



WASHINGTON STATE
UNIVERSITY

BERYLLIUM IN TISSUES OF FORMER NUCLEAR WORKERS

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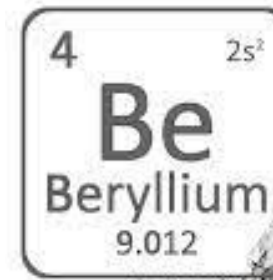
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Beryllium Facts

- Steel-grey alkaline-earth metal
 - ✓ stronger than steel and lighter than aluminum
 - ✓ high conductivity, melting point, and corrosion resistance
- Widely used in nuclear power industry and weapons production
 - ✓ as neutron reflector and neutron moderator
 - ✓ in plasma-facing components of fusion reactors
- Classified as a human carcinogen
- Prolonged inhalation can result in frequently fatal lung disease, berylliosis



<https://www.energylivenews.com/>



Beryllium Exposure

- Trace amounts of beryllium are present in air, water and food
- Estimated daily intake of 0.18–0.32 μg from food and drinking water^a
- Most human exposure occurs in the workplace via inhalation
- Limited published data available on beryllium in human body^{b,c,d,e}

^aFillipini *et al.* Expo Health 12: 641–655; 2020

^bForbes *et al.* J Biol Chem 209: 857–65; 1954

^cMeehan and Smythe. Environ Sci Technol 1(10): 839–844; 1967

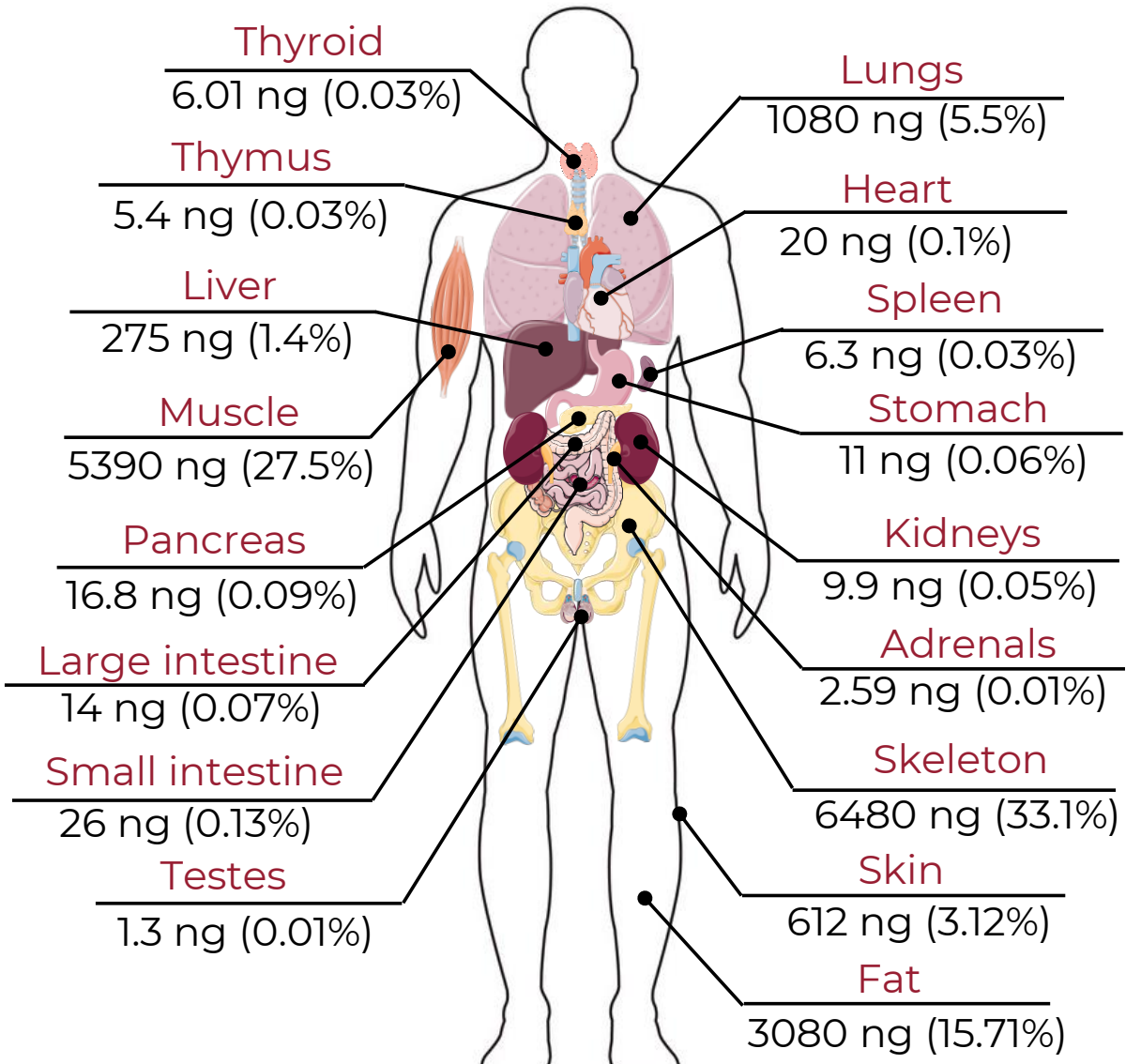
^dSchepers. Diseases Chest 42(6): 600–607; 1962

^eZhu *et al.* Health Phys 98(1): 61–73; 2010



Beryllium in Humans

- Zhu *et al.* (2010): 68 individuals
- Age: 20 – 60 y
- Body content: 19.6 μg



Paper

ELEMENT CONTENTS IN ORGANS AND TISSUES OF CHINESE ADULT MEN

Hongda Zhu,^a Neifen Wang,^b Yongbao Zhang,^c Quan Wu,^a Rusong Chen,^d Junquan Gao,^e Ping Chang,^f Qingfen Liu,^g Tijiang Fan,^h Juan Li,ⁱ Jixian Wang,^g and Jingyu Wang^g

Abstract—This study was undertaken to provide reference values for relevant parameters of Chinese Reference Man. Eighteen kinds of major organ or tissue samples, including muscle, rib, liver, and so on, were obtained from autopsies of 68 healthy adult men living in four areas of China with different dietary patterns (Hebei, Shanxi, Sichuan, Jiangxi or Jiangsu provinces, including Shanghai City) who had just encountered sudden deaths. At the same time, whole blood samples were collected from 10 volunteers living in each of these areas. The concentrations of 60 elements in these samples were detected by using inductively coupled plasma mass spectrometry (ICP-MS), inductively coupled plasma-atomic emission spectrometry (ICP-AES), neutron activation analysis (NAA), fluorimetry (FL), graphite furnace atomic absorption spectrometry (GF-AAS) techniques and necessary quality control (QC) measures. Based on obtained concentrations and reference values of these organ or tissue weights for Chinese Reference Man, the elemental burdens in these organs or tissues were estimated. As a summary report of a series of research studies for Chinese Reference Man, which included three steps (from 1996 to 2006), the concentrations of 60 elements in 18 main organs or tissues were determined and their elemental burdens in the organs or tissues and whole body were estimated. Furthermore, the organ or tissue distributions of some important elements for radiation protection were discussed. These results may provide more reliable and better representative bases than before for establishing related reference values of Chinese Reference Man and revising current reference values of International Commission on Radiological Protection (ICRP) Reference Man. These basic data will also be very valuable for many other applications in radiation protection and other scientific fields.

Health Phys. 98(1):61–73; 2010

Key words: dose, internal; radiation, background; biology; Reference Man

INTRODUCTION

CURRENT PARAMETERS of International Commission on Radiological Protection (ICRP) Reference Man 1975 and were primarily based on analytical samples from 150 Caucasian adult corp Europe and North America who had encountered death from accidents. The cadavers were from University of Tennessee and Oak Ridge National Laboratory around the year 1970 (ICRP 1975). At that time, it was difficult to provide quantitative data on so many elements. Since then there have been great changes in environment, dietary habits for human beings and developments for trace-element analysis technology, especially for nuclear analysis techniques and (QC) measures, making it possible to accurately measure ultra-trace elements than before. ICRP established a working group to work on revision of the parameters in 1984. G.V. Iyengar, who had been a member of the working group, based on collected data during this work, discussed how the technique had influenced the parameters of many elements in Reference Man and brought up his new concept (Iyengar 1998). Due to lack of the data population, from 1989 to 1998 the International Energy Agency (IAEA) organized the Coordinated Research Project (CRP) on "The Edition of Physiological and Metabolic Parameters of A Man," especially focusing on the seven elements in the field of radiation protection.

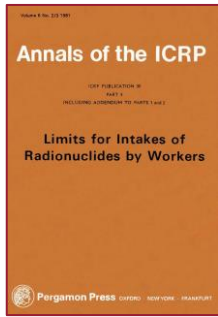
Since accomplishing the project for Reference Man, we have finished three successive projects for Chinese Reference Man from 1996 to 2006 to widen and deepen the IAEA research in a summary report of the series research content in main organs or tissues and whole body of Chinese adult men.

ANNALS OF THE ICRP PUBLICATION 151 Occupational Intakes of Radionuclides: Part 5

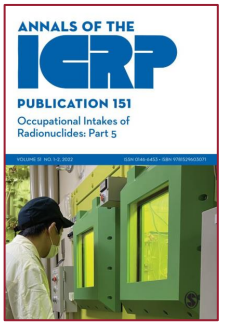
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DOI: 10.1097/HP.0b013e3181ba921





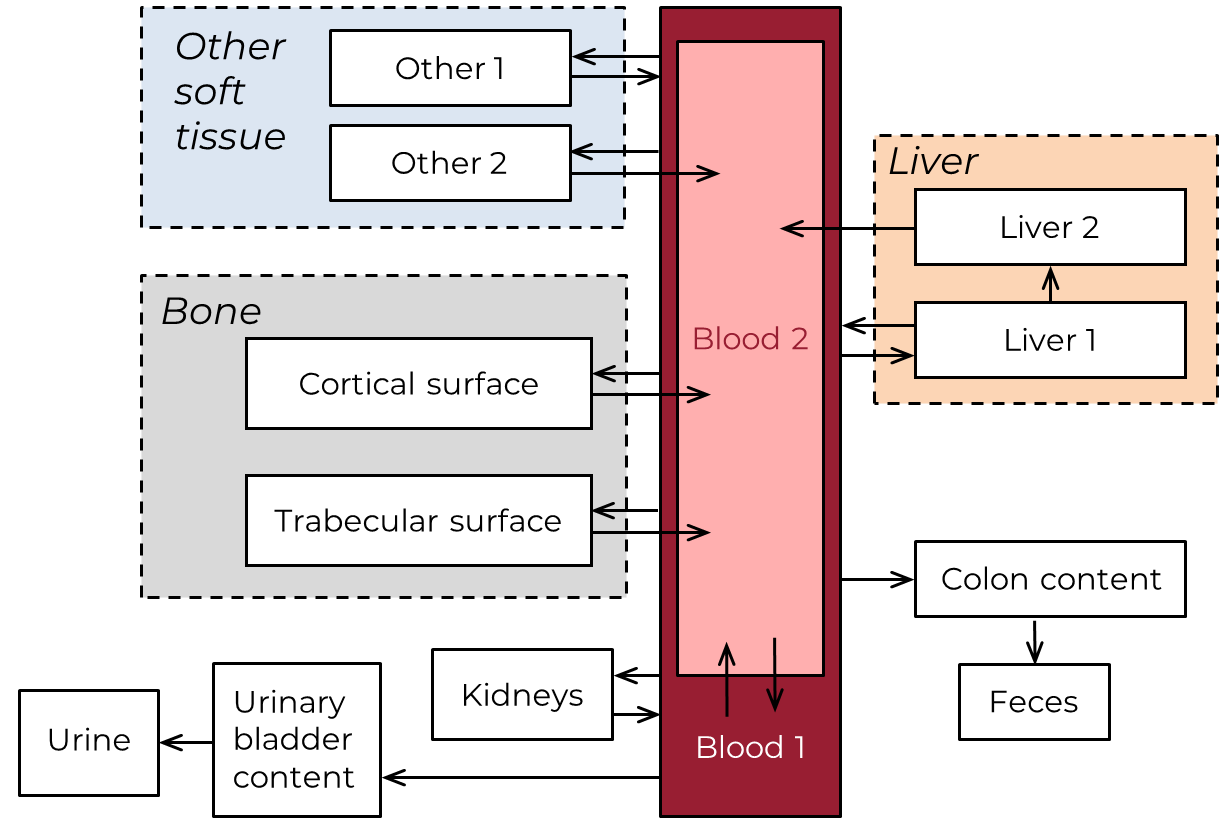
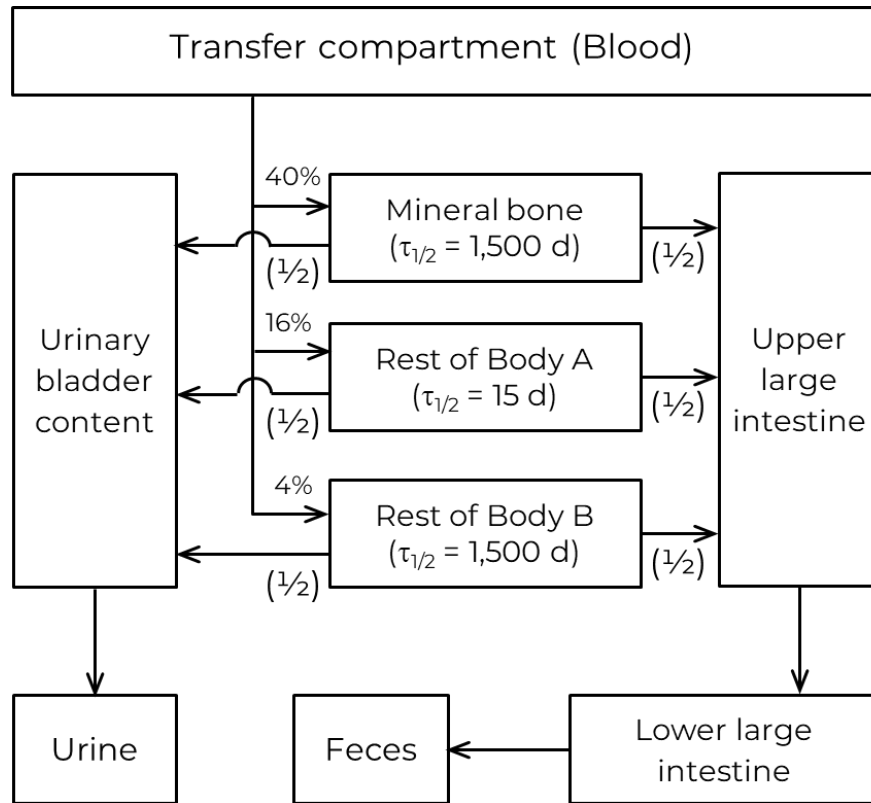
Beryllium Biokinetics



ICRP Publication 30, 1981

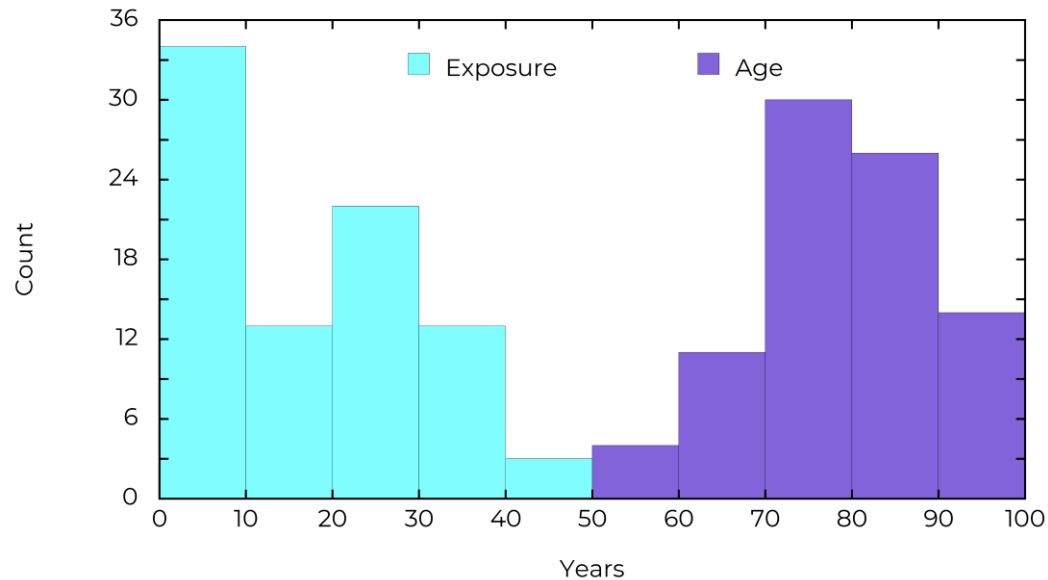


ICRP Publication 151, 2022



Beryllium at USTUR

- Self-reported exposure to beryllium: 106
- Exposure duration reported: 85
- Primary exposure: Pu (78), Am(1), U (6)
- Autopsy: 16 whole-body, 69 partial-body
- Age: 79 ± 10 y (50 – 99 y)



USTUR x Chemical Exposure x

Chemical Exposure

		From	To
Beryllium	<input type="checkbox"/> Y	1/1/1951	12/31/1955
Chlorinate Solvents	<input type="checkbox"/> Y		
Other Toxic chemicals	<input type="checkbox"/> N		
Asbestos	<input type="checkbox"/> N		
Benzene, Toluene	<input type="checkbox"/> Y	1/1/1968	12/31/1975

Self-reported work with, work around, or exposure to chemicals taken from USTUR questionnaires. A questionnaire was completed at intake and in 5-y intervals after intake.



Beryllium Tissue Analysis

- In-house tissue sample digestion
- No in-house measurement capabilities: non-radioactive element
- ^9Be measured using ICP-MS
- 'Full' analysis: USTUR Case 0706 (105 samples)
- Survey analysis: 13 USTUR cases (57 samples)
- Brain analysis: Radium Dial Painter (5 samples)



Anal Bioanal Chem (2012) 403:409–418
DOI 10.1007/s00216-012-5837-6

ORIGINAL PAPER

Detection of beryllium in digested autopsy tissues by inductively coupled plasma mass spectrometry using a high matrix interface configuration

Dominic Larivière · Mélodie Tremblay · Myriam Durand-Jézéquel · Sergei Tolmachev

JAAS

PAPER

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Cite this: *J. Anal. At. Spectrom.*, 2022, 37, 1369

Quadrupole and multi-collector ICP-MS analysis of ^{226}Ra in brain from a radium dial painter

D. L. Arbova,^a S. Y. Tolmachev^{id}^b and J. D. Brockman^{id}^{*ac}



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Survey Analysis Results

Case	Exposure (y)	⁹ Be Concentration (μg kg ⁻¹)						
		Respiratory system		Systemic soft tissues		Bones		
		Lung	LNTH	Liver	Kidney	Vert body	Rib	Femur MS
0262	8	0.210±0.006	6.18±0.07					0.015±0.003
0343	14	0.395±0.009	10.18±0.11	0.049±0.001	0.494±0.025	<DL	<DL	
0407	8	<DL	14.99±0.74	0.461±0.009	0.536±0.021	<DL	<DL	
0425	24		8.17±0.08		<DL	<DL	<DL	0.101±0.005
0720	23	0.104±0.002	83.2±0.8					0.094±0.004
0744	3	0.025±0.001	255±3					0.10±0.02
0806	15	1.16±0.41	<DL	<DL	1.49±0.52	21.3±7.3	5.1±1.5	
0817	38	0.082±0.005						0.159±0.007
0834	26	<DL	<DL	3.45±0.72	0.548±0.095	10.9±3.0	<DL	
0846	20		334±74	19.6±4.1		33448±347 [†]	68.1±12.3	
0990	20	8.67±1.08	148±44	812±15	2.99±0.53	15.9±1.0	6.39±1.19	
1002	27							0.033±0.004
GM (GSD)	16 (2)	0.29 (6.9)	41.6 (5.2)	4.16 (40.5)	0.92 (2.2)	15.4 (1.4)	13.0 (4.2)	0.065 (2.4)



Beryllium Distribution in Brain

- ^9Be content in brain: $0.27 \pm 0.01 \mu\text{g}$

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PAPER

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Quadrupole and multi-collector ICP-MS analysis of ^{226}Ra in brain from a radium dial painter

D. L. Arbova,^a S. Y. Tolmachev^b and J. D. Brockman^{a,*}

Two ICP-MS methods were developed to measure the radiotoxic isotope ^{226}Ra in brain from a radium dial painter worker. The first method was a direct analysis of acid digested quadrupole ICP-MS. The instrumental LOD of ^{226}Ra was 0.1 ng kg^{-1} . Polyatomic interferences were investigated and Fb was identified from a polyatomic interference in an in-house prepared from bovine brain, with a 226/208 formation ratio of 4×10^{-6} . The quadrupole method was also used to measure levels of beryllium, strontium, and uranium. A second method was developed that included cation-exchange chromatography to separate ^{226}Ra followed by a sector field MC-ICP-MS. The instrumental LOD for the cation exchange method was 0.5 pg kg^{-1} (0.9 mBq kg^{-1}). The measured concentrations of ^{226}Ra in brain regions ranged from $0.09\text{--}0.72 \text{ ng kg}^{-1}$ ($3.3\text{--}27 \text{ Bq kg}^{-1}$) and radium was non-uniformly distributed in the brain.

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Introduction

Radium is a radioactive alkaline earth metal produced through the natural radioactive decay chains. Among the radium isotopes, ^{226}Ra has the longest half-life of 1600 ± 7 years.¹ The ^{226}Ra decay chain produces 4 alpha particles and 4 beta particles before terminating at ^{206}Pb . Internal exposure to ^{226}Ra and its progeny are a human health concern due to effects of high linear energy transfer (LET) ionizing radiation.² Human exposure to radium occurs through consumption of food and water. The concentration of ^{226}Ra in natural waters ranges from $0.14\text{--}0.55 \text{ pg L}^{-1}$ ($0.5\text{--}20 \text{ mBq L}^{-1}$).³ Combustion of coal releases ^{226}Ra with concentrations in fly ash ranging from $1.21\text{--}63.6 \text{ ng kg}^{-1}$ ($44.3\text{--}2400 \text{ Bq kg}^{-1}$).⁴ Plants uptake ^{226}Ra through root and foliar processes.⁵ Animals are exposed through ingestion of food and water.⁶

The health effects of ^{226}Ra exposure have been studied using data from the United States Radium Dial Workers cohort.⁷ The watch dial painters, who were predominantly women, applied a luminescent mixture of $^{226}\text{RaSO}_4$ and ZnS onto watch dials and other instruments. Prior to 1926, it was common practice for the dial painters to "tip" or "point" the paintbrush using their lips leading to ingestion of radium.⁸ The ingested ^{226}Ra primarily accumulated in bone and the watch dial painters had an increased risk of developing osteomyelitis, osteosarcoma, and head carcinomas of the mastoid and paranasal sinuses.⁹ Watch dial painter's studies were used in the development of a radium biokinetic model published by the International Commission on Radiological Protection (ICRP).¹⁰

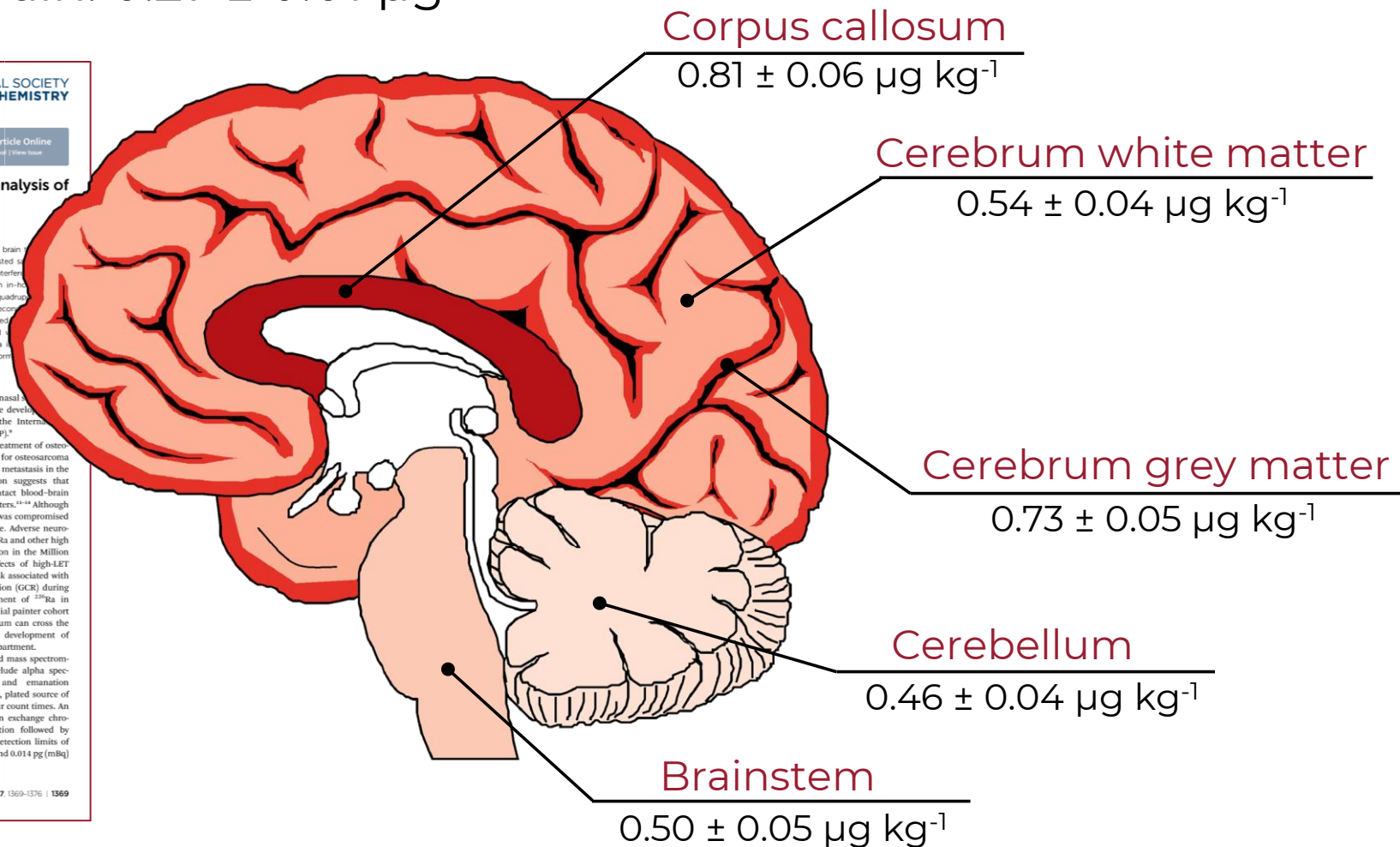
$^{223}\text{RaCl}_2$ is currently being used for the treatment of osteosarcoma. In one case study, a patient treated for osteosarcoma with $^{223}\text{RaCl}_2$ was observed to have shrunken metastasis in the cerebellum brain region.¹¹ This observation suggests that radium could be transported across the intact blood-brain barrier (BBB), potentially by calcium transporters.^{12–14} Although in this case it is unclear if the BBB integrity was compromised by cerebellar metastases or radiation damage. Adverse neurological effects associated with exposure to ^{226}Ra and other high LET emitters are currently under investigation in the Million Person Study (MPS).¹⁵ The neurological effects of high-LET radiation is also of interest for estimating risk associated with exposure to high-LET galactic cosmic radiation (GCR) during manned space flights.^{16,17} Direct measurement of ^{226}Ra in neurological tissue samples from the watch dial painter cohort would provide additional evidence that radium can cross the blood-brain barrier and provide data for development of a radium biokinetic model with a brain compartment.

^{226}Ra can be measured by radiometric and mass spectrometry methods.¹⁸ Radiometric techniques include alpha spectroscopy, liquid scintillation counting, and emanation counting. Alpha spectroscopy requires a thin, plated source of ^{226}Ra to minimize self-absorption and 48 hour count times. An alpha spectroscopy method that used cation exchange chromatography with selective complex formation followed by electrodeposition reported detection ^{226}Ra detection limits of 0.014 pg L^{-1} (0.5 mBq L^{-1}) in urine samples and 0.014 pg (mBq)

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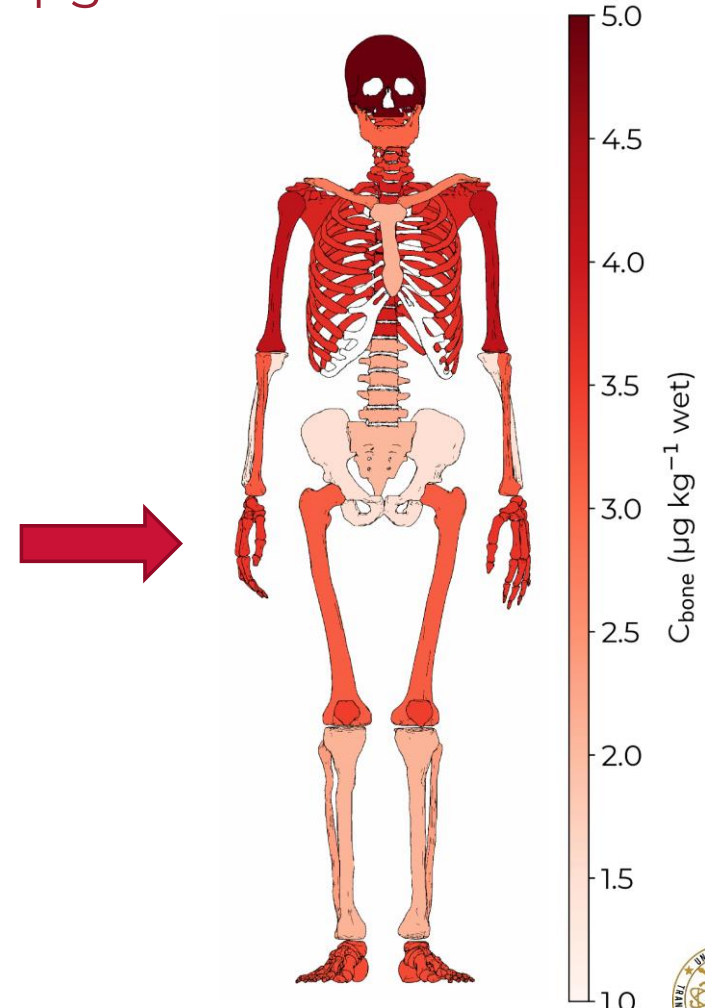
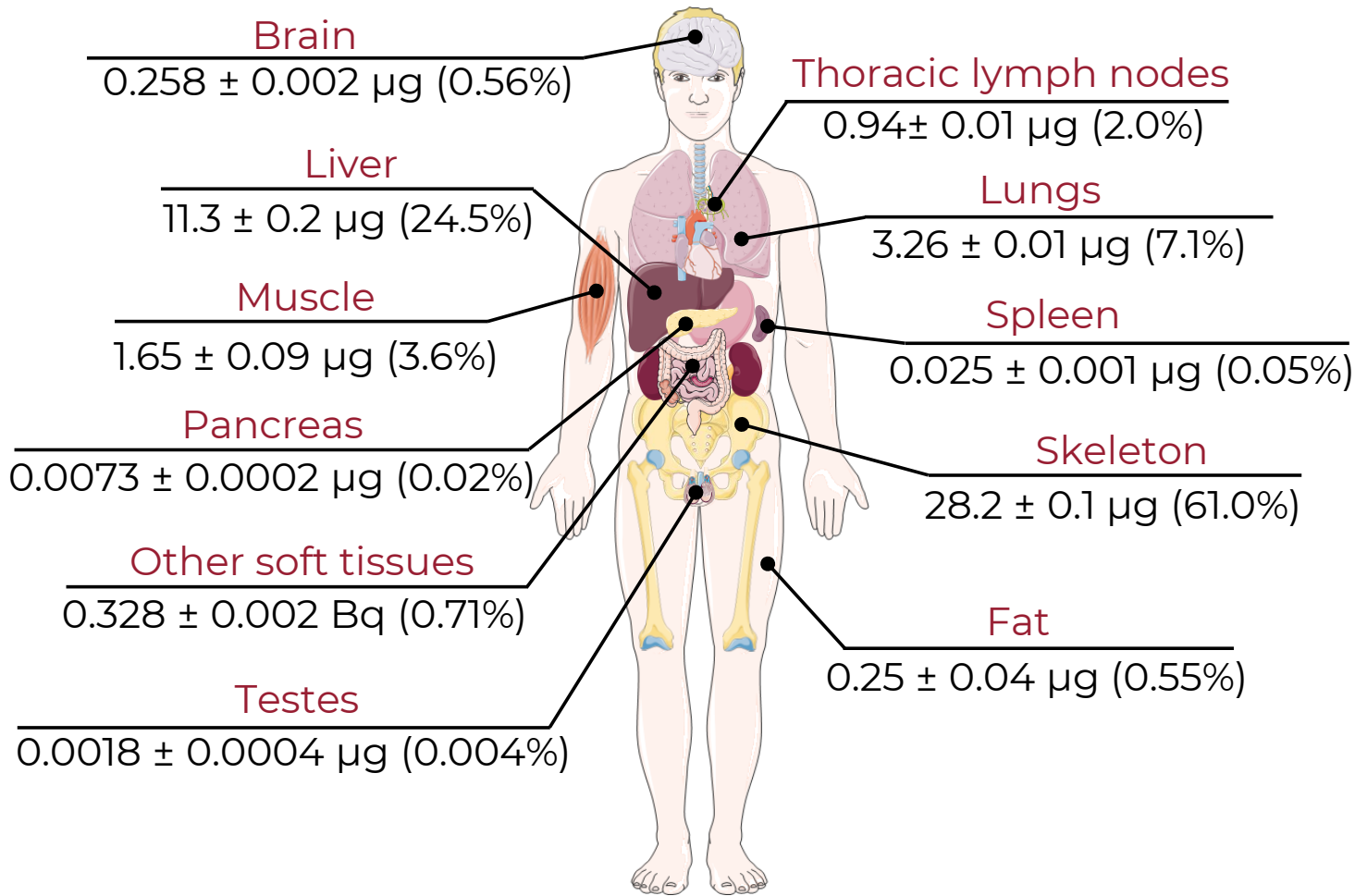
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Beryllium in USTUR Case 0706

- Self-reported exposure duration: 6 y
- Estimated total ⁹Be content in whole body: $46.3 \pm 0.2 \mu\text{g}$



Modeling USTUR Case 0706 Data

- Software: IMBA Professional Plus – USTUR research version
- Models: ICRP 130 HRTM, ICRP 151 Be systemic model
- Bioassay: Post-mortem contents in lungs, liver, and skeleton
- Intake scenario: Chronic inhalation
- Material type: 99.6% M and 0.4% S
- Estimated intake rate: $73.4 \mu\text{g d}^{-1}$

The screenshot displays the IMBA Professional Plus (USTUR) software interface. The main window shows the 'Intake Scenario' section with 'Chronic' selected and 'Inhalation' as the route. The 'Bioassay Calculations' window is open, showing 'Bioassay to Intake' and 'Intake to Bioassay' options. The 'Bioassay Calculations' window includes a table for 'Bioassay to Intake' and 'Intake to Bioassay' with columns for 'Ch' (Chromium), 'P' (Probability), and 'Degrees of freedom'. The 'Bioassay Calculations' window also includes a 'Statistics' dialog box with a table for 'Chromium' and 'Probability'.

Ch	P	Degrees of freedom
Whole body	0.0000	1
Lungs	0.0000	1
Liver	0.0000	1
Skeleton	0.0000	1

The 'Bioassay Calculations' window also includes a 'Statistics' dialog box with a table for 'Chromium' and 'Probability'.

Chromium	Probability
Whole body	0.0000
Lungs	0.0000
Liver	0.0000
Skeleton	0.0000

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Chromium	Probability
Whole body	0.0000
Lungs	0.0000
Liver	0.0000
Skeleton	0.0000

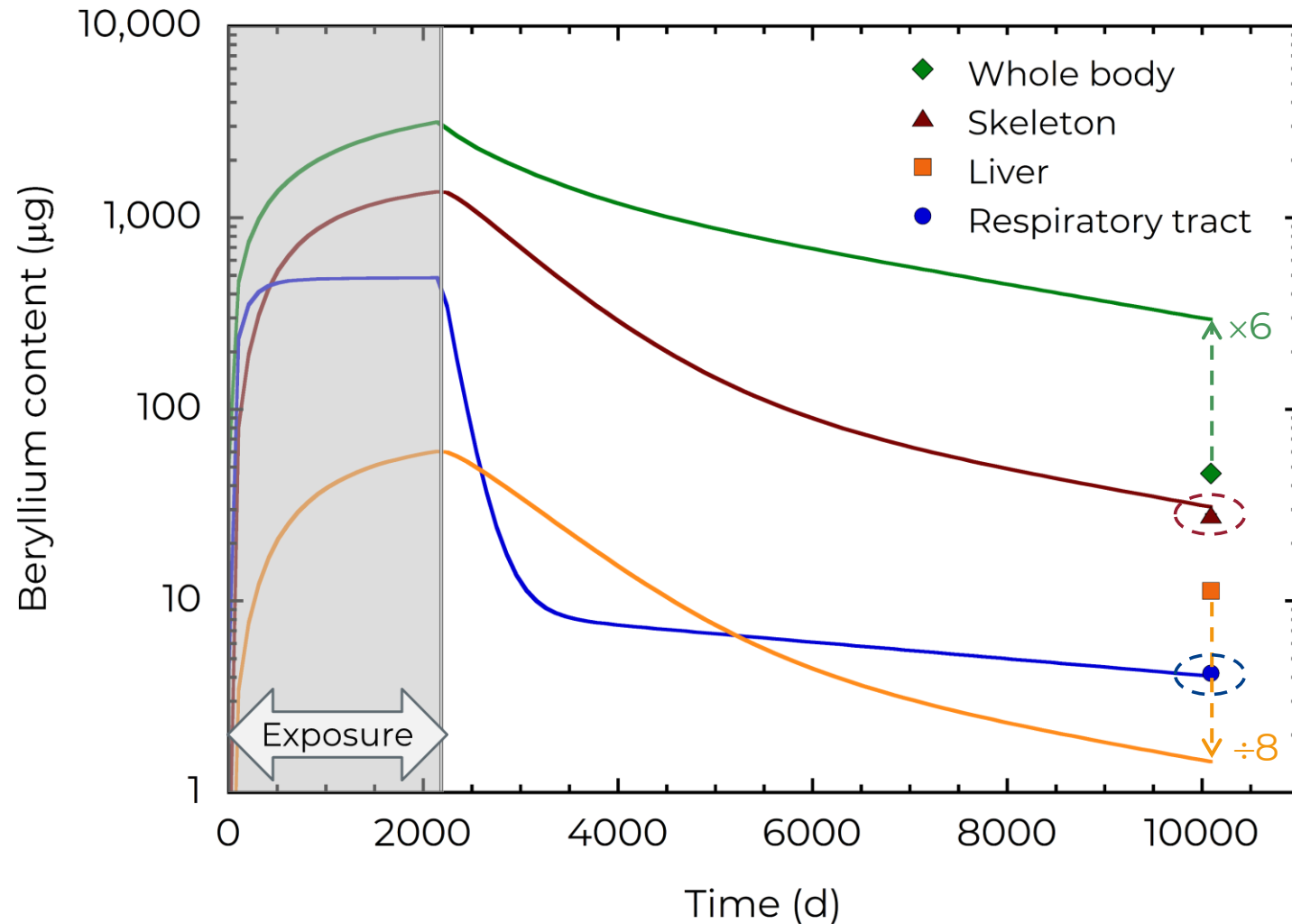
The 'Bioassay Calculations' window also includes a 'Statistics' dialog box with a table for 'Chromium' and 'Probability'.

Chromium	Probability
Whole body	0.0000
Lungs	0.0000
Liver	0.0000
Skeleton	0.0000



Tissue Retention: Model vs Measurement

ICRP 130 human respiratory tract and ICRP 151 systemic models:



- predict reasonably well respiratory tract and skeleton
- underestimate liver
- overestimate whole body

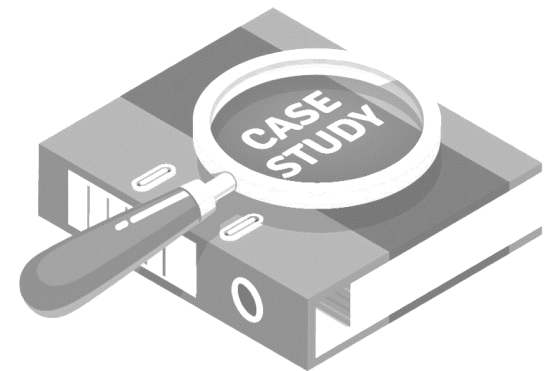


Summary

- Beryllium concentrations measured in tissues from former nuclear workers with self-reported occupational exposure
- First time, distribution and retention of beryllium was studied in whole body of exposed individual:

skeleton (61.0%) > liver (24.5%) > respiratory tract (9.1%) > other tissues (5.4%)

- ICRP 151 beryllium systemic model underestimates liver content and overestimates whole-body content
- Survey analysis indicated four potential cases for further study



QUESTIONS?



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