Motion Corrected Hepatic Scintigraphy: An Objective Clinical Evaluation

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An analogue motion-correction device was built for a scintillation camera. Corrected and uncorrected images were simultaneously recorded on Polaroid film during routine hepatic scintigraphy of 1,100 patients, selected without known bias. Autopsy, liver biopsy or inspection at laparotomy (and clinical followup in three patients with neither known malignancy nor benign liver disease) were considered to have established the true state of the livers of 49 patients with hepatic masses and 53 patients with normal livers. Five observers of varying experience in nuclear medicine independently evaluated the scintigrams for the presence of mass lesions, using a five-category rating scale, without knowledge of the true states. Results were expressed as receiver operating characteristic curves. For each observer, performance was better with motion correction, or when interpreting corrected and uncorrected studies together, than when reading the uncorrected studies alone. Analogue motion correction is an effective, inexpensive method for improving hepatic scintigraphy with a scintillation camera. The degree to which motion correction improves the detectability of mass lesions is a function of the size of the lesions, the performance parameters of the imaging system and the display medium, the depth of the subject's respirations, the counting rate, and the count density of the image, as well as of the proper adjustment of the motion-correction device itself.

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In 1971 Oppenheim described a digital method of correcting hepatic scintigrams for respiratory motion (*1*). In 1972 Hoffer and associates described an analogue version of Oppenheim's method, in which motion correction was achieved on-line with a relatively simple, inexpensive device (*2*). This device integrates Y-axis positioning signals over a short time interval. After correction for count rate, a DC signal is obtained, the voltage of which is proportional to the displacement of the centroid of radioactivity of the liver along the Y-axis of the detector. A bias voltage that is proportional in magnitude but opposite in polarity is then applied to the Y-axis deflection of incoming counts, displacing them in the direction opposite to that of the displacement of the centroid from the center of the detector. The effect of such a system is to hold the centroid, and hence the image of the liver, stationary in the center of the cathode-ray display during the entire imaging procedure. The time constant of integration of incoming Y-axis deflection signals must be relatively short, so as to avoid excessive error in position correction due to time lag between counts being collected and counts being repositioned. In addition, the counting

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rate must be adequate to ensure a statistically reliable estimate of the displacement of the centroid.

Reported here is a prospective experiment in which analogue motion-corrected hepatic scintigraphy was compared with uncorrected scintigraphy, in terms of observer performance, by means of receiver operating characteristic (ROC) curves (*3–5*).

MATERIALS AND METHODS

Instrumentation and scintigraphic procedure. A centroid-tracking device for motion-corrected hepatic scintigraphy along one axis* was designed and built for an Anger scintillation camera. The gamma camera was fitted with two independent display CRTs and Polaroid cameras, and the motion-correction device was connected to one of the CRTs. With this arrangement, both uncorrected and motion-corrected hepatic scintigrams could be recorded simultaneously during routine clinical scintigraphy.

The scintillation camera was fitted with a high-resolution, low-energy collimator and a prototype automatic peak-tracking device. The pulse-height analyzer was set for a 20% window about a centerline corresponding to an energy of approximately 140 keV.

The motion-correction device was calibrated with a radioactive line source (a fine polyethylene catheter filled with $Na^{99m}TcO_4$), which was placed under the scintillation camera on a specially designed respiratory-motion simulator (*6*) capable of moving back and forth in a manner similar to respiratory motion. An additional, stationary source was placed in the field of view of the camera to simulate stationary background activity. Failure to include such activity during calibration could lead, in theory, to incomplete motion correction during clinical studies because of damping of the observed motion of the centroid by stationary background in the patient. This effect, however, recently has been found to be negligible (*7*). With the line source moving back and forth at a rate of 16 cycles per minute and an amplitude of about 4 cm, the motion-correction device was adjusted until the sharpest image of the line source was obtained.

Patients selected as described below were given 7 mCi of Tc-99m sulfur colloid by i.v. injection, 10 min before the beginning of scintigraphy. Motion-corrected and uncorrected scintigrams of the liver and spleen were recorded simultaneously on Polaroid film in the anterior, posterior, and right and left lateral projections. Additional projections were obtained at the discretion of a nuclear medicine physician, after completion of the routine views. Patients were prone for the posterior views and supine for all other projections. One million counts were collected for all images. An effort was made to keep the exposures of the corrected and uncorrected scintigrams similar.

Selection of patients. Patients referred for hepatic scintigraphy were arbitrarily assigned by a scheduling clerk, without known bias, to undergo simultaneous motion-corrected and uncorrected scintigraphy. Between April 1/75 and July 1/76, about 1,100 patients, constituting 45% of all patients undergoing hepatic scintigraphy during that period, were so examined. Review of the records of these patients yielded 49 with one or more masses in the liver and 53 with normal livers, for whom the true state of the liver was considered to have been established by means other than hepatic scintigraphy.

The true states of all 49 livers classified as abnormal were established by inspection at laparotomy (with or without open liver biopsy), closed needle biopsy, or post-mortem examination. Forty-eight (98%) harbored primary or secondary carcinoma; one contained benign cysts. Confirmation of the presence of mass lesions in these livers was obtained within 2 mo of the scintigraphic procedure in 26

TABLE 1. MODE AND TIME OF DETERMINATION OF TRUE STATE OF 53 LIVERS CLASSIFIED AS NORMAL

	Maximum time (mo) before (—) or after (+) scintigram										
Mode of determination	−3	−2	−1	+1	+2	+3	+4	+5	+6	+7	Total
Laparotomy											
with biopsy	1	1		9	1						12
without biopsy	2		5	16		1					24
Autopsy				3	1		2				6
Closed liver biopsy				4	2				1	1	8
Clinical follow-up only*											3
Total											53

* Three patients with neither known malignancy nor benign liver disease, well at time of clinical followup by physician at 4, 12, or 13 mo after hepatic scintigram.

(53%) cases and within 3 mo in 35 (71%) cases: confirmation preceded scintigraphy by 3–6 mo in eight (16%), 10 mo in one (2%), 12–17 mo in four (8%) and 40 mo in two (4%) cases.

The mode of determination of the true state of the 53 livers classified as normal, and the times separating the determination from the scintigraphic procedure, are listed in detail in Table 1. In 50 cases the classification was based on inspection or biopsy of the liver at laparotomy, closed liver biopsy, or autopsy. Three patients were considered to have livers "proved" to be normal, as they had neither known malignancy nor evidence of any liver disease, and were well at a followup visit to their primary physicians 4, 12, and 13 mo after the scintigraphic procedure. Of the 53 patients with normal livers, 30 (57%) had various primary carcinomas. Ten patients (19%) had malignant lymphoma, and all of these underwent open or closed liver biopsy. One patient had a rhabdomyosarcoma, and 12 (23%) had neither known malignancy nor benign hepatic disease.

Interpretation of the images. The hepatic scintigrams of the 102 patients for whom the true state of the liver was considered known were interpreted independently by five observers, without knowledge of the patients' identities, the true state of the liver, or any other pertinent clinical information. Observers 1 and 2 were attending physicians with 13 and 2.5 yr of experience, respectively, in nuclear medicine. Observers 3, 4, and 5 were resident physicians with 5, 2, and 1 mo of experience, respectively, in nuclear medicine.

All images were viewed under the same physical conditions as those of routine nuclear medicine reporting sessions. The images were viewed, under adequite fluorescent lighting, either mounted on a radiographic view box (with back lights off) or held by the observer, at his discretion. Viewing distances and observation times were controlled by the observers. Reading sessions were about 2 hr long, with a rest break half way through each session.

The uncorrected scintigrams were presented to the observers first, in a random order. After all of the uncorrected scintigrams had been read, the corrected scintigrams were presented, also in a random order. After each corrected study was interpreted, the observers were given the patient's uncorrected scintigram, and together both studies were read again.

Since it was assumed that the benefit (if any) of motion correction would result from enhanced detectability of activity voids in the liver, the observers were asked to restrict their attention to this simple detection task. They were informed that the livers examined either contained mass lesions or were normal; patients with other liver diseases, such as cirrhosis, had been excluded. The observers were instructed not to make differential diagnostic decisions. They recorded each interpretation on a standard answer sheet, using a five-category rating scale to indicate their level of confidence that a mass lesion (or more than one) was present in the liver. The rating categories were: (a) definitely present, (b) probably present, (c) possibly present, (d) probably absent, (e) definitely absent. The use of this scale yields four operating points (on an ROC curve) which correspond to the four decision thresholds that distinguish the five categories. When viewing both types of study together, the observers considered structures that appeared sharper in the motion-corrected images to be most likely within the liver, whereas those that appeared less sharp in the corrected images were considered as probably extrahepatic.

Method of analysis. The true-positive fraction (TPF) (TPF = Number of abnormal livers called positive/Total number of abnormal livers) and false-positive fraction (FPF) (FPF = Number of normal livers called positive/Total number of normal livers), at each of the four decision thresholds implied by the five-category rating scale, were calculated for each observer interpreting (a) the uncor-

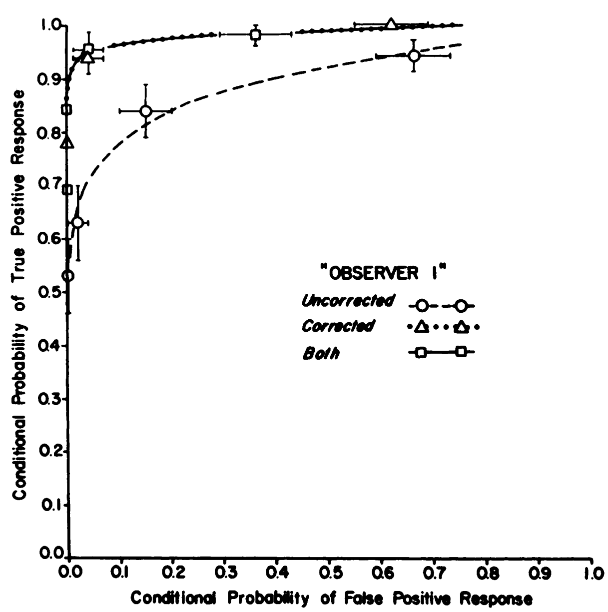

FIG. 1. ROC curves for Observer 1, who had 13 yr of experience in nuclear medicine. Motion correction resulted in dramatic improvement in observer performance. At conditional probability of false-positive response of 0.05, conditional probability of true-positive response increased from about 0.73 to about 0.95. No difference noted between reading of corrected scintigrams alone and corrected and uncorrected studies together.

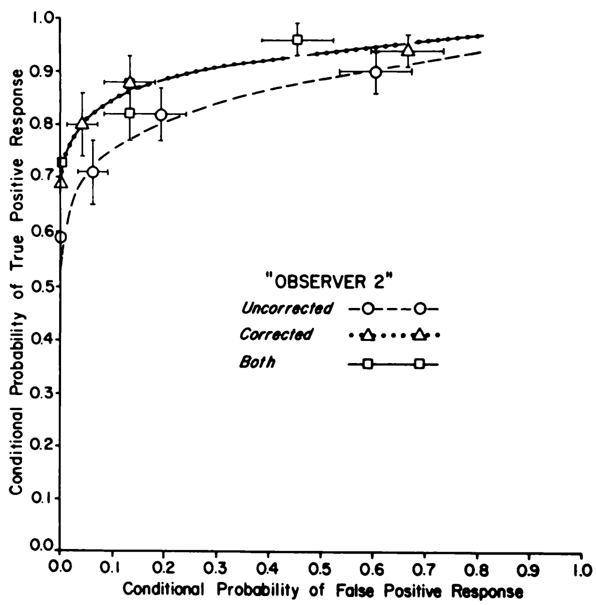

FIG. 2. ROC curves for Observer 2, who had 2.5 yr of experience in nuclear medicine. Observer performance improved with motion correction. No difference noted between reading of corrected scintigrams alone and corrected and uncorrected studies together.

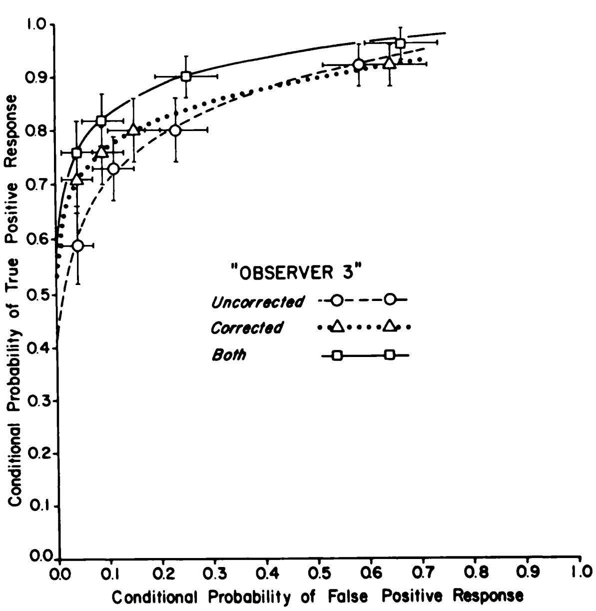

FIG. 3. ROC curves for Observer 3, who had 5 mo of experience in nuclear medicine. Performance was better reading corrected and uncorrected studies together versus corrected alone.

rected scintigrams alone, (b) the corrected scintigrams alone, and (c) the two types of images together; these fractions were computed in the customary manner (*3–5*). The resulting operating points were plotted for each observer in a separate coordinate space (ROC space) (Figs. 1–5). ROC curves were fitted by plotting the operating points on double-probability paper (*8*) and drawing a straight line through the points, visually dividing the errors. The resulting curves for each observer were then transferred to the corresponding ROC space. The right-hand portions of the curves for observer 4 reaching corrected studies alone and both studies together have been omitted, since the right-hand operating points did not fit a linear plot on double-

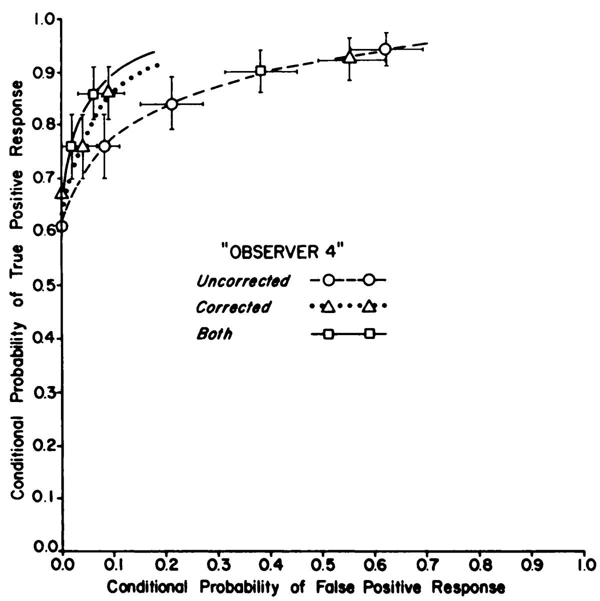

FIG. 4. ROC curves for Observer 4, who had 2 mo of experience in nuclear medicine. Right-hand portions of curves for reading of corrected studies alone and both studies together are omitted for reasons explained in text. Performance slightly better reading both types of study together than corrected study alone.

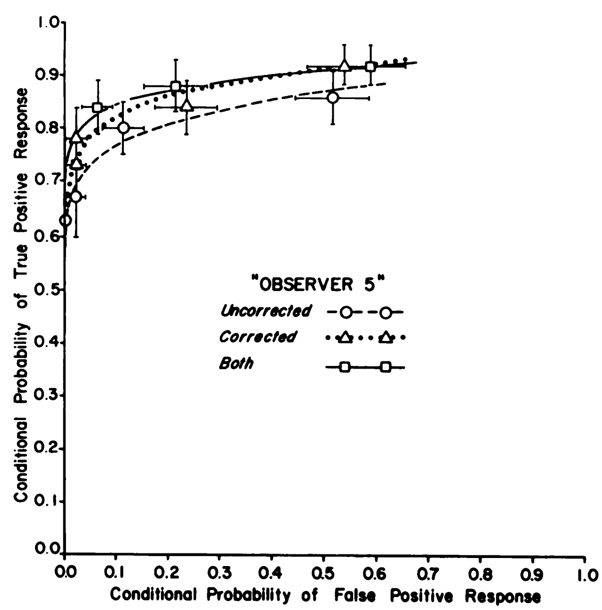

FIG. 5. ROC curves for Observer 5, who had 1 mo of experience in nuclear medicine.

probability paper. Error bars, which represent the square root of binomial variance, were fitted to all operating points (*9*).

RESULTS

Improvement in observer performance is indicated on an ROC graph by displacement of a curve upward and to the left (*3–5*). Hence, the ROC graphs (Figs. 1–5) show that the performance of each observer was better reading the motion-corrected studies alone, or both types of study together, than when reading the uncorrected studies alone. The greatest improvement with motion correction was achieved by Observer 1. For example, at a conditional probability of about 0.05 for a false-positive diagnosis, the conditional probability of making a true-positive diagnosis was about 0.73 without motion correction and 0.95 with motion correction.

Observers 1 and 2 exhibited little difference in performance when reading the corrected studies alone against both types of study together. Observers 3, 4, and 5, however, performed better reading the corrected and uncorrected scintigrams together than reading the corrected scintigrams alone, although the differences were quite small.

DISCUSSION

The results of this experiment suggest that analogue motion correction improves the detectability of mass lesions in the liver in clinical scintigraphy. Some observers may be aided in their interpretation of motion-corrected hepatic scintigrams by comparing them with simultaneously generated uncorrected scintigrams; motion correction reduces the blurring of intrahepatic structures, but it tends to smear out nonhomogeneity of the hepatic image caused by nonuniformity of detector response or overlying radioopaque material. Therefore, nonhomogeneity, or focal defects, that decrease in sharpness with motion correction can be taken as being the result of extrahepatic factors.

As of this writing, no entirely satisfactory statistical method has been described for the quantitative testing of the significance of the separation of ROC curves. It has been customary to fit ROC curves with error bars that represent the square root of binomial variance (*9*). A qualitative impression of the significance of curve separation can then be gained by visual inspection of the curves and associated error bars.

Binomial variance is related to several factors, one of which is uncertainty regarding the degree to which the sample population of patients (or, more generally, signal and noise events) is representative of the larger population from which it is drawn. Whether or not the sample population of patients in this experiment is representative of the larger population of patients who undergo hepatic scintigraphy, the corrected and uncorrected scintigrams were of identical patients. Although the curves taken singly are subject to the errors indicated by the error bars, they are generated from statistically dependent sets of observations and tend, therefore, to vary in the same direction; hence, it would seem that the separations of the curves in this experiment are somewhat more significant than is suggested by the error bars. This is of little consequence in the case of the data generated by Observer 1, since the curves for corrected and uncorrected scintigraphy are widely separated. It is an important factor in the interpretation of the graphs representing the data of the other four observers, however, whose analogous curve separations are less striking.

The degree to which analogue motion correction improves the image quality of hepatic scintigrams is dependent upon several factors, most of which have been discussed previously (*1*). The benefit of motion correction generally increases as improvements are made in spatial resolution, count density, and the properties of the display medium employed, since motion correction permits one to take full advantage of these improvements to identify small lesions. The benefit probably decreases as the uniformity of detector response is improved, since one has less need of motion correction's ability to smear out artifacts due to nonuniformity. The effectiveness of this method of motion correction increases as count rate and depth of respiration increase, and as respiratory rate decreases. Failure to optimize the time constant of integration of incoming positioning signals decreases the effectiveness of the method (*1*). The degree of benefit from motion correction will depend upon the size of the lesions to be detected, as shown in Fig. 6.

The striking performance of Observer 1, who achieved a TPF of 0.94 and a FPF of 0.04 reading motion-corrected scintigrams alone, deserves comment. One should recall that 36 (68%) of the "normal" livers were so classified on the basis of inspection at laparotomy, with or without open biopsy. Although this method of evaluating the liver for mass lesions is highly regarded in some quarters, Ozarda and Pickren have estimated that hepatic tumors may be missed at exploratory laparotomy in 15% of cases (*10*). Furthermore, eight (15%) of the "normal" livers were so classified on the basis of closed needle biopsy. Hence it is possible that some livers harboring inconspicuous metastases, missed at laparotomy or closed needle biopsy, were incorrectly classified as "normal." Thus, one cannot

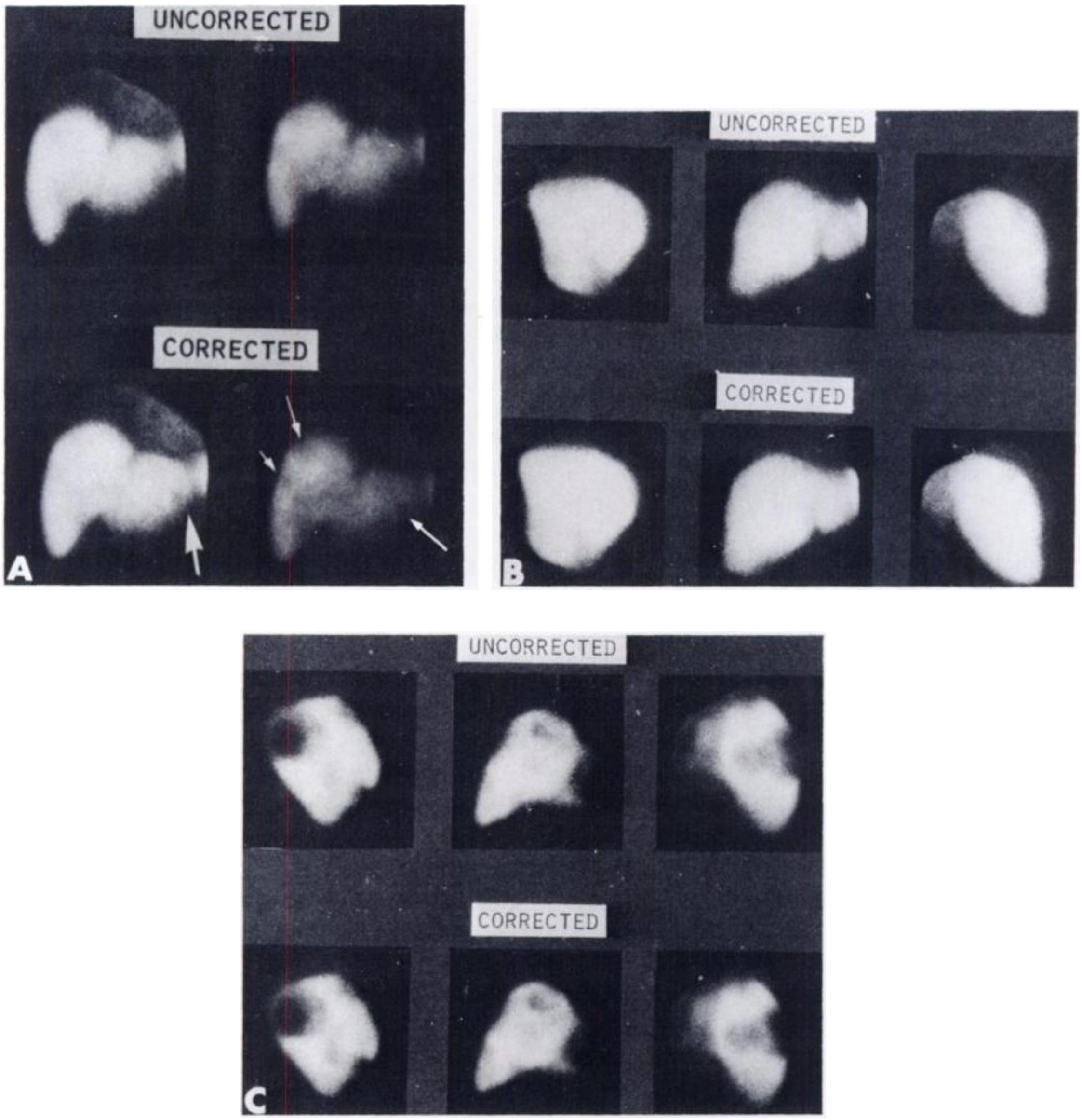

FIG. 6. The degree of benefit derived from motion correction depends in part on size of lesions. (A) Benefit is most obvious when lesions are of intermediate size. Note that lesions are difficult to see without motion correction, but easily seen in corrected images (arrows). Observers rated uncorrected images "definitely normal" to "possibly abnormal," whereas corrected images were rated "probably abnormal" or "definitely abnormal." (B) This liver harbored many tiny lesions. Because they are too small to see even with liver motionless, liver appears normal even with motion correction. (C) Large lesions are easily detected without correction. Hence, although margins of lesions are perhaps slightly sharper with motion correction, there is no diagnostic benefit.

contend that motion correction enabled Observer 1 to determine the "true" presence or absence of lesions with nearly perfect accuracy, but only that it enabled him to identify those cases in which lesions were found by biopsy or laparotory with nearly perfect accuracy.

The centroid-tracking motion-correction device employed in this experiment was designed to correct for motion only along the longitudinal axis of the body, which is the predominant axis of respiratory motion of the liver. It could have been designed to correct for transverse motion as well at moderate additional expense. Centroid-tracking motion correction cannot correct for rotational movement or change in hepatic shape, but it is our impression that these kinds of movement are important only in deep respiration.

All the images of the liver were automatically coded at the time they were recorded to indicate whether they were corrected or uncorrected. This was found necessary in order to avoid confusion of the two types of scintigram during clerical processing. As a result, the observers could easily tell which images were corrected and which were uncorrected. It is possible that this may have introduced a systematic bias, since the observers might have been motivated to interpret the corrected images more carefully than the uncorrected images. However, the performance of the two experienced observers (Observers 1 and 2) without motion correction was similar to that reported in three previously published series in which patients underwent hepatic scintigraphy with a scintillation camera (*11–13*): when the TPFs and FPFs from these series are plotted in ROC space, the resulting operating points cluster about the ROC curves generated by both observers without motion correction, and are clearly below the ROC curve generated by Observer 1 with motion correction. This suggests (but does not prove) that motivational bias did not seriously distort the results of the experiment.

In the final analysis, one must determine not only whether a new imaging procedure is effective, but whether or not it is cost effective. Although formal cost-against-benefit analysis has not been undertaken in this experiment, modification of hepatic scintigraphy by analogue motion correction should be expected to meet the latter test, since the additional cost of this modification per patient examined is trivial. The components for our system cost $850 in 1975. Hence, analogue motion correction can be recommended as an effective, inexpensive method for improving hepatic scintigraphy with a modern scintillation-camera system.

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FOOTNOTE

* Circuit diagrams will be supplied upon request.

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