



Radiotherapy utilization

Radiotherapy utilization in developing countries: An IAEA study



Eduardo Rosenblatt^{a,*}, Elena Fidarova^a, Eduardo H. Zubizarreta^a, Michael B. Barton^b, Glenn W. Jones^c, William J. Mackillop^d, Lisbeth Cordero^e, Joel Yarney^f, Gerard Lim^g, John V. Gan^h, Valentin Cerneaⁱ, Suzana Stojanovic-Rundic^j, Primoz Stojan^k, Lotfi Kochbati^l, Aldo Quarneri^m

^a International Atomic Energy Agency, Vienna, Austria; ^b Ingham Institute for Applied Medical Research, UNSW, Sydney, Australia; ^c The Cancer Centre Eastern Caribbean, St. John's, Antigua and Barbuda; ^d Division of Cancer Care and Epidemiology, Kingston, Canada; ^e Hospital Mexico, San Jose, Costa Rica; ^f Centre for Radiotherapy and Nuclear Medicine, Korle Bu Teaching Hospital, Accra, Ghana; ^g National Cancer Institute, Putrajaya, Malaysia; ^h Jose R. Reyes Memorial Medical Centre, Quezon City, Philippines; ⁱ Oncology Institute, Cluj-Napoca, Romania; ^j Institute of Oncology and Radiology of Serbia, Belgrade, Serbia; ^k Institute of Oncology, Ljubljana, Slovenia; ^l Institut National de Cancer Salah Azaiz, Tunisia; and ^m Hospital Pereira Rossell, Montevideo, Uruguay

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ABSTRACT

Background: The planning of national radiotherapy (RT) services requires a thorough knowledge of the country's cancer epidemiology profile, the radiotherapy utilization (RTU) rates and a future projection of these data. Previous studies have established RTU rates in high-income countries.

Methods: Optimal RTU (oRTU) rates were determined for nine middle-income countries, following the epidemiological evidence-based method. The actual RTU (aRTU) rates were calculated dividing the total number of new notifiable cancer patients treated with radiotherapy in 2012 by the total number of cancer patients diagnosed in the same year in each country. An analysis of the characteristics of patients and treatments in a series of 300 consecutive radiotherapy patients shed light on the particular patient and treatments profile in the participating countries.

Results: The median oRTU rate for the group of nine countries was 52% (47–56%). The median aRTU rate for the nine countries was 28% (9–46%). These results show that the real proportion of cancer patients receiving RT is lower than the optimal RTU with a rate difference between 10–42.7%. The median percent-unmet need was 47% (18–82.3%).

Conclusions: The optimal RTU rate in middle-income countries did not differ significantly from that previously found in high-income countries. The actual RTU rates were consistently lower than the optimal, in particular in countries with limited resources and a large population.

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In developed countries, approximately half of cancer patients have an indication for radiotherapy [1]. Countries that experience the need for radiotherapy infrastructure expansion – often painfully expressed in waiting lists – usually embark on a national strategy for a planned development of their radiotherapy capacity. In this scenario, knowing the radiotherapy utilization (RTU) rates in a country is necessary to inform planning models for future radiotherapy services. This planning requires a thorough knowledge of the national cancer epidemiology profile and a realistic future projection of these data [2,3].

The oRTU rate is the proportion of all cancers with an indication for radiotherapy. In the “Collaboration for Cancer Outcomes Research and Evaluation” (CCORE) model [1] used here, an

indication for radiotherapy was defined as a clinical scenario for which radiotherapy is recommended as the treatment of choice because there is evidence that it has a superior clinical outcome compared to alternative treatment modalities including no treatment. The superiority of radiotherapy over other treatment options could be due to better survival, local control, and quality of life or toxicity profiles. In clinical situations where radiation therapy had an equal outcome to other treatment options such as surgery or chemotherapy, all the treatment options were included in the model, and a sensitivity analysis was conducted to determine the range of proportion of patients for whom radiotherapy may be indicated. An evidence-based computation model was used based on data from high-income countries.

Estimates of RTU in developed countries based on expert opinion have found that the desirable RTU rate was in the order of 50% [4–6]. Patients in low-middle-income countries (LMICs) usually present with more advanced disease. This fact coupled with

* Corresponding author at: International Atomic Energy Agency, Wagramer Strasse 5 – A-1400, Vienna, Austria.

E-mail address: rosenblatt21@gmail.com (E. Rosenblatt).

URL: <http://www.iaea.org/> (E. Rosenblatt).

limited access to oncology surgery, result in higher demand for radiotherapy compared with high-income countries (HICs).

In this first study looking at RTU rates in nine middle-income countries following an evidence-based method, the aim was to estimate the actual RTU and compare it with the optimal, to determine the gaps in service provision in these countries.

The objectives of the study were to: (1) estimate the optimal radiotherapy utilization (oRTU) rate; (2) measure the actual rate of radiotherapy utilization (aRTU) in the same countries and (3) assess the characteristics of patient populations, disease profiles, and treatments administered in the participating countries.

Methods

Countries were selected for this study according to the following criteria: (1) middle-income nations as per the World Bank classification of economies based on a Gross National Income (GNI) per capita (Atlas method) of US\$ 1.026 – 12.475 in the fiscal year 2012 [7], when the study was initiated. (2) Countries located in the four IAEA regions; Africa, Asia, Europe and Latin America. (3) Countries with existing and operational radiotherapy centre(s), (4) with an operational cancer registry, and (5) where a reliable and motivated coordinator could be identified. The countries selected for the study were Costa Rica, Ghana, Malaysia, Philippines, Romania, Serbia, Slovenia, Tunisia, and Uruguay. Table 1 shows the level of robustness, availability and methods for cancer incidence data as per the Globocan-2012 classification. The table also shows the level of economic development (GNI-per capita) and the existence of an operational cancer control plan.

In the CCORE methodological approach, indications for radiotherapy for each cancer site were derived from evidence-based published treatment guidelines issued by reputed national and

international organizations. An optimal radiotherapy utilization tree was developed for each cancer site by combining clinical scenarios and epidemiological data using TreeAge Pro™ software. Patients requiring radiotherapy were counted only once even if they subsequently developed repeated indications for radiotherapy.

The distribution of tumour types for each country was taken from estimations of the International Agency for Research on Cancer (IARC) in their database Globocan-2012 [8]. This database lists 27 cancer types and the total. The list does not include sarcomas (except Kaposi's sarcoma), cancers of unknown primary (CUP) site or "other" categories.

The aRTU rate was calculated as the ratio of the number of new notifiable patients (no retreatments) treated with radiotherapy in 2012 in each country, to the total number of cancer patients diagnosed in the same year. Country coordinators reported separately the total number of new and carryover patients receiving radiotherapy in the index year 2012. They gathered the data from all operational RT centres in their respective countries.

The radiotherapy case-mix profile for each country was determined by prospectively registering 300 consecutive patients receiving radiotherapy at a leading RT centre in each country, capturing detailed data on patient, disease and treatment characteristics from this sample. Country coordinators conducted this prospective data collection filling an 18-item questionnaire for each one of 300 consecutive patients receiving radiotherapy in their respective centres (Appendix 1). This form was completed for each patient on treatment and forwarded to the IAEA Data Management Centre. The year 2012 was selected as the index year for calculations to allow correlation of the case-mix and radiotherapy data with estimates of cancer incidence from the Globocan-2012 database.

Table 1
Economic development, cancer incidence data and cancer control plans in the 9 target countries.

1.	2.	3.	4.	5.	6.	7.	8.
Country	GNI per capita 2018 (US\$)	Availability and methods of cancer incidence data	National cancer control strategy/plan	National cancer registry	Scope	Coverage	Last year of data
Costa Rica	11 824	High quality national data or high quality regional (coverage greater than 50%) Rates projected to 2012	Yes	Yes	Population-based	National	2010
Ghana	1 513	Frequency data. Age/sex specific rates for "all cancers" were partitioned using data on relative frequency of different cancers (by age and sex)	Yes	Yes	Hospital-based	Subnational	2012
Malaysia	9 508	High quality regional (coverage lower than 10%) Estimated as the weighted average of the local rates	Yes	Yes	Population-based	Subnational	2011
Philippines	2 951	High quality regional (coverage between 10% and 50%) Estimated as the weighted average of the local rates	Yes	Yes	Population-based	Subnational	2003
Romania	9 522	Regional data (rates) Estimated from national mortality estimates by modelling, using incidence mortality ratios derived from recorded data in local cancer registries in neighbouring countries	Yes	Yes	Population-based	Subnational	2010
Serbia	5 426	High quality regional (coverage between 10% and 50%) Estimated from national mortality estimates by modelling, using incidence mortality ratios derived from recorded data in local cancer registries in neighbouring countries	No	Yes	Population-based	Subnational	2010
Slovenia	21 650	High quality national data or high quality regional (coverage greater than 50%) Rates projected to 2012	Yes	Yes	Population-based	National	2010
Tunisia	3 688	High quality regional (coverage lower than 10%) Estimated as the weighted average of the local rates	No	Yes	Population-based	Subnational	2004
Uruguay	15 220	High quality national data or high quality regional (coverage greater than 50%) Most recent rates applied to 2012 population	Yes	Yes	Population-based	National	2008

Sources:

Column 2: GNI per capita: World Bank <https://data.worldbank.org/indicator/NY.GNP.PCAP.PP.CD?view=chart>.

Column 3: IARC/WHO Globocan-2012, Estimated cancer incidence, mortality and prevalence in 2012.

Columns 4–8: WHO Cancer Country Profiles 2014 – <http://www.who.int/cancer/country-profiles/en/#P>.

We calculated the “percent unmet need” as follows:

$$\text{Percent unmet need} = \frac{[(\text{optimal RTU rate} - \text{actual RTU rate})/\text{optimal RTU rate}] \times 100}{}$$

Results

Optimal RTU rate (oRTU)

The calculated oRTU rates based on countries incidence data as per Globocan-2012 have been previously reported [9] (Table 2). They were: Costa Rica 47%, Ghana 51%, Malaysia 53%, Philippines 53%, Romania 52%, Serbia 52%, Slovenia 48%, Tunisia 56% and Uruguay 52%. The median oRTU for the nine countries was 52% ranging from 47% in Costa Rica to 56% in Tunisia with a 9% difference between these two.

Actual RTU rate (aRTU)

Table 2 displays the optimal (column 10) and actual (column 11) RTU rates for comparison, the gap between them per country (column 12) and the calculated percent unmet need (column 13).

The median aRTU for these nine countries was 28%, compared to a median oRTU of 52%. The lowest aRTU rate was found in Ghana (8.7%), while the highest was found in Tunisia (46.5%).

Since the CCORE model, as well as Globocan-2012, excludes non-melanoma skin cancer, this disease entity was not included in the calculation of the actual RTU rates. However, in Table 3, – which reflects the characteristics of actual practice in these countries – the calculations include patients with non-melanoma skin cancer. In the two African countries (Tunisia and Ghana), this disease represents the 3rd and 8th most commonly irradiated cancers respectively.

Table 2 shows the total number of patients treated with radiotherapy in each nation (column 7) as well as the total number of new patients, as reported by country coordinators. The difference between these two values includes a small number of patients treated, which are the carryover from the previous year as well as re-irradiated patients.

Patients and treatments characteristics

Prospective registration of 18 variables in a series of 300 consecutive patients receiving radiotherapy in each participating

centre (Uruguay reported on 150 patients) allowed having an overview of the case-mix and stages treated in each country as well as the radiotherapy techniques used (Tables 2 and 3).

The mean age of patients treated in these nine centres was 55 years (median 56.7) and the ratio male to females 0.3.

“Centre’s delay” was defined as the time in days from the date of registration in the radiotherapy centre to the day of first radiotherapy session. It was a mean of 73 days (median: 28), from 14 days to 215 days.

The ratio curative versus palliative intention treatments was 0.6 meaning that 2/3 of patients were managed with curative intent.

Most patients (87%) were new patients while the median re-treatment rate for the nine countries was 11% with a range between 7% (Ghana) and 24% (Slovenia).

In four countries (Costa Rica, Ghana, Serbia, and Tunisia), sarcomas were among the ten most common cancers receiving radiotherapy. However, Globocan-2012 does not list sarcomas (except Kaposi’s sarcoma) among the 27 types of cancer reported.

Fifty-four percent of irradiated patients had had some invasive procedure (including biopsy) before RT. Twenty-one percent of patients were being treated with concomitant chemoradiotherapy.

Of a total of 2548 patients evaluable for treatment technique complexity, 49% were treated with 2D techniques, 42.6% with 3D-CRT, 3.2% with IMRT or equivalent and 5% with other methods. This represents a total of 46% of patients treated with conformal radiotherapy techniques including IMRT in these countries.

Thirty-four percent of all patients were treated with hypofractionation, defined as any radiotherapy regimen using daily fractions larger than 2.0 Gy.

Of a total of 2646 anatomic sites treated (Table 4) the distribution was as follows: CNS 11.4%, head-and-neck 12.3%, thoracic tumours 6.5%, abdominal 3.1%, pelvic 26.1%, breast 25.8%, and others including tumours of the limbs (13.5%). In Table 4, the sum of all sites irradiated for each country is higher than 300 due to some patients receiving treatment to more than one anatomic site.

Discussion

The proportion of patients who need RT and who actually receive it, best measures accessibility of radiotherapy in a country. Radiotherapy is prescribed to approximately 47% of new cancer patients in middle-income countries, while in 55.2% of patients the prescription is for combined modality therapy [10].

Table 2
Characteristics, radiotherapy infrastructure and RTU rates results in 9 middle-income countries.

1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.
Country	Population (millions)	New cancer cases 2012	No. RT centres	No. teletherapy machines (2012)	Teletherapy machines/1000 cancer cases (2012)	All RT patients in 2012	New RT patients in 2012	Re-irradiation rate (%)	Optimal RTU rate (%)	Actual RTU rate (%)	Diff. (10. minus 11.) (%)	Unmet need (%)
Costa Rica	4.793	8 900	4	8	0.89	3 487	3 138	10	47	35	12	25.5
Ghana	25.545	15 800	3	3	0.19	1 480	1 376	7	51	9	42	82.3
Malaysia	29.321	37 400	21	42	1.1	11 636	10 385	12	53	28	25	47
Philippines	96.471	98 200	27	34	0.34	10 894	10 087	7.4	53	10.3	42.7	80.5
Romania	21.387	78 800	16	23	0.29	19 490	17 346	11	52	22	30	57.6
Serbia	9.846	42 200	6	15	0.35	12 739	10 046	21	52	23.8	28	54
Slovenia	2.040	11 500	1	8	0.7	4 752	3 602	24	48	31	17	35.4
Tunisia	10.704	12 200	10	16	1.3	6 300	5 670	10	56	46	10	18
Uruguay	3.391	13 357	8	14	1.05	5 750	5 020	13	52	37	15	29
Median									52	28	24	47

Column 2 – UN Population Information Network.

Column 3 – Globocan-2012.

Column 13 – Percent unmet need = [(optimal RTU rate – actual RTU rate)/optimal RTU rate] × 100.

Table 3
Characteristics of patients and treatment techniques in nine middle-income countries.

Country	Number of patients assessed	Age (mean and median in years)	Gender (m/f)	Centre's delay (mean, median in days)	Intention (curative/palliative)	Mix (new pts./re-treatment)	Previous surgery	Concomitant chemo-rt	Techniques 2D/3D/IMRT/other	Use of hypofractionation (% of patients)
Costa Rica	300	57.02 (58.86)	0.44	51.46 (43)	0.80	0.91	0.65	0.19	1: 298: 1: 0	19.6
Ghana	300	52.77 (55.95)	0.28	215.2 (42)	0.61	0.91	0.48	0.22	246: 54: 0: 0	38.3
Malaysia	300	52.82 (54.22)	0.35	33.87 (32)	0.63	0.88	0.58	0.24	20: 214: 27: 38	58
Philippines	300	46.99 (47.06)	0.28	23.24 (20)	0.77	0.91	0.42	0.44	300: 0: 0: 0	9.3
Romania	300	56.16 (58.19)	0.32	80.53 (58)	0.75	0.90	0.50	0.22	238: 62: 0: 0	24.3
Serbia	300	56.91 (60.65)	0.36	14.38 (12)	0.58	0.82	0.60	0.16	149: 150: 0: 1	40.3
Slovenia	300	63.91 (64.22)	0.50	20.76 (20)	0.50	0.79	0.50	0.12	17: 142: 54: 87	65
Tunisia	299	52.06 (54.14)	0.42	86.6 (23)	0.70	0.93	0.55	0.094	269: 28: 1: 1	33.1
Uruguay	150	58.32 (60.81)	0.28	200.4 (24)	0.69	0.97	0.60	0.21	12: 138: 0: 0	8.7
Overall	2549	55.03 (56.78)	0.36	73.47 (28)	0.67	0.87	0.54	0.21	1252 (49%), 1086 (42.6%), 83 (3.2%), 127 (5%)	34.4

Hypofractionation was defined as any radiotherapy regimen using daily fractions larger than 2.0 Gy.

The oRTU rates represent an ideal scenario where all patients who need RT have access to it. In reality, aRTU rates do not reach 100% of those with an indication for it, even in developed countries, since current calculation models do not include patients' preference or medical contraindications.

Estimates of the need for radiotherapy have been reported using expert opinion including the Delphi panel method [4–6], epidemiological evidence-based assessment (EBEST) [1,11], and criterion-based benchmarking (CBB) [12–14].

The calculated oRTU rates in this group of nine middle-income countries based on their disease distribution (52%) did not differ from those found in developed countries; 48.3% for Australia, [11] 41.5% for Ontario [14] and 51% (47–53.2%) for Europe [15]. However, the actual RTU rates were consistently lower than oRTU rates.

The ESTRO-HERO group [15] calculated a 51% (unweighted average) oRTU in 41 European countries following the EBEST method. The actual utilization rates were variable among these countries between 55.3% (Montenegro) to 31.8% (Ireland). In the ESTRO-HERO study, Slovenia was reported to have a 32.3%, which is consistent with the 31% found in the present study. A large discrepancy was observed between the actual utilization and the optimal utilization of radiotherapy in European countries, with less than 17% of countries treating at least 80% of the optimal indications for radiotherapy and about 46% of the European countries not even reaching 70% of the patients optimally indicated. This ESTRO-HERO study illustrates that even in developed countries there is a gap between desirable and actual provision. The most critical impact on the RTU by country is due to changes in the relative frequency of tumours rather than disease stage at diagnosis. The effect of stage distribution is in the order of only 2% [15].

Zubizarreta et al. [16] calculated oRTU rates (EBEST method) as 54.3% for Africa, 53.3% for Latin America, 50.1% for Europe/Central Asia and 49.5% for the Asia-Pacific region. These regional calculations compare with data previously published for developed countries and are in general agreement with the results of the present study.

An essential purpose of the RTU rate calculation is establishing the gap between the desirable (oRTU) and the actual (aRTU) rates at the country level. This deficit can be expressed as the difference between rate values or, more meaningfully, as the percent of the unmet need for radiotherapy, namely, the percentage of patients who despite having an indication for radiotherapy, do not have access to it. In the present study, the median unmet need for the nine countries was 47% (18% Tunisia, 82.3% Ghana). The unmet need was particularly significant (>80%) in two countries with limited resources and a large population. In the two states re-classified as “high income” countries (Uruguay and Slovenia), the unmet need was 29% and 35.4% respectively. The two countries that revealed a most pressing situation were Ghana, with an aRTU of 9% and the Philippines with 10.3%.

In some countries, the aRTU for some specific diseases was surprisingly low compared with RTU rates reported from developed countries. For example, in Costa Rica, the aRTU for lung cancer was only 14.3% while the revised oRTU for lung cancer in Australia indicates 77% [11], 59% in British Columbia, Canada [17] and 77% globally [22]. This low aRTU in Costa Rica may reflect an under-referral of lung cancer patients for RT.

In Romania, the aRTU for prostate cancer was found to be 9% while it has been reported as 25% (initial) in the Netherlands [18], 58% in Australia [11] and 32% (initial), 61% (at 5-years) in British Columbia [18,19] and 58% globally [22] in the Netherlands [19]. The hypothesis is that in Romania most patients with localized prostate cancer are managed with surgery and hormone therapy.

Sarcomas were among the ten most commonly irradiated cancers in Costa Rica, Ghana, Serbia, and Tunisia. In a Swedish study

Table 4
Number of *anatomic sites* irradiated per country in a series of 300 consecutive patients prospectively registered.

Country	Central Nervous System	Head and Neck	Thorax	Abdomen	Pelvis	Breast cancer	Others (incl. limbs)	Total n of sites
Costa Rica	31	22	10	24	99	89	38	313
Ghana	22	27	5	16	117	93	38	318
Malaysia	33	66	13	10	76	71	47	316
Philippines	41	61	31	1	84	71	19	308
Romania	33	29	31	1	93	86	30	303
Serbia	46	32	14	3	80	52	78	305
Slovenia	48	38	61	23	58	55	39	322
Tunisia	37	42	27	4	35	108	52	305
Uruguay	10	9	12	1	49	58	17	156
Overall	301 (11.4%)	326 (12.3%)	173 (6.5%)	83 (3.1%)	691 (26.1%)	683 (25.8%)	358 (13.5%)	2646

The sum of all sites irradiated (2646) is higher than the total number of patients assessed (2549) due to some patients receiving treatment to more than one anatomic site.

[21], In a Swedish study [20], the observed RTU rate was 55% for sarcomas of bone and cartilage and 100% for soft-tissue sarcomas.

The ratio curative versus palliative-intention treatments was 0.6 meaning that 2/3 of patients were managed with curative intent. This finding contradicts the assumption that in developing countries the majority of radiotherapy patients are treated for palliation. However, one must consider that this is a selected group of countries some of which have high-income country features. This finding cannot be extrapolated to low-income countries.

A correlation was found between the aRTU rates and the number of teletherapy machines per 1000 cancer cases/year in each country (Fig. 1). This association confirms that, although other access factors may be at play, availability of RT machines in a country is an important factor in RT utilization. However, availability of RT machines in itself by no means reflects access to modern and more sophisticated techniques. Some of these countries have an acceptable number of teletherapy machines related to their population but are struggling to introduce conformal and image-guided techniques.

Regarding a high "centre's delay" in Ghana, in African countries, the definition of delay used here is often confounded by patients who abscond radiotherapy, only to come back for treatment later and not delay due to the centre's operations themselves.

Re-treatment (or re-irradiation) describes a situation where a patient who has previously received radiotherapy, is prescribed and given a second course. This can be either to the same or similar original volume (true re-irradiation) or a different anatomical region due to metastatic spread of the same cancer diagnosis. The re-treatment rate in Australia has been determined to be as high as 25% [22]. In the present study, the re-treatment rate was calculated by subtraction of the reported *new patients* in 2012 from the total number of patients irradiated in each country in the same year. The median retreatment rate was 11%. A possible explanation

may be a reluctance by radiation oncologists to prescribe a second course of radiotherapy to the same tissue volume in the face of a local recurrence, for concerns of excessive toxicity.

Atun et al. [23] have recently highlighted the obstacles facing radiotherapy availability worldwide and showed substantial health and economic benefits to investing in radiotherapy services. Steps to address this need include careful planning of radiotherapy services through international multisectoral partnerships and resource mobilization [2,3]. Not only will such planning ensure that all patients who could benefit from radiotherapy receive it, but will also potentially improve treatment results by reducing waiting times, which are known to have a detrimental effect on outcome in several cancer sites [24,25].

The case of Ontario, Canada [26], illustrates that radiotherapy utilization can be improved with a combination of a comprehensive capital investment strategy coupled with increased investment in human resource planning. The increased utilization rate outpaced the increasing cancer incidence and demonstrated the success of these strategies, providing better access to care in that province.

Population-based cancer registries have provided decisive contributions to cancer epidemiology and cancer control. In fact, cancer control planning without reliable data from cancer registries is prone to misplaced emphasis and wasted investment. All nine countries participating in this study have national cancer registries. The methods of estimation are country-specific, and the quality of the estimation depends upon the quality and the amount of the information available for each country. In theory, there are as many methods as countries, and because of the variety and the complexity of these methods, data from the Globocan-2012 database have been used.

A low aRTU rate and a high percent unmet need reflect problems with access to radiotherapy services. This is most likely due to a limited number of RT centres and/or megavoltage units (availability) relative to a large population. Other factors such as affordability, availability of diagnostic imaging and appropriate surgery, country geography, lack of awareness of patients and doctors, cultural beliefs and resorting to traditional forms of healing also play a role, but these factors were not the focus of this study.

Radiotherapy quality and access should be not only quantified but also monitored over time using appropriate radiation oncology quality indicators. National health authorities should conduct the long-range planning of cancer services including radiotherapy following international recommendations and the rich experience of countries that have already followed this path.

Limitations of this study include the selection of nine countries following pre-determined criteria. The GNI per capita was variable between 1513 US\$ (Ghana) to 21,650 US\$ (Slovenia). It has been previously shown that the level of economic development is correlated with the number of megavoltage machines (24).

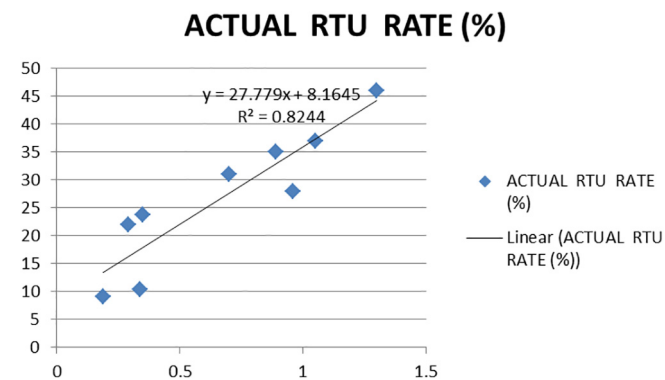


Fig. 1. Correlation between actual radiotherapy utilization rate (aRTU) and the number of megavoltage machines per 1000 cancer patients/year in 9 middle-income countries.

Finally, although this study did not include low-income countries, we can expect that in these countries, the aRTU rates will be even lower and the unmet need higher than those found here. Similar studies should be conducted in low-income countries identifying the factors that preclude access to radiotherapy services on a national level.

To conclude: actual RTU rates are lower than optimal RTU rates, and the level of unmet need for radiotherapy access is very significant in countries with limited resources and a large population.

Conflict of interest statement

The authors do not have any conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.radonc.2018.05.014>.

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