

## Collateral contamination concomitant to the polonium-210 poisoning of Mr Alexander Litvinenko

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### Abstract

Mr Litvinenko died on 23<sup>rd</sup> November 2006, having been poisoned with polonium-210 on 1<sup>st</sup> November, with evidence of a previous poisoning attempt during October 2006. Measurements of <sup>210</sup>Po in urine samples were made for a large number of people to determine whether they may have been contaminated. In the majority of cases, measured levels were attributable to the presence of <sup>210</sup>Po from normal dietary sources. For a small number of cases, elevated levels provided evidence of direct contamination associated with the poisonings. For one individual, while estimated doses were below thresholds for irreversible organ damage, a notably increased risk of cancer can be inferred. The use of the chelating agent, Unithiol, to increase <sup>210</sup>Po excretion in this case was only moderately effective in reducing doses received.

### 1. Introduction

Mr Alexander Litvinenko died on 23<sup>rd</sup> November 2006, following poisoning with polonium-210 on 1<sup>st</sup> November. The case has been the subject of a criminal investigation and a public inquiry chaired by Sir Robert Owen that reported on 21<sup>st</sup> January 2016 ([www.litvinenkoenquiry.org](http://www.litvinenkoenquiry.org)). The clinical case history has recently been published (Nathwani *et al* 2016), with separate publication of associated details of assessments of intake of <sup>210</sup>Po, organ doses and consequent rapid decline in physiological function leading to death (Harrison *et al* 2017). The results presented by Harrison *et al* (2017) include evidence of a previous poisoning attempt during October 2006. This paper considers the <sup>210</sup>Po contamination of other individuals, principally on the basis of measurements on urine samples.

Polonium-210 is an alpha particle (5.3 MeV) emitting radionuclide with a half-life of 138 days. It is a naturally-occurring radionuclide, present in our diets, body tissues and excreta as a member of the uranium-238 decay chain. Dietary intake varies substantially so that urinary excretion is also variable (Hodgson 2017). Interpretation of urine measurements to assess the probability of contamination from artificial sources must therefore take account of natural levels and their variability.

Polonium-210 contamination was found at the two London hospitals responsible for the care of Mr Litvinenko from 3<sup>rd</sup> November 2006, raising concerns that hospital staff may have become contaminated. The police investigation identified a number of contaminated locations, including parts of several hotels, restaurants, and office buildings. Twenty-four hour urine samples were taken from a large number of people judged to be at risk of contamination (over 800) in order to determine the extent of

any contamination (Bailey *et al* 2008, 2010, Maguire *et al* 2010). International follow-up of persons potentially exposed was reported by Shaw *et al* (2010).

The Litvinenko Inquiry was provided with reports on two additional contaminated individuals by an Expert Commission of the Federal Medical and Biological Agency (FMBA) of the Russian Federation. These reports provide measurements and interpretation for individuals referred to here as X (COM00181001) and Y (COM00182001) ([www.litvinenkoinquiry.org](http://www.litvinenkoinquiry.org)).

A detailed analysis of available data on natural concentrations of  $^{210}\text{Po}$  in urine (Hodgson 2017) is referred to here in the interpretation of measurements on urine samples taken in the UK during the months following Mr. Litvinenko's death. Use is also made of the data provided by FMBA. Estimates of radiation dose are presented for the two individuals and interpreted in terms of possible risks to health. The efficacy of intramuscular injections of Unithiol in accelerating excretion is also considered on the basis of the data provided.

## 2. Methods

### 2.1. Radioactivity measurements

A sensitive, but relatively rapid, method was developed to handle the large numbers of urine samples analysed during the poisoning incident response (Bailey *et al* 2008, 2010). It required 2–3 days from receipt of a 24-hour urine sample. The method was adapted from one that is in routine operational use for measurements on environmental samples, e.g. food, and is therefore capable of measuring natural levels of  $^{210}\text{Po}$  in many types of sample, including urine. In summary, concentrated nitric acid was added to a 1-litre sample of urine to break down organic matter. The mixture was evaporated slowly (overnight), the residue dissolved in hydrochloric acid, and the  $^{210}\text{Po}$  spontaneously deposited onto a silver metal disc for counting using an alpha spectrometer (typically overnight). The minimum detectable activity (MDA) varied between measurements according to the efficiency of the recovery of polonium, which was determined by adding a known amount of a different polonium isotope ( $^{209}\text{Po}$  or  $^{208}\text{Po}$ ) at the start of the process, and measuring the amount present at the end. MDAs of 1 – 10 mBq d<sup>-1</sup> were usually achieved, depending on recovery. Validation checks were performed with five laboratories in the UK and eight in other European countries. Some of these laboratories used different methods for the radiochemical isolation of polonium. The results obtained were all consistent.

### 2.2. Estimates of radiation doses

Bailey *et al* (2008, 2010) developed a methodology for dose assessment of the large number of results of urine measurements becoming available in the first weeks after it had been established that  $^{210}\text{Po}$  had been used to poison Mr Litvinenko and, that as a result, a number of places had been contaminated with  $^{210}\text{Po}$ . Essentially, three categories were identified: (1) urine measurements of < 30 mBq d<sup>-1</sup> that were possibly attributable to natural background  $^{210}\text{Po}$  levels, (2) effective doses of < 1mSv estimated by the application of standard conservative assumptions, and (3) effective doses of > 1 mSv estimated using more realistic assumptions applied to individual cases. The estimation of effective dose depended on the use of biokinetic and dosimetric models developed by the International Commission on Radiological Protection (ICRP 1993, 1994a,b, 1996, 2006) and ICRP values of effective dose per Bq inhaled or ingested. The ICRP models were implemented using the computer codes, IMBA (Birchall *et al* 2007) and PLEIADES (Fell *et al* 2007).

Excretion rates of  $\geq 30$  mBq d<sup>-1</sup> were taken as indicative of possible intake of an artificial source of <sup>210</sup>Po (see section 3.1). In all cases of recorded values  $\geq 30$  mBq d<sup>-1</sup>, an initial rapid assessment of possible dose was made using a standard set of assumptions that were either realistic (an activity median aerodynamic diameter, AMAD, of 5  $\mu$ m, moderate solubility of the aerosol in the respiratory tract (ICRP Type M), or tended to overestimate dose: intake entirely by inhalation rather than ingestion, acute intake on a fixed date as the earliest possible exposure rather than continuing chronic intake, and no subtraction of background levels attributable to natural <sup>210</sup>Po (Bailey *et al* 2008). With these standard assumptions, a set of conversion factors were calculated for estimation of dose from measured activity, dependent only on the duration between the assumed date of intake and the date of sample collection. For all estimates  $> 1$  mSv, a more detailed analysis was undertaken, in particular to take account of a more probable balance between intake by inhalation and ingestion (Bailey *et al* 2008, 2010).

The data provided to the Litvinenko Inquiry by an FMBA Expert Commission in the Russian Federation (reports COM00181001 and COM00182001, [www.litvinenkoinquiry.org](http://www.litvinenkoinquiry.org)) included measurements of <sup>210</sup>Po activity in urine and faecal samples and estimates of organ doses for two individuals, identified here as X and Y. Doses have been reassessed, using ICRP models, together with the systemic biokinetic model developed by Leggett and Eckerman (2001). The data on urinary and faecal excretion have also been used to assess the efficacy of intramuscular injections of Unithiol in accelerating excretion.

### 3. Results

#### 3.1 Natural background levels of <sup>210</sup>Po in urine

Hodgson (2017) presented a review and analysis of available data on background levels of <sup>210</sup>Po in urine. It was determined that 819 measurements could be considered to correspond to natural background levels, excluding a large number of values identified by the authors as potentially due to an artificial source or due to recognised enhancement of dietary intake. Almost 550 measurements were extracted from studies reported in the literature (Black 1956, Globel *et al* 1966, DeBoeck *et al* 1971, Bale *et al* 1975, Okabayashi *et al* 1975, Juan and Balleos 1976, Holtzman *et al* 1976, Spencer *et al* 1977, Clemente *et al* 1979, Helmkamp *et al* 1979, Okabayashi *et al* 1982, Irlweck 1983, Mancini *et al* 1984, Azeredo & Lipsztein 1991, Hunt and Allington 1993, Santos *et al* 1994, Santos *et al* 1995, Naumann *et al* 1998, Santos *et al* 2000, Thomas *et al* 2001, Schafer and Seitz 2005, Hunt and Rumney 2007, Manickam *et al* 2010). The additional measurements were contributions of previously unpublished data, acknowledged by Hodgson (2017). The analysis of the measurements gave mean and median values of 14 mBq d<sup>-1</sup> and 9 mBq d<sup>-1</sup>, respectively. Although not conforming statistically to a log-normal distribution, the majority of the measurements were found to be tightly clustered around the mean and median values but with a long asymmetric tail to the distribution. While the overall range was from 0.3 to 170 mBq d<sup>-1</sup>, more than 90% of the measurements corresponded to excretion rates less than 30 mBq d<sup>-1</sup>, 95% were less than 45 mBq d<sup>-1</sup> and 99% less than 70 mBq d<sup>-1</sup>.

Separate analysis of data for smokers and non-smokers suggested a modest increase in smokers of up to around 5 mBq d<sup>-1</sup>. Reflecting the importance of dietary differences such as seafood consumption, a marked difference between countries was observed in the range of results (Hodgson 2017). While for most countries, 95%

or more of results were below 30 mBq d<sup>-1</sup>, China and Italy were notable exceptions, with greater than 20% of values above this level.

### **3.2. UK Measurements to assess possible contamination in London during 2006**

The majority of the measurements of excretion rates (total of around 800) were below 30 mBq d<sup>-1</sup> and were most probably due to natural levels of <sup>210</sup>Po in diet, providing no evidence of exposure to an artificial source. The majority of measurements above 30 mBq d<sup>-1</sup> were assessed as corresponding to an effective dose of less than 1 mSv (86 cases identified by Bailey *et al* 2008, 2010). A total of 36 cases for which more detailed assessments were undertaken had estimated doses within the range of 1 – 6 mSv (Bailey *et al* 2010) or a total of 43 in the range 1 – 10 mSv. Doses in the range > 10 mSv – 100 mSv were recorded for a total of 8 people, mostly staff of one hotel.

### **3.3. Russian Federation measurements to assess contamination for two cases**

Assessments of intake and radiation doses have been made for comparison with those reported by FMBA. The results used were measurements on urine, blood and faecal samples taken prior to the administration of Unithiol to increase excretion. Estimates of <sup>210</sup>Po intake by individuals X and Y were made separately for each sample taken – urine, faeces and blood. As shown in Tables 1 and 2, estimates vary according to the assumed date and route of intake, and between the samples on which they are based. Values for X average about 4 MBq for either ingestion or inhalation on 1.11.06 and 6 – 7 MBq for ingestion or inhalation on 16.10.06 (Table 1). Values for Y are estimated to be an order of magnitude lower (Table 2).

Ratios of urinary to faecal excretion (U/F) for samples measured prior to administration of Unithiol were compared with model predictions to determine whether any conclusions could be drawn regarding route of intake. However, while difference in U/F ratios between inhaled and ingested <sup>210</sup>Po would be expected at shorter times after an intake, predicted values corresponding to the times of sample collection showed that there was not a large difference between expected ratios following inhalation and ingestion at these times. It is not possible, therefore, to use the excretion data provided to draw reliable inferences regarding the route(s) of intake in the two cases.

Tables 3 and 4 show estimated organ doses for X calculated using averaged values of intake from Table 1. Assuming intake by ingestion, organ doses are greatest for liver and kidneys at up to around 300 mGy and 400 mGy, respectively. Similar doses were estimated for liver and kidneys assuming intake by inhalation and in both cases (ingestion and inhalation), about half of the total organ doses were estimated to have been delivered in the first month after intake and a large proportion of these doses were estimated to have been delivered within three months. Lung doses after inhalation were estimated to be up to around 4 Gy for intake on 1.11.06 and 5 Gy for intake on 16.10.06.

Table 1. Polonium-210 intake estimates from sample measurements for individual X<sup>a</sup>

Sample	Sample date	Measurement (Bq/d or Bq)	Estimated intake, MBq			
			Ingestion on:		Inhalation on:	
			01/11/2006	16/10/2006	01/11/2006	16/10/2006
Urine 1	29/11/2006	550	2.9	4.6	3.0	4.4
Urine 2	30/11/2006	240	1.3	2.1	1.4	2.0
Urine 3	02/12/2006	459	2.6	4.2	2.7	4.0
Faeces	29/11/2006	3750	5.7	9.3	5.4	8.3
Blood	29/11/2006	30000	6.9	11.1	9.8	14.3

<sup>a</sup>Measurements reported by the Federal Medical Biological Agency of the Russian Federation to the Litvinenko Inquiry ([www.litvinenko inquiry.org](http://www.litvinenko inquiry.org) : COM00181001)

Table 2. Polonium-210 intake estimates from sample measurements for individual Y<sup>a</sup>

Sample	Sample date	Measurement (Bq/d or Bq)	Estimated intake, MBq			
			Ingestion on:		Inhalation on:	
			01/11/2006	16/10/2006	01/11/2006	16/10/2006
Urine 1	29/11/2006	31	0.2	0.3	0.2	0.3
Urine 2	30/11/2006	53	0.3	0.5	0.3	0.4
Faeces	29/11/2006	622	0.9	1.5	0.9	1.4
Blood 1	28/11/2006	2500	0.6	0.9	0.8	1.2
Blood 2	29/11/2006	2200	0.5	0.8	0.7	1.1

<sup>a</sup>Measurements reported by the Federal Medical Biological Agency of the Russian Federation to the Litvinenko Inquiry ([www.litvinenko inquiry.org](http://www.litvinenko inquiry.org) : COM00182001)

Table 3. Estimated absorbed doses to organs for X, assuming ingestion of <sup>210</sup>Po

Assumed day of intake	Integration period	Organ dose, mGy				
		RBM <sup>a</sup>	Liver	Kidneys	Spleen	Lungs
1.11.06	30 d	19	98	150	64	4
	100 d	33	160	240	100	7
	Total	37	170	260	110	7
16.10.06	30 d	30	160	240	100	6
	100 d	53	250	380	170	11
	Total	60	270	420	180	12

<sup>a</sup>RBM: Red Bone Marrow

Table 4. Estimated absorbed doses to organs for X, assuming inhalation of  $^{210}\text{Po}$

Assumed day of intake	Integration period	Organ dose, mGy				
		RBM <sup>a</sup>	Liver	Kidneys	Spleen	Lungs
1.11.06	30 d	14	74	150	48	2400
	100 d	27	130	250	86	3500
	Total	34	150	290	100	3700
16.10.06	30 d	21	110	230	71	3600
	100 d	41	190	370	130	5200
	Total	50	230	430	150	5500

<sup>a</sup>RBM: Red Bone Marrow

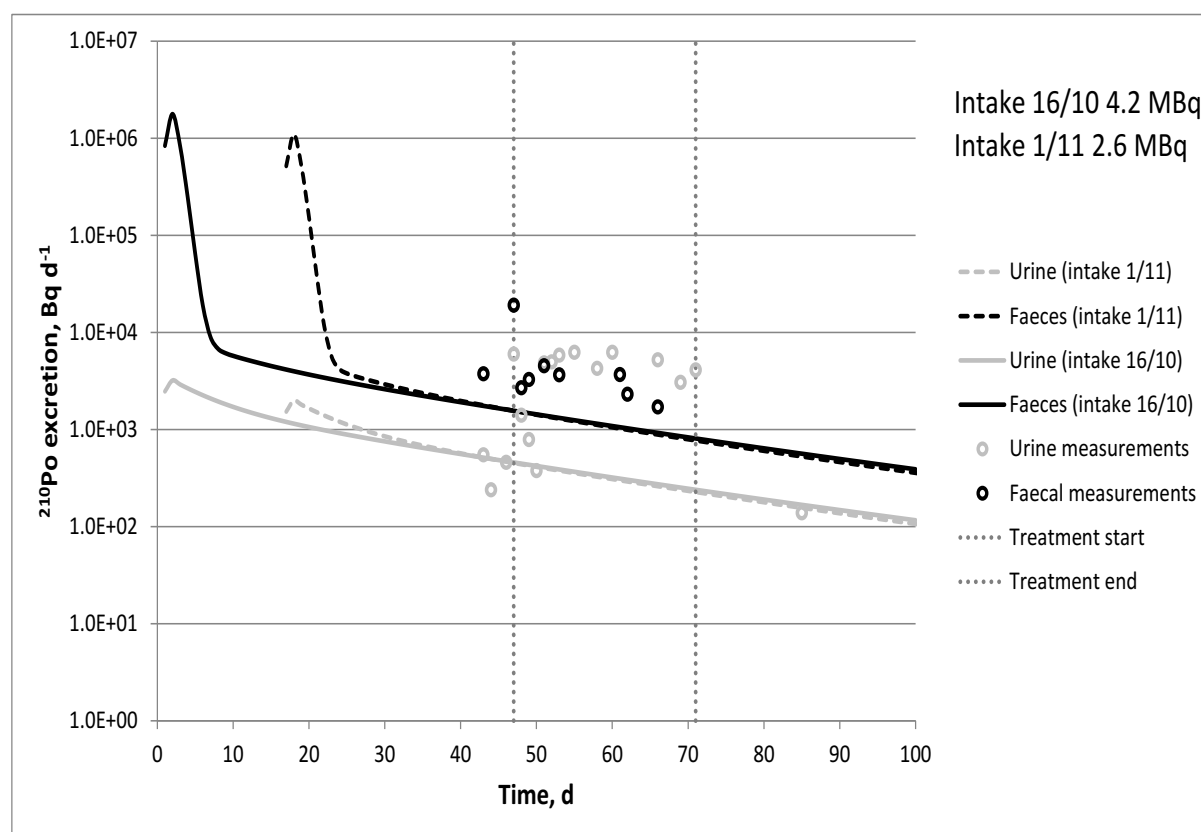


Figure 1. Urinary and faecal excretion of  $^{210}\text{Po}$  for X, comparing modelled excretion for inhalation or ingestion based on intake corresponding to urine sample 3 (Table 1), and measured values during Unithiol treatment

Table 5. Assessment of the efficacy of Unithiol treatment of X by comparison of predicted excretion of  $^{210}\text{Po}$  without treatment to measured excretion following administration of Unithiol

Sample	Assumed date of intake	Model <sup>a</sup>	Predicted excretion without treatment <sup>b</sup> , kBq	Observed excretion with treatment <sup>b</sup> , kBq	Actual/predicted
Urine	16/10/2006	U1	9.2	116	12.6
	01/11/2006	U1	9.1	116	12.8
	16/10/2006	U2	4.2	116	27.6
	01/11/2006	U2	4.1	116	28.5
	16/10/2006	U3	8.4	116	13.8
	01/11/2006	U3	8.1	116	14.2
	16/10/2006	F	18.6	116	6.2
	01/11/2006	F	17.8	116	6.5
Faeces	16/10/2006	U1	26.5	80.3	3.0
	01/11/2006	U1	26.5	80.3	3.0
	16/10/2006	U2	12.1	80.3	6.6
	01/11/2006	U2	11.9	80.3	6.8
	16/10/2006	U3	24.2	80.3	3.3
	01/11/2006	U3	23.7	80.3	3.4
	16/10/2006	F	53.7	80.3	1.5
	01/11/2006	F	52.0	80.3	1.5

<sup>a</sup>Model: the measurement in Table 1 on which estimates of intake and consequent urinary and faecal excretion were made, without consideration of the effect of Unithiol

<sup>b</sup>Considering only the treatment period

### 3.4. Effectiveness of Unithiol treatment to increase $^{210}\text{Po}$ excretion

Figure 1 illustrates analyses undertaken of the effect of Unithiol in enhancing excretion of  $^{210}\text{Po}$  in the case of X. FMBA physicians administered Unithiol intramuscularly over an extended period from 2<sup>nd</sup> December 2006 until X was discharged from hospital on 28<sup>th</sup> December 2006. Figure 1 shows modelled excretion curves for both urinary and faecal excretion of  $^{210}\text{Po}$ , for the two assumed times of intake, based on urine sample 3 taken on 2<sup>nd</sup> December (Table 1) before Unithiol treatment was started. Thus, the curves in Figure 1 show estimates of the normal

pattern of excretion without chelation therapy and the points are the measured excretion values.

Table 5 shows the results obtained by separate consideration of each intake estimate provided in Table 1, comparing model predictions of  $^{210}\text{Po}$  excretion in the absence of treatment and estimates of actual excretion as shown by measurements during the period of treatment. The possibility that the effects of Unithiol persisted beyond the treatment window was not pursued. As measurements were not available for every day during the treatment period, estimates of excretion on these days were interpolated using a cubic spline. The data indicate that urinary excretion was increased during the treatment period by an average of a factor of 15 and faecal excretion was increased by a factor of 4. Thus, it appears that continued intramuscular administration of Unithiol is effective in enhancing excretion. However, mainly because of the delay between the assumed time of intake and the commencement of treatment, the overall effect on retention and the averted dose attributable to treatment is modest at less than 10% (probably nearer 5%).

#### 4. Discussion

Mr Alexander Litvinenko died in a London hospital on 23<sup>rd</sup> November 2006, after having ingested an amount of  $^{210}\text{Po}$  on 1<sup>st</sup> November 2006, estimated to be around 4 GBq (Nathwani *et al* 2016, Harrison *et al* 2017). There is evidence of an earlier intake during October 2006 but at a substantially lower level that does not affect the interpretation of the fatal consequences of the intake on 1<sup>st</sup> November (Harrison *et al* 2017).

An analysis of over 800 measurements of natural background  $^{210}\text{Po}$  in urine gave mean and median excretion rates of 13.8 mBq d<sup>-1</sup> and 9.3 mBq d<sup>-1</sup>, respectively (Hodgson 2017). Consideration of results for individual countries indicated that UK values are generally lower, with a median of around 6 mBq d<sup>-1</sup>. The amount ingested by Mr Litvinenko was therefore about 10<sup>12</sup> times greater than natural daily intake levels.

Polonium-210 was not established as the cause of Mr Litvinenko's illness until the day of his death. From that time, an intensive survey of contamination of key London sites was initiated, together with a large programme of monitoring of people who may have become contaminated (Bailey *et al* 2008, 2010, Maguire *et al* 2010, Shaw *et al* 2010). Based on an early and rapid review of natural background levels of  $^{210}\text{Po}$  in urine, a value of 30 mBq d<sup>-1</sup> was chosen as an excretion rate above which intake was unlikely to be wholly attributable to natural dietary sources. The extensive analysis by Hodgson (2017) showed that while there was a very large range in individual values of from 0.3 to 170 mBq d<sup>-1</sup>, more than 90% of the measurements were less than 30 mBq d<sup>-1</sup>, supporting the early judgment. Separate analyses of data for individual countries showed that 95% or more of results were below 30 mBq d<sup>-1</sup> in most cases, including the UK, but that China and Italy were notable exceptions for which more than 20% of values were above this level.

More than 800 urine samples were analysed as part of the investigation of possible contamination resulting from direct contact with Mr Litvinenko or proximity during key events. The majority of the measured excretion rates were below 30 mBq d<sup>-1</sup>, providing no evidence of exposure to an artificial source. The majority of measurements above 30 mBq d<sup>-1</sup> were assessed as corresponding to an effective dose of less than 1 mSv (86 cases identified by Bailey *et al* 2008, 2010). A total of 43 individuals for whom more detailed assessments were undertaken had assessed



effective doses in the range 1 – 10 mSv. Effective doses in the range > 10 mSv – 100 mSv were recorded for a total of 8 people, mostly staff of one hotel.

The Litvinenko Inquiry was provided with reports on two additional contaminated individuals by an Expert Commission of the Federal Medical and Biological Agency (FMBA) of the Russian Federation (reports COM00181001 and COM00182001, [www.litvinenkoenquiry.org](http://www.litvinenkoenquiry.org)). The FMBA reports included estimates of intake and organ doses based on measurements of urinary and faecal excretion of  $^{210}\text{Po}$  and  $^{210}\text{Po}$  concentrations in blood samples. The data are reassessed in this paper, with essentially similar results. The two individuals are referred to here as X and Y. Estimates of intake by X averaged about 4 MBq for either ingestion or inhalation on 1.11.06 and 6 – 7 MBq for ingestion or inhalation on 16.10.06. Values for Y were estimated to be an order of magnitude lower. Assuming intake by ingestion, estimated organ doses for X reached maximum values of up to around 300 mGy for liver and 400 mGy for kidneys. Similar doses were estimated for liver and kidneys assuming intake by inhalation and in both cases (ingestion and inhalation), about half of the total organ doses were estimated to have been delivered in the first month after intake and a large proportion of these doses were estimated to have been delivered within three months. Assuming intake by inhalation, lung doses were estimated to be up to around 4 - 5 Gy. Estimated effective doses were around 1.5 Sv for X and 200 mSv for Y, assuming intake solely by ingestion, 9 Sv and 1 Sv, respectively, assuming intake by inhalation, and around 5 Sv and 800 mSv, respectively, assuming intake by both routes (1:1).

The chelating agent, Unithiol, was administered intramuscularly to both individuals during their time in hospital. Analysis of excretion rates for X indicated that urinary excretion was effectively increased during the treatment period by an average of a factor of 15 and faecal excretion was increased by a factor of 4. However, mainly because of the delay between the assumed time of intake and the commencement of treatment, the overall effect on retention and the averted dose attributable to treatment appeared to be less than 10% and probably nearer 5%. For a short commentary on the use of chelating agents to enhance excretion of  $^{210}\text{Po}$ , see Jefferson *et al* (2009).

The very different levels of  $^{210}\text{Po}$  intake experienced, ranging from the large intake suffered by Mr Litvinenko on 1<sup>st</sup> November 2006 to the natural background levels to which we are all exposed daily, is illustrative of the range of associated risks to health, from the certainty of death at the highest doses to the possibility of a very low and uncertain risk of cancer associated with the lowest doses.

Mr Litvinenko died three weeks after ingestion of an amount of  $^{210}\text{Po}$  estimated as around 4 GBq (400 MBq absorbed to blood). Death was the inevitable outcome of the radiation doses estimated to have been received by Mr. Litvinenko's red bone marrow, kidneys and liver (Nathwani *et al* 2016, Harrison *et al* 2017). Bone marrow failure is likely to have been an important contributory cause of death occurring within a few weeks of intake, as a component of multiple organ failure.

Autoradiography of hair samples from Mr Litvinenko provided evidence of an earlier intake of  $^{210}\text{Po}$  during October 2006 at a level of around 1% of the major intake on 1<sup>st</sup> November. As discussed by Harrison *et al* (2017), it is possible in principle that an intake by ingestion at this 1% level, of around 40 MBq (4 MBq absorbed to blood), could have proved fatal over a period of months or years, assuming that no medical intervention was instituted. Animal data reviewed by Harrison *et al* (2007) showed death occurring over a period of a few years as a result primarily of kidney damage at doses averaging around 1.5 Gy, which compares with an estimated kidney dose to

Mr Litvinenko from the first intake, if the second intake had not occurred, of a maximum of approaching 3 Gy.

The FMBA of the Russian Federation provided data to the Litvinenko Inquiry on two individuals with substantial  $^{210}\text{Po}$  contamination (reports COM00181001 and COM00182001, [www.litvinenkoinquiry.org](http://www.litvinenkoinquiry.org)). Estimates of intake of  $^{210}\text{Po}$  by the individual with the greatest contamination are about 1000 times less than estimated for the major intake by Mr Litvinenko, around 4 – 7 MBq (400 – 700 kBq absorbed to blood), depending on when the intake(s) occurred. Estimated organ doses were generally below levels that would be expected to cause acute clinically observable damage. Maximum estimates of kidney doses were about 400 mGy, below thresholds for irreversible acute damage. Lung doses could have been as high as 2 – 5 Gy if intake had been solely by inhalation and the inhaled chemical form had been moderately soluble in the respiratory tract (ICRP Type M). It is possible that such high doses to the lungs could result in clinically observable short-term effects. However, FMBA clinicians observed that no pathological change in lungs were detected (COM00181001 [www.litvinenkoinquiry.org](http://www.litvinenkoinquiry.org)).

Below threshold doses for acute deterministic effects, the concern is increased risk of stochastic effects, principally cancer. Effective dose is a risk-adjusted dosimetric quantity that is used for protection purposes and the control of exposures in relation to stochastic risks (ICRP 2007). Although not intended for the purpose of estimating risks of exposures, particularly for individuals, it can be used with caution to provide a rough indication of risk. Effective dose (Sv) is calculated as the doubly-weighted sum of absorbed doses (Gy) to organs and tissues, first using radiation weighting factors to correct for the relative biological effectiveness (RBE) of different radiation types (e.g. alpha particles compared with gamma rays) in relation to stochastic effects, and second, tissue weighting factors to represent fractional contributions of organs/tissues to overall detriment from stochastic effects. The nominal risk coefficient applied by ICRP to fatal cancer is 5% per Sv (ICRP 2007).

Using the ICRP nominal risk coefficient as an approximate indicator of risk in the case of X, estimates of effective dose of around 5 Sv, depending in particular on the assumed route of intake (ingestion or inhalation), correspond to a lifetime risk of fatal cancer of around 25%, applying as the estimated mortality in a population of people exposed at this level. In comparison, incidence rates in developed countries are around 40%, with overall fatalities accounting for very roughly half of cases, although incidence and survivability vary substantially between cancer types. A 25% increase in the risk of fatal cancer represents a substantial increase on background rates, approximately doubling lifetime risk. It should be noted that the ICRP risk coefficient of 5% per Sv (ICRP 2007) is intended to apply to low dose and dose rate exposures and is therefore of questionable applicability to the high organ doses in this particular case. However, while this consideration might lead to use of a somewhat higher value by up to a factor of two, it is also arguable that the use of a radiation weighting factor of 20 for alpha particles is generally conservative (Harrison and Muirhead 2003, Marsh and Harrison 2014). Ingestion seems a more likely route of intake than inhalation for both X and Y, leading to lower estimates of lung dose and effective dose (see above), although the possibility of airborne contamination cannot be excluded.

To obtain better estimates of risks of radiation-induced cancer, rather than using effective dose to provide an approximate indication of risk, requires the use of age-, sex- and population- specific risk factors for individual cancer types applied to organ absorbed doses (Gy), making due allowance for RBE of alpha particles relative to gamma rays for each cancer type. Such detailed analyses are beyond the scope of

this paper, but scoping calculations showed similar overall results when considering organ-specific risks, although with lower risks when considering age, sex and population (about 15% fatal cancer risk compared with about 25%).

In general terms, doses of around 100 mSv represent the limit of reliable direct epidemiological observations of statistically significant increases in cancer rates in studies of exposed populations (Boice 2014a,b, UNSCEAR 2012a,b). In addition to the uncertainties associated with the risk factors derived from such studies, applying largely to external exposures to gamma rays, there is the additional uncertainty in the present context of their application to internal  $^{210}\text{Po}$  exposures for which there is no direct information on cancer induction. Support for the assumption of equivalence of external radiation exposures and internal alpha particle irradiation, once account is taken for RBE, includes quantitative comparisons with risk factors for alpha particle emitting nuclides, notably lung cancer associated with inhalation of radon-222 and its progeny, but also inhaled plutonium-239, and leukaemia, liver and bone cancer induction by other nuclides (Harrison and Muirhead 2003, Marsh and Harrison 2014). These comparisons and available experimental evidence support the assumption that an estimated effective dose of the order of 100 mSv from  $^{210}\text{Po}$  is associated with a risk of cancer (around 0.5%) that may in principle be discernible in studies of large population groups but corresponds to a small additional risk to individuals. The large number of incident cancers in such a group would be very largely attributable to causes other than radiation (> 95%).

Effective doses of a few 10s of mSv and less are generally below levels for which there is direct evidence of harm in human populations. Studies at such doses have focussed on children because of their generally greater sensitivity to radiation-induced cancer and significant effects have been reported (Pearce *et al* 2012, Mathews *et al* 2013, Kendall *et al* 2013). However, caution is required in the interpretation of positive results for CT examinations (Pearce *et al* 2012, Mathews *et al* 2013) because of the potential for reverse causation (UNSCEAR 2013, Walsh *et al* 2014). Preliminary findings of an association between natural background gamma radiation and childhood leukaemia in Britain (Kendall *et al* 2013) await further study and confirmation. While it is important to pursue sources of direct epidemiological evidence of radiation effects in humans at low doses and dose rates (Boice 2014a,b), it will always be the case that estimates of risk at very low doses will depend on mechanistic understanding and projection of risk estimates derived at higher doses. The protection system recommended by ICRP adopts a linear non-threshold (LNT) dose response relationship in the control of exposures down to very low levels of dose. While this is a pragmatic and convenient approach that allows the addition of doses of different magnitude and different types, it is also difficult to challenge as the most plausible approach on the basis of our current scientific understanding of the mechanisms of radiation action (Preston *et al* 2003, UNSCEAR 2012c). The experimental data and theoretical considerations do not provide firm conclusions regarding deviation from linearity. While this issue is of critical importance to ensure that protection at low doses is sufficient but not unduly restrictive, in the present context of one-off exposures to  $^{210}\text{Po}$ , the inferred risk to health associated with doses of a few 10s of mSv and less should be regarded as very small and not of concern.

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