INVERTED COMPOUND EYE CAMERA FOR SECOND GENERATION MRI COMPATIBLE SPECT SYSTEM

BY

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THESIS

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ABSTRACT

In this work, we will evaluate a novel design of the second-generation MRI compatible SPECT system, MRC-SPECT-II, based on an inverted compound eye (ICE) gamma camera concept inspired by compound eyes often found in small invertebrates. The MRC-SPECT II system is constructed with a total of 24 ICE-camera panels that consists of a very large number (up to 1500) of independent micro-pinhole-gamma-camera-elements (MCEs) looking at the object. Each MCE only covers a narrow view angular through the object space. This system design offers several unique advantages for the MR-compatible SPECT imaging application. First, this design allows for a greatly improved system sensitivity over the more conventional pinhole SPECT system designs. Our Monte Carlo study showed that the MRC-SPECT-II system could deliver a peak geometry efficiency of around 1.5% (as compared to the typical levels of 0.1%-0.01% found in modern pre-clinical SPECT instrumentations), while maintaining an excellent spatial resolution of around 0.5 mm and a single-position field-of-view (FOV) of 1 cm. Second, the ICE camera design also allows for an ultra-compact detection system that helps to fit the MRC-SPECT-II system inside most of high-field pre-clinical MR system. Furthermore, given the very large number of micro-camera-elements pointing towards the object, the MRC-SPECT-II system design offers a super-rich angular sampling of the object. Finally, an ICE-camera-based SPECT system typically uses a highly de-magnifying geometry that requires a reduced detector volume, compared to typical pinhole SPECT system that relies on magnifying geometry to achieve a high spatial resolution. This offers the practical benefit of potentially lower construction cost. In this study, we used Monte Carlo studies to demonstrate the performance benefit of the MRC-SPECT-II system over the existing MRC-SPECT system that we have
developed in our lab. We have also expanded the Monte Carlo study to evaluate the use of the ICE-SPECT concept for imaging larger objects, human brain.

Keywords: CdTe semiconductor detector; SPECT/MRI; Compound Eye.
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1. Introduction

1.1 Application of Simultaneous SPECT/MRI and PET/MRI

Due to the complimentary natures of Single Photon Emission Tomography (SPECT) or Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI), simultaneous SPECT/MRI or PET/MRI shows great potential for both pre-clinical and clinical research and application. MRI has high spatial and temporal resolution capability but limited sensitivity, while SPECT and PET are highly sensitive molecular imaging tools with many specific targeted biochemical probes, which could assess the functional and molecular process of the studied objects. Without inducing extra dose like Computer Tomography (CT), high resolution MRI imaging could be used for partial volume correction(Fig.1.1), motion correction(Fig.1.2), as well

![Fig.1.1: Influence of MRI-based PVE correction on PET image contrast for normal brain. From left to right are shown MRI image used to automatically segment ROIs of multiple brain structures, original PET image, PVE correction factors for mean ROI values calculated via geometric transfer matrix method using segmented MRI and original PET images as inputs, and original PET image after application of recovery coefficients. Data were acquired on Brain- PET prototype at Martinos Center, Massachusetts General Hospital.(Courtesy of Spencer Bowen[1].) ](image-url)
Fig. 1.2: MRI-assisted PET motion correction in healthy volunteer using echo planar imaging–derived motion estimates. (Top) Plots of motion estimates: translations along (black) and rotations about (gray) 3 orthogonal axes. (Bottom) PET data reconstructed before (left) and after (right) motion correction. Substantial improvement in image quality can be observed after correction. Data were acquired on BrainPET prototype at Martinos Center, Massachusetts General Hospital [1].
as attenuate correction for PET and SPECT. Also, the simultaneous SPECT/MRI or PET /MRI could provide both spatial and temporal correlation of the signals of imaging object, creating a great number of research and application opportunities, such as cross-calibration and validation for cerebral perfusion, neuronal activation as well as brain baseline state, and brain tumor detection[1].

1.2 Technical Challenges for Simultaneous SPECT/MRI

While the PET/MRI has a great progress in technical and application aspects, combining SPECT and MRI lags behind, partially because of the tough technical challenge of integrating them – strong interferences between each other. Strong magnetic field inside MRI scanner will make the readout of conventional PhotoMultiplier Tube (PMT) detector impossible, while the ferromagnetic components of detector will distort the MRI B₀ field, which requires a uniformity of less than several ppm. Rapidly switching gradient magnetic field will induce eddy current to the aperture of SPECT and electronic circuit of detector, affecting the performance of detector, meanwhile the corresponding eddy current will distort the gradient field of MRI and B₁ field. The high power radiofrequency pulse influence the performance of detector electronics, at the same time, the functioning electronics of SPECT system may induce extra noise to MRI imaging. Also the limited space inside MRI elects one of convectional SPECT system design scheme, using large magnification to compensate poor resolution of detector. It requires high-resolution MRI compatible detector and highly compact system design and fabrication. In addition, the widely used rotation SPECT design scheme cannot implemented within high magnetics field without inducing artifacts of MRI imaging [2].

1.3 Research Efforts to Obtain Simultaneous SPECT/MRI
To solve those technical challenges, many groups have spent intensive research effort and proposed different solution.

1.3.1 System of Gamma Ideal Inc.

Fig. 1.3: a) detector for John Hopkins’ SPECT-MR system; b) detector ring design; c) install detector ring; d) SPECT system with MRI; d) resolution phantom(Figure are modified from [3])

John Hopkins, University of California, Ivine and Gamma Ideal worked together to achieve first simultaneous SPECT/MRI system. The team developed MRI compatible detector using CZT with pixel size of 1.5mm (as shown in Fig.1.3). They reported the design considerations of an MRI compatible SPECT system based on CZT detectors [3]. A prototype of MRI compatible SPECT system development by the same group has been reported in [3]. The first simultaneous SPECT/MRI was achieved by the same team. Poor resolution of detector(1.5mm) limited
performance of the system, which only achieved resolution between 1.7mm to 1.3mm [3]. It is far from sub millimeter resolution, which is critical preclinical application.

1.3.2 EU INSERT project

A big team in EU, including UCL, several groups in Italy, Germany, and company of Mediso, proposed INSERT project to develop integrated SPECT/MRI for enhanced stratification in radio-chemo therapy[4-6] in March 2013. The detector of the proposed systems, both for preclinical and clinical systems, is based on CsI scintillator coupled to Silicon PhotoMultipliers. Their simulation results claim that using 0.6mm resolution detector, for preclinical system has sub-millimeter resolution with sensitivity of 1.9x10^{-3}. And for clinical brain system, it could have sensitivity of 6.7x10^{-4} with resolution of 10mm. Those performance results are based on simulation. To build a true system, they still have a long way to go.

1.3.3 Research Effort in UI group

In the last five year, our group has also spent a lot of effort to develop simultaneous SPECT/MRI imaging. We developed first generation MRI compatible energy-resolved photon-counting (ERPC) CdTe detector. It offered spatial resolution of 0.35mm and energy resolution of 3-4kev[7]. A prototype MRI compatible system was built using this kind of detector and sub-500μm resolution imaging capability inside 3T clinical MRI has been demonstrated [8]. Based on previous efforts, we then constructed an ultrahigh resolution stationary MR compatible SPECT (MRC-SPEC-I, as shown in Fig.1.4) system for small animal imaging using second-generation ERPC detectors [9]. The system consisted of ten ERPC-II detectors and assembled in 3D printed compact gantry. The system provided 0.35mm resolution using the aperture, which consisted of 40 pinholes with diameter of 0.3mm [10]. And we have obtained 500μm spatial
resolution SPECT imaging with limited effect on MRI imaging inside a fully functioning Siemens Trio-I.

Fig. 1.4: MRC-SPECT-I: A is system design (40 pinhole inserted aperture was segmented into five pieces and electronically isolated with each other to reduce eddy current); B MRC-SPECT-I inserted in Siemens Trio-I 3T scanner; C) Dedicated hybrid transmit/receive birdcage coil shielded by 65μm copper foil.

3T scanner and system capability to track up 400 neural stem cells in mice brain, as shown in Fig.15.

Although MRC-SPECT-I is a state of art MRI compatible SPECT system, there are several aspects to be further improved. First, the system has an outer diameter of 25cm, which is still too large to be placed inside many pre-clinical MRI scanners (Bruker 9.4T MRI with Bore size 20cm). To take MRI/SPECT imaging, it has to sit on the side of pre-clinical MRI scanner. Second, the system geometry sensitivity, i.e., the probability of photon not blocked by aperture, is around 0.04% with 40 sampling angles, which would be limited for some functional imaging applications. So dramatically improved system sensitivity would be desired for future generation of the MRC-SPECT system.
Imaging studies without MRI

A: Resolution Phantom outside MRI; 1.5mCi Tc-99m; 1h Acquisition  
B: 400 Neural Stem Cells tagged with mesoporous silica nanoparticles (MSN)-$^{111}$In could be could be resolve in a 2-hour imaging

Simultaneous SPECT/MRI Imaging

A: SPECT imaging without magnetic induced distortion correction  
B: SPECT imaging with magnetic induced distortion correction;  
C: Corresponding MRI imaging  
D: MRI mice imaging with fully active SPECT

Fig. 1.5 MRC-SPECT-I imaging study results

1.4 Thesis Outline

To overcome these drawbacks, we have proposed a MR-SPECT-II system design that utilized an Inverted Compound Eye (ICE) design. In this thesis, the details about the system will be presented.

In Chapter Two, we will review the compound eye system and the advantage of this kind of eye system. And then we present the system design of MRC-SPECT-II based on Inverted Compound Eye (ICE). We also will talk about the detector we use for the system and DOI capability of the detector.
In Chapter Three, we will review basic principle of imaging system simulation and imaging reconstruction and discuss how to apply these tools to simulation of MRC-SPECT-I.

In Chapter Four, we discuss the simulation results of MRC-SPECT-II system, compare performance of MRC-SPECT-I and MRC-SPECT-II and evaluate DOI effects on imaging performance.

Conclusions and proposed future work are given in Chapter Five.
2. System Design of MRC-SPECT-II Based on Inverted Compound Eye

2.1 Compound-Eye

Compound eye is a common vision system founded in small invertebrates, like house fly (Fig. 2.1). It consists of thousands visual receptor units, called ommatidia [11]. Each ommatidium consists of a lens and a transparent crystalline cone, a light-sensitive visual receptor, as shown in Fig 2.2. Those units are located on convex surface and point in slightly different directions and accepted limited light from specific directions. There are two kinds of compound eye: apposition eye (Fig. 2.2-A) and superposition eye (shown in Fig. 2.2-B) [12]. The apposition eye has pigmented cells which separate an ommatidium from its neighbors and prevent the spread of light to its adjacent ommatidia. Each ommadidium forms an independent visual processing unit. The vision neuron system combines the multiple images from those ommatidia to perceive visual information. For superposition compound eye, the ommatidium does not have pigmented cells and the light from neighboring units could overlap and share the same light-sensitive visual receptor. The vision neuron system of a superposition eye gains a single erect, brighter but blurring image.

Fig. 2.1: compound eyes of fly, image courtesy of JJ Harison from wiki
Compared to a single eye system, the compound eye presents unique attributes: wide field-of-view, compact and sensitive to motion. Artificial implementation of compound eye has attracted a lot of research interest, because its unique attributes exhibits a huge potential application for medical, industrial, and military application[13]. Previous research effort focused on developing an optical imaging system. We will present a design for a nuclear imaging system inspired by compound eye in this chapter.

2.2 Inverted-Compound-Eye Gamma Camera

The proposed Inverted Compound Eye (ICE) gamma camera detector module is shown in Fig. 2.3. It consisted of an ultrahigh resolution gamma ray detector coupled to a special aperture that essentially defined an 8×8 array of closely packed micro-pinhole-camera-elements (MPCEs). The pinhole of each MPCE could confine the projection of the object into sub-area on the detector. The sub-area of detector units belonged to each MPCE had area of 3.2 mm in width. To ensure each MPCE to have a sufficient resolving power, the gamma ray detector used behind the collimator needed to have an ultrahigh intrinsic resolution, ideally below 100 μm. i.e., each element had 32×32 high resolution detecting pixels.

With the basic ICE camera concept, the shape of each pinhole could be designed to allow certain degree of projection overlapping, like the superposition compound eye, which could help to further improve the angular coverage of each MPCE, but at the same time reduced the information content per detected photon. As the ICE camera design offered an enormous amount of freedom in fine-tuning the aperture design, we would like to leave the aperture optimization problem to our future studies. Here we would focus on the non-overlapping aperture design, like
apposition compound eye and demonstrate the performance benefit of the ICE camera for SPECT applications.

![Fig. 2.2: Natural Compound Eye and Inverted Compound Eye (ICE) for SPECT imaging. (A) superpositional compound eye; (B) appositional compound eye; (C) one type of inverted compound eye, mimicking the nature superpositional compound eye](image)

![Fig. 2.3: (A) configuration of ICE module for SPECT imaging(a)Micro pinhole opening with limited angular coverage; b) ICE aperture made of platinum-iridium alloy; c) CdTe pixel detector, 2.56 cm x 2.56 cm, 100 μm x100 μm pixel; d) CMOS Readout ASIC and (e) Digital PCB.] (B) configuration for the ICE unit.](image)
2.3 MRC-SPECT-II System

The schematic of MRC-SPECT-II system is shown in Fig. 2.4. It had 8 ICE camera modules in transverse direction and 3 module rings along axial direction, i.e., and 24 modules for whole system. Each ICE module consisted of $2.56 \times 2.56 \, \text{cm}^2$ detector space and 64 micro-camera-elements (MPCEs) and total 1536 elements in the whole system. Since each MPCE only covered a small opening angle (Fig.2.3) and part of the FOV, how to design the distribution of MPCEs and their orientation was an essential issue to have the desired system FOV and to optimize the angular sampling. In the current design for the MRC-SPECT-II system, MPCEs are uniformly distributed along the sagittal direction and focused to the designated FOV area with diameter 1cm. In the transverse direction as shown in Fig.2.4, MPCEs did NOT focus on central of FOV. Instead, the orientation of MPCE will be designed so that the boundary of MPCE FOV will be tangent to the boundary of system FOV and each MPCE in the same ring will oriented to the same side of system FOV, say left of FOV in Fig.2.4, while the MPCE in the adjacent ring will be oriental opposite (for example, if MPCEs in first ring point to left side FOV, then the MPCE in the second ring will point to right side of the FOV). To further improve the angular sampling, every two rings are rotated $3^0$ related to previous ones.

2.4 MRC-SPECT-II System Detector and Depth of Interaction (DOI) Information

The resolution power of MPCEs and system performance relies heavily on the performance of the detector. In this design, we proposed to use 100µm CdTe detector with a hybrid pixel waveform readout system[14] consisting of a 2-D multi-pixel ASIC attached to the anode pixels to provide the X-Y positions of interactions (resolution down to 100µm), and a high-speed digitizer to
Fig.2.4 A is transverse view of IEC-SPECT(MRC-SPECT-II) system for mice imaging(four sample points are used to compared angular sampling and geometry sensitivity between MRC-SPECT-I and MRC-SPECT-II, position 1,2,3, and 4 are 0mm, 2.5mm, 5mm and 7.5mm away from center of FOV respectively.); brain model permission from[14,15] B is 3D Drawing of MRC-SPECT-II system
Fig. 2.5. Hybrid Waveform readout detector: A is design scheme; B is waveform sampled from cathode side (Courtesy of Dr. Liang Cai)[15]

sample the waveform induced on the cathode by the electron and hole movement inside CdTe crystal (Fig. 2.5). The waveform from cathode side not only could provide us energy information and also DOI information. Our previous published data[14] showed that using this scheme could achieve DOI resolution of 0.3mm in 2mm thickness CdTe detector. And our recent unpublished data demonstrated that we could achieve even better DOI resolution, down to 0.2mm. Here and after, 0.2mm resolution for DOI will be used.

The hybrid waveform readout detector benefits performance from the following aspects: a) the size of pixels (100μm) is comparable or smaller than the physical dimensions of the interaction-induced charge. The charge collection efficiency is very poor, because of charge lost in the pixel gap and also the charge cloud is shared by the neighboring pixels. Using Hybrid waveforms could gain much better energy performance and help system eliminate scattering events, and consequently improve system performance. b) as shown in Fig. 2.6, with DOI information, the FWHM of PSF through each pinhole is sharper than ones from none DOI
detector. With the existence of strong magnetic field and without DOI information, the FWHM of PSF becomes further broader, due to the fact that the charge drift in different depths is different. C) Although our design ensures detector units from each MPRE is not overlapped, this constrain is placed in the last layer of detector (far from the object) and without DOI information, there are still cross talk between neighboring detector units of MPCES, because the incident angle of the gamma ray in most cases is not zero and there is a finite thickness of detector, as shown in Fig.2.6.

**Fig. 2.6: Illustration of DOI effects**
2.5 Inverted Compound Eye for Human Brain System

To explore the benefits of the ICE for human SPECT imaging, we designed a human brain SPECT system for MRI/SPECT imaging, as shown in Fig.2.7. The micro-camera-elements (MPCEs) sensing area increased from $32 \times 32$ pixels to $64 \times 64$ pixels and the sensing thickness of the detector increased to 5mm. The number of MPCEs in each module was reduced to $4 \times 4$. The transverse had 40 modules, with size of 35cm and the sagittal direction had 12 modules, with length of 30.7cm. The system totally had 480 modules and 7680 MPCEs. The FOV of system was $150 \, \text{cm} \times 100 \, \text{cm}$ (Sag.). And the diameter of the pinhole was 0.5mm.
Fig. 2.7: Inverted Compound Eye For Human Brain SPECT Imaging: (A) transverse view of the system (brain model with permission from [16,17]); (B) configuration of one detection module.
3. Implementation of Monte Carlo Simulation for MRC-SPECT-II

To evaluate performance of MRC-SPECT-II using inverted compound eye, we will carry out Monte Carlo simulation using home developed code. As one of most widely used approaches for medical imaging system performance tests, Monte Carlo simulation, allows us detailed modeling and comprehensive evaluation for the system design.

In this chapter, we are going to talk about the basic procedure of Monte Carlo simulation for imaging system evaluation and apply this tool to MRC-SPECT-II.

Fig 3.1: An illustration of imaging study procedure

3.1 Procedure of Imaging Performance Study

Imaging study procedure should be dedicated modeled to represent the imaging process and physics behind this process. Without noise, the nuclear imaging system could be viewed as a linear system and it maps 3D object space to 2D detector space, described as:

$$\bar{y} = A \cdot x + r \quad (3.1)$$
where $\overline{y}$ is the noiseless projection in the detector space, $A$ is the system response function, $x$ is the pixelated object source, $r$ is the additional background events. An accurate imaging study involves carefully defining each term of this mapping process, statistical features of projection, i.e the distribution of the measured data with mean $\overline{y}$, how to use the measured data to estimate the parameters in the object space and ect. We will detail those processes for MRC-SPECT-II one by one in the following of this chapter.

### 3.2 Object Space Pixilation

The parameters, i.e, the number of the radioisotope decay events during the imaging time, in the object space are continuous function in 3D dimension. To access those parameters in real calculations, the gridding the object space is implemented. The object space is pixelated to $N$ cubic voxels, i.e., $x=[x_1, x_2, ..., x_N]^T$ with certain step size. The value of each element in this $N$ dimension vector represents total counts of the corresponding cubic voxel in object space during the imaging time. The step size of pixelization should be carefully considered. If we assume the parameters in the object is smooth enough (limited bandwidth in the frequency domain), according Nyquist’s rule, we could recover continuous function using step size less than half of one over $F$, where $F$ is the bandwidth limit. However, for an unknown object, whether the function has the bandwidth limit and what is the value of the bandwidth is hard to know. However, the nuclear imaging system works as a low passed filter and it truncates the function with a limited bandwidth in the frequency domain. Instead of accessing the true continuous space, we will access what is been seen by the imaging system, which has a limited bandwidth. We could pixelate the object with a step size less than half of the resolution of imaging system, which satisfies the Nyquist’s rule.
Fig. 3.2: illustration of imaging for SPECT (courtesy of Dr. Nan Li)

Fig. 3.3: imaging source used in Monte Carlo Simulation: from left to right are mice brain phantom, resolution phantom, human brain phantom and resolution phantom.

In our case, we used 4 objects as imaging sources, as shown in the Fig.3.3, the resolution phantom and the mice brain phantom for the mice system[15], the resolution phantom and the human brain phantom[16] for the human brain system. The step size of the mice system was 0.2mm (the target resolution of the system is 0.5 mm). The numbers of voxels in the object space is 100x100 x 100, i.e 1 million. For the human brain system, the voxel size is 0.8mm. The number of voxels in the object space is 16 x 180 x 180, i.e, ~0.6 million.

3.3 System Modeling
It is critical to model imaging system, i.e., to get accurate knowledge of response function matrix of A. The matrix is $M \times N$ dimension, where $M$ is the number of detector pixels. For the mice system of MRC-SPECT-II, $M$ is around 1.57 million and for the human system, the value is about 30 million and $N$ is the number of the voxels in the object space. Each element, $A_{i,j}$ of the system response matrix $A$, could be viewed as the probability that the $j^{th}$ cubic voxel in the object space emitted one photon is detected by the detector $i^{th}$ pixel. The matrix of $A$ for SPECT imaging is determined by the properties of object, including scatter and attenuation of the photon by the object (in small animal study, we could ignore those effects because of the small volume and the probability of scatter and attenuation is relatively small, compared to the detection probability), the collimator and the detector, including charges collection in the detector space, the signal formulation and processing, the geometry relationship of the object, the pinholes and the detector system. Without considering the object scattering and attenuation effect and with the assumption that the detector electronics could process every photon stopped in detector crystal, the condition that could be met in SPECT imaging, then we could analytical calculated each element of response matrix:

$$A_{i,j} = \iiint_{\text{detector volume of pixel } i} \frac{e^{-l_{1(i,r)}} \cdot e^{-l_{2(i,r)}}}{4 \cdot \pi} \cdot \mu_d \cdot dl_3 \cdot d\Omega. \quad (3.2)$$

where, $l_{1(i,r)}$ is the attenuation length of the aperture before photon interact with detector, $r_i$ is the position in the detector pixel $i$ where photon is absorbed, $r_j$ is the cubic voxel position in the object space where the photon emits. $\mu_p$ is the aperture attenuation coefficient. $l_{2(i,r)}$ is the length of photon passing the detector space before it is detected. $\mu_d$ is the detector attenuation coefficient. $dl_3$ is the length of detector crystal where photon being detected and $d\Omega$ is the corresponding solid angle.
Each column of the response matrix is defined as a point response function (PSF). Fig. 2.4 is the one eighth PSF of the object center voxel, corresponding to the elements of matrix for one detector of total 8 detectors for MRC-SPECT-II. It is reshaped and reordered to 2D detector space.

3.4 Measure Process

The imaging source is measured by the imaging system. The measure data, denoted by the vector $y = [y_1, y_2, \ldots, y_M]^T$, represents the number of detected photons by the imaging system. The expectation or the mean of measurement follows a linear relationship of (3.1):

$$\bar{y} = \mathbf{A} \cdot \mathbf{x} + \mathbf{r},$$

where the notations are the same as (3.1).

The statistical distribution of the measured data could be modeled by condition probability, $p(y|x)$, i.e, given the object source $\mathbf{x}$, the probability of detecting $y$ in the detector space. Each element of $y$ is views as number of success detection during certain number trials. When the count rate of the object is low enough that the event overlapping during imaging time could be ignored. This condition could be satified for SPECT imaging. Those process could be viewed as independent trials, with a constant success probability. The distribution could be described as binomial distribution. Further, since the detection probability is very small for each trial and the number of trials is very large. The distribution could be described as Poisson distribution:
\[ p_y(y|x) = \prod_{m} e^{-\tau_m} \frac{\bar{y}_m}{y_m!}, \quad m = 1\ldots M \quad (3.3) \]

where \( \bar{y}_m = \sum_{n} A_{m,n} x_n + r_m, \quad n = 1\ldots N \quad (3.4) \)

For Monte Carlo simulation, we could gain the mean projection by applying the Eq. (3.4) and get the “measured” data \( y \) using a random generator with Poisson distribution. Fig. 3.5 shows the mean projection (A) and the “measured” projection (B) of the resolution phantom for MRC-SPEC-II.

![Fig. 3.5: Projection profile of resolution phantom in Fig. 3.2: A is noisless data; B is projection with Poisson noise](image)

### 3.5 Reconstruction Process

With the measured data \( y \), we could solve equations of (3.3) and (3.4) with considering the noise effect. But a straightforward solution of the equations of (3.3) and (3.4) is very challenging or even impossible to implement since that the response matrix \( A \) is often singular and the size of matrix of \( A \) is very large.
The maximum-likelihood reconstruction method is commonly used for nuclear imaging reconstruction. We could reconstruct imaging, or estimate imaging, \( \hat{x}_{\text{ML}} \) by finding the solution, which maximizes the likelihood function in (3.3)[17], equivalently maximizing log of likelihood function:

\[
\hat{x}_{\text{ML}}(y) = \underset{x \geq 0}{\arg\max} \left[ L(x,y) \right] = \underset{x \geq 0}{\arg\max} \left[ \log p_r(y|x) \right] = \underset{x \geq 0}{\arg\max} \left[ \sum_m y_m \log \frac{y_m}{\bar{y}_m} \right] \tag{3.5}
\]

ML estimator is efficient, i.e., it could achieve the lowest variance in all unbiased estimators.
4. Monte Carlo Simulation Results

In the previous chapter, we talked about the procedure of doing Monte Carlo simulation for medical imaging system. In this chapter, we will apply this tool to evaluate the performance of MRC-SPECT-II system. Since the main propose of this study was to demonstrate that use of the ICE camera design could lead to a dramatically improved imaging performance, we specifically compared the MRC-SPECT-II system against MRC-SPECT-I, which is a state of art MRI compatible SPECT system developed in our lab.

4.1 MRC-SPECT-I System

MRC-SPECT-I system (Fig.4.1) consisted of ten second generation of energy resolve photon counting detectors, which had 4 ASIC modules, assembled as a compact ring. The distance between the opposite detectors was 15.6 cm and the detection area of each detector was $22.5 \times 45 \text{ mm}^2$. Each detector had four 300 to 500 µm pinholes and the object to pinhole distance was designed to be around 36 mm. Note that the modeling of MRC-SPECT-I system was fully validated with our experimental assessment of the actual MRC-SPECT-I system[10].

A small pixel CdTe detector module that we have recently developed was used to construct MRC-SPECT-I system. Each module consisted of CdTe crystal shaving with an overall size of $22.5 \times 11.2 \times 2 \text{ mm}^3$, divided into $64 \times 32$ pixels, the size of which is $0.35 \text{mm} \times 0.35 \text{mm}$. We previously reported the performance of the first generation ERPC ASICs[10]. The ASICs in the Gen-II ERPC detectors allowed for a much lower energy threshold and incorporated four gain levels for handling different gamma ray energies. The excellent energy resolution, high spatial
resolution as well as MR compatibility of the detector make a solid basis for MRC-SPECT-I providing promising imaging performance.

Two sets of Dual-FOV:
• Set1: FOV 42/22mm, pinhole size: 1/0.5mm
• Set2: FOV 36/12mm, pinhole size: 0.75/0.3mm
• Tungsten powder composite, segmented, electronically isolated to reduce Eddy current.
• Improved collimation for high-energy gamma rays (such as I-111)

Fig.4.1: System design of MRC-SPECT-I system

4.2 System Sensitivity and Angular Comparison

To evaluate the system performance, we evaluate system geometry sensitivity by calculating percentage of solid angle viewed by detector and it is equal to sum over column of response matrix

\[
p_n = \sum_{m} A_{m,n}, \quad m=1,\ldots,M \quad (4.1)
\]

Notations are the same as (3.2)
Using a pinhole with a diameter of 0.3mm, the peak sensitivity of MRC-SPECT-I could reach around 1.5% in the central FOV, as shown in Fig.4.2 and any points in central transverse slice could have sensitivity larger than 0.6%. In comparison, MRC-SPECT-I, the peak sensitivity was 0.04% for the 0.45 diameter pinhole.

To compare the angular sampling between MRC-SPECT-I and MRC-SPECT-II, four points were selected and they are center in central transverse plane and 0, 2.5mm, 5mm and 7.5mm away from the FOV. We calculated the sensitivity histogram along axial direction with step size 1° for both MRC-SPECT-I and MRC-SPECT-II system:

\[ p_n = \sum_m A_{m,n}, \quad m \in \{ \text{index of pixels in detector has } ith \text{ sampling angle} \} \quad (4.2) \]

The sensitivity histogram along transverse direction for the four selected points was shown in Fig.4.3. Fig4.3 also shows in angular sampling of corresponding points in MRC-SPECT-I(red bar). For MRC-SPECT-I, all four points are sampled by 30 to 40 pinholes. In comparison, we
could find the points inside the FOV could be uniformly sampled in $360^\circ$ by more units of MRC-SPECT-II. In the FOV center, it could be seen by all 64 micro-pinhole camera in each ring.

And at least four rings could see the central of FOV. The total number of sampling angles was 256 in the adjacent 4 twisted rings. The points away from the center of FOV and close to its boundary, like points 2.5mm and 5mm away from the FOV center, could be seen by half pinhole camera elements and totally 128 uniform distributed elements in the adjacent 4 twisted ring.

**Fig.4.3:** Four selected point (0, 2.5mm, 5mm and 7.5mm away from center of FOV in transvers plane) sensivity histogram over along axial direction, step size is 10. Red solid bar is for MRC-SPECT-I and Black solid bar is for IEC-SPECT(MRC-SPECT-II)
could see them. Outside the FOV, like the point 7.5mm away from the FOV center, the angular sample was limited and only the micro-pinhole camera elements in the region, which was closest to and furthest from them, could see those points.

4.3 Imaging Comparison

The reconstructed image is not only dependent on object, system, algorithm, initial imaging of the reconstruction, but also dependent on the interaction of reconstruction. For EM based reconstruction, with iteration increasing, the imaging resolution would increase but the imaging becomes noisier. The image resolution could be evaluated by local impulse response[17]:

$$L^j_k = \lim_{\delta \to 0} \frac{\tilde{\theta}_{(k, x_j(y), y_j(\theta + \delta))} - \tilde{\theta}_{(k, x_j(y))}}{\delta} \quad (4.3)$$

Where $y = [y_1, y_2, ..., y_N]^T$ is a Nx1(number of pixels in detector space) dimension Poisson random variable( here is projection of object) with mean of $\tilde{y}(\theta)$, $y = [\theta_1, \theta_2, ..., \theta_M]^T$ is Mx1 dimension parameters, here is the voxel counts of resolution phantom or brain phantom; $\delta e^j$ is the delta pulse in the $j^{th}$ voxel, $\tilde{\theta}_{(k, x_j(y))}$ is the reconstructed imaging in the $k^{th}$ iteration, with the projection of object, $\tilde{y}_{(\theta+j)}$, $\tilde{\theta}_{(k, x_j(y), y_j(\delta e^j))}$ is the reconstructed imaging in the $k^{th}$ iteration, with the projection of object $y_{(\theta)}$ pulsing $\tilde{y}_{(\delta e^j)}$, the mean projection of the delta impulse; $L^j_k$ is the local impulse response from the $j^{th}$ voxel and the $k^{th}$ iteration. If the $\delta$ is sufficient small, then

$$L^j_k \approx \frac{\tilde{\theta}_{(k, x_j(y), y_j(\delta e^j))} - \tilde{\theta}_{(k, x_j(y))}}{\delta} \quad (4.4)$$
To compare the imaging in similar resolution, we chose the reconstructed imaging of two system from the iterations, which have minimized difference between their local impulse response from center of FOV, i.e.,

\[ k'_{2} = \arg \min_{k_{2} \in \{1,...,K_{2}\}} \{ \text{norm}(L_{k_{1}}^{j} - L_{k_{2}}^{j}) \}, \text{ for fixed } k_{1} \]  \hspace{1cm} (4.5)

where \( L_{k_{i}}^{j} \) is the \( k^{th} \) iteration local impulse response of MRC-SPECT-I for the \( j^{th} \) voxel, here corresponding to the voxel in the center of FOV; \( L_{k_{i}}^{j} \) is the local impulse response from MRC-SPECT-II.

### 4.3.1 Imaging of Resolution Phantom for Mice System

The Monte Carlo simulation results of resolution phantom were shown in Fig. 4.4 and Fig.4.5. Fig 4.4 results for 100\( \mu \)Ci with 30mins acquisition case. We fixed iteration (100\textsuperscript{th}, 500\textsuperscript{th}, 1000\textsuperscript{th}) for MRC-SPECT-II without DOI information (the third row of Fig4.4). The reconstructed images of MRC-SPECT-I which had minimized difference of LIR with MRC-SPECT-I were from 31\textsuperscript{th}, 82\textsuperscript{th} and 159\textsuperscript{th} iterations respectively. And the ones from MRC-SPECT-II with DOI were from 69\textsuperscript{th}, 406\textsuperscript{th} and 863\textsuperscript{th} iterations. For 10\( \mu \)Ci case, we could find the iteration with the smallest difference between MRC-SPECT-I and MRC-SPECT-II, as shown in Fig.4.5.

Comparing images with and without DOI information, we could find that imaging with DOI could resolve boundary clearer, which were shown in both 100\( \mu \)Ci and 10\( \mu \)Ci cases. From 100\( \mu \)Ci phantom results, comparing imaging from MRC-SPECT-II NO DOI and MRC-SPECT-II with DOI, we could find that with DOI information, MRC-SPECT-II could resolve 0.45mm hot rod, while 0.45 hot rods became more blur without DOI. DOI could help achieve better resolution performance primarily because of two reason we mention in section 2.4, i.e, sharper PSF and smaller overlapping space than non-DOI detector.
Fig. 4.4: Resolution phantom imaging for 100uCi radioactivity in 30min imaging section

MRC-SPECT-I
100uCi, 31iter

MRC-SPECT-I
100uCi, 82iter

MRC-SPECT-I
100uCi, 159iter

MRC-SPECT-II
DOI
100uCi, 69iter

MRC-SPECT-II
DOI
100uCi, 406iter

MRC-SPECT-II
DOI
100uCi, 863iter

MRC-SPECT-II
NODOI
100uCi, 100iter

MRC-SPECT-II
NODOI
100uCi, 500iter

MRC-SPECT-II
NODOI
100uCi, 1000iter
Fig. 4.5: Resolution phantom imaging for 10uCi radioactivity in 30min imaging section
The much higher sensitivity ensures that in the same imaging time, MRC-SPECT-II could collect much more events and richer angular sampling immune the imaging performance of noise. Those advantages benefit system performance of MRC-SPECT-II over MRC-SPECT-I. When the noise did not heavily affect the imaging, as the case of 100μCi, MRC-SPECT-I and MRC-SPECT-II with DOI, have similar resolution, as shown in Fig. 4.4, we could find MRC-SPECT-II could resolve 0.45mm hot rods in 863\textsuperscript{th} reconstructed imaging, and MRC-SPECT-I could resolve corresponding hot rods. With radioactivity decreasing to 10μCi, the case that noise heavily affects imaging performance, MRC-SPECT-II still could resolve the 0.55mm hot rods while the reconstructed imagines of MRC-SPECT-I became much noisier and only the 0.65mm hot rods could be resolved.

4.3.2 Imaging of Brain Phantom for Mice System

High sensitivity and rich angular sampling effects also shows up in imaging of mice brain study. Images for mic brain phantom for 1mCi, 100uCi, 25uCi and 5uCi were shown in Fig.4.5-Fig.4.8. MRC-SPECT-II reconstructed imaging could resolved the detailed features of mice brain even in the case of 5uCi activity in whole brain with 30mins acquisition, while MRC-SPECT-I became very noisy after the radioactivity reduced to 100μCi.

4.4 Imaging Study for Human Brain System

For human brain SPECT system, it could achieve sensitivity of 0.1%. Using data from 3mCi activity and 30min scanning section, reconstructed imaging could resolve 2.5mm hot rods, as shown in Fig.4.10. With such high sensitivity and good space resolution, Holffmen brain phantom with 1mCi activity and 30mins acquisition, the protocol of which is commonly used in clinical practice, could be resolved clearly.
Fig. 4.6: Brain Imaging study using 1mCi Tc-99m during 30mins imaging section

Fig. 4.7: Brain Imaging study using 100uCi Tc-99m during 30mins imaging section
Fig. 4.8: Brain Imaging study using 25uCi Tc-99m during 30mins imaging section

Fig. 4.9: Brain Imaging study using 5uCi Tc-99m during 30mins imaging section
Fig. 4.10: imaging study for the human brain system: A is reconstructed resolution phantom with activity of 3mCi, 30mins acquisition time; B is the reconstructed imaging for 1mCi activity and 30mins acquisition
5. Conclusion and Future Work

In this report, we proposed the second generation MRI compatible system, MRC-SPECT-II, based on inverted compound eye. The system has size of 75mm (transverse) x78mm (sagittal), compact enough to put inside 9.4/14T preclinical MRI scanner. Monte Carlo simulation demonstrated that this system could achieve 1.5% peak geometry sensitivity while the system resolution could achieve sub millimeter in side 1cm FOV. We also explore the potential application of ICE for human brain SPECT system. The system achieved 0.1% sensitivity with resolution around 2.5mm.

To our knowledge, with similar resolution, both systems had 1 to 2 orders of magnitude higher sensitivity than current generation SPECT systems. The dramatic increase in sensitivity could potentially lead to a radical change in how we might employ SPECT imagining in both pre-clinical and (potentially) clinical practice, by offering much lower detection limit and allowing for new imaging procedures that would be difficult to implement with the current generation of SPECT instrumentation.

There are some concerns related to ICE for SPECT applications. One is the aperture fabrication. The aperture for mice has 1536 units and for human brain imaging, it has 7680 units. Those units have different shape and orientation. The conventional fabrication methods nearly impossibly construct such a complicated structure. Rapid additive manufacturing with selective laser melting [10] potentially solves this issue. Also the complicated aperture leads to a challenging task for system modeling. Ray tracing method to derive the response function is hard to achieve enough accuracy due to the discrepancy between the actual fabricated and designed geometry, difficulty in calibrating system parameters, like the pinhole position and orientation,
and the effect of small open angle. It seems system modeling based on experiment data could potentially solve this issue.

To evaluate feasibility and performance from experiment, we are going to build a prototype system based on this design. We will explore the technology of rapid prototyping for ICE aperture fabrication and develop new system modeling scheme. Those results will be published in the near future.
6. References


