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# Diagnosis and Treatment of Patients with early and advanced Breast Cancer

## Breast Cancer Surgery Oncological Aspects



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## Breast Cancer Surgery Oncological Aspects

- **Versionen 2002–2018:**  
**Bauerfeind / Blohmer / Böhme / Brunnert / Costa /  
 Fersis / Gerber / Hanf / Janni / Junkermann /  
 Kaufmann / Kühn / Kümmel / Nitz / Rezai / Simon /  
 Solomayer / Thomssen / Thill / Untch**
- **Version 2019:**  
**Möbus/Kühn**

### Screened data bases

Pubmed 1998 – 2018, ASCO 2018, SABCS 2018, ESMO 2018, EBCC 2018

Screened consensus conference:

- Goldhirsch A, Winer EP, Coates AS, et al. 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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# Breast Cancer Surgery Oncological Aspects

## AGO: ++

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



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## Pretherapeutic Assessment of the Breast and the Axilla

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

- **Clinical examination**
- **Mammography**
  - + Tomosynthesis (DBT)
- **Sonography**
  - Axilla CNB
- **Minimally invasive biopsy\***
- **MRI\*\***

\* Histopathology of lesions if relevant for treatment

\*\* MRI-guided vacuum biopsy is mandatory in case of MRI-detected additional lesions.  
Individual decision for patients at high familial risk, with dense breast (density 3-4/diagnostic assessability C-D), lobular invasive tumors, suspicion of multilocal disease. No reduction in reexcision rate.

### 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, Wobbles 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. Debold M, Abramian A, Nemes L, et al. Who may benefit from preoperative MRI? A single-center analysis of 1102 consecutive patients with primary breast cancer. Breast Cancer Res Treat 2015;153(3):531-537
4. Arnaut A, Catley C, Booth CM, et al. Use of preoperative Magnetic Resonance Imaging for breast cancer: A Canadian population-based study. JAMA Oncol 2015;1(9):1238-1250
5. Fancellu A, Turner RM, Dixon JM, et al. Metaanalysis of the effect of preoperative MRI on the surgical management of ductal carcinoma in situ. Brit J Surg2015;192(8)883-893
6. Houssami N, Turner R, Macaskill P, et al. An individual person data meta-analysis of preoperative magnetic resonance imaging and breast cancer recurrence. J Clin Oncol 2014;32(5):392-401
7. Vos EL, Voogd AC, Verhoef C, et al. Benefits of preoperative MRI in breast cancer surgery studied in a large population-based cancer registry. Br J Surg 2015;102(13)1649-1657

8. Lehman CD, Lee JM, DeMartini WS, et al. Screening MRI in women with a personal history of breast cancer. *J Natl Cancer Inst* 2016;108(3)
9. Wang SY, Long JB, Killelea BK, et al. Preoperative breast MRI and contralateral breast cancer occurrence among older women with breast cancer. *J Clin Oncol* 2015;Nov 30, epub ahead of print
10. Riedl CC, Luft N, Clemens B et al. Triple-modality screening trial for familial breast cancer underlines the importance of magnetic resonance imaging and questions the role of mammography and ultrasonography regardless of patient mutation status, age and breast density. *JCO* 2015;33(10):1128-1135
11. El Sharouni M, Postma EL, Menezes GLG et al. High prevalence of MRI-detected contralateral and ipsilateral malignant findings in patients with invasive ductolobular breast cancer: Impact on surgical management. *Clin Breast Cancer*. 2016 Aug;16(4):269-75.
12. Vriens BE, de Vries B, Lobbes MB, 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 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

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<ul style="list-style-type: none"> <li>History and clinical examination</li> </ul> <p>Only recommended in high metastatic potential and/or symptoms (in decision making for chemotherapy and/or Her 2 – therapy)</p>	Oxford		
	LoE	GR	AGO
	5	D	++
<ul style="list-style-type: none"> <li>CT scan of thorax/abdomen</li> </ul>	2a	B	+
<ul style="list-style-type: none"> <li>Bone scan</li> </ul>	2b	B	+
<ul style="list-style-type: none"> <li>Chest X-ray</li> </ul>	5	C	+/-
<ul style="list-style-type: none"> <li>Liver ultrasound</li> </ul>	5	D	+/-
<ul style="list-style-type: none"> <li>FDG-PET or FDG-PET /CT</li> </ul>	3a	C	+/-
<ul style="list-style-type: none"> <li>Whole body MRI</li> </ul>	4	C	+/-
<ul style="list-style-type: none"> <li>Liver – MRI in case of suspected liver metastases</li> </ul>	4	C	+

#### 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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## Evidence of Surgical Procedure

	Oxford LoE	GR	AGO
■ Survival rates after lumpectomy + XRT are equivalent to those after (modified) radical mastectomy	1a	A	
■ Local recurrence rates after skin sparing mastectomy are equivalent to those after mastectomy	2b	B	
■ Conservation of the NAC (nipple areola complex) is an adequate surgical procedure periphery of the gland and after tumor-free section, if R0 resection is achieved	2b	C	

### Evidence of surgical procedure (6/16)

#### 1. Statement: lumpectomy – mastectomy

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

Breast Conservation: Surgical Technical Aspects			
	Oxford		
	LoE	GR	AGO
 <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2019.1</p> <p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p>	<ul style="list-style-type: none"> <li>Non-palpable lesion <ul style="list-style-type: none"> <li>Wire guided localisation</li> <li>Radionuclide guided localisation</li> <li>Specimen radiography or ultrasound</li> </ul> </li> <li>Tumor-free margins required (also in unfavorable biology „no ink on tumor“ are enough)</li> <li>Immediate intraoperative re-excision for close margins (specimen radiography or ultrasound and/or intra-operative pathology)</li> <li>Re-excision required for involved margins (paraffin section)</li> <li>Therapeutic stereotactic excision alone</li> <li>Ultrasound guided surgery to prevent re-excision</li> <li>Intraop. margin evaluation with margin probe</li> </ul>		
	2b	B	++
	2b	B	+/-
	2b	B	++
	2a	A	++
	1c	B	++
	3b	C	+
	4	D	--
	1a	A	+/-
	1b	A	+/-

#### Statement: Wire guided ..

- 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
- 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.
- 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 ..

- 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.
- 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  $\geq 2$  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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## Breast Conservation Surgery (BCS)

Oxford		
LoE	GR	AGO
2b	B	+/-
2b	B	--
2b	B	--

- **Multicentricity**
- **Positive microscopic margins after repeated excision**
- **Inflammatory breast cancer**

**Surgery after neoadjuvant chemotherapy  
go to chapter „neoadjuvant chemotherapy“**

### Statement: Multicentricity

1. 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.
2. 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.
3. 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 ...

1. Tartter P. et al.: Lumpectomy margins, reexcision, and local recurrence of breast cancer. Amer J Surg, 2000, 179, 2, 81-85
2. 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

3. 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.
4. 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, Bognoux 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.

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li>Endpoint: Survival</li> <li>Endpoint Staging</li> <li>Endpoint: Locoregional control</li> </ul>	3 3 2a	D A A	- - +/-
<ul style="list-style-type: none"> <li>pN+ (pre-surgery) without neoadjuvant systemic therapy</li> <li>cN0 pN0(sn)(i+)</li> <li>cN0 pN1(mi)</li> <li>cN0 pN 1(sn) ( cT1/2 , &lt; 3 SN +, BCS + tangential radiation field, adequate systemic therapy)</li> <li>cN0 pN1 (sn) and mastectomy (no radiotherapy of the chestwall)</li> <li>cN0 pN1(sn) and mastectomy (T1/2, &lt;3SN+) (radiotherapy of the chestwall)</li> </ul>	2a 1b 2b 1b 1b 5	B A B B B D	+ -- -- - +* +/-*
<ul style="list-style-type: none"> <li>ALND indicated, but not feasible               <ul style="list-style-type: none"> <li>Irradiation according to AMAROS-trial</li> </ul> </li> </ul>	1b	B	+

\* Study participation recommended



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### Statement: Axillary lymph node dissection

1. 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.
2. Kuehn T, Bembenek A, Decker T. A concept for the clinical implementation of sentinel lymph node biopsy in patients with breast carcinoma with special regard to quality assurance. Cancer. 2005 Feb 1;103(3):451-61
3. Rudenstam CM, Zahrieh D, Forbes JF: Randomized trial comparing axillary clearance versus no axillary clearance in older patients with breast cancer: first results of International Breast Cancer Study Group Trial 10-93. J Clin Oncol 24(3): 337-344, 2006.
4. Van la Parra: The value of sentinel lymph node biopsy in ductal carcinoma in situ (DCIS) and DCIS with microinvasion of the breast. Eur J Surg Oncol. 2008 Jun;34(6):631-5
5. 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
6. 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.
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.

8. 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.
9. Galimberti V, Cole BF, Zurrada 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.
10. 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.
11. 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.
12. 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.
13. 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.
14. 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.
15. 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.
16. 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>
17. Morrow M, Jagsi R, Mcleod MC et al. Surgeons Attitudes toward the Omission of Axillary Dissection in Early Breast Cancer. *JAMA Oncol* 2018;4(11):1511-16
18. 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 2018;26(6):1084-1090

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.

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<h2 style="text-align: center;">Axillary Intervention and NACT</h2>						
SLNB before or after NACT bei cN0						
SLNB before NACT				2b	B	+/-
SLNB after NACT				2b	B	+
Further surgical procedures depending on SLNB status						
cN-Status (before NACT))	pN-Status (before NACT)	N-Status (after NACT)	Surgical Procedure (after NACT)			
cN0	pN0(sn)	-	Nihil	1a	A	+
cN0	pN+(sn) according to ACOSOG Z0011	ycN0	Nihil Re-SN alone ALND	5	D	+
				2b 3	B B	- -
cN0	pN+(sn) different from ACOSOG Z0011	ycN0	Re-SN alone ALND Axilla XRT	2b	B	-
				2b 2b	B B	+
cN0	Not done	ypN0(sn) ypN1(sn)	SN alone ALND ALND Axillary RT	2b 2b	B B	+
				2b 5	B B	- +
cN+	pN+ (CNB)	ycN0	SN alone TAD inkl. SN ALND	2b 3b	B C	+/- +
				2b	B	+/-
cN+	pN+ (CNB)	ypN1 (CNB)	ALND	2B	B	++

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.
5. Galimberti V, Cole BF, Zurrada 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.
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.
6. Boughey JC, Ballman KV, Le-Petross HAT et al. Identification and Resection of Clipped Node Decreases the False-negative Rate of Sentinel Lymph Node Surgery in Patients Presenting With Node-positive Breast Cancer (T0-T4, N1-N2) Who Receive Neoadjuvant Chemotherapy: Results From ACOSOG Z1071 (Alliance). Ann Surg. 2015 Nov 26. [Epub ahead of print]
7. Ryu JM, Lee SK, Kim JY, et al. Predictive Factors for Nonsentinel Lymph Node Metastasis in Patients With Positive Sentinel Lymph Nodes After Neoadjuvant Chemotherapy: Nomogram for Predicting Nonsentinel Lymph Node Metastasis. Clin Breast Cancer. 2017 Nov;17(7):550-55
8. Galimberti V, Ribeiro Fontana SK, 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 Surg Oncol 2016;42(3) 361-8
9. 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.



10. 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.
11. 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]
12. Sentinel lymph node biopsy without axillary lymphadenectomy after neoadjuvant chemotherapy is accurate and safe for selected patients: the GANEA 2 study. Classe JM, Loaec C, Gimbergues P et al. Breast Cancer Res Treat 2018; doi.org/10.1007/s10549-5004-7



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## Improvement of the False-Negative Rate of SLNB after NACT in Patients with pN+ (CNB)


	Oxford		
	LoE	GR	AGO
■ Removal of > 2 SLNs	3b	C	+/-
■ Combined tracer	3b	C	+/-
■ IHC and serial sections to detect micrometastases	2b	B	+
■ Exclusive LN localisation (Clip / Coil / Tattoo)	3b	C	+/-*
■ Targeted Axillary Dissection (SLNB + removal of localised lymph node, if ycN0)	3b	C	+*

TAD = Targeted Axillary Dissection;

\* Study participation recommended

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.
4. 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 2014;33:258-264
5. Caudle AS, Yang WT, Krishnamurthy S et al. Improved Axillary Evaluation Following Neoadjuvant Therapy for Patients With Node-Positive Breast Cancer Using Selective Evaluation of Clipped Nodes: Implementation of Targeted Axillary Dissection. J Clin Oncol 2016;34(10):1072-8
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]
8. Park S, Koo JS, Kim GM, et al.: Feasibility of Charcoal Tattooing of Cytology-Proven Metastatic Axillary Lymph Node at Diagnosis and Sentinel Lymph Node Biopsy after Neoadjuvant Chemotherapy in Breast Cancer Patients. *Cancer Res Treat*. 2017 Aug 17. doi: 10.4143/crt.2017.210.
9. van Nijnatten TJA, Simons JM, Smidt ML, et al. A Novel Less-invasive Approach for Axillary Staging After Neoadjuvant Chemotherapy in Patients With Axillary Node-positive Breast Cancer by Combining Radioactive Iodine Seed Localization in the Axilla With the Sentinel Node Procedure (RISAS): A Dutch Prospective Multicenter Validation Study. *Clin Breast Cancer*. 2017 Aug;17(5):399-402.
10. Hartmann S, Reimer T, Gerber B et al. Wire localisation of clip-marked axillary lymph nodes in breast cancer patients treated with primary systemic therapy. *Eur J Surg Oncol* 2018;44:1307-1311
11. Simons JM, Nijnatten TJA, van der Pohl CC. Et al. Diagnostic Accuracy of different surgical procedures for axillary staging after neoadjuvant systemic therapy in node positive breast cancer – a systematic review and meta-analysis. *Ann Surg* 2018; doi:10.1097/SLA.000000000000375
12. Siso C, de Torres J, Esgueva-Colmenarejo A et al. Intraoperative Ultrasound-Guided Excision of Axillary Clip in Patients with Node-positive Breast Cancer Treated with Neoadjuvant Therapy (ILINA Trial). *Ann Surg Oncol* 2018;25:784-791



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## Reduction of individual failures for SLNB in pN1ycN0

**The higher the probability for a ypN0 stage the lower is the individual failure risk from a specific false-negative rate**

- **Predictive Factors for conversion of the N-Stage**
  - Young age
  - Intrinsic Subtype (ER neg, HER 2 pos)
  - Grade 3
  - N1 (vs N2)
  - pCR (breast)

Kantor et al. Ann Surg Oncol 2018

This overview compares the different randomised trials comparing fertility preservation with GnRHanalogue without GnRHanalogue.

1. Gerber B, von Minckwitz G, Stehle H, Reimer T, Felberbaum R, Maass N, Fischer D, Sommer HL, Conrad B, Ortmann O, Fehm T, Rezai M, Mehta K, Loibl S; German Breast Group Investigators. [Effect of luteinizing hormone-releasing hormone agonist on ovarian function after modern adjuvant breast cancer chemotherapy: the GBG 37 ZORO study.](#) J Clin Oncol. 2011 Jun 10;29(17):2334-41. Epub 2011 May 2
2. Del Mastro L, Boni L, Michelotti A, Gamucci T, Olmeo N, Gori S, Giordano M, Garrone O, Pronzato P, Bighin C, Levaggi A, Giraudi S, Cresti N, Magnolfi E, Scotto T, Vecchio C, Venturini M. [Effect of the gonadotropin-releasing hormone analogue triptorelin on the occurrence of chemotherapy-induced early menopause in premenopausal women with breast cancer: a randomized trial.](#) JAMA. 2011 Jul 20;306(3):269-76.
3. Munster PN, Moore AP, Ismail-Khan R, Cox CE, Lacevic M, Gross-King M, Xu P, Carter WB, Minton SE. [Randomized Trial Using Gonadotropin-Releasing Hormone Agonist Triptorelin for the Preservation of Ovarian Function During \(Neo\)Adjuvant Chemotherapy for Breast Cancer.](#) J Clin Oncol. 2012 Jan 9. [Epub ahead of print]
4. Loibl S, Gerber B. [Gonadotropin-releasing hormone analogue for premenopausal women with breast cancer.](#) JAMA. 2011 Oct 26;306(16):1760; author reply 1760-1.

5. Moore HCF, Unger JM, Phillips K-A, et al. [Phase III trial \(Prevention of Early Menopause Study \[POEMS\]-SWOG S0230\) of LHRH analog during chemotherapy \(CT\) to reduce ovarian failure in early-stage, hormone receptor-negative breast cancer: An international Intergroup trial of SWOG, IBCSG, ECOG, and CALGB \(Alliance\). 2014 ASCO Annual Meeting](#); J Clin Oncol, 32 (suppl, LBA 505)

The ovarian failure rate at 2 years was statistically significant reduced from 22% without to 8% with GnRH treatment. Reassuringly the disease-free survival was not compromised by GnRH, in the contrary, the GnRH-group had a statistically significant improved DFS and (HR 0.49,  $p=0.04$ ) as well as OFS (HR 0.43;  $p=0.05$ ). The number of pregnancies (22 vs. 12) and babies born (18 vs. 12) was also improved by goserelin.

The study by Munster et al. Has not finished recruitment. Only 49 out of 124 planned pts were randomised. However, the results are in concordance with the ZORO study. Supporting the fact that the observed effect of LHRH is at its best small.

Sentinel Lymph Node Biopsy (SLNB): Indications I			
	Oxford		
	LoE	GR	AGO
▪ Clinically / sonographically neg. axilla (cN0)	1b	A	++
▪ Add./CNB of LN (clinical/sonogr. suspicious) in order to enable SLNB	2a	B	+
▪ T 1–2	2b	A	++
▪ T 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 the elderly	3b	B	+



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### 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
3. Ferrari A, Dionigi P, Rovera F. Multifocality and multicentricity are not contraindications for sentinel lymph node biopsy in breast cancer surgery. *World J Surg Oncol*. 2006 Nov 20;4:79
4. Boughey JC et al. Comparative analysis of sentinel lymph node operation in male and female breast cancer patients. *J Am Coll Surg* 2006 Oct;203(4):475-80.
5. Gentilini O et al. Sentinel Lymph Node Biopsy in Male Patients with Early Breast Cancer. *Oncologist* 2007;12;512-515
6. van der Ploeg IM, Nieweg OE, van Rijk MC Axillary recurrence after a tumour-negative sentinel node biopsy in breast cancer patients: A systematic review and meta-analysis of the literature. *Eur J Surg Oncol*. 2008 Dec;34(12):1277-84.
7. Van la Parra et al.: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

8. 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
9. Intra M, Rotmensz N, Veronesi P. Sentinel node biopsy is not a standard procedure in ductal carcinoma in situ of the breast: the experience of the European institute of oncology on 854 patients in 10 years. *Ann Surg*. 2008 Feb;247(2):315-9
10. Classe JM, Bordes V, Campion L: Sentinel Lymph Node Biopsy After Neoadjuvant Chemotherapy for Advanced Breast Cancer: Results of Ganglion Sentinelle et Chimiothérapie Neoadjuvante, a French Prospective Multicentric Study. *J Clin Oncol*. 2008 Dec 29. [Epub ahead of print]
11. Pugliese MS, Karam AK, Hsu M, et al. Predictors of Completion Axillary Lymph Node Dissection in Patients With Immunohistochemical Metastases to the Sentinel Lymph Node in Breast Cancer. *Ann Surg Oncol*. 2009 Dec 22. [Epub ahead of print]
12. Lyman GH, Temin S, Edge S 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
13. Charalampoudis P, Markopoulos C, Kovacs T.: Controversies and recommendations regarding sentinel lymph node biopsy in primary breast cancer: A comprehensive review of current data. *Eur J Surg Oncol*. 2017 Nov 13. pii: S0748-7983(17)30955-1. doi: 10.1016/j.ejso.2017.10.215. [Epub ahead of print]
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

1. Reimer T, Gerber B. Quality-of-life considerations in the treatment of early-stage breast cancer in the elderly. Drugs Aging. 2010 Oct 1;27(10):791-800.
2. Gerber B, Heintze K, Stubert J, et al. Axillary lymph node dissection in early-stage invasive breast cancer: is it still standard today? Breast Cancer Res Treat. 2011 Aug;128(3):613-24

#### Statement: 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.

Sentinel Lymph Node Excision (SNE): Indications II			
	Oxford		
	LoE	GR	AGO
▪ During pregnancy and / or breast feeding (no blue dye)	3	C	+
▪ After previous tumor excision	2b	B	+
▪ Previous major breast surgery (e.g. reduction mammoplasty)	3b	C	+/-
▪ Ipsilateral breast recurrence after prior BCS and prior SNE	4	D	-
▪ SN in the mammarian internal chain	2b	B	-
▪ After axillary surgery	3b	B	+/-
▪ Prophylactic bilateral / contralateral mastectomy	3b	B	--
▪ Inflammatory breast cancer	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

1. Avisar E, Molina MA, Scarlata M: Internal mammary sentinel node biopsy for breast cancer. Am J Surg. 2008 Oct;196(4):490-4.
2. Chen RC, Lin NU, Golshn M: Internal mammary nodes in breast cancer: diagnosis and implications for patient management -- a

systematic review. J Clin Oncol. 2008 Oct 20;26(30):4981-9.

3. Wouters MW, van Geel AN, Menke-Pluijmers M: Should internal mammary chain (IMC) sentinel node biopsy be performed? Outcome in 90 consecutive non-biopsied patients with a positive IMC scintigraphy. Breast. 2008 Apr;17(2):152-8.

#### Statement: prophylactic mastectomy

1. Dupont et al. The role of sentinel lymph node biopsy in women undergoing prophylactic mastectomy. Am J Surg 2000 Oct;180(4):274-7
2. Soran A et al.: Is routine sentinel lymph node biopsy indicated in women undergoing contralateral prophylactic mastectomy? Magee-Womens Hospital experience. Ann Surg Oncol 2007 Feb;14(2):646-51.
3. Boughey JC et al.: Decision analysis to assess the efficacy of routine sentinel lymphadenectomy in patients undergoing prophylactic mastectomy. Cancer 2007 Dec 1;110(11):2542-50

#### Statement: After previous tumor excision

1. Celebioglu et al.: Sentinel node biopsy in non-palpable breast cancer and in patients with a previous diagnostic excision. Eur J Surg Oncol 2007 Apr;33(3):276-80.

#### Statement: previous major breast surgery

1. Intra et al. Sentinel lymph node biopsy is feasible even after total mastectomy. J Surg Oncol 2007 Feb 1;95(2):175-9
2. Kaminski A, Amr D, Kimbrell ML: Lymphatic mapping in patients with breast cancer and previous augmentation mammoplasty. Am Surg. 2007 Oct;73(10):981-3
3. Karam A, Stempel M, Cody HS 3rd: Reoperative sentinel lymph node biopsy after previous mastectomy. J Am Coll Surg. 2008;207(4):543-8
4. Ruano R, Ramos M, Garcia-Talavera JR: Staging the axilla with selective sentinel node biopsy in patients with previous excision of non-palpable and palpable breast cancer. Eur J Nucl Med Mol Imaging. 2008 Jul;35(7):1299-304.

Statement: Ipsilateral breast recurrence after prior BCS and prior SLNB


1. Mattia Intra M, Triro G, Viale G: Second Biopsy of Axillary Sentinel Lymph Node for Reappearing Breast Cancer After Previous Sentinel Lymph Node Biopsy. *Ann Surg Oncol*. 2005;12(11):895-9
2. Intra et al. Second axillary sentinel node biopsy for ipsilateral breast tumour recurrence. *Br J Surg* 2007 Oct;94(10):1216-9
3. Schrenk P et al. Lymphatic mapping in patients with primary or recurrent breast cancer following previous axillary surgery. *Eur J Surg Oncol*. 2008 Aug;34(8):851-6.
4. Palit G, Jacqemyn ML, Tjalma W. Sentinel node biopsy for ipsilateral breast cancer recurrence: a review. *Eur J Gynecol Oncol* 2008;29:565-567
5. Intra M, Viale G, Vila J, et al. Second Axillary Sentinel Lymph Node Biopsy for Breast Tumor Recurrence: Experience of the European Institute of Oncology. *Ann Surg Oncol*. 2014 Dec 17.
6. Moffat FL Jr, Yakoub D.: Bilateral mastectomy and the retreat from breast-conserving surgery. *Breast Cancer Res Treat*. 2016 Aug;159(1):15-30.
7. Folli S, Falco G, Mingozzi M, et al. Repeat sentinel lymph node biopsy in patients with ipsilateral recurrent breast cancer after breast-conserving therapy and negative sentinel lymph node biopsy: a prospective study. *Minerva Chir*. 2016 Apr;71(2):73-9.

Statement: inflammatory breast cancer

1. Singletary SE. Surgical management of inflammatory breast cancer. *Semin Oncol*. 2008 Feb;35(1):72-7
2. 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]
3. Matro JM, Li T, Cristofanilli M, Hughes ME, et al. Inflammatory breast cancer management in the national comprehensive cancer network: the disease, recurrence pattern, and outcome. *Clin Breast Cancer*. 2015 Feb;15(1):1-7.

Statement: Others

1. Schwartz GF, Giuliano AE, Veronesi U; Consensus Conference Committee. Proceedings of the consensus conference on the role of sentinel lymph node biopsy in carcinoma of the breast, April 19-22, 2001, Philadelphia, Pennsylvania. *Cancer* 2002;94:2542-51
2. Kuehn T, Bembenek A, Decker T. A concept for the clinical implementation of sentinel lymph node biopsy in patients with breast carcinoma with special regard to quality assurance. *Cancer*. 2005 Feb 1;103(3):451-61
3. Golshan M et al. Sentinel lymph node biopsy for occult breast cancer detected during breast reduction surgery. *Am Surg* 2006 May;72(5):397-400
4. Schrenk et al. Symmetrization reduction mammoplasty combined with sentinel node biopsy in patients operated for contralateral breast cancer. *J Surg Oncol* 2006 Jul 1;94(1):9-15.
5. Lyman GH, Temin S, Edge SB, et al. American Society of Clinical Oncology Clinical Practice. Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. *Clin Oncol*. 2014 May 1;32(13):1365-83



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## Sentinel Lymph Node Excision (SNE): Marking

	Oxford		
	LoE	GR	AGO
■ <sup>99m</sup> Tc Kolloid	1a	A	++
■ Preoperative Lymphoscintigraphy	1b	B	+/-
■ Patent blue dye	1a	B	+/-
■ Methylen blue	4	D	-
■ Indocyanin green (ICG)*	2b	B	+/-
■ SPIO <sup>#</sup>	2b	B	+/-

# SPIO: Superparamagnetic Iron Oxide

### Statement radiotracer/blue dye

1. Krag DN, Anderson SJ, Julian TB, et al. National Surgical Adjuvant Breast and Bowel Project. Technical outcomes of sentinel-lymph-node resection and conventional axillary-lymph-node dissection in patients with clinically node-negative breast cancer: results from the NSABP B-32 randomised phase III trial. *Lancet Oncol.* 2007 Oct;8(10):881-8.
2. Rodier JF, Velten M, Wilt M, et al. Prospective multicentric randomized study comparing periareolar and peritumoral injection of radiotracer and blue dye for the detection of sentinel lymph node in breast sparing procedures: FRANSENODE trial. *J Clin Oncol.* 2007 Aug 20;25(24):3664-
3. Bines S, Kopkash K, Ali A, Fogg L, et al. The use of radioisotope combined with isosulfan Blue dye is not superior to radioisotope alone for the identification of sentinel lymph nodes in patients with breast cancer. *Surgery.* 2008 Oct;144(4):606-9; discussion 609-10.
4. Straver ME, Meijnen P, van Tienhoven G, et al. Sentinel node identification rate and nodal involvement in the EORTC 10981-22023 AMAROS trial. *Ann Surg Oncol.* 2010 Jul;17(7):1854-61.
5. Pesek S, Ashikaga T, Krag LE, et al. The false-negative rate of sentinel node biopsy in patients with breast cancer: a meta-analysis. *World J Surg* 2012;36(9): 2239-2251

6. Lyman GH, Temin S, Edge SB, et al. American Society of Clinical Oncology Clinical Practice. Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. Clin Oncol. 2014 May 1;32(13):1365-83
7. Ang CH, Tan MY, Teo C, et al. Blue dye is sufficient for sentinel lymph node biopsy in breast cancer. Br J Surg. 2014 Mar;101(4):383-9; discussion 389.
8. Ahmed M, Purushotham AD, Horgan K, et al. Meta-analysis of superficial versus deep injection of radioactive tracer and blue dye for lymphatic mapping and detection of sentinel lymph nodes in breast cancer. Br J Surg. 2015 Feb;102(3):169-81.

#### Statement: methylene blue

1. Varghese P, Mostafa A, Abdel-Rahman AT, et al. Methylene blue dye versus combined dye-radioactive tracer technique for sentinel lymph node localisation in early breast cancer. Eur J Surg Oncol. 2007 Mar;33(2):147-52.
2. Soni M, Saha S, Korant A, et al. A prospective trial comparing 1% lymphazurin vs 1% methylene blue in sentinel lymph node mapping of gastrointestinal tumors. Ann Surg Oncol. 2009 Aug;16(8):2224-30.
3. Kang SS, Han BK, Ko EY, et al. Methylene blue dye-related changes in the breast after sentinel lymph node localization. J Ultrasound Med. 2011;30(12):1711-21.
4. Kaklamanos IG, Birbas K, Syrigos K, et al. Prospective comparison of peritumoral and subareolar injection of blue dye alone, for identification of sentinel lymph nodes in patients with early stage breast cancer. J Surg Oncol. 2011 Jul 1;104(1):37-40.
5. Fattahi AS, Tavassoli A, Rohbakhshfar O, et al. Can methylene blue dye be used as an alternative to patent blue dye to find the sentinel lymph node in breast cancer surgery? J Res Med Sci. 2014 Oct;19(10):918-22.

#### Statement: ICG

1. Wishart GC, Loh SW, Jones L, Benson JR. A feasibility study (ICG-10) of indocyanine green (ICG) fluorescence mapping for sentinel lymph node detection in early breast cancer. Eur J Surg Oncol. 2012 Aug;38(8):651-6.
2. Samorani D, Fogacci T, Panzini I, et al. The use of indocyanine green to detect sentinel nodes in breast cancer: A prospective study. Eur J Surg Oncol. 2015 Jan;41(1):64-70.

3. Tong M, Guo W, Gao W. Use of Fluorescence Imaging in Combination with Patent Blue Dye versus Patent Blue Dye Alone in Sentinel Lymph Node Biopsy in Breast Cancer. *J Breast Cancer*. 2014 Sep;17(3):250-5.
4. Niebling MG, Pleijhuis RG, Bastiaannet E, et al: A systematic review and meta-analyses of sentinel lymph node identification in breast cancer and melanoma, a plea for tracer mapping. *Eur J Surg Oncol*. 2016 Apr;42(4):466-73.
5. Guo J, Yang H, Wang S, et al.: Comparison of sentinel lymph node biopsy guided by indocyanine green, blue dye, and their combination in breast cancer patients: a prospective cohort study. *World J Surg Oncol*. 2017 Nov 2;15(1):196.

#### Statement: SPIO

1. Rubio IT, Diaz-Botero S, Esgueva A, et al. The superparamagnetic iron oxide is equivalent to the Tc99 radiotracer method for identifying the sentinel lymph node in breast cancer. *Eur J Surg Oncol*. 2015 Jan;41(1):46-51
2. Thill M, Kurylcio A, Welter R, et al. The Central-European SentiMag study: sentinel lymph node biopsy with superparamagnetic iron oxide (SPIO) vs. Radioisotope. *Breast*. 2014 Apr;23(2):175-9.
3. Douek M, Klaase J, Monypenny I, et al. SentiMAG Trialists Group. Sentinel node biopsy using a magnetic tracer versus standard technique: the SentiMAG Multicentre Trial. *Ann Surg Oncol*. 2014 Apr;21(4):1237-45.

#### Statement: General


1. Ahmed M, Purushotham AD, Douek M. Novel techniques for sentinel lymph node biopsy in breast cancer: a systematic review. *Lancet Oncol*. 2014 Jul;15(8):e351-62.

#### Statement: Comparisons

1. Jung SY, Kim SK, Kim SW, et al. Comparison of sentinel lymph node biopsy guided by the multimodal method of indocyanine green fluorescence, radioisotope, and blue dye versus the radioisotope method in breast cancer: a randomized controlled trial. *Ann Surg Oncol*. 2014 Apr;21(4):1254-9.



2. Sugie T, Sawada T, Tagaya N, et al. Comparison of the indocyanine green fluorescence and blue dye methods in detection of sentinel lymph nodes in early-stage breast cancer. *Ann Surg Oncol*. 2013 Jul;20(7):2213-8. doi: 10.1245/s10434-013-2890-0. Epub 2013 Feb 21.



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## Procedure after Neoadjuvant Therapy

Oxford		
LoE	GR	AGO
5	D	++
2b	C	++
2	B	++
2	C	+

- Early Clip & Coil marking of tumor
- Surgical Removal of the tumor/tumor bed
- Microscopically clear margins
- Tumor resection in the new margins

For „Surgery after neoadjuvant chemotherapy“  
see chapter „Neoadjuvant chemotherapy“

### Statement: clip marking

1. Kuerer HM, Singletary SE, Buzdar AU, et al. Surgical conservation planning after neoadjuvant chemotherapy for stage II and operable stage III breast carcinoma. Am J Surg. 2001 Dec;182(6):601-8.
2. Thomassin-Naggara I, Lalonde L, David J, et al. A plea for the biopsy marker: how, why and why not clipping after breast biopsy? Breast Cancer Res Treat. 2012 Apr;132(3):881-93.


### Statement: operation and : tumor resection in new margins

1. Mauri D, Pavlidis N, Ioannidis JP. Neoadjuvant versus adjuvant systemic treatment in breast cancer: a meta-analysis. J Natl Cancer Inst. 2005 Feb 2;97(3):188-94.
2. Berruti A, Generali D, Kaufmann M, et al. International expert consensus on primary systemic therapy in the management of early breast cancer: highlights of the Fourth Symposium on Primary Systemic Therapy in the Management of Operable Breast Cancer, Cremona, Italy (2010). J Natl Cancer Inst Monogr. 2011;2011(43):147-51.
3. Kümmel S, Holtschmidt J, Loibl S. Surgical treatment of primary breast cancer in the neoadjuvant setting. Br J Surg. 2014 Jul;101(8):912-24

4. Ataseven B, Lederer B, Blohmer JU, et al. Impact of Multifocal or Multicentric Disease on Surgery and Locoregional, Distant and Overall Survival of 6,134 Breast Cancer Patients Treated With Neoadjuvant Chemotherapy. *Ann Surg Oncol*. 2014 Oct 9. [Epub ahead of print]
5. Early Breast Cancer Trialists Collaborative Group. Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: a metaanalysis of individual patient data from ten randomised trials. *Lancet Oncol* 2018;19(1):27-39

Statement: tumor free margins ...

1. Cendán JC et al., Accuracy of Intraoperative Frozen-Section Analysis of Breast Cancer Lumpectomy-Bed Margins. *J Am Coll Surg* 2005;201:194–198.
2. Cabioglu N, Hunt, Sahin et al: Role for Intraoperative Margin Assessment in Patients Undergoing Breast-Conserving Ann Surg Oncol. 2007 Apr;14(4):1458-71.
3. Ciccarelli G, Di Virgilio MR, Menna S. Radiography of the surgical specimen in early stage breast lesions: diagnostic reliability in the analysis of the resection margins. *Radiol Med (Torino)*. 2007 Apr;112(3):366-76.
4. Houssami N, Macaskill P, Marinovich ML, et al. Metaanalysis of the impact of surgical margins on local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy. *Eur J Cancer*. 2010 Dec;46(18):3219-32.
5. Harness JK, Giuliano AE, Pockaj BA, et al. Margins: a status report from the Annual Meeting of the American Society of Breast Surgeons. *Ann Surg Oncol*. 2014 Oct;21(10):3192-7.
6. Houssami N, Macaskill P, Marinovich ML, et al. The association of surgical margins and local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy: a meta-analysis. *Ann Surg Oncol*. 2014 Mar;21(3):717-30
7. Buchholz TA, Somerfield MR, Griggs JJ et al. Margins for breast-conserving surgery with whole-breast irradiation in stage I and II invasive breast cancer: American Society of Clinical Oncology endorsement of the Society of Surgical Oncology/American Society for Radiation Oncology consensus guideline. *J Clin Oncol*. 2014 May 10;32(14):1502-6.
8. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from randomised trials. (published online Dec 11.) *Lancet Oncol*. 2017; [http://dx.doi.org/10.1016/S1470-2045\(17\)30777-5](http://dx.doi.org/10.1016/S1470-2045(17)30777-5)



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## Adjuvant Therapy after Primary Surgery

	Oxford		
	LoE	GR	AGO
▪ <b>Start adjuvant systemic therapy and Radiotherapy (RT) as soon as possible (a.s.a.p.) after surgery</b>	1b	A	++
▪ <b>Start of adjuvant chemotherapy +/- Her2 therapy after surgery a.s.a.p., and prior to RT</b>	1b	A	++
<b>Without cytotoxic therapy +/- anti-HER2 therapy:</b>			
▪ <b>Start RT 6-8 weeks after surgery</b>	2b	B	++
▪ <b>Start endocrine therapy after surgery and a.s.a.p.</b>	5	D	++
▪ <b>Endocrine therapy concurrent with radiotherapy</b>	3b	C	+

### Statement: Timing of radiation and chemotherapy

1. Piroth MD, Pinkawa M, Gagel B et al. Sequencing chemotherapy and radiotherapy in locoregional advanced breast cancer patients after mastectomy - a retrospective analysis. BMC Cancer. 2008 Apr 23;8:114.
2. Tsoutsou PG, Koukourakis MI, Azria D, Belkacémi Y. et al. Optimal timing for adjuvant radiation therapy in breast cancer: a comprehensive review and perspectives. Crit Rev Oncol Hematol. 2009;71(2):102-16.
3. Balduzzi A, Leonardi MC, Cardillo A, et al. Timing of adjuvant systemic therapy and radiotherapy after breast-conserving surgery and mastectomy. Cancer Treat Rev. 2010;36(6):443-50.
4. Karlsson P, Cole BF, Colleoni M, et al; International Breast Cancer Study Group; Timing of radiotherapy and outcome in patients receiving adjuvant endocrine therapy. Int J Radiat Oncol Biol Phys. 2011;80(2):398-402.

### Statement: Tamoxifen concurrent with chemotherapy

1. Adamowicz K, Marczevska M, Jassem J. Combining systemic therapies with radiation in breast cancer. Cancer Treat Rev. 2009 Aug;35(5):409-16

2. Harris EE, Christensen VJ, Hwang WT, et al. Impact of concurrent versus sequential tamoxifen with radiation therapy in early-stage breast cancer patients undergoing breast conservation treatment. J Clin Oncol. 2005 Jan 1;23(1):11-6.
3. Pierce LJ, Hutchins LF, Green SR et al. Sequencing of tamoxifen and radiotherapy after breast-conserving surgery in early-stage breast cancer. J Clin Oncol. 2005 Jan 1;23(1):24-9.

#### Statement A1 concurrent with radiotherapy

1. Azria D, Belkacemi Y, Romieu G, et al. Concurrent or sequential adjuvant letrozole and radiotherapy after conservative surgery for early-stage breast cancer (CO-HO-RT): a phase 2 randomised trial. Lancet Oncol 2010;11(3):258-65
2. Chargari C, Castro-Pena P, Toledano I, et al. Concurrent use of aromatase inhibitors and hypofractionated radiation therapy. World J Radiol. 2012;4(7):318-23.
3. Ishitobi M, Shiba M, Nakayama T, et al. Treatment sequence of aromatase inhibitors and radiotherapy and long-term outcomes of breast cancer patients. Anticancer Res. 2014;34(8):4311-4.