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Image Quantification for Radiation Dose Calculations – Limitations and Uncertainties

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Abstract

Purpose—Radiation dose calculations in nuclear medicine depend on quantification of activity via planar and/or tomographic imaging methods. However, both methods have inherent limitations, and the accuracy of activity estimates varies with object size, background levels, and other variables. The goal of this study was to evaluate the limitations of quantitative imaging with planar and SPECT approaches, with a focus on activity quantification for use in calculating absorbed dose estimates for normal organs and tumors. To do this we studied a series of phantoms of varying complexity of geometry, with three radionuclides whose decay schemes varied from simple to complex.

Methods—Four aqueous concentrations of ^{99m}Tc, ¹³¹I and ¹¹¹In (74, 185, 370 and 740 kBq/ml) were placed in spheres of four different sizes in a water-filled phantom, with three different levels of activity in the surrounding water. Planar and SPECT images of the phantoms were obtained on a modern SPECT/CT system. These radionuclides and concentration/background studies were repeated using a cardiac phantom and a modified torso phantom with liver and ‘tumor’ regions containing the radionuclide concentrations and with the same varying background levels. Planar quantification was performed using the geometric mean approach, with attenuation correction (AC), and with and without scatter corrections (SC and NSC). SPECT images were reconstructed using attenuation maps (AM) for AC; scatter windows were used to perform SC during image reconstruction.

Results—For spherical sources with corrected data, good accuracy was observed (generally within $\pm 10\%$ of known values) for the largest sphere (11.5 ml) and for both planar and SPECT methods with ^{99m}Tc and ¹³¹I, but were poorest and deviated from known values for smaller objects, most notably for ¹¹¹In. SPECT quantification was affected by the partial volume effect in smaller objects and generally showed larger errors than the planar results in these cases for all radionuclides. For the cardiac phantom, results were the most accurate of all of the experiments, for all radionuclides. Background subtraction was an important factor influencing these results. The contribution of scattered photons was important in quantification with ¹³¹I; if scatter was not accounted for, activity tended to be overestimated using planar quantification methods. For the torso phantom experiments, results show a clear underestimation of activity when compared to previous experiment with spherical sources, for all radionuclides. Despite some variations that were observed as the level of background increased, the SPECT results were more consistent across different activity concentrations.

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Conclusion—Planar or SPECT quantification on state-of-the-art gamma cameras with appropriate quantitative processing can provide accuracies of better than 10% for large objects and modest target-to-background concentrations; however when smaller objects are used, in the presence of higher background, and for nuclides with more complex decay schemes, SPECT quantification methods generally produce better results.

Keywords

planar and SPECT images; activity quantification; phantom studies

I. INTRODUCTION

Image quantification in nuclear medicine with planar or tomographic methods is used to estimate activity in human subjects for the calculation of radiation dose in individuals undergoing radionuclide therapy and to study pharmacokinetics for approval of new radiopharmaceuticals (Sgouros, et al. 2003; Koral et al. 2003). In both applications, sufficient data must be obtained to characterize all significant phases of radiopharmaceutical uptake and elimination in all important source regions, as explained by Siegel et al. (1999). Performing quantitative imaging for dosimetry analyses may represent a significant time and financial burden on a medical facility, but such efforts are essential to establish reliable absorbed dose calculations to assess tumor response to radiation and to evaluate normal tissue toxicity, for treatment planning in radionuclide therapy (Pauwels et al. 2005).

In planar imaging, the external conjugate view method is commonly used to obtain quantitative data for radiation dose calculations (Siegel et al. 1999). In this method, activity in a source region can be determined as:

$$A = \sqrt{\frac{C_A C_P}{e^{-\mu T}}} \times \frac{1}{C} \quad \text{eq. 1}$$

where C_A and C_P are counts in regions of interest (ROIs) drawn on opposing (commonly anterior and posterior) images, μ is the effective attenuation coefficient in the ROI for the photon energy of interest, T is the body thickness and C is the calibration factor that expresses the sensitivity of the camera (e.g. counts/Bq-s)¹. This approach reduces the dependence of the measured values on the depth of activity in the body and has been shown to be useful for activity quantification in studies carried out with physical phantoms, simulated images employing Monte Carlo methods, and patient images.

Hammond et al. (1984) used planar imaging techniques and found activity quantification errors of 3–9% from known activity values of ^{131}I in spherical sources of 4 cm diameter. They found, however, higher errors (2–7 times greater) for 2 cm diameter spherical sources, a result that the authors attributed to the low activities in the spheres. Eary et al. (1989) showed that quantification errors were independent of source depth using the conjugate view method, and obtained errors within 5% for a well collimated system imaging ^{131}I in a large water-filled source (cylindrical bottle). They also achieved good accuracy in experiments using a realistic torso phantom; they calculated values of 92% and 102% of actual activity values in large structures in the torso phantom (liver and kidney). However, this study was carried out with

¹This equation may also apply a source region 'self-attenuation coefficient' $((\mu_e t/2)/\sinh(\mu_e t/2))$. In dosimetry studies, the thickness of individual organs is not usually known. If standard organ thicknesses are applied, this correction is usually of the order of a few percent, and is small compared to other uncertainties in the study. For this experiment, we were working mostly with small spherical objects for which this correction can reasonably be neglected.

no background activity, which is always present in clinical studies and which complicates activity quantification. In another phantom study, Norrgren et al. (2003) studied the influence of factors on the accuracy of activity quantification such as the effective attenuation coefficient (which could influence the estimation of activity by about $\pm 10\%$), body thickness ($\pm 10\%$) and device sensitivity ($\pm 5\%$). However, they noted that background activity was perhaps the most important factor, with differences in how background regions were defined contributing to as much as $\pm 20\%$ variation of the observed activity values from the known results.

Sjogreen et al. (2002) used planar imaging with ^{131}I to evaluate activity in organs and small tumors within simulated patient images, and employed novel pixel-wise correction methods for attenuation, scatter, septal penetration, background, and organ overlap. Estimated activity values were within $+15\%$ and -21% of known values for the major organs studied; agreement was poorer and consistently underestimated (up to -47%) for small tumors, believed to be due to partial-volume effects (inaccuracies in measured counts due to the finite resolution of the imaging system), combined with limited image contrast. Using patient images, Delpon et al. (2003) found overestimates of up to 120% over the actual value of whole body activity in patients, using only attenuation correction (using transmission images) on quantitative planar analyses. If scatter correction (using scatter window methods) was performed in addition to attenuation correction (AC), underestimates of $40\pm 10\%$ were observed. They concluded that in some of the cases analyzed, better accuracy was actually observed with no corrections to the original data. This may imply that the replacement of attenuated photons is quantitatively more significant than the subtraction of the scattered photons; however this work did not analyze the impact of these corrections on the accuracy of image-based quantification. Also it was not clear what impact background subtraction and superimposition of structures may have had; it is known that these corrections may represent a significant influence on the final activity quantification. He and Frey. (2006) combined quantitative method planar with 3D images of patients to create a new quantification method that they called the "Quantitative Planar" (QPlanar) method to image ^{111}In in organs of digitally simulated patient images. Using three dimensional organ VOIs and simulation models of the projection process, the method was designed to minimize errors due to overlap and background subtraction. The authors claimed a substantial increase in accuracy of organ activity estimates from planar images compared to conventional method of planar processing, and found that accuracies approached those of quantitative SPECT, but with lower acquisition and computation times.

Activity quantification with tomographic imaging e.g. Single Photon Emission Computed Tomography (SPECT) is theoretically superior to that with planar imaging, as problems of organ overlap may be overcome, contrast is increased for small regions, and generally more accurate information regarding activity (and thus ultimately radiation dose) may be obtained (Siegel et al. 1999). Tomographic data are also important in evaluating heterogeneous uptakes of activity in organs and resolving issues of under- or overlying background activity. But many effects complicate SPECT quantification, including that more effort is needed to obtain basic calibration data (conversion factors from counts to absolute activity), and accurately perform corrections for attenuation, scatter, and partial volume effects. Corrections for these effects can be incorporated into iterative reconstruction (IR) methods, and quantitative results using IR have been shown to be better than those using filtered back-projection (King and Farncombe, 2003; Dewaraja et al. 2005). However, IR methods take substantial computational time, as quantification is performed for dozens or hundreds of reconstructed image slices.

As with planar methods, SPECT quantification also has been evaluated by several authors in experimental studies (Jaszczak et al. 1981; Green et al. 1990; Gilland et al. 1994; Koral and Dewaraja, 1999). These studies have found results with various levels of accuracy, but it is often difficult to directly compare these results because investigators have used different levels of activity, different radionuclides, and different shapes and sizes of sources. All of the authors

agree that, due to the partial volume effect, underestimation of activity may occur when smaller volumes (below 20 ml on most imaging systems) are used. Zingerman et al. (2009) measured ^{99m}Tc , ^{111}In and ^{131}I activity in spherical, cubic, and cylindrical sources of varying size and volume. They noted the importance of subtracting background activity spill-in from neighboring area of source regions, as this may contribute ~12% (depending on the source/background ratio) to the total measured activity in spheres of volumes 2–16 ml (with aqueous solution of ^{99m}Tc).

Dewaraja et al. (2005) used simulated images to evaluate the accuracy of absorbed dose estimates for ^{131}I in a voxel phantom with organs and tumors of different sizes. This work illustrated the importance of choosing well designed phantoms for obtaining calibration factors (C) and of carefully performing attenuation and scatter corrections. Errors of $\pm 10\%$ were found for source region volumes ≥ 16 ml. However, errors of up to -35% were found for the smallest (7 ml) volumes, due to the partial volume effect. Another important result from this work was that increasing the number of iterations in the reconstruction process improves recovery, mainly for smaller tumors. Ljungberg et al. (2003) estimated ^{111}In and ^{90}Y activity in simulated SPECT projections and used them to define 3D dose distributions. Results were generally encouraging, some over- and underestimation of activity (up to 30–50%) occurred due to count spillover into and out of defined organ regions. He et al. (2005) imaged a torso phantom with known activities of ^{111}In in lungs, liver, heart, background and two spherical compartments of inner diameter 22 mm and 34 mm. They found good accuracy, within 6.5% for whole organs, but differences of 8–30% from true activity values for the spheres. Du et al. (2006) generated simulated images of various brain structures containing ^{123}I . They obtained results within about 3.5% of expected values using a model-based downscatter correction method. El Fakhri et al. (1999) measured levels of ^{99m}Tc in a left ventricle chamber of a cardiac phantom and a liver phantom. They evaluated the impact of various corrections on the accuracy of quantification and suggested a priority order of corrections for (1) attenuation, (2) partial volume correction, (3) scatter correction and (4) collimator response. Simulated imaging is a powerful tool used to assess data that cannot be obtained in experimental studies. The development of techniques for SPECT image simulation and quantification is an area of ongoing research and new tools for simulation of SPECT images have been developed that improve image quantification and may be useful in improving dose assessment in patient therapy (Autret et al. 2005).

Although many studies have been done to validate and improve quantification with imaging techniques, more data are needed to better characterize limitations regarding object size, background levels, and other variables. The goal of this study was to complement studies to date regarding limitations of quantitative imaging, by systematically studying quantification for several radionuclides of interest to dosimetry studies in the same series of phantoms of varying geometric complexity. Other studies, noted above, give results for particular radionuclides, and use different approaches to data quantification and reporting of values. We used both planar and SPECT approaches, and evaluated quantitatively how well activity levels were quantified in each case. Our ultimate interest was in evaluating how well concentrations in small organs and tumors may be estimated by the two methods for use in calculating absorbed dose estimates with nuclides of differing decay characteristics.

II MATERIALS AND METHODS

In image sets provided for dosimetry, there are situations in which organs or tumors are somewhat isolated and in regions of well defined ‘background’ (blood, muscle or other nonspecific uptake). In other situations, objects of varying concentrations may be near each other, and ‘background’ interferences may be more severe. The idea of this study was to evaluate the range of situations often seen in image data used to estimate radiation doses to

human subjects, for these different situations, and for nuclides of simple (^{99m}Tc) to more complex (^{111}In) decay schemes.

II.A Phantoms Employed

We estimated activity levels in a SPECT/CT systemⁱⁱ with phantoms containing known activity concentrations of three radionuclides important in clinical practice: ^{99m}Tc , ^{131}I , and ^{111}In . These nuclides were chosen for their importance in quantitative imaging and for their varying photon energy and complexity of decay scheme (Stabin and da Luz, 2002). ^{99m}Tc is used in many different diagnostic studies, including cardiac, pulmonary, and renal imaging (Sandler et al. 2002). ^{131}I is used in both diagnosis and treatment of thyroid diseases and is labeled to other therapeutic agents (Eary et al. 1997). ^{111}In is used as a diagnostic agent in a variety of studies and also as a surrogate for ^{90}Y , which is used in therapeutic applications (Conti, 2004). These radionuclides represent a range of relatively simple to more complex decay schemes (^{99m}Tc has one important photon emission, with no higher energy photons, ^{131}I has a principal imaging photon with higher energy photons that contribute downscatter, and ^{111}In has two photopeaks of interest, with the higher contributing scatter to the lower photopeak window). In this study we performed experiments with these nuclides in three water filled phantoms with varying geometric complexity (Figure 1 shows images of the three experimental phantoms), to evaluate the ability of the imaging methods to accurately quantify the activity under more and less difficult conditions.

II.A.1 Spherical sources—First we placed four different spheres of external diameter 1.5, 1.75, 2.5, and 3.0 cm (measured internal volumes of 1.4, 2.2, 6.0 and 11.5 ml respectively), in a water-filled cylindrical phantomⁱⁱⁱ. Experiments were performed first with a concentration of 74 kBq/ml in each of the four spheres and no background activity (clean water filling the rest of the phantom); all of the spheres were imaged simultaneously. We prepared a large volume solution (~500 ml) and measured the activity in a dose calibrator, then separated the amount needed for each sphere. For example, for the 74 kBq/ml concentration we placed 103, 163, 444 and 850 kBq in the four spheres (of 1.4, 2.2, 6.0 and 11.5 ml respectively). Then, the experiment was repeated with background concentrations of 0.5% and 1.0% of the sphere concentrations (using 2400 and 4800 kBq respectively) in the surrounding water, which had a total volume of 6393 ml. This situation is comparable to a clinical situation with 0.1–1% uptake of the total activity in small tumors and perhaps 10% uptake in other nearby tissues. Figure 1A shows a picture of the phantom and a lateral view of the phantom imaged with ^{99m}Tc , with the spheres in place and 1.0% background concentrations in the surrounding water. The phantom was laid on its side and lateral images were acquired to avoid the added attenuation of the table. The ^{99m}Tc study was then repeated three times using sphere concentrations of 185, 370 and 740 kBq/ml, for each of the three background concentrations of 0%, 0.5% and 1.0% of the sphere concentrations. This complete set of experiments was then performed with ^{111}In and ^{131}I , using the same sphere and background concentrations. We acquired planar and SPECT images for all studies, using the specifications described below. The objective of this experiment was to evaluate quantification accuracy in small objects, not only as a function of size, but also as a function of activity level in the spheres and level of ‘background’ activity in the images for each radionuclide.

II.A.2 Cardiac phantom—We then performed a series of experiments using a cardiac insert^{iv} in this same cylindrical phantom (Figure 1B). We used the same four concentrations (74, 185, 370 and 740 kBq/ml) of each nuclide (^{99m}Tc , ^{111}In and ^{131}I) in water to fill myocardial

ⁱⁱGeneral Electric Infinia Hawkeye

ⁱⁱⁱJaszczak SPECT Phantom, Biodex Medical Systems

^{iv}Cardiac Insert, Biodex Medical Systems

‘wall’ region of the phantom (with 116 ml), and for each concentration we used the same three background values in water surrounding the ‘wall’ region. In all cases only nonradioactive water was placed in the center of the myocardial compartment. Planar and SPECT images were acquired, using the specifications described below. The objective of this experiment was to evaluate the accuracy of quantification in objects with irregular geometry.

II.A.3 Torso phantom—Further experiments were performed using a torso phantom^V, with separate lung and liver chambers that were modified to allow mounting of the four spheres (representing tumors), two inside the liver (11.5 and 2.2 ml) and two outside (1.4 and 6.0), as shown in Figure 1C. The smaller sphere was placed in the outer cavity, to evaluate the interference of a large object (such as the hot liver region) on quantification of activity in small objects in the body. This experiment simulated activity uptake in isolated tumors or small organs, and was intended to evaluate detection of activity in complex geometries similar to those encountered in clinical imaging for dosimetry. In this experiment, the sphere and background (in the phantom cavity) concentrations were the same as those used before, with activity in the liver chamber *above* that in the background, but *below* that placed in the spheres. The sphere/liver ratios were 24:1, 16:1 and 12:1 when background levels were 0%, 0.5% and 1.0% respectively.

Thus, twelve separate acquisitions were performed with each radionuclide (four different sphere concentrations $\times$ three levels of background activity in the surrounding water) and for both imaging methods (planar and SPECT approaches). A total of 216 images were acquired, with 72 image sets for each experiment (36 planar and 36 SPECT). In the experiments, we ensured that we had an adequate number of counts in each image so that precision was high; we were able to thus evaluate accuracy of these imaging methods under the conditions of relatively low or high object concentrations, in low or high levels of background activity, for more simple to more complex groupings of objects.

II.B Acquisitions sets and Analysis

Images were obtained with a GE Infinia Hawkeye, a dual-detector SPECT/CT hybrid imaging system, using a low energy high resolution (LEHR) collimator for the ^{99m}Tc studies, a high energy general purpose (HEGP) for ^{131}I and a medium energy general purpose (MEGP) collimator for ^{111}In . Spatial resolutions cited for these nuclides at 10 cm for these crystals are 7.4, 9.4, and 10.7 mm. Effective attenuation coefficients (μ), as defined in Equation 1, were experimentally determined for each radionuclide. Individual gamma cameras have unique responses to individual nuclides that should be characterized for each situation (Seo et al. 2005), thus we felt that the use of literature reported ‘ideal’ attenuation coefficients for the different nuclides would not be sufficient. The coefficients were determined by placing a small (approximately point) source under one face of the camera and placing blocks of acrylic of varying (known) thickness between the source and camera head. Counts were obtained in each image by drawing a small circular ROI around the source, and the counts were fit to a single exponential function to determine the attenuation coefficient (slope of the line on a semilog plot). Counts from scatter windows (to be defined shortly) were subtracted from the images prior to fitting. The phantoms are a mixture of acrylic and water, to varying degrees. In the simple Jaszczak phantom with only the sphere inserts, the photon path length is primarily through water; in the torso and cardiac phantoms, more acrylic is present. The effect of using attenuation coefficients for pure acrylic for these situations was assumed to be small for the purposes of these experiments. The system sensitivity values ($\text{cts s}^{-1} \text{Bq}^{-1}$) were obtained from images of the source with no intervening acrylic, using the same conditions (collimation, matrix size and scatter correction) as used to collect the images of the phantoms for each nuclide.

^VAnthropometric Torso Phantom, Data Spectrum Technologies

Planar images were obtained using 5 minute acquisition times and matrix sizes of 256×256 pixels (pixel size 2.11 mm) for the sphere experiments and 1024×1024 pixels (pixel size 0.527 mm) for heart and torso experiments, which are similar to array sizes used in patient imaging studies at Vanderbilt. Regions of interest (ROIs) were drawn using CT images to determine the location and size of the sources. CT image data were also used to determine the thickness of the phantom at each location, for use in the regional attenuation corrections. Image quantification was performed using the MedDisplay software^{vi}. Activity was quantified according to the standard geometric mean method described in equation 1.

For scatter correction, energy windows were defined as follows: a primary photopeak window of 140 keV ±10% was defined for ^{99m}Tc, with a scatter window at 122–126 keV; TEW technique (Ogawa et al. 1991) was used for ¹³¹I, the primary window was defined at 364 keV ±10% and scatter windows at 320–326 keV and 401–409 keV; the primary windows were defined at 171 keV±10% and 245 keV±10%, for ¹¹¹In, with scatter windows at 125–145 keV and 198–208 keV. For scatter correction, counts from the scatter windows were subtracted, using a trapezoidal approximation to the area under the photopeak, with weighting factors that were proportional to the size of the windows relative to that of the primary photopeak window. For example, the photopeak for ¹³¹I was 73 keV wide. The scatter windows below and above the photopeak area were 6.5 and 8 keV wide. We multiplied the counts in the lower scatter window by ratios of the window sizes (73/6.5 times the value in the lower window and 73/8 time that of the upper window), then took the average of the two and subtracted it from the photopeak counts. Planar quantification was performed with and without scatter corrections (SC and NSC). Activity was quantified according to the standard geometric mean method described in equation 1. The correction was made before the geometric mean calculation was performed, to maintain depth independence for the objects, as suggested by King and Farncombe (2003).

SPECT Images were taken with a circular orbit at 3° intervals over 360° of rotation, with a matrix size of 256×256 pixels for all experiments, in step and shoot mode, with a radius of rotation chosen to be similar to that used for patient imaging. Acquisition times were typically 30 minutes. SPECT reconstructions were performed using inherent workstation Xeleris 2.0 software, using the Ordered Subset Expectation Maximization (OSEM) IR method with 1 iteration, 5 subsets and a Butterworth filter of 0.4 with cutoff of 10, as is typically used in reconstructing clinical images at Vanderbilt. An attenuation map generated by the workstation software, from a Hawkeye CT scan acquired immediately prior SPECT acquisition, was used in the reconstruction to perform attenuation correction (AC). Scatter corrections (SC) were performed by the software using the energy windows defined above. Default scatter window weights of 1.1 for ^{99m}Tc and 1.0 for ¹¹¹In and ¹³¹I were applied by the Xeleris software. Iterative reconstructions were performed using an attenuation map generated by the workstation software from a CT scan taken before SPECT acquisition for attenuation correction (AC) and scatter corrections (SC) performed by the software using the energy windows defined above. Regions of interest (ROIs) were drawn on individual SPECT slices, using CT images to determine the location and size of the sources. Image quantification for the SPECT image sets was carried out using the ImageJ software^{vii}, with activity determined according to equation 2, (contributions from all slices were added linearly).

$$A = \frac{\sum \text{counts}}{T_{\text{acquisition}}} \times C_{\text{system}}, \quad \text{eq. 2}$$

^{vi}MEDDisplay Systems Incorporated, Edmonton, Alberta, Canada

^{vii}National Institutes of Health, Bethesda, MD

where C_{system} is the system calibration constant.

Background subtraction correction in planar images, was performed as:

$$C = C_{ROI\ source} - \bar{C}_{ROI\ background} \times S_{source} \quad \text{eq. 3}$$

Where C gives the corrected counts in the region of interest in the source area, $C_{ROI\ source}$ is the number of the counts in the source region of interest, $\bar{C}_{ROI\ background}$ is the mean value of the counts/pixel in a background region drawn close to the source (examples are shown in Figure 2), and S_{source} is the source area in pixels. The subtraction was performed for each projection, I_a and I_p , before application of Equation 1. Equation 1 was used to estimate the activity in a drawn ROI, performing attenuation correction on the whole ROI. On some images background ROIs were also drawn far from the source area, to evaluate the effect of variability in the placement of background ROIs.

For SPECT images, background subtraction was performed using eq 3 as well. It was done to compensate the contribution of spurious numerical values that appear in all regions of the images after reconstruction and to compensate for background spill-in from the surround neighboring into the source area (Zingerman et al. 2009).

III. RESULTS

III.A Calibration factors

Figure 3 shows the curves used to establish the effective attenuation coefficients for ^{99m}Tc , ^{111}In , and ^{131}I ; the values were 0.162 cm^{-1} , 0.14 cm^{-1} and 0.118 cm^{-1} respectively, which were obtained using the same collimators and energy windows noted above for the planar acquisitions. Results for ^{111}In , and ^{131}I agree with values obtained in experimental studies presented by other authors (Hammond et al. 1984; Early et al. 1989; King and Farncomb, 2003). For ^{99m}Tc , result was slightly higher than those found in water for good geometry conditions ($\sim 0.15\text{ cm}^{-1}$). Besides the slight difference in material composition and density between water and acrylic, this value may be different due to the use of a high resolution collimator, and the scatter correction applied and ROI size used, which has been showed to influence values of the effective attenuation coefficient (Fernow et al. 1985). The system calibration factors were $61.0\text{ cts s}^{-1}\text{ MBq}^{-1}$ for ^{99m}Tc , $80.5\text{ cts s}^{-1}\text{ MBq}^{-1}$ for ^{111}In , and $17.5\text{ cts s}^{-1}\text{ MBq}^{-1}$ for ^{131}I .

III.A.1 Spherical sources—To analyze accuracy of the results, calculated activity values were divided by the known activity in the source regions for each experiment to determine recovery coefficients (RC) and were expressed as dimensionless ratios. Table 1 compares recovery coefficients (RC) found for planar and SPECT imaging for the spherical sources in the Jaszczak phantom. The results show small errors ($\pm 10\%$) for the largest sphere for both methods when ^{99m}Tc and ^{131}I are used. Results for ^{111}In quantification show the greatest differences from known values, and for both methods a dependence on concentration is evident, i.e. results improve as higher sphere concentrations are used.

Activity was detected in all spheres, even for the lowest concentrations values. For the highest activity concentration, the errors in activity estimates were larger for SPECT than planar quantification for the smallest spheres for all three radionuclides. For the larger spheres, the errors were generally comparable." Figure 4 shows inverse recovery coefficients ($1/\text{RC}$) curves, following a method suggested by Koral and Dewaraja (1999) to correct the partial volume effect as a function of sphere volume. The $1/\text{RC}$ curves were determined for each radionuclide separately and for each background level, using data from Table 1.

The impact of scatter correction was analyzed for the planar images. Figure 5 compares RC curves obtained with scatter correction (SC) and with no scatter correction (NSC) for planar images for all radionuclides at a concentration of 370 kBq/ml, for all background levels. This is representative of the general behavior for other nuclides. Similar differences were seen for ^{99m}Tc at all volumes, but larger differences were seen for ^{111}In in the two largest spheres and smaller impact was seen in general for ^{131}I .

Also we calculated results using background subtraction of regions that were drawn far from the sphere ROIs (calculations not shown) and found that activity values were overestimated by up to 30% for all radionuclides. This is an important aspect of image quantification, as drawing ROIs to correct for 'background' in patient images (which could be activity in blood pool or other surrounding tissues) is done differently by different investigators. There is no 'standard' method defined for drawing such ROIs; how it is done in each case is a matter of judgment by the investigator, and of course will impact reported results in any given case. Our investigations suggest the drawing of 'background' ROIs close to the source region of interest, as in Figure 2.

III.A.2 Cardiac phantom—Table 2 provides results for activity ratios (RCs) in the cardiac phantom for all nuclides. Due to the large size of the region containing the activity in these experiments (116 ml), and despite its somewhat irregular shape, activity ratios obtained using SPECT quantification for the cardiac phantom were the most accurate of all of the experiments, for all radionuclides and were fairly independent of the radionuclide concentration. An exception was the SPECT image results for ^{111}In obtained with lowest activity concentration, for which the results were somewhat worse. For planar images, results were good, but again for ^{111}In , results were generally underestimated by 10–30%.

As was done in the previous experiment, the results for planar imaging were also analyzed with no scatter correction (data not shown). Unlike the previous results, however, results for ^{99m}Tc , and ^{111}In were similar: activities were overestimated by up to about 35%. The largest differences were seen for ^{131}I , with values overestimated by up to 58%. For this phantom, use of background ROIs drawn far from the source region (again, results not explicitly shown here) resulted in activities in the myocardial region being overestimated by up to 10%.

II.A.3 Torso phantom—Table 3 summarizes RCs values determined for the studies in the modified torso phantom that simulated a more realistic situation, compared to what might be observed in real human imaging. Poor quantification can be observed in comparison to the original results with the spheres alone in the water-filled Jaszczak phantom, showing a clear underestimation of activity in many cases.

Using planar imaging, estimates of activity for the 11.5 ml and 2.2 ml spheres (placed inside of the liver region with an inhomogeneous activity distribution) had the greatest deviations from known results, for all levels of background. For the other spheres, of 6.0 ml and 1.4 ml placed in the phantom cavity (to study the effect of the interference of a large object (such as the liver) on quantification of other objects in the body, activity was significantly underestimated. Underlined results of the planar quantification in Table 3 represent values for which spheres were visualized only in one projection (anterior or posterior). In other cases, it was not possible to quantify the activity as these spheres could not be visualized in either projection (shown as 'NQ'). No estimate of activity was provided in these cases.

For SPECT methods, activity was sometimes underestimated as well, although to a lesser degree. Despite variations that were observed as the level of background increased, the results were more consistent across different activity concentrations than those obtained with planar images. For the smallest spheres, with the lowest activity concentrations of ^{131}I and highest

background levels, some NQ values were observed. Quantification for the liver region, being the largest object in the field (~1175 ml), had good accuracy, but also showed some dependence on background level for both planar and SPECT methods.

IV. DISCUSSION

There is inherent variability in any measurement of radioactivity due to Poisson distributed noise. As noted above, we ensured that we had an adequate number of counts in each image so that precision was high, so that our analysis focused on the accuracy of the imaging methods at low to high object concentrations, with varying levels of background activity, for the various objects of differing size and complexity.

It is important to note that we did not experiment with different approaches to optimize the quality of the quantifications, but to reflect what is routinely done in our treatment of data as is routinely supplied by the clinic. So, for example, the SPECT scatter window weights, numbers of iterations, and cutoff filters used to obtain data for dosimetry could perhaps be optimized by a more extensive study for a given nuclide, varying the window weights and observing changes in the results, in a separate study.

IV.A. Spherical objects

Planar images—In the planar imaging results, the most accurate quantification was obtained with ^{99m}Tc , and this was fairly independent of the radionuclide concentration. In general, for image quantification with ^{111}In , results were generally poorer, most so for the lowest concentration. We note that for spheres of the same size, activity concentration and background level, the impact of background subtraction was more important for ^{111}In than for ^{99m}Tc . Considering that the background in this experiment was uniform, we attribute this difference to the contribution of *spill-out* photons near the source where the background ROIs were placed. However, progressively better values were observed for higher concentrations. For ^{131}I , activity values were better than those for ^{111}In for lower concentrations, but were similar for the other studies. Significant variability was observed at smaller object and lower concentrations, which may be due to the effects of scatter in the (^{131}I) images.

For results not corrected for scatter, the contribution from scattered photons appears to somewhat compensate for the loss of counts due to the decreased signal-to-noise levels in the smaller objects in planar imaging. Thus, for objects 6 ml or less, activity was generally greater than that obtained from corrected data (Table 1). This explains (as with the work of Delpon et al. 2003.), why correction for scatter did not necessarily improve image quantification for smaller objects. However, for the larger objects, not correcting for scatter always resulted in an overestimation of activity, demonstrating the importance of performing scatter corrections in image quantification.

SPECT images—For larger spheres, ^{99m}Tc and ^{131}I results were obtained with good accuracy, for all concentrations. For ^{111}In , as was observed with planar images, results were better for higher concentrations. However, activity values were overestimated for the two higher concentrations (by up 21%).

Results for objects ≤ 6 ml were significantly affected by the partial volume effect. This did not improve when higher levels of activity were employed, for any radionuclide. Thus, partial volume effects are not really mitigated with higher concentrations, unless the effect is simply to more clearly distinguish the object from surrounding background. The poorest results were obtained with ^{131}I , with an inverse recovery coefficient of 5.8 for the 1.4 ml sphere (Figure 4), which is close to results presented by Koral and Dewaraja (1999) for their smallest object. The

results for ^{99m}Tc and ^{111}In , were slightly different for the 11.5 ml and 6.0 ml spheres, but greater variations were observed for the smaller spheres.

The subtraction of 'background' in SPECT images was performed to compensate for spurious counts and the 'spill in' effect. This is an approximate correction, and may have introduced some minor uncertainties in some of the more complex systems studied. The correction is important in general; by not correcting for background could result in better recovery coefficients in smaller objects, but could result in overestimation of activity for objects greater than 11.5 ml. This subtraction, done slice by slice, has a significantly smaller effect on the final results than in the case of planar images. For the largest sphere, the correction was of the order of about 20%.

IV.B Cardiac Phantom

Planar images—Estimation of activity in the planar images for ^{111}In was not as good as for ^{99m}Tc , as expected. Again, we note that background subtraction was most important for quantification with ^{111}In , suggesting that the ROI drawn on the cardiac region was affected by scattered photons from this source region, which may explain the consistently underestimated values. Again, significant variability from expected results were observed for the ^{131}I images, which may be due to the effects of scatter.

SPECT images—Results were reasonably accurate (within about 10%) for all radionuclides and were fairly independent of activity concentration, except for the lowest concentrations with ^{111}In . However, activity estimation was better than for planar imaging, as the contribution of spill-in photons could be reduced or eliminated from the central cavity of the chamber (filled with clean water). The contribution of this effect was most important for ^{131}I ; this explains the overestimation of activity in the planar images for this nuclide.

IV.C Torso Phantom

Planar images—For planar images, poor estimation of activity in the spheres in the outer cavity of the phantom can be attributed to the influence of activity in the liver, which contributes counts to regions near the spheres. This affected the results in two ways (a) reducing the contrast between objects and the background, which in some cases prevented quantification of small objects with low concentrations for some ^{131}I cases, and (b) causing background correction to be more important. Together, these factors caused activity to be not quantifiable (NQ) in some objects.

For spheres in the liver chamber, heterogenous activity distribution caused the largest error when performing background subtraction.

SPECT images—SPECT quantification proved superior in many cases. For spheres placed in the liver chamber (filled with a heterogeneous activity distribution), better activity quantification was seen for the largest sphere for all nuclides, but still results worsened as the sphere/liver activity ratio decreased. For the 2.2 ml sphere, background subtraction was more important, and poorer results with larger errors in activity estimates were seen. All of the spheres were detected, independent of size, activity concentration, or background level. The choice of background ROIs has a significant influence on the estimation of activity for these spheres. Choice of ROIs to correct background will influence activity quantification in tumors, should there be nearby regions with significant radionuclide uptake. These results suggest an expectation of better performance of SPECT imaging over planar imaging in detecting activity in smaller objects.

It is important to note that no explicit correction was made in this study for septal penetration of the ^{131}I photons (Dewaraja et al. 2000). Characterization of this phenomenon is an important factor to take into account for different source-to-collimator distances and will be the subject of further studies with our equipment.

IV.D Implications for Radiation Dosimetry

Modern imaging systems and quantification methods have limitations that complicate the accurate estimation of activity concentrations, and thus radiation dose, to structures of the body. A recent analysis discussed the numerous uncertainties that exist in any calculation of internal dose from radiopharmaceuticals (Stabin, 2008a). The conclusion of this analysis was that “The combined uncertainties in most radiopharmaceutical dose estimates will be typically at least a factor of 2 (standard of deviation as a fraction of the average) and may be considerably greater. In therapy applications, if patient-individualized absorbed doses are calculated, with attention being paid to accurate data gathering and analysis and measurement of individual organ volumes, many of the model-based uncertainties can be removed, and the total uncertainty in an individual radiation dose estimate can be reduced to a value of perhaps $\pm 10\%$ – 20% .” The results of the present study show that activity quantification in most major organs (such as in the cardiac phantom) may be quite good, within perhaps a few percent, with careful attention to background and scatter correction. Only in the case of planar imaging for ^{111}In was quantification poorer than $\pm 10\%$, this in the planar imaging studies at low organ concentration. For SPECT images of smaller organs (e.g. adrenals, gonads) or small tumors, quantification even with background and scatter correction, will require that some kind of partial volume compensation, perhaps with the use of recovery factors, factors be applied to account for the partial volume effect. If the objects are inside of organs or regions with high levels of background, estimation of recovery for objects smaller than a few ml will be problematic, and some uncertainty, perhaps significant, will remain in the estimation of activity (which is directly proportional to the absorbed dose ultimately received by the object), given current approaches to image reconstruction and compensation.

Characterizing radiation dose for individual patients is rarely of interest for radiopharmaceuticals labeled with $^{99\text{m}}\text{Tc}$, except during the new drug approval process (Stabin, 2008b). Our ability to quantify levels of activity in the various objects using $^{99\text{m}}\text{Tc}$ in these experiments was done to show the improved performance with radionuclides that have relatively simple decay schemes. Results for the more complex phantoms and small objects for ^{111}In and ^{131}I , particularly ^{111}In , were poorer than those for $^{99\text{m}}\text{Tc}$, which was expected. It is often necessary to use radionuclides of this nature to quantify activity for estimating radiation dose from radionuclides used in therapy. However, the use of nuclides with more simple decay schemes and photon emission energies in the range 100–170 keV is always more desirable. Differences in the resolution of the various collimators needed for imaging with the different nuclides, also affects partial volume effects and thus recovery coefficients.

V. CONCLUSIONS

Planar methods yielded reasonable estimates (values between 90–102% of the correct values, or variations between -10% and $+2\%$) of the activities for largest sphere (11.5 ml) with the low background level. But results were less reliable when a more complex experimental design was used (e.g. studies in the torso phantom), where the underestimation of activity for this sphere was more than 33%. Ratios of calculated to known activity were poorer in smaller objects, with higher background, and for nuclides with more complex decay schemes. Some inverse recovery coefficients for the smallest object (1.4 ml) were between 3–7, but for objects greater than 2 ml, were generally between 1.0–1.75. On the other hand, despite the partial volume effect in SPECT images, accuracy was more consistent across the background levels

studied than with the planar method. Corrections for scatter and attenuation effects were very important to obtain high accuracy, for both planar and SPECT methods. An inhomogeneous activity distribution in planar images causes the placement of background correction regions to be the largest source of uncertainty in the quantification, even for largest object. To perform high quality dosimetry studies, it is essential to carefully characterize the imaging system to establish attenuation and calibration coefficients, suitable window settings for collection of data for scatter correction and recovery factors for objects of different size, for any radionuclides used to obtain quantitative data. The size and location of small tumors in actual patients should be established using CT or MR images, to allow an accurate quantification of activity, if possible, in these regions which are important to evaluation of activity to optimize the therapeutic outcome. The results suggest that the use of SPECT imaging should be preferred over planar imaging, when performing dosimetry studies for smaller objects (<11 ml) and in situations involving complex backgrounds, more accurate results with greater independence from activity in the background and neighboring organs will be provided for calculating radiation dose estimates.

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Fig. 1. Images of the three physical phantoms used to carry out the experiments. A) Jaszczak SPECT Phantom with activity in four spheres, showing three levels of background activity employed (images using ^{99m}Tc). B) Cardiac phantom insert, activity solely in the wall chamber. C) 'Torso' phantom with activity in liver and 'background', modified to include four spheres in order 1, 2, 3 and 4 (11.5, 6.0, 2.2 and 1.4 ml respectively).

Fig. 2.
Examples of regions of interest (ROIs) and background ROIs used in the image quantification.

Fig. 3.
Curves used to establish the system effective attenuation coefficients.

Fig. 4. Plot of inverse of recovery coefficients for ^{99m}Tc , ^{111}In , and ^{131}I in spheres of various volumes

Fig 5.

Comparacao entre Uncorrected (NSC) ratios of calculated/known activity values and corrected values (SC) for planar images using spherical sources in the Jaszczak phantom

Table 1

Corrected ratios of observed/known values of activity (RCs) for experiments employing Planar and SPECT imaging of spherical sources in the water-filled cylindrical phantom.

Quantification Results - Spheres - Comparison of Planar and Spect																		
Radionuclide:	99mTc						111In						131I					
	Planar			SPECT			Planar			SPECT			Planar			SPECT		
Imaging method:	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%
Background level:																		
74 kBq/ml																		
Sphere Size:																		
11.5 ml	0.97	0.99	1.00	0.95	0.92	0.73	0.70	0.72	0.68	0.81	0.69	0.65	0.89	0.94	1.02	0.93	0.93	0.85
6.0 ml	0.91	0.92	0.87	0.90	0.89	0.61	0.60	0.60	0.57	0.64	0.44	0.45	0.52	0.68	0.84	0.62	0.64	0.50
2.2 ml	0.76	0.76	0.63	0.67	0.51	0.54	0.62	0.62	0.56	0.63	0.29	0.28	0.64	0.52	0.53	0.49	0.50	0.38
1.4 ml	0.63	0.57	0.57	0.26	0.23	0.24	0.40	0.39	0.40	0.28	0.10	0.10	0.41	0.22	0.12	0.19	0.21	0.11
185 kBq/ml																		
Sphere Size:																		
11.5 ml	0.97	0.98	1.00	1.05	1.01	0.95	0.84	0.80	0.78	1.09	1.02	0.78	0.95	0.93	0.96	0.97	0.95	1.04
6.0 ml	0.97	0.91	0.94	0.90	0.87	0.72	0.66	0.69	0.66	0.85	0.84	0.57	0.72	0.67	0.65	0.66	0.62	0.64
2.2 ml	0.79	0.79	0.73	0.69	0.74	0.62	0.62	0.58	0.56	0.73	0.58	0.49	0.53	0.49	0.50	0.58	0.51	0.36
1.4 ml	0.62	0.62	0.46	0.40	0.32	0.18	0.51	0.47	0.41	0.34	0.19	0.18	0.62	0.50	0.37	0.15	0.15	0.17
370 kBq/ml																		
Sphere Size:																		
11.5 ml	0.93	0.95	0.92	1.01	0.94	0.98	0.92	0.91	0.87	1.18	1.12	1.10	0.96	0.97	0.93	1.06	0.97	0.96
6.0 ml	0.95	0.88	0.85	0.89	0.81	0.77	0.78	0.73	0.73	0.93	0.91	0.78	0.76	0.80	0.78	0.78	0.67	0.65
2.2 ml	0.75	0.75	0.67	0.65	0.69	0.49	0.62	0.66	0.61	0.78	0.69	0.61	0.55	0.52	0.41	0.63	0.55	0.40
1.4 ml	0.48	0.47	0.39	0.38	0.26	0.16	0.54	0.49	0.41	0.35	0.27	0.29	0.46	0.38	0.33	0.18	0.17	0.13
740 kBq/ml																		
Sphere Size:																		
11.5 ml	1.01	1.02	1.02	1.02	1.05	1.01	0.93	0.89	0.88	1.21	1.14	1.09	0.94	0.94	0.94	1.09	1.08	1.06
6.0 ml	0.99	0.99	0.99	0.82	0.85	0.86	0.81	0.85	0.78	0.92	0.92	0.77	0.77	0.77	0.64	0.80	0.79	0.71
2.2 ml	0.83	0.81	0.73	0.70	0.69	0.60	0.67	0.65	0.63	0.81	0.66	0.58	0.68	0.53	0.53	0.61	0.55	0.46

QUANTIFICATION RESULTS - SPHERES - COMPARISON OF PLANAR AND SPECT																	
Radionuclide:		99mTc					111In					131I					
Imaging method:		Planar		SPECT			Planar		SPECT			Planar		SPECT			
Background level:		0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	
1.4 ml		0.69	0.63	0.54	0.29	0.29	0.22	0.54	0.51	0.50	0.35	0.40	0.40	0.37	0.22	0.17	0.21

Corrected ratios of observed/known values of activity (RCs) for experiments employing planar and SPECT imaging of the myocardial chamber in the cardiac phantom.

Table II

	QUANTIFICATION RESULTS – CARDIAC PHANTOM – CORRECTED														
	^{99m} Tc						¹¹¹ In						¹³¹ I		
	Planar			SPECT			Planar			SPECT			Planar		SPECT
Imaging method:	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%
Background level:															
Concentration:															
74 kBq/ml	0.93	0.92	0.93	1.03	1.05	1.02	0.80	0.72	0.70	0.87	0.85	0.84	1.20	1.15	1.17
185 kBq/ml	0.95	0.93	0.90	1.05	1.00	0.94	0.80	0.73	0.72	1.05	1.03	1.02	1.11	1.07	1.18
370 kBq/ml	0.95	0.93	0.97	0.97	0.95	1.05	0.86	0.77	0.71	1.10	1.08	1.04	1.09	1.06	1.05
740 kBq/ml	0.94	0.95	0.92	0.98	1.05	1.03	0.90	0.80	0.74	1.09	1.07	0.99	1.05	1.02	1.00

Table III

Corrected ratios of observed/known values of activity (RCs) for experiments employing planar and SPECT imaging of the liver region and spherical sources in the torso phantom.

QUANTIFICATION RESULTS - TORSO - PLANAR × SPECT																
Radionuclide:	^{99m} Tc						¹¹¹ In						¹³¹ I			
	Planar			SPECT			Planar			SPECT			Planar		SPECT	
Imaging method:	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	1.0%
Background level:																
74 kBq/ml																
Liver:	0.99	0.96	0.92	1.14	1.00	0.99	0.92	0.89	0.91	1.25	1.08	1.04	1.20	1.02	1.05	1.07
Spheres:																
11.5 ml	0.59	0.57	0.33	0.94	0.70	0.56	0.41	0.35	0.30	0.74	0.55	0.58	0.55	0.58	0.44	0.98
6.0 ml	0.52	0.64	0.53	0.73	0.69	0.66	0.63	0.43	0.47	0.67	0.44	0.47	0.40	0.42	0.46	0.63
2.2 ml	0.51	0.35	0.14	0.59	0.47	0.43	0.47	0.65	0.66	0.39	0.42	0.35	0.42	0.52	0.56	0.42
1.4 ml	0.21	0.29	0.29	0.32	0.21	0.18	0.19	0.19	0.13	0.28	0.14	0.20	NQ	NQ	NQ	0.16
185 kBq/ml																
Liver:	1.03	0.96	0.93	1.15	1.00	0.97	0.90	0.93	0.90	1.07	1.01	0.96	1.12	1.10	1.10	1.24
Spheres:																
11.5 ml	0.65	0.64	0.46	0.98	0.87	0.78	0.35	0.33	0.28	0.60	0.49	0.48	0.57	0.45	0.41	0.90
6.0 ml	0.71	0.69	0.67	0.92	0.90	0.89	0.46	0.41	0.35	0.55	0.44	0.42	0.54	0.62	0.63	0.59
2.2 ml	0.80	0.60	0.63	0.69	0.65	0.60	0.56	0.63	0.61	0.38	0.32	0.33	0.52	0.60	0.66	0.42
1.4 ml	0.30	0.25	0.37	0.33	0.29	0.24	0.20	0.14	0.20	0.21	0.20	0.16	NQ	NQ	NQ	0.25
370 kBq/ml																
Liver:	0.94	0.96	0.91	1.13	1.00	0.99	0.97	0.95	0.91	0.95	0.96	0.99	1.20	1.03	1.05	1.22
Spheres:																
11.5 ml	0.67	0.65	0.54	1.04	0.97	0.85	0.50	0.41	0.39	0.84	0.63	0.57	0.59	0.49	0.48	0.96
6.0 ml	0.74	0.68	0.69	0.93	0.99	1.03	0.47	0.46	0.49	0.72	0.57	0.48	0.56	0.71	0.53	0.70
2.2 ml	0.87	0.82	0.93	0.66	0.59	0.50	0.74	0.66	0.66	0.44	0.43	0.44	0.63	0.72	0.77	0.40
1.4 ml	0.27	0.38	0.31	0.31	0.29	0.27	0.26	0.22	0.15	0.27	0.21	0.25	0.32	0.08	0.11	0.24
740 kBq/ml																
Liver:	1.04	0.90	0.95	1.13	1.09	1.00	0.95	0.91	0.90	1.13	1.09	0.97	1.20	1.10	1.04	1.27
																0.96
																1.10

QUANTIFICATION RESULTS - TORSO - PLANAR × SPECT																		
Radionuclide:	99m Tc						111 In						131 I					
	Planar			SPECT			Planar			SPECT			Planar			SPECT		
Imaging method:	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%	0%	0.5%	1.0%
Background level:																		
Spheres:																		
11.5 ml	0.67	0.65	0.57	1.04	1.02	0.90	0.49	0.42	0.40	0.88	0.74	0.64	0.54	0.44	0.42	0.89	0.77	0.70
6.0 ml	0.70	0.73	0.68	0.96	0.94	0.92	0.51	0.51	0.42	0.74	0.66	0.53	0.62	0.51	0.56	0.65	0.58	0.64
2.2 ml	0.82	0.85	1.00	0.67	0.60	0.51	0.65	0.63	0.74	0.51	0.44	0.38	0.70	0.69	0.75	0.43	0.42	0.46
1.4 ml	0.32	0.35	0.17	0.31	0.30	0.29	0.26	0.27	0.20	0.25	0.21	0.23	0.19	0.10	0.08	0.26	0.21	0.18