RADIOISOTOPE-INDUCED XRF ANALYSIS
OF TUMOR-RELATED TISSUE SAMPLES

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Healthy and tumor-bearing mice have been analyzed in a trace element time dependent
study by employing two different radioisotope XRF systems. Results from these analytical
systems, using a point and an annular source, can be readily compared utilizing healthy tissue
samples as the normalizing standard. Normalized elemental ratios generated with the two
systems for similar tissue samples are in good agreement. The results reported use two of the
points generated in the time study of the disease progress, days zero and day 21.

Introduction

Normal trace element levels and their disease-related concentrations have been the
subject of a large number of investigations in recent years.1 -15 These previous
studies have been concerned with concentrations in biological tissues at time of biopsy
or death.6 -15 Therefore, determination of trace element concentration changes oc-
curring during the progress of the disease have not been deduced. In addition, sample
pretreatment16 and/or limitations with respect to the simultaneous measurement of a
variety of elements9,13,17 in a given sample has narrowed the scope of these studies.

An approach using radioisotope induced X-ray fluorescence (RIXRF) for multi-
element analysis has been designed to examine relative concentration changes during
the development of disease at ppm levels in mg weight tissue samples. The RIXRF
procedure for elemental analysis, if properly employed, attains the sensitivity needed
in studies of biopsy samples. Since the samples are small (<300 mg), and concentra-
tions can be in parts per million, it is more realistic to discuss concentrations and
sensitivity detection limits at the nanomole per sample level. Fig. 1, for example,
shows an RIXRF spectrum of 40 nanomoles of Cu in a synthetic protein. While
this represents a concentration of 100 ppm in this sample, the total sample weight
contains $24 \cdot 10^{15}$ atoms of Cu. Clearly the sensitivity is adequate for biological
analysis.

The advantages of using a radioisotope as the source of primary radiation in
an energy-dispersive XRF system have been discussed in previous works.18 -21

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Since these sources are virtually monochromatic, the background in the region of interest is substantially reduced over the bremsstrahlung distribution from an X-ray tube. Keeping in mind that concentration levels of less than 10 ppm in samples whose total weight is less than 100 mg are to be detected, any reduction in noise will result in a lower detection limit.

The strain of animals and disease models used in such studies are carefully controlled and selected for reproducibility in all aspects of their biological and physical natures. Therefore, tissue samples from healthy (or control) animals serve as the relative standard against which changes in elemental content of a given tissue type can be compared. In this way different X-ray detector systems (or any other analytical method) can be self-normalized. That is, results reported as deviation from normal can be comparable.

Biological samples are not of uniform size and thus, XRF system geometry effects associated with maximizing the primary flux and minimizing direct, as well as scattered radiation as seen by the detector, is essential. This is readily accomplished using point sources and appropriate collimation and shielding. The use of annular sources restricts the geometry options, but provides an easily reproducible set of parameters when multiple samples are to be examined. For example, the annular source, while limiting flexibility in source-sample-detector configuration does present a constant flux density and solid angle. A properly designed point source system, however, can be equally reproducible in this sense and allows for signal to noise (background) optimization. Both types of sources were used in these studies discussed in the following sections.