Present status of palliative radiotherapy

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Introduction

Radiotherapy plays a major role in the palliation of symptoms and signs in patients with uncontrolled cancer and should be an important treatment in any comprehensive palliative care programme [1]. Especially cancer-related bone pain, but also neurological deficits resulting from spinal cord compression and brain metastases as well as symptoms from bronchial obstruction, superior vena cava obstruction and other solid tumours can all be palliated effectively with radiotherapy. The aim of the treatment is to relieve and prevent impending symptoms, improve quality of life, and extend survival if possible (Table 1). It has been estimated that approximately 50% of all radiotherapy is given with palliative intent [1–3].

Many factors may influence the decision to give palliative radiotherapy such as expected survival time, severity and length of side-effects, potential hospitalisation for treatment of complications, and possible benefit and cost. Before deciding to give palliative radiotherapy it is important to establish and communicate the treatment goal, to determine the possible cause of symptoms and to consider the complexity of the treatment and patient conditions. If possible the treatment should give maximum benefit with minimum treatment.

A number of surveys among radiotherapists have worldwide shown great variation in the doses as well as fractionation schedules used for palliation [2,4–6]. However, recently an increasing number of prospective studies have been published especially in the treatment of bone metastases, and many cancer centres now base their strategy for palliation on results from these clinical trials rather than on tradition. On the other hand, a number of studies of patterns of practice have indicated that the use of palliative radiotherapy still varies markedly and is influenced by factors unrelated to the patient's needs such as resource limitations and oncology training [1,5,7]. Lievens et al. [8] analysed the impact of the radiotherapy financial system on palliative radiotherapy practice and found that the reimbursement systems indeed seem to influence radiotherapy practice. Thus, an effort is still needed to reduce the barriers for the use of palliative radiotherapy and to educate physicians about its potential benefits [1].

Table 1
The overall aim of palliative radiotherapy

AIM
Relieve pain
Prevent impending symptoms
Improve quality of life
Extend survival if possible

In this paper, the present status of palliative radiotherapy will be reviewed. The paper will primarily focus on palliative radiotherapy in the treatment of bone metastases, but will also discuss briefly its use in patients with spinal cord compression, brain metastases and other symptomatic solid tumours. Evidence-based radiation oncology is of the utmost importance and not least within the area of palliation. With the present data from the increasing number of randomised trials, there is now definite evidence for the use of palliative radiotherapy in patients with cancer-related symptoms. It is the hope that this paper will persuade more doctors to offer the treatment to their patients and thereby allow more patients to benefit from palliative radiotherapy.

Bone metastases

Bone metastases are often the first evidence of disseminated disease in cancer patients, and even though the long-term prognosis is poor, a proportion of the patients may survive for several months or even years (Fig. 1) and will require active treatment for their symptoms [9–12]. The commonest primary sites are the breast, prostate and lung [10,13]. In 75% of the patients with bone metastases pain is the dominant symptom [10]. Some patients develop pathological fractures, hypercalcaemia and spinal cord compres-

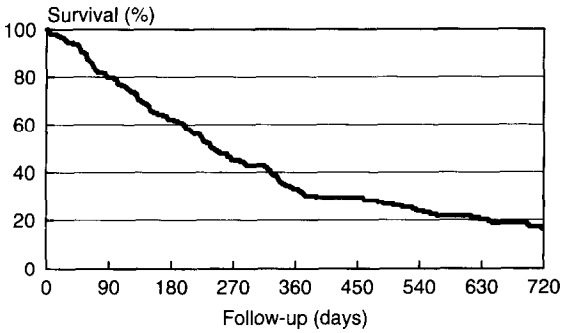

Fig. 1. Typical overall survival curve of patients treated with palliative radiotherapy for painful bone metastases. Based on data from the Danish bone trial [12].

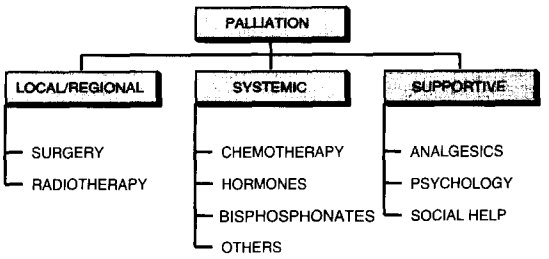

Fig. 2. The palliative treatment of bone metastases requires a broad approach. One or more of these possible treatment modalities should be used.

sion, which will further reduce their quality of life [13].

Treatment of bone metastases with a curative intent is only possible in a few cases, and in most patients the treatment is palliative. Therefore, the aims of treatment will primarily be to relieve pain, prevent the development of pathological fractures, improve mobility and function, and, if possible, to prolong survival. Treatment of bone metastases requires a broad approach (Fig. 2). Reduction of pain is one of the major goals. However, besides analgesics more specific treatments are often needed and among those radiotherapy is very effective, and bone metastases represent one of the most common conditions requiring radiotherapy today. Surgery, chemotherapy, endocrine therapy and bisphosphonates may also be indicated depending on the primary tumour. Social and psychological support is indicated in almost all patients.

Local external radiotherapy

Local radiotherapy of painful bone metastases unassociated with spinal cord compression or pathological fracture is very effective [14,15]. Relief of pain is obtained in the majority of the patients. The onset of pain relief occurs within a few days after treatment and reaches its maximum after 2–4 weeks. A large number of retrospective as well as an increasing number of prospective trials have reported that relief of pain is obtained in 50–80% of the patients, but various criticisms have been raised against these studies [10,11,15–17], i.e. problems related to patient selection, choice of end-points as well as definition of the precise contribution from radiotherapy to other co-interventions like analgesics and psychosocial support. The Radiation Therapy Oncology Group (RTOG) trials highlight the difficulty in controlling the many variables that may influence data evaluation. The original report concluded that there was no relationship between response and the number of fractions used [18]. A subsequent reanalysis of the same data [19], however, did demonstrate an association between the number of fractions and response. In contrast to the initial analysis, patients with solitary and multiple metastases were grouped together and analgesic requirements were included in the pain score.

Several studies have compared short fractionation with long fractionation radiotherapy [12,20–33]. The number of patients included in randomised trials evaluating the effect of single fraction radiotherapy has increased during the last 10 years (Fig. 3), and none of these straightforward two-arm trials (Table 2), comparing single doses with multiple fraction radiotherapy, have shown a difference between the treatment arms [11,12,17,23,26,27,30–33]. Price et al. presented one of the first studies pointing at the use of single fraction radiotherapy [23]. Since then a number of large trials have addressed the question of single fraction radiotherapy encompassing more than a thousand patients, and their findings are remarkably consistent, i.e. no advantage of the fractionated compared with the single fraction treatment (Fig. 4). In most patients, local radiotherapy for painful localised bone metastases can be given as a single treatment

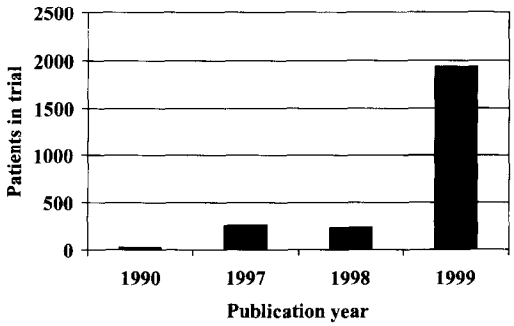

Fig. 3. Number of patients included in randomised-controlled trials of single versus fractionated palliative radiotherapy of bone metastases in the period 1990–99.

Table 2
Phase 3 randomised trials of palliative local radiotherapy in the period 1982–99

First author	Number of pts	Treatment #1	Treatment #2
Tong 1982 [18]	146	4 Gy × 5	2.7 Gy × 15
Madsen 1983 [24]	57	10 Gy × 2	4 Gy × 6
Price 1986 [23]	288	8 Gy × 1	3 Gy × 10
Okawa 1988 [25]	80	4.5 Gy × 5	2 Gy × 10–15
Cole 1989 [26]	29	8 Gy × 1	4 Gy × 6
Hoskin 1992 [27]	270	4 Gy × 1	8 Gy × 1
Rasmusson 1995 [28]	217	5 Gy × 3	3 Gy × 10
Niewald 1996 [29]	100	4 Gy × 4	2 Gy × 15
Gaze 1997 [30]	260	10 Gy × 1	4.5 Gy × 5
Nielsen 1998 [12]	241	8 Gy × 1	5 Gy × 4
Jeremic 1998 [31]	327	4 Gy × 1	6/8 Gy × 1
UK BPT 1999 [32]	765	8 Gy × 1	4 Gy × 5/3 Gy × 10
Steenland 1999 [33]	1171	8 Gy × 1	6 × 4 Gy
Total	3951		

pts, patients.

of about 8 Gy without unacceptable toxicity. Neither did relief duration, analgesic consumption and appearance of new painful sites differ between the single and fractionated regimens. In the latest studies, pain relief was evaluated up to one year post-treatment by the use of validated patient questionnaires [32,33].

In the literature, the reporting of adverse effects has generally been poor [17], but there are no obvious differences between the fractionation schedules studied, at least in the incidence of nausea, vomiting, diarrhoea and pathological fractures. Similarly, in the approximately 20% of patients living more than two years no increase in late morbidity after single fraction irradiation has been reported [12,17,32,33].

Recently, a meta-analysis was presented at the Second Consensus Workshop in Palliative Radiotherapy in London April 2000 (S. Bentzen, Gray Laboratory Cancer Research Trust, Northwood, UK). Single fraction and multiple fraction schedules were shown to be equally effective in reducing pain scores, providing further supporting data that for the majority of patients requiring local radiotherapy for metastatic bone pain unassociated with spinal cord compression or pathological fracture, a single fraction of 8 Gy is an effective and appropriate treatment [15]. There does not seem to be a correlation between the site of the primary and the likelihood of pain relief [12,23,32,33].

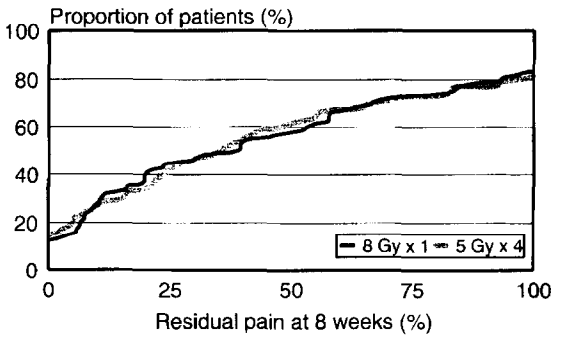

Fig. 4. The proportion of patients having a certain degree of pain at 8 weeks after treatment with either 8 Gy × 1 or 5 Gy × 4. The pain is given as the residual pain, i.e. the relative degree of pain at a given time interval after treatment compared with that measured prior to treatment. No significant difference was seen between the two treatments. Based on data from the Danish bone trial [12].

The importance of the single treatment dose has been studied in two studies. A single fraction of 4 Gy was either compared with 8 Gy [27] or with 6 and 8 Gy [31]. Both studies showed that these lower doses were effective, but the response rates obtained were lower and the relapse rate higher than that of 8 Gy suggesting a dose–response relationship between 4 Gy and 8 Gy.

Patients receiving a single fraction are more likely to have the same site re-irradiated compared with those treated with fractionated radiotherapy (Fig. 5). This higher retreatment rate has been explained by physician preference [12]. In addition, it has been shown that patients, who have responded initially, will have a similar probability of response after re-irradiation [34]. Recently, Jeremic et al. [35] have documented that the majority of those patients having pain relapse will benefit from a retreatment with single fraction radiotherapy. With the short survival expected in this group of patients the use of a single fraction will be a major advantage in palliative treatment by shortening overall treatment time while allowing retreatment in cases of pain recurrence.

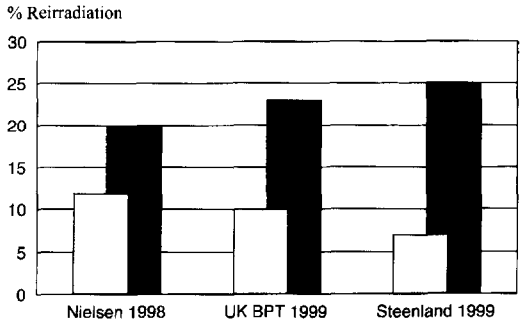

Fig. 5. Frequency of reirradiation in three randomised phase 3 studies: The Danish [12], the UK [32] and the Dutch [33] bone trials. Single fraction (black) and multifraction (grey) radiotherapy.

Unfortunately, there is still some scepticism about the use of single fraction radiotherapy [11,36]. In a review [11] of 12 published reports on randomised clinical trials the authors analysed treatment techniques, patient selection, end-points and data analysis. They concluded primarily based on the original RTOG data that higher dose fractionated regimens are the most effective. However, this analysis has been strongly criticised [37]. Their conclusion was based on extensive data-derived subgroup analysis, as well as on physician-based pain scores. In addition, their attempts to compare the levels of pain relief achieved in different trials are unreliable. Using logistic regression Bentzen et al. (S. Bentzen, Gray Laboratory Cancer Research Trust, Northwood, UK) did not find a significant dose-response by use of the same data. We still need more research into which patients, if any, are unlikely to benefit from local radiotherapy. Also the effect of 8 Gy on pain relief and bone healing beyond 12 months, as well as the management strategy of neuropathic pain in patients with bone metastases need to be further studied.

Wide-field radiotherapy

Most cancer patients have multiple bone lesions. Therefore, the use of half body irradiation (HBI) instead of multiple separate radiation fields has been tested [10,38]. Typically HBI is given as a single fraction of 6–7 Gy to the upper-half of the body or 7–8 Gy to the lower half of the body either alone, or sequentially with a 2–4 week interval [10,38]. Several retrospective studies have reported a useful palliative effect of HBI with partial relief of pain in 55–100% of the patients and complete relief in 5–50% [10,39–41]. The onset of pain relief occurs within 1–14 days of treatment with half of the patients noting pain relief within 48 hours. In more than half of the responding patients the pain relief lasts until death [10].

Administration of effective premedication, (5HT3 antagonists, steroids, hydration), has decreased toxicity considerably [10]. On the other hand, HBI should only be undertaken in centres familiar with the technique since experience is required both for dosimetry of large field treatments and for handling toxicity. With proper premedication it is possible to administer HBI even within the setting of a multicentre study. In a randomised RTOG study [39], local bone irradiation was compared with the same local treatment supplemented with HBI. HBI increased the time to new painful lesions and decreased the number of patients retreated at 1 year. Although HBI increased toxicity, it was acceptable in both treatment arms. Fractionated HBI has been evaluated as a way to further reduce toxicity and eliminate the need for premedication [40,41]. However, fractionated HBI did not seem to be more effective than single dose HBI [40]. With the present knowledge, HBI should be offered to more patients with multiple metastases and especially to patients with prostate cancer.

Radioisotopes

The administration of radioisotopes provides a means of delivering radiation systemically, i.e. Iodine-131 for thyroid cancer and yttrium-90, phosphorus-32 and strontium-89 for breast and prostate cancer [10,38,42]. Radioisotope therapy has been increasingly used in patients with disseminated painful bone metastases. Three randomised studies have tested the effect of strontium-89 [43–45]. In prostate cancer, it seems to give the same degree of pain relief as external irradiation [44] and a reduction in consumption of analgesics and in the development of new pain sites compared with both local and half body irradiation [45]. The toxicity of strontium-89 is acceptable [43–45] and in selected prostate cancer patients it could, despite being very expensive, be a useful alternative or more likely as an adjunct to external palliative radiotherapy. It has been suggested that strontium should be administrated in a higher dose than the 4 mCi recommended by the US government as the response rates obtained with this dose have in general been lower than that obtained in the randomised study with a dose of 10.8 mCi [36]. However, better-designed prospective studies are required before strontium-89 can be recommended in the clinical routine. It seems to be very important to select the right patients for the treatment: patients with very advanced bone disease rarely benefit from the treatment [15].

Phosphorus-32 has previously been evaluated extensively for palliation of diffuse bone pain, but due

to severe haematological toxicity its use is very limited [10]. Samarium-153 seems to provide a safe and effective treatment of bone metastases [46,47], but further data are needed. Rhenium-186 is another isotope under phase 2 and 3 investigation [48].

Mechanisms of pain relief after radiation

An unresolved, but important question is the relationship between pain relief, bone healing and tumour response after radiotherapy. However, this question is difficult to answer as long as the biological basis of pain relief from radiotherapy is unknown. The effect cannot be due entirely to tumour cell killing and shrinkage of macroscopic tumour, as this mechanism is unlikely to account for the pain relief which may occur within 48 hours of irradiation and after single doses as low as 4 Gy [38]. Similarly, the duration of response beyond 1 year after a single fraction of 8 Gy [32,33] is inconsistent with the expected short tumour growth delay at this dose. The pain relief in patients who respond quickly may be caused by a cytotoxic effect on normal bone cells, including macrophages and osteoclasts, thereby inhibiting the release of chemical mediators of pain [10,38]. Data have indicated that pain relief may be related to markers of osteoclast activity [32,49], which may also explain the pain-relieving effect of the bisphosphonates on bone metastases, being a chemical osteoclast inhibitor. On the other hand, in some patients pain relief is not achieved until 2–8 weeks after treatment, an interval which may indicate that some degree of killing and lysis of tumour cells may also be involved [10,12]. Obviously more data is needed.

Evaluation of response of bone metastases

Some of the criteria used to evaluate the response of bone metastases to treatment are listed in Table 3. The traditional biochemical and radiological methods may be poorly correlated with the clinical well being of the patient and are therefore of limited value for assessment of the results of palliative treatment of bone metastases. The primary aim is relief of symptoms and this is the context within which treatment should be judged. Symptoms are, by definition, subjectively experienced by the patient and, therefore, cannot be assessed without actively involving the patient [10,15,37,50].

There are a variety of potentially useful methods for evaluating pain and quality of life, all being tested for reliability, validity and responsiveness as well as acceptability [10]. The most used are those being simple and easily understandable based on linear analogue (LASA) scales, categorical scales, analgesic scores, and symptom checklists like the Rotterdam check list and European Organization for Research and Treatment of Cancer (EORTC) core 30 questionnaire [10,51]. Categorical and LASA pain scales give concordant results, whereas there may not be a clear-cut correlation between pain relief and quality of life in these patients (Fig. 6).

The primary response can be scored by various methods. Some studies have incorporated the analgesic consumption and/or quality of life in the response definition. The problem of defining response is illustrated in Fig. 7 showing that the complete response rate dropped after having incorporated analgesic consumption. If also quality of life was incorporated it dropped further (data not shown). Finally, the timing of response scoring is critical as illustrated by a markedly different response rate if scored at any time during the posttreatment follow-up or at a predetermined time interval (Fig. 7). A comparison of pain relief across the various trials on palliative radiotherapy could be dangerous and presently the international radiotherapy societies American Society for Therapeutic Radiology and Oncology (ASTRO) and European Society for Therapeutic Radiology and

Table 3
Criteria for evaluation of response to palliative local radiotherapy of bone metastases

Response criteria
Pain relief
Quality of life
Clinical examination
Radiology/scintigraphy
Biochemistry
Histology (biopsy)

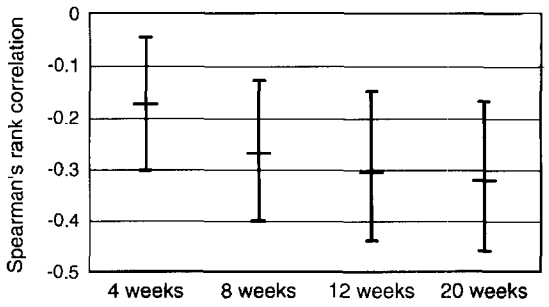

Fig. 6. The correlation between pain score and quality of life at 4 to 20 weeks after palliative radiotherapy. The analysis was based on data from 177 patients. Although the correlation seemed to be improved with increased post-treatment interval, no significant correlation was demonstrated. Based on data from the Danish bone trial [12].

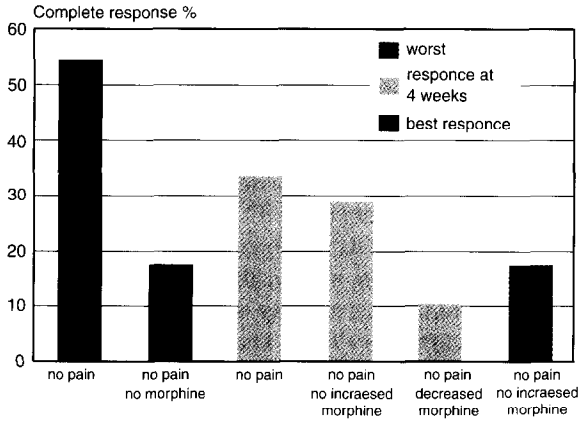

Fig. 7. The complete response rate after palliative radiotherapy of bone metastases as a function of timing of the response scoring: The worst score at any time, the best score at any time or at 4 weeks. The importance of incorporation of analgesic consumption (no morphine, increased morphine or decreased morphine) as well as quality of life (QoL) in the response definition is also illustrated. Based on data from the Danish bone trial [12].

Oncology (ESTRO) have set up a consensus group with the aim of obtaining an international standardisation of outcome measures. Hopefully this effort will be a success creating a standard set of outcome measures to be used in future studies on palliative radiotherapy.

Conclusion: radiotherapy of bone metastases

In a recent Cochrane analysis [52] it was concluded that radiotherapy is clearly effective in reducing pain from painful bone metastases and that there is no evidence of any difference in efficacy between different fractionation schedules. For treatment of generalised bone pain both hemibody irradiation and radioisotopes can reduce the number of painful new sites. The same conclusions were supported at the Second Consensus Workshop in Palliative Radiotherapy in London in April 2000 [15]. In the absence of any evidence for the superiority of multiple fractions in otherwise unselected patients with bone pain, the choice should be simple. With the present data most patients with uncomplicated metastatic bone pain should be treated with single dose radiotherapy. Since single dose radiotherapy is a very simple treatment schedule it should be available and offered to all patients with uncomplicated metastatic bone pain, and this treatment schedule will then allow more patients to benefit from palliative radiotherapy.

Spinal cord compression

Lesions in the spine can be managed provided that there is no neurological deficit or evidence of bony instability. However, once bony erosion jeopardises stability, then internal or external fixation may be needed [10]. Signs of developing spinal cord compression require urgent treatment [53]. More than 90% of the patients have a history of back pain, with or without a radicular component, which gradually intensifies and is associated with increasing neurological symptoms [10,53–55]. Despite the relatively subacute clinical course, less than half of the patients are able to walk at the time of initial evaluation. Thus early diagnosis is crucial. The majority of patients who are ambulatory at the time of treatment retain that ability. However, many patients are seen at later stages and the functional outcome is usually poor, regardless of which treatment is selected. In many series only about half of the patients either maintain or regain the ability to walk [10,54].

The optimal treatment of spinal cord compression is controversial: primary surgery or primary radiotherapy? The controversy stems from the lack of controlled clinical studies for directly comparing treatment modalities and an absence of standard criteria for evaluating response. The current approach incorporates the use of either radiotherapy alone or surgery often followed by postoperative radiation at least in cases of remaining pain. It is generally accepted that surgery should be used when patients have an unknown tissue diagnosis, when radioresistant tumours are involved, when patients have a fracture-dislocation of their vertebrae, and when the level of cord compression is in an area previously irradiated [10,53]. Patients with radio- or chemosensitive tumours should initially be managed with these modalities alone. However, these guidelines apply to only a minority of the patients, and the optimal treatment for the majority of patients with cord compression is unknown. The chosen treatment has often depended upon which speciality first sees the patient, and no firm recommendations are possible based on the present data.

The traditional aim of surgery in patients with cord compression has been decompression of the spinal canal by a posterior laminectomy and, occasionally, posterior stabilisation [10,53]. Recently, the efficacy of this treatment has been questioned, and several reports have described superior results with an anterior approach to the affected vertebrae, with removal of all gross disease and vertebral body reconstruction in selected patients [10]. If postoperative radiation is indicated a dose of 20–30 Gy given in 4–10 fractions has normally been used, but the

optimal dose has not yet been established [10,53,55]. Recently, short-course radiotherapy was shown to give a clinical outcome comparable with that resulting from more protracted regimens [55]. Thus, the use of a few large radiation fractions should be explored in future studies.

Brain metastases

The brain is a common site of metastases especially in patients suffering from lung, breast, kidney, and colon–rectum cancer as well as malignant melanoma [56]. The treatment of brain metastases has recently been discussed at the Second Consensus Workshop in Palliative Radiotherapy in London in April 2000 [57]. Possible treatment modalities include surgery, radiosurgery, radiotherapy and chemotherapy. Chemotherapy should be considered in patients with chemosensitive primaries. Initial treatment will often include corticosteroids. Because of their unfavourable prognosis, the standard treatment of patients with multiple brain metastases is palliative whole brain irradiation.

Many outcome measures have been used to measure the effectiveness of palliative radiotherapy of brain metastases, but at present there is no agreed criteria for response. The most important and most frequently reported endpoint is the relief of specific neurological symptoms, whereas quality-of-life has been measured in only a few studies [58]. The major radiation effect on brain metastases is an improvement of specific neurological symptoms. The expected effect will depend on the neurological function at the time of initiation of the radiotherapy [56]. In order to select the right group of patients for treatment, it is important to define clear pretreatment criteria based on factors such as performance status, age and active extracranial malignancy [57,59].

In patients with solitary metastasis, the primary treatment is either surgical excision or radiosurgery. For operable lesions, the two treatments are considered equivalent but they should be reserved for the patients in good condition and with well-controlled systemic disease and a metastasis in an easily accessible location [56,57]. Whether surgery should be combined with radiotherapy has not been settled. In patients with multiple brain metastases, whole brain radiotherapy is indicated. Based on the RTOG and the UK trials [57] 12 Gy/2 fractions should be considered for patients with a likely poor prognosis, whereas 20 Gy/5 fractions or 30 Gy/10 fractions should be considered standard treatment for patients with a more favourable prognosis.

Other symptomatic solid tumours

The number of phase 3 trials on palliative radiotherapy of other symptomatic tumours is much smaller than those on the treatment of bone metastases. However, the number has been increasing especially for the treatment of lung cancer.

Inoperable non-small cell lung cancer (NSCLC)

The strategy of radiotherapy of inoperable NSCLC differs significantly worldwide [60], both in the interpretation of the published data and in the approaches to treatment (Table 4). The strategy varies from a more radical attitude to treatment with the use of tumour doses of 50–60 Gy to a much more conservative policy of no immediate treatment or radiotherapy using one or two fractions. There is still a need for better-controlled clinical trials, but the present data from a number of randomised trials have in general shown no benefit from prolonged treatment regimens in palliating symptoms from NSCLC [61].

In the present paper, only palliative radiotherapy of patients with unfavourable stage 1–3B and all stage 4 NSCLC will be discussed. At the Second Consensus Workshop in Palliative Radiotherapy in London in April 2000, it was agreed that the intention of treatment in this group was palliation only [60]. For those with a better performance status, chemotherapy with or without local irradiation, may be appropriately based on the results of a meta-analysis demonstrating a 10% survival advantage at one year when compared with best supportive care [62]. However, given the uncertainty of response and the possible toxicity, chemotherapy should only be given within the confines of a carefully monitored study or a randomised clinical trial [60].

For patients with poor performance status and no or only minimal symptoms, there does not seem to be an advantage for immediate compared with delayed

Table 4
A survey of treatment strategy of NSCLC in Europe, Canada and USA. A total of 644 radiation oncologists responded to a questionnaire regarding the management of a 59-year-old man with a squamous cell carcinoma of the bronchus and mediastinal nodes. Data modified from Maher et al. [4]

	Europe	Canada	USA
Total dose (Gy)	56 (8–75)	40 (20–60)	60 (30–73)
No. fractions	28 (1–37)	15 (5–30)	32 (10–60)
Aim: Palliative	47%	69%	39%
Extend life	69%	37%	92%

NSCLC, non-small cell lung cancer.

irradiation and in the supportive care group, half of the patients die without the need for radiotherapy [60,63]. For those patients with symptoms, one or two fraction schedules such as 10 Gy × 1 or 8.5 Gy × 2 seem to be equivalent to more prolonged, higher dose regimens both in terms of symptom control and survival, but with a reduced risk of acute morbidity. At present, it is increasingly difficult to justify the use of more prolonged treatment regimens of palliative radiotherapy [60,61]. However, it is also apparent that much further work is required especially in the selection of patients for treatment. The need for radiotherapy is influenced by the particular symptoms present. Using relief assessment by the patients themselves, Rees et al. [61] demonstrated that haemoptysis and chest pain were the symptoms with the greatest chance of improvement, whereas improvement of other symptoms was slight. In patients with recurrent, persistent or new primary lung tumours, a recent study has indicated that reirradiation may be effective in palliating haemoptysis, pain, cough and dyspnoea [64]. The use of endobronchial brachytherapy as a palliative treatment option has also been tested, but seems to be inferior to external radiotherapy [65].

Superior vena cava syndrome

Almost all patients with superior vena cava syndrome have lung cancer, but a histological diagnosis is important to rule out the more successfully treated cancers [63]. Superior vena cava syndrome is the clinical expression of obstruction of blood flow through the superior vena cava. There is the possibility of the coincident occurrence of pulmonary embolism that may simulate progressive cancer. Palliative radiotherapy has been advocated as being the standard treatment for most patients with superior vena cava syndrome. As with lung cancer, conventional prolonged irradiation or large daily doses seem to produce similar results: 75% of the patients improve symptomatically [63].

Other symptomatic tumours

Choosing the optimal palliative treatment strategy for other symptomatic tumours such as tumours in uterus, bladder, oesophagus, colon–rectum, and skin is difficult due to the lack of controlled clinical trials. Many patients with visceral recurrences and metastasis will suffer from symptoms like pain, bleeding and obstruction [63]. Patients accepted for palliative irradiation should have symptoms and physical findings that correlate with the results of the imaging study and because there is no sound scientific evidence that irradiation for all metastases is effective, it is important to inform the patients about this uncertainty [63].

With the increasing support of using short treatment schedules in the palliative radiotherapy of bone and brain metastases as well as in NSCLC, the use of similar schedules in the treatment of other symptomatic tumours should be further evaluated. Until these data are available various treatment schedules are likely to be used, i.e. 8 Gy × 1, 4–5 Gy × 4–5, 3 Gy × 10 and in some cases, even higher doses depending on the site and volume to be irradiated.

Conclusion

Radiotherapy plays a major role in the palliation of patients with uncontrolled cancer and is important in any comprehensive palliative care programme. With the data from randomised clinical trials, there is definite evidence for its use in patients with cancer-related symptoms. Especially cancer-related bone pain, but also neurological deficits resulting from spinal cord compression and brain metastases, as well as symptoms from bronchial obstruction, superior vena cava obstruction and other solid tumours can all be palliated effectively with radiotherapy. Most patients with uncomplicated metastatic bone pain can be treated with single dose radiotherapy. Since single dose radiotherapy is a very simple treatment schedule it should be available and offered to all patients with uncomplicated metastatic bone pain, and this treatment schedule will then allow more patients to benefit from palliative radiotherapy. Many patients with other cancer-related symptoms are also likely palliated effectively with short radiotherapy schedules, but there is a need for more controlled clinical trials addressing this important question. In addition, future studies need to define better criteria for selecting the right patients for a given treatment and to create standardised outcome measures.

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