Diagnosis and Treatment of Patients with early and advanced Breast Cancer

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in der DGGG e.V.
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Guidelines Breast
Version 2020.1

Specific Sites of Metastases

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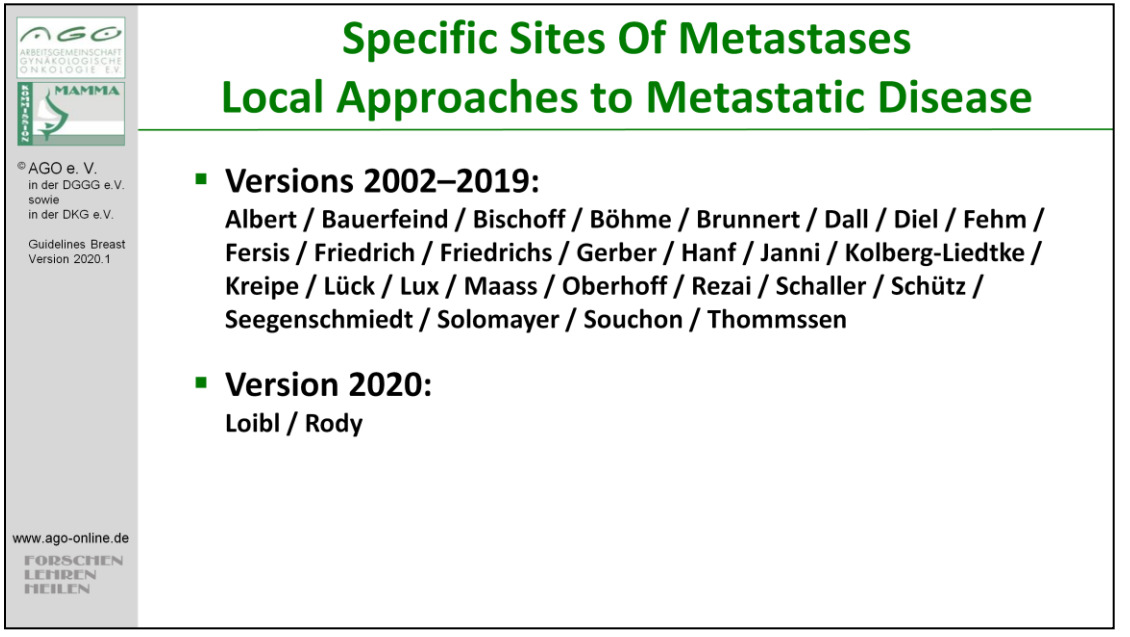
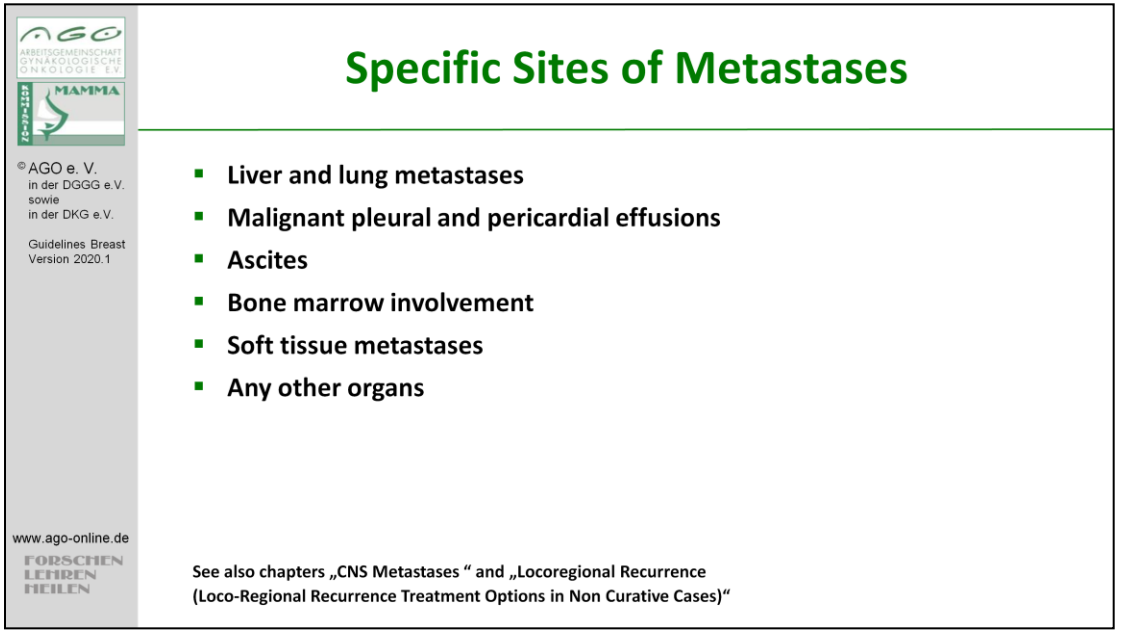
FORSCHEN
LEHREN
HEILEN



Pubmed 1.1.2014 bis 01.01.2019
Cochrane database

1. ABC 2: Cardoso F, Costa A, Norton L et al. ESO-ESMO 2nd international consensus guidelines for advanced breast cancer (ABC2). Ann Oncol. 2014 Oct;25(10):1871-88.
2. ABC 3: Cardoso F, Costa A, Senkus E et al. 3rd ESO-ESMO international consensus guidelines for Advanced Breast Cancer (ABC 3). Breast. 2017 Feb;31:244-259.



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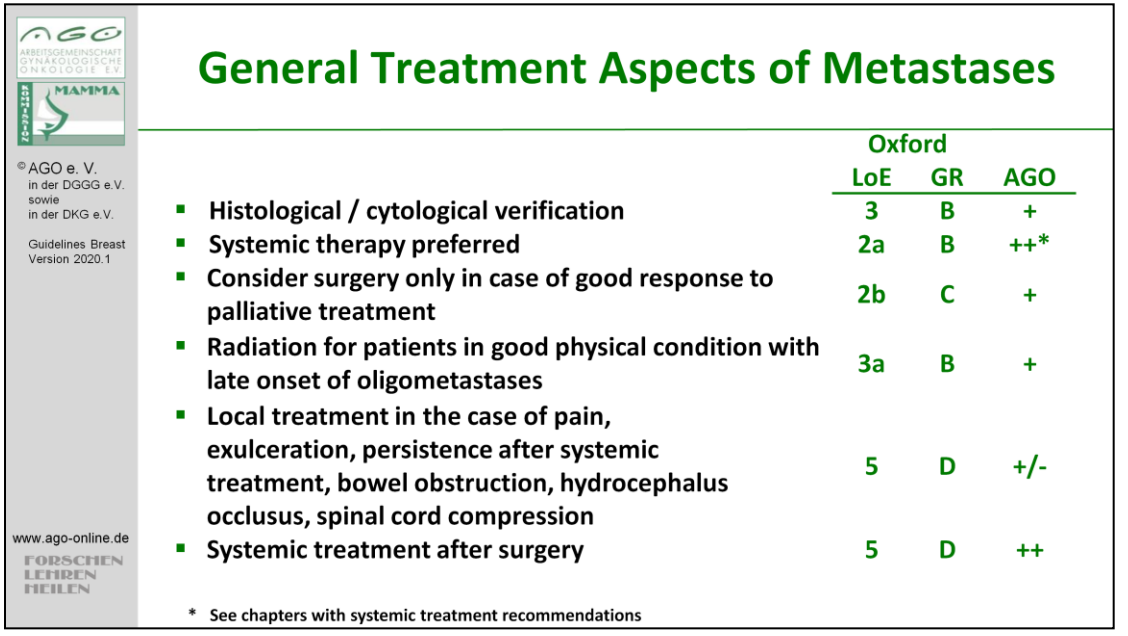
4. Badwe R, et al: Surgical removal of primary tumor and axillary lymph nodes in women with metastatic breast cancer at first presentation: A randomized controlled trial. SABCS [S2-02], 2013
5. Soran A et al. Early follow up of a randomized trial evaluating resection of the primary breast tumor in women presenting with de novo stage IV breast cancer; Turkish study (protocol MF07-01) SABCS [S2-03], 2013
6. Janssen S, Rades D. Primary Breast Cancer with Synchronous Metastatic Disease - Indications for Local Radiotherapy to the Breast and Chest Wall. Anticancer Res. 2015 Nov;35(11):5807-12. Review.
7. 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 Oncol. 2015 Oct;16(13):1380-8. doi: 10.1016/S1470-2045(15)00135-7. Epub 2015 Sep 9.



Local surgical

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.
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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.
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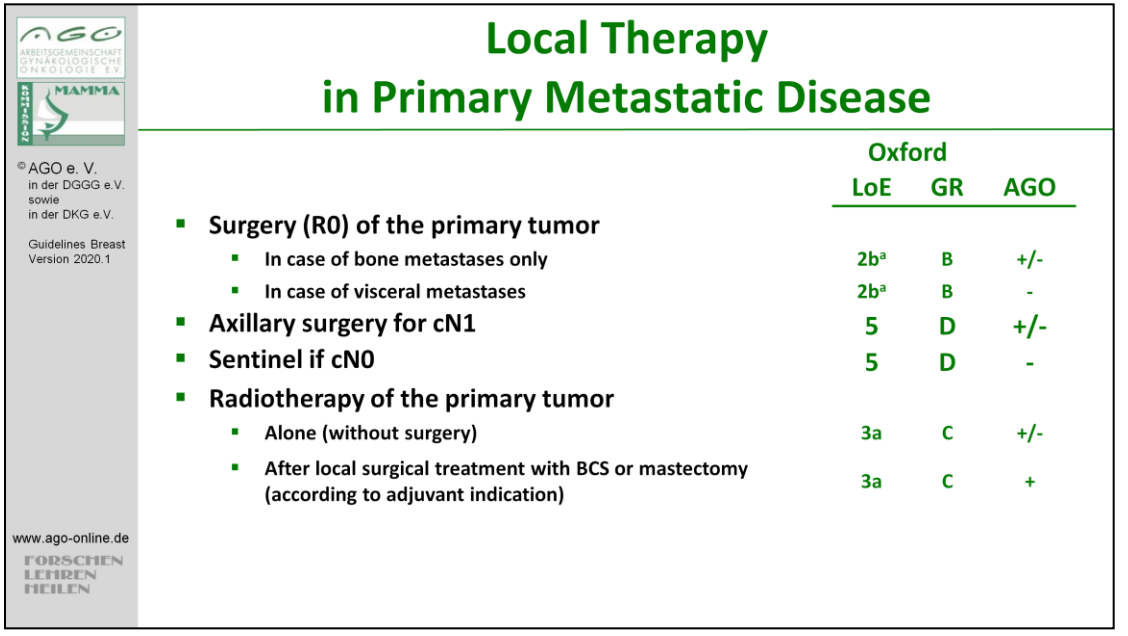
7. Barinoff J, Schmidt M, Schneeweiss A et al.: Primary metastatic breast cancer in the era of targeted therapy - Prognostic impact and the role of breast tumour surgery.Eur J Cancer. 2017 Sep;83:116-124.
8. Poggio F, Lambertini M, de Azambuja E. Controversies in Oncology: Surgery of the primary tumour 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

Oligometastasierung
Radical radiotherapy

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.

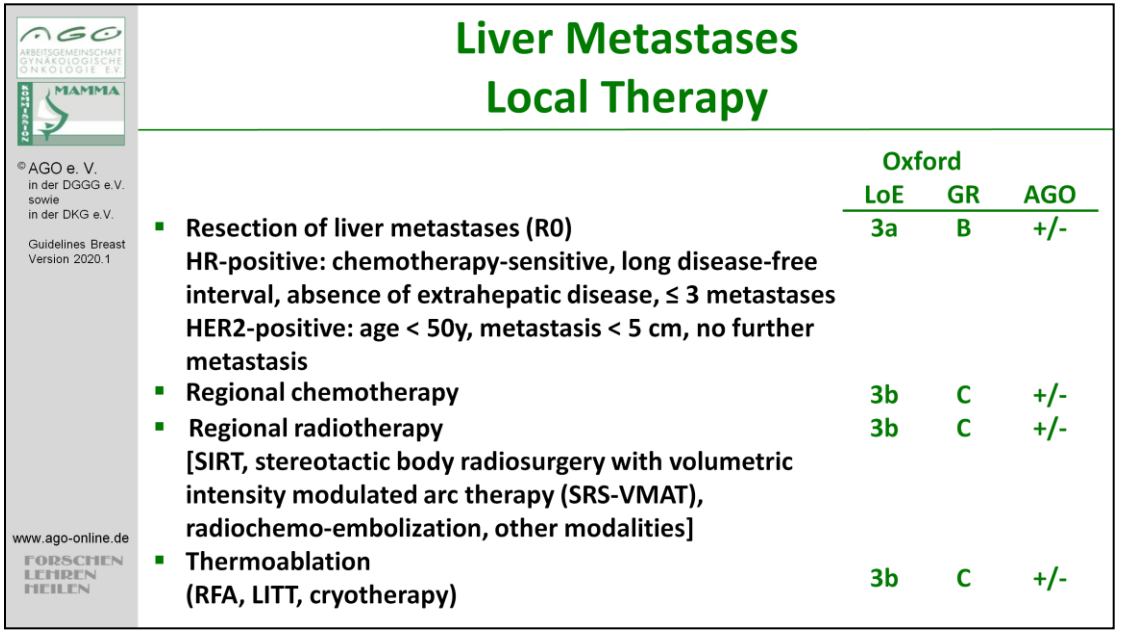


Operation (R0) des Primärtumors

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

Radiotherapy

1. Janssen S, Rades D. Primary Breast Cancer with Synchronous Metastatic Disease - Indications for Local Radiotherapy to the Breast and Chest Wall. Anticancer Res. 2015 Nov;35(11):5807-12.



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.

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. 2015 Oct 1. [Epub ahead of print]
4. BacalbaȘa 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.

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. Akhlaghpoor 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.
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6. 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.

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.
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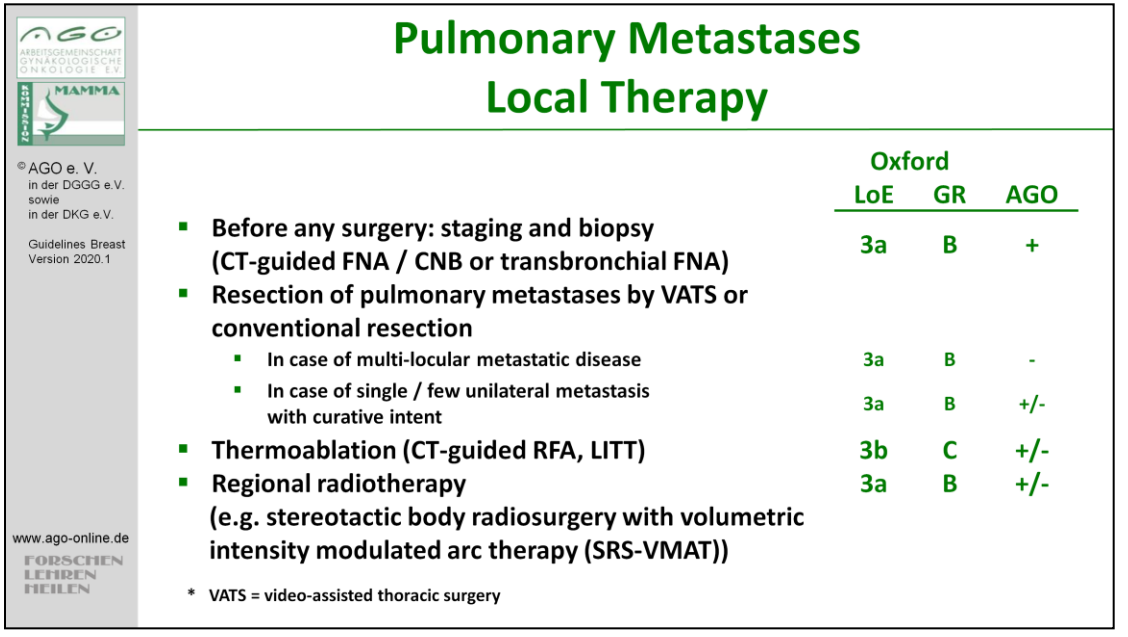
6. Xiao YB, Zhang B, Wi Yl. Radiofrequency ablation versus hepatic resection for breast cancer liver metastasis: a systematic review and meta-analysis J Zhejiang Univ-Sci B (Biomed & Biotechnol) 2018 19(11):829-843



Before surgery: staging and biopsy (fine-needle aspiration with CT-guidance or transbronchial needle aspiration)

Resection of pulmonary metastases by VATS or conventional resection
In case of multilocular metastatic disease
In case of single metastases on one side with curative intent

1. García-Yuste M, Pulmonary metastasectomy in breast cancer. J Thorac Oncol. 2010 Jun;5(6 Suppl 2):S170-1.
2. Nichols FC Pulmonary metastasectomy Thorac Surg Clin. 2012 Feb;22(1):91-9, REVIEW
3. 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
4. Kycler W, Laski P: Surgical approach to pulmonary metastases from breast cancer. Breast J. 2012 Jan;18(1):52-7.
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7. 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

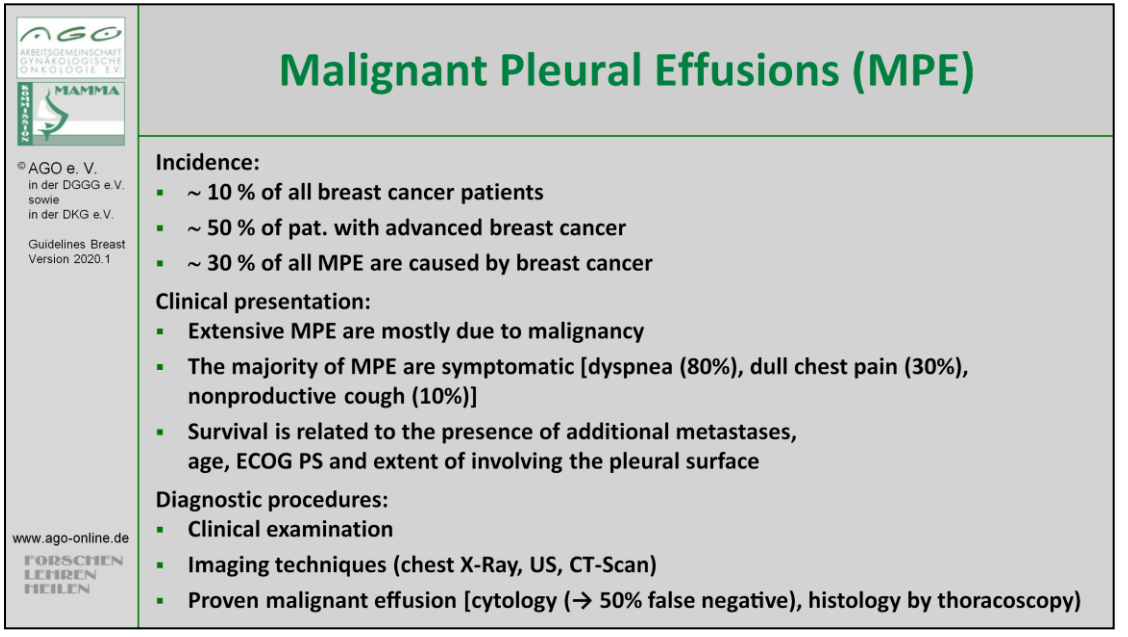
Metastasectomy.
8. Patrini D, Panagiotopoulos N, Lawrence D et al. Surgical management of lung metastases. Br J Hosp Med (Lond). 2017 Apr 2;78(4):192-198.
9. Meng D, Fu L, Wang L et al. Video-assisted thoracoscopic surgery versus open thoracotomy in pulmonary metastasectomy: a meta-analysis of observational studies. Interact Cardiovasc Thorac Surg. 2016 Feb;22(2):200-6.

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. 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
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



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.
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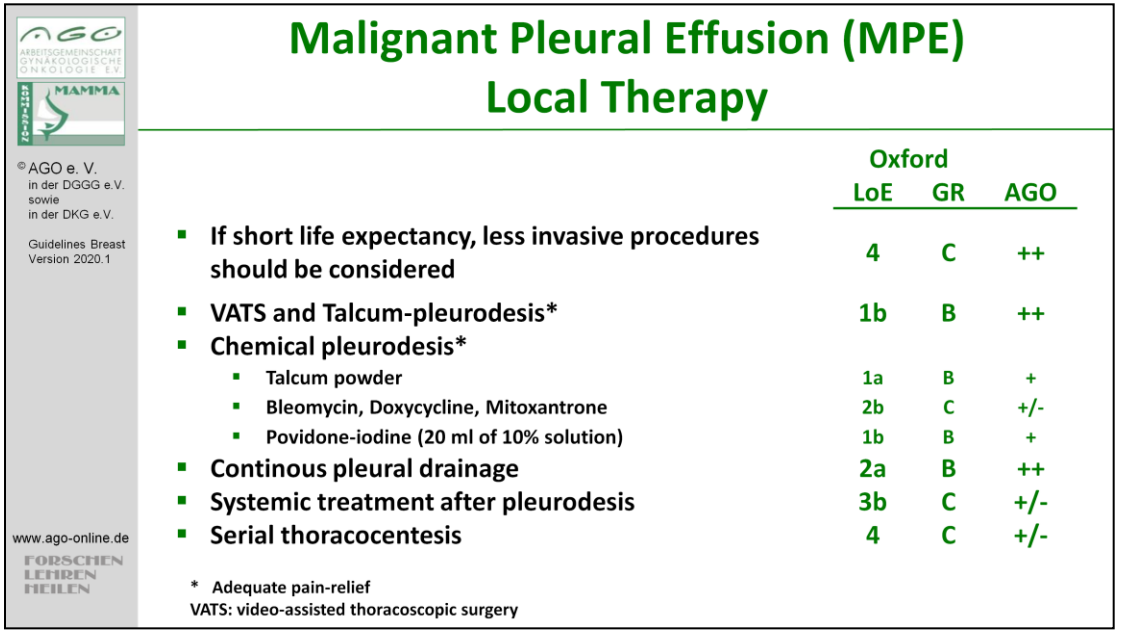
4. Li Z, Pantanowitz L, Khalbuss WE et al. Challenges in diagnosing metastatic breast carcinoma in fluid cytology. Diagn Cytopathol. 2014 Nov;42(11):1006-8. doi: 10.1002/dc.23067. Epub 2014 Mar 8.
5. Guerrini GP, Lo Faso F, Vagliasindi A et al. The Role of Minimally Invasive Surgery in the Treatment 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.



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.
3. Lombardi G, et al: Diagnosis and Treatment of Malignant Pleural Effusion: A Systematic Literature Review and New Approaches. Am J Clin Oncol. 2010 Aug;33(4):420-3.

4. Olden AM, Holloway R. Treatment of Malignant Pleural Effusion: PleuRx((R)) Catheter or Talc Pleurodesis? A Cost-Effectiveness Analysis. J Palliat Med. 2010 Jan;13(1):59-65.
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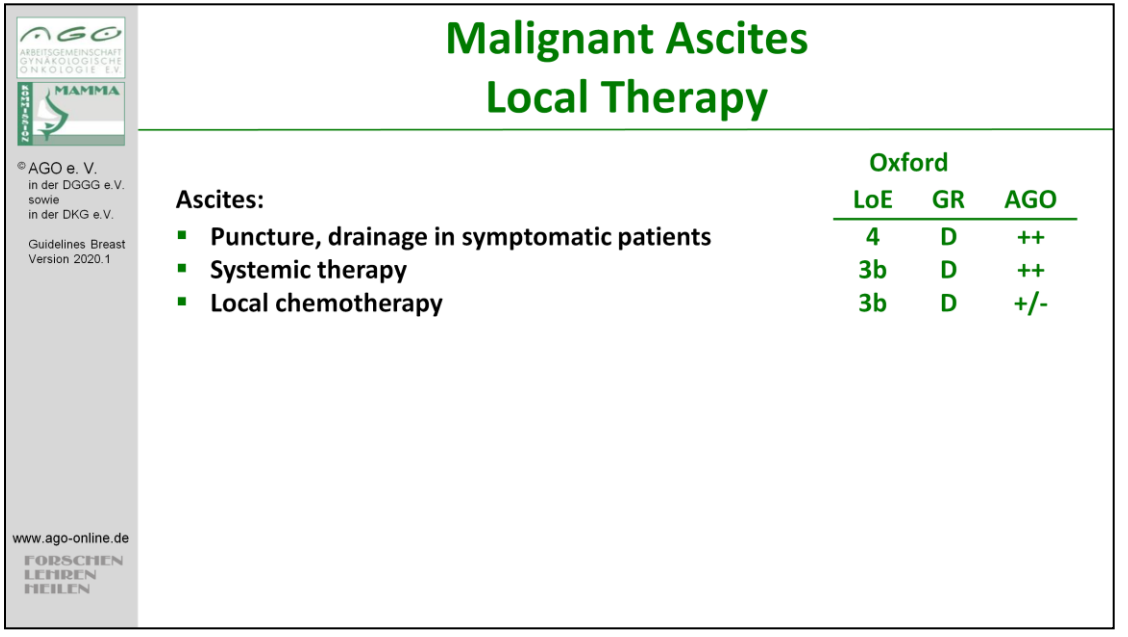
7. Ibrahim IM, Dokhan AL, El-Sessy AA et al. Povidone-iodine pleurodesis versus talc pleurodesis in preventing recurrence of malignant pleural effusion. J Cardiothorac Surg. 2015 May 1;10:64. doi: 10.1186/s13019-015-0270-5.
8. Thomas R, Fysh ETH, Smith NA et al. Effect of an Indwelling Pleural Catheter 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.
9. 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.

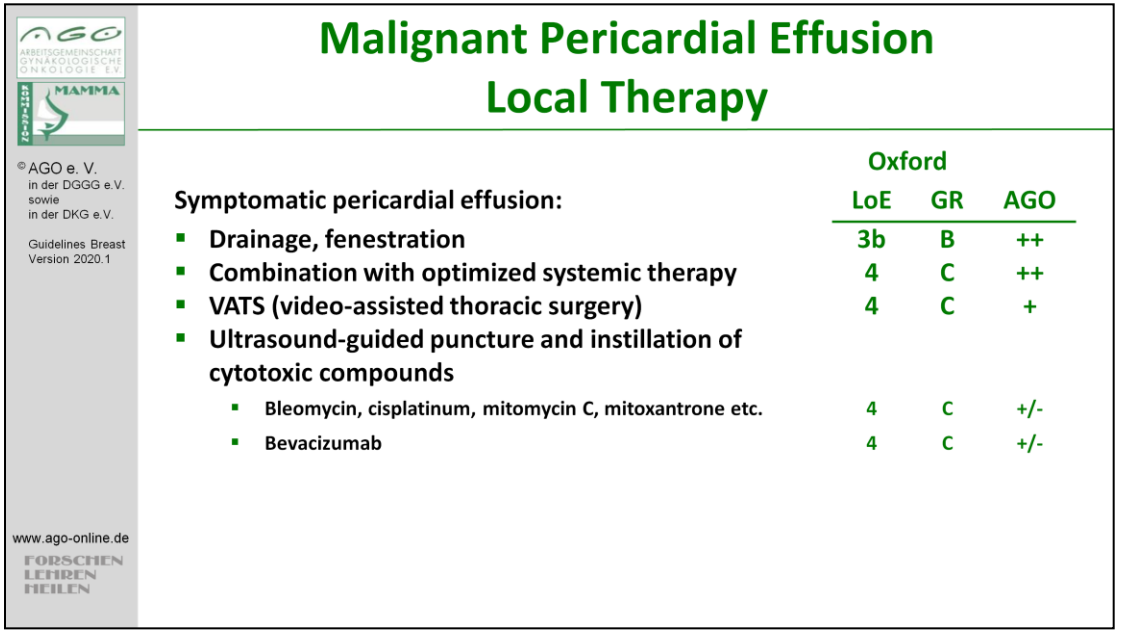
Statement: Continous pleural drainage

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.

Statement: Systemic treatment after pleurodesis



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.
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.
4. Kurbacher CM, Horn O, Kurbacher JA et al.: Outpatient Intraperitoneal Catumaxomab Therapy for Malignant Ascites Related to Advanced Gynecologic Neoplasms. Oncologist. 2015 Nov;20(11):1333-41.



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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
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.
4. El Haddad D, Iliescu C, Yusuf SW et al. Outcomes of Cancer Patients Undergoing Percutaneous Pericardiocentesis for Pericardial Effusion. J Am Coll Cardiol. 2015 Sep 8;66(10):1119-28
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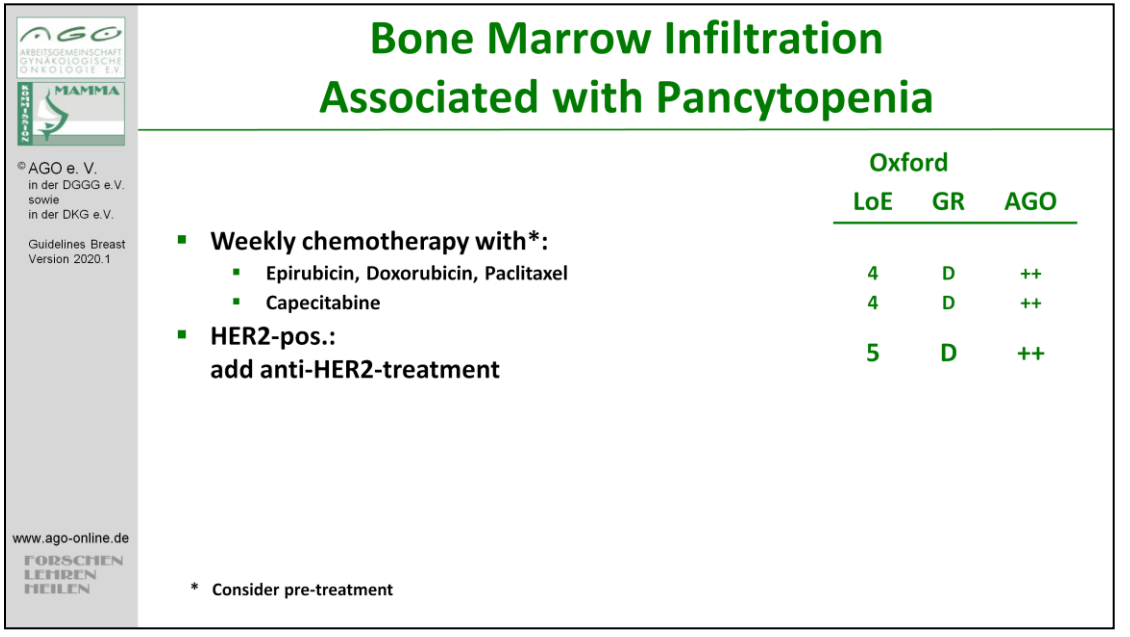
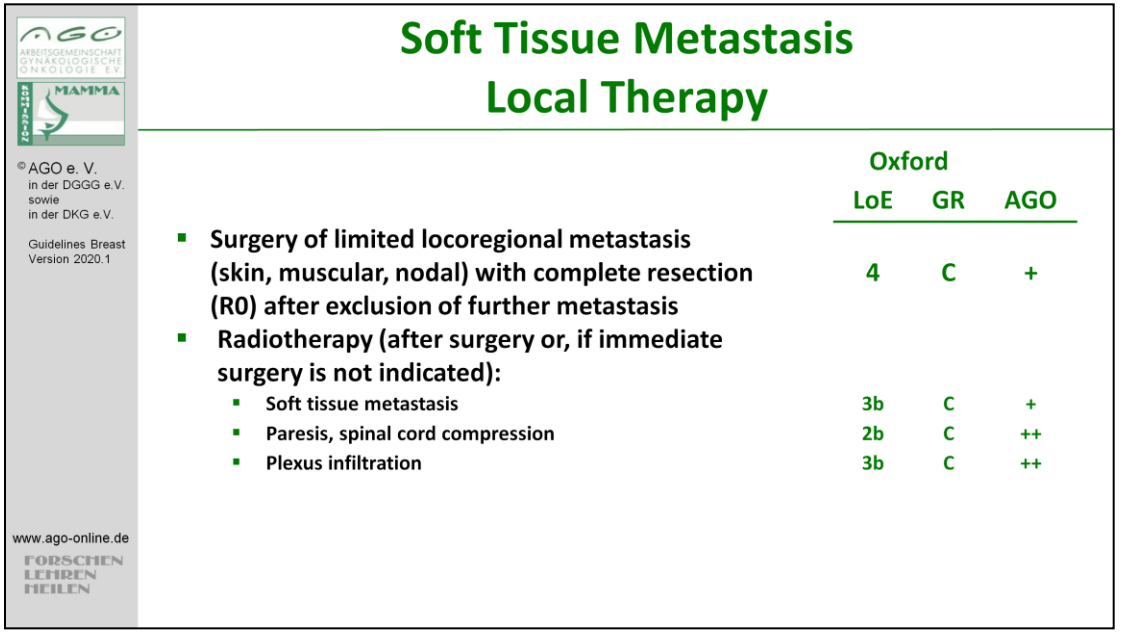
6. Numico G, Cristofano A, Occelli M et al. Prolonged Drainage and Intrapericardial Bleomycin Administration for Cardiac Tamponade Secondary to Cancer-Related Pericardial Effusion. Medicine (Baltimore). 2016 Apr;95(15):e3273



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.
7. 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.



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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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.