Quantification of Partial Volume Effects in Single Photon Emission Computed Tomography

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Abstract-- Introduction: Partial volumes effects (PVEs) are caused by the limited spatial resolution of the imaging system. They hinder accurate quantification of images of organs with diameters less than two-thirds times the full width half maximum of the imaging system. PVEs can manifest either spill-out or spill-in effects in non-radioactive and radioactive backgrounds respectively. Spill-out effects lead to underestimation of activity counts due "loss" of organ activity, spill-in effects results in overestimation due to movement of background activity counts into the organ. For successful implementation of diagnostic and therapeutic outcomes based on quantitative values, PVEs quantification must be prioritized. The objective of this study was to quantify PVEs in single photon emission computed tomography.

Methods: Images of spheres A, B and C of diameters 26 mm; 20 mm and 16 mm (filled with technitium-99m of activity concentration 74 kBq/ml) mounted inside a Jaszczak phantom were acquired with a gamma camera. Three background activities (0%; 0.5% and 1% activity of 74 kBq/ml) were used. Images were quantified using ImageJ software.

Results: Underestimation of image counts increased with decrease in sphere size. Quantification errors were: 54%; 55% and 66% in the order of decreasing sphere size for 0% background activity. For background activities 0.5% and 1% overestimation resulted in quantification errors of 65%; 61% and 55% and 58%; 53% and 46% respectively. Spill-out and spill-in effects cancelled out as background activity increased.

Conclusion: Quantification of PVEs should be prioritised when monitoring radionuclide therapy and where quantitative values are required to reach diagnostic conclusions.

Index Term-- Partial volume effects, quantification, spill-out, spill-in effects

1 INTRODUCTION
Image quantification is important for successful implementation of diagnostic and therapeutic outcomes. It has been a major objective in nuclear medicine from the early years of use. Quantification of nuclear medicine images acquired using planar, single photon computed tomography (SPECT) and positron emission tomography (PET) techniques allow functional and molecular characterization of in-vivo processes.

During treatment of patients with no-Hodgkin B-cell lymphoma using $^{90}$Y, quantification of nuclear medicine images of organs plays a significant role in determining specific patient internal dosimetry of the targeted organs as well as tumours at several imaging time points thus ascertaining successful therapy.

Accurate quantification of activity in voxels, tumours as well as in targeted organs is important also for approval of new imaging agents. SPECT images of tumours are required to evaluate the success of therapy and also in cases where monitoring of therapy is essential in order to arrive at a decision on whether to continue or discontinue therapy based on patient benefit. Therapy usually is discontinued in cases where toxicity to patient outweighs benefit. Accurate quantification of SPECT images is however hindered by partial volume effects (PVEs). The latter are attributed to the limited spatial resolution of the imaging system. PVEs may result in either loss or gain in activity counts within a targeted structure leading to failure to obtain accurate quantitative values from nuclear medicine images. Section 1.1 discusses PVEs in detail. Failure to prioritise PVEs when monitoring treatment of smaller tumours may portray them as less aggressive compared to a bigger ones when they are actually more aggressive. Pharmacokinetics studies also rely on quantification of activity for approval of new radiopharmaceutical drugs.

PVEs quantification can also be applied to optimise treatment of neuroendocrine tumours using Lutetium-177 (Lu-177) radionuclide. In order to optimize treatment whilst minimizing toxicity to kidneys, SPECT images of kidneys may be quantified so as to determine the radiation risks associated with the treatment. Without quantification of PVEs, quantitative values from kidney SPECT images remain inaccurate. They cannot be confidentially used to arrive at an informed decisions on the kidney toxicity. Ability to accurately quantify the accumulation of Lu-177 in the kidneys would enable clinicians to measure kidney toxicity and optimize treatment. Lu-177 emits a beta particles hence their excessive accumulation in the kidneys may lead to radiation injury.

Lastly but not least absolute quantification is important when using either planar or SPECT images to access the function of the parotid and salivary glands function post radiation therapy of head and neck tumours. The function of the glands can be equated to the image counts. However, absolute quantification in all the cases is hindered by some limitations among which include photon attenuation and scatter, spatial
resolution of the imaging system, patient motion, PVEs and statistical noise due to low photon count or detection.\textsuperscript{5}

Photon attenuation and scatter have since been successfully accounted for resulting in improved quantification.\textsuperscript{6} Attenuation correction relies on obtaining spatial distribution of attenuation coefficients to model the imaged object, often derived from computed tomography data to compensate for non-uniform attenuation. Scatter correction techniques for SPECT imaging include the use of the dual window method. The method makes use the energy window abutting the photo peak in lower energy, in order to estimate the scatter fraction in the photo peak. Choosing of a narrow energy window within a photo peak have the potential to minimize scatter contributions and achieves a better contrast of the image.\textsuperscript{7} Strategies have also been introduced to account for patient and organ motion, these include reduction of scanning time and increase in sensitivity of the detector. Much interests and effort have since been directed on cardiac respiratory gating. Although not available in routine imaging advanced techniques have made it possible to remove motion blur by combining all gates whilst keeping sensitivity.\textsuperscript{2}

A large number of improvements in the gamma camera imaging system, dedicated research that have been coupled with introduction and successful implementation of photon attenuation and scatter as well as strategies to account for patient motion have made quantification a reality in nuclear medicine. However, accurate quantification of activity distribution in small structures or organs with diameters less than a 2-3 times the full width half maximum (FWHM) of the imaging system still remains elusive due to the limited spatial resolution of the imaging system.

1.1 Partial volume effects
The limited spatial resolution contributes to formation of blurred images and underestimation of activity in small targeted organs,\textsuperscript{2,7} a phenomenon commonly referred to as PVEs.\textsuperscript{7} Apparent loss of radioactivity is due to increase in spatial resolution-related effects from loss due to tissue function and limited spatial resolution of the imaging system.\textsuperscript{9,10,11} Underestimation or overestimation of activity also depends on the effects of spill-out and spill-in respectively.\textsuperscript{2,10}

The PVEs may manifests as spill-out effects in a non-radioactive background or as both spill-out and spill-in effects in a radioactive background. Spill-out effects are a result of “loss” of activity from the organ of interest into the background resulting in underestimation of the regional distribution of organ activity. Figure 1 below, shows the concept of spill-out effect.

![Fig. 1. Spill-out results in “loss” of activity from the organ or structure of interest hence apparent decrease in activity in the structure](image)

Spill-in effects occur when activity from the neighboring structure or background blurs into the organ of interest leading to overestimation of the detected nuclear medicine signal. This effect occurs simultaneously with the spill-out effect in a radioactive background leading to cancellation of some spill-out and spill-in activity counts hence reduction in quantitative errors due overestimation.\textsuperscript{12,13,14} A pictorial representation of spill-out effects and spill-in effects occurring simultaneously is shown in figure 2.
The cancellation between spill-out and spill-in effects shown in figure 2 depends on the object size, the activity levels within the structure and background activities as well as the spatial resolution of the gamma camera.

In order to achieve accurate quantitative values of the distribution of the radionuclide it is agreeable that some form of PVEs quantification must be implemented. Previous several PVEs correction techniques have been implemented. These were designed for PET. However, none of them have since been co-opted into routine clinical imaging or may be considered as gold standard. Majority of these PVEs correction techniques originally intended for PET have since been applied in SPECT. Use of these PVEs correction techniques that were intended for PET will indeed not yield to absolute results when used in SPECT since PET and SPECT have fundamental differences. In PET the point spread function (PSF) is assumed to invariant yet it SPECT it is well known to vary with the distance from the collimator. For this reason, a PVEs correction technique designed for PET cannot be expected to yield desired results when used in SPECT imaging. This study therefore was aimed at implementing a PVEs quantification technique using ImageJ software specifically intended for SPECT images reconstructed using filtered back projection technique (FBP) technique.

1.2 The gamma camera

The quality of Nuclear Medicine images more than any imaging system relies on the skilful manipulation of the gamma camera by the nuclear medicine technologist. Furthermore, a gamma camera can only acquire good quality images if the medical physicists runs an effective quality control (QC) programme. The gamma cameras are manufactured by various companies among which include Siemens and Philips. Figure 3 shows a Siemens E-Cam dual head gamma camera. Although manufactured by different companies all gamma cameras are based on the scintillation principle by Hal O. Anger.
1.2.1 The gamma scintillation cameras are widely used in clinical imaging and research. During clinical imaging two dimensional (2D) or three dimensional (3D) images are acquired. These may be analysed quantitatively or quantitatively to answer a patient problem. All the nuclear medicine images are acquired from a process that involves introduction of a minute radionuclide into the body either by intravenous injection or inhalation or ingestion techniques. The radionuclide of choice should be organ specific, such that after complete biodistribution it accumulates mainly in the targeted organ. Decaying photons leaving the patient which originate from the targeted organ are then detected by the gamma camera mounted above the patient.20,21

The photons absorbed by the gamma camera crystal are converted into electrical signals by the electronic system before they are sent to the computer which comes interfaced to the gamma camera. These electrical signals are then converted into different intensities of varying radioactivity from varying colours and shades of grey to build images.

Quantification of these images give numerical values from which the patient diagnosis is completed.

A gamma camera can be used to acquire either planar or SPECT images depending on the imaging protocol used. During planar imaging, the gamma camera head is held in a fixed position above the patient.24 In this position, images in 2 D format are acquired. A single or dual head gamma camera may be used to acquire a static image. However, dynamic images may also be acquired. In this case, the gamma camera acquires a series of planar images showing the motion of the tracer over a short interval of time usually 1 to 10 s per frame. Acquisition of many projections makes it possible to observe animation of the tracer movement.20,21,22

During SPECT imaging, the gamma camera is rotated round the patient through 180° or 360° taking a series of planar images. Finally a computer is used to reconstruct the projections resulting in 3D images. These are superior to planar images in terms of contrast.20,21,22,23
2.1 Materials and Methods

Three hollow spheres A, B and C of diameters 26 mm; 20 mm, 16 mm were filled with technetium-99m (\(^{99m}\)Tc) activity of concentration 74 kBq/ml. \(^{99m}\)Tc was selected because this study served as a validation for a study in which SPECT images with PVEs quantification were used to evaluate the function of salivary glands (imitated using spheres) post radiation therapy of head and neck tumours. \(^{99m}\)Tc accumulates in the salivary glands soon after intravenous administration thus facilitating imaging of the major pairs of glands. The spheres were mounted inside Jaszczak phantom adjacent to the walls forming a V-shape (figure 3 shows top view of the Jaszczak phantom showing positioning of spheres A, B and C). The spheres were mounted adjacent to the walls further away from the centre of rotation because spatial resolution is better on the edges of the phantom. Three measurements were conducted, first with the phantom filled with activity free water, secondly with the phantom filled with a solution of water and 0.5% activity of the \(^{99m}\)Tc solution filled inside the spheres. Lastly the phantom was filled with a solution of water and 1% activity of the \(^{99m}\)Tc solution filled into the spheres. New activity concentration was prepared for each experiment.

During each of the three experiments, the phantom was imaged whilst laid on supine position using Siemens E-Cam dual head gamma camera as shown in figure 4. The Siemens E-Cam dual head gamma camera was fitted with low energy high resolution collimators. A Saturn nuclear medicine computer linked to the Siemens E-Cam dual head gamma camera collected the data.

The energy window of the Siemens E-Cam dual head gamma camera was fixed at 140 keV±15% so as to halt Compton scatter photons.
2.2 Image quantification

The images were reconstructed using FBP reconstruction technique. A Butterworth filter, cut-off frequency 0.9 and order of 9 was used. These parameters were deduced in an earlier study in which all default filters supplied with the Siemens E-Cam dual head camera were applied on the images of the three spheres leading to selection of the filtering parameters that gave the best FHWM for the central transaxial image slice.

Two regions of interests (ROI 1 and ROI 2) were drawn on each 2D transaxial SPECT image slice of each of the three spheres. ROI 1 was drawn tightly on the boundary of the image slice whilst ROI 2 was added such that it extended from the boundary of ROI 1 by the FWHM of the Siemens E-Cam dual head gamma camera. The FWHM was measured and found to be 4.2 pixels.

Figure 5 shows ROI 1 and ROI 2 used to quantify PVEs on 2D transaxial slices acquired whilst mounted in a Jaszczak phantom in which the background activity was activity free water. The similar quantification procedure was applied on the
2D transaxial SPECT images of the sphere acquired when the background activity in the Jaszczak phantom was 0.5% and 1% of the activity concentration added into the spheres.

3. RESULTS

Table 1 Image counts extracted pre and post PVEs quantification of 2D transaxial slices of spheres A, B and C acquired when filled with $^{99m}$Tc solution of activity concentration 74 kBq/ml.

4. DISCUSSION

We have presented an economic method for PVEs quantification that uses ImageJ, a licence free software. The method is applicable to SPECT transaxial images reconstructed using FBP technique. The method relies on the knowledge of the spatial resolution of the imaging system which was measured and found to be 4.2 pixels. This method is based on the assumption that the activity is uniformly distributed within the sphere, a scenario which may not be highly likely within tissues during clinical imaging. However, the procedure would still give good estimate values.

During quantification of image counts, ROI 2 was found to recover image counts that were spread outside the pixels of the image. In the absence of a radioactive background it was found that spill-out effects were responsible for underestimation of image counts (Table 1). Spill-out resulted in the spread of image counts outside the image pixels of spheres A, B and C. The column denoted recovered counts gives the image counts that were spread outside image pixels. These counts were responsible for the underestimation of the regional distribution of the activity in three spheres. The recovered image counts are obtained by subtracting ROI 1 image counts from ROI 2 image counts.

The study showed that the underestimation of the image counts increased with decrease of sphere size. The following quantification errors were found 55%; 61% and 69% in the order of decreasing sphere size for 0% background activity. For background activities 0.5% and 1% an overestimation of image counts was registered. This was attributed to the movement of background image counts into the peripheral boundaries of the sphere images. ROI 2 thus encompassed image counts and background activity counts thus resulting in overestimation quantification errors of 55%; 61% and 65% and also 46%; 53% and 58% respectively for background activities 0.5% and 1% respectively in the order of decreasing sphere size. From these results it became obvious that spill-out and spill-in effects cancelled as background activity increased. This is observed as the background was increased from 0.5% through to 1%. From the results of this study, it was also observed that as the background activity increased from 0.5% to 1%, the quantification errors attributed to overestimation decreased. This can be explained by the fact that more activity counts from the background (due to spill-in effects) cancelled with the activity counts from the spheres that spread to the outside the boundary of the sphere due to spill-out effect.

4.1 Comparison of ImageJ with other PVEs correction techniques

ImageJ software is specifically designed to quantify PVEs in nuclear images reconstructed using FBP technique. The software is licence free, can be installed on a personal laptop thus making it accessible to a large community of clinicians. Extra information required is only the spatial resolution of the imaging system which can be easily determined. This technique is also applicable to planar images. To our best knowledge this is the only economical quantification procedure specifically designed for quantification of PVEs in SPECT imaging.

Elanderson and Hutton, also came up with a partial volume correction technique designed for SPECT called p-PVC which also took into account the distance blurring associated with SPECT. The p-PVC method is however dependent on anatomical acquired using computed tomography (CT) and magnetic resonance imaging (MRI). This makes the procedure inaccessible to the large community owing to the cost of the co-registered systems that would give a structural image co-registered with the SPECT data. Furthermore the p-PVC technique is prone to mistakes arising from a series of data processing steps such as realignment of the image, parcellation and segmentation. This leaves PVEs quantification with ImageJ software as the only economically viable technique.

Quantification of PVEs using ImageJ remains favorable to previous partial volume correction (PVC) techniques. Some of the PVC techniques use anatomical information and they have been categorized as volume-of-interest (VOI),25 and voxel-based methods.26,27 One of the strengths of PVEs quantification using ImageJ is that it is specifically designed for SPECT images whilst previous PVC methods were designed for PET. These methods have been applied to SPECT. However, they cannot give good approximate values of PVEs since in SPECT spatial resolution varies as you move away from the collimator and it is well known that in PET spatial resolution is considered as invariant.21 This leaves our method as the most suitable since it takes into account the distant dependent blurring effect in SPECT.

5. CONCLUSION

ImageJ software provides the most economic means of quantifying PVEs in SPECT imaging. It is suitable for SPECT images reconstructed with FBP technique. However, presence of a radioactive background results in overestimation of quantitative values in an ideal clinical imaging scenario. This can be overcome by timing imaging such that it is performed when the radiopharmaceutical has reached its final biodistribution, this will guarantee minimum background activity (blood pool activity) and minimal errors due to overestimation.

REFERENCES


Table 1 Image counts extracted pre and post PVEs quantification of 2D transaxial slices of spheres A, B and C acquired when filled with $^{99m}$Tc solution of activity concentration 74 kBq/ml.

<table>
<thead>
<tr>
<th>Background Activity</th>
<th>Image Counts extracted from sphere A</th>
<th>Image Counts extracted from sphere B</th>
<th>Image Counts extracted from sphere C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counts before PVEs correction</td>
<td>Counts after PVEs correction</td>
<td>Recovered Counts</td>
<td>Counts before PVEs correction</td>
</tr>
<tr>
<td>0%</td>
<td>16870</td>
<td>63188</td>
<td>46318</td>
</tr>
<tr>
<td>0.5%</td>
<td>61934</td>
<td>135893</td>
<td>73959</td>
</tr>
<tr>
<td>1%</td>
<td>68882</td>
<td>152140</td>
<td>85258</td>
</tr>
</tbody>
</table>

Table 1 shows image counts extracted from 2D transaxial SPECT images of the spheres A, B and C acquired whilst mounted inside the Jaszczak phantom. Sphere images were acquired under three different background activities (0%; 0.5% and 1%) compared to the activity concentration of 74 kBq/ml filled into the spheres. The total image counts for each sphere was given by the sum of counts extracted from 2D transaxial slices that make up the sphere. Slices with negligible image counts were ignored.