No. 153

SELECTIVE SPECTRAL IMAGING OF DUAL FLUORESCENT/BIOLUMINESCENT REPORTER GENES *IN VITRO* AND *IN VIVO*

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Preclinical tumor studies require repetitive non-invasive assessment of tumor development *in vivo*. Optical imaging represents a powerful tool for longitudinal visualization of tumors in living subjects. We engineered and evaluated several dual reporter gene constructs for *in vitro* and *in vivo* studies. GFP or RFP genes linked to click beetle green/red (CBG/CBR), firefly (FLuc) or Renilla (RLuc) luciferases fusion reporter genes were produced in U87 glioma cells and *in vitro* fluorescent and bioluminescent characteristics were assessed. GFP/CBG, GFP/CBR and GFP/FLuc had maximal fluorescent signal at 510 nm, RFP/RLuc - at 580 nm. *In vitro* bioluminescence was measured using IVIS (Xenogen) (table). Cells bearing reporter construct were implanted subcutaneously in mice. GFP/CBG tumors had peak signal at 515-650 nm, GFP/CBR cells - at 575-875 nm, GFP/FLuc - at 515-875 nm and could be distinguished from RFP/RLuc based on lusiferase product substrate. Interestingly, substantial shift of peak detection toward red spectrum was detected for FLuc and CBG luciferases *in vivo*. Providing high sensitivity and quantitation, dual reporter genes allow for imaging of different cell populations in the same animal using different spectral channels and substrates. The shift of light spectrum of some luciferases should be taken into consideration for studies *in vivo*.

Bioluminescence *in vitro* (photons/sec/cm2/sr x109)

emission, nm	**wt**	**GFP/Fluc**	**GFP/CBG**	**GFP/CBR**	**RFP/Fluc**
515-575	0.07	5.74	3.64	0.54	2.12
575-650	0.11	10.11	1.76	8.94	4.68
695-770	0.02	0.63	0.04	1.13	0.31
810-875	0.02	0.04	0.02	0.05	0.03

No. 154

RESOLUTION IMPROVEMENT OF SMALL ANIMAL POSITRON EMISSION TOMOGRAPHY IMAGES USING A STEP AND SHOOT ROTATING SCANNER

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High cost of positron emission tomography (PET) scanners led to designs with reduced number of detectors, at the expense of sensitivity loss. Complete angular sampling is achieved rotating the detectors. The current generalization of iterative statistical methods of reconstruction, together with the fact that iterative methods are more tolerant to incomplete angular sampling allows us to explore different rotation schemes (i.e. continuous vs. step and shoot) of the detectors to obtain the best image resolution within the minimum reconstruction time. PET data are often arranged in sinograms, subsequently employed for analytical reconstruction methods, or in LOR-histograms, where the number of counts in every line of response is considered. These latter arrangement of data is better suited for iterative reconstructions, because the physical characteristics of the scanner are related to the nature and placement of the detectors that define every LOR, rather than by their corresponding position inside the sinogram. In general, the best way to reconstruct using iterative methods is LOR histograming, which allows for optimal evaluation of the response matrix of the system. Using Monte Carlo methods, we obtained simulated PET rotating scanner data which were reconstructed by 3-D-OSEM, and compare the resolution achieved and reconstruction time when employing sinograms, LOR histograms and LIST mode acquisitions. Different rotation strategies, such step-and-shoot with different overlaps or continuous mode rotation were compared. Our results show that resolution can be improves by up to 30 % just by modifying the configuration of the rotation motion and the histogramming method.

No. 155

QUANTIFICATION SOFTWARE FOR QUANTITATIVE MOLECULAR IMAGING

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We have previously developed COmpartment Model Kinetic Analysis Tool (COMKAT), a toolkit for analyzing pharmacokinetic data. We have extended COMKAT in several ways to create a more powerful tool for analyzing dynamic positron emission tomography (PET) images. First, we created a compiled MEX file model solver and linked it against CVODES, a robust differential equation solver written in the C language. This has significantly enhanced the speed of parameter estimation and output simulation. Second, we implemented support for customized kinetic rules that include, for example, enzyme-substrate kinetics and user-defined kinetic rules. Third, we implemented a graphical user interface for loading data, selecting a model and performing simulation and data fitting. Combined with the COMKAT IMAGETOOL, a component we developed for image viewing and processing, users may draw 2-D or 3-D regions and generate time activity curves (TACs). Users may simultaneously fit several TACs using one of the many preprogrammed models or a model of their own design. Finally, we established an integrated environment to support COMKAT developers. It includes a web site with upload and download functions. It includes a bug-tracking system for reporting, confirming and resolution tracking. It also includes Concurrent Version System (CVS) repositories to facilitate version tracking and concurrent development by multiple developers. The integrated environment enables developers from other groups to participate in developing and testing COMKAT. In summary, the improvements make COMKAT a more user-friendly and powerful software for quantitative analysis of PET images. COMKAT is made available without cost to not-for-profit researchers through the website: http://comkat.uhrad.com.

No. 156

COMPARISON ON TWO-DIMENSIONAL AND THREE-DIMENSIONAL IMAGING CHARACTERISTICS AND QUALITY OF A WHOLE BODY PET-CT SCAN

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The aim of the study was to compare the clinical utility and imaging quality of a whole body positron emission tomography (PET)/ computed tomography (CT) scan in three-dimensional (3-D) and two-dimensional (2-D) modes. The study group consisted of 60 patients (56 +/-15 yrs) with a suspected diagnosis of primary or recurrent malignancy consecutively scheduled for PET. Three sequential PET-CT scans (Discovery ST) were performed 50 minutes after 260-530 MBq 2-deoxy-2-[F-18]fluoro-D-glucose (FDG) i.v. of each patient. Every subject was studied in three standard modes: 2-D (3 or 4 minutes/ bed depending on patient weight over or under 70 Kg), long 3-D (3 or 4 min/bed) and short 3-D acquisition (1.5 or 2 min/bed). In order to avoid the influence of chronology in sequential studies, patients were included consecutively in six groups, including all the order possibilities. PET were reconstructed using iterative algorithm and one single attenuation correction CT was applied for the three studies in each patient. Two blinded observers analyzed the images and quality assessment was based on 4 items quantification (1 to 5 with 5 best): Image free of artifacts (IFA), Qualitative signal to noise (QSN), Lesion detectability (LD) and Overall image quality OIQ). Overall t-Student test for appeared samples was applied in order to detect significant differences