

ESTRO-HERO survey

The impact of cancer incidence and stage on optimal utilization of radiotherapy: Methodology of a population based analysis by the ESTRO-HERO project



Josep M. Borrás^{a,*}, Michael Barton^b, Cai Grau^c, Julieta Corral^d, Rob Verhoeven^e, Valery Lemmens^e, Liesbet van Eycken^f, Kris Henau^f, Maja Primic-Zakelj^g, Primož Strojjan^h, Maciej Trojanowskiⁱ, Agnieszka Dyzmann-Srokaⁱ, Anna Kubiakⁱ, Chiara Gasparotto^j, Noemie Defourny^j, Julian Malicki^k, Peter Dunscombe^l, Mary Coffey^m, Yolande Lievensⁿ

^a University of Barcelona, Spain; ^b CCORE, Ingham Institute for Applied Medical Research, UNSW, Liverpool, Australia; ^c Aarhus University Hospital, Denmark; ^d Doctoral Programme in Public Health, Department of Pediatrics, Obstetrics and Gynecology, Preventive Medicine and Public Health, Universitat Autònoma de Barcelona, Spain; ^e The Netherlands Cancer registry/Netherlands Comprehensive Cancer Organisation, The Netherlands; ^f Belgian Cancer Registry, Brussels, Belgium; ^g Cancer registry, Institute of Oncology Ljubljana, Slovenia; ^h Dept. of Radiation Oncology, Institute of Oncology Ljubljana, Slovenia; ⁱ Cancer Registry, Greater Poland Cancer Centre, Poznan, Poland; ^j European Society for Radiotherapy and Oncology, Belgium; ^k Electroradiology Dep. University of Medical Sciences, Greater Poland Cancer Centre, Poznan, Poland; ^l University of Calgary, Canada; ^m Trinity College, Dublin, Ireland; ⁿ Ghent University Hospital, Belgium

ARTICLE INFO

Article history:

Received 16 March 2015
Accepted 29 April 2015
Available online 19 May 2015

Keywords:

Radiotherapy
Optimal utilization
Cancer incidence
Stage
Cancer registry

ABSTRACT

Background and purpose: The impact of differences in the distribution of major cancer sites and stages at diagnosis among 4 European countries on the optimal utilization proportion (OUP) of patients who should receive external beam radiotherapy was assessed within the framework of the ESTRO-HERO project.

Materials and methods: Data from Australian Collaboration for Cancer Outcomes Research and Evaluation (CCORE) were used. Population based stages at diagnosis from the cancer registries of Belgium, Slovenia, the Greater Poland region of Poland, and The Netherlands were used to assess the OUP for each country. A sensitivity analysis was carried out.

Results: The overall OUP by country varied from the lowest of 48.3% in Australia to the highest of 53.4% in Poland; among European countries the variation was limited to 3%. Cancer site specific OUPs showed differences according to the variability in stage at diagnosis across countries. The most important impact on the OUP by country was due to changes in relative frequency of tumours rather than stage at diagnosis.

Conclusions: This methodology can be adapted using European data, thus facilitating the planning of resources required to cope with the demand for radiotherapy in Europe, taking into account the national variability in cancer incidence.

© 2015 Elsevier Ireland Ltd. All rights reserved. Radiotherapy and Oncology 116 (2015) 45–50

Radiotherapy is a key therapeutic approach in the multimodal treatment of cancer. The investment required to set up a radiotherapy facility, the time elapsed from the initial decision until the equipment is fully operational and the need for training highly skilled multi-professional teams are factors that have made the planning of radiotherapy a matter of discussion from a cancer policy making perspective. In order to proceed with such projects, the estimation of demand for radiotherapy is an essential component.

Classically, the demand for radiotherapy has been estimated as a percentage of the incident cancer cases with an adjustment for

re-treatment rates [1–3]. Traditionally the ‘50%’ estimate of incident cases benefitting from radiotherapy was the ‘ad hoc’ approach. However, this heuristic method has been replaced by three new approaches to the estimation of demand [4–9]:

- 1) an analysis of the utilization of radiotherapy in ‘optimal’ regions;
- 2) a criterion-based approach carried out for specific indications, and
- 3) an evidence-based evaluation of clinical guidelines, including all tumour sites with incidence of more than of 1%.

These approaches were reviewed within the framework of the QUARTS project [10]. The third approach was selected as being

* Corresponding author at: University of Barcelona – Hospital Duran i Reynals, Gran Via de l’Hospitalet, 199, 08908-Hospitalet del Llobregat, Barcelona, Spain.

E-mail address: jmborras@iconcologia.net (J.M. Borrás).

the most comprehensive due to its global coverage and the methodology used. An additional advantage of this approach is that the underlying data have been recently updated until 2012 [8]. This approach also allows for the calculation of the optimal utilization proportion (OUP) of external beam radiotherapy for all cancers together, a very convenient feature for planning purposes at the national or regional level. Using this updated model and Australian data on cancer incidence and stage, the authors obtained an optimal utilization proportion of 48.3% of all incident cancer cases in Australia that would benefit from radiotherapy during the course of the disease (excluding re-treatments, non-melanoma skin cancers and benign diseases).

In 2010 ESTRO initiated the HERO project (Health Economics in Radiation Oncology) with the aim of developing a knowledge-based model for the health economic evaluation of radiation oncology in different European countries [11]. Recently the current availability of equipment and staffing of radiotherapy services and of guidelines for planning purposes in individual European countries has been reported [12–14]. The next necessary component of the HERO project is to assess the evidence based demand for radiotherapy services in Europe, which is the objective of this study. This is pursued by adapting the Australian CCORE model to the epidemiological situation (distribution of major cancer sites and stages at diagnosis) in the European countries.

Materials and methods

The optimal utilization model is based on the careful review of the literature carried out for all tumour sites with more than 1% incidence by the Australian Collaboration for Cancer Outcomes Research and Evaluation (CCORE) group [7,8]. Briefly, the CCORE team reviewed all the relevant evidence based guidelines regarding indications for radiotherapy by tumour site and stage at diagnosis published by reputed national and international organisations and professional groups as well as other articles in the scientific literature, updated to 2012. An indication for radiotherapy was defined as meaning it was the treatment of choice because there was evidence that radiotherapy had a superior clinical outcome (measured by survival, quality of life, lower toxicity or better local control) compared to alternative modalities or no treatment, and the patient was fit enough to undergo treatment.

Based on the indications for radiotherapy for different cancer sites, the CCORE team developed a decision model to estimate, by tumour site and for all cancers overall, the proportion of patients for whom external beam radiotherapy should be recommended. In this way, the OUP defines the number of external beam courses of radiotherapy that should be foreseen for a certain cancer population (excluding re-treatments).

Pathway probabilities included the distribution of cancer incidence by tumour site, stage at diagnosis and relevant clinical characteristics of patients for each tumour. The structure of the decision trees for each cancer site as well as the evidence supporting each clinical alternative and the corresponding probability of occurrence are available in the original report [15]. It is necessary for the correct interpretation of the resulting OUPs that each patient is counted only once even if he or she subsequently required a re-treatment for the particular cancer. Brachytherapy indications were not considered in the present study but are available in the CCORE report.

A two-step approach

To assess the OUP of patients with an evidence-based indication for radiotherapy in European countries, epidemiological data from selected European countries were introduced into the CCORE decision trees. Two sets of information were used:

- i) country-specific distributions of cancer incidence by tumour site from the European Cancer Observatory for the year 2012, and
- ii) the stage at diagnosis as recorded in population-based cancer registries of the selected European countries.

Stage at diagnosis is collected for all cancer sites by only a few cancer registries [16], either due to the difficulties in ascertaining it in the clinical records or because of the resources required. Four population cancer registries were able to provide the data as required by the CCORE models: Belgium, the Netherlands, the Greater Poland region of Poland (covering about 10% of Poland [17]) and Slovenia. Data on stage correspond to the years 2010–11 for the Netherlands and Belgium, 2009–10 for Slovenia and 2010 for the Great Poland region. The average of two years was used when appropriate. Australian data were available for the year 2008 [18] and are used as a reference for comparison to assess the impact of changes in the distribution of cancer incidence or stage at diagnosis in the four European countries analysed. Cancer registries other than the four identified above were contacted, but were not able to provide stage data with sufficient detail or in a timely manner.

Sensitivity analysis

As there were missing values in the population based stage data, a sensitivity analysis was performed to examine the significance of these gaps. In addition to running the calculations on the stage data available, two other scenarios were also simulated: the worst case scenario, namely, assigning all the missing values to the most advanced stage considered for each tumour site; and the best case scenario where all missing cases were assigned to the earliest stage. In order to evaluate the independent impact of relative frequency of cancers compared to the impact of stage distribution on the OUP, we applied the stage distribution from the Australian data to the relative distribution of each of the European countries analysed here in the CCORE decision trees. All these calculations were carried out using TreeAge Pro software.

Results

Cancer incidence by tumour site

The distribution of cancer cases by tumour site among the four European countries analysed and Australia from 2012 is shown in Table 1. Differences by country among tumour sites were remarkable. For instance, breast cancer cases accounted for 16.1% of all cancers in the Netherlands and Belgium while in Poland it was only 10.5%; lung cancer also shows a marked difference of 8% (in this case, lower in Australia and higher in Poland). Perhaps most remarkable is the difference in incidence observed for prostate cancer (6.2% in Poland versus 18.4% in Australia).

Stage at diagnosis

In the annex ([Supplementary data available in the electronic version of this paper](#)), data on stage at diagnosis are shown for each cancer site consistent with the requirements of pathways adopted for CCORE decision trees. Significant differences can be observed. For instance, stage I–II oral cavity cancers showed a range from 30.6% in Poland to 52.4% in the Netherlands and there were also significant differences in stage distribution among the countries in the case of rectal cancer.

Optimal utilization proportion by country

Using the distribution of cancer incidence and the stage at diagnosis from each population-based cancer registry, the OUP by

Table 1
Distribution of cancer cases by tumour site (%).

Tumour	Australia	Belgium	Netherlands	Poland	Slovenia
Bladder	2.0	6.5	3.3	5.2	4.1
Brain	1.4	1.3	1.4	2.8	1.5
Breast	12.2	16.1	16.1	10.5	11.8
Cervix	1.0	1.1	0.9	2.6	1.9
Colon	8.4	8.3	9.2	6.7	7.5
Gall bladder	0.6	0.5	0.7	1.7	1.5
Head and neck	3.3	4.0	3.4	4.7	4.6
Lip	23.0	2.9	7.4	8.5	6.8
Oral cavity	24.0	31.8	33.8	20.1	28.2
Larynx	16.0	27.5	27.1	42.1	24.4
Oropharynx	17.0	14.5	11.1	9.3	18.4
Salivary gland	7.0	5.3	5.0	6.2	3.3
Hypopharynx	3.0	9.6	7.0	4.7	12.3
Paranasal sinus and Nasal cavity	5.0	4.6	5.7	3.8	4.4
Nasopharynx	3.0	2.1	2.5	3.2	2.0
Unknown primary	2.0	1.7	0.3	1.9	0.1
Kidney	2.3	2.2	2.3	3.7	2.7
Leukaemia	2.3	2.2	2.2	2.5	2.1
Lymphoid leukaemia	54.0	53.9	53.2	58.0	55.4
Myeloid leukaemia	46.0	46.1	46.8	42.0	44.6
Liver	1.2	0.8	0.5	1.2	1.6
Lung	9.0	11.7	13.1	17.0	12.7
Lymphoma	4.2	3.7	3.9	2.7	3.1
Hodgkin disease	12.0	13.1	13.2	23.4	16.2
Non-Hodgkin lymphoma	88.0	86.9	86.8	76.6	83.8
Melanoma	9.9	2.7	4.5	1.8	4.1
Myeloma	1.2	1.2	1.2	1.0	1.1
Oesophagus	1.2	1.5	2.0	0.9	1.0
Ovary	1.1	1.5	1.5	2.8	1.9
Pancreas	2.1	1.9	2.2	3.0	2.9
Prostate	18.4	15.4	11.9	6.2	9.2
Rectum	4.2	4.3	5.0	4.9	6.1
Stomach	1.8	2.3	2.6	4.7	5.0
Testis	0.8	0.5	0.8	0.7	1.0
Thyroid	1.8	1.1	0.6	1.4	1.4
Uterus	1.8	2.3	2.3	3.6	3.1
Vagina	0.1	0.1	0.1	0.1	0.1
Vulva	0.3	0.3	0.4	0.3	0.5
Unknown primary	2.4	2.0	3.5	4.5	3.2
Other	5.0	4.8	4.5	2.8	4.2
Anus	5.0	4.4	3.8	7.9	5.0
Biliary	6.0	0.0	0.0	0.0	0.0
Mesothelioma	11.0	8.4	13.2	4.9	7.4
Myelodysplastic Syndromes	18.0	30.5	27.5	2.5	29.3
Skin (non-melanoma, non SCC/BCC)	11.0	12.3	4.3	7.2	12.6
Small intestine	6.0	6.6	6.8	6.5	5.7
Soft tissue	8.0	11.4	14.3	19.5	11.8
Remaining rare cancers	35.0	26.3	30.1	51.5	28.2

country was estimated (Table 2 and Fig. 1). The overall OUP within each country, for which radiotherapy is indicated, varies from the lowest in Australia with 48.3% to the highest percentage of 53.4% in Poland, for an inter-country absolute variation of 5.1%. All four European countries included in this analysis showed a higher OUP of radiotherapy as compared to Australia.

The impact of varying stage distribution was evaluated using the frequency of tumours by country but including Australian stage data instead of country-specific data. The differences in the OUP between the two sets were minimal: Slovenia and Poland had a lower OUP using the Australian stage data, Belgium and The Netherlands had a higher OUP, with ranges between –1.3% and

+0.5% (Table 3). This suggests that with regard to the overall OUP estimation, the variability in the frequency of cancer distribution was more important than variability in stage.

Cancer specific OUP

The cancer specific OUP for each country showed differences according to the site and the stage at diagnosis. The most remarkable examples were cervical, rectal, vulva and pancreatic cancer (Table 2 and Fig. 1): these cancer types showed significant variability in case distribution among the different stages across the countries. For instance, in cervical cancer the lowest OUP was estimated for Slovenia with 62.4% of cancer cases being candidates for radiotherapy while in Poland the corresponding percentage was 82.3%. The higher proportion of early stage tumours in Slovenia and the higher percentage of advanced stages in Poland could explain this difference (Annex), which might be associated with screening uptake. The variation in OUP found in rectal cancer was also remarkable, with an OUP of 55.9% in the Netherlands and 72% in Poland, which again can be explained by the higher percentage of advanced cases in Poland (Annex). On the other hand, in some tumour sites such as breast or prostate cancer, in which variation in OUP might have a significant impact on RT services due to the high incidence and overall high utilization of radiotherapy, very similar results across countries were observed with variability of only 1.7–2.6% in the OUP.

Sensitivity analysis

In order to assess the potential impact of missing values in the stage at diagnosis data on the OUP calculation, a sensitivity analysis was carried out. As shown in Table 4, the differences in the overall OUP between scenarios are lower than 3% in all countries considered, with the least favourable scenario (Scenario 2) showing a slightly higher OUP than the most favourable scenario (Scenario 3) in all countries. The OUP by cancer type, however, shows a much larger variation in selected tumour sites, i.e. oesophagus and pancreatic cancer.

Discussion

The optimal utilization proportion (OUP) for external beam radiotherapy in the four European countries has been calculated using the distribution of cancer specific incidence by country and the population based stage at diagnosis. There was about 5.1% difference between the original Australian OUP and the highest European value observed in Poland. It is remarkable that the variation is only 3.1% among the European countries, although their epidemiological profiles showed significant differences both in the relative distribution of various tumour sites and stage at diagnosis. It therefore seems that the differences in both factors (frequency and stage) observed among these countries are compensating each other in some way, and this has resulted in a limited variation in the global value of the OUP of radiotherapy utilization. In fact, the largest systematic differences between Australia and the European countries are the higher proportions of colon cancer and melanoma in Australia, which reduce the demand for radiotherapy.

It is of interest that, according to our analysis, the most relevant factor in explaining the differences observed in OUPs is the relative frequency of cancers. Fortunately, the relevant frequency data are easily available from the estimations made by the European Cancer Observatory [19], while the less relevant in quantitative terms, stage data, are not available in many jurisdictions. This presents the opportunity of applying the methodology to the whole of Europe, even in the absence of widely available stage data. This is,

Table 2
Optimal utilization proportion by tumour site (expressed as % of incident cancer cases).

	Australia	Belgium	Netherlands	Poland	Slovenia	Range	
Bladder	46.6	47.1	49.4	50.7	46.7	46.6	50.7
Brain	80.1	92.0	89.1	80.1	90.7	80.1	92.0
Breast	87.2	86.2	87.0	87.3	85.6	85.6	87.3
Cervix	71.1	70.3	72.1	82.3	62.4	62.4	82.3
Colon	4.1	3.4	3.9	3.7	4.1	3.4	4.1
Gall bladder	16.5	20.4	16.0	13.3	11.7	11.7	20.4
Head and neck	73.9	82.8	78.8	84.4	83.2	73.9	84.4
Kidney	14.7	12.4	15.4	17.9	13.8	12.4	17.9
Leukaemia	3.9	3.0	3.6	4.9	3.4	3.0	4.9
Liver	-	-	-	-	-	-	-
Lung	77.1	76.9	78.0	77.7	81.9	76.9	81.9
Lymphoma	72.6	72.8	66.8	73.5	67.9	66.8	73.5
Melanoma	20.5	11.7	12.3	12.8	16.9	11.7	20.5
Myeloma	44.8	48.6	45.8	50.5	47.4	44.8	50.5
Oesophagus	70.7	72.6	74.0	76.5	72.9	70.7	76.5
Ovary	3.6	3.5	2.5	4.7	1.9	1.9	4.7
Pancreas	48.9	53.8	47.2	38.7	47.9	38.7	53.8
Prostate	58.4	58.5	59.7	61.0	58.7	58.4	61.0
Rectum	59.7	63.0	55.9	72.0	63.3	55.9	72.0
Stomach	27.3	30.4	28.0	26.6	28.3	26.6	30.4
Testis	7.0	3.4	6.5	7.9	7.1	3.4	7.9
Thyroid	3.7	5.9	9.4	6.5	4.5	3.7	9.4
Uterus	37.9	35.2	33.7	43.3	34.0	33.7	43.3
Vagina	94.3	95.0	95.7	98.6	98.2	94.3	98.6
Vulva	39.2	36.1	31.3	36.0	46.5	31.3	46.5
Unknown primary	61.3	61.3	61.3	61.3	61.3	61.3	61.3
Other	18.5	22.0	20.2	31.0	23.1	18.5	31.0
Overall OUP*	48.3	53.3	52.3	53.4	50.3	48.3	53.4

* OUP: optimal utilization proportion.

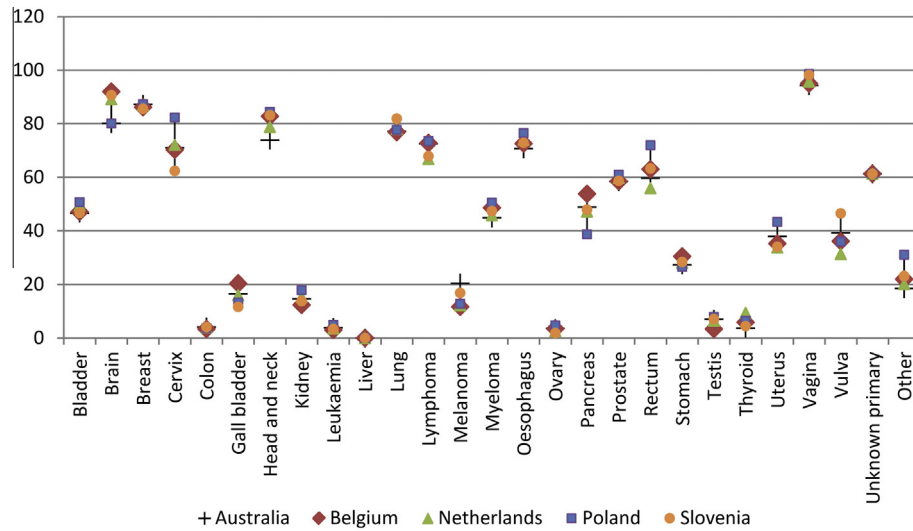


Fig. 1. Range of the optimal utilization proportion for cancer site according to the stage at diagnosis distribution.

Table 3
Optimal utilization proportion according to different stages of cancer.

	Australia	Belgium	Netherlands	Poland	Slovenia	Range	
Distribution of cancer cases by each country							
Population based stage at diagnosis from CCORE Australia	48.3	53.4	52.8	52.1	50.0	48.3	53.4
Distribution of cancer cases by each country							
Population based stage at diagnosis from country cancer registry	48.3	53.3	52.3	53.4	50.3	48.3	53.4

of course, under the assumption that the variation in the stages observed in the 4 cancer registries analysed here reflects the variation in the rest of the European countries and hence that the

impact of stage distribution will not be larger in the other European countries. Regarding this assumption, published data from other countries show that the range of values considered here

Table 4
Sensitivity analysis of the optimal utilization proportion.

Tumour	Belgium			Netherlands			Poland			Slovenia		
	Scenario 1	Scenario 2	Scenario 3	Scenario 1	Scenario 2	Scenario 3	Scenario 1	Scenario 2	Scenario 3	Scenario 1	Scenario 2	Scenario 3
Bladder	47.1	49.5	45.3	49.4	50.3	48.5	50.7	59.0	41.5	46.7	49.9	44.5
Brain	92.0	92.0	92.0	89.1	89.1	89.1	80.1	80.1	80.1	90.7	90.7	90.7
Breast	86.2	82.6	86.4	87.0	86.3	87.0	87.3	82.2	87.5	85.6	83.3	85.7
Cervix	70.3	77.9	54.8	72.1	75.6	64.3	82.3	87.4	62.7	62.4	63.7	59.8
Colon	3.4	3.4	3.4	3.9	3.8	3.9	3.7	3.3	3.9	4.1	3.9	4.1
Gall bladder	20.4	20.4	20.4	16.0	13.0	18.0	13.3	10.1	16.6	11.7	6.6	18.3
Head and neck	82.8	85.0	80.0	78.8	79.7	78.1	84.4	87.9	80.3	83.2	84.0	82.3
Kidney	12.4	12.4	12.4	15.4	17.8	14.8	17.9	21.9	16.2	13.8	17.5	13.1
Leukaemia	3.0	3.0	3.0	3.6	3.6	3.6	4.9	4.9	4.9	3.4	3.4	3.4
Liver	–	–	–	–	–	–	–	–	–	–	–	–
Lung	76.9	78.2	73.9	78.0	78.2	77.5	77.7	78.7	72.1	81.9	82.5	78.6
Lymphoma	72.8	72.8	72.8	66.8	65.1	70.0	73.5	70.1	70.4	67.9	65.6	70.7
Melanoma	11.7	18.5	11.6	12.3	13.0	12.2	12.8	12.8	12.8	16.9	18.7	16.9
Myeloma	48.6	48.6	48.6	45.8	45.8	45.8	50.5	50.5	50.5	47.4	47.4	47.4
Oesophagus	72.6	75.2	57.4	74.0	76.1	46.7	76.5	78.6	56.0	72.9	77.9	40.9
Ovary	3.5	6.3	2.3	2.5	3.9	2.2	4.7	6.0	3.9	1.9	3.1	1.7
Pancreas	53.8	46.2	62.2	47.2	38.2	62.3	38.7	35.6	48.4	47.9	35.8	67.2
Prostate	58.5	58.5	58.5	59.7	60.0	59.7	61.0	63.2	60.2	58.7	60.9	58.5
Rectum	63.0	58.1	57.1	55.9	52.6	51.9	72.0	71.6	69.7	63.3	58.9	58.0
Stomach	30.4	30.4	30.4	28.0	27.7	28.1	26.6	25.5	27.6	28.3	25.7	29.7
Testis	3.4	3.3	3.3	6.5	6.5	6.5	7.9	7.5	7.5	7.1	6.9	6.9
Thyroid	5.9	5.9	5.9	9.4	9.4	9.4	6.5	6.5	6.5	4.5	4.5	4.5
Uterus	35.2	44.5	33.3	33.7	35.1	33.4	43.3	52.1	40.7	34.0	40.8	32.3
Vagina	95.0	97.5	91.8	95.7	96.9	93.8	98.6	98.6	98.6	98.2	98.8	95.0
Vulva	36.1	51.6	30.8	31.3	42.8	28.5	36.0	48.3	31.9	46.5	54.3	41.8
Unknown primary	61.3	61.3	61.3	61.3	61.3	61.3	61.3	61.3	61.3	61.3	61.3	61.3
Other	22.0	22.0	22.0	20.2	20.2	20.2	31.0	31.0	31.0	23.1	23.1	23.1
Overall OUP*	53.3	53.4	52.2	52.3	52.1	51.8	53.4	54.1	51.1	50.3	50.1	49.8

Scenario 1: Missing cases not included.

Scenario 2: Missing cases included in advanced stage.

Scenario 3: Missing cases included in early stage.

* OUP: optimal utilization proportion.

from the four countries included is wide enough [20–22], with the possible exception of countries with no information available about incidence and survival [23].

Among the most important tumours from a radiotherapy perspective, that is, those with a high incidence and a high percentage of patients with evidence-based indications for radiotherapy (i.e. lung, prostate, rectum, breast and head and neck [8]), there are differences in the estimated OUP by tumour and country that may be relevant for capacity planning. Some tumour sites showed a large variation in OUP, such as rectal cancer (OUP ranging from 55.9% to 72%) or head and neck cancer (OUP ranging from 73.9% to 84.4%) due to different stage distributions. Prostate and breast cancer, on the contrary, showed very small variations in the estimated OUP by country, even though the differences observed in the stage distribution among the four population based cancer registries included in this study are not negligible (see annex), suggesting that stage distribution only has a small impact on the OUP for these tumours.

Less frequent tumours with inter-country differences higher than 10% are cervical cancer (OUP ranging from 62.2% to 82.3%) and brain tumours (OUP ranging from 80.1% to 92.0%). While this variation is also observed for vulva, uterus or pancreatic cancers, their OUP is lower (Table 2).

It should be acknowledged that similar levels of OUP -in total or by tumour type- may be associated with a different mix of palliative versus curative intent treatments, which in turn may impact the resources needed. When there is a shift towards more advanced stages, the complexity of radiotherapy is usually reduced. Moreover, more radiotherapy and less surgery could be indicated, as shown by the results of the sensitivity analysis in the worst-case scenario. The opposite could happen when a shift towards earlier stages occurs with the use of more protracted

and more complex radiation treatments. The complexity of radiotherapy will not affect the OUP as such, but it will impact on capacity planning as greater complexity treatments are typically more resource intensive and time consuming. This may, in part, be counterbalanced by the recent evolution towards more frequent use of hypo-fractionation.

The frequency by cancer site in each country was found to have a greater impact on the global OUP calculation than stage data. But the absolute impact of these various frequencies seems lower than expected. Even though the variation in OUP is small for some tumour sites, e.g. prostate or breast cancer, the observed differences in relative frequencies are substantial. This can be illustrated by the 18.4% of prostate cancers in Australia or 15.4% in Belgium as compared to only 6.2% in Poland. However, as the frequency of other tumours goes in opposite directions (for instance, the relative frequency of bladder cancer, 6.5% in Belgium versus 3.3% in the Netherlands; lung cancer also showing important inter-country variation), it may be assumed that it is this opposing nature of effects in different countries that explains the lower than expected impact on the global OUP.

Several factors should be taken into account when evaluating the results of this study. First of all, an advantage of our approach is that all stage categories were directly provided by population-based cancer registries and were adapted to the specific requirements of the decision trees structured by the CCORE team, thus avoiding the well-known problem of the comparability, at an international level, of stage data [24]. Secondly, in order to cope with the problem posed by missing values in the stage data, a sensitivity analysis was undertaken assuming the worst-case and best-case scenarios, namely, assigning all missing values to the most advanced or to the earliest stages. The impact on the OUP was rather small,

reinforcing the stability of the estimates. A third aspect is the limited number of countries included in this epidemiological assessment. As has been mentioned, it is not common for population based cancer registries to collect stage data for all cancer sites in a timely way and with enough detail for our purpose here. Several cancer registries contacted at the start of this study were unable to participate for these reasons. However, in all likelihood, the participating registries cover a great deal of the variability that would be observed across the European countries. Therefore, the range of calculated OUPs could be considered an acceptable representation of the consequences of the variability in stage data in most European countries with similar profiles of frequency in cancer incidence. Finally, population based stage data have some specific problems, such as the fact that classification of stage is not straightforward and there is a risk of misclassification. In addition, coding systems are not always easy to compare, and stage might only be available at the time of diagnosis, not at the time of recurrence. Related to the latter, available resources for diagnostic procedures may influence the accuracy of stage assignment at diagnosis.

This epidemiological assessment was carried out to gather information on evidence-based demand for radiotherapy in European countries. For planning purposes the OUP expressed as a single estimate for all cancers together is very convenient, and the calculated figures for the four countries included in this study were within a range of 3%, from 50.3% to 53.4%. However, differences are much more important when each tumour site is analysed separately. In fact, differences are significant among countries for specific tumour sites such as rectal cancer or lung cancer but they compensate each other during the weighted summation to calculate the global OUP.

The assessment of what proportion of cancer patients should benefit from radiotherapy is only the first step in the comprehensive estimation of the needs for radiotherapy services in the different European countries. The next step is to consider what the impact of these ranges of OUPs could be, either by tumour site or for all cancers together, on the evidence-based assessment of the need for radiotherapy equipment and staffing [25,26]. Other factors that would need to be taken into account are the impact of treatment complexity from evolving technology and dose fractionation, which are both in continuous evolution and certainly will have a specific impact on the present and future need for radiotherapy resources. Also, it should be mentioned that re-treatments need to be considered for planning purposes because they are not included in the CCORE model.

In conclusion, the differences in OUP were most dependent on the relative frequency of the cancer sites. The OUP by country showed a variation that could have an impact on the planning for radiotherapy needs of equipment and staffing. This information can be adapted using European data, allowing for planning the resources required to cope with the demand for radiotherapy in Europe, taking into account the national variability in cancer incidence.

Conflicts of interest

The authors have no conflict of interest.

Funding sources

This project was supported by the European Society for Radiotherapy and Oncology.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.radonc.2015.04.021>.

References

- [1] Erridge SC, Featherstone C, Chalmers R, Campbell J, Stockton D, Black R. What will be the radiotherapy machine capacity required for optimal delivery of radiotherapy in Scotland in 2015? *Eur J Cancer* 2007;43:1802–9.
- [2] Palacios A, Cabezas SG, Ugalde PF, et al. Characterization and adequacy of the use of radiotherapy and its trend in time. *Radiother Oncol* 2013;106:260–5.
- [3] IAEA. Planning radiotherapy services: a practical tool. Wien: IAEA, 2011.
- [4] Tyldesley S, Delaney G, Foroudi F, Barbera L, Kerba M, Mackillop W. Estimating the need for radiotherapy for patients with prostate, breast, and lung cancers: verification of model estimates of need with radiotherapy utilization data forms British Columbia. *Int J Radiat Oncol Phys* 2011;79:1507–15.
- [5] Tyldesley S, Boyd C, Schulze K, Walker H, Mackillop WJ. Estimating the need for radiotherapy for lung cancer: an evidence-based, epidemiologic approach. *Int J Radiat Oncol Biol Phys* 2001;49:973–85.
- [6] Jena R, Round C, Mee T, Kirkby N, Hoskin P, Williams M. The Malthus Programme – a new tool for estimating radiotherapy demand at a local level. *Clin Oncol* 2012;24:1–3.
- [7] Delaney G, Jacob S, Featherstone C, Barton M. The role of radiotherapy in cancer treatment: estimating optimal utilization from a review of evidence-based clinical guidelines. *Cancer* 2005;104:1129–37.
- [8] Barton MB, Jacob S, Schafiq J, et al. Estimating the demand for radiotherapy from the evidence: a review of changes from 2003 to 2012. *Radiother Oncol* 2014;112:140–4.
- [9] Kerba M, Miao Q, Zhang-Salomons J, Mackillop W. Defining the need for breast cancer radiotherapy in the general population: a criterion-based benchmarking approach. *Clin Oncol (R Coll Radiol)* 2007;19:481–9.
- [10] Bentzen SM, Heeren G, Cottier B, et al. Towards evidence-based guidelines for radiotherapy infrastructure and staffing needs in Europe: the ESTRO QUARTS project. *Radiother Oncol* 2005;75:355–65.
- [11] Lievens Y, Grau C. Health economics in radiation oncology: introducing HERO-ESTRO. *Radiother Oncol* 2012;103:109–12.
- [12] Dunscombe P, Grau C, Defourny N, et al. Guidelines for equipment and staffing of radiotherapy facilities in the European countries: final results of the ESTRO-HERO survey. *Radiother Oncol* 2014;112:165–77.
- [13] Grau C, Defourny N, Malicki J, et al. Radiotherapy equipment and departments in the European countries: final results from the ESTRO-HERO survey. *Radiother Oncol* 2014;112:155–64.
- [14] Lievens Y, Defourny N, Coffey M, et al. Radiotherapy staffing in the European countries: final results from the ESTRO-HERO survey. *Radiother Oncol* 2014;112:178–86.
- [15] Ingham Institute for Applied Medical Research (IIAMR) – Collaboration for Cancer Outcomes Research and Evaluation (CCORE). Review of optimal radiotherapy utilisation rates. CCORE report; 2013. Available from: tinyurl.com/pwkua34 [accessed 26-11-2014].
- [16] Siesling S, Kwast A, Gavin A, Balli P, Otter R. EUROCHIP-3. Availability of stage at diagnosis, cancer treatment delay and compliance with cancer guidelines as cancer registry indicators for cancer care in Europe: results of EUROCHIP-3 survey. *Int J Cancer* 2013;132:2910–7.
- [17] Dyzmann-Sroka A, Malicki J. Cancer incidence and mortality in the Greater Poland Region—Analysis of the year 2010 and future trends. *Rep Pract Oncol Radiother* 2014 Jul;9:296–300.
- [18] Australian Institute of Health and Welfare (AIHW). Australian Cancer Incidence and Mortality (ACIM) books. AIHW; 2011. Available from: <http://www.aihw.gov.au/acim-books/> [accessed 26-11-2014].
- [19] European Cancer Observatory. International Agency for Research on Cancer - WHO. <http://eco.iarc.fr/> [accessed 26-11-2014].
- [20] Lyratzopoulos G, Abel GA, Brown CH, et al. Socio-demographic inequalities in stage of cancer diagnosis: evidence from patient with female breast, lung, colon, rectal, prostate, renal, bladder, melanoma ovarian and endometrial cancer. *Ann Oncol* 2013;24:843–50.
- [21] Pavlik T, Majek O, Buchler T, et al. Trends in stage-specific population based survival of cancer patients in the Czech Republic in the period 2000–2008. *Cancer Epidemiol* 2014;38:28–34.
- [22] Walters S, Maringe C, Butler J, et al. Breast cancer survival and stage at diagnosis in Australia, Canada, Denmark, Norway, Sweden and the UK, 2000–2007: a population based study. *Br J Cancer* 2013;108:1195–208.
- [23] De Angelis R, Sant M, Coleman MP, et al. Cancer survival in Europe 1999–2007 by country and age: results of EUROCARE-5, a population based study. *Lancet Oncol* 2014;15:23–34.
- [24] Walters S, Maringe C, Butler J, Brierley J, Rached B, Coleman MP. Comparability of stage data in cancer registries in six countries: lessons from the International Cancer Benchmarking Partnership. *Int J Cancer* 2013;132:676–85.
- [25] Grau C, Borrás JM, Malicki J, et al. Radiotherapy capacity in Europe. *Lancet Oncol* 2013;14:e196–8.
- [26] Lievens Y, Dunscombe P, Defourny N. HERO (Health Economics in Radiation Oncology): a pan-European project on radiotherapy resources and needs. *Clin Oncol* 2014;27:115.