ESRF	**Experiment title:** Localisation of lanthanum in bone of chronic renal failure rats.	**Experiment number**: LS1709
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Report:

Introduction:

In patients with chronic renal failure, serum phosphorus levels increase due to insufficient renal excretion. To control serum phosphate levels, phosphate binding agents are given orally, in order to reduce gastro-intestinal phosphate uptake. Until recently, aluminium hydroxide was widely used, but accumulation in bone results in aluminium-related bone disease, characterised by a mineralisation defect. Using microanalytical and histochemical techniques, aluminium was localised at the mineralisation front, a region in bone critical for proper mineralisation. Lanthanum carbonate has been proposed as a new phosphate binding agent. However, being also a trivalent cation, and having some chemical similarities with aluminium, deposition of this element in bone can not be excluded. Due to the extremely low concentration of lanthanum in bone, more conventional microanalytical techniques are not sensitive enough to localise the element, and more sophisticated techniques were necessary.

Materials and methods:

Ultrastructural mapping of lanthanum distribution in rat bone was performed using the ID21 Scanning X-Ray Microscope, operated in fluorescence mode. The beam was focussed to a microprobe (< 1 µm) using a Fresnel zone plate, and the sample raster scanned to acquire 2D images. Different energy windows on the multichannel analyzer of the high energy resolution germanium solid state detector allowed the simultaneous mapping of lanthanum, calcium and phosphorus in the samples.

Rats in which renal failure was induced by a 5/6 nephrectomy have been loaded orally with lanthanum carbonate at doses ranging from 100 – 2000 mg/kg/day during 12 weeks. Tibial bone samples of these animals were embedded in methyl-methacrylate and cut into 'thick' sections of 0.5 mm and 'thin' sections of 10 µm. Due to the low concentrations, only sections from animals with the highest bulk lanthanum concentration were used for the mappings.

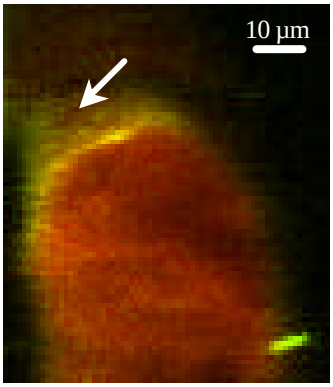


Figure 1

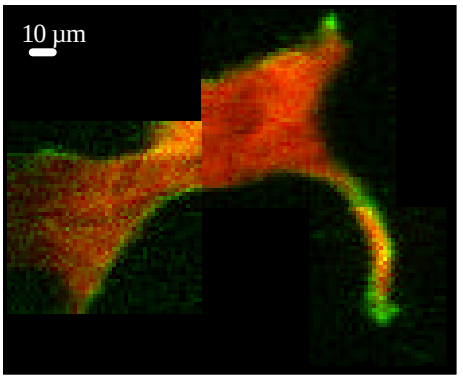
Chronic renal failure animal; bulk bone La content: 5613 ng/g wet weight

Combined calcium (red) and lanthanum (green) map of a 0.5 mm thick section. The image shows lanthanum to be localised at the edge of the calcified bone. The arrow indicates diffuse presence of calcium and lanthanum, probably caused by the thickness of the sample. The bright spot in the lower right is Ti or Ba contamination.

Figure 2

Chronic renal failure animal; bulk bone La content: 5613 ng/g wet weight

Combined calcium (red) and lanthanum (green) maps of a 10 µm thick section of the same animal as fig 1. Again, lanthanum appears to be localised at the edge of the calcified bone.



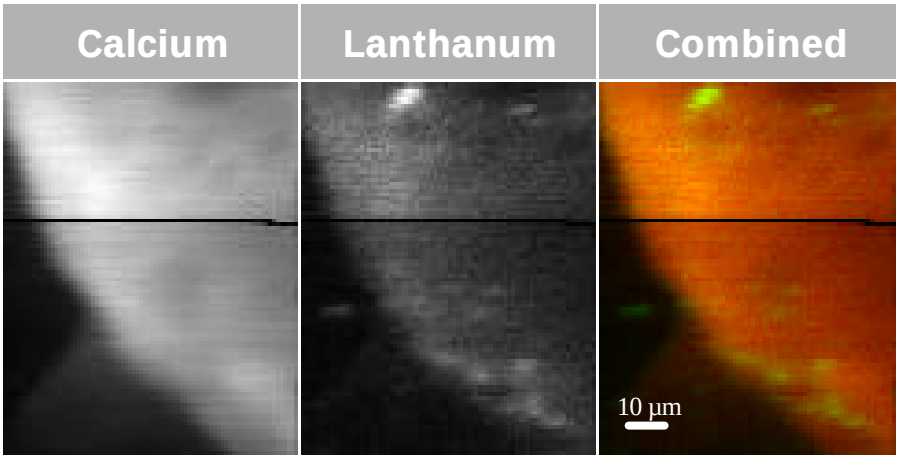


Figure 3

Normal renal function animal; bulk bone La content: 3874 ng/g wet weight.

Calcium, lanthanum and combined map of a 10 µm thick section of an animal which did not present histological evidence of bone disease. La does not appear to be present preferentially at the edge of the calcified bone.