Iterative versus filtered backprojection reconstruction for statistical parametric mapping of PET activation measurements: a comparative case study

Authors:

(Published in: NeuroImage 2002; 15(1): 175-181)
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Abstract

The significance of task-induced cerebral blood flow responses, assessed using statistical parametric mapping, depends, among other things, on the signal-to-noise ratio (SNR) of these responses. Generally, positron emission tomography sinograms of \( H_2^{15}O \) activation studies are reconstructed using filtered backprojection (FBP). Alternatively, the acquired data can be reconstructed using an iterative reconstruction procedure. It has been demonstrated that the application of iterative reconstruction methods improves image SNR as compared to FBP. The aim of this study was to compare FBP with iterative reconstruction, to assess the statistical power of \( H_2^{15}O \)-PET activation studies using statistical parametric mapping. For this case study, PET data originating from a bimanual motor task were reconstructed using both FBP and maximum likelihood expectation maximization (ML-EM), an iterative algorithm. Both resulting data sets were statistically analyzed using statistical parametric mapping. It was found, with this dataset, that the statistical analysis of the iteratively reconstructed data confirm the a priori expected physiological response. In addition, increased Z scores were obtained in the iteratively reconstructed data. In particular, for the expected task-related response, activation of the posterior border of the left angular gyrus, the Z score increased from 3.00 to 3.96. Furthermore, the number of statistically significant clusters doubled while their volume increased by more than 50%. In conclusion, iterative reconstruction has the potential to increase the statistical power in \( H_2^{15}O \)-PET activation studies as compared to FBP reconstruction.

Introduction

Positron emission tomography (PET) is an imaging method that provides the opportunity to study brain function during the performance of a specific task. Task-related neuronal activation is coupled to changes in regional cerebral blood flow (rCBF) which can subsequently be measured. An activation study includes the acquisition of several scans for each of the task conditions. The distribution of counts is based on the annihilation event of the positron and electron, which produces two photons in opposite direction and is detected in coincidence by a detector pair. Each coincidence detector pair forms a line of response. Every coincidence event is stored in the sinogram which is formed by all possible lines of responses. These sinograms are reconstructed to obtain a transaxial image which, after spatial transformation (mapping one image into another), can be statistically analyzed.

Differential neuronal processing, due to varying task demands, is reflected in the measurements as an increase or decrease in rCBF. The significance of these
differences in rCBF is assessed by using multiple univariate regression analyses: statistical mapping. Hypothesized differences in regional cerebral activity due to task-related region-specific effects can be tested by creating statistical parametric maps (SPMs) (Friston et al., 1991, 1995b). Such effects are tested against a null hypothesis. The null hypothesis states that there is no activation effect due to the task tested. A student $t$ test is performed on each voxel of the brain using regression parameters. Significant effects are shown as $Z$ scores (calculated, within SPM95, from the conversion of $t$ statistics to normal distribution) in the SPM.

Evidently, the statistical values in these SPMs are influenced by the signal-to-noise ratio (SNR) in the PET activation images. The sensitivity of a PET activation study may thus increase either by influencing signal levels or by controlling noise levels. Alternatively, data processing and analyses, especially in the field of intra-subject realignment and inter subject stereo-taxic normalization, will also determine the power of the statistical test. However, the latter approach will not be discussed here.

Items that can be optimized are the dose of $H_2^{15}O$, the number of scans, and scan time. One option to improve SNR is to obtain more signal. The amount of injected radioactivity and the sensitivity of the PET camera influence the SNR. Development of three dimensional PET scanners resulted in better SNR images as compared to two dimensional PET images for equal total injected activity (Li and Votaw, 1998).

A higher overall count rate is associated with a better SNR. However, due to count rate limitations of the camera, increasing count rate above a certain level is of no use or even counterproductive. For activation studies with the $H_2^{15}O$ bolus method, an optimal injection dose and an optimal scan duration can be obtained. The radio tracer concentration may reach the limits of the system in terms of dead time correction and accidental coincidence count rate (Sadato et al., 1994). For $^{15}O$ water activation PET measurements, Kanno et al. (1991) found an optimal scan duration of 90-120s for obtaining the maximal SNR.

Another way to improve SNR is to optimize the number of acquisition replications for each condition without changing the overall dose applied (Cherry et al., 1993; Sadato et al., 1994). Multiple acquisitions for each condition reduce the uncertainty in measured brain radioactivity uptake and thus increase statistical power of a brain region in SPM. However, increasing the number of scans implicates an increase in total session time, which is limited by subject comfort considerations. Special precautions have to be taken to minimize movement artifacts arising from multiple measurements. In the data analysis, a realignment procedure is one of the first steps in correcting for inter scan movement artifacts.

SNR improvement can also be achieved by using switched paradigms (Cherry et al., 1995). Switched paradigms can be used to maximize the difference signal in bolus injection activation studies by switching task execution from activation to
control during the activation scans and vice versa during the control scans, before
the washout phase. In this manner tracer distribution is manipulated by switching
task execution when the tracer concentration in the brain reaches a maximum.
This results in images that maximize the difference signal instead of seeking to
quantitate blood flow.

SNR can also be improved by reducing the amount of noise in the PET images.
One method for reducing noise levels in image data is to use a spatial smoothing
procedure. After realignment and spatial normalization, the PET images are spa-
tially smoothed (convolution with a Gaussian kernel). Various filter parameters can
be chosen for this spatial smoothing. These filter parameters, adjusted to camera
resolution as well as to the constraints imposed by the random Gaussian field
theory and stereo-taxic normalization considerations, influence the significance
scores in the SPM analyses.

Iterative reconstruction methods are known, in general, to improve recon-
structed image quality compared to filtered back projection (FBP) reconstruction,
especially in the case of relatively poor statistics. So a lower noise level (Liow and
Strother, 1994) can also be obtained by using an iterative reconstruction, instead
of the standard FBP reconstruction. The application of iteratively reconstructed
instead of FBP-reconstructed images into the statistical analyses might thus yield
higher significance scores or an increased number of statistically significant areas
in the statistical parametric maps.

Iterative reconstruction applications in emission tomography were introduced
by Shepp and Yardi (1982). It has been shown that maximum likelihood expecta-
tion maximization (ML-EM) images generally have a better SNR as compared to
images reconstructed with FBP (Liow and Strother, 1994; Liow et al., 1997; Comtat
et al., 1998; Nuyts et al., 2001; Qi and Huesman, 2001).

The major problem with ML-EM is the absence of an objective stop criterion.
Another disadvantage is that it is computationally time consuming. To overcome
the second problem an accelerated iterative reconstruction, using ordered subsets
of projection data, can be used to reduce computation time. An iteration of ordered
subsets EM (OS-EM) is defined as a single pass through all the subsets defined. The
OS-EM algorithm provides an acceleration over EM without losing quality (Hudson
and Larkin, 1994).

The aim of this study was to compare an iterative reconstruction algorithm
with a FBP algorithm, to assess the statistical power using statistical paramet-
ric mapping of \(^{15}O\)-PET activation studies. Therefore a PET activation study
published previously (de Jong et al., 1999) was reanalyzed after both FBP and
OS-EM reconstruction. Although this case study may show limited potential for
generalization, it should indicate whether it is worthwhile to pursue this line of
research.
Methods

PET data used for the comparison of different reconstruction methods originated from a bimanual motor task (de Jong et al., 1999). In that study a distribution of cerebral activations was described in relation to the change between two bimanual movement patterns.

Eight normal volunteers, each having four consecutive rCBF scans, participated in the study. Participants had to stretch and flex their fingers in alteration, paced by a regular auditory signal, in three conditions (A, B and C). In brief, both hands had to move in-phase in condition A, while in condition B anti-phase movements were made. In these two baseline conditions (A and B), an additional irregular auditory stimulus cued subjects to make an extra bimanual movement without changing phase. In condition C, subjects had to make the same stretching and flexing movements as in A and B, however, the secondary signal now indicated that they had to switch between the phase and anti-phase patterns (for more detail see: de Jong et al., 1999).

Data acquisition

The PET system used for the data acquisition was a Siemens ECAT 951/31 whole-body positron camera, which acquires 31 planes simultaneously over an axial length of 10.8 cm in 2D mode only. The PET scans were performed after a bolus injection of a fixed dose of 1.85 GBq of $H_2^{15}O$ for each scan. The tasks started just after the injection and continued during the scanning period. The scan was started when the $H_2^{15}O$ reached the brain, 20 s after injection generally, and lasted 90 s. Scans were made at 15-minutes intervals.

Image reconstruction

For the purposes of the present study the acquired sinograms were reconstructed in two ways: using the standard FBP algorithm and using the OS-EM iterative reconstruction algorithm. In both reconstruction algorithms images were attenuation corrected from a measured transmission scan and corrected for dead time and accidental coincidences. The FBP reconstruction algorithm applied a Hanning window with a cutoff of 0.5 cycle per pixel.

Different numbers of iterations (1,2,3,4 and 8) and subsets (1,2,4,8,16 and 32), were applied. These OS-EM-reconstructed images were visually compared with each other and with the FBP-reconstructed image. In the case of visually equivalent images, when the product of iterations and subiterations was equal, the minimum number of iterations was chosen because of computing efficiency. The OS-EM images were judged by three independent observers. The image reconstructed
with one iteration and 16 subsets (image C in figure 3.1) was unanimously selected as the best. These reconstruction parameters were subsequently used for all image reconstructions.

**Data analysis**

FBP- and OS-EM-reconstructed images were independently realigned and normalized, i.e. transformed into standard stereo-taxic space using the SPM95 software (Friston et al., 1995a; Talairach and Tournoux, 1988). Hypothesis testing was performed by use of statistical parametric mapping (SPM95 software from the wellcome department of cognitive neurology, London, UK). Statistical parametric mapping is the construction of spatially extended statistical processes to test a hypothesis on regionally specific effects in imaging data (Friston et al., 1991; Worsley et al., 1992; Friston et al., 1994). The SPM95 software was used to mimic the data analysis parameters of the original publication (de Jong et al., 1999). An additional argument was that the normalization procedure in SPM95 seems to be more appropriate for analyzing data from scanners with a smaller axial field of view, i.e. 10.8 cm, than more recent versions of SPM.

Similar to de Jong et al. (1999), the FBP scans were smoothed using an isotropic Gaussian kernel of 10 mm FWHM (full width at half maximum), resulting in a resolution of [x, y, z]=[11.0, 12.8, 11.6] mm FWHM, recorded from the SPM output, for the images used for the statistical analyses. Smoothing the OS-EM data with the same Gaussian kernel of 10 mm FWHM a resolution of [x, y, z]=[13.7, 12.7, 11.5] was obtained. FWHM in the y and z directions were about equal in both FBP and OS-EM data, but in the x-direction the FWHM differed by 2.7 mm. To obtain identical resolution of the iterative reconstructed images, the OS-EM images were filtered with an anisotropic Gaussian kernel (6.2, 10.3, and 10.2 mm FWHM). Subject and condition effects were estimated using the general linear model (Friston et al., 1995b). As in the original analyses, global activity was included as a nuisance covariate so the analysis was regarded as an ANCOVA. Images were scaled to a mean global activity of 50 ml/100ml/min.

Hypotheses about regionally specific condition effects were tested, comparing the estimates using linear compounds or contrasts. The resulting set of voxel values constitutes an SPM of the \( t \) statistics. These SPM\( t \) were transformed to the unit normal distribution SPM\( Z \). In addition to voxel based analyses, clusters of voxels can be examined. A cluster is defined as voxels which are spatially connected with each other in terms of edge, face, or vertex. The threshold of \( Z \geq 3.00 \) was used for the peak value voxel of a cluster to compare cluster information for the two reconstruction methods.
Figure 3.1: Different reconstructed images, from left to right: (A) FBP reconstructed image, (B) OS-EM reconstructed image using one iteration and eight subsets, (C) OS-EM reconstructed image using one iteration and sixteen subsets, and (D) OS-EM reconstructed image using one iteration and thirty-two subsets. The reconstruction parameters of image C were chosen for all image reconstructions.
Table 3.1: Brodmann areas with accompanying Talairach coordinates and Z score, thresholded at $Z \geq 3.00$, of the present statistical analysis with FBP reconstructed data.

<table>
<thead>
<tr>
<th>Brain area</th>
<th>L/R</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>$Z$</th>
<th>kE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial frontal gyrus</td>
<td>R</td>
<td>6</td>
<td>48</td>
<td>16</td>
<td>3.90</td>
<td>94</td>
</tr>
<tr>
<td>Superior temporal gyrus</td>
<td>R</td>
<td>60</td>
<td>-48</td>
<td>12</td>
<td>3.11</td>
<td>9</td>
</tr>
<tr>
<td>Parietooccipital sulcus</td>
<td>R</td>
<td>14</td>
<td>-80</td>
<td>32</td>
<td>3.08</td>
<td>8</td>
</tr>
<tr>
<td>Premotor cortex</td>
<td>R</td>
<td>20</td>
<td>14</td>
<td>48</td>
<td>3.06</td>
<td>46</td>
</tr>
<tr>
<td>Lateral parietooccipital sulcus</td>
<td>L</td>
<td>-28</td>
<td>-66</td>
<td>32</td>
<td>3.00</td>
<td>36</td>
</tr>
</tbody>
</table>

L/R = left or right hemisphere; (x,y,z) = Talairach coordinates in mm
kE = cluster size in voxels; BA = Brodmann area

**Results**

The statistical analysis method used to analyze the data sets was identical to the original statistical analysis (de Jong et al., 1999). Applying an uncorrected significance threshold of a $Z$ score of $\geq 3.00$, group rCBF analysis of the FBP-reconstructed images revealed five cortical foci of activation and group analysis of the OS-EM reconstructed images revealed ten cortical foci of activation. These areas, expressed in Talairach coordinates and Brodmann areas, and accompanying $Z$ scores are listed in table 3.1 for FBP reconstruction and in table 3.2 for OS-EM reconstruction. These activations are specifically related to the change between the two movement patterns (condition C) in comparison with baseline tasks A and B.

Increased rCBF using FBP-reconstructed data was observed over the right medial frontal gyrus (Brodmann area BA 9 and 10), the right superior temporal gyrus (BA 22), the right parietooccipital sulcus (BA 19 bordering precuneus BA 7), the right premotor cortex (BA 6), and along the sulcus demarcating the posterior border of the angular gyrus in the left inferior parietal lobe (BA 39). Coordinates are reported in table 3.1.

The original analysis (de Jong et al., 1999) showed four cortical foci of activation. Results were presented, uncorrected for multiple comparisons, which was allowed because of an *a priori* hypothesis (Friston et al., 1991), at a threshold of $P<0.001$, identifying all regions that included voxels with a $Z$ score $> 3.00$. These four areas with increased rCBF are indicated in table 3.3. The premotor and the posterior parietal areas were *a priori* expected to be activated significantly.
### Results

**Table 3.2:** Brodmann areas with accompanying Talairach coordinates and Z score, thresholded at $Z \geq 3.00$, of the statistical analysis with OS-EM reconstructed data.

<table>
<thead>
<tr>
<th>Brain area</th>
<th>L/R</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Z</th>
<th>kE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral parietooccipital sulcus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior border angular gyrus</td>
<td>L</td>
<td>-26</td>
<td>-66</td>
<td>32</td>
<td>3.96</td>
<td>91</td>
</tr>
<tr>
<td>Lingual gyrus</td>
<td>L</td>
<td>-22</td>
<td>-52</td>
<td>0</td>
<td>3.70</td>
<td>29</td>
</tr>
<tr>
<td>Inferior frontal gyrus</td>
<td>R</td>
<td>34</td>
<td>24</td>
<td>-12</td>
<td>3.32</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>R</td>
<td>44</td>
<td>16</td>
<td>-12</td>
<td>3.08</td>
<td></td>
</tr>
<tr>
<td>Precuneus</td>
<td>R</td>
<td>36</td>
<td>-62</td>
<td>44</td>
<td>3.22</td>
<td>29</td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>L</td>
<td>-32</td>
<td>50</td>
<td>-4</td>
<td>3.15</td>
<td>7</td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>R</td>
<td>34</td>
<td>30</td>
<td>40</td>
<td>3.14</td>
<td>11</td>
</tr>
<tr>
<td>Medial frontal gyrus</td>
<td>R</td>
<td>0</td>
<td>50</td>
<td>16</td>
<td>3.12</td>
<td>32</td>
</tr>
<tr>
<td>Frontal operculum</td>
<td>L</td>
<td>-44</td>
<td>8</td>
<td>8</td>
<td>3.11</td>
<td>15</td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>R</td>
<td>10</td>
<td>28</td>
<td>48</td>
<td>3.03</td>
<td>58</td>
</tr>
<tr>
<td>Left middle temporal gyrus</td>
<td>L</td>
<td>-38</td>
<td>-50</td>
<td>8</td>
<td>3.02</td>
<td>5</td>
</tr>
</tbody>
</table>

L/R = left or right hemisphere; (x,y,z) = Talairach coordinates in mm

**Table 3.3:** Brodmann areas with accompanying Talairach coordinates and Z score, thresholded at $Z > 3.00$, of the original (de Jong et al., 1999) statistical analysis with FBP reconstructed data.

<table>
<thead>
<tr>
<th>Brain area</th>
<th>L/R</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial frontal gyrus</td>
<td>R</td>
<td>6</td>
<td>48</td>
<td>16</td>
<td>3.46</td>
</tr>
<tr>
<td>Premotor cortex</td>
<td>R</td>
<td>20</td>
<td>12</td>
<td>48</td>
<td>3.42</td>
</tr>
<tr>
<td>Parietooccipital sulcus</td>
<td>R</td>
<td>14</td>
<td>-80</td>
<td>32</td>
<td>3.37</td>
</tr>
<tr>
<td>Posterior border precuneus</td>
<td>R</td>
<td>14</td>
<td>-80</td>
<td>32</td>
<td>3.37</td>
</tr>
<tr>
<td>Lateral parietooccipital sulcus</td>
<td>L</td>
<td>-28</td>
<td>-66</td>
<td>32</td>
<td>3.42</td>
</tr>
<tr>
<td>Posterior border angular gyrus</td>
<td>L</td>
<td>-28</td>
<td>-66</td>
<td>32</td>
<td>3.42</td>
</tr>
</tbody>
</table>

L/R = left or right hemisphere; (x,y,z) = Talairach coordinates in mm

BA = Brodmann area
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Table 3.4: General items of both FBP and OS-EM reconstructed statistically analyzed data, using the standard SPM threshold of $Z \geq 3.00$.

<table>
<thead>
<tr>
<th></th>
<th>FBP</th>
<th>OS-EM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regions</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Total cluster size</td>
<td>193</td>
<td>314</td>
</tr>
<tr>
<td>Resels *</td>
<td>574</td>
<td>596</td>
</tr>
<tr>
<td>Search volume §</td>
<td>58474</td>
<td>60840</td>
</tr>
</tbody>
</table>

§ in voxels
* resels = resolution elements

Increased rCBF using OS-EM-reconstructed data was found to be most prominent along the sulcus demarcating the posterior border of the left angular gyrus (BA 39). This focus and associated activations are reported with their locations in table 3.2. A noticeable result of OS-EM reconstruction was that the expected physiological response, reflecting activation of the posterior border of the left angular gyrus, appeared as the most significant area ($Z = 3.96$ table 3.2) in contrast with a fifth place ($Z = 3.00$ table 3.1) in FBP-reconstructed analysis.

Comparison of tables 3.1 and 3.2 revealed variations in the numbers of clusters and in cluster sizes, which can be a result of the two different reconstruction procedures. In the OS-EM situation more clusters reached the threshold of interest of $Z \geq 3.00$ uncorrected as compared to the FBP situation (ten versus 5). More general items for comparison are listed in table 3.4. It should be noted that with identical resolution, the number of clusters and the total cluster size, i.e. number of voxels included in the clusters, are larger in the iterative reconstruction situation.

In a subsequent experiment with slightly modified control conditions, included in the study of de Jong et al. (1999), activation at the left angular gyrus was replicated. In the present comparative study, the results of the statistically analyzed OS-EM-reconstructed data, with dominance of this left angular gyrus, activation is in better conformity with de Jong and colleagues major activation than the FBP-reconstructed results.

Discussion

Statistical results using the FBP-reconstructed images in this comparative case study showed only minimal differences from the originally published results. These small differences were probably due to a difference in the realignment procedure (AIR (Woods et al., 1992) vs SPM95). The second area (BA 22), as shown in table 3.1,
did not reach statistical significance in both the original publication and the OS-EM-reconstructed data. This may indicate that this area is only slightly activated, making it susceptible to small changes in statistical power.

It was hypothesized that, with identical spatial resolution, the statistical analysis of both OS-EM-reconstructed and FBP-reconstructed images should result in higher $Z$ scores for the OS-EM case. In the OS-EM-reconstructed images, as compared to FBP-reconstructed images, more statistically significant areas were found (ten vs five) and more voxels (314 vs 193) reached the significance threshold of $Z \geq 3.00$ (as shown in table 3.4). The expected physiological response, in the posterior border of the left angular gyrus, appeared at the fifth position in rank order ($Z = 3.00$ table 3.1) in the FBP case, while in the OS-EM situation it appeared with the highest statistical $Z$ score ($Z = 3.96$ table 3.2). This enhancement of the statistical inference situation is consistent with an improved SNR in the OS-EM-reconstructed data, resulting in more voxels and a larger number of clusters to reach the uncorrected threshold of $Z \geq 3.00$ (table 3.1, table 3.2 and table 3.4).

Furthermore, a larger number of resels were observed in the OS-EM data, representing a larger search volume (table 3.4). Thus a larger part of the brain is available for statistical analysis. Note that, due to the Gaussian random field theory, an increase in the number of resels should give a less significant result. However, despite this expanded search volume the statistical results are actually better in the OS-EM data. As the computed resolutions for both reconstruction methods are identical, the differences in search volume are probably due to differences in spatial transformations during the preprocessing steps.

In the original publication of de Jong et al. (1999), the left parietal activation was regarded as the dominant physiological response. One of the arguments for this was replication of this activation in a subsequently described experiment with slightly modified control conditions. Right premotor cortex activation was not replicated in the second experiment. de Jong et al. (1999) provided a consistent explanation for the differences between the two experiments. The right premotor activation was not significant in the OS-EM-reconstructed data. It remains to be shown whether this indicates a false-negative finding or rather a false-positive finding for the FBP-reconstructed data.

As discussed above, OS-EM reconstruction improves $Z$ scores as compared to FBP at a calculated resolution of 11.0 by 12.8 by 11.6 mm. This may not be the optimal filter parameters in terms of maximal $Z$ scores. Consequently, it can be argued that differences found in the statistical analyses of either OS-EM- or FBP-reconstructed data, are an artifact of non optimal filtering rather than an actual effect caused by differences in the reconstruction process. Using arbitrary resolution analysis it could be determined that the improvement in $Z$ scores is independent of resolution (data not shown), which strengthens the result that iterative reconstruction offers an option to improve statistical power in $H_2^{15}O$-PET activation studies.
Thus, OS-EM reconstruction not only showed an overall improvement in $Z$ scores, but also better confirmation of the \textit{a priori} expected physiological response which indicates that with the OS-EM reconstruction algorithm a real increase in statistical power, using SPM applied on this dataset, was obtained.

In contrast, Liow et al. (1997) found a decrease in the average $t$ values in comparing an iterative reconstruction procedure to standard FBP. This, however, in not in contrast with our study since they used different statistics, compared only two activated foci, and, most important, did not match resolution.

In our study the numbers of iterations and subiterations were visually optimized. It can be argued that the best combination of iterations and subiterations has to be acquired according to optimizing statistical $Z$ scores. However, this method may introduce artifacts, when using too many iterations, and is project dependent. Therefore, the acquired optimal combination has to be verified for other activation studies.

This case study has several limitations which need to be investigated in the future. In this chapter, bias variance or resolution variance issues, which characterize a reconstruction method's performance, are not introduced. The variance and the signal need to be investigated to identify the sources of the observed differences between FBP images and OS-EM images. Also, results of this case study were obtained with independently spatially transformed data; i.e., the spatial transformation parameters are not identical for the FBP- and OS-EM-reconstructed images. Consequently, the relative contributions of the different steps in the preprocessing (reconstruction, filtering, realignment, and spatial normalization) and the statistical analysis to the improvements in statistical power observed in this study cannot be specified. Although this may be unsatisfactory from a scientific viewpoint, it is the overall improved $Z$ scores which are of practical importance. Finally, since this is only a case study one should be cautious about the generalization of our results.

However, there are no apparent reasons why the improvements due to OS-EM instead of FBP reconstruction, as found in this study, should not hold in general. This includes acquisitions in 3D rather than 2D mode since, considering also count rate limitations, the increased sensitivity is generally used to increase the number of repetitions and, thus, improve the statistical power of the study, rather than to attempt to maximize the signal-to-noise ratio of the individual scan. Nevertheless, a more general and detailed study may be worthwhile to assess the pros and cons of OS-EM reconstruction and to assess the effect of OS-EM reconstruction on each single step of a PET activation study.

In conclusion, iterative reconstruction has the potential to improve statistical power in $H_2^{15}$O-PET activation studies as compared to FBP reconstruction.
References


