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Budget Impact Analysis for Proton Beam Therapy in adult population in Poland

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Abstract

Objective: The use of proton beam therapy (PBT) increases in the treatment of some cancers, especially in the critical organs. Contrary to traditional radiotherapy, protons limit the radiation of healthy tissues. Due to high cost of treatment and limited options, decisions to treat adults with PBT must be based on relative value compared to the current standard of care. The purpose of this publication is to assess the budgetary impact of using PBT in 8 selected oncology indications in Poland.

Methods: The budget impact analysis (BIA) was carried out in a 3-year time horizon. The 'new' scenario presents the estimated costs of PBT in adult population while the 'existing' scenario includes only other forms of radiotherapy – IMRT and stereotactic radiotherapy. Cost data reflect the estimated costs incurred by the public payer (NHF) in providing health benefits. Sources of data were: epidemiological data, opinions of clinical experts, scientific evidence and NHF data.

Results: Total incremental cost of the base case with PBT was about €34.6 million (€10.4 million, €11.5 million. and €12.7 million in each year of analysis). In comparison to 'existing' scenario cost increased approximately 2.75 times (total costs from €19.8 million to €54.4 million, cost per patient from €5,543 to €15,265). Sensitivity analysis revealed that total incremental costs in the minimum scenario were over 20% lower than in base case, while the cost in maximum scenario was similar to base case.

Conclusion: The expected costs of PBT in adult cancer patients in Poland significantly exceed the costs of treatment with IMRT and stereotactic radiotherapy.

INTRODUCTION

Proton beam therapy (PBT) is a radiation technique that delivers particles of protons in place of the X-rays used in conventional photon radiation therapy. The main advantage of PBT is the ability to deliver beam of proton particles precisely to the tumor tissue which results in almost no radiation affecting healthy tissue surrounding the tumor.[1]

The use of PBT is of particular importance in the case of children exposed for many years to the side effects of radiation, including secondary cancers. The indications for PBT in adults are less known comparing to pediatric population. In adults, PBT is mainly used for tumors close to critical structures (e.g. chordoma).[2] Taking into account the limitations, potential benefits and costs, adult patients should be qualified for PBT treatment on the 'not-routine' manner with particular focus on young adults with tumor located near critical organs.[3]

Currently, there are over 100 PBT treatment centers worldwide. Most of their activities started in last 10 years.[4] Despite the rapid development of the centers, the availability of treatment in relation to the number of sick patients is still limited. Apart from reimbursement and technical issues, major limitations in PBT access are related to determination of indications with proven advantages of PBT over other forms of radiotherapy.[5]

According to research, use of PBT will be increasingly important not only because of patient safety but also due to increasing cancer incidence rates. It is expected that by the end of 2025 the number of new cases in Poland will increase to 350,000 annually.[6]

MATERIALS AND METHODS

The BIA concerns the financial consequences of extending the use of PBT from the perspective of the Polish public payer (National Health Fund, NHF) in 8 indications including neoplasms located outside of the eye in adult population (table 1). The analysis was performed according to the recommendations for conducting BIA.[7,8,9]

The financial consequences of introducing the proposed changes were presented as an incremental cost expressed as the difference in costs between the 'new' and 'existing' scenario.

The 'existing' scenario presents the estimated costs of the NHF for two types of radiotherapy: intensity-modulated radiation therapy (IMRT) and stereotactic teleradiotherapy (stereotactic RT) in the above-mentioned indications. In this scenario the PBT is not available for treatment and is not financed by the NHF.

The 'new' scenario presents the estimated costs of PBT. Since some patients do not meet eligibility criteria for PBT, some of them will receive other forms of RT, i.e. IMRT or stereotactic RT. It is caused by:

- personal preferences of patients or their parents/guardians regarding the optimal form of radiotherapy,
- limited access to PBT (only one PBT center located in southern Poland).

The analysis was carried out in a 3-year time horizon. Cost data reflect the estimated costs incurred by the public payer in providing health benefits. The estimation of the financial consequences was based on the Polish current tariffs for the included benefits.

All costs are presented in EUR using the exchange rates as of June 23, 2022 of the National Bank of Poland (€1 = PLN 4.6590, £1 = PLN 5.4756, CAD 1 = PLN 3.4582, AUD 1 = PLN 3.0877 PLN). Amounts are shown in full values.No ethics committee review was required since this research did not include human subject data. Individual patient level information was not used, and the research relies purely on published or simulated data.

Data sources

Sources of data included into analysis were: opinions of clinical experts, scientific evidence and data received from NHF.

Population

The patient population for each indication was estimated based on the available epidemiological data and the opinion of clinical experts. The target population in both scenarios is equal due to:

- the same eligibility criteria for particular types of radiotherapy,
- no patients meeting eligibility criteria only in case of extension of the indications for PBT.

The parameters included in the analysis model are mainly based on expert opinions (based on the questionnaires and personal communications) as the best available data source due to fragmentation of information and high specificity of indications included in the BIA (table 1).

The analysis of the impact on the NHF budget also assumes an increase in the target population compared to the previous year (table 2).

Table 1. Estimation of the population for particular indications included in the analysis

Indication	Number of patients Scenario: 'new' or 'existing'		
	Year 1	Year 2	Year 3
Craniopharyngiomas, condition after incomplete surgical treatment or inability of surgical treatment of the primary or recurrent tumor (C75.2) (indication I)	13	15	17
Orbital sarcomas, condition after incomplete surgical treatment or inability of surgical treatment of the primary or recurrent tumor (C69.6) (indication II)	13	15	17
Orbital lymphomas requiring consolidation radiotherapy in the course of oncological treatment (C69.6) (indication III)	9	10	11
Meningiomas of the brain and spinal cord, WHO stages I and II, condition after incomplete surgical treatment or inability of surgical treatment of the primary or recurrent tumor (C70.0; C70.1; C70.9) (indication IV)	100	110	121
Adenomas of the pituitary gland, condition after incomplete surgical treatment or the inability of surgical treatment of the primary or recurrent tumor (C75.1) (indication V)	21	24	27
Tumors of the external auditory canal and middle ear, condition after incomplete surgical treatment or inability of surgical treatment of the primary or recurrent tumor (C43.2; C30.1) (indication VI)	21	24	27
Hodgkin and non-Hodgkin lymphoma that requires mediastinal irradiation (C30-C39) (indication VII)	600	660	726
Malignant neoplasms of various histopathology originating from the nasal cavity, paranasal sinuses or pharynx, infiltrating the natural orifices and/or bones of the skull base (diagnosis based on the MRI of the head and neck) (various types of cancer) (indication VIII)	200	220	242
Total	977	1,078	1,188

MRI – magnetic resonance imaging; WHO – World Health Organization

Table 2. Estimations of the population growth in the subsequent years of analysis in base case and sensitivity analysis

Parameter	Scenario		
	Minimal	Base	Maximum
Annual increase of population (%)	5	10	20

Types of costs included

The BIA includes costs related to the irradiation treatment itself, its planning and related hospitalization, i.e. the costs of:

- hospitalization,
- planning PBT,
- radiotherapy treatment (PBT, IMRT and stereotactic RT),
- treatment of adverse events (AEs) of Grade 3. or 4.

Table 3 presents detailed values concerning a valuation of health services related to radiotherapy in Poland by the NHF.

Table 3. Costs of the health procedures based on the NHF valuation

Procedure	Value [EUR]
PBT planning	3,650
PBT	9,230
IMRT	3,518
Stereotactic RT	3,128
Treatment of AEs Grade 3/per day	35
Treatment of AEs Grade 4/per day	46
Hospitalization/per day	76

AE – adverse event; IMRT – intensity-modulated radiation therapy; PBT – proton beam therapy; RT – radiation therapy

In order to correctly estimate the consequences of introducing the proposed changes, the analysis was based on variables related to radiotherapy, hospitalization during radiotherapy, adverse events and necessity of repeated radiotherapy in some cases. They are indicated in the table 4.

Table 4. Parameters used in the analysis with their values

Parameter	Scenario		
	Minimum	Base	Maximum
Parameters related to radiation therapy			
Percentage of patients receiving PBT	80	90	100
Percentage of patients receiving MRT/stereotactic RT – 'new' scenario	20	10	0
Percentage of patients receiving MRT/stereotactic RT – 'existing' scenario	100	100	100
Percentage of patients receiving IMRT in the group of patients receiving IMRT/stereotactic RT – 'new' and 'existing' scenario	85	85	85
Percentage of patients receiving stereotactic RT in the group of patients receiving IMRT/ stereotactic RT – 'new' and 'existing' scenario	15	15	15
Percentage of patients receiving PBT out of patients subject to planning procedure	100	100	100
Parameters related to hospitalization during radiotherapy			
Percentage of patients hospitalized during PBT	60	80	100
Percentage of patients hospitalized during IMRT/stereotactic RT	20	40	60
Hospitalization time - therapy (days)	42	56	65
Parameters related to adverse events			
Percentage of PBT patients with Grade 3 AEs	10	13	15
Percentage of PBT patients with Grade 4 AEs	0	2	5
Percentage of IMRT/stereotactic RT patients with Grade 3 AEs	25	33	40
Percentage of IMRT/stereotactic RT patients with Grade 4 AEs	15	18	20
Hospitalization time PBT/IMRT/stereotactic RT – Grade 3 AEs (days)	10	15	20
Hospitalization time PBT/IMRT/stereotactic RT – Grade 4 AEs (days)	15	20	25
Parameters related to the necessity of repeated radiotherapy			
Percentage of patients that undergo repeated PBT/ IMRT/stereotactic RT	5	10	10

AE – adverse event; IMRT – intensity-modulated radiation therapy; PBT – proton beam therapy; RT – radiation therapy

RESULTS

The results of the analysis were presented in table 5-6 (base case) and 7-8 (scenarios of the sensitivity analysis). The BIA was estimated as a total costs and costs of various forms of radiotherapy per patient. Total costs were calculated in scenario comprising costs of treatment with the PBT, IMRT or stereotactic RT with patients ratios according to values listed in table 4. In the base case 977 (year 1), 1,078 (year 2) and 1,188 (year 3) patients in 8 cancer indications were included. Total costs were shown in table 5. Costs of treatment per patient in 'existing' and 'new' scenario for all types of RT were presented in table 6.

Table 5. Results of the BIA

Indication	Year 1 [EUR]	Year 2 [EUR]	Year 3 [EUR]
'Existing' scenario			
I	79,265	91,459	103,654
II	79,265	91,459	103,654
III	54,876	60,973	67,070
IV	609,730	670,703	737,773
V	128,043	146,335	164,627
VI	128,043	146,335	164,627
VII	3,658,377	4,024,215	4,426,636
VIII	1,219,459	1,341,405	1,475,545
Total	5,957,057	6,572,884	7,243,586
'New' scenario			
I	218,291	251,874	285,457
II	218,291	251,874	285,457
III	151,124	167,916	184,707
IV	1,679,158	1,847,074	2,031,781
V	352,623	402,998	453,373
VI	352,623	402,998	453,373
VII	10,074,947	11,082,442	12,190,686
VIII	3,358,316	3,694,147	4,063,562
Total	16,405,373	18,101,322	19,948,396
Incremental cost			
I	139,026	160,414	181,803
II	139,026	160,414	181,803
III	96,249	106,943	117,637
IV	1,069,428	1,176,371	1,294,008
V	224,580	256,663	288,746
VI	224,580	256,663	288,746
VII	6,416,571	7,058,228	7,764,050
VIII	2,138,857	2,352,743	2,588,017
Total	10,448,316	11,528,439	12,704,810

Table 6. Costs per patient in scenarios: 'existing', 'new' and cost of PBT per patient

Average annual cost per patient [EUR]	
'existing' scenario	5,543
'new' scenario	15,265
'new' scenario' only PBT	16,351
PBT – proton beam therapy	

SENSITIVITY ANALYSIS

One-way sensitivity analysis was performed for all model inputs. Sensitivity analysis was presented as a minimum and maximum scenario. Values of parameters used were presented in table 4.

Sensitivity analysis (tables 7, 8) revealed that total incremental costs in the minimum scenario were over 20% lower than in base case. Interestingly, in the maximum scenario, the total incremental costs in the 3-year horizon were at the similar level compared to the base case (in absolute values, the difference amounts to €900thous.).

Table 7. Results of the sensitivity analysis – incremental costs in minimum and maximum scenario

Indication	Year 1 [EUR]	Year 2 [EUR]	Year 3 [EUR]
Incremental cost – minimum scenario			
I	115,027	123,876	132,724
II	115,027	123,876	132,724
III	79,634	88,483	97,331
IV	884,827	929,068	982,158
V	185,814	203,510	221,207
VI	185,814	203,510	221,207
VII	5,308,962	5,574,410	5,857,555
VIII	1,769,654	1,858,137	1,955,468
Total	8,644,760	9,104,870	9,600,373
Incremental cost – maximum scenario			
I	129,746	159,687	199,609
II	129,746	159,687	199,609
III	89,824	109,785	139,726
IV	998,044	1,197,653	1,437,183
V	209,589	259,491	319,374
VI	209,589	259,491	319,374
VII	5,988,264	7,185,917	8,623,100
VIII	1,996,088	2,395,306	2,874,367
Total	9,750,890	11,727,017	14,112,342

As part of the sensitivity analysis, the costs per patient were also estimated in the minimum and maximum scenarios. Results were presented in table 8.

Table 8. Costs per patient calculated in sensitivity analysis in minimum and maximum scenario

Average annual cost per patient [EUR]	
Minimum scenario	
'existing' scenario	4,499
'new' scenario	13,348
Incremental cost	8,848
Base case	
'existing' scenario	6,097
'new' scenario	16,792
Incremental cost	10,694
Maximum scenario	
'existing' scenario	9,768
'new' scenario	19,749
Incremental cost	9,980
PBT – proton beam therapy	

DISCUSSION

One of the most essential factors hampering the development of PBT is its high cost, including creating and operating of the PBT center. The majority of the economic studies comparing PBT with other forms of radiotherapy indicates that PBT cost is significantly higher – approximately 2-3 times vs. IMRT. This is also reflected in the costs estimated by the NHF, where PBT is 2.6 times more expensive than IMRT. However, more profound analysis taking into account also spendings for rehabilitation after therapy and treatment of adverse events results in diminishing the difference in costs due to lower complication rates after PBT, even with indicating PBT as a therapy with financial advantage.[11]

Due to the PBT's ability to deliver beam of proton particles precisely to the tumor tissue, the main advantage of this therapy consists in lower rates of adverse events comparing to other forms of RT. According to systematic reviews efficacy of PBT is similar to other innovative forms of RT (SBRT, IMRT or carbon ion RT) in several oncology indications including e.g.: non-small cell lung cancer,[12, 13] craniopharyngiomas[14] and various head and neck cancers.[15,16] However, since the main potential advantage of PBT over other RT forms includes long term safety issues further research addressing such evaluation, e.g. secondary cancers due to irradiation, shall be conducted. It should be also emphasized that the quality of currently available scientific evidence is relatively low, hence there is a necessity to conduct further randomized clinical trials of high quality.

Nevertheless PBT still remains costly therapy, hence its eligibility criteria must be determined strictly on the basis of scientific evidence with focus on the most promising indications. In Poland the initial list of neoplasms that could be treated with this method of radiotherapy included only seven diagnoses, although the original opinions (including the National Consultant's Team for Proton Radiotherapy) contained recommendations for significantly higher number of indications. In 2019 the list of indications was expanded by another nine groups of neoplasms located outside the eye.[17] Growing number of evidence led to conducting another analysis for potential widening eligibility criteria for PBT in Poland, which part is present BIA.

The BIA results indicate that out of 8 oncological indications, the highest costs of radiotherapy concern the indications IV (meningiomas), VII (Hodgkin and non-Hodgkin lymphomas) and VIII (neoplasms of various histopathology originating from the nasal cavity, paranasal sinuses or pharynx). Due to the assumption that the number of radiation doses taken by patients will remain unchanged, regardless of the indication, the highest costs for these indications result from the estimated population (respectively 10.2, 61.2 and 20.4% of the total number of patients included in the BIA).

According to the data obtained from the CCB, the number of PBT fractions taken by patients treated in this center varies in the range of 26-37 doses (average 32). We were unable to determine the dependence between the number of fractions and indications - it is selected individually, inter alia, based on the stage of the disease, the response/refractoriness of the neoplastic tissues to treatment or the patient's condition. However, since costs of PBT determined by NHF are not dependent on the number of doses, this inability do not influence the results of BIA.

The cost of PBT per patient calculated in BIA is approximately €16.3thous. while the same cost for entire 'new' scenario is slightly lower and amounts to €15.3thous. per patient. This difference is caused by lower cost of other forms of radiotherapy (IMRT and stereotactic RT) anticipated for use for the treatment of some patients. Estimated cost per patient in our BIA varies significantly from some analyses calculating costs in countries. In Canada, the average cost of PBT per patient is estimated at about €148,452, €117,527 in the United Kingdom and €132,548-€185,567 in Australia.[18] However these costs were estimated for the PBT treatment conducting outside of mentioned countries (e.g. in USA for Canadian patients) what, in fact, leads to their significant increase. Cost of PBT treatment of Canadian patients estimated for PBT center located within Canada greatly decrease this cost to about 29,711-35,790 EUR (depending on scenario including one- or four-room PBT center, respectively).[19] The result of this analyse indicates undoubtedly the cost-effectiveness of the PBT center operating within the country as long as adequate number of patients is eligible for proton treatment.

The cost of PBT per patient highly depends on the number of patients that are treated with the PBT, as well as which costs are included. Our BIA was based on costs of health services determined by the Agency for Health Technology Assessment and Tariff System (thus the cost that is paid by the NHF for the CCB as a fee for service) and does not include all costs of CCB functioning. The highest cost excluded from the analysis is the amortization cost. According to the data received from CCB this cost amounted to €8,498 thous. in 2019 and €4,683 thous. in 2020.

The BIA is subject to several limitations. One of them is the small size of the target population for some indications, which may potentially increase the uncertainty of cost estimates. However, this limitation is not a result of methodology used for BIA but it is caused by low preva-

lence of some cancers - in our BIA it concerns indications I, II, III, V and VI.

The time horizon adopted in the analysis (3 years) means that it does not include costs of treatment of late adverse events (e.g. secondary cancers due to irradiation of healthy tissues). It may potentially lead to underestimation of the advantages of PBT in comparison to other forms of radiotherapy, i.e. the likely better safety profile due to the physical properties of protons beam reducing irradiation of healthy tissues surrounding the tumor. The omission of this factor was caused by limited clinical data from low-quality studies with usually short follow-up periods. The BIA also does not take into account costs of terminal care (including best supportive care), costs from the patient's perspective (e.g. travel costs to a PBT center), costs from the social perspective (including indirect costs defined as costs of lost productivity of patients and their informal caregivers), the depreciation costs of the infrastructure (this applies to all types of radiotherapy included in the analysis) and costs of treating adverse events lower than grade 3.

It should also be noted that the analysis does not take into account the maximum capacity of the Polish PBT center. This means that the analysis includes the maximum number of patients for the indications covered by our BIA, which may exceed the capabilities of the CCB in Kraków. Finally, the analysis does not address the potential financial impact of an increase in the number of PBT patients on the treatment costs per patient (e.g. due to the division of fixed costs into a larger number of patients). It should be noted that in the event of a significant increase in the size of the population undergoing PBT, it may be necessary to re-calculate the actual costs.

CONCLUSION

The expected costs of PBT in adult cancer patients in Poland significantly exceed the costs of treatment with other forms of radiotherapy – IMRT and stereotactic RT. Both total costs of treatment and cost per patient are approximately 2.75 times higher in scenario with PBT comparing to scenario including only IMRT and stereotactic RT as available forms of radiotherapy in adult patients in 8 oncology indications covered by our BIA. The results obtained in our analysis may be useful for decisions in health care in Poland and to compare the costs of PBT with other countries.

AUTHORS' CONTRIBUTIONS

Radosław Rudź, PhD and Paweł Mońko, PhD – study design and all calculations; all authors – assisted in writing and editing of manuscript, data check-up, critical revision and final approval.

CONFLICT OF INTERESTS

The authors declare no conflicts of interest.

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