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DEVELOPMENTS IN DIGITAL COMPUTER IMPLEMENTATION IN NUCLEAR MEDICINE IMAGING

DONNER LABORATORY

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Developments in Digital Computer Implementation in Nuclear Medicine Imaging*

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ABSTRACT

The usefulness of a digital computer system for acquisition, manipulation and display of nuclear medicine or other medical two-dimensional images is enhanced by fast data acquisition of 80,000 cps in list mode (128 X 128) and 300,000 cps in histogram mode (64 X 64) with 3 μsec pulse pair resolution and dual isotope handling capabilities. Speed and ease of operation are important developments which lead to practical clinical application of research developments such as brain and heart blood-flow studies, Fresnel hologram reconstruction, three-dimensional reconstruction from multiple camera views, and display of functional images such as lung, heart, and kidney uptake and clearance rates.

INTRODUCTION

The clinical usefulness of digitizing and manipulating scintillation events for display of physiological function is in good part dependent upon the ease, accuracy, and speed of effecting the data acquisition and manipulation. The questions one might ask are: "Do the digital systems, now under the efficacy interrogation, do justice to the scintillation camera output; and if any limitations of these systems are overcome, what computer-assisted techniques would the clinician like to perform? Can these be conveniently executed on commercially available systems?" The answer to the first question is that most digital systems lose 20 to 40% of the data during high speed studies, and almost all the systems digitize the image without sufficient spatial resolution to represent properly the inherent resolution of the scintillation camera. The answer to the second question involves a list of procedures and desirable computer programs, some of which everyone agrees are needed. The third question is posed by the clinician who recognizes that processing data by digital computer might take 20 times longer than for similar processing by a specialized analog system (e.g., brain flow studies). The tedium of performing these procedures will diminish his enthusiasm, unless we also simplify the technical complexities and shorten by factors of 2 to 10 the time required for data manipulation. The clinician can understand and control the technical complexities, but cannot expend the time required to execute special studies.

This paper is an overview of how we attempted to overcome limitations many clinicians and computer scientists have encountered over the last eight years of experiments with computers in nuclear medicine. The hardware configuration of the system at Donner Laboratory is shown in Fig. 1. We present here how the hardware has been exploited. The entire system, including the software, can be duplicated through hardware acquisition and program sharing with us.

HARDWARE PHILOSOPHY

Analog to Digital Conversion

There are six important characteristics of the nuclear medicine ADC contained in the Hewlett-Packard system:

1. Pulse pair resolution less than 3 μsec,
2. Differential nonlinearity less than 1%,
3. 7-bit digitization in x and y (128 X 128),
4. Ability to move the field of view before digitizing,
5. Ability to zoom before digitizing,
6. Capability of acquiring information from physiological triggers, different energies or isotopes, or an additional camera looking at the same patient from a different view.

The speed and spatial resolution requirements are vital to any quantitative nuclear medicine system, and it is in this respect that we felt most digital systems had serious limitations. During the routine 10-mCi ^{99m}Tc-pertechnetate or albumin cardiac study, the data rate of the photopeak events is 40 kcps (thousand counts per second) during 2 to 3 seconds of the study. With a deadtime of 20 μsec the loss of data is 45%, and for 40 μsec, 62%. In fact, one can show that the maximum counting rate as the source isotope increases without limit is $(\text{deadtime})^{-1}$, which for a 40-μsec system is 25 kcps. Slow systems not only limit statistics, but give washout or flow curves that are distorted and must be corrected before they can be used for quantitative work. This is particularly important in cardiac flow studies. Correction of the observed count rate to the true count rate is dangerous, because the basic statistics cannot be improved (1).

The clock time of the dual ADC's used in the Hewlett-Packark system is 200 mHz, and the pulse pair resolution for each ADC digitizing 7 bits is 3

μsec. Although most Anger scintillation cameras have a pulse pair resolution greater than 6 μsec (Nuclear Chicago high performance camera, about 12 μsec), other imaging devices such as multicrystal NaI(Tl), multiwire gas- or liquid-filled xenon proportional chambers (2), or the pure germanium solid state camera can provide data at rates of 300,000 counts per second. In fact, the Anger scintillation camera can provide data with a pulse pair resolution of 3 μsec, and any scintillation camera can perform with a count rate in the crystal up to 500,000 cps (3), cf. Fig. 2.

Spatial resolution of the digitized data should be at least 128 X 128 for static imaging with the modern gamma cameras. The argument for setting up a system with a resolution of 64 X 64 or 32 X 32 is that it is convenient for a particular 12-bit or 16-bit word computer. As has been shown by Erickson and Brill (4) from the changes in the modulation transfer function, one needs more than 64 elements across a 10-inch crystal. Another argument, based on the uniform sampling theorem in a spatial domain, shows that more than 100 sampling points in each direction are required to faithfully represent the Anger camera data. Digitized resolution patterns show that a spatial resolution of 128 X 128 is required for a faithful reproduction of data available from the Anger scintillation camera.

The ability to zoom and the ability to move the field of view of our ADC's are useful for viewing high spatial resolution in small fields, such as the upper chest of a premature infant or the midbody of a child. The zoom capability allows one to acquire high spatial resolution at high frame rates; thus, by "looking" only at the center 1/4 area of the crystal, one can acquire data with equivalent 128 X 128 resolution with frame rates allowable for 64 X 64 frames. The zoom control involves no recalibration or complicated changes of the ADC's.

List Mode vs. Frame or Histogram Mode

In our system there is an option for data acquisition in two distinct modes, list and histogram. Each mode has its own advantages, and the choice of mode depends upon the type of study and the probable computer processing to be done.

In list mode the data are acquired with a spatial resolution of 128 X 128 and an effective frame rate of 100/sec. A flow study on a premature infant with a heart rate of 180 will yield good information if data are framed in 50-msec intervals. This figure is based on consideration of the wave shape of the time-activity curve over the precordium and the uniform-sampling theorem in the time domain. List mode is an appropriate solution to the difficulties of moving buffer data into and out of core with this time resolution. This mode also allows simultaneous acquisition of data and physiological information. Disc or drum data accumulation systems have the required speed to acquire data in the list mode, but tape systems are too slow for the cardiac flow studies we perform. In the list mode, the maximum data rate (without loss) is 80 kcps. The data are transferred to a raw data disc file of 1.3 million words, which is just adequate for most flow studies. A storage capacity of less than a million words will not suffice for nuclear medicine studies in list mode. We have found that list mode not only gives the required time resolution and, where desired, spatial resolution of 128 X 128, but also gives the operator-clinician the option of choosing, after the accumulation, the intervals and resolution for framing the data.

In the histogram mode, the data are acquired with spatial resolution of 64 X 64 (optionally 32 X 32) and frame rate of up to 20/sec (50/sec for 32 X 32), which must be chosen before the study. It should be noted that in the histogram mode the capability of acquiring and storing 128 X 128 frame sizes is not

present in most small computer systems, as this requires 16K of core dedicated to this task. A computer with 12K is adequate for most studies being performed in nuclear medicine; however, we have found it convenient to have more core available for buffer storage during experiments with new programs. We have just expanded the core to 32K to facilitate experimental programming. In the histogram mode, the maximum data rate (without loss) is 300 kcps, with no restrictions on the total number of counts in a study. The total number of histograms collected is limited to 330 by storage capacity of the disc. For a frame rate of 20/sec a study must be complete in 330/20 = 16.5 sec. For a frame rate of 4/sec, a study must be complete in 330/4 = 82.5 sec. If flow studies are done in histogram mode with a framing rate of 20/sec, it is likely that the accumulated histograms of sparse data will exceed the disc capacity before the end of the cardiac study. After 16.5 seconds the disc will be filled, and if the timing of the data acquisition commencement is not made at the proper moment after the injection, part of the study will be lost. Thus, the storage capacity is an extremely important consideration in the argument for list mode versus histogram mode in high-framing-rate studies using a disc.

METHOD OF DATA ACCUMULATION AND FILE STRUCTURE

Transfer of Raw Data to Disc

The moving-head disc consists of a series of disc platters which are rotating at 2400 rpm (40 rps) and for each platter two READ/WRITE heads on a movable arm. The heads are for each of the two surfaces of the platter (top and bottom). The arm has 203 fixed positions. When it is in any one of these positions it traces out a circle on the disc platter. This circle is referred to as a track. The collection of tracks for both heads, and for as many platters as there are, is called a cylinder. A track is divided into fixed-length sections, which may be individually read/written, and are called sectors.

The list mode accumulation of 80,000 events/sec requires an average computer-to-disc transfer of 80,000 words/sec. The achievement of these data rates should be possible in most computer-disc systems by proper organization of the disc driver and disc file. The system must, however, be completely dedicated to its accumulation task, since disc efficiency is based on head and disc platter position.

Disc transfer rates are frequently quoted as: (words/track)/(time/track) = (3072)/(1/40) = 122,880 words/sec. This performance figure is misleading, since a head cannot write indefinitely over one cylinder of the disc. After filling two tracks on a cylinder, the head must move to the next cylinder, and this track-track time is about 7 msec. In addition to the 7-msec track-track, one has to wait an additional 25 - 7 = 18 msec for the start of the cylinder before one can continue writing. A write operation cannot be effected without rotational delays. After the head is positioned over sector N, for example, full rotation plus one sector delay occurs before the write can be started on sector N+1; however, only one sector delay occurs before the write can be started on sector N+2. These delays must be taken into account when choosing a disc file organization. In this particular case, one can stop writing several milliseconds before the end-of-cylinder and start the track-track at that time. This allows one to switch cylinders without unnecessary rotational delays. In the general case, transfer speed depends completely on how the disc is utilized. To compare two systems, one must specifically ask what is the data transfer rate during system operation. We have measured a transfer rate of $\sim$ 82 kcps.

There are two disc platters in the system, the first 2/5 of the raw data file is stored on the upper (removable) platter, the remaining portion on the fixed disc platter (Fig. 3). The raw data disc file is blocked into 4096-word

records (32 sectors of 128 words each). Each record occupies sectors 0-23 of a cylinder (the entire track) on the top of a platter and sectors 0-7 of the same cylinder on the bottom of the platter. The remaining space on each cylinder is used for other files, such as frame files for 160 frames (4K) and special programs.

The data transfer takes place as follows. The first block (4096-word record) is transferred by a write request for 32 sectors. The hardware transfers data to sectors 0-23 on the top and automatically switches to the bottom to transfer data to sectors 0-7. The time for the transfer is 25 msec for the top and 8.3 msec for the bottom. At this point there is 25-8.3 = 16.7 msec time to switch to the next cylinder in order to be ready for the next write operation. Thus the data transfer rate is 4096 words in 25 + 8.3 + 16.7 = 50 msec or slightly over 80,000 words/sec. The slop time of 16.7 - 7.(track-track) - 1.4 (rotational delays) = 8.3 msec is important to allow for the problem of data transfer to a synchronous device (the disc) when running slightly below the 80-kcps rate.

METHOD OF GENERATING FRAMES FROM RAW DATA

The system has two distinct modes of data accumulation, list and histogram. Accumulated data are stored in a disc file, with identifier information specifying accumulation mode. The techniques of data acquisition in either mode leave the data in a form which cannot be viewed directly, thus a frame generation process must be employed on the raw data.

List mode

List mode describes a data accumulation mode where each event has its x, y coordinates digitized in 128 X 128 (7 X 7 bits) resolution. To this, two bits of isotope information are added, creating a 16-bit computer word. These raw data are saved as a list of events; that is, a computer word for each event without change of format. This list of raw data events has time events inserted as distinct words every 10 ms. These time events are distinguished

from camera data events as follows. There are four possible combinations of the two isotope bits. The three combinations ØØ, Ø1, and 1Ø are used to designate isotope. The fourth (11) is reserved for timing information. Only the 16-bit combination 1111111111111111 is used to indicate a 10-msec time event. As needs arise, other information may be inserted in the data list by using the isotope bits (11) and the remainder of the word for physiological parameters.

In list mode frame generation, the raw data are read from disc in buffers of 4K. From operator inputs, the original 128 X 128 raw data word is appropriately spatially reduced and offset in preparation for addition to the x, y word of the frame being generated. The frame being generated is limited to 4096 words (e.g., 64 X 64, 32 X 128) due to buffer size. When the appropriate time period (measured by the number of timing events) accumulates, the frame is written to disc and a new frame generation is started. Our system allows us to set x, y dimensions and offsets that use the full resolution capability of the list mode raw data. Thus four frames of 32 X 128 can be generated to form a montage of 128 X 128.

Histogram Mode

Histogram mode describes a data accumulation mode where each event is digitized in 64 X 64 (6 X 6 bits) or optionally in 32 X 32 (5 X 5 bits) format. These data are accumulated in core as a 64 X 64 (optionally four 32 X 32) histogram, similar to a frame image, and these histograms dumped to the raw data disc file at preselected intervals. For accumulation, two buffers are used, accumulating into one while the other is being dumped. The buffers are not cleared between dumps (this would add dead time). The raw data on disc appear as records, each being 64 X 64 histograms. These histograms cannot be directly interpreted as frames, in that they represent all the raw data to that time, accumulated in one of two buffers. The details of this accumulation were

chosen to avoid ADC dead time and data distortion (skew introduced by dumping and accumulating at the same time).

Histogram mode frame generation represents an easier task than a similar list mode operation. The total counts at any time are determined by adding the record dumped at that time to the previous record dumped (i.e., the other buffer). The frame for any time period is obtained by subtracting the total counts framed to the beginning of the time period from the total counts framed at the end of the period. Histogram mode frame generation is simply an iteration of this technique.

SYSTEM CONTROL AND CAPABILITIES

The computer system in a nuclear medicine laboratory can be as easy to operate as an Anger camera or rectilinear scanner. No special programming skills are required to run the system at Donner Laboratory.

The mode and language whereby the technician, clinician, or researcher communicates with a system is as important as any other aspect of the system design. Cumbersome computer language or mnemonics have been avoided, and most operations are under the control of a standard ASR-33 teleprinter keyboard, which has been labeled by an overlay shown in Fig. 4. Explanation of some of the functions is as follows:

CONTROL: (a) Select mode--sets the system in idle mode ready to accept a "core load" which consists of a set of instructions for particular modes of operation, such as accumulate or display. The computer memory is refreshed from the disc library in less than 1 sec.

(b) Enter--executes a valid command from elsewhere on the keyboard.

ACCUMULATE: A specific core load is read off the disc into computer core, thus putting the system in readiness for list mode or histogram mode accumulation of data. A switch on the ADC is set for list mode (7 bit) or histogram mode.

The study is started by depressing the key marked RUN and stopped by depressing PAUSE. Framing or regrouping the accumulated data is done by selecting a preset program initiated by depressing the keyboard program START or by entering framing parameters, using the key CREATE. One can accumulate data in either list mode or histogram mode with spatial resolution up to 256 X 256. Zoom control is simple to change, and the ADC will accept dual isotopes and physiological triggers after gating studies.

FORMAT: Display of any 4K block of a field of 128 X 128, and image orientation control. One can display 128 X 128 by using 4 exposures of 32 X 128.

FRAME CREATE: A "core load" which allows the user to transfer raw data into frames of any duration $\geq$ 10 msec, a specified count limitation if desired, and data into frames related to certain physiological markers or isotopes.

PATIENT READ & WRITE: Transfer of frame data to and from magnetic tape for permanent storage.

KEYBOARD PROGRAM: Preprogram various phases of operation such as format, framing intervals, etc. This facilitates data collection for routine clinical studies such as brain or liver.

TIME FUNCTION CREATE: When the key is pressed, a new "core load" enters the system and the user is able to create 1-16 time functions consisting of counts integrated over preselected areas of interest. These areas can be overlapping and become part of the permanent record along with the time functions.

AREA-OF-INTEREST AND TIME-ACTIVITY CURVES: Selection of regions for determining integral counts as a function of time can be performed readily for flow studies of brain, heart and lungs, kidney, as well as other organs--for example, parotid glands, thyroid, liver and bone. Measurement of ejection fraction (5-7), cardiac output (8 and 9), and intracardiac transit times (10 and 11) are easily effected by using this system. No special reduced lighting or skills are necessary for the light-pen operation.

One can use the time-activity curves to aid in the visualization of phases of physiological activity such as the second and third phase of the renogram or end systole and end diastole (Fig. 5) (1). In the latter, data from periods of minimum activity and periods of maximum activity over the left ventricle are separated and summed to give a statistically strong image of end systole and end diastole. The minimum and maximum activity frames are found by differentiating the time-activity curve with respect to time and selecting the frames corresponding to zeroes in the resultant function.

ARITHMETIC OPERATIONS: Addition, subtraction, multiplication, and division of 160-point time-activity curves or 4096-element frames by another time-activity curve or whole frame is accomplished by four key strokes. These operations take less than 0.5 sec and are performed by simple messages such as--

* F1 * 10 → F2

* F2/F3

which means multiply frame 1 by 10 and put the results in frame 2. Then divide frame 2 by frame 3.

The data for frames are accessed on disc automatically as part of the program, and these operations, including transfer of the calculation result

to a new frame, are accomplished in less than 1 sec. An example of image subtraction is shown for a pancreas study (Fig. 6). The activity over the liver for the ^{99m}Tc-sulfur colloid study is adjusted to that observed for the ^{75}Se-selenomethionine study by multiplying the respective frames by integers determined by the activity observed in selected liver regions in each study. Then the ^{99m}Tc-sulfur colloid normalized image is subtracted from the ^{75}Se-selenomethionine normalized image to give an image of the pancreas that supplements or clarifies, but does not supplant the information in the original view.

FIELD UNIFORMITY CORRECTION: This is a floating-point routine that corrects acquired images for field nonuniform response by using a reference flood field frame. A series of normalization frames appropriate for various energies and windows commonly used can be stored periodically for use in correcting images acquired during routine clinical studies. By depressing key "NORMALIZE" (Fig. 2) we start the routine that executes on the desired frames using the reference frame of choice:

NORMALIZE

MIN, MAX FRAMES: _____, _____

NORMALIZE FRAME: _____

This routine can be improved upon in terms of speed and accuracy by incorporating a means for excluding the edge effect in the calculation. It is known that the field uniformity is a function of energy, window position, count rate, collimator, and that the edge effect varies with these parameters as well as with the particular distribution of the source. The field uniformity system can be used to assist in the proper tuning of the camera and the investigation of changes with the variables listed above.

SMOOTHING: The method of smoothing presently implemented is a 9-point

(3 X 3) Hanning function smoothing algorithm. A Hanning function (weighting of 1/4, 1/2, 1/4 in one dimension) is commonly chosen when the sole desire is the reduction of high frequency additive noise in the image. This is the ideal 3-point (in each dimension) weighted smoothing function for reduction of high frequency additive noise. In these images, the noise contribution at a point is due to the counting statistics. The standard deviation of the noise term at a point is $\sqrt{N}$, where N = number of counts; hence, the noise term is not additive, and will not lend itself to this type of smoothing.

Some spatial averaging is necessary in order to simulate a continuous distribution from which the discrete counts arise. This procedure is to some degree justified from the fact that the distribution in the body is continuous, and smoothing operations will not prejudice the data if a smoothing function is varied to take into account the statistical significance of the data. Fixed-area smoothing, such a 9-point two-dimensional averages, weighted or un-weighted, will result in superfluous blurring. Since the points of low counts, hence low statistical significance, are treated the same as points of high counts, points of high statistical significance are inappropriately lowered. An appropriate technique is the variable spatial smoothing, which can be achieved by varying the radius of the smoothing domain inversely with the measured counts. Thus areas of high count rate where the statistical significance is great might require a 5-point smoothing function, whereas in areas of low count rate the 9-point smoothing is appropriate.

FRAME CREATION[‡]: Creation of a 64 X 64 image by using the light pen or other method of flagging picture elements. First a constant value (1, 10, 100, etc.) is placed in all 4096 elements. Then the image is drawn by flagging elements with the light pen. All elements other than those flagged are

zeroed by depressing teleprinter key "J." Frames also can be created using BASIC or FORTRAN (see below).

MASKING‡: Part or parts of an image frame can be removed by flagging the area-of-interest to be retained using the light pen, then depressing key "J," which will zero all picture elements outside that area.

AREA-OF-INTEREST PERIMETER EXPANDER‡: The perimeter of a flagged area-of-interest is automatically expanded by one element each time key "O" is depressed. Thus the outline of the left ventricle made by a single contour can be easily expanded into an annulus of any thickness. This routine aids in the implementation of ejection fraction by the method of Van Dyke et al. (5).

AUTOSCAN‡: A motion-picture effect using 2 to 160 frames is implemented by the rapid play-through of successive frames in selected groups. For example, 36 views of the head at 10 degree increments can be seen as the head rotating on the CRT. The program cycles through the 36 frames repeatedly until stopped by the operator. This routine is also used for following brain, heart, and kidney flow studies.

IMAGE ROTATE‡: The displayed image is rotated in 90° increments by depressing teleprinter key "=".

DISPLAY 128 X 64‡: A special program loaded as a separate "core load" allows one to display two successive frames simultaneously on the CRT. This program is used for displaying part of the 64 X 384 array from the digitized whole body scans (1).

The following capabilities are present in our system, and can be put in other systems by a system update which takes less than 60 sec and requires purchase of a disc ($99-$125). They will be explained under advanced applications.

DIGITAL TOMOSCANNING‡

IMPULSE RESPONSE‡

WASH-OUT TRANSFORM‡

2D FOURIER TRANSFORM‡

FRESNEL HOLOGRAM RECONSTRUCTION‡

MOTION IMAGE‡

Examples of BASIC (explained below) language programs applicable to operation on time functions are:

DECAY CORRECTION FOR TIME FUNCTIONS

END DIASTOLE AND END SYSTOLE IMAGES CREATION

CARDIAC OUTPUT

TELEPRINTER DISPLAY OF 3 TIME-ACTIVITY CURVES SIMULTANEOUSLY

FOURIER TRANSFORM ONE DIMENSION (two dimension is in FORTRAN)

UPTAKE-WASHOUT CURVE GENERATION

SQUARE ROOT, LOG, DERIVATIVE, INTEGRATION

OPERATIONS ON TIME-ACTIVITY CURVES

SIGNIFICANCE OF DIFFERENCE BETWEEN TWO TIME-ACTIVITY CURVES

PROGRAMMING LANGUAGES

BASIC

BASIC is a high level conversational computer programming language similar to FOCAL and, in the context of the nuclear medicine system, similar to NUTRAN, which is used by the Nuclear Data MED II system. These are easy languages for nonprogrammers to learn and use because programs are written using English or algebraic expressions, not cryptic computer codes. It is conversational in that it tells you when you make an error, and what and where the error is.

BASIC can be called up in our system with a single key stroke. This gives the researcher the capability of easily trying operations in the system,

which the original designers of the system did not anticipate (e.g., computation of the impulse response function of the heart). Once the BASIC program is written, no special knowledge of BASIC is required by the clinician to run the program. Simple BASIC CALL statements allow reading/writing of frames or time functions from their respective files on the disc. The BASIC statement, CALL READT (4,25,A(1)) will read from the disc file the first 25 points of time function 4 into the array A(1) ... A(25). Similar calls are made to write the time function back onto the disc where updating of the disc file is desired. All 160 points of time function X can be read in by specifying CALL READT (X,160,A(1)).

The problem of reading/writing frames is conceptually more difficult since the operation involves handling 4096 words of frame data. BASIC requires the data in floating point, which means two computer words are necessary for each array element. The 12K core was insufficient to handle this large an array. The solution was to have the two calls READF, WRITF for reading and writing a frame between computer core and disc files; and the calls GFD, PFD to get or put a frame element as a floating point word for BASIC. For example:

1. Add 1 to element (3Ø,6) in FRAME 1Ø.

```
DIM A(3Ø,69)
CALL READF (1Ø,A(1,1))
CALL GFD (3Ø,6,Z)
LET Z = Z+1
CALL PFD (3Ø,6,Z)
CALL WRITF (1Ø,A(1,1))
```

2. Clear FRAME 2.

```
DIM A(3Ø,69)
CALL READF (2,A(1,1))
FOR I = 1 to 4Ø96
```

```
CALL PED (I,1,Ø)
NEXT I
CALL WRITF (2,A(1,1))
```

Of course many operations on frames can be easily accomplished by the resident systems programs such as clearing a frame. In this case one enters--

```
Ø > F1
```

which clears frame 1 by placing a "Ø" in each picture element.

FORTRAN, ALGOL, Assembly Languages

FORTRAN and ALGOL are high level languages (similar to BASIC) that are compiled to produce an intermediate object paper tape, which may be considered to be a machine language equivalent of the program. The assembler produces a similar object tape. These intermediate object tapes must later be run through a special program provided with the system to produce an absolute machine language program, which may then be read into the system and run. This absolute program may also be made a part of the system and called up by a keystroke from the console.

The primary advantages of FORTRAN, etc. over BASIC is that computations will take place much faster (up to 500 times faster for some operations), since the FORTRAN program is compiled prior to execution, whereas each BASIC program step must be interpreted during execution. FORTRAN and ALGOL are more flexible, and may allow the performance of tasks that would be impossible in BASIC. BASIC programs will use more memory than similar FORTRAN programs, primarily due to the fact that the BASIC interpreter remains in core with the program.

The disadvantages of FORTRAN programming are primarily in the development and debugging of the program. In our system it involves prohibitive amounts of mechanical operations. First, the program must be punched on paper tape; then, load computer with FORTRAN Pass I; run this program, generating an intermediate

tape; load computer with FORTRAN Pass II; run this program, generating the object tape described above; load computer with FORTRAN-BCS; run this program with the object tape and FORTRAN libraries, finally producing an absolute paper tape. This tape may be loaded on the disc and called up whenever desired, but if there are errors one must go back to the original paper tape of the program and correct it by using a paper tape editor (another program to load and run!), and then start back at step one. This set of operations differs sharply from BASIC, where all the above operations are done in core with no paper tape handling.

The difficulties in FORTRAN program development discourage all but the most clear and pressing needs. In our system we have found it useful to do most of the research programming on large machines with data transmitted by magnetic tape from the HP 5407. Programs successfully developed and debugged can be later implemented on the system. As soon as the program has some utility, it is put into the system as a coreload, using assembly language or FORTRAN.

ADVANCED APPLICATIONS

Fresnel Hologram Digital Reconstruction

The efficacy of Fresnel zone-plate image coding over pinhole imaging has been emphasized for point sources; however, its value in nuclear medicine applications for sources extended over more than 5 to 6 cm has yet to be established (13-15). The signal-to-noise advantage for small sources such as the adrenal gland, or even parotid glands, does in theory give advantages over the pinhole collimator because the transmission of the Fresnel plate is hundreds of times greater than that of the pinhole. A digital reconstruction technique allows us to explore the tomographic potentials of this "lens." With Mr. Burns Macdonald (16) we explored techniques whereby the Fresnel hologram recorded by the scintillation camera can be directly transformed to an image by a small computer system such as the HP 5407. Application of this

routine can resolve the controversy regarding the efficacy of the Fresnel zone plate coding versus the pinhole coding for objects distributed in three dimensions. The cumbersome and nonquantitative aspect of the conventional Fresnel zone-plate reconstruction technique is the use of coherent light reconstruction. There is a large DC component and interference from the virtual image, which affect both the optical and the digital reconstruction; however, most of these problems are overcome by the digital technique, which we have been implementing on the HP 5407.

It can be shown that the image is related to the Fourier transform of the Fresnel hologram after an appropriate quadratic phase shift. This relationship is:

$$I(x,y) = \mathscr{F}\left[H(s_x,s_y)\, e^{\frac{-i\pi(s_x^2 + s_y^2)}{r_1^2}}\right], \tag{1}$$

where $H(s_x,s_y)$ is the two-dimensional scintigram of the Fresnel coded image, and r_1 is the radius of the inner ring of the Fresnel zone plate on the image plane. This is related to the distance between the Fresnel zone plate and the object, f, and the distance between the zone plate and the detector, S, as:

$$r_1 = r_0 \left(1 + \frac{S}{f}\right), \tag{2}$$

where r_0 is the actual radius of the zone plate. The digital reconstruction can be done in two ways. First, the acquired data (64 X 64) are placed in frame 1. The phase shift of Eq. (1) is effected and the complex Fourier transform made on the phase-shifted data. This is done 32 times each for a different object plane by incrementing r_1 by 0.5 for each operation. The transformed images are placed in frames 10 to 41, giving 32 planes through the object. The alternative technique involves writing the acquired digital frame onto Hewlett-Packard formatted tape and translating this tape to a CDC-66 or 7600 format. The Fourier transforms are done on arrays up to 1024 X 1024, and the

results translated back to the HP format for display and analysis. These techniques are convenient tools for determining the relative efficacy or sensitivity of the pinhole coding to Fresnel zone plate coding in nuclear medicine (Fig. 7).

Motion Image by Display of Fourier Coefficients

The periodic motion of an organ can be extracted from a study by a display of Fourier coefficients at frequencies corresponding to the periodic motion. For example, during a cardiac flow study after the injection of 10 mCi of ^{99m}Tc, the information can be framed into 64 (4K) frames at 100-msec intervals. Each of the 4096 pixels is then selected along with its corresponding pixel from the other 63 frames as a single dimension time domain vector, which is Fourier transformed with respect to time. The result of this transformation leads to 32 frequency values, which are placed in each frame in place of the real space counts. This is done for each of the 4096 pixels, and the result is a set of Fourier coefficients for each frame. Now the successive frames represent the amplitude of the frequency at first and successive harmonics. The result is an image of motion with applications to heart, lungs, and liver. For example, the frame representing frequency of 70/sec will show the highest amplitude in the left ventricle for a man with a heart rate of 70/min; and the frame which represents frequencies at 12/sec will show the edges of the lungs representing a patient with a respiratory rate of 12/min.

Impulse Response

During a flow study, one can expect the organ of interest to respond linearly during the first few moments of the passage of the isotope; i.e., the turnover function of the organ is invariant to the character of the input function. This turnover function is called the impulse response, and characterizes the frequency distribution of transit times. The turnover function can be determined using the observed input and output time-activity curves

by application of the Fourier convolution theorem. This system impulse response is the inverse Fourier transform of the system transfer function. The system transfer function is given by the quotient of the Fourier transform of the output function and the input function:

$$\mathcal{F}(\text{impulse response}) = \frac{\mathcal{F}(\text{out})}{\mathcal{F}(\text{in})} .$$

In practice this procedure is limited by poor statistics, inadequate definition of the input function, and the apparent nonlinear effects occasioned by recirculation (feedback). The program is a neat package that gives the response function as a time-activity curve after four minutes calculation (three Fourier transforms are involved). It has not been explored in clinical applications, except for determination of its relevance to cardiac flow studies.

Digital Tomography

By moving the pinhole collimator to multiple positions relative to the static distribution of an isotope, it is possible to perform a digital reconstruction of sections through the object at selectable levels. The information from other levels or planes will be superposed but defocused on the in-focus image from the selected level. The digital tomography algorithm involves shifting and expanding or contracting each pixel from each of, say, 36 images (6 X 6 grid) in order to reconstruct the information that would give rise to the 36 views if all the activity were in the selected plane. The amount of shifting and expansion of each pixel is determined from the pinhole divergence, distance between the camera and pinhole, and distance to the selected plane for viewing. The algorithm was developed by Dr. Lucine Mathieu (Lyon, France) in collaborative work at Donner Laboratory. The HP 5407 requires 3½ min to calculate each plane if 36 views (30,000 dots per view) are used. The results of digital tomography are as good or better than those from

the tomoscanner at Donner Laboratory in preliminary studies with 511 keV and 140 keV energies for bone, myocardium, and kidney imagery.

Three-Dimensional Reconstruction

There are 12 techniques known to us for three-dimensional reconstruction of the density or isotope distribution. Most of the techniques are easily implemented on a small digital computer, and we give here an overview of those techniques that can be implemented.

The back-projection technique, similar to section scanning pioneered in nuclear medicine by Kuhl (17 and 18) is a rapid and relatively simple method of delineating tumors within the head. Other methods such as the simultaneous iterative reconstruction technique proposed for microscopy (19), the Fourier transform technique (20), the algebraic reconstruction technique (21), the least-squares technique (22), or the orthogonal tangent correction method (23), are all, in general, equivalent and more accurate than the simple back-projection technique. Another technique, which is found to be equivalent to the Fourier transform technique, is the high-pass filter of the projections prior to back projecting used by the astrophysicists Bracewell and Riddle (24) and by Chesler (25) in nuclear medicine studies. Less well-known techniques involve the Hilbert transform of the first derivative of the projected images, followed by back projection and the technique of geometric means, which we have been exploring using multiple views somewhat similar to that of Schmidlin (26) with the additional modification of weighting by length of rays. All of these techniques are easily implemented in a small digital computer once the framework for mapping the projected densities or counts onto the array has been established (12). The rotation of the patient in front of the scintillation camera with a subsequent extraction of data along slices for reconstruction is shown in Fig. 8. A comparison of three direct methods for reconstruction is

shown in Fig. 9 (12). The on-going work includes a comparison of the least-squares technique with other techniques more easily implemented on small machines, such as the back-projection of the high pass filtered projections. To investigate these techniques we use the HP 5407 for data acquisition and display of reconstructed sections. The program development was done on large machines, after which the codes are transferred to the HP 5407.

DATA PRESENTATION

Contrast Enhancement and Background Subtraction

Contrast enhancement and thresholding, or background cutoff, are two of the most important features of a digital, or for that matter analog, data storage system. The match of the two-dimensional data array displayed on a cathode-ray tube to the human eye has been a problem from the earliest days of nuclear medicine imaging (27-29). Detection of lesions is aided by change in contrast and brightness of the display scope, but in some cases artifacts are enhanced. Control over the image presentation cannot always be obtained by simple integration of each dot on film using multiple f-stops as is usually done on the commercial scintillation cameras. Where the differences in detected counting rate between a region of interest and the surrounding normal tissues is only 15%, some background subtraction or thresholding is necessary for visualizing the difference. The digital computer allows one to present the same study as multiple images with different threshold or cutoff levels.

Enhancement by spatial filtering and digital smoothing certainly gives images more appealing to the eye; however, investigators (30) have not found these techniques to improve overall diagnostic accuracy. Results of image nonlinear restoration techniques such as adaptive filters (31-33) and histogram linearization procedures have not had clinical trials.

Techniques of contrast enhancement, and filtering by both smoothing and CRT defocusing, are illustrated (Fig. 10) for a heart image one hour after I.V. injection of 0.5 mCi ^{129}Cs. These well-known techniques are aids to the clinician who wishes to record an image which represents the optimal visual representation of his diagnostic impression. The dangers of enhancing artifacts by contrast enhancement of smoothed data are no greater than those experienced with other display techniques used with rectilinear cameras and scintillation cameras. The elective control of stored digital data can be obtained with special analog systems, but their cost is almost one-third that of an entire computer disc operating system.

Three-dimensional Display

An important potential of digital control of data is the ability to display three-dimensional images on a conventional oscilloscope by a computerized technique developed by Coulam and co-workers (34). By controlling the x-y position of the electron beam on the CRT and the beam intensity with a clever algorithm, a correct impression of the three-dimensional image data can be conveyed to the diagnostician. These algorithms have application to problems such as the display of the left ventricle shape at end diastole and end systole.

Projections and Profiles

The ability to show isometric projections and to display the profile of activity vs. position gives the clinician or investigator a means of evaluating the statistical significance of suspected lesions or abnormalities (Fig. 11). The accumulation of ^{129}Cs in the myocardium can be made to appear dramatically great relative to the accumulation in contiguous lung and muscle by contrast enhancement; however, the true relative distribution is forced on the observer by the pseudo-quantitative technique of viewing the isometric display. This maneuver is a hard-wired algorithm available on most nuclear medicine digital

computer or analog display systems. Our system can execute rotation of the image by 90° increments, which facilitates looking "behind" the image. The time required to effect these maneuvers is 1 sec, or almost as fast as a switch or key can be depressed.

Counts or activity levels of any magnitude can be delineated by adjusting a baseline and window width by controls on the display console. The picture elements having values lying within the window are intensified as illustrated in Fig. 11 (lower left).

Color

Color images have seven potentially useful applications in nuclear medicine. On a single scintiphoto, color gives the ability:

1. To give isocount or gray level delineation.
2. To represent different time intervals for a flow study.
3. To show respective spatial distribution of two isotopes.
4. To delineate relationships of transmission and emission studies on a single image.
5. To show relationships between ventilation or clearance and perfusion in the lung and heart studies.
6. To show relationship between static or anatomic image and the motion image (see above) by using color to represent each mode on the same print.
7. To facilitate stereoviewing with red and green images and red and green glasses.

We have found color very effective in delineating time relation and in demonstrating the difference in uptake of two or three isotopes. Uses 6 and 7 are still research studies. Important relations between right and left heart can be seen by employing color to delineate time relations. Other uses include

radionuclide cisternography, cerebral angiography, and renography. The color images are obtained with red, blue, and green filters handplaced between the P-31 phosphor of the Hewlett-Packard scope and Polaroid 180 film mounted on a Tetronics CRT-camera adaptor.

SUMMARY

The following clinically valuable adjuncts to nuclear medicine procedures are provided by a digital computer disc-operating system:

Control of image data presentation, including capability to use color, to correct for field nonuniformity, to enhance contrast, and to allow playback of the study for reviewing flow or reflex studies.

Creation of time-activity curves from flow studies of brain, heart, thyroid, kidneys, lungs, and liver.

Quantitation of counts or activity distribution.

Manipulation of data for determination of physiologic parameters such as cerebral flow transit times, cardiac left-to-right and right-to-left shunts, liver function, heart function, and kidney function.

By having a state-of-the art digital system at the technician's finger tips, one can provide patients with the benefits of the above data manipulation and reduction techniques and, in addition, can take advantage of 3-D reconstruction and motion extraction programs just now being implemented for small computers.

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FOOTNOTES

* Work done under the auspices of the U.S. Atomic Energy Commission.

† Consultant; present address: American-Asian Computer Service, P. O. Box 5225, San Francisco 94101.

‡ Programs or system modifications added to the standard HP5407.

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FIGURE LEGENDS

Fig. 1. Schematic diagram of the digital system configuration for acquisition and manipulation of data from the scintillation camera and the whole body scanner.

Fig. 2. The count rate performance of scintillation cameras from four different manufacturers. The curves were obtained by noting the time required for a million counts to be processed from a source of varying strength 48 in. from a bar pattern attached to the uncollimated crystal. A 30% window was used. The expected count rate is the count rate for an ideal system with no dead time.

Fig. 3. Schematic of the file structure on the disc. Data string on one cylinder flows from the top platter to the bottom platter, as signified by the break in the disc diagrams. (See text for details).

Fig. 4. Teletype keyboard overlay used to denote functions of keys.

Fig. 5. Example of retrospective gating where the time activity curve was generated at 50 msec intervals by using an area over the left ventricle for count integration. The sum of the frames at maximum activity gives an image at end diastole, and the frames at minimum activity give end systole.

Fig. 6. Pancreas image extraction by subtraction of ^{99m}Tc-sulfur colloid image from the ^{75}Se-methionine image after normalizing one to the other, using three regions-of-interest over the liver.

Fig. 7. Example of digital reconstruction of the two point sources from the Fresnel hologram. Hologram (middle) was transformed into the original two sources by using the algorithm of Eq. (1). Significant background subtraction was necessary to present the reconstructed images shown (bottom).

Fig. 8. Reconstruction of distribution through a section normal to the plane of viewing in a technetium pertechnetate study of the brain. The sections are

2.5 cm thick and reveal an abnormally high accumulation in the mid-brain, probably due to tumor. Data are from 30 sec views at 10 deg increments.

Fig. 9. Comparison of reconstruction techniques using a phantom 18 cm in diameter.

Fig. 10. Techniques of displaying scintiphoto data. Contrast enhancement, thresholding, and smoothing can be effected by digital manipulation or simply by changing contrast, brightness, and focus controls on the cathode-ray tube.

Fig. 11. Heart muscle accumulation of cesium-129 after intravenous injection of 500 μCi is shown to illustrate different techniques of display which allow semiquantative evaluation.

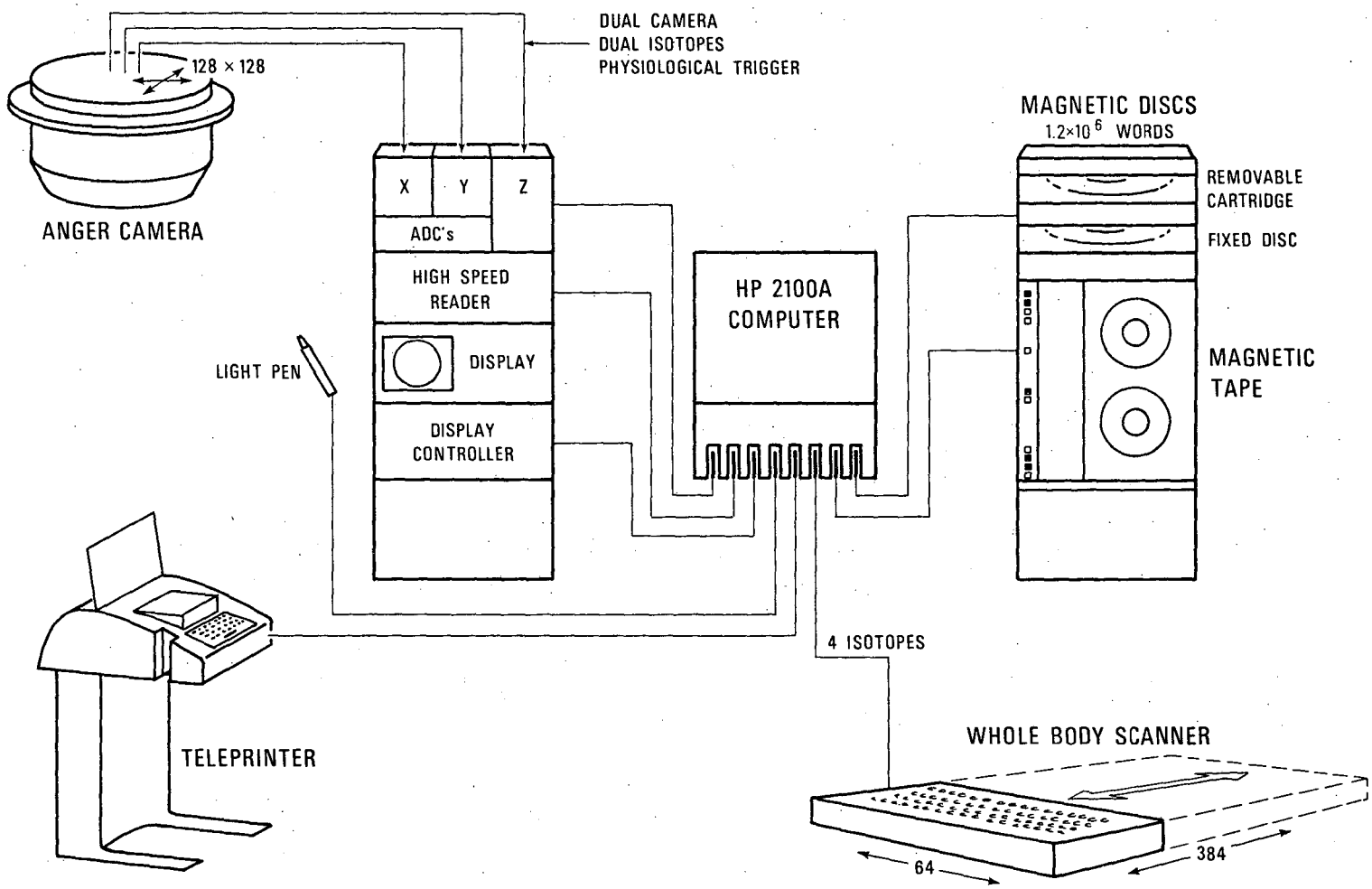
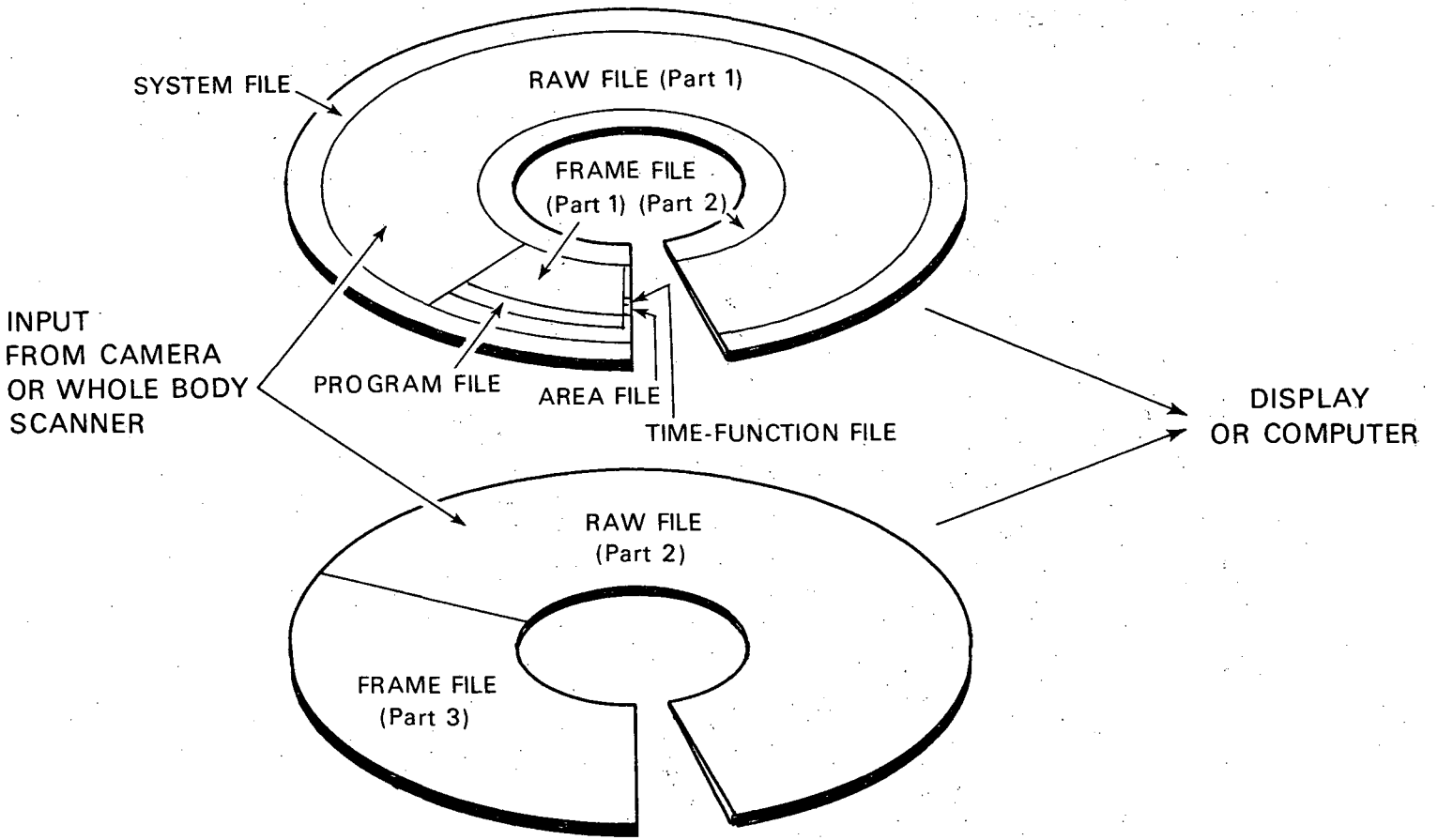

DUAL CAMERA
DUAL ISOTOPES
PHYSIOLOGICAL TRIGGER
128 × 128
ANGER CAMERA
X
Y
Z
ADC's
HIGH SPEED READER
DISPLAY
DISPLAY CONTROLLER
LIGHT PEN
HP 2100A COMPUTER
MAGNETIC DISCS
1.2×10 6 WORDS
REMOVABLE CARTRIDGE
FIXED DISC
MAGNETIC TAPE
TELEPRINTER
4 ISOTOPES
WHOLE BODY SCANNER
64
384
DBL 7210-5522

Fig. 1



DBL 737-5278

Fig. 2

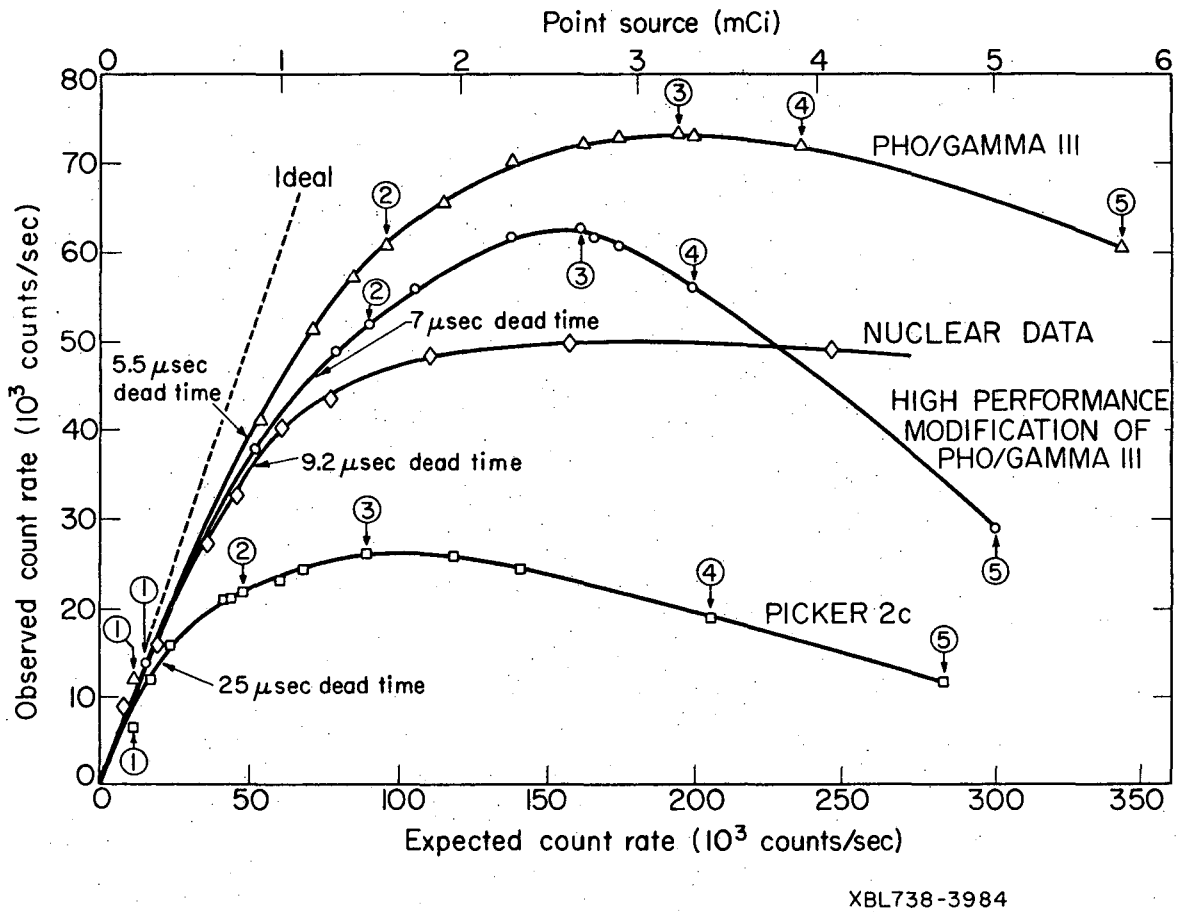

Point source (mCi)
0
1
2
3
4
5
6
80
70
60
50
40
30
20
10
0
Observed count rate (10^3 counts/sec)
Ideal
PHO/GAMMA III
NUCLEAR DATA
HIGH PERFORMANCE MODIFICATION OF PHO/GAMMA III
PICKER 2c
5.5 μsec dead time
7 μsec dead time
9.2 μsec dead time
25 μsec dead time
0
50
100
150
200
250
300
350
Expected count rate (10^3 counts/sec)
XBL738-3984

Fig. 3

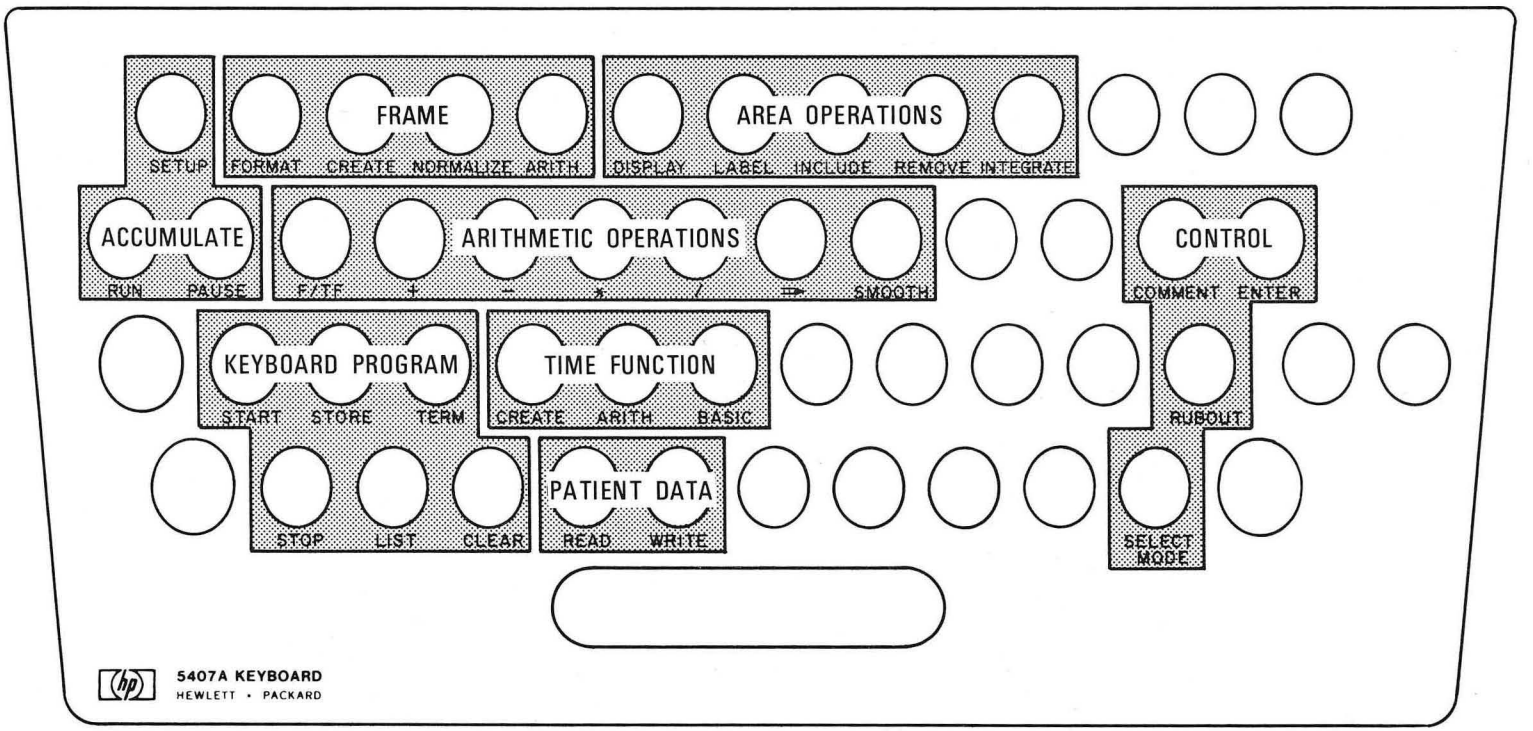


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Fig. 4.

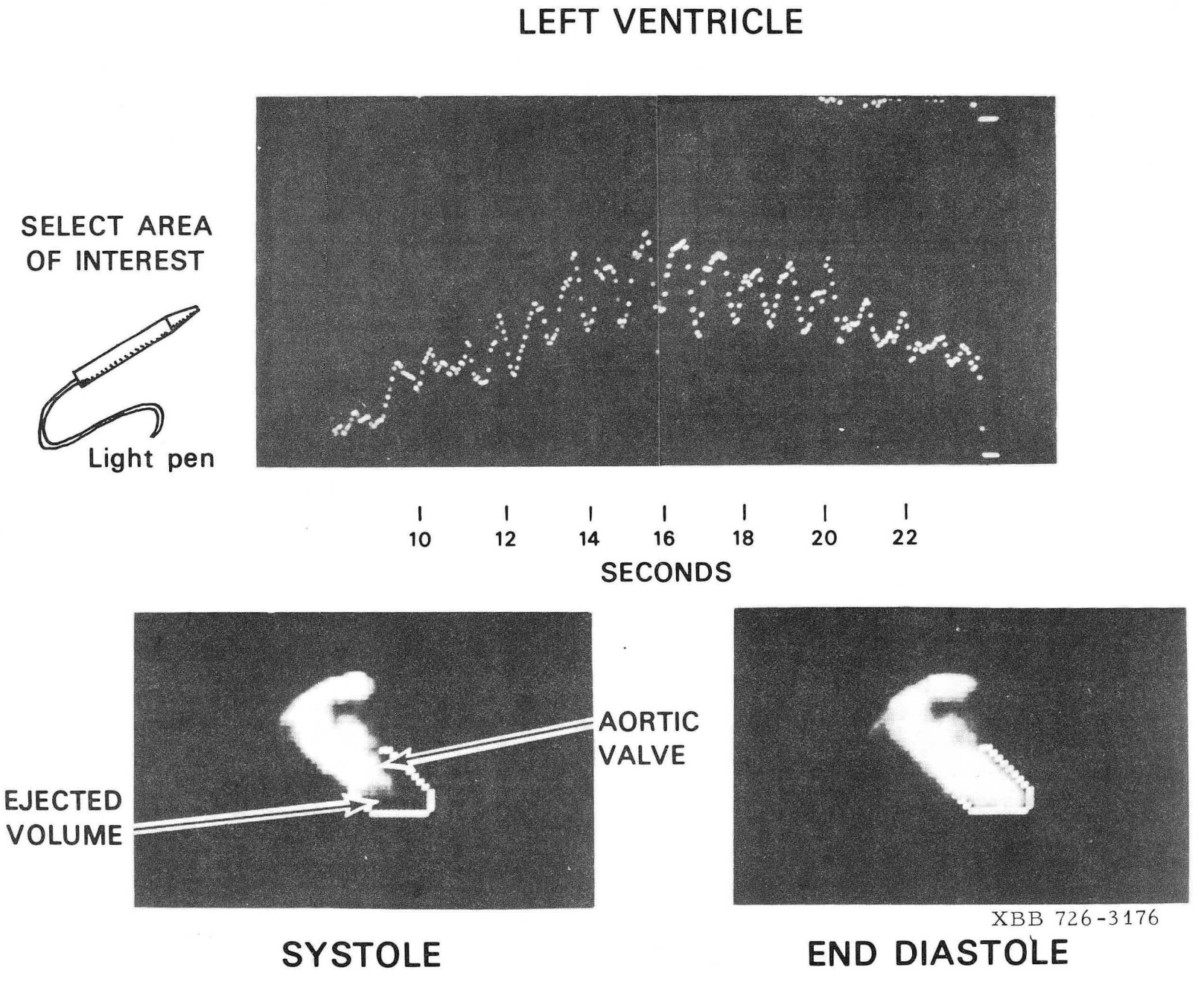
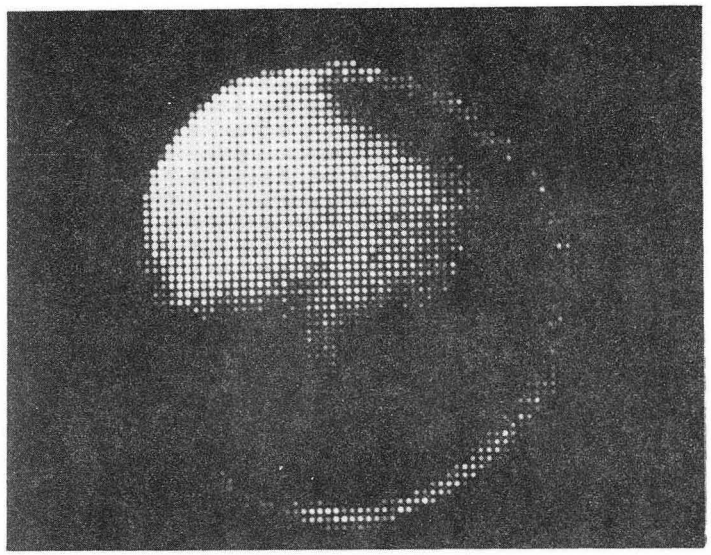
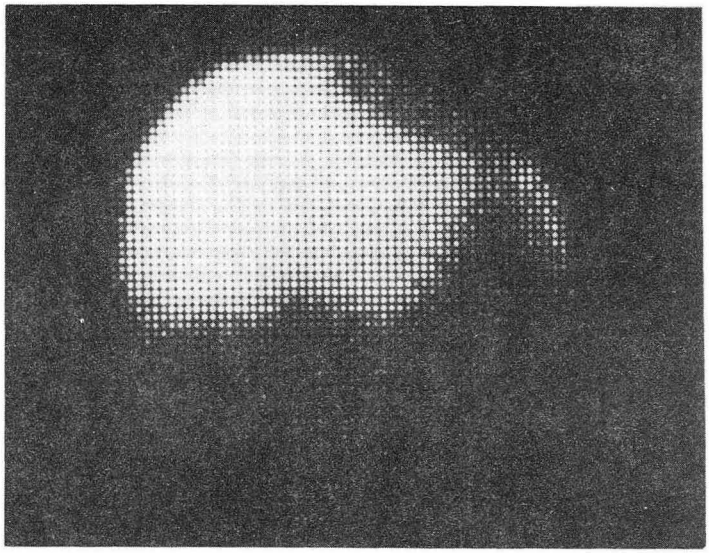

LEFT VENTRICLE
SELECT AREA OF INTEREST
Light pen
10
12
14
16
18
20
22
SECONDS
AORTIC VALVE
EJECTED VOLUME
XBB 726-3176
SYSTOLE
END DIASTOLE

Fig. 5.



^{75}Se-methionine



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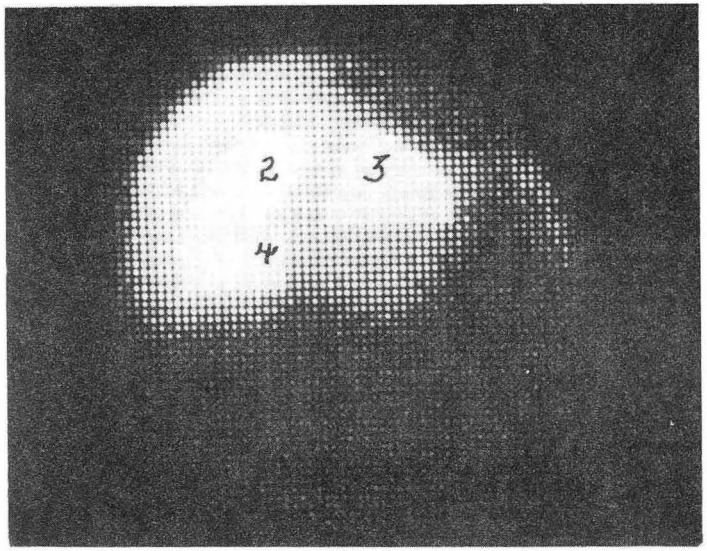
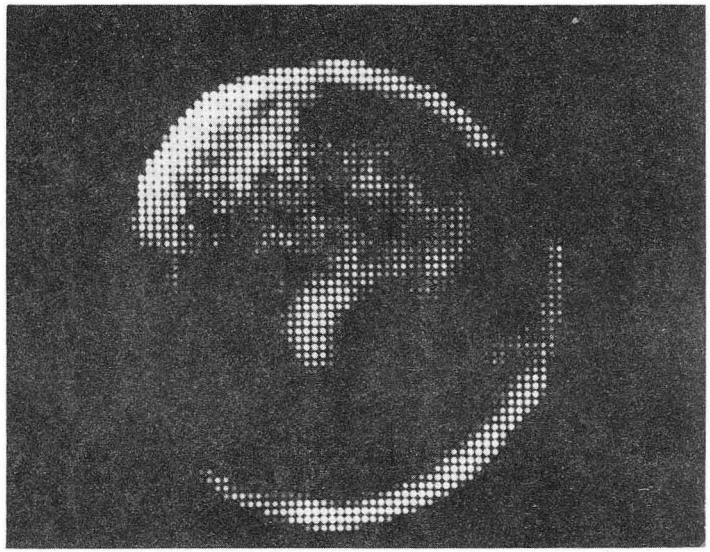


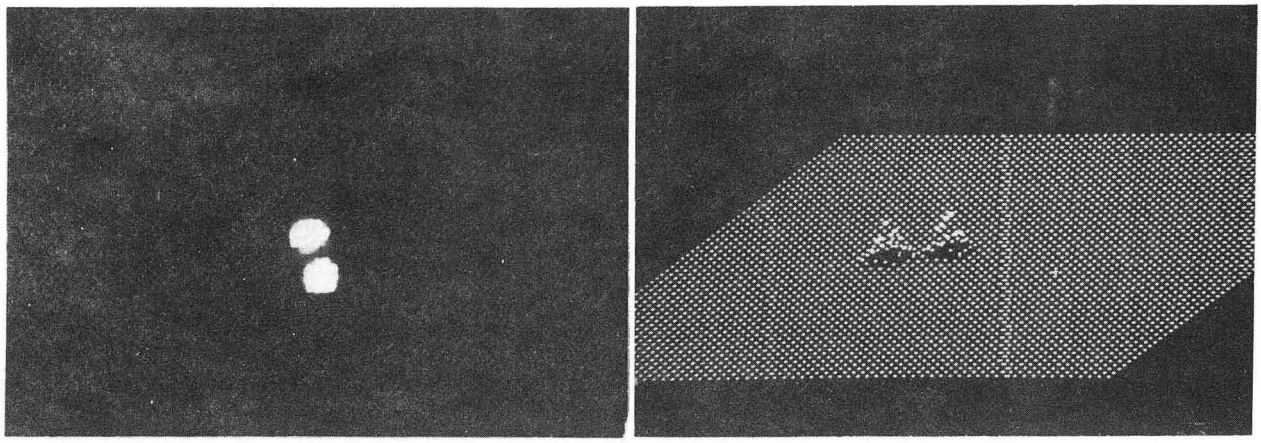
Normalization areas



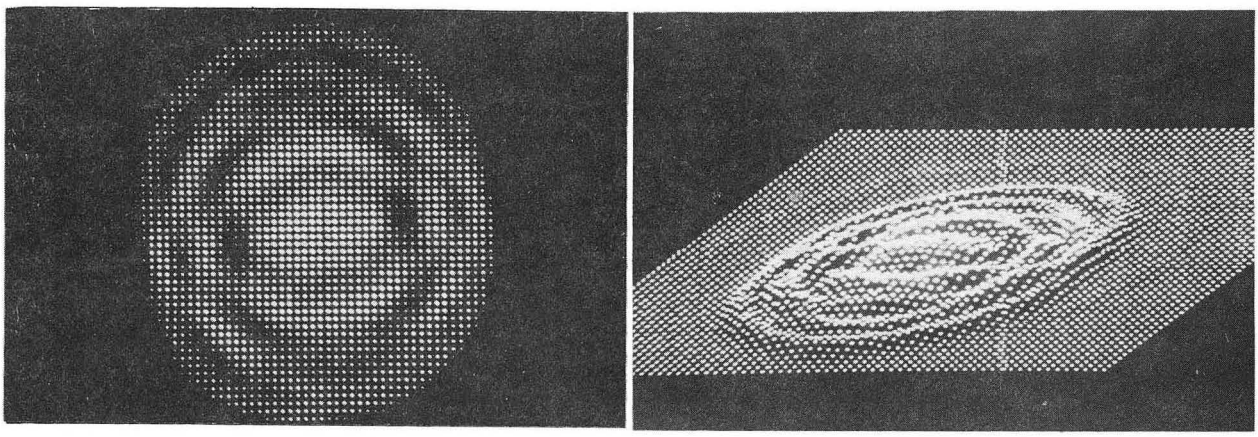
Subtraction after normalization

XBB 732-0603

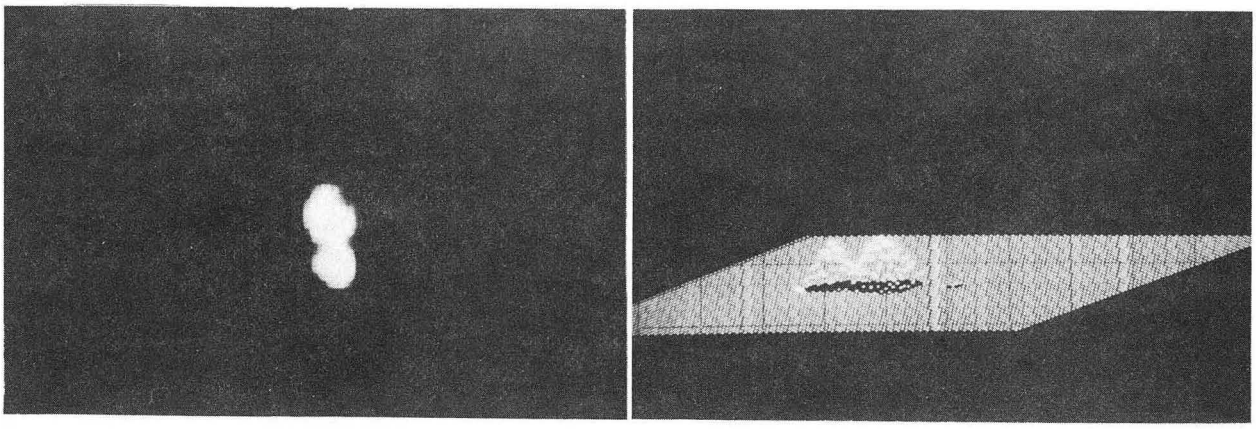
Fig. 6.



TWO SOURCES VIEWED BY PINHOLE



ABOVE TWO SOURCES VIEWED BY FRESNEL ZONE PLATE



DIGITAL COMPUTER RECONSTRUCTION OF ABOVE HOLOGRAM

XBB 739-5136

Fig. 7.

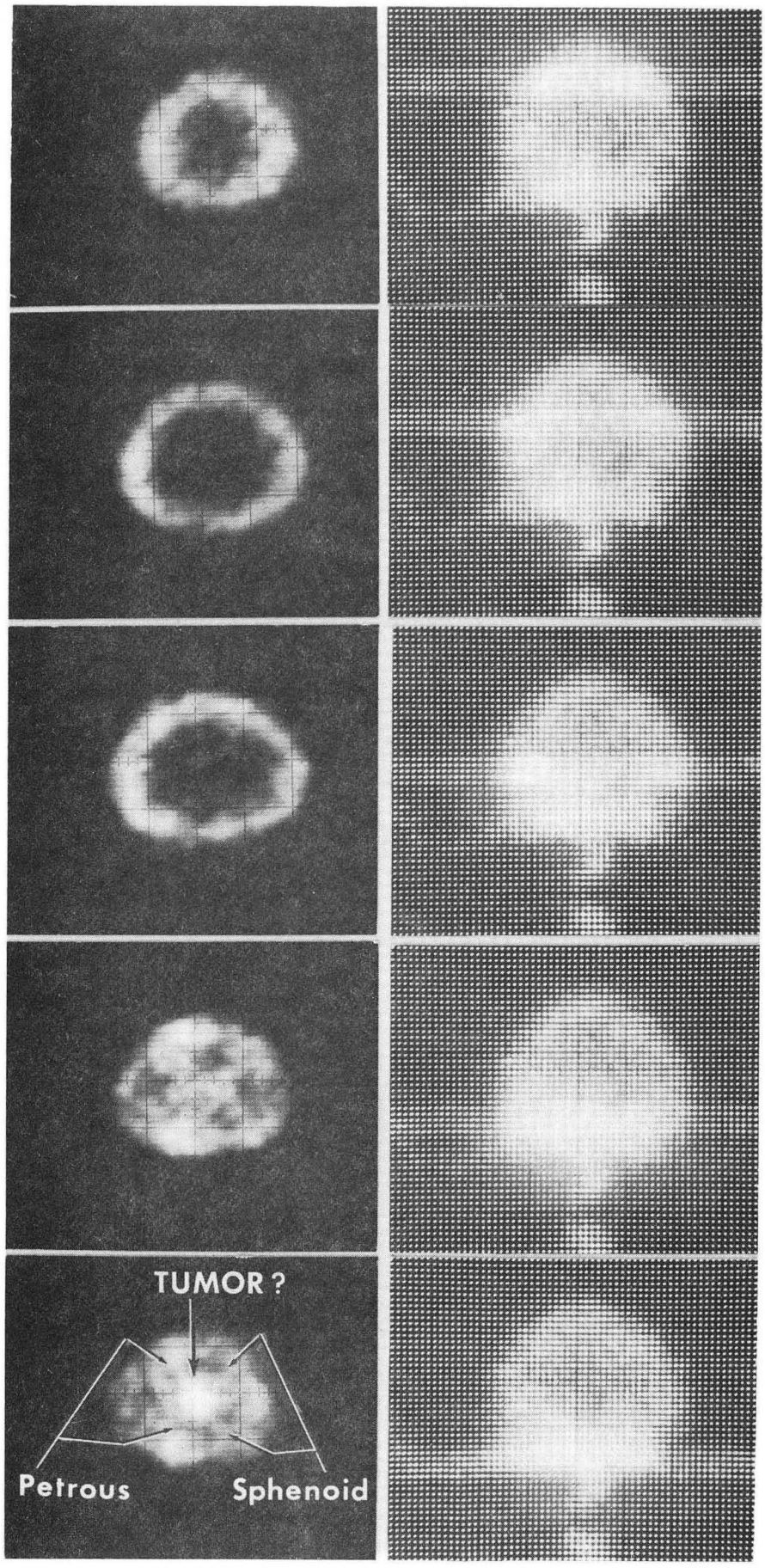


Fig. 8. XBB 739-5135

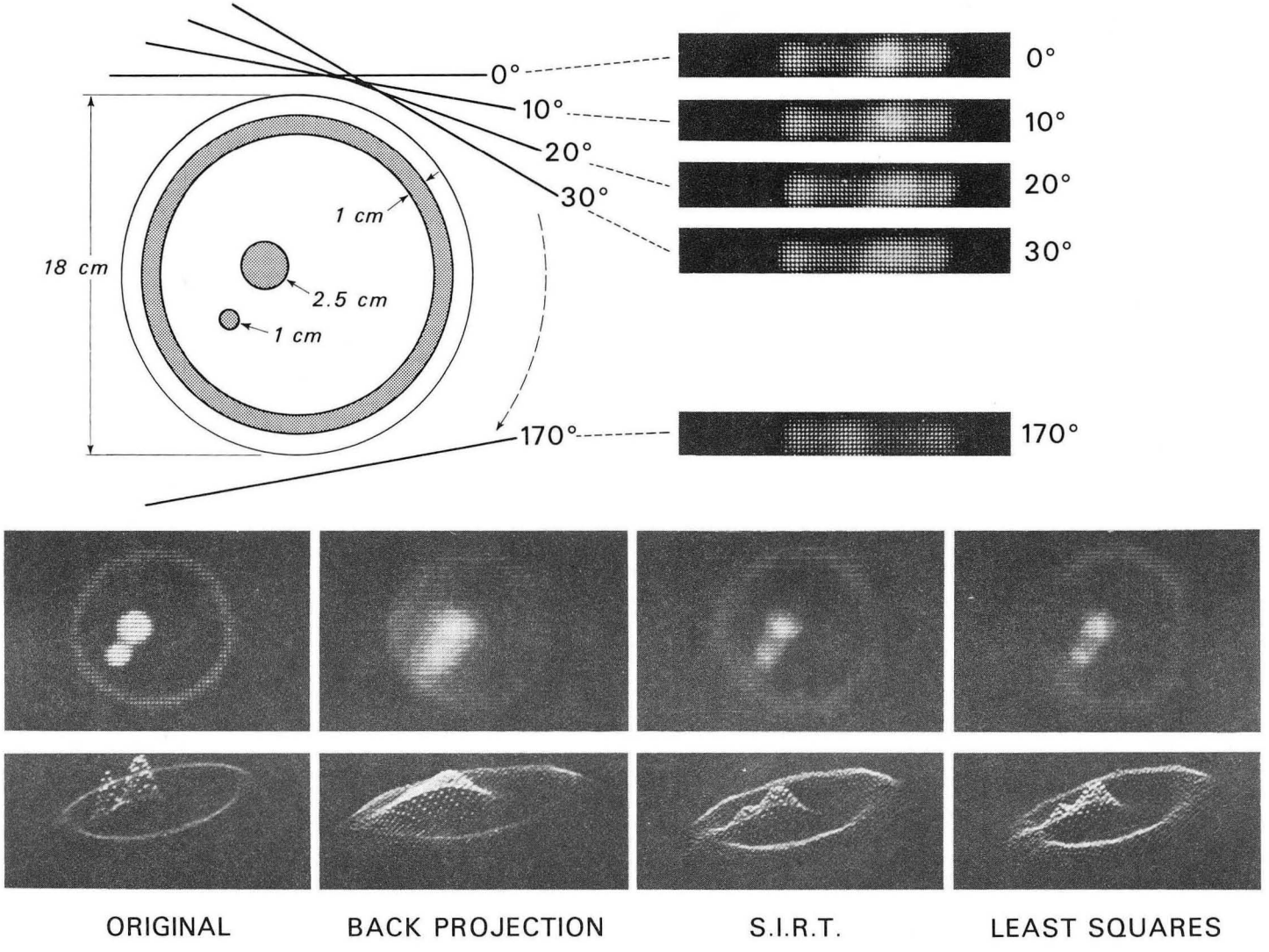
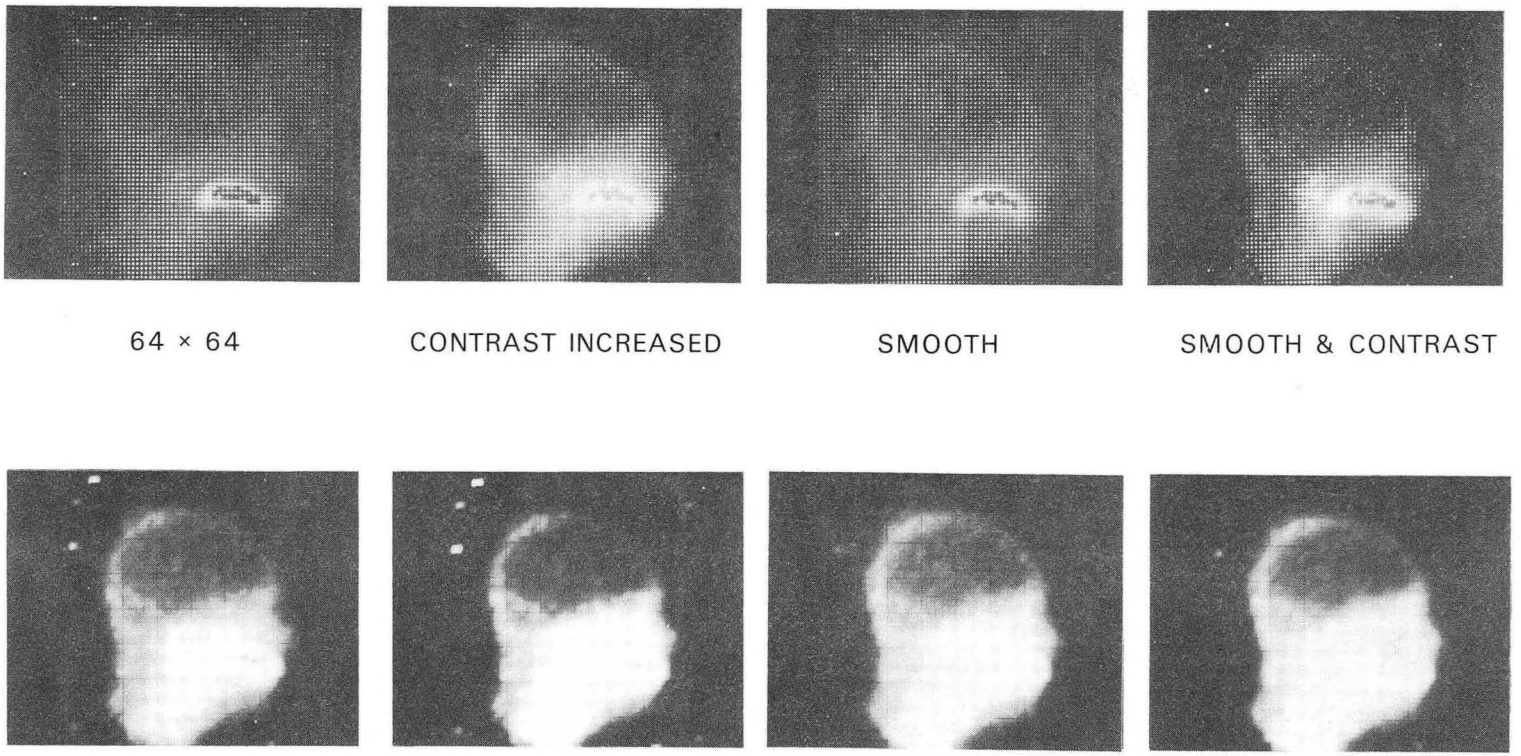


Fig. 9.

XBB 736-4065

MANIPULATION OF SCINTIPHOTO DATA



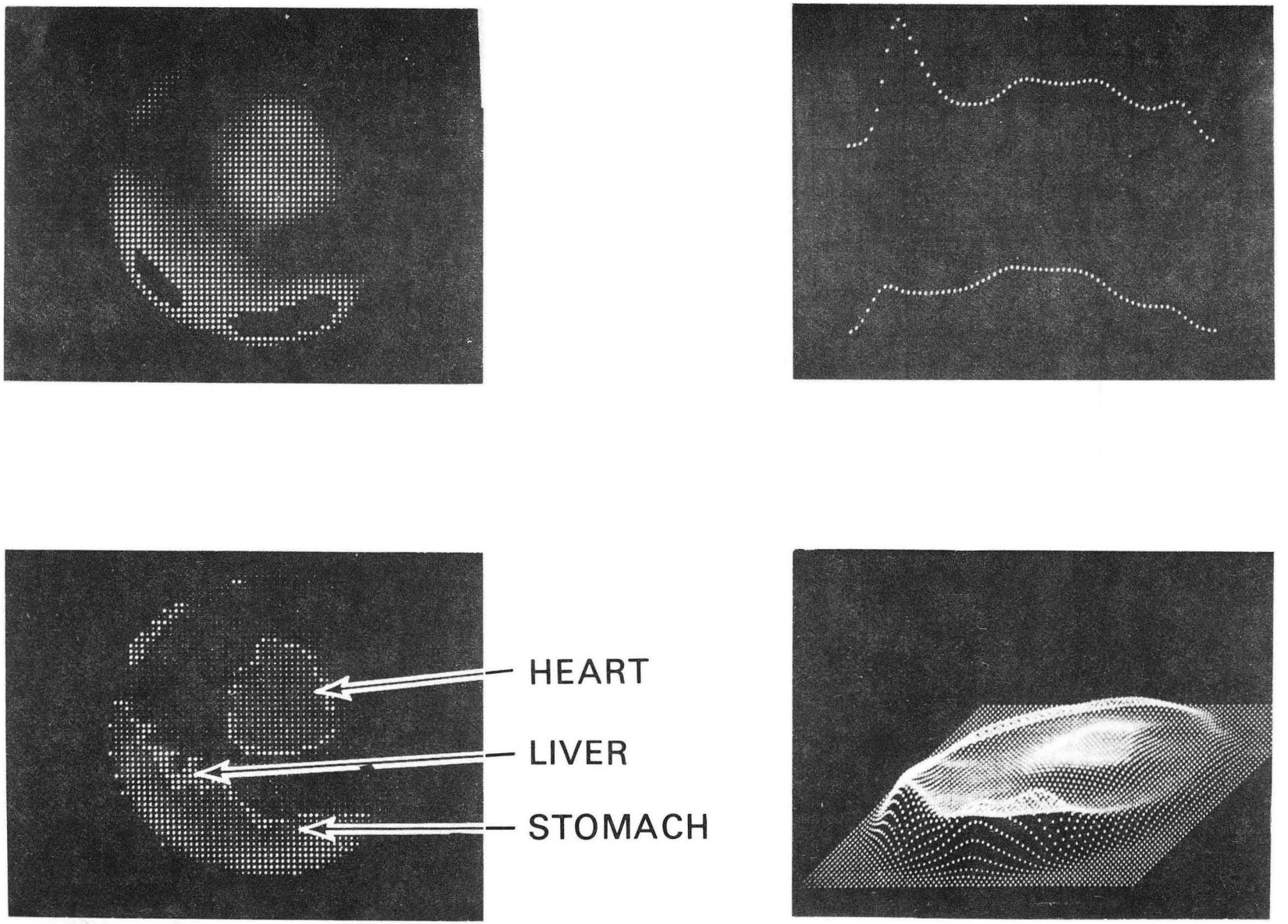
64 × 64 | CONTRAST INCREASED | SMOOTH | SMOOTH & CONTRAST

XBB 722-3518

DEFOCUS

Fig. 10.

^{129}Cs HUMAN



XBB 724-1756

Fig. 11.

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