Dual MRI-SPECT imaging system realized with Timepix pixel detector inserted into MR small animal scanner

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Abstract. Although MRI and SPECT are routine tools in medical imaging individually, the combination of these two modalities in multimodal imaging is still unexplored. By hybridizing high-resolution anatomical with functional imaging, combined MRI-SPECT could be a valuable addition to existing medical imaging methods, reducing overall scanning time and image co-registration errors. In contrast to PET, SPECT offers a cost-efficient range of applicable radioisotopes. This proof-of-principle study shows a modified experimental MRI-SPECT insert system consisting of an MR-compatible SPECT unit with hybrid semiconductor detectors Timepix. The insert system is equipped with CdTe pixelated sensors, tungsten collimators and a radiofrequency coil (RF). To increase the number of projections acquired, the setup is also equipped with an electromagnetic step motor Microcon SX 16-0503 for a sample rotation. Measurements were performed our own invented multimodal (¹H,⁹⁹mTc) inhomogeneous phantom filled with a liquid ⁹⁹mTc radiotracer, emitting 140.5 keV γ-rays inside the RF coil by the Bruker BioSpec 47/20 (4.7 T) MR animal scanner. For the evaluation of measured data, SPECT-back projection software was developed in Matlab. Our results pave the way for a preclinical MRI-SPECT insert system. This research was performed in the framework of the Medipix Collaboration.

1. Introduction

These Most of the nuclear imaging methods commonly used today are based on the injection of a solution containing molecules labelled by some radioactive isotope. Compared to the radiotracers used in PET (¹⁸F), solutions of ⁹⁹mTc or some form of Iodine are cheaper and also have a longer half-life. An overview of radioactive isotopes used for SPECT is in Table 1. SPECT imaging is mainly used in clinical practice for functional diagnostics of the brain, heart, and kidneys, or for the localization of tumours.

For patient examination, the activities of ⁹⁹mTc are typically in the range from ~100 MBq to ~1GBq. In experimental research on mice or phantoms, a much lower activity of ~10 MBq is typically used.
Table 1. Mostly used radiotracers in SPECT imaging.

| Radiotracer | Half-life | Photon energy [keV] |
|-------------|-----------|---------------------|
| Tc-99m      | 6.01 hours| 140.5               |
| In-111      | 2.8 days  | 171.28              |
| I-123       | 13.22 hours| 159                 |
| I-131       | 8.02 days | 364.49              |

Preclinical MRI-SPECT combines the high-resolution molecular information from SPECT with the excellent soft tissue contrast of MRI, together with localized chemical and physical information such as metabolite concentrations and water diffusion characteristics from MRI [1]. There is also the possibility of combining the chemical resolution of MRS with the sensitivity of the radiotracer. This would be a great tool in the study of drug pharmacokinetics and metabolism as well as therapeutic manipulations [2].

Karel Deprez et al have constructed an MRI compatible aperture using rapid additive manufacturing with selective laser melting of tungsten powder [3]. The main advantage of tungsten is high density and subsequent easy mechanical processing when it is mixed with polymer resin.

There are several groups in the Europe developed both preclinical and clinical SPECT insert systems based on SiPM detectors e.g. Hutton et al 2016 [4] or Carminati et al [5] who using the same type of material for multi-pinhole collimator as I do. Lai et al. proposed an inverted compound eye (ICE) camera design and a second-generation MRI compatible SPECT system (MRC-SPECT-II) based on hybrid pixel-waveform (HPWF) detector design that has been developed by our group over the past several years [1].

Nowadays there are practically two groups leading the development both based on CdTe or CZT sensors and pinhole collimators. Johns Hopkins University has developed an MRI-compatible pixelated CZT detector (256 pixels) providing excellent energy resolution of 3.8% at 140.5 keV and spatial resolution of 4 mm [6]. Second team is The company Gamma Medical Ideas, in collaboration with the University of California [7].

The first commercially available SPECT/MRI system is currently a preclinical in-line system by Mediso (nanoScan) combining 1 T MR with a traditional PMT-based SPECT [7]. Despite their excellent energy and spatial resolution, pixelated CdTe or CZT detectors are hardly scalable to static and MRI-compatible clinical systems because of cost and complexity (number of channels) issues.

1.1. Experimental MRI-SPECT insert system

Our MRI-SPECT insert system utilises hybrid semiconductor pixel detectors called Timepix. The main features and parts of the Timepix device including block diagram and description of individual measurement modes is summarized in [8]. These were equipped with 1 mm thick CdTe sensors with array of 1.41 x 1.41 cm, featuring 256 x 256 square pixels (55 µm x 55 µm) and a readout chip with an integrated preamplifier, discriminator and digital counter within each pixel. The functionality of detector Timepix in high magnetic field including characterization of charge collection direction inside the CdTe sensor and initial perspective for SPECT imaging is summarized in [9].

An illustration of the whole MRI-SPECT design based on the SPECT unit composed of Timepix detectors with CdTe sensors, MRI-compatible collimators and RF coil is shown in. The measured object - gelatine phantom (1H) with injected radio-isotopic gamma source (99Tc) - was inserted into the my own built RF coil (Ø = 35 mm, ω_01H = 200 MHz) [10] and placed into the developed MRI-SPECT system [Figure 1].
Figure 1. Experimental MRI-SPECT insert system for an MR animal scanner Bruker 47/20 composed of: a) SPECT unit equipped by two CdTe sensors Timepix (thickness 1mm), b) FITPix readout electronics, c) RF coil ($\Omega_{\text{inner}} = 1\,\text{mm}, f = 200\,\text{MHz}$), d) MRI-compatible collimator ($\Omega_{\text{outer}} = 1.29$, $\Omega_{\text{inner}} = 1\,\text{mm}$, $\Omega = 24.8\,\text{mm}$, thickness 8 mm, $\rho = 9\,\text{g cm}^{-3}$), e) Extension cable.

The data acquisition was performed by the Pixelman software [11]. A set of MRI-compatible collimators made from tungsten was placed directly above the CdTe sensors.

The whole small bore inset system (inner diameter of Bruker is 12 cm only!) was designed and made from MRI-compatible materials - conductive materials were replaced by different techniques (using of flexi cables, tungsten collimators, ...) or placed outside the gantry (FITPix device, electrolytic capacitors, ...). The influence of small parts (small sections of some electronic parts) exhibiting some magnetic properties has not been found [10].

2. Instruments and methods

In last work [10] shows a building of unique MRI-SPECT insert system based on CdTe pixelated sensors Timepix. It comprised design and construction of SPECT unit, collimator and Radiofrequency (RF) coil - everything MRI-compatible for operation in the high magnetic field of 4.7 T. Prosperous verification of the tungsten collimator for imaging (SPECT) and compatibility with MRI has been made. The whole insert system was composed and successfully tested on gelatine and tissue phantoms (1H) with an embedded radioisotopic source ($^{57}\text{Co} 122\text{keV} \gamma$ ray) inside the RF coil by the Bruker BioSpec 47/20 (4.7 T) MR animal scanner.

This paper is mainly focused on initial medical imaging of the small objects (~ 100 µm). It included design and realization of the multimodal ($^1\text{H}/^{99}\text{mTc}$) phantom idea, development and construction of the projection setup (motorization of the measured sample with own back-projection & fusing software) etc. Further the first simultaneous initial tests were made and mutual operation matters with their next possible solutions were explored.

For the purposes of this study, an MR animal scanner Bruker BioSpec 47/20 with high magnetic field of 4.7 T was used. This system is primarily intended for structural imaging based on proton density measurements with 200 MHz of resonant ($^1\text{H}$ nuclei) frequency.

2.1. SPECT back-projection software

While the MRI measurements were reconstructed by Bruker MRI software (Paravision 4.0), the reconstruction of the SPECT data were performed by custom back-projection software written in Matlab [12], retrieving size, shape and the location of the original radioisotopic source (for this case a distribution of volume activity) in the SPECT image. After independent reconstruction, the two resulting images were fused into a single hybrid MRI-SPECT image.

Before actual SPECT image reconstruction, each projection undergoes several pre-processing steps. An alpha-trimmed filter was used to reduce the salt and pepper-type noise caused by the low
quality of the gamma camera. This was followed by manual segmentation of the object and background. The whole background was then set to zero in order to enhance the contrast of the final result.

The SPECT image reconstruction is performed using filtered back projection (FBP). Even with a high number of projections (e.g. 180) the reconstructed image is still blurred. It is possible to reduce this effect by filtration (hence the name Filtered Back-projection) of each line of the sinogram. In this study, the Shepp-Logan filter was used [12].

The pre-processing and FBP were implemented in MATLAB with a self-developed graphical user interface (GUI). In the Projection window, it is possible to set SPECT parameters through several steps by using an Alpha-trimmed mean filter (AT filter), cut the image shape, centre the image, set image borders and set means with respect to shape. The Filtration window allows the choice of filter type, setting of parameters and to threshold adjustment (with respective to the size of the reconstructed object). The last Finalize window allows the fusion of MR images with the reconstructed SPECT image, transparency setting, and exporting of the final MRI+SPECT image.

2.2. Reconstruction of multimodal \(^1H/^{99m}Tc\) phantom

Due to the insert system arrangement (respectively the geometry of the used collimators) I designed and produce several \(^1H/^{99m}Tc\) inhomogeneous multimodal phantoms. The main idea and benefit to field of multimodal imaging is that \(^{99m}Tc\) is obtained from an elution generator in a form of physiological saline, containing a lot of free protons (\(^1H\)) which makes the main part of the phantom active not only for SPECT but also for MRI.

To verify the insert system for imaging of small-sized objects an eppendorf tube, embedded in a larger test tube was used as a multimodal \(^1H/^{99m}Tc\) phantom. This phantom was cast by standard boiled 4\% gelatine with gelatine pieces (to simulate living tissue) and the eppendorf tube was filled in three layers as shown in Figure 2. In the second layer, a cylinder made from Teflon (\(\varnothing = 600 \, \mu m, \ h = 6.5 \, mm\)) with the cavity filled by \(^{99m}Tc\) dissolved in saline solution was inserted.

![Figure 2](image)

**Figure 2.** Design of multimodal \(^1H/^{99m}Tc\) phantom: a) Test-tube (\(V = 50 \, ml, \ \varnothing = 29 \, mm\)), b) Eppendorf tube (\(V = 0.5 \, ml, \ \varnothing = 7.63 \, mm\)) filled in three layers: 1) Gelatine (\(V = 150 \, \mu l\)), 2) \(^{99m}Tc\) inside the cavity from teflon material, 3) gelatine (\(V = 150 \, \mu l\)).

Motorization of the SPECT unit in the presence of the high magnetic field is not a trivial task considering that the MR animal scanner Bruker is unshielded, this means it is not possible to operate typical electromagnetic motors inside or very close to the gantry.

A holder for electromagnetic step motor Microcon SX 16-0503 was constructed from wood and aluminium and placed at a distance of 80 cm beyond the tomograph Bruker (HW side). We have explored that at this distance the high magnetic field does not affect the motor’s operation or otherwise.

Connection between the motor and the insert system was made by use of fiberglass rod and brass bolts. This setup is intended for the rotation of the measured sample (in this case with weight about 50 g) embedded inside the insert system. It is feasible to perform projection angular steps every 2°. This yields up to 180 projections altogether from each sensor in one complete rotation.
2.3. MRI-SPECT measurements
The MRI measurements were performed by basic RARE (Rapid Acquisition with Relaxation Enhancement) sequence with different bandwidths. The measuring sequence was chosen to minimize the artifacts caused by used $^1$H/$^{99m}$Tc phantom and to increase the visibility of any artifacts given by the insert system.

To avoid the influence of the MRI measurement on the detector’s readout chip and also SPECT measurements on MR signal reception, the FITPix device was placed under the tomograph and measurements were performed in two steps:

1) Collect MRI data with unplugged SPECT detection setup (disconnected from voltage source and computer to prevent any influence on the homogeneity of the magnetic field);
2) After the MRI sequence, the SPECT measurement was performed by two CdTe sensors and double-pinhole tungsten collimators. Each projection was measured for 5 minutes, then the SPECT data was saved. After each angle rotation ($5^\circ$) of the insert system, the measurement continued. The angle rotation of $5^\circ$ was selected due to the best ratio between total measurement time and quality of result image.

3. Results
MR images (Figure 3) were obtained in Bruker scanner 4.7 T by RARE sequence ($TR = 3000 \text{ ms}, TE = 69.9 \text{ ms}, FA = 180^\circ$) with a total duration of 15 minutes per plane. Sagittal images are slightly burdened by artifacts in the form of stripes visible at the edges of the right part of each image, probably resulting from the wide bandwidth. Nevertheless, this small distortion of images has only negligible influence on the functionality of the system.

![Figure 3](image_url)

Figure 3. MRI of $^1$H/$^{99m}$Tc phantom: a) axial plane, b) sagittal plane wide bandwith ($BW = 100 \text{ kHz}$). Additionally, a wide bandwidth shortens the measuring period, which means that the higher gradient intensity leads to better suppression of inhomogeneities in the image.

SPECT data was obtained in 36 projections from two sensors (72 projections) by the electromagnetic step motor Microcon SX 16-0503, corresponding to gamma photons with energy higher than selected energetic threshold of 60 keV. Each projection was obtained recording 3000 frames with exposure time of 0.2 s at bias voltage -300 V with energetic resolution of 8.1777 keV [9]. Furthermore the data was evaluated, reconstructed (Figure 4a) and fused by SPECT-back projection software to the final 256 x 256 MRI-SPECT image (Figure 4b).
4. Conclusions & Future Work

Software for the evaluation of SPECT data (SPECT-back projection software) has been successfully developed. Reconstruction is independent from the number of used sensors in the SPECT unit. It is possible to fuse the reconstructed image with MRI data to the final MRI-SPECT image containing information from both modalities (for now, limited to 2D information).

Furthermore, a projection setup was designed and made with the intention of angular projections on the measured object - in this case, the novel multimodal ($^{1}$H/$^{99m}$Tc) phantom. The setup had to be considered utilizing magnetically-compatible materials with the possibility to perform 2° angular steps (SPECT projections) by the electromagnetic step motor placed out of reach of the high magnetic field.

Our goal was not to build an optimized preclinical insert system, but mainly to show the functionality of both methods operating in one common system inside a high magnetic field. This proof-of-principle concept was based on Timepix hybrid (prototype) technology available at the time and shows experimental confirmation. Nowadays, superior and thicker materials such as 2 mm CdTe or CZT sensors are accessible, as well as the newer Timepix 3 generations. These developments could bring possibilities of higher resolution, better homogeneity of the measured sample and shortening of the total measurement time.

Despite the above-mentioned issues, the MRI-SPECT insert system was modified and verified for imaging of an object in the size of 600 µm inside the MR animal scanner Bruker 47/20. MRI and SPECT images were consecutively obtained and successfully fused in a single image containing both structural and functional data.

Future steps will lead from this experimental insert into preclinical system mainly pertains to HW and SW modification. This includes using of new CdTe sensors which should bring better quality for whole gamma camera and shortening overall measurement time. Also the set of new collimators will be made and improving the other HW components of the insert system. Our main goal will be focused on 3D imaging of living objects (mice studies) and a further detailed exploration of the simultaneous operation of two different modalities.

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