Content Uniformity of Cobalt-57 Cyanocobalamin Capsules

TO THE EDITOR: We wish to share our experience of a drug product defect involving cobalt-57 cyanocobalamin capsules ([57]Co B-12) (Mallinckrodt, Inc.). We routinely utilize a well counter to "assay" each [57]Co B-12 capsule received (usually 10 – 20 capsules per order). Each capsule is counted for 1 min.

During 1987 and through August 1988, we have received 284 [57]Co B-12 capsules from 16 different lots. We conservatively calculate the capsule variation of each shipment as follows:

$$\text{Percent variation} = \frac{\text{Highest Capsule CPM} - \text{Lowest Capsule CPM}}{\text{Lowest Capsule CPM}}.$$

We accept the entire shipment if this value is <10%. When the percent variation exceeds 10%, the offending capsule(s) is/are identified and the percent variation is again recalculated using only the remaining capsules. Using this group of capsules, we calculate the mean capsule CPM and choose the capsule closest to this value for the preparation of a counting standard. The content variation from the mean of any unacceptable capsule(s) is/are then calculated.

The average percent variation for the 280 acceptable capsules was 3.23%. For the 16 shipments, the range in percent variation resulted in a minimum of 0.75% and a maximum of 7.06%. Ten years ago we encountered a capsule which measured 90% lower than the average capsule activity. We experienced no similar occurrence until August 1987. Since this time we have documented and reported through the Drug Product Problem Reporting Program of the USP/FDA, three separate instances, from three different lots, where the capsule content was lower than the average (−24.0%, −25.6%, and most recently, −39.9%). A fourth instance of a capsule measuring 11% low occurred, the capsule was not used but no report was filed in this case.

The NRC requires dose calibrator assay of photon emitting patient doses >10 μCi. Also, those which are intended to be <10 μCi must be assayed to verify that the activity is truly <10 μCi (1). However, compliance with these NRC regulations will not disclose a problem of the nature we describe.

The U.S.P. specifications require that each capsule contain not less than 90% nor more than 110% of the stated activity of [57]Co B-12 at the time of calibration. Additionally, the official U.S.P. content uniformity procedure (2), calls for the radioassay of ONLY 20 capsules from each lot. Thus, it is possible for the manufacturer to comply with this procedure and still release capsules which fall outside of the specifications. The subsequent administration of a capsule which varies by 25% or more from the average counting standard could result in a misdiagnosis or diagnostic confusion and patient inconvenience.

We believe that EACH capsule should be adequately assayed, preferably by the manufacturer. This is not unreason-

able given that: (a) radioassay is nondestructive, (b) there are relatively low number of capsules produced for each lot, and (c) we pay a notably high price for each capsule. In fact since 1984, when we observed no problems, the per capsule price has increased 92.6%.

However, in lieu of a U.S.P. monograph revision, which is unlikely, and improved quality control on the part of the manufacturer, we recommend that all [57]Co B-12 capsules received be assayed in a well counter. Problems should be reported to the U.S.P. Drug Product Problem reporting program (1-800-638-6725) or the Food and Drug Administration on form 3318 or call 1-800-FDA-1088.

1. Title 10 CFR Parts 35.53 (a) (b).
2. United States Pharmacopea XXI, cyanocobalamin [57]Co capsules, content uniformity, p. 239.

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Influence of Collimators on SPECT Center of Rotation Measurements

TO THE EDITOR: We read with interest the recent article by Cerqueira et al. (1) on the effect of collimator hole alignment on center of rotation (COR) measurements. They found that two of the four collimators they evaluated had variations in COR which made them unacceptable for single photon emission computed tomography (SPECT) studies. These results are similar to our own findings during acceptance testing of tomographic equipment. We employed a similar technique to that described by Cerqueira et al., but only performed three measurements of COR – one at the center of the field of view (FOV) and one at either extremity of the FOV along the axis of rotation. We then recorded the maximum variation of COR along the axis of rotation for each collimator. To date, we have evaluated a total of 22 collimators on SPECT gamma cameras manufactured by four different vendors. For tomographic studies, we currently specify that the collimators have <±1 mm variation in COR along the axis of rotation. These limits of variation in COR are similar to those recommended by Busemann-Sokole (2) and Chang et al. (3), from measurements of collimator hole angulation. They suggest limits of ~±0.3° for hole angle. This translates to a maximum variation of ±1.05 mm at a radius of rotation of 20 cm. These are slightly more stringent requirements than that recommended by Cerqueira et al. (maximum variation ± 1.5 mm); however, we feel that these requirements can be easily achieved with current manufacturing techniques.

Twenty-two collimators were evaluated: 11 all-purpose, seven high-energy, three medium-energy, and one slant hole. By the criterion of acceptance range of ≤2 mm (corresponding to ±1 mm), five collimators (23%) were rejected. Interestingly,

of those rejected, two were manufactured by cast and three by foil technique. This would indicate that poor quality control, rather than the manufacturing technique, may be the main culprit.

Although the techniques described by Busemann-Sokole (2) and Chang et al. (3) provide a more accurate mapping of collimator hole angulation over the entire field of view, we have found that the technique of Cerqueira et al. has the advantage of being simple and quick to perform, does not require any specialized test equipment, and provides a readily comprehensible indicator of collimator quality for SPECT. From our experience and the results of Cerqueira et al., it would appear that there are a large number of collimators in use on tomographic systems which are unsuitable for SPECT acquisition.

References

1. Cerqueira MD, Matsuoka D, Ritchie JL, Harp GD. The influence of collimators on SPECT center of rotation measurements: artifact generation and acceptance testing. *J Nucl Med* 1988; 29:1393–1397.
2. Busemann-Sokole E. Measurement of collimator hole angulation and camera head tilt for slant and parallel hole collimators used in SPECT. *J Nucl Med* 1987; 28:1592–1598.
3. Chang W, Li S, Williams JJ, Bruch PM, Wesolowski CA, Ehrhardt JC, Kirchner PT. New methods of examining gamma camera collimators. *J Nucl Med* 1988; 29:676–683.

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Automated Body Contour for Liver SPECT Using Photopeak Data

TO THE EDITOR: Recently Hosoba et al. (1) proposed a new method for detecting body surface contours for single photon emission computed tomography (SPECT) attenuation correction which uses only photopeak window data. Although alternative methods of external body contour determination have been described (2,3), the Hosoba method offers simplicity of implementation for routine clinical SPECT studies. We therefore attempted to apply the method to liver SPECT in combination with first order Chang attenuation correction, assuming uniform attenuation.

The Hosoba method employs a threshold search technique to determine edges in the projection images, which are then backprojected to define convex boundary points in the transaxial plane. The boundary points are fit with a fourth order Fourier series to yield smooth analytic contours which can be iteratively refined by adjusting the projection threshold until the major axis of the contour agrees with a directly measured value. The method works well for an Alderson body phantom containing background activity and a simulated liver (1), but we have found that it performs rather poorly for clinical liver SPECT as a result of a lack of peripheral activity in many of the transaxial sections of interest. We therefore abandoned the original approach of generating a separate contour for

each individual slice, and instead attempted to determine a single representative contour for each study (acquired as 64 × 64 word images in 64 views) from the projection data corresponding to an eight pixel wide slice centered on the spleen. A typical result for the "raw" boundary points obtained prior to fitting with the Fourier series is shown in Figure 1A.

The figure illustrates a general problem which exists in the anterior quadrant above the spleen, namely that a lack of activity in this region causes the boundary points there to fall inside the patient surface. Our first attempt to address the problem involved eliminating these points from the ensuing fitting procedure. It was not completely successful since some of the fitted contours continued to exhibit marked deformation in the anterior quadrant above the spleen. Eliminating the undesirable boundary points and further applying the constraint of bilateral symmetry rectified the problem, however. The symmetry constraint can be expressed as $R(-\theta) = R(\theta)$, where $R(\theta)$ describes the contour as a function of polar angle θ, measured from the vertical with origin at the geomet-
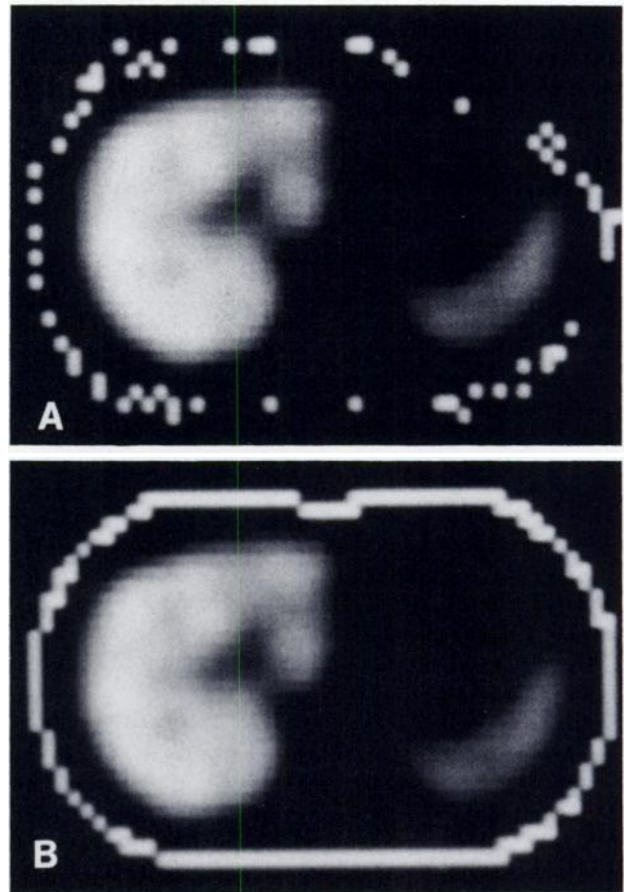

FIGURE 1

A: Transaxial body contour boundary points obtained by backprojecting edges determined from projection data using a modification of the method of Hosoba et al. (1).

B: Contour obtained by fitting the boundary points in A, exclusive of those in the upper left quadrant, with a fourth order polar Fourier series constrained to reflect bilateral symmetry. Note that the contour does not appear to be perfectly bilaterally symmetric because the origin of the polar coordinate system used for the fit does not coincide with the center of a pixel.