DUAL-RADIOISOTOPE TECHNIQUES AND DIGITAL IMAGE-SUBTRACTION METHODS IN PANCREAS VISUALIZATION

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The lack of any radiopharmaceutical specific to the pancreas has prompted many endeavors at "subtraction scanning" to visualize this organ.

Many reports are available concerning imaging in which rectilinear scanners were used. Then in 1968 Blanquet et al (*1,2*) reported the successful application of a gamma camera and multichannel analyzer to this problem using digital image-subtraction methods.

The earlier studies with rectilinear scanners had indicated value in the use of computer techniques for the associated data processing. However, Blanquet et al limited their data analysis to the processing facilities of the multichannel analyzer. While their results proved of clinical value, the question remained as to whether the results could be improved by digital-computer analysis.

Our study pertained to this question. We used similar equipment to Blanquet et al but augmented this with digital-computer methods for data smoothing, scan subtraction, and resulting image comparison.

Comparisons have been made between the original scintiphoto, the "immediate subtraction" image and a variety of computer-derived images for a series of 112 pancreas examinations obtained during the past 2 years.

EXPERIMENTAL METHODS

A schematic diagram of the experimental arrangement is shown in Fig. 1. One half hour before the study the patient received approximately 150 ml of milk. More elaborate methods of patient preparation have been proposed (*3–6*); however, these methods have not been shown to be particularly advantageous (*7,8*).

The patient was positioned supine under the gamma-camera detector (Nuclear-Chicago Corp.),

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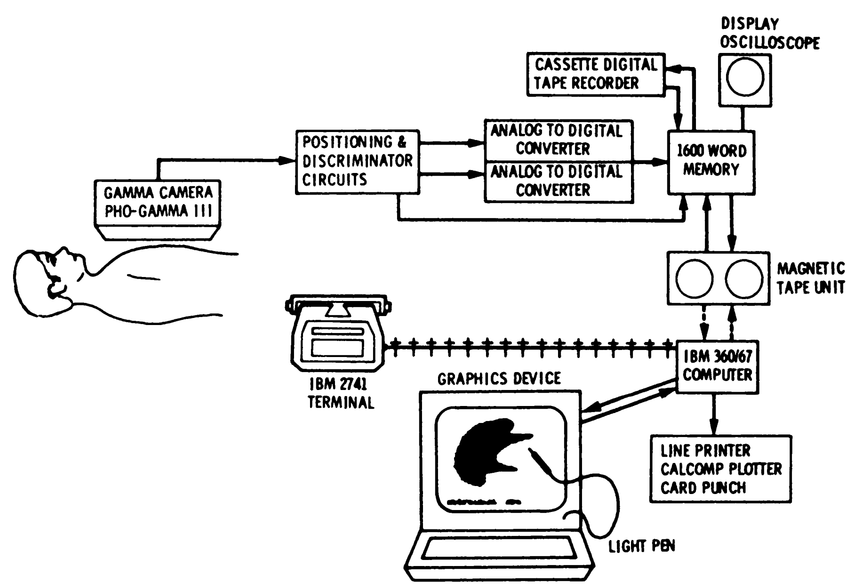

FIG. 1. Schematic diagram of experimental arrangement.

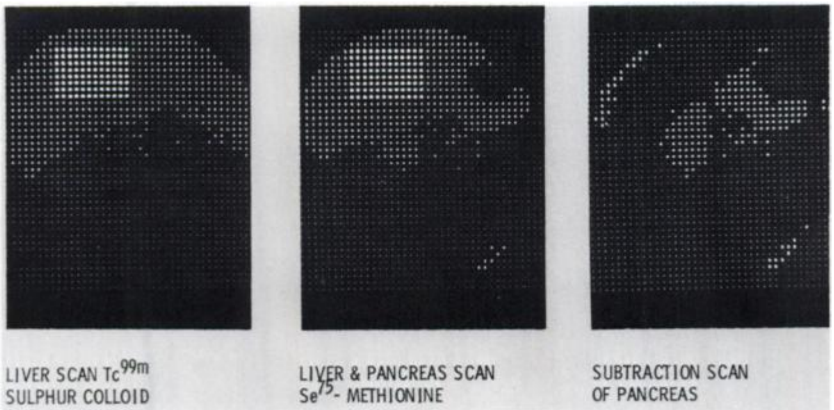

FIG. 2. Example of "immediate subtraction" procedure.

the surface of which was firmly placed against the abdomen with the center of the detector slightly to the left of midline and approximately half way between the umbilicus and xiphisternum. The detector was rotated cephalad to conform to the patient's abdominal surface and to "look under" the inferior hepatic margin. Gold-198-colloid, ^{99m}Tc-sulfur colloid, and ^{75}Se-selenomethionine were used for organ visualization.

In the early stages of our investigation ^{198}Au-colloid (100–200 μCi) was used for liver imaging. For reasons of gamma-ray energy discrimination it was necessary, using this material, to perform the liver-plus-pancreas scan with ^{75}Se-selenomethionine first to limit the degree of interference between the gamma-ray spectra of these two nuclides.

Subsequently in our study, and for the majority of cases considered in this paper, ^{99m}Tc-sulfur colloid was used as the liver-imaging agent. This material can be injected before ^{75}Se-selenomethionine and patient-detector positioning accomplished with greater accuracy. The use of ^{99m}Tc-sulfur colloid also provided greatly improved liver visualization with a significant reduction in radiation exposure to the patient (*9*).

With the present experimental method a decision on final positioning of the detector was made after an examination of the first short exposure following ^{99m}Tc-sulfur colloid injection. A scintiphoto, with between 100 and 200 K counts, was then obtained and the digital form of this image stored in the 1,600-word memory. This image was displayed as a 40 $\times$ 40 matrix on an oscilloscope, photographed, and stored on magnetic tape. Selenium-75-selenomethionine (200–300 μCi) was then injected and three or four serial scintiphotos obtained, each of approximately 10 min duration. The total number of events accumulated during these 10-min exposures ranged between 50 and 200 K. Following initial clearance of ^{75}Se-selenomethionine from the blood (approximately 10 min after injection), scintigraphic information was accumulated in the 1,600-word memory for approximately 30 min. Peak concentration of radionuclide in pancreatic parenchyma was achieved during this time (*10*). When accumulation of ^{75}Se-selenomethionine scintigraphic data was completed, the information was displayed and photographed, and stored digitally on magnetic tape.

DATA ANALYSIS

"Immediate subtraction" method. Using the region-of-interest (ROI) facility incorporated in the 1,600-word analyzer, an area of the ^{75}Se-selenomethionine (liver-pancreas) count matrix that related to the liver alone was delineated. (The relationship between the boundaries of this area and the liver-plus-pancreas outline, in one particular study, is shown in Fig. 2.) Total counts within this area were then obtained for both matrices, using the fast tape printout, and the ratio of response ^{99m}Tc/^{75}Se was calculated. Using the "data multiplier" incorporated in the cassette digital magnetic tape recorder, it was then possible to normalize the two matrices. For example, if the ratio ^{99m}Tc/^{75}Se was 3:1, the data multiplier was set at 1 and the ^{75}Se matrix was played back three times and stored in positive form; then the ^{99m}Tc matrix was played back a single time in negative form, thus subtracting the ^{99m}Tc (liver) matrix from the ^{75}Se (liver-plus-pancreas) matrix. The result—the "difference image" —was representative of the pancreas, although with some contribution from the kidneys, small bowel, and bladder. The result of such a subtraction is shown in Fig. 2.

Digital-computer image-subtraction techniques. As stated, all matrices were recorded digitally on magnetic tape. To facilitate the "immediate subtraction" described above, each matrix was stored initially on an individual cassette. At the conclusion of that procedure the paired matrices were recorded, with identification code, on seven-track computer-compatible tape.

The data on this tape were then processed numerically by computer program, using remote terminal control over processing. (A flow chart outlining the program is shown in Fig. 3.) Following the selection of a matrix pair the data were read into core. Artefacts, which were occasionally introduced during data transfer from cassette to computer tape, were eliminated by a data validity check, a point being replaced by the mean of its eight neighbors if it differed from this mean by more than 3 standard deviations. Data smoothing, using a method of variable spatial averaging (*11*), was then performed. Empirically determined "optimum" parameters were used in this smoothing process.

At the time of data transfer from cassette to computer tape, coordinates defining a region-of-interest specific to the liver were obtained by visual inspection of each matrix. These coordinates were provided to the computer program and average $^{99m}Tc/^{75}Se$ ratios were determined for the matrix subtraction procedure.

Several methods were considered for presentation of the "difference image"; examples for a particular matrix pair are shown in Fig. 4. The photographic presentation, Fig. 4A, was obtained by writing the "difference image" onto magnetic tape, reading this into the 1,600-word memory, and photographing the display oscilloscope with the nine-level gray scale in operation. In contrast, Fig. 4B shows a symbolic density plot obtained by line printer.

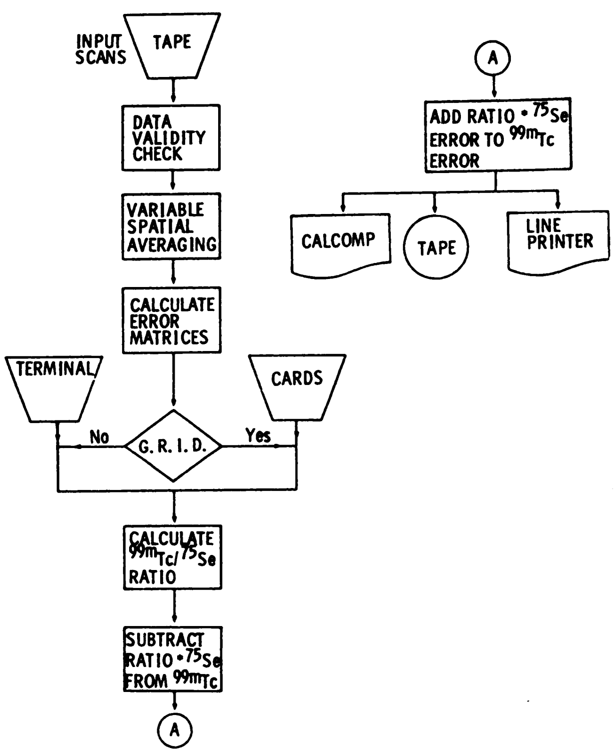

FIG. 3. Flow chart for computer processing.

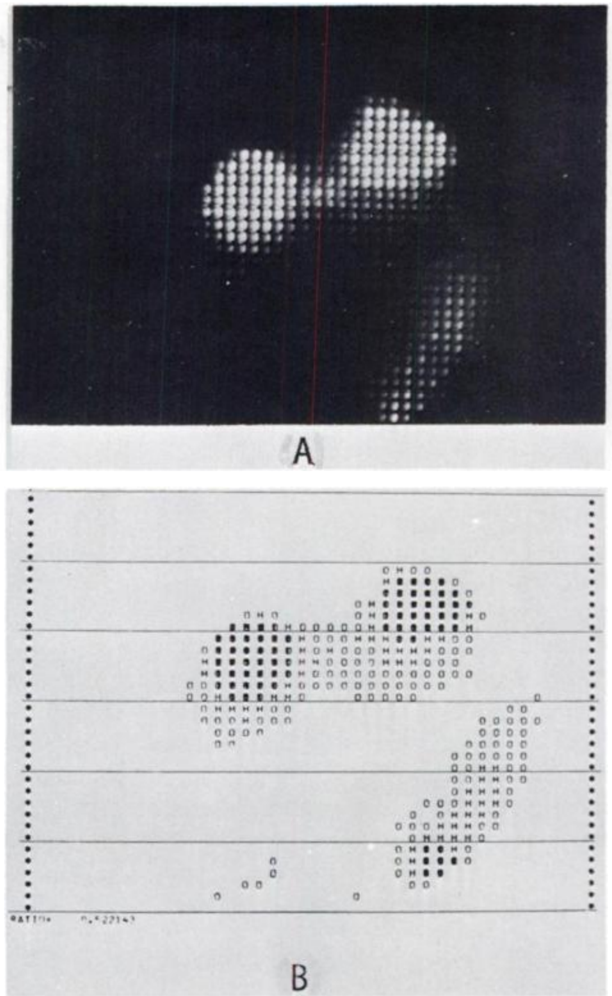

FIG. 4. Computer-processed "difference image" A is 1,600-word memory display with nine-level gray scale. B is symbolic density plot by line printer.

To estimate the validity of a computer-processed image symbolic density plots of the "difference image" with various levels of "background erase" were obtained. This effect was achieved by successive subtraction of 1 and 2 experimental standard deviations from the "difference image." This process is illustrated in Fig. 5 for two normal pancreas examinations.

"Interactive" computer graphics aids. An interactive graphics device (GRID, Control Data Corporation) connected "on line" to a large (IBM 360/67) computer was available to this investigation. The graphics device allowed boundary definition with a light pen—a technique that has proved particularly useful in region-of-interest selection for our pancreas "subtraction" studies.

The present computer operating system precludes truly "interactive" use, i.e. providing the region-of-interest boundaries to the subtraction programs and receiving the resulting "difference images" immediately on the screen display. We expect that this

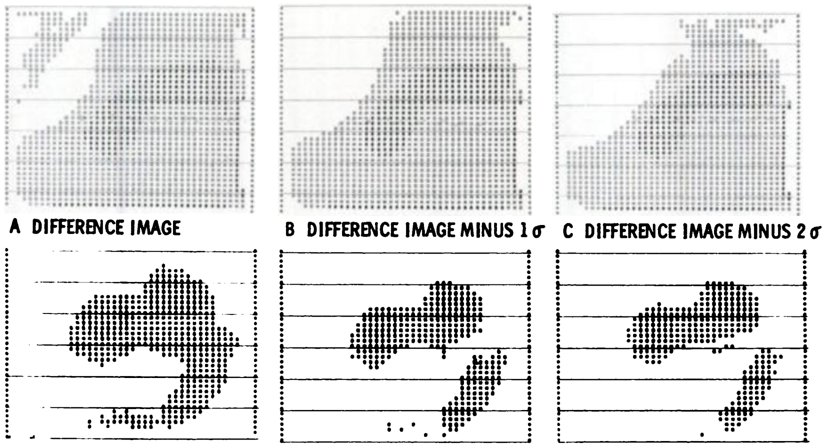

FIG. 5. "Difference images" for two normal pancreas examinations with subtraction of 1 and 2 experimental standard deviations.

facility, with its great flexibility in image manipulation, will be possible soon. For this study, matrices were displayed on the screen, boundaries defined with the light pen, and boundary coordinates punched on cards which were input to the processing program. The influence of boundary definition upon the "difference image" was also investigated. Three such images, corresponding to three different boundaries for a particular matrix pair, are illustrated in Fig. 6. In general, only small variations in the "difference image" were observed provided that the region-of-interest definition was representative of liver alone.

RESULTS AND DISCUSSION

One hundred and fifty pancreas examinations have been carried out over a period of 2 years. One hundred and twelve cases have had sufficient followup for a final diagnosis to be made.

Procedural errors, most of which were encountered early in the study, reduced the number of cases available for "immediate subtraction" to 91 and for computer processing to 86.

An abbreviated interpretation—normal, abnormal or equivocal—was assigned to each of the scintigrams (i.e. the original scintiphotos and, where applicable, the "immediate subtraction" and computer subtraction images).

These interpretations were compared to the final diagnosis for each case, and the results of this comparison are shown in Table 1.

An interpretation was labeled "correct" if the scintigram was considered to show abnormality in morphology and/or function and pancreatic disease was present or the scintigram was considered normal and no evidence of pancreatic disease was present at surgery, followup, or autopsy. An interpretation was labeled "incorrect" if the scintigram was considered normal and pancreatic disease was present or if the scintigram was considered abnormal and pancreatic

TABLE 1. CLINICAL CORRELATION

Experimental evaluation technique	Total number of examinations*	Diagnosis based on scintigrams compared to final clinical diagnosis† % correct	% incorrect	% equivocal
Original scintiphoto	112	47	13	40
	(86)	(48)	(12)	(40)
"Immediate subtraction"	91	71	9	20
	(86)	(73)	(8)	(19)
Computer subtraction	86	82	8	10

* A group of 86 examinations was processed by each of the techniques.
† See text for a detailed description of these classifications.

disease was not proven. (Some cases of pancreatitis will fall in this category when the scintigram was correctly interpreted as abnormal and the diagnosis could not be confirmed.)

Scintigrams were considered "equivocal" when pancreatic morphology and/or function could not be assessed due to incomplete visualization, e.g., as in some scintiphotos where liver overlap was present, or poor definition of pancreatic activity related to high adjacent background, e.g., due to activity in the bowel, kidney, or gastric tumor. The effectiveness of pancreas "subtraction scanning" is clearly demonstrated in the comparisons shown in Table 1.

Based upon the original scintiphoto alone, accuracy in diagnosis of the presence or absence of pancreatic disease was less than 50%. Improved visualization of pancreatic morphology, and thus an increased accuracy in diagnosis, results from the use of dual-radioisotope methods, even with the simple technique using a multichannel analyzer and cassette tape recorder.

Computer methods for pancreas scintigraphic data processing, such as that described in this paper, are seen to provide still further improvement in accuracy of interpretation.

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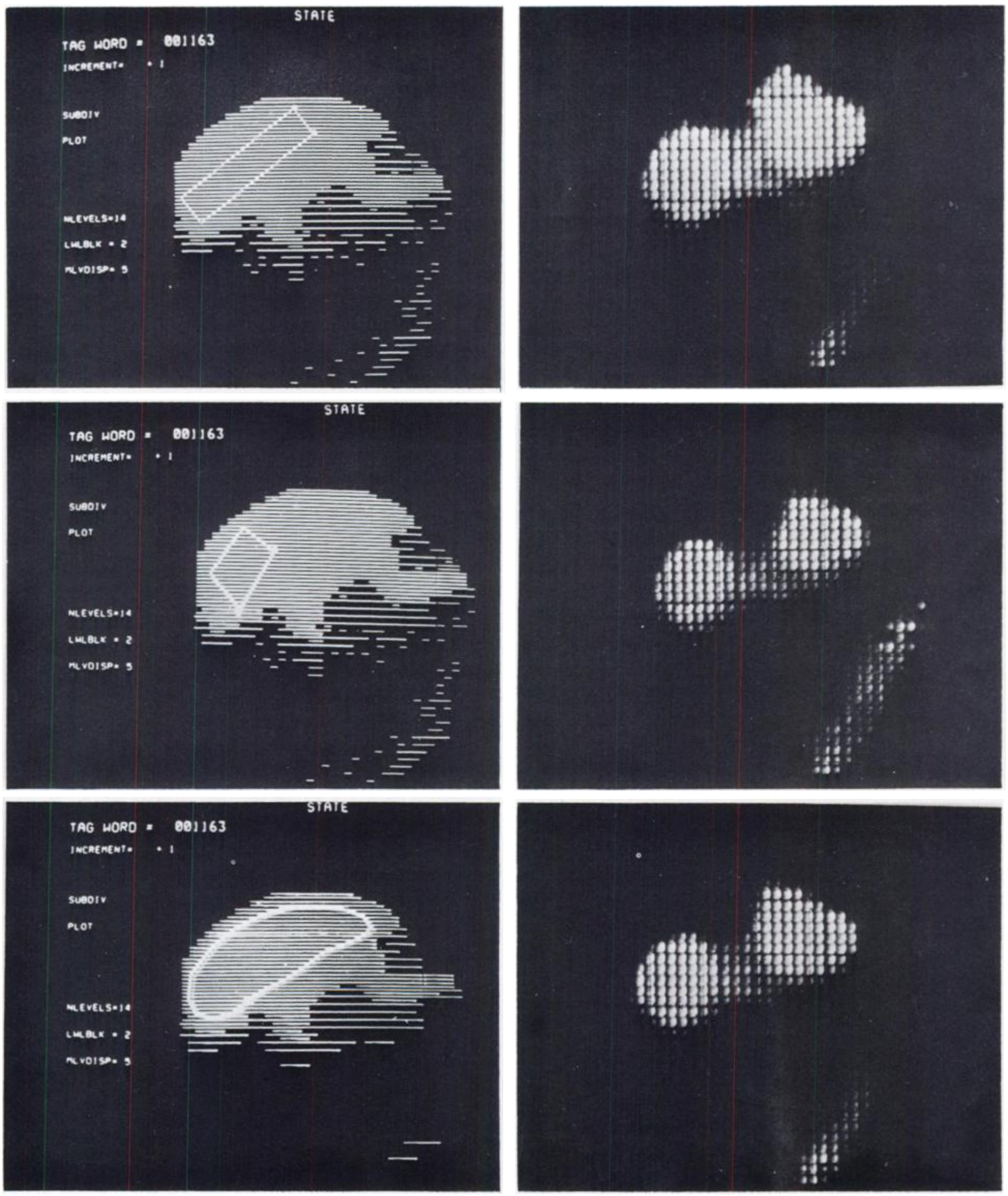

FIG. 6. Example of computer graphics representation of pancreas scintigram with light-pen specification of three distinct regions of interest. Three "difference images," obtained using ratios calculated with these three boundaries, show little variation.

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