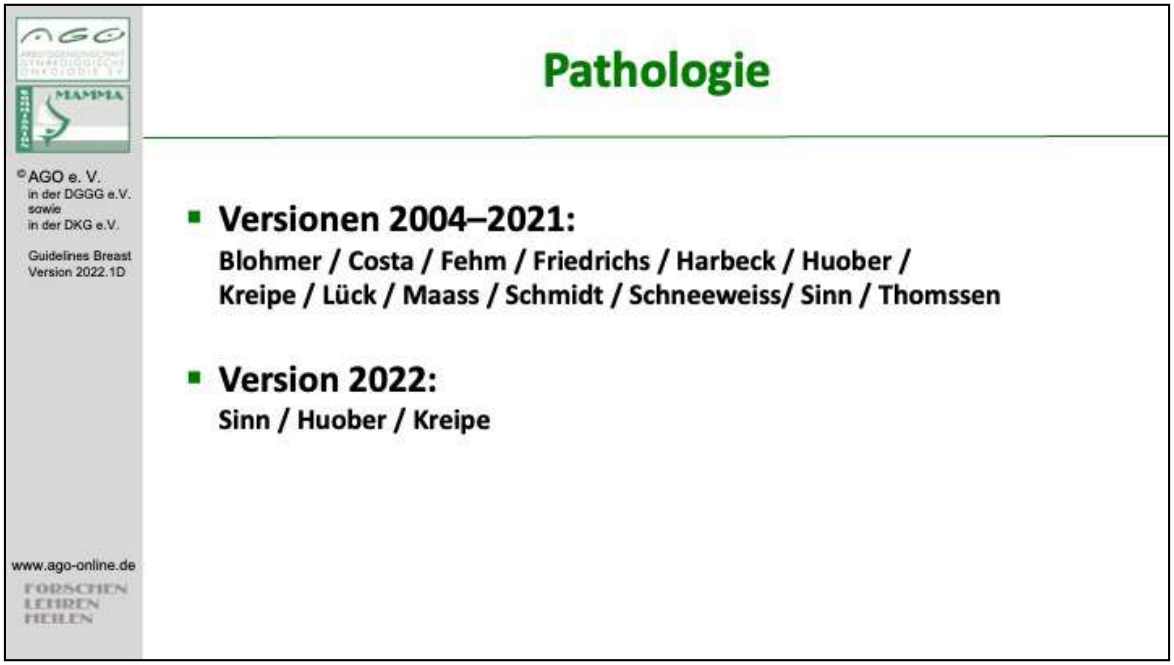
Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Guidelines Breast
Version 2022.1D

Pathologie



Screened data bases: PubMed 2021

Search Query:

(Breast Diseases/PA[mh] AND ("2011/01/01"[dp] : "2021/12/31"[dp])) AND ("english"[la] OR "german"[la])

Guidelines screened

1. WHO, Classification of Tumours Editorial Board. Breast Tumours: WHO Classification of Tumours Lyon (France): International Agency for Research on Cancer; 2019. DOI: 10.1111/his.14091

2. National Comprehensive Cancer Network (NCCN). Breast Cancer (Version 2.2022). http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed Jan 01, 2022

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4. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF). Interdisziplinäre S3-Leitlinie für die

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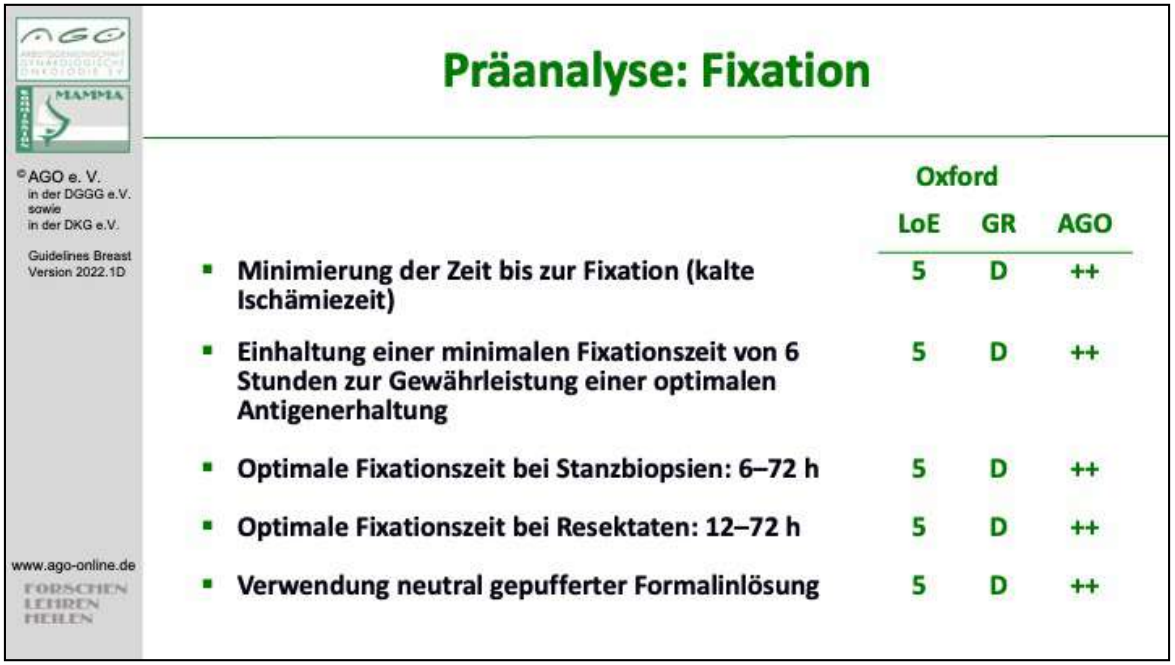
6. The Royal College of Pathologists. Pathology reporting of breast disease in surgical excision specimens incorporating the dataset for histological reporting of breast cancer. June 2016:1-160. https://www.rcpath.org/resourceLibrary/g148-breastdataset-hires-jun16-pdf.html

7. Schweizerische Gesellschaft für Pathologie (2017). Leitlinien zur Sicherung und Förderung der Qualitätskontrolle. https://sgpath.ch/docs/QRL/QRL_SGPath_Mamma_2017.pdf



Antigen preservation

1. Apple, S., Pucci, R., Lowe, A. C., et al. (2011). The effect of delay in fixation, different fixatives, and duration of fixation in estrogen and progesterone receptor results in breast carcinoma. American Journal of Clinical Pathology, 135(4), 592–598.
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3. Kalkman, S., Barentsz, M. W., & van Diest, P. J. (2014). The Effects of Under 6 Hours of Formalin Fixation on Hormone Receptor and HER2 Expression in Invasive Breast Cancer: A Systematic Review. American Journal of Clinical Pathology, 142(1), 16–22.
4. Lee, A. H. S., Key, H. P., et al. (2014). The effect of delay in fixation on HER2 expression in invasive carcinoma of the breast assessed with immunohistochemistry and in situ hybridisation. Journal of Clinical Pathology, 67(7), 573–575
5. Nagahashi, M., Shimada, Y., Ichikawa, H. et al. (2017). Formalin-fixed paraffin-embedded sample conditions for deep next generation sequencing. *The Journal of Surgical Research*, *220*, 125–132. http://doi.org/10.1016/j.jss.2017.06.077
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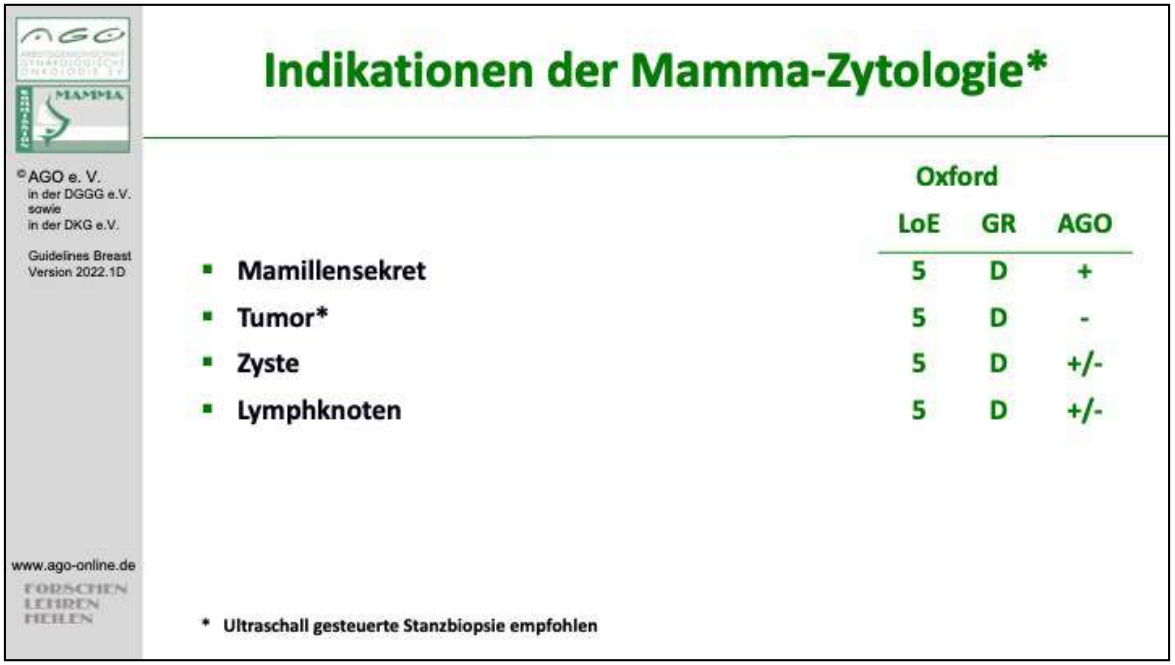
Retraction artifacts

1. Ragage, F., Debled, M., MacGrogan, G., et al. (2010). Is it useful to detect lymphovascular invasion in lymph node-positive patients with primary operable breast cancer? *Cancer*, *116*(13), 3093–3101.

2. Lester, S. C., Bose, S., Chen, Y.-Y., et al. (2009). Protocol for the examination of specimens from patients with invasive carcinoma of the breast. Arch Pathol Lab Med, 133(10), 1515–1538.



1. Day, C, N Moatamed, AM Fimbres, et al: A Retrospective Study of the Diagnostic Accuracy of Fine-Needle Aspiration for Breast Lesions and Implications for Future Use. Diagnostic Cytopathology 36, no. 12 (November 30, 2008): 855–60.
2. Pinder, S E, and J S Reis-Filho. Non-Operative Breast Pathology. Journal of Clinical Pathology 60, no. 12 (December 20, 2006): 1297–99. doi:10.1136/jcp.2006.040519.
3. Tse, G M K, T K F Ma, P C W Lui, et al. Fine Needle Aspiration Cytology of Papillary Lesions of the Breast: How Accurate Is the Diagnosis?. Journal of Clinical Pathology 61, no. 8 (August 2008): 945–49. doi:10.1136/jcp.2008.057489.
4. Ibrahim AE, Bateman AC, Theaker JM, et al. The role and histological classification of needle core biopsy in comparison with fine needle aspiration cytology in the preoperative assessment of impalpable breast lesions. J Clin Pathol 2001;54:121–5.
5. He, X., Wang, Y., Nam, G., et al. (2018). A 10 year retrospective review of fine needle aspiration cytology of cystic lesions of the breast with emphasis on papillary cystic lesions. *Diagnostic Cytopathology*. http://doi.org/10.1002/dc.24123
6. Bruzzone, M., Saro, F., Bruno, S. et al. (2018). Synergy of cytological methods in the pathological staging of breast cancer: Axillary fine-needle aspiration and intraoperative scrape cytology of the sentinel lymph node. *Diagnostic Cytopathology*, *46*(11), 919–926. http://doi.org/10.1002/dc.23995
7. Tiwari, P., Ghosh, S., & Agrawal, V. K. (2018). Evaluation of breast lesions by digital mammography and ultrasound along with fine-needle aspiration cytology correlation. *Journal of Cancer Research and Therapeutics*, *14*(5), 1071–1074.

http://doi.org/10.4103/0973-1482.191053

Statement: Routine workup in step sections

1. Hahn, M., Krainick-Strobel, U., Toellner, T. et al. (2012). Interdisciplinary consensus recommendations for the use of vacuum-assisted breast biopsy under sonographic guidance: first update 2012. *Ultraschall Med*, *33*(4), 366–371. http://doi.org/10.1055/s-0032-1312831
2. Sinn, Gerber, Brucker et al. (2017): DCIS und Risikoläsionen. In: AWMF: S3-Leitlinie Früherkennung, Diagnostik, Therapie und Nachsorge des Mammakarzinoms, S. 79 - 89.

Statement: Correlation with imaging

1. Heywang-Köbrunner SH, Sinnatamby R, Lebeau A, et al; Consensus Group. Interdisciplinary consensus on the uses and technique of MR-guided vacuum-assisted breast biopsy (VAB): results of a European consensus meeting. Eur J Radiol. 2009 Nov;72(2):289-94
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Statement: Frozen section diagnosis on core biopsies

1. Lebeau, Gerber, Brucker et al. (2017): Pathomorphologische Untersuchung. In: AWMF: S3-Leitlinie Früherkennung, Diagnostik,

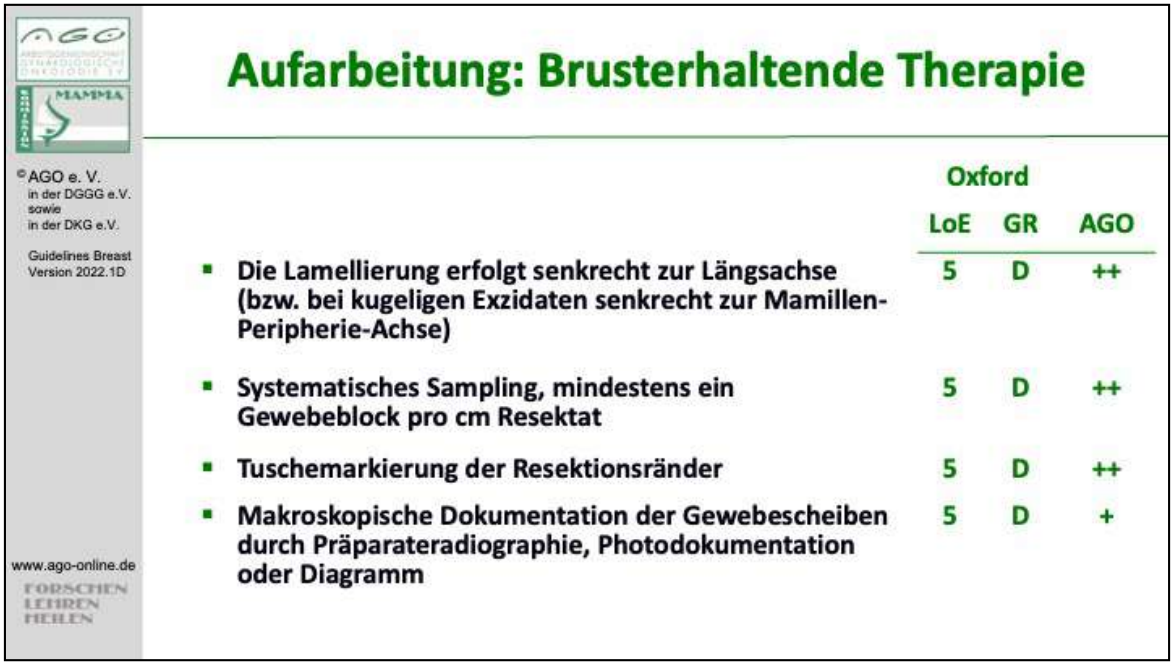
Therapie und Nachsorge des Mammakarzinoms, S. 100 - 139.
2. Dämmrich, M., Thomssen, C., Hillemanns, P. et al. (2012). Intraoperative pathologische Sofortuntersuchung in der Mammachirurgie. *Der Pathologe*, *33*(5), 424–429. http://doi.org/10.1007/s00292-012-1596-6

Statement: Routine evaluation of ER/PgR and HER-2 status

1. Dekker, T. J. A., Smit, V. T. H. B. M., Hooijer, G. K. J. et al. (2013). Reliability of core needle biopsy for determining ER and HER2 status in breast cancer. *Annals of Oncology*, *24*(4), 931–937. http://doi.org/10.1093/annonc/mds599
2. Meattini, I., Bicchierai, G., Saieva, C. et al. (2017). Impact of molecular subtypes classification concordance between preoperative core needle biopsy and surgical specimen on early breast cancer management: Single-institution experience and review of published literature. *European Journal of Surgical Oncology : the Journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology*, *43*(4), 642–648. http://doi.org/10.1016/j.ejso.2016.10.025

Statement: Turn-around time < 24h

1. Amendoeira I, Apostolikas N, Bellocq et al. Quality assurance guidelines for pathology: Open biopsy and resection specimens. In: Perry N, Broders M, de Wolf C, Törnberg S, Holland R, von Karsa L, Puthaar E (eds) European guidelines for quality assurance in breast cancer



Guidelines

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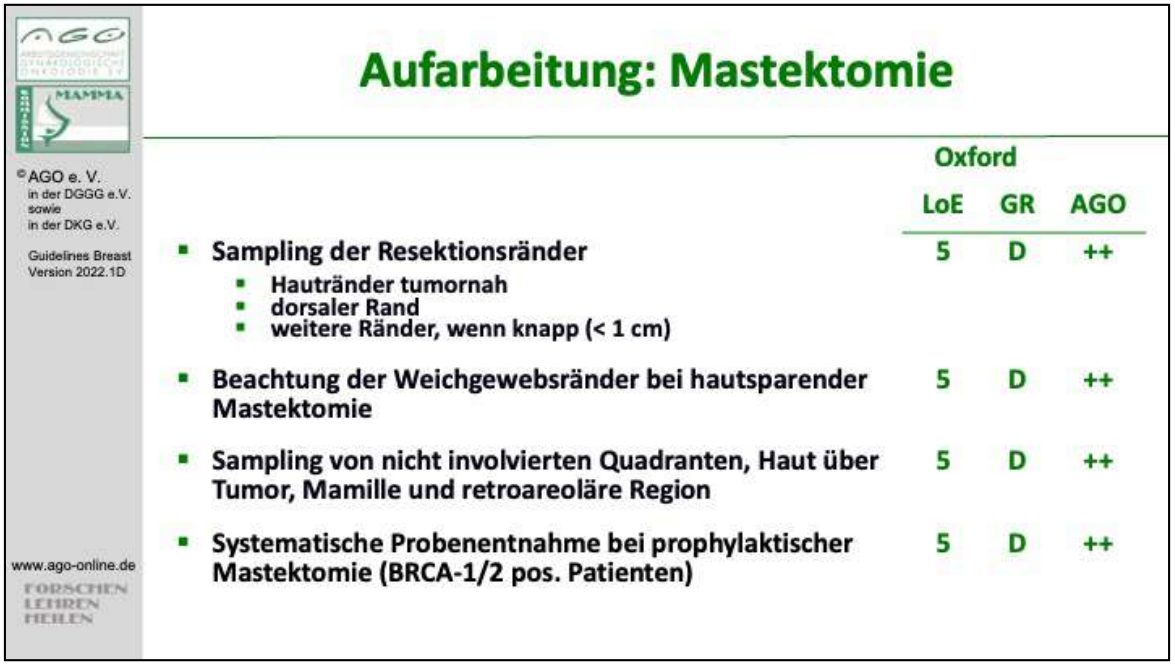
2. Schnitt SJ, Moran MS, Houssami N, Morrow M. The Society of Surgical Oncology-American Society for Radiation Oncology Consensus Guideline on Margins for Breast-Conserving Surgery With Whole-Breast Irradiation in Stages I and II Invasive Breast Cancer: Perspectives for Pathologists. *Arch Pathol Lab Med*. August 2014. doi:10.5858/arpa.2014-0384-ED.
3. Schweizerische Gesellschaft für Pathologie (2002). Leitlinien zur Sicherung und Förderung der Qualitätskontrolle. https://sgpath.ch/docs/QRL/QRL_SGPath_Mamma_2017.pdf
4. Lester SC, Bose S, Chen Y-Y, et al. Protocol for the examination of specimens from patients with invasive carcinoma of the breast. *Arch Pathol Lab Med*. 2009;133(10):1515-1538. doi:10.1043/1543-2165-133.10.1515.
5. Lester SC, Bose S, Chen Y-Y, et al. Protocol for the examination of specimens from patients with ductal carcinoma in situ of the breast. *Arch Pathol Lab Med*. 2009;133(1):15-25. doi:10.1043/1543-2165-133.1.15.
6. Fitzgibbons P, Connolly J, Page D. Updated protocol for the examination of specimens from patients with carcinomas of the

breast. Cancer Committee. *Arch Pathol Lab Med*. 2000;124(7):1026-1033.

Systematic Sampling

1. Ang SC, Tapia G, Davidson EJ, et al. Positive anterior margins in breast conserving surgery: Does it matter? A systematic review of the literature. *Breast*. 2016;27:105-108. doi:10.1016/j.breast.2015.12.013.
2. Molina MA, Snell S, Franceschi D, et al. Breast specimen orientation. *Ann Surg Oncol*. 2009;16(2):285-288. doi:10.1245/s10434-008-0245-z.
3. Sinn HP, Anton HW, Magener A, Fournier von D, Bastert G, Otto HF. Extensive and predominant in situ component in breast carcinoma: their influence on treatment results after breast-conserving therapy. *Eur J Cancer*. 1998;34(5):646-653. doi:10.1016/s0959-8049(97)10106-x.
4. Decker T, Ruhnke M, Schneider W. Standardisierte pathologische Untersuchung von Mamma-Exzisionspräparaten. Relevanz innerhalb eines interdisziplinären Praxisprotokolls für das Qualitätsmanagement der brusterhaltenden Therapie. *Der Pathologe*. 1997;18(1):53-59. doi:10.1007/s002920050196.



Guidelines

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3. Schweizerische Gesellschaft für Pathologie (2002). Leitlinien zur Sicherung und Förderung der Qualitätskontrolle. https://sgpath.ch/docs/QRL/QRL_SGPath_Mamma_2017.pdf
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breast. Cancer Committee. *Arch Pathol Lab Med*. 2000;124(7):1026-1033.

Skin sparing and nipple sparing mastectomy

1. Papassotiropoulos B, Güth U, Chiesa F, et al. Prospective Evaluation of Residual Breast Tissue After Skin- or Nipple-Sparing Mastectomy: Results of the SKINI-Trial. *Ann Surg Oncol*. 2019;26(5):1254-1262. doi:10.1245/s10434-019-07259-1.
2. Mota BS, Riera R, Ricci MD, et al. Nipple- and areola-sparing mastectomy for the treatment of breast cancer. *Cochrane Database Syst Rev*. 2016;11:CD008932. doi:10.1002/14651858.CD008932.pub3.
3. Zhang H, Li Y, Moran MS, Haffty BG, Yang Q. Predictive factors of nipple involvement in breast cancer: a systematic review and meta-analysis. *Breast Cancer Res Treat*. 2015;151(2):239-249. doi:10.1007/s10549-015-3385-4.
4. Wang J, Xiao X, Wang J, et al. Predictors of nipple-areolar complex involvement by breast carcinoma: histopathologic analysis of 787 consecutive therapeutic mastectomy specimens. *Ann Surg Oncol*. 2012;19(4):1174-1180. doi:10.1245/s10434-011-2107-3.
5. Petit JY, Veronesi U, Orecchia R, et al. Risk factors associated with recurrence after nipple-sparing mastectomy for invasive and intraepithelial neoplasia. *Ann Oncol*. January 2012. doi:10.1093/annonc/mdr566.
6. Weidong Li, Shuling Wang, Xiaojing Guo, et al. Nipple involvement in breast cancer: retrospective analysis of 2323 consecutive mastectomy specimens. *International Journal of Surgical Pathology*. 2011;19(3):328-334. doi:10.1177/1066896911399279.
7. Brachtel EF, Rusby JE, Michaelson JS, et al. Occult nipple involvement in breast cancer: clinicopathologic findings in 316 consecutive mastectomy specimens. *J Clin Oncol*. 2009;27(30):4948-4954. doi:10.1200/JCO.2008.20.8785.
8. Güth U, Wight E, Schötzau A, et al. Correlation and significance of histopathological and clinical features in breast cancer with skin involvement (T4b). *Hum Pathol*. 2006;37(3):264-271.
9. Torresan RZ, Santos dos CC, Okamura H, Alvarenga M. Evaluation of residual glandular tissue after skin-sparing mastectomies. *Ann Surg Oncol*. 2005;12(12):1037-1044. doi:10.1245/ASO.2005.11.027.
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11. Sikand K, Lee AHS, Pinder SE, Elston CW, Ellis IO. Sections of the nipple and quadrants in mastectomy specimens for carcinoma are of limited value. *SciMed Central*. 2005;58(5):543-545. doi:10.1136/jcp.2004.022665.

12. Love SM, Barsky SH. Anatomy of the nipple and breast ducts revisited. *Cancer*. 2004;101(9):1947-1957. doi:10.1002/cncr.20559.
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16. Lüttges J, Kalbfleisch H, Prinz P. Nipple involvement and multicentricity in breast cancer. A study on whole organ sections. *J Cancer Res Clin Oncol*. 1987;113(5):481-487.
17. Morimoto T, Komaki K, Inui K, et al. Involvement of nipple and areola in early breast cancer. *Cancer*. 1985;55(10):2459-2463.

Aufarbeitung: Sentinel-Lymphknoten

	Oxford LoE	Oxford GR	AGO
▪ Vollständige Aufarbeitung am Paraffinschnitt mit Schnittstufen von ≤ 500 µm	5	D	++
▪ Zytokeratin-Immunhistologie			
▪ zum Nachweis von Mikrometastasen, wenn suspekt	2b	B	+
▪ zum Nachweis von Mikrometastasen nach NACT	2b	B	+
▪ routinemäßig	5	D	+/-
▪ Schnellschnittuntersuchung (anschließender Paraffinschnitt erschwert)			
▪ bei klinischer Konsequenz	5	D	+
▪ bei nicht zu erwartender Konsequenz	5	D	-
▪ Abtupfzytologie anstatt oder zusätzlich zur Schnellschnittuntersuchung	3b	C	+/-
▪ RT-PCR zum Nachweis von Metastasen	4	D	-
▪ OSNA	3b	B	-

Statement: Evaluation of sentinel node biopsy

1. Maguire, A., & Brogi, E. (2016). Sentinel lymph nodes for breast carcinoma: an update on current practice. *Histopathology*, *68*(1), 152–167. http://doi.org/10.1111/his.12853
2. Liu L-C, Lang JE, Lu Y, et al. Intraoperative frozen section analysis of sentinel lymph nodes in breast cancer patients: a meta-analysis and single-institution experience. *Cancer*. 2011;117(2):250-258. doi:10.1002/cncr.25606.

Statement: Full workup using step sections of ≥ 500 µm on paraffin embedded tissue

1. Maguire, A., & Brogi, E. (2016). Sentinel lymph nodes for breast carcinoma: an update on current practice. *Histopathology*, *68*(1), 152–167. http://doi.org/10.1111/his.12853

Statement: Frozen section

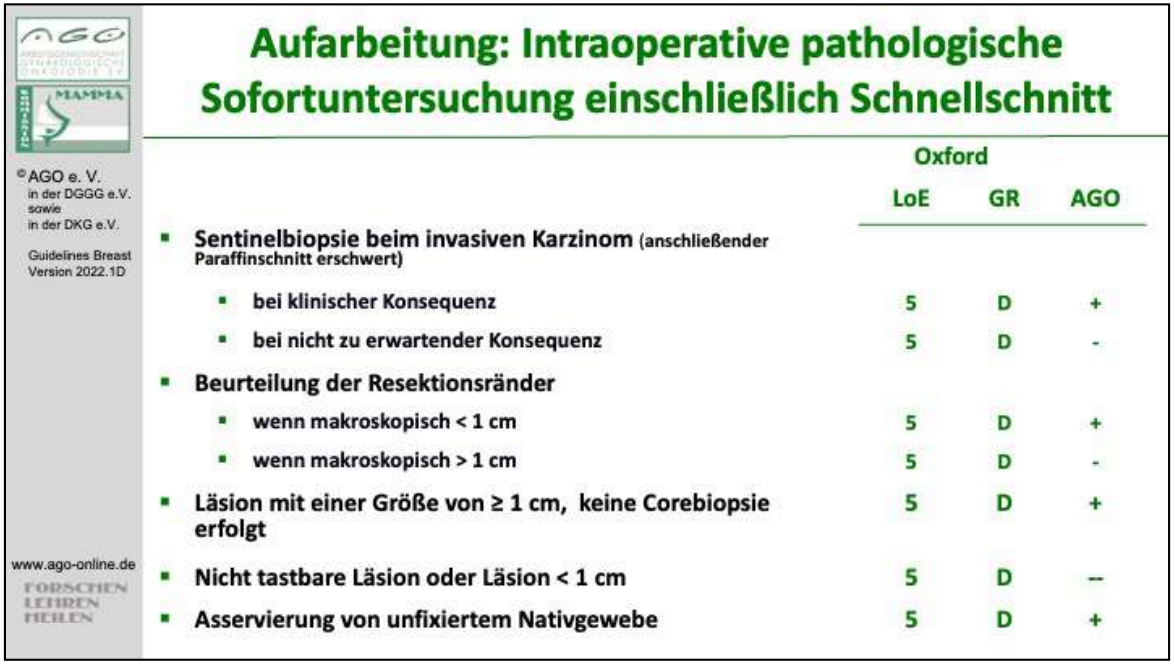
1. Langer, I., Guller, U., Berclaz, G. et al. (2009). Accuracy of frozen section of sentinel lymph nodes: a prospective analysis of 659 breast cancer patients of the Swiss multicenter study. *Breast Cancer Research and Treatment*, *113*(1), 129–136. http://doi.org/10.1007/s10549-008-9911-x

Statement: Imprint cytology instead or in addition of frozen section

1. Layfield et al. Intraoperative assessment of sentinel lymph nodes in breast cancer. The British journal of surgery (2011) vol. 98 (1) pp. 4-17
2. Upender, S., Mohan, H., Handa, U. et al. (2009). Intraoperative evaluation of sentinel lymph nodes in breast carcinoma by imprint cytology, frozen section and rapid immunohistochemistry. *Diagnostic Cytopathology*, *37*(12), 871–875. http://doi.org/10.1002/dc.21120

Statement: RT-PCR for epithelial genes

1. Layfield, D. M., Agrawal, A., Roche, H. et al. (2011). Intraoperative assessment of sentinel lymph nodes in breast cancer. *The British Journal of Surgery*, *98*(1), 4–17. http://doi.org/10.1002/bjs.7229
2. Visser, M., Jiwa, M., Horstman, A. et al. (2008). Intra-operative rapid diagnostic method based on CK19 mRNA expression for the detection of lymph node metastases in breast cancer. *International Journal of Cancer Journal International Du Cancer*, *122*(11), 2562–2567. http://doi.org/10.1002/ijc.23451



Aufarbeitung: Intraoperative pathologische Sofortuntersuchung einschließlich Schnellschnitt

	Oxford LoE	Oxford GR	AGO
▪ **Sentinelbiopsie beim invasiven Karzinom** (anschließender Paraffinschnitt erschwert)			
▪ bei klinischer Konsequenz	5	D	+
▪ bei nicht zu erwartender Konsequenz	5	D	-
▪ **Beurteilung der Resektionsränder**			
▪ wenn makroskopisch < 1 cm	5	D	+
▪ wenn makroskopisch > 1 cm	5	D	-
▪ **Läsion mit einer Größe von ≥ 1 cm, keine Corebiopsie erfolgt**	5	D	+
▪ **Nicht tastbare Läsion oder Läsion < 1 cm**	5	D	--
▪ **Asservierung von unfixiertem Nativgewebe**	5	D	+

Statement: Sentinel node biopsy for invasive cancer

1. Kühn T, Bembenek A, Decker T et al. A concept for the clinical implementation of sentinel lymph node biopsy in patients with breast carcinoma with special regard to quality assurance. Cancer 2005; 103: 451-461.
2. Grabau D, Rank F, Friis E. Intraoperative frozen section examination of axillary sentinel lymph nodes in breast cancer. APMIS 2005; 113: 7-12.
3. Van Diest PJ, Torrenga H, Borgstein PJ et al. Reliability of intraoperative frozen section and imprint cytological investigation of sentinel lymph nodes in breast cancer. Histopathology 1999; 35: 14-18.

Statement: Closest margin of resection

1. Reiner-Concin A, Lax S. Mammakarzinom. In: Manual der gynäkologischen Onkologie (Reinthaler R, Helfer L, Hrsg.). http://www.ago-manual.at/inhalt/i-mammakarzinom/15-pathologie/
2. Kraus-Tiefenbacher U, Scheda A, Steil V, et al.Intraoperative radiotherapy (IORT) for breast cancer using the Intrabeam system. Tumori. 2005;91:339-45

Statement: Lesions ≥ 1 cm, without core biopsy

1. Reiner-Concin A, Lax S. Mammakarzinom. In: Manual der gynäkologischen Onkologie (Reinthaler R, Helfer L, Hrsg.). http://www.ago-

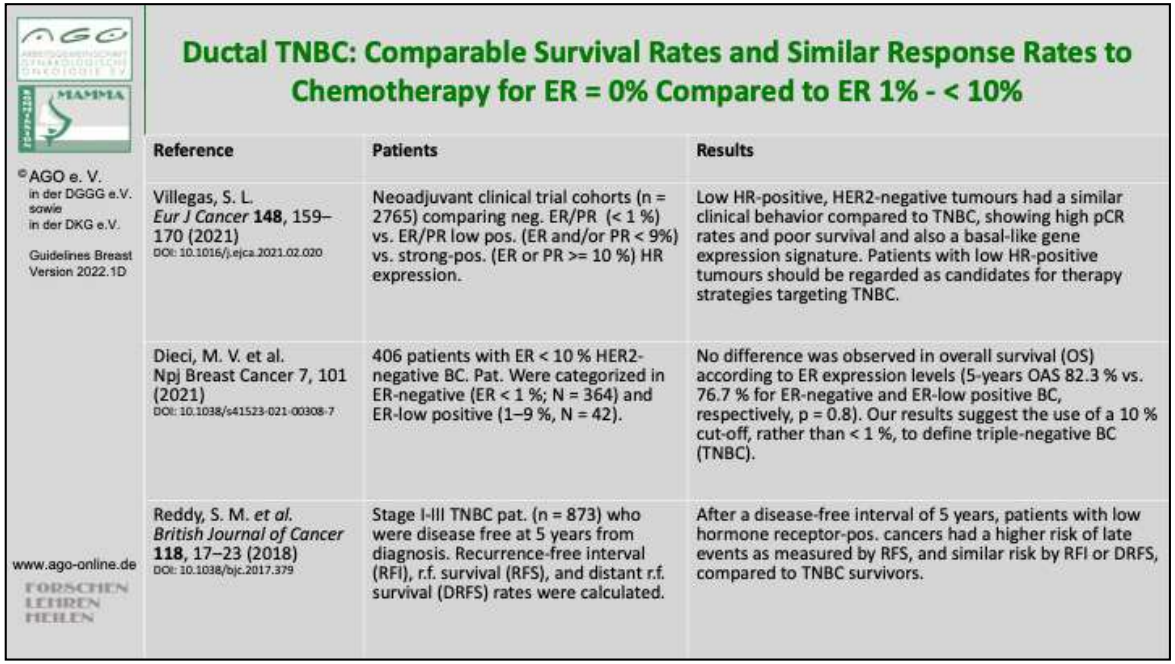
manual.at/inhalt/i-mammakarzinom/15-pathologie/
2. Fitzgibbons PL, Connolly JL, Page DL. Updated protocol for the examination of specimens from patients with carcinomas of the breast. Arch Pathol Lab Med 2000; 124:1026- 1033. (ACR)
3. Amendoeira I, Apostolikas N, Bellocq et al. Quality assurance guidelines for pathology: Open biopsy and resection specimens. In: Perry N, Broders M, de Wolf C, et al (eds) European guidelines for quality assurance in breast cancer screening and diagnosis; Office for Official Publications of the European Communities, Luxembourg, 2006, pp 256-311

Statement: Non-palpable lesions or lesions < 1 cm

1. Morrow M, Strom E, Bassett L et al. Standard for the management of ductal carcinoma in situ of the breast (DCIS). CA Cancer J Clin 2002; 52: 256-276.

WHO-Classification

1. Hoon TP, Ellis I, Allison K, et al. The 2019 WHO classification of tumours of the breast. *Histopathology*. February 2020. doi:10.1111/his.14091.
2. WHO. Breast Tumours: WHO Classification of Tumours. 5 ed. Lyon (France): International Agency for Research on Cancer; 2019.
3. Tan, P. H., & Ellis, I. O. (2013). Myoepithelial and epithelial-myoepithelial, mesenchymal and fibroepithelial breast lesions: updates from the WHO Classification of Tumours of the Breast 2012. Journal of Clinical Pathology, 66(6), 465–470. doi:10.1136/jclinpath-2012-201078
4. Viale, G. (2012). The current state of breast cancer classification. Annals of Oncology : Official Journal of the European Society for Medical Oncology / ESMO, 23 Suppl 10(suppl 10), x207–x210. doi:10.1093/annonc/mds326



Ductal TNBC: Comparable Survival Rates and Similar Response Rates to Chemotherapy for ER = 0% Compared to ER 1% - < 10%

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Reference	Patients	Results
Villegas, S. L. *Eur J Cancer* **148**, 159–170 (2021) DOI: 10.1016/j.ejca.2021.02.020	Neoadjuvant clinical trial cohorts (n = 2765) comparing neg. ER/PR (< 1 %) vs. ER/PR low pos. (ER and/or PR < 9%) vs. strong-pos. (ER or PR >= 10 %) HR expression.	Low HR-positive, HER2-negative tumours had a similar clinical behavior compared to TNBC, showing high pCR rates and poor survival and also a basal-like gene expression signature. Patients with low HR-positive tumours should be regarded as candidates for therapy strategies targeting TNBC.
Dieci, M. V. et al. Npj Breast Cancer 7, 101 (2021) DOI: 10.1038/s41523-021-00308-7	406 patients with ER < 10 % HER2-negative BC. Pat. Were categorized in ER-negative (ER < 1 %; N = 364) and ER-low positive (1–9 %, N = 42).	No difference was observed in overall survival (OS) according to ER expression levels (5-years OAS 82.3 % vs. 76.7 % for ER-negative and ER-low positive BC, respectively, p = 0.8). Our results suggest the use of a 10 % cut-off, rather than < 1 %, to define triple-negative BC (TNBC).
Reddy, S. M. *et al.* *British Journal of Cancer* **118**, 17–23 (2018) DOI: 10.1038/bjc.2017.379	Stage I-III TNBC pat. (n = 873) who were disease free at 5 years from diagnosis. Recurrence-free interval (RFI), r.f. survival (RFS), and distant r.f. survival (DRFS) rates were calculated.	After a disease-free interval of 5 years, patients with low hormone receptor-pos. cancers had a higher risk of late events as measured by RFS, and similar risk by RFI or DRFS, compared to TNBC survivors.

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Chemotherapy response and survival in low-ER BC vs. TNBC

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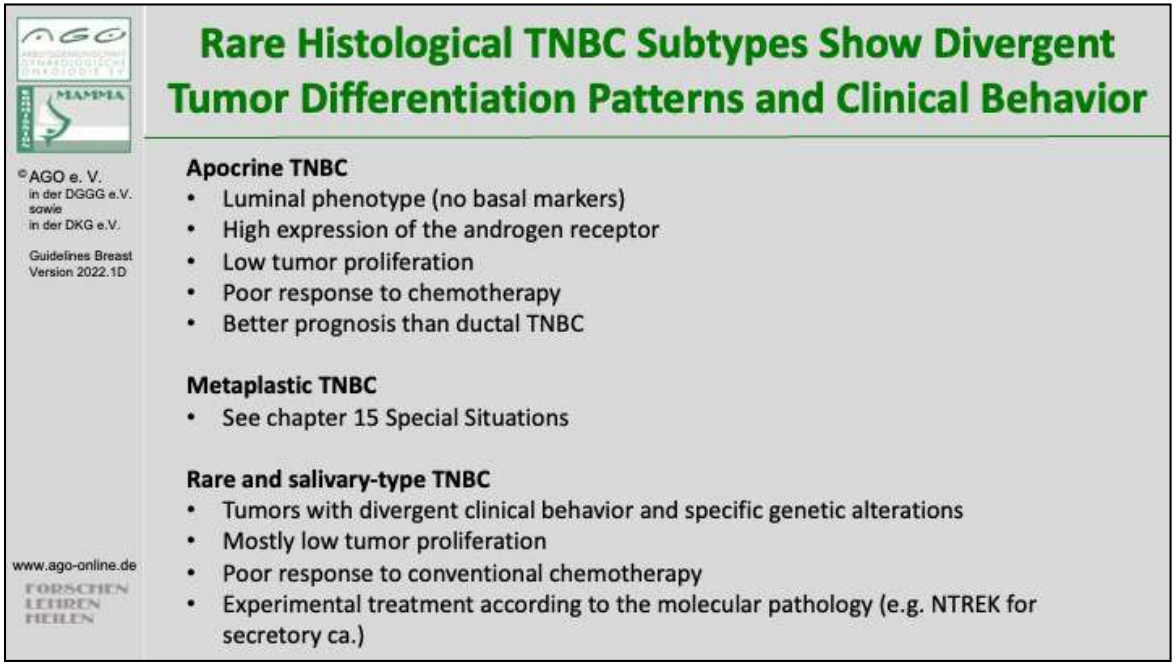

<u>Rare histological TNBC subtypes</u>

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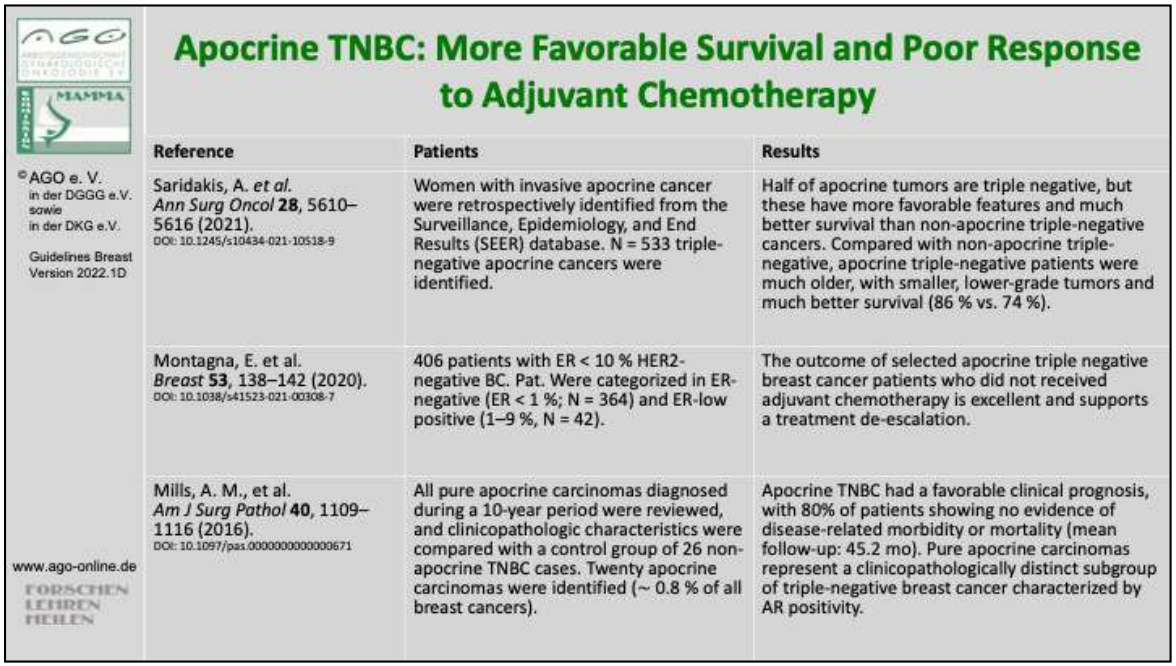

Apocrine TNBC: More Favorable Survival and Poor Response to Adjuvant Chemotherapy

Reference	Patients	Results
Saridakis, A. *et al.* *Ann Surg Oncol* **28**, 5610–5616 (2021). DOI: 10.1245/s10434-021-10518-9	Women with invasive apocrine cancer were retrospectively identified from the Surveillance, Epidemiology, and End Results (SEER) database. N = 533 triple-negative apocrine cancers were identified.	Half of apocrine tumors are triple negative, but these have more favorable features and much better survival than non-apocrine triple-negative cancers. Compared with non-apocrine triple-negative, apocrine triple-negative patients were much older, with smaller, lower-grade tumors and much better survival (86 % vs. 74 %).
Montagna, E. et al. *Breast* **53**, 138–142 (2020). DOI: 10.1038/s41523-021-00308-7	406 patients with ER < 10 % HER2-negative BC. Pat. Were categorized in ER-negative (ER < 1 %; N = 364) and ER-low positive (1–9 %, N = 42).	The outcome of selected apocrine triple negative breast cancer patients who did not received adjuvant chemotherapy is excellent and supports a treatment de-escalation.
Mills, A. M., et al. *Am J Surg Pathol* **40**, 1109–1116 (2016). DOI: 10.1097/pas.0000000000000671	All pure apocrine carcinomas diagnosed during a 10-year period were reviewed, and clinicopathologic characteristics were compared with a control group of 26 non-apocrine TNBC cases. Twenty apocrine carcinomas were identified (~ 0.8 % of all breast cancers).	Apocrine TNBC had a favorable clinical prognosis, with 80% of patients showing no evidence of disease-related morbidity or mortality (mean follow-up: 45.2 mo). Pure apocrine carcinomas represent a clinicopathologically distinct subgroup of triple-negative breast cancer characterized by AR positivity.

Apocrine TNBC

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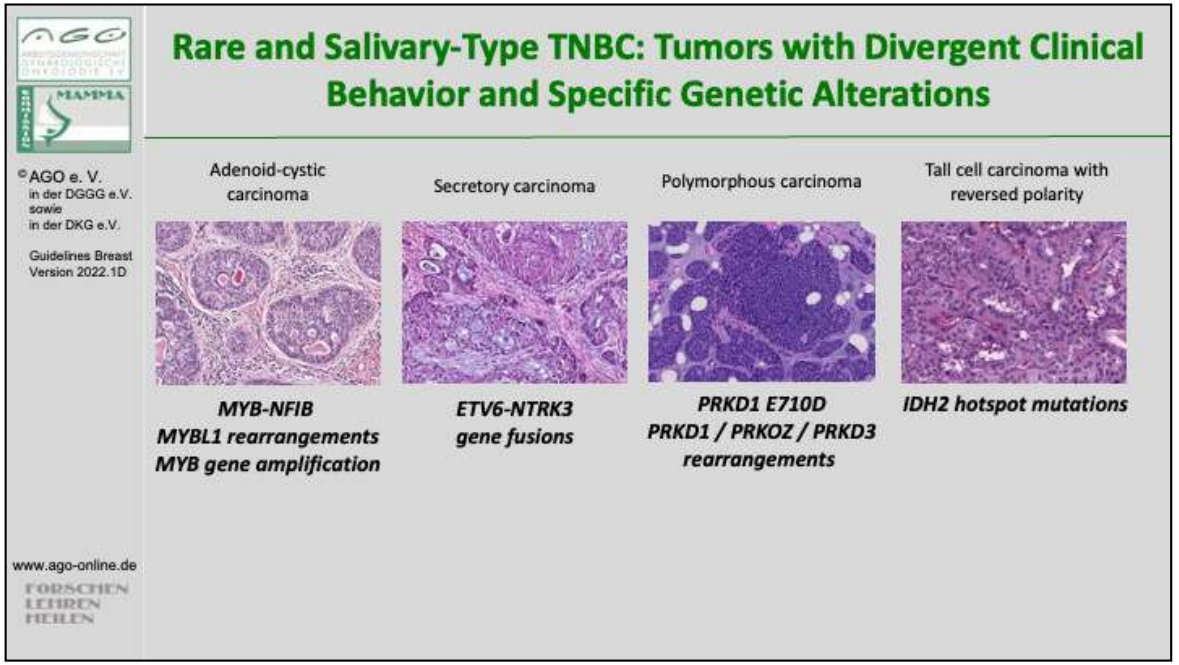

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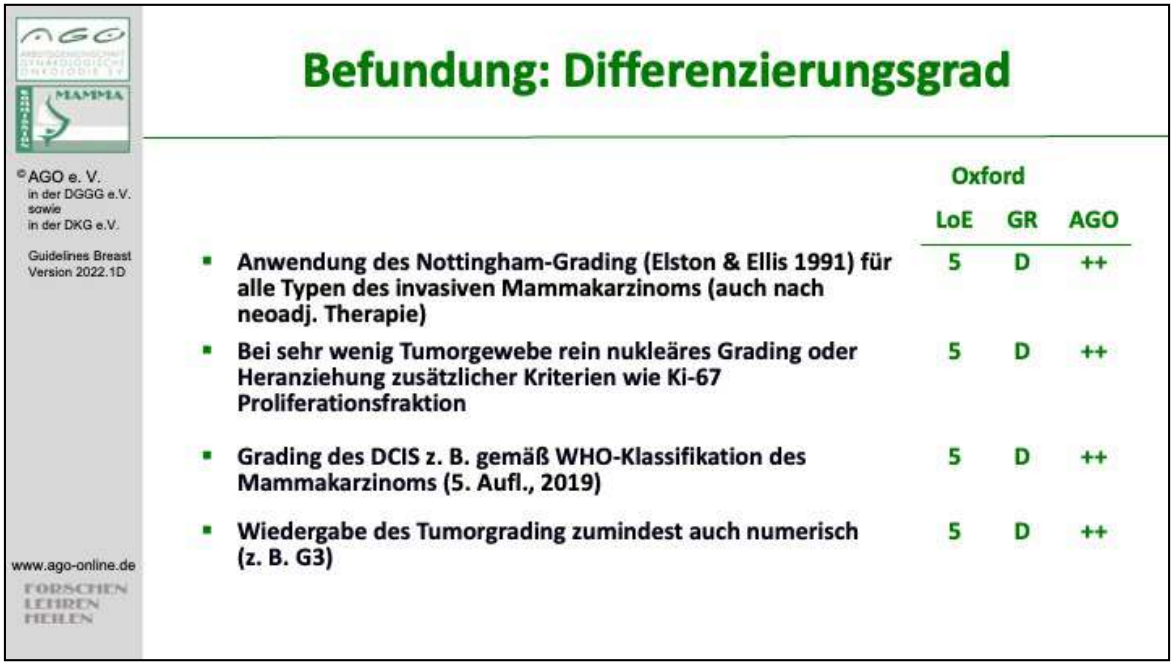

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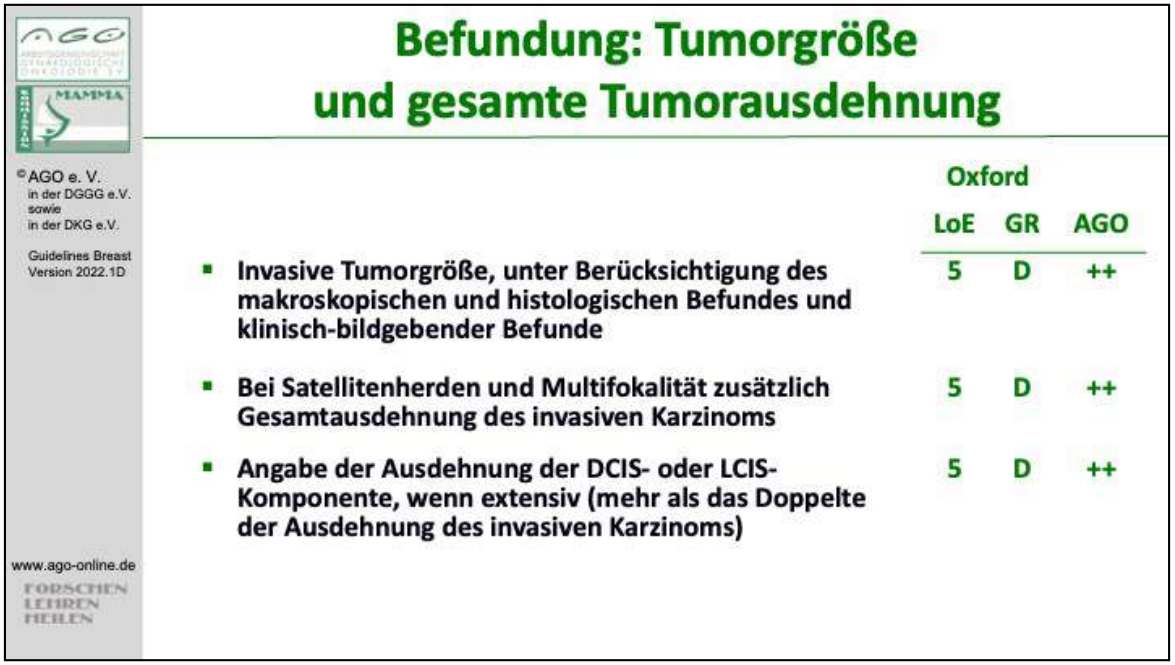

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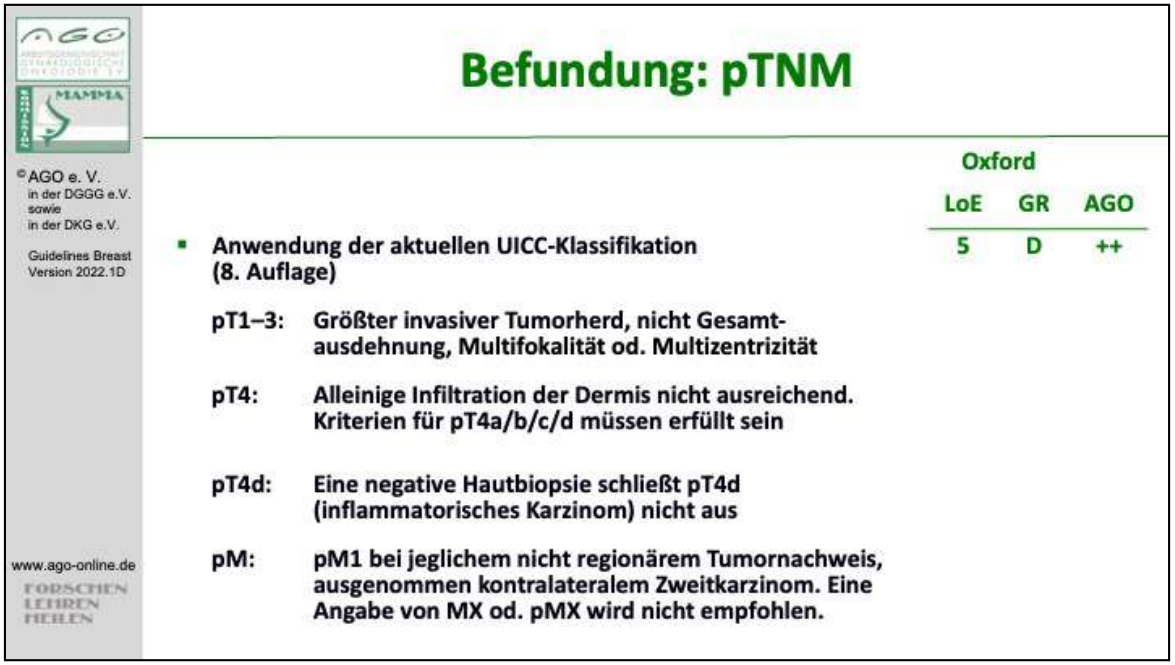

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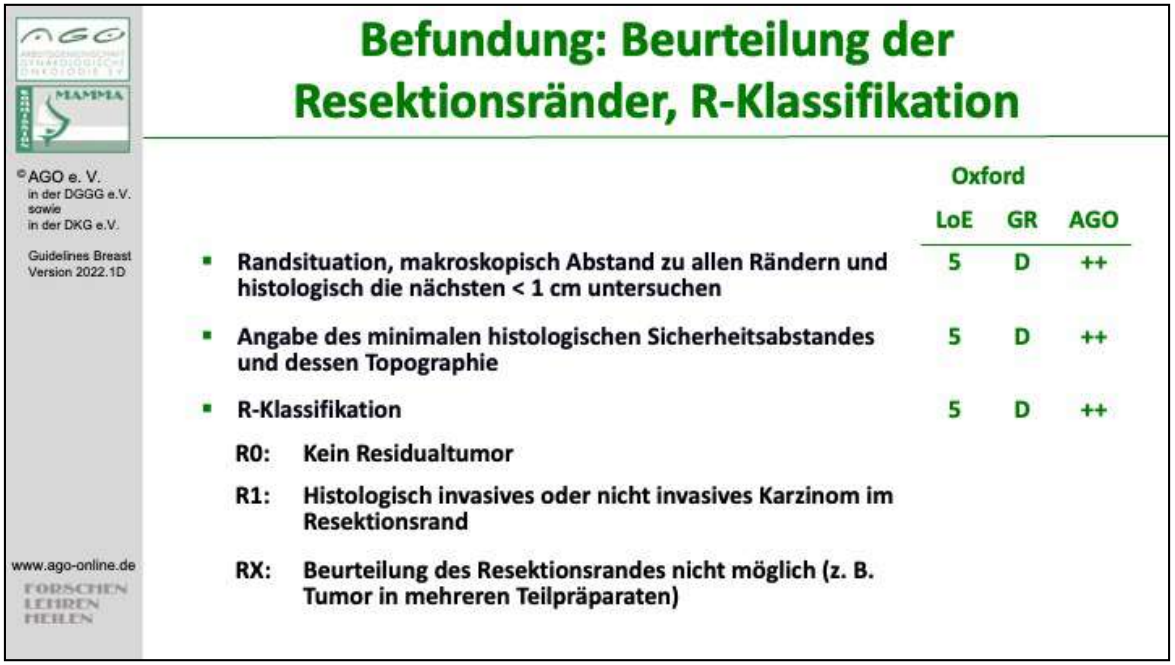

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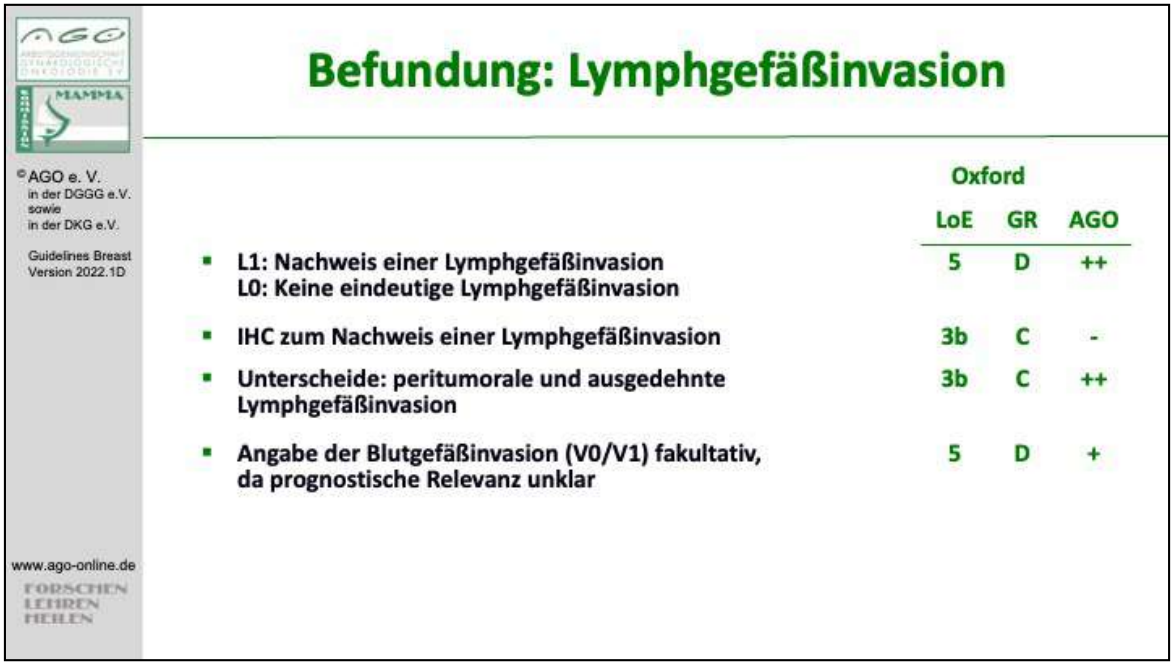

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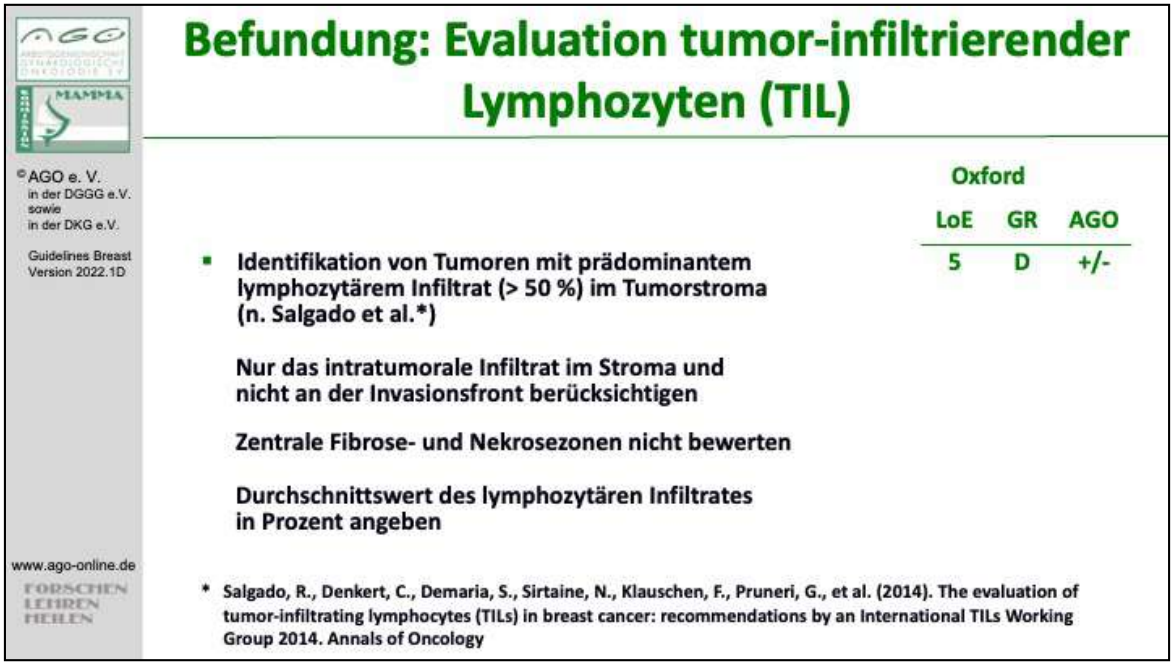

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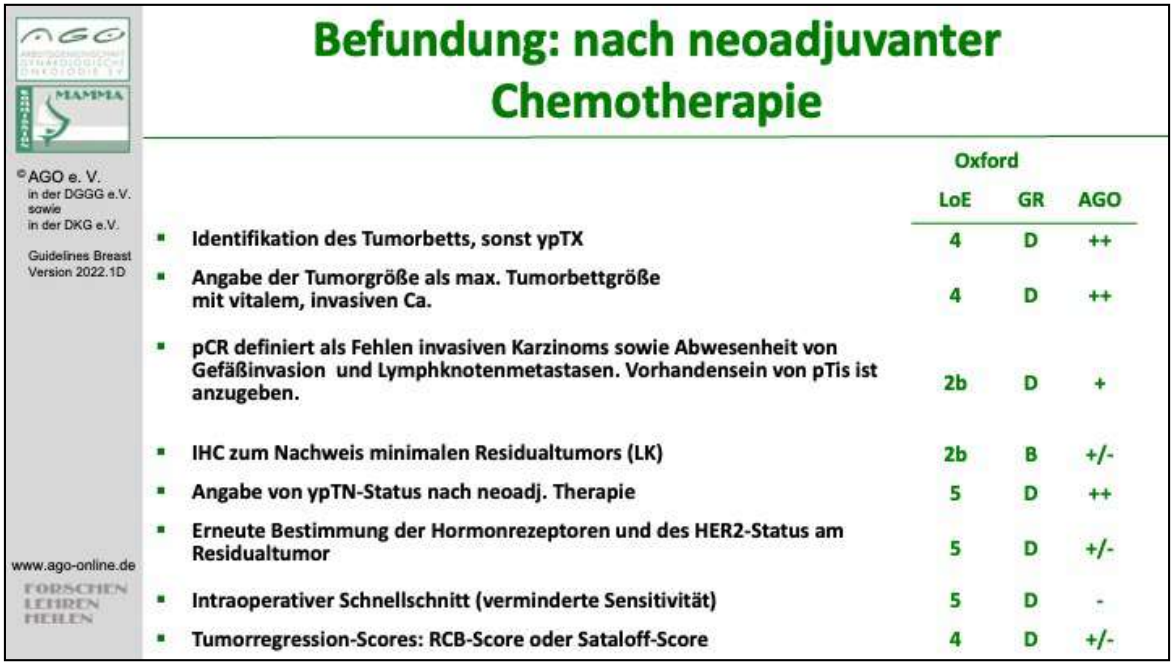

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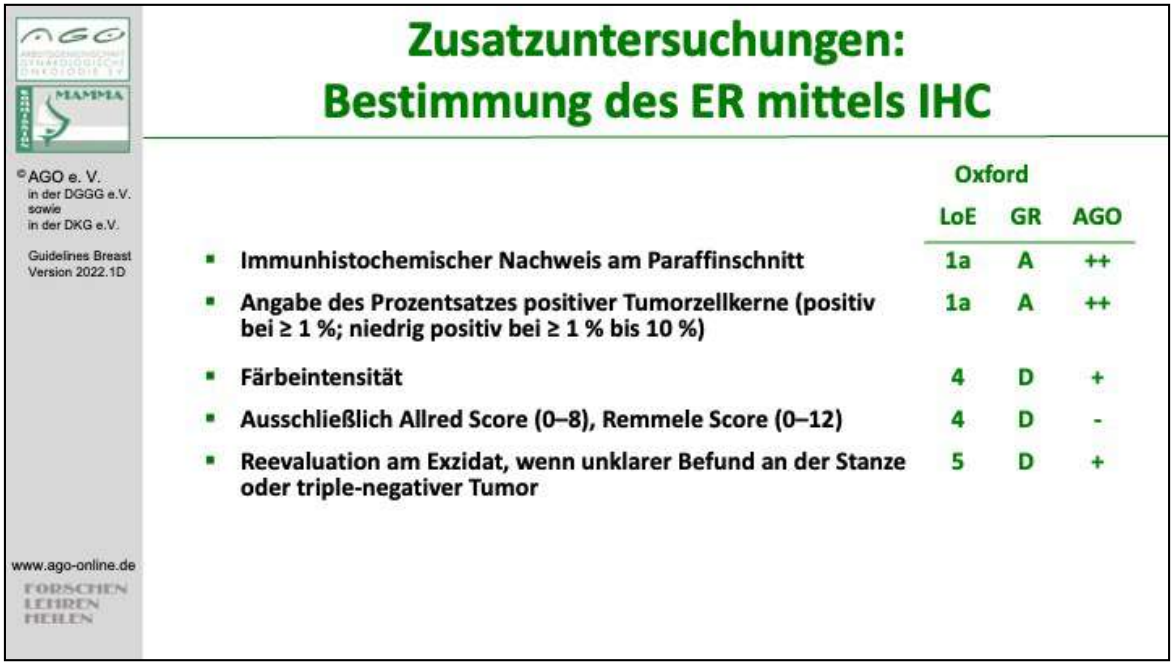

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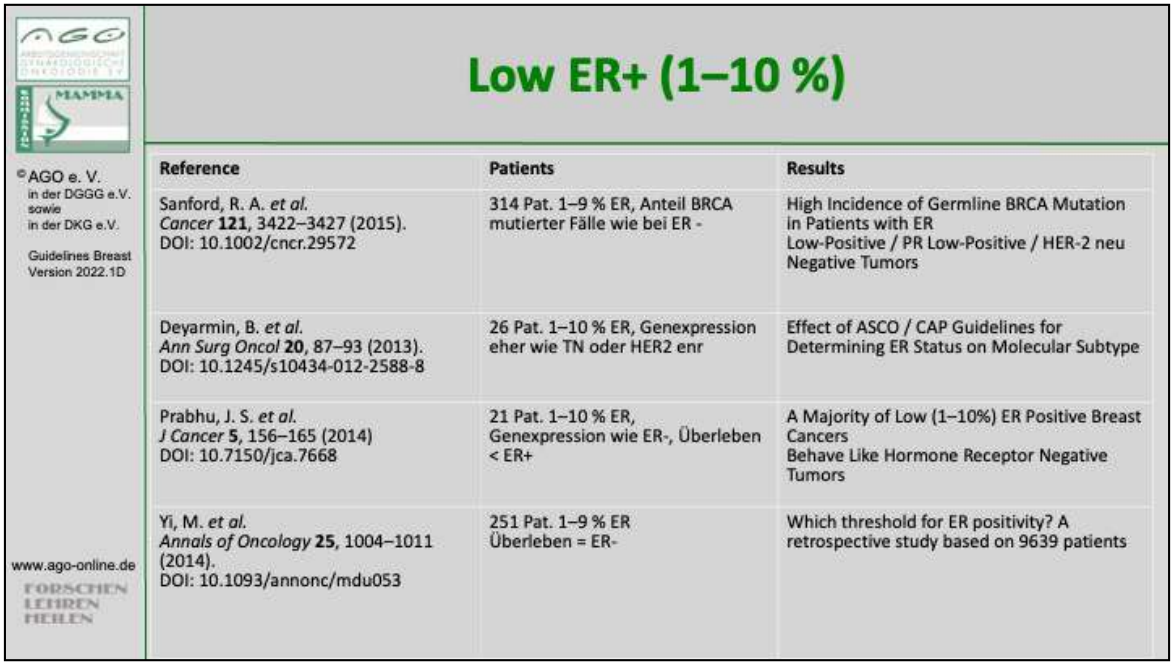

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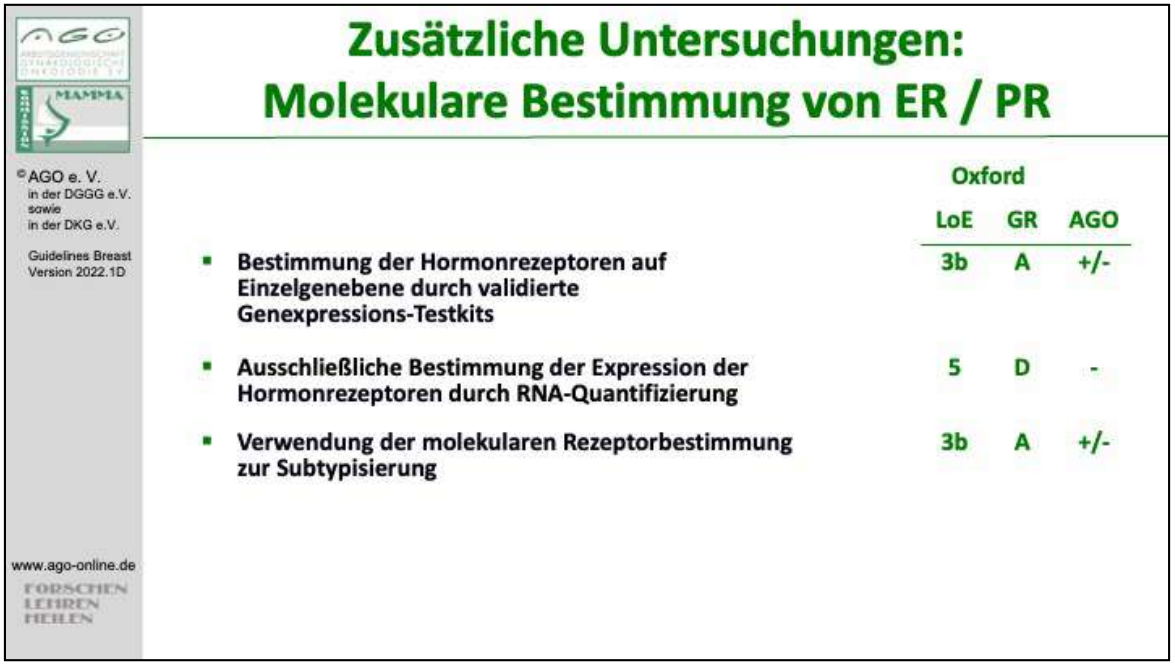

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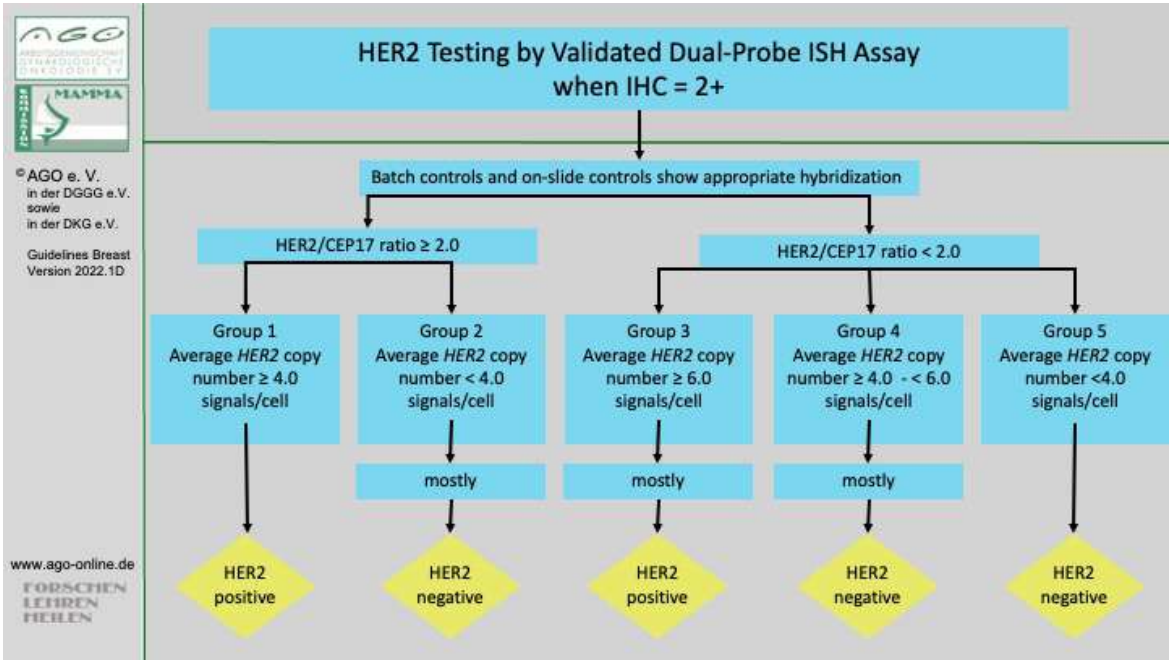

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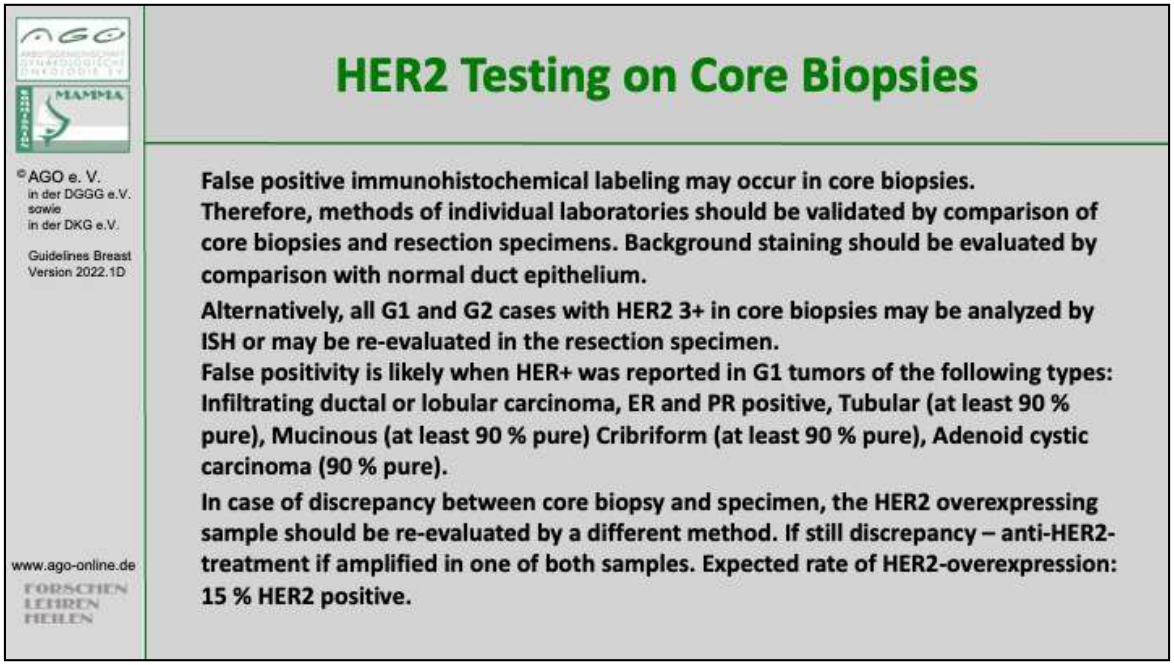

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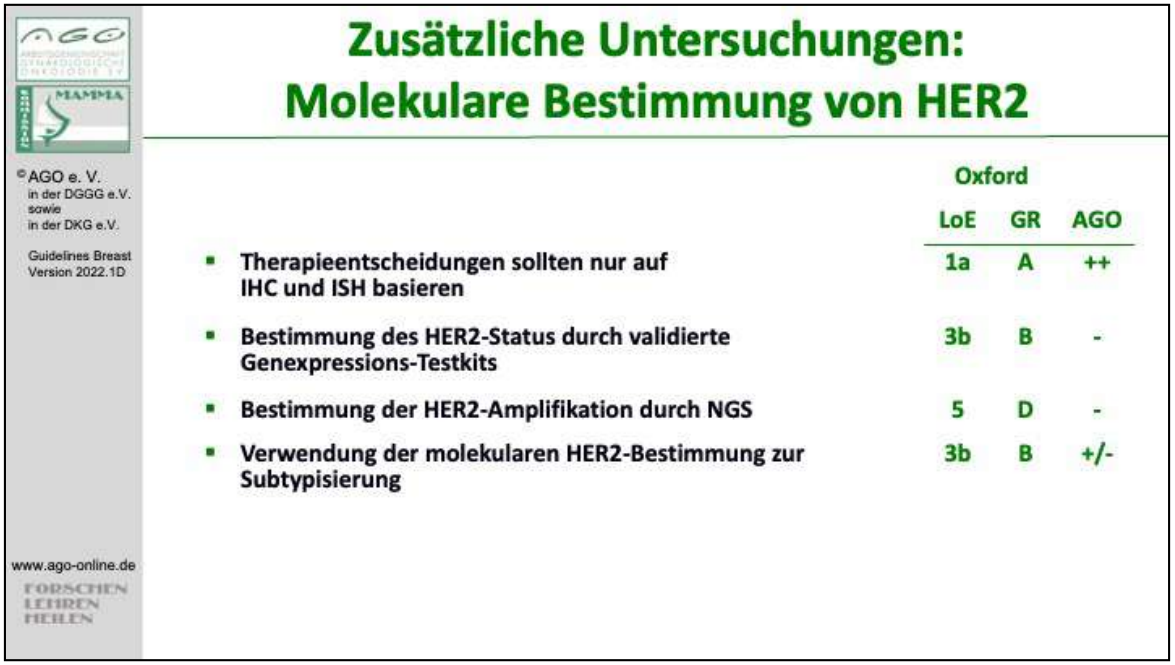

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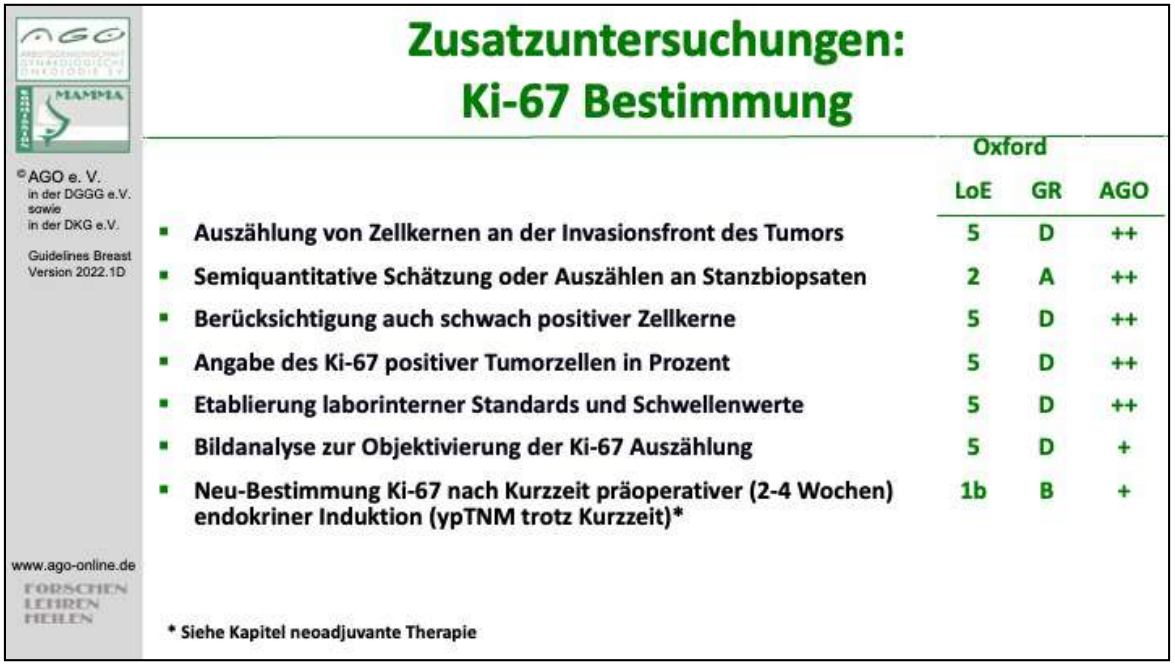

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<u>Ki67 als dynamischer Marker nach Kurzzeit endokriner Therapie</u>

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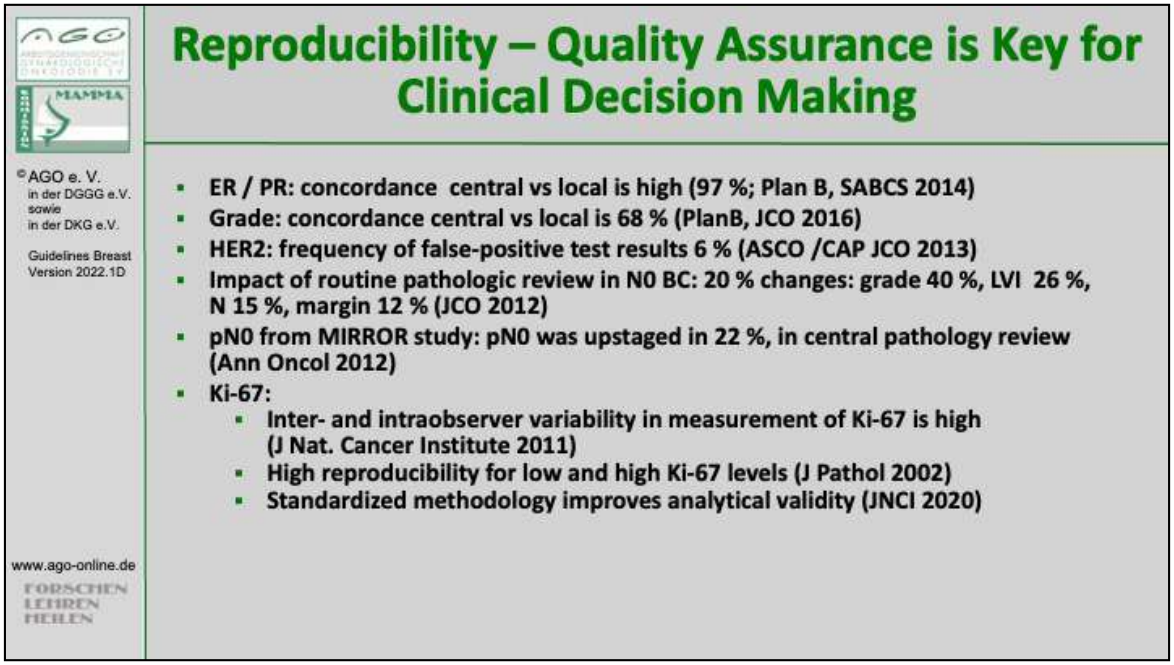

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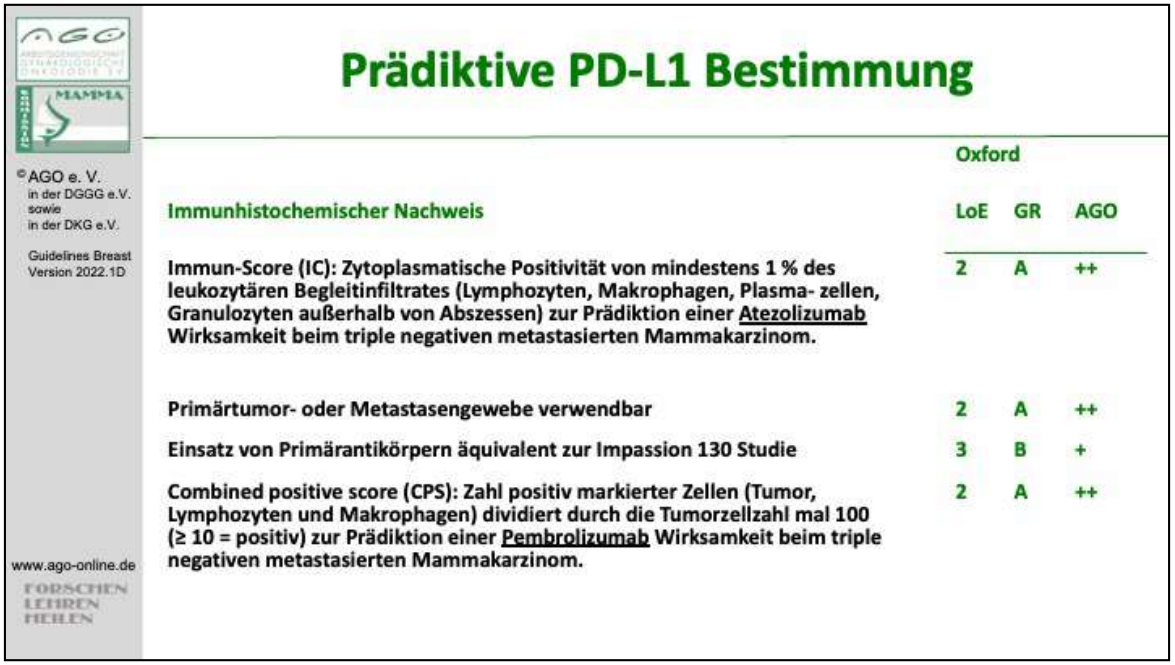

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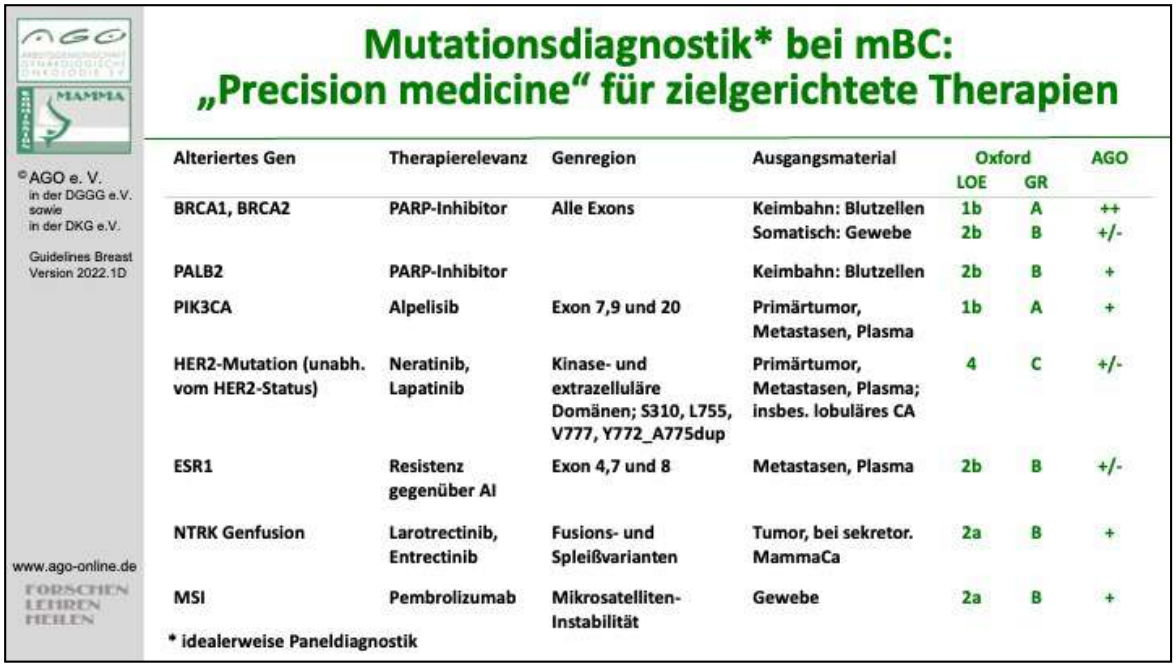

Mutationsdiagnostik* bei mBC: „Precision medicine“ für zielgerichtete Therapien

Alteriertes Gen	Therapierelevanz	Genregion	Ausgangsmaterial	Oxford LOE	Oxford GR	AGO
BRCA1, BRCA2	PARP-Inhibitor	Alle Exons	Keimbahn: Blutzellen	1b	A	++
			Somatisch: Gewebe	2b	B	+/-
PALB2	PARP-Inhibitor		Keimbahn: Blutzellen	2b	B	+
PIK3CA	Alpelisib	Exon 7,9 und 20	Primärtumor, Metastasen, Plasma	1b	A	+
HER2-Mutation (unabh. vom HER2-Status)	Neratinib, Lapatinib	Kinase- und extrazelluläre Domänen; S310, L755, V777, Y772_A775dup	Primärtumor, Metastasen, Plasma; insbes. lobuläres CA	4	C	+/-
ESR1	Resistenz gegenüber AI	Exon 4,7 und 8	Metastasen, Plasma	2b	B	+/-
NTRK Genfusion	Larotrectinib, Entrectinib	Fusions- und Spleißvarianten	Tumor, bei sekretor. MammaCa	2a	B	+
MSI	Pembrolizumab	Mikrosatelliten-Instabilität	Gewebe	2a	B	+

* idealerweise Paneldiagnostik

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