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ADAPTIVE SMALL-ANIMAL SPECT/CT

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Abstract

We are exploring the concept of adaptive multimodality imaging, a form of non-linear optimization where the imaging configuration is automatically adjusted in response to the object. Preliminary studies suggest that substantial improvement in objective, task-based measures of image quality can result. We describe here our work to add motorized adjustment capabilities and a matching CT to our existing FastSPECT II system to form an adaptive small-animal SPECT/CT.

Keywords

SPECT; SPECT/CT; adaptive SPECT

1. INTRODUCTION

In recent work, we have investigated the concept of adapting biomedical-imager configuration to optimize task-based image quality for a particular imaging subject rather than a population of subjects [1-3]. This involves acquiring and analyzing preliminary scout data and making *automated* decisions for setting the adjustable parameters in the system, which for SPECT may include choice of apertures, selection of magnification and field of view as determined by radial camera and aperture locations, and determination of overall acquisition trajectory [1].

We have completed a prototype single-camera adaptive SPECT system and tested it with phantoms [3]. In addition, we have developed a theoretical framework for the computations required to adapt a system optimally to a particular subject and task, and we have analyzed the benefits of creating feedback rules that involve data from a complementary modality, such as X-ray computed tomography (CT) [2]. These preliminary studies have led us to the conclusion that adaptive SPECT/CT represents a significant advance in molecular imaging that will have a positive impact in both laboratory and clinical settings.

[*]M. Freed is now with the U.S. Food and Drug Administration.

2. METHODS

We are now reconfiguring one of our most utilized imagers, FastPECT II [4], as an adaptive SPECT/CT system. FastSPECT II is a high-resolution, stationary SPECT imager that is housed in its own 284 sq.-ft. laboratory that is fully equipped as a small-animal SPECT facility (Figure 1).

FastSPECT II has 16 cameras that acquire SPECT projections simultaneously with a true-list-mode architecture designed in-house. Front-end list-mode event processors examine incoming free-running digital data streams for valid events and package the event measurements, including pulse-peak amplitudes and time, in a byte packet that comprises one list-mode data entry. Custom PCI-bus back-end boards accumulate the data, appending each valid event packet as it arrives from a front end to the appropriate list. Fast maximum-likelihood estimation algorithms running on networked PCs convert raw signals into image data in an optimal manner. The system is very powerful, digesting 48 gigabits of raw information per second, and produces intrinsically dynamic images.

Several unique capabilities of the FastSPECT II instrument have attracted attention in the molecular-imaging community [5, 10]. Among these are the ability to insert application-specific apertures, a feature that permits SPECT imaging at extremes of magnification (thereby resolution), field-of-view, and sensitivity, and the ability to perform dynamic, fully tomographic acquisitions at very short time scales. Example images that illustrate these capabilities are shown in Figures 2 and 3.

Figure 2 shows a standard whole-body mouse ^{99m}Tc-MDP bone scan acquired with a relatively conventional configuration: 1-mm pinholes with a geometric magnification around 3x that yields millimeter-scale resolution. Figure 2 also shows an imaging study with an 18x-magnification aperture and 100-μm pinholes that yield tenth-millimeter-scale resolution [6]. In fact, the ROI image on the right in Figure 2 shows just the distal end of a mouse femur with invasive neuroblastoma tumor.

Figure 3 illustrates one of the unique advantages of the FastSPECT imager geometry, the ability to acquire SPECT imaging sequences that reveal the complete dynamics of molecular-imaging tracers in the imaging subject: injection into the vascular system, uptake in the target tissue and background, and washout via biological clearance. Such complete kinetics information will be required (along with much better knowledge of specific activity) in order for SPECT to deliver absolute numbers for physiological values, such as concentration of a particular receptor in a volume of interest, while still adhering to the tracer principle.

3. CONVERSION TO ADAPTIVE IMAGING

Before we recognized the implications of adaptive SPECT, it seemed plausible to adjust FastSPECT II's radial camera positions and install a desired aperture manually. Indeed, we can currently set up a new configuration in a somewhat labor-intensive procedure lasting about an hour. This has been adequate for our research to date, which has employed fixed geometries for a given study. The adaptive imaging approach, on the other hand, requires

rapid, convenient configuration shifts that must take no more than a few minutes to accomplish.

We are therefore motorizing the camera location control with custom-designed camera stages. We have established specifications for positioning reproducibility, including three optically sensed home positions and a default safe state in the absence of power, that can be met with a combination of off-the-shelf components and a modest number of custom fabricated pieces. The current design concept is shown in Figure 4. We are specifying the use of controller/motor combinations that we use routinely in calibration systems and thus have libraries of motor-control software to draw from. We will de-energize all motors during acquisition to avoid effects on the detectors from magnetic fields and have therefore incorporated an electromechanical mechanism that locks camera position when motions are complete.

An adjustable aperture design is somewhat more subtle. Experience with the prototype adaptive system has revealed that a continuum of aperture locations and selections is not necessary for effective adaptation. A finite number of settings that sample the resolution-sensitivity-field-of-view configuration space suffices, and also permits us to continue to use fully-measured system imaging matrices (PSFs).

We have developed a conceptual design based on a set of three coaxial tungsten-alloy aperture cylinders that provide three center-to-pinhole distances, nominally 1″, 1.5″, and 2″. At each magnification setting, one of two apertures, which will be in the form of precision-machined gold inserts, can be selected. Our initial design premise is that one aperture insert will have a single pinhole commensurate with the magnification setting and intrinsic camera resolution, and one will increase sensitivity by having five similarly-dimensioned pinholes that project partially overlapping views [7-9].

The conceptual design shown above in Figure 4 illustrates a geometry under consideration. Three concentric cylinders designed to slide along the imager axis move to positions that allow one of six possible aperture configurations to illuminate the gamma cameras. The cameras can in turn be moved to at least three nominal radial positions to create a matrix of 18 different choices that provide nine different magnifications in the range of 3x to 18x, each with two choices of sensitivity (1S and 5S, where S is pinhole efficiency as determined by pinhole and cylinder diameters). Since FastSPECT II is a 16-camera, stationary SPECT system, the selection is really between 16 and 80 pinholes for system sensitivity.

4. COMPLEMENTARY ADAPTIVE CT

The combination of SPECT with an anatomical imaging modality has become standard in pre-clinical imagers [10]. Our first effort in this area was a very compact fixed-geometry CT/SPECT imager based on pixellated CdZnTe (CZT) [11]. We are now completing a helical-scan cone-beam X-ray CT with adaptive features that will physically mate to the FastSPECT II system.

Data from the CT will not only yield complementary anatomical information that provides context for SPECT images, but will also be used for multi-modality adaptive feedback rules

as discussed below and in more detail in a topical issue of the *Proceedings of the IEEE* [2]. This CT system uses an X-ray source with a 6-μm focal spot, programmable tube voltage (≤ 130 kVp), and programmable tube current (≤ .5 mA), and a 2048×1000-pixel CMOS detector with 48-μm pitch. The source and detector are mounted on a motorized beam that allows selection of cone-beam magnification as can be seen in Figure 5. A beam-forming aperture with four individual blades allows further control over exposure patterns.

We have used the FaCT system to acquire test data to evaluate the source and detector. Projection images of a mouse were taken at low, medium, and high magnification to show the range of adjustment available. Results are shown in Figure 6. One obvious aim for adaptive CT is to develop strategies for maximizing task-based image-quality metrics while minimizing radiation dose.

5. ADAPTIVE MULTIMODALITY IMAGING

In most current forms of multi-modality imaging, images are acquired and reconstructed completely independently and are combined only for presentation to the observer. If a large number of subjects are studied this way and there is some way of verifying the true diagnosis or parameter value, a receiver operating characteristic (ROC) curve or parameter mean-square error (MSE) can be computed, and a figure of merit (FOM) can be derived. In this case, the FOM characterizes both imaging chains and how well the observer uses the images jointly.

In adaptive multimodality imaging, the two imaging chains are not independent; information derived from either the raw projection data or a reconstructed image acquired with a first modality is used to alter the data-acquisition hardware or protocol for the second modality. The observer can utilize the resulting reconstructed image from the second modality alone, or can use both reconstructed images together to extract information. As before, if many subjects are studied and there is a way of determining truth, a FOM for either classification or estimation tasks can be computed, but now the FOM characterizes the observer, both modalities, and the adaptation rule by which the acquisition hardware or protocol for the second modality is altered in response to data from the first modality.

We have derived expressions for the ideal linear observers for estimation and classification tasks in adaptive systems, and have suggested a wide variety of possible adaptation rules [1,2]. In essence, the image from the first modality is used to narrow down the ensemble of subjects from which the particular subject could have been drawn, and the second modality is then optimized for this new ensemble, which we refer to as the *posterior ensemble* because it is constructed after acquiring the data from the first modality. Performance figures of merit, however, are computed with respect to the larger *prior ensemble*, representing what we know about all possible subjects that might be presented for particular imaging tasks.

6. CONCLUSIONS

When the reconfigured adaptive FastSPECT II system is interfaced to the adaptive FaCT system, we will be able to implement any combination of adaptive SPECT, adaptive CT, and

multimodality adaptive SPECT/CT imaging. We will be able to compute figures of merit for both estimation and detection tasks for each of these situations. The first experiments will be to test candidate adaptation rules and multi-modality configurations with physical phantoms that incorporate stochastic structure in the background as well as in the signal to be detected. We will be able to take advantage of the large volume of small-animal SPECT and CT studies performed routinely in our laboratories to assess the benefits in real biological problems.

ACKNOWLEDGMENTS

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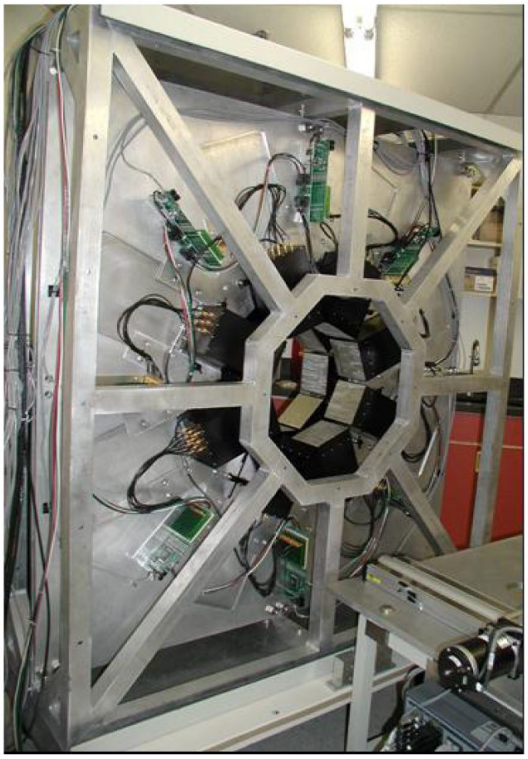

Fig. 1.
The FastSPECT II imager shown with shielding removed. The 16 stationary cameras are located in their low-magnification positions.

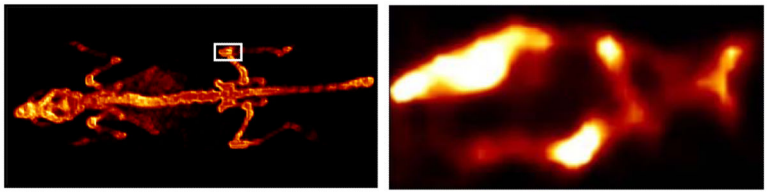

Fig. 2.

Sample ^{99m}Tc-MDP bone scan images from FastSPECT II in 3x (left) and 18x (right) magnification configurations. The field of view in the higher magnification image, as indicated on the 3x image, comprises just the distal end of the femur and the proximal tip of the tibia at far right.

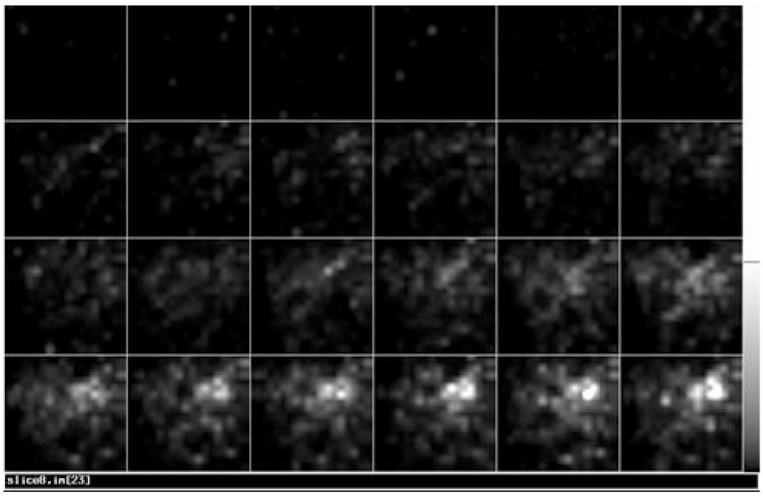

Fig. 3.

Dynamic FastSPECT II imaging of ^{99m}Tc-glucarate uptake in a mouse mammary-fat-pad tumor. The same tomographic slice is shown at 5-second intervals. Individual sub-millimeter tumor foci can be tracked.

Fig. 4.
SolidWorks™ rendering of adaptive configuration of FastSPECT II with independent camera stages and adjustable aperture assembly.

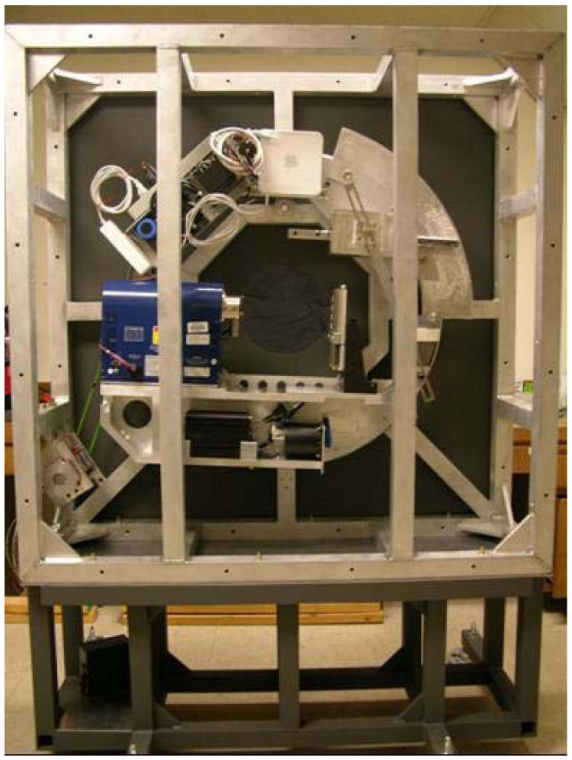

Fig. 5.
The FaCT helical-scan, cone-beam CT imager that mounts to FastSPECT II, shown with shielding removed.

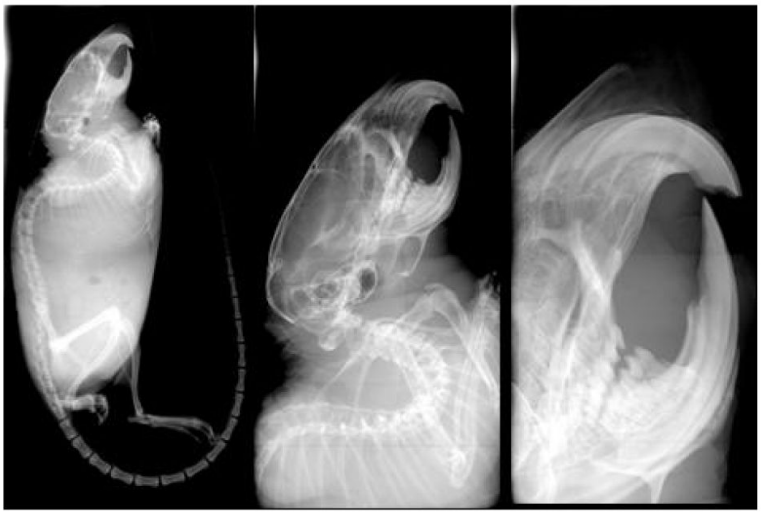

Fig. 6.
Planar mouse images from the FaCT CT system at: 1x, 2.5x , and 6x magnification settings.