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The Rutherford Appleton Laboratory's
Mark I Multiwire Proportional Counter Positron Camera

J E Bateman, J F Connolly, R Stephenson,
G J Tappern and A C Flesher

A small (30 cm x 30 cm) model of a proposed large aperture positron camera has been developed at Rutherford Appleton Laboratory. Based on Multiwire Proportional Counter technology it uses lead foil cathodes which function simultaneously as converters for the 511 keV gamma rays and readout electrodes for a delay line readout system. The detectors have been built up into a portable imaging system complete with a dedicated computer for data taking, processing and display. This has permitted evaluation of this type of positron imaging system in the clinical environment using both cyclotron generated isotopes (^{15}O , ^{11}C , ^{18}F , ^{124}I) and available isotopic generator systems (^{82}Rb , ^{68}Ga). At RAL we provided a complete hardware system and sufficient software to permit our hospital based colleagues to generate useful images with the minimum of effort. A complete description of the system is given with performance figures and some of the images obtained in three hospital visits are presented. Some detailed studies of the imaging performance of the positron camera are reported which have bearing on the design of future, improved systems.

1. Introduction

The development and application in medical research of tomographic imaging systems based on the detection of the collinear decay gamma rays from positron emitting isotopes is currently a vigorous and expanding field. Activity centres chiefly on the axial tomographic system or PECAT (Positron Emission Computed Axial Tomography) which utilises the analysis techniques of the X-ray scanner. However, in spite of the great success of this type of system in permitting more accurate physiological measurements than is possible with single photon emission techniques, there is concern over the limited sensitivity, spatial resolution (~ 12 mm fwhm in the best systems at present) and the spiralling costs of the new proposals for multiplane systems with new scintillation materials and phototubes. (See ref 1 for a review of the field of PECAT.) The chief conceptual problem with PECAT is that the narrow ring of detectors makes very poor use of the activity inside the patient, not only due to their small useful solid angle but also (and chiefly) due to the fact that 3 dimensionally variant data is integrated up to one dimensional projections from which the desired 3-D distribution must be recovered. In practice, of course, the PECAT restricts itself to the task of recovering 2-D information, the collimating slit eliminating the third dimension. It is clear on a cursory analysis that if one must (as is the case with positron annihilation gammas) reconstruct the target distribution from projections then the optimum solution is obtained by detecting the collinear events throughout the maximum angular range around the object (preferably over the whole sphere). The obvious solution of using large area position sensitive detectors to image the rays over a large cone of angles was tried out in practice by two groups initially, one using opposed Anger cameras⁽²⁾ and the other large area Multiwire Proportional Counters (MWPC)⁽³⁾. These early results, while indeed demonstrating the viability of the technique for producing high spatial resolution images (< 10 mm fwhm), rather tended to highlight the inherent problems of low rate capability and a poor signal to noise ratio in the fast coincidence channel due to pile-ups and Compton scatters. The Anger camera solution seemed to be eliminated by the long term fluorescent background light induced by the high singles rate in each NaI(Tl) crystal, the sensitivity of the latter to low energy radiation and the limited active area (~ 30 cm diameter), while the MWPC solution was limited

chiefly by poor detection efficiency. Since any viable clinical device required a large area detector (only $\sim 25\%$ of the area of a positron camera represents a useful field of view) the cheaper MWPC technology was taken up by two groups, the first at CERN⁽⁴⁾ and the second at RAL⁽⁵⁾. The two contrasting design philosophies are to be found described in references 4 and 5 and the current status of the CERN design is described in ref 6, and the RAL design was brought to the stage where useful clinical research trials could begin in 1981.

The rapidly dropping cost of computing power experienced in the late 1970's and early 1980's considerably facilitated the construction of a fully commissioned clinical type prototype positron camera with the local ability to process and display the images produced by the positron camera. The largely unresolved questions about the potential usefulness (or otherwise) of this type of positron camera in the true clinical situation with high accidental and scattering contributions made us decide at RAL to build a portable system for clinical trials which would allow us to take the positron camera, complete with its own computing power, to the patients and the cyclotrons. This report describes the RAL Positron Camera which is built into a transport container some 20 feet long and some of the results we have obtained with it during our visits to Hammersmith Hospital, Birmingham University Medical School and the Royal Marsden Hospital where in each case we operated in collaboration with the resident physics and medical staff. The clinical trials have taken place at intervals since June 1981 when the positron camera was first commissioned as a complete system.

2. An Overview of the Positron Camera System

In operation (as figure 1 shows) the two large area position sensitive gamma ray detectors are placed close on either side of a patient in whose tissue some ion labelled with a positron emitter is circulating. When a positron annihilates in the tissue two 511 keV gamma rays are emitted at $180^\circ \pm 0.25^\circ$ to each other. Simultaneous interception of these gamma rays in the two MWPC detectors permits off-line software to reconstruct a vector along which the original emission point must lie (ie the information derived is only projective in nature). The essential definition of a good event is a fast coincidence in the triggering of the two detectors and the familiar problem with such information is that the proportion of accidental (random or pile-up) coincidences increases very rapidly with the signal rate hitting the detector. In fact if R is the signal rate (true coincidence event rate S) to random rate ratio then

$$R = \frac{S_o}{S}$$

where $S_o = \frac{E^2}{2T}$ is the rate at which the system produces as many random coincidences as real ones. E is the Quantum Efficiency of each detector and 2T is the full width resolving time of the coincidence circuits ($\sim 2 \times$ the fwhm of the system timing performance). With the values quoted above for our detectors $S_o \sim 100$ kHz. This seems a very satisfactory value but, as shown below, in the practical clinical situation, scattering and background activity can have a rather severely degrading effect bringing S_o down to ~ 5 kHz in the worst cases.

The sensitivity of the system is simply given by

$$A = E^2 \frac{d\Omega}{2\pi}$$

where $d\Omega$ is the solid angle subtended at the source by the detector system. Typically $d\Omega$ is $\sim 0.15 \times 2\pi$ so that $A \sim 7 \times 10^{-4}$ (this is the absolute fraction of activity detected). In terms of familiar units this is 700 Hz/MBq (or 26 Hz/ μ Ci). In practice we found that we took data at about 50 - 70% of this sensitivity.

The essential details of the detection process are shown schematically in figure 1. A 511 keV gamma ray interacts with one of the stack of the lead

plastic laminated cathode foils generating a fast 'knock-on' electron which can escape into the MWPC gas volume. Attracted to the nearest anode wire, the free electrons generated by the knock-on electron generate an electron avalanche near the anode wire which generates in turn charge signals both on the anode wire itself and on the two nearest cathodes. The lead laminate is divided into mutually orthogonal strips which conduct the signal out to two delay line readout systems which in turn permit the measurement of the X and Y coordinates of the event. (See figure 2.) The anode plane trigger gives the Z coordinate which is necessary to correct parallax effects in the thick detector.

Figure 2 shows how the small charge pulses representing an event are transformed into digital images in a computer memory. The system hardware naturally divides into several separate and (to some extent) technologically distinct subsystems viz the MWPC detectors, the fast front end timing electronics, the data capture electronics (CAMAC), the analogue display system and the digital computer system.

The basic structure of the MWPC detector has already been described⁽⁵⁾ and the problem of extracting the small charge pulses ($\sim 5 \times 10^6$ electrons) from this very large sandwich of 20 anode planes and 21 cathode foils, described. Inside the gas envelope of the detectors are housed the delay line readout structures with their preamplifiers for the double-ended X and Y readouts (figure 2). The anode signals, connected in pairs, are taken on multiple coaxial cables to an external array of 10 preamplifiers with low impedance (50Ω) inputs. A summed output (analogue) is connected to a timing Constant Fraction Discriminator (CFD) for each detector, by which means the basic fast coincidence decision can be made in the Coincidence Detector. The presence of this coincidence signal is used to 'enable' the circuits providing the X, Y and Z coordinates.

Accurate timing pulses are provided from the delay lines by the dual CFD's and the double-ended readout. Offsets (equal to a delay line transit time) are provided by a multiple Surface Acoustic Wave (SAW) delay unit. A 200 MHz pulse train is gated into four fast CAMAC scalers by the CFD triggers from either end of each delay line to produce the four X and Y coordinates. The Readout Timer unit checks that for each event a complete set of coordinates is present, that multiple anode planes have not triggered and that the pulse

height selection criterion was met (see below). All this being 'true' a Look At Me is issued via the CAMAC interface module to the controlling computer program in the LSI-11/23. The data taking program then packs all the coordinates into a 511 event buffer in its memory and restores the Readout Timer to data taking mode ready for another event. When an event buffer is full in the memory it is dumped as a record on either a magnetic tape or the large capacity rigid disk (RL-01).

The generation and display of the collected events as images is an off-line exercise performed on the LSI 11-23 at the end of a data run. Generally the events are histogrammed into 5 planes of 128 x 128 pixels spaced as required within the analysis volume. Subsequent processing improves the quality of the images (as described below) and they are finally displayed on a TV monitor controlled by a video display system capable of showing 16 levels of grey or 16 colours. The final sets of 5 picture files are stored on 8 inch floppy disks. Given the time taken to generate the off-line display (~ 30 minutes) there is a vital need for an on-line display for patient positioning and operator feedback. This is achieved by means of an Analogue Computer which calculates the coordinates of the intersection of an event vector with any chosen plane parallel to the detectors (selected on a potentiometer). The Flat Field module imposes a uniform response function on the data for the analogue computer and a Display Interface module produces appropriate signals to store the image of each event on a Tektronix 611 storage oscilloscope. Other essential diagnostics are a Multi-Channel pulseheight Analyser (MCA) which is used to provide a 1 dimensional image of a test object (a point source say) from either of the system coordinates or to investigate the pulse height spectrum from the anode circuits. The count rates in the system were monitored by a Ratemeter for the LAM's to show the data taking rate and a quad scaler unit (not shown in figure 2) in which the singles rate in each detector and the 'raw' fast coincidence rate are monitored.

Figure 3 shows the whole system installed in its transport container. The MWPC detectors are to be seen in the background straddling the patient's bed. The electronics rack and the computer are seen on the right hand side of the picture. Out of sight are the computer terminal, the line printer and the gas supply rig. The only demand on services at a hospital is a single phase 250V mains supply of less than 30A.

3. The 511 keV Gamma Ray MWPC Detectors

The lead foil image converter screen is an old imaging technique in the technology of high energy X-ray imaging. It occurred to us some years ago that MWPC technology had matured to the point at which the problem of making an electronic imaging detector for high energy X-rays and gamma rays could be solved by the 'head on' approach of using a large stack of foil converters with MWPC anode planes interleaved to detect the 'knock-on' electrons. Positional readout could be achieved by laminating the metal converter foil onto plastic and dividing alternate foils into strips in mutually orthogonal directions. The electron avalanche induction signals induced on these could be read-out electronically on a common delay line readout system for each dimension and identification of the anode plane which triggered would give the depth of the gamma ray interaction in the detector and so permit removal of the parallax effect of such a thick detector. The early development work on this concept is described in several reports^(7, 5). Preliminary calculations and measurements indicated that the present design of 21 planes of 250 μm thick lead cathode foil interleaved with 20 anode planes would give a QE of ~ 0.13 for 511 keV gammas with a time resolution between detectors of ~ 25 ns fwhm and a spatial resolution of 6 mm fwhm. The present detectors have met our expectations in the latter parameters but the QE is found to be ~ 0.07 in practice (the early calculations were in error due to the use of an inaccurate formula for the range energy relation of electrons in lead).

The structure and detailed operation of a detector unit may be described briefly as follows. The whole detector consists of an interleaved sandwich of thin glass reinforced plastic (GRP) frames carrying anode wires and a further set of frames carrying stretched plastic/lead laminate material which form the cathodes. These consist of 125 μm thick lead foils laminated onto 75 μm thick kapton and etched so as to produce 3 mm wide strips which form the sensitive elements of the inductive x-y readout. (The isolating gap is 0.8 mm.) Between cathode planes is held a plane of 20 μm diameter gold plated tungsten wires on 2 mm spacing which perform the amplifying function. The full detector consists of 20 such sections with the cathode to anode spacing set at 2.5 mm and an active area of 30 cm x 30 cm is available.

The cathode laminates were first etched then stretched and glued onto rectangular GRP frames 1.5 mm thick with an inner window of 30 cm x 30 cm and

an outer dimension of 46 cm x 42 cm. The anode wires were wound and glued down onto similar frames which were held rigid while being wound. Spacers were glued onto the frames and when the stack of 20 sections (20 wire planes and 21 cathode planes) was pulled together with studs, the dimensional and wire tension tolerances stayed within acceptable bounds as evinced by the test which showed only a $\pm 12\%$ standard deviation in the gas gain for the 20 sections of a detector.

Care was taken with the dimensional tolerances between the planes (0.05 mm) and the wire tensions ($52 \text{ g} \pm 5\%$), and the final assembly was performed in a class 100 clean room.

The detector is housed in a large steel container with a flowing gas atmosphere (300 cc/min) of isobutane to which 0.1% of a freon (1,1,2 trichloro 1,2,2 trifluoro-ethane, trade name Fluorisol) is added to give stable operation. (The problem of adding such a small quantity of vapour to a gas held in the liquid form was solved by using an automotive injection system⁽⁸⁾.) The detectors deliver adequate signals to give the full spatial resolution and efficiency at an EHT of 3500V and have continued to do so without attention of any sort for 2 years. No ageing effects have so far been observed and a fully interlocked EHT and gas safety system has permitted the operation of the system by relatively inexperienced personnel over this period with no untoward effects.

The delay line readout system (chosen for reasons of convenience and economy) forms an intimate relationship with the MWPC structure and is housed within the gas enclosure (see figure 2). The strips on alternate cathodes point in the same direction and are bussed at the frame edge vertically down onto a readout board on which the delay line wand lies (see figure 2). The very large interstrip capacity ($\sim 200 \text{ pf}$) demands that an impedance transformer stage (in fact a common base transistor) be inserted in every vertical bus connection between the cathodes and the delay line. Combined with the necessary protection for the transistors against EHT breakdown this makes the readout board a fairly complex structure⁽⁵⁾. Nevertheless, all four have operated without failure to date. The delay line is a helically wound GRP wand with no compensation. When loaded by the readout assembly the

incremental delay is ~ 2.5 ns/mm on a characteristic impedance of 850Ω . Low noise wide band preamplifiers (Plessey) at each end of each delay line give a gain of $\times 4$ and an impedance transformation to a 50Ω cable to drive the signals to the external amplifier - constant fraction discriminator units.

The anode planes are connected together in pairs giving ten anode channels each with independent access to the external EHT distribution network. The anode preamplifiers are mounted externally to the gas enclosure (but in intimate contact) with the anode signals delivered to them through miniature coaxial cable. Again, due to the large capacity of each anode section (~ 500 pf) a low input impedance amplifier is used and matched to the signal cables (50Ω). An analogue summing channel provides the common signal from each detector which is used to generate the fundamental criterion of a positron annihilation event. These arrangements are indicated schematically in figure 2. The sensitivity of these preamplifiers (both cathode and anode) are such that the useful threshold in terms of the detected charge pulses is $\sim 10^6$ electrons/event and the useful dynamic range of pulse height $\sim 10:1$. This permits the electronics to meet the specifications given in section 2 as regards overall quantum efficiency, time resolution and spatial resolution. With such very low amplitude - high bandwidth signals very considerable attention must be paid to the earthing scheme otherwise radio frequency interference can seriously limit the system performance.

4. The NIM Readout Electronics

The task of producing useful data from the string of analogue pulses provided by the detectors is accomplished in a series of NIM modules designed and built at RAL specially for delay line readout systems by R Stephenson. (The current state of development of this instrumentation is reviewed in reference 9.) These modules are represented by the section of figure 2 immediately to the right of the MWPC's. The essential functions required of this circuitry may be defined as follows.

- (i) Derivation of accurate anode sum timing signals and performance of a fast coincidence between the two detectors.
- (ii) Derivation of accurate (amplitude independent) timing signals from the delay line pulses for subsequent use in Time to Amplitude Converters (TAC's) or Time to Digital Converters (TDC's).
- (iii) Control of the system deadtime and rejection of pile-ups which can corrupt the data at high rates.
- (iv) Encoding of the anode triggers to give a Z coordinate for the subsequent parallax correction (each detector is 10.4 cm deep).
- (v) Checking that all the parameters necessary to define a good event are present and rejection of incomplete events.
- (vi) Coordination of the timing of the detector electronics with the digital computer's data taking cycle.

Various control loops perform 'good housekeeping' functions between the various modules. Most of these have been omitted from figure 2 to enhance the clarity of the schematic.

The key timing function is performed by the Dual Constant Fraction Discriminator (PAG type 373). This single width NIM unit is described in reference 10. An amplifier of variable gain and variable (selectable) bandwidth precedes a constant fraction discriminator with variable fraction and delay to permit optimisation with any given delay line. Typically time slewing is ~ 1 ns for 40 db signal range with a 40 ns rise time pulse. The timing jitter is typically 1.8 ns fwhm with an input of 1 mV into 50 Ω . In double-ended

readout with the present delay lines the active width of the MWPC represents $2 \times 300 \times 2.5$ ns ie 1500 ns. The discriminators therefore do not limit the spatial resolution of the detectors, contributing at most a small fraction of a mm to the observed resolution of ~ 7 mm fwhm.

The basic fast coincidence is performed in the Coincidence Detector (PAG type 377A). This dual width NIM unit allows the coincidence overlap period (2T) to be set up and makes provision for a large delay to be inserted to measure the 'random rate'. Pile-up is also detected by a monostable-memory system and multiple pulses within the delay line readout period are rejected. Finally a deadtime corrected clock frequency is generated and made available for counting by the digital computer system.

It was found very early in our experience with this type of sandwich detector that large pulses are mostly due to knock-on electrons from the cathode scattered at large angles to the incident direction within a chamber section. Selection of the smaller pulses present (down to $\sim 50\%$ of all signals) fairly dramatically improves the spatial resolution of the system. This function was carried out on the anode signals by LeCroy type 620 multiple discriminator.

The two Z Encoders (single width NIM units) provide digital numbers (4 bits each) for the digital computer (via a CAMAC dual parallel register) to indicate which anodes have triggered and two analogue voltages for the Z inputs to the analogue computer. Checks are also made that no anode signals are missing and that multiple anode 'hits' are not present. Such events are rejected.

All the various housekeeping criteria are taken on board by the Readout Timer (a dual width NIM unit) which ensures that only valid and complete events are sent to the digital computer. This unit also controls the 'handshake' to the digital computer via a CAMAC interface module.

The final data taking task is the conversion of the relative delays between the 4 pairs of delay line outputs into a suitable form. First, one of each pair of signals is passed through the Surface Acoustic Wave Delay Unit which gives an accurate delay of 750 ns in each channel to offset the delay line length. Digital conversion is achieved by gating 4 independent clocks of approx 200 MHz into fast CAMAC scalers (type RL 433). Careful adjustment

of the clock frequency and the offset delays made the detector width exactly equal to 256 counts so minimising subsequent digital processing. The analogue X and Y signals necessary for the analogue computer are obtained from two Dual Time to Amplitude Converters of an in house design used at RAL for many years.

5. Data Capture

The storage on a secure medium (magnetic tape for example) of data for subsequent processing is the main function of the data capture part of the system. However, it was clear at an early stage that a simple 'on-line' form of display was essential for commissioning and monitoring the positron camera performance (and later it was found to be equally essential for patient positioning and monitoring). Accordingly an analogue computer was designed and built which takes the two triads of detector data (x_1, y_1, z_1 and x_2, y_2, z_2) and calculates the coordinates x and y at which this vector crosses the user selected plane z . This plane position (ie a plane parallel to the plane of the detectors) can be selected as a fraction of the detector separation on a potentiometer on the front panel. A second potentiometer permits the setting of the fraction T/D where T is the active detector depth (10.4 cm) and D is current detector separation. As figure 2 shows, the complete analogue display system consists of a suite of 4 (single width) NIM modules; first the two dual TAC's (discussed above) to produce the two pairs of x and y coordinates, second the Flat Field Module, third the Analogue Computer and fourth the Display Driver. The Flat Field Module applies the so-called 'limited angle' criterion to every event by inspecting the difference in each pair of coordinates, and gating the 'bright-up' pulse to the TX 611 storage oscilloscope. Rejection of vectors outside the chosen limit of angle produces an approximately flat response over the central region of the field of view of the detectors. The desired value is user-selectable on a potentiometer on the front panel. (A value of ~ 0.5 is routinely used, this giving a uniform response over the central 15 cm x 15 cm of the field of view in the central z plane.) The rate capability of the analogue display system is set at about 4 kHz by the TX 611 storage display oscilloscope, so that the TAC pulses are set to be $\sim 100 \mu\text{s}$ long and there are no settling problems with the analogue computer which comfortably achieves a precision of 1% of full scale. The Display Interface matches the +10V dynamic range of the analogue computer to the +1V dynamic range of the TX 611 with provision for variable gain and offset in the display. Most importantly, this unit also limits the slew rate of the driving pulses sent to the TX 611 to 100 μs for full scale, to prevent ringing of the magnetic deflection system. Figure 4a shows the TX 611 image produced by 2 line sources and figure 4b shows the histogram of the x coordinates of the reconstructed events as measured on the MCA (figure 2).

Digital data capture is managed using the CAMAC system. The LSI 11-23 speaks to the CAMAC bus via a dual width Q bus interface card (type 1104) and a Crate Controller (type 1100) supplied by Hytec Electronic Systems Ltd. The CAMAC interface operates by reserving 2K words of memory in the I/O page of the computer main memory through which data and commands can be transferred to any particular sub address of any CAMAC slot using MACRO-11 code. When a valid event is deemed to be present, the event data are stored as follows - a composite word containing z_1 and z_2 in the CAMAC parallel register and 4 scaler contents representing x_1 , y_1 , x_2 , y_2 . The data taking MACRO loads these as 5 individual words into a 2560 word long buffer (512 events), this process taking $\sim 120 \mu s$. When this buffer is full it is unloaded onto a permanent storage medium (either disk or tape) using a system DMA write. Figure 5 shows the flow chart for the data taking program (CAMDRV) which has the set up procedures written in FORTRAN with the data taking performed by a program (INDATA) written in MACRO 11. The handshake between the Readout Timer and the computer program is straightforward. A 'good event' criterion freezes the front end electronics and sends a level to a single slot CAMAC interface module which makes it generate a Look At Me. This is a convenient form of interrupt in the CAMAC canon which when received by INDATA initiates transfer of the 5 words to the buffer in the computer memory. On completion of this transfer an appropriate CAMAC command is sent to the interface which sends a clear level to the Readout Timer and opens the system up for data taking.

The state of data taking may be investigated by the operator at any time by hitting the terminal keyboard and any appropriate action taken (eg terminate data taking, continue or abort). As a further facility a real time clock installed in the CAMAC crate is read at the end of each data buffer and stored in the last word. This real time signal is valuable for correcting off-line short isotope half lives.

All subsequent processing of the acquired data is performed off-line as described below.

6. System Performance - Basic Parameters

As noted in section 2, the basic performance of the positron camera can be characterised by a few parameters viz, the Quantum Efficiency, the time resolution, the spatial resolution and the solid angle of the detectors. The solid angle depends only on the detector separation and at the minimum useful separation of ~ 40 cm (suitable, for example, for studying limbs) this is $\sim 0.25 \times 2\pi$ decreasing to half this value at a separation of just over 60 cm. The time resolution between the detectors is easily measured with a TAC to be 25 ns fwhm and a value of $2T$ (the coincidence resolving time) of some 54 ns was chosen so as to include $> 98\%$ of all events. The signal to noise parameter $E^2/2T$ is a factor of 2 lower than its maximum at this value of $2T$ but optimising this parameter would have led to a loss of $\sim 20\%$ of sensitivity. Clearly this parameter is one which it would be useful to be able to adjust to suit the experimental situation. The spatial resolution is also a variable parameter, as already noted, being controlled by the part of the pulse height spectrum selected for use. In practice a cut to include the lower 75% of each detector spectrum gives a spatial resolution of ~ 7 mm fwhm at a sacrifice of 50% of the total efficiency. A cut of 50% in each detector will give 5 mm fwhm but the loss in sensitivity ($\times 0.25$) is unacceptable in general. The final detector parameter, the Quantum Efficiency, is difficult to measure due to the scattering tendency of 511 keV gamma rays. However, our estimate of the QE from the number of events that contribute to the image of a point source is about 7%.

Figures 6 and 7 show the results of the calibration of the system performance using part sources placed at mid field in air with a detector separation of 43 cm. The curves show a satisfactory level of performance for the system: a gross sensitivity of 1081 Hz/MBq of positron emitter and a net sensitivity (ie the rate actually captured by the computer) of about half this value. This is an absolute efficiency of 0.05%. As the source activity increases above 1 MBq the accidental coincidences become noticeable and the LAM rate begins to show some deadtime losses (figure 6). Subtracting the accidental rate from the observed fast coincidence rate we see an excellent linear agreement between the observed rate and the source activity (figure 7). It is noted, however, that the true to random coincidence rate is much lower than predicted. The theoretical value $R = (E^2/T)/S$ is ~ 91 for a signal rate

of $S = 1000$ Hz (~ 1 MBq of activity). For the point source in mid field in air we measure (figure 7) a value of $R = 26$. The reason for this decrease is the substantial increase in scattering of gammas from the chamber structures and supports leading to an increase in the singles rates which (when squared) leads to a substantial increase in the accidental coincidence rate.

In the practical situation of imaging in extended human tissue the ratio R degrades very markedly. This arises from two principal effects (i) scattering in the tissue and (ii) the fact that the sensitivity of the camera to true coincidences drops rapidly to zero for activity located towards the edge of the detector field but the sensitivity for singles decreases hardly at all (by about 30%). These effects have been examined in a model calculation and some attempt made to quantify them⁽¹¹⁾. Table 1 shows the values of R realised in a variety of experimental situations. The R value of the image of the ^{18}F foot is better than that of the foot imaged with H_2O^{15} in the blood stream (inhaled as CO_2^{15}) because the activity is localised in a few lesions near the centre of the picture whereas the H_2O^{15} signal is widely disseminated over the field. The situation of a large object (the head) approximately uniformly filled with signal (in the form of CO^{11} labelling the blood pool) leads to a very poor signal to accidentals ratio of only 1:1. The consequence of this high random rate is (as will be shown below) to degrade the images but, due to the nearly uniform nature of the background it does not nullify the primary image as long as R remains $\gtrsim 1$. In this the positron camera is quite different from the PECAT which could not reconstruct an image from such data.

The performance of the system as seen from the analogue computer display system in a practical situation is shown in figure 8 where we see the images of the hands of two subjects at ~ 90 minutes after an intravenous injection of 200 MBq of ^{18}F . The upper image is of a case in which bone disease was not suspected and the lower of a case with a known history of an arthritic condition. The strong uptake of the ^{18}F in the arthritic lesions is clearly seen with reasonable definition of the fingers. The images shown in figure 8 represent ~ 10 minutes data collection at a rate of 200 Hz.

Digital data acquisition onto a magnetic storage medium is rate limited to ~ 1500 Hz onto magnetic tape ($\sim 10^6$ events per 2400 foot reel of tape) and 3000 Hz onto an RL01 ($\sim 10^5$ events). Table 1 shows some typical conditions

for clinical data runs. It is clear that in the clinical situation actual data capture rates (LAM's) rarely exceeded 1000 Hz, because at rates much above this the signal to noise ratio rapidly becomes so poor that the data is of little value. Also this range of LAM rates corresponds well to the radiation protection limits set for the patient in each type of study. Thus data taking to magnetic tape was generally employed with little loss of data.

Quantification of the positron activity in any area in the central field of view was achieved by measuring the system response to a calibrated point source. Thus in our thyroid studies with I^{124} (12) we were able to get reproducible values for the activity in the thyroid with the attenuation and the scattering calibrated out, by placing a calibrated point source on the thyroid location of the patient with no I^{124} present and using the measured sensitivity as our calibration.

7. System Performance - Fundamental Imaging Considerations

The process by which the Positron Camera realises an image of a source distribution of positron emitter is a complex one. If we look at the spatial resolution or more correctly the Point Source Response Function (PSRF) of the system, we can see that it depends on four readily identifiable factors viz (i) the physics of the interaction of the 511 keV gamma rays with the MWPC detectors, (ii) the ability of the readout electronics to amplify the small charge signals to a useful level without degrading the quality of the information, (iii) extrinsic factors such as the compton background induced by scattering material placed around the source distribution and by accidental pile-ups in the fast coincidence circuits, and (iv) the geometric distortions introduced by the fundamentally projective nature of the information obtained by the Positron Camera.

(i) The PSRF and the sensitivity of the Positron Camera are very much affected by the fact that the total cross section for the interaction of 511 keV gamma rays is almost 50/50 divided between the photoelectric absorption process (which gives high efficiency and high spatial resolution) and the compton scattering process (which gives low efficiency and low spatial resolution). The PSRF described for the positron camera is taken to be the observed distribution in a planar reconstruction in the central plane of the detector when a point positron emitting source is placed in the centre of the system. This is not the 'spatial resolution' of a single detector but is a geometrical convolution of that function as determined by the planar reconstruction process. The two functions are clearly closely related. The curves presented in figure 9 show radial areal density functions ($dN/dS(R)$) generated by the system relative to the ideal position of the point source. A simple physical model of the interaction of the gamma rays with the detector gives the PSRF (of one detector not of the positron camera) shown in figure 9 curve a. We see a high resolution part of fwhm 3 mm due to the photoelectrons escaping from a primary photoelectric absorption event. (The 3 mm fwhm correlates roughly with the half gap of the MWPC gas space.) A smaller contribution gives a wider base to the PSRF with a fwhm of ~ 7 mm due to the spread and detection of K shell fluorescent X-rays ($\sim 10\%$) from the primary photoelectric event. Finally there is a distribution of 15% of all events broadcast over the whole MWPC volume. This is the class of events in which the primary compton vertex is not seen (due to the failure of a low energy compton electron to escape from the lead cathode) but the compton scattered photon is subsequently detected elsewhere in the detector.

(ii) The extra circuitry necessary to extract the small charge signals from the chamber structure (ie the active readout assemblies) inevitably contribute extra electronic noise to the positional readout. Tests with a pulse generator show that with pulses of 10^6 electrons (measured in the anode circuit) the positional readout systems give a fwhm of 5 mm. The influence of pulse height selection on the observed fwhm of the detectors for the PSRF (viz, the smaller pulses give a narrower fwhm) is such as to imply that the physics limited fwhm and the electronics limited fwhm are approximately equal at ~ 5 mm.

(iii) The main factors affecting the PSRF which are extrinsic to the detectors are the compton scattering of the 511 keV gamma rays in the tissue of the patient and the associated pile-up generated in the fast coincidence circuit. The two effects are very closely linked in theory, but in practice show up in different 'channels'. The compton scattering noise consists of that class of events in which both annihilation gamma rays hit the detectors but one (or both) has been deflected from its original direction so leading to a wrong reconstruction in the computer. The simple model of reference 11 showed that for (say) a human head and detectors of our geometry ($d\Omega/2\pi \sim 0.2$) one can expect as much as 30% compton noise which is inevitably present in our data. In order to show the effect of this noise on the PSRF we ran a monte carlo simulation in which a point source was placed at the centre of a sphere of water (of adjustable diameter) and the scattered rays traced using the Klein-Nishina cross section. Curve (b) in figure 9 shows the calculated PSRF of the compton scattered events from a 20 cm dia sphere of water. (No limited angle selection was in force in this calculation but the effect on the distribution shape has been shown to be minimal in experimental tests.) The normalisation of this curve is of course entirely arbitrary. The conclusion to be drawn from the calculation is that the compton background is extremely broadcast in the reconstruction ie occupies very low spatial frequencies (of the order of the fundamental frequency of the field of view). Thus while the contrast in the image of activity in a scattering medium will be reduced, the basic imaging ability still remains in the shape of the unscattered events. Figure 10 shows some experimental demonstrations of this. The measured PSRF (in projection) of a point source is observed on the PHA (figure 2) in air (a), in the centre of a cylinder of water of 10 cm diameter (b) and in the centre of a 20 cm cube bath of water (c). As column 2 in

table 2 the fraction of signal in the central peak (the unscattered events) drops from 75% in air, to 42% in the 'limb' phantom and finally 22% in the 'belly' phantom. The nett effect of this degradation is to dramatically increase the counting statistics required to image through a large thickness of tissue, due to the contrast reduction caused in the image by this quasi uniform background.

As table 1 reminds us, we can expect to take data with not only up to $\sim 30\%$ compton noise but also up to $\sim 50\%$ pile-up (or random coincidence) noise. This noise arises from any process which turns a double event (true coincidence) into a single one (detector inefficiency and compton scattering), or generates uncorrelated single events (activity at the edge of the field). Fortunately, a simple monte carlo simulation of the effect of this noise on the projected PSRF for our standard point source shows a result similar to that for the compton scattering contribution. As curve (c) in figure 9 shows, the background generated by this effect is almost uniform and the main effect is to reduce the contrast in the picture. A feature of imaging with data governed by poissonian statistics is that the counting statistics required rise sharply as the contrast of the underlying image decreases. Thus the positron camera shows a very dramatic loss of picture quality as the signal to pile-up rate ratio approaches unity. In general we have not taken data with more than 30-40% of random coincidences in it.

(iv) The information available for each event in the positron camera system is limited to the direction of a vector somewhere along which the source nucleus lies. This means that the reconstructed data is a projected convolution of the actual source distribution. Much attention has been given to the problem of estimating the original distribution from the observed convolution of the data. See for example references 13, 14, 15, 16. With a static positron camera the missing range of projections is so great that any estimate of a genuinely 3 dimensional distribution (ie not entirely confined to a plane parallel to the detectors) is of limited value and prone to artefacts. (Recent work elsewhere⁽⁶⁾ has shown that when the range of projections is increased by multiple views the improvement in the unfolding process is dramatic.) This being the case and also in view of the problems (noted above) associated with scattering we elected to make our first studies on peripheral limbs (hands, feet and legs) where the source distributions

tend not to be complex and to occupy at most 10% of the detector separation. Depth effects can be clearly demonstrated with our data⁽¹⁷⁾ but it is a matter of 'focusing' on a certain plane rather than measuring the activity precisely at all points in a 3 dimensional volume. For our image processing then we chose a limited form in which we back project the data into 5 planes (the z position of each is user selectable) having first imposed a limited acceptance angle to produce a uniform geometric PSRF over the central part of the field of view. The processing now consists of a 2-D deconvolution of an experimental PSRF (preferably taken with the target limb in situ and with very good counting statistics) and the application of a high frequency roll-off filter in fourier space to damp down the high frequency noise from the pixel statistics. This simple approach appears to give almost as much useful information as a static positron camera can give since the lack of any discrimination of low spatial frequencies and the lack of any absolute normalisation makes more heroic attempts at the geometric problem unproductive. In fact we have implemented the geometric deconvolution system of reference 13 (which we chose because the computing time required looked acceptable on our microcomputer) but the response of the algorithm to low contrast, low statistics data is so artefactual that while the 'focusing' effect is definitely enhanced relative to our simple approach, the artefacts make the images unacceptable.

A final concern in the imaging performance of the system is the effect of attenuation (or to be more accurate) scattering in the patient on the observed images. As figure 10 and table 2 show we have both loss of counts (attenuation) and redistribution of counts from the peak of the PSRF to the tails (scattering) as the tissue thickness increases. The effects are clearly very significant and raise difficulties for any full geometrical deconvolution system and for the prospects of quantification. Figure 11 shows the results of a test in which a point source was moved across an axial diameter of a limb phantom (a long cylinder of water 10 cm in diameter mounted in mid field with the long axis parallel to the detector planes). The upper data points (x) show the total observed attenuation from this source in the total rate as it was scanned across the radius of the cylinder and the lower points (o) show the attenuation of the signal in the central peak only (figure 10). The solid line in figure 11 is the calculated attenuation (using the known total cross section for water) using the sagittal distance across the axial plane as the attenuating thickness and folding in the detector spatial resolution (only important at

the surface of the cylinder). This simple model appears to work extremely well and points out a route (essentially similar to that used in the PECAT) for the insertion of an attenuation correction. However it will be noted that it must only be applied to the higher spatial frequencies in the picture since, if we consider the 'tails' of the PSRF, we have a space varying PSRF to contend with. An interesting feature of figure 11 is the comparative flatness of the attenuation over the central 60-70% of the cylinder and the sharp change near the edge. This means that within the central region of a bolus of tissue there are no strong differential effects due to attenuation. However if there is activity in a surface feature (the plane of the surface being normal to the detector planes) then an abnormally high sensitivity is recorded due to lack of attenuation. This is sometimes referred to as 'skylining'. It also causes problems for the geometric deconvolution algorithms because the attenuation ought ideally to be included in the geometry. Two possible solutions are an experimental measure of attenuation performed on the patient at the time of a data run or the generation of a false (more tractable) scattering medium boundary by surrounding the patient with extra scattering medium.

8. Digital Image Processing and Display

The microcomputer hardware available to the positron camera is indicated in figure 2 in schematic form. The LSI 11-23 microcomputer has the full 256kbyte main memory, with a fast floating point arithmetic board, disk drive controllers and a quad serial interface to which the line printer, the console terminal and the video graphics system are connected. There is also a Q bus controller card for the magnetic tape drive (an EMI 8800 type running at 1600 bpi and 45 inches per second) and a Q bus to Unibus converter to allow the Analogic AP-400 array processor to communicate with the computer. The AP-400 is a fast 24 bit block floating point machine (approximately 4 floating point operations per μ s) fitted (in our case) with 8k of internal fast memory. This is insufficient to permit an 'in place' Fast Fourier Transform (FFT) to be performed on our 128 x 128 picture files. A line by line method takes about 5 seconds instead of ~ 0.25 seconds. However this is a dramatic improvement over the 2 minutes required by a FORTRAN FFT subroutine running in the 11-23 with the fast arithmetic board. The video graphics system is a very early model from Sigma Electronics with a resolution of 256 x 256 pixels and 4 bits (colours or grey scales) to a pixel.

The approach to the image processing problem was conditioned by two main factors (i) the performance limitations of the dedicated hardware (ie the microcomputer had to be capable of producing acceptable images in a time scale (~ 30 minutes) acceptable to the clinical user), and (ii) the inherent limitations in the usefulness of the data from a static camera (discussed in the previous section) meant that heroic number crunching would not bring any notable improvement in the images. We limited our efforts therefore to the simple scheme outlined above of reconstructing (or back projecting) into a small number of planes (usually 5) parallel to the detectors, deconvoluting a measured PSRF applying a roll-off filter in frequency space and displaying. If desired, the geometric deconvolution of Townsend⁽¹³⁾ could be inserted before the inverse FFT. Finally the processed images are displayed plane by plane on the video system. While a greater dynamic range of grey scales than the 16 of our system gives a softer image, the relatively poor pixel counting statistics in our data limits the effective dynamic range of the data to that which our video system can display effectively.

The work load indicated above is carried out by three separate program suites: (i) the reconstruction or back projection of the raw data into planes

is carried out by IMNEWA, (ii) the forward FFT's are carried out by APFFT, the deconvolution and filtering by TOMO and the inverse FFT by APINVT, and finally (iii) the five processed plane images are displayed by the program DISDIS. The programs are all written in FORTRAN and run under RT-11 with the Single Job monitor.

(i) In general the data from a positron camera exposure resides on a 2400 foot reel of magnetic tape in the form of 511 event records. The triads of coordinates for each event must be unscrambled, corrected for offsets in the TDC's and put into the range of 0 to 9 for z and 1 to 128 for the x and y coordinates. As figure 12 (the flow chart for IMNEWA) shows the operator having entered the current detector separation may select any 5 planes (normally uniformly spaced) into which the data will be back projected. The operator may also specify the limited angle criterion in the form of the maximum $(x_1 - x_2)$ or $(y_1 - y_2)$ difference accepted. (This is normally set to 64 giving the central 25% by area of the detector aperture a uniform geometric response.) The formula connecting the coordinates at which the event vector joining the detectors crosses the plane at position z is

$$\begin{array}{rcl} x & = & x_1 + \frac{(z + z_1)}{(D + z_2 + z_1)} (x_2 - x_1) \\ y & & y_1 + \frac{(z + z_1)}{(D + z_2 + z_1)} (y_2 - y_1) \end{array}$$

In order to save computing time the z correction factor is stored as a look up table of dimension 10 x 10 x 5 (ie 10 z coordinates in each detector and 5 z planes). Since our data is integer in nature the five planes are stored as 5 virtual integer arrays of dimension 128 x 128. The 128k word memory of the 11-23 comfortably accommodates this data file as well as the program and the system. On completion of the histogramming of the events from a selected number of event records into the five planes, the image arrays are saved to an 8 inch floppy disk as 5 files with an appropriate identifier. As a further refinement the real time clock running during the exposure can be read from the last 'event space' of each 512 event record on the tape and rates and source decay corrections calculated. The reconstruction process proceeds at the rate of 10,000 events/minute so an exposure total of 150,000 events requires 15 minutes for reconstruction. The limited angle criterion rejects ~ 60% of events so that our final data files contain (typically) 60,000 events and depending on the nature of the image the peak pixel contents vary from ~ 50 to ~ 300.

(ii) Calculation of the 2-D FFT's of our projection plane images is carried out in the AP-400 at the rate of 300 points per millisecond. However the need to do the job row by row involves access time and time for the LSI-11 to transpose the intermediate FFT. When disk access time is included the total time taken for a plane is approximately 1 minute. For implementation of the Townsend type processing, all five complex FFT planes must be held in memory simultaneously. This is clearly not possible as the storage required is ~ 655 kbytes. In practice the FFT program (known as APFFT) stores the 5 FFT planes in a number (user-selectable, but normally 16) of slices of frequency space, so that the corresponding region of frequency space of each FFT may be held simultaneously in the main memory.

The main part of the processing is done by the program TOMO. The first step is to read in a suitable PSRF FFT from a floppy disk and give the program the system geometry parameters (figure 13). Each amplitude in the large FFT file is then divided, plane by plane, by that of the corresponding amplitude of the PSRF FFT. This is, of course, performed on only 1/16 of the total data set. The noise induced in the data by poor pixel statistics is one of the dominating facts of life in the processing of positron camera. Consequently it is found desirable to put a high frequency roll-off filter on the FFT data to reduce high frequency visual noise (outside the 'physical' bandwidth of the detector system) and avoid instability at high frequencies when dividing by the PSRF. The shape of this filter is not critical and we have generally used one of the form $1/(1 + e^{k-k_c})$ where k_c is the 'cut-off frequency' at which the filter has the value 0.5.

The first stage of processing is now complete and one can now either store the FFT data back onto the disk ready for the inverse FFT operation or use it as the input to the full Townsend process⁽¹³⁾. The latter does not in fact require very much computing time. The calculation of the projection matrix $H_{ij}(k_x, k_y)$ and its pseudo inverse is simplified by the high degree of symmetry in the situation (the matrix is real symmetric and there is symmetry between k_x and k_y). In this case the amplitudes stored in the output slice file are linear combinations representing the inverse projection transformation.

Finally the large processed FFT file is treated to the inverse FFT process by a program called APINVT which having reconstituted the 5 planes separately, produces the final output 128 x 128 integer image. The final image is displaced in both dimensions by half a field pitch due to the translation

intrinsic in the PSRF function. This displacement is corrected before the image is written to a floppy disk file. At the end of this process which from beginning to end requires ~ 25 minutes ($\sim 50\%$ disk access time) we have 5 final processed 128×128 integer image ready for display.

(iii) Display of the processed image is controlled by a program called DISDIS which accepts a standard 128×128 integer array file from disk, finds the maximum and minimum pixel values, scales them for the video range of 0 - 15 and sends the result to the video memory. The user is able to specify the display range and select two types of display - linear or logarithmic. The former makes no alteration to the amplitudes sent to the video digital to analogue converters and, because of the power law response of the cathode ray tube gives a high contrast image with only the upper pixel values visible. Taking natural logarithms of the pixel values first leads to a flatter response with all grey scales visible. Four planes can be displayed simultaneously on the 256×256 display of video system.

Figure 14 shows the video displays of 3 differently processed planes of a thyroid imaged with I^{124} (12). These images represent the simplest form of processing noted above, ie deconvolution of a 2-D PSRF with a high frequency roll-off filter. The trade-off between increased detail (ie higher spatial resolution) and the appearance of statistical artefacts as the 50% filter frequency point is increased from 10 (harmonics of the field) in figure 14a through 12 (figure 14b) to 15 (figure 14c) corresponding to spatial resolution of ~ 15 mm fwhm, 10 mm fwhm and 7 mm fwhm.

The software system described above does not represent an optimal and polished solution to the processing of the positron camera data. However, we believe that it has, as shown in the next section, met the requirement of demonstrating the essential capabilities of the positron camera as a practical 'in vivo' imaging system up to the present state of development of the hardware. Clearly the next stage of using a rotating system requires a very substantial further input of programming effort.

9. Some Practical Imaging Results

In the course of three periods of clinical trials (extending over a period of 14 months) at the MRC Cyclotron Unit, Hammersmith Hospital, the General Infirmary Birmingham (Birmingham University) and the Royal Marsden Hospital at Sutton, a large variety of studies were undertaken in both human and animal subjects of which only a brief sample can be described in this report.

Figure 5 shows images of the type of most interest to our collaborators at Hammersmith Hospital who are particularly interested in measuring physiological function parameters using the PECAT technique. Figure 15a shows the image obtained in a lateral view by the positron camera of the foot of a healthy, active volunteer who is inhaling $C^{15}O_2$. The short half life of ^{15}O (2 mins) means that the equilibrium distribution of activity is proportional to the local blood flow in the region under study. Thus in the foot of an active individual (Figure 15a) the active muscles are in evidence with the strong arterial blood flows down the anterior and posterior tibial systems. In an inactive (but healthy) subject (Figure 15b) the active muscles are not seen and the posterior tibial arterial system is the main feature. The conditions for all the blood flow measurements remained substantially similar with the field of view presenting an equilibrium activity of ~ 3 MBq yielding a data rate of ~ 600 Hz of which $\sim 25\%$ were random coincidences. The lower blood flow in the inactive foot (Figure 15b) crudely indicated the proportionality of the blood flow measurement by yielding a data rate of $1/7$ of that of the active foot.

Imaging of the blood circulation in peripheral limbs with $^{15}O_2$ and $C^{15}O_2$ was carried out on patients suffering from gangrene of the foot (reported in detail elsewhere⁽¹⁷⁾) and lymphoedema of the lower limbs. During the same period images were obtained of arthritic lesions and other bone damage using ^{18}F . Animal work showed the usefulness of ^{82}Rb (from a generator) as a label for heart and kidney tissue and various tests were made with ^{68}Ga as a label (for example lungs were imaged with microspheres). Finally some work with ^{11}CO in human volunteers gave good images of the major blood vessels in peripheral limbs. The images of Figure 15 received only the lowest level of digital processing described in Section 8.

During the visit of the positron camera to Birmingham University where our collaborators were members of the Department of Immunology, it was hoped to demonstrate the imaging of particular tissue with specific antibodies labelled

with ^{124}I (4 day half life). The chemistry proved to be a problem not soluble within the time scale of the visit. However, the high specificity of the iodine for the thyroid gland enabled us to produce very good thyroid scans with low activity levels in the thyroid. Patients were given 3.7 MBq of ^{124}I orally and good images were obtained even in cases where uptake was as low as 8% at 24 hours. Figure 15 shows some sections of a large multinodular goitre as imaged by the positron camera with a $^{99\text{m}}\text{Tc}$ pertechnetate scan for comparison. Typically $1 - 2 \times 10^5$ events were collected in 15 - 30 minutes. This work is described in detail in Reference 12. Although imaging with labelled antibodies was not achieved during these experiments, the work with the thyroid gland helped to demonstrate that the 3 dimensional imaging potential of the positron camera can give a critical advantage in an application in which the intrinsic contrast available is expected to be very low.

The lack of an on-site cyclotron at the Royal Marsden Hospital meant that the studies undertaken there were largely confined to the use of ^{18}F and its compounds. At this hospital the emphasis is on tumour localisation and Figure 17 shows two images in which this is demonstrated. Figure 17a shows ^{18}F labelling the spine and bony structures of the head with an abnormal hot spot confirmed as a 2 cm lesion in the posterior brain by conventional $^{99\text{m}}\text{Tc}$ -glucoheptonate scintigraphy. 25 MBq of ^{18}F was administered by injection and 2.5×10^5 events were accumulated in ~ 40 mins. Figure 17b shows the visualisation of a tumour using 40 MBq of ^{18}F -fluorodeoxyglucose in which 5×10^5 events were accumulated in ~ 15 mins⁽¹⁸⁾.

Further studies at RMH involved the use of ^{52}Fe -citrate in patients with myeloproliferative disorders and included studies with ^{68}Ga solution in a liver phantom in which good imaging of this organ with this positron camera was demonstrated for the first time. The RMH group have developed new analysis software based on the general 3-D deconvolution of the system response which improves considerably on the version described in Section 8 above⁽¹⁹⁾.

The potential of the positron camera for quantitative and time resolved work was demonstrated in a small animal experiment with a collaborator from the Department of Immunology at Birmingham University. Approximately 3.7 MBq of ^{18}F was injected into the tail vein of a rat and the animal was imaged continuously thereafter for 30 minutes. Each record of 512 events on the magnetic tape was labelled with the elapsed time so that time resolved images

could be constructed off-line. It was found that statistics were adequate to permit 2 minute time slices. Figure 18 shows a polaroid photograph of a fairly early image in the sequence in which the ^{18}F is still to be found in the general blood pool and in the kidneys. Later the activity is completely confined to the skeleton (with strong uptake in the skull) and the bladder. Figure 18 shows the fraction of the total activity in each image which was found in the kidneys and the bladder. The steady purge of the fluorine into the bladder is clearly seen. An interesting result of this experiment was the observed behaviour of the normalised activity (suitably corrected for the half life of ^{18}F). It is clear that the filtering process used to produce the final images (described in Section 8) has some non-linear effects. The normalisation of the images varied from 1.08×10^5 to 1.25×10^5 over the 9 exposures showing a maximum full range error of less than 15%. Errors of this magnitude are not unacceptable and should be amenable to reduction by calibration procedures.

10. Current and Future Developments

The mission envisaged for the RAL Mark I positron camera (described in this report) was the exploration of the potential of the wide aperture positron camera (and in particular the MWPC form of that device) for 'in vivo' studies in nuclear medicine using positron emitting radionuclides. The production of a complete mobile clinical test system has allowed us to assess the performance envelope of the positron camera in strictly practical situations. Results have been obtained on two levels, the first level is that of indicating that clinically useful measurements can indeed be made with the current device and the second level is that of providing detailed numerical studies which will permit the design of a second generation device capable of giving results much superior to the imaging performance of the Mark I device. Our current development activities may be summarised as follows.

(i) Scanning the Positron Camera.

It has recently been shown that rotating a positron camera about a single axis during the data taking dramatically improves the quality and the quantitativity of the reconstructed images giving more truly 3 dimensional information⁽⁵⁾.

Accordingly, new camera supports have been engineered and a suite of software provided by our collaborators at the Royal Marsden Hospital which will allow rotating head scans to be performed on patients in the near future. Reconstructions of test phantoms in rotating mode have already demonstrated excellent results.

(ii) The Mark II Positron Camera.

The success of the Mark I device has permitted the development of a highly engineered Mark II device aimed initially at industrial testing applications but eventually at a clinical device. Using essentially the same technology as the Mark I device this system has twice the active area (60 cm x 30 cm) giving a useful operational volume of $30 \times 15 \times 15 \text{ cm}^3$. This is still rather small for a general purpose clinical tool and it is hoped that the first full scale medical model will have an aperture of at least 80 cm x 40 cm.

(iii) Improved Performance.

For a successful clinical device it is essential to have greater sensitivity and a better signal to randoms limit. This can be achieved most effectively by improving the quantum efficiency of the positron camera modules. Work is now in hand (in collaboration with our colleagues at RMH) to develop structured cathodes which could yield a factor of 2 in efficiency with a resulting factor

of 4 in sensitivity and in the signal to randoms ratio. Other options such as faster drift gases and an increased number of cathodes are also possible and under consideration.

Our conception of a final clinical system is that it would consist of two pairs of detectors (80 cm x 40 cm aperture) with improved cathodes which would take data around the complete circle with only one movement and have a sensitivity of approximately 40 times the Mark I device. Back projection calculations will be carried out in real time into a dedicated memory and the deconvolutions performed by a small dedicated array processor. Final images will be available to the clinician within 20 minutes of the end of data taking.

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At the Royal Marsden Hospital (Sutton) our collaborators are R J Ott, S Webb, O Khan, V R McCready, M A Flower, M O Leach and P Marsden. /

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Figure Captions

- Figure 1 Schematic diagram of the mode of operation of the positron camera showing the detector structure of multiple lead foil - MWPC sections. The upper bubble indicates the nature of the gamma conversion and detection process.
- Figure 2 This diagram is a general schematic of the positron camera electronics and the computer system which controls the data taking and processes the final images. Not shown is the detailed electronic logic which selects valid events.
- Figure 3 This photograph of the interior of the positron camera container shows most of the essential elements of the system: the detectors and patient couch, the control electronics and the tv monitor, the LSI-11/23 computer and its peripherals.
- Figure 4 (a) This shows the analog computer - storage oscilloscope image generated by two positron emitting line sources (^{22}Na) each 50 mm long, spaced 50 mm apart, placed in the central plane of the positron camera field.
- (b) This presents a histogram of the coordinates of the dots on the oscilloscope image, permitting a measurement of the line width response function (6 mm fwhm).
- Figure 5 Flow chart of the program CAMDRV which controls data taking from the positron camera and stores it in records of 512 events for subsequent processing.
- Figure 6 Basic performance curves of the positron camera in response to a point source in mid field with a detector separation of 43 cm. The data presented are (a) singles rate in one detector (θ), (b) the data capture rate or LAM's (Look At Me) (x), (c) the accidental rate in the fast coincidence circuit (o), and (d) the total rate in the fast coincidence circuit. All are plotted against the activity of the point source.

- Figure 7 This figure shows the proportionality of the fast coincidence rate to the point source activity when the accidental rate is subtracted ($\bullet$). Also shown is the behaviour of the true to random coincidence ratio as the source activity increases (o). The linear curve implies a sensitivity of 1081 Hz/MBq and the true to random ratio curve shown will reach a value of unity at ~ 26 MBq.
- Figure 8 Analogue computer images of two hand studies in which ~ 200 MBq of ^{18}F have been administered 90 minutes before the scan. Data has been acquired for about 10 minutes at ~ 200 Hz. (a) shows a hand in which disease is not suspected and (b) a hand in a patient with a known history of arthritic disease.
- Figure 9 This figure shows the various Point Spread Resolution Functions (PSRF) important in the image forming processes of the positron camera. Curve (a) shows the PSRF intrinsic to the detectors (ie the response of the camera to an infinitely small point source placed in mid field): curve (b) shows the PSRF of events compton scattered in a 20 cm diameter spherical bolus of water placed in mid field: curve (c) shows the PSRF of the 'random' events generated by accidental coincidences between unrelated vectors. The original source of events for curves (b) and (c) is a small point source in mid field. The curves come from mathematical models (montecarlo) run on a digital computer.
- Figure 10 Some experimental measurements of the PSRF of the positron camera under different conditions using a pulse height analyser to histogram one coordinate of the output of the analogue computer (a) point source in air, (b) point source in the centre of a cylinder of water of diameter 10 cm, and (c) point source in the centre of a 20 cm edge cube of water.
- Figure 11 Shows the results of a test in which a point source was moved across an axial diameter of a limb phantom (a long cylinder of water 10 cm in diameter mounted in mid field with the long axis parallel to the detector planes). The upper data points (x) show the total

observed attenuation from this source in the total rate as it was scanned across the radius of the cylinder and the lower points (o) show the attenuation of the signal in the central peak only (Figure 10). The solid line in Figure 11 is the calculated attenuation (using the known total cross section for water) using the sagittal distance across the axial plane as the attenuating thickness and folding in the detector spatial resolution (only important at the surface of the cylinder).

Figure 12 This is a flow chart of the reconstruction program IMNEWA which takes the stored raw data from magnetic tape, applies all the system calibrations and geometrical corrections (eg for detector parallax and limited angles) and histograms them into a series of planes (generally 5 in number) parallel to the positron camera detectors.

Figure 13 This is a flow chart of the program TOMO which takes the fourier transforms (FT) of the plane image (produced by a further suite of software controlling the AP-400 array processor) and performs the essential image processing functions viz (i) deconvolution of the 2-D PSRF of the system, (ii) application of a high frequency 'roll-off' filter, and (iii) implementation of the Townsend algorithm for unfolding the overlapping planes. The user may select the precise parameters required at the appropriate stage of processing.

Figure 14 In this figure we see the effect of changing the cut-off frequency of the low frequency pass filter during the image processing. The 50% frequency of the filter (CT) is varied from 10, (a) through 12, (b) to 15 (c). The frequency is measured in harmonics of the 30 cm field so that these frequencies have values of 0.33, 0.4 and 0.5 in units of cm^{-1} . The data comes from a ^{124}I labelled normal thyroid which, as the spatial resolution is increased, is shown to have, in fact, quite strong nodes. The original data set comprised 20,000 events.

Figure 15 This shows the positron camera images obtained when a lateral view is taken of the foot of a human subject inhaling C^{15}O_2 . The

equilibrium concentration of $C^{15}O_2$ (and hence of the positron activity) is proportional to the regional blood flow. (a) shows a healthy active foot with the main arteries and the active muscles clearly evident, whereas (b) shows a resting foot with only the two main arteries weakly visible. The scan in case (b) showed only 1/7 of the activity (and hence blood flow) of that exhibited in scan (a).

Figure 16 This figure shows the ^{124}I images taken at 24 hr after ingestion in a patient with a massive goitre. The uptake of ^{124}I is very nodal. The strongest nodes appear in all planes but the weaker ones reveal their depth by appearing best in different planes. Thus a small node bottom centre appears better in plane 5 (d) than in plane 3 (a). The 'linear' display of plane 5 (e) shows the 'hotter' parts of the picture with a clearer indication of the location of the active nodes. The contour plot of plane 3 is also given (c) and the pertechnetate scan of this patient for comparison (b).

Figure 17 (a) shows the lateral view given by the positron camera of the head of a patient given an intravenous injection of ^{18}F . The spine and boney tissue are clearly labelled and the 'hot spot' at the back of the head is confirmed by conventional ^{99m}Tc -glucoheptonate scintigraphy as a 2 cm diameter tumour. (b) shows a comparable brain scan of a patient with a known lesion in the posterior brain. The uptake of ^{18}F deoxyglucose gives a clear positive in the positron camera image.

Figure 18 (a) shows the anterior-posterior image obtained from a rat some 5 minutes after injection of 4 MBq of ^{18}F into the tail vein. The activity can be seen still in the blood pool but already concentrating into the bladder through the kidneys. (b) shows the kidney clearance curve obtained by integrating the total counts in both kidneys in two minute periods subsequent to the injection time. (Δ) Also shown are the total bladder counts (o) which, of course, increase as the kidneys function. The activity levels are expressed as a fraction of the total body count (the 10% level corresponds to counting statistics of 2500 giving very small statistical errors).

Table 1

Real rate/random rate ratios for various experimental configurations.

(The ratio is evaluated at a rate of 1000 Hz in the fast coincidence circuit.)

	Theoretical Value $\frac{E^2}{T} / 1000$	Point Source in Air	'in vivo' Foot (mean value) ^{18}F	'in vivo' Foot (mean value) H_2^{15}O	'in vivo' Head (mean value) C^{11}O
Real/Random Ratio	91	26	10	6.5	1.1
Total activity administered MBq		1	220	10/min	300
Data acquisition rate (LAMS) Hz		500	200 90 mins after injection	300	350 35 mins after inhalation

Table 2

Response of the positron camera to a point source placed inside various absorbers.
(Compare with curves of Figure 10.)

Absorber Configuration	Total Rate (Relative)	Fraction of Signal 'in' peak	Fraction of Signal 'under' peak	Rate 'under' peak relative to rate in air
Air	1	0.75	0.90	0.90
H ₂ O source at centre of a long cylinder of 10 cm diameter	0.67	0.42	0.58	0.39
H ₂ O source at centre of a cube of edge 20 cm	0.36	0.22	0.40	0.14

Figure 1

Figure 2

Figure 3

(a)

(b)

Figure 4

Figure 5

Figure 6

Figure 7

(a)

(b)

Figure 8

Figure 9

Figure 10

Figure 11

Figure 12

Figure 13

(a)

(b)

(c)

Figure 14

(a)

(b)

Figure 15

(a)

(b)

(c)

(d)

(e)

Figure 16

(a)

(b)

Figure 17

Figure 18