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#### Research article

## Factors affecting radiotherapy utilisation in geriatric oncology patients in NSW, Australia



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#### ABSTRACT

Background and Purpose: Large non-age-specific radiotherapy utilisation rate (RTU) studies have demonstrated that actual RTU is below the optimal recommended utilisation rate for both curative and palliative intent radiotherapy indications. The optimal utilisation rate for the geriatric oncology cohort of patients has not yet been determined. The purpose of this research was to examine the actual RTU for patients treated in New South Wales (NSW), Australia as a function of increasing age, and the relationship between RTU and tumour site, travelling distance and socio-economic status.

*Materials & Methods:* NSW Central Cancer Registry data (2009–2011) were linked to the NSW Radiotherapy Dataset (2009–2012). RTU was calculated for patients aged <80 years and  $\geq$ 80 years. RTU was defined as the proportion of patients receiving at least a single course of radiotherapy within 12 months of a cancer diagnosis.

Results: 110,645 patients were diagnosed with cancer, of whom 27,721 received at least one course of radiotherapy. The overall RTU was 25%. RTU for patients aged <80 years was 28% compared to 14% for patients aged 80+ years (p < 0.001). On both univariate and multivariate analysis, increasing age, residential address in disadvantaged socioeconomic areas and increasing distance to the nearest radiotherapy department were associated with a reduction in RTU.

Conclusion: Geriatric oncology patients are less likely to receive radiotherapy than their younger counterparts. Some of the reduction in RTU may be justifiable on the basis of limited life expectancy and comorbidity. Further research is required to determine the co-morbidity adjusted optimal RTU in older patients.

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#### Introduction

The population of older people for whom cancer treatment needs to be considered is increasing. This is in step with the ageing population and therapeutic advances in oncologic management. In Australia, it has been estimated that approximately 50% of people aged 65 years and above will develop cancer [1], and the overall proportion of people with cancer in this age group is projected to increase from 10-13% (1982–2007) to 17% by 2020 [2]. For patients

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aged 80–84 years, the number of new cases is projected to increase from 7570 to 9870 for males, and 5030 to 6120 for females, from 2011 to 2020 [2]. Worldwide, it is predicted that the proportion of cancer patients aged 65 years and above will increase from 47.5% (6.7 million patients) in 2012 to 60% (14 million patients) in 2035 [3]. However, there is under-representation of the geriatric ( $\geq$ 80 years) cohort in clinical trials, thus a need for further studies to examine and inform their care [4,5].

Radiotherapy is an important treatment option for older people with cancer. However, limited data are available on current and optimal radiotherapy utilisation (RTU) for older patients. Large, non-age specific RTU studies have demonstrated that actual RTU

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is below optimal utilisation for both curative and palliative intent radiotherapy schedules [6,7]. The shortfall in overall RTU appears to occur in all major tumour sites, including lung, breast, rectal and prostate cancer. There is evidence that an inappropriate reduction in RTU (non-treatment where evidence suggests benefit) results in decreased local control and overall survival [8–11]. The factors contributing to the reduction in RTU in older cancer patients have not yet been examined.

Improvements in radiotherapy technique are associated with a reduction in side effects [12]. Anecdotally, it is thought that older patients are generally 'fitter' in the current compared to previous eras. Furthermore, the disability-adjusted life year or DALY has reduced in patients aged 80+ years as reported in the Australian Bureau of Statistics disease burden and mortality estimates [13]. This is supported by the literature showing a reduction in functional disabilities in the modern era despite the number of medical co-morbidities increasing with advancing age [14]. Therefore, it is possible that a greater proportion of older patients may benefit from radiotherapy than predicted based on historical experience.

The objectives of this study were to analyse the factors that contribute to a reduction in RTU for people <80 and >80 years of age.

#### Materials and methods

All patients diagnosed with a notifiable cancer in New South Wales (NSW), Australia, from 2009-2011 were included in the study. NSW Central Cancer Registry data for this period were linked to the NSW Radiotherapy Dataset for 2009–2012. The NSW Central Cancer Registry includes all cancers except for non-melanomatous skin cancers. The radiotherapy dataset includes all patients treated in both the public and private sector. Performance status information was not available.

For the purpose of this research, the geriatric oncology patient group of interest was defined as those  $\geq 80$  years of age. In the geriatric oncology literature, the specific cut-off age is described variably. The International Society of Geriatric Oncology (SIOG) [15–18] uses 70 years and above. However, clinical treatment paradigms for radiotherapy often change when patients are  $\geq 80$  years of age, when the associated life expectancy is <10 years [19]. Therefore the  $\geq 80$  age group was considered of particular interest. Age was categorised into five age groups: <60, 60–69, 70–79, 80–89 and 90+ years.

The actual RTU was calculated by dividing the number of patients who received at least one course of radiotherapy within 12 months of diagnosis by the total number of cases of cancer in a particular population. This methodology has been reported previously [20,21]. The four most common primary cancer sites, breast, prostate, lung and rectal, were chosen to best reflect daily clinical practice, with the International Classification of Diseases, tenth revision (ICD-10) codes of C50, C61, C34 and C20 respectively. RTU rates were compared by age group, primary site, distance to the nearest radiotherapy department and socioeconomic status. Residential postcodes were classified using the census-based Socio-Economic Index for Area (SEIFA) categories based on the Index of Relative Socio-economic Disadvantage (IRSD) [22,23]. Distance to nearest radiotherapy department was examined as both a continuous and categorical variable; a cut-point of 100 km was chosen based on previous research that we have reported [21].

Descriptive statistics were carried out using the Chi-square test or Fisher's exact test for categorical variables. Univariate and multivariate logistic regression analyses were performed to examine the association of RTU with age after taking into account primary site, stage, degree of spread, sex, distance to the nearest radiotherapy department, remoteness and socioeconomic status [22]. Multicollinearity between geographic variables was assessed.

SPSS (SPSS Version 25. Armonk, NY: IBM Corp.), SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and ArcGIS (ESRI 2018. ArcGIS Desktop: Release 10.5 Redlands, CA, USA) were used in statistical analysis. *P* values < 0.05 were considered statistically significant.

#### **Ethics**

Ethics approvals were obtained from all relevant institutional and registry Human Research Ethics Committees.

#### Results

RTU and age

Overall, radiotherapy utilisation decreased with increasing patient age (Table 1). RTU for patients aged less than 80 years was 28% compared to 14% for patients aged 80 years and above (p < 0.001). In patients aged 70–79 years, the RTU was 25%. The drop off in RTU was most marked from the 80+ year age group.

RTU and tumour site

Radiotherapy utilisation decreased with increasing age from 60 years for all major tumour sites, except for patients with prostate cancer where the peak RTU (35.8%) was observed in the 70–79 year age group and declined thereafter (Fig. 1).

RTU and distance to the nearest radiotherapy department

Fig. 2 shows that for patients residing more than 100 km from the nearest radiotherapy department, patients aged 80 years and above were less likely to receive radiotherapy than younger patients (p < 0.001). The correlation was similar for all individual tumour sites.

RTU and socio-economic status (IRSD)

RTU was lowest for patients living in residential areas with the lowest socioeconomic status (Table 2). This effect was consistent for patients aged <80 years and patients aged 80+ years. For example, in patients with breast cancer aged  $\geq 80$  years, RTU was 29.6% in the least disadvantaged areas (IRSD-5), compared to 22.8% in the most disadvantaged areas (IRSD-1) (p < 0.001). For breast cancer patients younger than 80 years of age, RTU was 68.2% in the least disadvantaged area (IRSD-5) compared to 64.2% in the most disadvantaged areas (IRSD-1) (p = 0.001). There was no statistically significant interaction between socioeconomic status and age group on RTU (p = 0.38).

**Table 1**Radiotherapy utilisation within 1 year of diagnosis by patient age.

Age Group (years)	Total number of patients	Received radiotherapy	RTU rate
<60	33 088	9726	29.4 %
60-69	29 706	8271	27.8 %
70-79	26 868	6 812	25.4 %
80-89	17 955	2 679	14.9 %
90+	3 028	233	7.7 %
Total	110 645	27 721	25.1 %
<80 years	89 662	24 809	27.7%
80+	20 983	2 912	13.9%

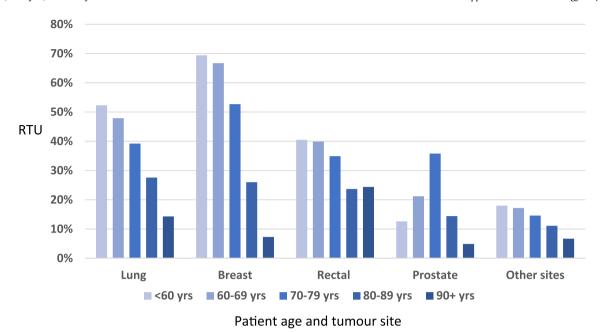
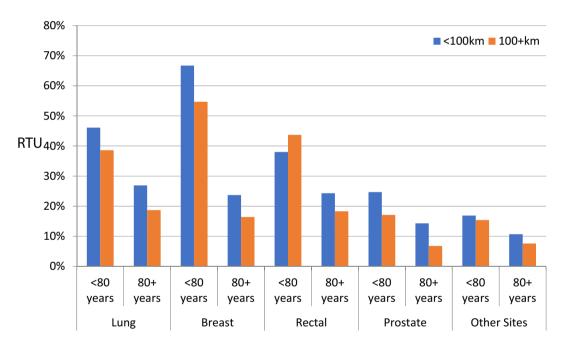


Fig. 1. Radiotherapy utilisation rates by tumour site and patient age.



Tumour site, patient age and distance to the nearest radiotherapy department

Fig. 2. Radiotherapy utilisation(RTU) rates by tumour site, patient age and distance to the nearest radiotherapy department.

#### Multivariate analyses

For all cancers combined, univariate analyses showed age, socioeconomic status and distance were associated with a reduction in RTU (Table 3). All factors significant on univariate analysis were included in the multivariate analysis (Table 4). The multivariate analysis demonstrated that increasing age, residence in areas of socioeconomic disadvantage and increasing distance to the nearest radiotherapy department were significantly associated with a reduction in RTU.

#### Discussion

Our Australian population-based research demonstrated a decrease in radiotherapy utilisation with increasing age across all tumour sites except prostate cancer, and with increasing distance to the nearest radiotherapy department. There was a decrease in RTU in older patients from lower compared to higher socioeconomic areas. On univariate and multivariate analysis, increasing age, lower socioeconomic status and greater distance and remoteness were all significantly associated with lower RTU. Our results

 Table 2

 Radiotherapy utilisation rates by tumour site patient age and Index of Relative Socioeconomic Disadvantage (IRSD).

Tumour site	IRSD*	Number of patients	<80 years	80 + years	p value
Lung	IRSD-1	2 369	42.0%	23.2%	<0.001
	IRSD-5	1 427	47.7%	27.6%	< 0.001
Breast	IRSD-1	2 322	64.2%	22.8%	< 0.001
	IRSD-5	3 088	68.2%	29.6%	< 0.001
Rectal	IRSD-1	784	41.5%	23.9%	< 0.001
	IRSD-5	576	29.6%	22.7%	0.17
Prostate	IRSD-1	3 676	27.0%	12.8%	< 0.001
	IRSD-5	4 331	18.9%	17.7%	0.52
Other	IRSD-1	12 887	16.4%	9.6%	< 0.001
	IRSD-5	12 430	16.0%	10.8%	< 0.001

<sup>\*</sup> IRSD-1 (most disadvantaged) IRSD-5 (least disadvantaged).

**Table 3**Univariate analysis of factors affecting RTU.

Variable	No. of patients	P-value	Odds ratio	95% C.I. for Odds ratio	
				Lower	Upper
Age - continuous	110,645	<0.001	0.986	0.985	0.987
Age - group		•			
< 45 years	9,145	< 0.001	2.265	2.132	2.406
45-59 years	23,943	< 0.001	2.714	2.587	2.847
60-69 years	29,706	< 0.001	2.396	2.287	2.510
70-79 years	26,868	< 0.001	2.109	2.011	2.213
80 + years	20,983		1.000		
Sex					
Males	62,641		1.000		
Females	48,004	< 0.001	1.496	1.456	1.538
Degree of spread					
Localised disease	45,429		1.000		
Regional disease	23,550	< 0.001	2.323	2.244	2.404
Distant disease	17,576	< 0.001	1.695	1.630	1.762
Indeterminate	24,090	< 0.001	0.643	0.616	0.671
Country of birth					
Australian born	45,590		1.000		
Overseas born	21,404	< 0.001	1.106	1.067	1.147
Unknown or missing	43,651	< 0.001	0.754	0.731	0.777
Socio-economic status (IRSD)					
IRSD-1 Most disadvantaged	22,038		1.000		
IRSD-2	22,334	0.306	0.978	0.936	1.021
IRSD-3	22,017	0.119	1.035	0.991	1.081
IRSD-4	22,172	0.001	1.078	1.033	1.125
IRSD-5 Least disadvantaged	21,852	0.854	0.996	0.954	1.040
Residential remoteness					
Major cities	78,191		1.000		
Inner regional	24,782	< 0.001	0.831	0.803	0.859
Outer regional	7,061	< 0.001	0.767	0.723	0.814
Remote & very remote	597	0.264	0.898	0.744	1.084
Residential distance from radiotherapy – continuous	110,624	<0.001	0.998	0.998	0.999
Residential distance from radiotherapy – group	•				
<100 km	100,031		1.000		
>100 km	10,593	< 0.001	0.765	0.728	0.803

IRSD, Index of Relative Socio-economic Disadvantage.

align with previous age and non-age specific radiotherapy utilisation studies as outlined below [11,31,32,35,36]. Although there has been increasing interest in the medical literature regarding geriatric oncology, reports of age-specific RTU are limited.

In the NSW 45 and Up Study, a reduction in RTU was noted in patients 80+ years of age, although age-specific RTU details were not the subject of this research [24]. The 45 and Up study was a population cohort study which utilised a questionnaire administered in 2006–2009 to 267 153 patients aged from  $\geq$ 45 years. This dataset was linked to the NSW Cancer Registry and other health databases. 3667 patients were aged 80+ years in this paper (21%) and 18% received radiotherapy (vs 33.8 % in the 60–69 year group). However, there is evidence that the 45 and Up cohort are healthier on average than the general population [25,26].

There is a potential for worsening general medical health and thus suitability and safety for receiving radiotherapy with advancing age. Guidelines have been published by the International Society of Geriatric Oncology (SIOG) on all the major tumour sites including breast, lung, rectal and prostate to guide management for geriatric patients [15–18]. These documents aim to support clinical decision making by increasing knowledge on geriatric oncology. The SIOG guidelines advise treatment recommendations based on a patient's medical co-morbidities and frailty rather than chronological age per se. For example, the breast cancer guidelines state that 'Age alone should not dictate any aspect of management of older individuals with breast cancer. All decisions should consider physiological age, estimated life expectancy, risks, benefits, treatment tolerance, patient preference and potential treatment barriers [15].'

**Table 4** Multivariate analysis of factors affecting RTU.

Variable	No. of patients	P-value	Odds ratio	95% C.I. for Odds ratio	
				Lower	Upper
Age -continuous	110,645	<0.001	0.986	0.985	0.987
Sex					
Males	62,641		1.000		
Females	48,004	< 0.001	1.331	1.294	1.369
Degree of Spread					
Local disease	45,429		1.000		
Regional disease	23,550	< 0.001	2.276	2.198	2.357
Metastatic disease	17,576	< 0.001	1.755	1.686	1.827
Indeterminate	24,090	< 0.001	0.695	0.665	0.725
Country of birth					
Australian born	45,590		1.000		
Overseas born	21,404	0.031	1.043	1.004	1.083
Unknown or missing	43,651	< 0.001	0.761	0.737	0.786
Socio-economic status					
IRSD-1 (most disadvantaged)	22,038		1.000		
IRSD-2	22,334	0.895	0.997	0.953	1.043
IRSD-3	22,017	0.811	1.006	0.961	1.052
IRSD-4	22,172	0.816	1.005	0.960	1.053
IRSD-5 (least disadvantaged)	21,852	< 0.001	0.912	0.870	0.956
Residential remoteness					
Major cities	78,191		1.000		
Inner regional	24,782	0.011	0.947	0.908	0.988
Outer regional	7,061	0.379	1.039	0.954	1.132
Remote and very remote	597	< 0.001	1.736	1.361	2.215
Residential distance from radiotherapy - continuous	110,624	< 0.001	0.998	0.998	0.999

However, there is little agreement about what performance assessment and scores should be used and there is likely to be high variability in fitness assessment.

Various performance scores may be used to assist in patient selection for treatment. The ECOG performance score, introduced in the 1960's, is well-established; assessing patient's function and independence and thus suitability of treatment [27]. Unfortunately, there is incomplete recording of patients' ECOG performance status in our dataset. Other methods may be used to assess functional status [28–30]. The multiple scoring systems highlight the importance of performance status and comorbidities in treatment decision making, but also the difficulty in attaining consensus criteria to help guide management and then train oncologists in their application, and no attempts to routinely collect these data.

In our research, a reduction in RTU was noted across different tumour sites. The following tumour-site specific articles in the literature also report a reduction in RTU across different tumour sites. Vinod et al., demonstrated a reduction in lung radiotherapy utilisation with increasing age, even in patients of good performance status (ECOG 0-2) [31]. McAleese et al. reported that the elderly, defined as age >70 years, were less likely to receive guideline-recommended curative intent treatment for non-small cell lung cancer compared to younger patients (40% vs. 60%) [32]. More recently, with advances in treatment techniques and greater access to specialised including stereotactic radiotherapy treatments, there is evidence of increased radiotherapy utilisation in elderly lung cancer patients, with utilisation increasing from 26% to 42% from 1999-01 to 2005-07 [33] as more elderly patients are offered curative radiotherapy as an alternative to surgery. Videtic et al. reported on their single institution experience of stereotactic radiotherapy in patients with lung cancer 90 years of age or older and concluded that radiotherapy is safe and effective in this age group [34].

The current literature also demonstrates a decrease in RTU for breast cancer with increasing age. Struikmans et al. reported a reduction in radiotherapy utilisation following breast-conserving surgery with increasing patient age, particularly in patients aged are  $\geq$ 75 years, finding an odds ratio of 0.13 for this patient group

versus patients less than or equal to 50 years of age [11]. Showalter et al. on examining the SEER database, demonstrated a reduction for adjuvant radiotherapy in stage I breast cancer patients 80 years of age and above following breast-conserving surgery, with a RTU of 6.4% [35].

Radiotherapy utilisation is reduced with increasing age in rectal cancer patients. Jobson et al. demonstrated, in a population-based study in the Netherlands 1997–2008, that pre-operative radiotherapy decreased to 17%-26% for patients aged 85–89 years compared with 47–69% in patients aged 60–64-years [36].

There is less data available in the literature on radiotherapy benefits for older patients with prostate cancer. Of note, the SIOG Task Force stated that if patients are elderly but fit, standard treatment is recommended [16]. Prostate RTU increased up until age 80 contrary to the findings for other cancers, perhaps because surgery is offered or accepted less frequently in prostate cancer patients with advancing age and low fitness. For the other major tumour sites, the radiotherapy offered is more frequently adjuvant therapy, and appears to be considered less important with increasing age. For some tumour sites such as breast cancer, this may be entirely appropriate when other competing adjuvant therapies may adequately reduce recurrence risk (such as early, ER-positive breast cancer being managed with adjuvant endocrine therapy in preference to radiotherapy) [37]. However, for other tumour sites, such as rectal cancer, this reduction in radiotherapy utilisation may or may not be appropriate depending on the predicted patient prognosis and their locoregional recurrence risk.

With regards to place of residence and distance to the nearest radiotherapy department, our results are similar to an earlier NSW study using a 2004–2006 dataset [21]. With an increase in the number of regional centres in recent years, it is expected that RTU may increase [7].

The duration of treatment, and the provision of shorter or 'hypo-fractionated' courses of radiotherapy may also increase the RTU in the older cohort of patients, with less treatment attendances required. Of note, certain hypo-fractionated radiotherapy schedules for specific cancer sites are considered standard of care for patients of all ages, for example, the breast cancer hypo-fractionated regimens [38,39].

Socioeconomic status is known to affect delivery of care and cancer outcomes and may also correlate with the presence of comorbidities. Galvin et al. in their systematic review, demonstrated that low socioeconomic status and advancing age were associated with poorer cancer specific and overall survival [40]. There are limited data on the relationship between socioeconomic status and RTU in older patients. Hui et al. reported on the socioeconomic status and patterns of care in NSW patients with lung cancer and found no difference in RTU rates based on IRSD categories [41]. However, less than 12% of patients were aged 70 years and above in this older study (with the patient population from January 1996-December 1996).

A concern by treating and referring clinicians may be the tolerance of radiotherapy toxicity in the elderly cohort of patients. There is research showing older patients can be safely treated with radiotherapy. A French multicentre retrospective study showed that radiotherapy was safe in patients 90 years of age or older [42]. This age group was reported to represent approximately 1% of patients treated in their centres. Kocik et al., reported that 41% of patients aged 90 years and above evaluated at their Austrian Cancer Centre (2005–2016) received definitive radiotherapy in their retrospective study [43], and 90% of these patients completed their course of treatment. The modern radiotherapy treatment techniques are also associated with a reduction in side effects, with an increase in the precision and accuracy of treatment [44].

Whilst appropriate treatment decisions are essential and expected, it is also important to note that if radiotherapy is withheld, the prognosis may be worse. The inferior clinical outcomes associated with the underutilisation of radiotherapy have been previously reported. In a younger cohort, of patients, there is a reduction in local control and survival if RT is not administered [20,45]. Hanna et al. reported that RT is associated with a 5-year improvement in local control in 10.4% and 5-year overall survival benefit in 2.4% in all patients [45]. The appropriate utilisation of radiotherapy is also potentially more important in geriatric patients if other treatment options, such as surgery and systemic therapies, are limited. Research exploring this topic is unfortunately limited.

The strengths of this research were the population-based study design, and the large number of cases. To our understanding, this is the first time that geriatric oncology RTU across multiple cancer sites using a large cancer registry has been reported in the literature. The limitations were the lack of ECOG performance status data and thus ability to determine the appropriate RTU in this cohort of patients. Other relevant data that were not present in this database include receipt of surgery, chemotherapy or targeted therapy, patient preference and caregiver availability.

#### Conclusion

Radiotherapy utilisation rates decreased with increasing age except for prostate cancer. This reduction in RTU rates occurs across the major tumour sites, in patients of lower socioeconomic status and with increasing distance from radiotherapy departments. Further research is required to estimate the appropriate proportion of geriatric patients who should receive radiotherapy and to examine reasons for any gap. The development of a co-morbidity/frailty adjusted score for optimal radiotherapy utilisation rate would assist in clinical decision making, especially in the era of personalised medicine.

#### **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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