VALUE IN HEALTH REGIONAL ISSUES 12C (2017) 84–89

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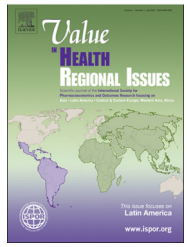

# Cost-Utility Analysis of Single-Fraction Versus Multiple-Fraction Radiotherapy in Patients with Painful Bone Metastases: An Iranian Patient's Perspective Study

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ABSTRACT

**Objectives:** To evaluate two of the various treatment strategies of bone metastasis— single-fraction radiotherapy and multiple-fraction radiotherapy. **Methods:** A multistage Markov decision model was applied to assess the incremental costs per quality-adjusted life-year (QALY) gained of single fraction against multiple fractions. The model had a monthly cycle length over a lifetime horizon with 1000 hypothetical cohort samples. The EuroQol five-dimensional questionnaire was used to estimate the health-related quality of life in patients. To cope with parameters of uncertainty, we conducted a probabilistic sensitivity analysis using a Monte-Carlo simulation technique. Both cost and utility variables were discounted by 3% in the base model. Strategies were assessed considering a willingness-to-pay threshold of US $6578 per QALY gained. **Results:** The expected mean cost and quality-adjusted life-years were, respectively, US $447.28 and 5.95 months for patients receiving single-fraction radiotherapy and US $1269.66 and 7.87 months for those receiving multiple-fraction radiotherapy. The incremental cost-utility ratio was US $428.38 per QALY. Considering the Iranian gross domestic product per capita (US $6578) as the recommended willingness to pay for 1 QALY gained, the multiple-fraction method was found to be a cost-effective strategy. **Conclusions:** Policymakers should advocate the multiple-fraction method instead of the single-fraction method in the treatment of patients with painful bone metastases.

*Keywords:* bone metastasis, cost-utility analysis, Markov modeling, Monte-Carlo simulation, radiotherapy.



## Introduction

Cancer is one of the leading causes of mortality in the world with an increasing trend of prevalence. So it is important to increase the financial resources of the health system for cancer care [1].

Cancers are the third leading cause of death in Iran after cardiovascular diseases and accidents. Because of the growing number of patients with cancer across the world, and even in Iran, today, cancer is a major problem for health systems. Furthermore, the growing death rate is the reason for more than 12% of deaths. Statistics show that the annual incidence of cancer in Iran is more than 70,000 [2], and more than 35,242 people die from cancers yearly [3]. With an increase in life expectancy and in the proportion of the aging population in Iran, it is expected that the prevalence of cancer will be doubled in the next two decades [4].

Approximately 60% of patients with cancer will experience metastasis during their illness [5]. Bone metastasis occurs in 70% of patients with prostate cancer and 30% of patients with lung, bladder, and thyroid cancers. This complication involves severe pain, metastatic spinal cord compression, pathological fractures, limitation in walking, drowsiness, and a significant decrease in quality of life [6]. A number of palliative treatments are available for treating bone metastatic cancer, including local therapy (external beam radiotherapy), systemic therapy (chemotherapy, systemic radionuclides, or bisphosphonates), and conservative treatment with pain medication. Palliative treatment choices depend on the cancer type and stage, the patient's age and health status, and the physician's discretion [7–9].

Patients with metastatic cancer need to be evaluated immediately for radiotherapy treatment because of the following reasons:

Conflicts of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

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2212-1099$36.00 – see front matter 

http://dx.doi.org/10.1016/j.vhri.2016.10.004

1. The bone pain caused by metastatic cancer is one of the most common syndromes that require treatment.
2. Patients with bone metastasis have more survival time than do those with visceral metastasis and so they experience disease complications for a longer time.
3. These patients have longer trouble and discomfort time than do patients with liver or lung metastasis and the disease develops earlier.
4. Bone metastasis complications are common (in one-third of patients) and will lead to severe disabilities.
5. Many problems are associated with the care of these patients [10–12].

In the past two decades, clinical evidence suggested that short-term treatment strategy or single radiation therapy (SRT) and long-term treatment strategy or multiple radiation therapy (MRT) have similar efficacy on controlling symptoms in patients with incurable cancer, especially in those with painful bone metastases [8,13,14].

In the single-fraction method, the total amount of radiation received by the patient is less and is given a limited number of times, but in the multiple-fraction method, the total amount of radiation received by the patient is high on a low dose in any fraction schedule used to achieve high local control of symptoms [15–17].

In the short-term treatment strategy, the number of visits is increased and the waiting time for radiotherapy is decreased. Evidence showed that in some clinical status, the long-term treatment (MRT) can be more effective than the short-term treatment (SRT) [18]. Patients with advanced cancer under a good treatment condition have higher life expectancy and these often occur in long-term palliation treatment (MRT) with a much higher amount of total dose irradiation [11,19,20].

Without palliative therapy, about 79% of patients will experience severe pain [7]. In some studies in Iran, the benefits of the two methods have been measured and evaluated [18]. According to the health policy perspective, the budget constraint of these treatments must be noticed and made more effective, and the lowest cost must be defined. For this purpose, one of the best methods is to conduct a cost-effectiveness analysis, which measures the benefits as well as costs [21].

The aim of this study was to perform an economic analysis comparing the single-fraction method with the multiple-fraction method for the first time in an Iranian setting.

## Methods

We used a previously published Markov model [22] for evaluating the cost-utility analysis of multiple fractions compared with that of a single fraction in the treatment of patients with painful bone metastases. The model used a monthly cycle length for a 5-year time horizon with 1000 hypothetical cohort samples. The EuroQol five-dimensional questionnaire (EQ-5D) was used to measure the quality of life of the patient and a Markov Monte-Carlo simulation method was used to compare the two methods.

The monthly transition probability assuming constant rates was calculated by using the following equation:

Monthly rate=[- ln(1 - Probe)/Time].

And the monthly probability of occurrence was calculated by using the following formula:

Monthly probability = 1−*exp*(−Monthly rate).

### *Study Population*

Through a pilot study the sample size for our study was estimated to be 100 patients. All the patients were referred to the Oncology and Radiotherapy Department of the Namazi Hospital in Shiraz between 2012 and 2013. Our inclusion criteria were as follows: 1) the patient had bone metastasis pain; 2) the patient was undergoing radiotherapy and oncology treatment continuously; 3) the patient was registered in the data register; 4) the patient had not undergone radiotherapy before; and 5) the patient's pain score was between 7 and 10, which represented severe pain on the Brief Pain Inventory. All the patients had signed the informed consent form and none of them was excluded during the study. The patients were divided into two groups on the basis of the type of therapy, and then within each group they were further categorized on the basis of the registry number. The samples were selected randomly among 247 patients.

### *Single- and Multiple-Fraction Radiation Therapy Models*

The models for both single fraction and multiple fractions were the same, as shown in Figure 1. The models were designed on the basis of the diagnostic stages of the disease and potentially had six states: No pain state 1 (after initial treatment), Pain medication (using MRT, SRT, or re-treatment), No pain state 2 (after re-treatment), and Death.

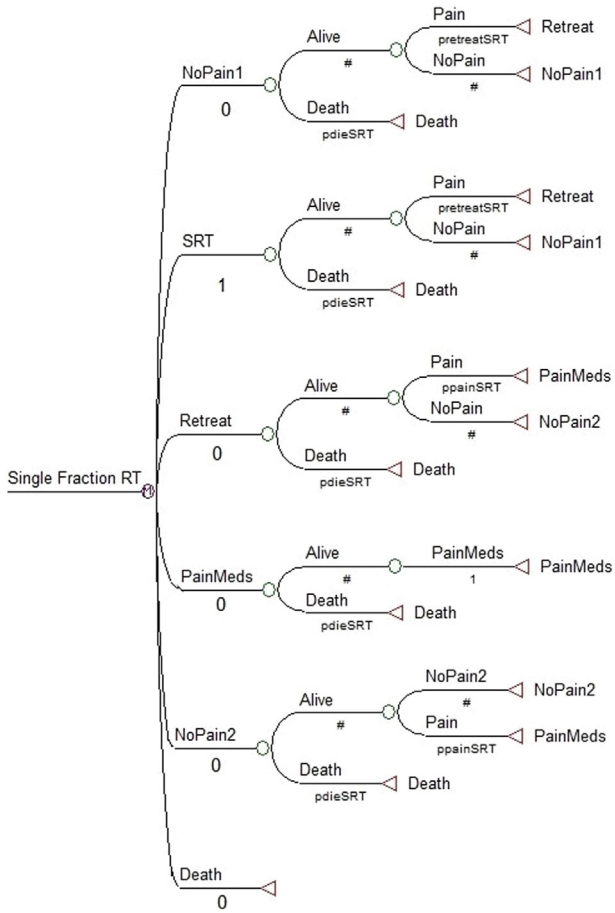


**Fig. 1 – The model for both SRT and MRT. MRT, multiple radiation therapy; RT, radiotherapy; SRT, single radiation therapy.**