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DEVELOPMENT AND EVALUATION OF A MULTI-PINHOLE SPECT METHOD FOR A SMALL ANIMAL SPECT IMAGING SYSTEM

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The purpose of this study is to develop a 3-D multi-pinhole (MPH) single photon emission computed tomography (SPECT) method for a small animal SPECT imaging system and to evaluate the effects of MPH collimator design and imaging geometry on the reconstructed image quality. In a Monte Carlo study, MPH projection data were generated from a digitized Defrise phantom and a realistic digital mouse phantom using MPH collimators with different pinhole numbers, hole patterns and imaging geometries. A Gamma Medica-Ideas X-SPECT small animal imaging system fitted with MPH collimators of different pinhole numbers and patterns were used in an experimental study. Projection data were acquired from a physical Defrise phantom, an ultra-resolution SPECT phantom and mice injected with Tc-99m MDP. All MPH projection data were reconstructed using an iterative 3-D OS-EM based MPH image reconstruction method with accurate correction for system misalignments. The 3-D MPH images from the simulation study were compared to the phantom images and were evaluated in terms of normalized mean square error and normalized standard deviation over selected regions-of-interests (ROIâ™s). Those from the experimental studies were compared to the corresponding SPH images for image artifact generation and image noise reduction. Our results indicate that MPH SPECT provides increased detection efficiency and lower image noise as compared to SPH with concomitant increased image artifacts and distortions which are also dependent on the pinhole pattern. We conclude that MPH SPECT with significant increase in detection efficiency and minimal artifacts and distortions is feasible with careful considerations of the different contributing factors.

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INITIAL RESULTS OF A POSITRON EMISSION TOMOGRAPHY/ COMPUTED TOMOGRAPHY SMALL-ANIMAL IMAGING DEVICE WITH CO-PLANAR GEOMETRY

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In this work we report initial results from a prototype of a small-animal positron emission tomography (PET)/ computed tomography (CT) system based on a common rotating gantry. The PET system consists of two detector modules based on MLS arrays and four large-area, flat-panel type PS-PMTs. The CT scanner uses a micro-focus X-ray tube and a semiconductor X-ray detector in a cone-beam geometry. Space for opposed PET detectors and the CT scanner has been allocated on the same face of the gantry disk, thus achieving a co-planar geometry that perfectly aligns the trans-axial and axial centers for both image modality systems. Shields around the detectors reduce cross modality contamination due to scatter in the sample when it is illuminated by the X-ray source. The gantry rotates 360 degrees to provide complete data sets for the CT image reconstruction program that implements a fast version of the FDK algorithm. OSEM algorithms (2-D and 3-D) as well as FBP are available for PET image reconstruction. Sequential acquisition protocols minimize the scan duration, and CT information can be used to implement PET imaging corrections. The co-planar geometry of this system provides intrinsically co-registered datasets, and eliminates the need for animal repositioning to change modality imaging. Avoiding undesired movement of the animal or attached accessories reduces the time required to perform the experiment and minimizes movement errors. The compactness and ergonomics of the system save space and enable direct visual monitoring of the animal.

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PARALLEL HOLE COLLIMATOR DESIGN FOR A DUAL PROJECTION IMAGING SYSTEM

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Several research groups have developed tomographic imaging systems for small animal research that combine anatomical images with physiological data from nuclear imaging modalities. The radiation dose associated with these imaging systems is often high, and imaging times can be quite long, ranging from several minutes to several tens of minutes for detailed applications. Many investigators make use of 3-D data from these tomographic imaging systems to compute single projections (sagittal or coronal) or a maximum intensity projection image (MIP) to demonstrate the distribution of radioactivity within the animal. A dual nuclear/X-ray projection imaging system which combines nuclear imaging using a parallel hole collimator (PHC) with X-ray radiography, has been designed in our laboratory. A single planar detector (BaFBr plate) captures a gamma-ray image on one side of the plate and an X-ray image on the other side. These images are co-registered and fused after analog to digital conversion is completed. This dual imaging system allows for high throughput imaging, and the low radiation levels permit investigators to obtain functional information more frequently in serial studies. A PHC designed specifically for small animal imaging will be manufactured using micro-fabrication lithography techniques. The optimal design of low energy and high energy parallel hole collimators has been studied using Monte Carlo simulations. A detector array with 50 μm square pixels and a collimator with square apertures have been modeled. The tradeoff between spatial resolution and sensitivity was assessed for PHCs with aspect ratios (height/aperture size) from 10:1 to 50:1.

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***IN VIVO* OPTICAL IMAGING OF TUMORS EXPRESSING CARCINOEMBRYONIC ANTIGEN (CEA) USING ENGINEERED ANTIBODY-LUCIFERASE FUSION PROTEINS**

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Two novel tumor targeting fusion proteins have been developed which consist of an engineered antibody fused to either an optimized *Renilla* luciferase (RLuc8) or *Gaussia* luciferase (GLuc), allowing for *in vivo* optical detection of the endogenous tumor marker carcinoembryonic antigen (CEA). The genetically engineered anti-CEA T84.66 diabody (Db), a dimer of the single-chain Fv, has previously exhibited high level tumor targeting in biodistribution and microPET imaging studies using a CEA-positive tumor model. The purified Db-RLuc8 and Db-GLuc fusion proteins remain bifunctional: able to bind to the antigen, CEA, and simultaneously emit light in the presence of the substrate, coelenterazine, as shown by bioluminescence ELISA assays. *In vivo* optical imaging of tumor bearing mice demonstrated specific targeting of Db-RLuc8 and Db-GLuc to CEA-positive xenografts. The Db-RLuc8 reached a maximum tumor:background ratio of 6.0 ± 0.8 in CEA-positive tumors at 6 hours after intravenous injection, compared to CEA-negative tumors at 1.0 ± 0.1 ($p < 0.05$, n=7). The Db-GLuc similarly targets only the CEA-positive tumor, although it demonstrates different clearance properties due to the lower molecular weight. Targeting and distribution was also evaluated by microPET imaging using ^{124}I-labeled fusions and confirmed that the optical signal was due to antibody-mediated localization of luciferase. These two luciferases, fused to biospecific sequences such as engineered antibodies, can be administered systemically to provide a novel, sensitive method for optical imaging based on expression of cell surface targets in living organisms.