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Uranium Hexafluoride Biokinetic Modeling

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Outline

- Motivation
- Case Description
- New Data
- Biokinetic Modeling
- Results
- Limitations
- Future Work

Motivation

Uranium Hexafluoride (UF_6)

- Most widely handled and transported chemical form of uranium (IAEA 1987)
- Limited number of published human data on acute exposure to UF_6
  - Howland 1949
  - Wing et al. 1966
  - Boback et al. 1966; 1975
  - Chalabreysse 1970
  - Kathren and Moore 1986
  - Fisher et al. 1991
- *New data from recent USTUR donation*

USTUR Case 1031

- Exposure: Acute Inhalation of UF_6
- Donation Type: Whole-Body
- Donation Year: 2010
- Cause of Death: Parkinson's Disease
- Age: 87 y
- Post-Intake: 65 y
- Smoking Status: Non-smoker

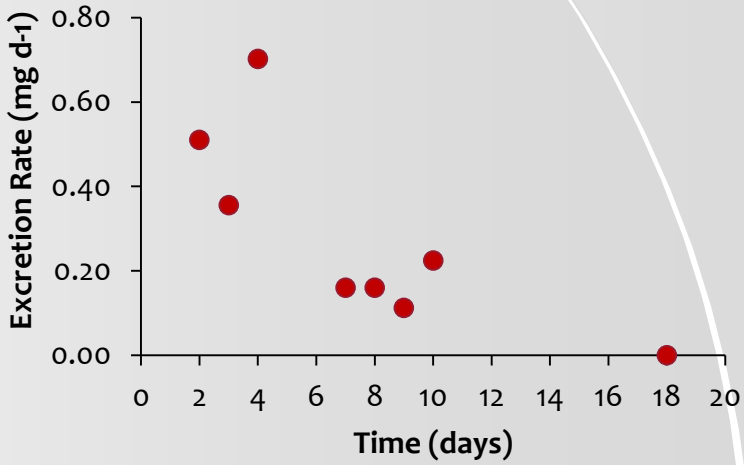
Accident

- Explosion involving UF_6
  - **0.85% ^{235}U**
- ~ 180 kg (400 lb) of UF_6 released:
  - Cloud of UF_6, UO_2F_2, HF covered area of 100-m radius
- Mean exposure time: 17 seconds

Follow-up Data

In vitro Bioassay:

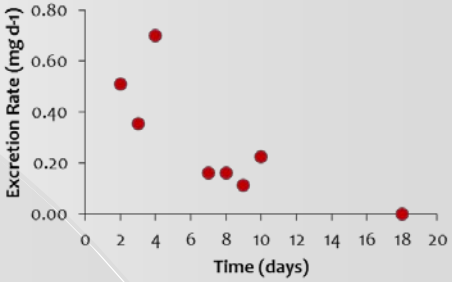
- Eight urinalyses from day 2 through day 18 post-intake
  - Excretion rate decreasing from 0.51 mg d^{-1} to 0
- Three additional urinalyses
  - 38 and 43 y post-intake
  - All results < MDA



In vivo Measurements:

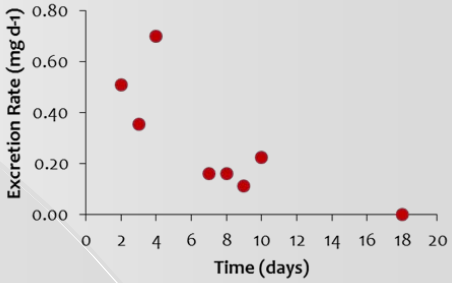
- Whole Body Count – 38 y post-intake
  - ^{235}U not detectable

Previous Evaluations (1)



- Kathren & Moore, 1986
  - Noted an unusual pattern in U urinary excretion
    - Manifested as slowed clearance
    - Believed to be a result of pulmonary edema due to HF
  - ICRP Publication 10 Model used to analyze urine data
  - Estimated Intake: 40-50 mg U
  - Natural U assumed: 0.005% ^{234}U; 0.72% ^{235}U; 99.275% ^{238}U
  - Committed Equivalent Dose to bone surfaces: 2 mSv

Previous Evaluations (2)



- Bailey & Davis, *Royal Society Report*, 2002
  - ICRP 66 HRTM and ICRP 69 U systemic model used
  - Fitting urine data with IMBA internal dosimetry software
  - Tested different scenarios including multiple intakes
    - Intakes on day 0, 4, 7, and 10
  - Estimated Intake: 50-70 mg U
  - Predicted maximum kidney concentration:
    - 1 μg U per g of kidney on day 3 post-intake

USTUR Evaluation

- Updating intake and dose estimates
  - Prompted by new data from autopsy tissue analysis

Autopsy Tissue Sample Analysis

- Analysis Method: *ICP-MS*
- Total of 33 tissue samples including:
  - *Respiratory Tract*:
    - Larynx, Trachea, Right Lung, LN_{TH}
  - *Other Soft Tissues*:
    - Liver, Kidney, Urinary Bladder, Brain, Heart, Spleen, Stomach, Esophagus, Tongue, Testes, Thyroid, Prostate, Pancreas, Axillary LN
  - *Bones*:
    - Skull, Vertebrae, Rib, Clavicle, Femur, Patella

Tissue Analysis Results

Tissue	Sample Weight, g	$^{235}U/^{238}U$	Concentration, $\mu g\ kg^{-1}$
Larynx	30.8	0.00741 ± 0.00003	8.730 ± 0.025
Trachea	14.5	0.00742 ± 0.00007	5.910 ± 0.020
Right Lung	372.0	0.00854 ± 0.00004	0.580 ± 0.001
Thoracic LN (4 samples)	11.7	0.00859 ± 0.00006†	44.82 ± 0.090‡
Liver	966.6	0.00761 ± 0.0002	0.505 ± 0.003
Right Kidney	138.2	0.00735 ± 0.0002	23.56 ± 0.090
Brain	558.1	0.00793 ± 0.0001	0.289 ± 0.001
Bones (8 samples)	502.4	0.00753 ± 0.0001†	8.336 ± 0.009‡

† Average; ‡ Weighted Average

Observations

- $^{235}U/^{238}U$ ratio in deep lungs and LN_{TH}: ~0.00856
  - Not consistent with NU: 0.00725
  - Consistent with LEU: 0.00861
- Retention of accidentally inhaled material in lungs
  - Not consistent with ICRP default Type F
- LN_{TH} to Lung Concentration Ratio: ≥ 20
  - Fraction of Insoluble material ??

Uranium Content in Critical Organs

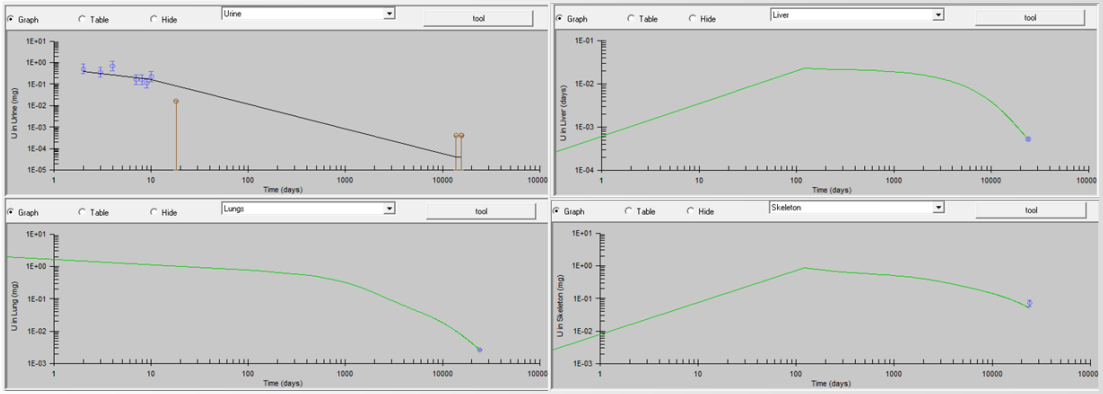
Calculated based on total tissue weights

- *Lungs incl. LN_{TH}:* 2.815 ± 0.004 µg
- *Liver:* 0.685 ± 0.004 µg
- *Skeleton:* 75.79 ± 0.08 µg
- *Kidneys:* 6.48 ± 0.03 µg
- *Whole Body:* 105.80 ± 0.10 µg

Uranium Content in Critical Organs

Used with urine data in biokinetic modeling

- *Lungs incl. LN_{TH}:* 2.815 ± 0.004 µg
- *Liver:* 0.685 ± 0.004 µg
- *Skeleton:* 75.79 ± 0.08 µg

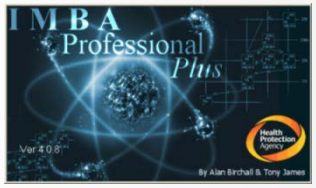


Biokinetic Modeling: Assumptions

- ❑ "Realistic" Intake Scenario
  - ➢ Occupational: UF_6 Accident
    - Acute Inhalation
    - Mixture of Type F, M, S
  - ➢ Environmental: U in diet & air
    - Chronic Ingestion
    - Chronic Inhalation: Type S

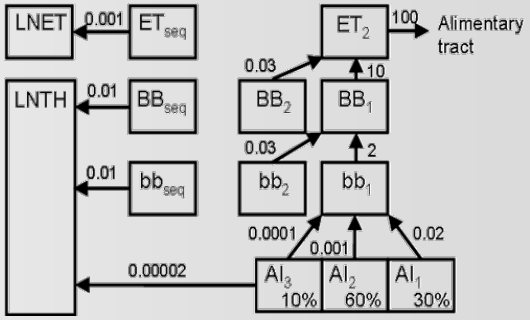
Biokinetic Modeling: Methods

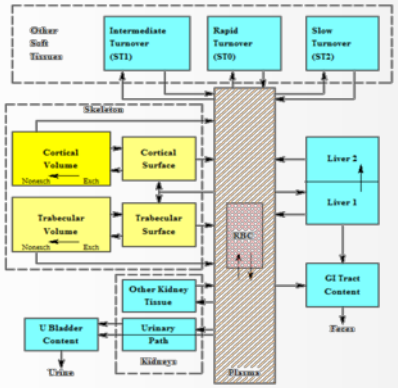
- Internal Dosimetry Software:



  - IMBA Professional Plus (IPP)

- Biokinetic Models:
  - ICRP 66 HRTM





  - ICRP 69 U Systemic Model

Evaluation Results

Acute Intake: Inhalation

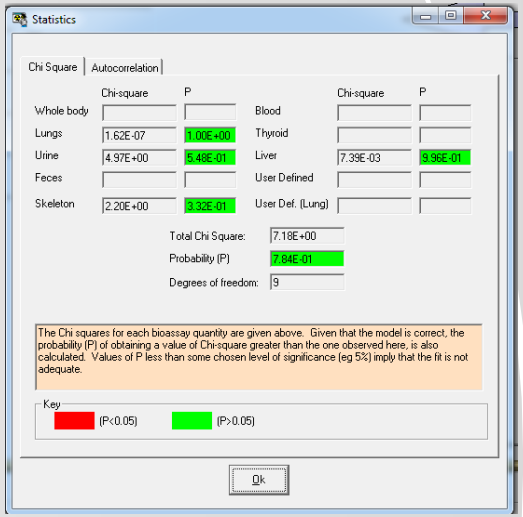
- Type F: 69.4 mg
- Type M: 0
- Type S: 10.5 mg

Chronic Intake

- Ingestion: 1.54 μg d^{-1}
  - ✓ US ref = 1.75 μg d^{-1} (*Wrenn 1985*)
- Inhalation: 2.8 ng d^{-1}
  - ✓ US ref = 1.5 ng d^{-1} (*Fisenne 1987*)

- Goodness-of-Fit Statistic:
  - χ^2/NDF = 0.8; P-value = 0.78
  - Autocorrelation P-value = 0.40

Plausible Fit !



Conclusions

- Accidental Inhalation of Uranium Hexafluoride
  - *Estimated Intake:* ~ 80 mg U
  - *Material:* 87% Type F; 13% Type S
  - *Compounds:* UF_6, UO_2F_2 *and U oxides ?*
  - *Composition:* *0.0068% ^{234}U; 0.845% ^{235}U; 99.148% ^{238}U*
  - *Committed Effective Dose:* 3 mSv ← *60% by lungs*
  - *Committed Equiv. Dose to Bone Surface:* 23 mSv
    - vs. 2 mSv (Kathren and Moore 1986)

Limitations

- Kidney not used in calculations as a bioassay quantity
- Standard biokinetic model underestimates uranium retention in kidney by two orders of magnitude
- Significant modification of transfer rates between plasma and kidney compartments is necessary

Podium Presentation

- 11th International Conference on the Health Effects of Incorporated Radionuclides
  - October 13-17, 2013; Berkeley, CA

Future Work

- Re-analyze the data using upcoming revision of ICRP Human Respiratory Tract Model
- Apply Bayesian analysis methods:
  - Define suitable priors for model parameters, as well as environmental intake rates
  - Use Monte Carlo simulation (WeLMoS, MCMC) to:
    - derive best estimates of intake and tissue doses given the measurement data
    - calculate uncertainties in model parameters as expressed by the posterior probability distributions


Thank you for your attention
Questions?