Establishing reference ranges of elements in human lung samples

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Elemental levels in lungs

Inhalation of small metal particles is common in workplaces such as welding
grinding
smelting.

Such exposures can lead to the development of respiratory disease and general ill health.

It is possible to identify exposures to a wide number of elements using established BM methods.

Occasionally in incident/historical/forensic cases lung samples are used.

Background metals in tissue samples

Most of the knowledge of trace element concentrations comes from autopsy studies

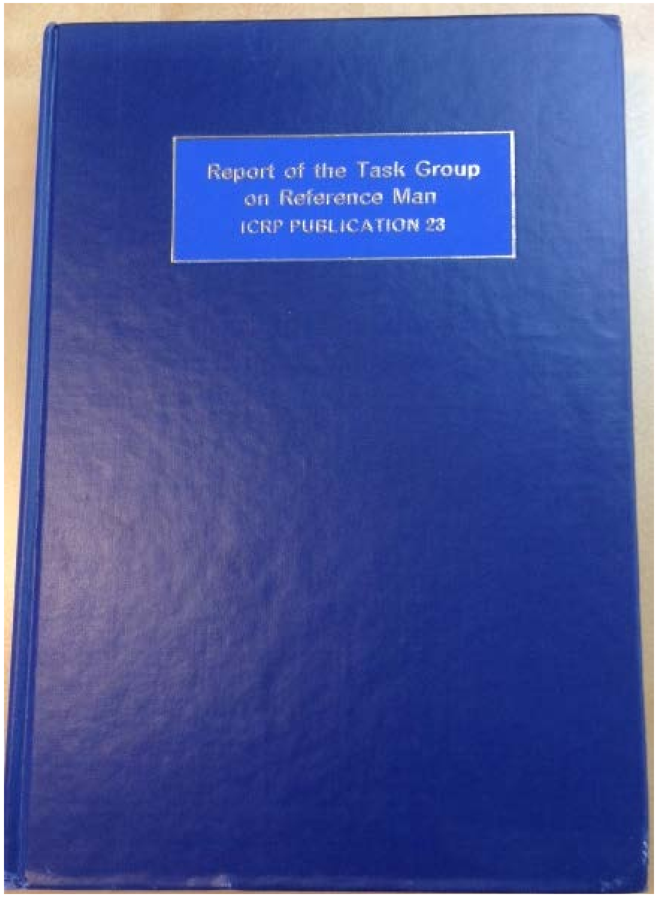
Reference man was published 40 years ago

Since then there has been

- Analytical improvements
- Quality control improvements
- Changes to samples collection and storage

Also major changes have occurred in environmental, occupational and dietary exposures in the past 5 decades

There is a need to establish current levels with up to date analytical methods.



Aim of the project

To establish current reference ranges of elements in lung samples from people not occupationally exposed to metals.

To use optimised collection and sample preparation methods

To use inductively coupled plasma mass spectrometry to analyse for a wide of elements

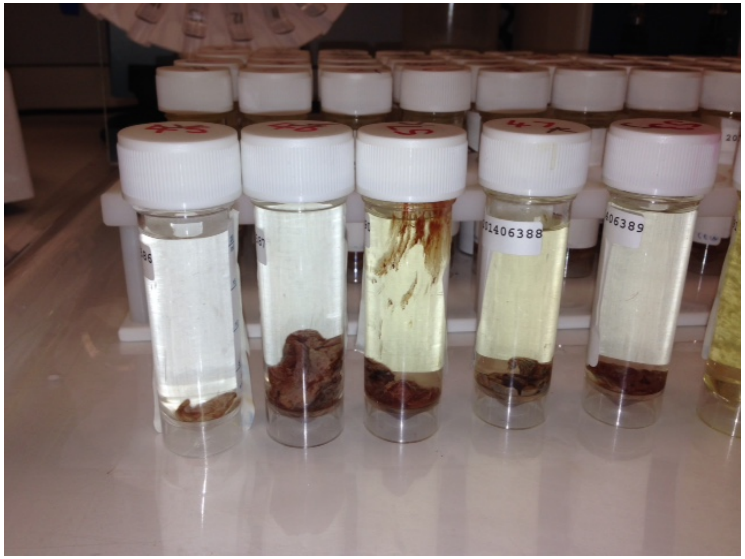
To analyse the data using mixed effect modelling for look for trends within the data

Source of samples

Ethical approval was obtained from a NHS REC committee (11/YH/0267) and Sheffield Teaching Hospitals STH Number 16163.

Lung tissue samples were collected from patients undergoing tumour removal surgeries.

The tissue used was routinely removed from surplus tissue surrounding excised tumour.



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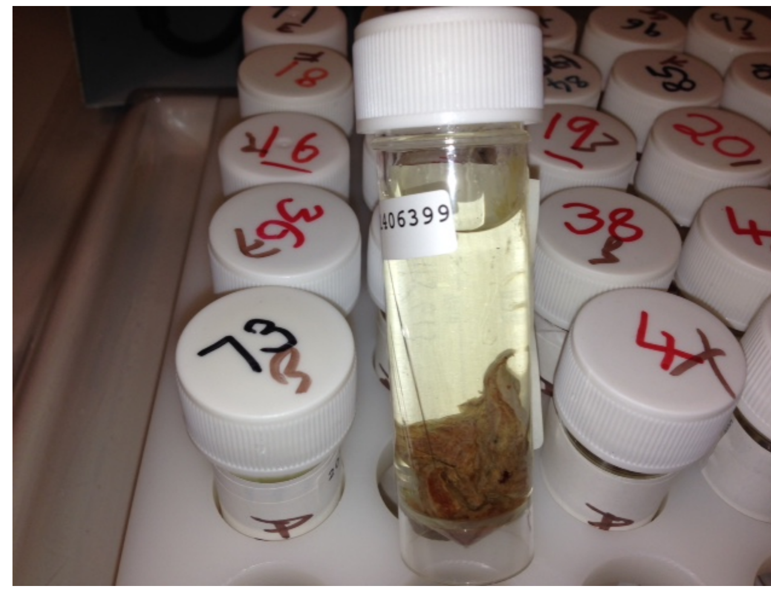
Sample cohort

Lung tissue was collected from 65 patients
54 were valid samples and analysed in this study

Samples were collected at Royal Hallamshire Hospital, Sheffield

31 male 23 female donors
Age range 18-83y, mean age 67.8y

15 stated they had worked with metals
14 smoked/had smoked

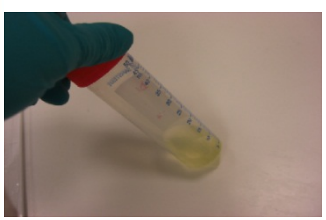


Analytical Method

Samples were stored in alcohol at 4°C → Dissected x3 with a ceramic blade → Dried to constant weight in oven → Approx. 10mg microwave digested in 2:1 nitric acid :$H_2 0_2$

Samples diluted for analysis → Analysis by ICP-MS →

1. Normal Mode
2. CCT mode
3. Low concentrations (rare elements)
4. Beryllium



Digestion and Analysis Results

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QC materials pig kidney and bovine liver CRMS were analysed with each digest
Digest samples were spiked and analysed for all elements
Average sample weight was 0.01 ±0.006g.

Element	Instrument	% recovery of digest matrix spiked with 0.5 µg/L (n=12) Mean ± SD	Mean certified reference material recovery % ERM-BB186	Mean certified reference material recovery % BCR-185R
^{93}Nb	ICAP Q	103.1 ± 1.8		
^{189}Os	ICAP Q	115.9 ± 10.1		
^{208}Pb	XSeries	94.4 ± 1.4	122.1 ± 46.3	90.4 ± 8.0
^{105}Pd	ICAP Q	102.5 ± 1.7		
^{195}Pt	ICAP Q	110.8 ± 2.1		
^{85}Rb	XSeries	98.4 ± 3.0		
^{185}Re	ICAP Q	118.5 ± 2.3		
^{101}Ru	ICAP Q	102.8 ± 1.5		
^{121}Sb	XSeries	89.8 ± 1.4		
^{82}Se	CCT XSeries	89.7 ± 5.0	60.4 ± 4.4	70.7 ± 9.7
^{147}Sm	ICAP Q	112.0 ± 2.7		
^{118}Sn	CCT XSeries	99.7 ± 5.7		
^{88}Sr	XSeries	98.4± 2.6		
^{181}Ta	ICAP Q	120.3 ± 7.2		
^{125}Te	ICAP Q	88.8 ± 4.4		
^{49}Ti	CCT XSeries	106.7 ± 7.7		
^{205}Tl	XSeries	94.1 ± 1.1		
^{169}Tm	ICAP Q	117.6 ± 2.2		
^{51}V	CCT XSeries	105.1 ± 4.0		
^{182}W	CCT XSeries	108 ± 3.4		
^{89}Y	ICAP Q	104.3 ± 1.8		
^{66}Zn	XSeries	102.6 ± 31.2	81.2 ± 10.0	79.9 ± 10.6
^{90}Zr	XSeries	93.4 ± 1.9		

Sample concentrations

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48 element … ent

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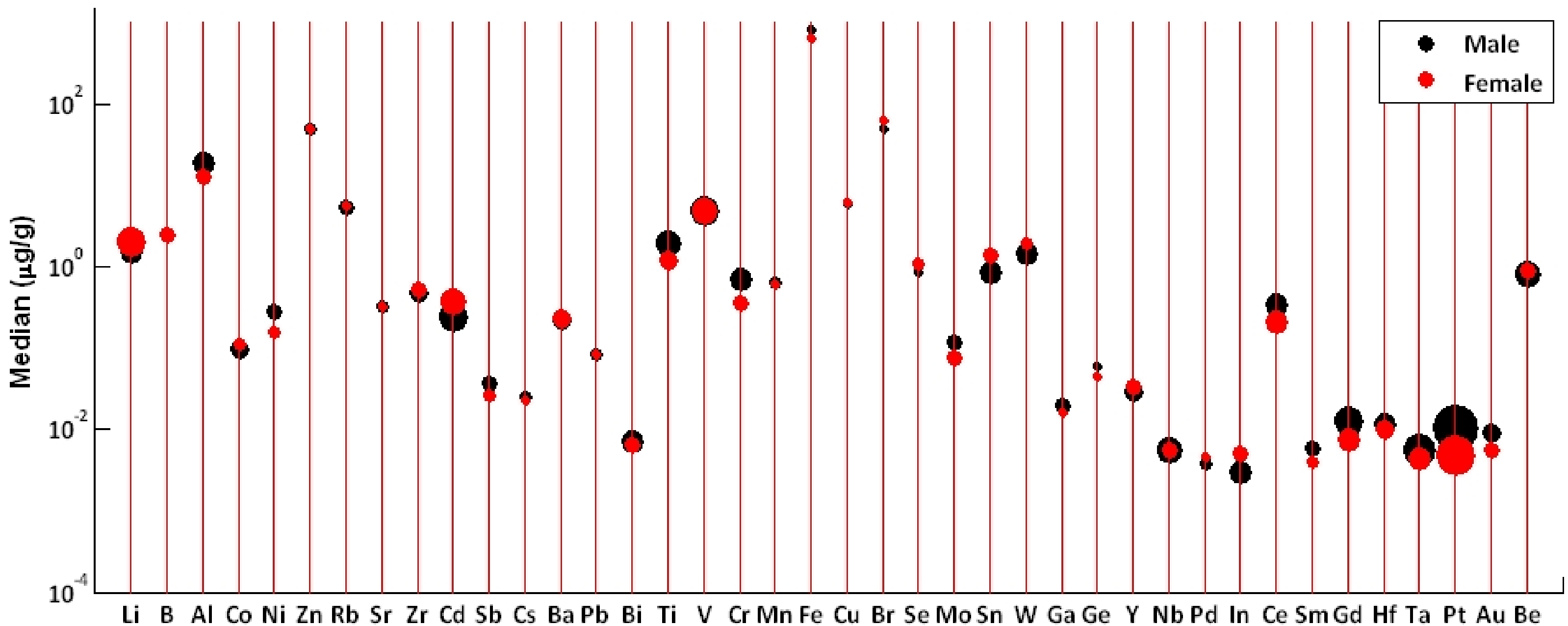
Element	%<LOD	Median in µg/g	95th prctile in µg/g
Al	1	14.27	116.64
As	52		0.168
Au	9	0.01	0.03
B	14	2.04	8.18
Ba	3	0.22	2.58
Be	28	0.00	0.01
Bi	14	0.01	0.04
Br	0	55.14	98.79
Cd	1	0.27	3.43
Ce	0	0.29	2.32
Co	2	0.11	0.42
Cr	0	0.48	5.18
Cs	4	0.02	0.06
Cu	0	6.02	10.51
Fe	0	745.56	1692.49
Ga	0	0.017	0.088
Gd	5	0.009	0.272
Ge	0	0.052	0.122
Hf	0	0.011	0.065
Hg	64		0.28
In	2	0.004	0.024
Li	3	1.637	5.929
Mn	0	0.621	2.015
Mo	16	0.080	0.522
Nb	0	0.006	0.084
Ni	1	0.221	1.127

Element	%<LOD	Median in µg/g	95th prctile in µg/g
Os	83		0.030
Pb	3	0.08	0.23
Pd	16	0.004	0.012
Pt	25	0.003	5.140
Rb	2	5.50	9.20
Re	96		
Ru	88		0.036
Sb	0	0.03	0.12
Se	8	0.89	2.37
Sm	30	0.00	0.02
Sn	1	1.01	6.66
Sr	1	0.32	0.83
Ta	22	0.0035	0.140
Te	71		0.023
Ti	1	1.59	15.71
Tl	45	0.0005	0.003
Tm	81		0.003
V	1	4.86	22.13
W	0	1.75	5.14
Y	0	0.03	0.14
Zn	0	49.44	82.95
Zr	2	0.51	1.76

Gender differences



Males were found to have significantly higher levels of Ni, Cr, Ge, Nb, Sm and Au than females, and significantly lower levels of In.

Trends using mixed effect modelling

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Smokers exhibited significantly higher levels Cd than non-smokers (five fold increase).

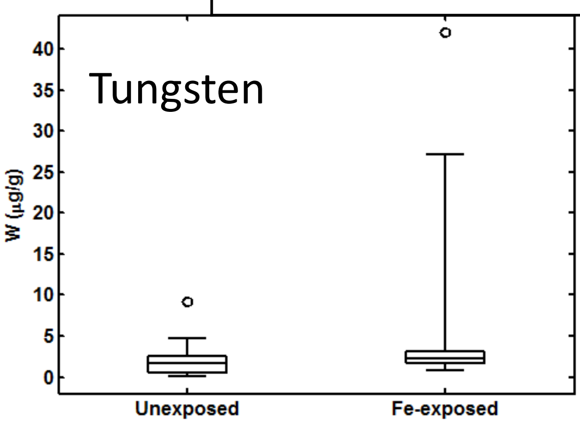
Effects of increased concentration with increased age, were observed for Be, Br, Ce, Co, Cr, Cs, Ga, In, Nb, Pb, Sb, Se, Sm Sn, Sr, Ti, and W.

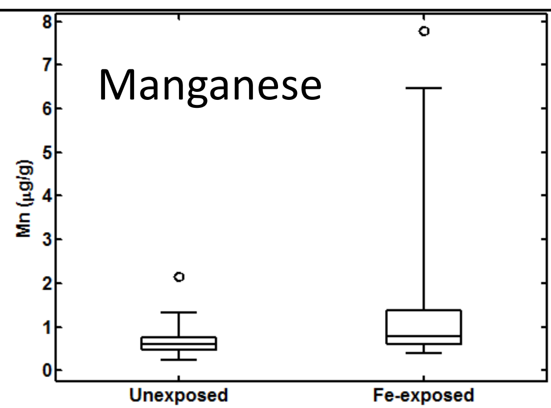
After adjusting for variation due to gender and smoking, the elements that displayed the greatest within person variation were Ti , Ba and Bi.
The lowest were Cu, Br, Cs, and Fe .

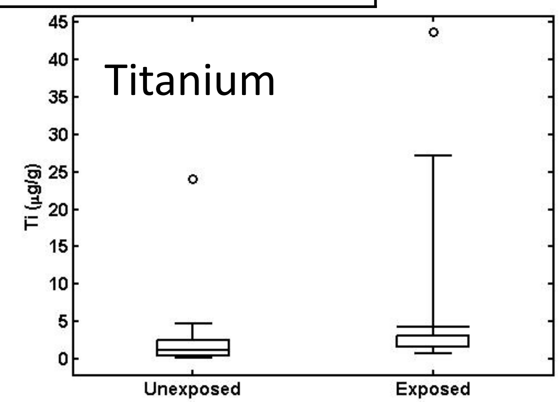
Between person variations were greatest for V, Li and Cd, and lowest for Cu.

Trends observed in ‘metal exposed’ workers

Element	95th percentile concentration in unexposed in µg/g	95th percentile concentration in ‘iron exposed workers’ in µg/g	Using ME model % increase in ‘iron exposed workers’
Iron	1380.4	2672.4	
Tungsten	4.66	27.1	119%
Manganese	1.31	6.47	73%
Titanium	6.15	25.12	150%







Summary

References ranges of these elements in lung samples collected from human donors have been established for 48 elements.

Typically variations within persons were lower for essential elements like copper, bromide and iron and higher for vanadium, lithium and cadmium.

Gadolinium and platinum levels are yet to be differentiated from treatments received.

Cadmium was the only element significantly associated with smoking status.

Donors who stated they had been occupationally exposed to metals showed elevated iron levels. Further analysis showed increased levels of tungsten, manganese and titanium with this exposed iron group.


Thank you for listening.