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Guidelines Breast
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**FORSCHEN
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Diagnostik und Therapie primärer und metastasierter Mammakarzinome

Operative Therapie des Mammakarzinoms unter onkologischen Aspekten



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Operative Therapie des Mammakarzinoms unter onkologischen Aspekten

- **Versionen 2002–2017:**
 Bauerfeind / Blohmer / Böhme / Brunnert /
 Costa / Fersis / Gerber / Hanf / Janni /
 Junkermann / Kaufmann / Kühn / Kümmel /
 Nitz / Rezai / Simon / Solomayer / Thomssen /
 Thill / Untch

- **Version 2018:**
 Bauerfeind / Gerber

Screened data bases

Pubmed 1998 - 2016, ASCO 2016, SABCS 2016, ESMO 2016, EBCC 2016

Screened consensus conference:

- Goldhirsch A, Winer EP, Coates AS, Gelber RD, Piccart-Gebhart M, Thürlimann B, Senn HJ; Panel members.
 Personalizing the treatment of women with early breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013.
 Ann Oncol. 2013 Sep;24(9):2206-23. doi: 10.1093/annonc/mdt303. Epub 2013 Aug 4.

Cochrane library:

- <http://onlinelibrary.wiley.com/cochranelibrary/search>



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Operative Therapie des Mammakarzinoms unter onkologischen Aspekten

AGO: ++

Die operative Therapie ist einer von mehreren Teilschritten bei der Behandlung des Mammakarzinoms. Daher ist sowohl eine diagnostische als auch eine onkologische Expertise unumgänglich und definitive Voraussetzung.



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Prätherapeutische Mamma- und Axilladiagnostik

		Oxford		
		LoE	GR	AGO
■	Klinische Untersuchung	5	D	++
■	Mammographie	2b	B	++
	■ Mammographie + Tomosynthese + Sonographie	3b	B	+
	■ Mammographie + Tomosynthese + Sonographie + MRT	3b	B	-
■	Sonographie	2b	B	++
	■ Axilla + FNP/CNB	2b	B	++
■	Minimalinvasive Biopsie*	1b	A	++
■	MRT**	1b	B	+/-

* Histologische Sicherung von Zusatzbefunden im Fall therapeutischer Relevanz.

** Die Möglichkeit der MRT-gestützten Biopsie ist Voraussetzung für die MRT-Untersuchung. MRT erwägen bei hohem familiären Risiko, eingeschränkter Beurteilbarkeit in MG & US (Beurteilbarkeit C/D), invasiv lobulärem Karzinom. Keine Reduktion der Nachresektionsrate.

* Histologische Sicherung von Zusatzbefunden im Fall therapeutischer Relevanz.
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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 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.


Biopsie

1. Chan KY, WiseberdFirtell, J, Jois HSR, et al. Localisation techniques for guided surgical excision of non-palpable breast lesions. Cochrane Database of Systematic reviews 2015;vol 12
2. Lourenco AP, Mainiero MB Incorporating imaging into the locoregional management of breast cancer. Semin Radiat Oncol 2016;26(1)
3. Mariscotti G, Houssami N, Durando M, et al. Accuracy of mammography, digital breast tomosynthesis, ultrasound and MR imaging in preoperative assessment of breast cancer. Anticancer Res. 2014 Mar;34(3):1219-25.


MRT

1. Mann RM, Loo CE, Wobbes T et al The impact of preoperative MRI on the re-excision rate in invasive lobular carcinoma of the breast. Breast Cancer Res Treat 2010; 119: 415-422
2. Houssami N, Turner R, Morrow M. Preoperative magnetic resonance imaging in breast cancer: meta-analysis of surgical outcomes. Ann Surg. 2013 Feb;257(2):249-55.
3. Debald M, Abramian A, Nemes L, et al. Who may benefit from preoperative MRI? A single-center analysis of 1102 consecutive patients with primary breast cancer. Breast Cancer Res Treat 2015;153(3):531-537
4. Arnaut A, Catley C, Booth CM, et al. Use of preoperative Magnetic Resonance Imaging for breast cancer: A Canadian population-based study. JAMA Oncol 2015;1(9):1238-1250
5. Fancellu A, Turner RM, Dixon JM, et al. Metaanalysis of the effect of preoperative MRI on the surgical management of ductal carcinoma in situ. Brit J Surg 2015;192(8):883-893
6. Houssami N, Turner R, Macaskill P, et al. An individual person data meta-analysis of preoperative magnetic resonance imaging and breast cancer recurrence. J Clin Oncol 2014;32(5):392-401
7. Vos EL, Voogd AC, Verhoef C, et al. Benefits of preoperative MRI in breast cancer surgery studied in a large population-based cancer registry. Br J Surg 2015;102(13):1649-1657
8. Lehman CD, Lee JM, DeMartini WS, et al. Screening MRI in women with a personal history of breast cancer. J Natl Cancer Inst 2016;108(3)
9. Wang SY, Long JB, Killelea BK, et al. Preoperative breast MRI and contralateral breast cancer occurrence among older women with breast cancer. J Clin Oncol 2015;Nov 30, epub ahead of print
10. Riedl CC, Luft N, Clemens B et al. Triple-modality screening trial for familial breast cancer underlines the importance of magnetic resonance imaging and questions the role of mammography and ultrasonography regardless of patient mutation status, age and breast density. JCO 2015;33(10):1128-1135

- 11.El Sharouni M, Postma EL, Menezes GLG et al. High prevalence of MRI-detected contralateral and ipsilateral malignant findings in patients with invasive ductolobular breast cancer: Impact on surgical management. Clin Breast Cancer. 2016 Aug;16(4):269-75.
- 12.Vriens BE, de Vries B, Lobbes MB, van Gastel SM, et al. INTENS Study Group. 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 Heal th 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



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MAMMA
ZS-PET-MRT

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Prätherapeutische Ganzkörperuntersuchung (Staging)

- **Anamnese und klinische Untersuchung**
Nur bei hohem Risiko für Fernmetastasen und / oder
Symptomen (bei geplanter Entscheidung zur
systemischen Chemo-/Antikörpertherapie)
- **CT Thorax/Abdomen**
- **Skelettszintigraphie**
- **Rö-Thorax**
- **Lebersonographie**
- **FDG-PET oder FDG-PET /CT**
- **Ganzkörper MRT**
- **Leber-MRT bei V.a. Metastasierung**

	Oxford		
	LoE	GR	AGO
	5	D	++
	2b	B	+
	2b	B	+
	5	C	+/-
	5	D	+/-
	3a	C	+/-
	4	C	+/-
	4	C	+

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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
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.
10. Gutzeit A, Doert A, Froehlich JM, et al. Comparison of diffusion-weighted whole body MRI and skeletal scintigraphy for the detection of bone metastases in patients with prostate or breast carcinoma. *Skeletal Radiol*. 2010 Apr;39(4):333-43.
11. Department of Health. Diagnosis, staging and treatment of patients with breast cancer. National Clinical Guideline No. 7. June 2015. ISSN 2009-6259
12. Bychkovsky BL, Lin NU: Imaging in the evaluation and follow-up of early and advanced breast cancer: When, why, and how often? 2017; 31, 318–324.
13. deSouza NM, Liu Y, Chiti A et al.: Strategies and technical challenges for imaging oligometastatic disease: Recommendations from the European Organisation for Research and Treatment of Cancer imaging group. *Eur J Cancer*. 2018 Jan 10. [Epub ahead of print].



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Stellenwert der operativen Optionen

- Die Überlebensraten nach BET (Tumorektomie + XRT) und MRM sind äquivalent
- Die Lokalrezidivraten nach „skin sparing mastectomy“ (SSM) und MRM sind äquivalent
- Die Erhaltung des Mamillen-Areola-Komplexes (MAK) bei MAK-fernem Tumor und tumorfreiem retroareolärem Gewebe ist onkologisch sicher

	Oxford		
	LoE	GR	AGO
	1a	A	
	2b	B	
	2b	C	

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Evidence of surgical procedure (6/16)

1. Statement: lumpectomy – mastectomy

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 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
3. Christiansen P, Carstensen SL, Ejlersen B, et al. Breast conserving surgery versus mastectomy: overall and relative survival-a population based study by the Danish Breast Cancer Cooperative Group (DBCG). Acta Oncol. 2017 Nov 23:1-7.
4. Hamelinck VC, Bastiaannet E, Pieterse AH, et al. prospective comparison of younger and older patients' preferences for breast-conserving surgery versus mastectomy in early breast cancer. J Geriatr Oncol. 2017 Sep 11. pii: S1879-4068(17)30175-3

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.
4. Simmons RM, Fish SK, Gayle L et al. Local and distant recurrence rates in skin-sparing mastectomies compared with non-skin-sparing mastectomies. *Ann Surg Oncol* 1999; 6:676-681.
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.
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.

Statement: Nipple sparing mastectomy

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.
2. Sacchini V, Pinotti JA, Barros AC et al. Nipple-sparing mastectomy for breast cancer and risk reduction: oncologic or technical problem? *J Am Coll Surg* 2006; 203:704-714.
3. Caruso F, Ferrara M, Castiglione G et al. Nipple sparing subcutaneous mastectomy: sixty-six months follow-up. *Eur J Surg Oncol* 2006; 32:937-940.
4. 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

5. Benediktsson KP, Perbeck L. Survival in breast cancer after nipple-sparing subcutaneous mastectomy and immediate reconstruction with implants: A prospective trial with 13 years median follow-up in 216 patients. *Eur J Surg Oncol* 2008; 34:143-148.
6. 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
7. 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.
8. Burdge EC, Yuen J, Hardee M, et al. Nipple skin-sparing mastectomy is feasible for advanced disease. *Ann Surg Oncol*. 2013 Oct;20(10):3294-302.
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
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.



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FOKUS MAMMA

Brusterhaltende Operation (BEO)

Vorgehensweise, Technische Aspekte

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▪ Nicht palpable Läsionen

- Bildgebend gestützte Drahtmarkierung
- Radionuklidmarkierung
- Präparateradiographie oder -ultraschall

▪ Tumorfremde Resektionsränder (auch bei ungünstiger Biologie reicht "no ink on tumor")

▪ Sofortige Nachresektion bei randbildendem Tumor in der Präparateradiographie oder -ultraschall und/oder intraoperativer patholog. Untersuchung

▪ Nachresektion bei Tumorausläufer bis in den Randbereich (Paraffinschnitt)

▪ Stereotaktische Befundentfernung als alleinige Therapie

▪ Intraop. Ultraschall zur Reduktion der Nachresektionsrate

▪ Intraop. Schnitttrandbeurteilung mit Margin probe

Oxford		
LoE	GR	AGO
2b	B	++
2b	B	+/-
2b	B	++
2a	A	++
1c	B	++
3b	C	+
4	D	--
1a	A	+/-
1b	A	+/-

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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.

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.

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.
2. 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.
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 ≥ 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
3. Vaz-Luis I, Ottesen RA, Hughes ME, et al. Outcomes by tumor subtype and treatment pattern in women with small, node-negative breast cancer: a multi-institutional study. *J Clin Oncol.* 2014 Jul 10;32(20):2142-50.
4. Pilewski M, Ho A, Orell E, et al. Effect of margin width on local recurrence in triple-negative breast cancer patients treated with breast conserving therapy. *Ann Surg Oncol.* 2014 Apr;21(4):1209-14.

Statement: ... re-excision ...

1. 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
3. McIntosh A, Freedman G, Eisenberg D: Recurrence rates and analysis of close or positive margins in patients treated without re-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

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
2. Gola S, Doyle-Lindrud S.: The MarginProbe® System: An Innovative Approach to Reduce the Incidence of Positive Margins Found After Lumpectomy. Clin J Oncol Nurs. 2016 Dec 1;20(6):598-599



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Brusterhaltende Operation (BEO) ohne neoadjuvante Therapie

	Oxford		
	LoE	GR	AGO
▪ Multizentrität	2b	B	+/-
▪ Histologisch befallene Resektionsränder trotz wiederholter Nachresektion	2b	B	--
▪ Inflammatorisches MaCa	2b	B	--

OP nach neoadjuvanter Chemotherapie
 siehe Kap. „Neoadjuvante Chemotherapie“

Statement: Multicentricity

- Gentilini O, Botteri E, Rotmensz N, et al. Conservative surgery in patients with multifocal/multicentric breast cancer. Breast Cancer Res Treat. 2009 Feb;113(3):577-83.
- 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.
- 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.

Statement: positive microscopic ...

- Tartter P. et al.: Lumpectomy margins, reexcision, and local recurrence of breast cancer. Amer J Surg, 2000, 179, 2, 81-85
- Cellini C, Huston T. Martins D. Multiple re-excisions versus mastectomy in patients with persistent residual disease following breast conservation surgery. Amer J Surg 2005, 189, 662-666
- 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.

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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
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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.
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.

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Axilläre Lymphknotendissektion (ALND) I

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■ Axilläre Lymphknotendissektion

- Endpunkt: Überleben (bei adäquater, multimodaler Therapie)
- Endpunkt: Staging
- Endpunkt: Lokoregionale Tumorkontrolle

■ Axilläre Lymphknotendissektion bei

- N+** (prä-OP) ohne neoadjuvante Systemtherapie
- DCIS
- SN positiv (cT1/2 cN0*, < 3 SN+, BET + tangentiale Radiatio, adäquate Systemtherapie)
- SN + (mic)
- SN (i+)
- SN + und Mastektomie (keine Radiotherapie der Thoraxwand)
- SN + und Mastektomie (Radiotherapie der Thoraxwand) bei T1-2 und 1-2 pos. SLN

■ Axilladissektion indiziert, aber nicht möglich

- Radiatio analog AMAROS-Studie

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

* Studienteilnahme empfohlen INSEMA

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Statement: Axillary lymph node dissection



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7. 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.

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Statement AMAROS-trial

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.


<div>  Operative Therapie der Axilla vor und nach NACT </div>						
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SLNB vor oder nach NACT bei cN0						
SLNB vor NACT				2b	B	+/-
SLNB nach NACT				2b	B	+
Weitere operative Therapie in Abhängigkeit von SLNB						
cN-Status (vor Therapie)	pN-Status (vor Therapie)	ycN-Status (nach Therapie)	operatives Vorgehen nach Therapie			
cN0	pN0(sn)	-	Nihil	1a	A	+
cN0	pN+(sn) analog ACOSOG Z0011	ycN0	Nihil Re-SN alleine ALND	5 2b 3	D B B	+ - +/-
cN0	pN+(sn) nicht analog ACOSOG Z0011	ycN0	Re-SN alleine ALND Axilla XRT	2b 2b 2b	B B B	- + +
cN0	Nicht durchgeführt	ypN0(SN) ycN0 ypN+(SN)	SN alleine ALND ALND	2b 2b 2b	B B B	+ +/- +
cN+	cN+ (CNB/FNA)	ycN0 ycN+ (CNB/FNA)	SN alleine ALND ALND	2b 2b 2b	B B B	+/- + ++

Complete Axillary lymph node dissection after positive sentinel lymph node may be ommitted in certain cases due to lack of benefit in pospectively 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.
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Statement surgical intervention in the axilla before or after neoadjuvant chemotherapy

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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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8. Martelli G, Miceli R, Folli S, et al. Sentinel node biopsy after primary chemotherapy in cT2 N0/1 breast cancer patients: Long-term results of a retrospective study. *Eur J Surg Oncol*. 2017 Nov;43(11):2012-2020.
9. Palmer JAV, Flippo-Morton T, Walsh KK, et al. Application of ACOSOG Z1071: Effect of Results on Patient Care and Surgical Decision-Making. *Clin Breast Cancer*. 2017 Oct 12. pii: S1526-8209(17)30492-5.
10. Fernandez-Gonzalez S, Falo C, Pla MJ, et al: The Shift From Sentinel Lymph Node Biopsy Performed Either Before or After Neoadjuvant Systemic Therapy in the Clinical Negative Nodes of Breast Cancer Patients. Results, and the Advantages and Disadvantages of Both Procedures. *Clin Breast Cancer*. 2017 Sep 4. pii: S1526-8209(17)30565-7. doi: 10.1016/j.clbc.2017.08.014. [Epub ahead of print]



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Verbesserung der Falsch-Negativ-Rate der SLNB nach NACT bei Patientinnen bei cN+ (gesichert durch CNB)


	Oxford		
	LoE	GR	AGO
Entfernung von > 2 SLNs	3b	C	+/-
Kombinierte Tracermethode	3b	C	+/-
Ultrastaging (IHC, Stufen)	2b	B	+
Clipmarkierung (MARI / TAD* / Tattoo)	3b	C	+/-**

* MARI = Marking Axillary LN with Radioactive Iodine Seeds; TAD = Targeted Axillary Dissection;
 ** Teilnahme an Studien empfohlen

1. Classe JM, Bordes V, Campion L: Sentinel Lymph Node Biopsy After Neoadjuvant Chemotherapy for Advanced Breast Cancer: Results of Ganglion Sentinelle et Chimiotherapie Neoadjuvante, a French Prospective Multicentric Study. J Clin Oncol. 2009 Feb 10;27(5):726-32.
2. 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.
3. 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.
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6. Galimberti V, Fontana SKR, Maisonneuve P. Sentinel node Biopsy after neoadjuvant treatment in breast cancer: Five year follow-up of patients with clinically node-negative or node positive disease before treatment. Eur J Clin Oncol 2016;42:361-368
7. Kim WH, Kim HJ, Jung JH, et al: Ultrasound-Guided Restaging and Localization of

Axillary Lymph Nodes After Neoadjuvant Chemotherapy for Guidance of Axillary Surgery in Breast Cancer Patients: Experience with Activated Charcoal. *Ann Surg Oncol*. 2017 Nov 13. doi: 10.1245/s10434-017-6250-3. [Epub ahead of print]

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Sentinel-Lymphknoten-Biopsie (SLNB) Indikationen I

	Oxford		
	LoE	GR	AGO
▪ Klinisch/ sonographisch neg. Axilla (cN0)	1b	A	++
▪ Zusätzliche FNA / Stanzbiopsie (klinisch/sonographisch suspekter axillärer Lymphknoten) um eine SLNB zu ermöglichen	2a	B	+
▪ Präoperative Lymphszintigraphie	1b ^a	B	+/-
▪ T 1-2	2b	A	++
▪ T 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	+
▪ Bei der älteren Patientin	3b	B	+

Statement: SLNB

1. Schwartz GF, Giuliano AE, Veronesi U; Consensus Conference Committee. Proceedings of the consensus conference on the role of sentinel lymph node biopsy in carcinoma of the breast, April 19-22, 2001, Philadelphia, Pennsylvania. Cancer 2002;94:2542-51
2. Kuehn T, Bembenek A, Decker T. A concept for the clinical implementation of sentinel lymph node biopsy in patients with breast carcinoma with special regard to quality assurance. Cancer. 2005 Feb 1;103(3):451-61
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14. Morrow M1, Van Zee KJ, Patil S, et al: Axillary Dissection and Nodal Irradiation Can Be Avoided for Most Node-positive Z0011-eligible Breast Cancers: A Prospective Validation Study of 793 Patients. *Ann Surg.* 2017 Sep;266(3):457-462.

Statement: präoperative Lymphszintigraphie

1. Sherko Kummel, Johannes Holtschmidt, Bernd Gerber, et al.: Randomized surgical multicenter trial to evaluate the usefulness of lymphoscintigraphy (LSG) prior to sentinel node biopsy (SLNB) in early breast cancer: SenSzi (GBG80) trial. DOI: 10.1200/JCO.2017.35.15_suppl.555 *Journal of Clinical Oncology* 35, no. 15_suppl (May 2017) 555-555.

Statement: DCIS

1. Tuttle TM, Shamliyan T, Virnig BA, et al. The impact of sentinel lymph node biopsy and magnetic resonance imaging on important outcomes among patients with ductal carcinoma in situ. *J Natl Cancer Inst Monogr.* 2010;2010(41):117-20.
2. Kotani H, Yoshimura A, Adachi Y, et al. Sentinel lymph node biopsy is not necessary in patients diagnosed with ductal carcinoma in situ of the breast by stereotactic vacuum-assisted biopsy. *Breast Cancer.* 2014 Jul 3. [Epub ahead of print]

3. van Roozendaal LM, Goorts B, Klinkert M, et al. Sentinel lymph node biopsy can be omitted in DCIS patients treated with breast conserving therapy. *Breast Cancer Res Treat.* 2016 Apr;156(3):517-525.
4. Bonev V, De Paz Villanueva CC, et al. Is Sentinel Lymph Node Dissection Necessary in All Patients with Ductal Carcinoma In Situ Undergoing Total Mastectomy? *Am Surg.* 2016 Oct;82(10):982-984.

Statement: elderly


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Statement: preoperative FNA / core biopsy of suspicious lymph nodes

1. Houssami N, Ciatto S, Turner RM, et al. Preoperative ultrasound-guided needle biopsy of axillary nodes in invasive breast cancer – a metaanalysis. *Ann Surg Oncol* 2011;254:243-251
2. Diepstraten SC, Sever AR, Buckens CF, et al. Value of preoperative ultrasound-guided axillary lymph node biopsy for preventing completion axillary lymph node dissection in breast cancer: a systematic review and meta-analysis. *Ann Surg Oncol.* 2014;21(1):51-9.
3. Nakamura R, Yamamoto N, Miyaki T, et al. Impact of sentinel lymph node biopsy by ultrasound-guided core needle biopsy for patients with suspicious node positive breast cancer. *Breast Cancer.* 2017 Jul 22. doi: 10.1007/s12282-017-0795-7. [Epub ahead of print]

Statement: Lymphedema

1. Miller CL, Specht MC, Skolny MN, et al. Sentinel lymph node biopsy at the time of mastectomy does not increase the risk of lymphedema: implications for prophylactic surgery. *Breast Cancer Res Treat.* 2012 Oct;135(3):781-9.



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Sentinel-Lymphknoten-Exzision Indikationen II

- Während Schwangerschaft oder Stillzeit
(nur Tc, keine Blaumarkierung)
- Nach vorausgegangener Tumorektomie
- Frühere „große“ Brust-Operation
(z.B. Reduktionsplastik, Mastektomie)
- Ipsilaterales intramammäres Rezidiv nach
vorheriger BET und vorheriger SNE
- SN entlang der A. mammaria interna
- Nach Axilla-Voroperation
- Prophylaktische bilaterale / kontralaterale
Mastektomie
- Inflammatorisches MaCa

	Oxford		
	LoE	GR	AGO
	3	C	+
	2b	B	+
	3b	C	+/-
	4	D	-
	2b	B	-
	3b	B	+/-
	3b	B	--
	3b	C	-

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Statement: pregnancy

1. Khera SY, Kiluk JV, Hasson DM Pregnancy-associated breast cancer patients can safely undergo lymphatic mapping. Breast J. 2008 May-Jun;14(3):250-4
2. Bergkvist L. Resolving the controversies surrounding lymphatic mapping in breast cancer. Future Oncol. 2008 Oct;4(5):681-8.
3. Classe JM, Loussouarn D, Campion L, et al. Validation of axillary sentinel lymph node detection in the staging of early lobular invasive breast carcinoma: a prospective study. Cancer. (2004); 100(5):935-41.
4. Han SN, Amant F, Cardonick EH, et al. International Network on Cancer, Infertility and Pregnancy: Axillary staging for breast cancer during pregnancy: feasibility and safety of sentinel lymph node biopsy. Breast Cancer Res Treat. 2017 Dec 12. doi: 10.1007/s10549-017-4611-z. [Epub ahead of print]

Statement: mammarian internal

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Sentinel-Lymphknoten-Exzision Markierung

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

- ^{99m}Tc Kolloid
- Patentblau
- Methylenblau
- Indocyaningrün (ICG)*
- SPIO#

SPIO: Superparamagnetic Iron Oxide

* Studienteilnahme empfohlen

Statement radiotracer/blue dye

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Statement: ICG

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Statement: General

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Operatives Vorgehen nach Neoadjuvanter Therapie

	Oxford		
	LoE	GR	AGO
▪ Rechtzeitige Clip-Markierung des Tumors	5	D	++
▪ Operation	2b	C	++
▪ Freie Resektionsränder	2	B	++
▪ Exzision in neuen Tumorgrenzen	2	C	+

OP nach neoadjuvanter Chemotherapie
siehe Kap. „Neoadjuvante Chemotherapie“

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Beginn adjuvanter Therapiemaßnahmen nach primärer Operation

	Oxford		
	LoE	GR	AGO
▪ Zeitnahe Anschluss systemischer Therapie und adjuvanter Radiotherapie (RT) nach OP	1b	A	++
▪ Beginn der Chemo- ± AK-Therapie nach OP baldmöglichst, vor Radiotherapie	1b	A	++
▪ Wenn keine Chemo- ± Antikörpertherapie:			
▪ Beginn der adjuvanten RT innerhalb von 6–8 Wochen nach OP	2b	B	++
▪ Beginn der endokrinen Therapie nach OP baldmöglichst	5	D	++
▪ Endokrine Therapie gleichzeitig mit Radiotherapie	3b	C	+

Statement: Timing of radiation and chemotherapy

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Statement: Tamoxifen concurrent with chemotherapy

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Statement A1 concurrent with radiotherapy

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