

# PALLIATIVE IRRADIATION OF BONE METASTASES: PATTERNS OF CARE WITH FOCUS ON SINGLE FRACTION TREATMENT

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## SUMMARY

**Objectives:** To evaluate the pattern of care in a large consecutive series of patients irradiated for bone metastases in one institution.

**Materials and method:** This series included 1754 bone metastases in 1165 patients treated between 1995 and 2002. The proportion of lesions assigned to one fraction or to fractionated radiotherapy was assessed in relation to periods of treatment and to clinical variables.

**Results:** Single fraction irradiation (8 Gy or 10 Gy) was applied in 327 locations (19%). The proportion of patients treated with one fraction was 28% in 2001-2002 as compared to 15-20% in previous periods ( $p < 0.01$ ). Single fraction was used more frequently in metastases to ribs (28%) and to long bones (21%) than in other locations (6-19%), and for small vs. large fields ( $p < 0.01$  for both comparisons). Lung and breast cancer patients were administered single fractions more frequently than prostate and renal cancer patients ( $p < 0.04$ ).

**Conclusion:** Despite clinical evidence of its efficacy, the use of a single fraction regimen in palliative radiotherapy of bone metastases has been increasing relatively slowly. This method is applied more frequently in patients with poor prognosis, in metastases to long bones and to ribs, as well as for small radiotherapy fields. Given the scarce resources of radiotherapy in Poland and satisfactory efficacy of single-fraction irradiation, this schedule should be recommended for wider use.

**Key words:** palliation, radiotherapy, bone metastases.

## INTRODUCTION

Bones are the most common location of metastases from malignant tumours and occur in 60-80% of patients dying from cancer [1]. Bone metastases frequently accompany breast cancer, lung cancer, renal cancer, thyroid cancer and malignant melanoma. In breast cancer, bone lesions are typically of osteolytic type, rarely mixed (osteolytic-osteoblastic) or osteoblastic [2], whereas in prostate cancer prevail osteosclerotic lesions. The areas most often affected by metastases are spine, pelvis, ribs, proximal epiphyses of femur and humerus [3]. Skeletal metastases are frequently associated with severe pain and pathological fractures. Vertebral fractures may lead to spinal cord compression and cause severe neurologic deficits, whereas multiple bone metastases may cause a life-threatening hypercalcaemia. Over 60%

of patients with bone metastases experience severe pain requiring treatment [4]. There is no correlation between intensity of pain caused by bone metastases and type of neoplasm, size or number of metastases [5].

Palliative treatment of bone metastases includes radiotherapy, endocrine therapy, chemotherapy, bisphosphonates and analgetic agents. Irradiation is highly effective in terms of pain relief and prevention of pathological bone fractures [6]. Traditionally, most commonly used radiotherapy schedules included 20 Gy in 4-5 fractions or 30 Gy in 10 fractions. More recently, numerous randomized clinical trials demonstrated that a similar pain-relieving effect can be obtained by the application of 8 Gy or 10 Gy in a single fraction [4, 7-10]. In this study, we analyzed the pattern of palliative bone metastases irradiation in a large consecutive series of pa-

tients treated in one institution, with particular focus on the use of one-fraction regimens.

## MATERIAL AND METHODS

This retrospective analysis included the records of 1754 painful bone metastases irradiated between 1995 and 2002 in 1165 consecutive patients admitted to the Department of Oncology and Radiotherapy, Medical University of Gdansk. The most common types of malignancies were breast cancer (n=621; 35%), lung cancer (n=334; 19%), prostate cancer (n=296; 17%), and renal cancer (n=174; 10%; *tab. 1*). In the statistical analysis, the chi-square test was used to compare categorical variables, and the non-parametric Mann-Whitney U test to compare continuous variables.

## RESULTS

Single fraction irradiation (8 Gy or 10 Gy) was used in 327 locations (19%). The proportion of patients irradiated in years 1995-2002 with one fraction varied between 15% and 28%. The proportion of patients administered one fraction in 2001-2002 was higher than in previous periods ( $p < 0.01$ ; *fig. 1*). The median number of radiotherapy fractions in the entire group was 5 (range, 1-25), and the median total dose was 24 Gy (range: 2-48 Gy).

Single fraction irradiation was used most often in metastases to ribs (28%) and to long bones (21%) as compared with other locations ( $p < 0.01$ ; *tab. 2*). One fraction was used most rarely for the irradiation of the cranium (6%). The median field sizes for one-fraction irradiation and fractionated therapy were 127 cm<sup>2</sup> and 144 cm<sup>2</sup>, respectively ( $p < 0.01$ ). One-fraction irradiation was used more often in bone metastases from lung cancer (22%) and from breast cancer (19%), as compared with those from prostate cancer (16%) and renal cancer (13%;  $p = 0.04$ ).

## DISCUSSION

The equivalence of single-fraction and fractionated radiotherapy for bone metastases was demonstrated in a series of randomized studies [4,7-10]. Nielsen et al [7]

in a series of 241 patients did not find any differences in the degree and duration of pain relief and the number of new painful sites between 8 Gy in one fraction and 20 Gy in four fractions. The results of a trial performed by the Bone Pain Trial Working Party are very similar [9]. Pain control, duration of pain relief and quality of life were analysed by Gaze et al [10] in a clinical trial including 280 patients. The aim of that study was to compare the efficacy, side effects, quality of life and performance status associated with two radiotherapy schedules of painful bone metastases - a single fraction of 10 Gy and 22.5 Gy in five fractions. Again, differences between groups were not statistically significant. Most recently, a Polish randomized study demonstrated that a single fraction of 8 Gy is as safe and effective as 20 Gy in 5 fractions in palliative irradiation of bone metastases [4]. Another problem is re-irradiation of painful bone metastases following single fraction radiotherapy. Jeremic et al [11] demonstrated that reirradiation with a single-fraction of 4 Gy was effective and non-toxic management after previous single-fraction radiotherapy.

Although single fraction radiotherapy is now recommended for routine use in European institutions [12], its implementation into practice vary for a number of reasons including institutional and national policies, as well as reimbursement systems [13]. Radiotherapy is considered a relatively expensive discipline, due to a very sophisticated equipment and facilities needed. On the other hand, the exclusive cost of treatment, particularly in palliative setting and on out-patient basis, is limited.

The results of our study indicate that the selection of an irradiation technique depends on the location of the primary tumour - single fraction was used most frequently in metastatic lung cancer, which carries a particularly poor prognosis. The therapeutic decision is also influenced by the location and size of the radiotherapy field. Single-fraction irradiation is used more often in metastases to ribs and long bones, as well as for smaller fields.

The optimal application of this technique in particular clinical situations warrants further clinical research.

In summary, single-fraction radiotherapy of bone metastases is strongly supported by the results of clinical trials [4,7-10]. Furthermore this technique is easy to administer, inexpensive and comfortable for pa-

tients. Its application should particularly be encouraged in Poland, given the scarce resources of radiotherapy equipment in this country.

Table. 1. Distribution of bone metastases according to the primary tumour location.

Primary tumour	Number of lesions (%)
Breast	621 (35)
Lung	334 (19)
Prostate	296 (17)
Renal	174 (10)
Unknown primary site	92 (5)
Colorectal	34 (2)
Bladder	31 (2)
Malignant melanoma	25 (1)
Stomach	17 (<1)
Uterine	16 (<1)
Other	98 (6)

Table 2. Distribution of single-fraction irradiation according to the location of bone metastases.

Area	Number of lesions	Number of one-fraction applications (%)
Spine	732	119 (16)
Pelvis	447	82 (18)
Ribs	190	54 (28)
Long bones	169	35 (21)
Cranium	31	2 ( 6)
Other	184	35 (19)

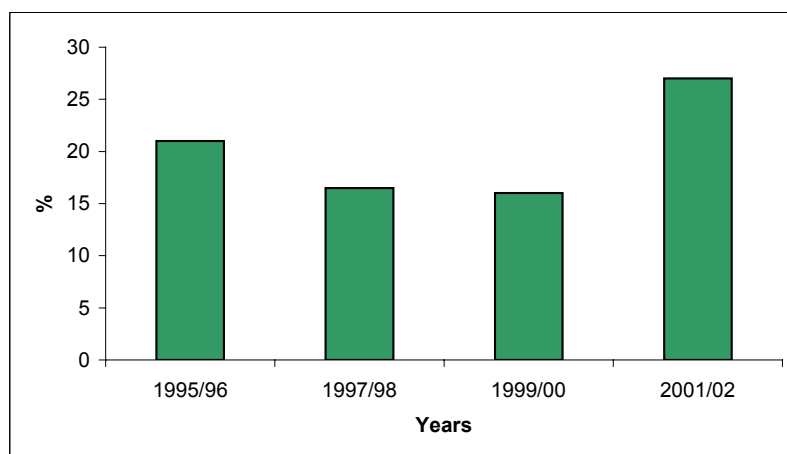


Fig. 1. The percentage of patients irradiated with one fraction in years 1995-2002.

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