

Estimation of the medical need for carbon-ion radiotherapy in Korea

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(Received 14 December 2017; revised 31 March 2018; editorial decision 15 May 2018)

ABSTRACT

The Korea Heavy Ion Medical Accelerator project focuses on the development of medical accelerator facilities for delivering carbon-ion beams to cancer patients. The purpose of the present study was to estimate the clinical need for carbon-ion therapy in Korea. Seven tumor sites, namely head and neck, liver, lung, colon and rectum, prostate, bone and soft tissue, and pancreas were selected as eligible sites for receiving carbon-ion radiotherapy (RT) by radiation oncologists of the Korea Institute of Radiological and Medical Sciences. Cancer incidence data for the selected tumor sites were obtained from the Korea National Cancer Incidence Database in order to estimate the potential medical need for carbon-ion RT. The carbon-ion RT adaption rate was assessed based on the clinical experience of other carbon-ion therapy facilities. An estimation model was constructed for estimating the medical need for carbon-ion RT, and from this, 25 606 patients were deemed to be potential candidates for carbon-ion RT. This estimated potential need corresponded to 10% of newly diagnosed cancer patients in Korea. The realistic estimation was calculated as ranging between 4000 and 6300 patients, depending on the carbon-ion RT adaptation rate. This estimated medical need corresponded to 2–3% of newly diagnosed cancer patients in Korea. Taken together, our findings suggest that there is a clear medical need for carbon-ion RT in Korea, with at least 4000 potential patients per year.

Keywords: medical need; radiotherapy; carbon-ion; patient number; KHIMA

INTRODUCTION

Cancer is a major health issue in Korea. According to a report of the Central Cancer Registry of Korea, the probability of a new cancer diagnosis has been increasing annually since 2010, with more than 200 000 people diagnosed each year [1–4]. Owing to the aging population, the increasingly westernized lifestyle, the development of more precise tools for diagnosing cancer, and the healthcare system of Korea, this trend is expected to continue into the future [5, 6].

Radiotherapy (RT) is a standard method for cancer treatment. A recent study found that the total estimated numbers of patients who underwent RT in Korea were 192 561 in 2009 and 225 343 in 2013. This corresponds to a total increase of ~17% over the 4-year period [7].

Carbon-ion beams have a potential advantage in the treatment of cancer because they have high dose conformity, high relative biological effectiveness characteristics, and a low oxygen enhancement ratio [8]. Their clinical efficacy and safety for cancer treatment have

been demonstrated by several international institutions over the past 20 years [9].

In view of the rapidly aging population in Korea, and the growing demand for advanced medical care, the construction of additional medical facilities has become necessary. Thus, prediction of the exact demand for medical facilities is an important factor in evaluating the cost-effectiveness of facility construction.

The construction and operation of a carbon-ion medical accelerator system is extremely expensive. The cost of constructing a particle facility is ~139 million Euros, and the operation costs and the patient burden are very high compared with those of conventional X-ray treatment [10]. In the case of the National Institute of Radiological Sciences (NIRS) in Japan, the treatment unit price is equivalent to 3.14 million yen per person (28 600 US dollars) [11]. Therefore, an estimation of the medical need for carbon-ion RT is a crucial piece of information for the establishment of a management plan for a huge treatment complex such as this.

The purpose of this study was to estimate the clinical need for carbon-ion RT in Korea. In order to estimate the medical demand, we considered the clinical attributes indicating carbon-ion RT, and the carbon-ion RT adaptation rate, in calculating the eligible number of patients. Subsequently, the number of potential and realistic candidates were calculated by using cancer statistics data in Korea and the carbon-ion RT adaptation rate. Finally, the numbers of patients eligible for carbon-ion RT were assessed with respect to seven different tumor sites.

MATERIAL AND METHODS

Data from the Korea National Cancer Incidence Database were used to estimate the medical need for carbon-ion RT [12]. Tumor sites suitable for carbon-ion RT were carefully considered by radiation oncologists of the Korea Institute of Radiological and Medical Sciences (KIRAMS), based on the results of over 20 years of clinical trials [9]. In this study, seven sites, namely the head and neck, liver, lung, colon and rectum, prostate, bone and soft tissue, and pancreas were chosen as eligible sites for carbon-ion RT.

An estimation model was constructed in order to estimate the realistic number of carbon-ion RT patients. First, we looked at the number of cancer patients for the seven selected tumor sites. The Korea National Cancer Incidence Database was used to identify newly diagnosed cancer cases [12]. Second, the incidence rates of the clinical attributes for the eligible tumor sites were multiplied to

estimate the number of potentially eligible patients. Third, the carbon-ion RT adaptation rates were carefully investigated and applied to the potential number of patients in order to estimate the realistic medical needs. The details of the selected tumor sites for carbon-ion RT are described in Table 1.

The carbon-ion RT adaptation rates for the selected tumor sites were investigated based on previous reports from two Japanese institutions: the Gunma Heavy Ion Medical Center (GHMC) and the NIRS [13, 15]. In the case of the GHMC, the adaptation rate was carefully identified before starting the GHMC project in many ways [16, 17]. Recently, the adaptation rates were updated and summarized in the interim report on the advanced cancer treatment facility project in Gifu prefecture [15]. The adaptation rates were identified at the NIRS and used to estimate the realistic medical need of carbon-ion RT in Japan. However, the clinical adaptation rate was revised for this study. For pancreatic cancer, the interim report showed a 1.7% adaptation rate for pancreatic cancer. In this study, the 1.7% adaptation rate was adjusted to 2% in expectation of the start of carbon-ion RT in Korea in the near future, because the clinical usage of carbon-ion beam will gradually increase. In the case of bone and soft tissue, cancer prevalence cases were used instead of the numbers of newly diagnosed patients in order to include inoperable bone and soft tissue cases. Thirty percent of bone and soft tissue cases were considered. The carbon-ion RT adaptation rates for selected tumor sites are summarized on Table 2.

Table 1. Number of patients potentially eligible for carbon-ion radiotherapy in Korea

Tumor site	No. of incident cancer cases in Korea (2013) ^a (a)	No. of patients potentially eligible for carbon-ion RT		
		Summary stage	Incidence ratio (%) (b)	Number of patients (a) × (b)/100
Liver	16 192	Localized	45.1 ^a	7309
Prostate	9515	Localized	55.0 ^a	5229
Lung	23 177	Localized	20.4 ^a	4730
Pancreas	5511	Localized, regional	44.8 ^a	2472
Colon and rectum	21 756	Recurrence in the pelvic area after curative treatment	10.0 ^b	2177
Connective and soft tissue	6831 (cancer prevalent cases)	Soft tissue sarcoma in the retroperitoneum or pelvis	30.0 ^b	2052
Bone and articular cartilage	4043 (cancer prevalent cases)	Bone sarcoma in the spine or inoperable cases	26.0 ^b	1051
Salivary glands	462	T1–4N0M0	75.2 ^b	347
Nose, sinuses, etc.	344	T1–4N0M0	70.0 ^c	241
Total				25 606

^aIncidence data from the Korea National Cancer Incidence Database were used to obtain the number of newly diagnosed cancer patients in 2013 [12].

^bCancer statistics data in Japan referred to the Gunma Heavy Ion Medical Center were also used in this study [13].

^cThe number of patients potentially eligible for carbon-ion radiotherapy was obtained from the product of the number of cancer incidence cases with a specific stage (a) and the corresponding incidence ratio (b) [14].

Table 2. Adaptation rates of carbon-ion radiotherapy and estimated medical needs in Korea

Tumor site	No. of patients potentially eligible for carbon-ion RT ^a	Carbon-ion radiotherapy adaptation rate (%)			Estimated patient number according to the adaptation rate		
		GHMC (2011) ^b	NIRS (2017) ^c	Estimated 2020 ^d	Using GHMC	Using NIRS	Using estimation
Liver	7309	25	12	12	1827	870	870
Prostate	5229	15	43	43	784	2243	2243
Lung	4730	10	14	14	473	672	672
Pancreas	2472		1.7	2.0 ^d		42	49
Colon and rectum	2177	25	8.4	8.4	544	183	183
Connective and soft tissue	2052	80		30 ^d	1640		615
Bone and articular cartilage	1051	80		30 ^d	841		315
Salivary glands	347	50	10	10	174	36	36
Nose, sinuses, etc.	241	25	10	10	60	25	25
Total	25 606				6344	4071	5008

^aData were obtained using the cancer statistics of the Korea National Cancer Incidence Database (2013) [12].

^bAIP Conf Proc 2011;1336:391–6 [13].

^cInterim report on introduction of advanced cancer treatment facilities in Gifu Prefecture [15].

^dThe data of the NIRS (2017) were adopted except for connective and soft tissue, bone and articular cartilage, and pancreatic cancers. The adaptation rates of connective and soft tissue and bone and articular cartilage sites were 30%. For pancreatic cancer, the adaptation rate was adjusted to 2% in view of the imminent commencement of carbon-ion RT in Korea.

RESULTS

According to the Korea National Cancer Incidence Database, 225 343 cancer cases were newly diagnosed in Korea in 2013. Among them, 25 606 patients were assessed as being potentially eligible for carbon-ion RT after considering the clinical attributes indicating carbon-ion RT.

Among the 25 606 identified patients, a total of 5008 patients were found to be eligible for carbon-ion RT. For localized liver cancer, prostate, and lung cancers, 12%, 43% and 14%, respectively, of patients were considered to be carbon-ion RT candidates. For pancreatic cancer, we assessed both localized and regional pancreatic cancer cases as being carbon-ion RT candidates, with an adaptation rate of 2%, owing to the fact that clinical trials for pancreatic cancer are still in progress. For colorectal cancer, we considered that 8.4% of patients with pelvic recurrence after curative treatment were realistic candidates for carbon-ion RT. For soft tissue sarcoma in the retroperitoneum or pelvis, 30% of the patients were considered carbon-ion RT candidates. For cases of bone sarcoma in the spine and inoperable bone sarcoma cases, 30% of patients were considered to be carbon-ion RT candidates. For both bone and soft tissue sarcoma cases, data on cancer prevalence were used instead of cancer incidence data, because patients with inoperable bone or soft tissue sarcoma are currently considered to be candidates for carbon-ion RT [18]. For head and neck cancer, we concluded that 10% of patients with localized salivary gland and sinus cancers were realistic candidates for carbon-ion RT.

Prostate cancer was estimated to be the most common indication for carbon-ion RT; a total of 2243 prostate cancer patients

were estimated to be carbon-ion RT candidates. The second and third most common cancers eligible for carbon-ion RT were bone and soft tissue cancer, and liver cancer, with 930 and 870 patients, respectively, indicated for carbon-ion RT. Taken together, these three cancer types accounted for 80% of the total estimated medical need for carbon-ion RT. A summary of the medical needs for carbon-ion RT for each cancer type is provided in Table 2.

In addition, the carbon-ion RT rates based on the GHMC and NIRS indications were calculated. According to the GHMC data, the need for carbon-ion RT was estimated at 6344 patients; this number did not include pancreatic cancer patients, owing to a lack of clinical trials. Based on the NIRS approach, 4071 patients were considered eligible, excluding bone and soft tissue cases. The realistic estimation ranged between 4000 and 6300 patients. Although the estimation depends on the carbon-ion RT adaptation rate for each institution, the realistic estimation corresponds to 2–3% of newly diagnosed cancer patients in Korea.

DISCUSSION

The study is based on the data of registered cancer patients in Korea. According to the data, 225 345 patients were newly diagnosed with cancer in 2013. The patients potentially eligible for carbon-ion RT are carefully selected based on the expected clinical outcomes. The number of potential patients is considered to be the potential medical need. In the present study, the potential medical need for carbon-ion RT was estimated at 25 606 patients. The

realistic medical need was calculated by considering factors such as the adaptation rate of carbon-ion RT. In this study, the adaptation rate refers to the clinical application rate of carbon-ion RT in Japan, because the major cancer incidence in Korea is similar to that in Japan, except for thyroid cancer [19]. However, the clinical adaptation rate was revised for this study. In particular, in order to reflect the results of recent clinical trials, pancreatic cancer was considered to be the major type of cancer for carbon-ion RT in Korea, despite not initially being treated with this modality. For bone and soft tissue cases, cases described as ‘inoperable were included in the data on the cancer prevalence, because this indicated that there was no other curative treatment except carbon-ion RT.

The realistic estimation of the medical need for carbon-ion RT in Korea was 5008 patients. This number corresponds to 8.1% of patients receiving RT, and 2.2% of newly diagnosed cancer patients. The estimated medical need for carbon-ion beams ranged between these estimations when calculated using the carbon-ion adaptation rates of GHMC and NIRS; the numbers of estimated patients were 4071 and 6344, respectively. Recently, Tsujii (2017) reported that the proportion of patients eligible for charged particle therapy per year was 15% of patients receiving RT [20]. This value corresponds to 9300 patients in Korea, based on the 2013 cancer statistics. This result includes patients requiring particle beam, proton, and carbon-ion RT. It may be reasonable to consider that approximately half of the estimated number may need carbon-ion RT; this would correspond to the results of the present study.

There may be several factors influencing the estimated number of patients eligible for carbon-ion RT. The current clinical indications for carbon-ion RT are continuously evolving, with the clinical factors and carbon-ion RT adaptation rates being based on the most recent and ongoing clinical trials. The current clinical protocols are gradually being applied to new tumor sites, and this will eventually be reflected in the new protocols [9]. The utilization rate of RT is another factor that needs to be considered when estimating the number of potential patients. The utilization rates of RT are ~50% in Europe and ~30% in Japan [21, 22], and a recent study showed an increasing trend for using RT for treating cancer patients in Korea [23]. According to the results of this previous study, the RT rate is increasing by 1% every year. If we project the reported rate to the present time, the RT utilization rate is currently ~30%. Therefore, the estimated number of patients indicated for carbon-ion RT might increase in the future with updated RT utilization ratios.

Several studies have estimated the number of patients suitable for carbon-ion RT. In the GHMC, the numbers of patients eligible for carbon-ion RT were estimated based on the regional population and cancer incidence ratio. As a result, ~1527 patients with head and neck, rectum, liver, lung, prostate as well as bone and soft tissue sarcoma, were estimated to be eligible for carbon-ion RT. This number corresponded to 2% of newly diagnosed cancer patients in Gunma and neighboring prefectures [13].

In Europe, the National Center for Oncological Hadron Therapy (CNAO) in Italy investigated the number of eligible patients for carbon-ion RT based on clinical trials conducted by the Heidelberg ion therapy center (HIT) [24]. A total of 3694 patients were considered as carbon-ion RT candidates, corresponding to 6% of newly diagnosed cancer patients in Italy. In the MedAustron

project in Austria, the author estimated realistic patient numbers based on the clinical results from the Heidelberg, Milano, Lyon, Vienna, and Innsbruck Universities [25]. Based on the epidemiological cancer incidence, the number of potential patients was estimated at 2044 per year. This result represents 6% of all newly diagnosed cancer patients in Austria. Of note, unlike in the GHMC and NIRS in Japan, the CNAO and MedAustron projects were designed to deliver both proton and carbon beams to cancer patients. The MedAustron project moreover used the results of former European clinical trials; thus, the clinical indications of the MedAustron project were similar to those of CNAO. In the case of the study from the CNAO, the author assessed carbon-ion RT candidates among patients with relatively radioresistant tumors and its indication as a boost after or prior to conventional RT [24]. Therefore, the estimated medical need for carbon-ion RT was lower than that in the present study.

The number of patients treated with carbon-ion RT in each above-mentioned institution is summarized in Fig. 1 [26]. The incremental increase in utilization of carbon-ion RT shows nearly linear behavior, indicating that there might be more medical need for carbon-ion RT in the near future. Based on a survey by the Japanese Society for Radiation Oncology, 251 000 patients received X-ray, γ -ray and electron RT in 2012. A total of 1315 (1%) patients were treated with carbon-ion RT in the same year, and this number was increased to 2047 in 2015 [22]. These data suggest a rapid increase in the use of carbon-ion beams for cancer treatment. According to the increase in the number of patients treated with carbon-ion beams, it may be expected that at least two or three more carbon-ion RT facilities will be needed in Korea in the near future.

In conclusion, the present study estimated the medical need for clinical utilization of carbon-ion RT in Korea, based on clinical indications for the Korea Heavy Ion Medical Accelerator project. We found that there is a clear medical need for carbon-ion RT in Korea, with at least 4000 patients per year indicated for this

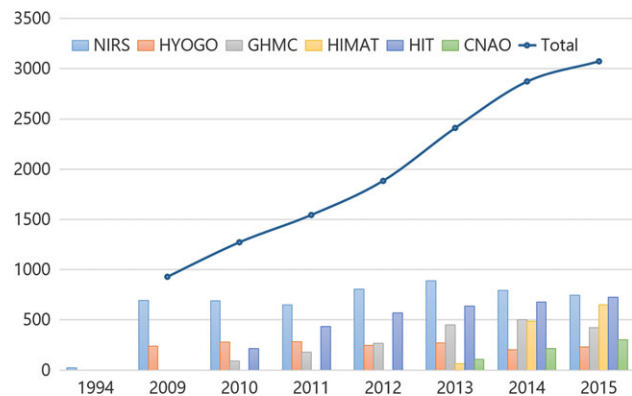


Fig. 1. Number of patients treated with carbon-ion radiotherapy in other facilities. NIRS = National Institute of Radiological Sciences, HYOGO = Hyogo Ion Beam Medical Center, GHMC = Gunma University Heavy Ion Medical Center, HIMAT = SAGA Heavy Ion Center Treatment Center, HIT = Heidelberg Ion Therapy Center, CNAO = National Center for Oncological Hadron Therapy.

treatment. This estimation will be helpful in developing a management plan for future facilities.

CONFLICT OF INTEREST

The authors state that they have no conflict of interest.

FUNDING

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIP) (No. NRF-2014M2C3A1029534). This study was supported by a grant of the Korea Institute of Radiological and Medical Sciences (KIRAMS), funded by Ministry of Science and ICT(MSIT), Republic of Korea No. 50532-2018. This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2018R1D1A1B07049174).

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