Exposure of patients to ionising radiation during lung cancer diagnostic work-up

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ABSTRACT

We examined the dose of radiation received during diagnosis of lung cancer as this may add to the risk of a second primary cancer. Patients undergoing surgery (n=40) or (chemo)radiotherapy (n=40) received comparable doses (28.6 mSv and 25.8mSv respectively), significantly higher than for supportive care (n=40; 15.1mSv). The effective dose of radiation received was higher for early stage disease than for those with metastatic disease. The mean lifetime attributable risk of malignancy for those receiving treatment with curative intent in our cohort was 0.059% and lung specific risk 0.019%.

INTRODUCTION

During work-up of patients with (suspected) lung cancer for treatment with curative intent, healthy tissues are exposed to ionising radiation. This may add to the risk of a future second primary cancer and is particularly pertinent to the growing number of younger long-term survivors. At present the total radiation dose received by patients during diagnostic work-up is not monitored or restricted and there remains a paucity of literature on the subject.

Given recent changes in investigation algorithms used in lung cancer [1] and the importance of understanding the risks associated with ionising radiation, we sought to evaluate diagnostic radiation exposure in a cohort of patients investigated through the Papworth and Addenbrookes Thoracic Oncology Service.

METHODS

The cumulative radiation dose received by patients undergoing investigation for treatment with curative intent for primary lung cancer at Papworth and Addenbrooke's Hospitals between December 2012 and March 2014 was calculated. Retrospective data were gathered from electronic reporting systems including patient demographics, stage and type of cancer and participation in clinical studies involving ionising radiation (supplementary Tables 1-4 online data). Information on all radiological investigations involving ionizing radiation between the first targeted investigation and the start of definitive treatment was gathered. Similar data for a group of patients (n=40) undergoing best supportive care (BSC) were also collected. If data on individual studies were not available, an estimate derived from local diagnostic reference levels was used. The total effective radiation dose was calculated for each patient and percentage lifetime attributable risk (LAR) estimated using conversion co-efficients in HPA-CRCE-028 and -012, NRPB-W67 and ICRP106 [2, 3, 4, 5].

Comparisons between groups were made using Student's t-test with a *P* value of <0.05 considered significant.

RESULTS

The mean cumulative dose of radiation received by 80 patients undergoing investigation for treatment with curative intent (surgery or radical (chemo)radiotherapy) was 27.6 mSv ± 0.9 (Table 1). Patients in the surgical and (chemo)radiotherapy groups received comparable doses - surgery 28.6 mSv, CRT 25.8 mSv; p=0.89 (Table 1 and Figure 1). This was significantly higher than those who received BSC (n=40; 15.1 mSv ± 1.4; $p<0.05$). When stratified by the stage of disease (Figure 2), the effective dose of radiation received was higher for early stage disease than for those with metastatic disease (μ = 26.9 mSv for stage I, 24.6 mSv for stage II, 22.3 mSv for stage III and 14.4 mSv for stage IV). As might be expected there was a correlation between body mass and effective dose (Supplementary Figure 1; r=0.44, $p<0.05$) but no significant correlation with patient age (Supplementary Figure 2; r=0.058, p=0.52). For patients undergoing treatment with curative intent the median number (range) of investigations undertaken was CT staging 1 (0-4); CT head 1 (0-2); CT guided biopsy 1 (0-3) and PET-CT 1 (0-2) (supplementary Table 5 on-line data).

The mean lifetime attributable risk (LAR) of malignancy for those receiving treatment with curative intent was 0.059% i.e. 5.9 in 10,000 long-term survivors would be expected to develop a second primary cancer as a direct consequence of diagnostic imaging investigations. The lung specific risk was 0.019% (Table 2).

DISCUSSION

Despite lung cancer being one of the most common cancers globally there is a paucity of information on the usual radiation dose patients receive during diagnostic work-up. We have shown that the mean cumulative dose of radiation received by patients undergoing investigation for treatment with curative intent (surgery, radical (chemo)radiotherapy) is around 28 mSv substantially lower than that identified by Stiles et al (2011) who found that in 94 patients, the three-year median estimated dose was 84.0 mSv and that the highest dose occurred in the pre-operative year [6]. In any one year 66% of their patients received more than 50 mSV while 19% received over 100 mSv. Only one of our 80 patients exceeded 50 mSv. Our finding that the radiation dose received by those who ultimately received treatment with curative intent was significantly higher than the dose received for those treated with BSC is not unexpected. This is because those being assessed for treatment with curative intent underwent additional investigations including PET-CT and CT head and some patients being assessed for surgical resection required coronary angiography and/or quantitative ventilation/perfusion scintigraphy. The overall reduction in radiation dose compared to the work by Stiles et al (2011) is most likely due to improvements in radiation technology over the last decade, which allows equivalent imaging at lower radiation doses [6].

Although we have estimated the associated LAR of malignancy this value remains difficult to interpret with regards to setting 'limits' of acceptability. Typically, LAR values are calculated in healthy subjects but the effect of radiation exposure in a high-risk tobacco exposed population may be greater. A number of factors should be considered. Age at presentation may be significant. For patients presenting over age 70 the risk of developing a second primary cancer as a result of previous radiation exposure is likely to be considerably lower than the risk conferred by previous/current cigarette smoking. However for younger

patients being treated with curative intent, thought should be given to LAR given that they will likely have longer life expectancy.

In conclusion, newer algorithms for investigating patients with suspected lung cancer, combined with improvements in imaging technology have reduced the average radiation dose in patients receiving definitive treatment to 28 mSv. Although this is considerably lower than previous reports it is still associated with a quantifiable mean LAR of malignancy of 0.059% in our patient cohort.

TABLES

Table 1 **Effective dose of radiation received/mSv**

Treatment Group	N	Mean/μ (95% CI)	SEM	SD/σ
Surgical	40	28.6 (26.0-31.2)	1.33	8.42
(Chemo)radiotherapy	40	25.8 (23.5-28.1)	1.19	7.50
Total curative intent	80	27.6 (25.8-29.4)	0.90	8.01
Best supportive care	40	15.1 (12.4-17.8)	1.36	8.60

Table 2 **Lifetime added risk of malignancy/%**

Treatment Group	N	Total			Lung		
		Mean/μ	SEM	SD/σ	Mean/μ	SEM	SD/σ
Surgical	40	0.062	0.00013	0.00082	0.019	0.00011	0.00072
(Chemo)radiotherapy	40	0.056	0.00015	0.00097	0.019	0.00026	0.00017
Total curative intent	80	0.059	0.00014	0.00090	0.019	0.000019	0.00012

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COMPETING INTERESTS

None

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None

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FIGURE LEGENDS

Figure 1

Effective radiation dose (mSv) received by patients during diagnostic work-up stratified by surgical, (chemo)radiotherapy (CRT) and best supportive care (BSC) groups.

Figure 2

Effective radiation dose (mSv) received by patients during diagnostic work-up stratified by stage of disease.

Supplementary Figures

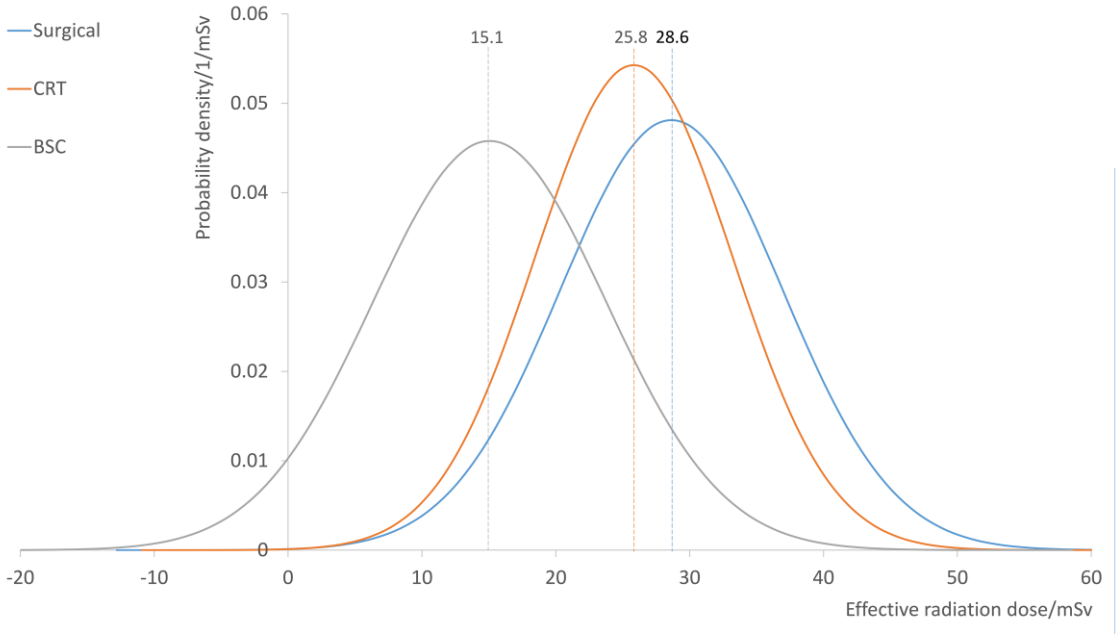
Figure 1

Effective radiation dose (mSv) as a function of weight (kg) for all patients (n=120).

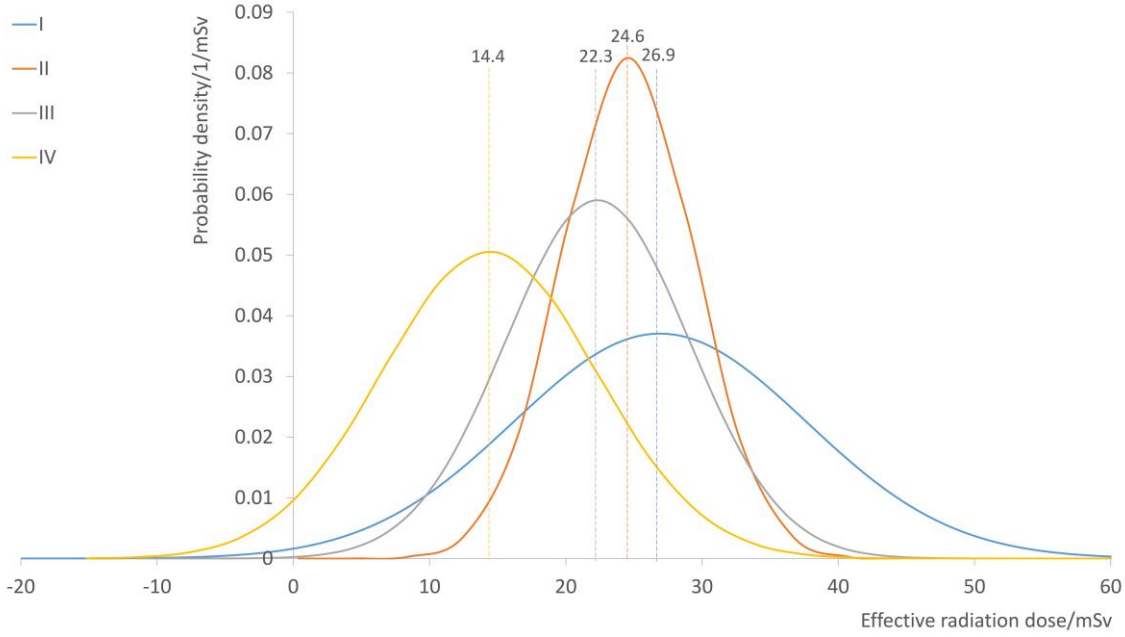
Figure 2

Effective radiation dose (mSv) as a function of age (yrs) stratified by stage of disease (I-IV).

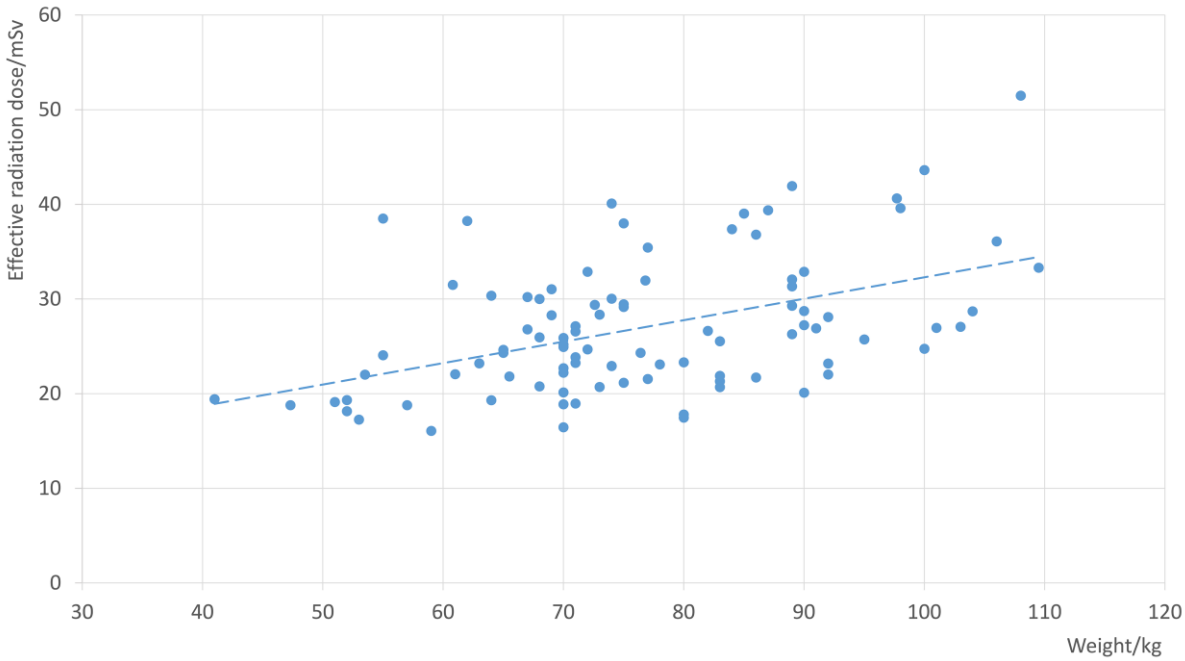
Main Figure 1



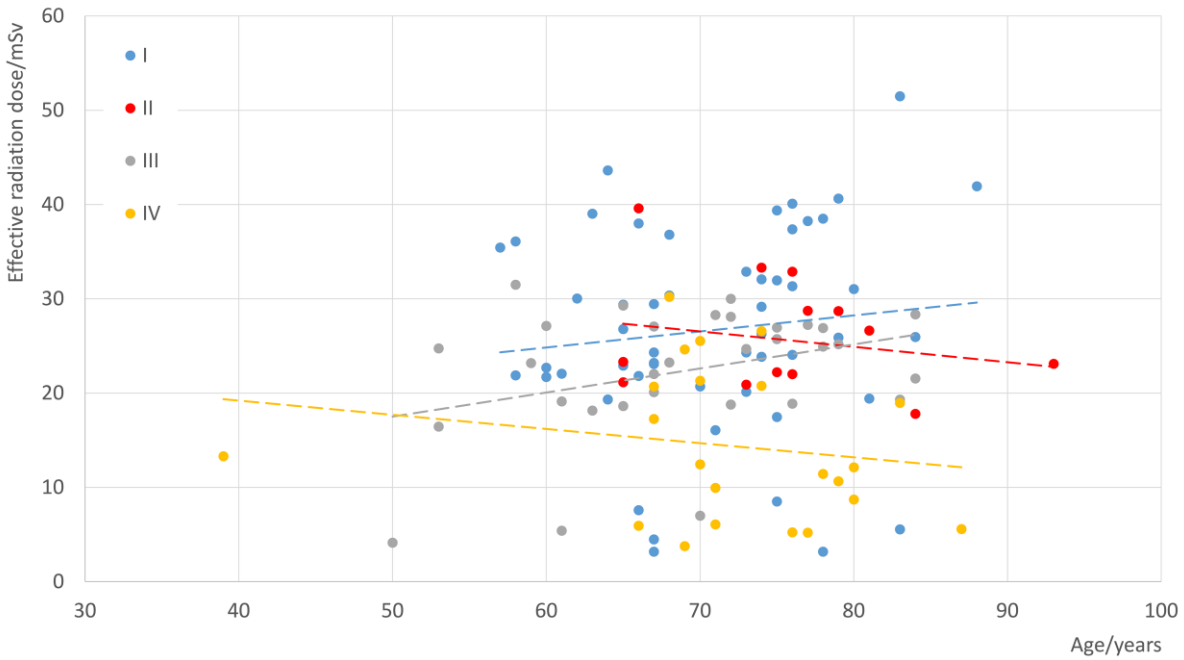
Main Figure 2



Supplementary Figure 1



Supplementary Figure 2



Supplementary Table 1 **Patient demographics**

Treatment Group	Sex/n		Median age/years
	Male	Female	
Surgical	24	16	71.5
Chemoradiotherapy	24	16	73
Total curative intent	48	32	72
Best supportive care	18	22	71
Total	66	54	72

Supplementary Table 2 **Stage of malignancy**

Treatment Group	Stage						
	1a	1b	2a	2b	3a	3b	4
Surgical	17	13	3	3	4	0	0
Chemoradiotherapy	10	8	3	2	14	3	0
Total curative intent	27	21	6	5	18	3	0
Best supportive care	0	5	1	2	5	5	22
Total	27	26	7	7	22	8	22

Supplementary Table 3 **Histological type of lung cancer**

Treatment Group	Type			
	NSCLC	SCLC	Mixed	Unknown
Surgical	39	0	1	0
Chemoradiotherapy	36	0	0	4
Total curative intent	75	0	1	4
Best supportive care	34	5	0	1
Total	109	5	1	5

Supplementary Table 4 **Clinical Trials**

Treatment Group	SPUTNIK	TIDAL	Lung-SEARCH	UKLS	None
Surgical	2	1	1	1	35
Chemoradiotherapy	2	0	0	1	37
Total curative intent	4	1	1	2	72
Best supportive care	2	0	0	0	38
Total	6	1	1	2	110

Treatment Group	CXR		CT Staging		CT Head		CT-guided biopsy		CTPA		PET-CT		Coronary angiogram		V/Q scan	
	Median (Range)	Mean/ μ	Median (Range)	Mean/ μ	Median (Range)	Mean/ μ	Median (Range)	Mean/ μ	Median (Range)	Mean/ μ	Median (Range)	Mean/ μ	Median (Range)	Mean/ μ	Median (Range)	Mean/ μ
Surgical	3 (1-7)	2.90	1 (0-4)	1.55	1 (0-2)	1.00	1 (0-2)	0.83	0 (0-1)	0.05	1 (0-1)	1.00	0 (0-1)	0.05	0 (0-1)	0.05
(Chemo)radiotherapy	2 (0-8)	2.33	1 (0-3)	1.45	1 (0-2)	1.00	0 (0-3)	0.54	0 (0-1)	0.05	1 (0-2)	1.05	0 (0-0)	0.00	0 (0-1)	0.13
Total curative intent	2 0-8)	2.62	1 (0-4)	1.50	1 (0-2)	1.00	1 (0-3)	0.68	0 (0-1)	0.05	1 (0-2)	1.03	0 (0-1)	0.03	0 (0-1)	0.09
Best supportive care	1 (0-8)	1.60	1 (0-3)	1.23	0 (0-1)	0.23	0 (0-2)	0.20	0 (0-1)	0.10	0 (0-1)	0.48	0 (0-0)	0.00	0 (0-1)	0.03

Supplementary Table 5 Median (range) number of investigations involving ionizing radiation performed for each treatment group.