Supplementary topics on Mayak worker dosimetry

Hyper-realisations
Lung clearance
Faecal samples

Bruce Napier &
Richard Bull

Project 2.4

- Alexander Efimov has given an excellent summary of this project
- The purpose of this presentation is to amplify some of the more technical aspects of Mayak worker internal dosimetry

Hyper-realisations

Using uncertainties in the dose calculations

Richard Bull

A standard calculation

- Assign default parameters to the biokinetic models.
- Run the models in forward mode to obtain a dose per unit intake
- To run in reverse mode use, for example, MLE to give the best estimate of intake, given a bioassay dataset and the set of default parameters. Multiply the MLE intake by the dose per unit intake to get best estimate of dose
- This method has been used for many years, but takes no account of uncertainties in parameter values

Hypermodels

- Take account of uncertainties in parameter values
- Assign probability distributions to each parameter
- Randomly select a set of values from each distribution
- Run the model in forward mode to produce a dose per unit intake – this is one realisation of the model
- Repeat for another random selection
- After many iterations, produce a probability distribution of dose per unit intake

Bayesian statistics

- To run a hypermodel in reverse is less straightforward.
- We can make a selection of values from the PDFs for each parameter and then fit the bioassay data to get an estimate of intake (obtained from MLE) and dose (by multiplying MLE intake by DPUI for this set of parameters)
- However, some selections of model parameters will give better fits to the data than others and we need to allow for this
- To do this calculation correctly requires the use of Bayesian statistics

Hyper-realisations

- Select a set of parameter values from the prior probability distributions of model parameters
- Use this set along with measurement data and a prior on intake for worker 1 to produce a Bayesian posterior probability distribution of dose
- Repeat this process for worker 2. Shared parameter values will remain the same as for worker 1, but unshared values will be different
- Repeat this procedure for all N workers in the cohort. This set of N posterior probability distributions of dose is a hyper-realisation

Multiple hyper-realisations

- Repeat this entire procedure for a new set of parameter values
- The shared parameter values will still be the same for each worker, but this shared value will be different from that used in the first hyper-realisation
- The procedure is repeated to produce, say, 1000 hyper-realisations
- This set is known as a multiple hyper-realisation

Welmos method

- The method described above can be implemented by the Markov Chain Monte-Carlo method
- This is very computationally intensive
- Welmos method has been devised (Puncher) to simplify the calculation
- In this method the intake distribution P(I) is weighted by P(M|L,I) to give the weighted likelihood WL.
- Here P(M|L,I) is the conditional probability to get measurements M, given intake I and a set L of model parameters

Complex intake regimes

- Welmos can be difficult to implement when the intake consists of a number of acute and chronic intake regimes
- One way of overcoming this is to construct a single intake consisting of a set of acute and chronic intakes each comprising a fixed fraction of the total intake.
- This is termed a complex intake regime (CIR).
- The total (CIR) intake is allowed to vary, but the individual acute or chronic components remain in fixed ratio to each other

Conclusion

- The output of this method is a set of 1000 hyper-realisations, where each of these is a set of probability distributions of dose
- The multiple hyper-realisation contains all of the information on parameter uncertainty
- Some simplification is needed to apply this to epidemiological studies
- See Birchall, Puncher, Vostrotin; RPD 2017 for details

Mayak Pu lung parameters

Evidence for a bound state and the slow dissolution rate

Richard Bull

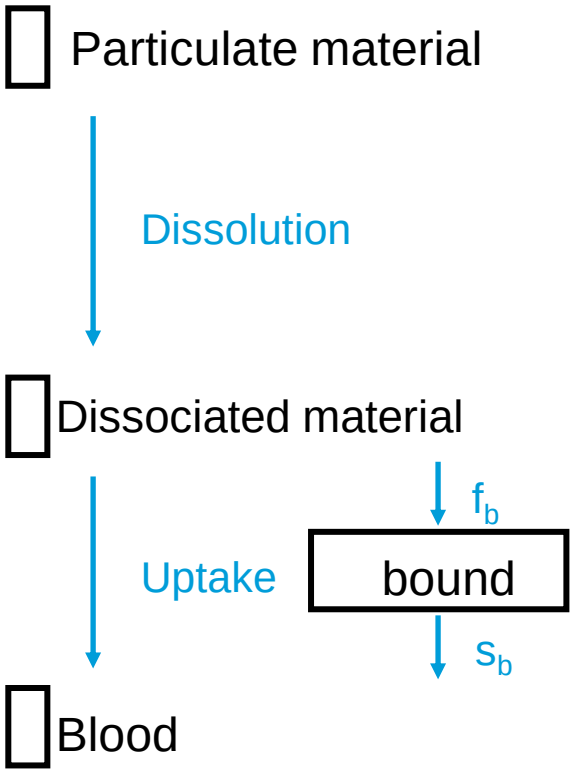
Plutonium lung parameters

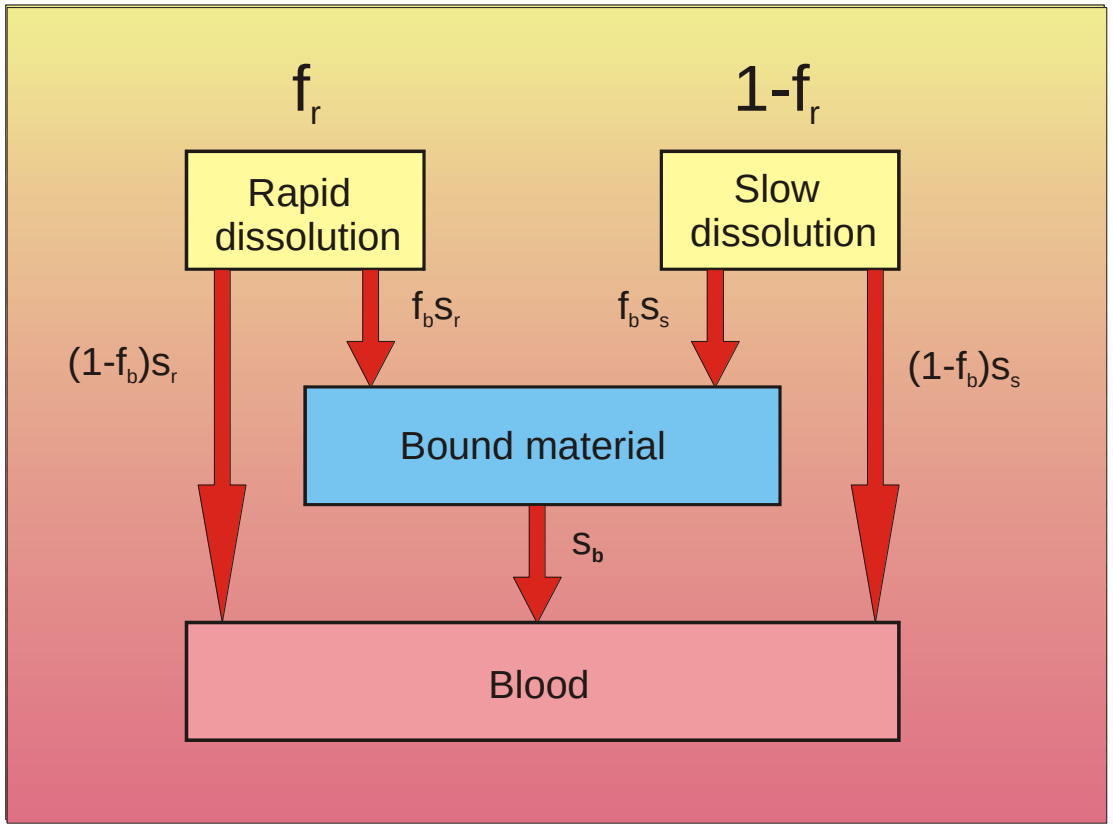
- Two features of clearance of plutonium from the lung were subject to detailed study for Mayak dosimetry
- For all regions of the lung (except ET1) a bound state is considered. A fraction f_b of initially deposited material is bound to lung tissue, from which it is cleared at rate s_b.
- A fraction $(1-f_r)$ of deposited material is cleared at a rate s_s.
- Both of these features of lung clearance can have a large influence on lung dose

3. Biokinetics

3.1 Respiratory tract model

CLEARANCE





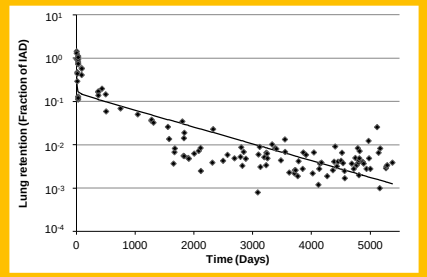
F_b & s_b indep't of compound Same for all regions of the RT

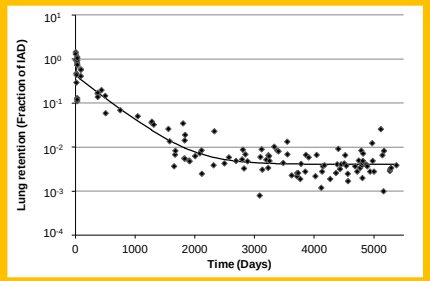
3. Biokinetics

3.1 Respiratory tract model

BOUND STATE:

1. Re-analysis of PNNL beagle dog data





0.2%

0.8%

2. Re-analysis of a USTUR case

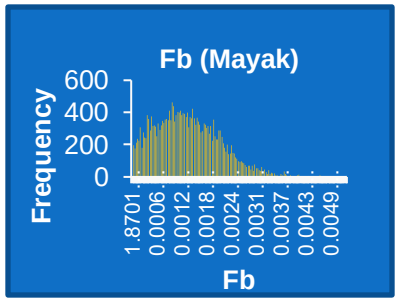
Full Bayesian analysis

0.7%

0.4%

CANNOT BE EXPLAINED WITHOUT A BOUND STATE

3. Simultaneous analysis of 20 Mayak worker autopsy cases



Bound Fraction
95% CI (0.01 to 0.3%)

$F_b \sim U(0, 0.4\%)$

Conclusions

- **Mayak study:**
- **Use a bound fraction of 0.2% for actinides**
- **Uptake rate from bound fraction 0 d^{-1}**
- **These values have also been used for actinides in the current OIR models**

Slow dissolution rate s_s for nitrates

- Important parameter for determining lung dose following inhalation
- Rather disparate values were available for Pu nitrates
- Puncher undertook a study to resolve these discrepancies

Some previous results

- Harwell volunteer study: 95% CI 19-23 x 10^{-4} d^{-1}
- A re-analysis of USTUR case 0269: Best estimate 48 x 10^{-4} d^{-1}
- BUT autopsies on 20 Mayak workers exposed to nitrate gave a CI 2.31 – 2.78 x 10^{-4} d^{-1} an order of magnitude lower!

Three hypotheses

- ***Slower dissolution rate in interstium:*** **Pu nitrate particles in alveoli walls start off with a high dissolution rate which decreases with time**

- ***An extra dissolution component:*** **Instead of just two dissolution rates, fast and slow, there is a third component with a very slow rate, labelled s_{ss}.**

- ***A mixture of compounds:*** **Instead of pure nitrate, Mayak workers were exposed to a mixture of nitrates and oxides**

Testing the hypotheses

Test vs the following datasets:

1. **Harwell volunteer data: subjected to Bayesian analysis**
2. **PNNL beagle dog data**
3. **USTUR nitrate exposure cases 0269, 0631, 0745 re-analysed.**

Conclusions

- The nitrate/oxide mixture can account for Mayak autopsy data without conflict with other studies
- Best-fit value for the oxide fraction is 0.14.
- Details of this work in RPD, v185, 201-207.
- Perhaps this topic could be revisited in the light of faecal data?

Faecal samples

Contribution to dose assessment

Richard Bull

Faecal excretion following intake

- Early faecal excretion arises from material entering the alimentary canal either via direct ingestion or the mucociliary escalator in the pulmonary system

- Plutonium in liver is sequestered in bile. In humans the bile reaches the small intestine via the gall bladder. Faecal excretion via this route dominates at later times after intake

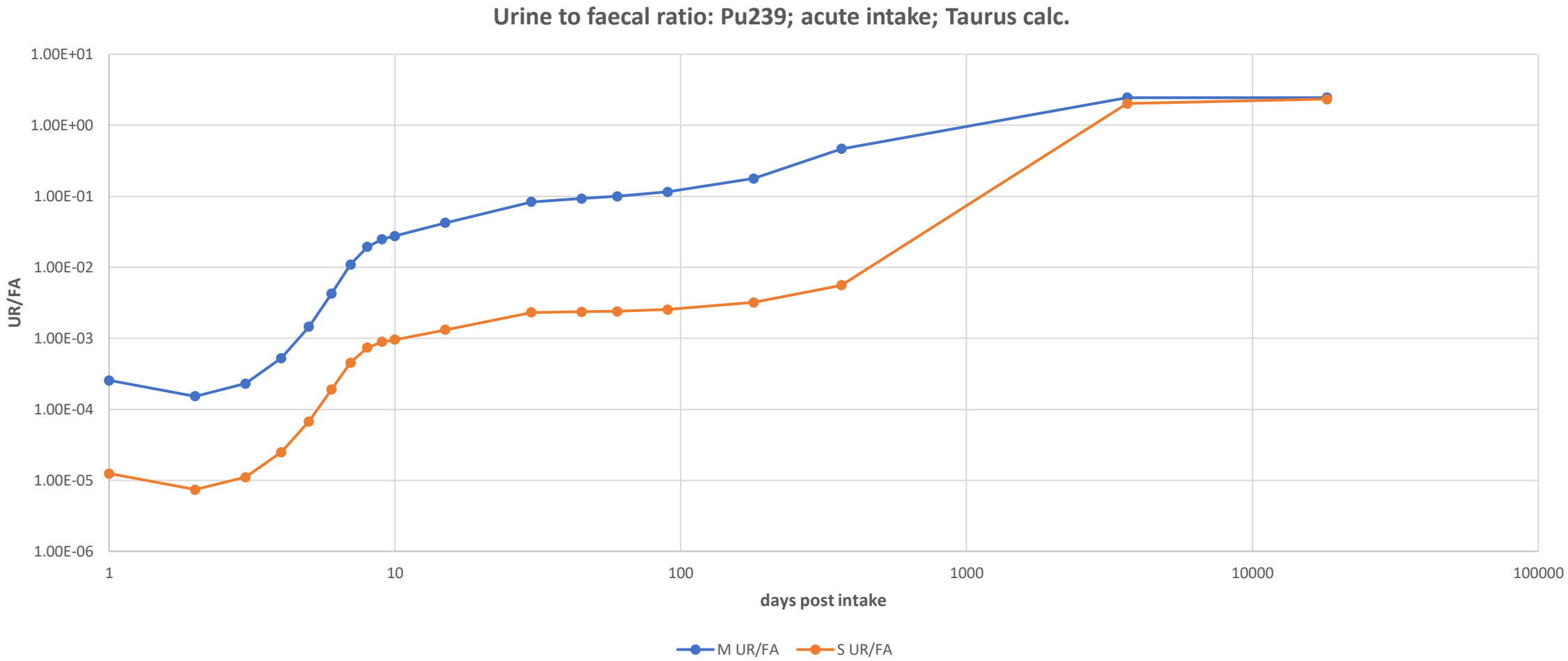
Faecal sampling at Mayak

- Faecal samples have not yet been used in Mayak worker dosimetry
- However, about 8000 faecal samples were collected from 2194 workers between 1958 and 2002.
- In most cases, urine samples were collected at the same time as faecal samples
- 58% of autopsy cases had previous faecal samples

What can be learnt from this data?

- The activity ratio of urine to faeces is very sensitive to solubility of the inhaled material
- A study of urine and faeces may help in validating assumptions about solubility in different workplaces
- The next slide illustrates this

Activity ratio UR/FA acute intake



Some early results from Mayak

- Large variation in daily faecal activities
- A selection of Mayak cases run with and without faecal data showed that inclusion of the latter usually increased the calculated dose
- Does this indicate the need for change in lung parameters?
- Or does this effect arise because the has been no correction for effect of Ca-DTPA on faecal excretion?
- Modelling using artificial datasets indicates that faecal data can be useful when there is uncertainty about lung solubility

Thanks for your attention

- **Any questions?**