

**PhD thesis:**  
**“Optimal Reconstruction Algorithms for High-Resolution Positron Emission Tomography”**

**Floris H.P. van Velden, PhD**

*Department of Nuclear Medicine & PET Research, VU university medical center, P.O. box 7057, 1007MB,  
Amsterdam, The Netherlands, email: f.vvelden@vumc.nl*

Supervision: Prof. Dr. A.A. Lammertsma (promotor) and Dr. Ronald Boellaard (co-promotor)

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The ECAT High-Resolution Research Tomograph (HRRT) is a dedicated human brain positron emission tomography (PET) scanner, with design features that enable high image spatial resolution combined with high sensitivity. The HRRT is the first commercially available scanner that utilizes a double layer of LSO/LYSO crystals to achieve photon detection with depth-of-interaction information. The HRRT consists of eight panel detectors, which are arranged in an octagon. Due to this geometry, gaps are present between detector heads, leading to missing data. Therefore, iterative reconstruction methods are the method of choice, as they do not require the missing data to be estimated prior to reconstruction. However, the 3D iterative reconstruction algorithm currently recommended by the supplier, ordinary Poisson ordered subsets expectation maximization (OP-OSEM), shows bias in short time frames due to non-negativity constraints. Consequently, implementation of analytical 3D filtered backprojection (3D-FBP) is of interest. To apply 3D-FBP, however, all missing data due to gaps between detector heads need to be estimated. Further improvements in HRRT image reconstruction might be expected when the variance on randoms is reduced. In previous studies, new iterative reconstruction algorithms, such as ordered subsets weighted least squares (OSWLS), showed promising results in bias reduction compared with OP-OSEM reconstruction. In this thesis, quantitative accuracy of various 3D iterative reconstruction and correction methods for the HRRT were assessed. The correction methods primarily concerned different attenuation correction methods (chapter 3), various strategies to estimate missing data (chapter 4) and random estimation techniques (chapter 5). Quantitative accuracy was assessed directly using both phantom and patient data. In addition, impact on pharmacokinetic analyses was assessed (chapters 6 and 7). Finally, performance of the HRRT was compared directly to that of a standard clinical whole-body PET scanner (ECAT EXACT HR+, chapters 2 and 8).

The thesis showed that attenuation and randoms correction methods for the HRRT are very accurate. Analytical 3D-FBP reconstructions in combination with a constraint Fourier space missing data estimation strategy can accurately predict activity concentrations, but still show high noise levels. In contrast, 3D iterative reconstruction techniques result in bias in short frames, which are typical for the early phase of a dynamic scan. This can lead to underestimation of pharmacokinetic values, such as the binding potential ( $BP_{ND}$ ), when a reference tissue method is applied. Nevertheless, accurate image derived input functions can be obtained, which can be attributed to the high spatial resolution of the HRRT. In summary, even with presently available software, the HRRT has excellent spatial resolution, sensitivity and reconstruction properties, with clinical results that are similar to those obtained with a standard clinical PET scanner when resolution is matched. As the HRRT can be operated at a much higher spatial resolution, results for smaller brain structures will be more accurate and, therefore, the HRRT should be the scanner of choice for human brain studies.