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

Breast Cancer Follow-Up



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Breast Cancer Follow-Up

- **Versionen 2002–2019:**

**Bauerfeind / Bischoff / Blohmer / Böhme / Costa / Diel / Friedrich /
Gerber / Hanf / Heinrich / Huober / Janni / Kaufmann / Kümmel / Lux
/ Maass / Möbus / Müller-Schimpfle / Mundhenke / Oberhoff / Rody /
Scharl / Solbach / Solomayer / Thomssen / Wöckel**

- **Version 2020:**

Kolberg-Liedtke/Möbus


Breast Cancer Follow-Up Objectives			
	Oxford		
	LoE	GR	AGO
Early detection of curable events			
▪ In-breast recurrence	1a	B	++
▪ Loco-regional recurrence*	1a	B	++
Early detection of contralateral cancers			
	1a	B	++
Early detection of metastasis			
▪ Early detection of symptomatic metastases	3b	C	+
▪ Early detection of asymptomatic metastases	1a	A	-
<p>* loco-regional recurrence is associated with a higher risk of mortality in node-positive, PR-negative, younger patients and in patients with a short time between primary diagnosis and recurrence</p>			

1. De Bock GH, Bonnema J, van Der Hage J et al., Effectiveness of Routine Visits and Routine Tests in Detecting Isolated Locoregional Recurrences After Treatment for Early-Stage Invasive Breast Cancer: A Meta-Analysis and Systematic Review. J Clin Oncol 2004; 22 (19): 4010-4018.
2. Margenthaler JA, Allan E, Cheng L, et al.. Surveillance of Patients With Breast Cancer After Curative-Intent Primary Treatment: Current Practice Patterns. Journal of Oncology Practice 2012; 8(2): 79 – 83.
3. Parmeshwar R, Margenthaler JA, Allam E, et al.. Patient Surveillance After Initial Breast cancer Therapy Variation by Physician Specialty. Am J Surg 2013; 206(2): 218-222.
4. Jochelson M, Hayes DF, Ganz PA. Surveillance and Monitoring in Breast Cancer Survivors: Maximizing Benefit and Minimizing Harm. ASCO Educational Book 2013 e13 – e18.
5. Khatcheressian JL, Hurley P, Bantug E, et al.. Breast Cancer Follow-up and Management After Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update . J Clin Oncol. 2013 March 1; 31(7):961-965.
6. Moschetti I, Cinquini M, Lambertini M et al., Follow-up strategies for women treated for early breast cancer. Cochrane Database Syst Rev. 2016 May 27;(5):CD001768.
7. NCCN Clinical Practice Guidelines in Oncology, Breast Cancer Version 3.17-10.17;

https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf

Statement: risk factors of mortality after loco-regional recurrence

1. Dent R, Valentini H, Hanna W, et al.. Factors associated with breast cancer mortality after local recurrence. Curr Oncol 2014; 21 (3): e418-25.



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Breast Cancer Follow-Up Objectives

	Oxford	
	LoE	GR
■ Improve quality of life	2b	B
■ Improve physical performance	2a	B
■ Reduction and/or early detection of therapy-related side effects (such as osteoporosis, cardiac failure, fatigue, neurotoxicity, lymphedema, sexual disorders, cognitive impairment, sterility, and secondary tumors) and start of necessary therapies	2b	B
■ Participation in interventional programs during follow-up for breast cancer survivors in order to maximize therapy adherence, assess life-style interventions, and improve quality of life	3b	B

Statement: Outcome measurements

1. Ong WL, Schouwenburg MG, van Bommel ACM et al.. A Standard Set of Value-Based Patient-Centered Outcomes for Breast Cancer: The International Consortium for Health Outcomes Measurement (ICHOM) Initiative. JAMA Oncol. 2017 May 1;3(5):677-685.
2. Browall M, Forsberg C, Wengström Y. Assessing patient outcomes and cost-effectiveness of nurse-led follow-up for women with breast cancer - have relevant and sensitive evaluation measures been used? J Clin Nurs. 2017 Jul;26(13-14):1770-1786.
3. Cheng KKF, Lim YTE, Koh ZM et al. Home-based multidimensional survivorship programmes for breast cancer survivors. Cochrane Database Syst Rev. 2017 Aug 24;8:CD011152.

Statement: Obesity, physical activity and quality of life

1. Bicego D, Brown K. Effects of Exercise on Quality of Life in Women Living with Breast Cancer: A Systematic Review. The Breast Journal 2009; 15(1): 45-51.
2. Carson JW, Carson KM, Porter LS et al.. Yoga of Awareness program for menopausal symptoms in breast cancer survivors: results from a randomized trial. Support Care Cancer 2009; 17: 1301-1309.
3. Vaskuil DW, van Nes JG, Junngeburt JM et al.. Maintenance of physical activity and body weight in relation to subsequent quality

of life in postmenopausal breast cancer patients. *Annals of Oncology* 2010; 21: 2094–2101.

4. Cramp F, Byron-Daniel J. Exercise for the management of cancer-related fatigue in adults. *Cochrane Database Syst Rev.* 2012 Nov 14;11:CD006145.
5. Bower JE, Garet D, Sternlieb B et al.. Yoga for persistent fatigue in breast cancer survivors: A randomized controlled trial. *Cancer* 2012; 118(15): 3766-75.
6. Cramer H, Lange S, Klose P et al.. Can yoga improve fatigue in breast cancer patients? A systematic review. *Acta Oncol* 2012; 51(4): 559 – 60.
7. Yang H, Brand JS, Fang F et al.. Time-dependent risk of depression, anxiety, and stress-related disorders in patients with invasive and in situ breast cancer. *Int J Cancer.* 2017 Feb 15;140(4):841-852.
8. Nagy AC, GulAcsi-Bardos P, CserEp Z et al..Late cardiac effect of anthracycline therapy in physically active breast cancer survivors - a prospective study. *Neoplasma.* 2017;64(1):92-100.
9. Baumann FT, Bieck O, Oberste M et al.. Sustainable impact of an individualized exercise program on physical activity level and fatigue syndrome on breast cancer patients in two German rehabilitation centers. *Support Care Cancer.* 2017 Apr;25(4):1047-1054.
10. NCCN-Guidelines Version 1.2017. Cancer-related Fatigue.

Statement: Obesity and breast cancer prognosis

1. Ewertz M, Jensen MB, Gunnarsdóttir KÁ et al.. Effect of obesity on prognosis after early-stage breast cancer. *J Clin Oncol* 2011; 29(1): 25-31.
2. Cespedes Feliciano EM, Kroenke CH, Bradshaw PT et al..Postdiagnosis Weight Change and Survival Following a Diagnosis of Early-Stage Breast Cancer. *Cancer Epidemiol Biomarkers Prev.* 2017 Jan;26(1):44-50.

Statement: Lymphedema

1. Soran A, Ozmen T, McGuire KP et al..The importance of detection of subclinical lymphedema for the prevention of breast cancer-related clinical lymphedema after axillary lymph node dissection; a prospective observational study.*Lymphat Res Biol* 2014;12(4):

289-9.


2. Basta MN, Wu LC, Kanchwala SK et al.. Reliable prediction of postmastectomy lymphedema: the Risk Assessment Tool Evaluating Lymphedema. Am J Surg. 2017 Jun;213(6):1125-1133.

Statement: sexual disorders and cognitive impairment:

1. Runowcz CD, Leach CR, Henry L et al.. American Cancer Society/American Society of Clinical Oncology breast cancer survivorship care guideline. CA Cancer J Clin 2016; 66: 43-73.
2. Janelins MC, Heckler CE, Peppone LJ et al.. Cognitive Complaints in Survivors of Breast Cancer After Chemotherapy Compared With Age-Matched Controls: An Analysis From a Nationwide, Multicenter, Prospective Longitudinal Study. J Clin Oncol. 2017 Feb 10;35(5):506-514.
3. Bernstein LJ, McCreath GA, Komeylian Z et al..Cognitive impairment in breast cancer survivors treated with chemotherapy depends on control group type and cognitive domains assessed: A multilevel meta-analysis. Neurosci Biobehav Rev. 2017 Dec;83:417-428.

Statement: Secondary tumors:

1. Hoekstra N, Fleury E, Merino Lara TR, et al. Long-term risks of secondary cancer for various whole and partial breast irradiation techniques. Radiother Oncol. 2018 Sep;128(3):428-433



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Breast Cancer Follow-Up Objectives

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

- **Evaluation of current adjuvant therapy**
 - incl. monitoring of adherence to endocrine therapies
- **Pro-active improvement of therapy adherence**
 - Patient information about efficacy data for 5-10 years endocrine therapy
 - Early therapy of side effects (sports, NSAIDs, vitamin D / calcium)

Evaluation of current adjuvant therapy

1. Hershman DL, Kushi LH, Shao T et al.. Early Discontinuation and Nonadherence to Adjuvant Hormonal Therapy in a Cohort of 8,769 Early-Stage Breast Cancer Patients. J Clin Oncol 2010; 28: 4120-4128.
2. Lueck H-J, Hadji P, Harbeck N et al.. 24 Months Follow-Up Results from PACT (Patient's Anastrozole Compliance to Therapy Programme), a Non-Interventional Study Evaluating the Influence of a Standardized Information Service on Compliance in Postmenopausal Women with Early Breast Cancer. SABCS 2011 [P5-17-05].
3. Neven P, Markopoulos C, Tanner M et al.. The impact of educational materials on compliance and persistence rates with adjuvant aromatase inhibitor treatment: first-year results from the compliance of aromatase inhibitors assessment in daily practice through educational approach (CARIATIDE) study. Breast. 2014 Aug;23(4):393-9.
4. Hershman DL, Kushi LH, Hillyer GC et al.. Psychosocial factors related to non persistence with adjuvant endocrine therapy among women with breast cancer: the Breast Cancer Quality of Care Study (BQUAL). Breast Cancer Res Treat. 2016 May;157(1):133-43.
5. Goss PE, Ingle JN, Pritchard KI et al.. Extending Aromatase-Inhibitor Adjuvant Therapy to 10 Years. N Engl J Med. 2016 Jul 21;375(3):209-19.
6. Nabieva N, Kellner S, Fehm T et al.. Patient and tumor characteristics and their influence on early therapy persistence with letrozole in postmenopausal patients with early breast cancer. Ann Oncol. 2017 Oct 10. doi: 10.1093/annonc/mdx630.

7. Laroche F, Perrot S, Medkour T et al.. Quality of life and impact of pain in women treated with aromatase inhibitors for breast cancer. A multicenter cohort study. PLoS One. 2017 Nov 8;12(11):e0187165.

Breast Cancer Follow-Up Objectives			
	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> ■ Psycho-social aspects of support and counseling <ul style="list-style-type: none"> ■ Pregnancy, contraception, sexuality, quality of life, menopausal symptoms, fear of recurrence ■ Inclusion of related persons (partner, family, friends, caregivers) ■ Second opinion regarding primary therapy ■ General counseling (e.g. genetics, HRT, prophylactic surgery, breast reconstruction) 	4	C	+
	2c	B	++
	2c	C	+



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Statement: Psycho-social aspects

1. Drolet M, Maunsell E, Brisson J et al. Not Working 3 Years After Breast Cancer: Predictors in a Population-Based Study. J Clin Oncol 2005; 23(33): 8305-8312.
2. Scheier MF, Helgeson VS, Schulz R et al.. Interventions to Enhance Physical and Psychological Functioning Among Younger Women Who Are Ending Nonhormonal Adjuvant Treatment for Early-Stage Breast Cancer. J Clin Oncol 2005; 23(19): 4298-4311.
3. Fors EA, Bertheussen GF, Thune I et al.: Psychosocial interventions as part of breast cancer rehabilitation programs? Results from a systematic review. Psycho-Oncology 2011; 20: 909-918.
4. Silva C, Caramelo O, Almeida-Santos T et al.. Factors associated with ovarian function recovery after chemotherapy for breast cancer: a systematic review and meta-analysis. Hum Reprod. 2016 Dec;31(12):2737-2749.
5. Luke B, Brown MB, Missmer SA et al.. Assisted reproductive technology use and outcomes among women with a history of cancer. Hum Reprod. 2016 Jan;31(1):183-9.
6. Gudenkauf LM, Ehlers SL. Psychosocial interventions in breast cancer survivorship care. Breast. 2017 Nov 20;38:1-6.
7. Rogers LQ, Courneya KS, Anton PM et al.. Effects of a multicomponent physical activity behavior change intervention on fatigue, anxiety, and depressive symptomatology in breast cancer survivors: randomized trial. Psychooncology. 2017 Nov;26(11):1901-1906.

8. Y Kim, DA Kashy, RL Spillers, et al: Needs assessment of family caregivers of cancer survivors: Three cohorts comparison Psychooncology 19:573–582,2010 Crossref, Medline, Google Scholar
9. Y Kim, RL Spillers, DL Hall: Quality of life of family caregivers 5 years after a relative's cancer diagnosis: Follow-up of the national quality of life survey for caregivers Psychooncology 21:273–281,2012 Crossref, Medline, Google Scholar
10. BA Given, CW Given, PR Sherwood: Family and caregiver needs over the course of the cancer trajectory J Support Oncol 10:57–64,2012 Crossref, Medline, Google Scholar

Statement: prophylactic surgery

1. Rhiem K, Engel C, Graeser M et al.. The risk of contralateral breast cancer in patients from BRCA ½ negative high risk families as compared to patients from BRCA1 or BRCA2 positive families: a retrospective cohort study. Breast Cancer Res. 2012; 14(6): R156..

Breast Cancer Follow-Up Recommended Interventions			
	Interventions regarding lifestyle risks and comorbidity in order to reduce an unfavorable impact on disease outcome		
	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> ■ Treatment of type II-diabetes (> 25% undetected DM in postmenopausal BC patients) 	5	D	++
<ul style="list-style-type: none"> ■ Weight intervention (if BMI < 18.5 and -> 30) 	2a	B	+
<ul style="list-style-type: none"> ■ Nightly fastening > 13h 	2b	B	+
<ul style="list-style-type: none"> ■ Reduction of dietary intake (at least 15 % calories from fat) in HR-negative BC is associated with improved overall survival 	2b	B	+
<ul style="list-style-type: none"> ■ Stop smoking (smoking causes 2-fold increase in BC-specific and 4-fold increase in not directly BC-associated mortality) 	2b	B	++
<ul style="list-style-type: none"> ■ Alcohol consumption reduction (below 6g/d) 	2b	B	+
<ul style="list-style-type: none"> ■ Moderate sport (in patients with reduced physical activity prior to diagnosis) 	1b	A	++
<ul style="list-style-type: none"> ■ Distress reduction 	3b	B	+

1. Onitilo AA, Donald M, Stankowski RV et al.. Breast and prostate cancer survivors in a diabetic cohort: results from the Living with DiabetesStudy. Clin Med Res. 2013 Dec;11(4):210-8.
2. Anderson C, Sandler DP, Weinberg CR et al.. Age- and treatment-related associations with health behavior change among breast cancer survivors. Breast. 2017 Jun;33:1-7.
3. Syrowatka A, Motulsky A, Kurteva S et al.. Predictors of distress in female breast cancer survivors: a systematic review. Breast Cancer Res Treat. 2017 Sep;165(2):229-245. Review.
4. Gudenkauf LM, Ehlers SL. Psychosocial interventions in breast cancer survivorship care. Breast. 2017 Nov 20;38:1-6. Review.
5. Mehra K, Berkowitz A, Sanft T.D et al.. Physical Activity, and Body Weight in Cancer Survivorship. Med Clin North Am. 2017 Nov;101(6):1151-1165. Review
6. Haykowsky MJ, Scott JM, Hudson K et al.. Lifestyle Interventions to Improve Cardiorespiratory Fitness and Reduce Breast Cancer Recurrence. Am Soc Clin Oncol Educ Book. 2017;37:57-64.
7. Chlebowski RT, Aragaki AK, Anderson GL et al. Low-Fat Dietary Pattern and Breast Cancer Mortality in the Women's Health Initiative Randomized Controlled Trial. J Clin Oncol. 2017 Sep 1;35(25):2919-2926.
8. Marinac CR, Nelson SH, Breen CI et al..Prolonged Nightly Fasting and Breast Cancer Prognosis. JAMA Oncol. 2016 Aug 1;2(8):1049-55.

Statement: for all statements see most recent literature see at Survivorship care guidelines of ASC and ASCO

1. Runowcz CD, Leach CR, Henry L et al.. American Cancer Society/American Society of Clinical Oncology breast cancer survivorship care guideline. CA Cancer J Clin 2016; 66: 43-73.

Weight intervention.

1. Chajès V, Romieu I. Nutrition and breast cancer. Maturitas, 2014; 77 (1): 7–11.

Moderate sport intervention when physical activity was reduced

1. Chlebowski RT. Nutrition and physical activity influence on breast cancer incidence and outcome. Breast 2013; Aug;22 Suppl 2: S30-7.
2. Patsou ED, Alexias GD, Anagnostopoulos FG et al.. Effects of physical activity on depressive symptoms during breast cancer survivorship: a meta-analysis of randomised control trials. ESMO Open. 2017 Dec 11;2(5):e000271

Nightly fasting

Prolonged nightly fasting improves prognosis in breast cancer patients

retrospective cohort study:

2413 BC-pat. (no diabetes), nightly fasting more or less than 13 hrs

Fasting < 13 hrs: HR 1.36, 36% increase of risk for recurrence
HR 1.21, n.s. increase of risk for mortality

**every 2-hrs-prolonged fasting was correlated with a 20% increase
of sleeping duration**

Marinac CR, Nelson SH, Breen CI et al. JAMA Oncol 2016; 2:1049-1055

Routine Follow-Up Examinations in Asymptomatic Patients			
	Oxford		
	LoE	GR	AGO
Tests:			
■ History (specific symptoms)	1a	A	++
■ Physical examination	1a	B	++
■ Breast self-examination	5	D	+
■ Mammography	1a	A	++
■ Sonography of the breast	2a	B	++
■ Routine MRI of the breast*	3a	B	+/-
■ Breast MRI if conventional imaging is inconclusive	3b	B	+
■ Pelvic examination	5	D	++
■ DXA-scan at baseline and repeat scan according to individual risk in women with premature menopause or women taking an AI	5	D	+

* Consider in case of increased risk (age <50y, HR-neg., diagnostic assessability C/D in mammography + ultrasound)

1. Margenthaler JA, Allan E, Cheng L, et al.. Surveillance of Patients With Breast Cancer After Curative-Intent Primary Treatment: Current Practice Patterns. Journal of Oncology Practice 2012; 8(2): 79 – 83.
2. Parmeshwar R, Margenthaler JA, Allam E et al.. Patient Surveillance After Initial Breast cancer Therapy Variation by Physician Specialty. Am J Surg 2013; 206(2): 218-222.
3. Jochelson M, Hayes DF, Ganz PA. Surveillance and Monitoring in Breast Cancer Survivors: Maximizing Benefit and Minimizing Harm. ASCO Educational Book 2013 e13 – e18.
4. Khatcheressian JL, Hurley P, Bantug E, et al.. Breast Cancer Follow-up and Management After Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update . J Clin Oncol. 2013 March 1; 31(7):961-965.
5. Bychkovsky BL, Lin NU. Imaging in the evaluation and follow-up of early and advanced breast cancer: When, why, and how often? Breast. 2017 Feb;31:318-324 Review.
6. Expert Panel on Breast Imaging: Moy L, Bailey L, D'Orsi C et al..ACR Appropriateness Criteria[®] Stage I Breast Cancer: Initial Workup and Surveillance for Local Recurrence and Distant Metastases in Asymptomatic Women. J Am Coll Radiol. 2017 May;14(5S):S282-S292.
7. Lam DL, Houssami N, Lee JM. Imaging Surveillance After Primary Breast Cancer Treatment. AJR Am J Roentgenol. 2017 Mar;208(3):676-686. Review.

Statement: Physical examination

1. Margenthaler JA, Allan E, Cheng L, et al.. Surveillance of Patients With Breast Cancer After Curative-Intent Primary Treatment: Current Practice Patterns. *Journal of Oncology Practice* 2012; 8(2): 79 – 83.
2. Khatcheressian JL, Hurley P, Bantug E, et al.. Breast Cancer Follow-up and Management After Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update . *J Clin Oncol*. 2013 March 1; 31(7):961-965.
3. Jochelson M, Hayes DF, Ganz PA. Surveillance and Monitoring in Breast Cancer Survivors: Maximizing Benefit and Minimizing Harm. *ASCO Educational Book* 2013 e13 – e18.
4. Parmeshwar R, Margenthaler JA, Allam E et al.. Patient Surveillance After Initial Breast cancer Therapy Variation by Physician Specialty. *Am J Surg* 2013; 206(2): 218-222.

Statement: Mammography

1. De Bock GH, Bonnema J, van Der Hage J et al.. Effectiveness of Routine Visits and Routine Tests in Detecting Isolated Locoregional Recurrences After Treatment for Early-Stage Invasive Breast Cancer: A Meta-Analysis and Systematic Review. *J Clin Oncol* 2004; 22(19): 4010-4018 .
2. Khatcheressian JL, Hurley P, Bantug E et al..Breast Cancer Follow-up and Management After Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update . *J Clin Oncol*. 2013 March 1; 31(7):961-965.

Statement: Sonography of the breast

1. Graf O, Helbich TH, Fuchsjaeager MH et al.. Follow-up of palpable circumscribed noncalcified solid breast masses at mammography and US: can biopsy be averted? *Radiology* 2004; 233(3): 850-6.
2. Dillon MF, Hill AD, Quinn CM et al.: The accuracy of ultrasound, stereotactic, and clinical core biopsies in the diagnosis of breast cancer, with an analysis of false-negative cases. *Ann Surg*. 2005; 242(5):701-7.
3. Karellas A, Vedantham S. Breast cancer imaging: a perspective for the next decade. *Med Phys* 2008; 35(11):4878-97. Review.

4. Jung Hyun-Yun., Min Jung Kim, Eun-Kyung Kim et al.. Imaging Surveillance of Patients with Breast Cancer after Primary Treatment: Current Recommendations. Korean J Radiol 2015;16(2):219-228.
5. Song SE, Cho N, Chang JM et al.. Diagnostic performances of supplemental breast ultrasound screening in women with personal history of breast cancer. Acta Radiol. 2017 Jan 1:284185117725779.

Statement: MRI of the breast

1. DeMartini W, Lehman C. A review of current evidence-based clinical applications for breast magnetic resonance imaging. Top Magn Reson Imaging 2008;19(3):143-50. Review.
2. Warner E. The role of magnetic resonance imaging in screening women at high risk of breast cancer. Top Magn Reson Imaging. 2008; 19(3):163-9. Review.
3. Lehman CD, Lee JM, DeMartini WB et al. Screening MRI in Women With a Personal History of Breast Cancer. J Natl Cancer Inst. 2016 Jan 7;108(3).
4. Shah C, Ahlawat S, Khan A et al.. The Role of MRI in the Follow-up of Women Undergoing Breast-conserving Therapy. Am J Clin Oncol. 2016 Jun;39(3):314-9.
5. Cho N, Han W, Han BK et al.:Breast Cancer Screening With Mammography Plus Ultrasonography or Magnetic Resonance Imaging in Women 50 Years or Younger at Diagnosis and Treated With Breast Conservation Therapy. JAMA Oncol. 2017 Nov 1;3(11):1495-1502.
6. Kim EJ, Kang BJ, Kim SH et al.:Diagnostic Performance of and Breast Tissue Changes at Early Breast MR Imaging Surveillance in Women after Breast Conservation Therapy.Radiology. 2017 Sep;284(3):656-666.
7. Tadros A, Arditi B, Weltz C et al.:Utility of surveillance MRI in women with a personal history of breast cancer.Clin Imaging. 2017 Nov - Dec;46:33-36.


Statement: Pelvic examination Expert Opinion

1. Cohen I, Beyth Y, Tepper R.: The role of ultrasound in the detection of endometrial pathologies in asymptomatic postmenopausal breast cancer patients with tamoxifen treatment. Obstet Gynecol Surv 1998; 53(7): 429-38.

2. Giorda G, Crivellari D, Veronesi A et al.: Comparison of ultrasonography, hysteroscopy, and biopsy in the diagnosis of endometrial lesions in postmenopausal tamoxifen-treated patients. *Acta Obstet Gynecol Scand* 2002; 81(10):975-80.
3. Robertson C1, Arcot Ragupathy SK, Boachie C et al.: The clinical effectiveness and cost-effectiveness of different surveillance mammography regimens after the treatment for primary breast cancer: systemic reviews registry database analyses and economic evaluation. *Health Technol Assess.* 2011;15(34): 1-322.
4. Geurts SM, de Vegt F, Siesling S et al. Pattern of follow up care and early relapse detection in breast cancer patients. *Breast Cancer Res Treat* 2012; 136(3): 859-68.
5. Khatcheressian JL, Hurley P, Bantug E et al.. Breast Cancer Follow-up and Management After Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update . *J Clin Oncol.* 2013 March 1; 31(7):961-965.

Statement: Dexa scan Expert Opinion

1. Mahon SM, Williams MT, Spies MA: Screening for second cancers and osteoporosis in long-term survivors. *Cancer Pract* 2000; 8(6): 282-90.
2. Runowcz CD, Leach CR, Henry L et al.:American Cancer Society/American Society of Clinical Oncology breast cancer survivorship care guideline. *CA Cancer J Clin* 2016; 66: 43-73.



Routine Follow-Up Examinations in Asymptomatic Patients

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- Routine biochemistry (incl. tumor markers)
- Ultrasound of the liver
- Bone scan
- Chest X-ray
- CT of chest, abdomen, and pelvis
- Detection of isolated / circulating tumor cells
- PET
- Whole body MRI

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

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1. Bychkovsky BL, Lin NU. Imaging in the evaluation and follow-up of early and advanced breast cancer: When, why, and how often? Breast. 2017 Feb;31:318-324 Review.
2. Lam DL, Houssami N, Lee JM. Imaging Surveillance After Primary Breast Cancer Treatment. AJR Am J Roentgenol. 2017 Mar;208(3):676-686. Review.
3. Expert Panel on Breast Imaging; Moy L, Bailey L, D'Orsi C, Green ED et al. ACR Appropriateness Criteria[®] Stage I Breast Cancer: Initial Workup and Surveillance for Local Recurrence and Distant Metastases in Asymptomatic Women. J Am Coll Radiol. 2017 May;14(5S):S282-S292.
4. Lafranconi A, Pylkkänen L, Deandrea S et al.. Intensive follow-up for women with breast cancer: review of clinical, economic and patient's preference domains through evidence to decision framework. Health Qual Life Outcomes. 2017 Oct 19;15(1):206.

Statement: Magnetic resonance imaging (MRI) of the breast

1. DeMartini W, Lehman C. A review of current evidence-based clinical applications for breast magnetic resonance imaging. Top Magn Reson Imaging 2008; 19(3):143-50. Review.
2. Warner E. The role of magnetic resonance imaging in screening women at high risk of breast cancer. Top Magn Reson Imaging.

2008; 19(3):163-9. Review.

3. Shah C, Ahlawat S, Khan A et al.. The Role of MRI in the Follow-up of Women Undergoing Breast-conserving Therapy. Am J Clin Oncol. 2016 Jun;39(3):314-9.

Statement: Routine biochemistry (incl. tumor markers)

1. McShane LM, Altman DG, Sauerbrei W et al..Statistics Subcommittee of the NCI-EORTC Working Group on Cancer Diagnostics. Reporting recommendations for tumor marker prognostic studies. J Clin Oncol 2005; 23(36): 9067-72.
2. Harris LN, Ismaila N, McShane LM et al..Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-stage Invasive Breast Cancer: American Society of Clinical Practice Guideline. J Clin Oncol 2016; 34(10): 1134-50.

Statement: Ultrasound of the liver

Statement: Bone scan

Statement: Chest X-ray

Statement: CT of chest, abdomen and pelvis

1. Emens LA, Davidson NE. The follow-up of breast cancer. Semin Oncol. 2003; 30(3): 338-48. Review.
2. Moschetti I, Cinquni M, Lambertini M et al..Follow-up strategies for women treated for early breast cancer. Cochrane Database Syst Rev 2005 Jan 25;(1) Review. Update in: Cochrane Database Syst Rev 2016; (5) CD001768.
3. Dull B, Linkugel A, Margenthaler JA, Cyr AE. Overuse of Chest CT in Patients With Stage I and II Breast Cancer: An Opportunity to Increase Guidelines Compliance at an NCCN Member Institution.J Natl Compr Canc Netw. 2017 Jun;15(6):783-789.


Statement: Detection of isolated/circulating tumor cells

1. Janni W, Vogl FD, Wiedswang G et al..Persistence of disseminated tumor cells (DTC) in bone marrow (BM) during Follow-up predicts increased risk for relapse – Up-date of the pooled European data. Clin Cancer Res 2011; 17(9): 2967-76.
2. Rack B, Schindlbeck C, Jückstock J et al.. Circulating tumor cells predict survival in early average-to-high risk breast cancer patients.

SUCCESS Study Group. J Natl Cancer Inst. 2014 May 15;106(5).

Statement: PET / WB-MRI

1. Ide M. Cancer screening with FDG-PET. Q J Nucl Med Mol Imaging 2006; 50(1): 23-7.
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Early Detection of Potentially Curable Events

	Oxford		
	LoE	GR	AGO
Locoregional recurrence (chest wall, in-breast):			
▪ Incidence 7–20% (depending on time of F/U)			
▪ Breast self-examination	5	D	+
▪ Physical examination, mammography & US	1a	A	++
▪ Magnetic resonance imaging (MRI)*	3a	B	+/-

* Consider in case of increased risk (age <50y, HR-neg., diagnostic assessability C/D in mammography + ultrasound)

Statement incidence


1. Perry NM. Quality assurance in the diagnosis of breast disease. EUSOMA Working Party. Eur J Cancer 2001; 37: 159-172
2. Wapnir IL, Anderson SJ, Mamounas EP et al.. Prognosis after ipsilateral breast tumor recurrence and locoregional recurrences in five National Surgical Adjuvant Breast and Bowel Project node-positive adjuvant breast cancer trials. J Clin Oncol 2006; 24:2028-2037

Statement breast self examination

1. Thomas DB, Gao DL, Ray RM et al.. Randomized trial of breast self-examination in Shanghai: final results. J Natl Cancer Inst 2002; 94(19): 1445-57.
2. Khatcheressian JL, Wolff AC, Smith TJ. American Society of Clinical Oncology 2006 update of the breast cancer follow-up and management guidelines in the adjuvant setting. J Clin Oncol. 2006 Nov 1;24(31):5091-7.
3. Montgomery DA, Krupa K, Cooke TG. Follow-up in breast cancer: does routine clinical examination improve outcome? A systematic review of the literature. Br J Cancer 2007; 97(12): 1632-41.

Statement physical examination, mammography & US & MRI

1. Beinart G, Gonzalez-Angulo AM, Broglio K. Clinical course of 771 patients with bilateral breast cancer: characteristics associated with overall and recurrence-free survival. Clin Breast Cancer 2007; 7(11): 867-74

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	Oxford		
	LoE	GR	AGO
Contralateral breast cancer:			
<ul style="list-style-type: none"> Relative risk: 2.5–5 Incidence: 0.5–1.0 % / year 			
▪ Breast self-examination	5	D	+
▪ Physical examination, mammography & US	1a	A	++
▪ Routine breast MRI*	3b	B	+/-
Male breast cancer: analogous to BC in women**			
	5	D	+
<p>* Consider in case of increased risk: age <50y, HR-neg., diagnostic assessability C/D in mammography + ultrasound.</p> <p>** See chapter “Breast Cancer Specific Situations”</p>			

Statement risk and incidence

1. Hooning MJ, Aleman BM, Hauptmann M et al.: Roles of radiotherapy and chemotherapy in the development of contralateral breast cancer J Clin Oncol 2008; 26(34): 5561-8.
2. Yerushalmi R, Kennecke H, Woods R et al.: Does multicentric/multifocal breast cancer differ from unifocal breast cancer? An analysis of survival and contralateral breast cancer incidence. Breast Cancer Res Treat 2009; 117(2): 365-70.
3. Bertelsen L, Mellekjær L, Christensen J et al.: Age-Specific Incidence of Breast Cancer in Breast Cancer Survivors and Their First-Degree Relatives. Epidemiology 2009; 20(2): 175 – 80.

Statement breast self examination


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2. Montgomery DA, Krupa K, Cooke TG et al.: Follow-up in breast cancer: does routine clinical examination improve outcome? A systematic review of the literature. Br J Cancer 2007; 97(12): 1632-41.
3. Khatcheressian JL, Hurley P, Bantug E et al.: Breast Cancer Follow-up and Management After Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2013 March 1; 31(7):961-965.

Statement physical examination, mammography & US&MRI

1. Beinart G, Gonzalez-Angulo AM, Broglio K et al.: Clinical course of 771 patients with bilateral breast cancer: characteristics associated with overall and recurrence-free survival. Clin Breast Cancer 2007; 7(11): 867-74.
2. Montgomery DA, Krupa K, Cooke TG et al.: Follow-up in breast cancer: does routine clinical examination improve outcome? A systematic review of the literature. Br J Cancer. 2007; 97(12): 1632-41.
3. Khatcheressian JL, Hurley P, Bantug E, et al.: Breast Cancer Follow-up and Management After Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update _ J Clin Oncol. 2013 March 1; 31(7):961-965.
4. Kim JY1, Cho N, Koo HR et al. Unilateral breast cancer: screening of contralateral breast by using preoperative MR imaging reduces incidence of metachronous cancer.Radiology. 2013 Apr;267(1):57-66.
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Statement surveillance of male breast cancer

1. Ferzoco RM, Ruddy KJ, Optimal delivery of male breast cancer follow-up care: improving outcomes, Breast Cancer: Targets and Therapy 2015;7 371–379
2. Auvinen A, Curtis RE, Ron E. Risk of subsequent cancer following breast cancer in men. J Natl Cancer Inst. 2002;94(17):1330–1332.



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Early Detection of Potentially Curable Events

Unrelated site carcinoma:

- MDS (RR 10.9), AML (RR 2.6–5.3), Colon RR 3.0; endometrium RR 1.6; ovary RR 1.5; lymphoma RR
- Screening for secondary malignancies according to current guidelines
- Pelvic examination and PAP smear
- Routine endometrial ultrasound / biopsy

Oxford

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Statement: Risk

1. Brown LM, Chen BE, Pfeiffer RM et al.: Risk of second non-hematological malignancies among 376,825 breast cancer survivors. Breast Cancer Res Treat 2007; 106(3): 439-51.
2. Kirova YM, De Rycke Y, Gambotti L et al.: Second malignancies after breast cancer: the impact of different treatment modalities. Br J Cancer 2008 Mar 11; 98(5): 870-4.
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Statement: Screening for secondary malignancies according to current guidelines

1. Khatcheressian JL, Hurley P, Bantug E et al.: Breast Cancer Follow-up and Management After Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update _ J Clin Oncol. 2013 March 1; 31(7):961-965.

Statement: Pelvic examination and PAP smear

1. Gerber B, Krause A, Müller H et al.: Ultrasonographic detection of asymptomatic endometrial cancer in postmenopausal patients offers no prognostic advantage over symptomatic disease discovered by uterine bleeding. Eur J Cancer 2001; 37(1): 64-71.
2. Fishman DA, Cohen L, Blank SV et al.: The role of ultrasound evaluation in the detection of early-stage epithelial ovarian cancer. Am J Obstet Gynecol 2005; 192(4): 1214-21.
3. Rieck GC, Lim K, Rogers MT et al.: Screening for familial ovarian cancer--management and outcome of women with moderate to high risk of developing ovarian cancer. Int J Gynecol Cancer 2006;16 Suppl 1: 86-91.
4. Chan JK, Manuel MR, Cheung MK et al.: Breast cancer followed by corpus cancer: is there a higher risk for aggressive histologic subtypes? Gynecol Oncol 2006; 102(3): 508-12.

Statement: Endometrial ultrasound / biopsy


1. Gerber B, Krause A, Müller H, et al.: Effects of adjuvant tamoxifen on the endometrium in postmenopausal women with breast cancer: a prospective long-term study using transvaginal ultrasound. J Clin Oncol 2000; 18(20): 3464-70
2. Barakat RR, Gilewski TA, Almadrones L et al.: Effect of adjuvant tamoxifen on the endometrium in women with breast cancer: a prospective study using office endometrial biopsy. J Clin Oncol 2000;18(20): 3459-63.
3. Fung MF, Reid A, Faught W et al.: Prospective longitudinal study of ultrasound screening for endometrial abnormalities in women with breast cancer receiving tamoxifen. Gynecol Oncol 2003; 91(1): 154-9.

Statement: Marrow neoplasms after adjuvant breast cancer therapy

1. Wolff AC, Blackford AL, Visvanathan K et al.: Risk of marrow neoplasms after adjuvant breast cancer therapy: the national comprehensive cancer network experience. J Clin Oncol. 2015; 33(4): 340-8.

Statement: Secondary lung tumors:

1. Hoekstra N, Fleury E, Merino Lara TR et al.: Long-term risks of secondary cancer for various whole and partial breast irradiation techniques. Radiother Oncol. 2018 Sep;128(3):428-433



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Follow-Up Care for Breast Cancer

Recommendations for asymptomatic pts.
(mod. according to ASCO-ACS recommendations 2016, NCCN 3.2017 und S3-guidelines 2017)

Clinical follow-up		Follow-up*				Screening/ Follow-up	
		1	2	3	4	5	> 5
Years after primary therapy		inv.: every 3 months			inv.: every 6 months		inv.: every 12 months
History, physical examination, counseling							
Self-examination		monthly					
Imaging modalities and biochemistry		indicated only if complaints, clinical findings, or suspicion of recurrence					
Mammo- graphy and additional sonography	BCT**	both sides: every 12 months					
	Mastectomy	contralateral every 12 months					

* Continued follow-up visits if still on adjuvant treatment
** In pts after breast-conserving therapy (BCT): First mammography 1 year after initial mammography or at least 6 months after completion of radiotherapy

1. Runowcz CD, Leach CR, Henry L et al.: American Cancer Society/American Society of Clinical Oncology breast cancer survivorship care guideline. CA Cancer J Clin 2016; 66: 43-73
2. Merkow RP, Korenstein D, Yeahia R et al.: Quality of Cancer Surveillance Clinical Practice Guidelines: Specificity and Consistency of Recommendations. JAMA Intern Med. 2017 May 1;177(5):701-709.
3. Muradali D, Kennedy EB, Eisen A et al.: Breast screening for survivors of breast cancer: A systematic review. Prev Med. 2017 Oct;103:70-75.
4. NCCN Clinical Practice Guidelines in Oncology, Breast Cancer Version 3.17-10.17;
https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
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Breast Cancer Follow-up Duration and Breast Nurses

	Oxford		
	LoE	GR	AGO
■ Duration of follow-up			
■ up to 5 years	1c	A	++
■ up to 10 years	1c	A	+
■ Surveillance by specialized breast nurses	2b	B	+/-*

* Studies recommended

1. Sheppard C. Breast cancer follow-up: literature review and discussion. Eur J Oncol Nurs 2007;11(4):340-7.
2. van Hezewijk M, Ranke GM, van Nes JG et al.: Patients' needs and preferences in routine follow-up for early breast cancer; an evaluation of the changing role of the nurse practitioner. Eur J Surg Oncol 2011; 37(9): 765-73.
3. Interdisziplinäre S3-Leitlinie für die Früherkennung, Diagnostik, Therapie und Nachsorge des Mammakarzinoms. Langversion 4.0 – Dezember 2017 AWMF-Registernummer: 032-045OL; http://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/LL_Mammakarzinom_Langversion_4.0.pdf
4. NCCN Clinical Practice Guidelines in Oncology, Breast Cancer Version 3.17-10.17; https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf



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Luminal-like, HER2-positive and Triple-negative Breast Cancer Patients

- **Intrinsic typing of breast cancer leads to the development of subgroups with different courses of disease**
- **Postoperative surveillance should be tailored to specific breast cancer type and their associated time periods of recurrence.**
- **ER-positive patients have a stable risk of recurrence of multiple years. Long term surveillance is recommended.**
- **In contrast, patients with HER2-positive disease and TNBC have an increased risk of recurrence in the early follow up phase. Surveillance should be adjusted accordingly.**

Ribelles et al. BCR 2013

1. Voduc KD, Cheang MC, Tyldesley S et al.: Breast cancer subtypes and the risk of local and regional relapse. J Clin Oncol 2010; 28(10): 1684-91.
2. Ribelles N, Perez-Villa L, Jerez JM et al.: Pattern of recurrence of early breast cancer is different according to intrinsic subtype and proliferation index. Breast Cancer Res 2013;15(5):R98.
3. Metzger-Filho O1, Sun Z, Viale G et al.: Patterns of Recurrence and Outcome According to Breast Cancer Subtypes in Lymph Node–Negative Disease: Results From International Breast Cancer Study Group Trials VIII and IX. J Clin Oncol 2013; 31(25): 3083-3090.
4. Benveniste AP, Dryden MJ, Bedrosian I et al.: Surveillance of women with a personal history of breast cancer by tumour subtype. Clin Radiol. 2017 Mar;72(3):266.e1-266.e6.
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