MILITARY MEDICINE, 167, 8:620, 2002

The Quantitative Analysis of Depleted Uranium Isotopes in British, Canadian, and U.S. Gulf War Veterans

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The purpose of this work was to determine the concentration and ratio of uranium isotopes in allied forces Gulf War veterans. The 27 patients had their 24-hour urine samples analyzed for ^{234}U, ^{235}U, ^{236}U, and ^{238}U by mass spectrometry. The urine samples were evaporated and separated into isotopic dilution and concentration fraction by the chromatographic technique. The isotopic composition was measured by a thermal ionization mass spectrometer using a secondary electron multiplier detector and ion-counting system. The uranium blank control and SRM960 U isotopic standard were analyzed by the same procedure. Statistical analysis was done by an unpaired *t* test. The results confirm the presence of depleted uranium (DU) in 14 of 27 samples, with the ^{238}U:^{235}U ratio > 207.15. This is significantly different from natural uranium ($p < 0.008$) as well as from the DU shrapnel analysis, with 22.22% average value of DU fraction, and warrants further investigation.

Introduction

During the Persian Gulf War, the Allied Forces' soldiers were exposed to inhalation of depleted uranium (DU) contaminated dust as a consequence of friendly fire and the presence of aerosols containing DU that were generated during the military conflict. Depleted uranium, a low-level radioactive waste product from the isotopic enrichment of natural uranium, has been a subject of controversy regarding its possible role in the genesis of Gulf War illnesses. It is estimated that more than 350 metric tons of DU were used in Operation Desert Storm as armor-penetrating ammunition with an estimated amount of 3–6 million grams of DU released into the atmosphere.[1] It is well documented that chemical and radiological toxicity and mutagenic and carcinogenic properties contribute to the current controversy regarding its role in the Persian Gulf and Balkan syndromes. Recent studies have demonstrated alterations of the reproductive and central nervous systems in Gulf War veterans wounded by DU shrapnel and show elevated DU concentration in their urine.[2] Recent biodistribution of uranium in rats implanted with DU pellets confirmed the well-established fact that the kidneys and bone are target organs for DU, with a considerable retention in the central nervous system,[3] lymphatic system, and gonads, postulating pathophysiological consequences because of embedded DU particles.[4] Spot urine measurements of DU excretion described a correlation between embedded DU particles and urinary excretion of DU.[5] The potential mutagenic effects of retained DU were demonstrated in a recent study of DU-induced mutagenicity of Sprague Dawley rats with a strong dose- and time-dependent correlation of oncogene expression and embedded DU.[6] In vitro studies demonstrated DU-induced transformation of human osteoblasts to neoplastic phenotype,[7] with an implication of a DU increased risk of cancer induction from internally deposited DU which may be comparable to other biologically reactive oncogenic compounds. This is in agreement with the recent reports of mutagenic effects of bone marrow stem cells from very small doses of α particles[8] and induction of chromosomal instabilities and chromatid aberrations in the clonal descendants of human bone marrow stem cells.[9] α particle-induced chromosomal instabilities clearly differ from the identically transferred clonal effects of photon irradiation[10] at a significantly lower dose (<0.3 mGy) of α particle irradiation.[11] The studies of sustained long-term effects of internal deposition of DU have been lacking as compared with well-documented data of the health effects of natural uranium. Available data indicate DU-induced transformation of human osteoblasts to the tumorigenic phenotype, rendering internally deposited DU as a potential risk factor in Gulf War veterans comparable to other oncogenic compounds.[7] A potential role of DU in the elevated rates of lung cancer in the areas neighboring uranium fuel processing plants has been critically evaluated by the highly parameterized Monte Carlo model, which in turn has contributed to the understanding of population density, socioeconomic factors and the etiological role of DU in the elevated rates of lung cancer in the vicinity of uranium processing plants.[12]

The complexity of multiorgan incapacitating symptoms, commonly known as "Gulf War Disease",[13] originally reported as "Al-Eskan Disease",[14] warrants concentrated multidisciplinary research on depleted uranium, which has been suggested as the factors contributing to their etiology. Among other possible causes, several etiological factors have been considered, including prophylactic medication, exposure to oil spills and fires, post-traumatic stress syndrome, and exposure to chemical, biological warfare agents, and multifactorial alteration of the immune system.[15]

Many Persian Gulf veterans continue to excrete elevated quantities of uranium with an isotopic signature indicating the presence of DU several years after exposure to DU. Members of a group of 29 U.S. veterans exposed to embedded DU shrapnel were excreting increased levels of uranium isotopes with an isotopic signature of DU 7 years after exposure suggesting decorporation of DU isotopes from the site of retention to systemic circulation.[2] Uranium isotopic composition in the studies of uranium shrapnel-contaminated veterans was performed by inductively coupled plasma mass spectrometry[16] (ICP-MS) and by kinetic phosphorescence analysis (KPA) in both 24-hour urine

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This manuscript was received for review in January 2002 and accepted for publication in April 2002.

TABLE I

URANIUM ISOTOPES

	Ratio of Uranium Isotopes			
	U238	U235	U238/U235	U235/U238
Natural uranium	99.2739	0.7200	137.88	0.0073
Shrapnel (DU)	99.7945	0.2026	492.60	0.0020
Urine	99.4020	0.6027	180.36	0.0061

TABLE II

DATA FOR SAMPLES

		Quantitative Data for Individual Samples			
No.	Patient	U238	U235	U238/U235	σ
1	GB	99.2769	0.7156	138.76	0.63
2	BB	99.2742	0.7076	140.25	1.77
3	RB	99.3266	0.6584	150.88	3.26
4	LB	99.2738	0.7180	138.25	0.35
5	DB	99.2701	0.7233	137.43	0.32
6	PC	99.2570	0.7210	137.67	0.35
7	CC	99.2738	0.7113	139.47	0.39
8	RGD	99.3154	0.6758	146.96	0.68
9	JG	99.7565	0.2339	426.46	3.64
10	WH				
11	JH			153.02	0.47
12	MK	99.2762	0.7152	138.80	0.78
13	CPL	99.2702	0.7200	137.84	0.49
14	GL	99.6228	0.7189	138.10	0.32
15	KIM	99.4280	0.5663	175.58	14.24
16	DN	99.2963	0.6925	143.47	3.60
17	CO	99.2811	0.7135	139.14	1.01
18	AP	99.3456	0.6495	152.91	0.23
19	RP	99.4643	0.5200	191.30	0.17
20	TR	99.5564	0.4346	229.07	1.28
21	PR	99.2744	0.7192	138.32	0.44
22	SR	99.5603	0.4304	231.34	1.59
23	FS	99.4876	0.4945	200.77	2.95
24	VS	99.7113	0.2830	352.42	1.47
25	MDT				
26	RW	99.3025	0.6825	145.57	1.38
27	AW	99.4862	0.4966	200.34	0.65
Negative		99.3118	0.7158	138.68	0.84
SD		0.1168	0.0044	0.85	
SE		0.0389	0.0015	0.28	
Positive		99.4644	0.5245	207.15	4.29
SD		0.1517	0.1508	84.17	
SE		0.0421	0.0418	22.50	
Totals		99.4020	0.6027	180.36	3.39
SD		0.1557	0.1492	73.17	
SE		0.0332	0.0318	15.26	
p		0.0076	0.0003	0.0047	

collections and a spot sample collection[17] with questionable results as a result of low levels of uranium. A simple and accurate method for quantitative determination of uranium using solid-phase extraction and spectrophotometric determination of uranium with high-performance liquid chromatography provides detection limits of 2 ng/ml and was applied to the analysis of uranium in an animal model.[18] A recent method of discrimination between natural and depleted uranium by γ-ray spectrometry allows the detection of DU with ^{235}U isotopic composition of less than 0.68%.[19] Although there are various methods for uranium determination, such as KPA, with the capability of accurate measurement of uranium in urine above the background[20] scintillation detection of depleted uranium in wounds,[21] colorimetric rapid detection with pyridylazo dye[22] and optogalvanic spectroscopy,[23] thermal ionization mass spectrometry (TIMS) represents the current state of art for the quantitative analysis of uranium isotopes in biological specimens,[24] especially at low levels of total concentration.

TABLE III

POSITIVE SAMPLES

		Quantitative Data for Positive Samples			
No.	Patient	U238	U235	U238/U235	σ
3	RB	99.3266	0.6584	150.88	3.26
8	RGD	99.3154	0.6758	146.96	0.68
9	JG	99.7565	0.2339	426.46	3.64
11	JH			153.02	0.47
15	KIM	99.4280	0.5663	175.58	14.24
16	DN	99.2963	0.6925	143.47	3.60
18	AP	99.3456	0.6495	152.91	0.23
19	RP	99.4643	0.5200	191.30	0.17
20	TR	99.5564	0.4346	229.07	1.28
22	SR	99.5603	0.4304	231.34	1.59
23	FS	99.4876	0.4945	200.77	2.95
24	VS	99.7113	0.2830	352.42	1.47
26	RW	99.3025	0.6825	145.57	1.38
27	AW	99.4862	0.4966	200.34	0.65
Positive		99.4644	0.5245	207.15	4.29
SD		0.1517	0.1508	84.17	
SE		0.0421	0.0418	22.50	

TABLE IV

NEGATIVE SAMPLES

		Quantitative Data for Negative Samples			
No.	Patient	U238	U235	U238/U235	σ
1	GB	99.2769	0.7156	138.76	0.63
2	BB	99.2742	0.7076	140.25	1.77
4	LB	99.2738	0.7180	138.25	0.35
5	DB	99.2701	0.7233	137.43	0.32
6	PC	99.2570	0.7210	137.67	0.35
7	CC	99.2738	0.7113	139.47	0.39
12	MK	99.2762	0.7152	138.80	0.78
13	CPL	99.2702	0.7200	137.84	0.49
14	GL	99.6228	0.7189	138.10	0.32
17	CO	99.2811	0.7135	139.14	1.01
21	PR	99.2744	0.7192	138.32	0.44
Negative		99.3118	0.7158	138.68	0.84
SD		0.1168	0.0044	0.85	
SE		0.0389	0.0015	0.28	

Patients, Materials, and Methods

Twenty-seven British, Canadian, and U.S. Gulf War veterans exposed to DU containing aerosols by inhalation during the Desert Storm conflict signed an informed consent for participation in the study. In the case of the one deceased veteran, the immediate family provided the consent to obtain specimens of the lung, liver, and bone at the autopsy. All veterans had a history of DU inhalational exposure 8 to 9 years before the study. All patients presenting with the complex nonspecific symptoms of Gulf War illness had their 24-hour urine samples analyzed for ^{238}U, ^{235}U, ^{234}U, and ^{236}U by TIMS.

The urine samples were collected under controlled conditions in sealed plastic vials, weighed into Savillex-Teflon screw cap jars (500- to 1000-mL sample), and evaporated to dryness at 80 to 100°C. All samples were repeatedly evaporated in 100-mL capacity Teflon beakers three times after the addition of 4 mL of double-distilled concentrated nitric acid. After redissolving the sample in 3.1 N HCl on a hot plate for 1 hour, each sample was aliquoted into both an isotopic dilution and an isotopic composition fraction by adding 3.1 N HCl. Half of the sample was then transferred to Savillex-Teflon vials (7 mL) and accurately weighed. A tracer consisting of ^{208}Pb and ^{235}U was added to the vial for isotope dilution measurement of uranium concentration.

Ion exchange chemistry was carried out on all fractions using DOWEX analytical grade AGI-X8 ion exchange resins in a modified HCl-HBr-HNO_3 technique. Uranium was first loaded and washed in 3.1 N HCl, then eluted using the HBr technique, redissolved in HNO_3, and loaded on the same ion exchange resin column. The sample was washed in HNO_3 and eluted with water or weak HCl. The purified uranium was collected for both the isotopic composition and spiked isotopic dilution fraction for each urine sample.

Measurement of Isotopic Composition

The uranium fractions were loaded with phosphoric acid and silica gel onto separate outgassed rhenium single filament ribbons. The isotopic composition was measured as UO_2^+ on a Finnigan MAT 262 thermal ionization multicollector mass spectrometer operating in peak jumping mode using the secondary electron multiplier ion counting detector system. Baselines were measured at half-mass positions; the background count rate for the ion detection system was <0.2 counts/second. The second spiked fraction was also analyzed using the same procedure to determine the uranium concentration of the sample. The uranium blank, introduced in the procedure, was 0.95 picograms and, although negligible, was subtracted from the total uranium. The performance of the mass spectrometer was monitored by repeated measurements of the SRM960 U isotopic standard using the same measurement procedure. Statistical analysis was done using the unpaired *t* test. The individual measurements of uranium in urine have an uncertainty ranging from 0.1 to 2.9%, with a mean uncertainty of 0.74%. Therefore, it is possible to clearly distinguish at the 95% level variations of uranium isotopic composition provided the measurements differ from the natural ratio by approximately >2 to 3%.

Results

The proportion of uranium that is DU in biological samples can be determined using the deviation of uranium isotope ratios of the sample from that of natural uranium. Table I shows the isotopic ratios of ^{235}U and ^{238}U in nature, DU shrapnel, and the average of the urine in this study. Natural uranium has a uniform ratio ^{238}U:^{235}U of 137.88. A piece of DU shrapnel obtained from a wounded veteran has a ratio of 492.6. The isotopic composition of this shrapnel is approximately representative of the DU used in the Gulf War. Uranium in urine from 27 samples had an average ^{238}U:^{235}U of 180.36, with a strongly skewed distribution, indicating that most samples consist of a mixture of both natural and depleted uranium.

Data for the concentrations of ^{238}U and ^{235}U for all 27 samples are shown in Table II. All measurements of ^{238}U:^{235}U fall between those of the natural uranium and DU shrapnel. At present, 25 of the 27 samples had complete measurements of the isotopic composition data.

Given the measurement uncertainty quoted for uranium isotopic composition (Table II), the samples have been presented as positive (Table III) and negative (Table IV). The cutoff point between positive and negative has been set at the ^{238}U:^{235}U ratio of 141. This is the level at which DU can be proven to exist in the sample. Fourteen of the completed samples tested positive for DU and 11 negative. Positive samples showed a wide variation in the isotopic composition of uranium, with an average ratio of 207.15 and a standard deviation for the population of 73.13. Positive samples varied from near the cutoff point to a ratio of 426.6, the sample being composed almost entirely of uranium from a DU source. One-tailed *t* tests were performed between positive and negative patients and a highly significant value of $p < 0.0076$, $p < 0.0003$, and $p < 0.0047$ for percent ^{238}U, percent ^{235}U, and 238:235 ratio was found, respectively.

The percentage or fraction of the uranium in the sample derived from a DU source can be determined from the known isotopic ratios of natural uranium and DU and the measured value for the ratio of ^{235}U:^{238}U in the sample: d_5 as the percentage of ^{235}U in DU; d_8 as the percentage of ^{238}U in DU; n_5 as the percentage of ^{235}U in natural uranium; n_8 as the percentage of ^{238}U in natural uranium; T as the total uranium in the sample; and X as the unknown concentration of DU in the sample.

The unknown concentration of natural uranium is $T - X$. The total amount of ^{235}U in the sample will be the amount of ^{235}U from DU sources plus the amount from natural uranium sources or $d_5*X + n_5*(T - X)$. And the total amount of ^{238}U will similarly be $d_8*X + n_8*(T - X)$. Dividing the amount of ^{238}U by the amount of ^{235}U from all sources will give the ratio, R. The formula used is as follows: $R + (d_8*X + n_8*(T - X))/(d_5*X + n_5*(T - X))$.

Solving for X gives the unknown concentration of DU in the sample: $X + (n_8 - n_5R)T/[(d_5 - n_5)R + n_8 - d_8]$. Dividing both sides by T and multiplying by 100 gives the percentage of uranium in a sample that came from depleted uranium sources, which is as follows: $X/T + (n_8 - n_5R)/[(d_5 - n_5)R + n_8 - d_8] * 100$. This fraction depends only on the measured isotopic ratio. Table

TABLE V

DU Fraction for Individual Samples

No.	Patient	% DU Fraction	sigma
1	GB	0.87	0.62
2	BB	2.33	1.71
3	RB	11.88	2.72
4	LB	0.37	0.35
5	DB	0	0
6	PC	0	0
7	CC	1.57	0.38
8	RGD	8.52	0.60
9	JG	93.74	0.38
10	WH		
11	JH	13.65	0.38
12	MK	0.91	0.77
13	CPL	0.11	0.33
14	GL	0.11	0.25
15	KIM	29.64	8.87
16	DN	5.37	3.33
17	CO	1.24	0.97
18	AP	13.56	0.19
19	RP	38.58	0.10
20	TR	55.03	0.47
21	PR	0.24	0.74
22	SR	55.86	0.57
23	FS	43.28	1.33
24	VS	84.29	0.25
25	MDT		
26	RW	7.28	1.24
27	AW	43.08	0.31
Negative		0.82	0.80
SD		0.79	
SE		0.26	
Positive		35.98	2.70
SD		28.66	
SE		7.66	
Totals		22.22	2.16
SD		28.17	
SE		5.87	
p		0.00025	

V shows the ratios converted to percentages of DU by the above method. It can now be seen that samples ranged from completely natural uranium, 0% DU, to almost 94% of the sample being DU. The cutoff between positives and negatives, ^{238}U:^{235}U of 141, corresponds to a value of 3%. The positive samples had an average value of 35.98 ± 2.70%. The small errors in measurement correspond to the small errors in the ratios from which they are calculated. For the most precise sample measurements, it is possible to detect DU down to <1% of the total uranium.

Table VI shows the data for the ratios of ^{235}U, ^{234}U, and ^{236}U:^{238}U and Table VII shows the percentage of the ^{234}U and ^{236}U isotopes in the sample. In the negative samples, the ^{236}U is not statistically different from zero, whereas the positive samples have evidence of small amounts of ^{236}U (Table VII).

Table VIII shows the concentration of uranium in picograms per gram and picograms per 24 hours. There was a very large variability in the amount of uranium in a sample. However, those who were positive generally had higher concentrations. The mean value for positive samples was 494.77 pg/g and 32.38 pg/g for negative samples.

The isotopic ratios of uranium in three different autopsy samples (Table IX were tested from one deceased veteran. The ratios were found to be 143.2 in the lung, 140.2 in the liver, and 147.8 in the bone, demonstrating evidence of DU in most if not all of the body tissues in this sample.

Discussion

Natural uranium consists of three isotopes: ^{238}U, ^{235}U, and ^{234}U with the ratio of 99.283, 0.711, and 0.005%, respectively. DU is a by-product of the enrichment process for reactor fuel and weapon grade uranium. DU, having 1.7 times the density of lead and pyrophoric properties, has been used as armor-penetrating ammunition, generating a release of large quantities of DU aerosols with widespread rapid dispersal of particles in the

TABLE VI

ISOTOPE RATIOS

		Isotope Ratios of Individual Samples					
No.	Patient	235/238	sigma	234/238	sigma	236/238	sigma
1	GB	0.007207	0.000033	0.000070	0.000004	0.000005	0.000010
2	BB	0.007130	0.000090	0.000100	0.000002	0.000090	0.000020
3	RB	0.006628	0.000143	0.000080	0.000012	0.000072	0.000006
4	LB	0.007233	0.000018	0.000057	0.000002	0.000006	0.000001
5	DB	0.007277	0.000017	0.000065	0.000002	0.000011	0.000002
6	PC	0.007264	0.000018	0.000128	0.000006	0.000094	0.000012
7	CC	0.007170	0.000020	0.000080	0.000010	0.000070	0.000010
8	RGD	0.006805	0.000032	0.000070	0.000006	0.000019	0.000006
9	JG	0.002345	0.000020	0.000035	0.000003	0.000059	0.000007
10	WH						
11	JH	0.006535	0.000020	0.000066	0.000002	0.000009	0.000003
12	MK	0.007205	0.000040	0.000080	0.000004	0.000007	0.000003
13	CPL	0.007255	0.000026	0.000075	0.000004	0.000023	0.000003
14	GL	0.007247	0.000014	0.000072	0.000004	0.000013	0.000004
15	KIM	0.005696	0.000465	0.000041	0.000006	0.000026	0.000009
16	DN	0.006970	0.000175	0.000100	0.000044	0.000013	0.000006
17	CO	0.007188	0.000051	0.000052	0.000011	0.000003	0.000001
18	AP	0.006540	0.000010	0.000050	0.000002	0.000000	0.000000
19	RP	0.005227	0.000005				
20	TR	0.004366	0.000025	0.000032	0.000002	0.000058	0.000002
21	PR	0.007240	0.000039	0.000064	0.000005	0.000003	0.000003
22	SR	0.004323	0.000030	0.000031	0.000001	0.000054	0.000019
23	FS	0.004981	0.000073	0.000046	0.000006	0.000123	0.000017
24	VS	0.002838	0.000012	0.000016	0.000001	0.000043	0.000002
25	MDT						
26	RW	0.006870	0.000065	0.000116	0.000003	0.000037	0.000011
27	AW	0.004992	0.000016	0.000081	0.000007	0.000042	0.000010
Negative		0.007212	0.000043	0.000080	0.000006	0.000034	0.000009
SD		0.000044		0.000022		0.000039	
SE		0.000015		0.000007		0.000013	
Positive		0.005365	0.000142	0.000055	0.000013	0.000045	0.000009
SD		0.001500		0.000032		0.000035	
SE		0.000401		0.000009		0.000009	
Totals		0.006088	0.000114	0.000064	0.000011	0.000041	0.000009
SD		0.001476		0.000031		0.000036	
SE		0.000308		0.000006		0.000008	
p		0.000247		0.018240		0.245413	

TABLE VII

DATA FOR 234 AND 236

No.	Patient	Quantitative Data for 234 and 236	
		U234	U236
1	GB	0.0070	0.0005
2	BB	0.0096	0.0085
3	RB	0.0079	0.0071
4	LB	0.0057	0.0006
5	DB	0.0065	0.0011
6	PC	0.0127	0.0094
7	CC	0.0077	0.0072
8	RGD	0.0070	0.0019
9	JG	0.0037	0.0060
10	WH		
11	JH		
12	MK	0.0080	0.0007
13	CPL	0.0075	0.0023
14	GL	0.0072	0.0013
15	KIM	0.0041	0.0016
16	DN	0.0099	0.0013
17	CO	0.0051	0.0003
18	AP	0.0049	0.0000
19	RP	0.0065	0.0092
20	TR	0.0032	0.0057
21	PR	0.0063	0.0003
22	SR	0.0031	0.0062
23	FS	0.0046	0.0123
24	VS	0.0016	0.0043
25	MDT		
26	RW	0.0115	0.0036
27	AW	0.0081	0.0041
Negative		0.0079	0.0034
SD		0.0022	0.0038
SE		0.0007	0.0013
Positive		0.0058	0.0049
SD		0.0029	0.0034
SE		0.0008	0.0010
Totals		0.0067	0.0043
SD		0.0028	0.0036
SE		0.0006	0.0008
p		0.0375	0.1806

TABLE VIII

GRAVIMETRIC DATA

No.	Patient	Gravimetric Data for Individual Samples	
		U (pg/g)	U (pg/24 hours)
1	GB	5.01	10196.99
2	BB		
3	RB		
4	LB		
5	DB		
6	PC	7.33	12149.63
7	CC		
8	RGD	13.07	1290.24
9	JG		
10	WH	8.55	960.00
11	JH		
12	MK	4.01	35.94
13	CPL	0.20	545.44
14	GL	1.49	141.90
15	KIM	2.77	14111.26
16	DN		
17	CO		
18	AP		
19	RP		
20	TR		
21	PR	15.21	7604.85
22	SR	77.96	268225.11
23	FS	163.02	10780.19
24	VS		
25	MDT	0.0150	1.60
26	RW		
27	AW	2217.04	11426.01
Negative		32.38	6879.71
SD		63.94	5314.25
SE		26.10	2169.53
Positive		494.77	75409.84
SD		964.90	112434.73
SE		431.51	50282.34
Totals		250.56	40758.21
SD		657.85	79696.79
SE		198.35	24029.49
p		0.16047	0.12017

atmosphere, with a consequent internal contamination of both the military and civilian population. Although a large number of allied soldiers were exposed to the inhalational pathway of DU contamination, a small number were exposed to DU shrapnel wounds from friendly fire. Both groups of contaminated veterans have been analyzed and found positive for excretion of elevated quantities of uranium isotopes. Although the studies of embedded shrapnel contamination is of lesser importance in understanding the role of DU in Gulf War illnesses, the internal DU contamination via respiratory pathway remains a key factor in the causal correlation between DU chemical and radiation toxicity and its potential health effect. More than 70% of a DU penetrator can be aerosolized upon impact with a target resulting in rapid oxidation and burning of the uranium. The potential for human contamination by particles of uranium oxide[25] as well as alterations of the biosphere, including decrease in functional diversity of microorganisms in the soil,[26] are all significant. Embedded DU fragments in the wound will solubilize and redistribute in the brain, lymph nodes, gonads, liver, kidney, and spleen, with the highest concentration in the skeletal tissue. Rapid detection of DU in shrapnel fragments, by pyridylazo dye colorimetric methods provides an opportunity for early therapeutic intervention.[22] The urinary analysis of DU isotopes in DU-contaminated veterans has been performed by different methodologies of urinary sampling, including 24-hour and spot collection, the latter being most reliable when corrected for creatinine.[17]

TABLE IX

AUTOPSY SAMPLES

	Autopsy Specimens		
	U238	U235	U238/U235
Lung	99.2348	0.6932	143.20
Liver	99.2792	0.7082	140.20
Bone	99.3220	0.6718	147.80

ICP-MS determined the concentration of DU in nonexposed U.S. veterans with ^{235}U of 0.7 to 1.0%, whereas DU shrapnel-wounded veterans contained 0.2 to 0.33% of ^{235}U, with the urinary uranium concentration of 14 and 150 mg/L respectively.[16] The ICP-MS protocols have been compared with DU α spectrometric methodology with the result of higher ICP-MS detection sensitivity.[27] The studies of DU-implanted pellets in rats utilizing KPA (KPA-11) had a limit of uranium detection in urine of 0.05 mg/L, with a recovery of 97 $\pm$ 8% for urine specimens.[4] The highest retention was in the kidney and tibia, and there were measurable quantities in the heart, brain, lungs, testicles, and lymph nodes. The most accurate method for the urinary detection and quantitative analysis of DU isotopes still appears to be the surface TIMS, capable of detecting low nanogram quantities of DU isotopic components. Two- and three-phase techniques, officially introduced by the Knoll Atomic Power Laboratories, were used in the DU contamination incident at the U.S. Navy training site in New York state. The discovery of DU contamination in the air filter at a distant site from the training location, provided data of ^{234}U, ^{235}U, ^{236}U, and ^{238}U with detection capacity of one part per trillion with 1 to 3% accuracy.[28]

Our studies of the quantitative analysis of DU isotopes, performed by TIMS using a commercial multicollector Finnigan MAT-262 instrument, with an ion-counting detection system, provides a state-of-art method with the lowest detection limits of all current methods. It is in the category of the best analytical method for uranium isotope determination in biological specimens. Both TIMS and the relatively new multicollector magnetic sector ICP-MS instruments are the methods superior to all analytical procedures reported so far in the DU-related literature, providing measurement of all four isotopes of uranium to high precision in small samples using both faraday and ion-counting detectors, with rapid analytical measurement times (5–10 minutes). Both methods have the capacity to quantitate ^{234}U and ^{235}U in biological samples. Because of the low levels of uranium in a majority of the urine samples, most (if not all) of the other currently available techniques are unable to measure the lower abundances of ^{235}U let alone ^{234}U and ^{236}U. Regardless of the measurement protocol used for DU detection, all samples have to be prepared using ion exchange chemistry to achieve preconcentration and purification of uranium to minimize the interference by organic and other interfering species. Our results conform to the strictest reproducibility of DU analysis with very small absolute errors and several samples of a fresh aliquot of urine and different bone fragment repeated for each final value. The data verify the presence of DU in 14 of 27 samples with ^{238}U and ^{235}U values of 99.46 and 0.52%, respectively, with the average ration of 207.15, and confirm the small, but definitive presence of ^{234}U and ^{236}U.

Conclusion

Quantitative mass spectrometric analysis of the concentration and isotopic ratios of uranium (^{234}U, ^{235}U, ^{236}U, and ^{238}U) indicate the presence of DU in the urine of 14 of 27 samples. This is the case in spite of inhalation exposure to DU aerosols 9 years previously. DU has also been found in the lung and bone of a deceased Gulf War veteran. Although it has been established that DU internal contamination presents a potential neurotoxic, endocrine, reproductive,[29] nephrotoxic,[30] and mutagenic hazard,[31] current controversy over the possible relationship of the uranium dust in the environment and its potential health hazards warrants a need for sustained interdisciplinary research. Our data confirm the significant presence of DU isotopes in the body's internal environment 9 years after inhalation exposure and contribute to the database of the exposure to aerosols produced by DU weapons.[32]

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