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Cost of particle therapy

How costly is particle therapy? Cost analysis of external beam radiotherapy with carbon-ions, protons and photons

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ABSTRACT

Purpose: Particle therapy has potentially a better therapeutic ratio than photon therapy. However, investment costs are much higher. This study provides an estimation and comparison of the costs of these therapies.
Methods: Within an extensive analytical framework capital and operational costs, cost per fraction, and four tumor specific treatment costs are calculated for three facilities: combined carbon-ion/proton, proton-only, and photon.
Results: Capital costs for the combined, proton-only and photon facilities are: € 138.6 million, € 94.9 million, € 23.4 million. Total costs per year are: € 36.7 million, € 24.9 million, € 9.6 million. Cost per fraction is: € 1128 (€ 877–1974), € 743 (€ 578–1300), € 233 (€ 190–407). Cost ratio particle/photon therapy is 4.8 for the combined and 3.2 for the proton-only facility. Particle treatment costs vary from € 10,030 (c-ion: lung cancer) to € 39,610 (proton: head & neck tumors). Cost difference between particle and photon therapies is relatively small for lung and prostate cancer, larger for skull-base chordoma and head & neck tumors.
Conclusion: Investment costs are highest for the combined carbon-ion/proton facility and lowest for the photon facility. Cost differences become smaller when total costs per year and specific treatment costs are compared. Lower fractionation schedule of particle therapy might further reduce its costs.
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Particle therapy is a promising treatment modality for cancer [1], but it is also questioned whether it is "too expensive to become true" [2]. The investment costs are considerably higher than for the conventional photon therapy [3]. Treatment with charged particles, such as carbon-ions and protons, offers improved dose distributions to the target volume as compared to photon radiotherapy, with better sparing of the surrounding healthy tissues [4]. Potential gains of particle therapy might be (1) a higher tumor control probability due to dose escalation, (2) less side-effects including fewer secondary cancers due to less radiation to normal tissue. However, at the moment there is a controversial view on whether particle therapy is too expensive for the potential improvements in outcome claimed, or not [5]. This may be the main reason why a decision to adopt particle therapy as a standard treatment is pending in a number of countries. Cost-effectiveness analyses can give a decisive information on whether the extra costs are worth the extra effects [6]. An increasing number of studies report on the clinical effectiveness of particle therapy [7–10]. There is an ongoing debate on the cost issue as well [11,12]. The reported studies on cost-effectiveness of particle therapy differ substantially in terms of methodology and assumptions [13]. In order to determine whether the extra effects of particle therapy are worth the extra costs, an insight into the investment and operational costs of the facilities for particle therapies is crucial.

The present study specifies in detail the costs of radiotherapy and provides as such an input for future cost-effectiveness analyses. The aim was to determine the integral costs of external beam radiotherapy with carbon-ions, protons, and photons. The research objectives were to (1) develop an analytical framework for an integral cost calculation, (2) estimate the capital and operational costs of the facilities and the relative cost per fraction of carbon-ion and proton therapy as compared to photon therapy, (3) identify factors that influence the cost per fraction, and (4) calculate treatment costs for specific tumor sites.

Methods

Framework for cost calculation

To identify relevant cost items to be incorporated in the framework for the cost calculation the literature was searched for articles

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on costs and cost-effectiveness of particle therapy. The search revealed four relevant papers [3,14–16]. Through contacts with other researchers in the field additionally one report on hadrontherapy [17] and one extra cost article [18] were found. The cost results of these studies recalculated to the 2007 price level, using the consumer price index figures, are given in Table 1. Only one cost analysis was found, that compared particle therapy with intensity-modulated photon therapy [3]. This latter study includes detailed cost calculations with a large number of input parameters. Its format was used as a starting point for the development of the framework for the cost calculation in the present study.

Calculation sheet

The calculation sheet is developed in Excel™. Costs can be calculated for three types of facilities: (1) combined carbon-ion and proton (further referred to as a combined facility), (2) proton-only, and (3) photon. The spreadsheet contains several sub-sheets with input parameters from which derived variables can be computed and from these finally the integral costs can be determined for each facility. The yearly throughput of patients is modelled in a detailed operational model. By adapting the input parameters a sensitivity of the calculated costs to any parameter change can be assessed.

Breakdown of costs

Costs are divided into two main categories: capital and operational costs. *Capital costs* consist of construction costs, costs of particle therapy equipment, and medical equipment costs (including linear accelerators – linacs for photon therapy, planning devices, computers, software etc.) *Operational costs* consist of costs for energy and utilities (water, heating, electricity); hard facility operating costs (maintenance of the: building, particle therapy equipment, medical equipment); soft facility operating costs (cleaning, insurance, administration, others); renewal costs (building, particle therapy equipment, medical equipment); and personnel (administration, clinical staff).

Financial plan

The whole-life costs for three different facilities are modelled and compared regardless of which sector is involved, private or public. An interest rate of 5% on the original initial funding, paid over 20 years, is included. This is added to the yearly operational costs. The lifetime of the facilities is expected to be 30 years plus. Within this period, parts of the facilities need to be replaced. It is modelled that all three facilities are being constantly renewed, including regular equipment replacement. For example, an annual renewal cost of 10% of the original funding for medical equipment allows, among others, a replacement of linacs in the photon facility every 10 years, which is the average estimated lifetime of a linac. For the renewal of particle therapy equipment a 2% and 1% annual rate is included for the combined facility and the proton facility, respectively (in addition to the 7% and 4% annual rate for regular maintenance).

Sources of estimates

The estimates for the input parameters are retrieved from different sources: literature, business plan Maastro Clinic [19], and a Belgian report on hadrontherapy [17]. Data on workflow, staffing, and personnel costs are customary to The Netherlands [20,21]. A detailed overview of the personnel costs can be viewed in Appendices 1 and 2. Costs are valued from a hospital perspective. Construction costs are based on previous projects by Turner & Townsend, construction and management consultants. Costs for equipment are average benchmark prices as given by Turner & Townsend for commercially available equipment.

Basic assumptions

The following assumptions are incorporated in the model: (a) There is a sufficient number of patients to make use of a maximum capacity of the facilities. (b) Cost per fraction is calculated for the following patient mix: (1) For particle therapy facilities – patients with special treatment category tumors, which are assumed

Table 1
Overview of the costs of particle therapy: outcomes of this study and costs found in the literature.

Study	Type of study	Capital costs	Operational costs/year	Cost per fraction			Cost per treatment			
		Mean (million €)	Mean (million €)	Beam	Mean cost (€)	Range (€)	Beam	Mean cost (€)	Range (€)	Treatment description
Combined facility										
KCE report, [17]	Cost description	159.6	17.5	–	–	–	C-ion or proton	24,700	15,000–40,000	Average
Jakel et al. [14]	Cost-effectiveness analysis	–	–	C-ion	1030	–	C-ion	20,560	–	Skull-base chordoma; 20 fractions (including planning)
Perrier et al. [18]	Cost description	–	–	C-ion	1130	980–1290	C-ion	22,590	16,930–28,240	Average
								22,100	–	Prostate
								14,800	–	Lung (including planning)
Proton-only facility										
KCE report, [17]	Cost description	75.2	–	Proton	–	–	Proton	19,100	–	Average
Konski et al. [15]	Cost-effectiveness analysis	–	–	Proton	–	–	Proton	44,510	30,380–56,960	Prostate
Lundkvist et al. [16]	Cost-effectiveness analysis	66.7	–	Proton	–	–	Proton	–	10,790–11,750	Medulloblastoma, Breast; 25 fractions
								–	13,760–14,280	Prostate; 35 fractions
Goitein and Jermann, [3]	Cost analysis	67.5	16.5	Proton	1110	–	Proton	27,660	–	Average
								15,880	–	Average (business costs excluded)

€ = euro (all costs are recalculated to the 2007 price level).
C-ion = carbon-ion.

eligible for particle therapy [20]. (2) For the photon therapy facility – a mix of standard and complicated cases as common in practice. (c) Treatment costs are calculated specific to each tumor, including the most sophisticated photon treatment. (d) Initial capital costs are evenly distributed/paid back over the assumed facility lifetime period. (e) Interest rate of 5% on the original initial funding is included. (f) The following costs are not included in the analysis: taxes (VAT), inflation and price changes over time, staff training, contingency, and demolishing works. (g) High standard service level for the hard and soft facility management services is assumed, resulting in a high technical availability of treatment rooms. (h) High treatment room utilization is based on: (1) A combined facility containing three treatment rooms, two of them equipped with either a proton gantry or a pair of fixed beams, third room equipped with a horizontal beam, a linac and synchrotron for acceleration, and a robotic patient positioning system. (2) A proton-only facility containing three treatment rooms, two of them equipped with a proton gantry, third room equipped with a horizontal beam, a cyclotron for particle acceleration, and a robotic patient positioning system. (3) A photon facility containing two treatment rooms equipped with standard linacs, in line with Goitein and Jermann [3]. (i) All facilities have equal image-guided equipment. (j) All reported costs are in euros (€), 2007 price level.

Analyses

Base-case analysis

Cost per fraction for each facility is calculated as total costs per year divided by the number of fractions per year. *Total costs* per year are a sum of the capital costs divided by the lifetime of the facility (30 years) and the yearly operational costs. *Number of fractions* per year is calculated in an operational model. In this model, first the maximum number of fractions per year per treatment room is calculated, as a ratio of the time available for treatment and the average time needed per fraction. This maximum number of fractions per room is then adjusted for the number of treatment rooms, the technical room availability, and the room utilization (limited by the accelerator availability; see Table 2). Capital costs for building, costs for maintenance, energy, water supply, cleaning, etc. depend on the gross floor area. This is explicitly calculated for all three facilities. To illustrate a number of patients expected to be treated per year in a facility, the total number of fractions per year is divided by the estimated average number of fractions per patient, specific for each facility (see Table 2). For a photon facility the estimation of the average number of fractions per patient is based among others on data from our clinic. For the particle facil-

Table 2
Base-case analysis: operational model and cost estimates.

Operation	Particle facility		Photon facility	Source
	Combined (carbon-ion and proton)	Proton-only		
Number of rooms	3 rooms[a]	3 rooms[b]	2 rooms[c]	Assumption
Treatment category[d]	Special	Special	Standard	Assumption
Working days per week	5	5	5	Assumption
Hours/day available for treatment	14	14	14	Assumption
Days of operation/year	250	250	250	Assumption
Time/fraction (average)	18 min	18 min	10 min	Assumption
Number of fractions/room	11,667	11,667	21,000	Outcome
Treatment room utilization	98%	98%	100%	Assumption
Treatment room availability	95%	98%	98%	Assumption
Total number of fractions/year	32,585	33,614	41,160	Outcome
Number of fractions/patient (average)	18	20	18	Maastro, data on file; Ref. [20]; Expert opinion
Total number of patients/year	1810	1681	2287	Outcome
Costs (€)				
Capital costs				
Medical equipment and IT	13,750,000	11,250,000	14,250,000[e]	T&T, data on file
Particle therapy equipment	90,000,000	60,000,000	–	T&T, data on file
Building	34,850,000	23,680,000	9,180,000	T&T, data on file
Total capital costs	*138,600,000*	*94,930,000*	*23,430,000*	–
Assumed lifecycle	30 years	30 years	30 years	Assumption
Capital costs/year	4,620,000	3,164,333	781,000	–
Operational costs				
Cost of operation/year	10,952,350	5,736,450	2,758,350	T&T, data on file
Cost of renewal/year	3,697,750	2,080,200	1,562,700	T&T, data on file
Cost of staff/year	6,366,304	6,366,304	2,599,716	See Appendix
Yearly interest for financing (5% over 20 years)	11,121,623	7,617,429	1,880,084	Assumption
Operational cost/year	32,138,027	21,800,383	8,800,850	–
Total costs/year	36,758,027	24,964,716	9,581,850	–
Cost/fraction	1128	743	233	–
Ratio to photon	4.8	3.2	–	–

T&T = Turner & Townsend GmbH, construction and management consultants.
Maastro = Maastricht Radiation Oncology (Maastro Clinic), The Netherlands.
[a] 3 treatment rooms with 2 treatment rooms equipped with a gantry or a pair of fixed beams, third room equipped with a horizontal beam, a linear accelerator and synchrotron for acceleration, robotic patient positioning system.
[b] 3 treatment rooms with 2 treatment rooms equipped with a gantry, third room equipped with a horizontal beam, and cyclotron for acceleration, robotic patient positioning system.
[c] 2 treatment rooms equipped with standard linear accelerators (in line with Goitein en Jermann [3]).
[d] Treatment categories for radiotherapy as given by Slotman and Leer [20].
[e] Including the cost of linear accelerators (linacs).

ities the estimations are based on opinion of experts from particle facilities, backed up by evidence pointing out that the average number of fractions for carbon-ion treatment tends to be lower than the number of fractions for proton treatment, as shown in the trials.

Sensitivity analyses

The following items are varied to investigate their influence on the cost per fraction: (1) capital costs, (2) operational costs, (3) lifetime of the facilities, (4) patient throughput, (5) time per fraction, (6) treatment hours per day, (7) treatment room availability, (8) treatment room utilization, (9) energy costs, (10) interest rate, and (11) patient mix. With regard to the last: patients who require special treatments bring along higher costs due to a longer time per fraction and the use of sophisticated equipment. In The Netherlands teletherapy treatments are categorized into four groups, from T1 'simple' category (short radiation course) to T4 'special' category (e.g., 3D-conformal therapy with intensive megavoltage imaging and in vivo dosimetry, stereotactic radiotherapy, intensity-modulated radiotherapy – IMRT, and intra-operative radiotherapy) [20]. Slotman and Leer [20] calculated that for special category treatments (T4) the amount of resources is 2.9 times higher than for a standard treatment (T2 equivalent). In a sensitivity analysis this standard-to-special-treatment factor is varied between 1.5 and 5.

Treatment scenarios

To illustrate the actual treatment costs, these are calculated for four tumor indications: prostate, lung, head & neck, and skull-base chordoma. In Table 4 the number of fractions and time to deliver a single fraction as used for the cost calculation for each tumor type are given. Treatment costs are calculated for a range of fractions based on actual clinical study protocols [22–51]. A linear relation between the number of fractions and the cost per fraction is assumed. No threshold value for fixed costs, e.g., for preparation of the treatment, is taken into account. Proton costs are calculated separately for a combined facility and a proton-only facility.

Results

Base-case analysis

A combined facility is most costly, with total costs per year of € 36.7 million, followed by a proton-only facility with € 24.9 million, and a photon facility with € 9.6 million. Total yearly costs for the combined and proton-only facilities are 3.8 and 2.6 times higher as for the photon facility.

In the particle facilities approximately 87% of the annual costs are due to the operational and 13% due to the capital costs. In the photon facility this is 92% and 8%, respectively. Here not only the capital and operational costs are substantially lower, but also the total number of fractions per year is 18–21% higher. Cost per fraction is highest for the combined facility with € 1128, followed by the proton-only facility with € 743, and the photon facility with € 233. Cost per fraction for the combined and proton-only facilities is 4.8 and 3.2 times higher as for the photon facility. The cost estimates are listed in Table 2.

Sensitivity analyses

A change in capital costs of ±20% leads to a change in the cost per fraction of ±2.5% for the particle and ±1.7% for the photon facilities. A change in operational costs of ±20% leads to a change in the cost per fraction of ±17% for the particle and ±18% for the photon facilities. This has only a small impact on the cost ratios. A shorter lifetime of a facility leads to a larger cost difference between particle and a photon facilities. A ±20% change in the number of treated patients changes the cost per fraction with −17% to +25%, assuming that the capital costs and operational costs have remained unchanged. When 30% less patients are treated the cost per fraction increases with 43%. Halving of the number of patients doubles the costs. Shortening the time per fraction in the particle facilities with 4 min (14 min instead of 18 min) causes a major reduction in the cost per fraction, notably in a combined facility. The cost ratios drop from 4.8 to 3.8 and from 3.2 to 2.5. Variation of the hours available for treatment, treatment room availability, and increased energy costs have a small impact on the cost ratios. When treatment room utilization for particle therapy is reduced from 98% to 90% the cost ratios increase to 5.3 and 3.5. Exclusion of the interest payment for financing reduces the cost per fraction with 30% for the particle and 20% for the photon facility. Cost per fraction for a photon facility increases from € 233 to € 676 when a value of 2.9 for the standard-to-special-treatment factor is applied [20]. The cost ratios decrease to 1.7 and 1.1. The sensitivity analyses outcomes are presented in Table 3.

Treatment scenarios

Cost difference between particle and photon therapies is relatively small for the lung and prostate tumors, and larger for skull-base chordoma and head & neck tumors. The lowest particle therapy costs are for inoperable stage I non-small cell lung cancer, namely € 10,030 for treatment with c-ions and € 12,380 for a proton treatment in a proton-only facility (€ 18,800 in a combined facility). For this indication, the costs for photon treatment are € 8150 for 3DRT and € 3720 for SBRT. The highest particle therapy costs are for head & neck tumors, € 30,080 for a c-ion treatment, € 39,610 for a proton treatment in a proton-only facility (€ 60,160 in a combined facility). Costs for IMRT with photons for head & neck tumors are € 11,520. In Figs. 1–4, the relation between the treatment costs and the number of fractions used is illustrated. Ranges around the average number of fractions, as given in Table 4, are used for these figures.

Discussion

In the presented study radiotherapy costs are determined for three different facilities: a combined carbon-ion and proton, a proton-only, and a photon facility. The best currently available information on most important factors contributing to and influencing the costs is incorporated. Construction costs, costs for running a facility, and throughput of patients are jointly used to calculate the cost per fraction for each facility. Additionally, specific treatment costs are determined for four cancer indications: prostate, lung, head & neck, and skull-base chordoma. The calculated cost per fraction is: € 1128 (€ 877–1974) for a combined facility, € 743 (€ 578–1300) for a proton-only facility and € 233 (€ 190–407) for a photon facility. This gives a cost ratio to photon of 4.8 for a combined facility and 3.2 for a proton-only facility. Cost per fraction is sensitive to changes in operational costs and patient throughput. The tumor specific treatment costs for particle therapy range from € 10,030 for lung cancer treatment with c-ions to € 60,160 for head & neck tumors treatment with protons in a combined facility.

The calculated figures are inevitably associated with uncertainty. A high number of input variables is included, based on information from the literature, business data and expert opinion. The given cost ratios most likely approach reality better than the absolute costs. The above mentioned approach was chosen because

Table 3
Sensitivity analyses: estimates of cost per fraction.

	Particle facility				Photon facility
	Combined carbon-ion and proton	*Ratio to photon*	Proton-only	*Ratio to photon*	
Capital costs					
Base case scenario	€ 138,600,000		€ 94,930,000		€ 23,430,000
Optimistic scenario (−20%)	€ 110,880,000		€ 75,944,000		€ 18,744,000
Pessimistic scenario (+20%)	€ 166,320,000		€ 113,916,000		€ 28,116,000
	Cost per fraction		Cost per fraction		Cost per fraction
Base case scenario	€ 1128	4.8	€ 743	3.2	€ 233
Optimistic scenario (−20%)	€ 1100	4.8	€ 724	3.2	€ 229
Pessimistic scenario (+20%)	€ 1156	4.9	€ 762	3.2	€ 237
Operational costs					
Base case scenario	€ 32,138,027		€ 21,800,383		€ 8,800,850
Optimistic scenario (−20%)	€ 25,710,421		€ 17,440,306		€ 7,040,680
Pessimistic scenario (+20%)	€ 38,565,632		€ 26,160,459		€ 10,561,020
	Cost per fraction		Cost per fraction		Cost per fraction
Base case scenario	€ 1128	4.8	€ 743	3.2	€ 233
Optimistic scenario (−20%)	€ 931	4.9	€ 613	3.2	€ 190
Pessimistic scenario (+20%)	€ 1325	4.8	€ 872	3.2	€ 276
Lifecycle of a facility	Cost per fraction		Cost per fraction		Cost per fraction
Base case: 30 years	€ 1128	4.8	€ 743	3.2	€ 233
5 years	€ 1837	5.6	€ 1213	3.7	€ 328
40 years	€ 1093	4.8	€ 719	3.2	€ 228
No. of patients per year[a]					
Base case scenario	1810		1681		2287
Optimistic scenario (+20%)	2172		2017		2744
Pessimistic scenario (−20%)	1448		1345		1829
Pessimistic scenario (−30%)	1267		1176		1601
Pessimistic scenario (−50%)	905		840		1143
	Cost per fraction		Cost per fraction		Cost per fraction
Base case scenario	€ 1128	4.8	€ 743	3.2	€ 233
Optimistic scenario (+20%)	€ 940	4.8	€ 619	3.2	€ 194
Pessimistic scenario (−20%)	€ 1410	4.8	€ 928	3.2	€ 291
Pessimistic scenario (−30%)	€ 1612	4.8	€ 1061	3.2	€ 333
Pessimistic scenario (−50%)	€ 2256	4.8	€ 1485	3.2	€ 466
Average time per fraction (particle)	Cost per fraction		Cost per fraction		Cost per fraction
Base case: 18 min	€ 1128	4.8	€ 743	3.2	–
Optimistic scenario (−4 min)	€ 877	3.8	€ 578	2.5	–
Pessimistic scenario (+4 min)	€ 1379	5.9	€ 908	3.9	–
Hours per day available	Cost per fraction		Cost per fraction		Cost per fraction
Base case: 14 h/day	€ 1128	4.8	€ 743	3.2	€ 233
8 h/day	€ 1974	4.8	€ 1300	3.2	€ 407
16 h/day	€ 987	4.8	€ 650	3.2	€ 204
Treatment room availability	Cost per fraction		Cost per fraction		Cost per fraction
Base case: 95%, 98%, 98%	€ 1128	4.8	€ 743	3.2	€ 233
90% all facilities	€ 1191	4.7	€ 809	3.2	€ 253
Treatment room utilization (particle)	Cost per fraction		Cost per fraction		Cost per fraction
Base case: 98%	€ 1128	4.8	€ 743	3.2	–
90%	€ 1228	5.3	€ 809	3.5	–
Energy costs	Cost per fraction		Cost per fraction		Cost per fraction
Base case: 100 € /MWh/a	€ 1128	4.8	€ 743	3.2	€ 233
150 € /MWh/a	€ 1147	4.9	€ 749	3.2	€ 236
200 € /MWh/a	€ 1165	4.9	€ 755	3.2	€ 238
Interest payment	Cost per fraction		Cost per fraction		Cost per fraction
Base case: 5% over 20 years	€ 1128	4.8	€ 743	3.2	€ 233
5% over 25 years	€ 1089	4.8	€ 716	3.1	€ 228
5% over 30 years	€ 1063	4.7	€ 700	3.1	€ 224
No interest payment	€ 787	4.2	€ 516	2.8	€ 187
T4 category photon treatments only [20]	Cost per fraction		Cost per fraction		Cost per fraction
Base case: standard treatment	€ 1128	4.8	€ 743	3.2	€ 233
Weight factor 1.5	–	3.2	–	2.1	€ 350
Weight factor 2.9	–	1.7	–	1.1	€ 676
Weight factor 5.0	–	1.0	–	0.6	€ 1165

[a] Assuming an average number of fractions per patient (specific for each facility).

at the moment there are no fully operational combined facilities in Europe that would allow an activity based costing, which would possibly give more accurate results [52]. The framework for calculation is however, set up in detail and extensive sensitivity analyses account for potential variations in the estimates.

The construction and operation of a radiotherapy facility depends on many local factors. The financial plan, budgetary conditions, construction/vendor market providing the facility and the equipment might differ internationally and even within one country. The presented model is a simplified reflection of a complex sit-

Table 4
Number of fractions, time to deliver a single fraction, and corresponding treatment costs, as calculated by the model, for four different tumor indications.

RT treatment per tumor indication	Number of fractions (average and range)	Time per fraction (min)	Source	Facility	Cost per treatment (€)
Prostate					
C-ion	20 (16–26)	10	Ref. [22]	Combined	12,530 (10,030–16,290)
Proton	39 (34–44)	10	Refs. [23–25]	Proton-only	16,090 (14,030–18,160)
				Combined	24,450 (21,320–27,590)
IMRT	39 (20–41)	20	Refs. [26–29]	Photon	18,160 (9310–19,090)
3DCRT	36 (20–40)	10	Refs. [23,26,29,30]	Photon	8380 (4660–10,240)
Lung[a]					
C-ion	4 (1–18)	40 (inclusive gating)	Ref. [31]	Combined	10,030 (2510–45,120)
Proton	10 (10–20)	30 (inclusive gating)	Refs. [32,33]	Proton-only	12,380 (12,380–24,760)
				Combined	18,800 (18,800–37,600)
SBRT	4 (1–10)	40	Ref. [34]	Photon	3720 (930–9310)
3DRT	35 (20–44)	10	Ref. [35]	Photon	8150 (4660–10,240)
Head & neck					
C-ion	16 (16–24)	30	Ref. [36]	Combined	30,080 (30,080–45,120)
Proton	32 (26–40)	30	Refs. [37–39]	Proton-only	39,610 (32,180–49,510)
				Combined	60,160 (48,880–75,200)
IMRT	33 (25–35)	15	Refs. [40–45]	Photon	11,520 (8730–12,220)
Skull-base chordoma					
C-ion	20 (16–38)	20	Refs. [46,47]	Combined	25,070 (20,060–47,630)
Proton	37 (25–42)	20	Refs. [48–50]	Proton-only	30,530 (20,630–34,660)
				Combined	46,380 (31,340–52,640)
FSRT	30 (28–38)	20	Ref. [51]	Photon	13,970 (13,040–17,690)

IMRT = intensity-modulated radiation therapy.
3DCRT = three dimensional conformal radiation therapy.
SBRT = stereotactic body radiation therapy.
3DRT = three dimensional radiation therapy.
FSRT = fractionated stereotactic radiation therapy.
[a] Inoperable stage I non-small cell lung cancer.

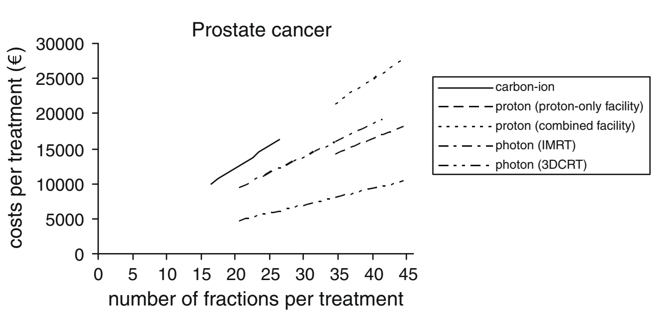

Fig. 1. Prostate cancer (A linear relation between the number of fractions and the cost per fraction is assumed. Although no threshold values for fixed costs, e.g., for preparation of the treatment, were taken into account in the model, for illustration, an expected minimal treatment cost of € 2500 was used in the figures. IMRT = intensity modulated radiation therapy 3DCRT = three dimensional conformal radiation therapy.

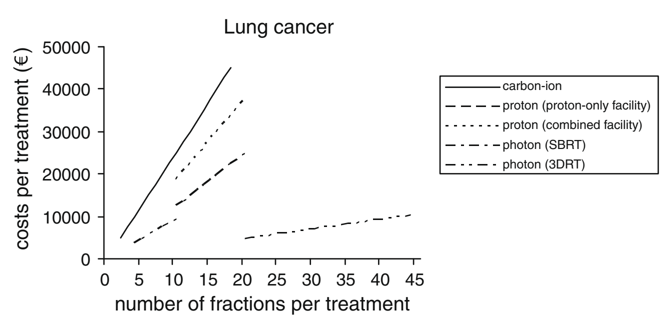

Fig. 2. Lung cancer (A linear relation between the number of fractions and the cost per fraction is assumed. Although no threshold values for fixed costs, e.g., for preparation of the treatment, were taken into account in the model, for illustration, an expected minimal treatment cost of € 2500 was used in the figures. SBRT = stereotactic body radiation therapy. 3DRT = three dimensional radiation therapy.

uation. Initial capital costs are evenly distributed over the assumed life cycle period of the facilities and an interest rate of 5% on the original funding is included. Both assumptions represent a conservative approach. Cost per fraction without interest payment is calculated to be € 787, € 516, and € 187 for the combined, proton-only, and photon facility, respectively. This is about 70% of the base-case figures for the particle therapy and 80% for the photon therapy.

The main input parameters are varied in the sensitivity analyses. Apart from the market developments and technical issues, changes in a facility operation have an impact on the cost per fraction. There are at least two issues which influence the operational costs that are associated with running a new facility. First is the optimal use of a facility's capacity. In the present study a maximum capacity use is modelled. However, in practice it will presumably take some years before such a situation is reached. Cost per fraction will be higher before a facility is fully operational. Second issue is the learning effect. Costs of new health technologies tend to fall with time as the efficiency improves through experience. This has been showed in radiotherapy previously, for instance for

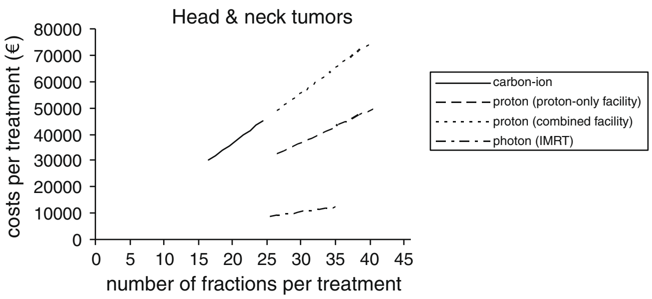

Fig. 3. Head & neck tumors (A linear relation between the number of fractions and the cost per fraction is assumed. Although no threshold values for fixed costs, e.g., for preparation of the treatment, were taken into account in the model, for illustration, an expected minimal treatment cost of € 2500 was used in the figures. IMRT = intensity modulated radiation therapy.

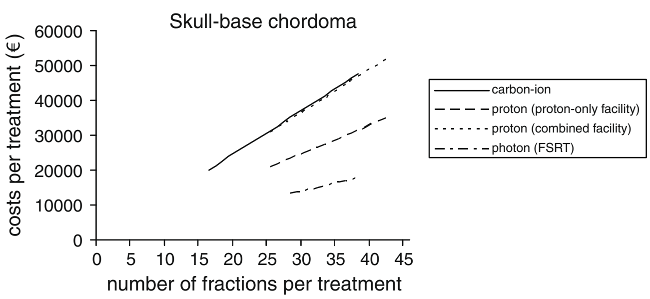

Fig. 4. Skull-base chordoma (A linear relation between the number of fractions and the cost per fraction is assumed. Although no threshold values for fixed costs, e.g., for preparation of the treatment, were taken into account in the model, for illustration, an expected minimal treatment cost of € 2500 was used in the figures. FSRT = fractionated stereotactic radiation therapy).

IMRT [53]. The above mentioned issues have an opposite effect on the costs. In the present study this is not explicitly modelled, but the operational costs have been varied, as has been the patient throughput.

Another issue to consider in a cost comparison of different facilities is the patient mix. The number of fractions delivered per year in a facility depends on the patient mix because this determines the average time per fraction. Complicated treatments often require more time per fraction than standard treatments. It can be assumed that once a facility is built, only patients are going to be treated who are qualified for treatment in such facility. For a photon facility this inevitably means a mix of standard and complicated cases. For a particle facility this will be mainly the complicated cases, at least at present. To demonstrate the average cost difference between the facilities, in the base-case analysis an *average cost per fraction* for each facility is calculated, assuming a mix of standard and complicated cases in a photon facility and complicated cases in a particle facility. For a comparison of the *tumor specific treatment costs*, the corresponding tumor specific treatment costs are calculated, including the most sophisticated photon treatment at present.

In the chosen three facility scenarios particle therapy is compared to photon therapy, consistent with the objective of this study. A rationale to combine c-ion and proton therapy in one combined facility is the technical advantage of using the same accelerator. A construction of an 'all inclusive' facility including treatment with c-ions, protons and photons is not included in this study. This might be of interest considering that some proton facilities (Boston, Loma Linda) use mixed beam treatment schedules, combining photon and proton radiation, e.g., for high risk prostate cancer patients [24,25,54].

Regarding the specific treatment costs there are several points to discuss. Treatment scenarios for particle therapy are still in development. The fractionation schedules used in this study are based on the conducted trials. It is feasible that in the future treatments can be given with much fewer fractions than at present. This will reduce the treatment costs of particle therapy. Ultimately, the treatments' efficacy and toxicity will determine the cost-effectiveness of particle therapy as compared to photon therapy. However, in theory, any cost-effectiveness ratio will be more favourable for particle therapy in case fewer fractions per patients are used.

The actual impact of a reduced fractionation on costs, depends on how treatment costs are defined and valued. Number of fractions, time to deliver a single fraction, logistic aspects of treatment are all factors to which different weight might be attributed. Moreover, in practice different fixed cost thresholds are used. In the present paper the calculations are simplified, assuming linearity, without any threshold values for fixed costs. A tumor specific time per fraction is taken to calculate the cost per fraction, which is then multiplied by the number of fractions. This gives large treatment costs for tumors which require a large number of fractions and a long time to deliver a fraction at the same time. Therefore, treatment costs for head & neck tumors, and the IMRT costs for prostate cancer are relatively high. Further, the calculated treatment costs roughly correspond with the costs found in the literature, as shown in Table 1.

The estimates of the cost per fraction correspond to the figures found in the literature (recalculated to the 2007 price level). For a combined particle facility no estimates could be found. Two studies reported a cost per fraction for a carbon-ion facility, € 1030 [14] and € 1130 [18]. These figures correspond to our estimate of € 1128. The cost per fraction of € 1110 for proton therapy calculated by Goitein and Jermann [3] is higher than our estimate of € 743, based on relatively high patient throughput in the particle facilities. In a recently published review on radiation costs, a maximum cost per fraction of photon therapy is € 190 [55]. The cost calculated in this study is € 233. The cost per fraction of photon IMRT was estimated by Goitein and Jermann [3] as € 460. In our study the cost per photon fraction for special treatment category, such as IMRT, is € 676.

This study is a first cost analysis that compares the costs per fraction and the costs per treatment for carbon-ion, proton and photon therapy. The estimated investment costs for a particle facility are much higher than for a photon facility, but this difference becomes smaller when the total yearly costs over the lifetime of the facilities are compared. Cost per fraction and also treatment specific costs are highly dependent on patient mix and throughput. The difference in treatment costs between particle and photon therapy is further reduced through the advantage of particle therapy to give treatments with fewer fractions. Ultimately, the clinical effectiveness of the treatments with charged particles will decide whether such treatments are cost-effective compared to photon therapy. Based on the results of this study, we can point out that depending on the indications selected for particle therapy, when a sufficient number of patients is available, and a facility is run efficiently, particle therapy may not be "too expensive to become true".

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Appendix 1

Table A1. Staffing plan for the facilities.

Staff	Required personnel particle facility (FTE)	Required personnel photon facility (FTE)	Cost per FTE (€/ year)
Director	2	1.5	132,516
Physician	8.2	4.2	132,516
Financial manager	1.4	0.8	59,448
Research fellow	4.2	4.2	61,249
Physicist	15.5	1.6	96,779
Biologist	1.5	0.1	96,779
Technician	15.7	1.5	51,174
Radiation technologist	35.1	19.0	45,420
Secretary	7.6	7.6	35,812
Total	91.3	40.4	

FTE = full time equivalent. Working hours per physician per week = 48. Working hours per all other FTE per week = 36. Productive hours/total working hours per FTE = 80%.
Data based on Refs. [20,21] and Maastro Clinic, Maastricht, The Netherlands.

Appendix 2

Table A2. Total costs for staff for the facilities.

Costs for staff	Particle facility (k€)	Photon facility (k€)
Cost for personnel	6016	2428
Cost for scientific committee	50	50
Contingency (5%)	301	121
Total costs staff per year	6366	2600

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