

Diagnostik und Therapie primärer und metastasierter Mammakarzinome

Früherkennung und Diagnostik

Früherkennung und Diagnostik

- **Versionen 2005–2017:**
Albert / Blohmer / Fersis / Junkermann /
Maass / Müller-Schimpfle / Scharl / Schreer
- **Version 2018:**
Albert / Müller-Schimpfle

Screened data bases

Pubmed	2013 - 2017
Medline	2013 - 2017
Cochrane	2013 - 2017

Guidelines

S3 Diagnostik, Therapie und Nachsorge des Mammakarzinoms

2015 ACS Update Breast Cancer Screening for women at average risk

IARC Handbook 2016

European Commission 2016

(<http://ecibc.jrc.ec.europa.eu/recommendations/list/3;Update> 24.11.2016, Abruf 20122016)

Screened: Metaanalyses/ Systematic reviews / RCT / Cohort studies

Früherkennung Mammographie

Alter	Intervall	Oxford		AGO
		LOE	GR	
< 40	na	-	-	--
40–49	12–24	1b	B	+
50–69*	24	1a	A	++
70–74	24	1a	A	++
> 75**	24	4	C	+

* Nationales Mammographie-Screening-Programm

** Abhängig von Gesundheitszustand + Lebenserwartung mehr als 10 Jahre

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Tomosynthese

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Radiation Dose

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Mammography density assessment

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2. *Radiology*. 2017 Feb;282(2):348-355.

Brustkrebs Mortalitätsreduktion

Metaanalyses

RR 95%CI

Independent UK Panel, 2012

13-year metaanalysis 0.80 (0.73–0.89)

Cochrane Review, 2011

Fixed-effect metaanalysis of 9 RCT-trials 0.81 (0.74–0.87)

As above, but excluding women <50 years 0.77 (0.69–0.86)

Canadian Task Force, 2011

Women aged 50–69 years 0.79 (0.68–0.90)

Duffy et al, 2012

Review of all trials and age groups 0.79 (0.73–0.86)

1. Broeders M, Moss S, Nyström L et al. The impact of mammography screening on breast cancer mortality in Europe: a review of observational studies. J Med Screen 2012; 19(Suppl 1):14-25
2. Canadian Task Force on Preventive Health Care. Recommendations on screening for breast cancer in average-risk women aged 40-74 years. CMAJ 2011; 183:1991-2001
3. Duffy S, Ming-Fang Yen A, Hsiu-Hsi Chen T, et al. Long-term benefits of breast screening. Breast Cancr Management 2012; 1:31-38
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Brustkrebs Mortalitätsreduktion

Metaanalyses

RR 95%CI

Case-Control Studies

Broeders et al	Screening Mx	0.46 (0.4 – 0.54)
	Corr. for self selection	0.52 (0.42-0.65)
	Invited for screening	0.69 (0.57-0.83)

Incidence-based Mortality Studies

Broeders et al	Screening Mx	0.62 (0.56-0.69)
	Invited to screening	0.75 (0.69-0.81)

Randomized Clinical Trials

Gotsche and Jorgenson	Screening Mx	0.81 (0.74-0.87)
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Breast cancer mortality reduction

1. Morrell S, Taylor R, Roder D, et al. Mammography service screening and breast cancer mortality in New Zealand: a National Cohort Study 1999-2011. Br J Cancer. 2017 Mar 14;116(6):828-839
2. Johns LE, Coleman DA, Swerdlow JA, Moss SM, et al. Effect of population breast screening on breast cancer mortality up to 2005 in England and Wales: an individual-level cohort study Br J Cancer 2017;116: 246 -252
3. Sankatsing VDV, van Ravesteyn NT, Heijnsdijk EAM, et al. The effect of population-based mammography screening in Dutch municipalities on breast cancer mortality: 20 years of follow-up. Int J Cancer. 2017 Aug 15;141(4):671-677
4. Beau AB, Lynge E, Njor SH, et al. Benefit-to-harm ratio of the Danish breast cancer screening programme Int J Cancer. 2017 Aug 1;141(3):512-518.

Brustkrebs Mortalitätsreduktion

Age Group (yrs)	NNS	
	Mortality Reduction	
	20%	40%
40 - 49	1770	753
50 - 59	1087	462
60 - 69	835	355

4 systematic reviews of 8 RCTs,
1 systematic review of 7 cohort studies and metaanalysis
of case-control studies

Oeffinger KC et al JAMA 2015;314

1. Myers ER, Moorman P, Gierisch JM, et al. Benefits and harms of breast cancer screening: a systematic review. JAMA 2015;314(15)1615-1634
2. Oeffinger KC, Fontham ETH, Etzioni R, et al. Breast Cancer Screening for women at average risk. 2015 Guideline Update from the American Cancer Society. JAMA 2015; 314:1599-1614



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Guidelines Breast
Version 2018.1D

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**FORSCHEN
LEHREN
HEILEN**

Mammographie-Screening Vor und Nachteile

Grundgesamtheit: per 10.000 gescreente Frauen über 10 Jahre
Breast Cancer Surveillance Consortium Registry Data

Lebensjahr	40-49	50-59	60-69	70-74
Vermiedene Brustkrebstodesfälle (CI95%)	3 (0-9)	8 (2-17)	21 (11-32)	13 (0-32)
Falsch-positive Fälle (n)	1212	932	808	696
Brustbiopsien (n)	164	159	165	175
Falsch-negative Fälle (n)	10	11	12	13

Siu AL on behalf of the USPSTF 2016, 164:279-296

Siu AL, on behalf of the U.S. Preventive Services Task Force
Screening for Breast Cancer: U.S. Preventive Services Task Force
Recommendation Statement. Ann Internal Med 2016 vol 164: 279-296

Breast Cancer Screening

ACS Guideline Update 2015

American Cancer Society Guideline for Breast Cancer Screening, 2015

These recommendations represent guidance from the American Cancer Society (ACS) for women at average risk of breast cancer: women without a personal history of breast cancer, a suspected or confirmed genetic mutation known to increase risk of breast cancer (eg, *BRCA*), or a history of previous radiotherapy to the chest at a young age.

The ACS recommends that all women should become familiar with the potential benefits, limitations, and harms associated with breast cancer screening.

Recommendations

1. Women with an average risk of breast cancer should undergo regular screening mammography starting at age 45 years. (*Strong Recommendation*)
 - 1a. Women aged 45 to 54 years should be screened annually. (*Qualified Recommendation*)
 - 1b. Women 55 years and older should transition to biennial screening or have the opportunity to continue screening annually. (*Qualified Recommendation*)
 - 1c. Women should have the opportunity to begin annual screening between the ages of 40 and 44 years. (*Qualified Recommendation*)
2. Women should continue screening mammography as long as their overall health is good and they have a life expectancy of 10 years or longer. (*Qualified Recommendation*)
3. The ACS does not recommend clinical breast examination for breast cancer screening among average-risk women at any age. (*Qualified Recommendation*)

- ^a A strong recommendation conveys the consensus that the benefits of adherence to that intervention outweigh the undesirable effects that may result from screening. Qualified recommendations indicate there is clear evidence of benefit of screening but less certainty about the balance of benefits and harms, or about patients' values and preferences, which could lead to different decisions about screening.

1. Oeffinger KC, Fontham ETH, Etzioni R, Herzig A, Michaelson JS et al Breast Cancer Screening for women at average risk. 2015 Guideline Update from the American Cancer Society (ACR). JAMA 2015; 314:1599-1614

Breast-Cancer Screening- Viewpoint of the IARC Working Group

Method	Strength of Evidence
Reduces breast-cancer mortality in women 50-69 yr of age	Sufficient
Reduces breast-cancer mortality in women 70-74 yr of age	Sufficient
Reduces breast-cancer mortality in women 40-44 yr of age	Limited
Reduces breast-cancer mortality in women 45-49 yr of age	Limited
Detects breast cancer that would never have been diagnosed or never have caused harm if women had not been screened (overdiagnosis)	Sufficient
Reduces breast-cancer mortality in women 50-74 yr of age to an extent that its benefits substantially outweigh the risk of radiation-induced cancer	Sufficient
Produces short-term negative psychological consequences when the result is false positive	Sufficient
Has a net benefit for women 50-69 yr of age who are invited to attend organized mammographic screening programs	Sufficient

1. Lauby-Secretan B, Scoccianti C, Loomis D, et al; International Agency for Research on Cancer Handbook Working Group: Breast-cancer screening–viewpoint of the IARC Working Group. N Engl J Med 2015;372:2353-2358
2. IACR Handbook 2016: Website for the IARC publications:
<http://publications.iarc.fr/Book-And-Report-Series/Iarc-Handbooks-Of-Cancer-Prevention/Breast-Cancer-Screening-2016>

Mammographie-Screening Frauen 40–49 Jahre

RR (eingeladene Frauen)	0.74 (95%CI 0.66-0.83)
40–44 J	0.83 (95%CI 0.67-1.00)
45–49 J	0.68 (95%CI 0.59-0.78)
Teilnehmerinnen	0.71 (95%CI 0.62-0.80)
NNS	1252 (95%CI 958-1915)
(1 live saved / 10 years screening)	

Hellquist BN et al. Cancer 2011; 117(4) : 714-722

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Recommendations from the Society of Breast Imaging and the ACR on the use of mammography, breast MRI, breast ultrasound and other technologies for the detection of clinically occult cancer. J Am Coll Radiol 2010; 7; 18-27

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Früherkennung Sonographie

- **Screening-Mammasonographie**
 - Autom. 3D-Sonographie
- Als Ergänzung bei:
 - **Dichtem Parenchym**
(Dichte 3–4/Beurteilbarkeit: C-D)
 - Erhöhtem Risiko
 - **Mammographischer Läsion**
 - **Zur Abklärung susp. Läsionen im MRT**

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

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6. Kolb T, Lichy J, J.Newhouse J. Comparison of the performance of screening mammography, physical examination and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations, Radiology 2002; 225: 165-175
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ABUS/AVUS

1. Golatta M, Franz D, Harcos A, et al. Interobserver reliability of automated breast volume scanner (ABVS) interpretation and agreement of ABVS findings with hand held breast ultrasound (HHUS), mammography and pathology results. *Eur J Radiol*. 2013 Aug;82(8):e332-6.
2. Wojcinski S, Gyapong S, Farrokh A, et al. Diagnostic performance and inter-observer concordance in lesion detection with the automated breast volume scanner (ABVS). *BMC Med Imaging*. 2013 Nov 12;13:36. doi: 10.1186/1471-2342-13-36.
3. Golatta M, Baggs C, Schweitzer-Martin M, et al. Evaluation of an automated breast 3D-ultrasound system (ABUS) by comparing it with hand-held ultrasound (HHUS) and mammography. *Arch Gynecol Obstet* 2014 Oct 14.
4. Choi WJ, Cha JH, Kim HH, et al. Comparison of automated breast volume scanning and hand- held ultrasound in the detection of breast cancer: an analysis of 5,566 patient evaluations. *Asian Pac J Cancer Prev*. 2014;15(21):9101-5.
5. Golatta M, Baggs C, Schweitzer-Martin M, et al. Evaluation of an automated breast 3D-ultrasound system by comparing it with hand-held ultrasound (HHUS) and mammography. *Arch Gynecol Obstet* 2015;291:889-895
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11. Wilczek B, Wilczek HE, Rasouliyan L, et al. Adding 3D automated breast ultrasound to mammography screening in women with heterogeneously and extremely dense breasts: Report from a hospital-based, high-volume, single-center breast cancer screening program. *Eur J Radiol.* 2016 Sep;85(9):1554-63
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US-Screening

1. Gartlehner G, Thaler KJ, Chapman A, et al. Mammography in combination with breast ultrasonography versus mammography for breast cancer screening in women at average risk. *Cochrane Database Syst Rev.* 2013 Apr 30;4:CD009632.
2. Health Quality Ontario. Ultrasound as an Adjunct to Mammography for Breast Cancer Screening: A Health Technology Assessment. *Ont Health Technol Assess Ser.* 2016 Jul 1;16(15):1-71.
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Dense Breast

1. American College of Radiology (ACR): ACR BIRADS fifth edition: Breast imaging reporting and data system, Breast Imaging Atlas. American College of Radiology, Reston, VA, 2013
2. Müller-Schimpfle M. et al. BI-RADS die 5.–Eine Kurzmitteilung aus deutsch-/österreichischer Sicht. *Fortschr Röntgenstr* 2016; 188: 346–352 ;*Geburtshilfe Frauenheilkd* 2016; 76(05): 490-496;
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5. *Ont Health Technol Assess Ser.* 2016; 16(15):1-71

Elevated Risk

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2. Berg WA, Blume JD, Adams AM, et al. Reasons women at elevated risk of breast cancer refuse breast MRI imaging screening: ACRIN 6666. *Radiology.* 2010;254(1):79–87.

3. Health Quality Ontario.. Ultrasound as an Adjunct to Mammography for Breast Cancer Screening: A Health Technology Assessment.
4. Ont Health Technol Assess Ser. 2016; 16(15):1-71

Recommendations International

1. Oeffinger KC, Fontham ETH, Etzioni R, et al. Breast Cancer Screening for women at average risk. 2015 Guideline Update from the American Cancer Society (ACR). JAMA 2015; 314:1599-1614
2. Lauby-Secretan B, Scoccianti C, Loomis D, et al; International Agency for Research on Cancer Handbook Working Group: Breast-cancer screening–viewpoint of the IARC Working Group. N Engl J Med 2015;372:2353-2358
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<http://publications.iarc.fr/Book-And-Report-Series/Iarc-Handbooks-Of-Cancer-Prevention/Breast-Cancer-Screening-2016>
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Früherkennung

Klinische Untersuchung

Als alleinige Untersuchung

- Selbstuntersuchung
 - Klinische Untersuchung (CBE) durch ärztliches Personal
 - CBE wegen mammo/sonographischer Läsion
- CBE in Kombination mit Bildgebung**

Oxford		
LoE	GR	AGO
1a	A	-*
3b	C	-*
5	D	++
BCP		++

* Kann Brust-Bewußtsein erhöhen

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Abklärung von Symptomen

- **Klinische Untersuchung**
- **Mammographie**
 - Tomosynthese
- **Sonographie**
 - Elastographie (Shear wave)*
 - Autom. 3D-Sonographie
- **Minimalinvasive Biopsie**
- **MRT****

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

* Zusatzuntersuchung

** Wenn klinische, mammographische und sonographische Diagnostik inkl. Nadelbiopsie keine endgültige Diagnose erlauben.

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MRT

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Prätherapeutische Untersuchung von Brust- und Axilla

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

* Histologische Sicherung von Zusatzbefunden im Fall therapeutischer Relevanz.

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

Combined DM + DBT + US + MRI

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US-Axilla +FNA/CNB

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MRT

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MRT: Präoperatives Staging

- **9 ausgewählte Studien
(2 randomisiert; 7 Kohortenstudien)**
- **3112 Patientinnen mit Mammakarzinom**
- **MRT versus kein-MRT:**
 - **Initiale Mastektomie 16,4% versus 8,1%**
[OR, 2,22 (P < 0,001); adjusted OR, 3,06 (P < 0,001)]
 - **Nachresektion nach initialer BET 11,6% versus 11,4%**
[OR, 1,02 (P = 0,87); adjustiert OR, 0,95 (P = 0,71)]
 - **Gesamt Mastektomie 25,5% versus 18,2%**
[OR, 1,54 (P < 0,001); adjustierte OR, 1,51 (P < 0,001)]

N Houssami et al. Ann Surg 2013; 257

1. 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.
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3. 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

MRT: Präoperatives Staging bei Lobular Invasive Breast Cancer

- **766 patients with invasive lobular cancer (ILC)**
 - Initial mastectomy: 31.1% versus 24.9%
[OR, 1.36 (P = 0.056); adjusted OR, 2.12 (P = 0.008)]
 - Re-excision after initial breast conservation 10.9% versus 18.0%
[OR, 0.56 (P = 0.031); adjusted OR, 0.56 (P = 0.09)]
 - Overall mastectomy 43.0% versus 40.2%
[OR, 1.12 (P = 0.45); adjusted OR, 1.64 (P = 0.034)]

N Houssami et al. Ann Surg 2013; 257

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MRT Screening (Hoch-Risiko-Gruppe) Nutzen

- **Frühe Erkennung von Mammkarzinomen zusätzlich zur konventionellen Bildgebung**
- **Prognoseverbesserung?
(Mortalitätsreduktion? Reduktion der Intervallkarzinome?)**

MRT Screening bei Frauen mit hohem familiärem Risiko

Autor	Hochrisiko / Mutation	Anzahl Frauen	Anzahl Karzinome	MRT		Mammographie	
				Sensitivität (%)	Spezifität (%)	Sensitivität (%)	Spezifität (%)
Kriege 2004	M	1909	50	80	90	33	95
Warner 2004	M	236	22	77	95	36	99
Hagen 2004	M	491	25	86	-	50	-
Leach 2005	H / M	649	35	94	77	40	93
Riedl 2007	H / M	327	28	50	98	85,7	92
Kuhl 2010	H / M	687	27	93	98,4	33	99,1
Rijnsburger 2010	M	594	97	77,4	89,7	41	-
Sardanelli 2011	H / M	501	52	91	97	50	-
Passaperuma 2012	M	496	57	90	97	19	97
Gareth 2014	H / M	649	139	93	63	60	-

Prospective study results for MRI screening in women with high familiar risk (H) and mutation carriers (M)

- Chiarelli AM, Prummel MV, Muradali D et al. Effectiveness of Screening With Annual Magnetic Resonance Imaging and Mammography: Results of the Initial Screen From the Ontario High Risk Breast Screening Program. J Clin Oncol 2014; 32: 2224-22302
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MRT-Screening (Hoch-Risiko-Gruppe) Probleme

MRT zusätzlich zur Mammographie	RR
Abklärung benigner Läsionen	3,43–4,86
Biopsien mit benignem Befund	1,22–9,50
Operative Eingriffe benignen Befunde (MARIBS)	2
Falsch-negatives MRT (MRISC)	22%

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MRT und DCIS

Studie	Anzahl Untersuchungen	Zuverlässigkeit (%)	Sensitivität (%)	Spezifität (%)
Gilles et al 1996	172	70	95	51
Westerhof et al 1998	63	56	45	72
Bazzocchi et al 2006	112	80	79	68
Kuhl et al 2007	75	-	88	-
Baur et al. 2013	58		79,3	

„Ein negativer MRT-Befund kann nicht als Beweis für Gutartigkeit gewertet werden.“

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Guidelines Breast
Version 2018.1D

Prätherapeutisches Staging

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

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

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FORSCHEN
LEHREN
HEILEN

Statement: history and physical examination

1. GCP

Statement: high metastatic potential / symptoms

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