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Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Behandlungen in Abhängigkeit der Lokalisation der Metastasierung



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- **Versionen 2002–2021:**
 Albert / Bauerfeind / Bischoff / Böhme / Brunnert / Dall / Diel / Fehm /
 Fersis / Friedrich / Friedrichs / Gerber / Hanf / Janni / Kolberg-Liedtke /
 Kreipe / Loibl / Lück / Lux / Maass / Mundhenke / Oberhoff / Park-Simon
 / Rezai / Rody / Schaller / Schütz / Seegenschmiedt / Solomayer /
 Souchon / Thomssen

- **Version 2022:**
 Kolberg-Liedtke / Solbach

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Metastasenlokalisationen

- **Leber- und Lungenmetastasen**
- **Maligne Pleura- und Perikardergüsse**
- **Aszites**
- **Knochenmarkinfiltration (Verdrängungsmielopathie)**
- **Weichteilmetastasen**
- **Kontralaterale Axillametastase**

Siehe auch Kapitel „ZNS-Metastasen“ / „Lokoregionäres Rezidiv-Behandlungsoptionen bei nicht kurativen Fällen“



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Distribution of Breast Cancer Metastasis

Risk of breast cancer metastases

- is approx. 20%
- is dependent on molecular breast cancer subtype (i.e., lower in luminal A and higher in HER2-enriched and basal-like breast cancer)
- is decreasing due to more efficacious therapeutic regimens
- about 6% of new breast cancer diagnosis are stage IV and have an estimated 5-y OS rate of 27%

Pattern of breast cancer metastases

- Bone metastases are most common metastases (30-40%), followed by lung (20%) pleura (8%) and liver metastases (isolated liver metastases approx. 5%). Other locations are rare
- Breast cancer is the most common origin of cutaneous metastases and is considered to be the most prevalent primary tumor of all metastases to the orbit
- Metastatic pattern strongly depends on breast cancer molecular biology and efficacy of (targeted) therapy (i.e., compared with luminal A tumors, luminal/HER2 and HER2-enriched tumors are associated with a significantly higher rate of brain, liver, and lung metastases, while basal-like tumors show a higher rate of brain, lung, and distant nodal metastases but a significantly lower rate of liver and bone metastases)
- Pattern of breast cancer metastases is one of several factors determining disease prognosis

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Allgemeine Aspekte der Metastasentherapie			
	Oxford		
	LoE	GR	AGO
■ Histologischer / zytologischer Nachweis der Metastasierung	3	B	+
■ Bevorzugung systemischer Therapien	2a	B	++*
■ Metastasenresektion nur bei gutem Therapieansprechen der systemischen Therapie, Oligometastasierung	2b	C	+
■ Stereotaktische Radiotherapie bei Patientinnen mit Oligometastasierung	2a	B	+
■ Lokale Behandlung bei Schmerzen, Exulzeration, Ileus, persistierender(n) Metastase(n) nach Abschluss der Systemtherapie, Hydrocephalus occlusus, spinalem Kompressionssyndrom	5	D	+/-
■ Systemische Behandlung nach Chirurgie	2c	B	++

* Siehe auch Kapitel zur Systemtherapie in der metastasierten Situation

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Wording

Stereotactic Therapy can be referred to as:

SBRT

Stereotactic Body Radiation Therapy

SABR

Stereotactic Ablative Radiotherapy

IGRT

Image Guided Radiation Therapy

Histology

1. Kasraeian S, Allison DC, Ahlman ER et al. A comparison of fine-needle aspiration, core biopsy, and surgical biopsy in the diagnosis of extremity soft tissue masses. Clin Orthop Relat Res. 2010;468:2992-3002.

Local surgery

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Radiotherapy in oligometastatic breast cancer

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Combined surgery of the primary side and metastasis

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Lokale Therapie in der primär metastasierten Situation			
	Oxford		
	LoE	GR	AGO
Operation (R0) des Primärtumors (individuelles Vorgehen bei Oligometastasierung) <ul style="list-style-type: none"> Bei alleiniger ossärer Metastasierung Bei viszeralen Metastasen 	1b	B	+/-
Axillaoperation bei cN1	3b	B	+/-
Sentinellymphonodektomie bei cN0	5	D	-
Radiotherapie des Primärtumors <ul style="list-style-type: none"> Ohne Operation Nach brusterhaltender Operation oder nach Mastektomie (analog der adjuvanten Situation) 	3a 2c	C B	+/- +

Surgery of the primary tumor (R0)

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Axillary surgery

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Primary metastatic breast cancer - Locoregional therapy (local RT vs. surgery + RT vs. surgery)

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Randomized Phase III Trials ST +/- Surgery of the Primary Tumor					
Trial	n	Therapy prior to randomization	Local Control	Improved OS Primary Endpoint	QoL
ECOG 2108 * ^{1,2} (USA/Kanada) 2001-2016	256	4-8 months systemic therapy	yes	no	ns
Tata Memorial Hospital * ³ (India) 2005-2012	350	chemotherapy	yes	no	-
MF07-01 * ^{4,5,6,7} (Turkey) 2008-2012	278	no systemic therapy	no 10 y LRP: LRT 1% vs. 14% ST, s	10 y fu OS: LRT 19% vs. ST 5%, s (HR+, Her2-, < 55 y, solitary bone only metastasis)	ns
ABCSG-28#* ^{8,9} (Austria) 2010-2019	90	no systemic therapy	yes	no	ns
JCOG 1017 (Japan) 2011-2018	410	primary ST	Completed, results not reported so far		

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ns not significant, s: significant #trial terminated due to poor recruitment
ST = systemic therapy, LRT= locoregional therapy, LRP = locoregional progression

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2. Kahn SA. Educational Session SABCS 2021, Thursday 9th Dec; Session: Local Therapy of the Primary and Beyond in Patients with Advanced Disease, Presentation: Local therapy of the primary tumor in de novo Stage IV breast cancer.
3. Badwe R, Hawaldar R, Nair N et al. Locoregional treatment versus no treatment of the primary tumour in metastatic breast cancer: an open-label randomised controlled trial. Lancet 2015 Oct;16(13):1380-8.
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Prospective Registry Study (Bone only)

Trial	n	Randomization	Local Control	Improved OS Primary Endpoint	QoL
BOMET MF 14-01# 2014-	505	ST vs. LRT (LRT+ST vs. ST+LRT)	yes	3y fu: improved OS in the LRT group (HR 0.40) HR+, Her2-; Her2+ subgroups, no benefit in triple neg. patients	-

ST = systemic therapy, LRT = locoregional therapy,

1. Soran A, Dogan L, Isik A et al. The Effect of Primary Surgery in Patients with De Novo Stage IV Breast Cancer with Bone Metastasis Only (Protocol BOMET MF 14-01): A Multi-Center, Prospective Registry Study. Ann Surg Oncol. 2021;28(9):5048-5057.

Diagnostics

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Overview

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Local surgery

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Statement: Regional chemotherapy

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Statement: Regional radiotherapy

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Statement: Thermoablation

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Lungenmetastasen Lokale Therapie			
	Oxford		
	LoE	GR	AGO
<p>■ Vor einer lokalen Therapie histologische Sicherung der Metastasierung bei therapeutischer Konsequenz Staging und Biopsie (CT-gesteuert/e FNA / CNB o. transbronchiale FNA, EBUS, VATS)</p> <p>■ Resektion mittels VATS* oder konventionell</p> <ul style="list-style-type: none"> ■ multilokulärer Metastasen ■ Solitärer / weniger unilateraler Metastasen mit kurativer Intention <p>■ Thermoablation (CT-gesteuert RFA, LITT)</p> <p>■ Regionale Radiotherapie (stereotaktische Radiotherapie mittels SRS-VMAT)</p>	3a	B	+
	3a	B	-
	3a	B	+/-
	3b	C	+/-
	2a	B	+/-

* VATS = video-assistierte Thorakoskopie

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Overview

1. Lin S, Mo H, Li Y et al. Clinicopathological characteristics and survival outcomes in patients with synchronous lung metastases upon initial metastatic breast cancer diagnosis in Han population. BMC Cancer. 2021 Dec 14;21(1):1330.

Resection of pulmonary metastases by VATS or conventional resection

1. García-Yuste M, Pulmonary metastasectomy in breast cancer. J Thorac Oncol. 2010 Jun;5(6 Suppl 2):S170-1.
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Statement: Thermoablation (CT-guided RFA, LITT)

1. Vogl TJ, et al: Microwave ablation therapy: clinical utility in treatment of pulmonary metastases. Radiology. 2011 Nov;261(2):643-51.
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Statement: Regional Radiotherapy

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Maligner Pleuraerguss Lokale Therapie			
	Oxford		
	LoE	GR	AGO
▪ Wenn die erwartete Lebenszeit kurz ist, sollten weniger invasive Prozeduren in Betracht gezogen werden	4	C	++
▪ VATS und Talkum-Pleurodese*	1b	B	++
▪ Kontinuierliche Pleuradrainage	2a	B	++
▪ Medikamentöse Pleurodese*			
▪ Talkumpulver	1a	B	+
▪ Bleomycin, Doxycyclin, Mitoxantron	2b	C	+/-
▪ Povidon-Jodid (20 ml 10 % Lösung)	1b	B	+
▪ Systemtherapie nach Pleurodese	3b	C	+/-
▪ Wiederholte Pleurapunktionen	4	C	+/-

* Adäquate Schmerztherapie
VATS = video-assistierte Thorakoskopie

If expected survival is short, less invasive procedures should be considered

1. Zamboni MM, da Silva CT Jr, Baretta R et al. Important prognostic factors for survival in patients with malignant pleural effusion. BMC Pulm Med. 2015 Mar 28;15:29.

VATS and Talcum-pleurodesis

Chemical pleurodesis

Talcum powder

Bleomycin, Doxycycline, Mitoxantrone

Povidone-iodine (20 ml of 10% solution)

Serial thoracocentesis

1. Hirata T et al: Efficacy of pleurodesis for malignant pleural effusions in breast cancer patients. Eur Respir J. 2011 Dec;38(6):1425-30
2. Mohsen TA et al: Local iodine pleurodesis versus thoracoscopic talc insufflation in recurrent malignant pleural effusion: a prospective randomized control trial. Eur J Cardiothorac Surg. 2011 Aug;40(2):282-6.
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11. Dipper A, Jones HE, Bhatnagar R, et al. Interventions for the management of malignant pleural effusions: an updated network meta-analysis. Eur Respir Rev 2021; 30: 210025.

Statement: Continuous pleural drainage

1. Cases E, et al: Use of indwelling pleural catheter in the outpatient management of recurrent malignant pleural effusion Arch Bronconeumol. 2009 Dec;45(12):591-6.
2. Demmy TL, Gu L, Burkhalter JE et al. Cancer and Leukemia Group B. Optimal management of malignant pleural effusions (results of CALGB 30102). J Natl Compr Canc Netw. 2012 Aug;10(8):975-82.
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Maligner Aszites Lokale Therapie			
	Oxford		
	LoE	GR	AGO
Aszites:			
▪ Punktion, Drainage bei Symptomen	4	D	++
▪ Kontinuierliche Drainage bei persistierendem Aszites	3b	D	+
▪ Systemische Therapie	3b	D	++
▪ Lokale Chemotherapie	3b	D	+/-

1. Saâda E, et al: Pathogenesis and management of refractory malignant ascites. Bull Cancer. 2011 Jun;98(6):679-87.
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3. Petrelli F, Borgonovo K, Lonati V et al.: Regression of liver metastases after treatment with intraperitoneal catumaxomab for malignant ascites due to breast cancer. Target Oncol. 2013 Dec;8(4):291-4.
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6. Lew M, Cantley R, Heider A et al. Diagnosis and categorization of malignant effusions: A 6-year review from a single academic institution. Diagn Cytopathol. 2021 May;49(5):615-621.

Maligner Perikarderguss Lokale Therapie			
	Oxford		
	LoE	GR	AGO
Symptomatischer Perikarderguss			
▪ Drainage, chirurgische Fensterung des Perikards	3b	B	++
▪ Kombination mit optimierter systemischer Therapie	4	C	++
▪ Video-assistierte Thoraxchirurgie (VATS)	4	C	+
▪ Ultraschall geführte Punktion und Instillation von zytotoxischen / zielgerichteten Substanzen			
▪ Bleomycin, Carboplatin, Cisplatin, Mitomycin C, Mitoxantron, Bevacizumab	4	C	+/-

1. Pokieser W, Cassik P, Fischer G et al. Malignant pleural and pericardial effusion in invasive breast cancer: impact of the site of the primary tumor. Breast Cancer Res Treat. 2004 Jan;83(2):139-42.
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3. Jeon HW, Cho DG, Park JK et al. Prognostic factors affecting survival of patients with cancer-related pericardial effusion managed by surgery. World J Surg Oncol. 2014 Aug 5;12:249.
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Verdrängungsmyelopathie / Knochenmarksinfiltration (mit Panzytopenie)			
	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> Wöchentliche Chemotherapie*: <ul style="list-style-type: none"> Epirubicin, Doxorubicin, Paclitaxel Capecitabin HER2 pos.: <ul style="list-style-type: none"> zusätzlich anti-HER2 Therapie Hormonzeptor-positiv: <ul style="list-style-type: none"> endokrin-basierte Therapie 	4	D	++
	4	D	++
	5	D	++
	4	C	+

* Beachte Vorbehandlung

1. Kopp HG, et al: Symptomatic bone marrow involvement in breast cancer-clinical presentation, treatment, and prognosis: a single institution review of 22 cases. Anticancer Res. 2011 Nov;31(11):4025-30.
2. Freyer G, et al: Palliative hormone therapy, low-dose chemotherapy, and bisphosphonate in breast cancer patients with bone marrow involvement and pancytopenia: report of a pilot experience. Eur J Intern Med. 2000 Dec 20;11(6):329-333.
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Weichteilmetastasen Lokale Therapie			
	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> ■ R0-Resektion (bei lokoregionär limitierten Metastasen (Haut, Muskel, Lymphknoten) nach Ausschluss weiterer Fernmetastasen) 	4	C	+
<ul style="list-style-type: none"> ■ Bestrahlung (postoperativ oder primär) (Ausnahme: unmittelbare Indikation zur Operation) bei: <ul style="list-style-type: none"> ■ Weichteilmetastasen ■ Rückenmarkskompression, Parese ■ Plexusinfiltration 	3b 2b 3b	C C C	+ ++ ++




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1. Wilson B, et al: Resolution of extensive leptomeningeal metastasis and clinical spinal cord compression from breast cancer using weekly docetaxel chemotherapy. Breast Cancer Res Treat. 2012 Jan;131(1):343-6. Epub 2011 Oct 26.
2. Tancioni F et al: Surgery followed by radiotherapy for the treatment of metastatic epidural spinal cord compression from breast cancer. Spine (Phila Pa 1976). 2011 Sep 15;36(20):E1352-9.
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Oligometastasierung: Kontralaterale Axillametastase

“OLIGO-METASTATIC DISEASE in CONTRALATERAL AXILLA Contralateral axillary nodal metastasis (in the absence of contralateral primary) as initial diagnosis of recurrent disease is considered stage 4 metastatic breast cancer.

However, after prior local therapy to ipsilateral axilla for early breast cancer, subsequent metachronous contralateral axillary nodal metastasis, either alone or concurrent with an in-breast ipsilateral recurrence, could be considered and treated as a regional metastasis (due to altered lymphatic drainage), and has the potential for long survival or cure with a multidisciplinary approach”

ABC6 2021: LoE: Expert opinion/NA (85%)

1. Magnoni F, Colleoni M, Mattar D et al. Contralateral Axillary Lymph Node Metastases from Breast Carcinoma: Is it Time to Review TNM Cancer Staging? Ann Surg Oncol. 2020 Oct;27(11):4488-4499.
2. Díaz-Roldán J, Eguía-Larrea M, Rubio-Sánchez T et al. Systematic review of synchronous contralateral axillary metastases in breast cancer: really M1 disease? Breast Cancer. 2021 Oct 15. doi: 10.1007/s12282-021-01293-2. Online ahead of print. Review.
3. Nash AL, Thomas SM, Plichta JK et al. Contralateral Axillary Nodal Metastases: Stage IV Disease or a Manifestation of Progressive Locally Advanced Breast Cancer? Ann Surg Oncol. 2021 Oct;28(10):5544-5552.
4. SABCS 2021 Educational Session Local Therapy of the Primary and Beyond in Patients with Advanced Disease