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# SOME MEDICAL APPLICATIONS OF PIXE USING CYCLOTRON BEAM

G. Robaye*, I. Roelandts**, A. Collignon***, J.M. Delbrouck*, G. Weber*, P. Bartsch***, Yu-Jie Jian****

University of Liège - Institut de Physique Nucléaire, B-15, Sart-Tilman par Liège 1, Belgium.
* Experimental Nuclear Physics.
** Geochemistry.
*** Internal Medicine.
**** General Research Institute for N-F Elements MMI Peking, China.

Abstract : 1) Lung content in trace metals : 35 lungs pairs obtained at autopsy from patients randomly selected have been investigated by Pixe for overall and regional elemental contents ; in each case the interbronchial lymph node was simultaneously processed. While homogeneous distribution has been constantly observed for K, Ca, Fe, Cu, Zn and Rb, very different pattern was recorded regarding Ti, Cr, Ni and Sr. The signification of these results is discussed with regard to pollution hazards. Regional accumulation of this second set of elements seems related to pollution hazards peculiar to our city.

2) Serum content in trace elements in chronical renal insufficiency : the sera of patients submitted to iterative dialysis for renal insufficiency have been studied before and after epuration and compared to 27 sera of normal subjects. Expected data have been collected : depletion of K and increase of Ca during the dialysis. Besides these well known facts, all patients exhibit a very low bromine concentration which tends to reach lower values after the dialysis. Copper concentrations for normal as well as for dialysed subjects are very largely dispersed. We do not confirm an elsewhere mentioned chronic deficiency of zinc content associated with renal disease.

1. Introduction.- As trace element analysis raises up more and more interest in the medical field, Pixe facilities have been developed in the University of Liège near to the Cyclotron Research Centre (C.R.C). Pixe (short for charged Particle Induced X Ray Emission Spectrometry) [1] [2] has proved to be a suitable method for studying in a short time the elemental composition, even at the p.p.m. level, of small samples of biomedical materials. This technique has been used here to study two types of biological problems : the elemental analysis of lung parenchyma and lymph nodes and the elemental analysis of sera of hemodialysed patients.

2. Sample preparation.- The target preparation scheme for lung samples has been fully described elsewhere [3] and the value of Pixe method for obtaining quantitative results demonstrated. Fig. 1a summarizes the preparation method. Different procedures are available for preparing serum ssmples[2]. Fig. 1b presents a way to avoid the loss of volatile elements such as bromine. Yttrium nitrate solution is added as an internal standard to one ml of serum. After homogeneization the sample solution is lyophilized and the powder obtained is pressed at 4000 kg/cm$^2$ to give a suitable 13 mm diameter pellet. Contamination by the mould during the compression phase is avoided by using a 4 µm thick polypropylene foil protecting the pellet face choosen to be irradiated. This protecting foil is withdrawn and the pellet mounted on an aluminum sheet in a standard slide frame. The pellet is maintained in the centre of the frame by means of a thin (4 µm), contamination free polypropylene foil. A small pin is used to create several holes throughout the Al foil all around the pellet to avoid problems encountered when placing the sample under vacuum. The aluminum foil is mandatory to provide a suitable electrical contact between the sample and the sample holder. This target preparation and irradiation at a pressure of $10^{-2}$ torr eliminate secondary bremsstrahlung generation during Pixe measurement.

3. Irradiation.- The irradiation set-up is shown in ref. 4. The 3.12 MeV proton cyclotron beam is homogeneized by passing through an aluminum foil and a 20 nA, 2.5 MeV proton beam hits the target with an 8 mm diameter spot for pellets and 11 mm diameter spot for lung samples in order to cover the whole target in the latter case. This procedure avoids the problem of selective ion migration along the cellulosic Gelman filter used as a backing. The X-Rays produced are detected with a 12 mm$^2$ Si(Li) detector, the resolution of which is 151 eV FWHM at 5.9 keV. The detector is placed at 135° LAB at a distance of 31 mm from the centre of the target.The vacuum in the chamber is maintained at $10^{-2}$ torr as explained above. A 620 µm thick mylar absorber is placed between target and detector. The chamber window is a 30 µm thick mylar foil.

4. Results and discussion.

a) Lung samples : The first aim of this research was to prospect the capability of Pixe to study possible professional or environmental contamination of the lungs. To determine the sampling method it was at first necessary to answer the following questions : 1) how many samples are necessary for the characterization of the trace element content of lungs ? 2) Is the interbronchial lymph node content different from that of the corresponding pair of lungs and worth while to study ? 3) What is the appropriate size for the samples ? The size of the samples was determined by considering the local homogeneity of highly probably uncontaminated lungs from young animals (pigs). Results of this preliminary work are presented in table 1. Samples of about 2g (wet weight) were consequently adopted. 35 lungs pairs obtained at autopsy from patients randomly selected were then investigated. Table 2 summarizes the data obtained for K, Ca, Fe, Cu, Zn, Rb, Ti, Cr, Ni and Sr. The striking feature is that the distribution of these elements is not the same for all of them. Homogeneous distribution has been systematically observed for K, Ca, Fe, Cu, Zn and Rb but a very different pattern characterizes Ti, Cr, Ni and Sr the concentration of which

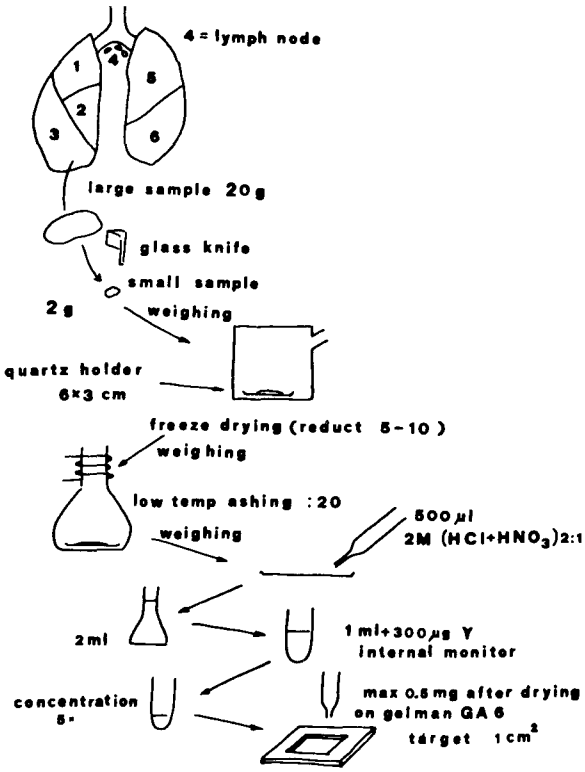



Fig. 1a Lung sample preparation

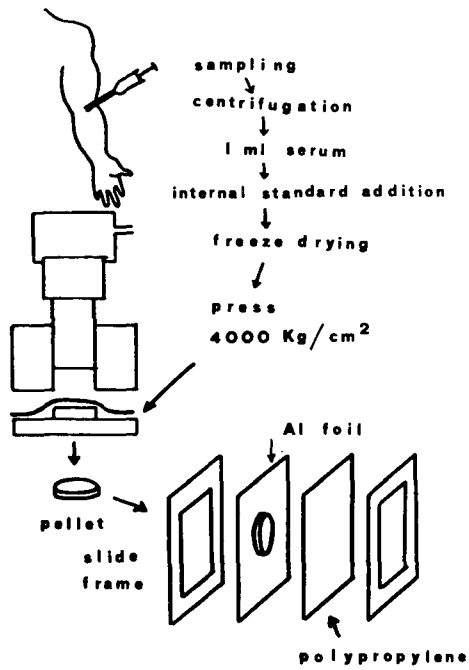



Fig. 1b Serum sample preparation

| Sample N° | K | Ca | Fe | Ni | Cu | Zn | Rb |
|---|---|---|---|---|---|---|---|
| 1 | 13338 | 426 | 256 | 2.27 | 11.5 | 89.0 | 25.6 |
| 2 | 11852 | 414 | 257 | 2.32 | 11.5 | 80.4 | 24.3 |
| 3 | 12570 | 422 | 270 | 2.89 | 13.4 | 85.5 | 25.8 |
| 4 | 12659 | 366 | 256 | 2.58 | 13.0 | 81.3 | 22.8 |
| 5 | 13958 | 459 | 235 | 2.50 | 13.2 | 91.0 | 26.1 |
| 6 | 13358 | 513 | 262 | 3.45 | 14.2 | 89.3 | 24.0 |
| Mean | 12956 | 433 | 256 | 2.67 | 12.8 | 86.1 | 24.8 |
| ST | 744 | 49 | 12 | 0.44 | 1.1 | 4.4 | 1.3 |

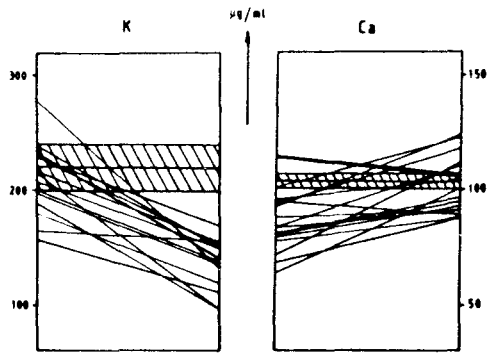
Table 1 : Concentration of elements in different parts of a pig lung.

increases significantly from base to apex.This constatation associated to the fact that the correlated lymph nodes concentrations and the shape of the concentration distributions are also very different for the two groups of elements leads us to the conclusion that Ti, Cr,Ni and Sr are most probably external contaminants. Air pollution of Liège area where the subjects had lived for decades has been recently studied[5] .It is characterized by a particularly high concentration in these elements. In conclusion to this research one can say that Pixe is suitable for that kind of study, that it is necessary to study at least one sample in each lobe of both lungs in order to characterize external contaminants, that 2g samples appear to be an adequate size and that the lymph node study gives useful indications to confirm the contamining nature of elements detected. Such a study gives the average level of trace element concentration as well as their fluctuations in the lungs of an unselected population in a given area. It could furnish provisional reference values for future studies about professionaly exposed people in the same geographic area. It is evident that a considerable lot of work would be necessary if more informations such as precise medical history recording, living area, smoking habits, local airborne pollution and professional exposure would be taken into account to constitute more specific groups. That could reduce the statistical fluctuations within the different groups and make further diagnosis more efficient. However such a large study seems to require a collaboration between several Pixe groups in order to reduce the delay of achievement.

b) Sera from dialysed patients: Because of the easy procesure available to obtain suitable targets from small serum samples, Pixe method was used to study the variation in the composition of sera from patients submitted to hemodialysis. Sera from 27 volunteers taking no drugs and in good health were proceeded simultaneously as controls. Fig. 2 summarizes the results obtained before and after dialysis. The horizontal line gives the mean concentration for each element measured on the control group and the hachured region represents $\pm 1\sigma$ of the mean value. As well known lowering of the K concentration and increase of the Ca concentration can be observed. Zn : our results do not confirm the low values of Zn of renal insufficiency suffering subjects observed by Cornelis et al.[6]. Our patients did not indeed present the symptoms of Zn deficiency reported by Fornari[7] , consisting in a loss of taste sense. If we compare the mean of the present results to the results obtained by Cornelis et al. (Table 3) we can see that the difference between the two studies lies in the value of the mean concentration in Zn for the reference groups. As a matter of fact, R. Cornelis observes a Zn deficiency but no corresponding change in the sense of taste in the hemodialysed peoples studied.

| | K | Ca | Ti | Cr | Ni | Fe | Cu | Zn | Rb | Sr |
|---|---|---|---|---|---|---|---|---|---|---|
| AREA 1 | 0.98 ± 0.12 | 1.14 ± 0.50 | 1.39 ± 0.53 | 1.40 ± 0.63 | 1.41 ± 0.92 | 1.08 ± 0.35 | 0.97 ± 0.21 | 1.00 ± 0.15 | 1.00 ± 0.20 | 1.20 ± 1.06 |
| AREA 2 | 1.09 ± 0.17 | 0.99 ± 0.35 | 1.04 ± 0.56 | 0.96 ± 0.44 | 1.04 ± 0.68 | 0.92 ± 0.27 | 0.99 ± 0.26 | 1.09 ± 0.16 | 1.09 ± 0.22 | 1.06 ± 1.16 |
| AREA 3 | 0.98 ± 0.14 | 0.98 ± 0.33 | 0.67 ± 0.42 | 0.69 ± 0.34 | 0.67 ± 0.45 | 1.01 ± 0.24 | 0.99 ± 0.16 | 0.95 ± 0.14 | 0.94 ± 0.19 | 0.83 ± 0.86 |
| AREA 5 | 0.97 ± 0.11 | 0.95 ± 0.23 | 1.18 ± 0.57 | 1.13 ± 0.42 | 1.03 ± 0.76 | 0.97 ± 0.27 | 0.98 ± 0.18 | 0.97 ± 0.13 | 0.97 ± 0.17 | 1.14 ± 1.33 |
| AREA 6 | 0.98 ± 0.14 | 0.94 ± 0.34 | 0.72 ± 0.39 | 0.82 ± 0.38 | 0.84 ± 0.58 | 1.02 ± 0.25 | 1.06 ± 0.34 | 0.99 ± 0.24 | 1.00 ± 0.25 | 0.76 ± 0.88 |
| AREA 4 | 0.55 ± 0.30 | 0.54 ± 0.30 | 3.98 ± 3.07 | 2.77 ± 3.48 | 2.33 ± 2.24 | 0.74 ± 0.43 | 0.55 ± 0.32 | 0.56 ± 0.29 | 0.61 ± 0.37 | 0.70 ± 0.82 |

Table 2. Mean values of the ratio between the lobar and ganglionar results and the mean value of the corresponding lung pair.



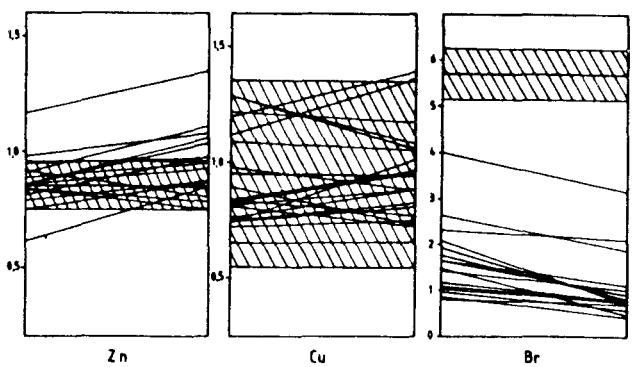




Fig. 2. Elemental concentration before and after dialysis.

Cu : the concentrations for healthy as well as for dialysed peoples are so dispersed that no significant evolution can be found.
Br : a substantial deficiency in Br exists for all dialysed peoples studied here and a further lowering in Br concentration during dialysis is systematically observed. R.D. Vis et al,[8] have demonstrated an easy passage of Br ions through the dialysis membrane.From "in vitro" studies they have shown that using a dialysis fluid enriched in calcium bromide it is possible to reach rapidly (10 minutes) normal values in Br concentrations.

| | Cornelis et al n = 10 | This work n = 17 |
|---|---|---|
| Before Dialysis.A | 0.86±0.26 | 0.87±0.12 |
| After Dialysis.B | 0.97±0.25 | 0.94±0.14 |
| Variation $\frac{B-A}{B}$ x100 | 12 % | 8 % |
| Reference Serum | 1.13±0.2 | 0.85±0.1 |

Table 3. Variation of Zn concentration.

5. General conclusions : Pixe is a powerful tool allowing simultaneous determination of most of the elements above Ar in small biological samples such as biopsies, serum, hair and lung alveolar cells from bronchio-alveolar lavages.

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