

A Review of Activity Quantification by Planar Imaging Methods

Collie Miller, Larry Filipow and Stuart Jackson

Department of Radiology and Diagnostic Imaging, MacKenzie Centre, University of Alberta Hospitals, Edmonton, Alberta

Objective: The purpose of this paper is to provide information on the nature and magnitude of the problems encountered in activity quantification by planar imaging in nuclear medicine and provide an understanding of several methods of activity quantification.

Methods: This paper presents a critical examination of several methods that have been applied or proposed for use in the quantification of radioactivity in the body using planar images in nuclear medicine. Outlined in this paper are the uses and limitations of each method in quantifying activity in the body, along with errors associated with each method, and suggestions for improving the accuracy of activity quantification.

Results: Absorption and scatter of gamma photons in the body have significant influence on the accuracy of activity quantification.

Conclusion: Accurate activity quantification will require the use of a method that can adequately correct for errors including those due to source inhomogeneity, the presence of nontarget organ activity, and for overlapping discrete regions of activity uptake.

Key Words: quantification; attenuation absorption and scatter; buildup factor; activity; planar imaging

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The increasing use of sophisticated gamma camera systems and a number of relatively new radiopharmaceuticals in nuclear medicine has generated much interest in activity quantification. Unfortunately, nuclear medicine images are degraded by several factors which limit the quantitative ability of this modality. These factors include clearance of radioactivity during acquisition, poor spatial resolution, motion, absorption and scatter. Absorption and scatter probably have the most influence on the accuracy of quantification of radioactivity distributed in the human body.

Absolute quantification of the in vivo distribution of radioactivity is important in clinical research and for understanding many physiological processes. It provides significant diagnostic and therapeutic information on patient dosimetry and has potential applications that may influence patient management.

Several methods have been proposed for quantifying radioactive uptake by an organ from planar images. Planar imaging methods are based on counts acquired either from a single image or combined from a pair of opposing images. For each method, quantification requires that correction be made for absorption and scatter in the body. This is generally done either by comparison with a phantom that approximates the organ in shape, size, depth and tracer distribution or by direct measurement.

Essentially, the correction methods used by most investigators in planar imaging quantification can be placed into three broad categories. The first employs the use of energy window techniques to exclude or correct for scatter (1-5). The second utilizes a broad beam linear attenuation coefficient in the attenuation correction term and includes a term to correct for radionuclide distribution (6-11). The third uses a buildup factor for correction (12-14). The accuracy of any of the methods depends on its ability to correct for scatter. At present, none of the scatter correction methods has been adopted as the standard method for clinical use.

Most of the investigations in organ activity quantification are currently carried out using SPECT instead of planar imaging. Undoubtedly SPECT has the potential to improve quantification and, in particular, it can be used to estimate the uptake in a small, localized region. However, the magnitude of uptake following some procedures, such as the intravenous administration of radiolabelled antibodies, indium-111 leukocytes and gallium-67 citrate, is too small for satisfactory SPECT imaging. Whole body activity quantification by SPECT would require unacceptable acquisition time. Certainly, there are limitations with planar imaging methods also, but they are easier to implement, require shorter acquisition and processing times, and produce images that are less noisy than SPECT images with the same activity and distribution.

For reprints and correspondence contact: Mr. Collie Miller, MSc., Dept. of Radiology and Diagnostic Imaging, MacKenzie Centre, University of Alberta Hospitals, Edmonton, Alberta, T6G 2B7 Canada.

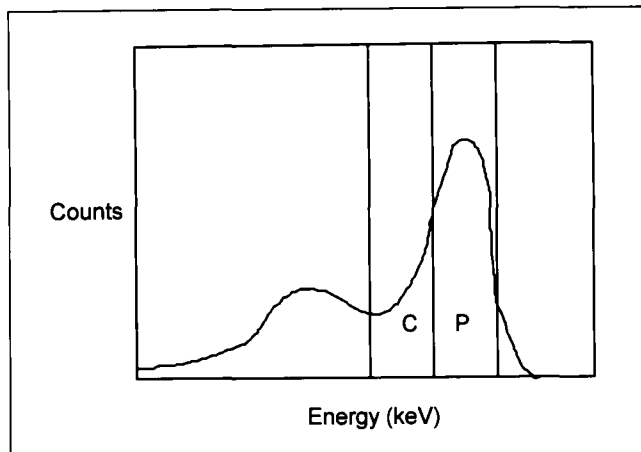


FIGURE 1. Dual energy windows with lower energy scatter window, C, and photopeak window, P.

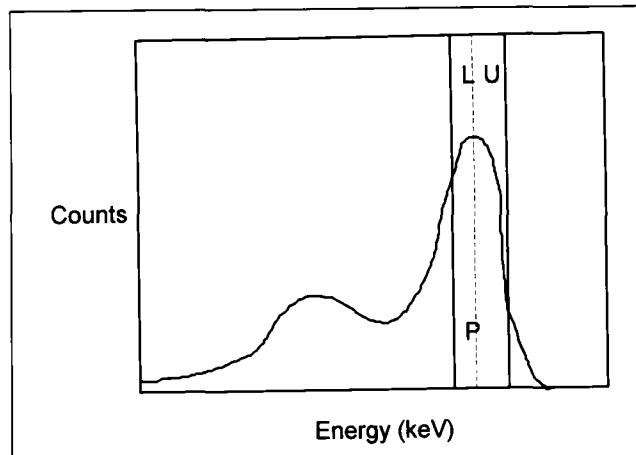


FIGURE 2. Asymmetric energy windows with lower photopeak window, L, and upper photopeak window, U.

APPROACHES TO ACTIVITY QUANTIFICATION

Accurate activity quantification requires that proper correction be done for attenuation and scatter. Consequently, several methods to compensate for these factors have been proposed and are discussed below.

Use of Secondary Energy Window

Ehrhardt and Oberley (1) proposed the use of dual energy windows to correct for Compton scatter. This can be achieved by simultaneously obtaining images in two energy windows, a photopeak window and a lower-energy scatter window (Fig. 1). These energy intervals are obtained by assuming that the Klein-Nishina equation for single Compton scatter adequately describes the spectrum. Compton corrected count rates can then be obtained by subtracting a fraction, k , of the Compton region count rate from the photopeak count rate. The corrected count rate, C_{cor} is given by:

$$C_{cor} = C_{pp} - k * C_{scat} \quad \text{Eq. 1}$$

where C_{pp} is the photopeak count rate, C_{scat} is the scatter window count rate and C_{cor} is the Compton corrected count rate. This secondary energy window method is based on the assumption that the events detected in the scatter window are correlated to the scatter component of the events detected in the photopeak window. Bloch and Sanders (2) adopted this method for liver phantom imaging and reported satisfactory results. Van Reenen et al. (4) have reported errors of $0.1 \pm 8.5\%$ for spleen activity and $3.8 \pm 6.4\%$ for liver activity when the method was applied to planar imaging.

The accuracy of the correction will depend, to a large extent, on the value of k . This will vary with scatter distribution within the spectrum which is dependent on source geometry. Filipow et al. (15) reported the change in proportion of scatter in different energy intervals with source depth. In addition, distortion is introduced in the spectrum when distributed sources are used and background activity is present (16). Also there is significant difference in the scat-

ter/photopeak ratio for different organs (17). Furthermore, the estimated scatter distribution from the lower energy window is not identical to the shape of the scatter distribution within the photopeak window, hence it is difficult to achieve accurate correction (18–20).

The primary objective of this method is to determine the value of k that optimizes the correction procedure for a specific class of source geometry and energy window settings. The value of k can be determined experimentally using line sources and phantoms or by Monte Carlo simulations of the systems. However, a variable k value might be necessary in order to improve accuracy.

Use of Asymmetric Energy Windows

Another window method that has been applied for reducing scatter is the use of asymmetric windows (5,21–23). Essentially, the energy discriminators are set so that the energy window is shifted slightly to the higher energy region of the photopeak. In other words, the lower energy cutoff is closer to the photopeak energy than the higher energy cutoff (Fig. 2). The rationale is that Compton scattering will reduce the energy of the scattered photons enough to allow discrimination through energy window selection. However the energy loss from each scattering event is not large enough to allow for discrimination of all scattered events through energy window settings. For example, ^{99m}Tc photons (140 keV) undergoing scatter of angles up to 45° will still be within an energy interval that is only 7% below the photopeak energy. Thus, there exists great likelihood for scatter to be included even when a narrow window is selected.

In fact, given the energy resolution of a NaI(Tl) gamma camera (10–15%), scattered events would be detected even with the lower baseline value set at the photopeak energy. Another problem with this technique is that primary photons are being eliminated while excluding scatter, thus reducing the sensitivity of the system. Furthermore, if the window is made too narrow in an effort to reduce scatter, then a compromise would have to be made between poor counting

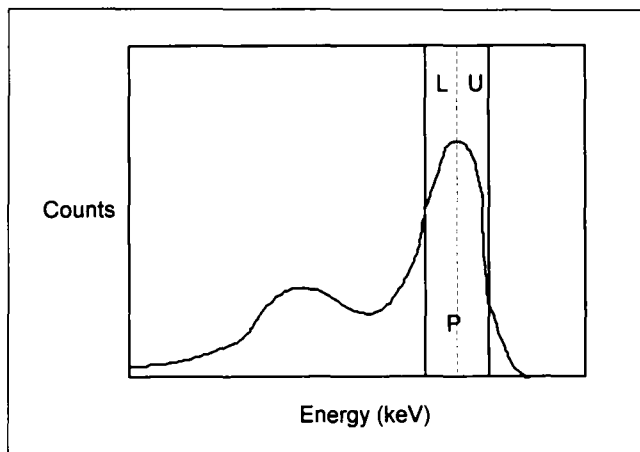


FIGURE 3. Dual-photopeak windows with lower half, L, and upper half, U.

statistics and significantly increased acquisition time, neither of which is desirable.

Dual-Photopeak Window Method

King et al. (24) proposed the possible use of a dual-photopeak window (DPW) method for Compton scatter correction in SPECT and planar imaging. The basis of this method of scatter correction is that Compton scattered photons contribute more to the lower energy portion of the photopeak than to the high energy side (19,25-28). In this method the photopeak window (20% symmetric energy window) is divided into upper and lower halves (Fig. 3) and a regression relationship established between the ratio of counts within each of the halves and the scatter fraction for the counts within the total photopeak window.

This method has potential applications for scatter correction in organ activity quantification. However, for low count images it may produce scatter estimates that are noisy since only half of the photopeak events are used for forming each image. For good counting statistics, increased imaging time would be required which would increase the likelihood of patient motion artifacts and reduce the number of cases that can be done when compared to similar camera systems employing the full photopeak window for each image.

A common limitation presented by this method is the increased number of energy windows that are required for simultaneous acquisition of radionuclides of multiple energy photons, such as ^{67}Ga , ^{201}Tl and ^{111}In , which cannot be achieved on most of the currently available gamma cameras.

Activity quantification by energy window methods produces acceptable results when applied to a single-point or line source in a homogeneous medium. However, when applied to volume or distributed sources in a nonhomogeneous medium (as in the case of the human body), they are limited. This is because the methods are incapable of correcting for errors due to source and attenuating medium characteristics. These include variation in source size, inhomogeneity of radioactivity distribution within the source, and attenuating medium inhomogeneity.

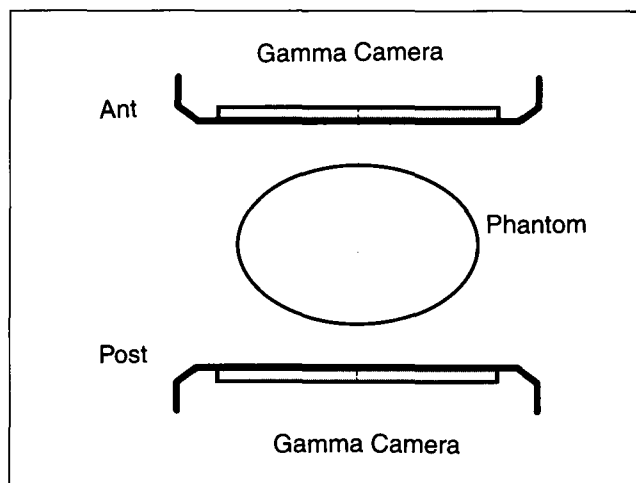


FIGURE 4. Geometry of phantom and dual head gamma camera.

Geometric Mean Method

This method has been used to determine organ activity from the geometric mean anterior and posterior gamma camera count rates as indicated in Figure 4 (9,29,30) using the relationship:

$$A = [(C_a * C_p)^{1/2}/E] * \exp(\mu T/2) \quad \text{Eq. 2}$$

where A is the activity of the organ, C_a and C_p are the anterior and posterior counts respectively, T is the total thickness of the patient, μ is the broad beam linear attenuation coefficient, and E is the sensitivity of the camera. The attenuation correction term can be derived from a transmission source using the relationship:

$$C_i = C_o * \exp(-\mu T) \quad \text{Eq. 3}$$

where C_i is the count rate obtained with the patient between the source and the camera and C_o is the count rate without the patient. Macey and Marshall (9) showed that when Equation 2 was applied to activity quantification for lung tissue (density = 0.3 g/cc) of thickness up to 15 cm, less than 3% error would be introduced by ignoring correction for source thickness. However, for soft tissue (density = 1.0 g/cc) and bone (density = 1.8 g/cc), the error introduced increases significantly with increased thickness. For example, with soft tissue thickness of 5 cm, the error would be about 2%, but for 15-cm thickness the error would be about 15%. For bone of 5-cm thickness, the error would be about 6%, increasing to 12% error for 8 cm of bone. If correction for source thickness effect is applied, then accuracy will improve.

Equation 2, in its current form, cannot be used to accurately quantify activity distributed in isolated regions, particularly those separated vertically, such that their projected anterior and posterior images are superimposed. Overestimation of activity of up to 40% has resulted from $^{99\text{m}}\text{Tc}$ point sources separated vertically by a distance of 14 cm in a perspex phantom (unpublished work by author). There are

reports of overestimation of activity for both spleen and liver by 42.6–50.9% using ^{111}In as a tracer (29) and up to 20% for distributed $^{99\text{m}}\text{Tc}$ sources (31).

Certainly the method has useful applications as demonstrated in lung activity quantification (9,30). However, its accuracy is limited to specific clinical situations. Perhaps the most fundamental drawback with this method is the fact that it assumes constant attenuation of photon intensity with source depth, hence it does not correct for the contribution of scatter to the counts obtained. This assumption is not valid for the relatively wide window settings used in nuclear medicine. It has been shown that the broad beam attenuation coefficient, μ , varies from 0.081 cm^{-1} for a source at 1-cm depth to 0.122 cm^{-1} for a source at 15-cm depth in tissue equivalent material using a 30% window (11). In addition, the method does not take into consideration the effects of source thickness and inhomogeneity of the attenuating medium. Source thickness and inhomogeneity effects *in vivo* may be as high 20% each (32).

Use of Anterior, Posterior and Lateral Views

Errors obtained using the geometric mean method can be reduced by applying anterior, posterior and lateral imaging. Fleming (8) applied a method that corrects for source thickness using the equation:

$$A = [(C_a * C_p)^{1/2}/E] * \exp(\mu T/2) * (\mu x/2)/(\sinh \mu x/2) \quad \text{Eq. 4}$$

where x is source thickness and the other terms are as before. Patient and organ thicknesses can be determined from lateral images. Fleming (8), using a liver phantom, reported a 3.2% error as the best result that could be obtained with the method and pointed out that in a clinical situation the error could be as much as 5–10%. Some of the problems associated with this method include the need for accurate thickness measurement from the lateral image. An error of 1 cm in patient thickness results in 5% error in activity quantification (32). The method cannot correct for errors due to the presence of activity in regions surrounding or overlying the organ of interest. In fact, accurate organ activity quantification in such situations cannot be achieved from anterior, posterior and lateral images. Also, Fleming's equation makes no provision to correct for error due to non-uniform distribution of radioactivity within the source.

The authors of this paper adopted the model of Sorenson (32) to correct for errors due to source inhomogeneity using the equation:

$$A = [(C_a * C_p)^{1/2}/E] * \exp(\mu T/2) * (\mu x/2)/(\sinh \mu x/2) * 1/\cosh[(f - x)\mu/2] \quad \text{Eq. 5}$$

where f is the sum of the distance separating the sources and the thickness of each source. This method was applied to two $^{99\text{m}}\text{Tc}$ point sources in a cylindrical perspex phantom. Increasing vertical separation from 2 cm to 16 cm gave an average measured activity of $102\% \pm 2\%$ (unpublished data).

Transmission-Emission Method

The use of transmission measurement for error correction was first described by Evans (33) for whole body counting. Since then the method has been adopted by several investigators to measure organ or whole body radioactivity by counting and planar imaging procedures (6, 9, 10, 30–32, 34). Perhaps the most thorough investigation of the application of this method to planar imaging quantification has been carried out by Thomas et al. (6). They examined the effects on lesion activity quantification in regions of differing attenuation coefficients and non-target organ activity in tissue surrounding the lesion.

In a clinical situation, however, the parameters required to make corrections in the equations of Thomas et al. (6) are unknown and cannot be accurately determined from planar images. Also, it is difficult, if not impossible, to determine the thickness and homogeneity of an internal distribution and, therefore, analytically determined correction cannot be employed.

In the clinical application of this method, the attenuation correction term (Eq. 2), can be derived from the patient by measuring the transmitted radiation from a uniformity source through a region of interest (ROI). The accuracy will depend on variation of thickness and attenuation across the ROI. Errors can be reduced by dividing the ROI into several small regions and separately quantifying uptake in each.

Some investigators, that have adopted this technique, have used the same radionuclide as the transmission and emission sources. They therefore used the attenuation coefficient calculated from the transmission source as the emission source attenuation coefficient. Strictly, this is not correct because the measuring conditions are different. The effects of scattered radiation are considerably greater for an internal source than an external source and will produce different attenuation coefficients (32). Thus accurate quantification requires that the various exponential coefficients be determined separately. In addition, whenever transmission and emission scans are done separately, care must be taken to ensure accurate spatial correlation between both. If possible, simultaneous transmission–emission scans should be done instead.

Buildup Factor Methods

The attenuation of photons in nuclear medicine imaging involves broad beam conditions (Fig. 5). Under such conditions a considerable amount of scattering occurs in the attenuating medium surrounding or overlying the radiation source. Harris et al. (35) have reported the variation in linear attenuation coefficient values with energy window settings and source depth under broad beam conditions. The buildup factor is the factor by which transmission is increased in the broad beam conditions, relative to narrow beam conditions (36). The buildup factor, $B(d)$, is defined as:

$$B(d) = (C/C_0) * \exp(\mu_n d) \quad \text{Eq. 6}$$

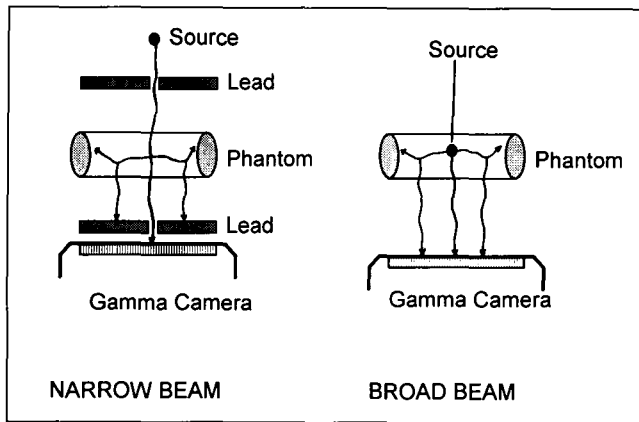


FIGURE 5. Example of narrow and broad beam geometries.

where C is the count rate measured for depth, d , in a phantom; C_0 is the count rate measured in air at the same source to collimator distance; and μ_n is the narrow beam linear attenuation coefficient. Two buildup factor methods have been developed to correct for the contribution of scatter. These are the depth-dependent buildup factor (DDBF) and the depth-independent buildup (DIBF) methods (12,13,14). The methods require the use of anterior and posterior view count rates and the use of a set of derived buildup factors to correct for the effects of scatter. There are reports of successful applications of the buildup factor methods for cardiac studies (13), activity quantification in patients with hepatic disorders (37), activity quantification in lungs (30) and for kidney activity uptake (38).

Depth-Dependent Method. Wu and Siegel (12) have described activity quantification by the depth-dependent buildup factor method using the following equations:

$$A_{\text{ant}} = C_a [E * B(d) * \exp(-\mu_n d)] \quad \text{Eq. 7}$$

and

$$A_{\text{post}} = C_p [E * B(T - d) * \exp(-\mu_n(T - d))] \quad \text{Eq. 8}$$

where A_{ant} and A_{post} are the activity estimates from the anterior and posterior view count rates, respectively, and the other terms are as before. Using a set of derived buildup factors from phantom measurements, the equations are then solved by an iterative technique to determine the activity and source depth.

The significant difference with this approach from the others is that the buildup factor removes the requirement in the exponential term for correction due to scatter contribution and replaces it by a simple multiplicative factor. Thus, the linear attenuation coefficient used is that of narrow beam conditions and is independent of source depth, window width and other parameters that influence linear attenuation coefficients under the broad beam conditions imposed by nuclear medicine. Wu and Siegel (12) showed that the method provides less than 5% error and Forge et al. (30) have reported average uptake of $100\% \pm 3\%$ for lung activity

using this method. The use of the buildup factor obviates the need for an external source to measure patient transmission and enables depth measurement to be obtained without the use of lateral views.

However, there are limitations in applying the method. The buildup factor is dependent upon the energy of the radionuclide used, source depth, source size, source thickness, collimator type, window width and geometry of measurement (12).

Van Rensburg et al. (29) have reported errors ranging from 22.5% to 4.7% for spleen and 5.3% to -14.7% for liver using ^{111}In , depending on which one or both of the two different energy photons (172 keV and 247 keV) were used. Wu and Siegel (12) compared buildup factors for a 15×15 -cm source and a 2×2 -cm source at a depth of 12 cm in tissue equivalent material and reported a difference of 13%.

This means that in order to apply this method, knowledge of the dimensions of the specific organ under investigation is required so that a source approximating the actual organ dimensions can be used to establish a set of buildup factors necessary for correction. It is difficult to achieve this clinically, without significant errors and this would be required for each patient and for each organ. However, Monte Carlo simulation could be used to generate appropriate buildup factors for correction (39). Unfortunately, the method does not correct for inhomogeneity of source distribution within the organ or inhomogeneity within the attenuating medium, either of which can introduce significant errors in activity quantification as indicated earlier.

Depth-Independent Method. Siegel et al. (14) have proposed that the commonly used transmission factor, $TF = \exp(-\mu d)$, should be replaced by:

$$TF = 1 - (1 - \exp(-\mu d))^{B(\infty)} \quad \text{Eq. 9}$$

where $B(\infty)$ is the buildup factor at infinite depth. $B(\infty)$ can be determined by using a nonlinear least-squares algorithm obtained from a graph of transmission factors versus source depth in a phantom. The relationship, $TF = \exp(-\mu d)$, suggests that a semilogarithmic plot of TF versus depth would be linear. This is true only for a window width that approaches zero which is never the case in nuclear medicine imaging (12-14). This method can be used to improve accuracy in activity quantification over the DDBF method because $B(\infty)$ is independent of source size for a constant energy window. Van Rensburg et al. (29) have reported errors of -1.5% to 1.8% in using this method.

A fundamental drawback with this method, however, is that the parameter, TF [$TF = 1 - (1 - \exp(-\mu d))^{B(\infty)}$], was derived for a thin source and is not suitable for a volume source. Kojima et al. (40) suggested the use of a transmission factor, TF_v , for a volume source, obtained by integrating Equation 9 over the thickness, t , of the volume. Thus, the transmission factor is given by:

$$TF_v = 1 - (1/t) \int_d^{d+t} [1 - \exp(-\mu x)]^{B(\infty)} dx \quad \text{Eq. 10}$$

TABLE 1
Summary of Methods Used for Correction in Activity Quantification and Errors Reported

Authors	Methods	Investigations	Errors
Van Reenen et al. (4)	Dual-energy window	Liver Spleen	3.8 ± 6.4% 0.1 ± 8.5%
Myers et al. (31)	Geometric mean approach	Liver/Spleen and distributed sources	20% overestimation of activity
Van Rensburg et al. (29)	Geometric mean approach	Liver/Spleen	42.6% to 50.9% overestimation of activity
Fleming (8)	Use of ant, post and lat views	Liver phantom	*3.2%
Macey and Marshall (9)	Transmission-emission	Lung Soft tissue Bone Phantom	† <3% (for up to 15 cm thickness) approx. 15% (for 15 cm thickness) approx. 12% (for 8 cm thickness) <5%
Wu and Siegel (12)	DDBF	Lung	100% ± 3% activity uptake
Forge et al. (30)	DDBF	Liver	5.3% to -14.7%
Van Rensburg et al. (29)	DDBF	Kidney phantom	<5%
Kojima et al. (40)	DIBF	Liver/Spleen	1.8% to -1.1%
Van Rensburg et al. (29)	DIBF		

* The author indicated that 5–10% error is likely in clinical situations.
† These are the estimated errors when correction for source thickness is ignored.

However, the attenuation coefficient, μ , varies with cross sectional area of the source by the relationship:

$$\mu = \mu_n * \exp(-kA)$$

where A is the cross sectional area of the source and k a constant. Therefore, before the method is applied, determination of organ cross sectional area is required. This cannot be accurately achieved from anterior, posterior and lateral images, hence μ cannot be accurately determined for the correction procedure. Also the parameters $B(\infty)$ and k would have to be predetermined under conditions consistent with the clinical situation to which they are to be applied. This, undoubtedly, presents a fundamental limitation in that the method can only be applied to situations for which predetermined values can be obtained. Furthermore, the solution for volume sources proposed by Kojima et al. (40), is only true for volume sources with uniform activity distribution because the integration was done assuming TF for a thin source with uniform activity distribution. The method may have useful applications to specific organs such as the kidneys (38), but certainly needs further testing and evaluation. The relationship makes no provision for error corrections under the clinical conditions already mentioned and in its present form cannot be used for accurate whole-body quantification.

SUMMARY AND DISCUSSION

Despite the fact that several methods have been proposed for error correction in planar imaging quantification, none has been adopted as the standard method for clinical use. Those methods that have been reported to produce accurate results (less than 5% error), are limited to specific organs and clinical situations. Table 1 gives a summary of some of the

methods used and errors reported. Correction by energy discrimination can reduce the effects of scatter in radioisotope imaging. However, with low energy isotopes such as ^{99m}Tc and the limited energy resolution of NaI(Tl) gamma cameras, only imperfect discrimination against scattered photons can be achieved. Additional limitations of these methods are the need for a number of energy windows and the influence of noise on the estimation of scatter or increased imaging time. Monte Carlo simulation, has been employed to develop and evaluate scatter correction methods by analyzing energy and spatial distributions of scattered photons (25).

The geometric mean of anterior and posterior view counts in activity quantification of volume sources will always give an overestimation of activity since the source thickness correction term, $[\sinh(\mu l/2)]/(\mu l/2)$, in Equation 4 will always be greater than one and gets worse with increased source thickness. Therefore, those methods that correct for errors due to source thickness will improve accuracy over the geometric mean method. However, they are limited by their inability to correct for errors due to source inhomogeneity, the presence of nontarget organ activity and for overlapping discrete regions of activity uptake, such as the spine as it overlaps the liver. The buildup factor methods also suffer from these limitations, though they have demonstrated improved quantification for a limited range of source geometries.

In view of the foregoing limitations, it is obvious that there is need for further work on the development of a method for accurate whole-body activity quantification by planar imaging. Consequently, research continues in this area with the hope of developing a method that will accurately correct for errors such as those due to the presence of nontarget organ activity and activity uptake in overlapping discrete regions of the body.

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