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Original article

Evidence-based optimal number of radiotherapy fractions for cancer: A useful tool to estimate radiotherapy demand

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ABSTRACT

Background and purpose: The recently updated optimal radiotherapy utilisation model estimated that 48.3% of all cancer patients should receive external beam radiotherapy at least once during their disease course. Adapting this model, we constructed an evidence-based model to estimate the optimal number of fractions for notifiable cancers in Australia to determine equipment and workload implications.

Materials and methods: The optimal number of fractions was calculated based on the frequency of specific clinical conditions where radiotherapy is indicated and the evidence-based recommended number of fractions for each condition. Sensitivity analysis was performed to assess the impact of variables on the model.

Results: Of the 27 cancer sites, the optimal number of fractions for the first course of radiotherapy ranged from 0 to 23.3 per cancer patient, and 1.5 to 29.1 per treatment course. Brain, prostate and head and neck cancers had the highest average number of fractions per course. Overall, the optimal number of fractions was 9.4 per cancer patient (range 8.7–10.0) and 19.4 per course (range 18.0–20.7).

Conclusions: These results provide valuable data for radiotherapy services planning and comparison with actual practice. The model can be easily adapted by inserting population-specific epidemiological data thus making it applicable to other jurisdictions.

Radiotherapy services planning requires a reliable estimate of radiotherapy demand. Actual radiotherapy utilisation (RTU) rates vary substantially throughout Australia and internationally [1]. Delaney et al. [2] constructed an evidence-based optimal RTU model which estimated that 52.3% of all cancer patients should be treated with external beam radiotherapy at least once during their disease course. Recent update of the model estimated an optimal RTU rate of 48.3% due to changes in epidemiological data and radiotherapy indications, and refinements of the model structure [3]. Further work is required to determine equipment and workload implications of the model.

A treatment fraction is a fundamental unit of radiotherapy productivity. The average number of fractions per radiotherapy course in a department will depend on the proportion of patients receiving radical versus palliative treatment. Number of fractions has been used for radiotherapy services planning. Morgan et al. [4] estimated that an extra 50 linear accelerators were required in Australia and New Zealand in 2009 to achieve a 52.3% RTU rate, based on 19 fractions per treatment course which reflected actual practice. Williams et al. [5] modelled the radiotherapy activity required to deliver an evidence-based radiotherapy service and compared with actual radiotherapy activity in the UK in 2005. A 33% increase in activity was required to achieve a 52% RTU rate. A further increase of 37% in activity was required when guideline-recommended evidence-based dose-fractionation schedules [6] were taken into consideration.

Substantial variation in radiotherapy fractionation practices has also been observed. The average number of fractions per treatment course ranged from 9.1 to 23.5 in the 24 Radiation Oncology centres in New South Wales (NSW) in 2013 [7]. The overall average number of fractions per course in NSW was 19. In comparison, the average number of fractions per course was 13.7 in Scotland in 2003 [8]. Variation was also observed in the five Radiation Oncology departments in Scotland (ranging from 11.7 to 17.3 fractions per course) [8] and in the UK (ranging from 13.0 in England to 17.8 in Ireland) [9]. Casemix alone does not account for all fractionation variations.

An evidence-based optimal radiotherapy fractionation (RTF) model was constructed to estimate for the first course of radiotherapy: (i) the optimal number of fractions per cancer patient and per treatment course, (ii) the proportion of patients that should receive radical versus palliative radiotherapy, (iii) the optimal number of

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fractions per radical and per palliative radiotherapy course if all cases were treated according to national and international guidelines.

Materials and methods

The updated RTU model [3] was used as the basis of this study. As the purpose of the RTU model was to determine the proportion of cancer patients who have at least one indication for radiotherapy at some time in their disease course, patients requiring radiotherapy were counted once, even if they had multiple indications at different stages in their illness. The current study was limited to the first course of radiotherapy. We recently published the breast cancer RTF model based on the original RTU model, and the methodology was discussed in detail [10]. The same methodology has been applied to all cancer sites of the updated RTU model. The recommended dose-fractionation schedules were derived from evidence-based treatment guidelines published between January 2000 and December 2014.

An indication for radiotherapy was defined as a clinical situation for which radiotherapy was recommended as the treatment of choice on the basis of published evidence that radiotherapy has a superior clinical outcome compared to alternative treatment modalities (including no treatment), and where the patient was suitable to undergo radiotherapy based on an assessment of performance status and co-morbidities. Radiotherapy indications were derived from evidence-based treatment guidelines issued by reputed national and international organisations.

In the RTU model, patient and tumour-related attributes were used to define specific radiotherapy indications, so each branch point represented a particular radiotherapy indication. For this study, some of the RTU model branches were split to model more specific clinical situations where the fractionation schemes vary between branches. Proportions of patients with the different attributes associated with additional branches were obtained by performing Medline searches, manual bibliographic searches and examination of review articles. Australian data were used if available as the primary purpose was to apply this model to the Australian population.

TreeAge Pro Suite 2009™ was used to construct the RTF model as a decision tree. "Chance nodes" (represented by circles) were used to depict different clinical scenarios. A node's branches represented the outcomes or alternatives associated with each clinical scenario, the number underneath each branch representing the proportion of patients with that attribute. The recommended number of fractions, derived from evidence-based treatment guidelines, was added at each "terminal node" (represented by a triangle) as the final outcome, referred to as the "payoff". If the guidelines did not adequately address dose-fractionation schedules, other sources including meta-analyses and randomised controlled trials were identified. The quality of evidence was assessed according to the National Health and Medical Research Council hierarchy of levels of evidence [11].

When a range of fractions was recommended, the number of fractions best supported by evidence was used in the calculations. If there were a number of sources of equal quality that recommended different fractionation schedules, the Australian guidelines recommendation was used if available, as the primary purpose was to make recommendations for radiotherapy services in Australia. When fractionation recommendations were not in the Australian guidelines, the lowest of the range of fractions recommended in the other guidelines was used. The effect of higher fraction numbers on the model was tested by sensitivity analysis.

The decision tree was analysed from right to left. For each cancer site, the optimal number of fractions per patient, depicted by the number at the left most node, represented a weighted mean taking into account all the payoffs (recommended numbers of fractions at the terminal nodes) and the probability of each clinical scenario. By dividing this number by the proportion of patients with that particular cancer recommended to have radiotherapy, the optimal number of fractions per treatment course was calculated. The overall optimal number of fractions was the weighted average of the optimal number of fractions for all cancer sites, taking into account the different proportions of these cancers. For patients with an indication of radiotherapy, further analysis was performed to determine the proportion of patients recommended to have radical versus palliative radiotherapy, and the optimal number of fractions per radical and per palliative course.

For each branch with a range of recommended number of fractions or a range of epidemiological data, one-way sensitivity analysis was conducted to assess the effect on the optimal estimate for each cancer site and for the entire tree.

Results

There are 27 cancer sites in the RTF model (Table 1). For each cancer site, the optimal number of fractions ranged from 0 to 23.3 per cancer patient. As an example, the rectal cancer RTF model is shown in Fig. 1, with the optimal number of fractions per patient being 14.4. For the entire cancer population, the optimal number of fractions was 9.4 per cancer patient. This was a weighted average of all indications including radical, palliative and cases in which radiotherapy was not recommended.

The last column of Table 1 shows the optimal number of fractions per radiotherapy course, considering only the patient population for whom radiotherapy was recommended. This ranged from 1.5 to 29.1, with the highest being brain, prostate and head and

Table 1
Optimal radiotherapy utilisation rate and number of fractions.

Cancer site	Proportion of all cancers in Australia (%)	Optimal radiotherapy utilisation (%)	Optimal number of fractions per cancer patient	Optimal number of fractions per treatment course
Bladder	2.0	47	4.9	10.4
Brain	1.4	80	23.3	29.1
Breast	12.2	87	14.3	16.4
Cervix	1.0	71	15	21.1
Colon	8.4	4	0.1	2.5
Gallbladder	0.6	17	4.1	24.1
Head and neck	3.3	74	20	27.0
Kidney	2.3	15	0.3	2.0
Leukaemia	2.3	4	0.3	7.5
Liver	1.2	0	0	–
Lung	9.0	78	12.1	15.5
Lymphoma	4.2	73	10.4	14.2
Melanoma	9.9	21	3.9	18.6
Myeloma	1.2	45	1.6	3.6
Oesophagus	1.2	71	10	14.1
Ovary	1.1	4	0.3	7.5
Pancreas	2.1	49	10.3	21.0
Prostate	18.4	58	16.3	28.1
Rectum	4.2	60	14.4	24.0
Stomach	1.8	27	5.0	18.5
Testis	0.8	15	2.2	14.7
Thyroid	1.8	4	0.5	12.5
Unknown primary	2.4	61	0.9	1.5
Uterus	1.8	32	7.1	22.2
Vagina	0.1	94	20.7	22.0
Vulva	0.3	39	9.4	24.1
Other	5.0	19	3.5	18.4
Total	100.0	48.4	9.4	19.4

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