Aus dem Institut für Strahlenschutz

Helmholtz Zentrum München

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Estimating the absorption of ingested soil-derived uranium and the resulting internal dose to humans: Development and application of a new method

Dissertation

zum Erwerb des Doktorgrades der Naturwissenschaften

an der Medizinische Fakultät

der Ludwig-Maximilians-Universität zu München

vorgelegt von

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München

2020

Mit Genehmigung der Medizinischen Fakultät

der Universität München

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Tag der mündlichen Prüfung: 22.04.2021

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1 Contents

2 Abbreviations

$C_{soil,I}$	Average concentration of a radionuclide *i* in the ingested soil
CT	Computed tomography
DC_i	Effective dose coefficient of an ingestion radionuclide i
DF	Bioaccessibility; the fraction of uranium, which is soluble in the alimentary tract and therefore potentially available for absorption
E	Committed effective dose
ED	Duration of the exposure period
f_A; f_1	Bioavailability; the fraction of ingested uranium which is absorbed from the alimentary tract into the circulatory system; data on bioavailability taken from the literature are denoted as f_1, bioavailability data received by this thesis are denoted as f_A
f_A^{sol}	Expression of the relation between bioaccessibility and bioavailability of soil-derived uranium
GM	Geometric mean
GUM	Guide to the Expression of Uncertainty in Measurement
$H_{T,female}$; $H_{T,male}$	Committed equivalent dose of an organ or tissue of the reference female or male
ICP-MS	Inductively coupled plasma mass spectrometry
ICRP	International Commission on Radiological Protection
I_{soil}	Average daily amount of the soil ingested during the exposure period
LOQ	Limit of quantification
U	Expanded uncertainty
u(y)	Standard uncertainty of a quantity y
$u_c(y)$	Combined standard uncertainties

3 Abstract

The main objective of this thesis was the development of a method to estimate the bioavailability of ingested soil-derived uranium and the resulting internal dose to humans.

The ingestion of small amounts of soil by humans occurs involuntarily and deliberately. For the involuntary ingestion of soil, for example via food, the amount of soil ingestion differs between 10 mg/day and 100 mg/day for adults and children, respectively. For the deliberate ingestion of soil, e.g. healing soil, amounts of up to 40 g/day over several weeks are reported. Uranium is ubiquitous in soil, and involuntary or deliberate soil ingestion is therefore accompanied by the ingestion of uranium. This leads to an increase of the internal dose due to the ionizing radiation from the radioactive decay of ingested uranium and its progeny.

To estimate the internal dose after ingestion of soil-derived uranium, its bioavailability must be known. However, when work on this PhD started, no method was available to reliably determine the bioavailability of uranium for such a scenario. Therefore, a new method was developed. First, an already established *in vitro* solubility assay was used to determine the bioaccessibility (DF) of uranium of an edible soil low in uranium. Second, the actual bioavailability (f_A) of uranium of this soil was determined by means of a human study. In this study, ten human volunteers ingested a specific amount of this soil and the bioavailability (f_A) of uranium was estimated for all ten volunteers from their urinary excretion. By determining bioaccessibility (DF) and bioavailability (f_A), it was possible to calculate the f_A^{sol} factor, which is the ratio of f_A and DF, and which describes the transfer of soluble uranium to the circulatory system. The f_A^{sol} factor was calculated to be 0.53% (GM) ranging from 0.06% (2.5^{th} percentile) to 4.43% (97.5^{th} percentile). Knowing f_A^{sol} it is possible to obtain realistic data on the bioavailability (f_A) of uranium from virtually any soil, without the need of further human studies. Only the same *in vitro* solubility assay, which was applied in the current study, has to be performed for any soil of interest to determine its specific bioaccessibility (DF). The corresponding bioavailability (f_A) is thereafter simply calculated by adopting the f_A^{sol} factor determined earlier.

The f_A^{sol} factor obtained was compared to values from the literature and found to be in good agreement. It can therefore be assumed that the f_A^{sol} factor does not depend on the duration of exposure or the amount of ingested uranium. In other words, it can be used for acute as well as chronic ingestion scenarios with high and low amounts of soil-derived uranium. Thus, in the course of this

thesis a robust method was developed to estimate the bioavailability and the resulting internal dose for different ingestion scenarios with different amounts of soil-derived uranium.

Finally, this newly developed method was applied on highly uranium-contaminated soils, i.e., on original soils from former uranium mining sites located in Eastern Germany. The bioavailability of uranium from these soils was determined and used to calculate internal doses after an assumed realistic scenario of soil ingestion. Based on the assumed exposure scenario a committed effective dose of 0.6 µSv (GM) ranging from 0.3 µSv (2.5^{th} percentile) to 3.0 µSv (97.5^{th} percentile) was estimated for the most uranium-contaminated soil. It is concluded that this ingestion of soil-derived uranium does not imply any major health risk to humans due to the additional internal dose.

4 Zusammenfassung

Ziel dieser Dissertation war die Entwicklung einer Methode zur Abschätzung der Bioverfügbarkeit von ingestierten, uranhaltigen Erden/Böden und der damit verbundenen internen Strahlenexposition des Menschen.

Menschen nehmen bewusst und unbewusst kleine Mengen Erde auf. Unbewusst werden dabei zwischen 10 mg/Tag und 100 mg/Tag Erde durch Erwachsene bzw. Kinder aufgenommen. Auch die bewusste Ingestion von bis zu 40 g/Tag Heilerde ist dokumentiert. Da Uran in allen Erden/Bodenarten vorkommt, geht sowohl die beabsichtigte als auch die unbeabsichtigte Ingestion von Erde mit einer gewissen Ingestion von Uran einher. Im Ergebnis führt dies aufgrund des radioaktiven Zerfalls von Uran und dessen Folgeprodukten zu einer Erhöhung der internen Strahlendosis.

Um die interne Strahlendosis, die sich aus der Ingestion von uranhaltigen Erden/Böden ergibt, abschätzen zu können, muss deren Bioverfügbarkeit bekannt sein. Da es für deren Bestimmung bisher keine verlässliche Methode gab, wurde in dieser Dissertation dafür eine neue Methode entwickelt. Dabei wurde in einem ersten Schritt, mit Hilfe eines bereits etablieren *in vitro* Löslichkeitstests, die Biozugänglichkeit (DF, bioaccessibility) des Urans einer mäßig uranhaltigen Erde bestimmt. Anschließend wurde in einer Humanstudie die tatsächliche Bioverfügbarkeit (f_a, bioavailability) des Urans in dieser Erde ermittelt. Anhand dieser zwei Parameter, Biozugänglichkeit (DF) und Bioverfügbarkeit (f_a), konnte der f_A^{sol}-Faktor, welcher das Verhältnis aus f_a und DF darstellt, ermittelt werden. Dieser beträgt 0,53% (GM) und reicht von 0,06% (2,5tes Perzentil) bis 4,43% (97,5tes Perzentil). Bei Kenntnis dieses f_A^{sol}-Faktors ist es möglich, realistische Daten zur Bioverfügbarkeit von nahezu jeder Erde/Bodenart zu erhalten, ohne dafür weitere Humanstudien durchführen zu müssen. Lediglich der in dieser Studie benutzte *in vitro* Löslichkeitstest wird zur Bestimmung der Biozugänglichkeit einer beliebigen Erde herangezogen. Die dazugehörige Bioverfügbarkeit wird dann mit Hilfe des bereits bestimmten f_A^{sol}-Faktors berechnet.

Der in dieser Dissertation ermittelte f_A^{sol}-Faktor stimmt gut mit vergleichbaren Literaturdaten überein. Dies deutet darauf hin, dass der hier bestimmte f_A^{sol}-Faktor unabhängig von der Dauer der Ingestion und der Menge des aufgenommenen Urans ist. Dieser Faktor ist somit für Ingestionsszenarien mit akuter oder chronischer Ingestion von kleinen oder großen Mengen uranhaltiger Erde geeignet. Die hier entwickelte Methode liefert damit erstmals die Möglichkeit, die Bioverfügbarkeit und die damit

verbundene interne Strahlendosis für verschiedene Ingestionsszenarien mit verschiedenen Mengen uranhaltiger Erde verlässlich zu bestimmen.

Im Weiteren wurde diese Methode auf verschiedene, stark uranhaltige Bodenproben von ehemaligen Uranabbaugebieten aus Ostdeutschland angewandt. Die Bioverfügbarkeit des Urans in diesen Proben wurde bestimmt, um damit die interne Strahlendosis zu berechnen, die sich aus einem angenommen Ingestionsszenario ergeben würde. Für die am stärksten mit Uran kontaminierte Bodenprobe wurde eine interne Strahlendosis bzw. effektive Folgedosis von 0,6 µSv, mit einem Bereich von 0,3 µSv (2,5tes Perzentil) bis 3,0 µSv (97,5tes Perzentil), bestimmt. Die Ergebnisse wurden mit Literaturdaten vergleichen. Aus den Ergebnissen kann geschlussfolgert werden, dass von der zu erwartenden erhöhten internen Strahlendosis kein nennenswertes Gesundheitsrisiko ausgeht.

5 Introduction

The main objective of this thesis was to study the bioavailability of uranium from ingested soils in humans and to estimate the resulting internal dose. In the following, the basic concept of the thesis is introduced.

5.1 Soil ingestion

The ingestion of small amounts of soil by humans, either involuntarily or deliberately, occurs worldwide. For instance, soil is an important constituent of house dust (Abrahams 2002), which can be found in virtually every dwelling. The ingestion of this form of dust takes place mainly indirectly, in particular by inhalation, followed by mucociliary clearance of the lung and swallowing of the dust particles. Thus, the ingestion of very small quantities of soil cannot be avoided and is characteristic for all humans. Additional scenarios of involuntary soil ingestion by humans are via food products, which are not properly washed, and via outdoor (sports) activities. For children aged between 1 and 5 years, increased soil ingestion is reported due to increased outdoor activities (van Wijnen et al. 1990). In 2007, a meta-analysis reported for children aged below 11 years an indoor hand-to-mouth frequency of up to 28.0 contacts/hour and an outdoor hand-to-mouth frequency of up to 14.5 contacts/hour, respectively (Xue et al. 2007). Hence, hand-to-mouth activities by young children might be the main route of soil ingestion.

Geophagy, the deliberate ingestion of soil, can also be found around the world (Sing and Sing 2010). In Africa the ingestion of soil is a common practice among pregnant women (Njiru et al. 2011), but is also reported for men and children (Golden et al. 2012). In Germany geophagy is practiced to cure moderate alimentary tract related symptoms like acid reflux. For this purpose so-called healing soil or medical soil is ingested (Höllriegl et al. 2010).

For the involuntary ingestion of soil, which is the most common form of soil ingestion, the amount of ingested soil differs between 10 mg/day and 100 mg/day for adults and children, respectively. For the deliberate ingestion of soil, amounts of up to 40 g/day over several weeks are reported (Stanek III et al. 1997; Höllriegl et al. 2010; UNSCEAR 2013).

Soil ingestion can be accompanied by different health effects. Healing soil is a medical product by which acid-induced gastric disorders like pyrosis or diarrhea are treated. Beside its anti-diarrheal effects, some soils are also acting as detoxifying agents by absorbing glycoalkaloids and other toxic

compounds, and also as a possible source of nutritive minerals (Sing and Sing 2010). Negative health effects of soil ingestion might be due to the ingestion of pathogenic organisms like endogenous parasites, heavy metals and radioisotopes like uranium, which is the subject of the present study.

Uranium is ubiquitous in soil and its ingestion, whether involuntarily or deliberately, is therefore accompanied by the ingestion of uranium. Accordingly, it is also accompanied by an increase of the internal dose due to the ionizing radiation from the radioactive decay of uranium and its progeny.

5.2 Radiation exposure

Humans are exposed to artificial and natural sources of radiation. For example, in Germany the public is exposed to artificial sources of radiation resulting in an annual effective dose of about 1.9 mSv/a, and to natural sources of radiation radiation resulting in an annual effective dose of about 2.1 mSv/a, respectively. The effective dose is a dosimetric quantity by which the radiation exposure of humans is related to radiation risk. It takes into account different biological effectiveness of different radiation types and differences of the sensitivities of organs and tissues to stochastic health effects like cancer. Today, artificial sources of radiation are mainly medical diagnostic applications (1.9 mSv/a) like CT (computed tomography) scans, while the nuclear accident of Chernobyl from 1986, for example, contributes less than 0.011 mSv/a (BfS 2015). The chest CT scan of a patient typically results in a dose of about 10 mSv (Grupen 2008). Natural sources of radiation include cosmic radiation (0.3 mSv/a) and terrestrial radiation (1.8 mSv/a). Besides, numerous so-called cosmogenic radionuclides are produced by cosmic radiation. In terms of public exposure, the isotope ^{14}C is the most relevant of such radionuclides and adds about 12 µSv/a by internal exposure. Terrestrial radiation is caused by internal radiation sources and by external radiation sources like ^{40}K, ^{238}U, ^{232}Th, and its progeny, which are present in trace amounts in the human body and in soils (UNSCEAR 2008). Internal radiation exposure results mainly from inhalation and ingestion of radionuclides, which virtually cannot be avoided. The main contributor is ^{222}Rn and its progeny which contribute about 1.1 mSv/a (BfS 2015). The human body contains also an activity of about 9,000 Bq, mainly ^{40}K (4,200 Bq) and ^{14}C (3,800 Bq) (Grupen 2008). From incorporated ^{40}K the resulting annual equivalent dose is about 0.185 mSv and 0.165 mSv for children and adults, respectively. Due to the more or less uniform distribution of ^{40}K within the body, the same values are considered to be appropriate for the effective dose (UNSCEAR 2008). Ingestion of radionuclides adds about 0.3 mSv/a (BfS 2015).

The average daily intake of uranium is about 1.25 µg. This intake results from uranium in food and liquids, which was estimated for milk products (1 mBq/kg), meat products (2 mBq/kg), grain products (20 mBq/kg), leafy vegetables (20 mBq/kg), root vegetables and fruits (3 mBq/kg), fish products (30 mBq/kg), and drinking water (1 mBq/kg), respectively (UNSCEAR 2000). Accordingly, the retention of ingested ^{238}U in liver (3 mBq/kg), kidney (30 mBq/kg), bone (100 mBq/kg), muscle and other tissues (5 mBq/kg) were estimated (UNSCEAR 2000). The resulting masses of uranium in liver (0.435 µg), kidney (0.75 µg), bone (44.3 µg), muscle and other tissues (7.75 µg) were also calculated

based on anatomical data provided by ICRP (International Commission on Radiological Protection) (Li et al. 2005). Eventually, for ^{238}U the average daily intake of uranium from food and liquids results in a committed effective dose of about 0.25 µSv (UNSCEAR 2000). The committed effective dose is a dosimetric quantity by which the radiation exposure from incorporated radionuclides and its progeny is related to radiation risk. It takes into account different biological effectiveness of different radiation types and differences of the sensitivities of organs and tissues to stochastic health effects. The commitment period is taken to be 50 years for adults and 70 years for children (ICRP 2007). Note that ^{238}U accounts for 99.27% of ingested uranium in terms of percentages by mole fraction; 0.0054% and 0.72% account for ^{234}U and ^{235}U, respectively (Berglund and Wieser 2011). The committed effective dose of ^{234}U and ^{235}U is about 0.28 µSv and 0.011 µSv, respectively. Accordingly, the committed effective dose of uranium (^{234}U, ^{235}U, and ^{238}U) from intake of food and liquids accumulates to about 0.5 µSv (UNSCEAR 2000).

5.3 Uranium and toxicity

Naturally occurring uranium comprises the three radioisotopes ^{234}U, ^{235}U, and ^{238}U. All three radioisotopes are alpha-particle-emitting heavy metal with half-lives of 245,500 (^{234}U), 704,000,000 (^{235}U), and 4,468,000,000 years (^{238}U) (ICRP 2008). In nature, ^{234}U, ^{235}U, and ^{238}U occur with percentages by mole fraction of 0.0054, 0.72, and 99.27%, respectively (Berglund and Wieser 2011).

The naturally occurring radionuclides ^{238}U and ^{234}U belong to the radium series whereas ^{235}U belongs to the actinium series. The radium series starts with the primordial alpha emitter ^{238}U followed by the beta emitters ^{234}Th and ^{234}Pa with short half-lives below one month. The series is continued by the two alpha emitters ^{234}U and ^{230}Th with half-lives of at least 75,000 years. The actinium series starts with the alpha emitter ^{235}U followed by the beta emitter ^{231}Th with a half-life of 25.52 hours and is followed by the alpha emitter ^{231}Pa with a half-life of about 33,000 years. Both the radium series and the actinium series are continued by numerous alpha and beta emitters and are ending with the stable isotopes ^{206}Pb and ^{207}Pb, respectively (ICRP 2008; Krieger 2012). For dosimetric consideration of ingested ^{234}U, ^{235}U, ^{238}U, and its subsequent internally arising progeny, the respective decay chain can be truncated at ^{234}U, ^{231}Th, and ^{234}Pa, respectively (ICRP 1983). Compared to the human life span, the half-lives of the decay daughters of ^{234}U, ^{231}Th, and ^{234}Pa are extremely long and therefore do not add a noticeable amount to the calculated internal dose.

The concentration of naturally occurring uranium in soil is about 3 mg/kg but can be artificially increased (Bleise et al. 2003). Agriculture activities are the main source of uranium contamination of cultivated soils due to an increased amount of uranium in phosphate fertilizer. Thereby between 1951 and 2011 a cumulative application of 1 kg uranium per hectare on agriculture land was estimated on average for Germany (Schnug and Lottermoser 2013). In some regions, uranium contamination of soils is also a result of uranium mining. Uranium production was ceased in Germany in 1990 but

remediating of former uranium mining sites is still ongoing. However, due to natural processes like capillary rise re-contamination of already remediated areas was reported (Langella et al. 2014). Since global uranium production has still increased over the last years to 60,000 tons in 2013, further uranium contamination of soil can be expected (WNA 2014). Elevated uranium concentrations of soils can also be due to nuclear incidents like the Chernobyl accident in 1986 or the Fukushima Daiichi incident in 2011 (Shinonaga et al. 2014). The military use of depleted uranium (DU) is another source for soil contamination (Bleise et al. 2003).

Naturally occurring uranium comprises chemical and radiological toxicity. The chemical toxicity of uranium is similar to the chemical toxicity of nickel and chromium and is the primary concern regarding environmental health hazard. Chemical toxic effects of uranium generally occur at concentrations whereas radiological effects are still small, because of the low specific activity of uranium. From animal studies and human epidemiology various health effects of uranium like developmental and reproductive defects and DNA damage are known (Brugge and Buchner 2011).

Notably, only a very few publications used different isotopic compositions of uranium (depleted and enriched uranium), in order to distinguish chemical from radiological effects. Thereby, for different isotopic compositions of uranium, different patterns of brain pro-/anti-oxidant activity have been shown for rats (Lestaevel et al. 2009). The influence of the isotopic composition of uranium on its genotoxic profile has also been demonstrated (Darolles et al. 2010).

5.4 Biokinetics of uranium

The uptake, distribution, and deposition of radionuclides in tissues and organs and their excretion from these tissues, organs, and the whole body can be simulated by biokinetic models. These biokinetic models consist of several compartments which represent functional units (e.g. “soft tissue”), entire organs (e.g. “stomach”) or even certain cell types (e.g. “red bone marrow”). The transport of radionuclides between these compartments is assumed to follow first-order kinetics, is individually quantified and is referred to as transfer rate. For uranium ICRP provides a biokinetic model that has a structure which is based on the generic model structure of the alkaline earth metals (ICRP 1992, 1995a). The corresponding transfer rates are based on human data or, if human data are not available, on animal data. The human data are based on studies on several human individuals who were intravenously injected with uranium. The administered uranium mass per body mass ranged from 6.3 µg/kg to 1 mg/kg. Blood, excretion, and postmortem measurements were performed up to 566 days after the injection of uranium whereas most samples were taken within several days or weeks. Most human individuals involved in those studies were patients who suffered from various diseases or who were in terminal phases of diseases of the central nervous system. These studies are referred to as the Boston study, the Bassett study, and the Terepka study (Leggett 1994). Data on long-term distribution of uranium in the human body were received from several other postmortem measurements of uranium in tissues of occupationally and environmentally exposed human subjects.

Various aspects of the biokinetics of uranium have also been received from animal data involving baboons, dogs, rabbits, rats, and other species. Transfer rates were later estimated in the awareness of the health status of the human subjects. For animal data, preference was generally given to baboons and dogs over other animals and preference was generally given to data from relatively low uranium uptake (Leggett 1994).

The biokinetic model of uranium comprises kidney, liver, skeleton, and blood. Remaining organs and tissues are assigned to several soft tissue compartments. For the alimentary tract a separate biokinetic model is provided by ICRP (ICRP 2006). For quantification of the uptake of uranium from the alimentary tract into the blood numerous human studies mostly using drinking water with high concentrations of soluble uranium were considered. From these data an f_1 value of 0.02 is assumed for adults (ICRP 1995a). Since no sufficient experimental data are available for children of one year or older, the f_1 value for adults was adopted. For the 3 month old infant a f_1 value of 0.04 is assumed. The bioavailability (f_1) of uranium is defined here as the fraction of ingested uranium which is absorbed from the alimentary tract into the circulatory system. In this thesis data on bioavailability taken from the literature are denoted as f_1 while bioavailability data received by this thesis are denoted as f_A. This was done in compliance with ICRP, which recently changed the notation of the bioavailability from f_1 to f_A (ICRP 2006; Ruby et al. 1999). In adults the transfer of uranium from blood to kidney, liver, skeleton, and other soft tissues is about 8%, 1%, 10%, and 35%, respectively. About two-thirds of uranium are excreted via urine within three days after ingestion. For infants the transfer of uranium from blood to kidney, liver, and other soft tissues is similar, in particular 5%, 1%, and 33%, respectively. The transfer of uranium from blood to skeleton is simulated to be about 31% for infants (ICRP 1995a).

5.5 Internal dosimetry

Involuntary or deliberate ingestion or inhalation of radionuclides, the contamination of wounds by radionuclides, and the injection of radionuclides is always accompanied by a certain internal radiation exposure. The purpose of internal dosimetry is to quantify the received dose from this internal radiation exposure by means of calculation. The current study focused on the internal exposure from ingested soil-derived uranium.

For a scenario by which soil-derived radionuclides are ingested the committed effective dose is calculated by Eq. 1 (Simon 1998).

$$D_{soil} = \sum_i C_{soil,i} \times I_{soil} \times ED \times DC_i \qquad 1$$

Thereby $C_{soil,i}$ is the average concentration of a radionuclide i in the ingested soil (Bq/g), I_{soil} is the average daily ingestion of this soil during the exposure period (g/day), and ED is the exposure duration

(day). DC_i is the ingestion effective dose coefficient of a radionuclide i (Sv/Bq), which quantifies the effective dose per activity intake of a radionuclide i.

ICRP provides ingestion dose coefficients for several radionuclides. These ingestion dose coefficients are based on certain predefined bioavailabilities. For uranium the bioavailability (f_1 value) is assumed to be 2% (ICRP 1995a), assuming soluble uranium.

It is emphasized here that the purpose of the current study was to estimate soil-specific bioavailabilities by which sample-specific ingestion effective dose coefficients and finally the sample-specific internal dose can be calculated. Accordingly, the effective dose coefficients for ingestion were determined as follows.

The ingestion effective dose coefficients of a radionuclide i (DC_i) is derived from Eq. 2.

$$DC_i = \frac{E}{A_i} \qquad 2$$

E is the committed effective dose (Sv) and A_i the activity of the ingested radionuclide (Bq).

The committed effective dose (E) is calculated by Eq. 3.

$$E = \sum_T w_T \left(\frac{H_{T,male} + H_{T,female}}{2}\right) \qquad 3$$

The committed equivalent dose of an organ or tissue of the reference male ($H_{T,male}$) is averaged with the committed equivalent dose of an organ or tissue of the reference female ($H_{T,female}$) (ICRP 2007). The radiation sensitivity of certain organs and tissues is taken into account by the tissue weight factor (w_T) (ICRP 1991).

The committed equivalent dose of an organ or tissue of the reference male ($H_{T,male}$) or reference female ($H_{T,female}$) is calculated by Eq. 4.

$$H_{T,sex} = \sum_N \sum_{r_S} \tilde{A}(r_S, T_{50}, sex, N) S_w(r_T \leftarrow r_S, sex, N) \qquad 4$$

$\tilde{A}(r_S, T_{50}, sex, N)$ is the cumulated activity of a radionuclide or progeny (N) in a source region (r_S). For male or female (sex) $\tilde{A}(r_S, T_{50}, sex, N)$ is calculated over 50 years (T_{50}). $\tilde{A}(r_S, T_{50}, sex, N)$ is derived from biokinetic models.

Mathematically, biokinetic models are described by systems of first-order linear ordinary differential equations and are based on experimental animal and human data. By these models the uptake, distribution, and deposition of certain radionuclides in organs and tissues and their excretion from these organs, tissues, and the whole body are simulated. For internal dosimetry the biokinetic simulations are performed for a period of 50 years for adults and 70 years for children, respectively. The purpose of these calculations is to derive the cumulated activity of the source regions (r_S).

To simulate the ingestion of uranium, the systemic model of uranium is combined with the human alimentary tract model (HATM) (ICRP 2006). The resulting combined model was built for the radioisotopes ^{234}U, ^{235}U, and ^{238}U (ICRP 1995a). The systemic models and the alimentary tract models were connected by the bioavailability values obtained in this thesis, rather than by the ICRP pre-defined bioavailability of 2%. The built models were further expanded by their radiologically relevant progeny thorium, protactinium, and protactinium (meta) (ICRP 1979, 1995b). The decay constants by which the parent nuclide is connected with its relevant progeny were used accordingly (ICRP 2008). The biokinetic models were numerically solved by using the SAAM II software (Barrett et al. 1998).

$S_w(r_T \leftarrow r_S, sex, N)$ is the sex-specific (sex) radiation-weighted S factor, which is calculated for a radionuclide or progeny by Eq. 5.

$$S_w(r_T \leftarrow r_S, sex, N) = \sum_R w_R S(r_T \leftarrow r_S, E_R, sex, N) \qquad 5$$

$S(r_T \leftarrow r_S, E_R, sex, N)$ is the specific energy of a radiation type R (E_R), which is absorbed in a target region (r_T) emitted from a source region (r_S), per nuclear transformation of a radionuclide or its progeny (N). It is multiplied with the appropriate radiation-weighting factor (w_R) as suggested by ICRP (ICRP 1991).

The S_W values (formerly SEE values) were provided by the current SEECAL software which was developed at Oak Ridge National Laboratory. SEECAL is used worldwide for dose estimations concerning the incorporation of radionuclides into the human body. Thereby, S_W values are still based on the ORNL mathematical phantoms, not on the voxel based S_W values, which are not yet officially published by ICRP.

5.6 Estimating the absorption of soil-derived uranium

The internal dose caused by the ingestion of a certain amount of uranium cannot be determined directly but is estimated by means of tabulated radiological information and biokinetic models. Using these mathematical models the uptake of uranium as well as its distribution and deposition in the human body is simulated. Information concerning the excretion rate of ingested uranium can be also obtained from these biokinetic models. ICRP has published appropriate biokinetic models, which were used in the current thesis (ICRP 1995a, 1995b, 2006). Beside information on the distribution of uranium within the human body another very important parameter is provided by the ICRP for these biokinetic models. This is the bioavailability (f_1) of uranium. Data on the bioavailability of uranium in the human body published by ICRP are based on experimental evidence using drinking water, i. e. data are based on soluble uranium in drinking water. However, unlike uranium in drinking water, soil-derived uranium is just partially soluble in the human gastro intestinal tract, which results in a decreased bioavailability compared to soluble uranium from drinking water. Therefore, bioavailability data published by ICRP are not applicable on the ingestion of soil-derived uranium.

However, so far no method was available to determine the bioavailability of soil-derived uranium. For this reason, a method was needed to determine the bioavailability of uranium for a scenario by which soil-derived uranium was ingested. Different *in vitro* solubility assays are published in the literature by which the bioavailability (f_A) can be determined at least indirectly via determining first the bioaccessibility (DF). The bioaccessibility (DF) of uranium is defined here as the fraction of uranium, which is soluble in the alimentary tract and therefore potentially available for absorption. However, the different available *in vitro* solubility assays are known to provide different results on the bioaccessibility even for the very same soil. This was exemplary reported in 2002 for the soil contaminates As, Cd, and Pb by applying five different *in vitro* solubility assays and, for example, bioaccessibility values for Cd between 6% and 99% were found for the very same soil (Oomen et al. 2002). Different bioaccessibility values were also reported for soil-derived uranium and thorium based on two different *in vitro* solubility assays. Thereby bioaccessibility values for uranium between 10% and 14% were found (Höllriegl et al. 2010). Beside these different results, which obviously depend on the performed *in vitro* solubility assays, several methods can be found in the literature by which bioavailability (f_A) is derived from bioaccessibility (DF). As an example, Frelon et al. 2007 proposed that 100% of bioaccessible uranium is absorbed by the gastro intestinal tract and therefore they equate bioaccessibility with bioavailability (Frelon et al. 2007). In contrast, Höllriegl et al. 2010 assumed only 0.2% to 5% of bioaccessible uranium to be absorbed by the gastro intestinal tract and is therefore bioavailable (Höllriegl et al. 2010). Both of the described problems were solved by the concept developed in the present thesis.

In this thesis an *in vitro* solubility assay was used to determine the bioaccessibility (DF) of an edible soil low in uranium. The applied *in vitro* solubility assay was already established in the lab and was chosen out of several assays, due to its realistic physiological properties. The same edible soil was also used to determine the actual bioavailability (f_A) of uranium of this soil by a human study. This study included ten human volunteers who ingested a specific amount of this edible soil. The bioavailability (f_A) of uranium of all ten volunteers was estimated from their urinary excretion. By determining these two parameters, bioaccessibility (DF) and bioavailability (f_A), it was possible to calculate the f_A^{sol} factor ("sol" abbreviates "soluble"). The f_A^{sol} factor describes the relation between the bioaccessibility and the bioavailability of soil-derived uranium. It is expressed by Eq. 6:

$$f_A^{sol} = \frac{f_A}{DF} \qquad 6$$

Again, the obtained f_A^{sol} factor describes the relation between the bioaccessibility (DF) of soil-derived uranium in the alimentary tract obtained by the applied *in vitro* solubility assay, and the bioavailability (f_A) of soil-derived uranium in the human body obtained by the performed human study. Once this f_A^{sol} factor is determined for a specific *in vitro* solubility assay it is possible to make use of the actual advantage of this proposed concept, which is receiving realistic data on the bioavailability (f_A)

of uranium of virtually any soil, without the need of further human studies. Only the same *in vitro* solubility assay, which was applied in the current thesis, has to be performed for any soil of interest to determine its specific bioaccessibility (DF). The corresponding bioavailability (f_A) is thereafter simply calculated by adopting the f_A^{sol} factor (Eq. 7).

$$f_A = DF \times f_A^{sol} \qquad 7$$

By using this method, especially soil samples from uranium mining sites, which are chemically processed and highly contaminated with uranium and further heavy metals and radionuclides, can be investigated without hesitation. Thereby realistic data on the bioavailability of soil-derived uranium from even those soils can be received.

5.7 Measurement of ^{238}U by ICP-MS

For the current thesis a measurement technique was needed to determine ^{238}U in several urine, artificial gastrointestinal fluid, and microwave-assisted digested soil samples, at low concentrations.

In theory, radioisotopes can be detected by the radiation emitted after radioactive decay. As an alpha emitter with energies between 4.038 and 4.198 keV ^{238}U can be measured by alpha-spectroscopy. However, beside the very long half-life of ^{238}U, for alpha-spectroscopy of trace elements, comprehensive and therefore time-consuming and error-prone sample preparations have to be performed. Therefore, alpha-spectroscopy is not the proper application for routine analysis of ^{238}U as a trace element. Gamma-spectroscopy is also not a proper application because of similar disadvantages. Besides, ^{238}U emits only low energy gamma rays of about 50 and 114 keV with low yields of about 0.06 and 0.01%, respectively (IAEA 2017). In principal, indirect measurement of ^{238}U by gamma-spectroscopy could be performed e.g. via its progeny ^{234}Pa.

For measurements of trace elements like ^{238}U in liquid samples ICP-MS is frequently chosen and no specific time-consuming or error-prone sample preparations have to be performed (Heitland and Koster 2006a, b; Oeh et al. 2007; Höllriegl et al. 2010; Callan et al. 2013). Instead, urine or artificial gastrointestinal fluid samples only have to be diluted on a routine base. An internal standard like ^{103}Rh or ^{193}Ir of a known concentration and of a similar element mass and ionization energy like the investigated radionuclide is added, to correct for potential matrix effects. For the determination of ^{238}U in urine, calibration can be done by applying the standard addition method. By this method the matrix of the standard and the matrix of the sample are the same, which further minimizes uncertainties (Träber et al. 2014).

In principle, ICP-MS measurements can also be affected by polyatomic and isobaric interferences. Isobaric interferences are not expected for measurements of ^{238}U because it is the only naturally occurring isotope with an atomic mass of ^{238}U. Polyatomic interferences would be of interest if uranium isotope ratios like ^{235}U/^{238}U are analyzed by ICP-MS (Gwiazda et al. 2004; Xiao et al. 2014).

Yet in this thesis isotopic ratios of uranium were not analyzed by ICP-MS. Solely the concentration of ^{238}U was determined by ICP-MS.

Like for the urine and the artificial gastrointestinal fluid samples measured in the present thesis, uranium in the soil-samples was also measured via ICP-MS. For these samples a microwave-assisted digestion with HF was performed to dissolve the whole soil sample, in order to determine the total amount of ^{238}U in these soils (Träber et al. 2015).

5.8 Measurement uncertainty

A measurement value of a measurand cannot be exactly known, because of various reasons like finite instrument resolution, imperfect realization of the definition of the measurand or limited measurement capability of the measurement system. The measurement value is therefore only an approximation or estimate of the measurand. The guide to the expression of uncertainty in measurement (GUM) provides guidance to estimate the uncertainty which is associated to the result of a measurement (JCGM 2008). The measurement uncertainty is a parameter which characterizes the dispersion of the measurement values of a measurand. It gives a range within the true measurement value of a measurand is found with a certain level of confidence.

According to the concept of GUM there are two different ways of evaluating uncertainty components which are denoted as Type A and Type B. Type A standard uncertainty is obtained by statistical means and therefore from repeated measurements; Type B standard uncertainty is obtained from available knowledge like previous measurement data, manufacturer's specifications or experience or general knowledge. Both types are based on probability distributions. The Type A standard uncertainty u(y) of a quantity y is expressed as the standard deviations of the mean $s(\bar{q})$ of n individual observations q_k (Eq. 8).

$$u(y) = s(\bar{q}) = \sqrt{\frac{\sum_{k=1}^{n}(q_k - \bar{q})^2}{n(n-1)}} \qquad 8$$

For measurement result obtained from the values of a number of uncorrelated quantities, the combined standard uncertainty is used. Thereby the standard uncertainties of these uncorrelated quantities are used to calculate the combined standard uncertainties $u_c(y)$ (Eq. 9).

$$u_c(y) = \sqrt{\sum_{j=1}^{n}\left(\frac{\partial f}{\partial x_i}\right)^2 u^2(x_i)} \qquad 9$$

From the combined uncertainty the expanded uncertainty (U) can be obtained by multiplying the coverage factor (k) with the combined uncertainty. In the current study the level of confidence is about 68% which corresponds to a coverage factor of 1.

6 Introduction to the publications

The aim of the thesis was

1. to set up a method by which reliable data on the bioavailability of uranium from ingested soils are received and
2. to apply this method to estimate the internal dose for ingested and highly uranium-contaminated soils from former uranium mining sites.

This effort resulted in two publications (Träber et al. 2014; Träber et al. 2015). In the first publication the newly developed method which allows to obtain reliable data on the bioavailability of soil-derived uranium by means of a simple *in vitro* solubility assay is presented. This method was developed by combining an *in vitro* solubility assay and a human study, using the same edible healing soil for both studies. By the *in vitro* solubility assay and the human study the bioaccessibility (DF) and the bioavailability (f_A) were determined, respectively. By combining the results of both studies it was possible to calculate the f_A^{sol} factor (see Eq. 6). Using f_A^{sol} factor and the mentioned *in vitro* solubility assay, the bioavailability of uranium from any other soil can be obtained (see Eq. 7). Thereby, this method eliminates the need for further human soil-ingestion studies to receive reliable data on the bioavailability of soil-derived uranium. The f_A^{sol} factor was compared with data from the literature. From this comparison it can be concluded that the developed method can be applied on soils slightly or highly contaminated with uranium. Thereby it is also irrelevant whether the intake of uranium-contaminated soils is acute and chronic. The published method therefore provides a robust possibility to determine the bioavailability and the resulting internal dose for different ingestion scenarios with different amounts of uranium in various types of soil. The method was developed based on adult volunteers and, therefore, the results are only valid for adults.

In the second publication the application of the developed method on soil highly contaminated with uranium is presented. Original soils from former uranium mining sites were investigated; one soil sample was from a heap of a former uranium mining site near Dresden, Germany. The bioavailability of uranium from these soils was determined and used to calculate the resulting internal doses. This was done by applying the biokinetic models published by ICRP. A conceivable ingestion scenario was assumed by which a reasonable amount of the investigated uranium-contaminated soils would have been ingested. The results were compared with data from the literature.

7 Träber et al. 2014: Estimating the Absorption of Soil-Derived Uranium in Humans

The aim of the first part of this thesis was to set up a method by which reliable data on the bioavailability of uranium from ingested soils are received. The method was developed by combining an *in vitro* solubility assay and a human study, using the same edible healing soil for both studies, to obtain the f_A^{sol} factor (see Chapter 5.6).

The applied *in vitro* solubility assay based on the German method DIN 19738 (DIN 2000), which provides guidance on how to simulate the human gastrointestinal tract. This assay was once developed to estimate the bioaccessibility of different pollutants from contaminated soils. Here this *in vitro* solubility assay was used to determine the bioaccessibility (DF) of uranium for the used healing soil. The conducted human study was an ingestion study on ten human volunteers who ingested the same healing soil as it was also used for the *in vitro* solubility assay. The bioavailability (f_A) of healing soil-derived uranium was determined based on the urinary excretion of uranium.

7.1 *In vitro* solubility assay

Determination of bioaccessibility (DF)

To determine the bioaccessibility (DF) of uranium of the used healing soil, an in vitro solubility assay based on the German method DIN 19738 was performed. By this assay, the human gastrointestinal tract is simulated using artificial gastric and intestinal fluids and physiological incubation times and temperature. In practice, 2 g of healing soil were incubated in artificial gastric fluid for 2 hours at 37 °C ± 1 °C. The gastric pH was adjusted to pH 2.0 ± 0.2. After 2 hours artificial intestinal fluid was added. The pH status was adjusted to 7.5 ± 0.2 for another 6 hours at 37 °C ± 1 °C. Thereafter, a fraction of the suspension was centrifuged, filtered at 0.2 µm and stored at 4 °C until measurement by ICP-MS was performed. The bioaccessibility (DF) of the used healing soil was 7.7% ± 0.2% (mean ± SD). The result was applied to Eq. 6.

7.2 Human study

Determination of bioavailability (f_A)

The human study was conducted on healthy volunteers according to the principles of the Declaration of Helsinki, under the ethical authorization of the competent review boards (Technical University Munich, Germany, Ethical Commission), and with patients' written consent. Six female and four male volunteers aged between 22 and 55 years participated. The author of this thesis participated three times and his results were averaged to avoid overrepresentation. The study was conducted over six days and all ten volunteers had to collect their complete 24-h-urine. Urine was collected starting with first void urine in the morning until the following day without first void urine. Soil ingestion took place at day four at around 8:00 a.m. after a 10 hours overnight fast. After 2.5 hours the volunteers were provided with a standard breakfast and were thereafter allowed to eat and drink ad libitum. All ten volunteers ingested 20 g of healing soil mixed in 400 mL water which contained about 52 µg of ^{238}U. For comparison, adults are instructed to ingest up to 40 g/day of healing soil to cure health problems (Höllriegl et al. 2010). Note also that the average daily intake of uranium by food and drinking is 1.25 µg (UNSCEAR 2000).

To estimate the bioavailability (f_A) for all ten volunteers the urinary soil-derived uranium excretions were determined. Thereafter the individual bioavailability was estimated based on the systemic biokinetic compartmental model for uranium (ICRP 1995a).

Total ^{238}U excretion (m_{te}) after ingestion of healing soil was determined by subtracting the amount of excreted ^{238}U cumulated over three days before healing soil ingestion (m_b) from the amount of excreted ^{238}U cumulated over three days after healing soil ingestion (m_a) (see Eq. 10).

$$m_{te} = m_a - m_b \qquad 10$$

Incidentally, the daily urinary uranium excretion over three days before healing soil ingestion ranged from 11.4 ng/day to 12.7 ng/day (median values). These blank values of unexposed volunteers are in good agreement with a study on another 113 German unexposed volunteers which showed a daily urinary uranium excretion of 14.4 ng/day (median).

The total urinary systemic excretion of ^{238}U over three days after ingestion amounts to 68.5% (ICRP 1995a). Accordingly, the total amount of absorbed healing soil-derived ^{238}U (m_{ta}) was calculated by Eq. 11.

$$m_{ta} = \frac{m_{te} \times 100\%}{68.5\%} \qquad 11$$

The bioavailability (f_A) was calculated by Eq. 12 with m_{ti} as the amount of ingested healing soil-derived ^{238}U, which was 51.8 µg.

$$f_A = \frac{m_{ta}}{m_{ti}} \qquad 12$$

The bioavailability (f_A) was calculated for each volunteer. For one female volunteer a negative bioavailability of -0.01% was calculated due to a relatively high urinary blank value at day 1. Therefore this result was not included in further calculations. Based on the already mentioned study of urinary uranium excretion from 113 German unexposed volunteers, a log-normal distribution was assumed for the current human study (Oeh et al. 2007). Hence, the geometric mean (GM) and the geometric standard deviation (GSD) were calculated. The 95% confidence interval was considered by calculating the 2.5th percentile ($Q_{2.5th}$) and the 97.5th percentile ($Q_{97.5th}$) by Eq. 13 and Eq. 14, respectively.

$$Q_{2.5th} = \frac{GM}{GSD^2} \qquad 13$$

$$Q_{97.5th} = GM \times GSD^2 \qquad 14$$

The bioavailability (f_A) expressed as geometric mean was calculated to be 0.04%, the 2.5th percentile and the 97.5th percentile were calculated to be 0.0049% and 0.34%, respectively. The results of the bioavailability (f_A) which were obtained by the human study were applied to Eq. 6.

7.3 Calculation of the f_A^{sol} factor, options, and limitations

F_A^{sol} was determined based on *in vivo* data of the human study and on *in vitro* data of the solubility assay. The two data sets are connected because the same edible healing soil was used for both experiments. The results which were obtained by the *in vitro* solubility assay (DF) and the human study (f_A) were applied to Eq. 6. This resulted in a f_A^{sol} of 0.53% (GM) ranging from 0.06% (2.5th percentile) to 4.43% (97.5th percentile). By the f_A^{sol} factor and the used *in vitro* solubility assay the bioavailability of uranium from any other soil can be determined. Thereby, this method avoids the need for any further human soil-ingestion studies to receive reliable data on the bioavailability of any soil-derived uranium.

This advantage is not only of importance for ordinary soils, which may contain human pathogenic organisms, but especially for uranium-contaminated soils of uranium mining sites. These soils not only contain uranium but also various heavy metals which might be more bioavailable due to chemical and mechanical processing compared to ordinary soils. Therefore, human studies with these soils should be avoided and replaced by an *in vitro* solubility assay.

It should be noted that the bioavailability (f_A) determined in the current human study is assumed to be a log-normal distribution whereas the bioaccessibility (DF) is assumed to be a normal distribution. The log-normal distribution of the bioavailability (f_A) is a relatively wide distribution of over three orders of magnitude. In contrast, the bioaccessibility (DF) is characterized by a relatively narrow distribution.

Therefore, the bioaccessibility (DF) was approximated as an absolute term for the calculation of f_A^{sol}. Accordingly f_A^{sol} was assumed to also be log-normally distributed.

Data on the bioavailability of uranium as found in most of the available literature are based on the ingestion of drinking water which contains only soluble uranium. In contrast, in the current thesis the bioavailability was not determined from drinking water but from ingested soil-derived uranium which contains only a fraction of soluble uranium. Consequently, the available data from the literature were compared with the calculated f_A^{sol} factor results, because equal to drinking water f_A^{sol} represents only the soluble fraction of soil-derived uranium, which is absorbed by the alimentary tract into the circulatory system. In the literature, for an acute ingestion of up to 270 µg of uranium or a chronic ingestion of uranium of 0.37 to 2775 µg/day over at least 15 days bioavailabilities between 0 and 7% are reported (Wrenn et al. 1989; Harduin et al. 1994; Leggett and Harrison 1995; Karpas et al. 1998; Limson Zamora et al. 2003; Karpas et al. 2005). This data are in good agreement with those obtained in this thesis for f_A^{sol} of 0.53% (GM) ranging from 0.06% (2.5^{th} percentile) to 4.43% (97.5^{th} percentile). Based on these data it is assumed that the f_A^{sol} factor does not depend on the duration of exposure or the amount of ingested uranium, and that it can be used for acute as well as chronic ingestion scenarios with high amounts of soil-derived uranium.

In the present thesis, the f_A^{sol} factor was determined based on the German method DIN 19738. This is of importance since soil contaminants like As, Cd, Pb, and U are reported to result in different bioaccessibilities depending on the performed *in vitro* solubility assays. Bioaccessibility values between 6% and 99% were reported for soil contaminates of the same sample (Oomen et al. 2002; Höllriegl et al. 2010). Accordingly, for applying the f_A^{sol} factor determined in the present thesis on other soils the *in vitro* solubility assay developed in the present thesis has to be performed. Otherwise the bioaccessibility values obtained would probably result in misleading bioavailability values.

In the current human study female and male volunteers aged between 22 and 55 years participated. The resulting f_A^{sol} values might therefore by representative for the majority of the population. It is noted that the participants of the human study were adult volunteers, but children and pregnant women, and therefore unborn children, were not considered. The results of the current thesis must therefore not be directly applied to these vulnerable groups. Compared to adults, children exhibit higher soil ingestion rates. In particular, small children exhibit hand-to-mouth behavior by which small amounts of soils might directly be ingested. Higher soil ingestion rates by children compared to adults are also likely due to different outdoor activities. These higher soil ingestion-rates could be considered using Eq. 1. Additionally, children are also assumed to exhibit higher uranium absorption rates compared to adults. Hence, a higher fraction of uranium is absorbed from the pediatric intestine into the circulatory system. This is not be accounted for in the current thesis. Beside the increased absorption of uranium, children are also reported to exhibit uranium net retention, meaning uranium intake exceeds uranium excretion. This might be especially pronounced during periods of growth

(Leggett and Harrison 1995; Harrison et al. 2001; Chen et al. 2011). Like for the previous aspect this is not considered in the present thesis.

The study is described in detail in Träber et al. 2014 (see Chapter 8).

8 Träber et al. 2014

Estimating the Absorption of Soil-Derived Uranium in Humans

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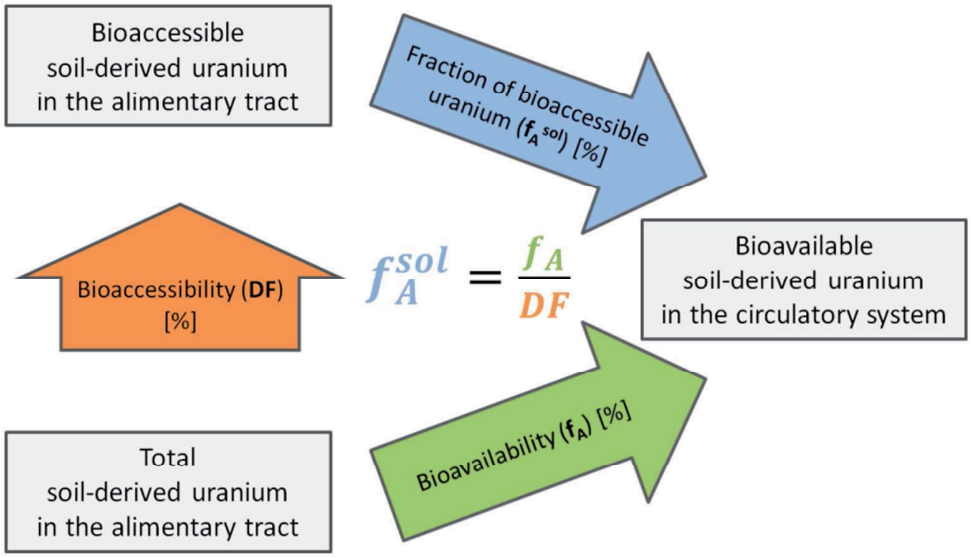
Environmental Science & Technology 2014 48 (24), 14721-14727

DOI: 10.1021/es504171r

Estimating the absorption of soil-derived uranium in humans

Journal:	*Environmental Science & Technology*
Manuscript ID:	es-2014-04171r.R1
Manuscript Type:	Article
Date Submitted by the Author:	24-Oct-2014
Complete List of Authors:	Träber, Stephan; Helmholtz Zentrum München, Research Unit Medical Radiation Physics and Diagnostics Hoellriegl, Vera; Helmholtz Zentrum München, Research Unit Medical Radiation Physics and Diagnostics Li, Wei Bo; Helmholtz Zentrum München, Research Unit Medical Radiation Physics and Diagnostics Czeslik, Uta; Nuclear Engineering and Analytics Inc., Rühm, Werner; Helmholtz Zentrum München, Institute of Radiation Protection Oeh, Uwe; Helmholtz Zentrum München, Research Unit Medical Radiation Physics and Diagnostics Michalke, Bernhard; Helmholtz Zentrum München, Research Unit Analytical BioGeoChemistry



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Estimating the absorption of soil-derived uranium in humans

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ABSTRACT

The aim of the present study was to improve the estimation of soil-derived uranium absorption in humans. For this purpose, an *in vitro* solubility assay was combined with a human study by using a specific edible soil low in uranium. The mean bioaccessibility of the soil-derived uranium,

18 determined by the solubility assay in artificial gastrointestinal fluid, was found to be 7.7% with a
19 standard deviation of 0.2%. The corresponding bioavailability of the soil-derived uranium in
20 humans was assumed to be log-normal distributed with a geometric mean of 0.04% and a 95%
21 confidence interval ranging from 0.0049% to 0.34%. Both results were used to calculate a factor,
22 denoted as f_A^{sol}, which describes the relation between the bioaccessibility and the bioavailability
23 of soil-derived uranium. The geometric mean of f_A^{sol} was determined to be 0.53% with a 95%
24 confidence interval ranging from 0.06% to 4.43%. Based on f_A^{sol}, it is possible to estimate more
25 realistic values on the bioavailability of uranium for highly uranium-contaminated soils in
26 humans by just performing the applied solubility assay. The results of this study can be further
27 used to obtain more reliable results on the internal dose assessment of ingested highly uranium-
28 contaminated soils.

29 INTRODUCTION

30 The aim of the present study was to improve the estimation of soil-derived uranium absorption
31 in humans.

32 Ingestion of small amounts of soil by humans can be observed around the world. It occurs
33 involuntarily or deliberately. Involuntary routes of soil ingestion are via inhalation and
34 swallowing of dust, via food and via hand-to-mouth activities of young children. Deliberate
35 ingestion of soils, which is also called geophagy, is reported, e.g. in Africa, Asia and South
36 America.[1, 2] In European countries like Germany some people also practice geophagy by eating
37 soils called healing soil or medical soil.[3] These soils can be purchased without a prescription and
38 are used to cure moderate alimentary tract related symptoms like acid reflux.

39 Recent values concerning the amount of soils ingested by children are varying from 26 mg/day
40 to 100 mg/day.[4, 5] The average soil ingestion by adults is assumed to be 10 mg/day, whereas

deliberate ingestion of soils like healing soil can amount from 6 g/day to 40 g/day over several weeks.[3, 6]

Uranium, as a naturally occurring radioactive material (NORM), occurs ubiquitously in soils at concentrations of about 3 mg/kg and comprises the radio-isotopes ^{234}U, ^{235}U and ^{238}U with percentages by mole fraction of 0.0054%, 0.72% and 99.27%, respectively.[7, 8] In some areas, the amount of uranium in soils is technologically enhanced (TENORM) e.g. due to uranium refining, agriculture activities and presumably also as a result of nuclear incidents like the Chernobyl accident in 1986 or the Fukushima Daiichi incident in 2011.[9-11] Consequently, soil ingestion leads to a certain internal dose enhancement.

The internal dose caused by ingested uranium is calculated by using the current biokinetic compartmental model reported by the International Commission on Radiological Protection (ICRP).[12] This biokinetic model describes the uptake, distribution and deposition of uranium in tissues and its excretion from the human body. One important parameter within this model is the so-called f_1 value, which quantifies the bioavailability of uranium. The bioavailability (f_1) of uranium is defined as the fraction of ingested uranium which is absorbed from the alimentary tract into the circulatory system.[13]

It is noted, however, that the f_1 value of uranium was established by the ICRP for ingestion scenarios of soluble uranium, especially considering the uptake of uranium from drinking water.[12] To estimate the bioavailability (f_1) of uranium from a highly uranium-contaminated soil, human soil ingestion studies e. g. of soils from uranium mining sites are inappropriate. Instead, *in vitro* solubility assays, which mimic the alimentary tract conditions, are applied. By these assays only the bioaccessibility but not the bioavailability of uranium can directly be estimated. The bioaccessibility (DF) of uranium is defined as the fraction of uranium, which is soluble in

the alimentary tract and therefore potentially available for absorption.[13] To derive the bioavailability (f_1) of uranium from the bioaccessibility (DF) data, some investigators assumed that the total fraction of bioaccessible uranium is absorbed into the circulatory system, hence equating bioavailability with bioaccessibility.[14] Others estimated a proportion of only 0.2% - 5% of bioaccessible uranium to be absorbed by the alimentary tract into the blood.[3] As a consequence, these differences ended up in a high variation of the estimates of the f_1 value for uranium of up to three orders of magnitude.

Additionally, different established solubility assays like the solubility assay "DIN 19738" and the “US P”- method showed varying estimates of the bioaccessibility for uranium despite using an identical soil.[3] These differences in the bioaccessibility data are expected to be the result of the different composition of those assays, which further increases the uncertainty of the bioaccessibility and consequentially the uncertainty of the estimated bioavailability.

For the reasons mentioned above, the aim of this study was to set up a method which enables the assessment of more reliable data on the bioavailability for soil-derived uranium. The idea was to combine a solubility assay with a human study by using an edible healing soil as a model soil for both investigations. Thereby, the bioaccessibility value and the corresponding bioavailability value of the healing soil-derived uranium can be obtained experimentally. Both values can then be used to calculate a factor, which describes the relation between the bioaccessibility and the bioavailability of soil-derived uranium.

This factor can be further used to obtain more realistic data on the bioavailability of uranium dissolved from various soils by just performing a solubility assay. Thereby, especially highly uranium contaminated soils and potentially also industrial forms of uranium can easily be

86 investigated to determine realistic bioavailabilities. Finally, more reliable data on the internal
87 dose due to soil ingestion can be obtained.

88 EXPERIMENTAL SECTION

89 Experimental design and calculation of f_A^{sol}

90 The notation of the bioavailability has changed from f_1 to f_A by the ICRP.[15] Therefore, the
91 results on bioavailability obtained in this study are denoted as f_A, while data on the
92 bioavailability from previous studies are still denoted as f_1.

93 The present work was designed to determine a factor, denoted as f_A^{sol}, which connects the
94 bioaccessibility DF and the bioavailability f_A for soil-derived uranium. This factor (f_A^{sol}) is
95 defined as the fraction of bioaccessible uranium, which is absorbed from the alimentary tract into
96 the circulatory system. It can be determined as previously published by:[3]

97 $$f_A^{sol} = \frac{f_A}{DF} \qquad (1)$$

98 Hence, f_A^{sol} can be derived by using the same edible soil for a solubility assay and a human
99 study to evaluate DF and f_A, respectively. The relation of the bioavailability (f_A), the
100 bioaccessibility (DF) and the factor f_A^{sol} is depicted in Figure 1.

101 Healing soil

102 In the present study, the healing soil "Luvos®Heilerde ultrafein" (Luvos Just GmbH&Co,
103 Friedrichsdorf, Germany) was selected as the model soil for the solubility assay and the human
104 study because it fulfills all necessary requirements. An important aspect here is that the healing
105 soil "Luvos®Heilerde ultrafein" is a medical product which is suitable for ingestion by humans.
106 It can easily be purchased in sufficient quantities without a prescription and is ultra-fine (<1 μm)
107 and therefore homogeneous, which ensures a constant quality during the whole study. The
108 healing soil "Luvos®Heilerde ultrafein" contains a small concentration of the naturally occurring
109 radionuclide ^{238}U.[3]

110 Determination of ^{238}U in healing soil

For the analyses of total ^{238}U in healing soil 139.2 mg of healing soil were mixed with 5 mL of HNO_3 (65%), 1 mL of HCl (30%) and 1 ml HF (40%). The mixture was microwave-assisted digested in a Multiwave 3000 (Anton Paar, Austria); power: ramp for 15 min up to 1400 W, hold for 30 min at 1400 W, cooling down for 15 min. After the subsequent addition of 6 mL of H_3BO_3 to neutralize free fluorides the solution was placed again in the Multiwave system, applying a 5 min ramp up to 900 W, hold for 15 min and cooling down for 15 min. Thereafter, the solution was stored at 4 °C until measurement of ^{238}U using ICP-MS (Supporting Information, Section S.1).

Gastric pH-metry – Determination of the gastric pH

To ensure that the solubility assay DIN 19738 (see below) realistically reproduces the gastric pH-conditions and therefore presumably provides more realistic data on the bioaccessibility for healing soil-derived uranium, the *in vivo* gastric pH after soil ingestion had to be determined. For this purpose, a volunteer test with a 29-year-old male was performed where the gastric pH status after healing soil ingestion was measured by means of a standard gastric pH-metry. After an overnight fast, a pH glass probe (F8/IR BLUE LINE, SMT Simtec GmbH, Switzerland) was inserted via nose, throat, and esophagus into the stomach. This was carried out under medical supervision in the clinic Rechts der Isar, TU München, Germany. The probe was connected during the whole experiment to a portable recorder (DL 70, Standard Instruments GmbH, Germany). The setup enabled the volunteer to eat, drink and act as usual. One hour after probe insertion, 20 g of healing soil slurried in 400 mL water (MilliQ) were quickly ingested, according to the standard healing soil ingestion protocol. The pH data were recorded during the whole experiment and noted as “physiological”. However, the pH-metry data were only available as raster graphics image and therefore redigitized by using the WinDIG 2.5 program.[16] Thereby

mean pH values over about 1.5 min were obtained with estimated standard uncertainties of the mean pH values (U_m) of 0.2.

Solubility assay – Determination of DF

To determine the bioaccessibility of uranium within the alimentary tract, an *in vitro* solubility assay was performed based on the German method DIN 19738.[17] This solubility assay included artificial gastric and intestinal fluids composed of organic and inorganic compounds. The composition of these fluids was already presented elsewhere.[3] Incubation times, temperature and partly pH values were also adapted from the DIN 19738. As the absorption of uranium from the gastrointestinal tract into the systemic circulation occurs mainly in the small intestine,[18] only the entire incubation mixture (gastric and intestinal) was used for the quantification of soluble ^{238}U.

The *in vitro* solubility experiments were performed by incubating 2 g of healing soil in 100 mL of artificial gastric fluid for 2 h using a pH status of 1.0 ± 0.2, 2.0 ± 0.2 or the "physiological" pH-status as assessed in the investigation described in the previous section. The pH status was adjusted with HCl (10%). The suspension was held at 37 °C ± 1 °C and was constantly stirred at about 500 rpm to avoid sedimentation. Thereafter, 100 mL of artificial intestinal fluid were added and the pH was adjusted to 7.5 ± 0.2 and held by the addition of $NaHCO_3$ and HCl, respectively. The suspension was stirred for another 6 h at 37 °C ± 1 °C. After a total of 8 h, 50 mL-fractions were taken and centrifuged at 5000 rpm (Hettich Universal 32R). Three aliquots of 10 mL were taken. From these samples, two aliquots were further filtered at 0.45 µm or 0.2 µm (sterile filter, Millipore). A fourth sample was directly taken from the suspension and filtered at 0.2 µm without centrifugation. For each solubility experiments, extractions were prepared in triplicates. To correct for the background of ^{238}U the solubility assays were run without soil. The

156 samples were stored at 4 °C until measurements of ^{238}U were performed using an inductively
157 coupled plasma mass spectrometer (ICP-MS) (Supporting Information, Section S.1).

158 Human Study – Determination of f_A

159 The human study was conducted on healthy volunteers according to the principles of the
160 Declaration of Helsinki, under the ethical authorization of the competent review boards
161 (Technical University Munich, Germany, Ethical Commission), and with patients' written
162 consent.

163 Ten volunteers (6 females, 4 males, aged 22-55 years) without chronic disorders participated in
164 the human study, which was performed between 2011 and 2013. Nine volunteers participated
165 once. One male volunteer (Volunteer 1) participated three times. These three investigations were
166 done to investigate any possible individual variations. Only averaged results of all three
167 investigations were used for further calculations. Therefore, every volunteer is equally
168 represented in the current study.

169 All volunteers had to collect their complete 24-h-urine over three days before (day 1, day 2,
170 day 3) and three days after (day 4, day 5, day 6) a single ingestion of 20 g of healing soil mixed
171 in 400 mL water (MilliQ). The soil ingestion was at day 4 around 8:00 a.m. after a 10 h
172 overnight fast. After 2.5 hours the volunteers were provided with a standard breakfast (bread roll,
173 jam, and tea, water or coffee). Afterwards, the volunteers were allowed to eat and drink ad
174 libitum.

175 The amounts of applied healing soil were not considered to pose any health risk to the human
176 volunteers. The volunteers were never knowingly exposed through ingestion or inhalation to any
177 other increased levels of uranium. All participants were provided with polyethylene bottles of 3

178 L capacity (Sarstedt, Nümbrecht, Germany) and were given instructions on how to collect their
179 urine.

180 The total weights of all 24-h-urine samples were recorded. Subsamples of 20 mL were drawn,
181 acidified with subboiled distilled nitric acid in a sterile polystyrene test tube and stored frozen at
182 −20°C until analysis by ICP-MS (Supporting Information, Section S.2). Daily urine volumes
183 were calculated by dividing the weighed urine masses by the urine specific density factor of
184 1.020 g/mL ± 0.015 g/mL.[19]

185 To determine the bioavailability (f_A) of soil-derived ^{238}U for the human volunteers, the current
186 systemic biokinetic compartmental model for uranium published by the ICRP[12] together with the
187 measured urinary excretion data of ^{238}U were used.

188 Total daily ^{238}U excretion of volunteers was calculated by multiplying the concentrations of
189 ^{238}U in the 24-h-urine samples with the corresponding urine volumes. To correct for the
190 background of dietary uranium excretion total healing soil-derived ^{238}U excretion (m_{te}) was
191 estimated for a period of 3 days after soil ingestion by $m_{te} = m_a - m_b$, where m_a is the
192 cumulated amount of excreted ^{238}U over 3 days after soil ingestion and m_b is the cumulated
193 amount of excreted ^{238}U obtained over 3 days before soil ingestion. According to the current
194 biokinetic compartmental model for uranium, the urinary systemic excretion of absorbed
195 uranium over 3 days amounts to 68.5% in total.[20] Therefore, the total amount (100%) of
196 absorbed soil-derived uranium (m_{ta}) was calculated by $m_{ta} = m_{te} \times 100/68.5$.

197 Finally, based on the total amount of ingested ^{238}U from 20 g of healing soil (m_{ti}) f_A was
198 calculated by:

199 $$f_A = \frac{m_{ta}}{m_{ti}} \qquad (2)$$

200 The applied 68.5% of urinary excreted uranium over three days does not account for the slight
201 delay of uranium excretion due to the transition time of healing soil in the upper gastrointestinal
202 tract after ingestion. However the conducted urinary sample collection over three days is
203 sufficiently long to compensate for this delay.

RESULTS AND DISCUSSION

Gastric pH-metry – Determination of the gastric pH

In accordance with the physiological conditions of the alimentary tract, the procedure of the solubility assay DIN 19738 recommends a sequential incubation of soil in artificial gastric and intestinal fluid with a pH value of 2 over 2 hours and a pH value of 7.5 over 6 hours, respectively.

However, these standard conditions may not be valid for the specific case of ingestion of healing soil, since one characteristics of the healing soil in humans is its capability to neutralize gastric acid after ingestion. Moreover, preliminary results of the solubility assay DIN 19738 had shown that the gastric pH-value is a sensitive parameter when assessing the solubility of healing soil-derived ^{238}U (a 60% decrease in solubility was observed when varying the pH-value from 2 to 4; data not shown). Yet, it remained unknown to which extent the ingested healing soil was actually capable to neutralize the real gastric acid. Therefore, it was important to find out the *in vivo* gastric pH status after healing soil ingestion. For this reason, a standard gastric pH-metry was done on a 29-year-old male volunteer while ingesting the healing soil. The gastric pH status was recorded for the initial two hours after soil ingestion (Figure 2).

After an overnight fast, the pH value of the volunteer was about 1.0 ± 0.2. After healing soil ingestion, the gastric pH-metry revealed a rapid increase of the gastric pH up to 5.1 within 6 min, followed by a slow decline. About 30 min after soil ingestion, the gastric pH was at 2.0 and further declined towards pH 1.0 within the next 60 min. For the remaining 30 min, the gastric pH level stayed at about 1.0 ± 0.2. From these data gastric pH values of 1.6 (mean) and 1.3 (median) can be evaluated.

Solubility assay – Determination of DF

As a conclusion from the gastric pH-metry, two alternative gastric pH courses were applied in addition to the recommended stable gastric pH of 2 for the solubility assay DIN 19738, while all other parameters of the solubility assay were not altered. The first alternative gastric pH course was directly adopted from the gastric pH-metry. In this case, the complete pH pattern over 2 hours, shown in Figure 2, was mimicked. This pH pattern represents the most physiological gastric pH conditions regarding healing soil ingestion. In the second alternative, the gastric pH value was set constant at 1.0, which represents the long-term limit of the measured gastric pH by the gastric pH-metry (Figure 2). Both stable gastric pH values (i.e. 2.0 and 1.0) include the mean and median value of 1.6 and 1.3 of the gastric pH-metry data, respectively.

The results of the solubility assays using different gastric pH statuses are shown in Figure 3. The indicated bioaccessibility values are based on the ^{238}U concentration of 2.59 mg/kg ± 0.08 mg/kg (mean ± SD) in the healing soil measured by ICP-MS after HF digestion. By using the stable gastric pH of 2, 7.6% ± 0.5% (mean ± SD) of healing soil-derived ^{238}U was soluble in the synthetic gastrointestinal fluid after centrifugation. Additional filtration steps (0.45 µm and 0.2 µm) did not markedly alter the bioaccessibility. Importantly, the bioaccessibility of ^{238}U did not change by adopting the alternative gastric pH status "physiological" from the gastric pH-metry, regardless of whether or not additional filtration steps were applied. A stable gastric pH value of 1 had no notable influence on the bioaccessibility of healing soil-derived uranium either. The bioaccessibility of the non-centrifuged but filtered samples also showed no obvious variations.

The results clearly demonstrate that there are no substantial changes of the estimated bioaccessibilities neither among the different gastric pH statuses used nor among the filtered or unfiltered samples. The bioaccessibility data obtained by using the stable gastric pH of 2, the

249 centrifugation and the filtration step at 0.2 μm was applied as the reference value. This resulted
250 in a DF value of 7.7% ± 0.2% (mean ± SD).

251 Human Study – Determination of f_A

252 The ten volunteers who participated in the study ingested once a single amount of 20 g of
253 healing soil which contained 51.8 μg ± 1.6 μg (mean ± SD) of ^{238}U. The daily urinary excretion
254 of ^{238}U of the volunteers is shown in Figure 4. These data were further used to determine the
255 volunteer-specific bioavailability f_A of healing soil-derived ^{238}U. The daily urinary excretion of
256 ^{238}U over 3 days before healing soil-ingestion ranged from 11.4 ng/day to 12.7 ng/day (median
257 values). This is in reasonable agreement with the results of a study on 113 German unexposed
258 volunteers aged from 3 to 92 years, where a daily urinary excretion of ^{238}U of 14.4 ng/day
259 (median) was measured.[21] Median excretion of ^{238}U after healing soil ingestion (day 4) was
260 increased by about 6.4 ng ^{238}U compared to day 3 and was accompanied by an increased inter-
261 individual variability. Over the next two days (day 5, day 6) the daily ^{238}U excretion declined
262 towards blank values.

263 To determine the bioavailability (f_A) of healing soil-derived ^{238}U for each of the ten human
264 volunteers, the current uranium biokinetic model published by the ICRP[12] together with the
265 obtained urinary excretion data of ^{238}U were applied. A negative bioavailability of -0.01% was
266 obtained for one subject due to a relatively high blank value of urinary ^{238}U at day 1, which
267 presumably illustrates the strong intra-individual variation of dietary uranium excretion. This
268 value was not included in further calculations. The results of the remaining nine volunteers are
269 shown in Figure 5 (left graph). Similar to a former publication on daily urinary excretion of
270 uranium[21], a log-normal distribution was assumed. Therefore, the f_A values are presented by a
271 log-scaled probability plot in Figure 5 (right graph). Accordingly, geometric mean (GM) and

geometric standard deviation (GSD) were calculated to be 0.04% and 2.9, respectively. To cover a 95% confidence interval of f_A values, the 2.5th percentile and the 97.5th percentile were calculated by:[22, 23]

$$Q_{2.5th} = \frac{GM}{GSD^2} \quad (3)$$

and

$$Q_{97.5th} = GM \cdot GSD^2 \quad (4)$$

Thus, the 2.5th percentile and the 97.5th percentile amount to 0.0049% and 0.34%, respectively. The indicated range of f_A over three orders of magnitude implies a relatively high inter-individual variability.

The bioavailability (f_A) value of soil-derived uranium obtained in this experimental study is, to our knowledge, the first experimentally derived value in the literature. As mentioned, most of the former bioavailability (f_1) values obtained from human studies were from investigations on soluble uranium from drinking water. For this reason, these f_1 values are inappropriate for a direct comparison with f_A because of the relatively high proportion of insoluble uranium in soil. It is therefore more suitable to compare the f_1 values with the calculated f_A^{sol} values (see below). Similar to the dissolved uranium from drinking water, f_A^{sol} represents only the amount of soluble soil-derived uranium, which is absorbed from the alimentary tract into the circulatory system.

As already mentioned, to investigate any possible individual variations one male volunteer (Volunteer 1) participated three times. An interval of at least 2 months between the studies was maintained to avoid any interference. Thereby, the daily urinary excretion values of ^{238}U over 3 days before healing soil-ingestion were 3.9 µg/day ± 1.5 µg/day, 8.1 µg/day ± 0.6 µg/day and 9.0 µg/day ± 1.2 µg/day (mean ± SD). Similar variations are reported in the literature.[24] The corresponding f_A values were 0.024% ± 0.001%, 0.003% ± 0.001% and 0.044% ± 0.002% (f_A

295 value ± combined uncertainty). This limited data set suggests an intra-individual variation of the
296 f_A of about one magnitude, which was independent from the urinary ^{238}U status before healing
297 soil ingestion. This finding might indicate a general intra-variability of the uptake of uranium by
298 the alimentary tract.

299 Determination of f_A^{sol}

300 In the present study, the bioaccessibility and the corresponding bioavailability of healing soil-
301 derived ^{238}U were measured by a solubility assay and a human study. The bioaccessibility and
302 the bioavailability amounted to 7.7% ± 0.2% (mean ± SD) and 0.04% (GM) with a GSD of 2.9,
303 respectively. By adapting these results to eq. 1, f_A^{sol} results to 0.53% (GM) ranging from 0.06%
304 (2.5^{th} percentile) to 4.43% (97.5^{th} percentile).

305 The factor f_A^{sol} was established by using a healing soil, which contains only small amounts of
306 uranium. On the basis of a DF of 7.7%, the volunteers of the current study who ingested 20 g of
307 healing soil were only exposed to a small amount of soluble soil-derived uranium of about 4 µg.
308 However, the intention was to apply the f_A^{sol} to soil ingestion scenarios with high levels of
309 uranium. This raised the question as to whether f_A^{sol}, which was established by acute and low
310 levels of uranium, is also applicable to chronic and high level scenarios, or as to whether f_A^{sol}
311 might vary in these cases.

312 In this regard, the data on f_A^{sol} established in the present study was compared with the values
313 available in the literature on the absorption of high levels of soluble uranium in humans. As
314 already mentioned, f_A^{sol} and f_1 are suitable for comparison because both represent soluble
315 uranium, which is absorbed from the alimentary tract into the circulatory system. Table 1 gives
316 an overview on f_1 ranges for soluble uranium compounds obtained in different human studies
317 compared to the present value of f_A^{sol}. Three studies on acutely ingested uranium revealed f_1

values ranging from 0% to 5%. Three studies on chronic ingestion of soluble uranium showed similar data on f_1 ranging from 0.02% to 7%.

Table 1. Summary of bioavailabilities of ingested soluble uranium in humans

	Ingestion of soluble uranium	f_A^{sol} (present study) or f_1 for soluble uranium compounds (other studies)
Present Study	4 µg[a]	0.06% - 4.43%[c]
Karpas et. al. 1998[25]	100 µg[a]	0.14% - 1.56%
Harduin et. al. 1994[26]	162 µg[a]	0.5% - 5% [d]
Wrenn et. al. 1989[27]	~270 µg[a]	0% - 3.5% [d]
Harduin et. al. 1994[26]	81 µg/day[b]	0.3% - 2%[d]
Limson Zamora et. al. 2003[28]	0.37 to 573 µg/day[b]	0.1% - 6.3%
Karpas et. al. 2005[29]	10 - 2,775 µg/day[b]	0.02% - 7%

[a]Acute ingestion of uranium at one day. [b]Chronic ingestion of uranium, at least over 15 days. [c]Range for f_A^{sol} with a confidence interval of 95%. [d]Indicated ranges are based on interpretation of Leggett and Harrison et. al.[30]

Table 1 demonstrates that there are no major differences between the range of f_A^{sol} obtained in the present study and the ranges of the bioavailabilities (f_1) of former studies, no matter what levels, low or high, of uranium were acutely or chronically ingested. Based on the results in Table 1 it is assumed that the f_A^{sol} value does not depend on the amount or the exposure time of ingested uranium and can thus be used for soils highly contaminated with uranium. Additionally, similar to the human data, the bioavailability of soluble uranium e. g. in rodents ranged from 0.7% to 2.8%.[31, 32]

For the estimation of f_A and f_A^{sol}, only adult volunteers were considered. Hence, the derived data on f_A^{sol} should not be directly applied to children, since the latter might exhibit increased absorption and net retention of uranium, especially during periods of growth.[12, 15, 30, 33, 34] In this

334 regard, the derived value of f_A^{sol} is very likely to underestimate the actual bioavailability of non-
335 adults.

336 Based on the f_A^{sol} value, it is possible to estimate more realistic f_A values for other soils as
337 well. Assuming that the absorption from the alimentary tract does not depend on the chemical
338 speciation of soluble uranium, only the solubility assay DIN 19738 has to be performed for a
339 specific soil to gain the soil specific DF value.[35] A more realistic f_A value could then be achieved
340 by directly applying eq. 1, without the need of performing additional human studies.

341 The resulting bioavailability f_A can be used in the biokinetic compartmental model of uranium
342 to improve the internal dose assessment after soil ingestion. Currently we are working on the
343 assessment of the internal dose after ingestion of some highly uranium-contaminated soils by
344 applying the introduced concept.

345 ASSOCIATED CONTENT

346 Supporting Information

347 Section S.1: details on the determination of urinary ^{238}U by ICP-MS. Section S.2: details on the
348 determination of ^{238}U from the solubility assay and the microwave-assisted digested healing soil
349 by ICP-MS. This material is available free of charge via the Internet at http://pubs.acs.org.

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354 Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

The authors would like to thank all volunteers for their participation. Thanks also to Prof. Dr. H. Feußner and H. Wirnhier (Department of Surgery, Klinikum rechts der Isar, Technische Universität München, Munich, Germany) for enabling us to conduct a gastric pH-metry. The present work was mainly funded by the German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung, BMBF), Berlin, Germany (Contract No. 02NUK015B).

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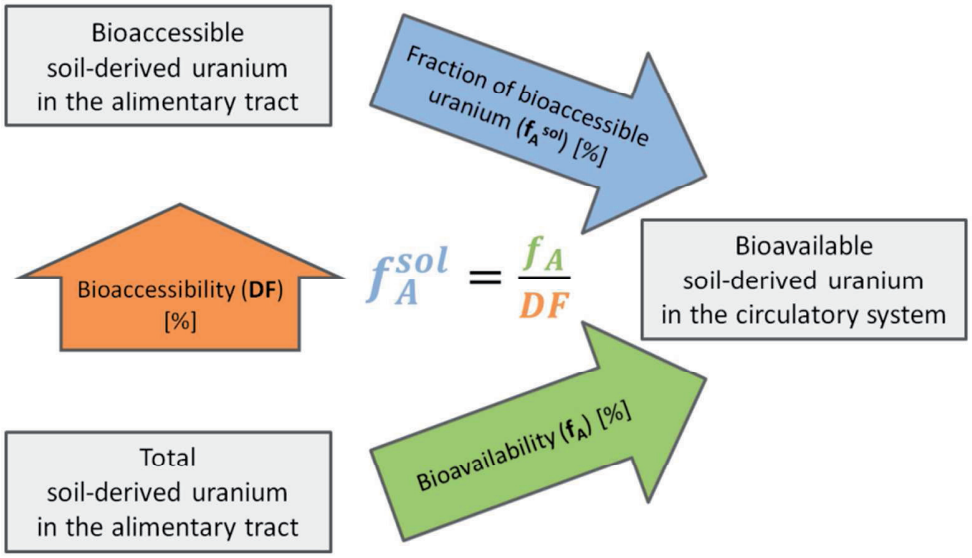

Figure 1. Scheme of the relation of bioavailability (f_A), bioaccessibility (DF) and the f_A^{sol} factor.
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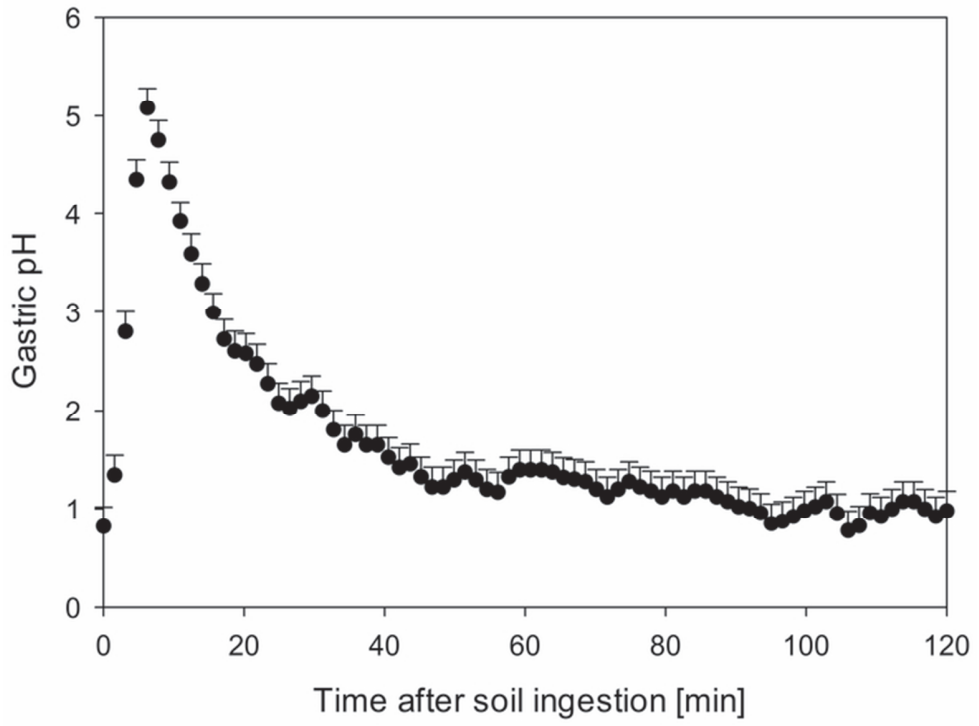

Figure 2. Gastric pH over 2 hours after a single initial ingestion of healing soil (20 g) by a male volunteer (mean + standard uncertainty).
63x47mm (300 x 300 DPI)

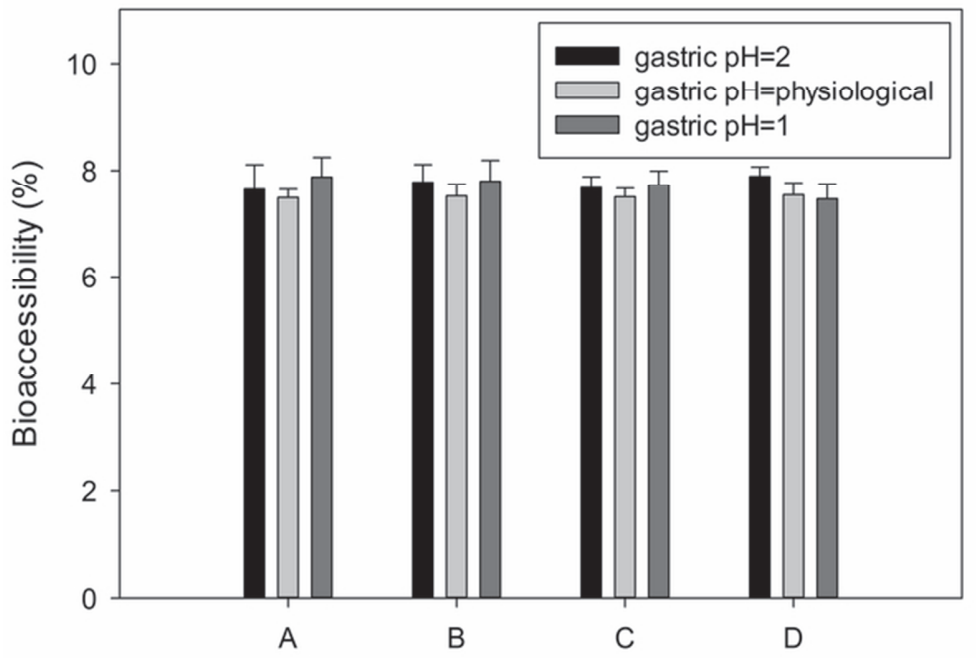

Figure 3. Bioaccessibility (DF) of healing soil-derived ^{238}U in gastrointestinal fluid (mean + SD, n=3). Before measurement via ICP-MS, the samples were (A) centrifuged, (B) centrifuged and filtered at 0.45 µm, (C) centrifuged and filtered at 0.2 µm or (D) non-centrifuged, but filtered at 0.2 µm.
57x39mm (300 x 300 DPI)

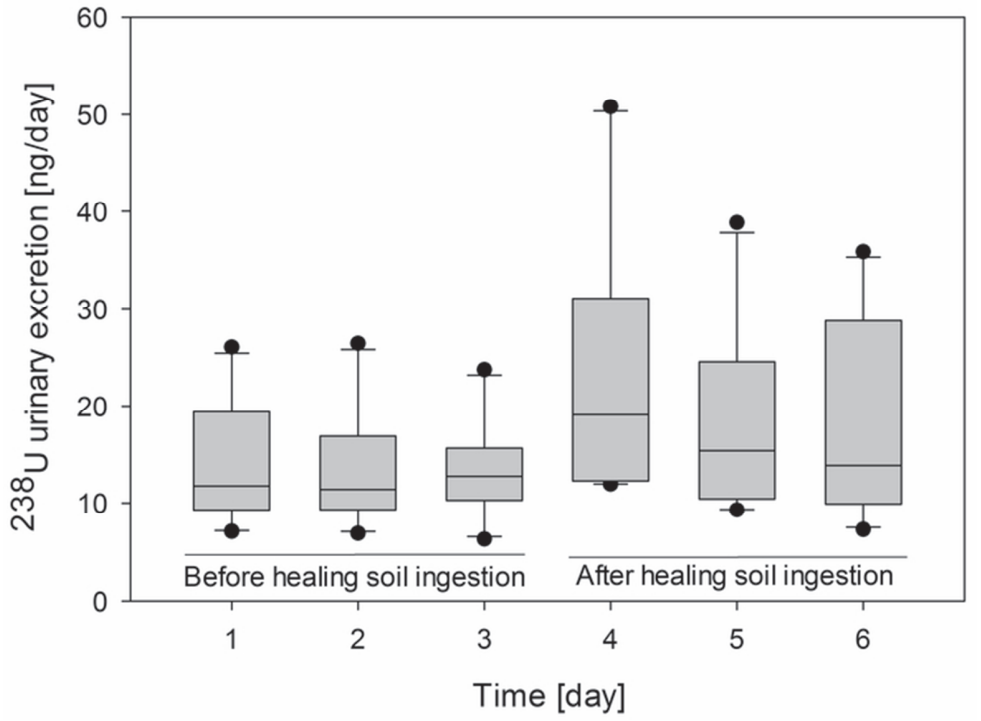

Figure 4. Daily urinary excretion of ^{238}U by ten volunteers. At the beginning of day 4, all volunteers ingested 20 g of healing soil, equal to 51.8 µg of ^{238}U. Box plot with following statistical values: 5th percentile (lower circle), 10th percentile (lower whiskers), 25th percentile (lower boundary of the box), median (solid line within the box), 75th (upper boundary of the box), 90th (upper whiskers) and 95th percentile (upper circle).
62x46mm (300 x 300 DPI)

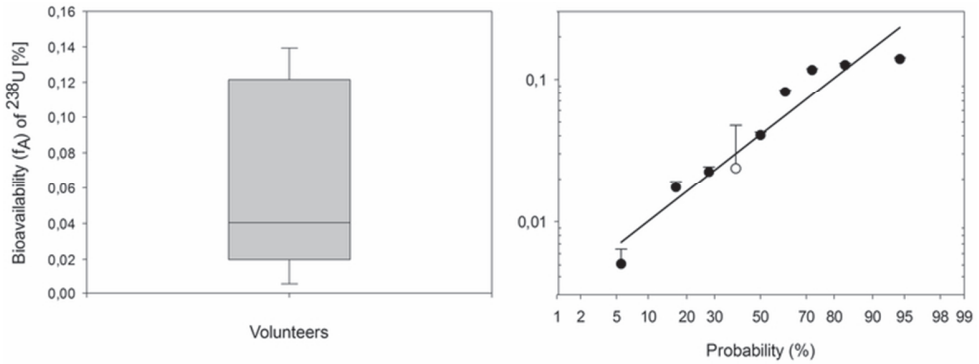

Figure 5. Bioavailability f_A of ^{238}U as experimentally derived on human volunteers ingesting healing soil (n=9). Left graph: box plot with following statistical values: 10th percentile (lower whisker), 25th percentile (lower boundary of the box), median (solid line within the box), 75th (upper boundary of the box), 90th (upper whisker). Right graph: probability plot, including experimental data with combined standard uncertainty (black dots with whiskers), Volunteer 1 with SD (open dot with whisker) and fitted curve (black line).
66x24mm (300 x 300 DPI)

SUPPORTING INFORMATION

Estimating the absorption of soil-derived uranium in humans

Stephan C. Träber, Vera Höllriegl, W.B. Li, Uta Czeslik, Werner Rühm, Uwe Oeh, Bernhard Michalke*

Section S.1:

For the analysis of ^{238}U an Element 1 ICP-SF-MS instrument (Thermo, Bremen, Germany) in low resolution mode was used. The samples of the solubility assay were diluted 1:2 with diluted nitric acid (5%, final concentration). The sample of the microwave-assisted digested healing soil was diluted 1:2 with diluted nitric acid (1%, final concentration). An internal standard solution (1 µg/L ^{193}Ir, final concentration) was added to each sample to correct for matrix interferences. For each sample three replicates were measured. Sample transport to nebulizer was realized by a peristaltic pump at a flow rate of 0.5 mL/min. Sample introduction to ICP-MS was performed by a Meinhard nebulizer fitting into a cyclone spray chamber. Uranium was determined at m/z = 238. RF power was 1200 W, nebulizer gas (Ar) was daily optimized and usually set to 0.8 L/min. Plasma gas: Ar, 15 L/min. Auxiliary gas: 0.8 L/min. runs: 3 patterns: 3, 12 samples per peak. The instrument was calibrated using a 7 point calibration between blank and 2000 ng/L. After ten measurements regularly three blank determinations and a control determination of a certified standard were performed. Calculation of results was carried out on a computerized lab-data management system, relating the sample measurements to calibration curves, blank determinations and control standards. The detection limit, calculated as blank + 3 times the blank standard deviation (SD) was 1.5 ng/L, the limit of quantification (LOQ) calculated as blank + 10 x SD was 4.5 ng/L.

Section S.2:

The determination of urinary ^{238}U was carried out according to the DIN EN ISO 17294-2 by inductively coupled plasma mass spectrometry on an Element 2 (Thermo Scientific).[1] For the determination of the ^{238}U concentration in urine, the calibration and data evaluation were carried out by applying the standard addition method. Thus, the elimination of disturbing influences was assured as far as possible by the usage of the same matrix as the real sample. For the standard addition six aliquots of one urine sample were diluted with 1.5% nitric acid in a 1:10 ratio. In five dilutions, uranium was added to yield concentrations from 0.005-0.025 µg/L. The resulting calibration curve was checked with the reference material SeroNorm Trace Elements Urine. Subsequently, the real samples were diluted with 1.5% nitric acid in a 1:10 ratio and measured several times. ^{103}Rh was used as the internal standard.

REFERENCES

1. DIN, Water quality - Application of inductively coupled plasma mass spectrometry (ICP-MS) - Part 2: Determination of 62 elements (ISO 17294-2:2003); German version EN ISO 17294-2:2004. In 2005-02; Vol. DIN EN ISO 17294-2:2005-02.

Environmental Science & Technology

Addition/Correction

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Correction to Estimating the Absorption of Soil-Derived Uranium in Humans

Stephan C. Träber, Vera Höllriegl,* W. B. Li, Uta Czeslik, Werner Rühm, Uwe Oeh, and Bernhard Michalke

Environ. Sci. Technol. **2014**, *48*, 14721−14727; DOI: 10.1021/es504171r

In the text, at page 14725, right column, line 19 and 20, the units are incorrectly given (μg/day instead of ng/day). The amended sentence is

"Thereby, the daily urinary excretion values of ^{238}U over 3 days before healing soil ingestion were 3.9 ng/day ±1.5 ng/day, 8.1 ng/day ±0.6 ng/day and 9.0 ng/day ±1.2 ng/day (mean ± SD)."

Published: January 20, 2015

DOI: 10.1021/acs.est.5b00177
Environ. Sci. Technol. 2015, 49, 1982−1982

9 Träber et al. 2015: Calculation of internal dose from ingested soil-derived uranium in humans: Application of a new method

The aim of the second part of this thesis was to estimate the internal dose for ingested and highly uranium-contaminated soils from former uranium mining sites by applying the previously developed method (see Chapter 7).

Two soils and additionally one fertilizer contaminated with uranium were investigated. The sample-specific bioaccessibilities and subsequently the corresponding bioavailabilities were determined. The bioavailability results were included into biokinetic models of uranium. Finally, the results were used to estimate the internal dose for a conceivable ingestion scenario.

The committed effective dose for a specific ingestion scenario is calculated by Eq. 1. Accordingly, the following information is needed:

- the average daily amount of the soil ingested during the exposure period (I_{soil}; see Chapter 9.1),
- the duration of the exposure period (ED; see Chapter 9.1),
- the average concentration of a radionuclide i in the ingested soil ($C_{soil,i}$; see Chapter 9.2),
- the effective dose coefficient of an ingested radionuclide i (DC_i; see Chapter 9.4).

9.1 Amount (I_{soil}) and duration (ED) of soil ingestion

For the exposure scenario explored here, a ingestion of 10 mg/day of soil (I_{soil}) lasting one year (ED) was assumed. Daily ingestion of 10 mg of soil is based on the average soil ingestion experimentally determined in a study on adults, aged between 22 and 45 years (Stanek III et al. 1997). In comparison, soil ingestion of children is higher and is estimated to vary from 26 mg/day to 100 mg/day, due to hand-to-mouth, outdoor and other activities (van Wijnen et al. 1990; Xue et al. 2007; Stanek III et al. 2012; UNSCEAR 2013). For this exposure scenario, the entire daily ingested amount of soil was assumed to be uranium-contaminated soil. While this assumption seems to be a worst-case scenario, it should kept in mind that uranium mining can actually take place near inhabited regions. As an example, the E1 sample was from a heap of a former uranium mining site near Dresden, Germany. Since mining and milling processes are accompanied by the formation of dust, the assumed ingestion of 10 mg/day of soils over one year might even be a realistic rather than a worst-case scenario.

9.2 Concentration ($C_{soil,i}$) of uranium in the samples

Two original uranium-contaminated soil samples were used for the present thesis. Note that no soil samples artificially spiked with uranium were used, to reflect the original characteristics of uranium-contaminated soils resulting from mining and milling processes and to describe a realistic scenario. One sample named "Gauern" was taken at a former uranium mining site in the eastern part of Thuringia, Germany. The second soil sample named "E1" was taken from a heap of a former uranium mining site near Dresden, Germany. Additionally, one phosphate fertilizer named "Fertilizer" was investigated, since phosphate fertilizers are known to be often contaminated by uranium and therefore agriculture activities are the main source of uranium contamination of cultivated soils (Schnug and Lottermoser 2013).

The concentrations of ^{238}U of the three samples Gauern, E1, and Fertilizer were determined by ICP-MS after a microwave assisted acid digestion. Uranium concentrations of the soil samples Gauern, E1, and Fertilizer were 553 ± 9 mg/kg, 456 ± 3 mg/kg, and 23.3 ± 0.5 mg/kg (mean ± SD), respectively. Concerning the two soil samples Gauern and E1, this is an increase of about two orders of magnitude compared to the average concentration of uranium in soils which is only about 3 mg/kg (Bleise et al. 2003). Therefore the samples are considered as highly uranium-contaminated.

Based on the experimentally determined concentrations of ^{238}U of the three samples, the concentrations of ^{234}U and ^{235}U were deduced from literature data on typical isotopic ratios (Berglund and Wieser 2011). Therefore, the average concentrations of all three radionuclides (^{234}U, ^{235}U, and ^{238}U) of the ingested soils were available ($C_{soil,i}$).

The concentrations of ^{234}U and ^{235}U could be derived from literature data since all samples, while physically and chemically processed, still kept the natural abundance of the uranium isotopes.

9.3 Determination of bioaccessibility (DF) and bioavailability (f_A)

Like for the original healing soil sample (see Chapter 7.1) the bioaccessibilities for the three uranium-contaminated samples were determined in accordance to the German method DIN 19738. The bioaccessibilities of ^{238}U of the healing soil was about 10%, whereas the bioaccessibilities of ^{238}U of the three samples Gauern, E1, and Fertilizer were about 53% ± 3%, 33% ± 3%, and 24% ± 3% (mean ± SD), respectively.

The high bioaccessibility of the two soils from uranium mining sites might be due to the intensive chemical (leaching) processing, which had been applied to maximize the dissolution of uranium from soils. Another reason for an increased bioaccessibility might be the mechanical processing (milling) of theses soils. Thereby the average grain size of the soil particles is reduced. Thus, the surface area of the particles is increased which results in a higher accessibility of uranium for dissolution and therefore in an increased bioaccessibility (Jovanovic et al. 2012). As mentioned the examined soil

samples originated from uranium mining sites and were not artificially spiked with uranium. Therefore, the results plausibly suggest a general elevated bioaccessibility of uranium from processed soils, as compared to natural soils.

The experimentally determined bioaccessibilities (DF) and the previously determined f_A^{sol} factor were applied to Eq. 7 to calculate the bioavailabilities (f_A) of each investigated soil. Hence, for the samples Gauern, E1, and Fertilizer, bioavailabilities of 0.28, 0.18, and 0.13% (GM) were determined. The corresponding 2.5th percentile and 97.5th percentile of the bioavailability for these samples were determined to be 0.03 to 2.34%, 0.02 to 1.48%, and 0.01 to 1.07%, respectively.

9.4 Committed effective dose coefficients (DC_i)

Based on the calculated bioavailabilities of the three samples Gauern, E1, and Fertilizer (see Chapter 9.3), the committed effective dose coefficients (DC_i) were calculated for all three samples by Eq. 2 as explained in Chapter 5.5. For each sample, all three isotopes ^{234}U, ^{235}U, ^{238}U, and their radiologically relevant progeny were taken into account. For naturally occurring uranium in soils almost half of the activity accounts for ^{238}U (48.6%). The remaining sum of activity of naturally occurring uranium accounts for ^{234}U (49.2%) and ^{235}U (2.2%) (Mkandawire 2013).

9.5 Committed effective dose

The committed effective doses were calculated for all three samples for the same exposure scenario. Therefore, resulting committed effective doses only differ because of two parameters; the average concentration of a radionuclide i in the ingested soil ($C_{soil,i}$) and the committed effective dose coefficient of an ingested radionuclide i (DC_i). Among the three samples, Gauern is characterized by the highest concentration of uranium and also by the highest committed effective dose coefficient, which resulted from the highest bioaccessibility among all three samples. Consequently, the highest committed effective dose was calculated for the sample Gauern and therefore only this result is discussed below.

For the Gauern sample a committed effective dose of about 0.6 µSv (GM) ranging from 0.3 (2.5th percentile) to 3.0 µSv (97.5th percentile) was calculated, based on the assumed exposure scenario. This resulting committed effective dose, here presented as geometric mean and 97.5th percentile, can be classified as very low. Accordingly, this also applies for the committed effective doses deduced for the remaining two samples.

In comparison, the effective dose from the average daily intake of 1.25 µg of uranium by food and drinking water is estimated to be about 0.5 µSv/a for adults, based on a bioavailability of 2% (UNSCEAR 2000). This is in good agreement even with the 97.5th percentile of the by this study assumed scenario, which is 3.0 µSv/a. This 6-fold increase is mainly due to the different uranium intakes. For the exposure scenario considered here, a daily ingestion of 10 mg of the Gauern soil for

one year was assumed which equals a daily ingestion of 5.57 µg of uranium. This is about five times higher compared to the daily intake of 1.25 µg uranium from food and drinking. In addition, in comparison to the 2% bioavailability which is assumed by the ICRP, the 97.5th percentile was calculated based on a bioavailability of about 2.34%. Finally, the estimated effective dose for the daily intake of 1.25 µg of uranium was rounded to only one significant figure, which further increases the deviation.

The calculated annual dose of 3.0 µSv/a (97.5th percentile) is about three orders of magnitude lower than the annual effective dose by which the public is exposed on average (2.4 mSv), due to natural radiation (UNSCEAR 2008).

The study is described in detail in Träber et al. 2015 (see Chapter 10).

10 Träber et al. 2015

Calculation of internal dose from ingested soil-derived uranium in humans: Application of a new method

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Radiation and Environmental Biophysics (2015) 54: 265.

DOI: 10.1007/s00411-015-0602-9

Radiation and Environmental Biophysics

Calculation of internal dose from ingested soil-derived uranium in humans - Application of a new method

--Manuscript Draft--

Manuscript Number:	REBS-D-14-00151R1
Full Title:	Calculation of internal dose from ingested soil-derived uranium in humans - Application of a new method
Article Type:	Original Paper
Keywords:	Uranium; biokinetic modeling; internal dosimetry; humans; soil
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Funding Information:	German Federal Ministry of Education and Research (BMBF) (02NUK015B) — Stephan Christian Träber
Abstract:	The aim of the present study was to determine the internal dose in humans after the ingestion of soil highly contaminated with uranium. Therefore, an in vitro solubility assay was performed to estimate the bioaccessibility of uranium for two types of soil. Based on the results, the corresponding bioavailabilities were assessed by using a recently published method. Finally, these bioavailability data were used together with the biokinetic model of uranium to assess the internal doses for a hypothetical but realistic scenario characterized by a daily ingestion of 10 mg of soil over 1 year. The investigated soil samples were from two former uranium mining sites of Germany with 238U concentrations of about 460 mg/kg and 550 mg/kg. For these soils, the bioavailabilities of 238U were quantified as 0.18% and 0.28% (geometric mean) with 2.5th percentiles of 0.02% and 0.03%, and 97.5th percentiles of 1.48% and 2.34%, respectively. The corresponding calculated annual committed effective doses for the assumed scenario were 0.4 µSv and 0.6 µSv (GM) with 2.5th percentiles of 0.2 µSv and 0.3 µSv, and 97.5th percentiles of 1.6 µSv and 3.0 µSv, respectively. These annual committed effective doses are similar to those from natural uranium intake by food and drinking water, which is estimated to be 0.5 µSv. Based on the present experimental data and the selected ingestion scenario, the investigated soils - although highly contaminated with uranium - are not expected to pose any major health risk to humans related to radiation.

Calculation of internal dose from ingested soil-derived uranium in humans – Application of a new method

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KEYWORDS

Uranium; biokinetic modeling; internal dosimetry; humans; soil

CONCISE AND INFORMATIVE TITLE

Internal dose from ingested soil-derived uranium in humans

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ABSTRACT

The aim of the present study was to determine the internal dose in humans after the ingestion of soil highly contaminated with uranium. Therefore, an *in vitro* solubility assay was performed to estimate the bioaccessibility of uranium for two types of soil. Based on the results, the corresponding bioavailabilities were assessed by using a recently published method. Finally, these bioavailability data were used together with the biokinetic model of uranium to assess the internal doses for a hypothetical but realistic scenario characterized by a daily ingestion of 10 mg of soil over 1 year. The investigated soil samples were from two former uranium mining sites of Germany with ^{238}U concentrations of about 460 mg/kg and 550 mg/kg. For these soils, the bioavailabilities of ^{238}U were quantified as 0.18% and 0.28% (geometric mean) with 2.5th percentiles of 0.02% and 0.03%, and 97.5th percentiles of 1.48% and 2.34%, respectively. The corresponding calculated annual committed effective doses for the assumed scenario were 0.4 µSv and 0.6 µSv (GM) with 2.5th percentiles of 0.2 µSv and 0.3 µSv, and 97.5th percentiles of 1.6 µSv and 3.0 µSv, respectively. These annual committed effective doses are similar to those from natural uranium intake by food and drinking water, which is estimated to be 0.5 µSv. Based on the present experimental data and the selected ingestion scenario, the investigated soils - although highly contaminated with uranium - are not expected to pose any major health risk to humans related to radiation.

INTRODUCTION

Uranium is the heaviest naturally occurring element. It occurs ubiquitously in soils at concentrations of about 3 mg/kg (Bleise et al. 2003) and comprises three isotopes with percentages by mole fraction of 0.0054% (^{234}U), 0.72% (^{235}U) and 99.27% (^{238}U) (Berglund and Wieser 2011). All three isotopes are alpha emitters with half-lives of 245,500 years (^{234}U), 704,000,000 years (^{235}U) and 4,468,000,000 years (^{238}U) (ICRP 2008), respectively. The corresponding percentages by radioactivity of naturally occurring uranium are about 49.2% (^{234}U), 2.2% (^{235}U) and 48.6% (^{238}U), respectively (Mkandawire 2013).

Elevated uranium concentrations in soils are mostly of anthropogenic nature. In agriculture, for example, uranium-contaminated phosphate fertilizers are the main source of uranium contamination of soils. About 14,000 tons of uranium were deposited between 1951 and 2011 on agricultural land in Germany, which equals about 1 kg of uranium per hectare (Schnug and Lottermoser 2013). Uranium mining is another source of potential uranium contamination of soils (Brugge and Buchner 2011). The global uranium production has increased from about 36,000 tons in 2002 to 60,000 tons in 2013, whereby the top five uranium producers in 2013 were Kazakhstan, Canada, Australia, Niger, and Namibia (WNA 2014). Even for remediated former uranium mining sites elevated uranium concentrations are reported, since these sites are re-contaminated due to natural processes like capillary rise of contaminated ground water (Langella et al. 2014). A third notable source of environmental uranium contamination is by the military use of depleted uranium (DU) penetrators, leading to DU dust formation after impact (Bleise et al. 2003).

The unintended ingestion of small amounts of soils by humans via various routes is observed all over the world (Abrahams 2002, Sing and Sing 2010) Thereby, the average ingestion rate of soil by adults is assumed to be about 10 mg/day (Stanek et al. 1997). Since uranium ubiquitously occurs in soil, soil ingestion is always accompanied by the ingestion of uranium. To estimate the resulting internal dose, the bioavailability (f_1) of soil-derived uranium has to be assessed. The bioavailability (f_1) is the fraction of uranium which is absorbed from the human alimentary tract into the circulatory system. In practice, the bioavailability of uranium from highly contaminated soils is not directly assessed by human soil ingestion studies, but is indirectly assessed by *in vitro* solubility assays. However, by these assays only the bioaccessibility (DF) of soil-derived uranium can directly be estimated. The bioaccessibility (DF) quantifies the fraction of soil-derived uranium in human alimentary tract, which is soluble and therefore potentially

available for absorption. Consequently, the bioavailability is usually estimated based on bioaccessibility data. However, there are different solubility assays and different estimation methods described in the literature which can lead to varying estimated bioavailabilities for one particular soil of up to three orders of magnitude (Träber et al. 2014). In response to that, Träber et al. 2014 recently reported a solubility assay-specific factor (f_A^{sol}) (Fig. 1), which was based on a human study and by which more reliable data on the bioavailability of soil-derived uranium can be deduced from the bioaccessibility data. Using this method, only a solubility assay has to be performed e.g. for a highly uranium-contaminated soil to receive more reliable data on its bioavailability.

The aim of the present study was to estimate the internal dose in humans after a potential ingestion of soils highly contaminated with uranium by applying the recently published method (Träber et al. 2014). Two types of soil highly contaminated with uranium and additionally one pure fertilizer were investigated. Thereby more reliable data on the uptake of uranium in humans were obtained from highly contaminated soils than previously available. Consequently, more reliable data on the internal dose enhancement can be obtained for the risk assessment of potential ingestion scenarios.

MATERIALS AND METHODS

Samples

In the present study, two types of soil and additionally one fertilizer were analyzed. The soil sample "Gauern" was selected from a former uranium mining site in the east of Thuringia, Germany. It was taken from the surface (0-10 cm) of a hot spot, a supposed former ore terminal, near the former heap "Gauernhalde". The soil sample "E1" was taken from a heap of a former uranium mining site (Coschütz/Gittersee) near Dresden in Saxony, Germany. Both soil samples were sieved at 2 mm. The fertilizer "Blaukorn NovaTec" (COMPO Gesellschaft GmbH & Co. KG, Germany), with an indicated mass fraction of P_2O_5 of 7%, was bought at retail.

For the analyses of total soil-derived ^{238}U 250.0 mg of each soil was mixed with 1.5 mL of HNO_3 (65%), 4.5 mL of HCl (30%) and 1 mL HF (40%). The mixture was digested in a Multiwave 3000 microwave device (Anton Paar, Austria); power: ramp for 5 min up to 1400 W, hold for 30 min at 1400 W and cooling down for 20 min. Thereafter 6 mL of H_3BO_3 were added to neutralize free fluorides and the solution was placed a second time in the Multiwave system; power: ramp for 5 min up to 1400 W, hold for 15 min and cooling down for 15 min. For the analyses of total fertilizer-derived ^{238}U 118.1 mg fertilizer was mixed with 1.0 mL of HNO_3 (65%) and heated at 160 °C overnight under pressure (Schramel et al. 1980). All solutions were stored at 4 °C until measurement of ^{238}U by using inductively coupled plasma mass spectrometry (ICP-MS, see below).

Determination of bioaccessibility (DF) and bioavailability (f_A)

The bioaccessibility (DF) of the soil-derived ^{238}U and of the fertilizer-derived ^{238}U in the relevant part of the alimentary tract, which is the intestine (Frelon et al. 2007), was estimated by an *in vitro* solubility assay. In accordance to the previous study, the same *in vitro* solubility assay based on the German DIN 19738 (DIN 2000) was performed; the assay is described in detail elsewhere (Träber et al. 2014).

Briefly, 2 g of soil or fertilizer was incubated under physiological conditions, using an artificial gastric fluid with a pH of 2 followed by the addition of an artificial intestinal fluid with a pH of 7.5. After 8 h of incubation an aliquot was withdrawn, centrifuged at 5000 rpm (Hettich Universal 32R) and filtered at 0.2 µm (sterile filter, Millipore). All experiments were repeated three times independently. The solutions were stored at 4 °C until measurement of ^{238}U using ICP-MS (see below).

The bioaccessibility (DF) was calculated as the percentage of soluble ^{238}U based on the total concentration of soil-derived ^{238}U or fertilizer-derived ^{238}U.

The sample-specific bioavailabilities were calculated for the two soil samples and the fertilizer by the previously published relation Eq. (1) (Höllriegl et al. 2010).

$$f_A = f_A^{sol} DF \qquad (1)$$

Note that for the current study the bioavailability is denoted as f_A, since the notation of the bioavailability has changed by the International Commission on Radiological Protection (ICRP) from f_1 to f_A (ICRP 2006). DF was derived from the applied solubility assay whereas the f_A^{sol} factor was directly adopted from the previous work being 0.53% (geometric mean, GM) and ranging from 0.06% (2.5^{th} percentile) to 4.43% (97.5^{th} percentile) (Träber et al. 2014). The f_A^{sol} factor quantifies the fraction of bioaccessible uranium which is absorbed into the circulatory system. It is emphasized here again that the data on f_A^{sol} are based on human data.

Measurement of ^{238}U by ICP-MS

For the analysis of ^{238}U a NexIon ICP-MS instrument (Perkin-Elmer, Rodgau-Jügesheim, Germany) in standard mode was used. The samples of the solubility assay were diluted between 1:2 and 1:100 with diluted nitric acid (5%, final concentration). The samples of the microwave-assisted digested soils were diluted 1:2 with diluted nitric acid (3 %, final concentration). An internal standard solution (1 µg/L ^{193}Ir, final concentration) was added to each sample to correct for matrix interferences. For each sample three replicates were measured. Sample transport to nebulizer was realized by a peristaltic pump at a flow rate of 0.5 mL/min. Sample introduction to ICP-MS was performed by a Meinhard nebulizer fitting into a cyclone spray chamber. A uranium stock standard solution of 1 g/L purchased and certified by SPEX (USA) was used for calibration. Uranium was determined at m/z = 238. RF power was 1250 W, nebulizer gas (Ar) was daily optimized and usually set to 0.92 L/min. Plasma gas: Ar, 15 L/min. Auxiliary gas: 0.8 L/min, dwell time 300 ms, 3 readings per replicate. The instrument was calibrated using a 7-point calibration between blank and 2000 ng/L. After ten measurements regularly three blank determinations and a control determination of a certified standard were performed. Calculation of results was carried out on a computerized lab-data management system, relating the sample measurements to calibration curves, blank determinations and control

standards. The detection limit, calculated as blank + 3 times the blank standard deviation (SD) was 1.5 ng/L, the limit of quantification (LOQ) calculated as blank + 10 x SD was 4.5 ng/L.

Biokinetic model

To model the biokinetics of ingested soil-derived ^{238}U, the systemic model for uranium (ICRP 1995a) and the human alimentary tract model (HATM) (ICRP 2006) were coupled. These two models were connected by the alimentary tract transfer rate, which was quantified in the present study for two soils and one fertilizer. For internal dose assessment of ^{238}U, the radiologically relevant progeny ^{234}Th, ^{234}Pa, and ^{234m}Pa were also taken into account (ICRP 1979). Similar to the parent ^{238}U, the systemic models of thorium, protactinium and protactinium (meta) as decay products, which were published by ICRP in Publication 71 in Annex C (ICRP 1995b), were also coupled to the human alimentary tract model. Thereby, each systemic model of a progeny was connected to one human alimentary tract model. The corresponding alimentary tract transfer rates were adopted from ICRP Publication 100 (ICRP 2006). The resulting four ingestion models (Fig. 2) were interconnected in accordance with the ^{238}U decay series by the corresponding decay constants (ICRP 2008).

As the biokinetic models of different radionuclides are independent, their transfer rates and especially their compartment structures are not necessarily identical. For a proper interconnection of biokinetic models with varying compartment structures, like the biokinetic model of uranium and the biokinetic model of thorium as a progeny, two approaches are proposed by ICRP (ICRP 1995b). By the first approach the biokinetics of a radionuclide of a chain are calculated by using the biokinetic descriptions given by ICRP (ICRP 1995b). Thereafter, necessary, non-existing compartments representing source regions receive a portion of nuclear transformations which are partitioned by mass fraction from the so-called “Other” tissue. This “Other” tissue represents all systemic tissues, which are not explicitly specified in a biokinetic model. In the present work, however, the second approach was applied because this approach will be adopted by the forthcoming ICRP Publications on “Occupational Intakes of Radionuclides, Part 1”. By this approach, prior to biokinetic modeling, the biokinetic model of a radionuclide of a chain is expanded for the necessary, non-existing compartments and transfer rates, respectively. In the present work, only the biokinetic model for uranium had to be expanded for the compartments gonads, cortical marrow, and trabecular marrow, to match with its progeny biokinetic model of thorium. The structures and transfer rates of the protactinium

model and the protactinium (meta) model were assigned to the biokinetic model of thorium (ICRP 1995a, ICRP 1995b).

As an example, for the biokinetic model of ^{238}U the transfer rate from the blood compartment to the newly created cortical marrow compartment is calculated from the corresponding transfer rate of the so-called "Other" tissue compartment by its mass-fraction. The transfer rate from the blood compartment to the "Other" tissue compartment is reduced accordingly. Since the uranium model contains three soft tissue compartments with different transfer rates, three new cortical marrow compartments were integrated into the uranium model. As a part of a decay series, all three cortical marrow compartments were connected to the single cortical marrow compartment of thorium by their decay constant. Finally, nine additional compartments were integrated into the biokinetic model of the parent radionuclide ^{238}U.

Beside the transfer rates of the systemic model, the transfer rates for "total diet" of the HATM model were adopted from ICRP (ICRP 2006) for male and female, which resulted in two sex-specific biokinetic models for ^{238}U. In addition, sex-specific biokinetic models for ^{234}U and ^{235}U with their corresponding progeny were implemented. Thereby the radiologically relevant progeny of ^{235}U is only ^{231}Th, whereas ^{234}U has no progeny with relevant dosimetric contribution (ICRP 1979).

With these six models, the sex-specific biokinetics of the three naturally occurring isotopes of uranium and their progeny are described by a system of first-order linear ordinary differential equations, which were numerically solved by using the commercially available software SAAM II (Barrett et al. 1998) (The Epsilon Group VA, USA). For internal dose assessment of adults, the integrated activity of the ingested uranium and its progeny in all compartments over a 50-year period was calculated.

Calculation of the committed effective dose

The committed equivalent dose (H_T) and the committed effective dose (E) were calculated based on the time-integrated activity ($\tilde{A}$) in so-called source regions (r_S) and radiation-weighted factors (S_w) and the appropriate tissue-weighting factors (w_T) (Bolch et al. 2009, ICRP 1989). In the present calculation, only adults were considered for the internal dose calculation because only the f_A^{sol} value for adults was established (Träber et al. 2014).

The committed equivalent dose ($H_{T,sex}$) for female and male was calculated by Eq. (2) as the sum of a radionuclide and its progeny (N):

$$H_{T,sex} = \sum_N \sum_{r_S} \tilde{A}(r_S, T_{50}, sex, N) S_w(r_T \leftarrow r_S, sex, N) \quad (2)$$

Where $\tilde{A}(r_S, T_{50}, sex, N)$ is the cumulated activity ($\tilde{A}$) of a radionuclide or progeny (N) in a source region (r_S) over 50 years (T_{50}), which is sex-specific (sex); $\tilde{A}$ was calculated by the biokinetic models as described above.

$S_w(r_T \leftarrow r_S, sex, N)$ is the radiation-weighted S factor calculated for a radionuclide or progeny for both sexes (sex) by Eq. (3).

$$S_w(r_T \leftarrow r_S, sex, N) = \sum_R w_R S(r_T \leftarrow r_S, E_R, sex, N) \quad (3)$$

Where w_R is the radiation weighting factor and $S(r_T \leftarrow r_S, E_R, sex, N)$ is the specific energy of a radiation type R (E_R), which is absorbed in a target organ (r_T) emitted from a source region (r_S), per nuclear transformation of a radionuclide or its progeny (N). S_w was calculated as the sum of all radiation types per nuclear transformation of a radionuclide or its progeny (N) by using the SEECAL program (Oak Ridge National Laboratory, Oak Ridge, TN, USA). Since S_w factors are not yet available for a few organs like the prostate, the "splitting rule" in the treatment for remainder tissues was applied in the current work as recommended in ICRP Publication 60 (ICRP 1991). Accordingly, the appropriate radiation weighting factors (w_R) and tissue weighting factors (w_T) were adopted from ICRP Publication 60 (ICRP 1991).

Finally the committed effective dose (E) was calculated by Eq. (4) by averaging the effective dose of male and female (ICRP 2007):

$$E = \sum_T w_T \left(\frac{H_{T,male} + H_{T,female}}{2}\right) \quad (4)$$

Dose calculation for ingestion scenarios

By the introduced committed effective dose calculation (see above), sample-specific ingestion effective dose coefficients were assessed by adopting the corresponding sample-specific alimentary tract transfer rates to the biokinetic models and assuming a single uptake of 1 Bq of ^{234}U, ^{235}U or ^{238}U.

Based on the sample-specific ingestion effective dose coefficients the committed effective dose can be simply obtained for different ingestion scenarios by Eq. (5) (Simon 1998).

$$D_{soil} = \sum_i C_{soil,i} \times I_{soil} \times ED \times DC_i \quad (5)$$

D_{soil} committed effective dose from soil-derived radionuclides (Sv)

$C_{soil,i}$ average concentration of radionuclide *i* in soil (Bq/g)

I_{soil} average daily ingestion of soil during the exposure period (g/day)

ED exposure duration (d)

DC_i ingestion effective dose coefficients of radionuclide *i* (Sv/Bq)

RESULTS AND DISCUSSION

Concentration of ^{238}U in samples

The concentration of ^{238}U in the three samples "Gauern", "E1" and "Fertilizer" was determined (see Table 1). The soil samples "Gauern" and "E1" revealed elevated concentrations for ^{238}U of about two orders of magnitude compared to the average concentration of ^{238}U in soils of about 3 mg/kg (Bleise et al. 2003).

Bioavailability (f_A) of soil and fertilizer samples

To calculate the sample-specific f_A values for ^{238}U, first the bioaccessibilities (DF) for ^{238}U of all three samples were determined by the mentioned solubility assay. The results are given in Fig. 3 based on the corresponding total concentrations of ^{238}U (Table 1).

The sample "Fertilizer" showed the lowest bioaccessibility for ^{238}U of about 24%, while the two soil samples revealed higher bioaccessibilities of about 33% and 53%, respectively. In comparison, the bioaccessibility of the previously examined healing soil with a uranium concentration of about 2.6 mg/kg was below 10% (Träber et al. 2014). The different bioaccessibilities among the healing soil and the here investigated soil samples might be a result of the different mining processes. Whereas healing soil is a pure natural product, soils from uranium mining sites are intensively chemically processed (leaching) to dissolve more uranium. This might also increase the bioaccessibility of uranium of these processed soils. Apart from that, different particle sizes of soil samples may also explain different bioaccessibilities; for samples with similar uranium concentrations, smaller particle sizes are accompanied by a larger total surface by which more uranium is accessible for dissolution (Jovanovic et al. 2012).

Based on the determined bioaccessibilities (DF), the sample-specific bioavailabilities (f_A) were calculated by Eq. (1). The results are given in Table 2 and reveal bioavailabilities between 0.13% and 0.28% (GM). These data are similar to ICRP data, by which a bioavailability of uranium of 0.2% for relatively insoluble compounds is assumed (ICRP 2006). In Table 2 the 2.5th percentile and the 97.5th percentile of the bioavailabilities are also given to cover a 95% confidence interval.

Committed effective doses

The committed effective dose was estimated by Eq. (5) for all three samples, for a conceivable exposure scenario by which 10 mg of soil or fertilizer are daily ingested over one year. For that, besides the average daily ingestion (I_{soil}) of soil or fertilizer and the exposure duration (ED), the sample-specific ingestion dose coefficients (DC_i) of the radionuclides ^{234}U, ^{235}U, and ^{238}U are needed. Therefore, the sample-specific alimentary tract transfer rates (Table 3) were calculated from the sample-specific bioavailability data (Table 2) (ICRP 1997) and applied to the used biokinetic models. The resulting sample-specific ingestion effective dose coefficients (DC_i) of the radionuclides ^{234}U, ^{235}U, and ^{238}U are given in Table 4. For the dose calculation using Eq. 5, the data on the sample-specific average concentrations ($c_{soil,i}$) of the radionuclides ^{234}U, ^{235}U and ^{238}U are also needed. The sample-specific activities of ^{238}U are based on our measurements (Table 1) whereas the proportional sample-specific activities of ^{234}U and ^{235}U are based on literature data (Berglund and Wieser 2011). The resulting sample-specific average concentrations ($c_{soil,i}$) of the radionuclides ^{234}U, ^{235}U and ^{238}U are given in Table 5.

Our assumption of 10 mg of soil or fertilizer that are daily ingested over 1 year is assumed to be a realistic worst case scenario. The investigated uranium-contaminated soil sample E1, for example, was from a heap of a former uranium mining site nearby the city of Dresden, Germany. In the worst case scenario, the whole amount of daily ingested soil or fertilizer (10 mg) is assumed to be from a uranium or phosphate mining site.

The sum of the calculated sample-specific annual committed effective doses of the isotopes ^{234}U, ^{235}U and ^{238}U and their radiologically relevant progeny are given in Table 6. The soil sample “Gauern” revealed the highest total concentration of uranium (553 mg/kg, Table 1) as well as the highest bioaccessibility of uranium (53%, Fig. 3) and therefore the highest annual committed effective dose among all samples, with about 0.6 µSv (GM) ranging from 0.3 µSv (2.5th percentile) to 3.0 µSv (97.5th percentile). Besides, a daily ingestion of 10 mg of the soil sample “Gauern” would equal a daily ingestion of 5.57 µg of uranium. These results are similar to those from the daily intake of 1.25 µg uranium by food and drinking water, which is estimated to be 0.5 µSv for adults (UNSCEAR 2000). Furthermore, the calculated annual committed effective dose of about 3.0 µSv (97.5th percentile) for the assumed scenario is about three orders of magnitude lower than the average annual natural background effective dose of 2.4 mSv (UNSCEAR 2008).

The present results are not appropriate to be applied to children who are expected to exhibit a two- to tenfold increased soil ingestion rate compared to adults (Stanek et al. 2012, UNSCEAR 2013). As reported by ICRP (ICRP

1995a), the committed effective dose coefficients of uranium for children are 1.5 to 2.7 times greater than that of adults; this increase is based on an assumed bioavailability of uranium of 2% for adults and children. Moreover, a 2.4-fold increase of the bioavailability of uranium can be concluded from recent data for children aged between 1 and 7 years compared to adults (Chen et al. 2011). Therefore, an increased effective dose of about one to two orders of magnitude might be considered for children.

Quality assurance of dose calculations

The calculated effective dose coefficients of the ingested naturally occurring isotopes ^{234}U, ^{235}U and ^{238}U, and their radiologically relevant progeny, were compared with the effective dose coefficients given by ICRP (ICRP 1995a) (Table 7), based on an exemplary intake of 1 Bq of ^{234}U, ^{235}U or ^{238}U and an alimentary tract transfer factor for uranium of 2% (ICRP 1995a). As reported by ICRP, the difference of both approaches for treatment of decay products in the dose calculation are less than 5% (ICRP 1995b). From Table 7 it is evident that the effective doses calculated in the present work are not more than 4% different, for all three isotopes, from those given by ICRP. It is implied that the present method of dose calculation is consistent with that proposed by ICRP.

CONCLUSION

Based on the experimental data and the assumption of a daily soil or fertilizer ingestion of 10 mg over 1 year, neither the uranium-contaminated fertilizer nor the investigated highly uranium-contaminated soils are expected to pose any major health risk to humans related to radiation. It is worth to note that the present results are based on values for the f_A^{sol} factor, which were derived from a study on healthy volunteers aged between 22 and 55 years (Träber et al. 2014). Therefore, the low health risk refers only to adults and not to children who are expected to exhibit an increased soil ingestion rate and a higher bioavailability for uranium as well as a higher committed effective dose coefficient.

ACKNOWLEDGEMENTS

This work was supported by the German Federal Ministry of Education and Research (BMBF) with the contract number 02NUK015B. The contents are solely the responsibility of the authors.

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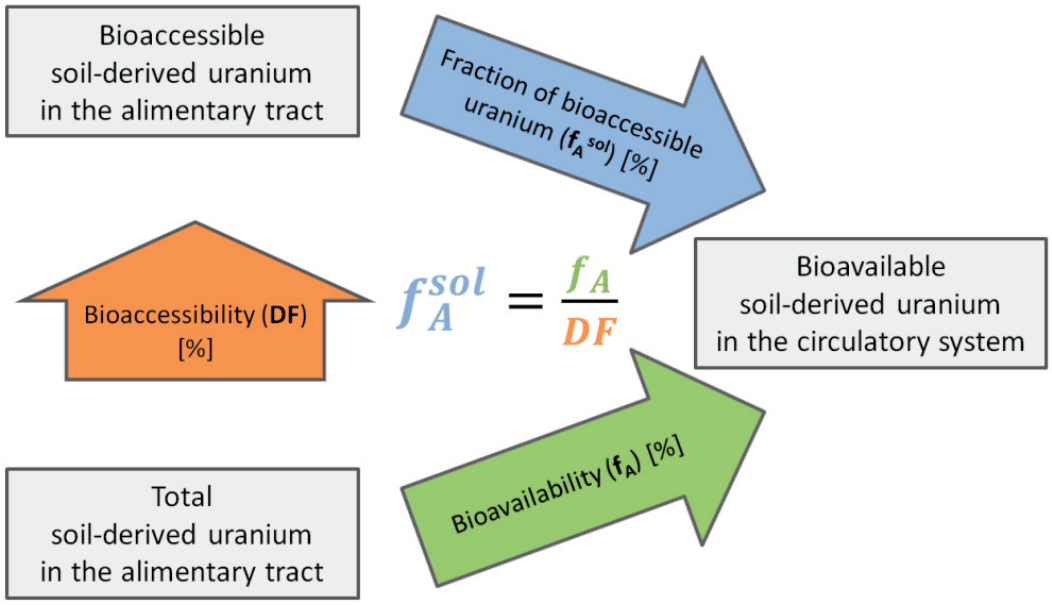

Fig 1 Scheme of the relation of bioavailability (f_A), bioaccessibility (DF) and the f_A^{sol} factor. The figure is reprinted (adapted) with permission from Träber SC, Höllriegl V, Li WB, Czeslik U, Rühm W, Oeh U, Michalke B (2014). Estimating the Absorption of Soil-Derived Uranium in Humans. Environ Sci Technol 48 (24):14721-14727. Copyright 2015 American Chemical Society

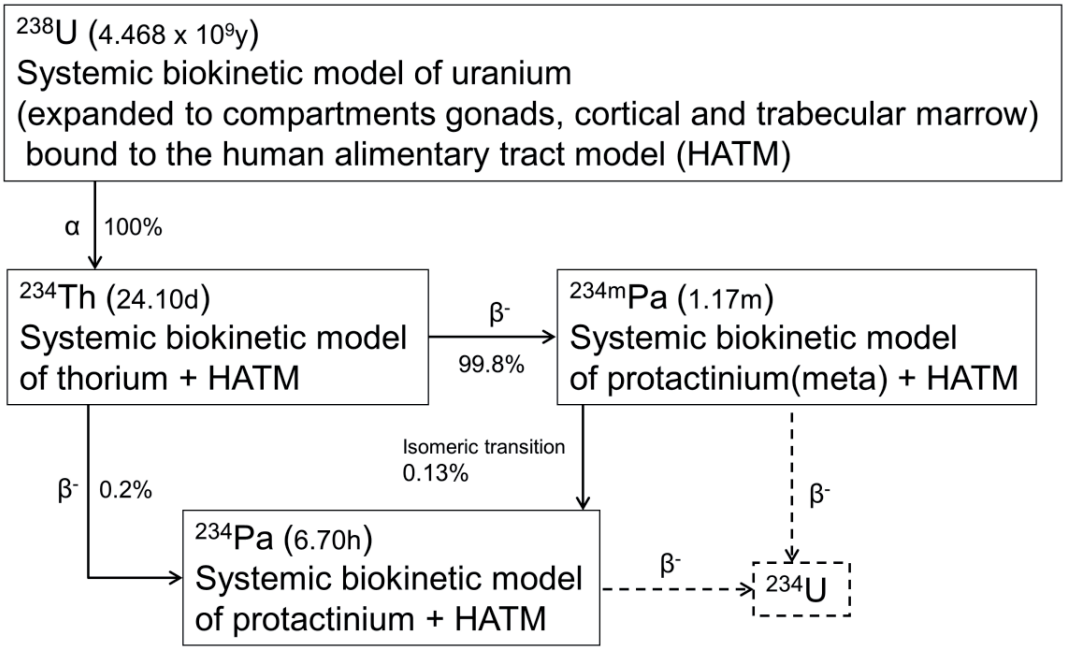

Fig 2 Interconnection of the biokinetic models (for ingestion) of uranium and its radiologically relevant progeny ^{234}Th, ^{234}mPa and ^{234}Pa (half-lives given in brackets)

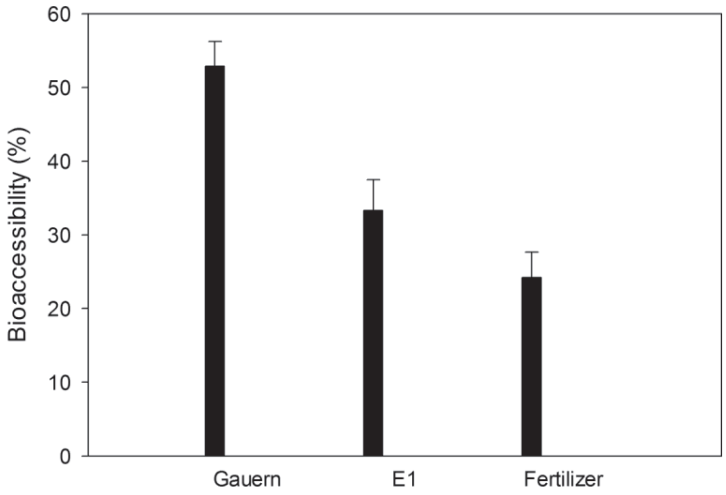

Fig 3 Bioaccessibility (DF) of soil-derived (Gauern, E1) and fertilizer-derived (Fertilizer) ^{238}U in artificial gastrointestinal fluid (mean ± SD, n=3)

Table 1 Concentration of ^{238}U in soil samples (Gauern, E1) and fertilizer

	Total concentration of ^{238}U (mean ± SD) in mg/kg
Gauern	553 ± 9
E1	456 ± 3
Fertilizer	23.3 ± 0.5

SD - standard deviation of three measurements per sample

Table 2 Sample-specific bioavailabilities f_A of ^{238}U

	GM (%)[A]	$P_{2.5th}$ (%)[B]	$P_{97.5th}$ (%)[C]
Gauern	0.28	0.03	2.34
E1	0.18	0.02	1.48
Fertilizer	0.13	0.01	1.07

[A]Geometric mean, [B]2.5th percentile, [C]97.5th percentile

Table 3 Sample-specific alimentary tract transfer rates

	GM $(d^{-1})^A$	$P_{2.5th}$ $(d^{-1})^B$	$P_{97.5th}$ $(d^{-1})^C$
Gauern	1.69×10^{-2}	1.90×10^{-3}	1.44×10^{-1}
E1	1.06×10^{-2}	1.20×10^{-3}	8.99×10^{-2}
Fertilizer	7.70×10^{-3}	8.70×10^{-4}	6.49×10^{-2}

[A]Geometric mean, [B]2.5th percentile, [C]97.5th percentile

Table 4 Sample-specific committed effective dose coefficients (ingestion)

	GM (Sv/Bq)[A]	$P_{2.5th}$ (Sv/Bq)[B]	$P_{97.5th}$ (Sv/Bq)[C]
Gauern			
^{234}U	1.21×10^{-8}	6.30×10^{-9}	6.02×10^{-8}
^{235}U	1.15×10^{-8}	6.18×10^{-9}	5.61×10^{-8}
^{238}U	1.09×10^{-8}	5.73×10^{-9}	5.41×10^{-8}
E1			
^{234}U	9.68×10^{-9}	6.03×10^{-9}	4.00×10^{-8}
^{235}U	9.31×10^{-9}	5.93×10^{-9}	3.74×10^{-8}
^{238}U	8.76×10^{-9}	5.48×10^{-9}	3.60×10^{-8}
Fertilizer			
^{234}U	8.55×10^{-9}	5.90×10^{-9}	3.05×10^{-8}
^{235}U	8.26×10^{-9}	5.81×10^{-9}	2.86×10^{-8}
^{238}U	7.74×10^{-9}	5.37×10^{-9}	2.75×10^{-8}

[A]Geometric mean, [B]2.5th percentile, [C]97.5th percentile

Table 5 Sample-specific activities of ^{234}U, ^{235}U and ^{238}U

	^{234}U (Bq/g)	^{235}U (Bq/g)	^{238}U (Bq/g)
Gauern	6.93	3.21×10^{-1}	6.88
E1	5.72	2.65×10^{-1}	5.67
Fertilizer	2.92×10^{-1}	1.35×10^{-2}	2.90×10^{-1}

[A]Geometric mean, [B]2.5th percentile, [C]97.5th percentile

Table 6 Sample-specific committed effective doses (ingestion of 0.01 g over 1 year)

	GM (Sv)[A]	$P_{2.5th}$ (Sv)[B]	$P_{97.5th}$ (Sv)[C]
Gauern			
^{234}U	3.06×10^{-7}	1.59×10^{-7}	1.52×10^{-6}
^{235}U	1.35×10^{-8}	7.24×10^{-9}	6.57×10^{-8}
^{238}U	2.74×10^{-7}	1.44×10^{-7}	1.36×10^{-6}
$\sum$	5.94×10^{-7}	3.11×10^{-7}	2.95×10^{-6}
E1			
^{234}U	2.02×10^{-7}	1.26×10^{-7}	8.34×10^{-7}
^{235}U	8.99×10^{-9}	5.73×10^{-9}	3.61×10^{-8}
^{238}U	1.81×10^{-7}	1.14×10^{-7}	7.45×10^{-7}
$\sum$	3.92×10^{-7}	2.45×10^{-7}	1.62×10^{-6}
Fertilizer			
^{234}U	9.12×10^{-9}	6.29×10^{-9}	3.25×10^{-8}
^{235}U	4.08×10^{-10}	2.87×10^{-6}	1.41×10^{-9}
^{238}U	8.20×10^{-9}	5.68×10^{-9}	2.91×10^{-8}
$\sum$	1.77×10^{-8}	1.23×10^{-8}	6.30×10^{-8}

[A]Geometric mean, [B]2.5th percentile, [C]97.5th percentile, $\sum$ is the sum of the sample-specific committed effective doses of the isotopes ^{234}U, ^{235}U and ^{238}U and their radiologically relevant progeny

Table 7 Committed effective dose coefficients (ingestion)

	ICRP (ICRP 1995a) (Sv/Bq)	Present method (Sv/Bq)
^{234}U	5.0×10^{-8}	5.2×10^{-8}
^{235}U	4.7×10^{-8}	4.9×10^{-8}
^{238}U	4.5×10^{-8}	4.7×10^{-8}

11 Conclusion and outlook

In the course of this thesis a general method was developed allowing for the quantification of the bioavailability of uranium from ingested soils. The first part of the thesis includes an *in vitro* solubility assay and a human study, to obtain the so-called f_A^{sol} factor. By this factor and the mentioned *in vitro* solubility assay the bioavailability of uranium from any other soil can be obtained, without the need for any further human soil-ingestion studies. The results of the human study by which the f_A^{sol} factor was deduced, were compared with literature data. From this comparison it is concluded that the developed method can be applied on soils slightly or highly contaminated with uranium. The results can be used both for acute and chronic ingestion. The developed method therefore offers a robust means to determine the bioavailability of uranium from theoretically or potentially ingested uranium-contaminated soils.

The method developed here was applied to soils highly contaminated with uranium, in particular to original soils from former uranium mining sites. The bioavailability of uranium in these soils was determined and used to calculate the resulting internal committed effective doses. A conceivable ingestion scenario was assumed which would lead to the ingestion of a realistic amount of the investigated uranium-contaminated soils. The results were compared to data from the literature. Based on the results obtained for the corresponding internal radiation dose it is concluded that ingestion of these soils is not expected to pose any major health risk to humans. However, two aspects have to be kept in mind if these methods are applied.

First, this thesis focused on the bioavailability of ingested soil-derived uranium and its subsequent resulting internal dose caused by uranium itself and its radiologically relevant progeny. Original soils from former uranium mining sites highly contaminated with uranium were investigated. However, soils of active and former uranium mining sites are not only contaminated with uranium but also with the respective progeny of the radium and the actinium series. Ingestion of uranium-contaminated soils is therefore accompanied by the ingestion of several additional radionuclides and, consequently, by additional sources of internal exposure. Clearly, investigation concerning the quality and quantity of the uptakes of these additional radionuclides and the corresponding contributions to dose are also of interest. The same strategy which was applied in this thesis to obtain reliable data on the bioavailability of uranium from ingested soils might be applicable to quantify the bioavailability of other radionuclides as well.

Second, the participants of the human study were adult volunteers. The results of this thesis can therefore be applied to the majority of the population. However, children, pregnant women, and the unborn child were not considered in this thesis, but of course are also of interest. For those individuals only limited data can be found in the literature, as discussed below. Note that a biokinetic model of uranium for pregnant women is not published by ICRP.

In 2005, urine samples of 72 children and 87 adults were examined for 30 trace elements including uranium (Heitland and Koster 2006a). The urine samples were from unexposed inhabitants of the surrounding areas of Aachen, Erkelenz and Bremen, Germany. The mean measured concentrations of uranium were 4 ng/L and 5 ng/L with 95%-percentiles of 8 ng/L and 10 ng/L for children and adults, respectively. For these results no uncertainties were indicated, and about 80% of the uranium concentration values for children and adults were below the limit of quantification (LOQ), which was 4 ng/L in that study. Consequently, uranium concentrations below the LOQ were calculated as LOQ/2. Based on these very limited data, children appear to exhibit a lower urinary uranium concentration compared to adults. No information concerning diet, especially uranium uptake was given by the authors, wherefore an equal ingestion of uranium among all children and adults is assumed. In general, the assumption is made that the daily urinary excretion of uranium is equal to the absorbed amount of daily ingested uranium (Leggett and Harrison 1995). A lower daily urinary excretion of uranium by children compared to adults might therefore support the assumption of a net retention of uranium by children (Leggett and Harrison 1995; Harrison et al. 2001). For the unborn, no information concerning the prenatal uranium absorption was found in the literature. However, as uranium qualitatively tends to follow the behavior of calcium, the demand of calcium by the unborn should be kept in mind when the quantitative behavior of uranium in the unborn is to be estimated (ICRP 1995a). The demand of calcium by the fetus accumulates to about 13 to 33 mg over pregnancy, wherefore the maternal bioavailability of calcium is increased among other physiological changes (Givens MH 1933; Naylor et al. 2000). Like for the unborn, this increased calcium absorption might be accompanied by a certain uranium accumulation by the pregnant woman.

Like for children, only limited data concerning the biokinetics of uranium in pregnant women are available. A recent study reported on measured uranium concentrations in blood and urine of pregnant women (Callan et al. 2013). For blood a mean concentration of 70 ng/L with a 95-percentile of 130 ng/L was found. In comparison, a study on 130 (non-pregnant) adults reported a measured mean concentration of < 3 ng/L with a 95-percentile of only 4 ng/L in blood (Heitland and Koster 2006b). Uranium concentrations below the LOQ were calculated by these authors again as LOQ/2. For uranium in urine a mean concentration of 13 ng/L with a 95-percentile of 40 ng/L was found for pregnant women (Callan et al. 2013). In comparison, a study on 87 (non-pregnant) adults found a mean concentration of 5 ng/L with a 95-percentile of only 10 ng/L (Heitland and Koster 2006a). Based on these limited data and compared to non-pregnant adults, pregnant women exhibit notably higher

uranium concentrations in blood, which are accompanied by relatively low urinary uranium concentrations. Like for children the mentioned blood and urine data seem to indicate an increased uranium retention by pregnant woman compared to the general adult population.

Future studies on the biokinetics of uranium in pregnant women should also take into account possible variations of the biokinetics of uranium within the trimesters of pregnancy. Recently, a study on 489 women found statistically significant differences of metal concentrations in urine between the first and the third trimester (Fort et al. 2014). These differences could be linked to physiological changes rather than to changes of metal ingestion. Increasing lead concentrations in blood taken close to the end of the pregnancy were also found (Gulson et al. 2004). This study revealed an increase of lead in blood by 10 to 50%, as compared to minimal values at the beginning of pregnancy. Placental transfer of lead from the maternal blood was also concluded from data on the isotopic lead ratio in maternal and cord blood.

Based on the cited literature, further investigations on children, pregnant women and the unborn are necessary to gain reliable biokinetic data on uranium of these vulnerable groups.

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13 Publications and presentations

13.1 Publications

Träber SC, Höllriegl V, Li W, Czeslik U, Rühm W, Oeh U, Michalke M (2014) Estimating the Absorption of Soil-Derived Uranium in Humans. Environ Sci Technol 48 (24) (24):14721-14727

Träber SC, Li WB, Höllriegl V, Nebelung K, Michalke B, Rühm W, Oeh U (2015) Calculation of internal dose from ingested soil-derived uranium in humans: Application of a new method. Radiat Environ Biophys 54 (3):265-272. doi:10.1007/s00411-015-0602-9

13.2 National and international presentations

2011 Workshop KVSF II, Rheinbach

2012 EURADOS Annual Meeting, Wien (VIC), Austria

2012 Workshop KVSF II, Neuherberg

2012 VKTA, Rossendorf

2012 Workshop KVSF II, Jena

2013 1. Projektstatusgespräch zur BMBF-geförderten nukl. Sicherheitsforschung, Karlsruhe

2013 Workshop KVSF II, Neuherberg

2013 HEIR 2013, Berkeley, USA

2014 Workshop KVSF II, Hannover

14 Eigenanteile

14.1 Eigenanteil bei Träber et al. 2014

Folgender Teil wurde von Stephan Träber (teilweise unter Diskussion/Anleitung durch die Co-Autoren) erstellt/erarbeitet:

- Erstellung des überwiegenden Teils der Publikation Träber et al. 2014 inkl. Abbildung 1
- Solubility Assay - Determination of DF
    - Planung/Durchführung der Löslichkeitsversuche zur Heilerde, Interpretation der ICP-MS-Daten des Partnerlabors (HMGU) inkl. Erstellung der Abbildung 3
- Human Study - Determination of f_A
    - Organisation der Studie (Anleitung und Betreuung der Probanden); Sammlung und Verarbeitung der 24h-Urinproben für den Versand an das Partnerlabor (VKTA)
    - Interpretation der ICP-MS-Rohdaten des Partnerlabors (VKTA) inkl. Erstellung der Abbildung 4
    - Interpretation/Berechnung der probandenspezifischen Bioverfügbarkeit f_A inkl. Erstellung der Abbildung 5
    - Berechnung des GM bzw. GSD/Perzentile und Interpretation/Diskussion der Daten
- Determination of f_A^{sol}
    - Berechnung des f_A^{sol}-Faktors und Interpretation der Daten anhand der verfügbaren Literaturdaten inkl. Erstellung der Tabelle 1

14.2 Eigenanteil bei Träber et al. 2015

Folgender Teil wurde von Stephan Träber (teilweise unter Diskussion/Anleitung durch die Co-Autoren) erstellt/erarbeitet:

- Erstellung des überwiegenden Teils der Publikation Träber et al. 2015
- Bioavailability (f_A) of soil and fertilizer samples
    - Durchführung der Löslichkeitsversuche, Interpretation der ICP-MS-Daten inkl. Erstellung der Abbildung 3
    - f_A-Berechnung inkl. Erstellung der Tabelle 2
- Committed effective doses

- Berechnung der *sample-specific alimentary tract transfer rates* inkl. Erstellung der Tabelle 3
- Berechnung *sample-specific ingestion effective dose coefficients (DC_i)* inkl. Erstellung der Tabelle 4
- Berechnung *sample-specific average concentrations ($c_{soil,i}$) of the radionuclides ^{234}U, ^{235}U and ^{238}U* inkl. Erstellung der Tabelle 5
- Berechnung *sample-specific annual committed effective doses* inkl. Erstellung der Tabelle 6

- Quality assurance of dose calculations
  - Berechnung/Vergleich der *effective dose coefficients* inkl. Erstellung der Tabelle 7

15 Danksagung

Ich bedanke mich bei Prof. Dr. Christoph Hoeschen und Dr. Uwe Oeh für die Möglichkeit in dem Forschungsbereich der Biokinetik von Radionukliden/internen Dosimetrie zu arbeiten.

Besonders möchte ich Dr. Vera Höllriegl, Dr. Weibo Li und Prof. Dr. Werner Rühm für die Unterstützung in Labor und bei der Humanstudie, für die Anleitung bei der Dosimetrie- und Unsicherheitsberechnung sowie für die zielgerichteten Diskussionen und Ratschläge und die Unterstützung auch über meine aktive Zeit am HMGU hinaus ganz herzlich danken. Deswegen und wegen des stets sehr hilfsbereiten und kollegialen Umfelds innerhalb des AMSD/ISS denke ich gerne an diese Zeit zurück.

Ebenso bedankte ich mich bei Prof. Dr. Bernhard Michalke und den Mitgliedern des Kompetenzverbund Strahlenforschung (KVSF) Uta Czeslik und Katja Nebelung für die Durchführung der ICP-MS-Messungen und für die Bereitstellung der Erdprobe „Gauern“.

Ich danke meiner Familie, Ivette, unseren Kindern, meinen Eltern und meinem Bruder für die Geduld und Unterstützung während der gesamten Zeit.

Die Arbeit wurde finanziert vom Bundesministerium für Bildung und Forschung (BMBF), Förderkennzeichen: 02NUK015B.