PIXE analysis of biological samples treated with quantum dots

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Abstract

Particle induced X-ray emission (PIXE) is an excellent tool for multi-elemental analysis of a wide variety of samples and can provide elemental distribution in the sample using a beam scanning technique. Thus, PIXE plays an important role in various fields of research such as material engineering, environmental science and life science.

In biological and medical fields, it is important not only to evaluate elemental concentration in the sample but also to understand its biological mechanism, whereas PIXE provides only elemental information of the sample. In order to study relationships between elemental distribution and vital function, I aimed to apply Quantum dots (QD) as a biological tracer to PIXE analysis. QD is a semiconductor nanocrystal having unique optical and electronic properties, such as size-and composition-tunable fluorescence emission. In addition, its surface is coated with PEG. Therefore, QD can be conjugated with biological substances such as molecule and antibody associated with biological response.

In this work, QD was applied as a blood-flow tracer in tumor bearing mice treated with the vascular disrupting agent AVE8062. I administered AVE8062 at a single dose of 10mg/kg or 40mg/kg into C3H/HeSlc mice that were transplanted with NFSa fibrosarcoma cells. QD

(10pmol/kg) was injected into the tail veins of the mice 24h after AVE8062 administration. The tumors were excised and frozen immediately with powdered dry ice. Tumor samples were for conventional PIXE analysis as well as fluorescent observation. We also prepared kidney samples in the same way as the tumors. We used Qtracker® of Invitrogen as QD. Because the PEG surface does not contain reactive functional groups, Qtracker® is retained in circulation longer period of time. The conventional PIXE analysis were performed at Nishina Memorial Cyclotron Center (NMCC), while elemental distribution in the sample tissue sections were evaluated from the PIXE analysis using the submillimeter-sized proton beam (submilli-PIXE) at the Fast Neutron Laboratory, Tohoku University.

In the case of the control mouse, fluorescence of QD was observed clearly in both its tumor and kidney samples. I could also observe the elemental distribution of Cd and Se, which are component of QD, in the submilli-PIXE analysis. Althogh fluorescence was not observed in the tumors and kidney samples of the AVE8062 treatment group (40 mg/kg), the elemental distribution of Cd and Se was observed in only kidney samples.

The results of the present analysis indicate the following points：

(1) QD was not observed in tumors of the two mice treated with AVE8062 because of tumor blood-flow interrupting effect.

(2) it is possible to observe fluorescence of QD, even if Cd concentration is under the detection limit in PIXE analysis.

(3) The relationships between elemental distribution and vital function can be derived by comparing fluorescence images and PIXE images.

In conclusion, I performed both PIXE analysis and fluorescent observation using QD for the same samples. It was difficult to apply Qtracker® of Invitrogen as the blood-flow tracer for PIXE analysis because the elemental concentration concerning the QD is under the level of the detection limit in PIXE analysis. It is suggested that if QD conjugated with biological substances is used, the QD can be detected by PIXE analysis as a biological tracer because concentration of QD in bio-samples is expected to increase.