Medical Application

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1. Introduction

The main subjects of our research group is characterization of trace elements in biological systems through X-ray Fluorescence analysis (XRF). The trace elements have important role because they act as catalysts in metabolic processes. They serve as constituents of various metalloproteins and enzymes, which are indispensable for maintenance of biological activity. Examination of a trace element level in human body can be an important indicator for various diseases, because nutrition and metabolism have a large influence on the level. Moreover, a study of the interactions between toxic and essential elements is an approach to elucidate the metal-promoted toxicity.

The analysis of the trace elements in biological samples requires a development of a XRF technique with ultra high sensitivity and high spatial resolution, together with capability in nondestructive, nonvacuum, and simultaneous multielemental analyses. The experimental facility installed at BL39XU will be satisfactory for these requirements. We expect sensitivity of fg or ppb and X-ray microbeam with sub-micron size using a combination of focusing mirror and pin hole or capillary. SR-XRF analysis of biological and medical samples will represent an important step in understanding the role of trace elements in biological systems.

2. Activity of Medical application group in 1996.

Our group share the experimental station with the spectrochemical analysis group. We have joined the planning of the construction of the experimental station. Our research activity in 1996 in the field of SR-XRF was carried out at the Photon Factory, KEK and the literatures in the field of SR-XRF so far published are listed in the end of this paper.

3. Overview of our previous activities and our research projects at SPring-8 in 1997.

Medical application of SR-XRF technique will be carried out in the scheme shown in Fig. 1. It consists of two approaches: one is application of X-ray micro-beam and the other is total reflection analysis of trace elements.

3-I. X-ray Microprobe Analysis

The important application of X-ray micro-beam is XRF imaging of organs and tissues to determine trace element distributions (#1A and B). Since SR-XRF analysis does not cause any damage to samples, we are able to combine this method with histological examination. This technique is useful for toxicology[1-3] environmental exposure and industrial health monitoring[4-6] clinical science[7,8], and so on. We expect that focused micro-beam of submicron size from the SPring-8 light source allows us to clarify elemental distribution in a single cell (#1C). Another application of X-ray micro-beam is analysis of metal binding in metalloprotein (#2). As developed recently, a combination method (#2A) [9,10] of gel electrophoresis to clarify change in protein structure and SR-XRF line analysis for the detection of metal

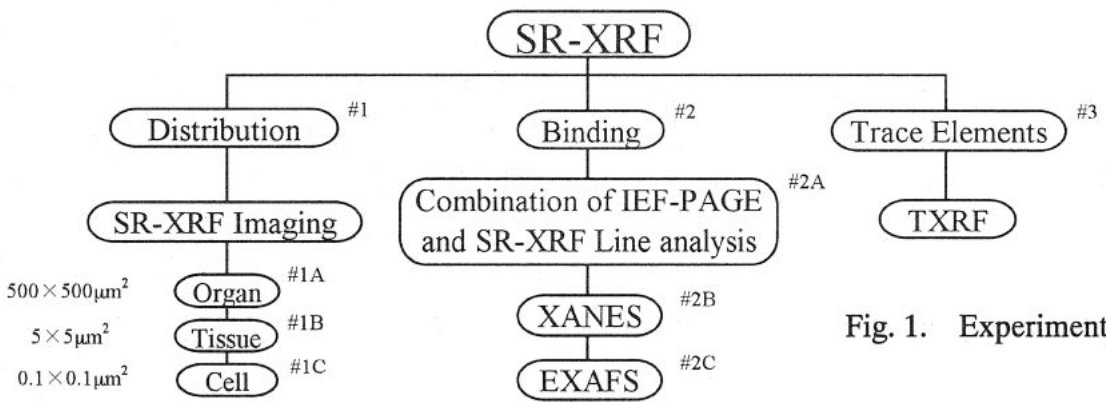

Fig. 1. Experimental plan

will become a convenient method for protein chemistry 11). Interaction Mechanism between metalloprotein and metal will be revealed by XANES (#2B) and EXAFS (#2C) techniques.

The first experimental target at SPring-8 in 1997 is "Development of a combination analysis of SR-XRF microbeam imaging and TUNEL staining technique and its medical applications". Apoptosis is a physiological mode of cell death mediating precisely controlled deletions of "unwanted cells". It is a marked phenomena in medical and biological sciences. Recently, toxicant-induced apoptosis has been reported for toxic metals, but few data are available for a dose-response relationship between induction of apoptosis and the metal distribution after the exposure. In this study, we attempt to develop a new method for simultaneous determination of metal and apoptotic cells in situ at a submicron level. SR-XRF imaging is used for determination of metal distribution and TUNEL staining for detection of apoptotic cells[12,13]. Since apotosis is characterized as enzymatic fragmentation of DNA occurred in nuclei, the elemental imaging, which is capable of distinguishing among various organelles in a cell, should be required.

Furthermore, multi-elemental analysis will provide us better understanding of apoptotic phenomena because most of endonucleases, which are key enzymes involved in apoptosis, are controlled by divalent metal ions, such as Ca^{2+}, Zn^{2+} , and Mg^{2+}.

3-II. Total Reflection Analysis

Another important medical application of the SR-XRF technique is Total reflection X-ray Fluorescence (TXRF) analysis[14,15]. This technique enables us to carry out quantitative analysis of ultra trace elements using trace amount of samples such as a sample obtained by biopsy. Trace element analysis of biopsy samples represents a difficult analytical problems due to the small masses of the samples. Advantages of TXRF analysis over conventional XRF analysis include extremely 10w back ground conditions, extremely small amount (volume) of a sample required (a few microliters), and multi-elemental analysis technique. Combined with these advantages, natural collimation of SR beam and extremely high intensity of the X-rays from SPring-8 offer an ideal light source for TXRF analysis of trace elements in biopsy samples.

We are now designing the TXRF experimental system installed at BL39XU in 1997. With an automatic sampler, it would be possible to analyze 10 samples/hr, i.e. more than 100 samples/day, which is appropriate for medical application of this technique. A future plan for constructing a medical center at the SPring-8 cite will be beneficial to each other.

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