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Simulation study of the second-generation MR-compatible SPECT system based on the inverted compound-eye gamma camera design

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Abstract

In this paper, we presented the simulation studies for the second-generation MRI compatible SPECT system, MRC-SPECT-II, based on an inverted compound eye (ICE) gamma camera concept. The MRC-SPECT-II system consisted of a total of 1,536 independent micro-pinhole-camera-elements (MCEs) distributed in a ring with an inner diameter of 6 cm. This system provided a FOV of 1 cm diameter and a peak geometrical efficiency of approximately 1.3% (as compared to the typical levels of 0.1%–0.01% found in modern pre-clinical SPECT instrumentations) while maintaining a sub-500 μm spatial resolution. Compared to the first-generation MRC-SPECT system (MRC-SPECT-I) [1] developed in our lab, the MRC-SPECT-II system offered a similar resolution, but a dramatically improved sensitivity and a greatly reduced physical dimension. The latter allowed the system to be placed inside most clinical and pre-clinical MRI scanners for high-performance simultaneous MRI and SPECT imaging.

1. Introduction

Because of the complementary nature of MRI and emission tomography, a combination of SPECT or PET with MRI shows great potential for both pre-clinical and clinical applications. MRI has excellent spatial and temporal resolutions, as well as exquisite soft-tissue contrast, but limited sensitivity. SPECT and PET are highly sensitive molecular imaging modalities, but offer little structural information. While combined imaging studies of SPECT and MR could be carried out with sequential SPECT-MR scanners, simultaneous SPECT/MR imaging allows for dynamic, multi-parametric imaging studies that could reveal molecular changes related to physiology with high-resolution functional and anatomical images aided by an exquisite soft tissue differentiation. Also, acquiring SPECT and MR images simultaneously allows for real-time spatial and temporal image co-registration, as well as MR-guided motion and partial-volume corrections, which could help to improve imaging resolution and data quantification. These aspects would be particularly important for small animal studies that require ultra-high spatial resolution SPECT and MR images co-registered with a precision greater than the spatial resolution of both modalities. In the longer run, simultaneous SPECT and MR image acquisition could benefit clinical cardiac imaging applications, which are confounded by dynamic, functional, geometric, and metabolic indices of the heart, and challenges associated with complex cardiac and respiratory motion [2, 3, 4].

While PET/MRI instrumentation has greatly progressed [5, 6, 7], the development of combining SPECT and MRI instrumentation, especially systems allowing for simultaneous SPECT and MR imaging, has been lagging. This is partially due to the special technical challenges of integrating SPECT with MR scanners, including potential interferences between modalities. First, the strong magnetic field could potentially affect the operation of SPECT detectors, such as MR-induced noise degraded energy and spatial responses [8]. Second, the electronic and metallic components of the SPECT system could also cause distortions and degradation in MR image quality [9, 10]. Furthermore, the limited space inside MRI scanners would pose practical challenges for using the conventional pinhole SPECT system designs that typically require large magnification to ensure reasonable trade-offs between spatial resolution and sensitivity [9].

In recent years, several groups have devoted intensive effort in developing combined SPECT and MR imaging systems. Most notably, Wagenaar *et al.* have reported the design considerations of an MRI compatible SPECT system based on CZT detectors [11]. Tsui *et al.* have presented a prototype of a MRI compatible SPECT system based on similar CZT detectors [12]. A consortium consisting of several groups in EU proposed and developed both preclinical and clinical SPECT inserts using SiPM based detector [13, 14, 15, 16]. Karel Deprez *et al.* have constructed an MRI compatible aperture using rapid additive manufacturing with selective laser melting of tungsten powder [17]. And J. Zajicek *et al.* have presented a MR-SPECT insert using Timepix detectors [18].

We have reported an ultrahigh resolution stationary MR compatible SPECT system (MRC-SPECT-I) for small animal imaging [1]. The MRC-SPECT-I detector ring has a diameter size of 156 mm and consists of ten energy-resolving photon-counting (ERPC) CdTe detectors [19, 20]. The CdTe in each detector has a sensing volume of $22.5 \times 45 \times 2 \text{ mm}^3$ and is divided by 64 by 128 pixels, each with a 0.35 mm width. MRC-SPECT-I consists of forty 300/500 μm -diameter pinholes in a 66-mm diameter ring. We have demonstrated its ability to achieve a sub-500 μm resolution in simultaneous SPECT/MRI mode while working inside the Siemens Trio 3T clinical scanner [21].

Despite the success in developing the MRC-SPECT-I system, the preliminary evaluation revealed several limitations of the system, which limit the use of the system in many practical SPECT/MR imaging applications. First, the system has a relatively low geometrical sensitivity of around 0.02% with 40 pinholes of 350 μm diameter and 0.05% with 500 μm pinholes, which would be insufficient for potential dynamic SPECT imaging applications. Second, since the MRC-SPECT-I system was designed to have a reasonable magnification ratio to ensure an excellent imaging resolution, the system has a large outer diameter of 25 cm, which cannot be placed inside many pre-clinical MRI scanners for high-performance MR imaging [22].

In this paper, we proposed an Inverted Compound Eye (ICE) camera design and the second-generation MRI compatible SPECT system (MRC-SPECT-II) based on ultrahigh-resolution detector technologies. We will present the results from a comprehensive simulation study to demonstrate the tremendous performance benefit given by the ICE camera design and the MRC-SPECT-II system design over the existing MRC-SPECT-I system.

2. Method and materials

2.1. Design of the inverted-compound-eye gamma camera and the MRC-SPECT-II system

We have recently proposed an Inverted-Compound Eye (ICE) gamma camera design for use with the MRC-SPECT-II system (Fig. 1). Each ICE camera used the CZT or CdTe detector with a sensor area of $2.56 \times 2.56 \text{ cm}^2$ coupled to an aperture with 8×8 pinholes, each with a diameter of 300–500 μm (300 μm in this study). The shape of each pinhole restricted the projection from the object to a small area of around $3.2 \text{ mm} \times 3.2 \text{ mm}$ on the detector. Each pinhole and its corresponding effective detector area formed a micro-pinhole-camera-element (MCE). In our current design, each single ICE camera module has 64 MCEs.

The current design of the MRC-SPECT-II system was also shown in Fig. 1. It had three detector rings along the axial direction and each ring has eight ICE-camera modules. This led to a total of 24 modules and 1,536 MCEs. Since each MCE had a small open angle and covered a fraction of the FOV, the distribution of the MCEs and their orientation could be critical for achieving a reasonable FOV and an adequate angular sampling.

Within the eight ICE camera modules in a ring, there were in effect 8 rings of MCEs along the axial direction. These rings focused on a FOV with a 1 cm diameter in the axial direction and provided a relatively uniform angular coverage. In the transverse direction, the MCEs in the first ring were all designed so that the left boundaries of their individual angular coverage were always tangential to the left boundary of the system FOV of a 1 cm diameter. For each MCE in the second ring, the right boundary of its FOV is tangential to the right boundary of the system FOV. The 1st, 3rd, 5th and 7th rings of the MCEs were designed in a similar way to bias towards the left-hand-side of the system-FOV, and the 2nd, 4th, 6th and 8th rings of the MCEs were designed to bias towards the right-hand-side of the system-FOV. As we will show later in Sec. 3.1, this design offered a relatively uniform angular sampling in an ultra-compact detection system.

2.2. Considerations on gamma ray detectors

To facilitate the specific ICE camera design, we have compared CZT detectors with small pixels of 100 μm to 400 μm pitch, and without DOI resolution and with a DOI resolution 500 μm . A gamma-ray imaging detector satisfying such requirements could be readily available by adopting existing electronics and detector technologies that have been developed and experimentally verified by our group, many other research groups, and commercial companies [25, 26, 27, 28, 29, 30].

In this study, we proposed to use the hybrid pixel-waveform (HPWF) detector design that has been developed by our group over the past several years [25, 26, 27, 28]. In an HPWF detector, we use pixel readout circuitry to read out small anode pixels and digital waveform sampling circuitry working in coincidence with the anode readout circuitry to record the cathode waveform and to derive the DOI and energy information.

We have previously studied the performance benefit of using the cathode waveform to extract the energy and DOI information for gamma-ray interactions inside semiconductor detectors [25, 26]. We have also constructed several prototype HPWF detector modules

based on the ERPC CdTe detectors with 350 μm anode pixels [27] and experimentally evaluated these detectors for single photon imaging applications [28] and for coincidence (PET) imaging applications [27].

In order to provide a detector that offered an imaging resolution of 100 μm , we proposed to combine a cathode sampling circuitry with existing photon counting ASICs, such as the XC225 ASIC from AJAT/XCounter [29] or the Medipix series ASICs [30]. Please note that both the XC225 (with 100 μm pixel pitch) and the Medipix 3/4 (with 55 μm pixel pitch) ASICs implement various forms of charge sharing correction techniques to integrate the charge induced on neighboring (say 2×2) pixels. These schemes could significantly reduce the impact of charge sharing effects on the effective spatial resolution for small pixel detectors (Fig.6 and Fig.7 in [29]) and also help to alleviate the impact of charge-sharing (and incomplete charge collection) on the effective detection efficiency of the detectors.

Since these ASICs (XC225/Medipix) are designed for x-ray imaging and have a very high counting capability, the maximum count rate of the HPWF detector is limited by the cathode readout time. For a 2 mm CdTe detector with a bias voltage of 400 V, the maximum time of hole drifting is around 0.5 μs , and considering the shaping and other post-processing, the time (t_p) needed to process one event could be extended to 2.5 μs . The maximum count rate will be around 400 k (*i.e.*, $\frac{1}{t_p}$). Consider that 1 mCi activity is concentrated at the center of

the FOV, and the total detection efficiency of the MRC-SPECT-II system is 1%, then the entire system would detect 3.7×10^5 photons per second distributed over 24 detectors. Each detector would receive an average of 1500 photons per second. So, the 400 k allowance (the photon flux allowed without inducing substantial dead time) is several orders of magnitude over the expected the photon flux for the MRC-SPECT-II applications.

2.3. Comparison with the MRC-SPECT-I system

In this study, we used our MRC-SPECT-I system [1] as a benchmark to evaluate the MRC-SPECT-II system. The design parameters of MRC-SPECT-I and MRC-SPECT-II were summarized in Table. 1 and further detailed below.

Detectors: MRC-SPECT-I used an energy-resolved photon-counting CdTe detector. Each CdTe detector had an active volume of $22.5 \times 45 \times 2 \text{ mm}^3$ and the anode side of the detector was divided into 64×128 pixels with 0.35 mm pitch.

By comparison, the MRC-SPECT-II system design outlined above was based on the CdTe detector with an active volume of $25.6 \times 25.6 \times 2 \text{ mm}^3$. To evaluate different detector options, we compared the MRC-SPECT-II system with three different detector configurations. The first one, named MRC-SPECT-II-A, used the prototype HPWF, providing a DOI resolution of 0.5 mm and a pixel size of 0.4 mm (the original pixel size is 0.35 mm; here we used 0.4 mm to match the detector width, *i.e.*, 25.6 mm). The second one, called MRC-SPECT-II-B, used the ultra-high photon counting anode ASIC without cathode readout, which had x-y spatial resolution of 0.1 mm but no DOI resolving power. And the third one, called MRC-SPECT-II-C, used the proposed HPWF detector and it had a pixel size of 0.1 mm and a DOI resolution of 0.5 mm.

System design: The MRC-SPECT-I system consisted of ten detectors in a closely packed ring with an inner diameter of 15.6 cm (the distance between two opposite detectors and an axial length of 2.25 cm. Inside the detector ring, there was a single ring of 40 pinholes of 300 μm or 500 μm diameter. The distance between the pinhole and the axis of the system is 33 mm) [1, 21]. MRC-SPECT-I was designed to offer a FOV of around 16 mm diameter and 20 mm actual length. In this simulation study, we used 0.45 mm diameter pinholes for the MRC-SPECT-I system to match the intrinsic resolution of MRC-SPECT-I and MRC-SPECT-II-C.

By comparison, the MRC-SPECT-II system consisted of 24 detectors in three rings (eight detectors per ring). Within each ring, the distance between the opposite detectors was around 60 mm and the total length of the MRC-SPECT-II detection system was 8 cm. Each detector of 2.56 cm $\times$ 2.56 cm was coupled to a cluster of 8 $\times$ 8 pinholes that were all positioned in a plane parallel to the detector surface. The current design of the MRC-SPECT-II system had 1,536 MPCEs, each with a single pinhole. The distance between the detector front surface to the pinhole aperture plane was 9.7 mm and the distance between the aperture plane to the axis of the system was 21.6 mm. This system design allowed for a FOV of around 10 mm diameter by 10 mm in axial length.

2.4. System modeling, simulation, and reconstruction

In this simulation, the system response matrices (H) of MRC-SPECT-I and MRC-SPECT-II were pre-calculated using the line-trace method.

$$H_{mn} = \int_{\mathbf{r}_d \in V_m} \left\{ \frac{\mu_d}{4\pi|\mathbf{r}_d - \mathbf{r}_n|^2} \exp[-\mu_d l_d(\mathbf{r}_d, \mathbf{r}_n) - \mu_p l_p(\mathbf{r}_d, \mathbf{r}_n)] \right\} dV \quad (1)$$

, where H_{mn} is the probability of a photon emitted from the n^{th} object voxel detected by the m^{th} detector pixel; we calculated the probability at $\mathbf{r}_d$ for the object voxel at $\mathbf{r}_n$ and then integrated over the sensing volume belonging to the m^{th} detector pixel, *i.e.*, $\mathbf{r}_d \in V_m$ (For MRC-SPECT-I, the sensing volume of each detector pixel is $0.35 \times 0.35 \times 2.0 \text{ mm}^3$; for MRC-SPECT-II-A, $0.40 \times 0.40 \times 0.5 \text{ mm}^3$; for MRC-SPECT-II-B, $0.1 \times 0.1 \times 2.0 \text{ mm}^3$; for MRC-SPECT-II-C, $0.1 \times 0.1 \times 0.5 \text{ mm}^3$). μ_d and μ_p are the linear attenuation coefficients of CdTe and the aperture at 140 KeV respectively; l_d and l_p represent the distance that the photon travels in the aperture and the CdTe crystal before it is detected at $\mathbf{r}_d$.

The line-trace method does not take into account detector energy resolution and energy window effect, nor Compton scattering. However, these simplifications would not significantly affect this method's reliability for the pre-clinical SPECT modeling. Most gamma rays with 140 keV and below would interact with CdTe and CZT materials through photoelectric interaction, and the fraction of photoelectric effect is even higher for interactions of these gamma rays in collimator materials (Pt-90%/Ir-10%, density 21 g/cm³). Furthermore, for imaging a mouse's brain, the effect of Compton scattering and attenuation in the small object (1.5 cm in diameter) is negligible, given that the mean free path of a 140 Kev photon is around 6.6 cm in water. For this imaging application, one could assume that

most gamma-rays reaching the detector are coming directly from their originating emission site.

To experimentally evaluate the model, we compared the simulated pinhole response (the projection of a point source of 250 μm diameter through a given pinhole onto a CdTe detector of 2 mm thickness) to the pinhole response experimentally measured with identical geometry. In addition, we have also compared the phantom images reconstructed with simulated and measured data under the same calibrated geometry. The simulated pinhole response matched reasonably well with the experimental response. On the other hand, image qualities of the simulated phantom degraded compared to the corresponding experimental results. We will discuss the potential reasons causing this degradation in Sec. 4. Nevertheless, the simulation presented in this paper evaluated the potential performance MRC-SPECT-II could achieve.

After calculating the system matrix, we generated the noise free projection ($\mathbf{g}$) by

$$\bar{\mathbf{g}} = \mathbf{H}\mathbf{f} \quad (2)$$

where $\mathbf{f}$ is a digital phantom. In this study, we evaluated the system designs using three digital phantoms. The first one was a resolution phantom that had four groups of hot rods with different sizes, which were surrounded by a uniform background. The radioactivity concentration in the hot rods was ten times that of the background. The second one was a uniform phantom, and the third one was a mouse brain phantom developed by Beekman et al. [31]. For all three phantoms, the region with activity was confined to within a roughly 1 cm diameter. They were all divided into 64 voxels in each dimension with a voxel size of 0.2 mm. More details of the digital phantoms could be found later in Fig. 5 and Fig. 6.

The noise projection $\mathbf{g}$ then is generated using Poisson noise model based on the noise free projection. And the images were reconstructed using post-filtered maximum-likelihood estimation [32, 33]:

$$\hat{\mathbf{f}}_{ML} = \arg \max_{\mathbf{f}} \left\{ \log[P(\mathbf{g}|\mathbf{f})] \right\} \quad (3)$$

and then:

$$\hat{\mathbf{f}}_{PF-ML} = \mathbf{F}\hat{\mathbf{f}}_{ML} \quad (4)$$

where $\hat{\mathbf{f}}_{ML}$ is a maximum-likelihood ($P(\mathbf{g}|\mathbf{f})$) estimator and $\hat{\mathbf{f}}_{PF-ML}$ is post-smoothed $\hat{\mathbf{f}}_{ML}$, which is derived by using a 3-D Gaussian post-filter, $\mathbf{F}$.

2.5. Numerical performance indexes for comparing different system designs

In this study, we used resolution-variance trade-offs [34, 35, 36, 37], to evaluate the proposed MRC-SPECT-II system design. We evaluated the spatial resolution and variance properties at different locations of FOV. By selecting reconstructed images at different EM iterations, we arrived at different trade-offs between imaging variance against spatial resolution, which are then plotted to obtain so-called resolution-variance trade-off curves for comparing different system designs.

In this study, the spatial resolution was presented by the FWHM of the local-impulse response (LIR) [38], $I_j(f)$, for a given pixel (j^{th}) as:

$$I_j(f) = \lim_{\delta \rightarrow 0} \frac{\bar{\hat{f}}(f + \delta e_j) - \bar{\hat{f}}(f)}{\delta} \quad (5)$$

where $\bar{\hat{f}}(f)$ is the mean of reconstructed images, and δe_j is a small impulse on the voxel j . The reconstructed image mean and pixel-wise variance were both derived by simulation through 500 random realizations for resolution-variance trade-off studies.

3. Results

3.1. MRC-SPECT-II design dramatically improved sensitivity and angular sampling with an ultra-compact detection system

In Fig. 3, we studied angular sampling provided by the MRC-SPECT-II system at 4 points-of-interest (POIs, shown with red dots in Fig. 1-C) and compared it against corresponding sampling provided by the existing MRC-SPECT-I system. The MRC-SPECT-II system had 1,536 pinholes covering FOV with a diameter of 10 mm. As a result, POI 1 was "seen" by all MCEs in four adjacent rings with a total of 256 pinholes. POIs 2 and 3 were seen by at least a half of the MCEs in four adjacent rings with >128 pinholes uniformly distributed across the 360 degrees around the axis. By comparison, the MRC-SPECT-I system had only 40 pinholes distributed around the object. Therefore, the MRC-SPECT-II system provided much better angular sampling without any translation of the object or the SPECT detection system.

The MRC-SPECT-II system design achieved better angular sampling with a highly compact geometry. The aperture-to-object distance was 21.6 mm for MRC-SPECT-II versus 36 mm for MRC-SPECT-I. More pinholes for seeing the FOV and shorter distance between the pinholes and the axis enabled the MRC-SPECT-II system to provide a dramatically improved system sensitivity over the MRC-SPECT-I system. As we showed in Fig. 4, using pinholes with a diameter of 0.3 mm, the peak sensitivity of the MRC-SPECT-II reached around 1.3% in the central FOV, and any point in the central transverse slice had sensitivity larger than 0.5%. Due to the highly focused geometry, the sensitivity had a large spatial variation. In the axial direction, the sensitivity at the boundary of FOV decreased to around 0.3%. By comparison, using 40 pinholes with a diameter of 0.45 mm, MRC-SPECT-I had a peak sensitivity of around 0.04%, which was about 30 times less than MRC-SPECT-II.

It was equally important, from the MR-compatible SPECT view point, that the improved sensitivity and angular sampling were achieved with a greatly reduced system dimension (6 cm inner diameter for the MRC-SPECT-II detector-ring versus 15.6 cm diameter for the MRC-SPECT-I system). This enabled the MRC-SPECT-II system to be integrated into a wide variety of high-magnetic-field MR scanners [22].

3.2. Resolution phantom studies

In order to evaluate the imaging performance of MRC-SPECT-II and different configurations, we have carried out a series of simulation studies and the results are shown in Fig. 5

In Fig. 5, we found that the detector resolution played a significant role in improving the imaging qualities of MRC-SPECT-II. Given 1000 μCi activity, the features of the 0.65 mm hot rods were blurred by MRC-SPECT-II with the prototype HPWF (MRC-SPECT-II-A), while the features of the 0.45 mm hot rods were clearly resolved by MRC-SPECT-II with the proposed HPWF (MRC-SPECT-II-C). When the activity was reduced to 10 μCi , the reconstructed images of MRC-SPECT-II-A were distorted but ones of the proposed HPWF still could resolve features of 0.55 mm. Comparing the results of MRC-SPECT-II-B and MRC-SPECT-II-C, we could find that DOI information allowed the system to resolve high resolution features. In the 1000 μCi case, DOI information (MRC-SPECT-II-C) could improve the system resolution from 0.55 mm to 0.45 mm.

In Fig. 5, we also compared images obtained with MRC-SPECT-I and MRC-SPECT-II. At high activity (1000 μCi), MRC-SPECT-II-C with proposed HPWF detector could achieve a resolution of around 0.45 mm, while MRC-SPECT-I only delivered 0.55 mm resolution images at the similar variance. When the phantom activity was reduced to 10 μCi , all of the hot rods in MRC-SPECT-I were distorted, while MRC-SPECT-II still could resolve features of 0.55 mm. Clearly, high system sensitivity and rich angular sampling made MRC-SPECT-II more immune from noise.

3.3. Mouse brain phantom studies

Compared to the resolution phantom used above, the brain phantom described in Sec. 2.4 had a much broader distribution of activity and allowed us to further evaluate the capability of MRC-SPECT-II. In Fig. 6, we simulated the phantom filled with different activity levels ranging from 1 mCi to 5 μCi and compared the reconstructed images at similar spatial resolution of around 0.5 mm. Given the > 30 times greater sensitivity, the MRC-SPECT-II system offered a greatly reduced imaging noise. With a very low activity of 5 μCi in the whole brain, MRC-SPECT-I image became very noisy and virtually unusable, while the MRC-SPECT-II image retained reasonable qualities.

3.4. Quantitative Studies

In Fig. 7, we quantitatively evaluated benefits of an ultra-high pixel resolution detector. For the target spatial resolution in the range between 0.7 mm and 1.0 mm, the image variance at the center of the FOV using the proposed HPWF detectors (MRC-SPECT-II-C, 100 μm detector pixels) was around 5 times less than that of the prototype HPWF detectors (MRC-

SPECT-II-A, 400 μm pixels). Fig. 7 also demonstrated that it was challenging for the prototype HPWF detector system (MRC-SPECT-II-A) to get resolution better than 0.7 mm.

Fig. 7 also assessed the performance benefit of DOI effect. We showed that for the target spatial resolution in the range between 0.5 mm and 1 mm, the image variance at the center of the FOV obtained with DOI resolution of 500 μm was more than 2 times less than that without DOI information.

Compared with MRC-SPECT-I (Fig. 7 and Fig. 8), the image variance obtained with the MRC-SPECT-II system (MRC-SPECT-II-C) at the center of FOV was more than 20 times less when the target spatial resolution was in the range between 0.5 mm and 1 mm. The non-uniformity of MRC-SPECT-II's sensitivity led to appreciable difference in the resolution-variance trade-offs for different spatial locations. As shown in Fig. 8, the variance increased by 50% when it was moved away from the center by 3.2 mm. Nevertheless, the MRC-SPECT-II system consistently allowed for a reduction in imaging variance by an order of magnitude at a given spatial resolution, when compared to the MRC-SPECT-I system.

4. Discussions and conclusions

In this paper, we proposed and evaluated the design of the second-generation MR-compatible SPECT system (MRC-SPECT-II) based on an inverted-compound-eye gamma-camera design. The ultra-high 3D resolution of the detector enabled MRC-SPECT-II to use a demagnification design without sacrificing resolution and allowed the system to pack a large number (1,536 in the current design) of micro-pinhole cameras around the object. Compared to the MRC-SPECT-I system, this configuration offered a dramatically improved detection efficiency, greatly enriched angular sampling, and a significantly reduced physical dimension. As we demonstrated by simulation studies, these improvements enabled the MRC-SPECT-II system to offer a dramatically improved image quality over the MRC-SPECT-I system with a compact detection system that could be inserted in most pre-clinical MR scanners. Also, the performances of MRC-SPECT-II in terms of sensitivity and resolution were significantly better than current generation commercial scanners [39, 40, 41], even though designing an MR-compatible SPECT system that allowed for simultaneous SPECT-MR studies would be subject to many extra constraints than those for designing a regular SPECT system.

As one may have noticed, the current design of MRC-SPECT-II led to spatially variant sensitivity and angular sampling and non-uniform image quality across the FOV. This issue could be readily resolved by re-distributing the pinhole positions and their angle of orientations, to direct more pinholes to cover the regions that have lower sensitivity in the current sensitivity profile shown in Fig. 4. Given the large number of degrees of freedom associated with the ICE camera design, one could fine-tune the design of the MRC-SPECT-II system. However, a systematic optimization will be computationally expensive, and the optimization should be highly specific to the imaging tasks. We would leave this optimization study to our future studies. Nevertheless, there is no doubt that the MRC-SPECT-II system design would lead to a dramatically improved imaging performance compared to the MRC-SPECT-I system.

Regarding the viability for constructing the MRC-SPECT-II system, most of the hardware components, such as the system gantry and collimators, can be readily produced with 3-D printing techniques [1, 17, 21, 42]. As we previously discussed in Sec. 2.2, we are currently developing the HPWF detector for use in the MRC-SPECT-II system. Given the recent advances in semiconductor detector and readout electronics, a detector with nearly perfect detection efficiency (as defined by the physical stopping power of CZT material and not degraded by the readout electronics), an excellent energy resolution could be achieved with this newer generation of CZT detectors. From experience learned from developing the MRC-SPECT-I hardware and from much other recent developments in CdTe/CZT detector technologies, we believe that a detector with the performance matching that being simulated in this study could be readily developed. The related progress will be presented in our future publications.

In Sect. 2.4, we showed that the image qualities of the simulated phantom degraded compared to the experimental one. One of the potential causes was a mismatch between the calibrated and actual imaging geometry, including pinhole position, pinhole shape, *ect.* This issue will potentially become more critical in MRC-SPECT-II, given the large number of the micro-pinholes and the limited mechanical precision of current 3-D printing techniques. In such a case, we could experimentally measure and validate the system response function by using a point source scanning across the object space [42]. This would allow us to incorporate the mechanical imperfections into the system model and therefore minimize the impact of related systematic errors on imaging quality.

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Figure 1.

Initial design of the ICE module for SPECT imaging. In sub-figure (A), a) the micro pinhole; b) the ICE aperture with 8×8 pinholes; c) the cone of pinhole restricting the projection to $3.2 \text{ mm} \times 3.2 \text{ mm}$ sensing area; d) a CZT/CdTe detector with an area of $2.56 \times 2.56 \text{ cm}^2$. (B), cross section of the ICE unit. (C), transverse view of the MRC-SPECT-II system. The four selected points are used to study angular sampling and geometrical sensitivity. Point 1, Point 2, Point 3, and Point 4 are 0 mm, 2.5 mm, 5 mm, and 7.5 mm away from the center of the FOV; the brain model is used with permission of Allen Institute for Brain Science [23, 24]. (D) 3D drawing of the MRC-SPECT-II system.

Figure 2.

A comparison between simulated and experimentally measured system responses: (A) The simulation point response function (PRF) around the FOV center of MRC-SPECT-I; (B) the corresponding experiment PRF; (C) the reconstructed image using a simulation phantom; (D) the reconstructed image using experimental data acquired using MRC-SPECT-I system. The system and phantom geometries remained the same for both the simulation study and actual experimental measurements, where MRC-SPECT-I used forty $300\ \mu\text{m}$ pinholes.

Figure 3.

Comparing angular sampling of MRC-SPECT-I (red circles) and MRC-SPECT-II (blue diamond) at four locations shown in Fig. 1-C as Point 1, Point 2, Point 3, and Point 4 respectively. Sample angle in x-axis defines a gamma ray's emission direction in the transverse plane, *i.e.*, the azimuthal angle with the reference center at the sample point (Point 1, Point 2, *ect*). And the angle is discretized with a step size of 0.5° . Sensitivity in y-axis is the probability of the gamma ray being detected by the system at the corresponding sample angle.

Figure 4.

Transverse and axial geometrical sensitivity profiles for the MRC-SPECT-I and MRC-SPECT-II. Note that the profiles of the MRC-SPECT-I were scaled by a factor of $\times 20$. The geometrical sensitivity is defined as the probability of a gamma ray emitted in a sampled point and going through pinholes.

Figure 5.

Images of a resolution phantom reconstructed with similar variance level; the filter FWHMs for the MRC-SPECT-II-C images at 1 mCi, 100 μ Ci, and 10 μ Ci were 0.3 mm, 0.4 mm, and 0.5 mm respectively. We varied the filter size of other systems to ensure their variance in the ROI (the four square regions, each having $4 \times 4 \times 10$ (axial) voxels) similar to that of the corresponding MRC-SPECT-II-C images.

Figure 6.

Reconstructed images of the mouse brain phantom; the reconstructed images had the similar resolution for each activity level; MRC-SPECT-II with the proposed HPWF (MRC-SPECT-II-C) was used. The resolution was evaluated in terms of LIR (Eq. 5) at the center of the FOV. The filter FWHM of MRC-SPECT-II was fixed at 0.5 mm, and we varied the filter size of MRC-SPECT-I to minimize the LIR difference with MRC-SPECT-II.

Figure 7. Resolution-variance trade-off curves. The results were derived by selecting different-iteration images of a uniform phantom. Resolution and variance were evaluated at the center of FOV and obtained through simulation with 500 realizations.

Figure 8.

Resolution-variance trade-off curves at different locations. P1 is at the center for FOV, P2 and P3 are 3.2 mm away from the FOV center in the transverse and axial direction respectively; the same simulated data sets of MRC-SPECT-I and MRC-SPECT-II-C were used as the ones in Fig. 7.

Table 1

System parameters of MRC-SPECT-I and MRC-SPECT-II

parameters/systems	MRC-SPECT-I	MRC-SPECT-II ^{N1}
# of detector	10 in one ring	24 in three rings
Detector to object center	78 mm	30.9 mm
Detector volume	$22.5 \times 45 \times 2 \text{ mm}^3$	$25.6 \times 25.6 \times 2 \text{ mm}^3$
Detector pixel size	0.35 mm	0.4/0.1/0.1 mm ^{N1}
DOI resolution	2.0 mm ^{N2}	0.5/2.0/0.5 mm ^{N1,N2}
Number of pinhole	40 in total, 4 per detector	1536 in total, 64 per detector
Aperture to object center	36 mm	20.6 mm
Pinhole diameter	0.45 mm	0.3 mm
FOV (mm)	$\phi 16 \text{ mm} \times 20 \text{ mm}$ ^{N3}	$\phi 10 \text{ mm} \times 10 \text{ mm}$

^{N1} For MRC-SPECT-II, we simulated three systems, *i.e.*, MRC-SPECT-II-A, MRC-SPECT-II-B, and MRC-SPECT-II-C. These systems were equipped with different detectors, and the corresponding detector parameters are given in the rows of "Detector pixel size" and "DOI resolution" in this table.

^{N2} Non-DOI detector had DOI information equal to the detector thickness, *i.e.*, 2 mm;

^{N3} The aperture design of MRC-SPECT-I allowed projection overlapping, and the non-overlapping region in the FOV was around $\phi 12 \text{ mm} \times 20 \text{ mm}$