Report MD710: Chemical imaging to investigate Fe and Cu metabolism in human lung tissue after asbestos exposure and in vitro human mesothelial cells.

The lung tissue reaction to asbestos fibres is an issue at today that needs deep investigation not only for the understanding of physico-chemical properties that confer a specific toxicity to this material but also in order to prospect diagnostic and therapeutic interventions in the asbestos-related diseases [1]. The research greatly depends from the availability of high sensitive techniques that could allow assessing the distribution of the asbestos fibres in possibly untreated histological samples and that can help the understanding of the formation mechanisms of the asbestos bodies. These structures consist of asbestos fibres coated by iron containing proteins and other organic material and that are the histological hallmark of asbestos exposition. The proposal intended to further investigate Fe metabolism around these formations. Differently the possible involvement of Cu is of interest for possible diagnostic/therapeutic intervention in asbestos-related diseases.

The present beamtime activity allowed to complete previous activities (MD546) and further explore features of Fe mobilization in lung tissue that is clearly related to asbestos presence. The analyses results complemented previous experiments at ESRF and are published in Scientific Reports (Pascolo L, et al. Sci Rep. 2013;3:1123),

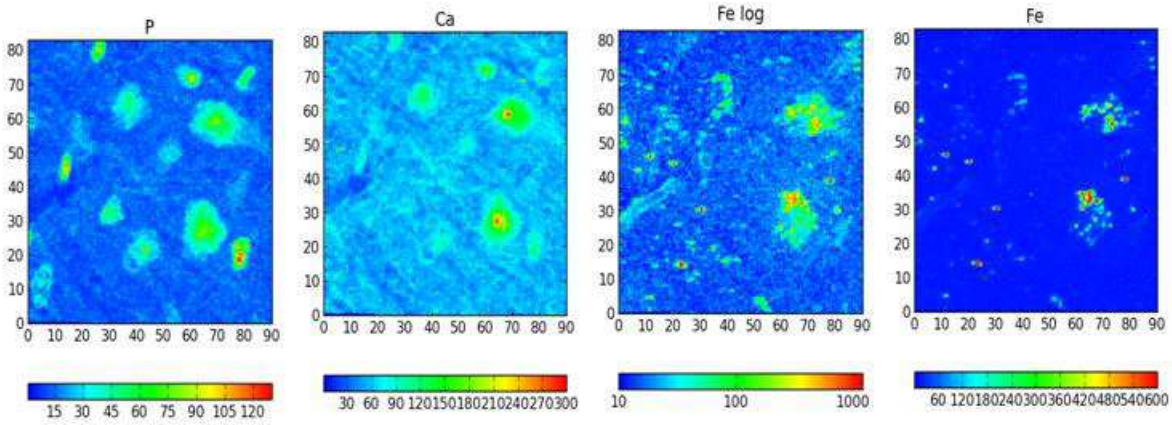
Differently the attempt to resolve Cu presence in lung tissue and mesothelial cells was not greatly successful. At ID21 the sensibility for this element is limited and result need further elaboration. At ID22 the sensibility for Cu is good but the beamtime suffered of many technical problems and at today we are not able to elaborate part of the data. The limited time we had and the poor performance of the beam (absent for many hours) prevented good results.

However the beamtime was very successful at ID21, not only for the new results on Fe metabolism, but also for testing the feasibility of two new projects:

1) The possibility to follow in animal models nanodrug disposition and brain targeting

2) Investigating Fe presence in the cells of a genetically tractable organism such as Dictyostelium, helpful in the investigation of Fe related pathologies.

The figure 1 shows a typical result obtained from the analyses of brain tissue slices of mice administered with polymer-coated iron nanolarticles that are properly functionalized to cross the blood brain barrier. The results clearly demonstrate the feasibility of the approach and a dedicated beamtime will be requested for this project.



XRF microscopy maps obtained at ID21 on a selected brain area of a NPs treated mice -.

A 7.3 keV incident X-ray beam was focused onto the sample and images were acquired by raster scanning the samples at a step size from 0.25 to 0.5 m. P distribution allows to identify cell structures, while Ca is present in few structures, possibly mainly nuclear districts. Fe presence is shown both in linear and logarithmic scale in order to better highlight the high presence of the element and the clear intracellular localization in a brain section of NPs treated animals. Map dimensions are in micron.

Similarly, the XRF approach is greatly successful to reveal the endogenous presence of Fe in the Dictyostelium cells and a dedicated beamtime will be proposed for this project.

The FTIR analyses at ID21 had the aim of revaling possible changes in the protein content of asbestos containing lung tissues. From the first analyses it appears that asbestos affects the structure (beta component increase) of the proteins arown asbestos fibres. Further complementary analyses are however needed.