Multi-Centre Assessment of HRRT Image Uniformity via $^{68}$Ge and $^{18}$F Cylindrical and Anthropomorphic Phantoms

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Abstract—To date, the high resolution research tomograph (HRRT) still offers the highest resolution PET imaging capability of the human brain. Spatial uniformity of the images is of paramount importance, as many radioligand studies require either accurate regional dynamic quantification or, at the very least, accurate measurement of relative activities between regions. Often uniform cylinders, of $^{68}$Ge or $^{18}$F, are used for quality control and calibration purposes. This work examines the spatial uniformity obtained in reconstructed images of uniform cylinders from seven different HRRT centres, using either $^{68}$Ge or $^{18}$F, and also considering a head and brain phantom filled with $^{18}$F scanned at three of the centres. To account for varying activity levels used in each centre’s data acquisition, and possibly different image reconstruction parameters, a progressive smoothing method was used to analyze image uniformity, with metrics designed to assess non-uniformity in image planes as well as in randomly selected region of interest pairs. Unusually high image non-uniformities were found for germanium cylinders at two centres, but of greater concern was the fact that uniformity for the brain phantom was found to be notably inferior at two of the three centres which scanned the phantom. A change of mu-map reconstruction parameters, and minor adjustment of a parameter used in the single scatter simulation, was shown to remedy the issue (reducing relative region errors to <5%).

I. INTRODUCTION

FULLY 3D dynamic PET imaging with the high resolution research tomograph (HRRT) [1] provides the highest resolution human brain PET imaging available anywhere in the world. Time sequences of 3D images are used to estimate either 3D parametric functional images (e.g. neuroreceptor binding potential (BP) maps) or to find these functional parameters for specific volumes of interest (e.g. BP in the striatum). For these functional parameter estimates to be reliable, spatial uniformity in the reconstructed images is extremely important, whether absolute quantification is desired or whether a reference tissue method is used [2, 3]. Although previous HRRT multi-centre comparisons have been done [4], this work initiates a specific focus on reconstructed spatial uniformity for the HRRT at different centres, using uniform cylinders (filled either with $^{68}$Ge or with $^{18}$F) and also a realistic anthropomorphic head and brain phantom (filled with $^{18}$F) [5]. This phantom has the advantages of complex realistic attenuation and scatter properties, whilst also providing a simple large uniform volume (~1200 mL) for a straightforward analysis. Seven HRRT centres have so far contributed data: Aarhus (Denmark), Baltimore (USA), Cologne (Germany), Copenhagen (Denmark), Montreal (Canada), Turku (Finland) and Vancouver (Canada). Since each centre is likely to use slightly different reconstruction parameters for the emission data and scan a different level of radioactivity in the scanner field of view (FOV), a particular challenge is to assess uniformity in a way which is insensitive to these less-important variations between centres, whilst preserving any issues arising from other more-important differences between centres (such as the quality of the attenuation and scatter corrections, or the scanner setup).

II. METHODS

The following analysis seeks to minimize the effect of phantom activity and the emission image reconstruction parameters on the uniformity metrics considered, through use of progressive smoothing levels applied to the emission images. Increased smoothing (with careful control for edge effects) reduces the impact of count level and reconstruction method/parameters, whilst leaving the basic structure of any low-spatial frequency non-uniformities intact. Low-spatial frequency non-uniformities are expected to arise within a given volume (which should otherwise be uniform) if the attenuation and scatter correction are inaccurate.

First, based on the $\mu$-map, a major central sub volume of the emission image, which is expected to be uniform, was identified, staying at least several voxels clear from the edges. Having identified a sub volume, analysis was carried out without smoothing, and then with progressive degrees of smoothing. Each 3D smooth of a reconstructed emission image $f$ used a 3D Gaussian convolution kernel $g$, (full width
at half maximum (FWHM) of 5.73 mm) and was normalized to reduce edge effects:

\[ f_{SM}^{j} = m_{j} \left( f \ast g \right)_{j} + (1 - m_{j}) f_{j} \]  

(1)

where \( m \) is a 3D mask image containing values of 0 or 1 only, with the values of 1 indicating which of the \( j=1\ldots J \) voxels are in the sub volume of interest. The smoothed image result \( f_{SM}^{j} \) is effectively smoothed by a shift-variant (due to truncation) Gaussian kernel at the edges of the sub volume, by a shift-invariant kernel within the sub volume, and not smoothed at all outside the sub volume. All centres used ordered subsets expectation maximization (OSEM) [6] [7] to reconstruct their emission data into 3D image arrays of 256×256×207 voxels (voxel side length 1.21875 mm), but with potentially different numbers of iterations, and use or non-use of image-space point spread function (PSF) modeling [8-10].

Two uniformity analysis procedures were performed for the image obtained at each smoothing level. In the first analysis, 10 million random voxel pairs were selected from the sub volume. The ratio of any pair of voxel values is expected to be equal to 1.0 for a uniform volume. With increased smoothing, the value in any given voxel corresponds to a regional average (according to the kernel used to smooth), and so this first analysis also gives a useful insight into relative uniformity between larger sized regions of interest (ROIs). Statistical noise due to limited counts, imperfect reconstruction and data corrections will all cause deviations from a value of 1.0 for the ratio test. The ratio analysis was repeated for 3 iterations of smoothing (example results are shown much later in this work).

The second uniformity analysis, which in fact forms the main focus for what follows, considered voxel values in three sets of sequential planes: the average voxel value in sagittal planes, coronal planes and transverse planes. For each case, only the values in the planes which intersected the sub volume were considered. The mean of the voxel values in a plane should not change with respect to the position of the plane in the reconstructed volume, and so calculating the coefficient of variation (CV) of these planar means gives an indication of non-uniformity for the three sets of planes under consideration (transverse CV, coronal CV and sagittal CV). As for the first analysis, this analysis was carried out for no smoothing, and for three iterations of image smoothing to seek to reduce the impact of activity concentration in the phantom (example results of this analysis are shown later in Fig. 4).

In addition to assessing uniform cylinders, a uniformly filled anthropomorphic head and brain phantom was used for the analysis (Fig. 1), which is commercially available (RSD/Capintec). One acquisition of 60 minutes of the brain phantom was considered (using ~1 mCi \(^{18}\)F to fill the main brain volume), followed optionally by 10 hours of further acquisition (this optional acquisition was used for just part of the following analysis, for which only Montreal data were considered).

**III. RESULTS**

Figs. 2 and 3 demonstrate first that the planar non-uniformity CV measures used in this work are relatively invariant to OSEM iteration number, use of PSF modeling, and also the quantity of radioactivity in the scanner FOV. This important result means that uniformity can be compared between different centres.

Fig. 4 shows example results for the planar non-uniformity measure for the three sets of planes for a Montreal germanium cylinder.
Fig. 3. Example non-uniformity measurements from the head and brain phantom filled with $^{18}$F scanned with the Montreal HRRT, for 21 different scan frames (frame 1 of 60 minutes duration, and frame/scans 2-21 of 30 minutes duration each (10 hours total)). Over a period >10 hours, the planar CV measures are approximately invariant, so data acquired at different count levels from different centres can be pooled together for comparison when using the planar CV non-uniformity measures (TR=transverse, CO=coronal, SA=sagittal).

Fig. 4. Example results for the planar non-uniformity measures: the solid central red line in each plot indicates the mean of the planar means, and the dashed red lines indicated +/- 5% deviation from this mean. The coefficient of variation (CV) can therefore be found for each set of planes.

Fig. 5 compares uniformity for cylinders acquired at seven centres: Montreal (shown by crosses), Aarhus (AARH), Baltimore (BALT), Cologne (COLO), Copenhagen (COPE), Turku (TURK) and Vancouver (VANC). The uniformity performance for the 322 Montreal cylinder reconstructions looks good, in that the non-uniformity CV values found cover a range of CV values which are competitive with those from other HRRT centres.

Some centres however, Cologne and Baltimore, show inferior uniformity for the large $^{68}$Ge cylinders, and this is expected to be due to:

1. The single scatter simulation [11] parameter (“layer background energy ratio”, LBER, %) used for generating the scatter sinograms for use with the ordinary Poisson OSEM reconstruction algorithm. This LBER parameter, which compensates for the fact that the HRRT energy window seems to accept more low-energy events than expected, was tuned
using smaller $^{18}$F cylinders, filled with water rather than gel. This means that the LBER would not necessarily be optimal for uniformity over a larger volume of the FOV (such as that covered by a large 8 litre $^{68}$Ge cylinder), and furthermore, lack of usage of germanium cylinders by a centre may mean that a centre’s reconstruction of the $\mu$-map for the germanium cylinder may not be accurate. The $\mu$-value is expected to be 0.102 cm$^{-1}$ for the solid germanium phantoms, and this can be imposed through use of correct prior parameters with the MAP-TR reconstruction algorithm [12].

2. Some centres do not use plane calibration factors – thereby leaving a higher axial non-uniformity (manifested as high transverse plane CV / non-uniformity).

3. Scanner setup / performance can be different between centres, for example the Cologne scanner does not have the same specification as the HRRTs at other centres.

Fig 6. shows the reconstructions of the head and brain phantom from the three centres which scanned the phantom, along with the differing $\mu$-maps. Fig. 7 compares the non-uniformity measures for the brain phantom reconstructions, placing the results alongside results for the uniform cylinders obtained by the same 3 centres. The chosen uniform cylinder for the Montreal results corresponds to the germanium cylinder which was scanned on the same day as the brain phantom. It is immediately apparent that there are issues for the brain phantom reconstruction for the Montreal data: the uniformity is clearly impaired in the coronal and transverse planes (i.e. a larger coronal CV and transverse CV), in comparison to results from Copenhagen. Furthermore, there is a similar, but less emphatic, problem with the Vancouver results.

![Fig. 6. OSEM reconstructions of the head and brain phantom (transverse, coronal and sagittal sections) from the three centres which scanned the same phantom, along with a sagittal section of the $\mu$-map (mu map) from each centre.](image)

Fig. 8. shows the uniformity profiles for the sets of planes for the different centres, clearly showing where the coronal and transverse plane non-uniformity comes from: there is a gradient in the mean values of the planes for the coronal and transverse planes, for both the Montreal and the Vancouver data, which is not seen for the Copenhagen data. It is important to note that this issue was not revealed by the uniform cylinder analysis (previous Fig. 5), but only by analyzing the brain phantom. As a consequence, a number of changes were explored for the Montreal data. The single scatter simulation was changed to a newly released fully 3D version for the HRRT data [13], but as reported in that work, there was little impact on uniformity. However, changing the $\mu$-map reconstruction parameters (which affect both the attenuation and scatter correction) to match those of the Copenhagen reconstruction (see specific details in Fig. 9) did have a significant impact on uniformity, as demonstrated in Fig. 10. Fig. 11 shows the effect of changing the LBER for the single scatter simulation, with Fig. 12 justifying the change to LBER=9% for the new $\mu$-map reconstruction parameters, through use of the voxel-pair ratio uniformity measure (described earlier in section II and illustrated in Fig. 13).

![Fig. 7. Non-uniformity measures for OSEM reconstructions of the head and brain phantom (shown as red squares) from the three centres which scanned the same phantom, placed alongside cylinder results. For the comparison to be meaningful with the uniform cylinders, the uniformity was assessed only over a sub volume of the uniform cylinders which matched the uniformity analysis sub volume for the brain phantom. “MTL” = Montreal.](image)
Fig. 8. Mean values in planes for the head and brain phantom for the three centres. There is clearly a gradient in the coronal and transverse planes for the Montreal and Vancouver data, particularly for the case of the transverse planes for the Montreal data. Note the units for the average voxel value for the Vancouver data are kBq/mL (and Bq/mL for Copenhagen and Montreal).

Fig. 14 shows the \( \mu \)-maps reconstructed with the new parameters, and their impact on the emission reconstruction is shown in Fig. 15 (the gradient in the transverse and coronal planes is now nearly removed).

Fig. 16 pools together the non-uniformity measures for the 3 centres, for both cylinder data and the brain phantom data, importantly using a common sub-volume for the uniformity analysis (the sub volume expected to be uniform in the brain phantom was also used to re-assess uniformity in the same sub volume of the uniform cylinders).

Fig. 17 (with Fig. 18) demonstrates the impact of the non-uniformity, and its correction for the Montreal data: without the correction, errors as large as 10% could be obtained in relative region analysis (pertinent to reference region methods for BP estimation). With the correction, these errors are now below 5%. Finally Fig. 19 shows the new emission reconstructions for the Montreal data.

Fig. 9. Reconstruction parameters which were in use in Montreal for the \( \mu \)-map of the head and brain phantom alongside the new parameters used (based on those from Copenhagen).

Fig. 10. Transverse and coronal plane non-uniformity is improved by the new \( \mu \)-map (but with a minor change in the LBER from 7% to 9%). With the old \( \mu \)-map, CV is greater than 4% for transverse planes. The graph actually considers not just the 60 minutes of emission data, but also the 10 hours of further data (as was the case for the previous Fig. 3).

Fig. 11. For the new \( \mu \)-map: shows the change in planar non-uniformity is small for a change of LBER from 7 to 9. In fact, whatever the LBER (from 0 to 50), the CV is <2% for the transverse planes. Therefore the major improvement in uniformity seen in Fig 10 was found by changing the \( \mu \) map (old \( \mu \)-map showed ~4.5% transverse CV in Fig. 10).
Fig. 12. The reason why LBER 9 was chosen with the new reconstruction parameters (minimizes a non-uniformity measure based on voxel-pair ratios).

Random voxel pair ratios, HRRRT, head & brain phantom

![Graph showing voxel-pair ratio distribution FWHM (%)](image)

Fig 13. Random voxel pairing analysis for a Montreal germanium 68 cylinder, demonstrating the metric (FWHM of the voxel-pair ratio distribution) used to optimize for uniformity in Fig. 12. The distribution shows the ratios of 10 million randomly chosen voxel pairs. The sub volume used is shown by the smoothed region. The edge preserving smoothing of the sub volume means that ratios of 1.0 are still expected even for smoothed data.

![Images of coronal, transverse, and sagittal slices with smoothed and unsmoothed regions](image)

Fig 14. μ-map reconstructions. Top row: CT-based μ-map (not available as part of an HRRT acquisition). Middle row: standard Montreal parameters. Bottom row: parameters changed to those from Copenhagen.

Coronal plane number
Average voxel value in plane

CV of most smoothed case=1.84%

Transverse plane number

CV of most smoothed case=1.71%

Fig. 15. Impact of the change of μ-map, and the returned LBER. These profiles are to be compared with those in the middle row of the previous Fig. 8. It is evident that the gradient has been largely removed.

![Graphs showing sagittal plane variation (CV%) and coronal plane variation (CV%) for different conditions](image)

Fig. 16. Same as the previous Fig. 7, but now also importantly including the “Modified Montreal” result – which achieved superior uniformity compared to the “Standard Montreal” result. The uniformity for the modified result now compares well with the uniformity obtained in uniform cylinders.
Fig. 17. This figure demonstrates the motivation for improving the uniformity of the Montreal head and brain phantom data. Four regions in the head and brain phantom were selected (see Fig. 18 for the colour code and legend), and the ratio of the ROI means taken. Errors are reduced from ~10% to less than 5% with the new $\mu$-map reconstruction parameters for the Montreal data.

Fig. 18. The regions selected for the relative region analysis of Fig. 17.

Fig. 19. Analogous to the previous Fig. 6, but now with inclusion of the new emission reconstruction which uses the new $\mu$-map for Montreal’s data.

IV. DISCUSSION AND REQUIRED DIRECTIONS

The analysis of $^{68}$Ge uniform cylinders implied all was well between different HRRT centres except for two centres (which use smaller, water-filled $^{18}$F cylinders for scatter tuning). It is suspected that for those two centres, the $\mu$-value for the germanium cylinder is incorrect, and furthermore that the LBER parameter has been tuned for a smaller sub volume of the FOV (pertaining to the volume used for brain imaging). The task of reconstructing a large germanium cylinder cannot be performed well if the $\mu$-value is wrong (attenuation correction inaccuracy will give non-uniformity) and if the LBER is not accurately tuned to accommodate a larger volume of the FOV. It is worth noting that liquid and solid germanium cylinders (scanned at Aarhus) delivered comparable uniformity (previous Fig. 5), implying, at least for that centre, that the solid germanium cylinder did not have inherent low-spatial frequency non-uniformities in its radioactivity concentration.

The anthropomorphic head and brain phantom revealed significant issues for the Montreal data (a gradient from -5% to +5% in planar values along the axis of the scanner), and similar concerns (-4% to +5%) for the Vancouver data. These issues were resolved by changing the parameters of the $\mu$-map reconstruction and retuning the LBER parameter for the single scatter simulation. Whilst these adjustments worked well for the phantom, it is still not necessarily the case that these
parameters would be optimal for human brain data (e.g. the μ-value should be close to 0.099 cm\(^{-1}\) for the main brain volume [12]). As already mentioned, problems can arise when using \(^{68}\)Ge cylinders for tuning of LBER, as the μ-map can be inaccurate (and a wrong attenuation correction leads to a wrong LBER), and more of the FOV is considered with germanium cylinders (so the LBER is tuned to accommodate most of FOV, rather than just the brain volume).

It is clearly advantageous to use phantoms with realistic levels of attenuation and scatter rather than uniform cylinders, and it is likewise essential to make unambiguous recommendations to all HRRT centres concerning μ-map reconstruction parameters and the phantom to use for LBER tuning. Perhaps a good way forward would be to use the head and brain phantom for routine adjustment of the LBER value, using a method similar to that proposed here in Figs. 12 and 13. This metric relates closely to the task of interest for HRRT imaging: relative mean values in variously located brain regions, focusing only on the sub-volume of the scanner FOV which is actually used during a subject scan.

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**REFERENCES**


