A Bayesian Analysis of Uncertainties on Lung Doses Resulting from Occupational Exposures to Uranium

M Puncher and A Birchall *(1)*

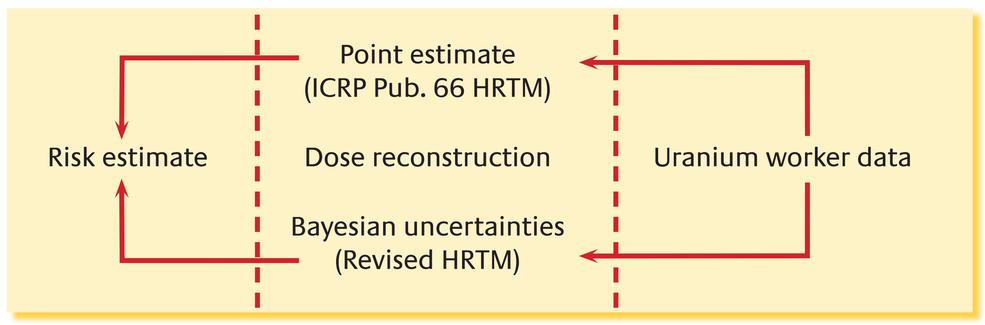
RK Bull *(2)*

Introduction

Epidemiological studies that estimate cancer risk from internal exposures are often based on point estimates of dose that ignore uncertainties in the biokinetic and dosimetric models used to calculate doses to target tissues.

In a recent epidemiological study of European uranium workers[1], lung doses resulting from occupational exposures to uranium-bearing aerosols were estimated from urine bioassay data. Two sets of calculations were performed in the study:

- **Point Estimates of Dose** were calculated using current International Commission on Radiological Protection (ICRP) reference models for calculating doses from occupational exposures; these use the standard ICRP Publication 66 Human Respiratory Tract model (HRTM). The point estimates will be used in a preliminary analysis of possible association between lung dose and lung cancer incidence.
- **Uncertainties on Doses** were calculated using Bayesian inference and will be used in a final analysis of risk. The calculations produced probability distributions of doses which included uncertainties on model parameter values and intakes. They also used an updated version of the particle transport clearance model described in the HRTM. The updated version is based on one being used by ICRP in its forthcoming publication on occupational intakes of radionuclides. .



This study compares the differences between the uncertainties on doses and the point estimates of dose that were calculated for former uranium workers of the United Kingdom Atomic Energy Authority (UKAEA) facilities, who were members of the study cohort.

Bayesian Inference

In the Bayesian approach, uncertainties are provided for all important model parameters. In this study, empirical distributions were derived for HRTM parameters and intake; distributions for lung absorption parameters were derived from a review of published *in vivo* studies.

Parameter	Point Estimates	Bayesian Estimates	
	Value	Distribution	Median (GSD/range)
Lung deposition			
AMAD	5	Log normal	4.4 (1.8)
GSD	2.5	Log normal	2.2 (1.5)
Lung absorption			
f_r	Mixture of ICRP	Stepped-uniform	0.1 (0.001 - 0.1)
s_r	Type F, M and S	Log normal	1 (4)
s_s	solubilities	Log normal	0.002 (4.2)
Intakes	Maximum likelihood	Log normal	Case specific
Lung particle transport model	ICRP Pub. 66	Revised model	

Comparison of Dose Estimates

Bayesian uncertainties were calculated for 118 UKAEA uranium workers using an established Monte Carlo method[2].

To compare uncertainties with point estimates, sample statistics from the posterior distribution of intake or dose for each worker were divided by the corresponding point estimate.

Geometric Means of Ratios of Bayesian Estimates : Point Estimates

Bayesian statistic	Intake	Lung
Mean	3.8	7.8
Median	2.3	2.8
2.5%	0.6	0.2
97.5%	16.8	49.5

Results

- The uncertainties on doses were approximately lognormal and covered a broad range, being greater than two orders of magnitude for some lung tissues.
- The median values of the distributions of lung dose were on average 3 times higher than the point estimates.
- The mean values of the distributions of lung dose were on average 8 times higher than the point estimates; a result of the elevated median values and the high degree of positive skewness in the distributions of lung dose (caused by the large uncertainties).
- Additional calculations suggest that it is the uncertainties on lung absorption parameters that are responsible for the large uncertainties on lung doses.

Why are the Median Values Greater than the Point Estimates?

To answer this question, new point estimates of intake and dose were obtained for the same workers using the revised HRTM and the median values of the priors. It was found that these were around 6-fold higher than the original point estimates. This suggests that the median values of the posterior distributions of lung dose are greater than the point estimates provided for the epidemiology study because either

(a) the median values of the prior distributions are different to the parameter values used to obtain the original point estimates, or
(b) the revised calculations used a different lung model, or
(c) a combination of these effects.

A sensitivity analysis was performed to determine if the cause was (a), (b) or (c). This was achieved by recalculating the original point estimates after substituting parameter values with their corresponding median values from the Bayesian prior, either individually, in combination with each other, or in combination with the revised HRTM; and then comparing the revised point estimates with the original to see if the substitution caused an increase in dose comparable to the 6-fold increase.

Sensitivity Analysis

	Intake	Lung
Lung absorption	+++	+++
Lung deposition	—	+
Revised HRTM	No effect	No effect

+++ Large increase in the point estimate of intake or dose comparable to the revised point estimate: original point estimate ratio of 6

— A reduction in the point estimate of intake or dose

Results

- It is the lung absorption parameter values that produce the observed increase in dose (posterior medians versus point estimates).
- The deposition parameters had a small effect, but the revised HRTM model had no effect.

Conclusion

- Bayesian methods provide a useful framework for calculating uncertainties on doses for workers for epidemiology.
- Point estimates of lung dose ignore significant uncertainties in the model describing deposition and clearance of inhaled uranium materials from the lungs.
- Precise knowledge of the lung absorption parameter values for uranium materials are required to obtain accurate and unbiased estimates of dose and risk from occupational exposures to uranium *for epidemiology*.
- The point estimates of dose provided for the epidemiology study appear to, on average, underestimate lung dose. However, it should be noted that these estimates apply only to the assessments provided for this study, where central estimates of dose were sought. ADS assessments are unlikely to yield significant underestimates, as pessimistic assumptions of lung solubility would almost always be used.

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References

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(1) Health Protection Agency, Centre for Radiation, Chemical and Environmental Hazards, Chilton, Didcot, Oxon OX11 0RQ, UK
(2) Nuvia Limited, 351.15 Harwell Oxford, Didcot, Oxon, OX11 0TQ, UK

matthew.puncher@hpa.org.uk