

Consortium



University of Modena and Reggio Emilia
LABORATORY of BIOMATERIALS



INFN - Istituto Nazionale
per la Fisica della Materia



Johannes Gutenberg University
Institute of Pathology



UNIVERSITY OF
CAMBRIDGE

Department of Materials and Metallurgy

biomatech

France



FEI COMPANY™

THE STRUCTURAL PROCESS MANAGEMENT COMPANY

Italy

Project Coordinator

Dr. Antonietta M. Gatti
Laboratory of Biomaterials
University of Modena and Reggio Emilia
Via del Pozzo, 71 - 41100 Modena Italy
e-mail: gatti@unimore.it
e-mail: biomat@nanopathology.it
web page: www.nanopathology.net

Project Administrator

Dr. Emanuela Arata
INFN - The National Institute for the Physics
of Matter

Commission's Scientific Officer

Dr. Ana Nieto
European Commission- DG Research,
Unit E-2: Health, Food, and Environment
Brussels - Belgium
e-mail: ana.nieto@cec.eu.int

Partners

Prof. C. James Kirkpatrick
University of Mainz, Germany
e-mail: Kirkpatrick@pathologie.klinik.uni-mainz.de

Prof. William Bonfield
University of Cambridge, UK
e-mail: wb210@hermes.cam.ac.uk

Dr. Rosy Eloy
Biomatech SPA, France
e-mail: i.china@biomatech.fr

Dr. Alberto Tinti
FEI Italia, Italy
e-mail: atinti@it.feico.com



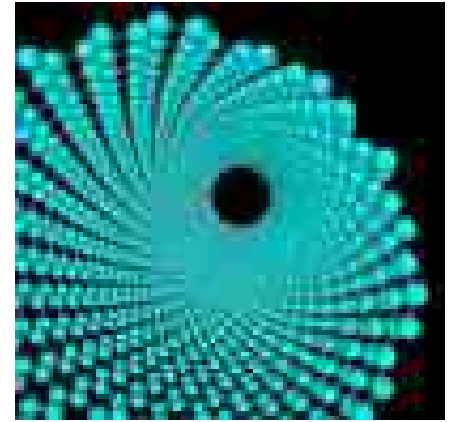
An RTD project funded by
the European Commission

Nano pathology

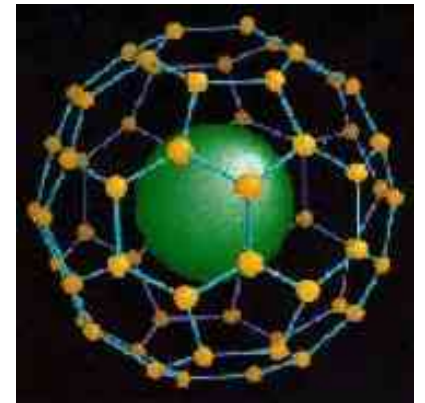
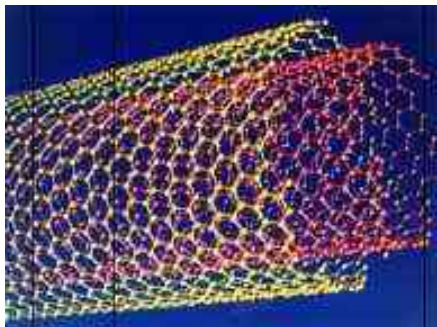
The Role of Micro
and Nanoparticles in
Biomaterial-Induced
Pathology

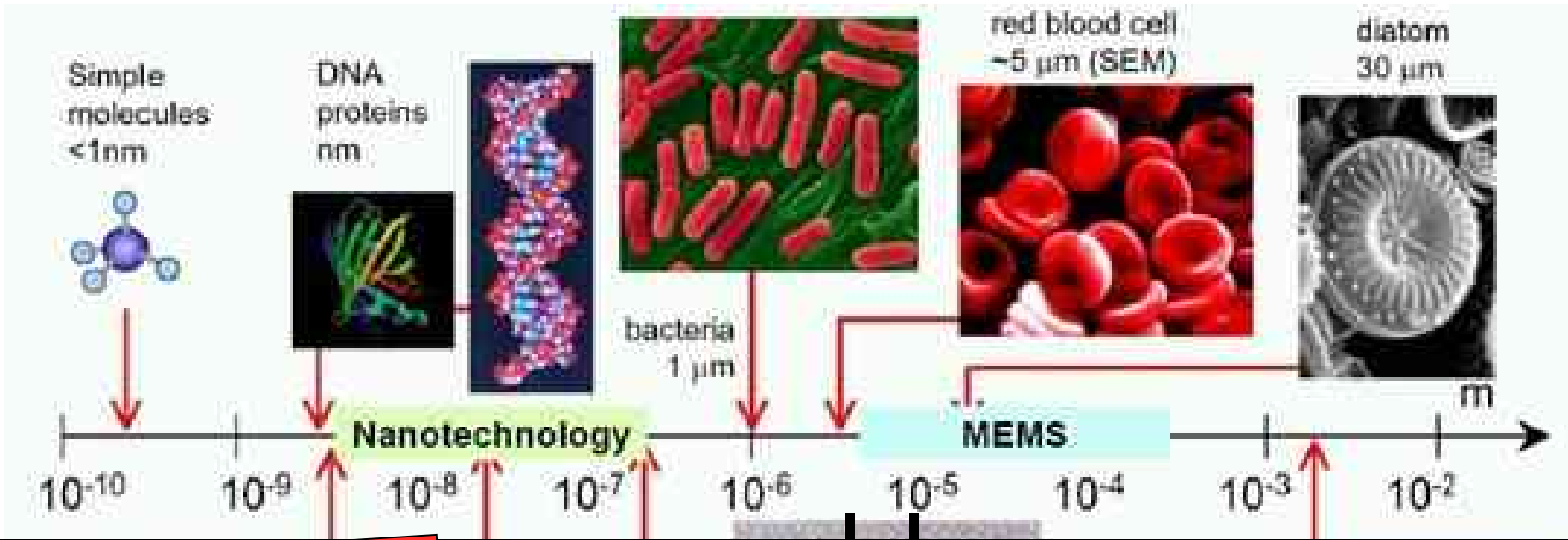
Project
QLRT-2002-147
(2002-2005)

Nanopathology



is the branch of learning that deals with how the organism reacts to the presence of micro- and nano-particles





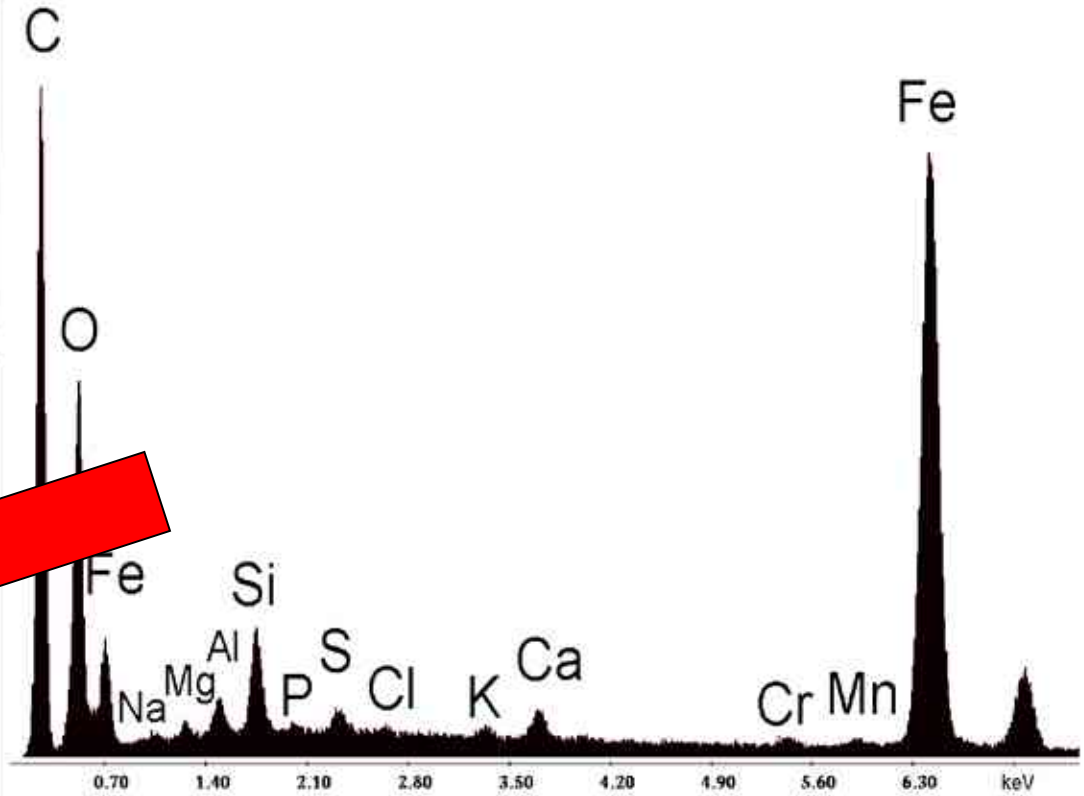
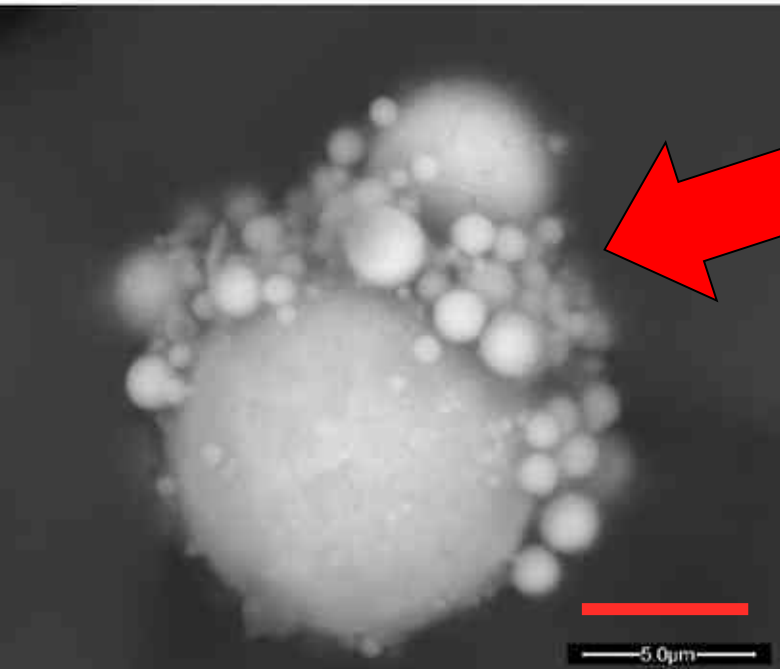
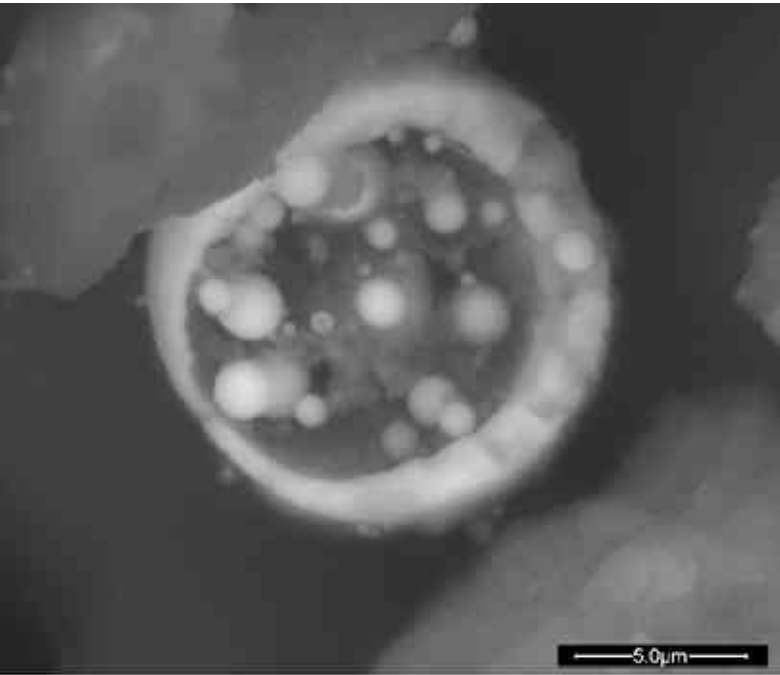
Nanoparticle

PM10

Red cells

Scale of dimensions of biological and synthetic materials

Examples of environmental pollution from a foundry



5 micron

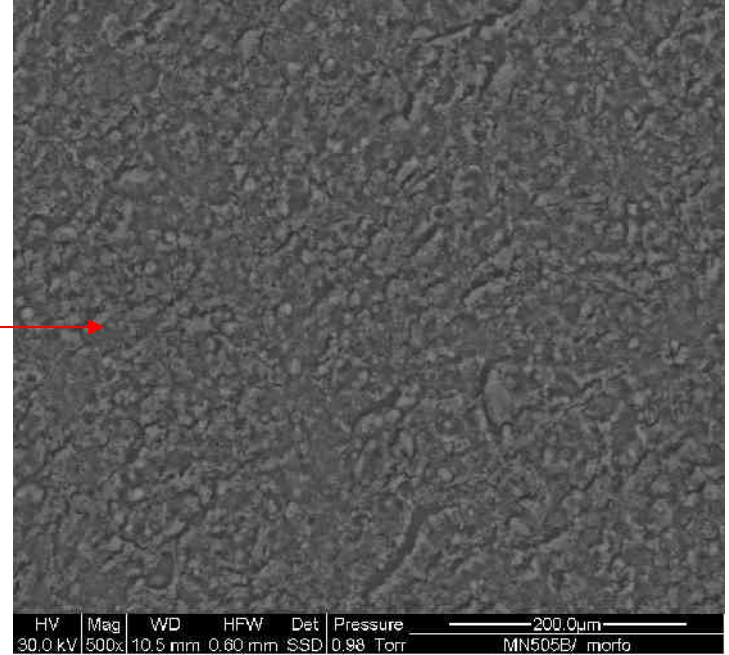
	<u>Pathologies</u>	<u>No. Cases</u>
I	Anencephalic birth	7
II	Anomalies	10
III	Neu-Lexova	6
IV	Leukemia	2
V	Control	6

Analyzed samples:

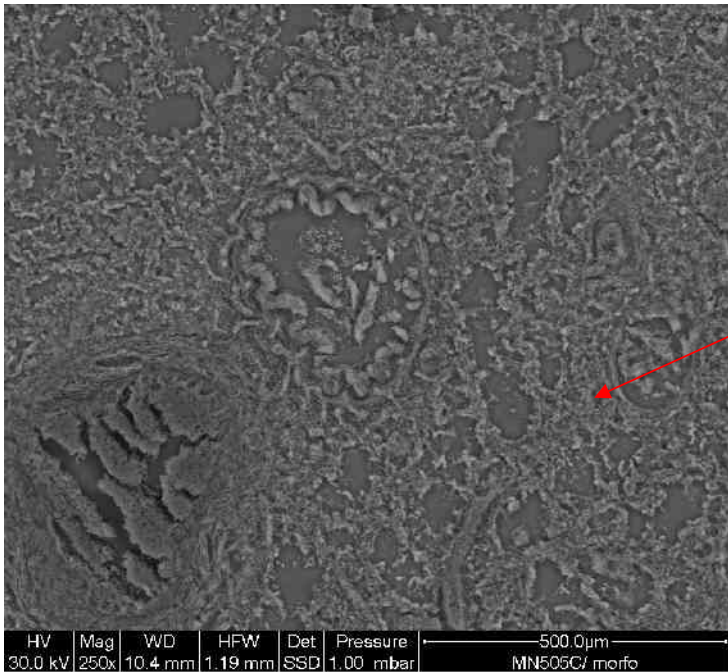
liver, kidney, lung, bladder, gonads, brain, placenta

Control samples

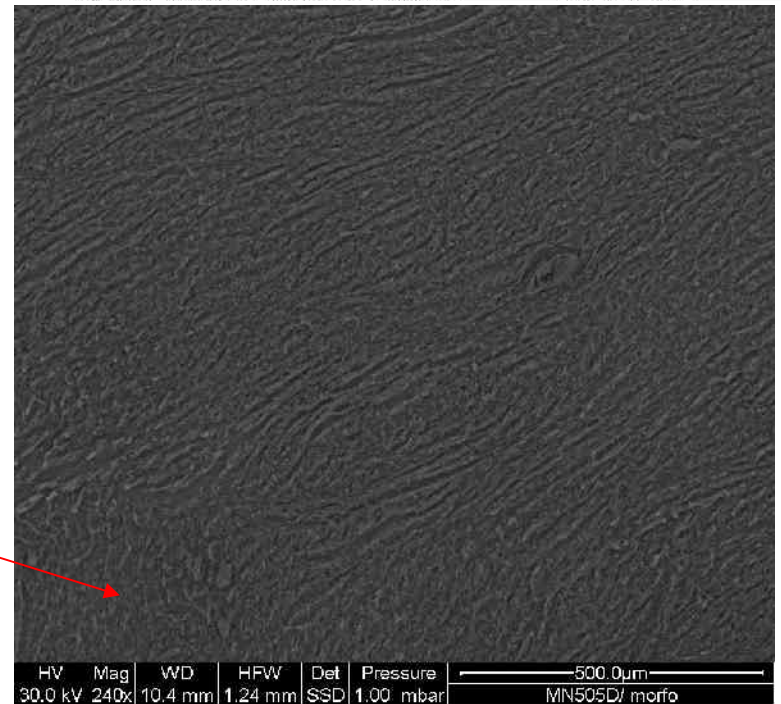
Liver →

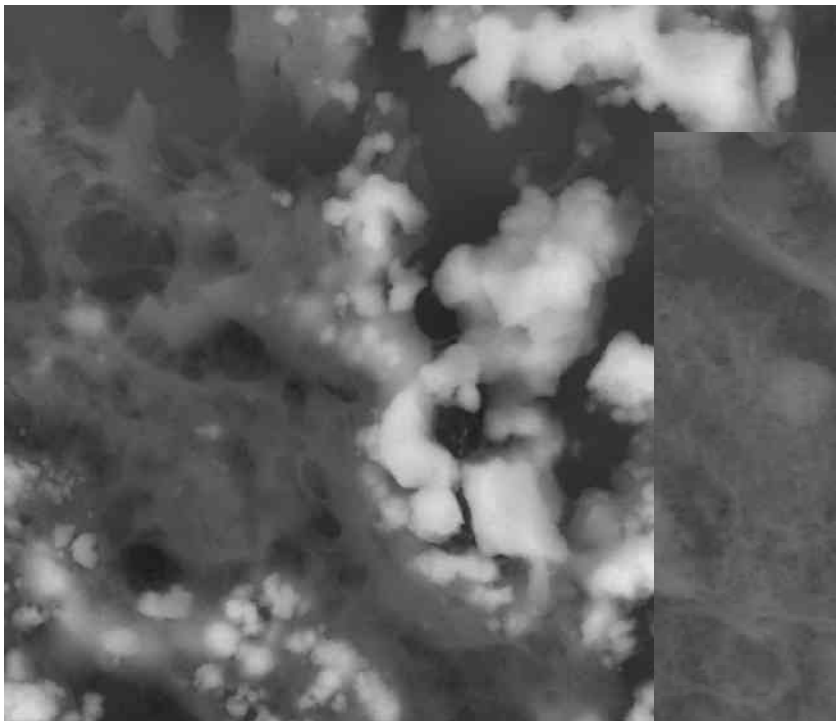


Lung →

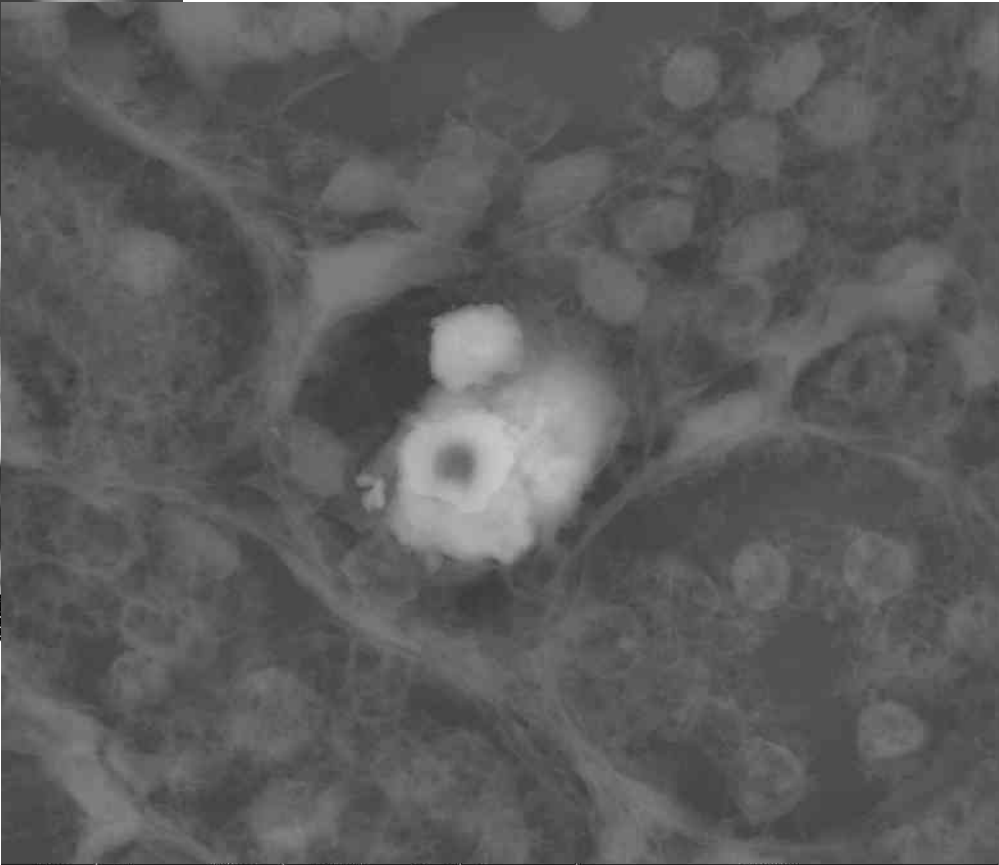


Heart →

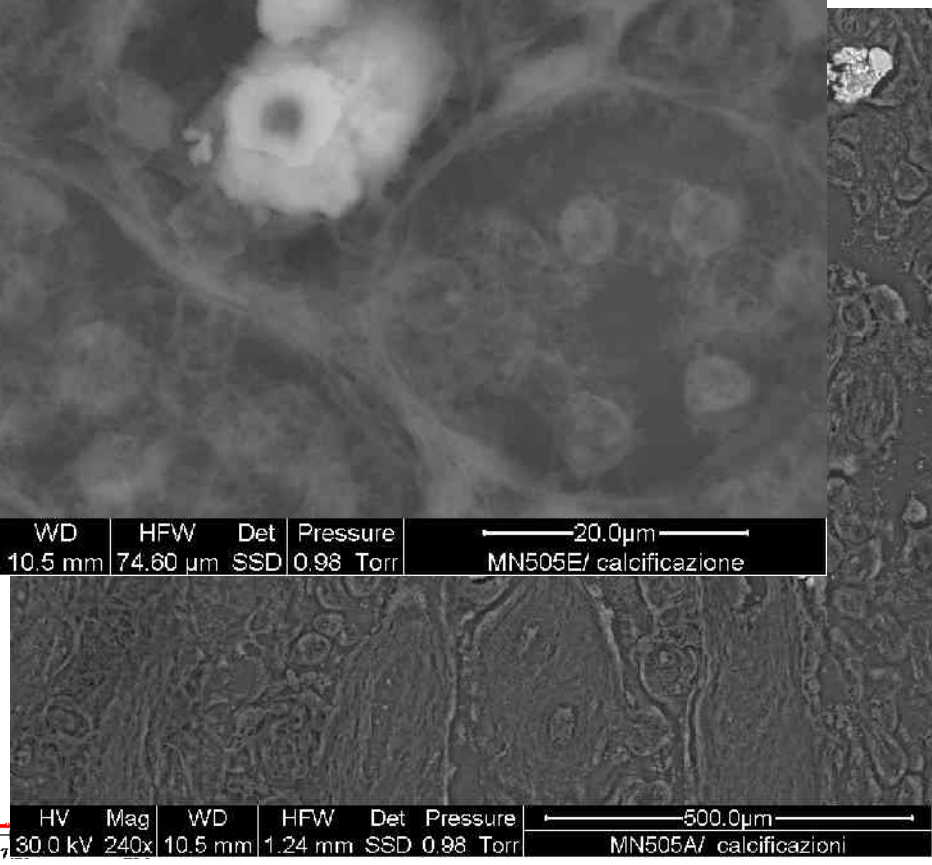
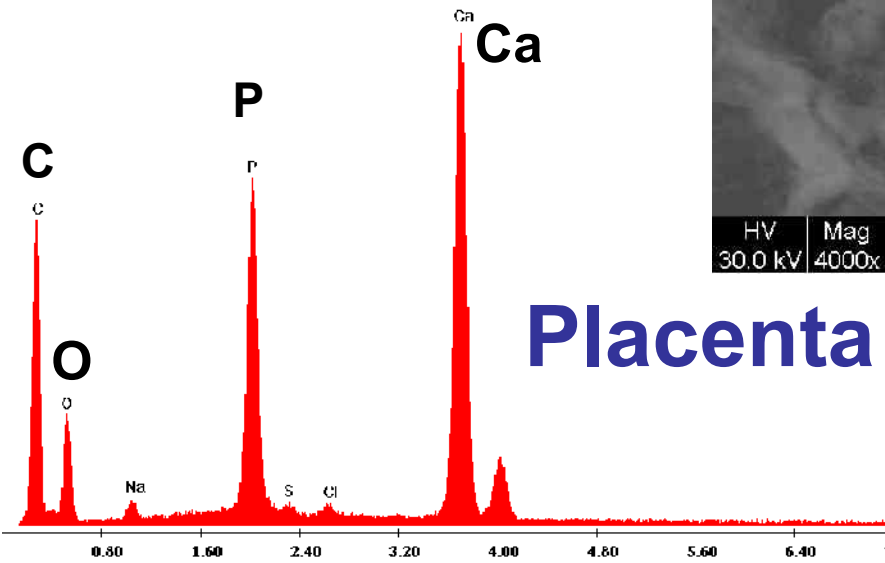




HV	Mag	WD	HFWD	Det	Pressure	20.0
30.0 kV	4000x	10.6 mm	74.60 μm	SSD	0.98 Torr	MN505A/ c

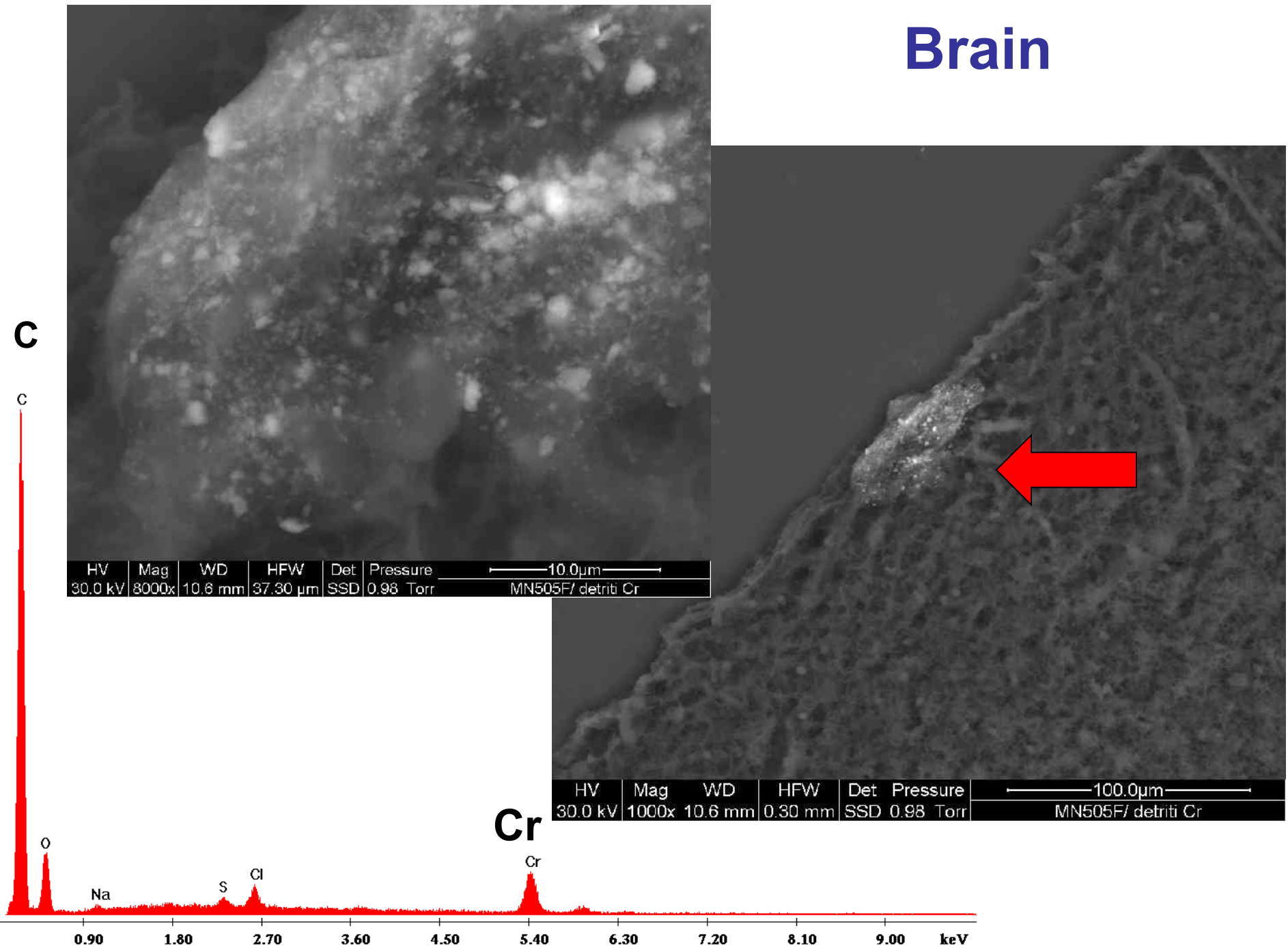


HV	Mag	WD	HFWD	Det	Pressure	20.0 μm
30.0 kV	4000x	10.5 mm	74.60 μm	SSD	0.98 Torr	MN505E/ calcificazione



HV	Mag	WD	HFWD	Det	Pressure	500.0 μm
30.0 kV	240x	10.5 mm	1.24 mm	SSD	0.98 Torr	MN505A/ calcificazioni

Brain



Acute Mieloid Leukemia from Mantua (n. int. 478 MN - 481 MN)

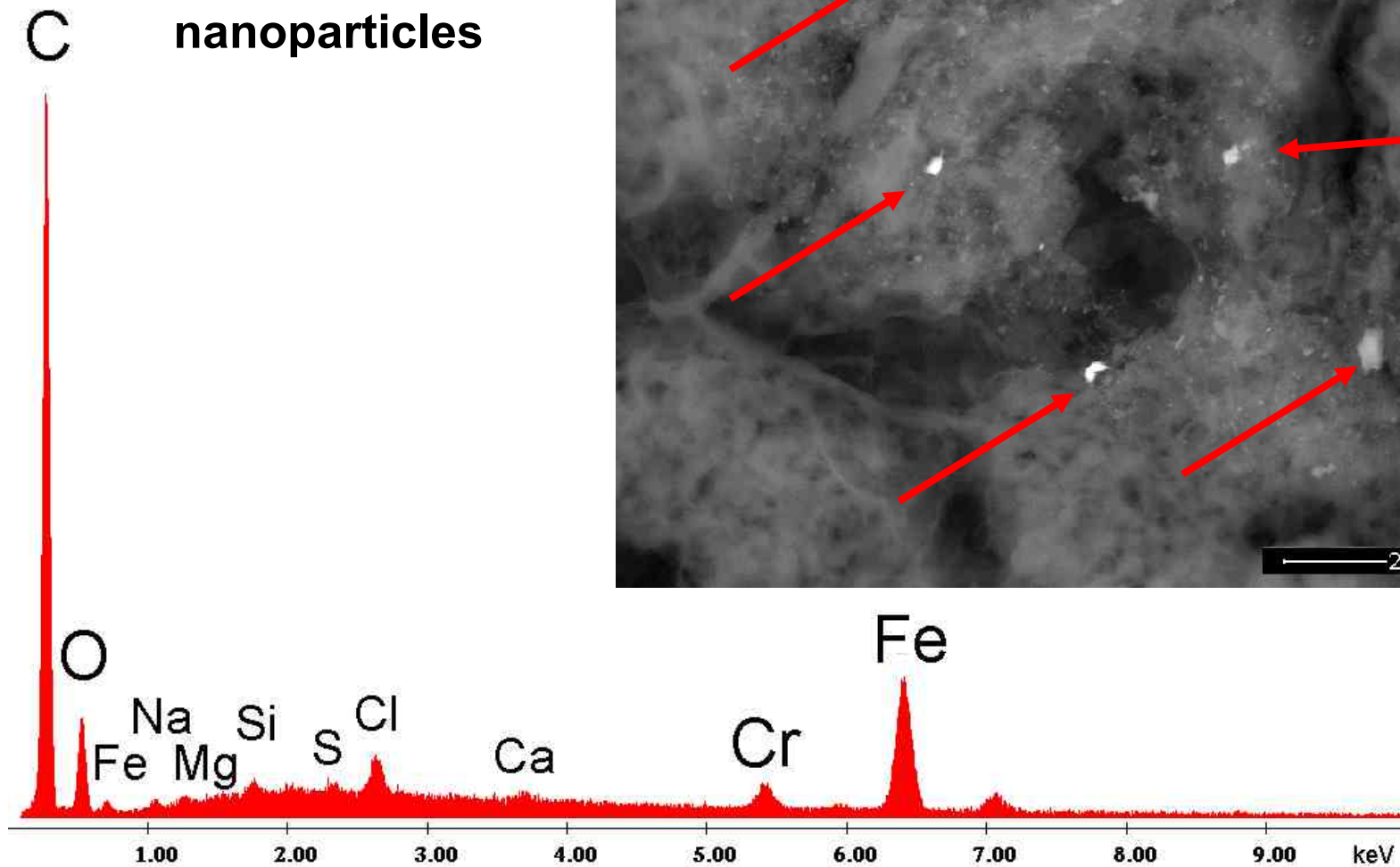
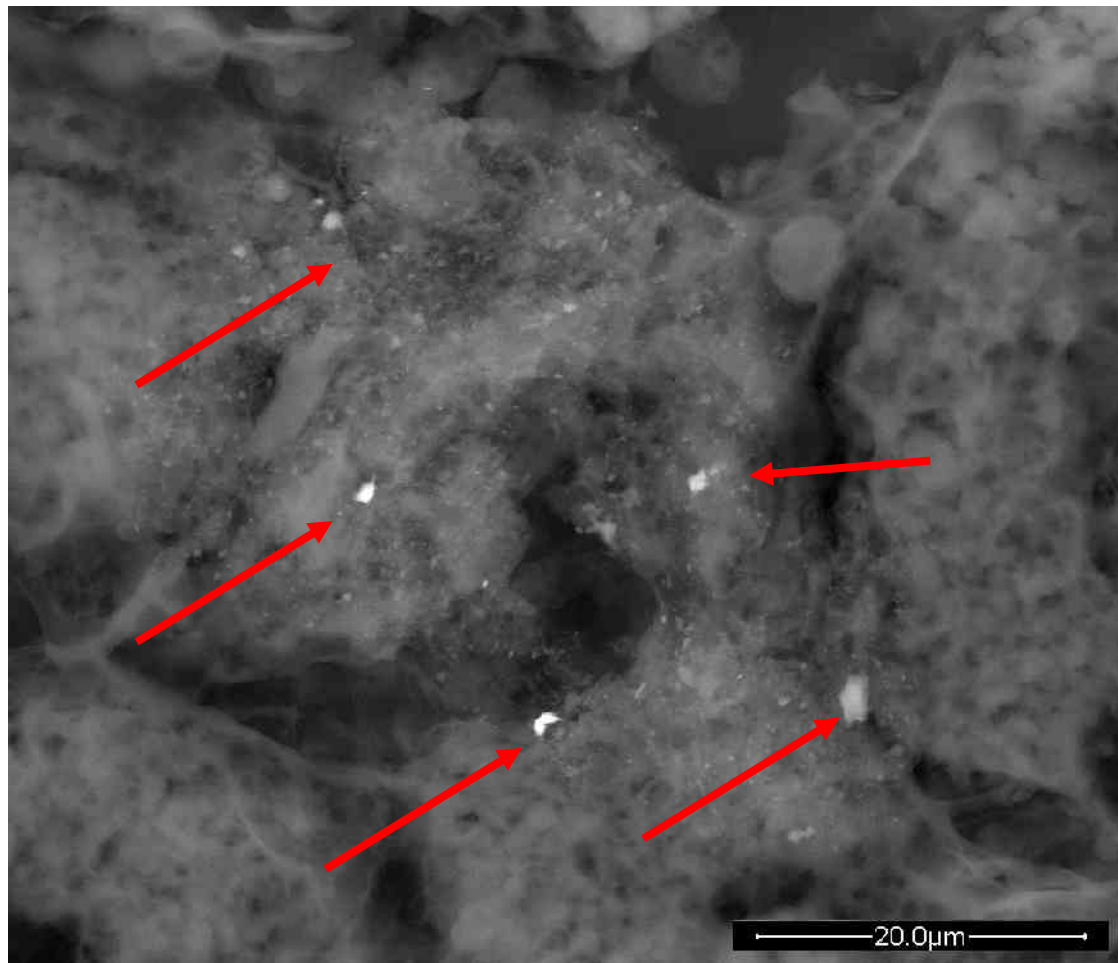


Kidney

N° Analysis	Morphology	Chemical elements
1	Biological tissue	C,O,Cl,Na,S,P,N
2	Debris 2 µm	C,O,Cl,Fe,S,P,Cr,Na,N
3	Debris 2 µm	C,O,Cl,Fe,S,Na,P,N
4	Debris 2 µm	C,O,Fe,Na,P,S,Cl,N
5	Debris 5 µm	C,Si,O,Na,Ca,K,Cl,P,N,s
6	Debris 7 µm	C,O,Si,Cl,Ca,S,Na,P,Al,K,Fe,Mg
7	Debris 2 µm	C,Cr,O,Cl,S
8	Debris 0,2 µm	C,Fe,O,Cl,Cr,S,Si,Ca,Na,Mg
9	Cluster of debris	C,Fe,O,Cl,Cr,S,Si,Ca,Na,Mg
10	Debris 0,5 µm	C,Bi,O,Na,P,Si,N
11	Cluster of Debris	C,P,O,Ca,Na,Cl,S,Fe,Zn
12	Cluster of Debris	C,O,Si,Cl,Ca,S,Na,P,Al,K,Fe,Mg
13	Debris	C,P,O,CaZn,S,Cl,Fe

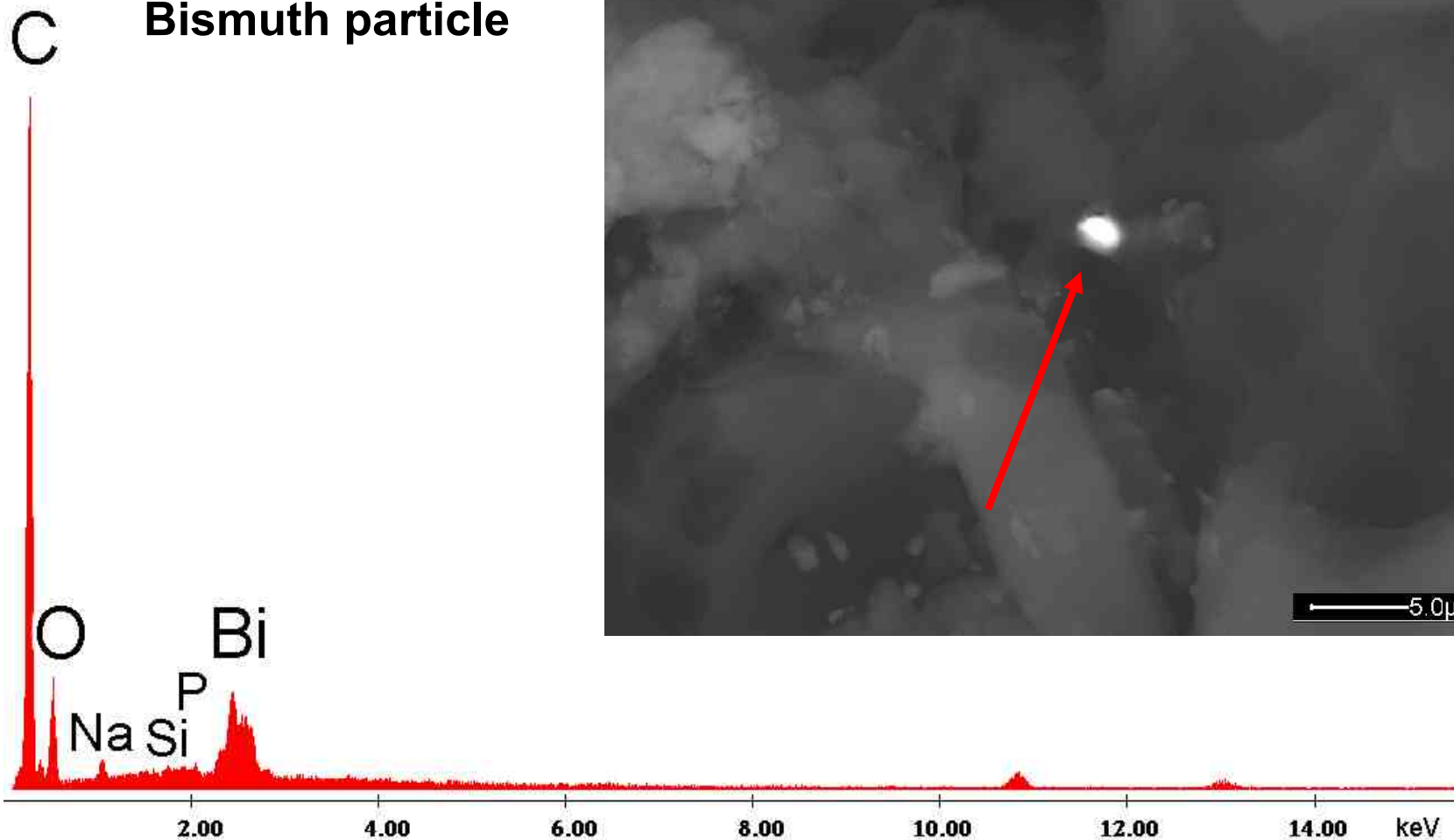
Kidney

Stainless steel nanoparticles

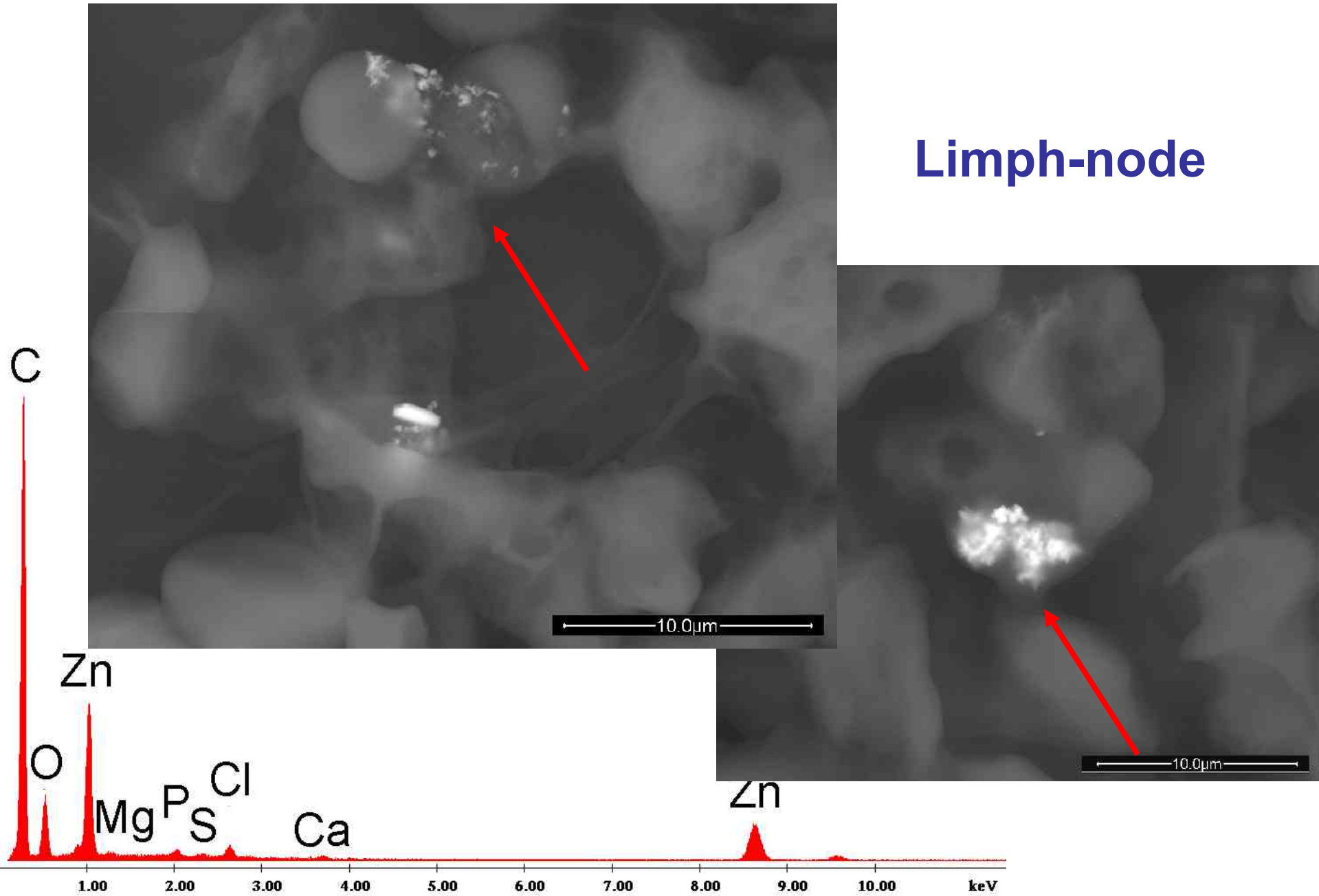


Kidney

Bismuth particle



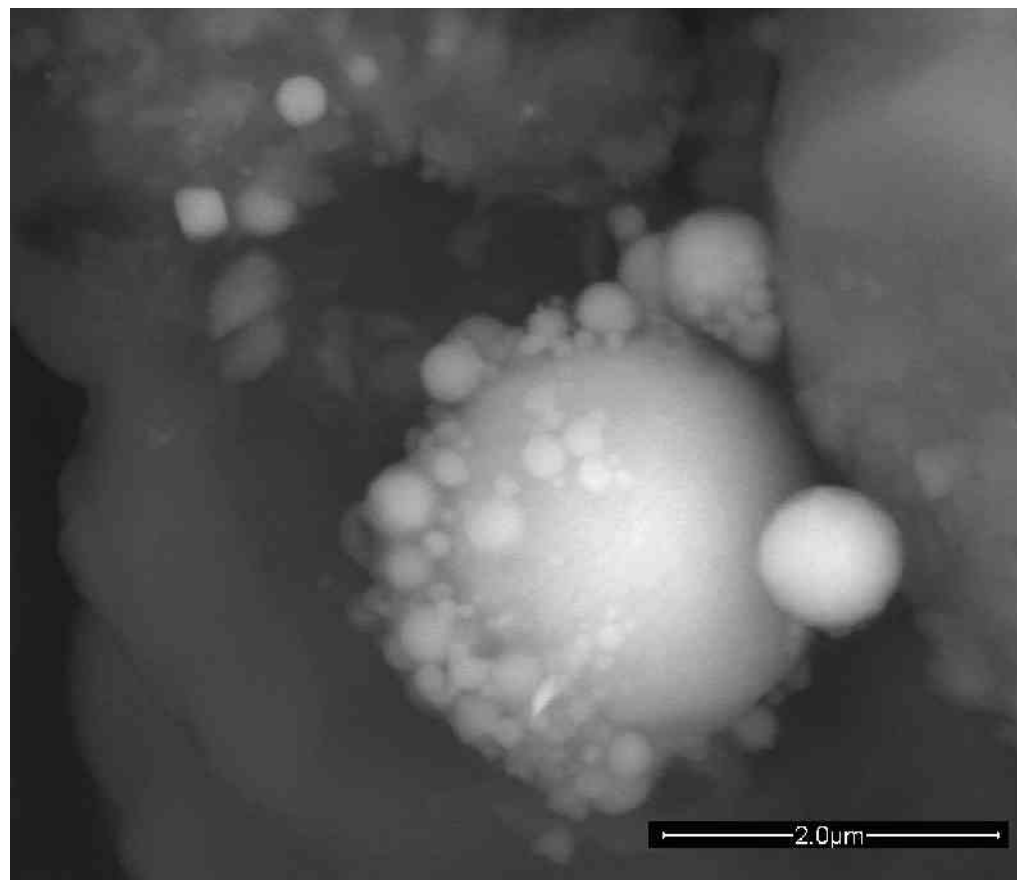
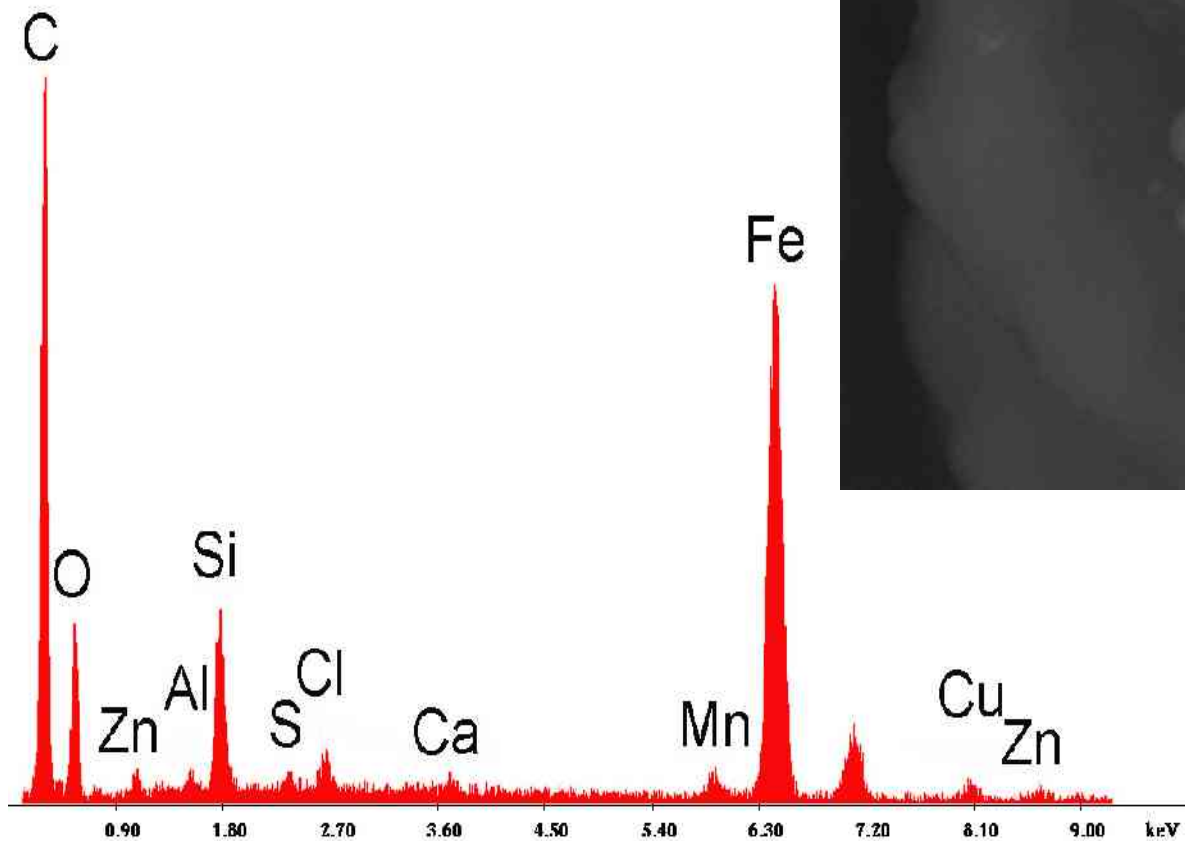
Lymph-node



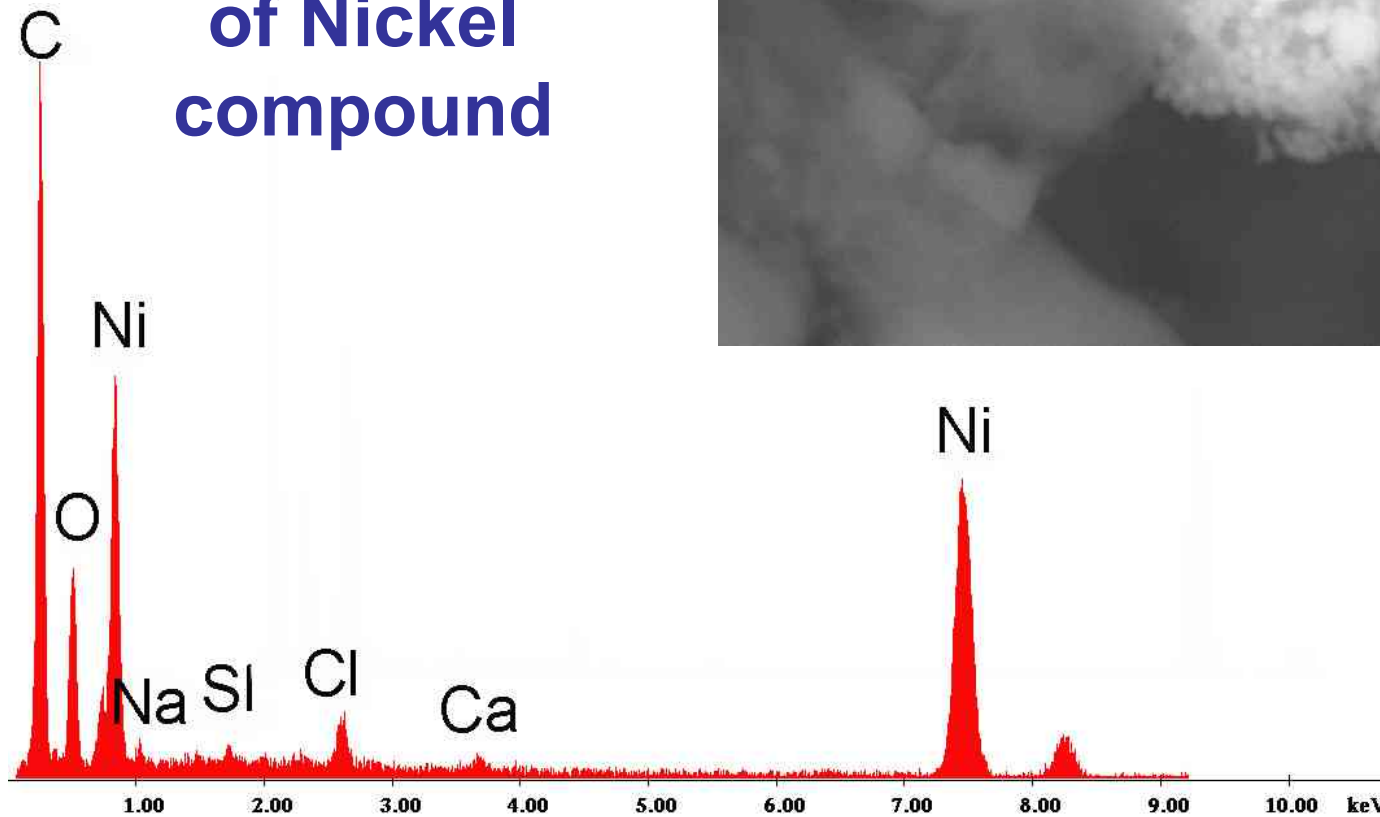
Heart

N° Analisi	Morphology	Elements
1	Biological tissue	C,O,Cl,Na,S,P
2	Cluster of 2 µm spherules	C,Ni,O,Cl,Si,Ca,Na
3	1 - 4 µm debris	Si,C,O,Na,Cl,Al,Ca,K,Mg, Fe
4	0,1 - 2 µm spherules	C,Fe,Si,O,Cl,Mn,Zn,Cu,S, Al,Ca
5	7 µm debris	C,Zn,P,S,Cl,Ca

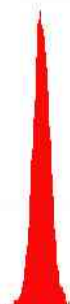
Heart Debris of Iron- Manganese-Copper- Zinc



Heart Cluster of nanoparticles of Nickel compound

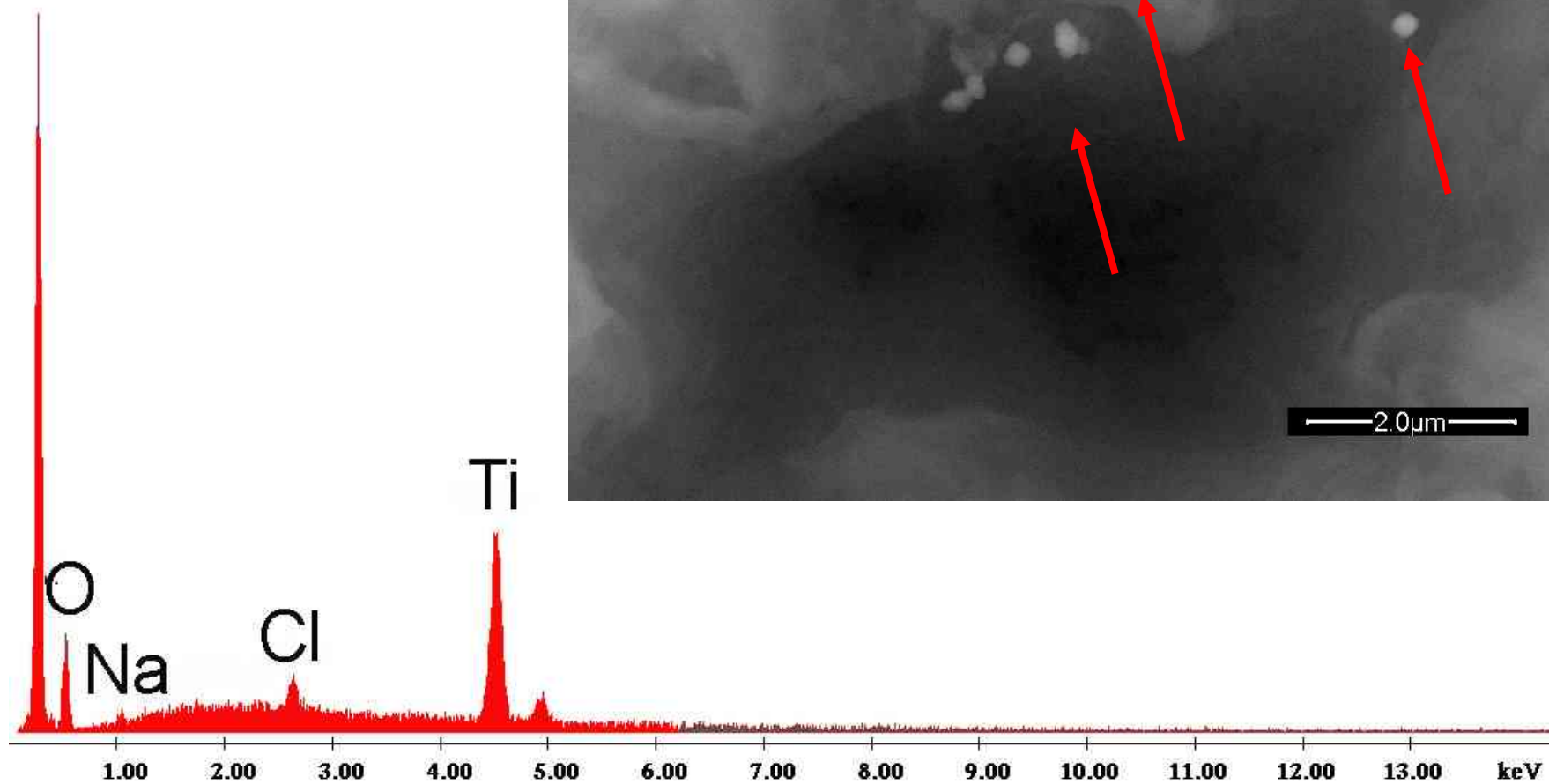


Ni



Brain with Titanium nanoparticles

C nanoparticles

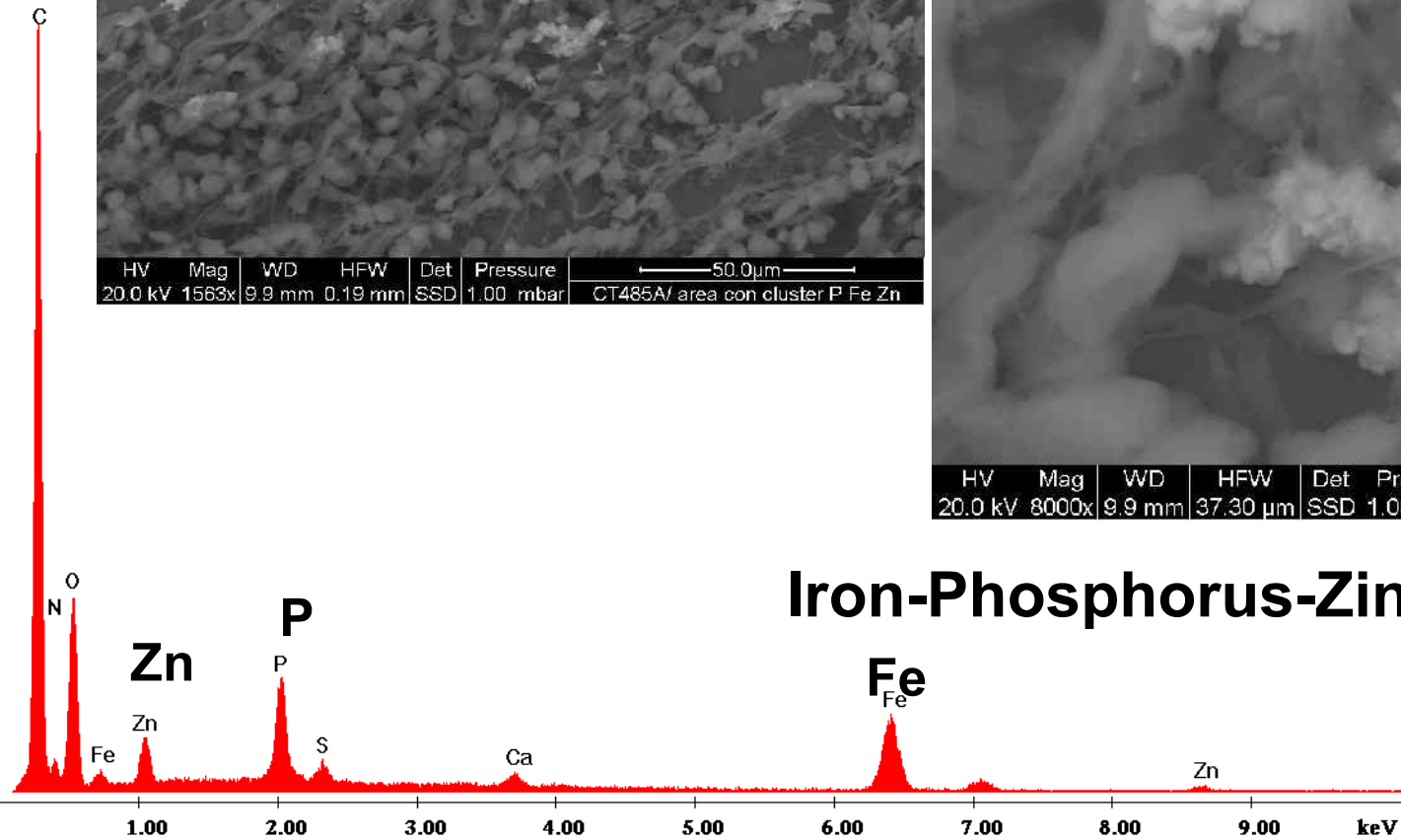
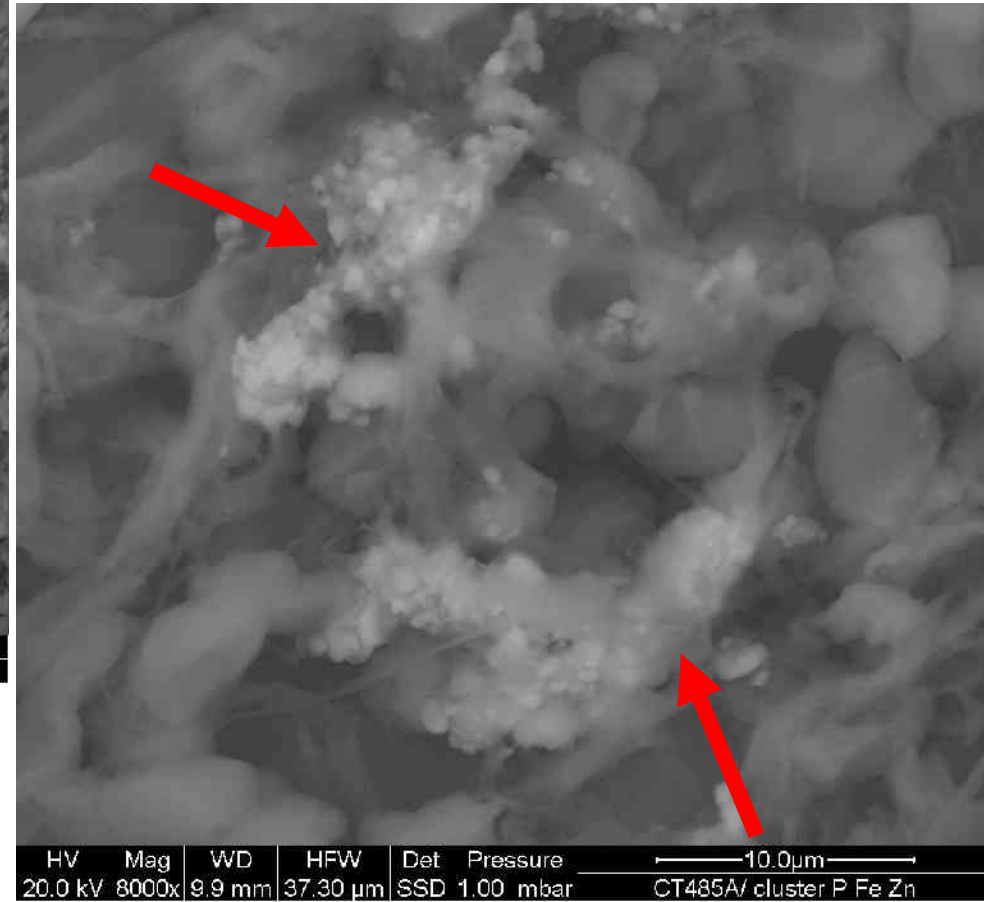
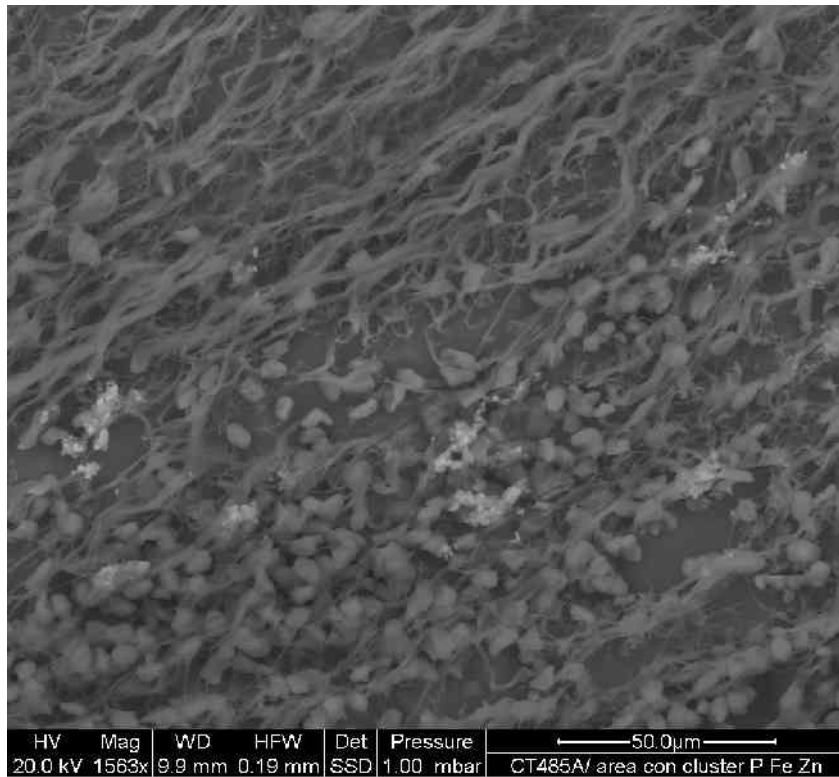


Spleen of a spina byphida case

CT 485 A

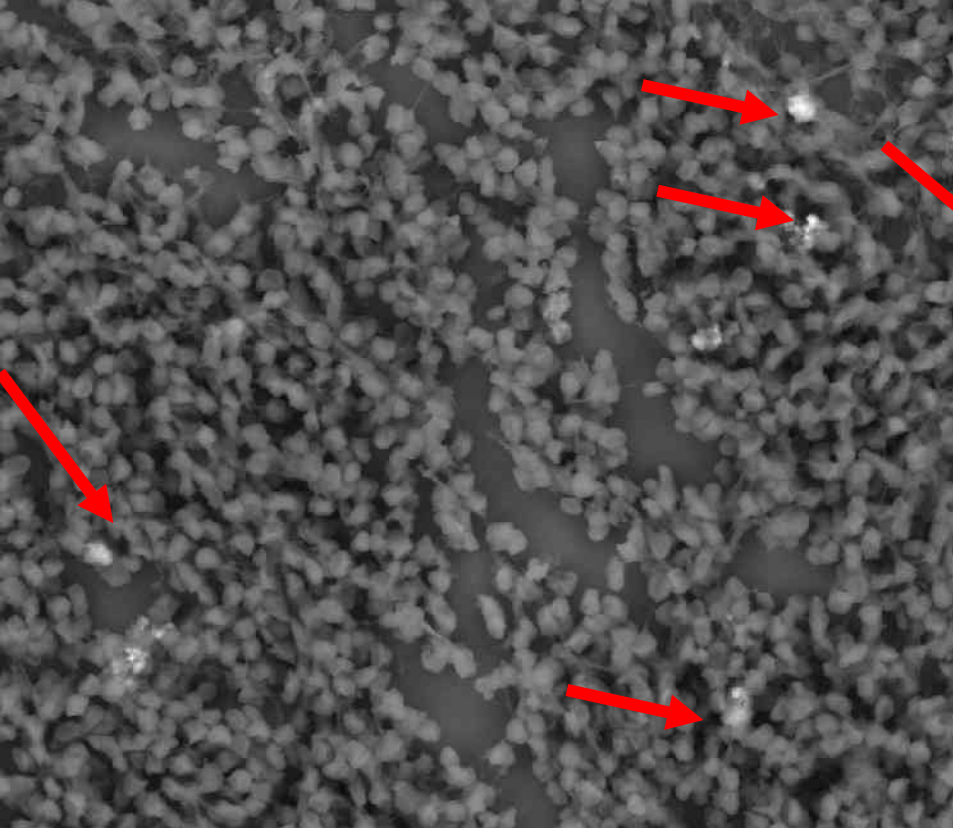
Analysis	Morphology	Elements
1	Biological tissue	C,O,S,P,Na,N
2	5 µm debris	C,Si,O,Al,Na,Ca,P,S,N
3	clusters	C,O,P,Fe,Na,Ca,Mg,S
4	7 µm debris	Si,C,O,P,P,Na,S,N
5	0,5 - 2 µm clusters	C,O,P,Fe,Zn,Ca,S,N
6	2 µm debris	C,O,Fe,Si,Al,Na,S
7	10 µm clusters	C,O,Ba,S,Ca,Si,Al,Na,Fe
8	5 µmclusters	C,Ca,O,Si,Ti,Al,P,S,Cl,NaK, Fe,Mg
9	100 µm clusters	C,P,O,Fe,Na,Ca,S,Mg

Spleen



Iron-Phosphorus-Zinc Precipitates

Kidney

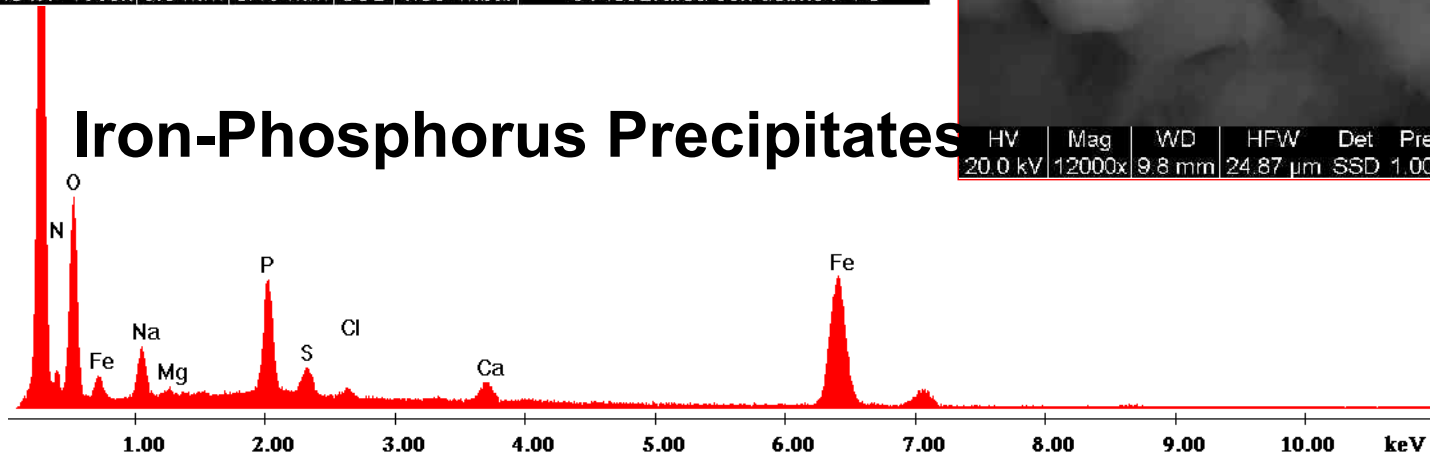


HV 20.0 kV Mag 1563x WD 9.8 mm HFW 0.19 mm Det SSD Pressure 1.00 mbar
50.0µm
CT485B/area con debris P Fe

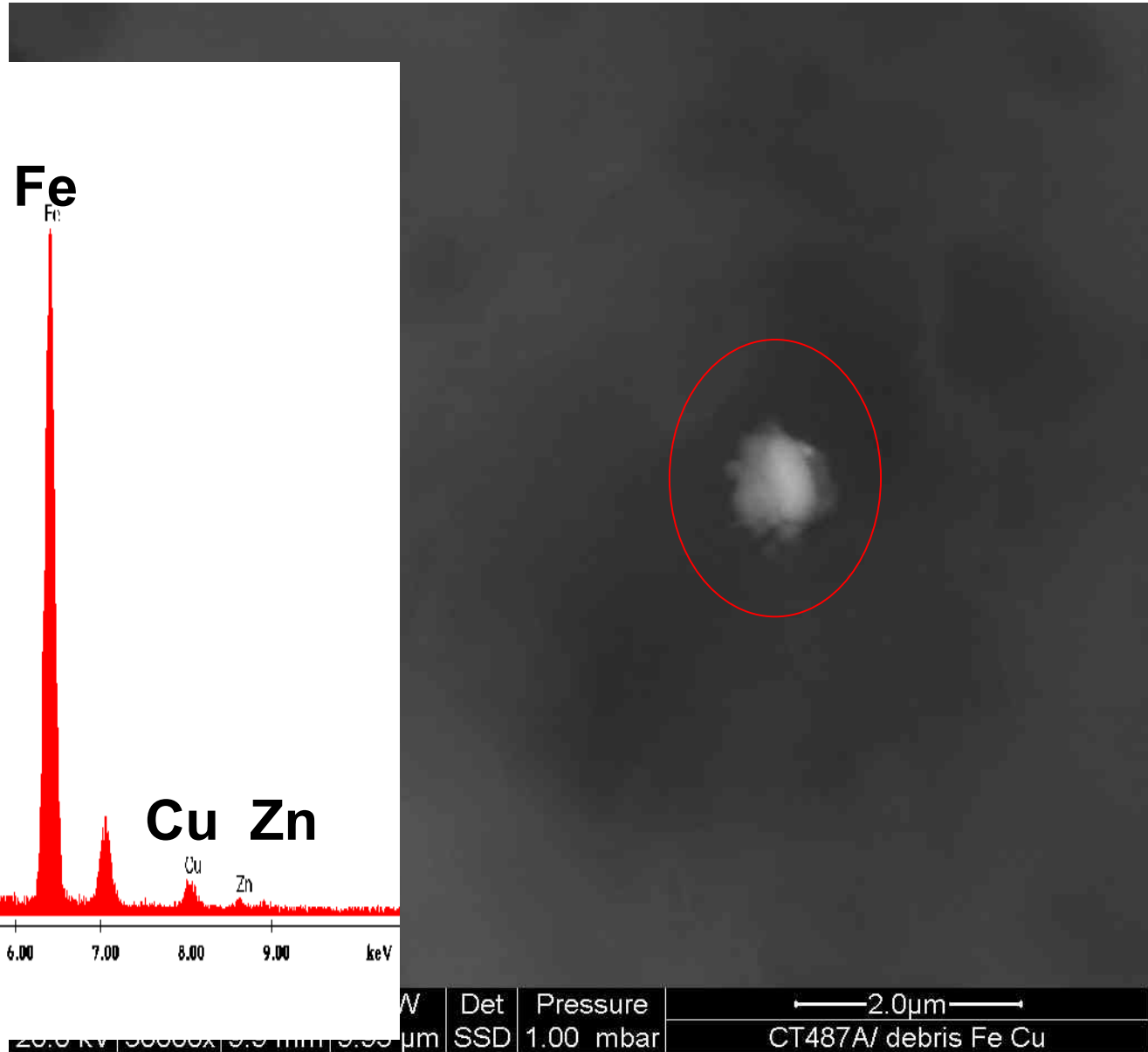
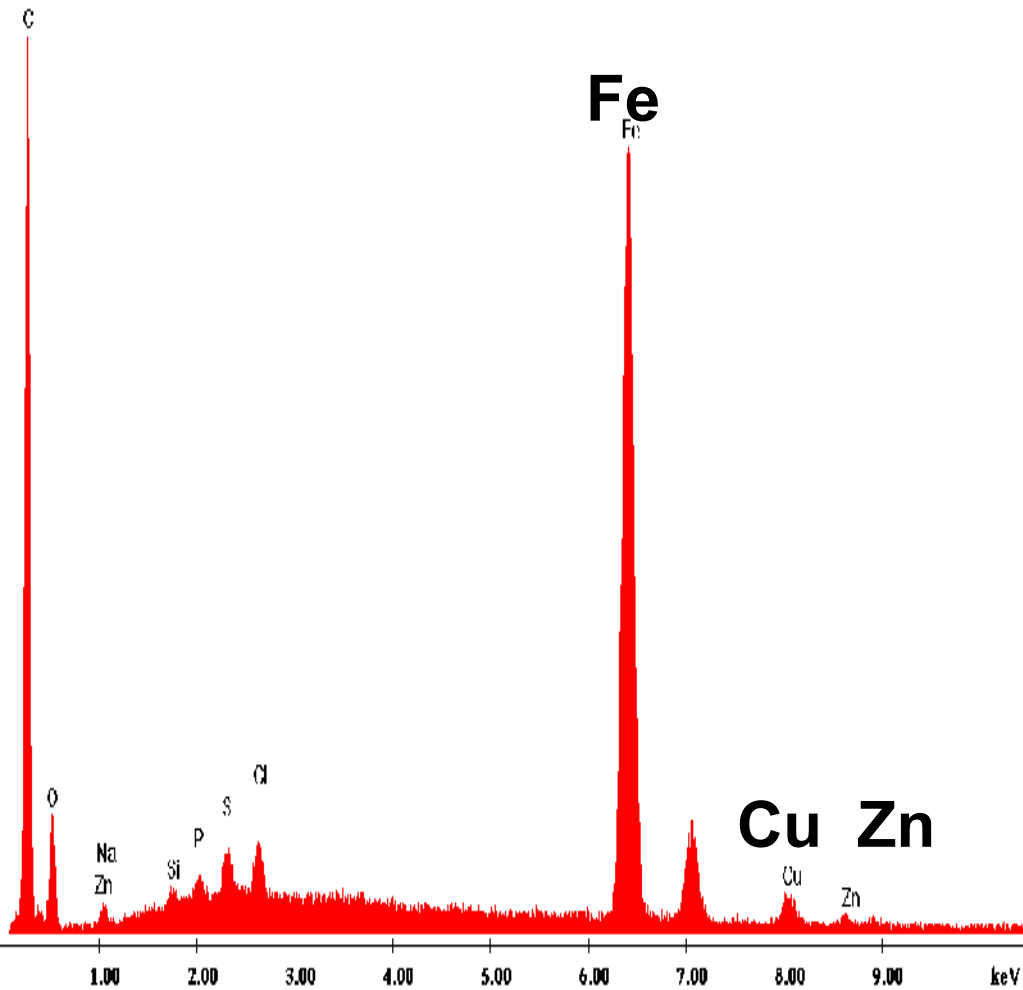


HV 20.0 kV Mag 12000x WD 9.8 mm HFW 24.87 µm Det SSD Pressure 1.00 mbar
10.0µm
CT485B/area con debris P Fe

Iron-Phosphorus Precipitates



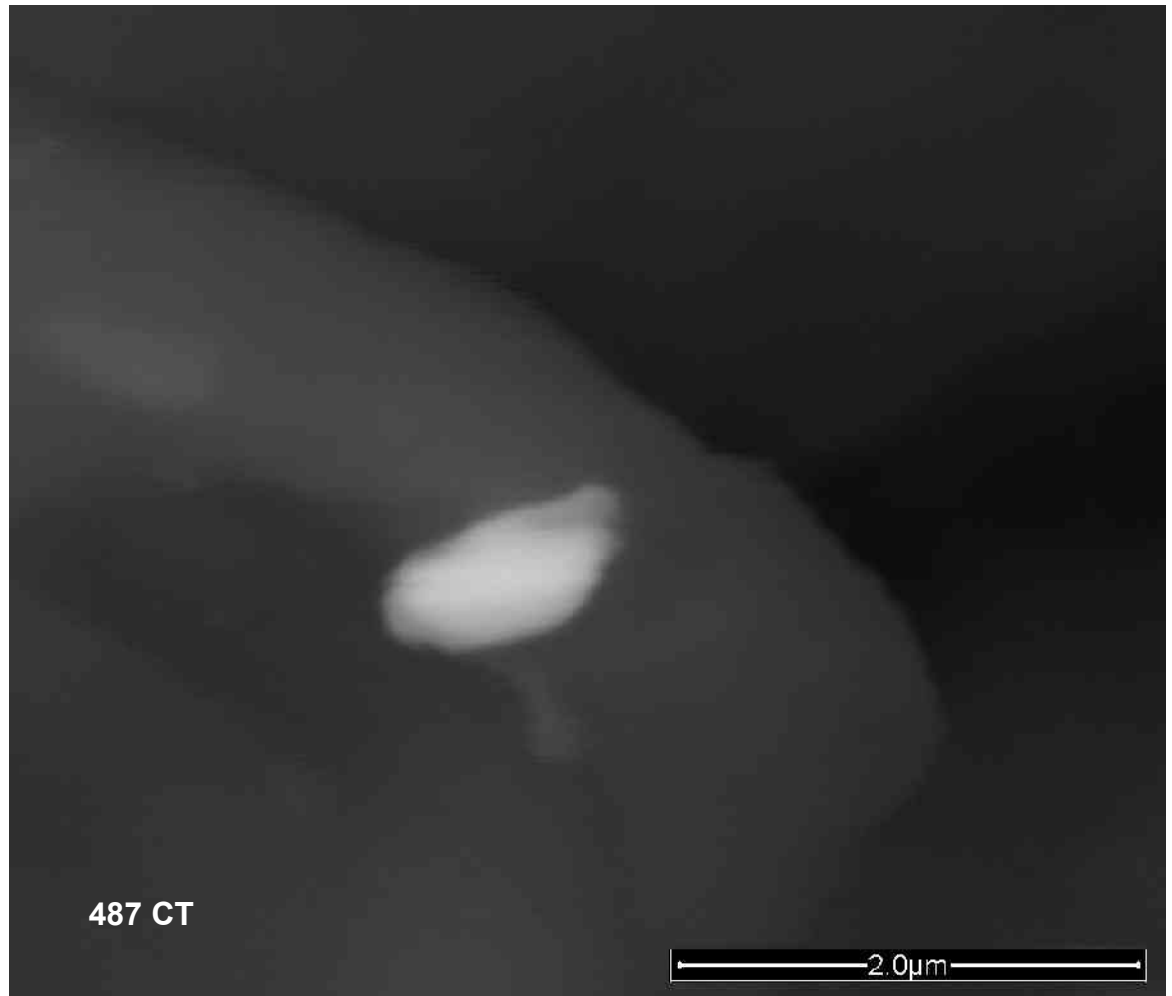
Liver





Spina Byphida Kidney

B 46/06 CT 487 B



C

O

Si

Al

Pb

Zn

P

Ca Ti

Fe

Zn

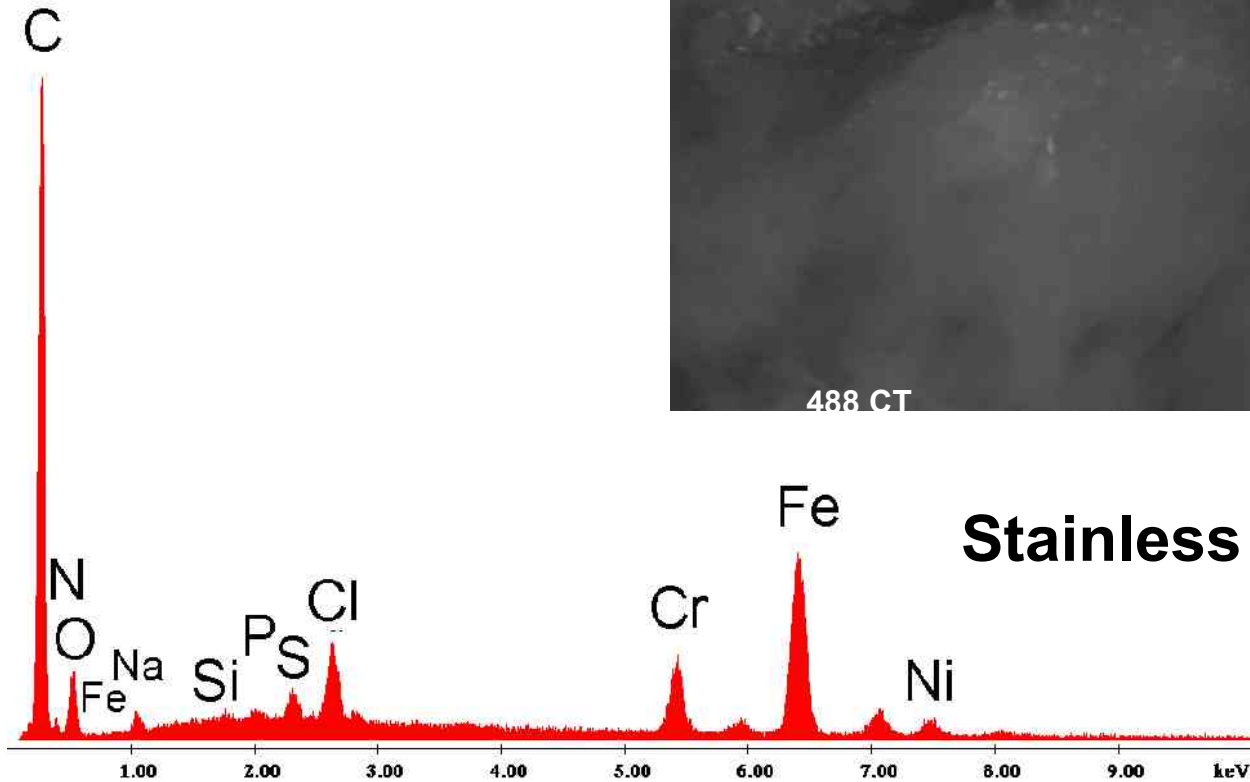
Pb

1.00 2.00 3.00 4.00 5.00 6.00 7.00 8.00 9.00 10.00 11.00 12.00 keV

800-nm toxic particle of Lead



Spina byphida Liver A 251/06



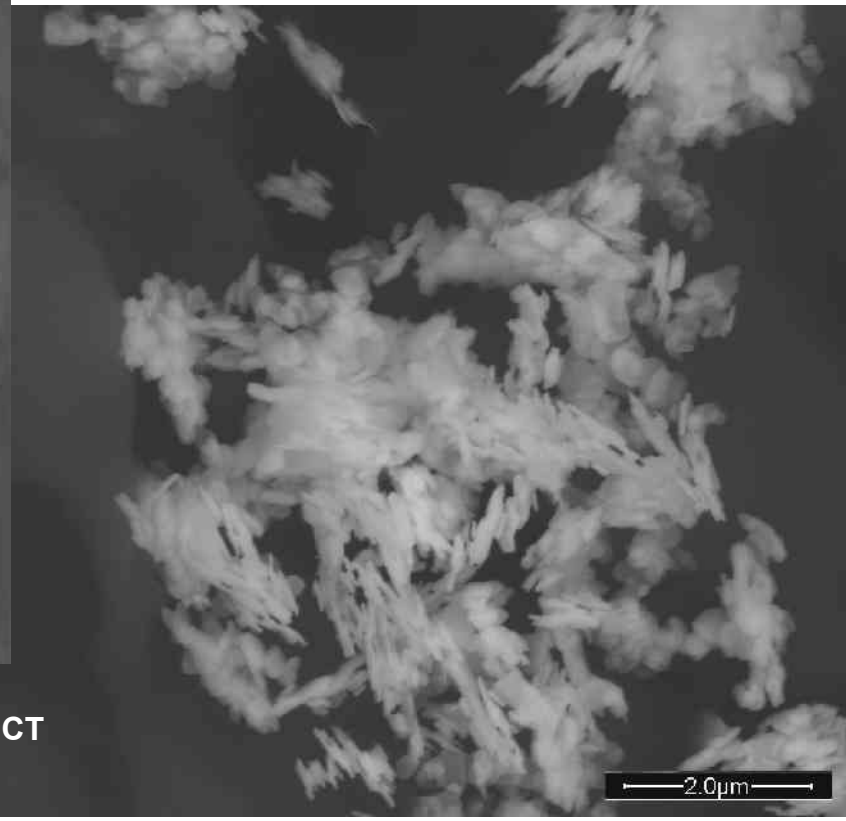
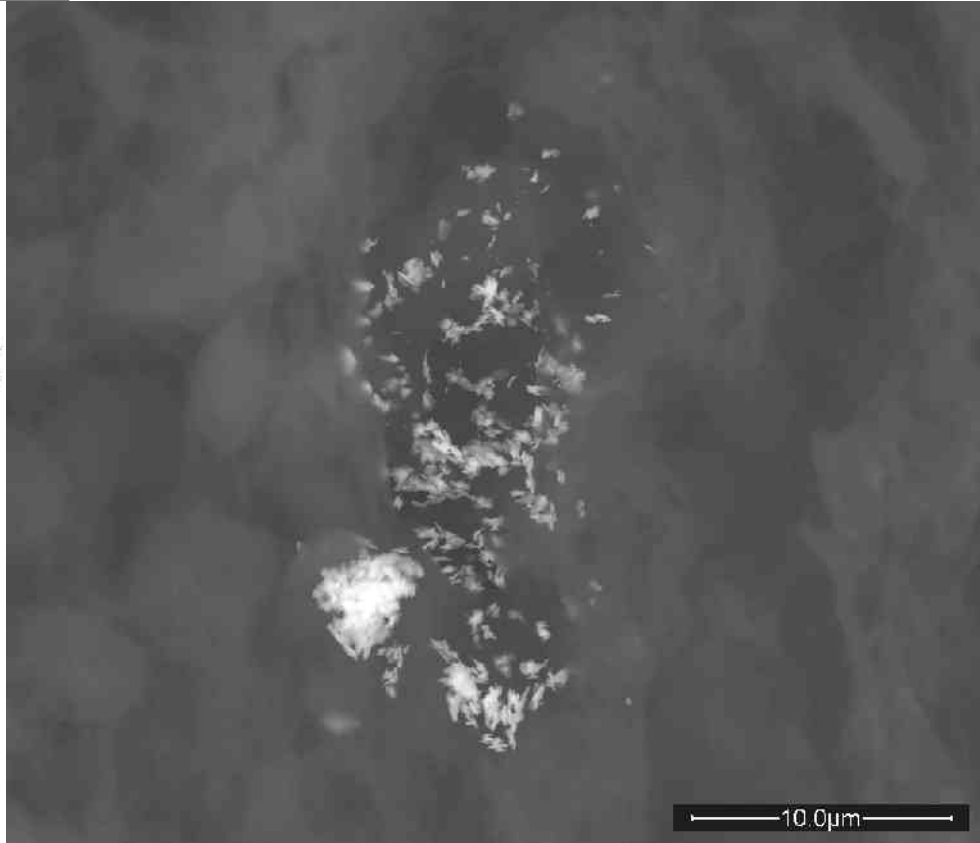
Stainless steel Nanoparticle



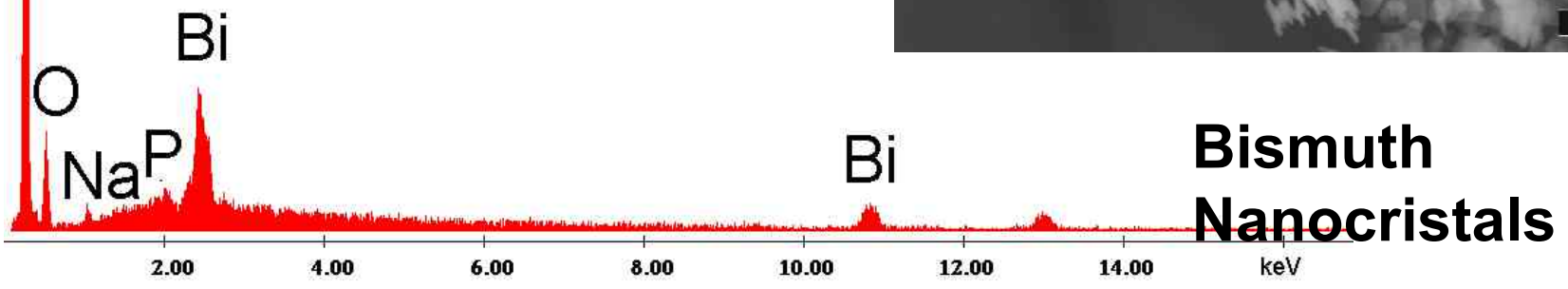
Spina byphida Liver

B 251/06 488 B

C

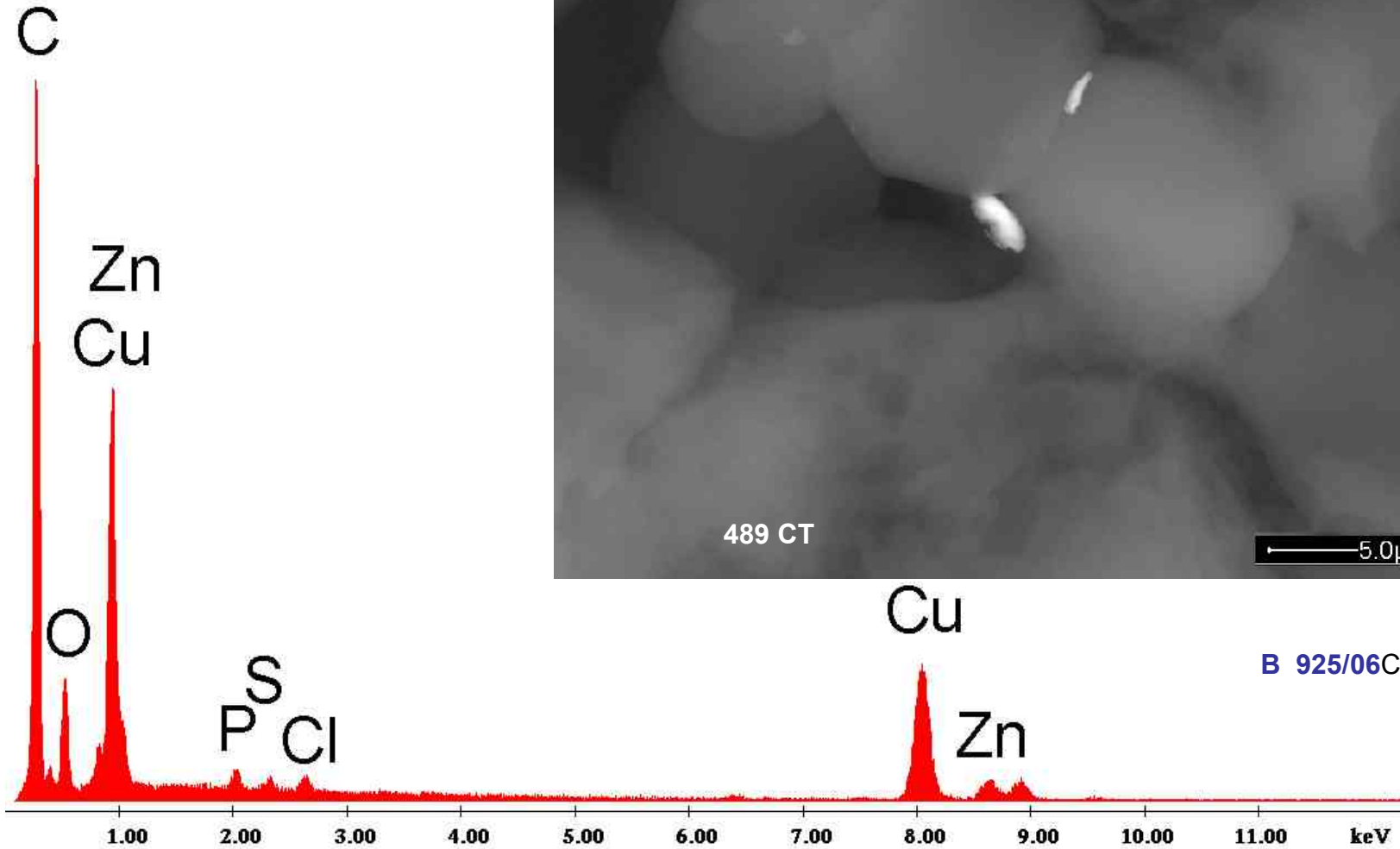
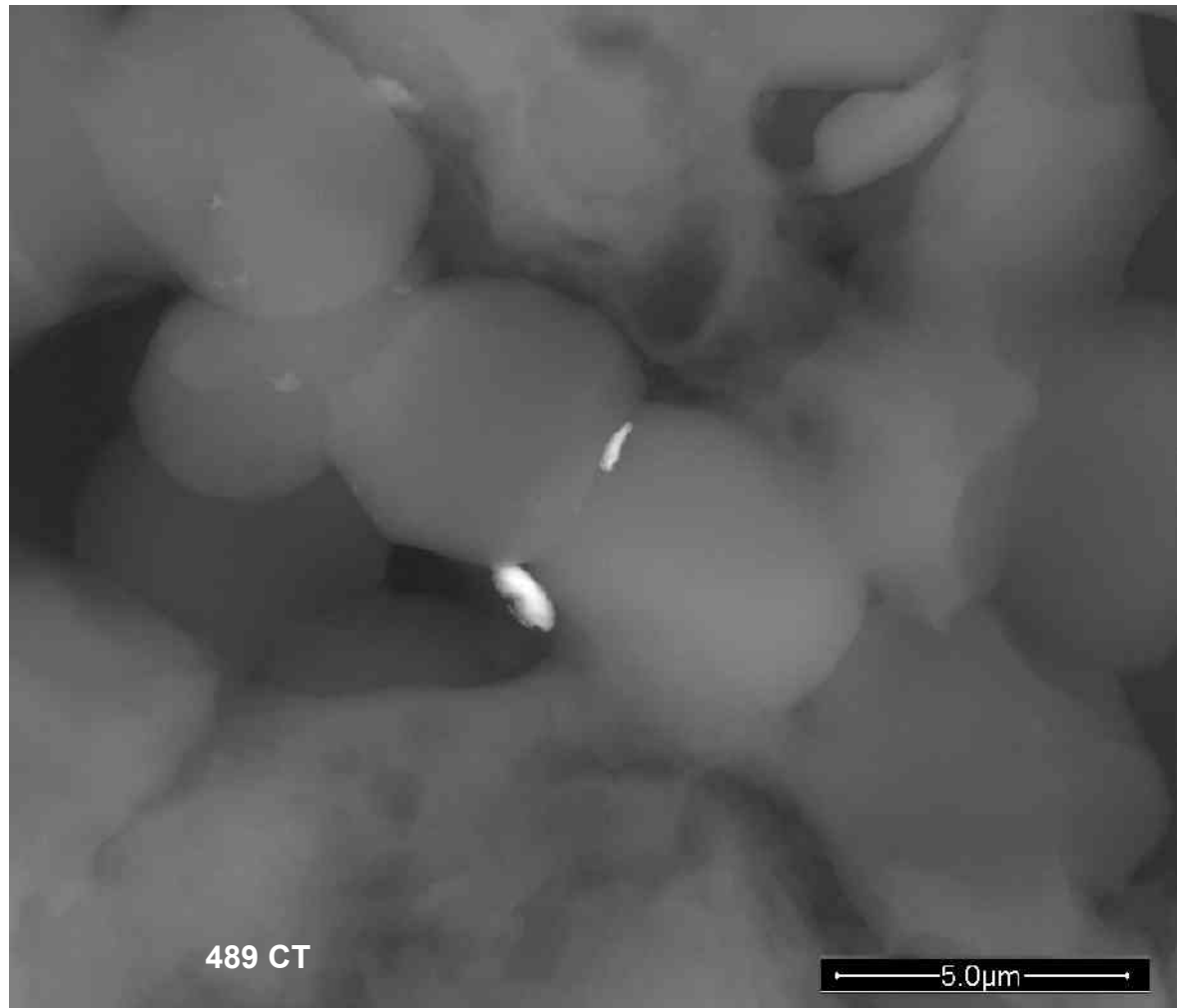


488 CT



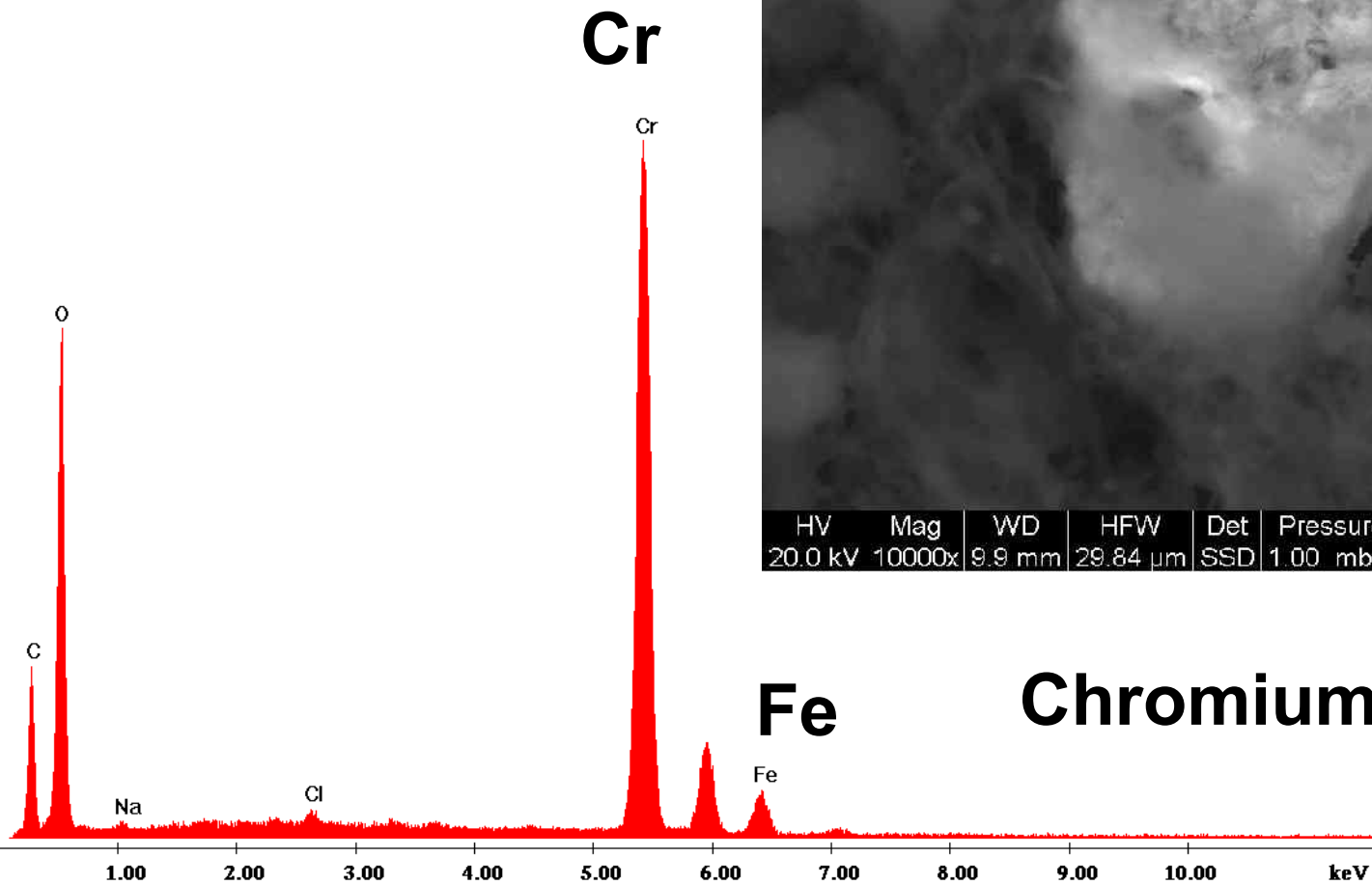


Spleen

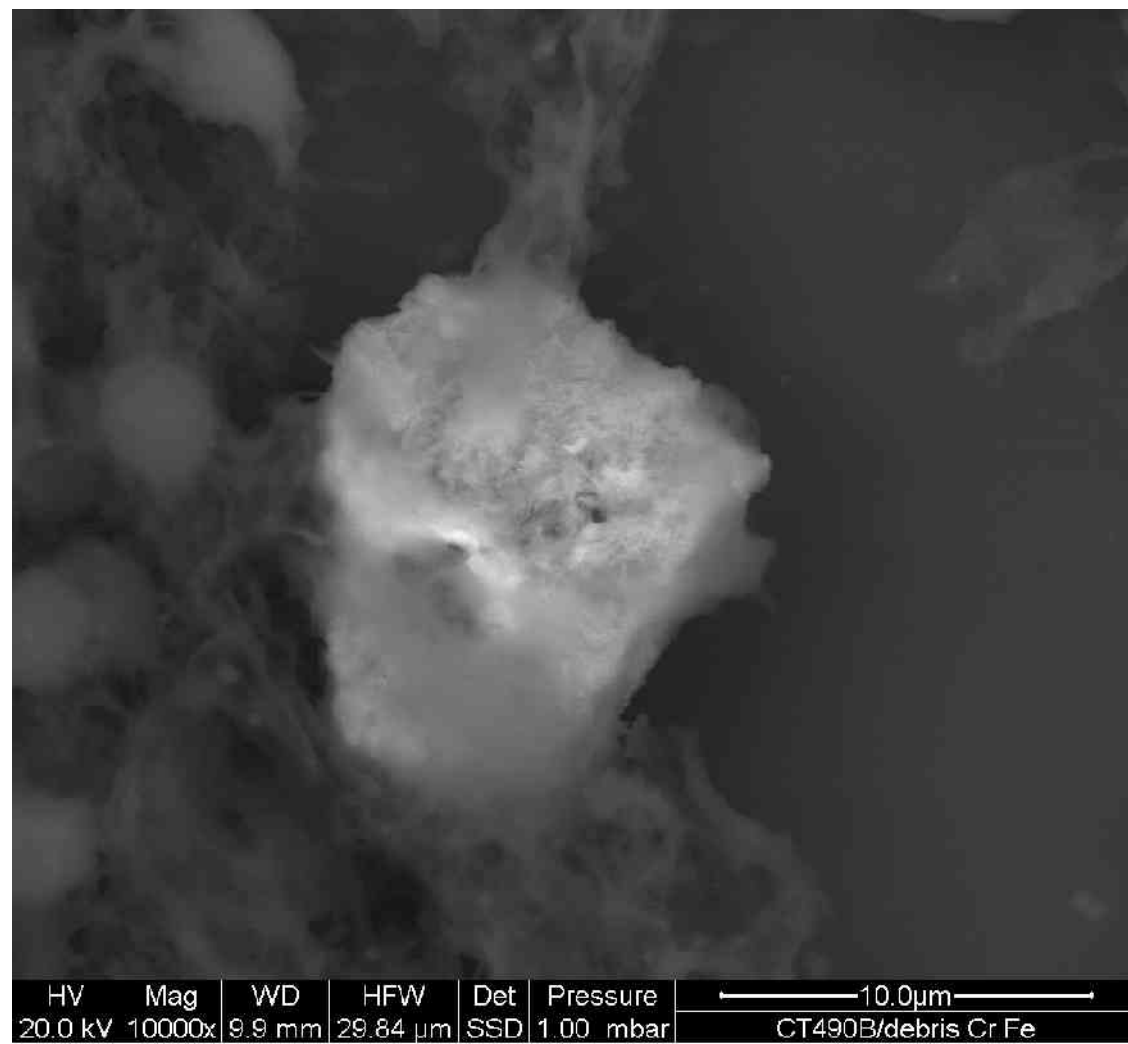


B 925/06CT 489 B

Spleen



Cr



Fe

Chromium-Iron Debris

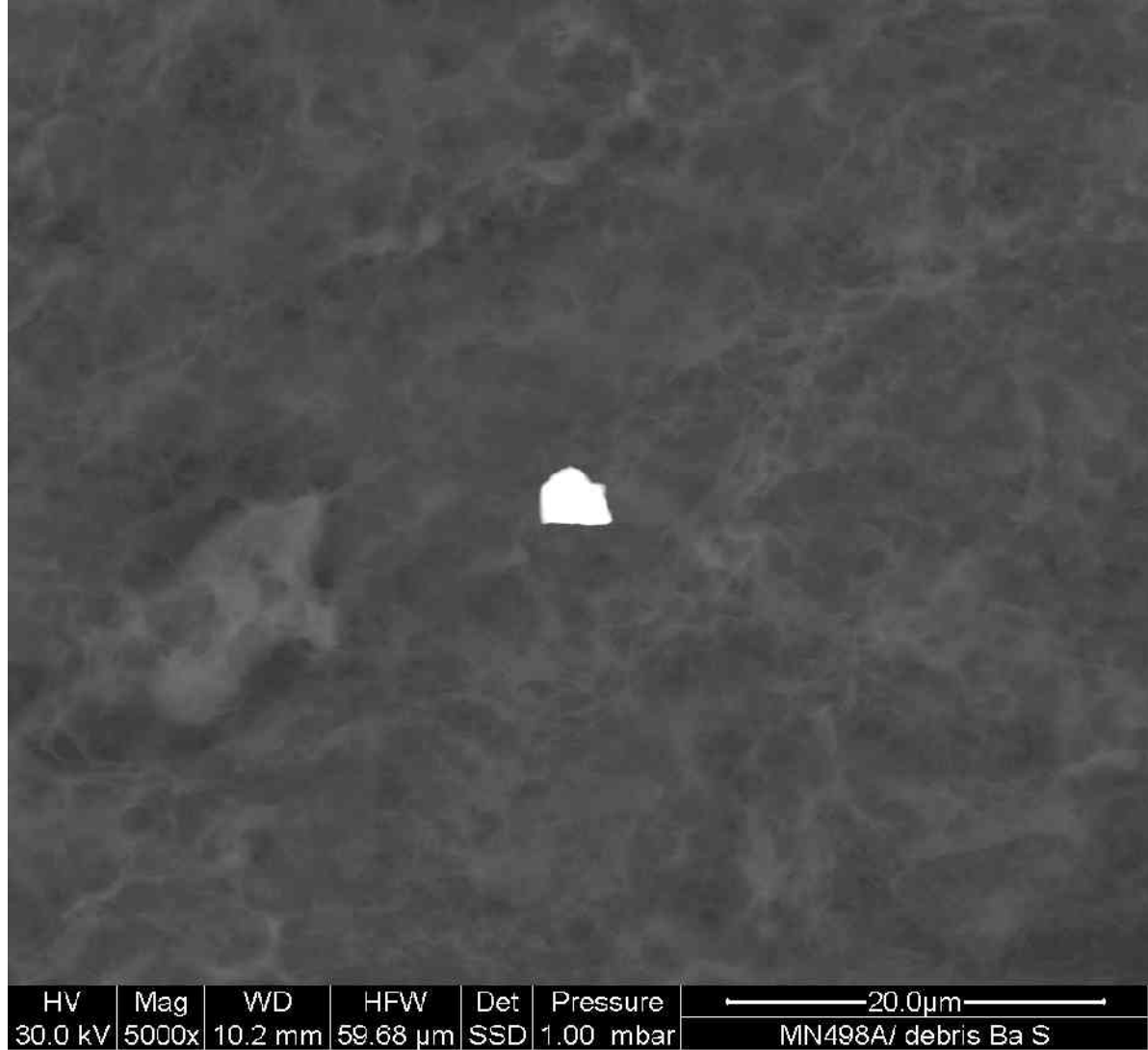
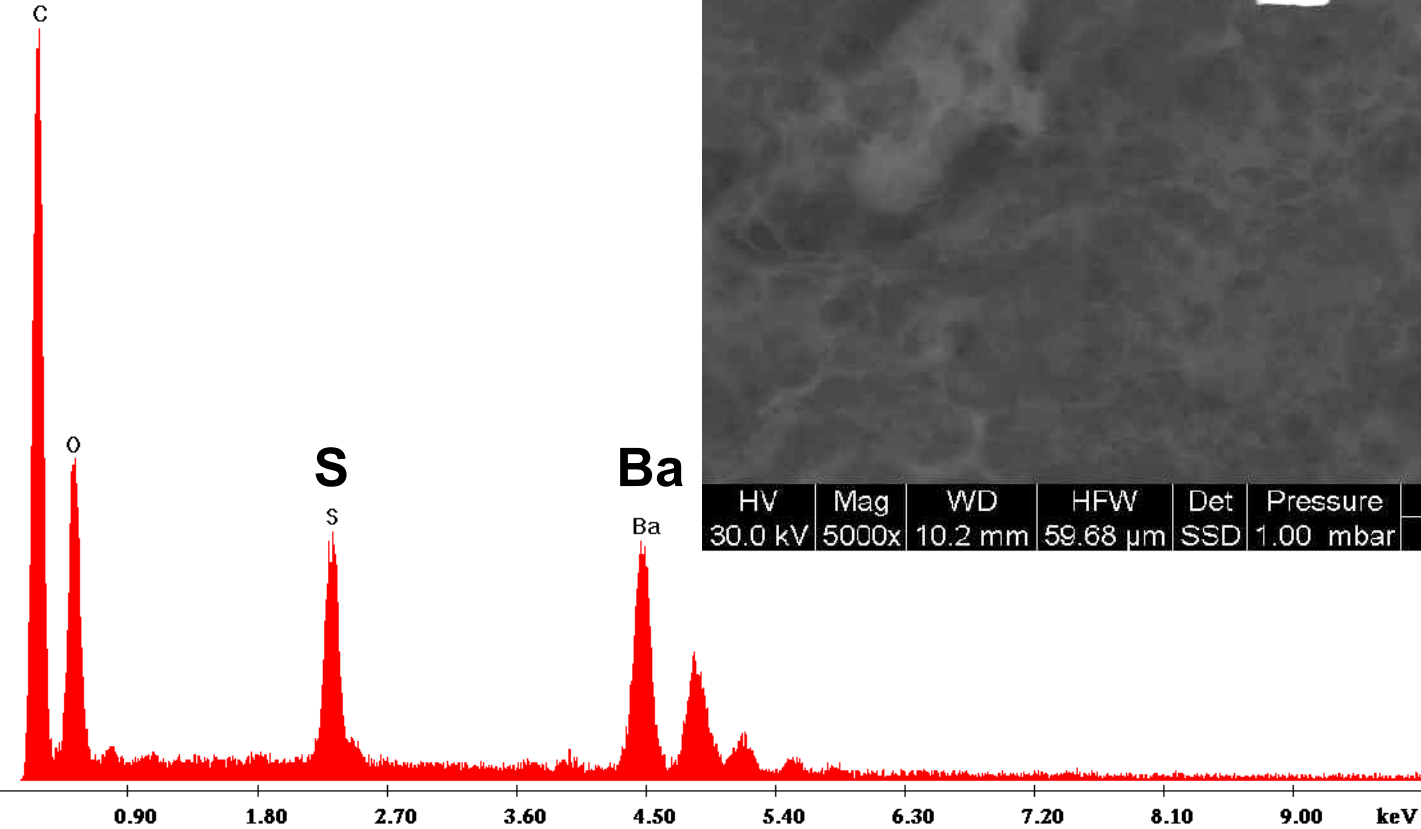
20-week Foetus of uncertain sex

MORRIS SYNDROME

Placenta (MN 498 A)

Analysis	Morphology	Elements
1	placenta	C,O,S,Na
2	calcification	Ca,P,C,O,S,Zn,Fe
3	3 μm debris	C,O,S,Ba
4	calcification	Ca,P,C,O,S,Zn,Fe

PLACENTA



MN 498 A)

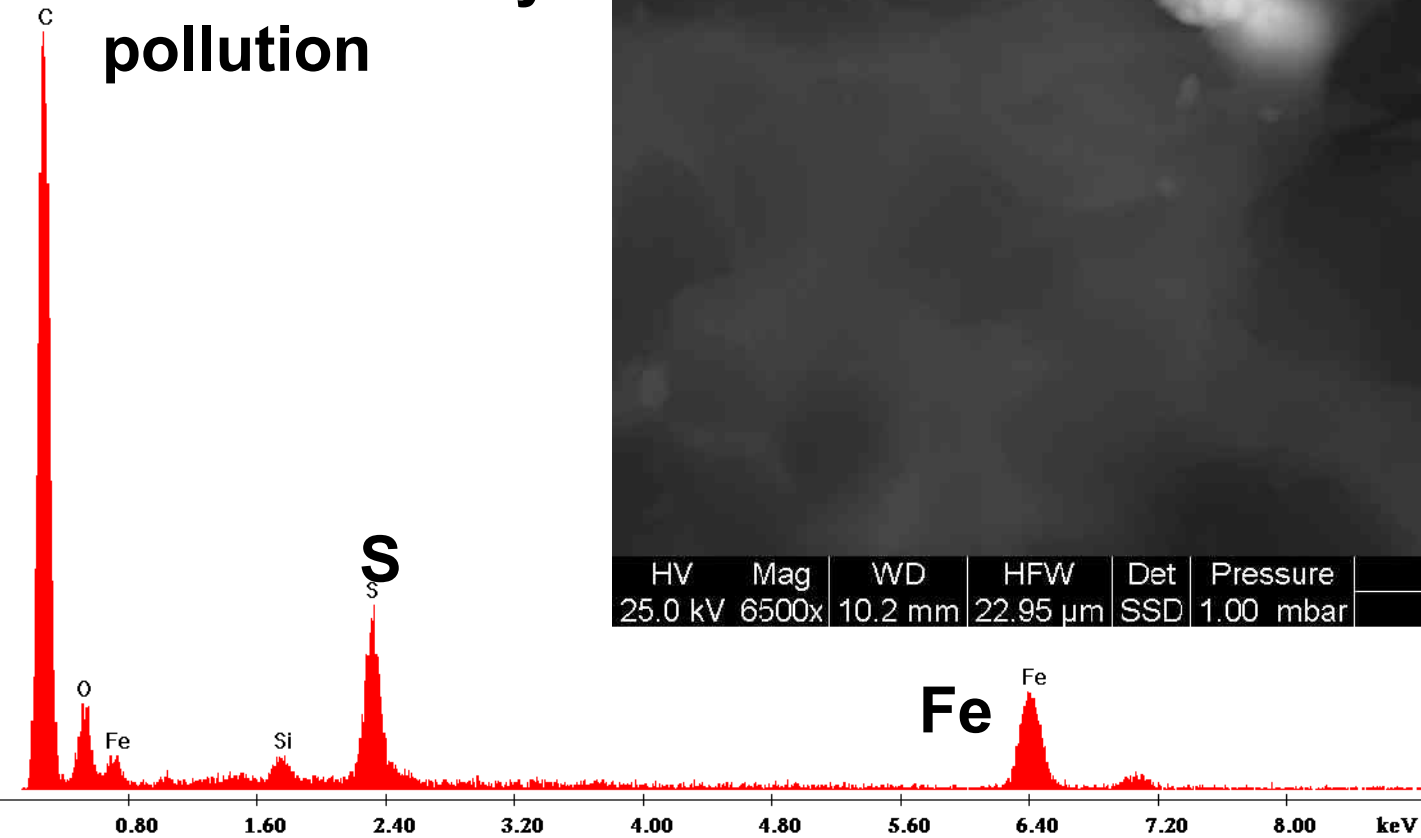
Brain

(MN 498 B)

Analysis	Morphology	Elements
1	Tissue	C,O,S,Na,P
2	3 μm debris	C,Fe,O,Na
3	0,2 μm-4 μm cluster	C,S,Fe,O,Si
4	1 -10 μm debris	C,Ca,O

Brain

Nanoparticles
of Sulphur-Iron
from a refinery
pollution



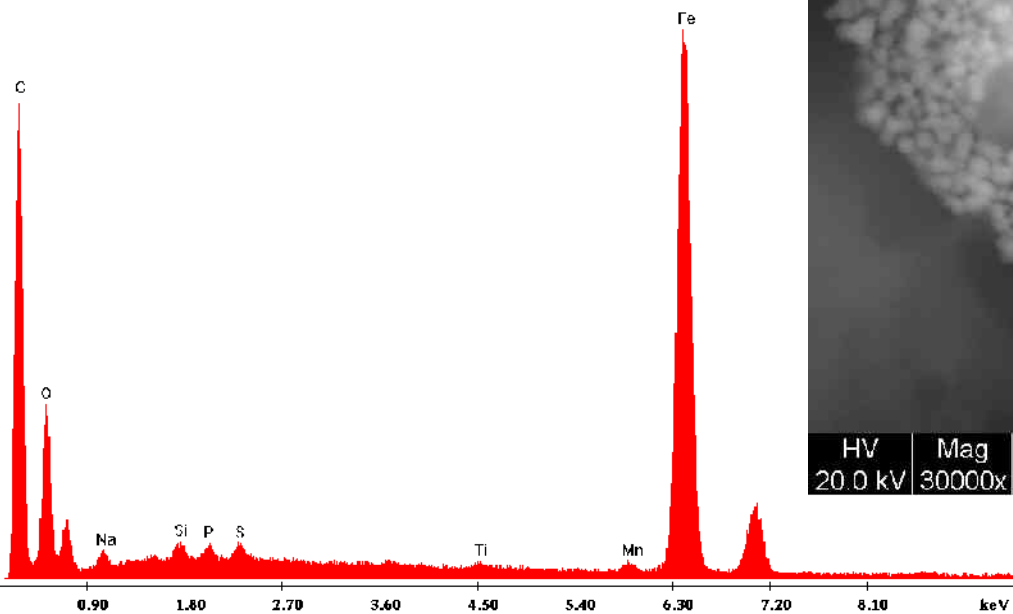
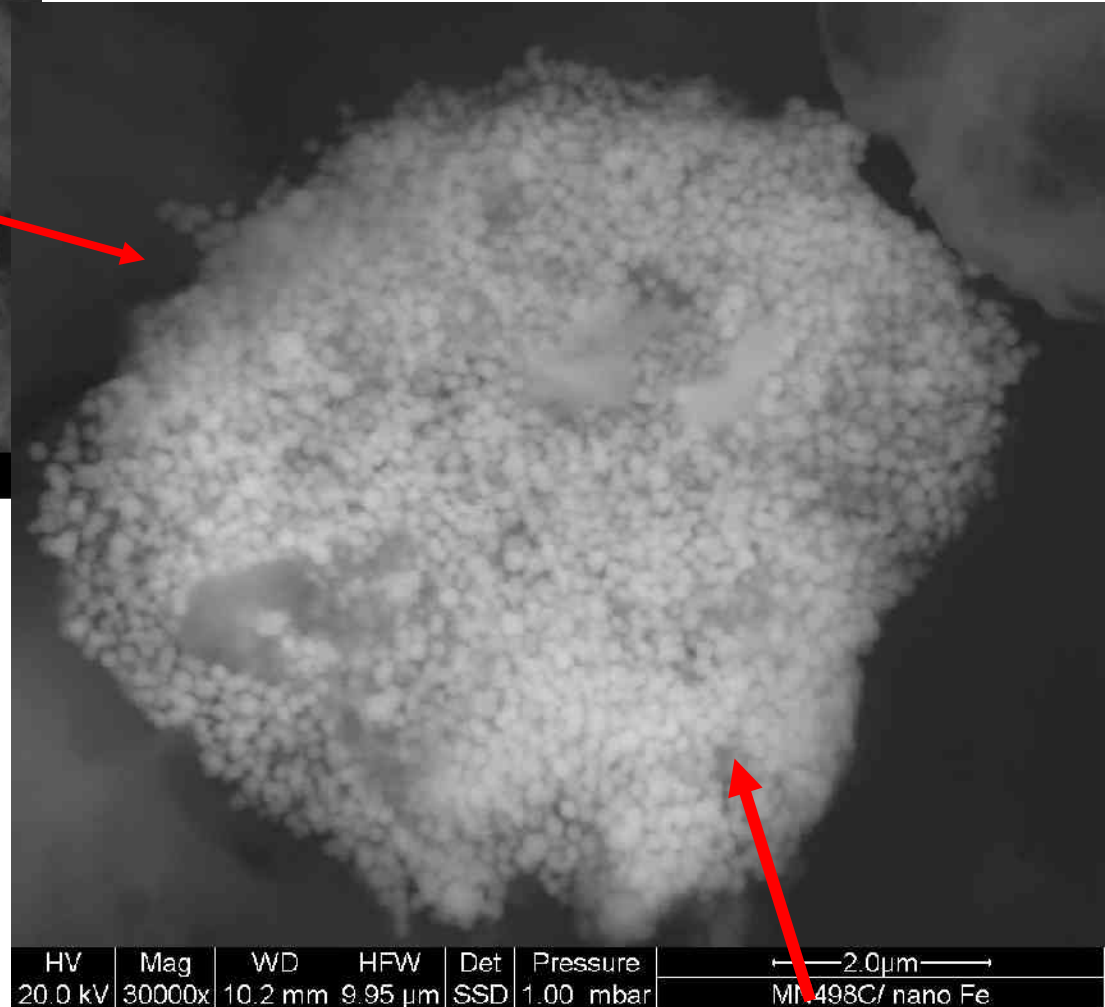
(MN 498 B)

Lung

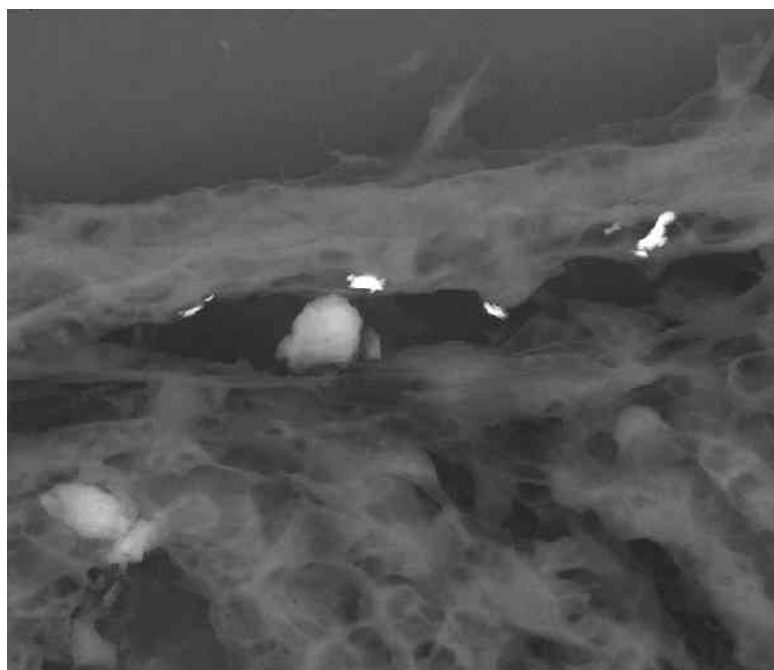
(MN 498 C)

Analysis	Morphology	Elements
1	tissue	C,O,P,S,Na
2	0,2 μm-10 μm cluster	Fe,C,O,Si,P,S,Ti,Mn
3	2 μm debris	C,Fe,O,Cr,Ni,Si,P,S,Na
4	nanoparticles	Fe,C,O,Si,P,S,Ti,Mn
5	0,5 μm debris	C,O,Bi,Na,P,S
6	cluster	Zn,Al,C,O

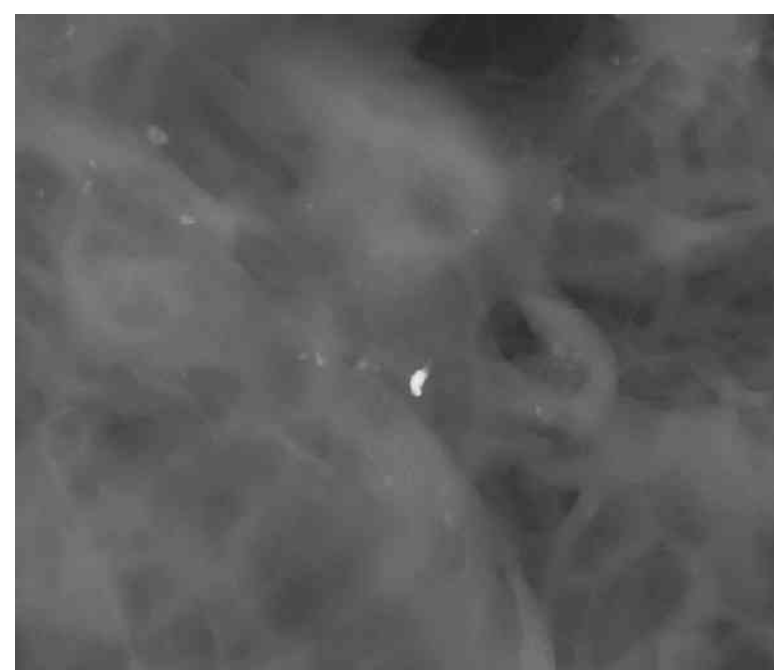
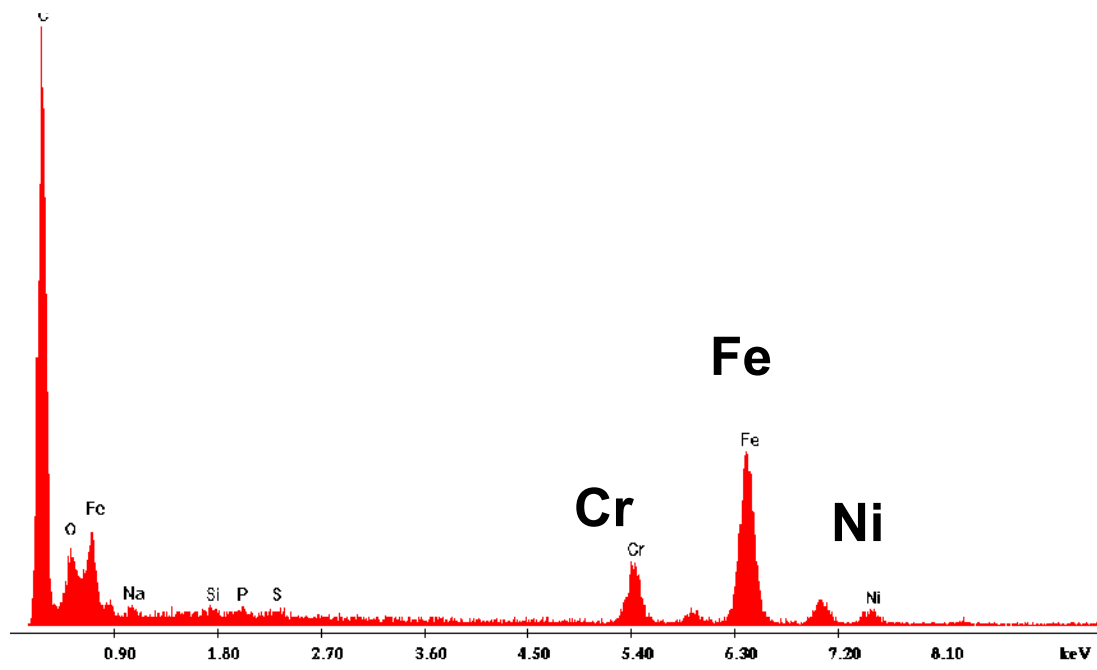
Lung



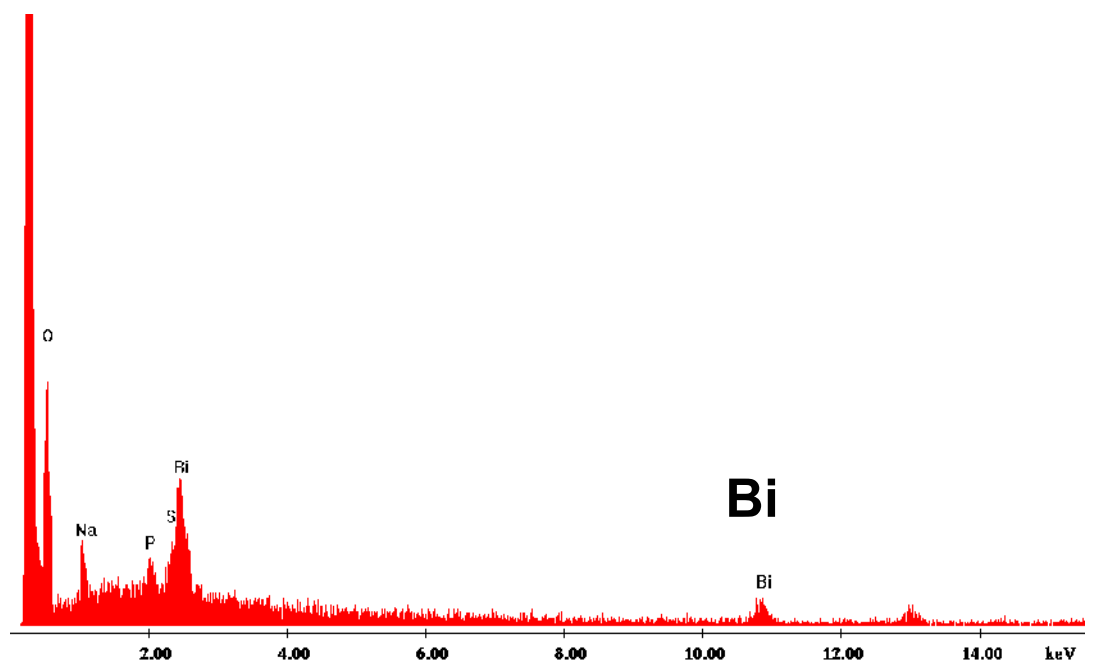
Nanoparticles of Iron



HV	Mag	WD	HFW	Det	Pressure	20.0 μm
25.0 kV	4000x	10.2 mm	74.60 μm	SSD	1.00 mbar	MN498C/ debris Fe Cr Ni



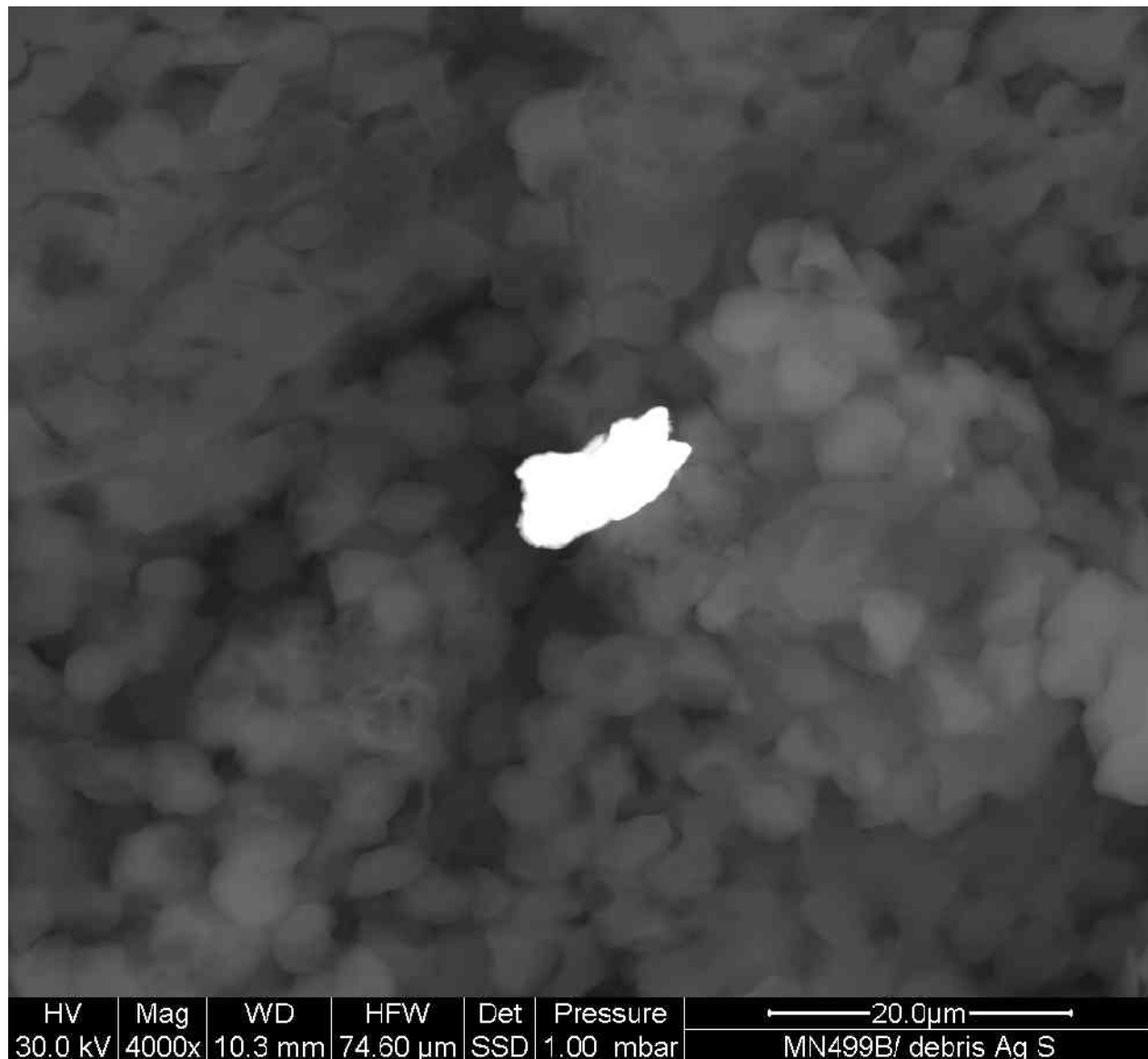
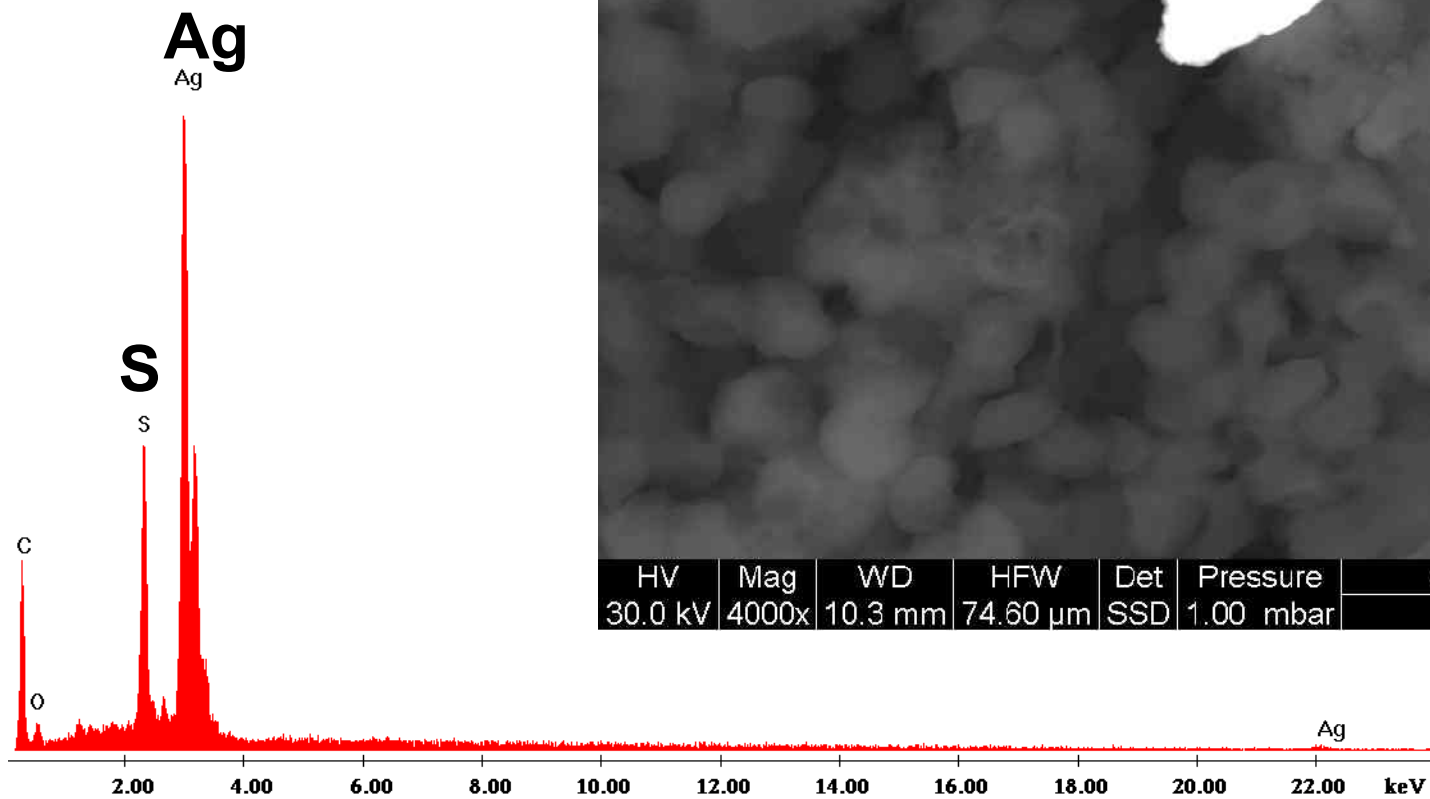
HV	Mag	WD	HFW	Det	Pressure	5.0 μm
25.0 kV	15000x	10.2 mm	19.89 μm	SSD	1.00 mbar	MN498C/ debris Bi



21-week male Foetus
Spontaneous Delivery with corionamnionite.

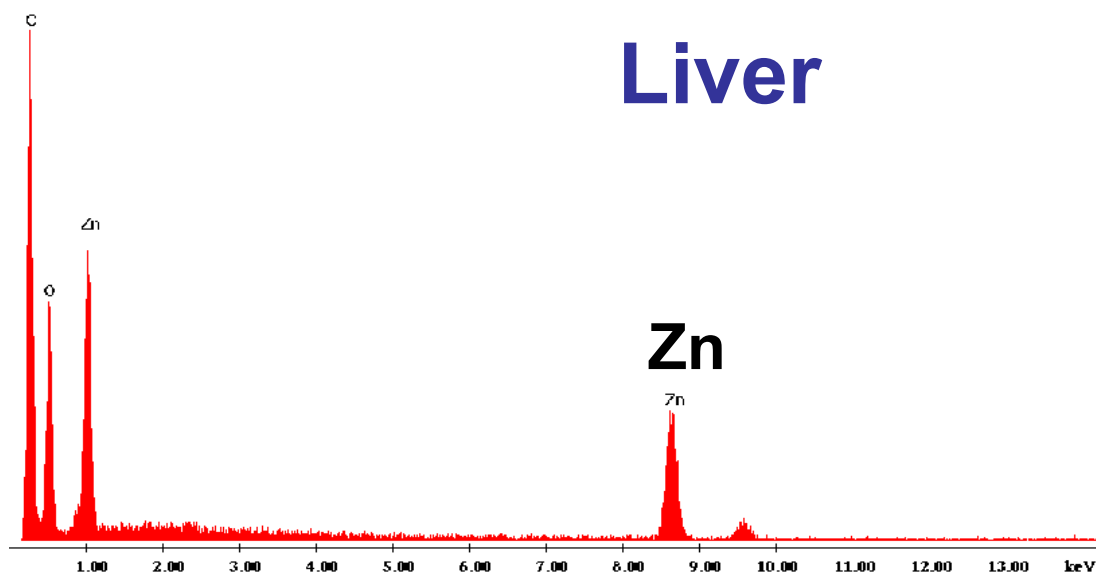
Found particles of
Zinc,
Lead-Calcium-Bromide,
Cerium-Phosphorus,
Gold-Sulphur
Silver-Sulphur
Tin
in placenta, liver and lung

Heart

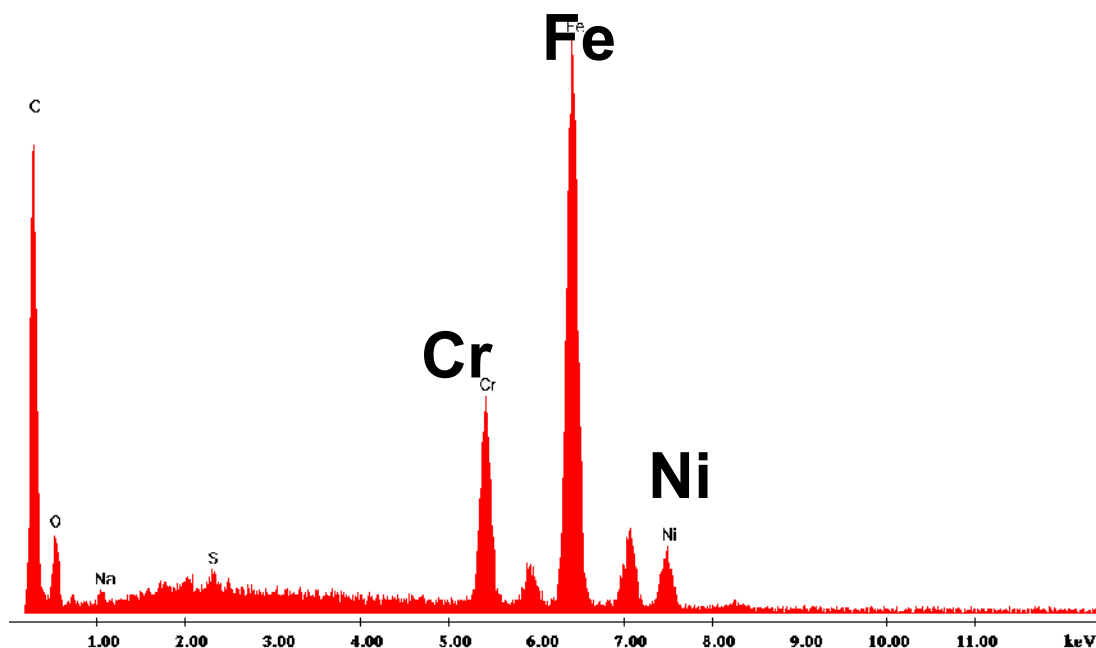




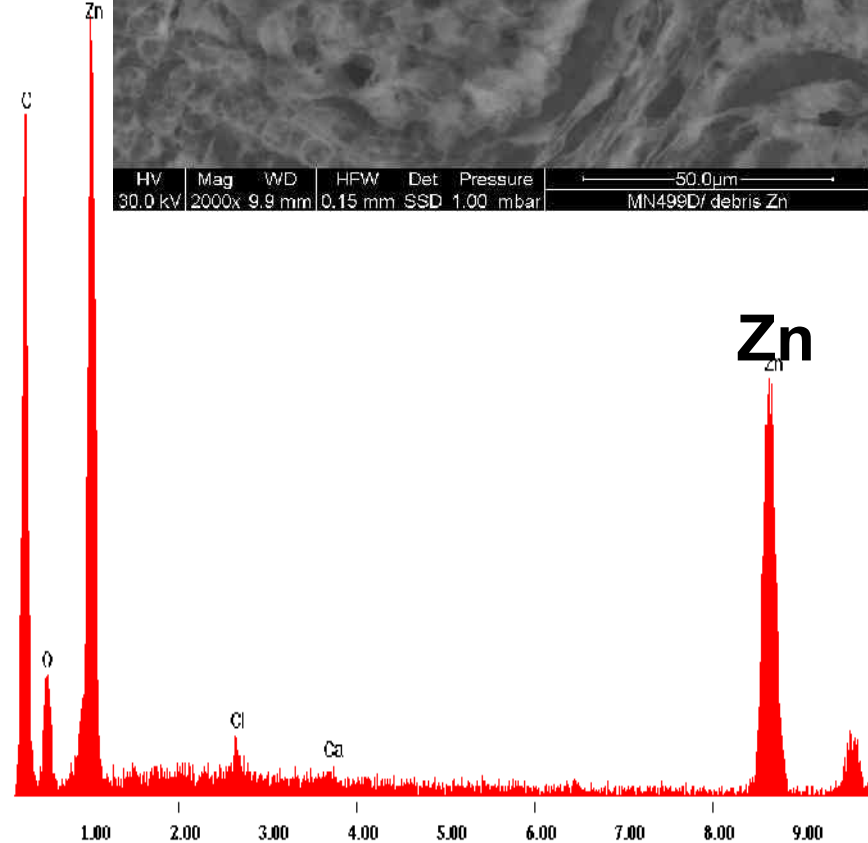
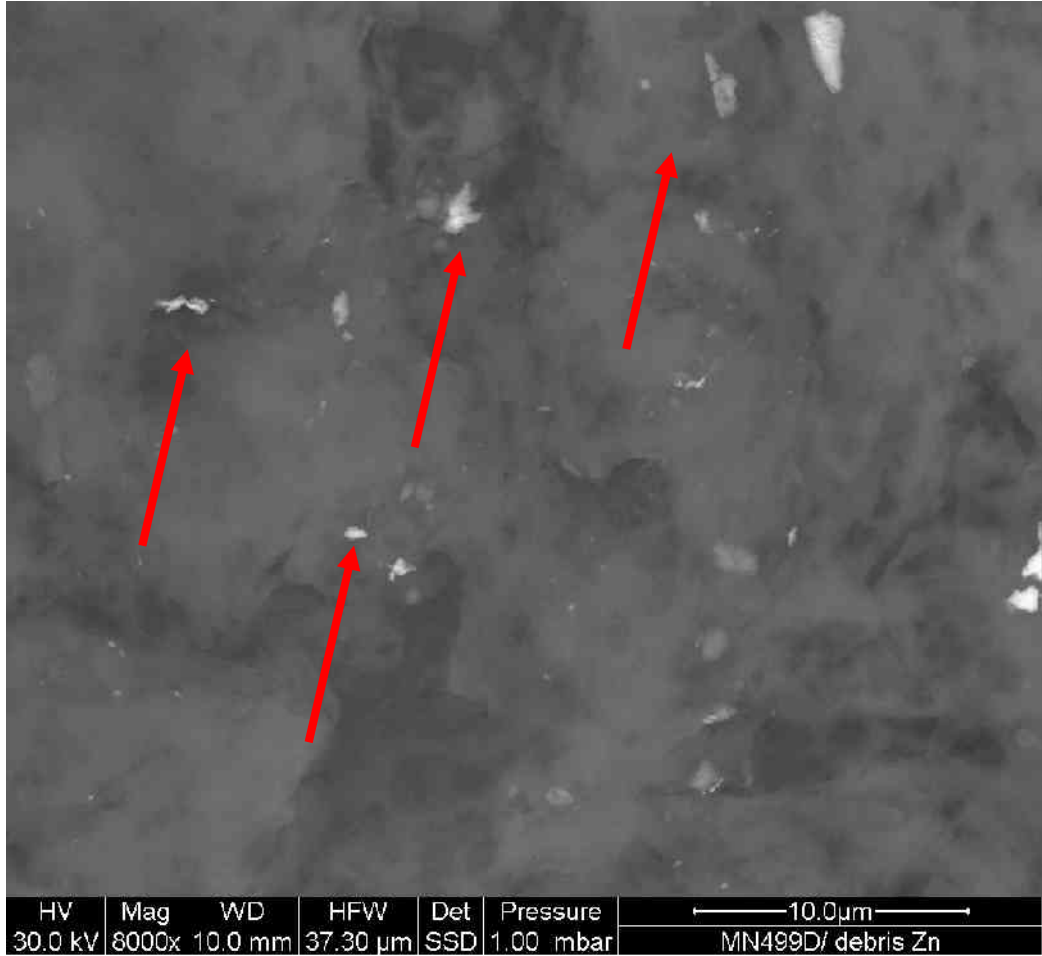
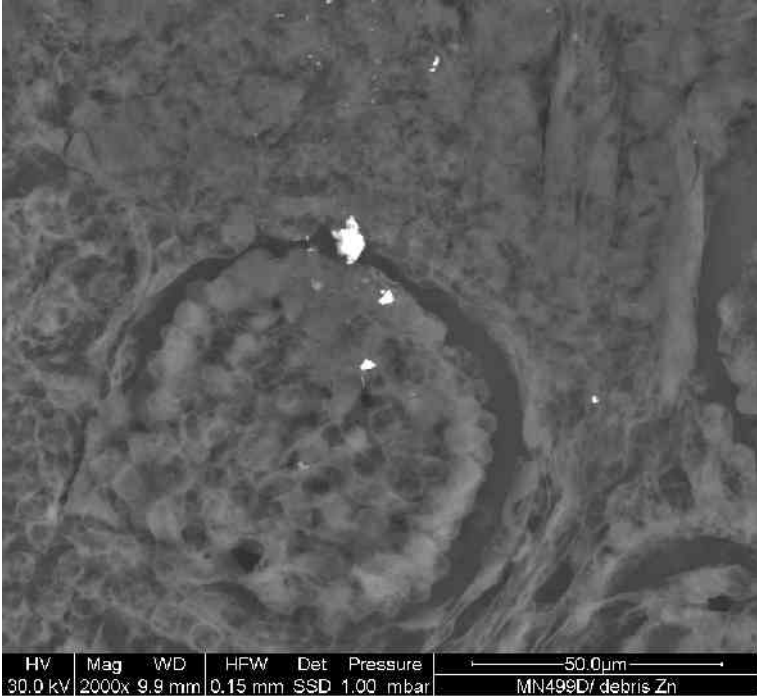
HV	Mag	WD	HFW	Det	Pressure	20.0µm
30.0 kV	4000x	10.2 mm	74.80 µm	SSD	1.00 mbar	MN499C/ debris Zn



HV	Mag	WD	HFW	Det	Pressure	20.0µm
30.0 kV	5000x	10.0 mm	59.68 µm	SSD	1.00 mbar	MN499C/ debris Fe Cr Ni



Kidney



19-week male foetus with
16-CROMOSOMIC TRISOMIA

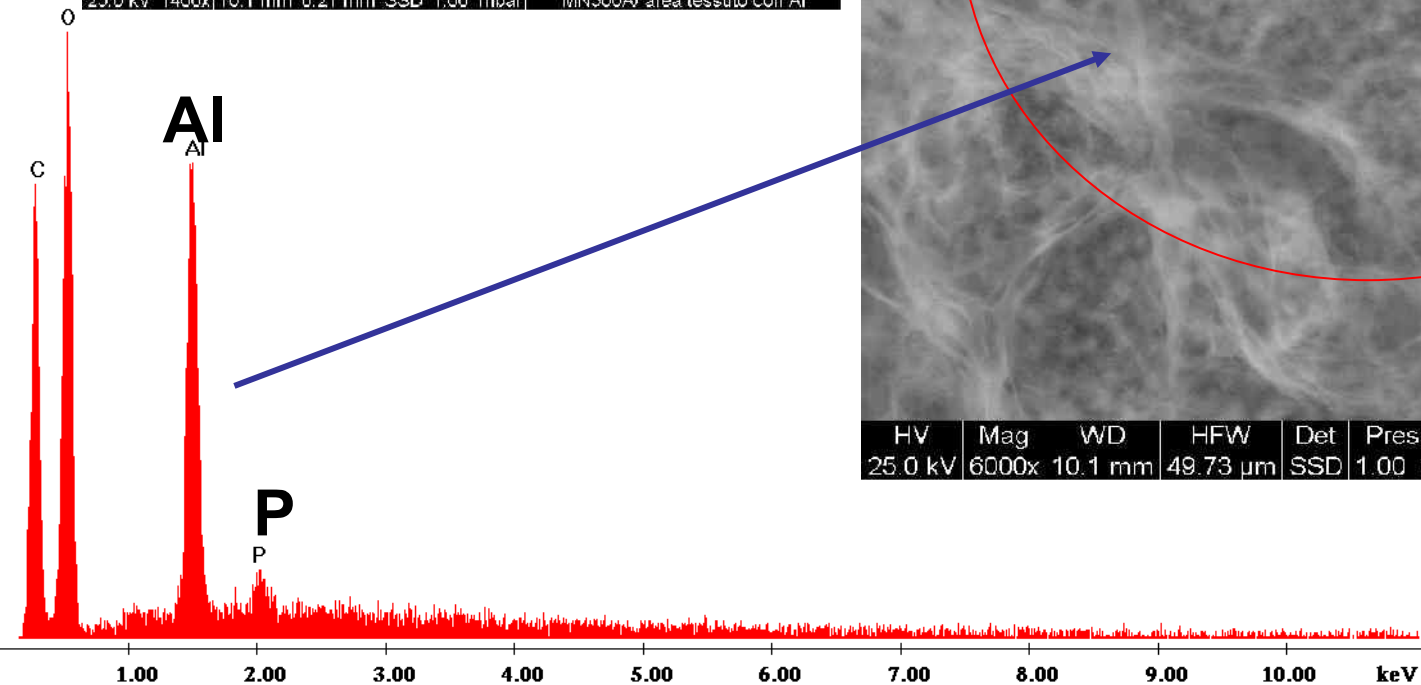
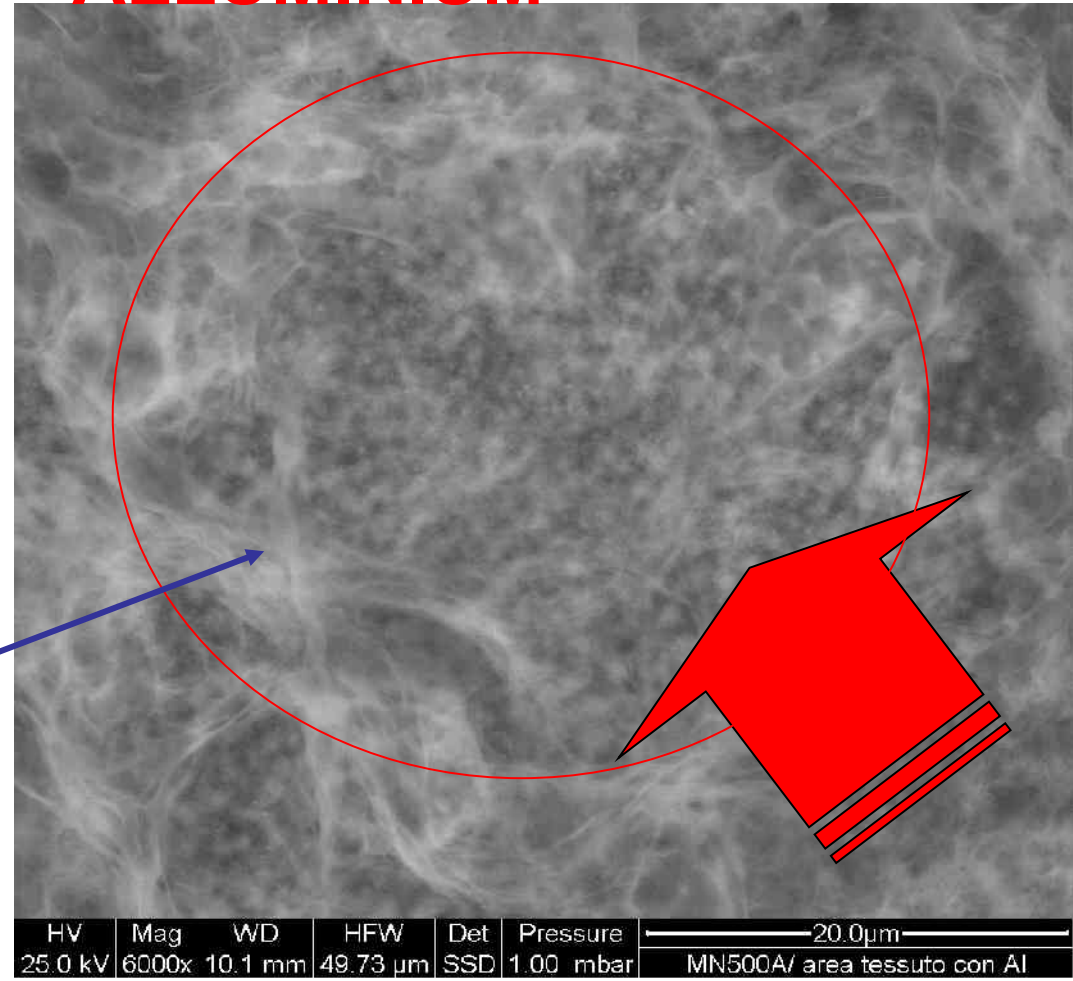
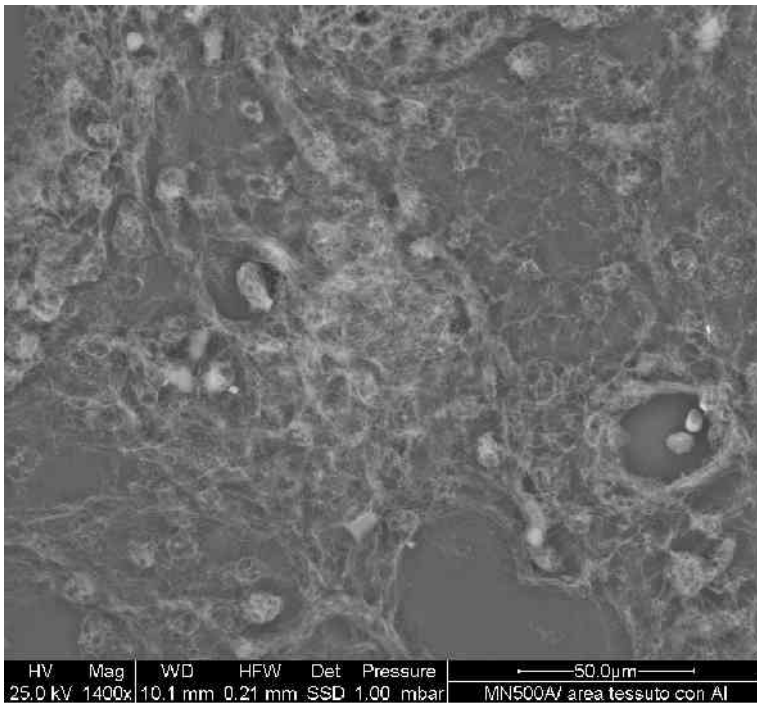
Found particles and precipitates of
Aluminium
Titanium-Antimony,

MN 500

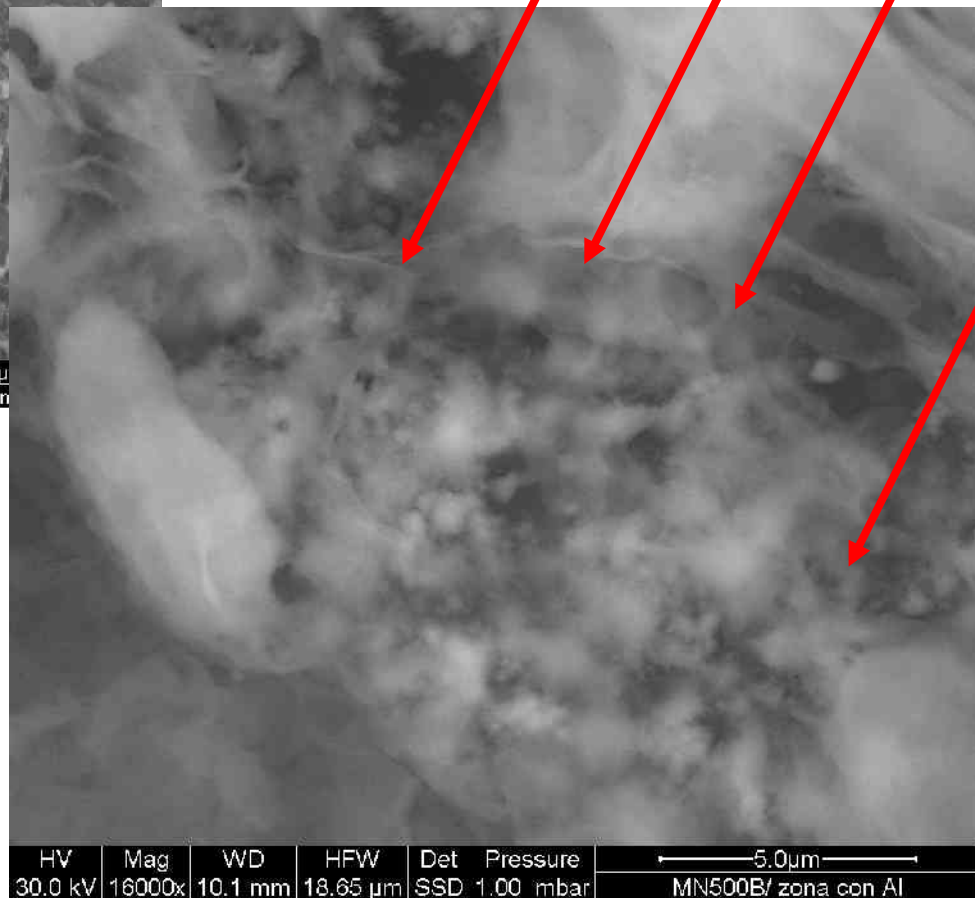
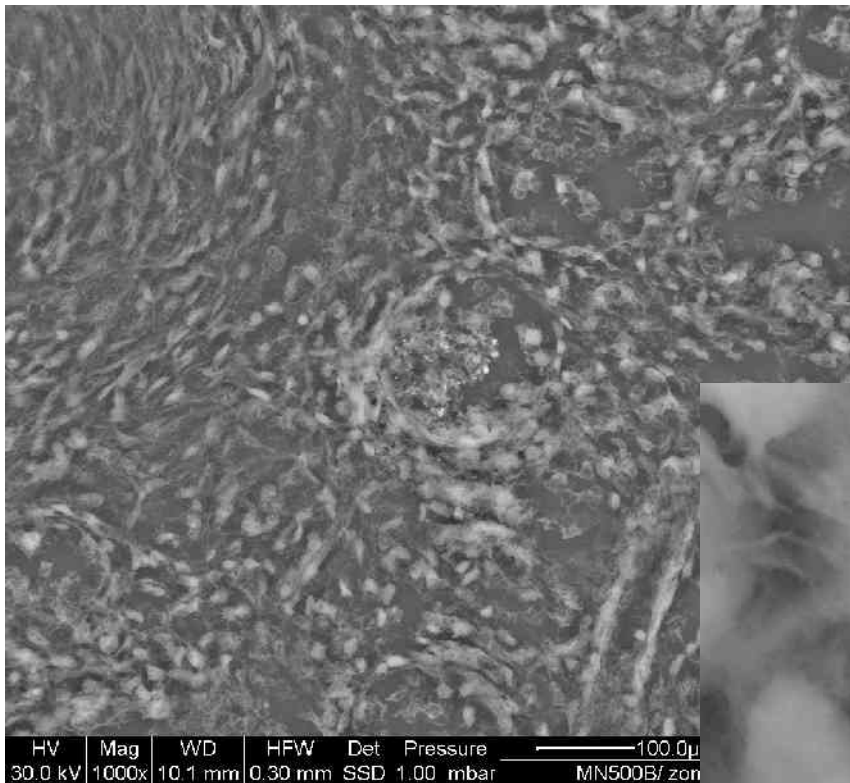
Placenta (MN 500 A)

Analysis	Morphology	Elements
1	placenta	C,O,S,Na
2	2 μm debris	C,Fe,O,P,Si,Na
3	5 μm debris	Ti,C,O,Sb,Cr,P,Na
4	precipitates	C,P,Ca,Fe,Na,S,Zn
5	0,1 -5 μm debris	O,Cr,C,S
6	area with Alluminium	O,Al,C,P
7	1-5 μm debris	C,Zr,Si,O,Na,Fe

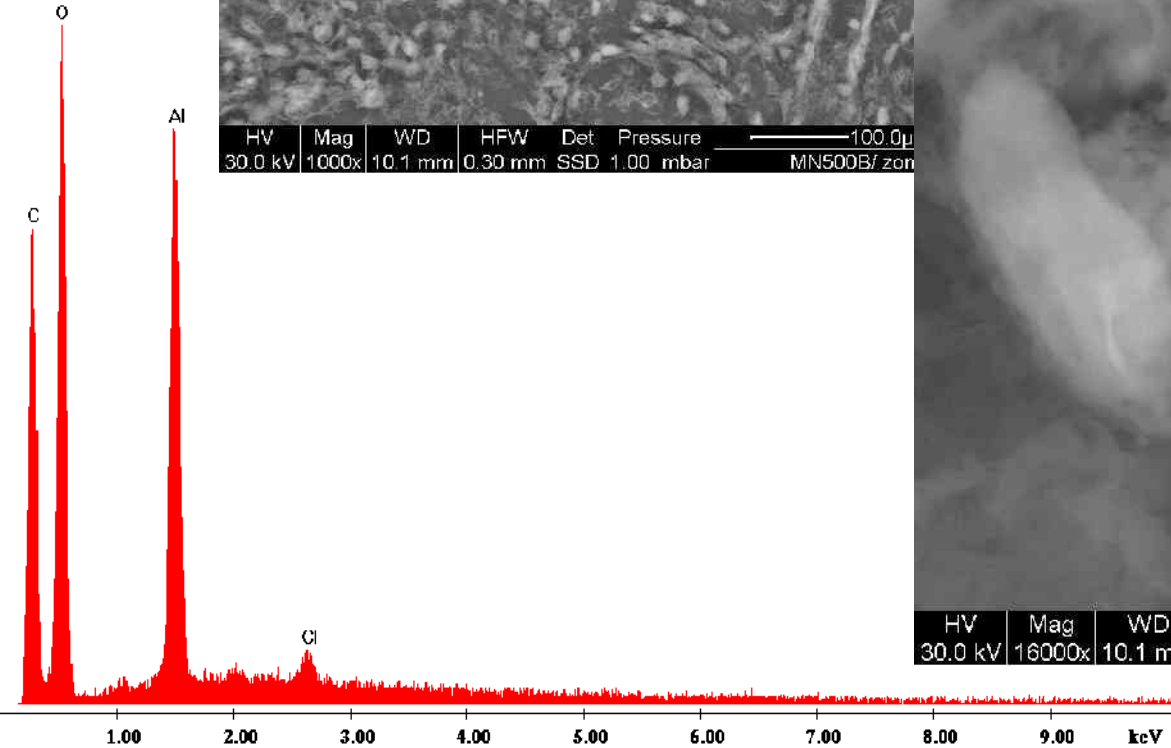
PLACENTA is full of ALLUMINIUM



Lung



Al



Heart

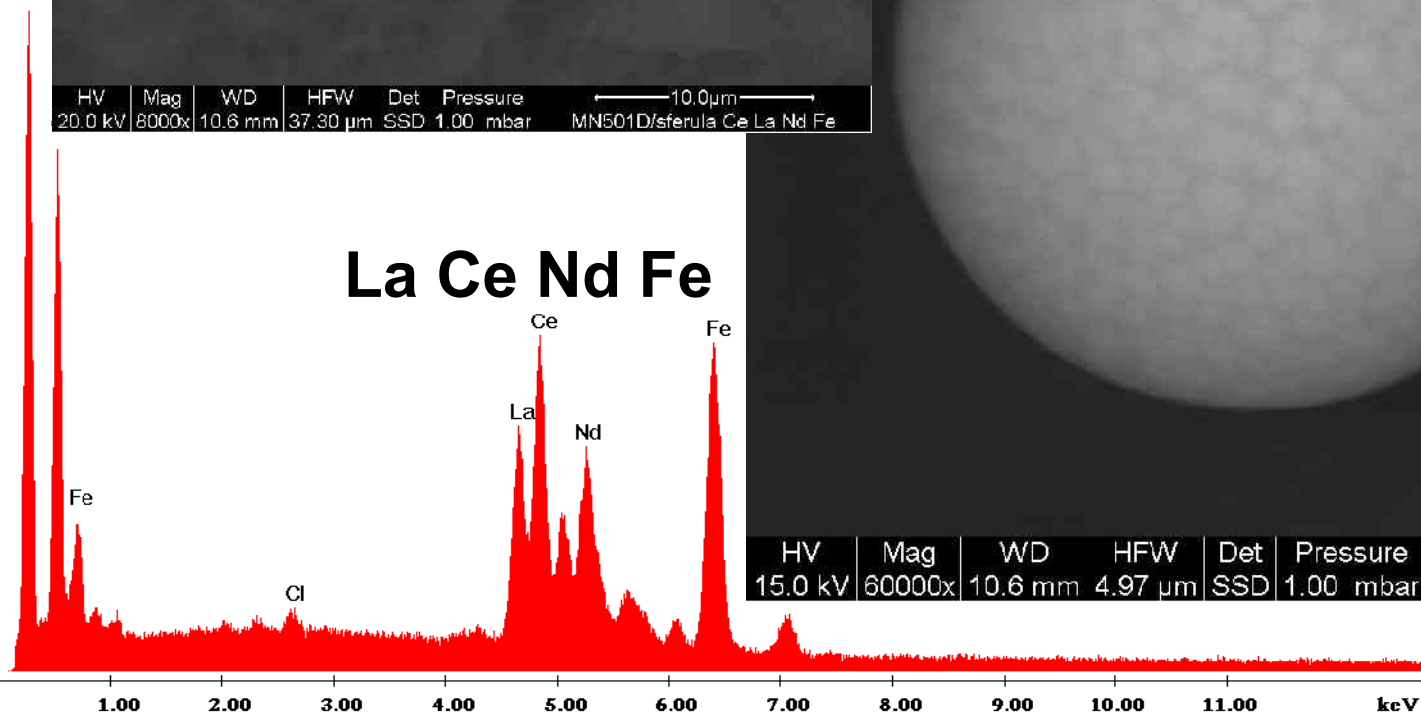
(MN 501 D)



C

HV	Mag	WD	HFWD	Det	Pressure	10.0 μm
20.0 kV	8000x	10.6 mm	37.30 μm	SSD	1.00 mbar	MN501D/sferula Ce La Nd Fe

La Ce Nd Fe



HV	Mag	WD	HFWD	Det	Pressure	2.0 μm
15.0 kV	60000x	10.6 mm	4.97 μm	SSD	1.00 mbar	MN501D/sferula Ce La Nd Fe

Neu-Laxova syndrome

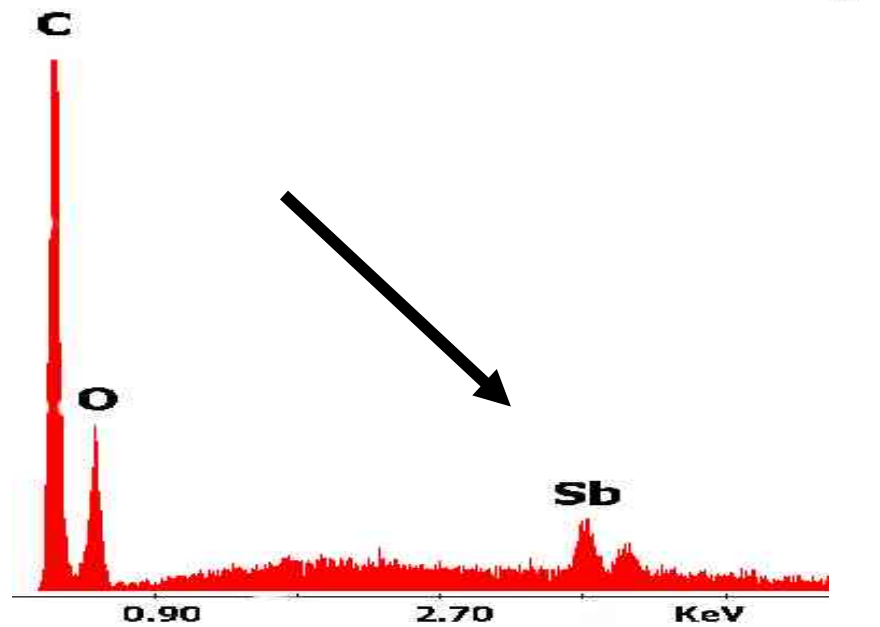
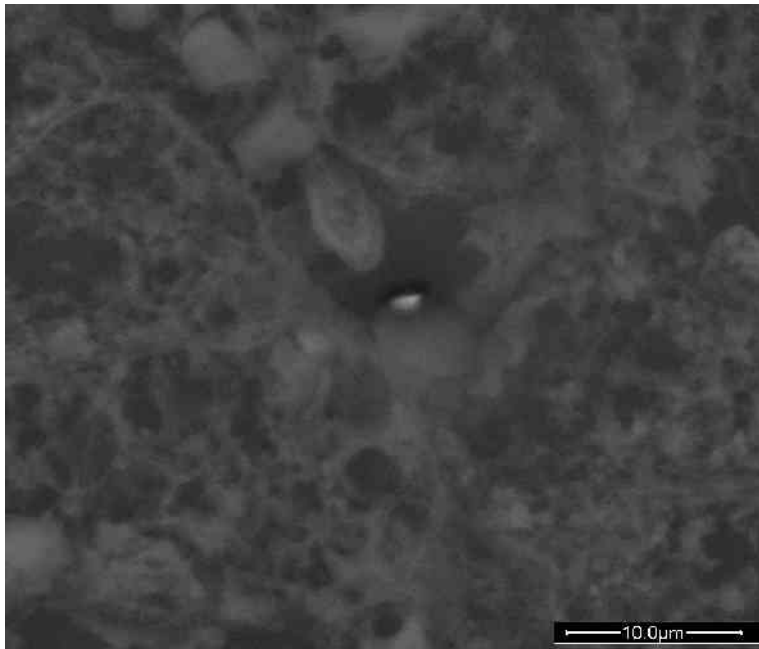
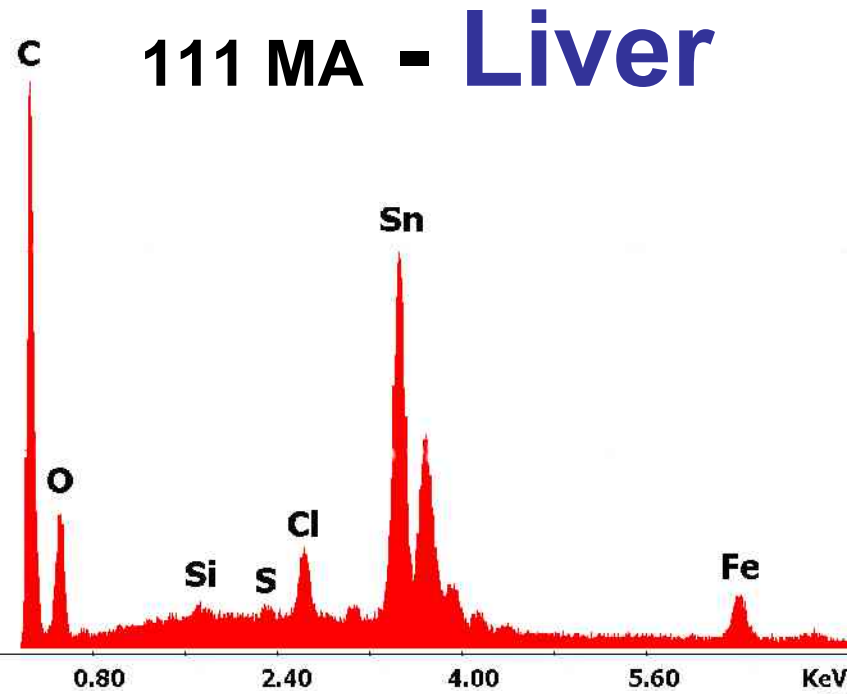
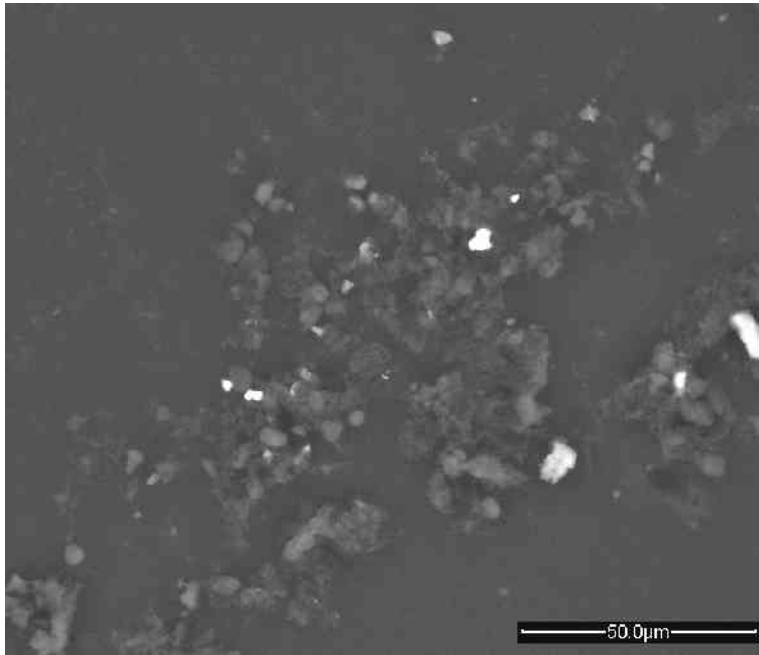
Neu-Laxova syndrome is a rare congenital abnormality characterised by intrauterine growth restriction, microcephaly, facial dysmorphism, short neck, edema, scaly skin and perinatal death.

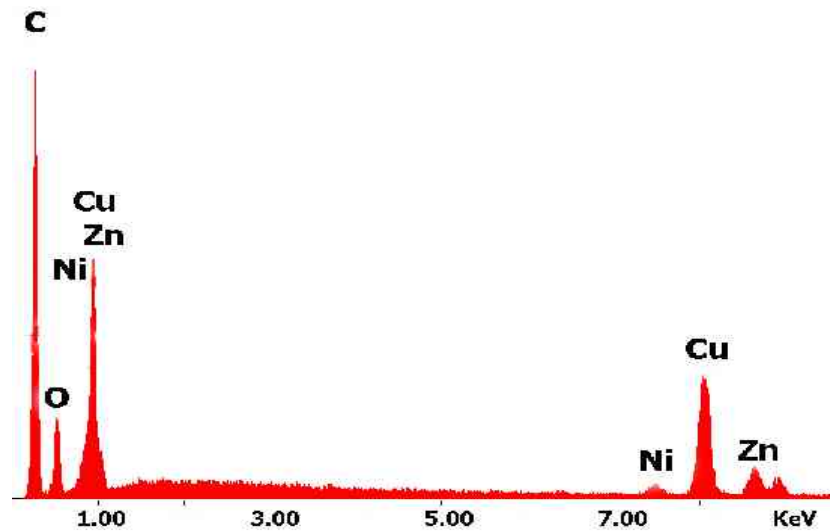
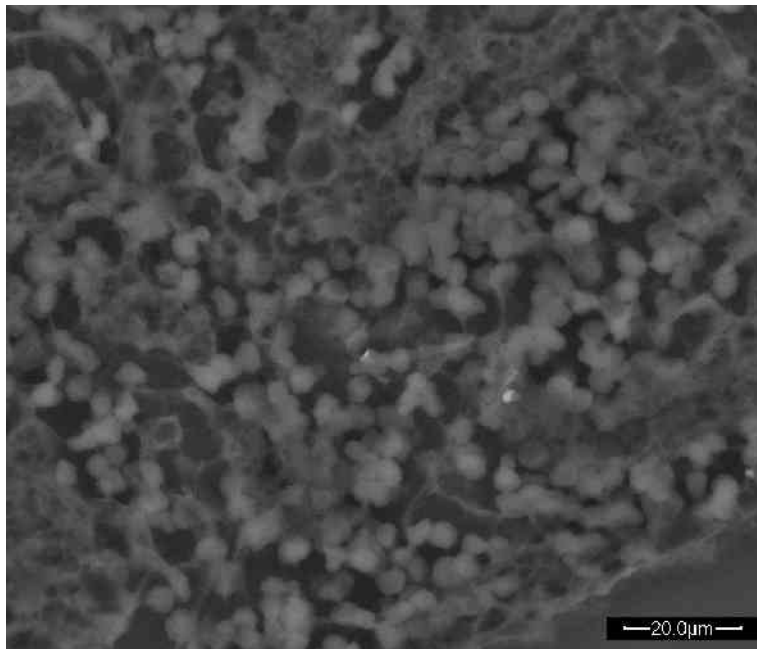
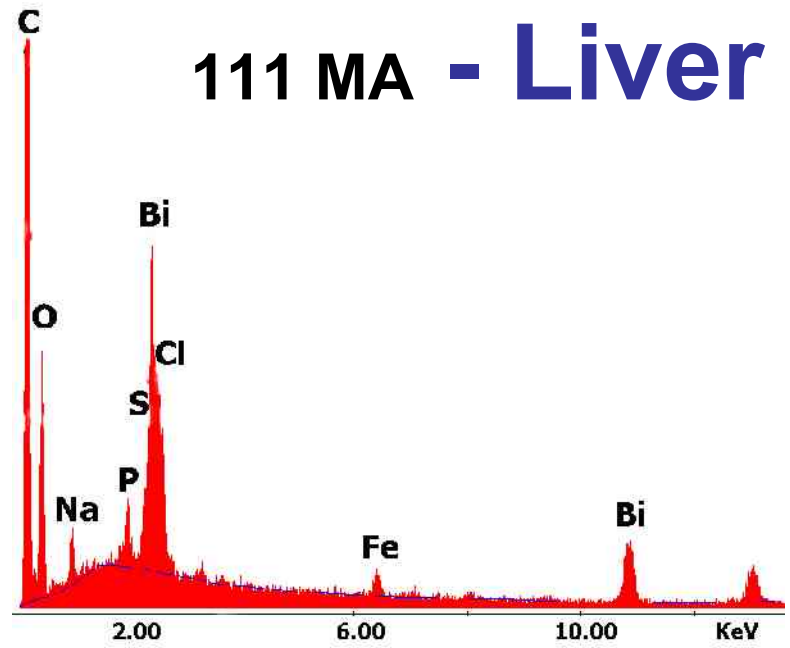
Additional features such as spina biphida, cryptorchidism and shallow orbital cavities have been reported. Chromosomal analysis in reported cases has revealed a *normal karyotype* and an *autosomal recessive inheritance* has been postulated.



The 6 cases of Neu-Lexova
occurred within 20 months
present similar contamination

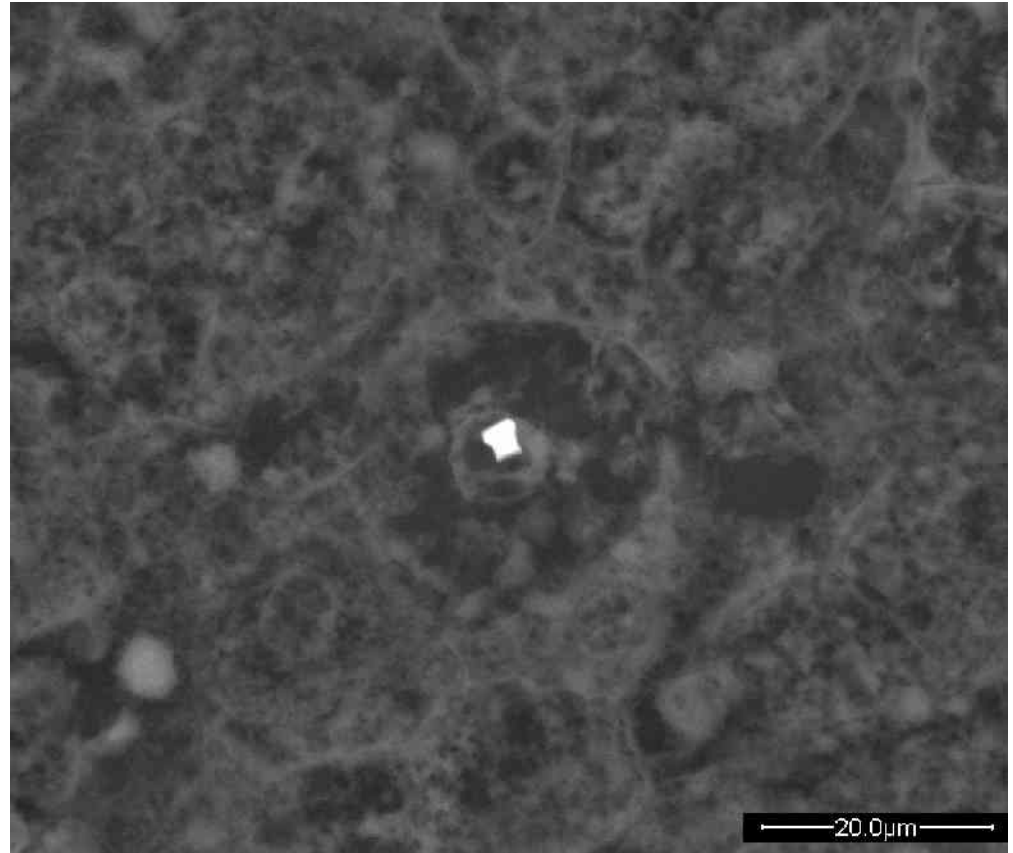
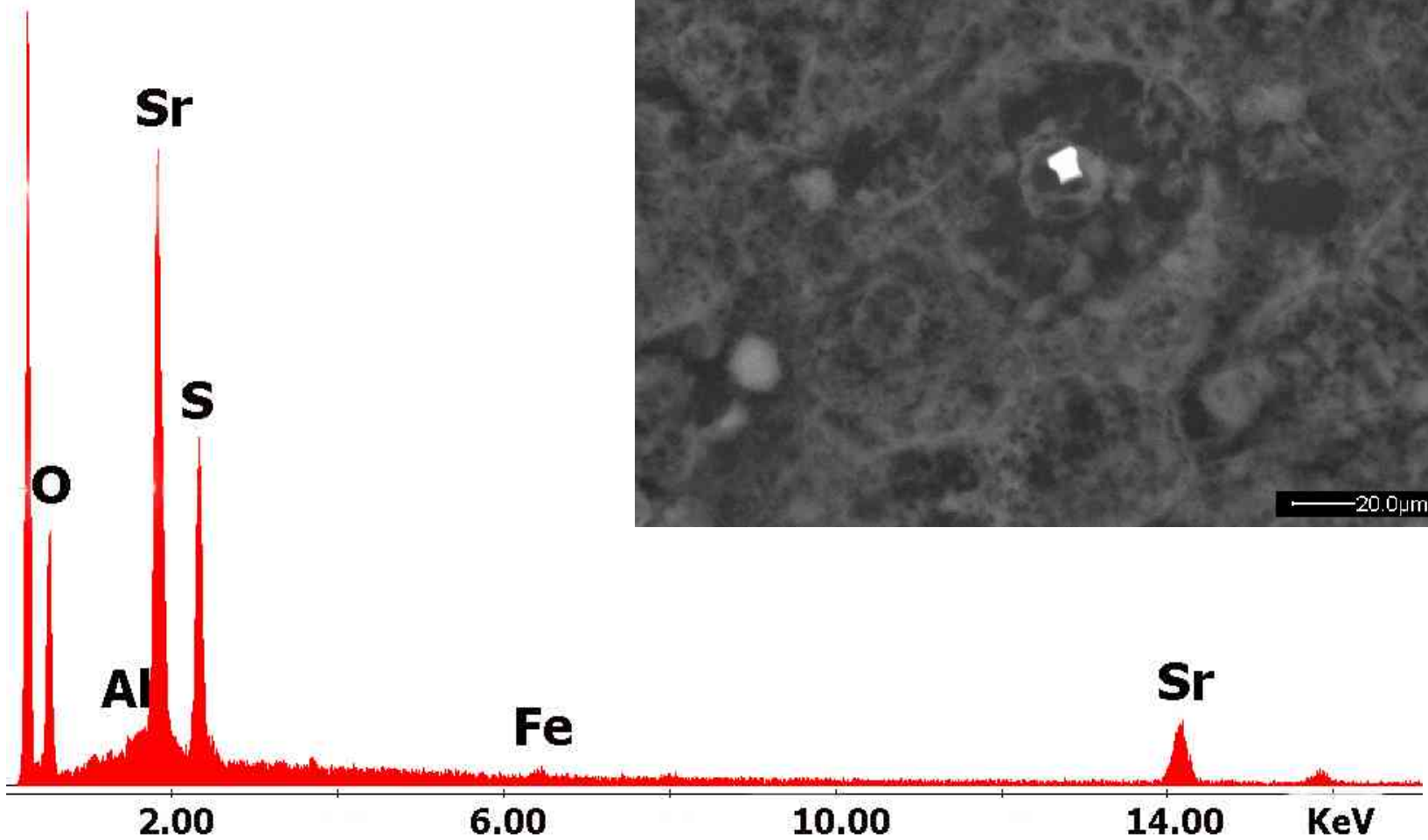
- Particles of **Antimony**
- **Tin and Stainless steel**
- **Bismuth-Chlorine**
- **Strontium-Sodium**
- **Lead-Bismuth and Zinc**

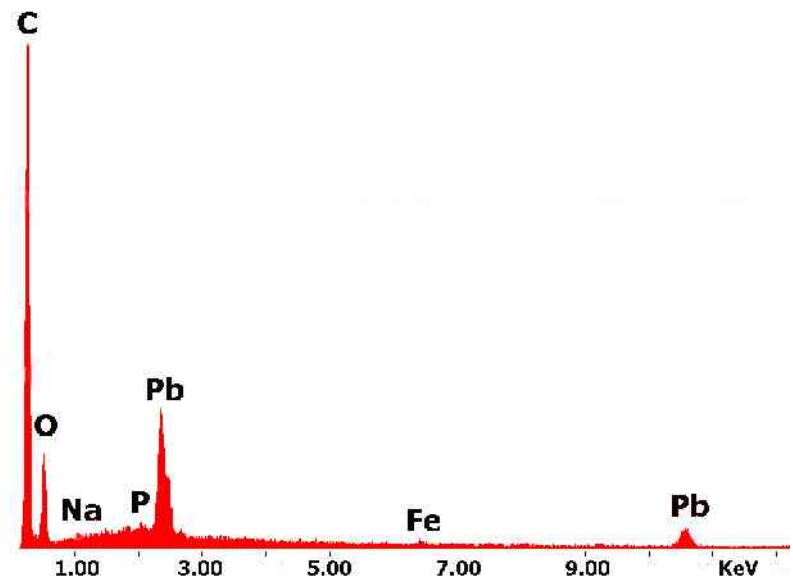
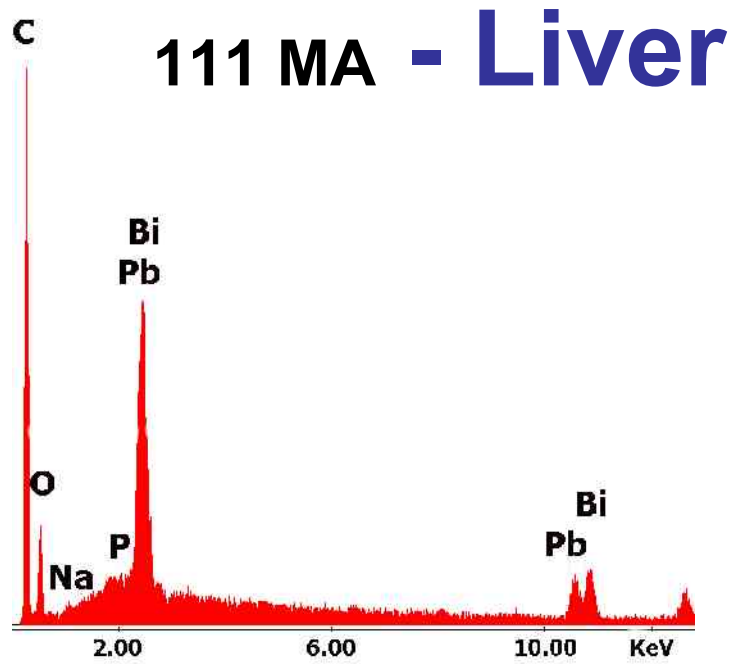
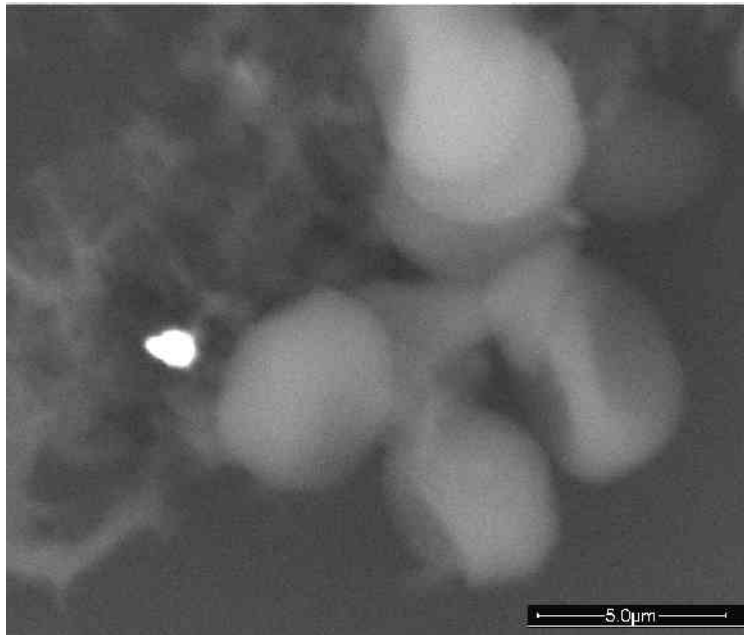




111 MA - Liver

C

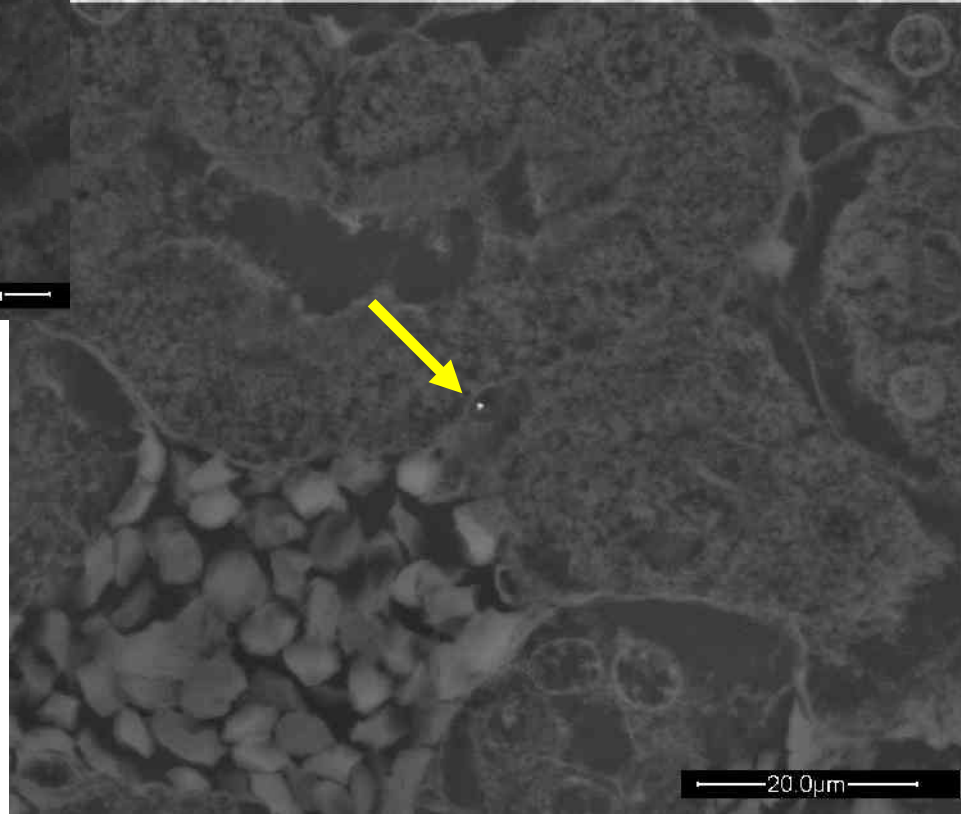
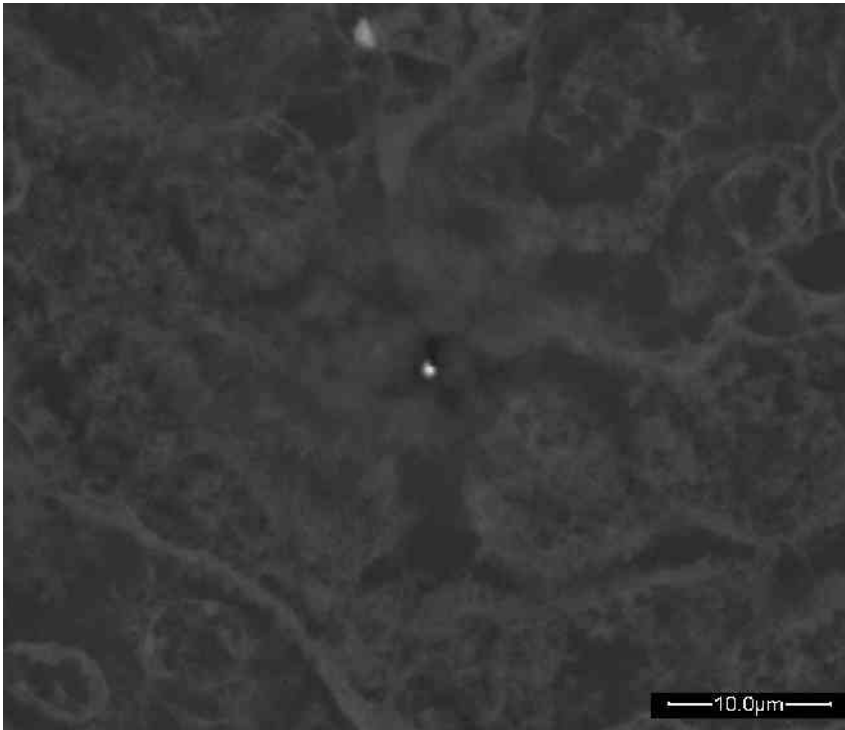




111 MA

Kidney

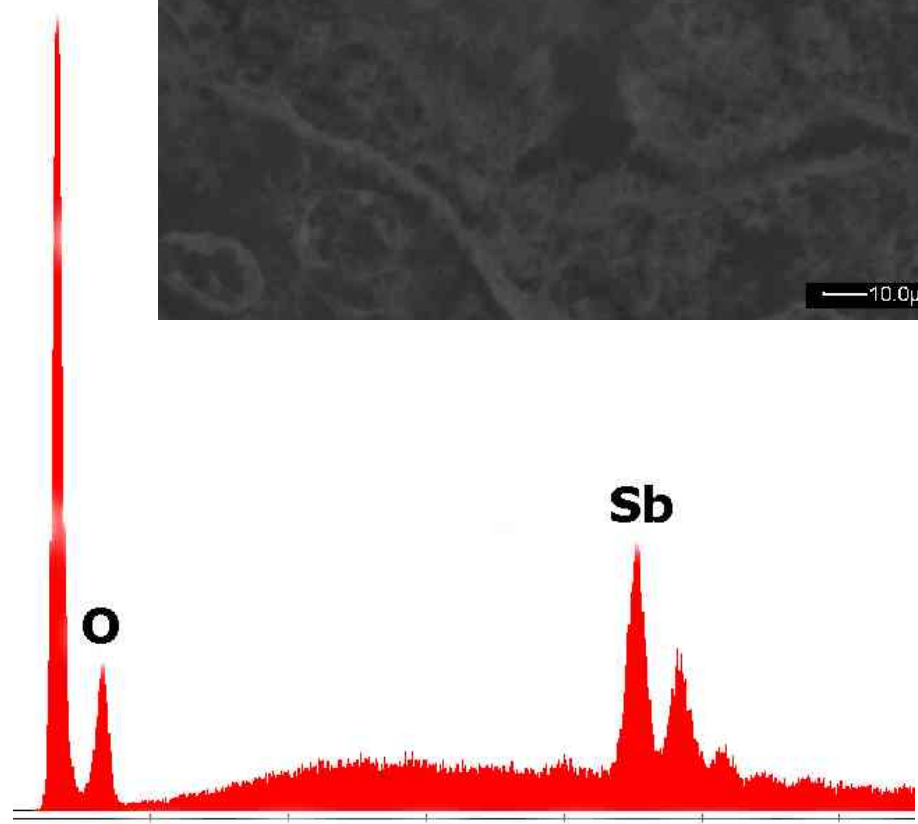
C



Sb

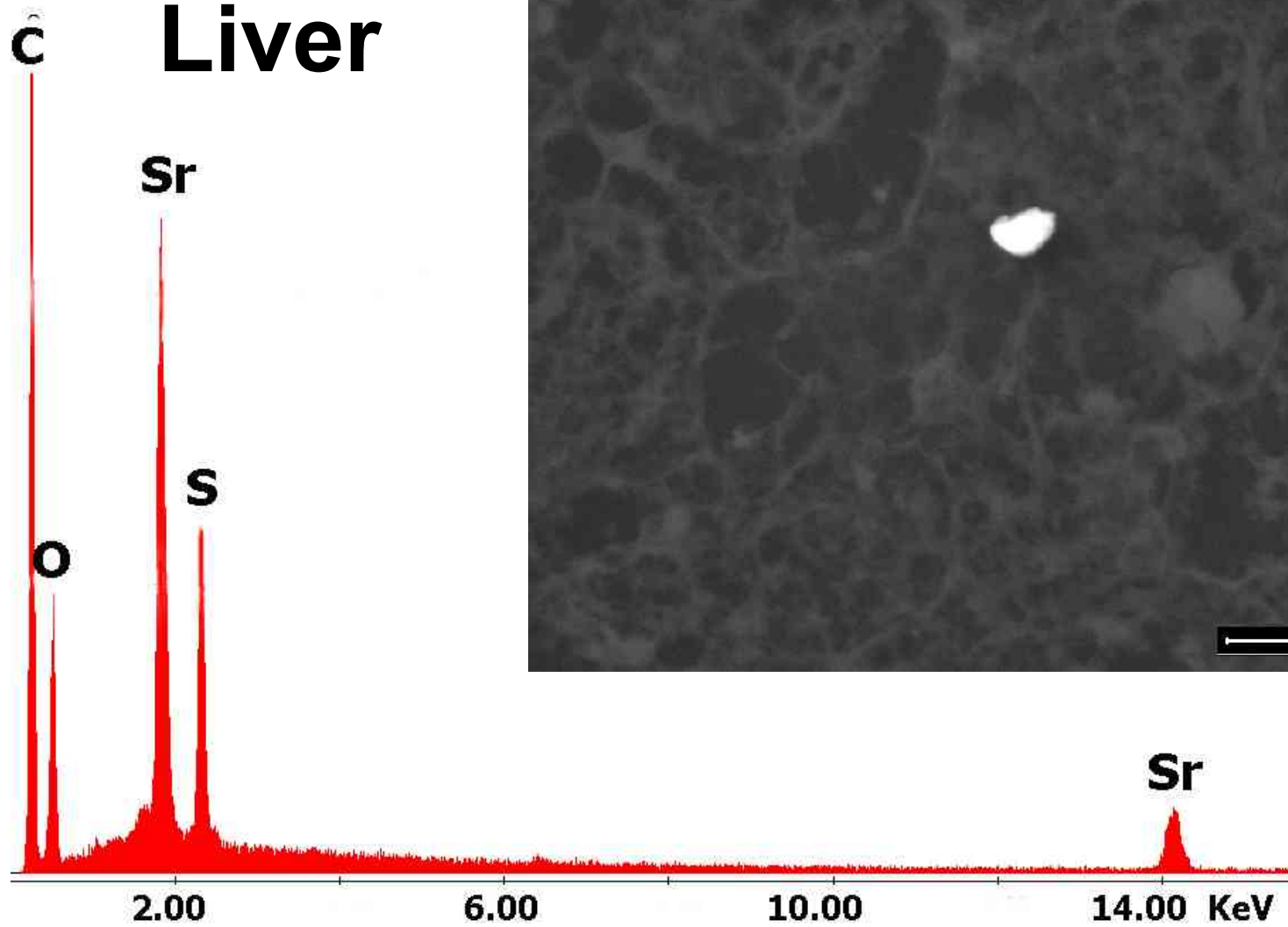
O

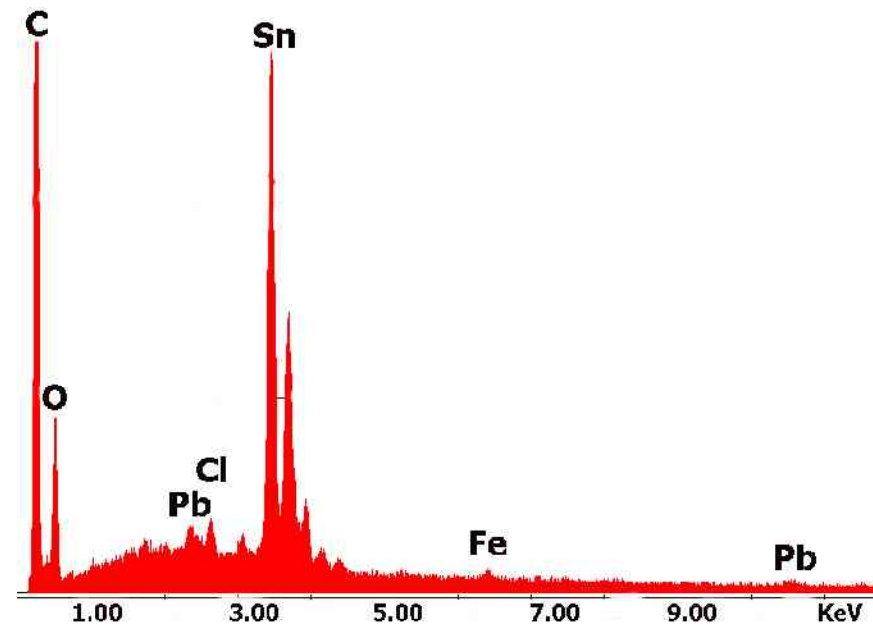
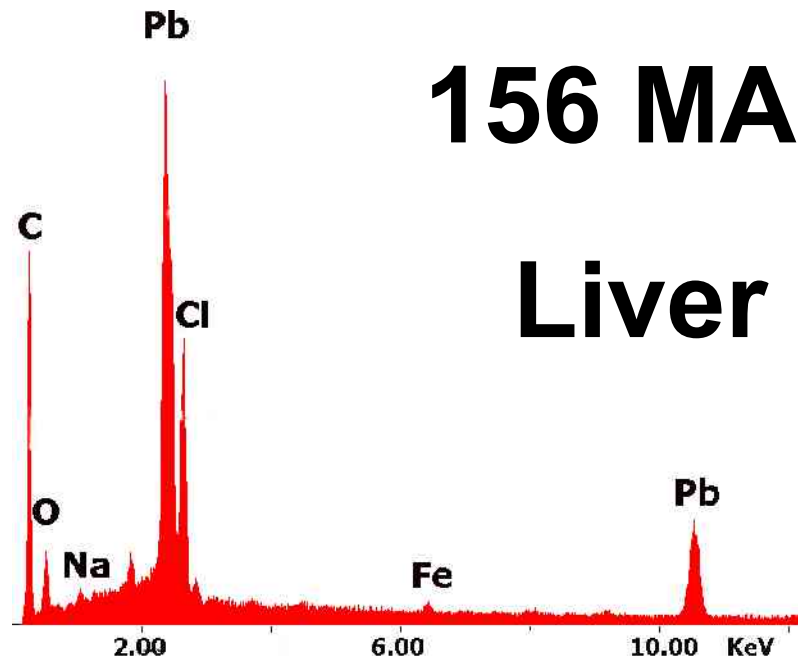
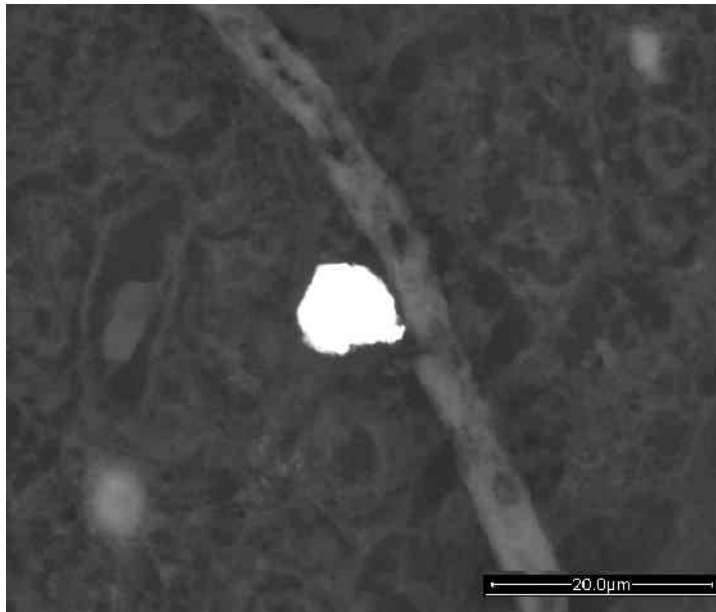
0.80 2.40 4.00 KeV

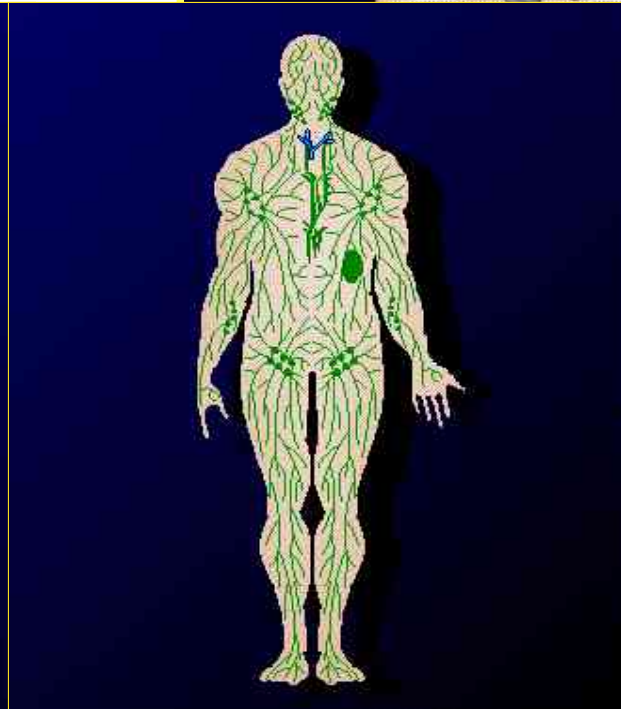
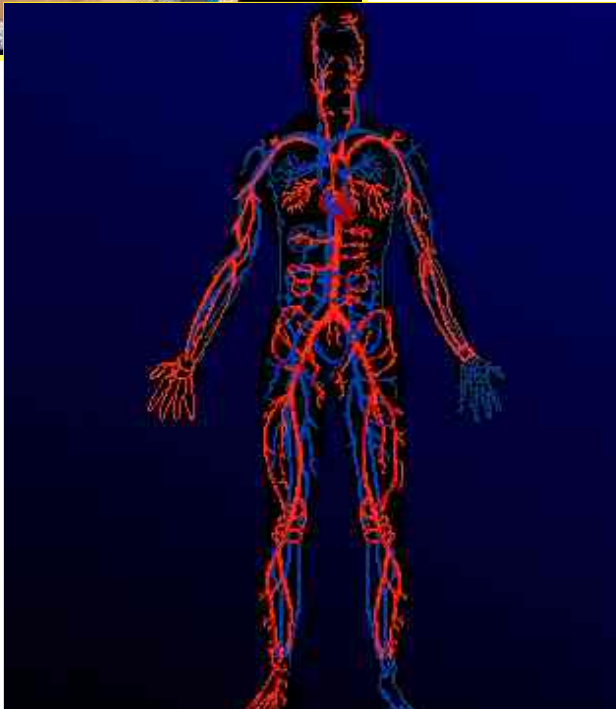
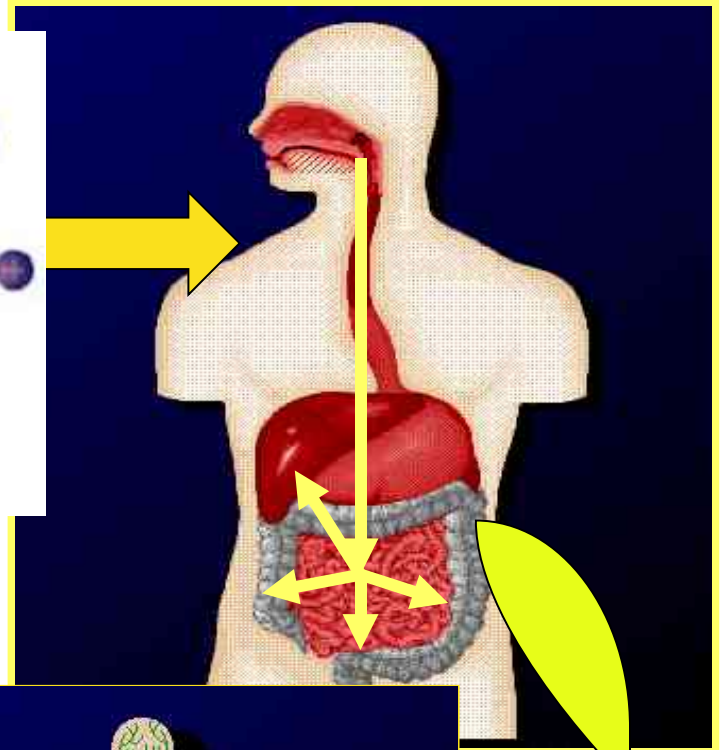
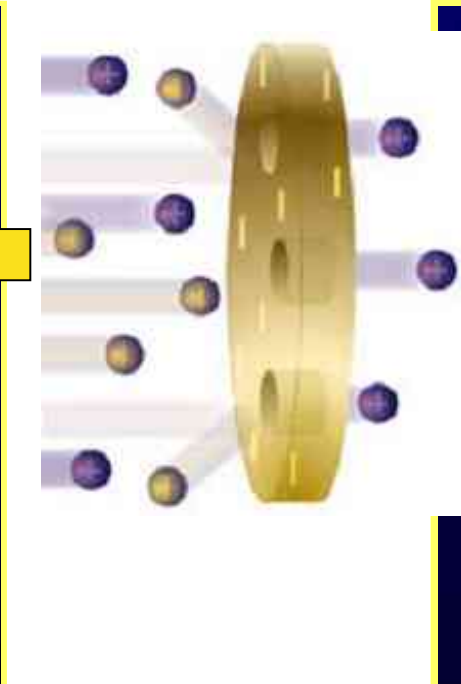
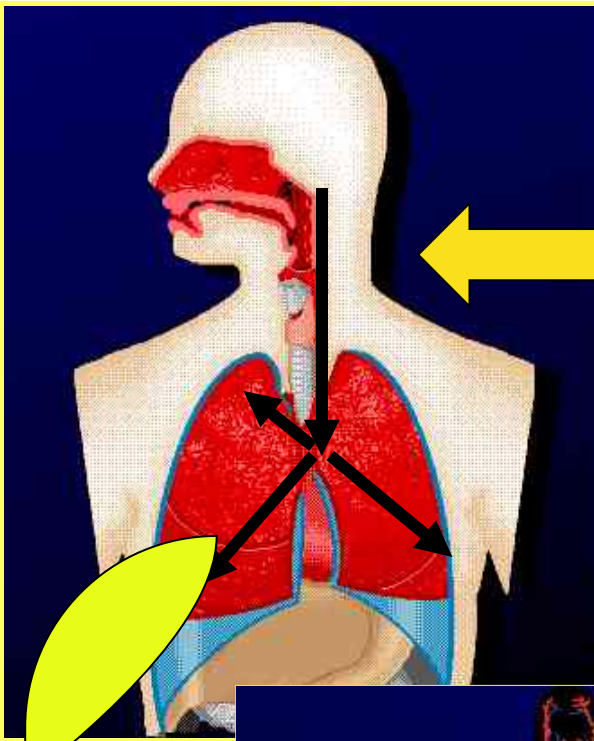


156 MA

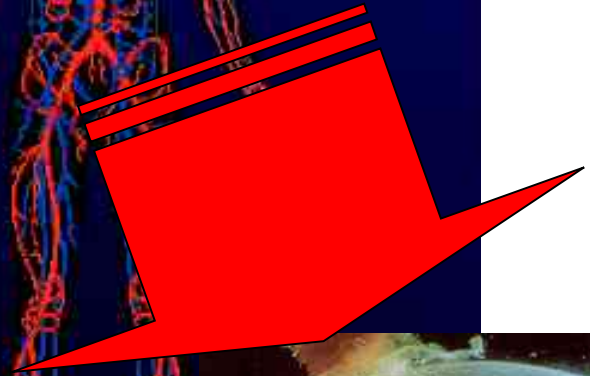
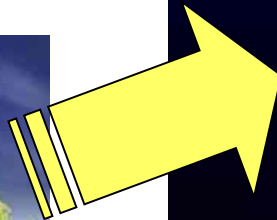
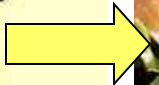
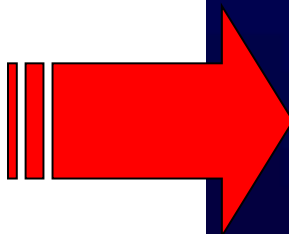
Liver



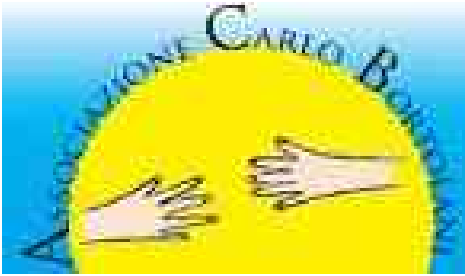




Impact of the environmental nanopollution



The study was supported by



**Associazione Carlo
Bortolani Onlus**



**The group of
Nanopathology**

*The ability to think differently today from yesterday
distinguishes the wise man from the stubborn.*

J.Steinbeck (Nobel Prize 1962)

THANKS