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Guidelines Breast
Version 2023.1D

FORSCHEN
LEHREN
HEILEN

Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Behandlungen in Abhängigkeit der Lokalisation der Metastasierung

Behandlungen in Abhängigkeit der Lokalisation der Metastasierung

■ Versionen 2002–2022:

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 / Solbach / Solomayer / Souchon / Thomssen

■ Version 2023:

Lüftner / Solomayer

1. Cardoso F, Paluch-Shimon S, Senkus E et al. 5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5). Ann Oncol. 2020 Dec;31(12):1623-1649.



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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“

Allgemeine Aspekte der Metastasentherapie

	Oxford		
	LoE	GR	AGO
▪ Histologischer Nachweis der Metastasierung	3	B	++
▪ Zytologischer Nachweis der Metastasierung, wenn histologischer Nachweis nicht möglich	3	B	+
▪ Bevorzugung systemischer Therapien	2a	B	++*
▪ Metastasenresektion bei gutem Therapieansprechen der systemischen Therapie, Oligometastasierung	2b	C	+/-
▪ Stereotaktische Radiotherapie bei Patientinnen mit Oligometastasierung	2b	B	+/-
▪ Lokal-interventionelle ablative Maßnahmen	3b	C	+/-
▪ 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

Wording

Sterotactic 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

1. Warschkow R, Güller U, Tarantino I et al. Improved Survival After Primary Tumor Surgery in Metastatic Breast Cancer: A Propensity-adjusted, Population-based SEER Trend Analysis. Ann Surg. 2016 Jun;263(6):1188-98.

2. Yoo TK, Chae BJ, Kim SJ et al. Identifying long-term survivors among metastatic breast cancer patients undergoing primary tumor surgery. *Breast Cancer Res Treat.* 2017 Aug;165(1):109-118
3. Barinoff J, Schmidt M, Schneeweiss A et al.: Primary metastatic breast cancer in the era of targeted therapy - Prognostic impact and the role of breast tumour surgery. *Eur J Cancer.* 2017 Sep;83:116-124.
4. Lane WO, Thomas SM, Blitzblau RC et al. Surgical Resection of the Primary Tumor in Women With De Novo Stage IV Breast Cancer: Contemporary Practice Patterns and Survival Analysis. *Ann Surg.* 2019 March ; 269(3): 537–544.
5. Poggio F, Lambertini M, de Azambuja E. Controversies in Oncology: Surgery of the primary tumour in patients presenting with de novo metastatic breast cancer: to do or not to do? *ESMO Open* 2018;3:e000324. doi:10.1136/esmoopen-2018-000324
6. 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
7. Soran A, Ozmen V, Ozbas S et al. Randomized Trial Comparing Resection of Primary Tumor with No Surgery in Stage IV Breast Cancer at Presentation: Protocol MF07-01. *Ann Surg Oncol.* 2018 Oct;25(11):3141-3149.
8. Fitzal F, Bjelic-Radisic V, Knauer M et al. Impact of Breast Surgery in Primary Metastasized Breast Cancer: Outcomes of the Prospective Randomized Phase III ABCSG-28 POSYTIME Trial *Ann Surg.* 2019 Jun;269(6):1163-1169.
9. Khan SA Plenary Session ASCO 2020 Late Breaking Abstract 2
10. Lopez-Tarruella S, Escudero MJ, Pollan M et al. Survival impact of primary tumor resection in de novo metastatic breast cancer patients (GEICAM/El Alamo Registry). *Sci Rep.* 2019 Dec 27;9(1):20081.
11. Amabile MI, Frusone F, De Luca A et al. Locoregional Surgery in Metastatic Breast Cancer: Do Concomitant Metabolic Aspects Have a Role on the Management and Prognosis in this Setting? *J Pers Med.* 2020 Nov 13;10(4):227.
12. Soran A, Ozmen V, Ozbas S et al. MF07-01 Study Group. Primary Surgery with Systemic Therapy in Patients with de Novo Stage IV Breast Cancer: 10-year Follow-up; Protocol MF07-01 Randomized Clinical Trial. *J Am Coll Surg.* 2021 Dec;233(6):742-751.
13. Stahl K, Wong W, Dodge D et al. Benefits of Surgical Treatment of Stage IV Breast Cancer for Patients With Known Hormone Receptor and HER2 Status. *Ann Surg Oncol.* 2021 May;28(5):2646-2658.
14. Chen YQ, Xu JW, Xu XF et al. Predicting the survival benefit of local surgery in patients aged 70 years or older with stage IV breast cancer: A population-based analysis. *Breast.* 2021 Oct;59:124-134.

[Radiotherapy in oligometastatic breast cancer](#)

1. Trovo M, Furlan C, Polesel J et al.: Radical radiation therapy for oligometastatic breast cancer: Results of a prospective phase II trial. *Radiother Oncol.* 2018 Jan;126(1):177-180.
2. Thelen WSME, Peulen HMU, Lalezari F et al. Effect of pembrolizumab after stereotactic body radiotherapy vs pembrolizumab alone on tumor response in patients with advanced non—small cell lung cancer: results of the PEMBRO-RT phase 2 randomized clinical trial. *JAMA Oncol* 2019; 5:1276–1282
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4. Palma DA, Olson R, Harrow S et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. *Lancet.* 2019 May 18;393(10185):2051-2058.
5. Olson R, Mathews L, Liu M et al. Stereotactic ablative radiotherapy for the comprehensive treatment of 1-3 Oligometastatic tumors (SABR-COMET-3): study protocol for a randomized phase III trial. *BMC Cancer* 2020 May 5;20(1):380
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7. Dunst J. [Curative radiotherapy of oligometastatic cancer: long-term results of the SABR-COMET phase II trial]. *Strahlenther Onkol.* 2021 Apr;197(4):365-367.
8. Wijetunga NA, Dos Anjos CH, Zhi WI et al. Long-term disease control and survival observed after stereotactic ablative body radiotherapy for oligometastatic breast cancer. *Cancer Med.* 2021 Aug;10(15):5163-5174.
9. Chmura S, Winter KA, Robinson C et al. Evaluation of Safety of Stereotactic Body Radiotherapy for the Treatment of Patients With Multiple Metastases: Findings From the NRG-BR001 Phase 1 Trial. *JAMA Oncol.* 2021 Jun 1;7(6):845-852.
10. Sogono P, Bressel M, David S et al. Safety, Efficacy, and Patterns of Failure After Single-Fraction Stereotactic Body Radiation Therapy (SBRT) for Oligometastases. *Int J Radiat Oncol Biol Phys.* 2021 Mar 1;109(3):756-763.
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Overviews

1. Bale R, Putzer D, Schullian P. Local Treatment of Breast Cancer Liver Metastasis. *Cancers (Basel).* 2019 Sep; 11(9): 1341.
2. Caswell-Jin JL, Plevritis SK, Tian L, et al. Change in survival in metastatic breast cancer with treatment advances: meta-analysis and

systematic review. 2018. <https://doi.org/10.1093/jncics/pky062>.

3. Cardoso F, Paluch-Shimon S, Senkus E et al. 5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5). *Ann Oncol*. 2020 Dec;31(12):1623-1649.
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8. 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.

Combined surgery of the primary side and metastasis

1. Bilani N, Yaghi M, Singh Jabbar I et al. Survival benefit of a combined surgical approach in patients with metastatic breast cancer. *J Surg Oncol*. 2021 Dec;124(8):1235-1241.
2. Bilani N, Elson L, Liang H et al. Effect of Surgery at Primary and Metastatic Sites in Patients With Stage IV Breast Cancer. *Clin Breast Cancer*. 2021 Jun;21(3):170-180.

Lokale Therapie in der primär metastasierten Situation

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

Surgery of the primary tumor (R0)

- Xiao W, Zou Y, Zheng S et al. Primary tumor resection in stage IV breast cancer: A systematic review and meta-analysis. Eur J Surg Oncol. 2018 Oct;44(10):1504-1512.
- Tosello G, Torloni MR, Mota BS et al. Breast surgery for metastatic breast cancer. Cochrane Database Syst Rev. 2018 Mar 15;3:CD011276. doi: 10.1002/14651
- Soran A, Ozmen V, Ozbas S et al. Randomized Trial Comparing Resection of Primary Tumor with No Surgery in Stage IV Breast Cancer at Presentation: Protocol MF07-01. Ann Surg Oncol. 2018 Oct;25(11):3141-3149.
- Fitzal F, Bjelic-Radisic V, Knauer M et al. Impact of Breast Surgery in Primary Metastasized Breast Cancer: Outcomes of the Prospective Randomized Phase III ABCSG-28 POSITIVE Trial Ann Surg. 2019 Jun;269(6):1163-1169.
- Khan SA Plenary Session ASCO 2020 Late Breaking Abstract 2
- Lopez-Tarruella S, Escudero MJ, Pollan M et al. Survival impact of primary tumor resection in de novo metastatic breast cancer patients (GEICAM/El Alamo Registry). Sci Rep. 2019 Dec 27;9(1):20081.
- Amabile MI, Frusone F, De Luca A, et al. Locoregional Surgery in Metastatic Breast Cancer: Do Concomitant Metabolic Aspects Have a Role on the Management and Prognosis in this Setting? J Pers Med. 2020 Nov 13;10(4):227.
- 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.


9. Peng P, Chen JY, Han YT et al. Impact of surgery on survival in breast cancer with bone metastases only: a SEER database retrospective analysis. BMC Surg. 2021 Oct 26;21(1):378.

Axillary surgery

1. Bitencourt A, Rossi Saccarelli C, Morris EA et al. Regional Lymph Node Involvement Among Patients With De Novo Metastatic Breast Cancer. JAMA Netw Open. 2020 Oct 1;3(10):e2018790.
2. De Wit A, Arbion F, Desille-Gbaguidi H et al. Role of surgery in patients with synchronous metastatic breast cancer: Is there a need for axillary lymph node removal? J Gynecol Obstet Hum Reprod. 2021 Apr;50(4):101771.

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

1. Choi SH, Kim JW, Choi J et al. Locoregional Treatment of the Primary Tumor in Patients With De Novo Stage IV Breast Cancer: A Radiation Oncologist's Perspective . Clin Breast Cancer. 2018 Apr;18(2):e167-e178.
2. Pons-Tostivint E, Kirova Y, Lusque A. Survival Impact of Locoregional Treatment of the Primary Tumor in De Novo Metastatic Breast Cancers in a Large Multicentric Cohort Study: A Propensity Score-Matched Analysis. Ann Surg Oncol. 2019 Feb;26(2):356-365.
3. Wang W, Liu J, Wang J et al. Impact of Locoregional Treatment on Prognosis of de novo Stage IV Breast Cancer: A Retrospective Long-Term Study of Chinese Population. Gynecol Obstet Invest. 2019;84(3):248-258.
4. Bourgier C, Khodari WA, Vataire AL et al. Breast radiotherapy as part of loco-regional treatments in stage IV breast cancer patients with oligometastatic disease. Radiother Oncol. 2010 Aug;96(2):199-203
5. Stahl K, Wong W, Dodge D et al. Benefits of Surgical Treatment of Stage IV Breast Cancer for Patients With Known Hormone Receptor and HER2 Status. Ann Surg Oncol. 2021 May;28(5):2646-2658.
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<div>  <h2>Randomized Phase III Trials ST +/- Surgery of the Primary Tumor</h2> </div>					
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

1. Khan SA Plenary Session ASCO 2020 Late Breaking Abstract 2
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.
4. Soran A, Ozmen V, Ozbas S et al. Randomized Trial Comparing Resection of Primary Tumor with No Surgery in Stage IV Breast Cancer at Presentation: Protocol MF07-01. Ann Surg Oncol. 2018 Oct;25(11):3141-3149.
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6. 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.
7. Soran A, Soyder A, Ozbas S et al. The role of loco-regional treatment in long-term quality of life in de novo stage IV breast cancer patients: protocol MF07-01Q. Support Care Cancer. 2021 Jul;29(7):3823-3830.
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9. Bjelic-Radisic V, Fitzal F, Knauer M, ABCSG. Primary surgery versus no surgery in synchronous metastatic breast cancer: patient-

reported quality-of-life outcomes of the prospective randomized multicenter ABCSG-28 Positive Trial. BMC Cancer. 2020 May 6;20(1):392.



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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.

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> Resektion (R0) <ul style="list-style-type: none"> HR positiv: Chemotherapie-sensibel, langes DFS, keine extrahepatischen Metastasen, ≤ 3 Metastasen HER2 positiv: Alter < 50 Jahre, Metastase < 5 cm, keine weiteren Metastasen 	3a	B	+/-
<ul style="list-style-type: none"> Interventionelle regionale Chemotherapie (TACE)* 	3b	C	+/-
<ul style="list-style-type: none"> Interventionelle regionale Radiotherapie (SIRT / TARE)* 	3b	C	+/-
<ul style="list-style-type: none"> Stereotaktische Radiotherapie mittels SRS-VMAT, andere Bestrahlungsverfahren* 	2a	B	+/-
<ul style="list-style-type: none"> Regionale ablative Verfahren Thermoablation (RFA, MWA) <ul style="list-style-type: none"> IRE, LITT, and HIFU Kryoablation 	3b 5 3b	C D C	+/- - -

* Interdisziplinäre Indikationsstellung

CA = cryoablation
HIFU = high-intensity focused ultrasound
IRE = irreversible electroporation
LITT = laser-induced interstitial thermotherapy
MWA = microwave ablation
RFA = radiofrequency ablation
SIRT = selective internal radiotherapy = TARE
SRS = stereotactic radiosurgery with volumetric modulated arc therapy (VMAT)
TACE = transarterial chemoembolization
TARE = transarterial radioembolization

Statements:

Resection of liver metastasis (R0)
 HR positive: chemotherapy sensible, long disease-free interval, absence of extrahepatic disease, ≤ 3 metastases
 Her2 positive: age < 50 y., metastasis < 5 cm, no further metastases

Diagnostics

1. van Dam PJ, van der Stok EP, Teuwen LA et al. International consensus guidelines for scoring the histopathological growth patterns of liver metastasis. Br J Cancer. 2017 Nov 7;117(10):1427-1441.

Overview

1. Bale R, Putzer D, Schullian P. Local Treatment of Breast Cancer Liver Metastasis. Cancers (Basel). 2019 Sep; 11(9): 1341.
2. Kent CL, McDuff SGR, Salama JK. Oligometastatic breast cancer: where are we now and where are we headed?-a narrative review. Ann Palliat Med. 2020 Sep 10;apm-20-1128.
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5. Bilani N, Yaghi M, Main O et al. Metastasectomy versus radiation of secondary sites in stage IV breast cancer: Analysis from a national cancer registry. Breast. 2021 Dec;60:185-191.

Local surgery

1. Golse N, Adam R. Liver Metastases From Breast Cancer: What Role for Surgery? Indications and Results. Clin Breast Cancer. 2017 Jul;17(4):256-265
2. Yoo TG, Cranshaw I, Broom R et al. Systematic review of early and long-term outcome of liver resection for metastatic breast cancer: Is there a survival benefit? Breast. 2017 Apr;32:162-172
3. Labgaa I, Slankamenac K, Schadde E et al. Liver resection for metastases not of colorectal, neuroendocrine, sarcomatous, or ovarian (NCNSO) origin: A multicentric study. Am J Surg. 2018 Jan;215(1):125-130.
4. Wen J, Ye F, Xie F, Liu D et al. The role of surgical intervention for isolated breast cancer liver metastasis: Results of case-control study with comparison to medical treatment. Cancer Med. 2020 Jul;9(13):4656-4666.
5. Franzese C, Comito T, Viganò L et al. Liver Metastases-directed Therapy in the Management of Oligometastatic Breast Cancer. Clin Breast Cancer. 2020 Dec;20(6):480-486.
6. Chun YS, Mizuno T, Cloyd JM et al. Hepatic resection for breast cancer liver metastases: Impact of intrinsic subtypes. Eur J Surg Oncol 2020; 46: 1588-1595.
7. Xiong Y, Shi X, Hu Q et al. A Nomogram for Predicting Survival in Patients With Breast Cancer Liver Metastasis: A Population-Based Study. Front Oncol. 2021 Jun 2;11:600768.

Statement: Regional chemotherapy

1. Liberchuk AN, Deipolyi AR. Hepatic Metastasis from Breast Cancer. *Semin Intervent Radiol* 2020; 37(5): 518-526.
2. Duan XF, Dong NN, Zhang T et al. Treatment outcome of patients with liver-only metastases from breast cancer after mastectomy: a retrospective analysis. *J Cancer Res Clin Oncol* 2011; 137: 1363-1370.
3. Vogl TJ, Nour-Eldin NA, Hammerstingl RM et al. Microwave Ablation (MWA): Basics, Technique and Results in Primary and Metastatic Liver Neoplasms – Review Article. *Rofo* 2017; 189: 1055-1066.
4. Lin YT, Médioni J, Amouyal G et al. Doxorubicin-Loaded 70-150 μ m Microspheres for Liver-Dominant Metastatic Breast Cancer: Results and Outcomes of a Pilot Study. *Cardiovasc Intervent Radiol* 2017; 40: 81-89.
5. Aarts BM, Muñoz FMG, Wildiers H et al. Intra-Arterial Therapies for Liver Metastatic Breast Cancer: A Systematic Review and Meta-Analysis. *Cardiovasc Intervent Radiol*. 2021 Dec;44(12):1868-1882

Statement: Regional radiotherapy

1. Chang J, Charalel R, Noda C et al. Liverdominant Breast Cancer Metastasis: A Comparative Outcomes Study of Chemoembolization Versus Radioembolization. *Anticancer Res* 2018; 38: 3063-3068.
2. Trovo M, Furlan C, Polesel J et al. Radical radiation therapy for oligometastatic breast cancer: Results of a prospective phase II trial. *Radiother Oncol*. 2018 Jan;126(1):177-180.
3. Onal, C.; Guler, O.C.; Yildirim, B.A. Treatment outcomes of breast cancer liver metastasis treated with stereotactic body radiotherapy. *Breast* 2018, 42, 150–156.
4. Mahadevan, A.; Blanck, O.; Lanciano, R et al. Stereotactic Body Radiotherapy (SBRT) for liver metastasis-clinical outcomes from the international multi-institutional RSSearch(R) Patient Registry. *Radiat. Oncol*. 2018, 13, 26.
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6. Franzese C, Comito T, Viganò L et al. Liver Metastases-directed Therapy in the Management of Oligometastatic Breast Cancer. *Clin Breast Cancer*. 2020 Dec;20(6):480-486.
7. Ridouani F, Soliman MM, England RW et al. Relationship of radiation dose to efficacy of radioembolization of liver metastasis from breast cancer. *Eur J Radiol*. 2021 Mar;136:109539.
8. Helmberger T, Golfieri R, Pech M et al. On behalf of the CIRT Steering Committee; On behalf of the CIRT Principal Investigators. Clinical Application of Trans-Arterial Radioembolization in Hepatic Malignancies in Europe: First Results from the Prospective

- Multicentre Observational Study CIRSE Registry for SIR-Spheres Therapy (CIRT). Cardiovasc Intervent Radiol. 2021 Jan;44(1):21-35.
9. Schatka I, Tschernig M, Rogasch JMM et al. Selective Internal Radiation Therapy in Breast Cancer Liver Metastases: Outcome Assessment Applying a Prognostic Score. Cancers (Basel). 2021 Jul 27;13(15):3777.
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Statement: Thermoablation

1. Xiao YB, Zhang B, Wi YI. Radiofrequency ablation versus hepatic resection for breast cancer liver metastasis: a systematic review and meta-analysis J Zhejiang Univ-Sci B (Biomed & Biotechnol) 2018 19(11):829-843
2. Bale R, Richter M, Dünser M et al. Stereotactic Radiofrequency Ablation for Breast Cancer Liver Metastases. J Vasc Interv Radiol. 2017 Dec 19. pii: S1051-0443(17)30911-9
3. Bai XM, Yang W, Zhang ZY et al. Long-term outcomes and prognostic analysis of percutaneous radiofrequency ablation in liver metastasis from breast cancer. Int J Hyperthermia. 2019 Jan 1;35(1):183-193.
4. Franzese C, Comito T, Viganò L et al. Liver Metastases-directed Therapy in the Management of Oligometastatic Breast Cancer. Clin Breast Cancer. 2020 Dec;20(6):480-486.

Lungenmetastasen Lokale Therapie

■ **Vor einer lokalen Therapie histologische Sicherung der Metastasierung, auch zum Ausschluss von Zweittumoren**

■ **Resektion mittels VATS* oder konventionell**

- multilokulärer Metastasen
- Solitärer / weniger unilateraler Metastasen

■ **Thermoablation (CT-gesteuert RFA, LITT)**

■ **Regionale Radiotherapie**
(stereotaktische Radiotherapie mittels SRS-VMAT)

* VATS = video-assistierte Thorakoskopie

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

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. Patrini D, Panagiotopoulos N, Lawrence D et al. Surgical management of lung metastases. Br J Hosp Med (Lond). 2017 Apr 2;78(4):192-198.
2. Meng D, Fu L, Wang L et al. Video-assisted thoracoscopic surgery versus open thoracotomy in pulmonary metastasectomy: a meta-analysis of observational studies. Interact Cardiovasc Thorac Surg. 2016 Feb;22(2):200-6.
3. Endoh M, Shiono S, Yamauchi Y et al. Pulmonary metastasectomy for pulmonary metastasis of breast cancer has a limited prognostic impact: a multi-institutional retrospective analysis. J Thorac Dis. 2020 Nov;12(11):6552-6562.
4. Bilani N, Yaghi M, Main O et al. Metastasectomy versus radiation of secondary sites in stage IV breast cancer: Analysis from a national cancer registry. Breast. 2021 Dec;60:185-191.

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.

2. Ewert R, Opitz C. Pulmonary function testing before ablative methods] Radiologe. 2004 Jul;44(7):708-10. 4.
3. Diederich S, Hosten N: Percutaneous ablation of pulmonary tumours: state-of-the-art 2004 Radiologe. 2004 Jul;44(7):658-62.

Statement: Regional Radiotherapy

1. Ricco A, Davis J, Rate W et al. Lung metastases treated with stereotactic body radiotherapy: the RSSearch® patient Registry's experience. Radiation Oncology (2017) 12: oi: 10.1186/s13014-017-0773-4
2. Lehrer EJ, Singh R, Wang M et al. Safety and Survival Rates Associated With Ablative Stereotactic Radiotherapy for Patients With Oligometastatic Cancer: A Systematic Review and Meta-analysis. JAMA Oncol. 2021 Jan 1;7(1):92-106.
3. Viani GA, Gouveia AG, Alexander V Louie AV et al. Stereotactic body radiotherapy to treat breast cancer oligometastases: A systematic review with meta-analysis. Meta-Analysis Radiother Oncol. 2021 Nov; 164:245-250.

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	+
▪ 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. Thomas R, Fysh ETH, Smith NA et al. Effect of an Indwelling Pleural Catheter vs Talc Pleurodesis on Hospitalization Days in Patients With Malignant Pleural Effusion: The AMPLE Randomized Clinical Trial. JAMA. 2017 Nov 21;318(19):1903-1912.
2. Bibby AC, Dorn P, Psallidas I, et al. ERS/EACTS statement on the management of malignant pleural effusions. Eur J Cardiothorac Surg. 2019 Jan 1;55(1):116-132.
3. Kapp CM, Lee HJ. Malignant Pleural Effusions. Clin Chest Med. 2021 Dec;42(4):687-696. Review
4. 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. Warren WH, Kalimi R, Khodadadian LM et al. Management of malignant pleural effusions using the Pleur(x) catheter. Ann Thorac Surg. 2008 Mar;85(3):1049-55.
2. Hak CC, Sivakumar P, Ahmed L. Safety of indwelling pleural catheter use in patients undergoing chemotherapy: a five-year retrospective evaluation. BMC Pulm Med. 2016 Mar 11;16:41.

Maligner Aszites Lokale Therapie

Aszites:

- Punktion, Drainage bei Symptomen
- Kontinuierliche Drainage bei persistierendem Aszites
- Systemische Therapie
- Lokale Chemotherapie

Oxford		
LoE	GR	AGO
4	D	++
3b	D	+
3b	D	++
3b	D	-

1. Korpi S, Salminen VV, Piili RP et al. Therapeutic Procedures for Malignant Ascites in a Palliative Care Outpatient Clinic. J Palliat Med. 2018 Jun;21(6):836-841.
2. 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. Strobbe A, Adriaenssens T, Bennett J et al. Etiology and Long-Term Outcome of Patients Undergoing pericardiocentesis. J Am Heart Assoc. 2017 Dec 23;6(12). pii: e007598.
2. Numico G, Cristofano A, Ocelli M et al. Prolonged Drainage and Intrapericardial Bleomycin Administration for Cardiac Tamponade Secondary to Cancer-Related Pericardial Effusion. Medicine (Baltimore). 2016 Apr;95(15):e3273
3. Lambert A, Salleron J, Kieffer A, Raymond P, Geoffrois L, Gavaille C. Intrapericardial instillation of bleomycin prevents recurrence of malignant pericardial effusions: Series of 46 cases and comprehensive literature review. Bull Cancer. 2020 Jul-Aug;107(7-8):756-762.
4. Kotake M, Imai H, Kaira K, Fujisawa T, Yanagita Y, Minato K. Intrapericardial carboplatin in the management of malignant pericardial effusion in breast cancer: a pilot study. Cancer Chemother Pharmacol. 2019 Sep;84(3):655-660. .
5. Chen D, Song X, Shi F et al. Greater efficacy of intracavitary infusion of bevacizumab compared to traditional local treatments for patients with malignant cavity serous effusion. Oncotarget. 2017 May 23;8(21):35262-35271.
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.

Verdrängungsmyelopathie / Knochenmarksinfiltration (mit Panzytopenie)

Wöchentliche Chemotherapie*:

- Epirubicin, Doxorubicin, Paclitaxel
- Capecitabin

HER2 pos.:

- anti-HER2 Therapie

Hormonzeptor-positiv:

- endokrin-basierte Therapie

LoE	Oxford	
	GR	AGO
4	D	++
4	D	++
5	D	++
3b	C	+

* Beachte Vorbehandlung

1. Pahouja G, Wesolowski R, et al, Stabilization of bone marrow infiltration by metastatic breast cancer with continuous doxorubicin, Cancer Treat Commun. 2015 ; 3: 28–32.
2. Artac M, Koral L, Toy H et al. Complete response and long-term remission to anti-HER2 combined therapy in a patient with breast cancer presented with bone marrow metastases. J Oncol Pharm Pract. 2014 Apr;20(2):141-5.
3. Pahouja G, Wesolowski R, Reinbolt R et al. Stabilization of bone marrow infiltration by metastatic breast cancer with continuous doxorubicin. Cancer Treat Commun. 2015;3:28-32.
4. Yamaguchi T, Masumoto M, Sakurai U et al. Disseminated Carcinomatosis of the Bone Marrow from Occult Breast Cancer Responding to a Sequence of Endocrine Therapy. Case Rep Oncol. 2020 Feb 24;13(1):193-199.

Weichteilmetastasen Lokale Therapie

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> R0-Resektion (bei lokoregionär limitierten Metastasen, z.B. Haut, Muskel, Lymphknoten, nach Ausschluss weiterer Fernmetastasen) 	4	C	+/-
<ul style="list-style-type: none"> Bestrahlung (postoperativ oder primär) bei*: <ul style="list-style-type: none"> Weichteilmetastasen Rückenmarkskompression, Parese Plexusinfiltration 	3b 2b 3b	C C C	+/- ++ ++

*Ausnahme: unmittelbare Indikation zur Operation

- Kong JH, et al: Patterns of skin and soft tissue metastases from breast cancer according to subtypes: relationship between EGFR overexpression and skin manifestations. Oncology. 2011;81(1):55-62. Epub 2011 Sep 16.
- Berlière M, Duhoux FP, Taburiaux L et al. The place of extensive surgery in locoregional recurrence and limited metastatic disease of breast cancer: preliminary results. Biomed Res Int. 2015;2015:782654. doi: 10.1155/2015/782654. Epub 2015 Mar 18.

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