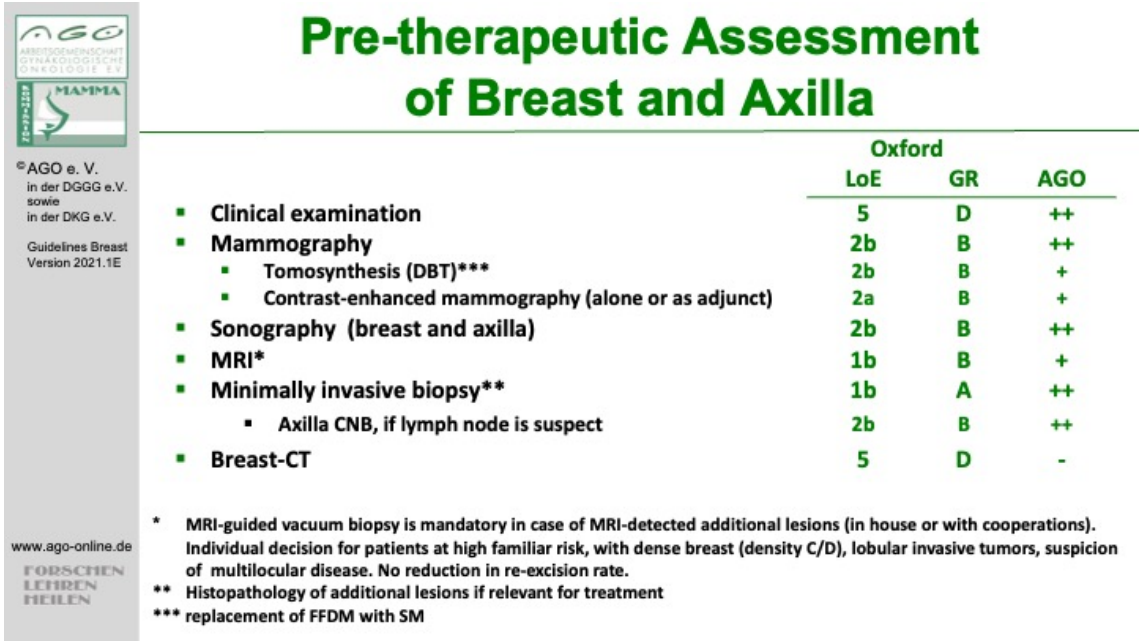

Pre-therapeutic Assessment of Breast and Axilla

	Oxford LoE	GR	AGO
▪ Clinical examination	5	D	++
▪ Mammography	2b	B	++
▪ Tomosynthesis (DBT)***	2b	B	+
▪ Contrast-enhanced mammography (alone or as adjunct)	2a	B	+
▪ Sonography (breast and axilla)	2b	B	++
▪ MRI*	1b	B	+
▪ Minimally invasive biopsy**	1b	A	++
▪ Axilla CNB, if lymph node is suspect	2b	B	++
▪ Breast-CT	5	D	-

* MRI-guided vacuum biopsy is mandatory in case of MRI-detected additional lesions (in house or with cooperations). Individual decision for patients at high familiar risk, with dense breast (density C/D), lobular invasive tumors, suspicion of multilocular disease. No reduction in re-excision rate.
** Histopathology of additional lesions if relevant for treatment
*** replacement of FFDM with SM

Combined DM + DBT + US + MRI

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

US-Axilla +FNA/CNB

1. Diepstraten SC, Sever AR, Buckens CFM, et al. Value of preoperative ultrasound guided

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
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9. Wang SY, Long JB, Killelea BK, et al. Preoperative breast MRI and contralateral breast cancer occurrence among older women with breast cancer. J Clin Oncol 2015;Nov 30, epub ahead of print
10. Riedl CC, Luft N, Clemens B, et al. Triple-modality screening trial for familial breast cancer underlines the importance of magnetic resonance imaging and questions the role of mammography and ultrasonography regardless of patient mutation status, age and breast density. JCO 2015;33(10):1128-1135
11. El Sharouni M, Postma EL, Menezes GLG et al. High prevalence of MRI-detected contralateral and ipsilateral malignant findings in patients with invasive ductolobular breast cancer: Impact on surgical management. Clin Breast Cancer. 2016 Aug;16(4):269-75.

12.Vriens BE, de Vries B, Lobbes MB, et al. Ultrasound is at least as good as magnetic resonance imaging in predicting tumour size post-neoadjuvant chemotherapy in breast cancer. Eur J Cancer. 2016 Jan;52:67-76.
13.Health Quality Ontario. Magnetic Resonance Imaging as an Adjunct to Mammography for Breast Cancer Screening in Women at Less Than High Risk for Breast Cancer: A Health Technology Assessment. Ont Health Technol Assess Ser. 2016; Nov 1;16(20):1-30
14. Lobbes MB, Vriens IJ, van Bommel AC, et al. Breast MRI increases the number of mastectomies for ductal cancers, but decreases them for lobular cancers. Breast Cancer Res Treat. 2017;162:353-364.
15.Houssami N, Turner RM, Morrow M. Meta-analysis of pre-operative magnetic resonance imaging (MRI) and surgical treatment for breast cancer. Breast Cancer Res Treat. 2017 Sep;165(2):273-283
16.Achim Wöckel, Jasmin Festl, Tanja Stüber, et al: Interdisciplinary Screening, Diagnosis, Therapy and Follow-up of Breast Cancer. Guideline of the DGGG and the DKG (S3-Level, AWMF Registry Number 032/045OL, December 2017) – Part 1 with Recommendations for the Screening, Diagnosis and Therapy of Breast Cancer. Geburtshilfe Frauenheilkd. 2018 Oct; 78(10): 927–948.

Reviews CESM:

1. Dromain, C., N. Vietti-Violi, and J.Y. Meuwly, Angiomammography: A review of current evidences. Diagn Interv Imaging, 2019.
2. Patel, B.K., M.B.I. Lobbes, and J. Lewin, Contrast Enhanced Spectral Mammography: A Review. Semin Ultrasound CT MR, 2018. 39(1): p. 70-79.
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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.
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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.
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8. Gluskin J, Rossi Saccarelli C, Avendano D, Marino MA, Bitencourt AGV, Pilewskie M, et al. Contrast-Enhanced Mammography for Screening Women after Breast Conserving Surgery. Cancers (Basel). 2020;12(12).
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10. González-Huebra I, Malmierca P, Elizalde A, Etxano J, Vejborg I, Uhlenbrock D, et al. The accuracy of titanium contrast-enhanced mammography: a retrospective multicentric study. Acta Radiol. 2020;61(10):1335-42.
11. Åhsberg K, Gardfjell A, Nimeus E, Rasmussen R, Behmer C, Zackrisson S, et al. Added value of contrast-enhanced mammography (CEM) in staging of malignant breast lesions-a feasibility study. World journal of surgical oncology. 2020;18(1):100.
12. Sumkin JH, Berg WA, Carter GJ, Bandos AI, Chough DM, Ganott MA, et al. Diagnostic Performance of MRI, Molecular Breast Imaging, and Contrast-enhanced Mammography in Women with Newly Diagnosed Breast Cancer. Radiology. 2019;293(3):531-40.
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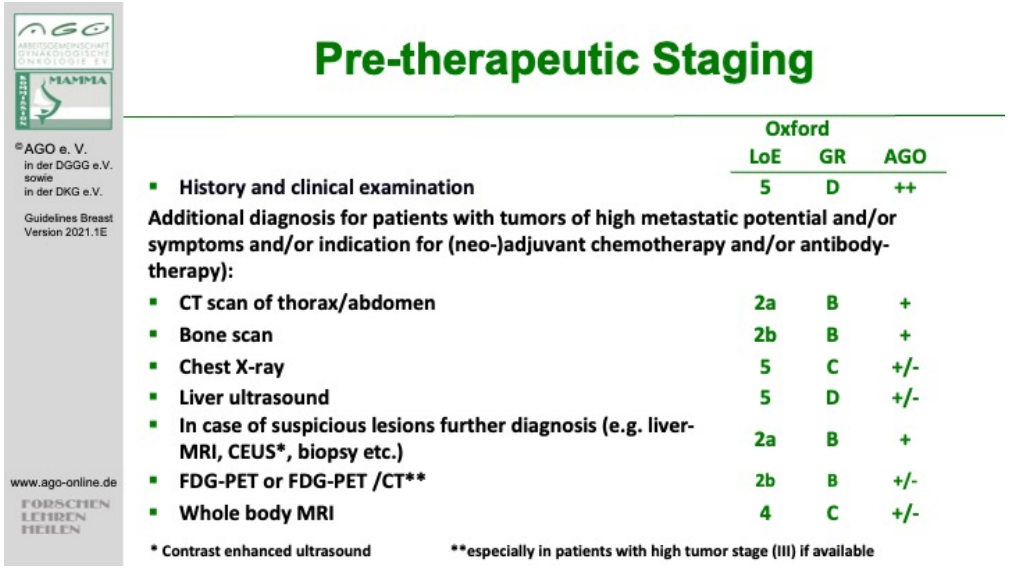

Pre-therapeutic Staging

	Oxford LoE	GR	AGO
▪ History and clinical examination	5	D	++
Additional diagnosis for patients with tumors of high metastatic potential and/or symptoms and/or indication for (neo-)adjuvant chemotherapy and/or antibody-therapy):			
▪ CT scan of thorax/abdomen	2a	B	+
▪ Bone scan	2b	B	+
▪ Chest X-ray	5	C	+/-
▪ Liver ultrasound	5	D	+/-
▪ In case of suspicious lesions further diagnosis (e.g. liver-MRI, CEUS*, biopsy etc.)	2a	B	+
▪ FDG-PET or FDG-PET /CT**	2b	B	+/-
▪ Whole body MRI	4	C	+/-

* Contrast enhanced ultrasound **especially in patients with high tumor stage (III) if available

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
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9. Hong S, Li J, Wang S. 18FDG PET-CT for diagnosis of distant metastases in breast cancer patients. A meta-analysis. Surg Oncol. 2013 Jun;22(2):139-43.
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16. Zhang L, Zhang L, Wang H, Chen L, Sui G. Diagnostic performance of contrast-enhanced ultrasound and magnetic resonance imaging for detecting colorectal liver metastases: A systematic review and meta-analysis. Dig Liver Dis. 2019 Sep;51(9):1241-1248.
17. Ulaner GA, Castillo R, Goldman DA, et al. 18F-FDG-PET/CT for systemic staging of newly diagnosed triple-negative breast cancer. Eur J Nucl Med Mol Imaging 2016; 43:1937–1944
18. Ulaner GA, Castillo R, Wills J, Gönen M, Goldman DA. 18F-FDG-PET/CT for systemic staging of patients with newly diagnosed ER-positive and HER2-positive breast cancer. Eur J Nucl Med Mol Imaging 2017
19. Groheux D, Giacchetti S, Espié M, et al. The yield of 18F-FDG PET/CT in patients with clinical stage IIA, IIB, or IIIA breast cancer: a prospective study. J Nucl Med 2011; 52:1526–1534
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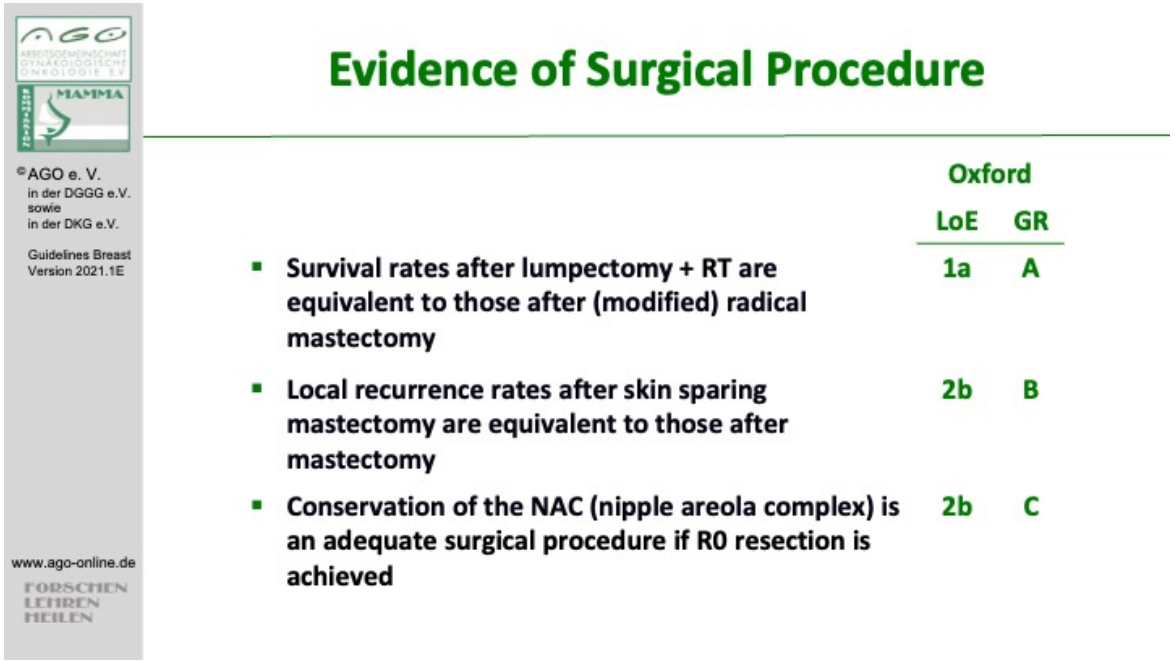

Evidence of surgical procedure

Statement: lumpectomy – mastectomy

1. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer (2002) N Engl J Med 347:1233-1241
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Statement: skin sparing mastectomy

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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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9. Patani N, Devalia H, Anderson A et al. Oncological safety and patient satisfaction with skin-sparing mastectomy and immediate breast reconstruction. Surg Oncol 2007; 17:97-105.
10. Paepke S, Schmid R, Fleckner S, et al. Subcutaneous mastectomy with conservation of the nipple-areola skin: broadening the indications Ann Surg. 2009;250(2):288-92
11. Gerber et al.: Skin-sparing mastectomy with conservation of the nipple-areola complex and autologous reconstruction is an oncologically safe procedure. Ann Surg 2009 Mar;249(3):461-8
12. Lanitis S1, Tekkis PP, Sgourakis G, et al.: Comparison of skin-sparing mastectomy versus non-skin-sparing mastectomy for breast cancer: a meta-analysis of observational studies. Ann Surg. 2010 Apr;251(4):632-9.

<u>Statement: Nipple sparing mastectomy</u>

1. Petit JY, Veronesi U, Orecchia R et al. Nipple-sparing mastectomy in association with intra operative radiotherapy (ELIOT): A new type of mastectomy for breast cancer treatment. Breast Cancer Res Treat 2006; 96:47-51.
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treatment options. Plast Reconstr Surg 2006; 117:1381-1386
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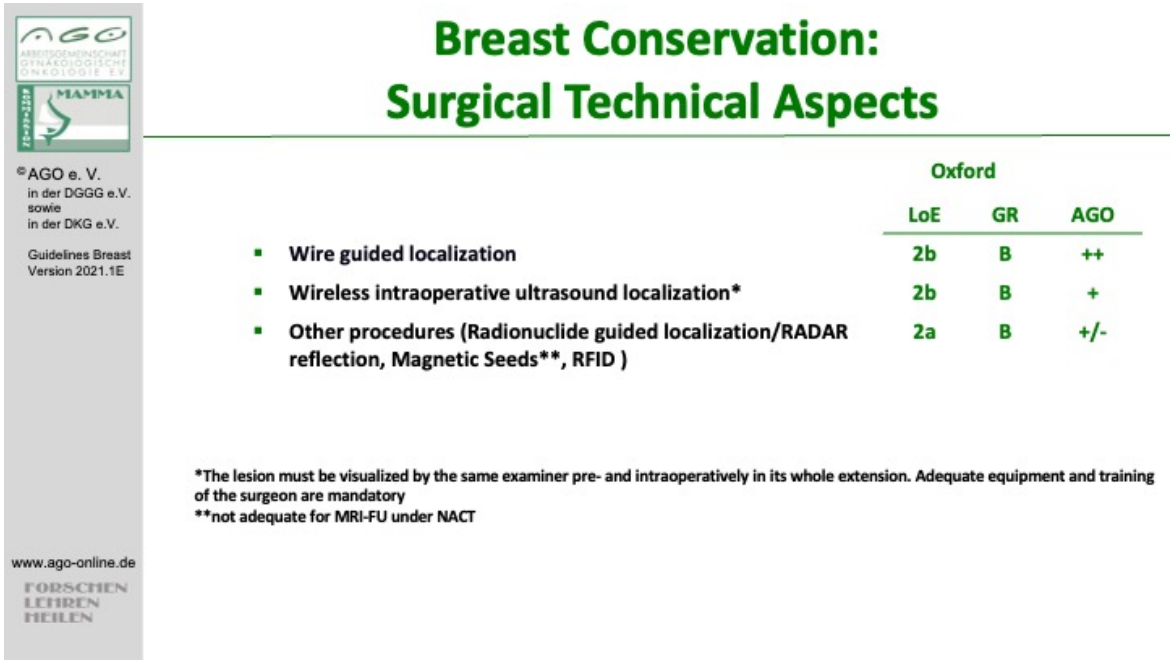
10. Muller T , Baratte A, Bruant-Rodier C, et al. Oncological safety of nipple-sparing prophylactic mastectomy: A review of the literature on 3716 cases. Ann Chir Plast Esthet. 2017 Oct 10 pii: S0294-1260(17)30137-1.



Statement: Wire guided ..

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

Intraoperative ultrasound-guided:

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

Statement: Radioguided ..

1. van der Ploeg IM, Hobbelink M, van den Bosch MA: 'Radioguided occult lesion localisation' (ROLL) for non-palpable breast lesions: a review of the relevant literature. Eur J Surg Oncol. 2008 Jan;34(1):1-5.
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palpable breast cancers. Breast Cancer Res Treat. 2013 Jul;140(2):241-52
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5. Kapoor MM, Patel MM, Scoggins ME. The Wire and Beyond: Recent Advances in Breast Imaging Preoperative Needle Localization. Radiographics. 2019 Nov-Dec;39(7):1886-1906
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8. Kasem I and Mokbel K: Savi Scout Radar-Localization of non-palpable breast lesions: systematic review and pooled analysis of 842 cases.

Statement: Magseed

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Statement: Intraoperative ultrasound..

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

5. Karadeniz Cakmak G, Emre AU, Tascilar O, et al: Surgeon performed continuous intraoperative ultrasound guidance decreases re-excisions and mastectomy rates in breast cancer. Breast. 2017 Jun;33:23-28
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Breast Conservation: Surgical Technical Aspects

	Oxford LoE	Oxford GR	AGO
▪ **Tumor-free margins required** (also in unfavorable biology, „no ink on tumor" is sufficient)	2a	A	++
▪ **Re-excision required for involved margins (paraffin section)**	3b	C	+
▪ **Therapeutic stereotactic excision alone**	4	D	--
▪ **Ultrasound guided surgery to prevent re-excision**	2a	B	+
▪ **Intraoperative margin evaluation (with Margin Probe®)**	1b	A	+/-
▪ **Specimen radiography or ultrasound**	2b	B	++

Statement: Wire guided ..

1. Hanna et al.: The use of stereotactic excisional biopsy in the management of invasive breast cancer. World J Surg. 2005 Nov;29(11):1490-4
2. Köhler J, Krause B, Grunwald S, et al. Ultrasound and mammography guided wire marking of non-palpable breast lesions: analysis of 741 cases. Ultraschall Med. 2007 Jun;28(3):283-90.
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Statement: Radioguided ..

1. van der Ploeg IM, Hobbelink M, van den Bosch MA: 'Radioguided occult lesion localisation' (ROLL) for non-palpable breast lesions: a review of the relevant literature. Eur J Surg Oncol. 2008 Jan;34(1):1-5.
2. Ahmed M, van Hemelrijck M, Douek M. Systematic review of radioguided versus wire-guided localization in the treatment of non-palpable breast cancers. Breast Cancer Res Treat. 2013 Jul;140(2):241-52
3. Ong JSL, Teh J, Saunders C, Bourke AG, et al: Patient satisfaction with Radioguided Occult Lesion Localisation using iodine-125 seeds

('ROLLIS') versus conventional hookwire localisation. Eur J Surg Oncol. 2017 Dec;43(12):2261-2269.

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6. Srour MK, Kim S, Amersi F et al. Comparison of wire localization, radioactive seed, and Savi scout® radar for management of surgical breast disease. Breast J. 2019 Aug 25.

Statement: specimen radiography

1. Singletary: Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. Am J Surg. 2002 Nov;184(5):383-93.
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3. Tan KY et al. Breast specimen ultrasound and mammography in the prediction of tumour-free margins. ANZ J Surg. 2006 Dec;76(12):1064-7.
4. Kunos C, Latson L, Overmoyer B Breast conservation surgery achieving>or=2 mm tumor-free margins results in decreased local-regional recurrence rate, Breast J. 2006 Jan-Feb;12(1):28-36

Statement: tumor free margins ...

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

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

Statement: tumor free margins in intrinsic subtypes

1. Sioshansi S, Ehdaivand S, Cramer C, et al.Triple negative breast cancer is associated with an increased risk of residual invasive carcinoma after lumpectomy. Cancer. 2012 Aug 15;118(16):3893-8
2. Gangi A, Chung A, Mirocha J et al. Breast-conserving therapy for triple-negative breast cancer. JAMA Surg. 2014 Mar;149(3):252-8
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Statement: ... re-excision ...

1. Kitchen PR, Cawson JN, Moore SE: Margins and outcome of screen-detected breast cancer with extensive in situ component. ANZ J Surg. 2006 Jul;76(7):591-5
2. Schouten van der Velden AP, Van de Vrande SL, Boetes C: Residual disease after re-excision for tumor-positive surgical margins in both ductal carcinoma in situ and invasive carcinoma of the breast: The effect of time. J Surg Oncol. 2007 Dec 1;96(7):569-74
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excision before radiation for breast cancer. Am J Clin Oncol. 2007 Apr;30(2):146-51.

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

Statement: stereotactic excision alone ...

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

Statement: Intraoperative ultrasound..

1. Ahmed M; Douek, M. Intra-operative ultrasound versus wire-guided localization in the surgical management of non-palpable breast cancers: systematic review and meta-analysis. Breast Cancer Res Treat. 2013 Aug;140(3):435-46.
2. Pan H, Wu N, Ding H, et al. Intraoperative Ultrasound Guidance Is Associated with Clear Lumpectomy Margins for Breast Cancer: A Systematic Review and Meta-Analysis. PLOS One 2013;8(9), e74028
3. Eggemann H, Ignatov T, Beni A, et al. Ultrasonography-guided breast-conserving surgery is superior to palpation-guided surgery for palpable breast cancer. Clin Breast Cancer. 2014 Feb;14(1):40-5.
4. Karanlik H, Ozgur I, Sahin D et al: Intraoperative ultrasound reduces the need for re-excision in breast-conserving surgery. World J Surg Oncol. 2015 Nov 24;13:321.
5. Karadeniz Cakmak G, Emre AU, Tascilar O, et al: Surgeon performed continuous intraoperative ultrasound guidance decreases re-excisions and mastectomy rates in breast cancer. Breast. 2017 Jun;33:23-28

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

Statement: Margine probe

1. Freya Schnabel, Susan K. Boolbol, Mark Gittleman, et al: A Randomized Prospective Study of Lumpectomy Margin Assessment with Use of MarginProbe in Patients with Nonpalpable Breast Malignancies Ann Surg Oncol (2014) 21:1589–1595
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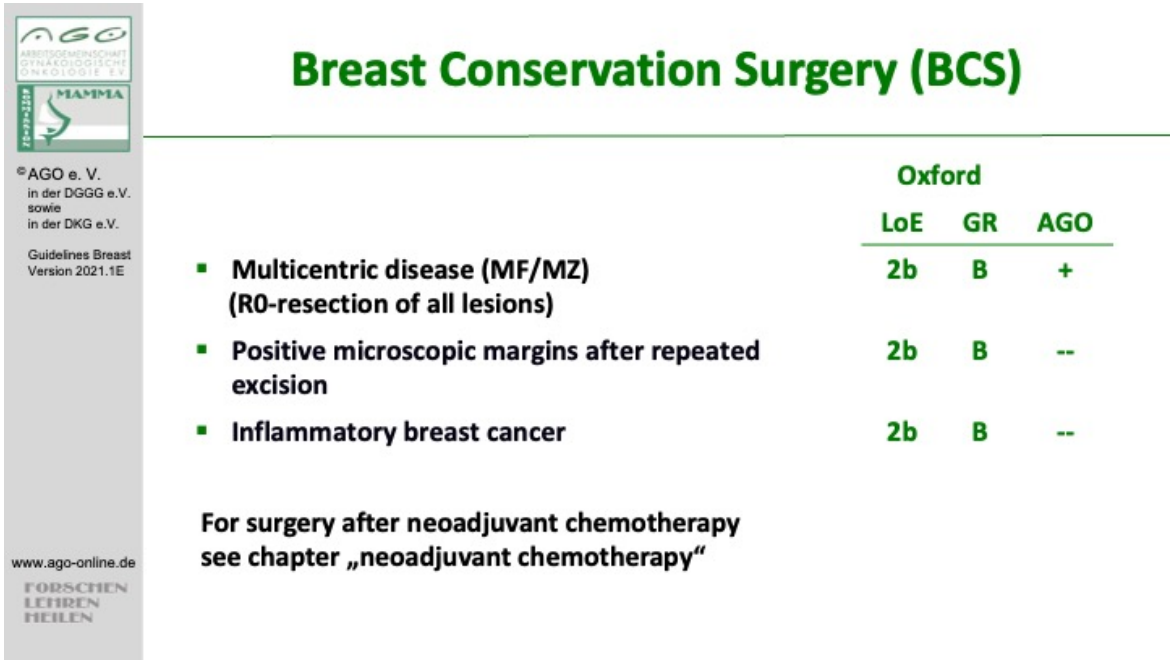


Statement: Multicentricity

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

Statement: positive microscopic margins

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

Mar;21(3):717-30.
2. Marinovich ML, Azizi L, Macaskill P, et al: The Association of Surgical Margins and Local Recurrence in Women with Ductal Carcinoma In Situ Treated with Breast-Conserving Therapy: A Meta-Analysis. Ann Surg Oncol. 2016 Nov;23(12):3811-3821

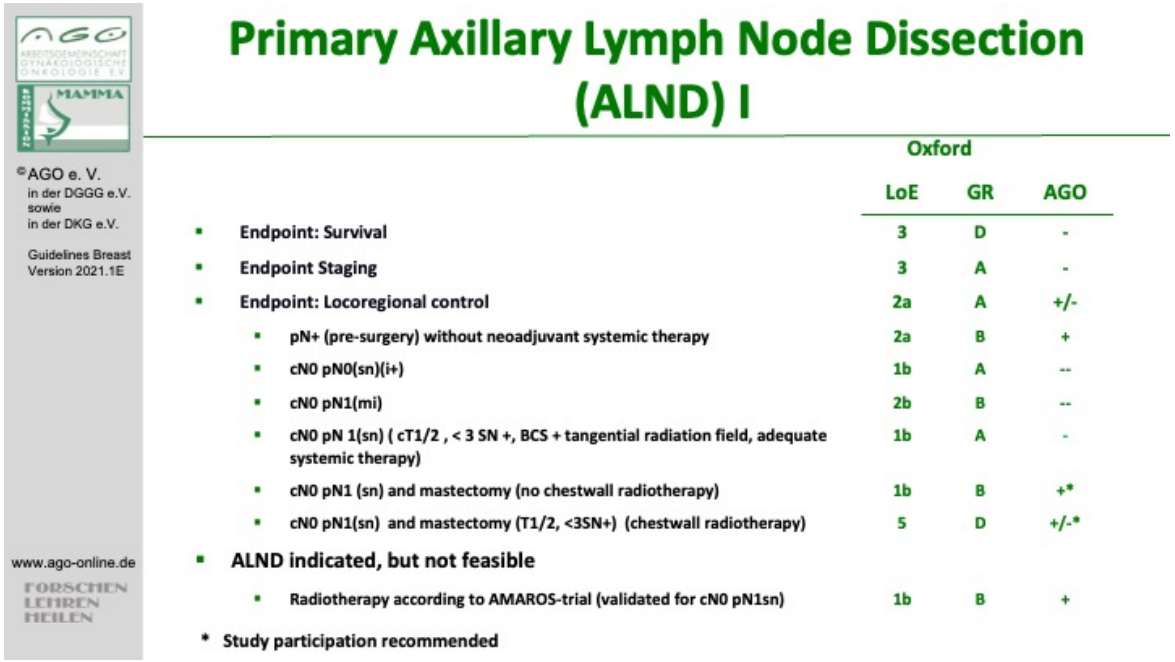
Statement: Inflammatory Carcinoma

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

Statement: general

1. Marret H, Perrotin F, 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.



Primary Axillary Lymph Node Dissection (ALND) I

	Oxford LoE	GR	AGO
▪ Endpoint: Survival	3	D	-
▪ Endpoint Staging	3	A	-
▪ Endpoint: Locoregional control	2a	A	+/-
▪ pN+ (pre-surgery) without neoadjuvant systemic therapy	2a	B	+
▪ cN0 pN0(sn)(i+)	1b	A	--
▪ cN0 pN1(mi)	2b	B	--
▪ cN0 pN 1(sn) (cT1/2 , < 3 SN +, BCS + tangential radiation field, adequate systemic therapy)	1b	A	-
▪ cN0 pN1 (sn) and mastectomy (no chestwall radiotherapy)	1b	B	+*
▪ cN0 pN1(sn) and mastectomy (T1/2, <3SN+) (chestwall radiotherapy)	5	D	+/-*
▪ ALND indicated, but not feasible			
▪ Radiotherapy according to AMAROS-trial (validated for cN0 pN1sn)	1b	B	+

* Study participation recommended

Statements: Axillary lymph node dissection I

Statement: Axillary lymph node dissection

1. Kuehn T, Bembenek A, Decker T. A concept for the clinical implementation of sentinel lymph node biopsy in patients with breast carcinoma with special regard to quality assurance. Cancer. 2005 Feb 1;103(3):451-61
2. Rudenstam CM, Zahrieh D, Forbes JF: Randomized trial comparing axillary clearance versus no axillary clearance in older patients with breast cancer: first results of International Breast Cancer Study Group Trial 10-93. J Clin Oncol 24(3): 337-344, 2006.
3. Van la Parra: The value of sentinel lymph node biopsy in ductal carcinoma in situ (DCIS) and DCIS with microinvasion of the breast. Eur J Surg Oncol. 2008 Jun;34(6):631-5
4. D'Angelo-Donovan DD, Dickson-Witmer D, Petrelli NJ. Sentinel lymph node biopsy in breast cancer: A history and current clinical recommendations. Surg Oncol. 2012 Jan 9.
5. Reimer T, Gerber B. Quality-of-life considerations in the treatment of early-stage breast cancer in the elderly. Drugs Aging. 2010 Oct 1;27(10):791-800.
6. Gerber B, Heintze K, Stubert J, et al. Axillary lymph node dissection in early-stage invasive breast cancer: is it still standard today?

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

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

Endpoint: Survival LoE 3D AGO-

-

Endpoint: Staging LoE3A AGO -

-

Endpoint: Locoregional control LoE 2aA AGO+/-

-

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

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

cN0 pN0(sn)(i+)LoE 1b A AGO –

1. Rutgers EJ. Sentinel node biopsy: interpretation and management of patients with immunohistochemistry-positive sentinel nodes and those with micrometastases. J Clin Oncol. 2008 Feb 10;26(5):698-702.

2. Li Y, Zhang H, Zhang W, et al: A competing risk analysis model to determine the prognostic value of isolated tumor cells in axillary lymph nodes for T1N0M0 breast cancer patients based on the surveillance, epidemiology, and end results database. Frontiers in Oncology 10:572316, 2020

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

1. Mamtani A, Patil S, Stempel M, et al. Axillary Micrometastases and Isolated Tumor Cells Are Not an Indication for Post-mastectomy Radiotherapy in Stage 1 and 2 Breast Cancer. Ann Surg Oncol. 2017 Aug;24(8):2182-2188.
2. Cserni G, Gregori D, Merletti F: Meta-analysis of non-sentinel node metastases associated with micrometastatic sentinel nodes in breast cancer. Br J Surg 91(10): 1245-1252, 2004.
3. Rutgers EJ. Sentinel node biopsy: interpretation and management of patients with immunohistochemistry-positive sentinel nodes and those with micrometastases. J Clin Oncol. 2008 Feb 10;26(5):698-702
4. Galimberti V, Cole BF, 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
3. Morrow M, Jagsi R, Mclead MC et al. Surgeons Attitudes toward the Omission of Axillary Dissection in Early Breast Cancer. JAMA Oncol 2018;4(11)1511-16
4. Poodt IGM, Spronk PER, Vugts G et al. Trends on Axillary Surgery in Nondistant Metastatic Breast Cancer Treated Between 2011 and

2015: A Dutch Population based Study in The ACOSOC Z0011 and AMAROS Era. Ann Surg Oncol 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. Jung J, Han W, Lee ES et al. Retrospectively validating the results of the ACOSOG Z0011 trial in a large Asian Z0011-eligible cohort. Breast Cancer Res Treat. 2019 May;175(1):203-215
7. Barrio AV, Downs-Canner S, Edelweiss M et al. Microscopic Extracapsular Extension in Sentinel Lymph Nodes Does Not Mandate Axillary Dissection in Z0011-Eligible Patients. Ann Surg Oncol. 2019 Dec 9.

cN0 pN1 (sn) and mastectomy (no chestwall radiotherapy) LoE 1b B AGO +*

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

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

-

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

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

Axillary Surgery and NACT

	Oxford		
	LoE	GR	AGO
SLNE after NACT	2b	B	++
SLNE before NACT	2b	B	-

cN-Status (before NACT)	pN-Status (before NACT)	cN-Status (after NACT)	Surgical procedure (after NACT)	pN-Status (after NACT and Surgery)	Surgical consequence from histology**			
cN0	—	ycN0	SLNE alone	ypN0 (sn)	—	2b	B	++***
				ypN0 (i+) ypN1$_{mic}$ (sn)	ALND	2b	C	+ (+/- at i+)
					none **	5	D	+/-
				ypN1 (sn)	ALND	2b	C	++
					none **	5	D	+/-
cN+	pN+$_{CNB}$	ycN0	SLNE alone* TAD (TLNE + SLNE)* ALND*	ypN0 ypN0 ypN0	—	2b 2b 2b	B B B	+/-*** +*** +***
			SLNE alone* TAD (TLNE + SLNE)*	ypN+ incl. ypN0 (i+)	ALND	2b	B	+ (+/- at i+)
			ALND	ypN+	—	2b	B	++
			none	n.d.	none**	5	D	-
cN+	pN+$_{CNB}$	ycN+	ALND	ypN+ incl. ypN0 (i+)	—	2b	B	++
			none	n.d.	none**	5	D	-

*Study participation (Axsana) recommended; ** s. Recommendations chapter Radiotherapy, irradiation alone is not recommended in case of pN1(sn) and pN+ ; ***recommendation grade concerning to staging at cN0 and cN+ ypN0

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

1. Reimer T, Gerber B. Quality-of-life considerations in the treatment of early-stage breast cancer in the elderly. Drugs Aging. 2010 Oct 1;27(10):791-800.
2. Tuttle TM, Shamliyan T, Virnig BA, et al. The impact of sentinel lymph node biopsy and magnetic resonance imaging on important outcomes among patients with ductal carcinoma in situ. J Natl Cancer Inst Monogr. 2010;2010(41):117-20. Review.
3. 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.
4. D'Angelo-Donovan DD, Dickson-Witmer D, Petrelli NJ. Sentinel lymph node biopsy in breast cancer: A history and current clinical recommendations. Surg Oncol. 2012 Jan 9.
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6. 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.

Statement surgical intervention in the axilla before or after neoadjuvant chemotherapy

1. Kuehn T, Bauerfeind I, Fehm T, et al.: Sentinel-lymph-node biopsy with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective multi-center cohort study. Lancet Oncol 2013;14(7):609-18.
2. 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(14):1455-61.
3. Fu JF, Chen HL, Yang J, et al. Feasibility and accuracy of sentinel lymph node biopsy in clinically node-positive breast cancer after neoadjuvant chemotherapy: a meta-analysis. PLoS One. 2014 Sep 11;9(9):e105316
4. Lee HD, Ahn SG, Lee SA, et al. Prospective Evaluation of the Feasibility of Sentinel Lymph Node Biopsy in Breast Cancer Patients with Negative Axillary Conversion after Neoadjuvant Chemotherapy. Cancer Res Treat. 2014 Aug 29. doi: 10.4143/crt.2013.208. [Epub ahead of print]
5. Boileau JF, Poirier B, Basik M, et al. Sentinel Node Biopsy After Neoadjuvant Chemotherapy in Biopsy-Proven Node-Positive Breast Cancer: The SN FNAC Study. J Clin Oncol. 2015;33(3):258-264.
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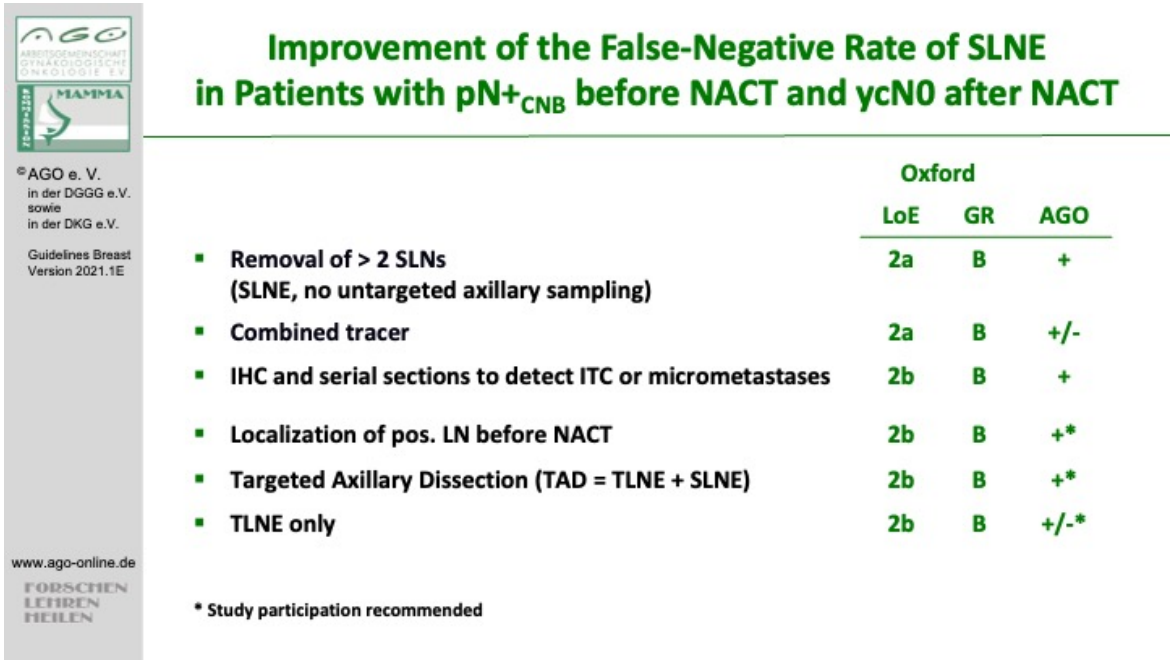

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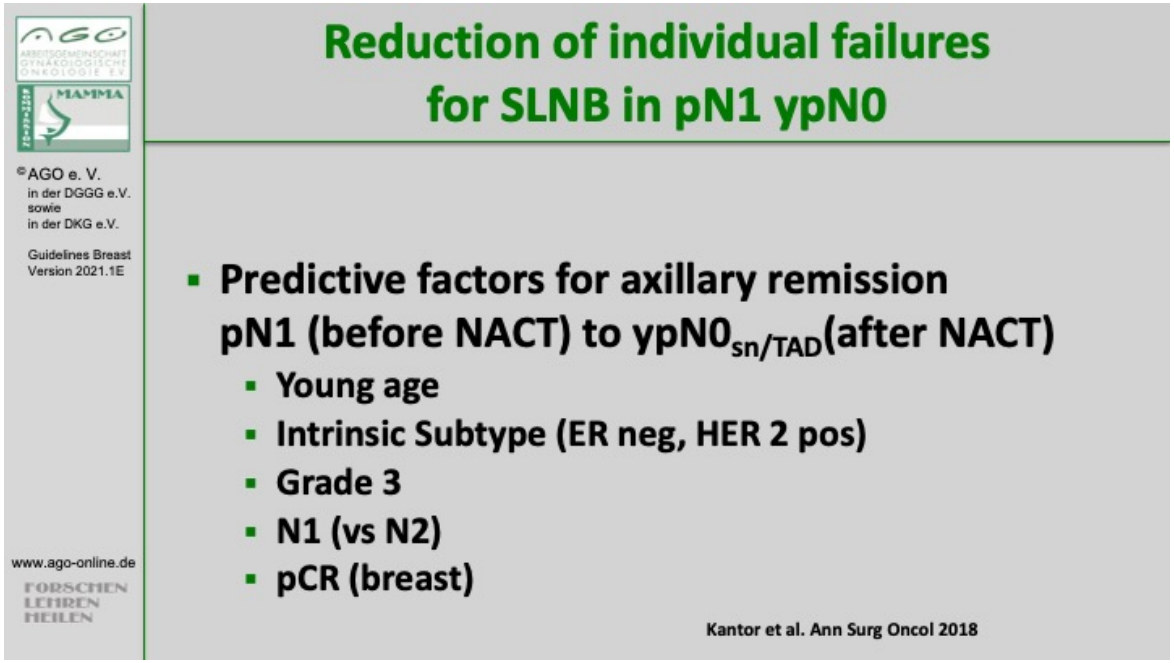

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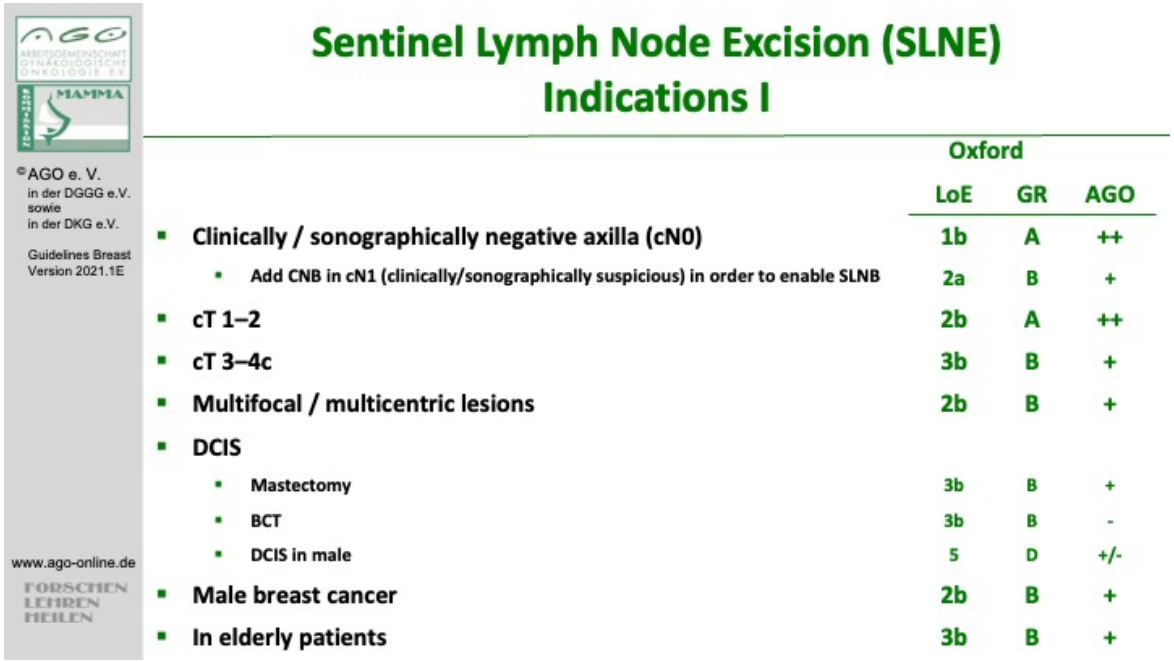

Sentinel Lymph Node Excision (SLNE)
Indications I

	Oxford LoE	GR	AGO
▪ Clinically / sonographically negative axilla (cN0)	1b	A	++
▪ Add CNB in cN1 (clinically/sonographically suspicious) in order to enable SLNB	2a	B	+
▪ cT 1–2	2b	A	++
▪ cT 3–4c	3b	B	+
▪ Multifocal / multicentric lesions	2b	B	+
▪ DCIS			
▪ Mastectomy	3b	B	+
▪ BCT	3b	B	-
▪ DCIS in male	5	D	+/-
▪ Male breast cancer	2b	B	+
▪ In elderly patients	3b	B	+

Statement: SLNE

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

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Statement: Multifocal / multicentric MaCa

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Statement: Male

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Statement: Elderly

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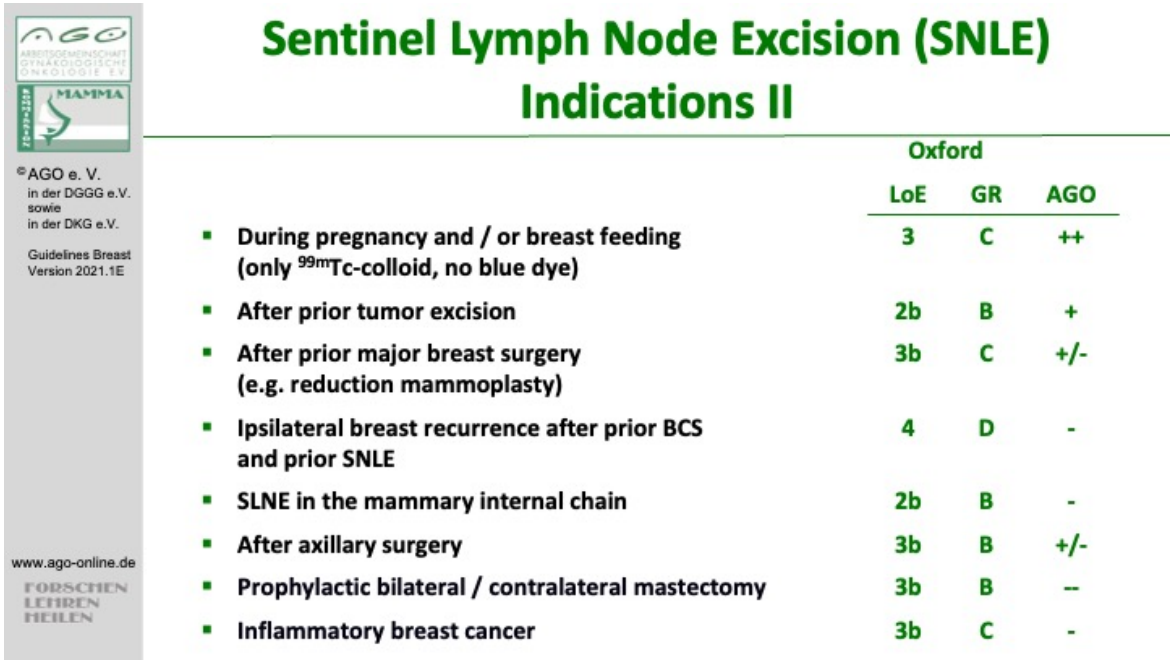

Statement: pregnancy

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Statement: internal mammarian

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Statement: prophylactic mastectomy

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Statement: After previous tumor excision

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Statement: previous major breast surgery

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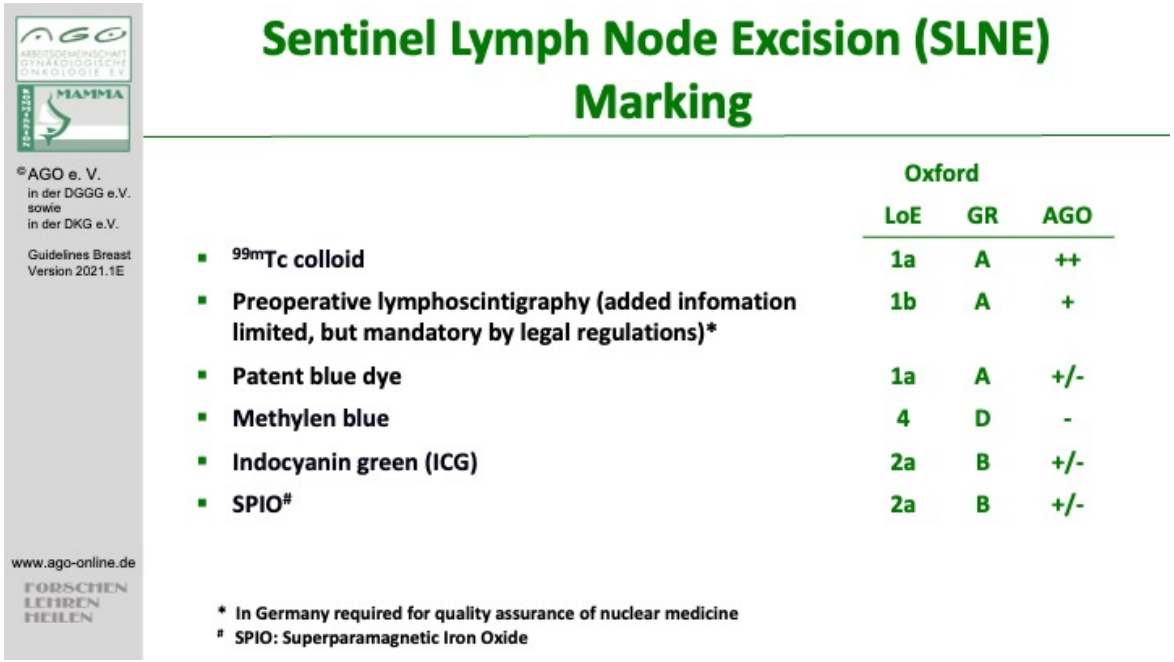

Sentinel Lymph Node Excision (SLNE) Marking

	Oxford		
	LoE	GR	AGO
▪ ^{99m}Tc colloid	1a	A	++
▪ Preoperative lymphoscintigraphy (added infomation limited, but mandatory by legal regulations)*	1b	A	+
▪ Patent blue dye	1a	A	+/-
▪ Methylen blue	4	D	-
▪ Indocyanin green (ICG)	2a	B	+/-
▪ SPIO#	2a	B	+/-

* In Germany required for quality assurance of nuclear medicine
\# SPIO: Superparamagnetic Iron Oxide

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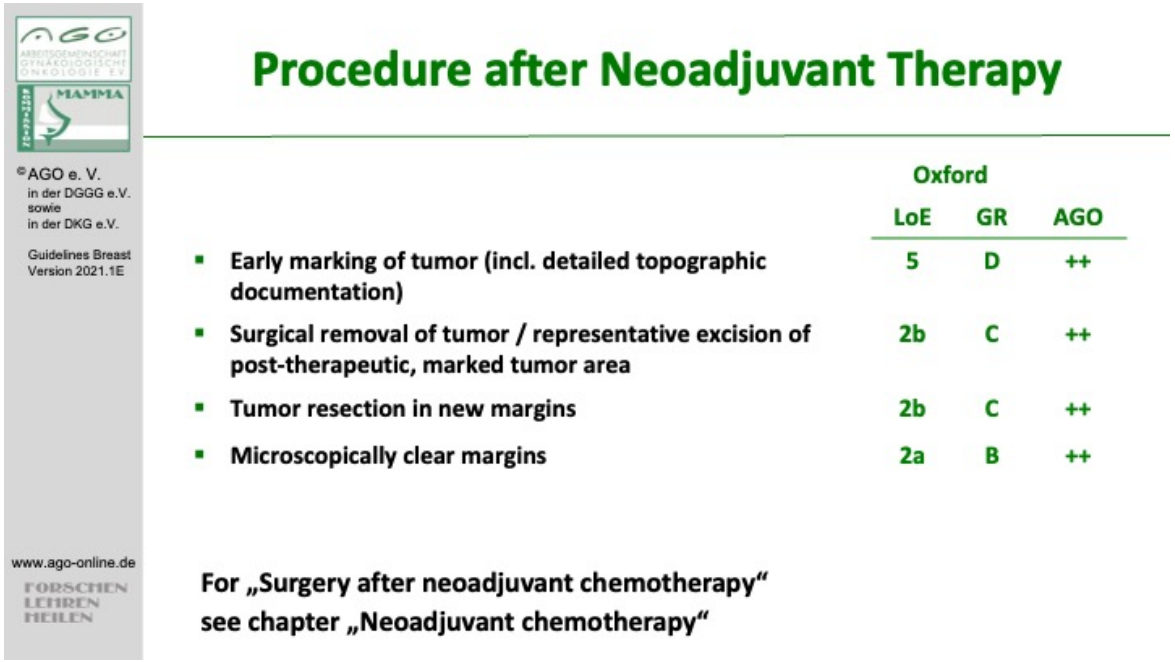

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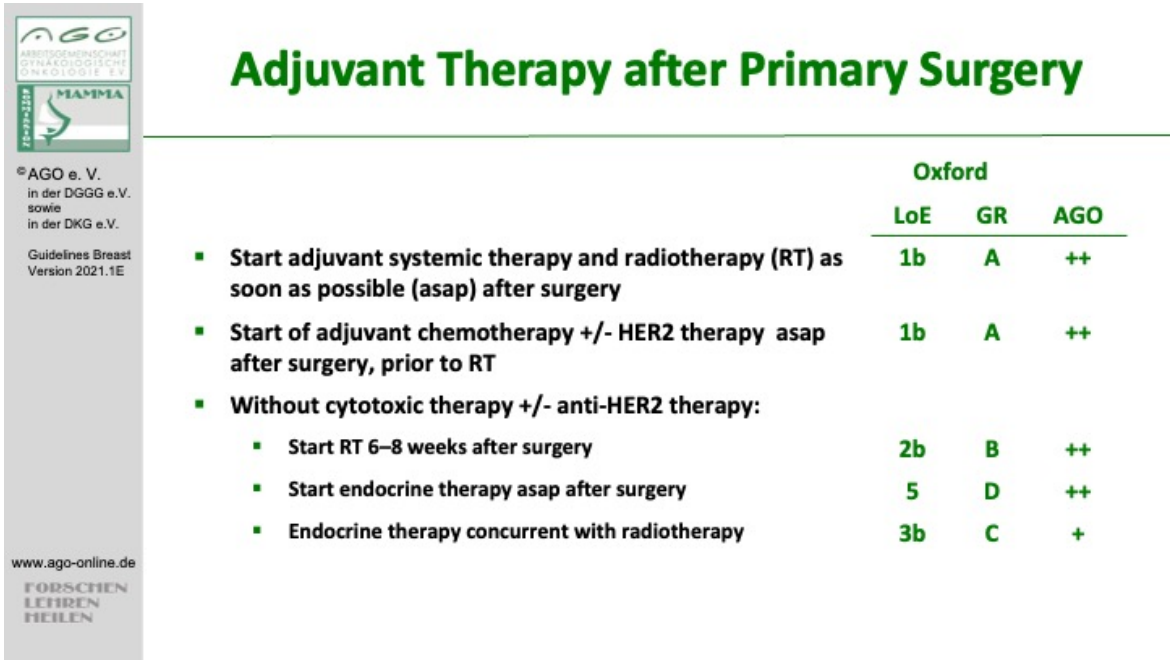

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