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Improving the Quantification Accuracy of Tc-99m Mibi Dual-Phase Parathyroid Spect/Ct: A Monte Carlo Simulation Study

Research Article

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Abstract

Quantitative parathyroid SPECT imaging is a technique used in assessing primary hyperparathyroidism that may have potential in the identification and differentiation of parathyroid lesions as well as the estimation of disease severity. Studying the effect of data acquisition parameters on the quantification error is important for maximizing the accuracy of this diagnostic technique. In this study, the effects of different data acquisition parameters, namely the type of collimator, scatter correction status, and reconstruction iteration number on the quantification accuracy were examined using computer simulation. The SIMIND Monte Carlo Simulation and CASToR iterative reconstruction program was used to simulate a commercially available SPECT camera (Siemens Symbia Intevo Gamma Camera) with a crystal size of 29.55cm and 128x128 matrix size. A digital cylindrical phantom filled with water was constructed. A 0.36 cm radius spherical adenoma filled with a uniform 1MBq radioactivity is placed within the phantom. Low-Energy High Resolution (LEHR) and Low Energy Ultra High Resolution (LEUHR) collimator models are tested along with the presence of Scatter correction and differing iteration numbers (x16, x32). An image FOV-based calibration method was used to gather quantitative information and check against the input radioactivity. The inclusion of scatter correction resulted in a 15-20% relative improvement in quantification accuracy while the optimal number of iterations yielded a 10% improvement. Overall, accuracies as high as 7% were observed. The optimization of parameters can provide a significant improvement in quantification accuracy.
Keywords: SPECT, Monte Carlo Simulation, Quantification, Hyperparathyroidism.

1. INTRODUCTION

Primary hyperparathyroidism (PHPT) is among the most common endocrine disorders in the world. The disorder can cause the overproduction of parathyroid hormones (PTH) and an increase of plasma calcium levels in the blood [13]. It presents itself in the form of irregularities and over-release of PTH. Symptomatic representation of PHPT is commonly seen around the renal system and skeletal structures, with patients suffering from fragility in bones, renal nephrocalcinosis, and renal insufficiency. However, with the improvements in modern medicine and the ability to screen serum calcium levels, it is possible for physicians to gradually shift the PHPT presentation form from symptomatic to asymptomatic presentations [9]. Around 80% to 85% of hyperparathyroidism is caused by parathyroid adenomas, with primary parathyroid hyperplasia (15%) and parathyroid carcinoma (5%) less commonly linked with the disorder [13, 54]. Most patients exhibit adenomas on a single gland while about 20% percent of patients have multiple adenomas on their glands [40].

In normal circumstances, parathyroids are too small to detect, but PHPT causes the glands to increase in size, resulting in an enlarged state that allows imaging [54]. Patients with enlarged glands are generally advised to undergo surgery for the removal of the adenoma. For those patients who are not seen as fit for surgical operation, according to relevant guidelines [9], physicians can follow more conservative approaches such as newer, less invasive surgical interventions [40].

Parathyroid glands are rather small (generally 5x3x1 mm [54] and situated right behind the thyroid glands [22]. This makes imaging difficult. Sonography and Tc99m-Sestamibi scintigraphy are the imaging modalities used for imaging parathyroid glands [54]. Tc99m-Sestamibi is a known substance used in parathyroid imaging and is absorbed by both the adenomas and the thyroid glands. The substance then washes off the thyroid glands and provides a good vision of the adenomas in parathyroids [24].

Quantification of a medical image means gathering not only visual but also numeric information on biological structures such as the concentration of radioactive material within a certain biological structure in units of kilo becquerels per cubic centimeter This allows the user to further understand the properties of pathologies. Research has highlighted the benefits of quantification. [50] uses quantification to observe the effect of delay in Tc99m SPECT/CT imaging of secondary hyperparathyroidism patients. Another study on thyroid imaging Lee et al. ([31]) found that quantitative SPECT/CT measurements were more accurate than the thyroid uptake system (TUS). Some articles in the literature describe quantitative imaging as one of the most promising practices in nuclear medicine [1, 26, 28, 30].

In the case of an adenoma, quantification allows for the observation of not only the radioactivity level, but also properties such as size, shape, position, and volume in a much more precise way. Furthermore, it is possible to assess disease severity [23, 47].

The detection and quantitative analysis of parathyroid adenomas is a studied field that encompasses many approaches. Namely, Listewnik et al. ([32]) used particle swarm optimization with random neighbor topology to achieve 3% voxel size with heavily reduced processing times. Havel et al. ([19]), Khouli et al. ([27]), Robin et al. ([46]), and Wang et al. ([51, 52]) have used quantitative methods to gather information on optimal timing, standard uptake by time, and washout of radionuclides during imaging. Ma et al. ([36]) have employed a semi-quantitative method to analyze the degree of hyperplasia of the parathyroid gland pre-operation. Harris et al. ([17]) were able to localize adenomas with an accuracy within 19mm, demonstrating the viability of quantitative techniques for non-invasive analysis. Razavi et al. ([44]) has used quantitative analysis of parathyroid imaging to test the co-registration combinations of the early and delayed SPECT/CT scans to achieve the most viable pair along with operator variability. Khouli et al. ([29]) has successfully used quantitative analysis in the localization of adenomas.

The consensus is that the accurate acquisition of quantitative data is a critical step in dosimetry and treatment planning in nuclear medicine. However, inaccurate calculation of quantitative measures can cause mistreatment and potential adverse side effects [10]. With the addition of iterative imaging methods that allow for corrections during reconstruction, quantitative imaging has become increasingly prevalent in SPECT imaging.

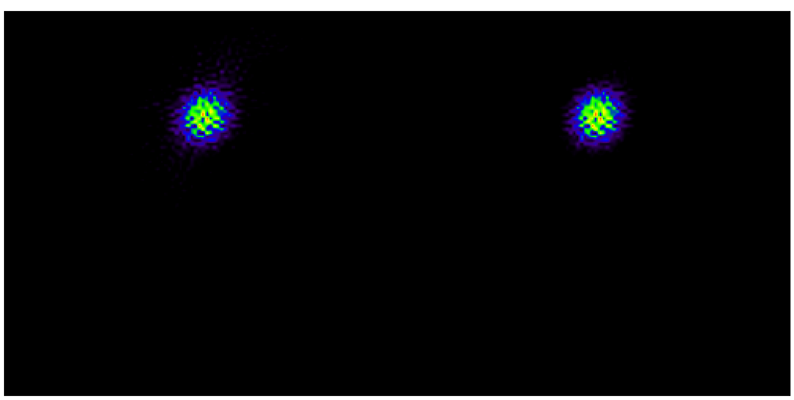
Single photon emission computed tomography (SPECT) visualizes the radioactivity distribution across the human body on a field of view (FOV). Traditionally, SPECT is seen as a qualitative imaging technique that has low special resolution and high noise in regions of interest [45, 41]. Since the recent development of

iterative reconstruction algorithms, SPECT has joined others as a quantitative imaging modality providing an accurate quantitative representation of radioactivity in the body. Corrections should be performed for maximum accuracy against naturally occurring physical phenomena, such as scattering and attenuation. These phenomena cause inaccuracies in radioactivity readings. Studies show that iterative reconstruction methods paired with correction methods can give much higher quantitative accuracy than their non-iterative counterparts (e.g., filtered back projection) [3, 4, 45]. When performing a SPECT scan, there are many factors to consider: detector properties, collimator models, and randomly occurring physical events such as scattering and attenuation [2]. Furthermore, when simulating a system such as SPECT, the ability to simulate randomly occurring events becomes paramount. Monte Carlo simulation is one algorithm that allows the user to simulate these events and its use in Nuclear Medicine is well documented [11, 55]. Monte Carlo uses random sampling and different numbers of probability density functions (pdf) to model, simulate, and predict complex systems [18].
As quantification becomes important for parathyroid SPECT/CT studies, there is a clinical need to identify the best acquisition and processing parameters that will yield the optimum accuracy. This study aims to address this need for the first time by using a Monte Carlo simulation platform for the Tc-99m sesta-MIBI dual-phase parathyroid SPECT/CT imaging protocol. Monte Carlo simulation allows the determination of optimal parameters while eliminating experimental errors and the expense and inconvenience of using physical systems.

2. METHODS

The following steps have been followed in our study:

A. Use the previously validated cylindrical digital phantom ([53]) along with the Simind platform to enable multiple parameter testing. An illustration of images obtained using SIMIND is shown in Figure 1.
B. Define processing acquisition parameters based on previous similar studies.
C. Analyze the results quantitatively, then find the optimal parameters.
D. Compare results with previously obtained research findings.



(a) (b)

Figure 1. Examples of Siemens Symbia Gamma camera image outputs in transaxial view using LEUHR(a) and LEHR(b) collimators, with a spherical source.

Imaging Modalities that are Simulated

The dual-phase parathyroid Tc-99m-MIBI SPECT imaging protocol was used per previous parathyroid studies [40, 41]. Specifically, Siemens Symbia Intevo Gamma Camera was chosen for the study. Table 1 and Table 2 give the parameters that were selected based on previous studies.

Table 1. SPECT camera specifications used in simulations per previous studies [41].

Camera Parameters	Value
Photon Energy(keV)	140
Upper Window Threshold(keV)	147
Lower Window Threshold(keV)	133
Energy Resolution(140keV)	9.9%
Intrinsic Resolution (140 keV) (cm)	0.3
Source Activity (MBq)	13629
Image Matrix Size	128x128
Number of SPECT Projections	48
SPECT Rotation (3=180)	3
Pixel Size(cm)	0.24
Crystal Thickness	0.95
Crystal Half Length/Radius(cm)	29.55

Siemens Low-Energy High Resolution (LEHR) and Low-Energy ultra-high-resolution (LEUHR) collimators have been used to see the effect of the collimator model on the quantification process (Table 2) [48].

Table 2. Siemens Collimator specifications including septal properties. Sensitivity is set according to Tc99m [41].

Collimator	Hole length (mm)	Septal Thickness (mm)	Hole Diameter (mm)	Sensitivity (cpm/µCi)	System Resolution (100mm)	Septal Penetration (%)
LEHR	24.05	0.16	1.11	202	7.5	1.5
LEUHR	35.08	0.13	1.16	100	6	0.8

A digital cylindrical phantom (Figure 2) was selected for the study. The phantom was chosen for its cylindrical shape to simulate the neck and upper torso area. The phantom has an 11cm cross-section and 30 cm height, which is in line with previous anthropometric measurements of the neck and torso [49]. This allows for simulation of the neck and upper torso area without using an anthropomorphic phantom. The simulated phantom was filled with water. The pixel size for the phantom was 0.24mm according to previous studies ([40, 41]) while the entire phantom is sized 128x128x128 pixels. The adenoma is simulated as a uniform sphere with an offset ~1.5cm from the center situated on the upper central portion of the cylinder. The sphere was sized around a radius of ~0.3 cm. The sphere was filled with approximately 1MBq/cc.

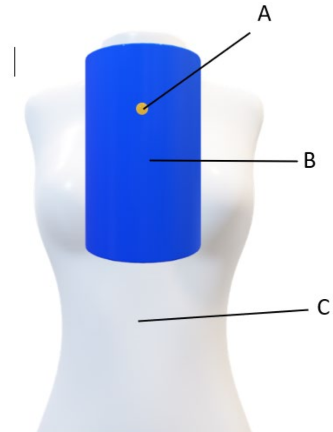


Figure 2. An approximate representation of the way the cylindrical phantom simulates the head and neck area. (A)The radioactive matter (B)The cylindrical phantom (C)A model human torso.

SIMIND (Ljungberg n.d.) was selected as the simulation platform for this study. It is a validated simulation platform that utilizes Monte Carlo Simulation. SIMIND enables users to simulate photon emissions through Monte Carlo simulation with possible reconstruction [15].

Simulated imaging studies allow us to test many parameters during testing without the need to travel to medical facilities or use radioactive material, thus being time and cost-effective. These parameters that are used during SPECT imaging such as Energy window, collimator type, etc., can be changed within SIMIND. This allows a comprehensive study of how the image quality behaves concerning acquisition parameters. It is used by ([2]) to simulate a single photon emission as well as being used in quantitative studies [34, 35, 38].

The software Customizable and Advanced Software for Tomographic Reconstruction (CASToR) ([37]) was used for the reconstruction of the images created by SIMIND simulation, CASToR, an open-source project, is created for the iterative reconstruction of emission (SPECT, PET) data. The OSEM algorithms can use differing number of iterations. In this study, 16 and 32 iterations were used with 8 subsets.

Three parameters were chosen for testing their impact on quantification error in hyperparathyroid imaging (Table 3): Collimator type (Low Energy-Ultra High Resolution, Low Energy-High Resolution), iteration number (16, 32), and presence of scatter correction.

Table 3. The simulation/reconstruction process parameters that are being tested in regard to their effect on quantification accuracy. With parameter Scatter Correction given binary coding. (0-not used,1-used).

Parameters		
Collimator	**Iteration**	**Scatter Corr.**
siemens-leuhr	16	0
siemens-leuhr	16	1
siemens-leuhr	32	0
siemens-leuhr	32	1
siemens-lehr	16	0
siemens-lehr	16	1
siemens-lehr	32	0
siemens-lehr	32	1

Attenuation Correction

All SPECT images suffer from attenuation artifacts due to the varying attenuation values of the object between the source and the detector surface. These artifacts affect the quantification of the images and applying methods to correct this effect is a must. To correct this effect, the attenuation coefficients of the object in question need to be known during the reconstruction stage of the image [45]. With the advent of SPECT/CT, which allows the acquisition of both imaging modalities for the patient with presumably shared positional information, gathering attenuation maps has become much more available [43]. During reconstruction, CASToR can perform attenuation correction. This correction has been featured in all images within this study.

Scatter Correction

One of the many factors affecting the SPECT imaging is Compton photon scattering. The Triple-Energy-Window (TEW) method, proposed by Koichi Ogawa, is one of the simplest methods to correct this effect [7, 39]. According to this method, the scattering effect on a certain energy window could be corrected by subtraction of the counts observed in the two neighboring energy windows [7]. This technique allows us to administer scatter correction after the reconstruction, thus giving us a chance to compare it against its non-scatter corrected counterpart. Three energy windows were set-up with the primary photopeak at 140 keV [41].

Table 4. Energy windows utilized in the study. With the central window 133-147 keV and the two neighboring energy windows used in the scatter correction process. The window-with represents the distance between the 140 keV mark and the upper and lower limits of the windows.

Window	Window Limits(keV)	Window Width
1	133-147	%10
2	147-168	%15
3	112-133	%15

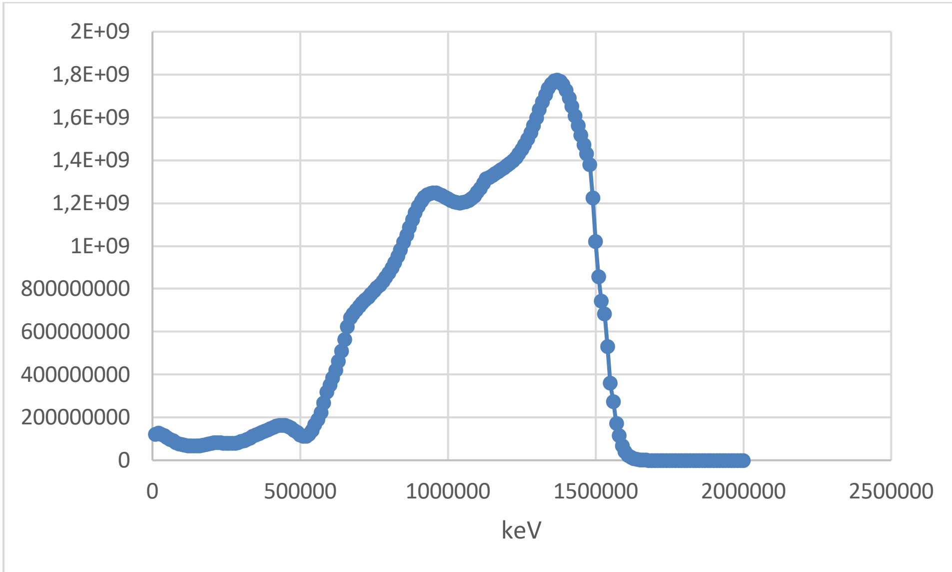


Figure 3. The energy Spectra of the Siemens Symbia Intevo Gamma Camera for LEUHR Collimator, where the triple energy window centered around the 140 keV peak can be observed within the main window and every dot representing an event.

Calibration

In the field of nuclear medicine, there is a significant need for the standardization of dosimetry and characterization of the imaging system. Since there is an abundance of factors that could influence the resulting counts in the output, calibration of the system is crucial for quantitative imaging [10, 14, 16, 53]. In this study, a previously validated image-based calibration protocol was used. This calibration method proposed by ([16]) uses the count numbers in each pixel to create an image-based calibration factor $S_{std.}$ The calibration factor for each image was determined by calibrating the number of counts found in the images to the known input radioactivity. System calibration factor S_{tot} was found by pooling the individual calibration factors gathered from each image.

$$S_{std} = \frac{N_{SPECT}}{Amean\ x\ \Delta Tacq} \tag{1}$$

Halty et al. ([16]) suggests using the equation (1) to calculate the individual calibration factor S_{std}. The Halty equation was slightly modified to calibrate the images on a Bq/cc basis. Which might offer a better insight regarding adenomas that are not uniform.

$$S_{std} = \frac{N_{Bq/cc}}{Amean\ x\ \Delta Tacq} \tag{2}$$

$$N_{\mathrm{Bq}/\mathrm{cc}} = \frac{N_{SPECT}}{N_{Voxel}\ x\ 76.62} \tag{3}$$

$N_{Bq/cc}$: The number of counts per cc in the adenoma. The adenoma should be segmented before this measurement is made (as given in the "Segmentation" section).

N_{voxel}: The number of voxel that adenoma spans. This value along with the $N_{Bq/cc}$ could be found by using quantitative reporting and segmentation algorithms. This value is multiplied by 76.62 to reflect the voxel to cc change in equation (3).

Amean: Mean activity over the acquisition duration $\Delta Tacq$.

ΔTacq: The acquisition duration of the image. (33s for this study)

Using equation (2) the individual calibration factors for every image can be found. It was chosen to pool these factors to get a cohesive understanding of the system and gather a singular pooled calibration factor S_{tot}. It was discovered that for better accuracy all image types should be counted in this average, such as images with and without scatter correction, lower and higher iteration, and other image-altering settings.

$$S_{tot} = \frac{\sum_{i=0}^{n} Sstd_i}{n} \quad (4)$$

Here, n represents the number of images that are being pooled.
One thing to keep in mind with this method is ensuring consistency in iteration numbers when dealing with components such as scatter correction. This means for example if one uses iteration number a with scatter correction, then he/she should also use iteration number a without scatter correction.

Segmentation

For the analysis and segmentation of the radioactive sphere placed within the phantom 3D-Slicer was used [12]. Using various plugins such as quantitative reporting and radiomics, it was possible to observe: the mean radioactivity per voxel, the voxel-wise size of the adenoma, the coordinates of the adenoma center, etc. For segmentation, an auto segmentation algorithm, the OTSU 3D Segmentation algorithm was used[6, 8, 20, 25]. Otsu is a popular non-parametric method in image segmentation and has precedent in the use of medical imaging [6]. The selection to use an auto-segmentation algorithm was made to eliminate the human factor in segmentation, in favor of mathematical algorithms for the most objective segmentation and quantification accuracy.

3. RESULTS

The results (Table 5) show that the change of parameter sets can result in a nearly 20% relative improvement in quantification error, from the highest error rate of 8.7% to the lowest error rate of 7%. The quantification error for the simulated images was found to be around 9% or below which is in line with the desired results of a sub-10% error. When low energy-ultra high-resolution collimator was used with scatter correction and 32 iterations, the error was found to be as low as 7%.

Table 5. Quantification accuracy results of Siemens Symbia Intevo Gamma Camera Using LEUHR and LEHR collimators along with the corresponding process parameter combinations.

Parameters			Quantification Error
Collimator	**Iteration**	**Scatter Corr.**	**MBq/cc**
siemens-leuhr	16	0	7.5%
siemens-leuhr	16	1	7%
siemens-leuhr	32	0	7.3%
siemens-leuhr	32	1	7.1%
siemens-lehr	16	0	8.3%
siemens-lehr	16	1	7.6%
siemens-lehr	32	0	8.5%
siemens-lehr	32	1	8.7%

4. DISCUSSION

This study aims to simulate and observe the effects of differing simulation and processing parameters on the quantification accuracy of hyperactive parathyroid glands using Tc-99m MIBI dual-phase parathyroid SPECT/CT.

According to Hwang et al. (2008), the presence of attenuation and scatter correction can cause a 25 percent difference in the observed radioactivity level in water-filled phantoms which is consistent with our results. A consistent improvement in accuracy was observed when scatter correction was applied to experiments. While the absence of both is stated to cause a nearly 50 percent error rate (Hwang et al. 2008), we consider this as a plausible possibility. Zeintl et al. ([56]) report that using commercial tools a quantification accuracy of 1-4 percent can be achieved. This is consistent also with our observations of around a 7 percent accuracy improvement made with open-source programs such as SIMIND and CASToR.

This study has been conducted with three different simulation and process parameters: the collimator, iterative reconstruction number, and the presence of scatter correction. During the simulation, a uniform adenoma within a digital cylindrical phantom filled with water was used. These experiments with rather simple parameter sets were selected to showcase the quantification capabilities of SPECT imaging and can become a basis for any further studies looking to experiment with other parameters as well as more complicated phantoms and reconstruction algorithms.

An anthropomorphic phantom could be used in this study to better examine real life situations. The current cylindrical phantom provides advantages in having uniform density and low background activity facilitating easier segmentation of the adenoma. However, its lack of biological structures and attenuation poses another limitation of this study.

The number of iterations has also been observed to be effective in improving accuracy. This is reasonable considering the optimization-based reconstruction algorithms (OLEM) used. However, higher iterations also certainly mean higher process times and delayed outputs. Therefore, users should be encouraged to keep a balanced approach when tackling this issue. Therefore, the processing power of the system is seen as highly affecting the processing time, so this should also be considered.

The type of collimator also makes a difference. It was observed that the higher resolution LEUHR collimator results in higher accuracy than LEHR. We observed an accuracy difference of around 1-1.5% percent in relative comparison between these types of collimators. The collimator has shown a consistent difference in accuracy with LEUHR having an accuracy of lower 7 percent while LEHR achieved an accuracy of around 8.5 percent. These results give us an idea about the impact of septal properties on quantitative accuracy, with both collimators operating on low energy. The most significant differences in properties are hole length and septal penetration percentage (Table 2).

Scatter correction influenced the results, by 1-1.5 percent in certain instances. When put into perspective, this is around a 15 percent improvement relative to the accuracy without scatter correction. This puts forward the capabilities and importance of this correction method, as scattering is a factor present in every imaging modality involving photon radiation. In further studies, the importance of scatter correction might be emphasized particularly with biological structures having different attenuation coefficients. Additionally, within the open-source programs SIMIND and CASToR, it is not possible to employ resolution recovery, dead time correction, and partial volume correction which is another limitation in our study. In conclusion, it can be stated with confidence, that the results show that parameters used in imaging have a considerable impact on quantification accuracy.

5. CONCLUSION

This study undertakes for the first time the optimization of quantitative parathyroid SPECT using computer simulation. This study has the potential to advance the use of this technique by improving accuracy.

Quantification is shown to be a method that holds immense potential for the future of medical imaging. It gives the user the ability to identify an adenoma in a precise and accurate manner.

In this study, it was concluded that instrumentation and processing parameters have observable effects on quantification accuracy. The results show that the presence of scatter correction, the number of iterations, and the collimators have impactful effects on quantification accuracy. All parameter values have achieved a sub-10 percent quantification accuracy, demonstrating the viability of SPECT as a quantitative imaging modality.

Resolution recovery, a correction method, used to reduce the necessary dose for imaging during the reconstruction process. It is only available alongside iterative reconstruction. Images created by resolution recovery provide better contrast and resolution while needing less acquisition and processing time [42]. This method should be further examined for its effect on quantification accuracy.

Other correction methods such as dead time correction and partial volume correction may also improve the quality of the image which is proven to be very important in quantitative studies and should be employed in future studies.

The addition of anthropomorphic phantom types to the testing can improve our understanding of this study with scenarios closer to real-life circumstances. It also introduces further challenges, such as segmentation alongside background activity and attenuation.

Simulating and testing different gamma camera models would expand the spectrum of this study encompasses. Since most gamma camera models have different imaging parameters, their effects could also be studied. More clinical studies are also needed to establish the technique.

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