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Guidelines Breast
Version 2021.1D

FORSCHEN
LEHREN
HEILEN

Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Besondere Situationen und Lokalisationen in der metastasierten Situation

Besondere Situationen und Lokalisationen in der metastasierten Situation

■ Versionen 2002–2020:

Albert / Bauerfeind / Bischoff / Böhme / Brunnert / Dall / Diel / Fehm /
Fersis / Friedrich / Friedrichs / Gerber / Hanf / Janni / Kolberg-Liedtke /
Kreipe / Loibl / Lück / Lux / Maass / Oberhoff / Rezai / Rody / Schaller /
Schütz / Seegenschmiedt / Solomayer / Souchon / Thomssen

■ Version 2021:

Mundhenke / Park-Simon / Thomssen

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.

Besondere Metastasenlokalisationen

- **Leber- und Lungenmetastasen**
- **Maligne Pleura- und Perikardergüsse**
- **Aszites**
- **Knochenmarkinfiltration (Verdrängungsmielopathie)**
- **Weichteilmetastasen**
- **Lokalisationen in anderen Organen (Augen, Haut, Nebennieren, Ovarien, Uterus, Magen, Darm, ...)**

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

Allgemeine Aspekte der Metastasentherapie

	Oxford		
	LoE	GR	AGO
▪ Histologischer / zytologischer Nachweis der Metastasierung	3	B	+
▪ Systemische Therapie bevorzugt	2a	B	++*
▪ Operative Therapie nur bei gutem Therapieansprechen der systemischen Therapie, Oligometastasierung	2b	C	+
▪ Radiatio bei Patientinnen in gutem Zustand mit spät aufgetretener Oligometastasierung	3a	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	5	D	++

* Siehe auch Kapitel zur Systemtherapie in der metastasierten Situation

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
2. Ortop Relat Res. 2010;468:2992-3002.

Local surgery

1. Badwe R, et al: Surgical removal of primary tumor and axillary lymph nodes in women with metastatic breast cancer at first presentation: A randomized controlled trial. SABCS [S2-02], 2013
2. Cameron D. Removing the primary tumour in metastatic breast cancer. Lancet Oncol. 2015 Oct;16(13):1284-5.
3. Criscitiello C, Giuliano M, Curigliano G et al.: Surgery of the primary tumor in de novo metastatic breast cancer: To do or not to do? Eur J Surg Oncol. 2015 Oct;41(10):1288-92. doi: 10.1016/j.ejso.2015.07.013. Epub 2015 Jul 29. Review.
4. Soran A et al. A randomized controlled trial evaluating resection of the primary tumor in women presenting with de novo stage IV breast cancer; Turkish study (MF07-01). J Clin Oncol 34, 2016 (suppl; abstr 1005)
5. 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.
6. 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
7. 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.
 8. 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.
 9. 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
 10. 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.
 11. 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.
 12. 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.
 13. Khan SA Plenary Session ASCO 2020 Late Breaking Abstract 2
 14. 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.
 15. 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.

Radiotherapy in oligometastatic breast cancer

1. Scorsetti M, Franceschini D, De Rose F et al.: Stereotactic body radiation therapy: A promising chance for oligometastatic breast cancer. *Breast.* 2016 Apr;26:11-7.
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. Weykamp F, König L, Seidensaal K et al. Extracranial Stereotactic Body Radiotherapy in Oligometastatic or Oligoprogressive Breast Cancer. *Front Oncol.* 2020 Jun 26;10:987.
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

Overviews

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.
3. Liberchuk AN, Deipolyi AR. Hepatic Metastasis from Breast Cancer. Semin Intervent Radiol. 2020 Dec;37(5):518-526.

Lokale Therapie in der primär metastasierten Situation

	Oxford		
	LoE	GR	AGO
▪ Operation (R0) des Primärtumors (ohne OS Vorteil)*	1b	B	-
▪ Bei Beschwerden durch den Primarius	5	D	+/-
▪ Bei alleiniger ossärer Metastasierung	2b	B	+/-
▪ Bei viszeralen Metastasen	2b	B	-
▪ Axillaoperation bei cN1	5	D	+/-
▪ Sentinel bei cN0	5	D	-
▪ Radiotherapie des Primärtumors			
▪ Ohne Operation	3a	C	+/-
▪ Nach brusterhaltender Operation oder nach Mastektomie (entsprechend adj. Indikation)	3a	C	+

*Individuelles Vorgehen bei Oligometastasierung


Operation (R0) des Primärtumors

1. 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.
2. Headon H, Wazir U, Kasem A et al. Surgical treatment of the primary tumour improves the overall survival in patients with metastatic breast cancer: A systematic review and meta-analysis. Molecular and Clinical Oncol. 2016;4;863-867
3. 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.
4. 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
5. 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.
6. 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.
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8. 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.

9. 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.

Lokoregionäre Therapie (alleinige Bestrahlung vs OP+Bestrahlung vs OP) bei primär metastasiertem Mammakarzinom

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



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Randomized Phase III Trials

Trial	n	Prior to Randomization	Local Control	Improved OS Primary Endpoint	QoL
ECOG 2108	256	4-8 months systemic therapy	yes	no	ns
Tata Memorial Hospital	350	chemotherapy	yes	no	-
MF07-01	278	no systemic therapy	yes	no in post analysis evaluation improved OS (notably in solitary bone mets.)	-
ABCSG-28*	90	no systemic therapy	yes	no	ns
JCOG 1017	410	Completed, results not reported so far			

ns not significant *trial terminated due to poor recruitment



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1. 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.
2. 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 POSYITIVE Trial Ann Surg. 2019 Jun;269(6):1163-1169.
3. Khan SA Plenary Session ASCO 2020 Late Breaking Abstract 2
4. 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.

Lebermetastasen Lokale Therapie

	Oxford		
	LoE	GR	AGO
Resektion (R0) HR positiv: Chemotherapie-sensibel, langes DFS, keine extrahepatischen Metastasen, ≤ 3 Metastasen HER2 positiv: Alter < 50 Jahre, Metastase < 5 cm, keine weiteren Metastasen	3a	B	+/-
Regionale Chemotherapie	3b	C	+/-
Regionale Radiotherapie (SIRT, stereotaktische Radiotherapie mittels SRS-VMAT, Radiochemoembolisation, andere Bestrahlungsverfahren)	3b	C	+/-
Thermoablation (RFA, LITT, Kryotherapie)	3b	C	+/-

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.
3. Liberchuk AN, Deipolyi AR. Hepatic Metastasis from Breast Cancer. Semin Intervent Radiol. 2020 Dec;37(5):518-526.

Local surgery

1. van Walsum GA, de Ridder JA, Verhoef C et al. Dutch Liver Surgeons Group Resection of liver metastases in patients with breast cancer: survival and prognostic factors. *Eur J Surg Oncol*. 2012 Oct;38(10):910-7. doi: 10.1016/j.ejso.2012.04.015. Epub 2012 Jun 7.
2. Abbott DE, Brouquet A, Mittendorf EA et al. Resection of liver metastases from breast cancer: estrogen receptor status and response to chemotherapy before metastasectomy define outcome. *Surgery*. 2012 May;151(5):710-6..
3. Sadot E, Lee SY, Sofocleous CT et al. Hepatic Resection or Ablation for Isolated Breast Cancer Liver Metastasis: A Case-control Study with Comparison to Medically Treated Patients. *Ann Surg*. 2016 Jul;264(1):147-154.
4. Bacalbaşa N, Balescu I, Dima S et al. Long-term Survivors After Liver Resection for Breast Cancer Liver Metastases. *Anticancer Res*. 2015 Dec;35(12):6913-7.
5. Vertriest C, Berardi G, Tomassini F et al. Resection of single metachronous liver metastases from breast cancer stage I-II yield excellent overall and disease-free survival. Single center experience and review of the literature. *Dig Surg*. 2015;32(1):52-9.
6. 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
7. 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
8. 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.
9. 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.
10. 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.

Statement: Regional chemotherapy

1. Martin RC et al. Optimal outcomes for liver-dominant metastatic breast cancer with transarterialchemoembolization with drug-eluting beads loaded with doxorubicin. *Breast Cancer Res Treat*. 2012;132(2):753-63.
2. 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*. 2012 Nov 30
3. Eichler K et al. Transarterial chemoembolisation (TACE) with gemcitabine: phase II study in patients with liver metastases of breast cancer. *Eur J Radiol*. 2013;82(12):e816-22
4. Ang C et al. Hepatic arterial infusion and systemic chemotherapy for breast cancer liver metastases. *Breast J*. 2013;19(1):96-9.

5. Camacho LH, Kurzrock R, Cheung A et al. Pilot study of regional, hepatic intra-arterial paclitaxel in patients with breast carcinoma metastatic to the liver. *Cancer*. 2007 Jun 1;109(11):2190-6.
6. Vogl TJ, Zangos S, Scholtz JE et al. Chemosaturation with percutaneous hepatic perfusions of melphalan for hepatic metastases: experience from two European centers. *Rofo*. 2014 Oct;186(10):937-44. doi: 10.1055/s-0034-1366081. Epub 2014 Apr 11.

Statement: Regional radiotherapy

1. Hoffmann RT, et al: Radiofrequency ablation after selective internal radiation therapy with Yttrium90 microspheres in metastatic liver disease-Is it feasible? *Eur J Radiol*. 2010 Apr;74(1):199-205
2. Vogl TJ, Farshid P, Naguib NN et al. Thermal ablation therapies in patients with breast cancer liver metastases: A review. *Eur Radiol*. 2012 Oct 13. [Epub ahead of print]
3. Akhlaghpour S, Aziz-Ahari A, Amoui M et al. Short-term effectiveness of radiochemoembolization for selected hepatic metastases with a combination protocol. *World J Gastroenterol*. 2012 Oct 7;18(37):5249-59.
4. Macchia G, Deodato F, Cilla S et al. Volumetric intensity modulated arc therapy for stereotactic body radiosurgery in oligometastatic breast and gynecological cancers: feasibility and clinical results. *Oncol Rep*. 2014 Nov;32(5):2237-43. doi: 10.3892/or.2014.3412. Epub 2014 Aug 18.
5. Saxena, A.; Kapoor, J.; Meteling, B.; Morris, D.L.; Bester, L. Yttrium-90 radioembolization for unresectable, chemoresistant breast cancer liver metastases: A large single-center experience of 40 patients. *Ann. Surg. Oncol*. 2014, 21, 1296–1303.
6. Pieper, C.C.; Meyer, C.; Wilhelm, K.E.; et al. Yttrium-90 Radioembolization of Advanced, Unresectable Breast Cancer Liver Metastases- A Single-Center Experience. *J. Vasc. Interv. Radiol*. 2016, 27, 1305–1315.
7. 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.
8. 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.
9. 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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11. 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.

Statement: Thermoablation

1. Dwivedi DN, Pal S, Pande GK. Management of liver metastases: cut, cryo, coagulate or chemotherapy. Trop Gastroenterol. 2001 Apr-Jun;22(2):57-64. Review
2. Seifert JK, et al. Cryotherapy for liver tumors: current status, perspectives, clinical results, and review of literature. Technol Cancer Res Treat. 2004 Apr;3(2):151-63.
3. Vogl TJ, et al. MR-guided laser-induced thermotherapy (LITT) of liver tumours: experimental and clinical data. Int J Hyperthermia. 2004 Nov;20(7):713-24
4. Keil S, et al. Radiofrequency Ablation of Liver Metastases-Software-Assisted Evaluation of the Ablation Zone in MDCT: Tumor-Free Follow-Up Versus Local Recurrent Disease. Cardiovasc Intervent Radiol. 2009 Aug 18.
5. Vogl TJ, et al. Magnetic resonance-guided laser-induced interstitial thermotherapy of breast cancer liver metastases and other noncolorectal cancer liver metastases: an analysis of prognostic factors for long-term survival and progression-free survival. Invest Radiol. 2013;48(6):406-12.
6. Xiao YB, Zhang B, Wi YL. 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
7. 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
8. 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.
9. 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

	Oxford		
	LoE	GR	AGO
▪ Vor einer Operation: Staging und Biopsie (CT-gesteuert/e FNA / CNB o. transbronchiale FNA, EBUS)	3a	B	+
▪ Resektion mittels VATS* oder konventionell			
▪ multilokulärer Metastasen	3a	B	-
▪ solitärer/weniger unilateraler Metastasen mit kurativer Intention	3a	B	+/-
▪ Thermoablation (CT-gesteuert RFA, LITT)	3b	C	+/-
▪ Regionale Radiotherapie (z.B. stereotaktische Radiotherapie mittels SRS-VMAT)	3a	B	+/-

* VATS = video-assistierte Thorakoskopie

Vor Operation: Staging und Biopsie (fine-needle aspiration with CT-guidance or transbronchial needle aspiration)

Resektion pulmonaler Metastasen (VATS oderr konventionelle Resektion García-Yuste M, Pulmonary metastasectomy in breast cancer. J

Thorac Oncol. 2010 Jun;5(6 Suppl 2):S170-1.

1. Nichols FC Pulmonary metastasectomy Thorac Surg Clin. 2012 Feb;22(1):91-9, REVIEW
2. Omar M. Rashid and Kazuaki Takabe The evolution of the role of surgery in the management of breast cancer lung metastasis. J Thorac Dis. 2012 August; 4(4): 420–424. REVIEW
3. Kyler W, Laski P: Surgical approach to pulmonary metastases from breast cancer. Breast J. 2012 Jan;18(1):52-7.
4. Meimarakis G et al. Prolonged overall survival after pulmonary metastasectomy in patients with breast cancer. Ann Thorac Surg. 2013;95(4):1170-80.
5. Fan J, Chen D, Du H et al. Prognostic factors for resection of isolated pulmonary metastases in breast cancer patients: a systematic review and meta-analysis. J Thorac Dis. 2015 Aug;7(8):1441-51. doi: 10.3978/j.issn.2072-1439.2015.08.10.
6. Lumachi F, Mazza F, Del Conte A et al. Anticancer Res. 2015 Jun;35(6):3563-6. Erratum in: Anticancer Res. 2015 Jul;35(7):4371. Short-term Survival of Patients with Lung Metastases from Colorectal and Non-colorectal Cancer Who Underwent Pulmonary Metastasectomy.
7. 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.


8. 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.
9. 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.

Statement: Thermoablation (CT-gesteuert 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: Regionale Radiotherapie

1. Macchia G, Deodato F, Cilla S et al. Volumetric intensity modulated arc therapy for stereotactic body radiosurgery in oligometastatic breast and gynecological cancers: feasibility and clinical results. *Oncol Rep*. 2014 Nov;32(5):2237-43.
2. 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



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Malignant Pleural Effusion (MPE)

Incidence:

- ~ 10 % met. breast cancer
- ~ 17-30 % of MPE caused by breast cancer

Symptoms:

- Extensive MPE predominantly caused by malignant disease
- Most MPE cause symptoms [dyspnea (80%), chest pain (30%), non-productive cough (10%)]
- Survival is associated with the site of metastases, ECOG PS, age and extent of pleural carcinomatosis

Diagnostic Procedure:

- Physical examination
- Chest X-ray, ultrasound, CT-scan
- Histology/cytology by ultrasound-guided puncture or video-assisted thoracoscopy (⇒ 50% false negative).

1. Bielsa S et al: Tumor type influences the effectiveness of pleurodesis in malignant effusions. *Lung*. 2011 Apr;189(2):151-5.
2. Ried M, Hofmann HS.: The treatment of pleural carcinosis with malignant pleural effusion. *Dtsch Arztebl Int*. 2013 May;110(18):313-8.
3. 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..
4. Li Z, Pantanowitz L, Khalbuss WE et al. Challenges in diagnosing metastatic breast carcinoma in fluid cytology. *Diagn Cytopathol*. 2014 Nov;42(11):1006-8. doi: 10.1002/dc.23067. Epub 2014 Mar 8.
5. Guerrini GP, Lo Faso F, Vagliasindi A et al. The Role of Minimally Invasive Surgery in the Treatment of Lung Metastases. *J Invest Surg*. 2016 Oct 3:1-6.
6. Meyer C, Bartsch D, Mirow N et al. Video-Assisted Laser Resection of Lung Metastases-Feasibility of a New Surgical Technique. *Thorac Cardiovasc Surg*. 2017 Jan 22.
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J. 2020;2020:2950751

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. doi: 10.1186/s12890-015-0025-z.

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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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.
3. Davies HE et al., Effect of an indwelling pleural catheter vs chest tube and talc pleurodesis for relieving dyspnea in patients with malignant pleural effusion: the TIME2 randomized controlled trial. JAMA. 2012 Jun 13;307(22):2383-9. doi: 10.1001/jama.2012.5535.
4. 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.
5. 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. Saâda E, et al: Pathogenesis and management of refractory malignant ascites. Bull Cancer. 2011 Jun;98(6):679-87.
2. Barni S, et al: A novel perspective for an orphan problem: old and new drugs for the medical management of malignant ascites. Crit Rev Oncol Hematol. 2011 Aug;79(2):144-53.
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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 Substanzen			
▪ Bleomycin, Carboplatin, Cisplatin, Mitomycin C, Mitoxantron etc.	4	C	+/-
▪ 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.
2. Çelik S, Lestuzzi C, Cervesato E et al. Systemic chemotherapy in combination with pericardial window has better outcomes in malignant pericardial effusions. J Thorac Cardiovasc Surg. 2014 Nov;148(5):2288-93
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7. Lambert A, Salleron J, Kieffer A, Raymond P, Geoffrois L, Gavoille 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.
8. 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. .

9. 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.

Verdrängungsmyelopathie / Knochenmarksinfiltration (mit Panzytopenie)

	Oxford		
	LoE	GR	AGO
▪ Wöchentliche Chemotherapie*:			
▪ Epirubicin, Doxorubicin, Paclitaxel	4	D	++
▪ Capecitabin	4	D	++
▪ HER2 pos.:			
▪ zusätzlich anti-HER2 Therapie	5	D	++
▪ Hormonzeptor-positiv:			
▪ endokrin-basierte Therapie	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.
3. Ardavanis A, et al: Low-dose capecitabine in breast cancer patients with symptomatic bone marrow infiltration: a case study. Anticancer Res. 2008 Jan-Feb;28(1B):539-41.
4. Krockenberger M, et al: Prolonged clinical benefit from platinum-based chemotherapy in a patient with metastatic triple negative breast cancer. Eur J Gynaecol Oncol. 2009;30(4):449-51. 2.
5. 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.
6. 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.
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Weichteilmetastasen Lokale Therapie

- **Chirurgische R0-Resektion***
- **Bestrahlung bei folgenden Indikationen**:**
 - Weichteilmetastasen
 - Parese, Rückenmarkskompression
 - Plexusinfiltration

Oxford		
LoE	GR	AGO
4	C	+
3b	C	+
2b	C	++
3b	C	++

* bei lokoregionär limitierten Metastasen (Haut, Muskel, Lymphknoten)
nach Ausschluss weiterer Fernmetastasen

** als postoperative Bestrahlung oder primär, falls keine unmittelbare
Operations-Indikation besteht

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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.
3. Tancioni F, et al: Multimodal approach to the management of metastatic epidural spinal cord compression (MESCC) due to solid tumors. Int J Radiat Oncol Biol Phys. 2010 Dec 1;78(5):1467-73. Epub 2010 Mar 16.
4. 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.
5. 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.