

Value of High-dose Radiation Therapy for Isolated Osseous Metastasis in Breast Cancer in Terms of Oligo-recurrence

YUZURU NIIBE¹, MASARU KURANAMI², KEIJI MATSUNAGA¹,
MAMIKO TAKAYA¹, SATOKO KAKITA¹, TOSHIMASA HARA¹,
KENJI SEKIGUCHI³, MASAHIKO WATANABE² and KAZUSHIGE HAYAKAWA¹

Departments of ¹Radiology and ²Surgery, Kitasato University School of Medicine,
1-15-1, Kitasato, Sagamihara, Kanagawa 228-8555;

³Department of Radiation Oncology, St. Luke's Hospital, 9-1, Akashi-cho, Chuo-ku, Tokyo 104-8560, Japan

Abstract. *Background:* For many years, patients with recurrent or distant metastatic cancer have been considered to be at the last stage of their lives because it was considered that the cancer had spread throughout the whole body. However, the development of methods for the early detection of recurrence or distant metastases allows the detection of limited site recurrence or single organ metastases, called oligometastases or oligo-recurrence. Additional local treatment for oligometastatic or oligo-recurrent lesions such as radiation therapy could be efficacious. The purpose of the current study was to evaluate radiation therapy for solitary osseous metastasis of breast cancer in terms of oligometastasis and oligo-recurrence. *Patients and Methods:* One hundred and thirteen breast cancer patients were treated with radiation therapy for osseous metastases at Kitasato University Hospital, Japan between January 1998 and March 2003. Out of them, seven patients had solitary osseous metastases with primary and other sites controlled. These patients were registered in the current study, three had lumbar spine metastases, three pelvic and one thoracic spine. The median time between the initial treatment of the primary lesions and diagnosis of the osseous metastases was 44 months (range: 10-95 months). The median total radiation dose was 46 Gy (30-50 Gy; BED: biological effective dose, 39-60 Gy₁₀). *Results:* The median follow-up time was 40 months (range: 11-80 months). All the patients were alive at the last follow-up. Only one patient relapsed in terms of

pain from the osseous metastasis. This patient was treated with 30 Gy (BED 39 Gy₁₀) irradiation, the lowest total dose among the seven patients. *Conclusion:* Radiation therapy for solitary osseous metastasis might be efficacious and moreover, high dose could be useful for long-term pain relief of osseous metastasis.

For many years, patients with recurrent or distant metastatic cancer have been considered to be at the last stage of their lives because it was considered that the cancer had spread throughout the whole body via the hematogenous route. However, the development of methods for early detection of recurrence or distant metastases, such as computed tomography (CT), magnetic resonance imaging (MRI), positron-emission tomography (PET) and serum biochemical markers for anticancer antigens, allows the detection of limited site recurrent or single organ metastatic cancer, called oligometastasis (1) or oligo-recurrence (2, 3).

Oligometastasis was first reported by Hellman *et al.* in 1995 (1). The concept of oligometastasis suggested that local treatment such as radiation therapy or surgery of one or several distant metastatic or recurrent carcinogenic lesions could be efficacious for survival. In 2006, Niibe *et al.* proposed oligo-recurrence, more strictly defined criteria of oligometastasis, in which one or several metastatic or recurrent lesions occurred with controlled primary lesions, the local treatment of which could be efficacious for survival (2, 3). The latter definition ruled out patients with failure of primary lesions, making strict evaluation of survival possible.

The purpose of the current study was to evaluate the significance of radiation therapy for solitary osseous metastasis of breast cancer in terms of oligo-recurrence.

Patients and Methods

One hundred and thirteen breast cancer patients were treated with radiation therapy for osseous metastases at Kitasato University Hospital, Japan between January 1998 and March 2003. Out of them,

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Correspondence to: Yuzuru Niibe, MD, Ph.D., Department of Radiology, Kitasato University School of Medicine, 1-15-1, Kitasato, Sagamihara, Kanagawa 228-8555, Japan. Tel: +81 42 778 8111, Fax: +81 42 778 9436, e-mail: joe-n@hkg.odn.ne.jp

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Table I. Patient characteristics.

Age at the recurrence (years)	44-73 (median: 56)
Time to recurrence (months)	10-95 (median: 44)
Recurrent site (n)	
Lumbar spine	3
Pelvic bone	3
Thoracic spine	1
Total dose (Gy)	30-50 (median: 46)
Biological effective dose (BED; Gy ₁₀)	39-60 (median: 55.2)
Overall treatment time (OTT; days)	14-36 (median: 36)

Table II. Treatment outcomes.

Pt No.	Start of initial RT	Diagnosis of recurrence	Site of recurrence	Total radiation dose	Pain	Outcome
1	3.15.95	2.25.03	Lumbar spine	40 Gy (48 Gy ₁₀)	Controlled	Alive
2	10.20.97	4.22.02	Lumbar spine	30 Gy (39 Gy ₁₀)	Relapsed (11.2005)	Alive
3	11.22.96	3.13.01	Pelvic bone	50 Gy (60 Gy ₁₀)	Controlled	Alive
4	11.24.95	1.11.99	Lumbar spine	40 Gy (48 Gy ₁₀)	Controlled	Alive
5	4. 5.96	12.9.99	Pelvic bone	50 Gy (60Gy ₁₀)	Controlled	Alive
6	9.11.01	12.20.02	Pelvic bone	40 Gy (48 Gy ₁₀)	Controlled	Alive
7	11.28.02	9. 1. 03	Thoracic spine	46 Gy (55.2 Gy ₁₀)	Controlled	Alive

seven patients had solitary osseous metastases with primary and other sites controlled. These patients were registered in the current study. The characteristics of these patients are listed in Table I.

Radiation therapy was performed using one port postero-anterior field for the spine and 2 ports antero-posterior parallel opposed fields for the legs and pelvic bone. The energy of radiation therapy was 6 or 10 MV X-rays.

Results

The patient outcomes are listed in Table II. The median total dose was 46 Gy (range; 30-50 Gy). The median BED was 55.2 Gy₁₀ (range; 39-60 Gy₁₀) if α/β of 10 was applied. The median follow-up time was 40 months (range; 11-80 months).

All the patients were alive at the last follow-up. Only one patient had a pain relapse although she was free from pain for 40 months after the radiation therapy for osseous metastasis. This patient was treated with a total of 30 Gy (BED 39 Gy₁₀) irradiation, the lowest total dose among the seven patients.

Discussion

Recently, 8 Gy per fraction radiation therapy for painful osseous metastases has been reported to be sufficient (4-8). The RTOG study of the palliation of symptomatic osseous metastases concluded that the total dose and fractionation had no impact on the pain relief of osseous metastases in 1982 (9). This study indicated that 40.5 Gy in 15 fractions

was equal to 20 Gy in 5 fractions if the osseous metastasis was solitary and, moreover, that 30 Gy in 10 fractions, 15 Gy in 3 fractions, 20 Gy in 5 fractions and 25 Gy in 5 fractions were equal to each other if the osseous metastases were multiple. RTGO9714, a recent phase III study regarding prostate cancer and breast cancer with osseous metastases, revealed 8 Gy per 1 fraction was equal to 30 Gy in 10 fractions for the pain relief of osseous metastases (10). However, these studies have given rise to many problems for practice.

Firstly, the RTOG in 1982 and others are old studies and the concepts of oligometastases and oligo-recurrence, and results of recent improvements in diagnostic imaging and serum-anticancer agents had not been proposed at that time. In addition, because the patients in these studies were often given prognoses worse than those given to patients with oligometastases and oligo-recurrence, short-term pain relief alone was the goal of the older studies. Moreover, the recent phase III RTOG 9714 study evaluated pain relief of the osseous metastases at three months after the irradiation. In the current study, the oligo-recurrence patients have survived beyond 10 months. Therefore, a three-month symptom-free period is meaningless and longer symptom-free periods must be evaluated. The survival benefit of high-dose radiation therapy for osseous metastases, however, has not been clarified in the current study, since the long periods of survival were largely due to chemotherapy. However, it was suggested that high-dose irradiation could give patients long-

term pain relief and contribute to maintaining quality of life for an extended period.

The number of the patients in the current study was limited. Larger studies will be required to evaluate the precise usefulness of high-dose radiation therapy for solitary osseous metastasis of breast cancer in terms of oligo-recurrence.

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