Development and evaluation of quantitative imaging for improved estimation of radiopharmaceutical bio-distribution in small animal imaging

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Quantitative imaging techniques like Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT) are an essential part of the treatment planning based on dosimetry in targeted radiation therapy. Apart from Fluorine-18 (^{18}F), the potential of various other radionuclides with respect to the development of new radiopharmaceuticals which can be used for both diagnostic and therapeutic applications are increasingly under investigation. Three such radionuclides that are attractive for further research are Gallium-68 (^{68}Ga), Copper-64 (^{64}Cu)_and Zirconium-89 (^{89}Zr). To determine the performance of a PET or a SPECT, the National Electrical Manufacturing Association (NEMA) has published a standard set of protocols. However, there are limitations with the NEMA method with respect to the determination of the spatial resolution. Firstly, it does not take into account the overall behavior of the point spread function (PSF). Secondly, it has a very limited scope for a validation or a quality check criterion and thus the error of the calculated full width at half maximum (FWHM) cannot be determined.

In the first part of this work, the aim was to quantitatively develop, evaluate and improve the performance characteristics of the PET and SPECT subsystem of the Albira II pre-clinical tri-modal system (Bruker BioSpin MRI GmbH, Ettlingen, Germany) for the radionuclides ^{18}F, ^{68}Ga, ^{64}Cu and ^{89}Zr (PET) and ^{99m}T (SPECT). In this study, the sensitivity and spatial resolution characteristics of the systems based on a developed point source phantom were furthermore investigated for each of the radionuclides and compared with the NEMA protocol results based on measurements with a ^{22}Na point source. In addition, a new set of protocols was developed for quantitative image reconstruction with the respective systems.

In the second part of this work, an alternative method to accurately determine the PSF of an imaging system was developed to improve quantification accuracy in dosimetry. The developed method is based on 3-dimensional Gaussian fit functions taking into account the correction for the pixel size and the source dimension. Additionally, the effect of inaccurate determination of the PSF on the partial volume correction and hence the quantification of small structures in a diagnostic image was investigated.

The ability of quantitative image reconstructions was determined based on the recovery coefficients that showed that upto 95% and 60% activity values could be recovered with the PET and SPECT systems, respectively. Overall the system performed satisfactory with respect to the linearity for the activity range (8-10) MBq generally used for pre-clinical imaging for all the investigated radionuclides.

With respect to the determination of the system PSF, the method includes fitting of 3-dimensional functions, validation of fitting quality and choosing the best fit function based on the Akaike information criterion (AIC). The proposed method has advantages that it can better take into account the 3D distribution of the data and additionally yields an estimate for the error of the FWHM calculated from the estimated PSF. Furthermore, the investigation demonstrated that the PSF determined using the NEMA or another inadequate fit function can lead to a relative deviation of more than 40% for the recovery correction of small structures. Thus, the general method developed here can be used for obtaining robust and better reproducible PSFs for performing recovery corrections in PET/SPECT quantification studies and thus is a prerequisite for optimal evaluation of biokinetics in small animal studies.