INSTITUTE OF PHYSICS PUBLISHING PHYSICS IN MEDICINE AND BIOLOGY

Phys. Med. Biol. **51** (2006) R99–R115 doi:10.1088/0031-9155/51/13/R07

REVIEW

The early years of single photon emission computed tomography (SPECT): an anthology of selected reminiscences

Ronald Jack Jaszczak

Duke University Medical Center, Durham, NC 27710, USA

E-mail: R.Jaszczak@ieee.org

Received 1 February 2006, in final form 6 April 2006
Published 20 June 2006
Online at stacks.iop.org/PMB/51/R99

Abstract

The origin of SPECT can be found in pioneering experiments on emission tomography performed approximately 50 years ago. This historical review consists of a compilation of first person recollections from nine trailblazing scientists who shaped the early years of SPECT instrumentation during the 1960s and 1970s.

(Some figures in this article are in colour only in the electronic version)

1. Introduction

The origin of SPECT can be found in the groundbreaking experiments on emission tomography performed approximately 50 years ago by David Kuhl and Roy Edwards (Kuhl and Edwards 1963). For this historical review on SPECT, I have invited a select group of pioneering scientists to share their personal reminiscences of SPECT instrumentation research in its early years (i.e., circa 1960 through the early 1980s).

This historical account cannot be all-inclusive; rather, I wish to share with the interested reader some of the key events that occurred during this critical period of immense technological changes. Unfortunately, it is impossible, in the limited space available, to include the personal accounts of all of the fantastic scientists, physicians and engineers who have made significant contributions to SPECT instrumentation and reconstruction. I must, by necessity, leave the reminiscences of those outstanding investigators of the more recent past to a future compiler. To those who have been precluded from participating, particularly my many esteemed international colleagues from Japan and other countries, I offer my honest apologies.

I would like to sincerely thank the following distinguished scientists for participating in this compendium: A Bertrand (Randy) Brill, Thomas F Budinger, John W Keyes Jr, David E Kuhl, Stig A Larsson, John R Mallard, Gerd Muehllehner and W Les Rogers. It is only through their efforts that this historical account exists at all.

2. A selected listing of early SPECT milestones

To set the stage for the narratives that are to follow, a few of the most important scientific achievements relating to the development of SPECT imaging systems are briefly described in this section.

2.1. Fundamental pre-SPECT instrumentation developments

In the early days of nuclear medicine, scans were performed by manually positioning a simple Geiger counter (Geiger and Walther 1928) above the organ of interest. An improvement in sensitivity came with the development of the scintillation detector and scanner (Cassen *et al* 1951, 1950). A major breakthrough followed with the invention of the Anger scintillation camera (Anger 1958, 1964). The Anger camera viewed the entire organ of interest at one time; thus, it provided a marked improvement in gamma ray detection efficiency.

2.2. Longitudinal emission tomography (i.e., focal-plane tomography)

Longitudinal tomography uses techniques that focus on a particular plane of interest; however, because of incomplete angular sampling, these methods cannot provide an artefact-free image; activity located above or below the plane is blurred. Crandall and Cassen developed a longitudinal tomographic scanner that used a highly focusing collimator placed on a large crystal-matrix detector (Crandall and Cassen 1966). In 1969, Anger invented a sophisticated longitudinal tomograph that used a scanning scintillation camera (Anger 1969). This method is similar to the method of x-ray laminography, where motion of the x-ray tube and film can be used to select a particular focal plane. Anger's tomographic scanner was later named the 'Pho-Con', and was sold for several years by Searle Radiographics. Gerd Muehllehner described a longitudinal tomographic approach that used a rotating slant-hole collimator (Muehllehner 1970, 1971).

2.3. Transaxial section tomography

2.3.1. Discrete detector approaches. In the early 1960s, Kuhl and Edwards investigated both longitudinal and transaxial tomography, and they were the first investigators to describe a true transaxial approach for emission tomography (Kuhl and Edwards 1963, 1964). During the period of 1963 through 1976, Kuhl and his colleagues developed a series of transaxial tomographs (Kuhl and Edwards 1964, 1970, Kuhl *et al* 1974, 1976). Kuhl's Mark II (Kuhl *et al* 1974) is shown in figure 1. This device consisted of two scintillation detectors and used a translate-rotate motion of the detectors. Kuhl's final tomograph was the Mark IV (Kuhl *et al* 1976). Each detector array had a linear array of eight discrete scintillation detectors. Kuhl even investigated the use of transmission computed tomography (CT) in 1966 (Kuhl *et al* 1966).

During the late 1960s and the early 1970s, John Mallard's remarkable research group at the University of Aberdeen introduced their version of an emission tomograph (figure 2) that used discrete scintillation detectors, the Aberdeen Section Scanner (ASS) (Bowley *et al* 1973). Also, during this period, Patten, Brill and their colleagues developed a novel scanner (figure 3) that used a scanning array of eight focusing detectors to obtain sectional images (Patton *et al* 1969). Their investigations influenced the multiple detector tomograph that was developed by Stoddart and Stoddart (1979).

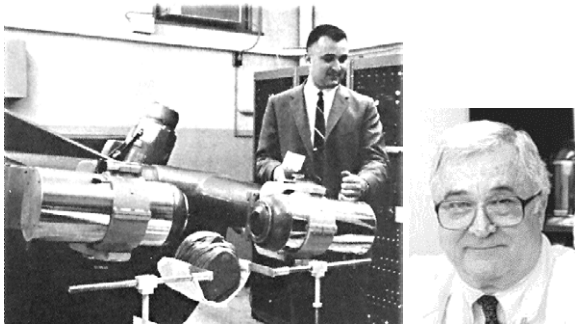

Figure 1. David Kuhl and the Mark II scanner. (Photograph of scanner reprinted by permission of the Society of Nuclear Medicine from (Silver 1996). Photographs courtesy of Dr D E Kuhl.)

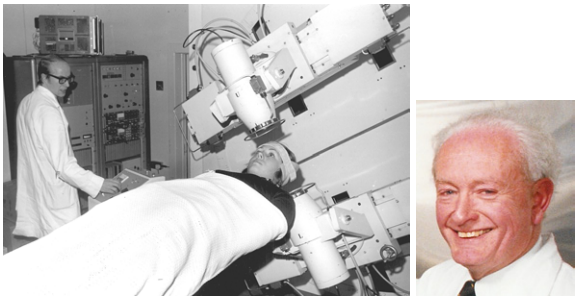

Figure 2. John Mallard and the Aberdeen Section Scanner (ASS) Mark I. Professor Mallard's former colleague, W I Keyes, is shown operating the scanner. (Photographs courtesy of Dr J R Mallard.)

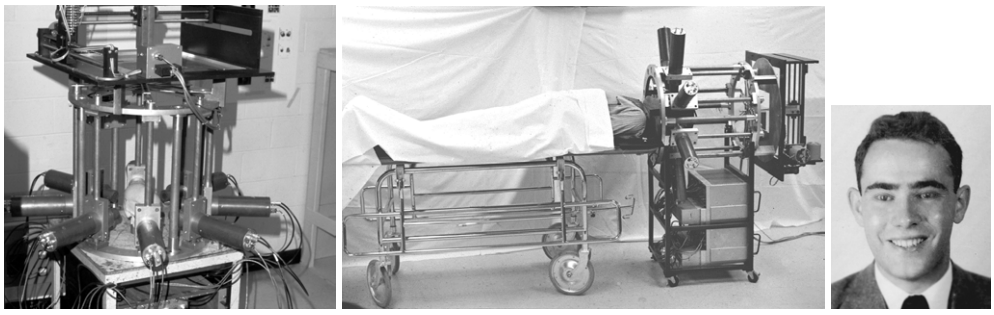

Figure 3. Randy Brill and the Vanderbilt cylindrical geometry tomograph. (Photographs courtesy of Dr A B Brill.)

2.3.2. SPECT using the Anger scintillation camera. Paul Harper and colleagues at the University of Chicago were the first investigators to explore the use an Anger camera for transaxial tomography (Harper *et al* 1965). In 1968, Gerd Muehllehner first investigated a transaxial tomographic approach that used a rotatable chair placed in front of a stationary Anger camera (figure 4) (Muehllehner 1968, Muehllehner and Wetzel 1971). In the early

Figure 4. Gerd Muehllehner and the Searle rotating-chair SPECT method. (Photographs courtesy of Dr G Muehllehner.)

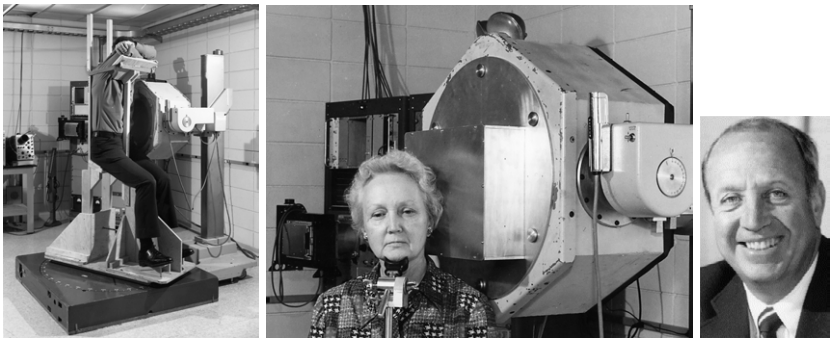

Figure 5. Tom Budinger and the Berkeley rotating-chair SPECT approaches: (left) chair on a rotating platform for cardiac imaging; (middle) chair with bite mouth piece for brain imaging. (Photographs courtesy of Dr T F Budinger.)

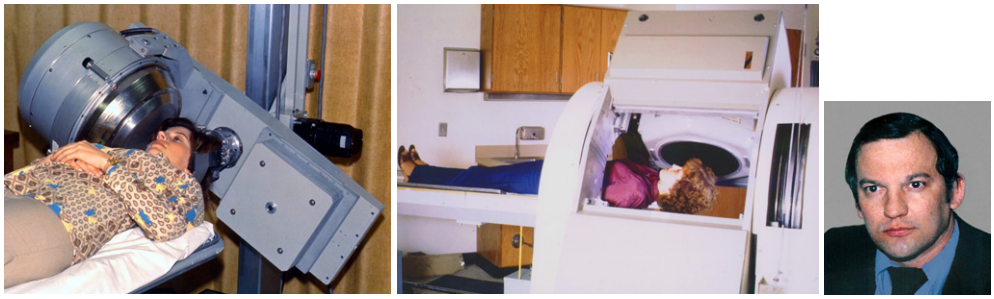

Figure 6. Ron Jaszczak and the Searle rotating-camera SPECT scanners: (left) brain imager; (middle) dual-camera, whole-body SPECT system.

1970s, a rotatable chair approach (figure 5) was also investigated by Tom Budinger, Grant Gullberg and Ron Huesman (Budinger and Gullberg 1974). Independently in 1976, I and John Keyes Jr and our respective colleagues developed SPECT systems that used an Anger camera mounted on a gantry that rotated about a recumbent patient (figures 6 and 7). Results obtained with these SPECT scanners were presented at the 1976 Annual Meeting of the Society of Nuclear Medicine (SNM) (Jaszczak *et al* 1976, Keyes *et al* 1976); subsequently, they were described in detail in the same issue of the *Journal of Nuclear*

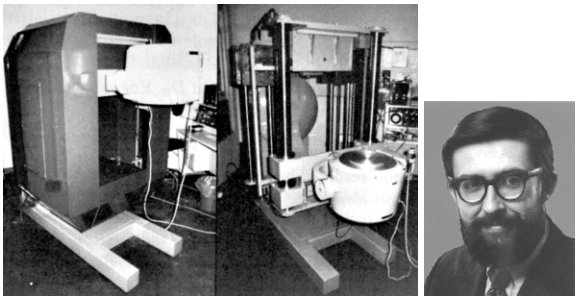

Figure 7. John Keyes and the Humongotron SPECT scanner. (Gantry photograph reprinted with permissions by Dr Keyes and the Society of Nuclear Medicine from (Keyes *et al* 1977). Dr Keyes portrait courtesy of Dr W L Rogers.)

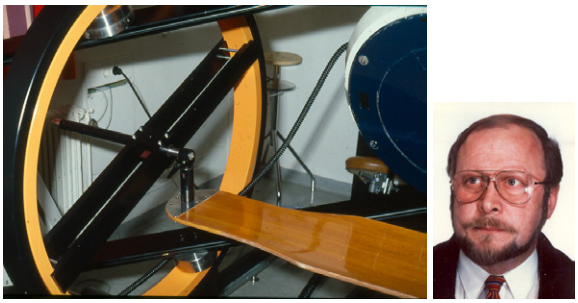

Figure 8. Stig Larsson and the first prototype gantry from GE. Note: the rotating chair can partially be seen in the background. (Photographs courtesy of Dr S A Larsson.)

Medicine (Jaszczak *et al* 1977, Keyes *et al* 1977). During 1976, 1977 and 1978, my Searle colleagues and I developed and clinically evaluated the first whole-body SPECT system that used multiple Anger cameras (figure 6). This system was clinically evaluated in 1978 at the Baylor College of Medicine (Murphy *et al* 1978). We described the Searle dual-camera, whole-body SPECT system in detail in this journal (Jaszczak *et al* 1979). In Europe during the late 1970s, Stig Larsson at Karolinska University in Stockholm was evaluating a prototype (figure 8) rotating-camera SPECT system (Larsson 1980). During the 1980s, other research groups evaluated rotating-camera SPECT systems and proposed both hardware and data processing approaches to improve the performance of these devices. Many of these important contributions were published in *Physics in Medicine and Biology* (PMB). Selected PMB articles on SPECT include Flower *et al* (1981, Chesser and Gemmell (1982), Todd-Pokropek (1983), Myers *et al* (1983), Webb *et al* (1983), Tanaka *et al* (1984), Webb (1985), Axelsson *et al* (1987), Floyd *et al* 1987, Laird and Williams (1987), Mills and Delchar (1988).

2.3.3. SPECT using stationary detector configurations. In the late 1970s and the 1980s, Les Rogers and his colleagues at the University of Michigan developed a series of SPECT tomographs (Williams 1979, Knoll and Williams 1979, Rogers *et al* 1982). A later multi-slice version called the SPRINT II (figure 9) used NaI(Tl) bar-detectors (Rogers *et al* 1988). Later, in the 1980s, Genna and Smith at Digital Scintigraphics, Inc. developed a SPECT brain scanner (ASPECT) that used an stationary annular crystal and a rotating collimator (Genna and Smith 1988).

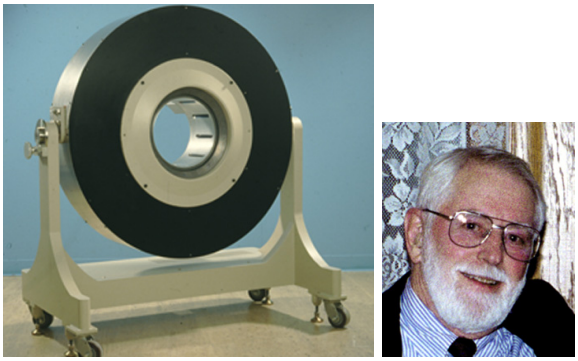

Figure 9. Les Rogers and the SPRINT II system. (Photograph of scanner reprinted from Rogers *et al* (1988). Photographs courtesy of Dr W L Rogers.)

3. The reminiscences

3.1. David E Kuhl, MD

'My research grant experience began as a first year radiology resident in 1958. I asked the physicist Dr John Hale for $5 to purchase ping-pong balls, which could serve as tumour models for phantom experiments of emission tomography. He balked and said I should ask the radiologist Dr Antolin Raventos for $20. Raventos balked and said I should apply to the school's American Cancer Society [ACS] Institutional Grant for "seed" money, but I should ask for $200. I applied for $2,000 and got it. The ACS committee chair, Dr David Goddard, said such an award assumed I would seek external funding and he gave me an NIH [National Institutes of Health] RO1 grant application form. I completed this form, asking for $15,000 annually for three years. When told that Vice President Isadore Ravdin should sign the front sheet for the University, I naively cornered him in the dressing room of his operating suite, had him sign it, and mailed the forms directly to NIH, completely bypassing the proper University channels. The application was funded. The University grants personnel were appalled to have no record of the submission. Finally, the University accepted the award, but only after I promised never to bypass them again, and also to leave Dr Ravdin alone. This NIH grant funded my early work with emission tomography. Its direct descendants have been funded continuously since then, a period of over 40 years. (I did buy the ping-pong balls. I still have some of them.)

In the months that followed, I worked out the scan strategies for transverse and longitudinal emission tomography, and drew up a scanner design (Mark II) which the shop director, Roy Edwards, felt confident he could build. The most important mode, cross-sectional or transverse section imaging required completely new backprojection apparatus which we finally got to work correctly on 21 August 1959, when Roy and I worked through the night to perform successfully the world's first transverse section emission tomography. The machine shop's Bridgeport Milling Machine served as our "scanner" and a radioactive plastic bottle in a water bath was our "patient".

Over the next 15 years, in the basement of Radiology, in the Hospital of the University of Pennsylvania, we invented a series of computerized emission tomographs and procedures that introduced cross-sectional reconstruction tomography to medicine and were the true forerunners of present day SPECT, PET and CT. I am fortunate to have been a part of this.' [Kuhl D E, written communication, June 1999]. [Reprinted with permission by Dr Kuhl and by the Radiological Society of North America from Potchen (2000).]

3.2. John R Mallard, PhD

'Tomography was first carried out in 1964 by Dr Dave Kuhl, a nuclear medicine specialist in Philadelphia, by an analogue technique. My team in Aberdeen built the first digital CT for radio-isotope distributions from 1967 to 1969. (This was some five years before the technique was applied to X rays by Godfrey Hounsfield, which revolutionized X ray diagnosis, and for which he received the Nobel prize.) In essence, two opposed scintillation counters, detecting the gamma rays, translate across the patient, and their axis is then rotated through 15 degrees; the counters are then passed back over the patient, rotated through 15 degrees again crossed again, and so on, completely around the patient. All the passes of the counters are in the same transverse plane. The method is known as translate-rotate. In the computer, the counting rate along the line joining the counters is recorded and summed, so that with each pass of the counters over the tumor, the tumor "hot spot" is increased, while the more random background elsewhere becomes averaged, thereby increasing the tumor contrast. This method is known as back projection. The resultant image is the transverse-section view, or CT (computed tomography) view.

Tumors that were difficult to see in conventional antero-posterior and lateral views were much more easily detected and localized with the CT view, and when the CT view was added to the diagnostic work-up, brain lesion detection improved to 92 percent. By 1973, much more precise radiotherapy treatments began to be prescribed from the scans. One of the prominent uses of the section scanner was to begin a trial to evolve a positive diagnosis of epilepsy from imaging, in addition to the complex symptomatic tests. At the beginning, it could never have been expected that the radioisotope work of physicists would lead to a step forward in the battle against mental disorders. Perhaps this was the fulfillment of a medieval dream that a machine could exist that would suck out all of a patient's dementias.

A commercial version of the Aberdeen section scanner was produced for a few years by a small company called J and P, Ltd., of Reading, and an American company, Cleon, also entered the field. During this period, we built a second version of the scanner that gave better images, but it was not until the rotating gamma cameras for SPECT had been widely and fully explored that the multinational medical imaging companies really took up the technology in a big way. SPECT became popular from the mid-1980s onwards. Peter Sharp, who became my successor, pioneered the use of a radioactive drug (*HMPAO*) with tomography to image blood flow in the brain, and this technique is still used to distinguish between, for example, Huntington's chorea and Alzheimer's dementia. Gamma-camera images nowadays are superb. Leading teaching hospitals worldwide, as well as the better general hospitals in the West, now have a nuclear medicine service. About 15,000 tests are performed per million population served, with about 20 different tests being available, and approximately half of the examinations involving SPECT use commercial gamma cameras. These tests have had a very beneficial effect upon patient management.' [Excerpted from: John R Mallard "The Evolution of Medical Imaging: from Geiger Counters to MRI—A Personal Saga". *Perspectives in Biology and Medicine* **46** (3) (Mallard 2003), pp 354, 355. ©The John Hopkins University Press. Reprinted with permission of the The John Hopkins University Press. The evolution of medical imaging *Perspect. Biol. Med.* **46** 349–70.]

3.3. A Bertrand (Randy) Brill, MD, PhD

'My work with radioisotopes as a nuclear medicine physician/scientist dates back to a summer job in 1948 in Keith Cannon's Biochemistry Department at NYU, on what would now be called a molecular biology project. Turned on to science, I went on to get a PhD in Biophysics from Berkeley (Donner Lab), and an MD from Utah, following which I joined Bob Heyssel in 1964

at Vanderbilt University in what was then Division of Nuclear Medicine and Biophysics. The program had been started by Paul Hahn and George Meneely who moved from Rochester University to Vanderbilt in 1943. Paul was an established investigator whose PhD in 1936 was on iron metabolism using Fe-59, followed shortly by publications of the work with E.O. Lawrence, G.W. Whipple, and W. Bale, all distinguished pioneers in the field. Paul continued his work on iron metabolism at Vanderbilt, and did pioneering work on radiocolloids for cancer therapy. George was a skilled clinician/innovative researcher who used tracers in many cardiopulmonary applications. An early instrumentation project of note was presented in 1954 at an American Physics Society meeting in Knoxville, TN which was published with the title: "A Rotating Sphere Solid Angle Scanner for Gamma Rays". The device used a rotating oscillating collimator that allowed radiation to reach a NaI detector with the direction of the incoming collimator-defined beam recorded by coupling the collimator motion to that of an oscilloscope readout device. The device had very low sensitivity and the only published illustration is a liver and spleen scan of a cancer patient who received a therapeutic dose of Au-198 colloid. Ten years later, a similar coupling of a moving optical readout device was used by Paul Harper and Hal Anger independently to display whole body images from limited field of view scanning gamma cameras. Meneely left Vanderbilt in 1962 and Bob Heyssel, who was then in charge of nuclear medicine sought to acquire a nuclear medicine scanner that was then sold by Picker. The money was hard to come by, as it cost more than Dave Kuhl's ping pong balls. Bob went to the Chairs of four related Departments, with the story that he had all but a quarter of the price of the device which may have cost $20,000–$40,000, and no one failed to come through. When I arrived in 1964, the device was in place and used with I-131 for thyroids, and Hg-203 for brain scanning, which was fine with meningiomas, but confidence in localizing other brain tumours was marginal at best.

At Vanderbilt, we tracked Kuhl's tomography developments with great interest and pored over his system and the computer coupling during the SNM meeting in Philadelphia in the mid 1960s. On return, we developed a digital logic patch panel programmable front end for controlling all of our input and output devices. Meneely had gotten AEC support for his whole body counter R&D applications. That support lasted through 1979 and during my 15 years at Vanderbilt it provided the flexible support needed for many clinical applications tests, and explorations of novel instrumentation. Apart from controlling the large, heavily shielded NaI(Tl) whole body scanner with multiple collimators, we collected digital data from Ohio Nuclear dual-opposed scanners, Anger cameras, and later the PhoCon. My first year at Vanderbilt, I gave a talk at the annual June meeting for returning alumni about the excitement raised by non-invasive section scanning. By that time I was aware of the proposed use of a standard scanner with the detector oriented horizontally, scanning back and forth, as the patient sat on a rotating barber chair for brain imaging. We and others explored this approach with little success. In subsequent years, our group developed an eight detector cylindrical array system for emission tomography and for fluorescence imaging of x-rays from stable bismuth that was picked up by brain tumours. Jon Erickson and Jim Patton were mostly responsible for that system. Dave Pickens and Paul King developed a 12 crystal section scanning instrument that collected planar data from coronal, sagittal, and transverse orientations. Unfortunately, the system used experimental self contained detector modules, and we never had all 12 detectors working at the same time. The people from Cleon came and looked at the system closely, and their commercial implementation took advantage of some of the key features of the system. I left in 1979 for Brookhaven, and the Radiology research at Vanderbilt turned more and more to MRI developments, that have moved far in the ensuing years.

Nuclear medicine was and is able to keep up (e.g., acquire and process in real time the relatively low data rates from gamma-emitting tracers in patients), and lessons learned

have translated well into the development of 3-, 4-, and 5-D imaging in a variety of *in vivo* applications. Nuclear medicine tracers have the highest process-specific signal content of all modalities for use in patient studies, with optical tracers a close second for *in vitro* application, especially for small animal studies. Advances in molecular medicine can only increase the range and scope of the benefits derived from nuclear imaging of patients.' [Brill A B, written communication, January 2006.]

3.4. Gerd Muehllehner, PhD

'I received my PhD in nuclear physics in 1966, and at that time had to choose between developing better nuclear bombs and working in the field of nuclear medicine. It was not difficult to decide to be constructive instead of destructive, even though it represented a move to the application of nuclear technology in a different field. While my initial task at Searle Radiographics (my first employer) was to improve the Anger scintillation camera—via better collimators and better analogue and digital signal processing—my interest in methods to better visualize the 3-D aspect of radioisotope distributions started shortly thereafter.

It must be remembered that 1966 was before the digital world had started. Nevertheless, I tried in 1967 to create a 3-D representation of a radioisotope distribution by subtracting counts from over- and underlying structures, rather than by merely blurring them. I attempted this by combining the data from eight views around the patient using an iterative algorithm (Muehllehner 1968), which did indeed give transverse section images—before the CT scanner and before Kuhl's orthogonal tangent correction algorithm. At that time, a large data matrix consisted of 40 by 40 pixels, and it required a major computing effort on an IBM 360 mainframe to produce the images. The clinical evaluation required shipping a "large" data acquisition system to a hospital, and then sending the data (all 25 kbytes) via large nine track tapes back to the computing centre for processing (Muehllehner and Wetzel 1971). The awkward process of getting the patient's shoulders out of the way and to position a large detector head close to the brain not only prevented us from using more than eight views, but also gave rise to the development of the special detector head used several years later by Ron Jaszczak to get his excellent brain transverse sections—of course, using more angles and a "proper" reconstruction algorithm also helped.

After realizing that the use of a computer to calculate 3-D images was impractical, and seeing the excellent longitudinal images from Hal Anger's tomoscanner, I was motivated to build a rotating collimator attachment to the Anger camera, which did indeed give tomographic images, processed with analogue electronics, and recorded on Polaroid film to show four longitudinal slices simultaneously (Muehllehner 1970, Muehllehner 1971). While this was more practical, given the fact that we were still living in an analogue world, its clinical benefit did not justify the extra effort. Since overlying and underlying activity was merely blurred instead of subtracted, the resulting images had low contrast.

By the mid-seventies my interests shifted to PET, and have remained there ever since. However, during the seventies I implemented a few improvements in the Anger camera; noteworthy is linearity correction, also called digital distortion removal (Muehllehner *et al* 1980, Muehllehner 1973), because it is a good example of an idea that was tested on a large computer in 1971, but had to wait until 1980 for the digital processing and data storage methods to become compact and inexpensive enough to allow the method to be used routinely.

One way to look at the benefit of SPECT is that SPECT uses time as an additional coordinate, by collecting different information as a function of time and translating this into spatial information. Of course, rectilinear scanners did this as well: the detector has no position information and all spatial information is gathered as a function of time. We can measure

time with superb precision—down to microseconds. It has always been my ambition to find a device incorporating scanning motion that makes better use of our ability to measure time in order to give higher quality images of static radioisotope distributions. Now that I am retired, I am frustrated by this failure and keep scanning the literature, hoping to read that a younger and brighter investigator has reached that goal.' [Muehllehner G, written communication, January 2006.]

3.5. Thomas F Budinger, PhD, MD

'My early work as an oceanographer involved exploring the water of the Arctic and the Antarctic regions studying the topography of the ocean floor and tracking movement of sea ice and icebergs. It became apparent that these concepts could be applied to mapping of the function of the human body in health and in disease. Combined with my interests in physics and mathematics, this led to our work in creating the instruments and mathematical methods to determine these functions.

While still in medical school, I became convinced that there should be no technological impediment to the detection of abnormal human processes by 3-dimensional triangulation methods similar to those I used in the study of iceberg motion and special methods of navigation. Thus, it seemed then, as it does now, that we have the capability to discover the physical and biochemical causes of diseases by using these techniques, which allow us to probe the human body using physical methods such as x-rays, isotope detection, magnetic resonance, and ultrasound. My work came to focus not only on chemical function of the body, but also on the navigational methods required to more accurately map these processes in different parts of the body.

My first work in medical science involved the use of digital computers and principles of physical optics to measure fundamental aspects of electron wave scattering on thin objects relevant to biological studies with Professor Robert Glaser. Application of these theories to imaging body function using radioisotopes was a result of my association with the Donner Laboratory, founded by Professor John Lawrence. The proximity of this facility to the Lawrence Berkeley Laboratory created an environment to develop the tools and procedures for exploring and quantitating disease processes in the body.

One of the first important applications of these techniques was the development in 1970 of a high-speed digital computer system for the acquisition and display of dynamic processes in the body. My colleague Professor David Kuhl did early work on 3-dimensional tomography in nuclear medicine. The contribution of our group was in the development of mathematical techniques to give a quantitative description of the dynamics of flow and metabolic processes in the body in 3-dimensions.

We recognized that in order to truly see quantitative chemical functions in the body we needed better instruments for radioisotope detection. In addition, improvements were needed for the processing and analysis of data. In 1975 my colleagues, Drs. Grant Gullberg, Stephen Derenzo and Ronald Huesman along with chemist Yukio Yano worked as a team to develop high-speed dynamic radionuclide emission imaging tomography and appropriate radioisotopes for the study of ischemic heart disease, stroke, epilepsy, and brain tumours. By 1980 my colleagues, Drs. Friedland and Jagust were essential partners in the discovery of a specific pattern of human brain glucose metabolism defects and corresponding blood flow abnormalities in Alzheimer's patients.

These studies caused us to focus in the 1980s on the development of a dynamic positron emission tomographic system with a resolution of 2.6 mm.' [Budinger T F, written communication, January 2006.]

3.6. Ronald J Jaszczak, PhD

'Early in 1971, I felt fortunate to have found a research position at Searle Radiographics in Des Plaines, IL. I recall that I was extremely nervous when I made my first presentation at the 1972 Annual Meeting of the Society of Nuclear Medicine (SNM), where I described a filter-scanning technique (Jaszczak 1974) to eliminate the effect of intrinsic spatial resolution on image quality. After my presentation, a soft-spoken gentleman approached me and spent about 30 minutes asking me to explain some details about this technique. When I learned later that the quiet gentleman was the famous Hal Anger, I was deeply humbled and honoured.

I first worked on a couple of longitudinal tomographic approaches; however, it soon became apparent that transaxial computed tomography using a rotating Anger camera could acquire more completely sampling data. Around 1973, my colleagues and I experimented with some SPECT scans of a skull phantom placed on a manually rotated turntable. Then, during 1974 and 1975, we designed and built a rotating-camera SPECT system that could acquire patient brain scans. We decided to first build a brain-imager, since the degrading effects of attenuation would be less for brain imaging than for body imaging. Also, I had access to an existing compact gamma camera with a 10 inch field of view that could be brought very close to the patient's head without shoulder interference.

The SPECT brain-imager was shipped to Baylor College of Medicine in Houston, where John Burdine was Director of Nuclear Medicine and Paul Murphy was the Medical Physicist. On November 16, 1975, I became the first human volunteer to be scanned with the Searle SPECT brain-imager. I returned to Des Plaines with the projection data (stored on one-inch video tape), and used our laboratory computer to perform the reconstructions. At first, I was somewhat concerned that my brain scan was abnormal, but the nuclear medicine physicians assured me that the "abnormality" was due to uptake in the parotid glands. We acquired dozens of patient scans and described our initial results at the 1976 SNM Annual Meeting.

In the period 1976 through 1978, we designed, built and clinically evaluated a whole body SPECT system that used two large field of view Anger cameras. When visitors came to our laboratory and saw our system, they thought it was a dual-camera positron system. I would have to explain to them that it did not detect coincidence photons; rather, it detected photons sequentially, or singly, one at a time. Thus, I coined the acronym SPECT (Single Photon Emission Computed Tomography) to describe this new dual-camera tomograph so that it would not be confused with a positron camera. Our dual-camera SPECT system had corrections for attenuation and scatter; it was also capable of acquiring body contour information and gated cardiac data. We presented our initial clinical results at the 1978 SNM Annual Meeting. I must acknowledge the important contributions of my talented fellow Searle colleagues, for example, Gerd Muehllehner, Bill White, Lee-Tsui Chang, Chun Bin Lim and Tony Smudde. They, and many other distinguished members of the Searle Research Department, were terrific.

In 1979, Searle Radiographics' Chief Executive Officer, Donald Rumsfeld, while in the process of selling off Searle (eventually to Siemens), ordered that all long term research on SPECT be stopped. Candidly, I am most beholden to Mr. Rumsfeld to have given me the opportunity in August, 1979, to start a new, productive, and priceless career in academia at Duke University Medical Center in Durham, North Carolina.

In 1981, Siemens allowed us to install the dual-camera prototype SPECT system in the Department of Radiology, where we used it productively for several years. In 1988, we replaced it with a Triad triple-camera SPECT system from Trionix Research Laboratory, a company founded by my former Searle colleague, Chun Bin Lim. Also, in 1981, my wife Nancy and I founded Data Spectrum Corporation, a company dedicated to providing research

and quality control phantoms for SPECT, PET and MRI. The original phantom has even been called the "Jaszczak" phantom!

During my early years at Duke, my very first NIH R01 grant application (entitled "*In Vivo* Radionuclide Quantitation Using Emission CT") was deferred for a project site visit by the Study Section. The reviewers cited the "enormous budget requested". Fortunately, the grant was funded following the site visit. In fact, all competing renewal applications have been funded on their first submission, and this series of grants was continuously funded for a 23 year period. I am much appreciative to the distinguished members of the original Site Visit team.

My career has been shaped by my esteemed nuclear medicine colleagues such as Tom Budinger, Grant Gullberg, Ron Huesman, Mike King, Dave Kuhl, Charles Metz, Steve Moore, Ben Tsui, Henry Wagner, and too many others to acknowledge here.

At Duke, I have had the opportunity to work with many fine faculty colleagues, research associates and students, for example, Ed Coleman, Craig Harris, Konstantin Bobkov, Jim Bowsher, Carey Floyd, Dave Gilland, Dinko Gonzalez Trotter, Leszek Hahn, Jianying Li, Jerome Liang, Steve Manglos, Scott Metzler, Joerg Peter, Mark Smith, Charles Tenney, Martin Tornai, Tim Turkington, Huili Wang and others. I am most grateful to Kim Greer, an extraordinary nuclear medicine technologist. I have found my research career in SPECT a most rewarding experience; it is one that I will always look back upon with pleasant reminiscences.' [Note: the author (rjj) has learned that, regrettably, some Europeans have changed from using the acronym SPECT to SPET so as to be similar to PET.]

3.7. John W Keyes Jr, MD

'My interest in nuclear medicine actually dates back to my grade school days. I distinctly remember reading an article in Colliers magazine about the use of radioactive mercury to localize brain tumours. This was in the early 1950s and long before the existence of the first scanners and nuclear medicine as a specialty.

They were using Geiger probes placed directly on the brain. I was intrigued. Many years later, several years out of medical school, I read an article by Bill Beierwaltes in the *New Physician* about this neat new specialty called nuclear medicine. Remembering the old article, I was hooked, and went on to do a residency in nuclear medicine with Beierwaltes at the University of Michigan.

We started experimenting with SPECT techniques in the early 1970s, using the newly developed techniques of filtered back-projection and a rotating chair. At Michigan, we had the physics shop build us a large rotating platform with degree marks indexed around the perimeter. An object (or patient) could be placed on this, and rotated manually in front of a gamma camera to acquire data. We quickly learned that with a PhD, an MD, and a graduate student all helping to rotate the platform, nobody could keep track of how many projections we had acquired. Furthermore, stabilizing a patient in front of the camera was a real nightmare. It was obvious that the answer was to lay the patient down and rotate the camera around the patient and let the computer keep track of everything. Using grant money from NIH, this led to the eventual development of the Humongotron in 1976.

The Humongotron owes its name to Les Rogers, and is of course based on the slang term "humongous" which became popular about that time. And humongous it was. We had been scratching our heads over how to mount a heavy gamma camera head and collimator so that it could rotate through 360 degrees and move in and out from the axis of rotation to allow for different sizes of patients. One day one of Les' graduate students mentioned that he had been out at the University's surplus warehouse and had seen a machine that looked like what we

had been picturing. This turned out to be an old caesium therapy machine which was designed to rotate the heavily shielded caesium source around a patient during radiation treatments. Bingo! We had this shipped to the physics shop, which removed the old therapy head and manufactured an elaborate dual post support to hold the gamma camera while allowing it to both rotate and move in and out. This was completed and shipped to the University Hospital Nuclear Medicine Clinic during the Christmas holidays of 1975—an undertaking in itself considering the size and weight of this "gadget". The heritage of the Humongotron can still be seen in virtually all of today's commercial SPECT devices.

There is a last note about the name. When we submitted our paper on the Humongotron to the *Journal of Nuclear Medicine*, one of the reviewers and the editor objected to the name as being too frivolous for a serious journal. I replied that if John Mallard, who had been working on alternative approaches to SPECT in Scotland and had published a paper describing the Aberdeen Section Scanner, i.e. "ASS", then we could call our machine pretty much anything we liked. And Humongotron it remained.' [Keyes J W Jr, written communication, January 2006.]

3.8. Stig A Larsson

'I entered the world of 3D tomographic imaging from the design of a dual detector system for screening brain tumours (1968–1972). This was far away from 3-D imaging, but two complete computerized systems were designed and manufactured during 1968 to 1972 before the project became obsolete when the x-ray CT entered the scene. The CT technique was introduced very early at the Karolinska Hospital, which obtained the 9th EMI-scanner in the world. It was installed in the neuroradiology department, headed by Prof. Torgny Greitz. He needed a physicist on the team, so he asked me to join his group. That was a very exciting period of my life and became my start in the tomographic world of medicine.

In 1974 I was appointed senior physicist and chief of nuclear medicine physics at the Karolinska Hospital. A 100,000 USD grant for a new gamma camera and a computer system was reserved for the build-up of a modern nuclear medicine facility. When the Maxicamera, with its 40 cm diameter field of view, was released by the General Electric Co in Copenhagen, Denmark in 1975, we selected this camera due to its large field of view. The choice of computer system was between the French Intertechnique and the DEC-system (Digital Equipment Corp. USA), operating with the GAMMA 11 program for nuclear medicine applications. The DEC-system was selected due to its widespread applicability in many different research areas. The computer system was only utilized for dynamic studies and for correction of camera non-uniformity—not a very efficient use of an advanced computer system. In 1975, I received a grant giving me the opportunity to visit some advanced nuclear medicine centres in the US—the Mallincrodt Institute (Terpogossian, Phelps and Hoffman), NIH (DiChiro), Mass. General Hospital and University of Philadelphia (D. Kuhl). On my way back home from this trip I made the very first drawings of a tomographic gamma camera device.

My research group at that time was very small—consisting of myself and two engineers and a few MD colleagues. Later the group was extended with two PhD students. In 1977, we started to develop what would be the SPECT system by putting in the filtered backprojection reconstruction code into the PDP11/34 computer, equipped with 32 kword RAM and two 1.2 Mbyte hard-disc drives. By means of a rotating chair, we could demonstrate the great advantages of the tomographic technique from the images obtained with four "hot" ^{99m}Tc-cylinders in a trash-bag with ^{99m}Tc as background activity. The hot cylinders were not visible on planar images—but were visible on the reconstructed images. Clinical studies

were performed by positioning the patient on a rotating chair with angular indications. In order to control the position within the field of view, we developed a device with marker sources and two sticks on each side of the patient. When the patient moved from the original position, the pins with their marker sources (close to the collimator to achieve the best possible definition) moved in the same way, thus allowing an adjustment of the images before reconstruction.

After demonstrating the tomographic images to the director (K. Lange) of GE in Copenhagen, they designed a rotating prototype gantry that we received in September 1978. The couch coupled to the gantry was made of wood and needed a support at the table-end.

Some basic problems were of course present in the very beginning.

- A computer interface and a motor control unit for the rotation had to be designed by ourselves.
- At a very early stage we observed a shift of the peak position during camera rotation by about 12 keV. The reason was the lack of mu-metal shields around the PM-tubes. This introduced non-uniformity artefacts which were eliminated using a set of 16 floods obtained at separate angles 0–360°.

The first clinical results were presented at many national conferences in Europe during late 1978. Apart from many manufacturers, we also had many scientists visiting us, for instance John Keyes, Jr. and James Richie (Washington Univ.). John Keyes wanted us to extend our 64×64 acquisition/reconstruction matrix (reconstruction time per slice was 30 s) to 128×128, which might have been favourable for studies of the brain, but less important for whole-body. Richie brought an IOWA-heart phantom which he wanted to scan in order to compare the results with the 7-pin-hole technique. He was quite sure that we did not need to fill the smallest defect of the phantom wall with pure water—we would not detect it. I insisted that we should include this defect in our study and to his great surprise—it was clearly visible.' [Larsson, SA, written communication, January 2006.]

3.9. W Les Rogers, PhD

'At the nadir of the physics job market in 1967 I received a PhD in physics from Case Institute. By chance I learned that Bendix Aerospace in Ann Arbor was looking for someone to develop a gamma-ray camera for some physician in nuclear medicine at the University of Michigan. I had never heard of nuclear medicine but it sounded intriguing.

The doctor turned out to be Bill Beierwaltes, and his collaborators were Glenn Knoll in nuclear engineering, Larry Jones in physics, and two physicians who had trained in nuclear medicine, John Keyes and Deaver Thomas. The job was offered, instantly accepted, and unknown to me, a lifetime career had begun.

The camera, similar to one under investigation by John Mallard in Aberdeen, consisted of a high gain image intensifier tube that viewed a 10 inch diameter NaI crystal through an $f/0.7$ lens. The output images were recorded with a Polaroid camera. Spatial resolution was 1–2 mm but sensitivity was abysmal. Nevertheless, one could marvel at cosmic rays as they traversed the crystal. Focusing two lenses and setting the high voltage to focus the tube was quite an exercise, especially when the output lens got too close to the anode and a 10,000 volt arc would jump with a resounding crack that would cause the heart to skip a beat.

In 1970 the project and I moved to nuclear medicine at University of Michigan, and Don Strange, a student of Glenn's, joined the project. At that time the imaging equipment consisted of several rectilinear scanners, and an Anger camera—Nuclear Data 50/50 system. This was a DEC PDP-8 computer interfaced to a multi channel pulse-height analyzer for collection of

digital camera images. To start the system required toggling in a bootstrap program to read the program from paper tape. When tired, or after a beer, toggling in the bootstrap could easily require a half dozen tries or more.

By 1971 it was clear that the image intensifier camera was doomed by poor sensitivity, but when we heard of Harry Barrett's work with Fresnel zone plates that offered orders of magnitude increase in sensitivity along with "tomographic" response, it appeared that this might be the answer. We visited Emmett Leith and Juris Upatnieks in electrical engineering and they set us up in their lab with a laser and optical bench and showed us how to develop holographic plates exposed by the intensifier camera. Point sources were beautiful, but performance degraded with larger sources. Also, the photographic process and optical reconstruction were tricky and time-consuming. Around 1973 Glenn Knoll suggested that we consider using time-modulated neutron chopper codes that could be reconstructed digitally. A translating lead code plate was constructed for an Anger camera and surprisingly good limited angle tomographic thyroid images and even a set of dynamic cardiac images were obtained. Jim Thrall, then at Michigan, was skeptical about the imaging application but really liked the appearance of the lead code plate and suggested that we make leather belts with that pattern and sell them at the SNM meeting.

Around 1979 Glenn Knoll and his student, Jay Williams, built a bench-top single slice ring tomograph with a rotating coded aperture ring and discrete NaI detectors. Thus was born SPRINT, to be followed by Son of SPRINT with NaI bar detector modules and real-time maximum likelihood position estimation designed and constructed by Neal Clinthorne, Ken Koral and myself. Some of these detectors are in use today in experimental Compton cameras in Slovenia, Spain, and even Ohio State.

Of course the fondest memories are of the people: faculty colleagues, graduate students, and nuclear medicine technologists. Bill Beierwaltes was the ultimate optimist and always encouraged and supported the ongoing research in the division. The spirit of collaboration and collegiality flourished between the basic scientists and the medical faculty and with the faculty in nuclear engineering, electrical engineering, physics, and bioengineering. It was a very good time.' [Rogers W L, written communication, January 2006.]

4. Conclusions

The reminiscences by these trailblazing scientists impart a meaningful understanding into the evolution of SPECT instrumentation as a valuable diagnostic imaging modality, and provide an intuitive insight into the inner workings of their research teams. It is clear that several distinguished research teams contributed significantly during the early years of SPECT.

Physics and Medicine and Biology (PMB) played an important role in publishing seminal SPECT manuscripts. For example, several early PMB SPECT articles are cited in section 2.3.2. Over the years, such a large number of SPECT papers have appeared in PMB that it is inconceivable that they could all be cited here.

References

Anger H O 1958 Scintillation camera *Rev. Sci. Instrum.* **29** 27–33

Anger H O 1964 Scintillation camera with multichannel collimators *J. Nucl. Med.* **5** 515–31

Anger H O 1969 Multiplane tomographic gamma-ray scanner *Medical Radioisotope Scintigraphy* ed G Freedman (Vienna: International Atomic Energy Agency) pp 203–16

Axelsson B, Israelsson A and Larsson S A 1987 Studies of a technique for attenuation correction in single photon emission computed tomography *Phys. Med. Biol.* **32** 737–49

Bowley A R, Taylor C G, Causer D A, Barber D C, Keyes W I, Undrill P E, Corfield J R and Mallard J R 1973 A radioisotope scanner for rectilinear, arc, transverse section and longitudinal section scanning (ASS—the Aberdeen Section Scanner) *Br. J. Radiol.* **46** 262–71

Budinger T F and Gullberg G T 1974 Three-dimensional reconstruction in nuclear medicine emission imaging *IEEE Trans. Nucl. Sci.* **21** 2–19

Cassen B, Curtis L, Reed C and Libby R 1951 Instrumentation for I-131 use in medical studies *Nucleonics*. **9** 46–50

Cassen B, Curtis L and Reed C W 1950 A sensitive directional gamma-ray detector *Nucleonics* **8** 78–81

Chesser R and Gemmell H 1982 The interfacing of a gamma camera to a DEC Gamma-11 data processing system for single-photon emission tomography *Phys. Med. Biol.* **27** 437–41

Crandall P and Cassen B 1966 High speed section scanning of the brain *Arch. Neurol.* **15** 163–71

Flower M A, Rowe R W, Webb S and Keyes W I 1981 A comparison of three systems for performing single-photon emission tomography *Phys. Med. Biol.* **26** 671–91

Floyd C E J, Jaszczak R J and Coleman R E 1987 Convergence of the maximum likelihood reconstruction algorithm for emission computed tomography *Phys. Med. Biol.* **32** 463–76

Geiger H and Walther M 1928 The electron counting tube *Phys. Z.* **29** 829–41

Genna S and Smith A P 1988 The development of ASPECT, an annular single crystal brain camera for high efficiency SPECT *IEEE Trans. Nucl. Sci.* **35** 654–8

Harper P V, Beck R M, Charleston D E, Brunsten B and Lathrop K A 1965 Three dimensional mapping and display of radioisotope distributions *J. Nucl. Med.* **6** 332

Jaszczak R J 1974 Line spread response for a scintillation camera and movable filter plate system *Phys. Med. Biol.* **19** 362–72

Jaszczak R J, Chang L-T, Stein N A and Moore F E 1979 Whole-body single-photon emission computed tomography using dual, large-field-of-view scintillation cameras *Phys. Med. Biol.* **24** 1123–43

Jaszczak R, Huard D, Murphy P and Burdine J 1976 Radionuclide emission computed tomography with a scintillation camera *J. Nucl. Med.* **17** 551

Jaszczak R J, Murphy P H, Huard D and Burdine J A 1977 Radionuclide emission computed tomography of the head with ^{99m}TC and a scintillation camera *J. Nucl. Med.* **18** 373–80

Keyes J W Jr, Orlandea N, Heetderks W J and Leonard P F 1976 The humongotron—a gamma camera transaxial tomograph *J. Nucl. Med.* **17** 552

Keyes J W, Orlandea N, Heetderks W J, Leonard P F and Rogers W L 1977 The humogotron: a scintillation-camera transaxial tomograph *J. Nucl. Med.* **18** 381–7

Knoll G F and Williams J J 1979 Application of a ring pseudorandom aperture for transverse section tomography *IEEE Trans. Nucl. Sci.* **245** 581–6

Kuhl D E and Edwards R Q 1963 Image separation radioisotope scanning *Radiology* **80** 653–62

Kuhl D E and Edwards R Q 1964 Cylindrical and section radioisotope scanning of the liver and brain *Radiology* **83** 926–35

Kuhl D E and Edwards R Q 1970 The Mark III scanner: a compact device for multiple-view and section scanning of the brain *Radiology* **96** 563–70

Kuhl D E, Edwards R Q and Ricci A R 1974 Transverse section scanner at the University of Pennsylvania *Tomographic Imaging in Nuclear Medicine* ed G S Freedman (New York: Society of Nuclear Medicine) pp 19–27

Kuhl D E, Edwards R Q, Ricci A R, Yacob R J, Mich T J and Alavi A 1976 The Mark IV system for radionuclide computed tomography of the brain *Radiology* **121** 405–13

Kuhl D E, Hale J and Eaton W L 1966 Transmission scanning: a useful adjunct to conventional emission scanning for accurately keying isotope deposition to radiographic anatomy *Radiology* **87** 278–84

Laird E E and Williams E D 1987 The optimum technique for 201T1 tomography of myocardium: an investigation using phantoms *Phys. Med. Biol.* **32** 985–99

Larsson S A 1980 Gamma camera emission tomography: development and properties of a multi-sectional emission computed tomography system *Acta Radiol. Suppl.* **363** 1–75

Mallard J R 2003 The evolution of medical imaging; from Geiger counters to MRI—a personal saga *Perspect. Biol. Med.* **46** 349–70

Mills J A and Delchar T A 1988 Origin of the false defect in longitudinal emission computed tomography of the left ventricle *Phys. Med. Biol.* **33** 969–73

Muehllehner G 1968 Radioisotope imaging in three dimensions *J. Nucl. Med.* **9** 337

Muehllehner G 1970 Rotating collimator tomography *J. Nucl. Med.* **11** 347

Muehllehner G 1971 A tomographic scintillation camera *Phys. Med. Biol.* **16** 87–96

Muehllehner G 1973 Radiation imaging device *US Patent Number* 3,745,345

Muehllehner G, Colsher J G and Stoub E W 1980 Correction for field nonuniformity in scintillation cameras through removal of spatial distortion *J. Nucl. Med.* **21** 771–6

Muehllehner G and Wetzel R A 1971 Section imaging by computer calculation *J. Nucl. Med.* **12** 76–84
Murphy P H, Burdine J A, Moore M, Jaszczak R J, Thompson W and DuPuey G 1978 Single photon emission computed tomography (SPECT) of the body *J. Nucl. Med.* **19** 683
Myers M J, Sokole E B and de Bakker J 1983 A comparison of rotating slant hole collimator and rotating camera for single photon emission tomography of the heart *Phys. Med. Biol.* **28** 581–8
Patton J, Brill A B, Erickson J, Cook W E and Johnston R E 1969 A new approach to mapping three-dimensional radionuclide distributions *J. Nucl. Med.* **10** 363
Potchen E J 2000 Reflections on the early years of nuclear medicine *Radiology* **214** 623–9
Rogers W L, Clinthorne N H, Shao L, Chiao P, Ding Y, Stamos J A and Koral K F 1988 SPRINT II: a second generation single photon ring tomograph *IEEE Trans. Med. Imaging* **7** 291–7
Rogers W L, Clinthorne N H, Stamos J, Koral K F, Mayans R, Keyes J W, Williams J J, Snapp W P and Knoll G F 1982 SPRINT: a stationary detector single photon ring tomograph for brain imaging *IEEE Trans. Med. Imaging* **1** 63–8
Silver S 1996 'Father of emission tomography' receives 1996 Cassen Prize [news] *J. Nucl. Med.* **37** 23N–24N
Stoddart H F and Stoddart H A 1979 A new development in single gamma transaxial tomography Union Carbide focused collimators scanner *IEEE Trans. Nucl. Sci.* **26** 2710–12
Tanaka E, Toyama H and Murayama H 1984 Convolutional image reconstruction for quantitative single photon emission computed tomography *Phys. Med. Biol.* **29** 1489–500
Todd-Pokropek A 1983 Non-circular orbits for the reduction of uniformity artefacts in SPECT *Phys. Med. Biol.* **28** 309–13
Webb S 1985 Comparison of data-processing techniques for the improvement of contrast in SPECT liver tomograms *Phys. Med. Biol.* **30** 1077–86
Webb S, Flower M A, Ott R J and Lech M O 1983 A comparison of attenuation correction methods for quantitative single photon emission computed tomography *Phys. Med. Biol.* **28** 1045–56
Williams J J 1979 Design and investigation of a circular ring emission tomograph *PhD Thesis* University of Michigan

Biography

Ronald J Jaszczak received his BS degree with High Honors from the University of Florida (UF) in 1964, ranking 4th in a class of 980. After receiving his PhD degree from UF in 1968, he was awarded an Atomic Energy Commission Fellowship at Oak Ridge National Laboratory. He remained there as a physicist until 1971, when he joined Searle Radiographics as a Research Scientist. He became Chief Scientist in 1977. In 1979, he was recruited to Duke University, and is currently a tenured Professor of Radiology and Biomedical Engineering. He has co-authored over 300 publications. He received the 2000 Paul C. Aebersold Award from the Society of Nuclear Medicine, and in 2004, the Outstanding Alumni Award from the University of Florida. He is a Fellow of the IEEE.