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PET/CT Imaging of Tuberculosis with 68ga-Citrate

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Abstract

Objective: The impact of tuberculosis (TB) on mortality and morbidity is indisputable worldwide and even more so in countries with a high prevalence of Human Immunodeficiency Virus (HIV) co-infection. The development of a non-invasive diagnostic tool that is capable of early and accurate detection, staging and follow-up evaluation of tuberculosis is crucial in minimizing its devastating effects. We evaluated PET/CT imaging with a novel tracer, 68Ga-citrate,in this setting.

Methods: Thirteen patients with tuberculosis were included in this prospective pilot study and were imaged with 68Ga-citrate. A diagnosis of TB was reached with bacteriological or histopathology studies (n=8) or based on a combination of clinical data, biochemistry and imaging (n=5). PET images were acquired at 60 minutes (and 120 minutes where possible) and analyzed qualitatively (relative to the liver) and semi-quantitatively (using SUVmax and change in SUVmax). PET findings were also compared to that of CT.

Results: All 13 patients demonstrated abnormal tracer accumulation in the lungs or extra-pulmonary or both. 68Ga-citrate accumulated in every lung lesion noted on CT in six cases (46%). In seven cases (54%) some of the lung lesions noted on CT were not 68Ga-citrate avid, which is suggestive of non-active tuberculosis lesions. Ten patients (77%) demonstrated extra-pulmonary involvement, which included various lymph node groups, skeletal lesions, pleural-, splenic- and gastro-intestinal tract involvement. More extra-pulmonary lesions were detected on PET compared to CT in eight cases (80%). The results of dual-time point imaging varied significantly amongst study participants.

Conclusion: Pulmonary and extra-pulmonary tuberculosis lesions demonstrate 68Ga-citrate accumulation; with more extra-pulmonary lesions detected on PET compared to CT. 68Ga-citrate PET may also provide a way of distinguishing active from inactive lesions for treatment response evaluation.

Key words: 68Gallium-citrate, PET/CT, tuberculosis
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^{131}I Labeled Zinc Oxide Nanoparticles: Synthesis, Labeling with ^{131}I and in Vitro Uptake Studies on U87-Mg Cells

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Abstract

Objective: A protein to aequorin (the chemiluminescent protein from Aequorea named jellyfish) green fluorescent protein (GFP) has become established as an important tool in drug discovery and biological research (1). It consists of 238 amino acids and its molecular mass is 27-30 kDa. GFP fluorescence occurs without cofactors and this property allows GFP fluorescence to be utilized in nonnative organisms. Genetically engineered cells with GFP expression have provided a valuable tool for automated analysis, and can be adapted for high-throughput systems (2). Inorganic NPs, including metal oxides, are promising materials for applications in medicine, such as cell imaging, biosensing, drug/gene delivery, and cancer therapy. Zinc oxide (ZnO) NPs belonging to a group of metal oxides are characterized by their photocatalytic and photo-oxidizing ability against chemical and biological species. In recent times, ZnO NPs have received much attention for their implications in cancer therapy (4). ZnO nanoparticles have even been shown to specifically target cancer cells and can possibly be developed as an alternative anticancer therapeutic agent. Although several studies have already characterized the toxicology of ZnO nanoparticles in vitro

with a variety of mammalian cell lines, most of these studies focused on the cytotoxicity of ZnO nanoparticles as a means of assessing biocompatibility (5). ZnO utilizes a multifunctional nanoplatform that bombards malignant cells from the outside. On the other hand, ZnO nanoparticles propose new opportunities including the improvement of the specific drug delivery and also manipulating cell membranes. No cytotoxic effects of ZnO nanoparticles were found in human glioma cells. ZnO nanoparticles are known to be one of the multifunctional inorganic nanoparticles with effective antibacterial activity (6).

Methods: In this study, ZnO/GFP was synthesized previously, used in cell imaging studies for targeting and labeling platform. In the synthesis procedure, initially ZnO/GFP was conjugated through crosslinker. The bonding of GFP to the ZnO nanoparticles yield was detected by High Performance Liquid Radio Chromatography. The complex was labeled with ^{131}I via iodogen method. The yield of radiolabeling of ZnO/GFP was determined by Thin Layer Radio Chromatography. ^{131}I labeled ZnO/GFP (^{131}I/ZnO/GFP) was added to the glioma cells in order to investigate its optical signals. Cytotoxicity studies were carried out on Human glioblastoma cells (U87-MG), 24 hour by MTT method.

Results: The sizes of ZnO were change by the incubation time. Radiolabeling yield of ^{131}I/ZnO/GFP was 98.42±0.90%. There are no toxicity till to concentration 1000 ng/ml limit. U87-MG were used to determinate the time dependent incorporation of ^{131}I, ^{131}I/ZnO and ^{131}I/ZnO/GFP. Due to investigation time dependent incorporation of ^{131}I 0.037 MBq (1.0 µCi/mL) labeled components, the cells were incubated for 1, 2, 4 and 24 hour at 37 °C. Two hour was found as the maximum uptake time.

Conclusion: All experimental results suggest that ^{131}I labeled GFP/ZnO compound can be used in the applications of Nuclear Medicine as a radiolabeled agent for imaging both optical and radioisotopical.

Key words: Green Fluorescent Proteins (GFP), zinc oxide nanoparticles, ^{131}I, glioma cells (U87-MG)
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The Effects of (^{99}mTc) Hm-Pao Labeling on Lymphocyte Functions

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Abstract

Objective: (^{99}mTc) HM-PAO labeled leucocytes have been used as a standard diagnostic procedure for the detection of infection and inflammation. Although, some investigators have already pointed out that labeling of leucocytes with (^{99}mTc) HM-PAO has detrimental effects on the cells, still very little is known regarding the effects of ionizing radiation on lymphocyte functions.

Methods: In this study, we evaluated the effects of (^{99}mTc) HM-PAO labeling on lymphocyte adhesion, proliferation, migration and apoptosis. We used NC-NC lymphoblastoid cell line as the lymphocyte population. (^{99}mTc) HM-PAO labeling decreased cell adhesion, proliferation and motility whereas induced apoptosis, and cell cycle arrest. Proliferation assays were performed both using MTT and ELISA tests with 24 hours intervals following labeling.

Results: It was recorded that the rate of decrease in proliferation was up to 70% by the 4th day after labeling. (^{99}mTc) HM-PAO labeling led a 35% decrease on adhesion ability of the cells on fibronectin. By using Boyden chamber motility assay, we showed that both spontaneous and MCP-1 induced lymphocyte motility were potently blocked by (^{99}mTc) HM-PAO labeling. The rate of decrease in motility was approximately five times. In addition, we observed a 12 times increase in the apoptosis rate within the (^{99}mTc) HM-PAO treated cells compared to the control cells. Besides it was observed that cell cycle arrest was induced starting from 3rd day after (^{99}mTc) HM-PAO treatment.

Conclusion: Based on our data (^{99}mTc) HM-PAO labeling has damaging effects on lymphocyte functions including cell adhesion, proliferation, motility and viability in in vitro.

Key words: ^{99}mTc HM-PAO, apoptosis, migration, adhesion
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