

A Preliminary Study on the Estimation of the Number of Cancer Patients Eligible for Hadron Therapy in Iran and Fars Province

Mohammad Amin Hosseini¹, PhD;
Mohammad Mohamadianpanah^{2,3}, MD;
Mohammad Zare-Bandeamiri³, MSc;
Mohammad Amin Mosleh-Shirazi^{1,3}, PhD

¹Ionizing and Non-Ionizing Radiation Protection Research Center (INIRPRC), Shiraz University of Medical Sciences, Shiraz, Iran;

²Colorectal Research Center, Shiraz University of Medical Sciences, Shiraz, Iran;

³Department of Radiotherapy and Oncology, Nemazee Hospital, Shiraz University of Medical Sciences, Shiraz, Iran

Correspondence:

Mohammad Amin Mosleh-Shirazi PhD;
Department of Radiotherapy and Oncology, Nemazee Hospital,
Postal code: 71936-13311, Shiraz, Iran
Tel/Fax: +98 71 36474320

Email: mosleh_amin@hotmail.com
amosleh@sums.ac.ir

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What's Known

- Hadron therapy is an advanced radiotherapy technique for inaccessible and resistant tumors as well as many pediatric indications.
- There is currently no hadron therapy center in Iran.

What's New

- The total number of new patients eligible for hadron therapy in Fars and Iran is estimated to be at least 351 and 5,756 cases/year, respectively.
- Based on the number of patients, establishing two hadron therapy centers in the northern and southern parts of Iran is justifiable.

Abstract

Hadron therapy (HT) with protons and carbon ions is an advanced radiotherapy technique. As the first report addressing this topic, the present study aimed to estimate the number of patients eligible for HT in Fars province and the whole of Iran. The data were collected through direct inspection of medical records of the patients treated at the Radiotherapy Department, Namazi Hospital, Shiraz, Iran in 2014. The patients who were treated with external-beam radiotherapy and declared to be a resident of Fars province were extracted from the medical records. After classification based on appropriate indications and factors, the number of eligible patients in Iran was calculated by scaling (Iran: Fars population). Of the 2,932 medical records, 1,943 patients were treated with external-beam radiotherapy, among which 1,536 were from Fars. The total number of patients eligible for HT in Fars was >351 cases/year (22.9% of the treated patients). The cancer site distribution of the eligible Fars residents was central nervous system primary tumors (n=31), brain metastases (n=64), eye (n=7), head and neck (n=28); thyroid (n=4), lung (n=17), breast (n=56), esophagus (n=5); pancreas (n=5), gastric (n=32), liver and bile duct (n=0), rectum and anus (n=26); prostate (n=27), bladder (n=8), cervix (n=6), soft tissue (n=17); kidney (n=1), Hodgkin lymphoma (n=9), non-Hodgkin lymphoma (n=4), and bone metastases (n=4). A total number of 5,756 cases/year was estimated for the entire country. Considering the experiences of other countries, these results suggest that establishing at least two HT centers (covering the northern and southern parts of Iran) is justified based on the total number of patients. Further accurate estimations and cost evaluations are recommended.

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Keywords • Proton therapy • Carbon ion radiotherapy • Patient selection • Treatment costs • Hospitals

Introduction

Hadron therapy (HT) is regarded as an advanced radiotherapy (RT) technique, where energetic light ions (heavy particles, in particular protons and carbon ions) are used to kill cancer cells. Due to the physical and radiobiological properties of these ions, some clinical advantages are observed in HT compared to the conventional X- or gamma-ray RT. Therefore, HT is usually indicated in the treatment of radioresistant neoplasms, tumors located near vital organs, pediatric patients, etc.¹

The demand for hadron therapy is increasing sharply in recent years. Japan and China are the pioneers in this field. According to a recent report, other Asian countries such as India, Saudi Arabia, and Qatar intend to acquire this technology in the near future.² Unfortunately, there are no HT centers in Iran despite a large number of cancer patients. Despite attempts in recent years to set up a reliable nationwide cancer registration system³ in Iran, there are still many limitations and bottlenecks in obtaining reliable and accurate data concerning the number of eligible patients for this treatment.⁴ This scenario instigated a study in Iran and Fars province (where the data were collected from) to indicate the extent of the need for HT. To the best of our knowledge, this is the first scientific report on the estimation of the number of eligible cases for HT in Iran.

Materials and Methods

In the present descriptive-analytical study, the data were collected from the medical records of the patients who referred to the Department of Radiotherapy and Oncology, Namazi Hospital, Shiraz, Iran in 2014. This department is the first and currently the sole RT center in Fars province and serves as the only RT and oncology referral center. It has the longest-established cancer registry office in the country. Fars province is in the southern part of Iran with Shiraz as its capital city. According to official reports by the Statistical Center of Iran, the population of Fars province in 2014 was 4,735,146, which accounts for 6.1% of the total population of the entire country.⁵

The number of patients was estimated in two stages, as described below.

- i. Initially, the medical records of all patients who referred to this center were examined by the census method. Data, including patients' national ID number, place of residence, diagnosis, and treatment, were collected and carefully recorded in a specially designed form by direct inspections of the records. The use of the national code prevented double entries in the collected data, and cases without pathological confirmation were excluded. Additionally, based on the declared place of residence, patients from regions other than Fars province were excluded.
- ii. In the second stage, the refined data were categorized into different indications based on the anatomical location of the tumor. This classification method is according to a study in which the number of eligible patients for HT was estimated based on the data from

five university hospitals in Germany, Italy, France, and Austria.⁶ The mean coefficients for each indication were extracted from the same study. Therefore, in the present study, previously-derived indications and mean coefficient values have been adapted and applied to our collected data. The estimated number of patients suitable for HT in six previous studies is summarized in table 1.

Results

Of the total of 2,932 cases in the archives of 2014, medical records of 1,943 patients who underwent conventional RT were used for data analysis. Among them, 1,536 records (male: 628 (41%) and female: 908 (59%)) of those residing in Fars province were selected. The age distribution of the patients is shown in figure 1. Then, 1,536 indications suitable for HT were classified, as shown in table 2. In this table, the category of indications is shown in the first column, and their corresponding distribution in Fars province and the coefficients used in the previous study⁶ are shown in the adjacent columns. Multiplying each coefficient by the corresponding number in the previous column determines the absolute number of indications (last column) suitable for HT. Hence, the total number of patients who reside in Fars and are eligible for HT is 351 cases/year. Multiplying this value by the proportion of the Fars population with respect to the entire country (1/16.4), the estimated eligible patients in the whole country (i.e., 16.4×351) is 5,756 cases per year.

Discussion

Despite the frequent and relatively reliable data available on the construction of HT centers and patients who have been treated, limited access to the methods for estimating the number of patients eligible for HT still poses a challenge. Most of these reports have been published

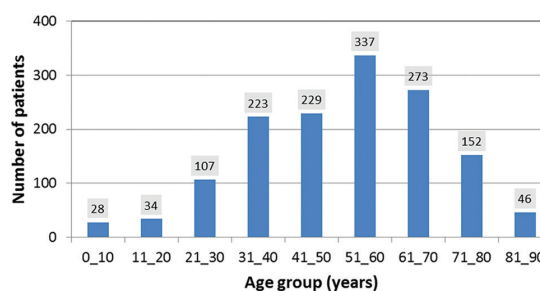


Figure 1: Age distribution of patients treated at the Radiotherapy Department of Namazi Hospital and residing in Fars province in 2014.

Table 1: Estimated values of hadron therapy indications reported in previous studies

Publication	Year	Center	Reported number
Mayer et al. ⁶	2004	MedAustron, Austria	2,044 cases/year
Orecchia et al. ⁷	1997	CNAO, Italy	10,825 cases/year
Engels et al. ⁸	1999	MedAustron, Austria	13,145 cases/year
Baron et al. ⁹	2004	ETOILE, France	5,320 indications/year for carbon ions
Krengli et al. ¹⁰	2004	CNAO, Italy	3,694 cases/year for protons 1,885 cases/year for carbon ions
Patin et al. ¹¹	2013	Rhône-Alpes, France	8.5 (incidence/100,000 inhabitants/year)

Table 2: Distribution of patients in terms of indications appropriate for hadron therapy in Iran and fars province

Category	Number of residents in fars treated with radiotherapy (% of all radiotherapy patients)	Suitable for hadrons based on ref. ⁶ (%)	Number of patients eligible for hadron therapy living in fars
Primary central nervous system tumors	156 (74)	20	31
Brain metastases	64 (85)	100	64
Eye tumors	10 (83)	67	7
Head and neck tumors	112 (79)	25	28
Thyroid cancer	8 (72)	45	4
Lung metastases	17 (89)	100	17
Breast cancer	563 (79)	10	56
Esophagus cancer	18 (62)	28	5
Pancreas cancer	24 (82)	20	5
Gastric cancer	74 (77)	43	32
Liver and bile duct cancer	0 (0)	46	0
Rectum and anus cancer	126 (84)	21	26
Prostate cancer	98 (88)	28	27
Bladder cancer	36 (88)	22	8
Cervix cancer	26 (76)	23	6
Soft tissue tumors	46 (75)	38	17
Kidney cancer	4 (37)	14	1
Hodgkin lymphoma	48 (69)	19	9
Non-Hodgkin lymphoma	20 (68)	19	4
Bone metastases	82 (83)	5	4
Total	1,536 (79)	693	351

between 1998 and 2002.⁶⁻¹⁰ A literature review has been reported in a recent study published in 2013.¹¹ Given the significance of finding a useful method for estimating the number of patients, who are eligible for HT, some of these studies are discussed in more detail.

In a study by Baron et al., the statistics for one-day referral of eligible patients for HT in five RT centers in the east of France were reported. Assuming the treatment period for such patients lasts 5-7 weeks and applying a factor of 10, the total number of patients admitted per year was estimated at 5,320. This estimate showed a fairly good agreement with the actual number of patients (6,300). Finally, the authors concluded 770 appropriate indications for HT.⁹ Krengli et al. studied the predicted equipment and facility requirements for the CNAO installation in Italy by considering the capacity to treat 900 patients

per year. The study showed that, on a yearly basis, 25,000 new cases are added to the number of cancer patients in Italy. Given that 10-15% of such patients would probably need to undergo HT, the number of candidates for HT was estimated at 3,000-4,000 patients.¹⁰ Mayer et al. conducted a feasibility study of patients as candidates for the Austrian National Center for HT (MedAustron). All patients who were candidates for RT (a total of 3,783 patients in three months) were studied. The total number of such patients was multiplied by 4 to derive 15,132 patients eligible for HT during a year.⁶ They estimated the mean values from five European university hospitals and multiplied the calculated values by indications collected during a whole year and found that 2,044 patients were eligible for HT. Accordingly, they underlined the urgent need for establishing a national HT in

Austria.⁶ Note that, the mean coefficients were calculated in the same manner (third column in table 2) as in the present study. The need for an HT center in Rhône-Alpes (France) was evaluated in 2010. The patients' data were collected from 34 centers and the estimated value of 8.5 (incidence/100,000 inhabitants/year) was calculated. Without commenting on the need for establishing an HT center in the region, the authors recommended further research to be carried out in the region under analysis.¹¹ In another study published in 2013, the feasibility study of an HT center in Belgium was performed in collaboration with several universities, hospitals, and leading experts.¹²

The present study estimated appropriate indications for HT in Fars province and the whole of Iran by inspecting the medical records of patients treated at Namazi Hospital in 2014. Based on the presented data, the total number of eligible patients for HT in Fars was 351 cases per year, accounting for 29.4% of the treated patients in 2014. A total number of 5,756 cases per year was estimated at the nationwide level. Indications eligible for HT are also discussed in table 2.

Although the exact figures are not accurately known, it is well established that the utilization rate of RT in Iran is below the worldwide average. This means that, at present, a smaller fraction of Iranian cancer patients undergo RT compared to developed countries. Therefore, the total number of patients used in the current analysis is an underestimate of the real number requiring RT. Consequently, the number requiring hadron therapy is also an underestimate.

In addition to the evaluation and approximation of the number of patients (as carried out in the present study), other factors should also be taken into consideration for the establishment and development of HT centers. Although the design and operational stages of these centers are almost the same in all countries, other factors can play important roles in the success of HT projects, including the existence of strong infrastructures that can greatly increase the chance of success.¹³ As developing countries are moving towards implementing HT,² some important recommendations need to be considered by such countries, including the establishment of a strong RT infrastructure, annual patient throughput, accurate patient estimates that allow a project to be financially sustainable, and even the assessment of the number of treatment sessions that can be done per day. To maximize health benefits, it is recommended to implement work plans and feasibility studies. This issue is particularly important in the sense that in most

reports the final cost is estimated up to \$100M and the maintenance costs of these centers should also be added.^{13,14} However, it should be emphasized that new technologies such as laser accelerators^{1,15} and the use of linear accelerators¹⁶ have reduced the costs. Also, the introduction of single-room centers^{1,17} can be very useful for research and development purposes too. Therefore, substantial cost reduction seems feasible. Moreover, providing training programs for radiation oncologists, medical physicists, and radiotherapy technologists alongside a skilled management team is highly recommended.¹³

To sum up, in the present study, an evaluation of the number of patients eligible for HT was conducted for the first time in Iran; supported by data from previous studies in other countries. Based on the number of patients and benefiting from the experiences of HT centers in other countries, the need for at least two HT centers was indicated. Geographically spreading the two centers is sensible for better patient access. However, given an increase in the incidence rate of cancer in Iran, further research that includes health economic evaluation is required in this field.

Conclusion

Given the estimated number of total indications for HT in Fars province and Iran, establishing at least two HT centers (covering the northern and southern parts of Iran) is justified in terms of patient numbers. However, there is a need for further detailed studies to provide more accurate data for the entire county by considering cost-effectiveness and other economic and cultural factors.

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Conflict of Interest: None declared.

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