The role of local management in locally recurrent and metastatic breast cancer

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Introduction

It is very well accepted that the treatment strategy in early breast cancer should be a multidisciplinary approach. The same strategy is also relevant in the treatment of loco-regional recurrent and metastatic breast cancer to obtain maximal disease control and alleviation of symptoms and thereby improve quality of life and prolong survival.

For decades, numerous trials have been performed with the aim of developing effective systemic treatment of recurrent breast cancer. As a result, these trials have provided solid evidence about the indication and effect of systemic therapy of metastatic breast cancer. However, when it comes to trials addressing the role of local management in locally recurrent and metastatic breast cancer, the literature is much sparser, and there are very few trials that specifically focus on this issue. This is a pity because it does not reflect either the common use of local therapy in most cancer centres or the importance of such treatment. Several retrospective studies of the pattern of recurrence in breast cancer have shown that roughly one-third of all stages of breast cancer will develop loco-regional recurrence at some time, and further, that a large number of patients presenting with disseminated disease also have dominating symptoms and signs from one or more metastatic sites, which require prompt local therapy before or during a systemic treatment [1].

The aim of this paper is to outline the indications for local management in breast cancer, to review relevant literature addressing the issue, and to give guidelines for treatment strategies in frequently occurring clinical situations (Fig. 1).

Definition of end points

The definition of local recurrence is any reappearance of cancer in the ipsilateral regio mammaria, i.e. residual breast, chest wall or skin overlying the chest wall after initial treatment. Regional recurrence refers to tumour involving the ipsilateral axillary lymph nodes, supra/infraclavicular lymph nodes or internal mammary lymph nodes. In addition, the terms "limited loco-regional recurrence without distant metastases" and "advanced loco-regional recurrence with and without distant metastases" will be used. Metastatic breast cancer is defined as any reappearance of breast cancer outside the ipsilateral loco-regional area, either alone or together with loco-regional recurrence.

Presenting symptoms

Local recurrence after mastectomy often appears as one or more asymptomatic cutaneous or subcutaneous nodules in or near the scar of mastectomy. A few patients present with multiple nodules or diffuse disease with infiltration of the skin and subcutaneous tissue of the chest wall, with spread of tumour beyond the area for standard surgery or radiation therapy. Simultaneous recurrence occurs in regional nodal sites in about one-third of patients. Regional recurrence alone is less common, but there are great variations in studies depending on the extent of primary treatment (surgery ± radiotherapy), primary stage, and aggressiveness of the disease (Table 1). A special unpleasant presentation of regional recurrence is brachial plexopathy and severe lymph oedema of ipsilateral arm due to respectively tumour infiltration of the brachial plexus and in the periclavicular nodal area.

Local recurrence after breast-conserving surgery is often detected solely by follow-up mammography in up to 50% of the cases. The remaining recurrences are found by the patients due to new symptoms and signs in the breast or at routine follow-up where physical examination revealed suspicious changes [2]. Clearly, the quality of routine follow-up after

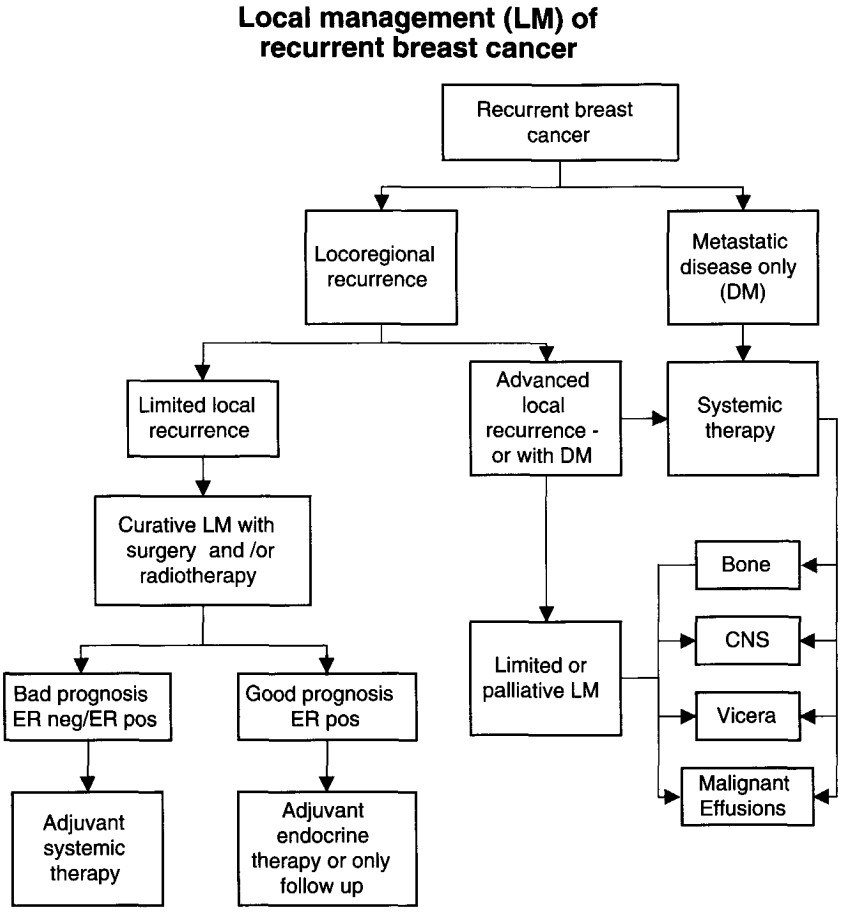

Fig. 1. Decision tree for local management of recurrent breast cancer. ER, oestrogen receptor; pos, positive; neg, negative; CNS, central nervous system.

breast-conserving therapy may have an important influence on the possibility of salvage treatment in such patients.

The presenting symptoms of metastatic breast cancer include a large range of different symptoms and signs in relation to sites of recurrence. Of relevance for the present paper are pain from bone metastases, neurological deficits due to central nervous system (CNS) metastases, and respiratory symptoms due to lung and pleural metastases [1].

Table 1
Factors of importance for the rate of loco-regional recurrences

Primary stage
Tumour characteristics
Age
Extent of primary surgery
Postoperative irradiation
Adjuvant systemic therapy
Years of follow-up (actuarial)
Type of recurrences recorded

Pre-treatment investigations

It is very important to make a careful restaging of the patient before making the final decision of a treatment. Pre-treatment evaluation should include medical history, including previous antineoplastic treatment, physical examination, performance status, blood tests, chest X-ray, bone scintigraphy, and ultrasound scanning of the liver. Further, X-rays, computerised tomography (CT) scan or magnetic resonance imaging (MRI) scans should be used to clarify all suspicious lesions and symptoms. Finally, biopsy is mandatory if there is only one site of recurrence.

Loco-regional recurrent breast cancer

Loco-regional recurrence after mastectomy without distant metastases

Approximately one-third of patients treated with initial mastectomy will develop loco-regional recur-

Table 2
Treatment of local recurrence after primary mastectomy

Study	Treatment	*N*	Follow-up (months)	Local control (%)	Survival (%)	5-yr (%)	10-yr (%)	Diss. rate (%)	5-yr (%)	10-yr (%)	Prognostic factors
Haylock, 2000	Ex. + RT	120			57	82–74	57		25–39	58	
Kamby, 1999	Ex. + RT	99	123	57	39	60	38		50	72	Node status, haemoglobin at first recurrence
van Tienhoven, 1999	Ex. + RT	67		62	58						pN and pT category, vascular invasion
Willner, 1997	Ex. + RT	145	107	86		42		57		64	Site, number of nodules, time to recurrence
Faneyte, 1997	CWR	44	3	80		45 (58%)		39	65		
Dahlstrom, 1993	WLE	98	36	55	52						
Salvadori, 1992	WLE	39	48	82	54						
Probstfeld, 1989	Various	106		75				55			Size of primary tumour, no. nodules, time to recurrence

Ex, excision; RT, radiotherapy; CWR, chest wall resection; WLE, wide local excision; yr, year..

rence during the course of disease. The frequency of recurrences after mastectomy differs substantially in different published series [3]. The reasons for this variation are listed in Table 1. Advanced stages, less extensive surgery, no radiotherapy, no adjuvant systemic therapy, long follow-up time, and cumulative registration of all loco-regional recurrences are all factors which will increase the incidence. More than 50% of recurrences occur on the chest wall, about 30% in the axilla, and the remaining 10–20% in the periclavicular and internal mammary areas [3]. The treatment of loco-regional recurrences varies substantially in the reported series. This is partly influenced by the extent of primary treatment, but also by institutional preferences [2,3]. Therefore, it is very difficult to draw any definite conclusions with respect to optimal local management. In most studies of "limited loco-regional recurrence" after mastectomy, a treatment approach with curative intent has been chosen either by surgery alone, radiotherapy alone or a combination [2]. The results of radiation therapy alone show complete regression of disease in most patients, but a large proportion of patients will suffer from reappearance of loco-regional disease when limited target volumes and low doses have been used [2]. When large chest wall fields and appropriate nodal irradiation as well as sufficient total dose are used, the chance of infield tumour recurrence diminishes substantially, especially in patients with small residual tumours and in patients who had complete excision of recurrent tumour before radiotherapy [4]. Similarly, results of surgery show that the chance of new local treatment failure is very high (60–70%) if only limited local excision has been used [2]. If more radical surgical approaches are used, persistent local tumour control has been obtained in most patients as illustrated in Table 2 [5,6], which also includes other retrospective and prospective studies of carefully selected patients treated with surgical resection of recurrent tumour followed by radiotherapy. Persistent local tumour control in 55–86% of patients as well as long-term survival in 39–57% of patients can be obtained [7–12]. As mentioned earlier, there are no clinical trials comparing different combinations of treatment modalities or the extent of these. Therefore, the best evidence for treatment decisions in such patients stem from a few comprehensive single institution studies of a treatment strategy used over a time period, and where sufficient follow-up is available.

Prognosis

Most retrospective studies of the outcome of treatment of local recurrence are more focused on the general prognosis of local recurrence after mastectomy than on the effect of the treatment intervention itself. Overall, the conclusion of the results is that despite aggressive local treatment, a large number of patients with local recurrence after mastectomy will eventually develop distant metastases [2–4]. However, the results shown in Table 2 indicate that a curative treatment strategy in carefully selected patients matters — at least by obtaining persistent local tumour control, when this cannot be reached by use of very limited local therapy or systemic therapy alone. The prognosis of local recurrence after mastectomy is in fact influenced by some of the same factors which define the risks for recurrence. Thus, patients with unfavourable prognostic factors at the time of primary treatment (positive nodes, large tumour and

Table 3
Indicators of poor prognosis after treatment for loco-regional failure

Primary node-positive
Hormone receptor-negative
High malignancy grade (including HER2-positivity)
Short interval from primary treatment
Multiple nodules or recurrence in more than one site
Young age
Insufficient treatment of loco-regional recurrence

grade III) will not only have a higher risk for developing loco-regional recurrences, but they will also have a worse prognosis, even after curative salvage treatment. A short interval from primary treatment to recurrence has proved to be significantly related to a poor prognosis in all studies [8,9,12]. In contrast, patients with more favourable characteristics at primary treatment and who develop local recurrences often after a long delay will have a much better prognosis after curative local treatment for recurrence [2]. These results indicate that the occurrence of loco-regional relapse may be part of dissemination in some patients and, therefore, the treatment of such patients should include systemic therapy to obtain overall disease control as long as possible. The most important poor prognostic factors are listed in Table 3. Such factors could form the basis for future clinical trials addressing the question about the effect of adjuvant systemic therapy in addition to local therapy. At the moment, there is very little information about this issue.

The prognosis of the patient is also related to the site of local recurrence. Thus, most studies indicate that isolated local recurrences on the chest wall carry the best prognosis, whereas recurrence in nodal areas and in more than one site or in multiple nodules is much more difficult to control. With respect to recurrence in the supra/infraclavicular area, there seems to be some controversy. On the one hand, the supraclavicular area is regarded as a regional nodal area and is therefore also included in the target volume for postoperative radiotherapy as well as comprehensive radiotherapy after local recurrence. On the other hand, according to the American Joint Committee on Cancer Manual for Staging of Cancer (1988), the disease in the supraclavicular area is classified as metastatic disease. This is in agreement with studies where the prognosis of recurrence in the supraclavicular area is shown to be as poor as for other distant metastases [13]. However, in the latest Manual for Staging of Cancer (2002), the disease in the supraclavicular area is no longer classified as distant metastases. A single study of combined modality therapy for locally advanced breast cancer with ipsilateral supraclavicular metastases confirms that these patients have similar prognosis to those with stage IIIB breast cancer. It is likely that a similar optimistic approach could be applied to patients who have developed recurrence in the supraclavicular area, especially if this is the only site of recurrence. There is a need to explore this aspect further to see whether a more aggressive multimodality therapy can lead to "cure" in some of these patients or can reduce the number of patients with uncontrolled loco-regional disease as described below.

Unfortunately, there is a general lack of clinical trials which can help us to select the optimal treatment for loco-regional recurrence in relation to prognostic parameters and previous treatment. On the basis of the brief review and discussion of relevant literature as described above, the following conclusions can be drawn regarding treatment strategy for local recurrence after mastectomy.

Patients with "limited loco-regional recurrence after mastectomy without distant metastases" should be offered curatively intended loco-regional treatment. If postoperative radiotherapy was previously given, the preferred treatment would be radical surgery with radical resection of all tumour tissue on the chest wall and/or in the axilla. If there was no previous radiotherapy, an optimal strategy would be a combined approach with excision of recurrent tumour followed by comprehensive loco-regional irradiation (50 Gy in 25 fractions to the whole target plus 10–25 Gy in 5–12 fractions to sites of recurrence).

Radiation therapy alone to patients with macroscopic residual tumour will only occasionally result in persistent tumour control even if high doses are used. Therefore, this category of patients where clinically radical surgery before irradiation is not feasible may belong to the group with "advanced local recurrence" as described below. Precise description of curability criteria is needed in every cancer centre treating these patients.

Recurrence after breast-conserving therapy without distant metastases

The local recurrence rate after breast-conserving surgery is around 13% when postoperative radiotherapy has been used, and up to 42% after surgery alone [3,4]. Most local recurrences occur in residual breast, with more than 50% in the tumour bed area [14]. In most series of breast-conserving therapy, the incidence of regional recurrences is very low. This is because this treatment is primarily offered in the very early stages of breast cancer and because axillary node dissection has been the standard in most patients. Thus, in the large EORTC study (boost trial), the re-

Table 4
Treatment of local recurrence after breast-conserving therapy

Study	Treatment	*N*	Follow-up (months)	Local control (%)	Survival (%)	5-year (%)	Diss. rate (%)	5-year (%)	Prognostic factors
McBain, 2003	Mastectomy	101		75	62	23-39-57*			
van Tienhoven, 1999	Mastectomy	66		63	59				pN and pT category, vascular invasion
Salvadori, 1999	Mastectomy/Ex.	191	73	83		74			
Voogd, 1999	Mastectomy	266	52	75	56	61	52	53	Skin and LN involvement, grade of primary tumour
Dalberg, 1998	Mastectomy	85		73		66		41	
Abner, 1993	Mastectomy	123	39				41		
Fourquet, 1989	?	46	103			73			

Ex, excision; LN, lymph node.
*For recurrences diagnosed <2, 2–4 and >4 years after primary surgery, respectively.

gional recurrence rate is less than 1% at 5 years [14]. Like the mastectomy series, the loco-regional recurrence rates after breast-conserving therapy is also influenced by the variables listed in Table 1. It is well known that patients with ipsilateral breast tumour recurrence (IBTR) are candidates for a curatively intended treatment approach, which will include radical surgery alone or limited surgery ± radiotherapy [3,4,15]. Most often a salvage mastectomy is performed, and, as shown in Table 4, the 5-year relapse-free survival after such treatment is around 60–75% [9,16–21]. Subsequent chest wall recurrence occurs in less than 10%. Some patients with very small recurrences in the breast may be candidates for new breast-conserving surgery either alone or followed by irradiation if this was not used in the primary treatment. The results of such limited surgery alone, however, show that at least one-third of these patients will have further local failure by 5 years [2]. Re-irradiation after wide excision in breast recurrences has also been used in selected patients with interstitial implantation or external irradiation to a small volume. Long-term follow-up of such patients, however, reveals that a rather large number of patients will either develop new recurrences or will have inferior cosmetic results.

Some patients with failure after breast-conserving therapy may have a desire for breast reconstruction at the time of salvage mastectomy. The fact that most of these patients have had prior radiation, however, may increase the risk of complications and reduce the cosmetic outcome. Immediate reconstruction with a myocutaneous flap offers the most satisfactory result in these situations.

The treatment of regional node recurrences in patients treated initially with breast-conserving surgery is in principle the same as after mastectomy. However, most patients have received postoperative irradiation after conservative surgery, and usually the radiation fields have included part of the infraclavicular and axillary regions. Therefore, regional recurrences in these areas should primarily be treated with radical surgery where possible.

Prognosis after IBTR

The general belief is that the prognosis after IBTR is better than after a local recurrence after mastectomy. However, in the randomised European Organisation for Research and Treatment of Cancer (EORTC) 10811 trial which compared breast-conserving therapy with mastectomy, the prognosis following local relapse was similar in both treatment groups [9]. This was later confirmed in a joint re-evaluation of the EORTC 10811 trial together with the Danish TM 82 Study. The re-analysis showed the same loco-regional failure rate and survival after mastectomy and breast-conserving therapy [17]. This may suggest that the risk of subsequent distant metastasis and death may be independent of the loco-regional treatment. Therefore, it may be of concern that in a subgroup of young patients (<35 years), the local recurrence rate after breast-conserving treatment was five times higher than after mastectomy, although only a non-significantly higher distant metastasis rate has been observed in this subgroup so far. Also, after neoadjuvant chemotherapy and breast-conserving therapy in more advanced disease, a much higher rate of IBTR and subsequent distant metastases was observed, higher than normally seen in the classical randomised series. Again this supports the idea that IBTR may be a significant risk factor for the development of distant disease [17,22].

Furthermore, Dalberg et al. reported long-term results of salvage treatment after IBTR. They found that 13% of such patients will ultimately suffer from uncontrolled loco-regional disease [23]. Thus, there is

accumulating evidence that salvage treatment of IBTR will not always be successful, and that there seem to be limits for the use of breast-conserving therapy. This, of course, is a challenge to salvage treatments, but naturally also to reconsider optimal selection and optimal initial treatment of such patients.

The prognosis after treatment for IBTR is influenced by a number of factors including patient characteristics at primary treatment, the extent of primary treatment, as well as the time interval from primary treatment to recurrence. Patients with a new primary tumour had a better prognosis than patients with true recurrences [2–4,17,23]. The indicators for a poor prognosis as shown in Table 3 are also true in relation to IBTR, and knowledge about these factors might be helpful when considering adjuvant systemic therapy.

Loco-regional recurrence together with distant metastases

As previously mentioned, about 25% of patients with loco-regional recurrence after mastectomy and about 10% of patients with recurrence after breast-conserving surgery will concurrently have distant metastases. Such patients may not be candidates for extensive curatively intended loco-regional treatment since such treatment will not influence the final survival rates. Loco-regional therapy could be indicated anyway: first, the appearance of loco-regional disease is often very distressing for the patient; second, systemic therapy will seldom eradicate the loco-regional recurrent disease [2]. Limited surgical resection of all loco-regional recurrent tumour tissue would be preferable, on the assumption that this procedure can be included in the overall treatment plan where priority will usually be given to systemic therapy. Radiation therapy should be reserved as palliation for patients with progressive local symptoms.

Patients presenting with diffuse or advanced loco-regional recurrences not eligible for surgery are candidates for systemic therapy. However, such patients often have very painful and unpleasant symptoms (ulcerations, bleeding), which indicate treatment that can offer immediate relief. Patients with tumour infiltration of the brachial plexus will often suffer from severe and progressing pain in addition to neurological deficits. Patients who have not previously been irradiated should be considered for radiation therapy. A dose of 30 Gy in 10 fractions to a limited target area has resulted in significant palliation [24]. However, in patients treated with doses up to 50 Gy in 25 fractions, in general a better response has been reported [2]. The reason for the different outcome could be the fact that severe neurological injury is not reversible, and therefore such patients will need additional analgesic treatment, which may vary in the different studies. In previously irradiated patients with recurrent tumour around the brachial plexus, re-irradiation may not be an attractive solution due to risk of worsening of the nerve injury, but the pros and cons must be balanced on an individual basis.

Recurrent tumour in the upper axilla and periclavicular area can cause severe lymph oedema of the ipsilateral arm. Patients who have not been previously irradiated will respond well to palliative radiotherapy to a limited area [24]. Palliative treatment concurrently or sequentially combined with a systemic endocrine or non-endocrine therapy can often significantly relieve symptoms and stabilise the disease for some time. However, iterative local recurrences and uncontrolled loco-regional disease remain a difficult problem in spite of more effective systemic therapies. Patients with local recurrent disease, even with extensive disease with involvement of the skin and soft tissue of the chest wall, often including the shoulder and the axilla (carcinoma "en cuirasse"), will often survive for a long time. Unfortunately, surgery and/or radiotherapy can only alleviate the symptoms for a limited time period, but not profoundly control the disease once it has reached this stage. Therefore, there is a need to explore how to avoid such loco-regional disease progression. As mentioned, there is evidence that insufficient primary loco-regional treatment as well as insufficient salvage treatment at the time of local recurrence will increase the number of such cases.

Metastatic breast cancer

At the time of occurrence of metastatic disease, most patients will have symptoms from one or more foci of metastatic disease. In such situations, there could be indications for local therapy with surgery and/or radiotherapy. Metastatic breast cancer is a chronic disease, often lasting for years with shorter or longer treatment-induced time periods of remission and repeating relapses. Therefore, local management of focal symptoms and signs will often be needed again and again along with systemic therapy during the course of the disease. Below, the role of local management is described in relation to the most common sites of metastatic disease.

Bone metastases

Bone metastases are a significant problem in breast cancer. More than 80% of patients who die from breast cancer have bone involvement. The most

common site for bone metastasis is in the axial skeleton, most often the spine, but the pelvis and proximal femora are also frequent sites. The consequence of bone metastases is often pain, which leads to impaired physical performance. Further, progression of bone metastases can lead to hypercalcaemia, pathologic fractures, and spinal cord compression, which will further debilitate the patient and could even shorten survival. Surgery is obviously indicated when pathologic fracture has occurred. Thereby rigid fixation of pathologic fractures can be obtained and this again will lead to resumption of ambulation and improved fracture healing. The indications for prophylactic fixation of impending fractures have not been clearly defined. The reason for that is the difficulty to radiographically assess the criteria for impending fractures. Operative treatment for bone lesions in the spine is reserved for patients with bony collapse and instability or vertebral body collapse that results in retropulsion of bone and disc fragments directly into the cord. Advances in spinal surgery have resulted in better methods for stabilisation of vertebral body collapse from metastatic disease, and such surgical procedures are increasingly used in patients with extensive metastases in the spine [25].

However, a majority of patients with bone metastases will not need surgery, but pain and disease control can be obtained with a course of palliative radiotherapy along with systemic therapy. Many women will experience several courses of palliative radiotherapy, and since breast cancer is the most common malignancy in women throughout the world, the total consumption of radiotherapy needed for such treatment is very large. There are several clinical prospective studies evaluating optimal palliative radiotherapy of bone metastases [25,26]. It is shown that significant relief of pain can be obtained in 50–80% of patients. The onset of pain relief occurs within a few days after treatment and reaches its maximum after 2–4 weeks. Several studies have compared short fractionation schedules with longer fractionation schedules, and the conclusion of these trials is that a single treatment of about 8 Gy gives similar response as fractionated regimens in most situations. Therefore, a single fraction dose of 8 Gy is now regarded by many European institutes as the standard palliative treatment for bone metastases. Such treatment is also shown to be acceptable with regard to toxicity, and one single fraction dose is easy to incorporate in between cycles of chemotherapy. However, the subject is still a matter of controversy, and in the treatment of solitary bone metastases and in patients with neuropathic pain due to bone metastases, the optimal dose and fractionation remains to be determined, as does the more frequent use of re-irradiation after a single fraction compared to fractionated radiotherapy. In relation to re-treatment of vertebral metastases, the risk of radiation myelitis is of special concern [26]. However, toxicities in other tissues treated with larger doses and large volumes, as part of the initial treatment (skin, brachial plexus, lung, heart), should also be taken into account when deciding to offer re-irradiation.

CNS metastases

CNS manifestations of systemic cancer are becoming increasingly evident as patients live longer. Intracranical metastases represent the most common site for CNS manifestation. Epidural metastases most often arise from metastases to the vertebral column. Generally, systemic therapy will only have a minor effect on intracranial, leptomeningeal, and spinal cord metastases. However, there is good evidence that significant palliation can be obtained by radiation therapy alone or in combination with surgery. In the treatment of intracranial metastases, radiotherapy is preferable to surgery when widespread metastases occur throughout the body. There are a number of studies of different dose fraction schemes for whole-brain irradiation therapy in such situations. Thus, schedules with a few fractions, 20 Gy in 4–5 fractions or 15 Gy in 2 fractions, compared to 40 Gy in 20 fractions, have a similar response. Since median survival from the time of diagnosis of brain metastases until death ranges from 3–6 months, time is precious, and therefore a short-fractionation scheme would be preferable. In most institutes, such short fractionation schedules have been accepted [27]. Less than 10% of patients are alive one year after diagnosis. Some patients may be candidates for re-treatment, and there are studies showing significant response to a second course of palliative radiotherapy. Both in the initial treatment of solitary brain metastases, and with the need for re-treatment, stereotactic radiosurgery should be considered. Surgical therapy of brain metastases plays a role, especially when a patient recurs with a solitary brain metastasis without distant disease. In these situations, surgery is indicated to verify the diagnosis. If the lesion can be removed completely, surgery could serve as the only treatment. There is evidence, however, that combined surgery and radiation therapy in such patients is superior to surgery or radiation therapy alone [27–29].

Epidural spinal cord compression is a neurological emergency which calls for immediate local management. Because the prognosis for good functional outcome is dependent on the degree of impairment at

the time of treatment, it is important for the clinician to be aware of early symptoms of this disorder. The treatment of epidural cord compression has for many years primarily been decompressive laminectomy, with or without radiation therapy. Such treatment will lead to improvement in symptoms in 30–40% of patients [29]. However, there is also some evidence that radiation alone is as good as laminectomy plus radiation. The question about the efficacy of combined surgery and radiotherapy versus radiotherapy alone has been addressed in a randomised trial [30]. This study concluded that radical direct decompressive surgery plus radiotherapy leads to the regaining of the ability to walk more often than radiotherapy alone. Also, the duration of neurological symptom control was significantly better after the combined treatment.

The development of newer surgical methods as mentioned above now allows resection of the vertebral body in selected patients, and preliminary results of such series have been encouraging. Both in the treatment of brain metastases and spinal cord compression, it is optimal to have a close collaboration between the neurosurgical and oncological teams.

Visceral metastases

The role of local management in the treatment of visceral metastases is usually minor. However, in situations where the patients present with bronchial obstruction, bile duct obstruction or tumour infiltration around intestine or ureters, immediate local therapy is indicated. Different endoscopic and surgical methods are available to give immediate relief and outlet, thereby allowing initiation of systemic therapy to obtain proper regression and stabilisation of metastatic disease.

Occasionally, patients present with a solitary lung metastasis or solitary liver metastasis which has persisted in spite of systemic therapy. Such patients, who otherwise have disease control and are in a good performance status, might be candidates for surgical removal or stereotactic irradiation of residual tumour [29,31]. However, there is no evidence that such complete eradication of residual visible tumour will improve the long-term outcome.

Malignant effusion

Malignant effusion is common in metastatic breast cancer, especially pleural effusion. The local treatment consists of either intermittent drainage with a percutaneous thoracocentesis along with systemic therapy. However, in more resistant cases with continuous re-accumulation of pleural effusion, a more effective local therapy would be thoracotomy and sclerosis. Different chemotherapy agents have been used in the hope that a direct anti-neoplastic effect would be seen. However, several studies have revealed that installation of talc, which causes an intense pleuritis, gives superior results [32].

Pericardial effusion can lead to constrictive or effusive pericardial tamponade and thus result in cardiovascular collapse, and such a situation calls for immediate treatment with percutaneous pericardial drainage. To avoid re-accumulation of pericardial effusion, surgical placement of a pericardial window and pericardial stripping are useful methods.

Ascites can occur either from peritoneal serosal implants or from extensive hepatic metastases. Intermittent drainage of ascites can relieve symptoms. However, without control of the basic tumour, ascitic fluid re-accumulates and it can be difficult to relieve the symptoms.

Interaction of local therapy with systemic therapy

When using a multidisciplinary treatment approach, it is always important to consider immediate and long-term interactions between the different treatment modalities, as well as the toxicity to each treatment. The complexity of these problems is even more pronounced in heavily pretreated patients, which is often the case regarding metastatic breast cancer, and it therefore represents an important challenge and responsibility for the decision-maker.

Conclusions

Loco-regional recurrent breast cancer is a common event and a large number of these patients are potentially curable if they receive appropriate treatment. Although some of the salvage procedures are widely used and regarded as standards (i.e. mastectomy after IBTR), there seems to be a striking lack of good clinical trials which can provide the necessary evidence for precise treatment guidelines. Implementation of new local treatment approaches in the primary setting, such as omitting axillary dissection on the basis of sentinel node technique and increasing use of breast-conserving therapy with reduced or no postoperative irradiation, are expected to increase the number of patients with loco-regional recurrences. Optimal salvage treatment in such situations needs to be defined according to data from prospective clinical trials on this issue.

In patients with metastatic disease there are numerous examples of painful and disabling symptoms,

which can immediately be relieved from local therapy along with effective systemic therapy. Acknowledgement of the benefits and potentials of the use of local therapies in metastatic breast cancer may also inspire further research to clarify the many uncertainties of such treatment modalities along with the trials on systemic therapy.

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