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Guidelines Breast  
Version 2022.1D

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# Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

## Früherkennung und Diagnostik



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## Früherkennung und Diagnostik

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▪ **Versionen 2005–2021:**  
**Albert / Blohmer / Fallenberg / Fersis / Gerber / Junkermann /  
Maass / Müller-Schimpfle / Scharl / Schreer**

▪ **Version 2022:**  
**Fallenberg / Wöckel**

### Screened data bases

Pubmed	2018 - 2021
Medline	2018 - 2021
Cochrane	2018 - 2021

### Guidelines

S3 Diagnostik, Therapie und Nachsorge des Mammakarzinoms:

1. Wöckel A, Festl J, Stüber T et al. Interdisciplinary Screening, Diagnosis, Therapy and Follow-up of Breast Cancer. Guideline of the DGGG and the DKG (S3-Level, AWMF Registry Number 032/045OL, December 2017) - Part 1 with Recommendations for the Screening, Diagnosis and Therapy of Breast Cancer. Geburtshilfe Frauenheilkd. 2018 Oct;78(10):927-948. doi: 10.1055/a-0646-4522. Epub 2018 Oct 19.
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Epub 2018 Nov 26.

European Commission Initiative on Breast Cancer (ECIBC)

European guidelines on breast cancer screening and diagnosis

<https://healthcare-quality.jrc.ec.europa.eu/european-breast-cancer-guidelines>

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 bei asymptomatischen Frauen durch Mammographie				
Alter	Intervall (Monate)	Oxford		AGO
		LOE	GR	
< 40	na	-	-	--
40-44	na	1b	B	-
45-49	24-36	1a	B	+ <sup>#</sup>
50-69*	24	1a	A	++
70-74	24	1a	A	+ <sup>#</sup>
> 75**	24	4	C	+/- <sup>#</sup>

\* Nationales Mammographie-Screening-Programm  
 \*\* Abhängig von Gesundheitszustand + Lebenserwartung mehr als 10 Jahre  
 # Cave: rechtfertigende Indikation ist notwendig

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<http://www.cancer.org/acs/groups/content/documents/document/acspc-046315.pdf>. Zugriff am 11.August 2016
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3. ([https://healthcare-quality.jrc.ec.europa.eu/sites/default/files/Guidelines/EtDs/ECIBC\\_GLS\\_EtD\\_screening\\_40-44.pdf](https://healthcare-quality.jrc.ec.europa.eu/sites/default/files/Guidelines/EtDs/ECIBC_GLS_EtD_screening_40-44.pdf))
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Früherkennung bei asymptomatischen Frauen Tomosynthese			
	Oxford		
	LOE	GR	AGO
<b>Digitale Tomosynthese (DBT ± SM)*</b>	<b>1a</b>	<b>B</b>	<b>+</b>
<b>Ersatz der DM durch synthetische MG + DBT**</b>	<b>1a</b>	<b>B</b>	<b>++</b>

Es muss immer auch der komplette Datensatz der Tomosyntheseschichten zur Beurteilung zur Verfügung stehen, die alleinige synthetische Mammographie ist nicht ausreichend.

\* Sign. höhere Sensitivität, heterogene Spezifität und höhere Kosten [Gerät, Befunder, Archivierung] der digitalen Brust-Tomosynthese (DBT) im Vgl. zur digitalen Mammographie (DM)  
Dosisreduktion durch Berechnung einer synthetischen Mammographie (SM) statt DM

\*\* Evaluation für D in randomisierter prospektiver Studie (TOSYMA)

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Brustkrebs Mortalitätsreduktion	
Metaanalysen	RR 95% CI
<b>Independent UK Panel, 2012</b> 13-year metaanalysis	0.80 (0.73–0.89)
<b>Cochrane Review, 2011</b> 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)
<b>Canadian Task Force, 2011</b> Women aged 50–69 years	0.79 (0.68–0.90)
<b>Duffy et al, 2012</b> Review of all trials and age groups	0.79 (0.73–0.86)
<b>Duffy et al, 2020</b> Review of 549,091 Women (30% eligible Swedish screening population)	0.59 (0.51–0.68) mortality 0.75 (0.66–0.84) advanced BC

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Brustkrebs Mortalitätsreduktion		
Metaanalysen		RR 95% CI
<b>Case-Control Studies</b>		
Broeders et al	Screening Mx Corr. for self selection Invited for screening	0.46 (0.4 – 0.54) 0.52 (0.42–0.65) 0.69 (0.57–0.83)
<b>Incidence-based Mortality Studies</b>		
Broeders et al	Screening Mx Invited to screening	0.62 (0.56–0.69) 0.75 (0.69–0.81)
<b>Randomized Clinical Trials</b>		
Gotsche and Jorgenson	Screening Mx	0.81 (0.74–0.87)
<b>ECIBC</b>		
	Screening MX	
	45-49	0.88 (0.76 - 1.02)
	50-69	0.77 (0.66 - 0.90)
	70-75	0.77 (0.54 - 1.09)

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## Brustkrebsinzidenz und Mortalität

- Annual incidence of breast cancer and mortality in the EU (GLOBOCAN 2012)

Age	Incidence / 1000	Mortality / 1000
40 to 44	1.2	0.1
45 to 49	1.7	0.2
50 to 69	2.7	0.5
70 to 74	3.0	0.8

From: <http://gco.iarc.fr/>

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# 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 (CI 95 %)	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

Früherkennung (normales Risiko) Sonographie / MRT			
	Oxford		
	LoE	GR	AGO
■ Screening-Mammasonographie alleine	5	D	--
■ Autom. 3D-Sonographie	3a	C	--
■ Mammasonographie als Ergänzung bei:			
• Dichtem Parenchym (inhomogen dicht, extrem dicht)	2a	B	++
• Erhöhtem Risiko	1b	C	++
• Mammographischer Läsion	2b	B	++
• Zur Abklärung susp. Läsionen im MRT	2b	C	++
■ MRT bei neg. MG und extrem dichter Brust* 50-75 LJ	1b	B	+

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\* Definition von extrem dicht entspricht BIRADS-Dichtekategorie D inhomogen dicht Kategorie C nach ACR BI-RADS-Atlas 5. ed. 2013

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Früherkennung			
Klinische Untersuchung (clinical breast examination; CBE)			
	Oxford		
	LoE	GR	AGO
<b>Als alleinige Untersuchung</b>			
▪ Selbstuntersuchung (BSE)	1a	A	-*
▪ Klinische Brust-Untersuchung (CBE) (außerhalb der Krebsfrüherkennungsuntersuchung (KFU))	1a	C	-*
▪ Klinische Brust-Untersuchung (CBE) (im Rahmen der KFU)	1a	B	++
▪ Medizinisch-taktile Untersuchung durch Blinde / Sehbehinderte	3b	C	-
CBE wegen klinisch- / mammo- / sonographischer Läsion	5	D	++
CBE in Kombination mit Bildgebung	1a	A	++

\* Kann Brust-Bewußtsein erhöhen

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Abklärung von Symptomen			
	Oxford		
	LoE	GR	AGO
■ Klinische Untersuchung	3b	B	++
■ Mammographie	1b	A	++
■ Tomosynthese***	2a	B	+
■ Kontrastmittel-mammographie (alleine oder zusätzlich)	2a	B	+
■ Sonographie	2b	B	++
■ Elastographie (Shear wave)*	2b	B	+
■ Automat. 3D-Sonographie	3b	B	+/-
■ Minimalinvasive Biopsie	1b	A	++
■ MRT**	3a	B	+

\* Zusatzuntersuchung  
 \*\* Wenn klinische, mammographische und sonographische Diagnostik inkl. Nadelbiopsie keine endgültige Diagnose erlauben.  
 \*\*\* Ersatz der DM durch synthetische Mammographie (SM)

#### 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.

#### 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
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### MRT

1. Mann RM, Loo CE, Wobbes T et al The impact of preoperative MRI on the re-excision rate in invasive lobular carcinoma of the breast. Breast Cancer Res Treat 2010; 119: 415-422
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3. Debal 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
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1. Luczynska, E., et al., Comparison of the Mammography, Contrast-Enhanced Spectral Mammography and

- Ultrasonography in a Group of 116 patients. *Anticancer Res*, 2016. 36(8): p. 4359-66.
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Prätherapeutische Mamma- und Axilladiagnostik			
	Oxford		
	LoE	GR	AGO
■ <b>Klinische Untersuchung</b>	5	D	++
■ <b>Mammographie</b>	2b	B	++
■ + Tomosynthese***	2b	B	+
■ Kontrastmittelmammographie (alleine oder zusätzlich)	2a	B	+
■ <b>Sonographie (Mamma/Axilla*)</b>	2b/2a*	B	++
■ <b>MRT*</b>	1b	B	+
■ <b>Minimalinvasive Biopsie Mamma** (CNB, VAB)</b>	1b	A	++
■ Axilla CNB, wenn auffälliger LK-Befund	2b	B	++
■ <b>Mamma-CT</b>	5	D	-
■ <b>PET für die Axilla</b>	2b	B	-

\* Möglichkeit der MRT-gestützten Biopsie (in domo oder im Rahmen einer Kooperation). MRT erwägen bei hohem familiärem Risiko, eingeschränkter Beurteilbarkeit in MG & US (Beurteilbarkeit C/D), invasiv lobulärem Karzinom. Keine Reduktion der Nachresektionsrate.  
 \*\* Histologische Sicherung von Zusatzbefunden im Fall therapeutischer Relevanz.  
 \*\*\* Ersatz der DM durch synthetische Mammographie (SM)

### 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.
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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.

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### Biopsie

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1. Luczynska, E., et al., Comparison of the Mammography, Contrast-Enhanced Spectral Mammography and Ultrasonography in a Group of 116 patients. *Anticancer Res*, 2016. 36(8): p. 4359-66.
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Sensitivitäten CESM (contrast enhanced spectral Mammography)						
Author	N	MG	CESM	MRI	US	Analyse
Dromain 2011	110	78	92			Per patient
Fallenberg 2014	118	77.9	94.7			Per patient
Mokhtar 2014	60	93.2	97.7			Per patient
Lobbes 2014*	113	96.9	100			Per patient
Perez 2015 ECR	98		78		66	Per lesion
Luczynska 2014	152	91	100			
Jochelson 2012	52	81 59	96 83	96 93		Per patient Per lesion
Fallenberg 2013	80	81	100	97		Per patient
Fallenberg 2016	155	81 55	94 72	95 76		Index Per Lesion
Lalji 2016*	199	93	96,9			Per patient 10 reader
Tennant 2016	100	84	95			
Luczynska 2016	116	90	100		92	
Xing 2019	235		91,5	91,5		Per lesion

CESM is comparable to MRI regarding index, a bit inferior for additional lesions

\* Recall from Screening

© AGO e. V.  
in der DGKG e.V.  
sowie  
in der DKG e.V.  
Guidelines Breast  
Version 2022.1D

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FORSCHEN  
LEBEN  
HELEN

#### CESM Originalarbeiten:

1. Luczynska, E., et al., Comparison of the Mammography, Contrast-Enhanced Spectral Mammography and Ultrasonography in a Group of 116 patients. Anticancer Res, 2016. 36(8): p. 4359-66.
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4. Fallenberg, E.M., et al., Contrast-enhanced spectral mammography vs. mammography and MRI - clinical performance in a multi-reader evaluation. Eur Radiol, 2017. 27(7): p. 2752-2764.
5. Jochelson, M.S., et al., Comparison of screening CEDM and MRI for women at increased risk for breast cancer: A pilot study. Eur J Radiol, 2017. 97: p. 37-43.
6. Xing D, Lv Y, Sun B, et al. Diagnostic Value of Contrast-Enhanced Spectral Mammography in Comparison to Magnetic Resonance Imaging in Breast Lesions. Journal of computer assisted tomography. 2019;43(2):245-51.

Prätherapeutisches Staging			
	Oxford		
	LoE	GR	AGO
■ Anamnese und klinische Untersuchung	5	D	++
<b>Nur bei hohem Risiko für Fernmetastasen und/oder Symptomen und/oder Indikation zur (neo-)adjuvanten Chemo- / Antikörpertherapie:</b>			
■ CT Thorax / Abdomen	2a	B	+
■ Skelettszintigraphie	2b	B	+
■ Röntgen-Thorax	5	C	+/-
■ Leberzonographie	5	D	+/-
■ Weiterführende Diagnostik je nach Befund (z. B. Leber-MRT / CEUS* / Biopsie etc.)	2a	B	+
■ FDG-PET oder FDG-PET-CT**	2b	B	+/-
■ Ganzkörper MRT	4	C	+/-

\* Contrast enhanced ultrasound  
\*\* vorzugsweise bei hohem Stadium (III), wenn verfügbar

#### 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.
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- 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.
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  17. Ulaner GA, Castillo R, Goldman DA, et al. <sup>18</sup>F-FDG-PET/CT for systemic staging of newly diagnosed triple-negative breast cancer. *Eur J Nucl Med Mol Imaging* 2016; 43:1937–1944
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<https://doi.org/10.1007/s00259-017-3745-x>
  26. <https://healthcare-quality.jrc.ec.europa.eu/european-breast-cancer-guidelines/staging-breast-cancer>