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REVIEW ARTICLE

The origins of SPECT and SPECT/CT

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Abstract Single photon emission computed tomography (SPECT) has a long history of development since its initial demonstration by Kuhl and Edwards in 1963. Although clinical utility has been dominated by the rotating gamma camera, there have been many technological innovations with the recent popularity of organ-specific dedicated SPECT systems. The combination of SPECT and CT evolved from early transmission techniques used for attenuation correction with the initial commercial systems predating the release of PET/CT. The development and acceptance of SPECT/CT has been relatively slow with continuing debate as to what cost/performance ratio is justified. Increasingly, fully diagnostic CT is combined with SPECT so as to facilitate optimal clinical utility.

Keywords Single photon emission tomography · SPECT · SPECT/CT

Introduction

Since the early introduction of radioactive tracers for use in medicine, there has been the desire to visualize the true distribution of the tracer and to quantify 3-D uptake in the body. It is therefore not surprising that emission tomography was explored at an early stage of nuclear medicine's development and continues to be one of the primary challenges in technological development. There is evidence of early research on transverse axial X-ray tomography in the 1940s and 1950s following on from even earlier work on focal plane X-ray tomography. It was, however, in the 1960s and 1970s that single photon emission computed tomography (SPECT) developed to the stage of being clinically applicable and more widely available as a commercial product, along with both X-ray computed tomography (CT) and positron emission tomography (PET) (and magnetic resonance imaging, MRI) (Table 1). It is of course a misnomer to include 'computed' at a time that predates the use of computers for reconstruction; early reconstruction was achieved using optical methods. The term 'SPECT' was introduced at a later date, and in some cases the method was referred to as single photon emission tomography (SPET).

The development of clinical SPECT has involved much innovation, but in practice the emphasis has largely been on designing a flexible instrument with broad clinical application for both planar imaging and SPECT. Inevitably this has resulted in certain constraints on design, somewhat different from the parallel development of PET, which has traditionally involved dedicated tomographic instruments (with exception of very early coincidence counting systems). The combination of modalities into a single multimodality instrument occurred much more recently, with SPECT/CT being commercially introduced slightly ahead of PET/CT. Once again the need to provide a flexible and low-cost instrument, until recently, has tended to dominate this development. This article tracks the development of SPECT and its later integration with CT. Readers may be interested in other general articles on SPECT and SPECT/CT [1–4] and in particular the excellent comprehensive historical coverage in *From the Watching of Shadows* by Webb [5].

Early pioneers

There is no doubt that Kuhl and associates made a significant impact on the early development of emission tomography. They undertook early research based on pioneering work in X-ray tomography to explore stereoscopic acquisition as well as multiview angled acquisition to achieve focal plane tomography (see section Focal plane tomography). But it is

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Table 1 Timeline for the development of SPECT and SPECT/CT

Year	Description	References
1958	Invention of the gamma camera	[10]
1963	First SPECT system described	[6]
1966	First transmission scan	[7]
1967–74	SPECT using a rotating chair	[11–13]
1968–72	Early focal plane emission tomography	[19, 22, 24]
1970–73	Clinical SPECT using translating detectors	[8, 9]
1973–75	First clinical studies using CT leading to the first commercial CT system	[125, 126]
1977–80	SPECT using a rotating gamma camera	[15, 16, 17]
1977–83	First description of Compton cameras	[79–81]
1978–79	Development of Cleon/Harvard brain scanner	[33–35]
1980–86	Various dedicated brain SPECT systems: SPRINT, Tomomatic, Headtome	[37, 38, 41, 43]
1984–87	Transmission scanning using a flood source	[97, 98, 100, 101]
1990–92	First SPECT/CT designs	[111, 112]
1992–93	Early simultaneous emission/transmission: scanning line source	[105, 107]
1999	First commercial SPECT/CT: Hawkeye	[114]
2009–10	Commercial CZT-based cardiac SPECT	[54, 55, 57, 58]

their development of SPECT designs based on linear motion of probe systems at each of a set of projection angles that truly introduced SPECT [6] (Fig. 1b), a development that essentially foreshadowed the initial single-slice CT (see Webb [5] for details of the early work of Kuhl and associates based on personal communication received in 1989). Reconstruction involved back projection without filtering based on optical techniques, and so the initial images had poor contrast, but their work included the first-in-man tomographic studies (transmission and emission acquired simultaneously [7]). Initially a scanning dual probe system was designed but this was later extended to the use of multiple probes [8]. A similar transverse tomography single-slice device was built in Aberdeen, UK (Fig. 1c) and was used for early brain SPECT studies [9]. These systems were the predecessors of many dedicated brain imaging systems that evolved in the subsequent decades (see section Other early novel designs). However the introduction of the gamma camera [10] in many respects formed the basis for clinical SPECT, and it continues today to be the most widely used system.

Initially tomographic acquisition on a gamma camera was achieved by rotating the patient in front of a stationary camera, a technique still used on one commercial cardiac imaging system. This method was introduced by Anger (Fig. 1a) in 1968 at the Donner Laboratory [11] and then continued in the same laboratory by Budinger and Gullberg [12] and colleagues, as well as Muellehner in Philadelphia [13]. The Donner Laboratory researchers were also noted for their early development of reconstruction algorithms, developing the widely used open-source RECLIB library [14]. It was not until 1977 that Keyes and colleagues in Michigan demonstrated the first rotating gamma camera [15]. This was accompanied by the first commercial rotating-camera SPECT system developed by Jaszczak and colleagues at Searle Radiographics (formerly Nuclear Chicago and subsequently Siemens Gammasonics) in conjunction with staff at Baylor College of Medicine [16], initially for dedicated brain imaging and later for whole-body application. Similar pioneering work was undertaken by Larsson with the introduction and evaluation of the cantilever design popularized by GE in the early 1980s (Fig. 1d). The lengthy treatise on SPECT by Larsson in 1980 [17] demonstrates the already highly developed understanding of SPECT at that time. There were many problems associated with early SPECT systems as the requirements for stringent quality control and robust rotation were not fully understood. Early systems suffered from variability in camera performance with rotation, imprecise rotation with unstable centre-of-rotation and inadequate planar uniformity. Unfortunately, these led to an early lack of confidence in SPECT and contributed to rather slow acceptance of SPECT as part of standard clinical practice. Fortunately, gamma camera performance and stability have improved and sturdy, reliable gantries are typical of current SPECT system designs (Fig. 1e, f).

Clearly a single gamma camera has limited sensitivity and so several suppliers developed multidetector systems that involved three (or four) detectors arranged so as to have a variable radius to accommodate whole-body or brain SPECT (initially introduced by Trionix, Picker and Toshiba). These systems were essentially dedicated SPECT systems rather than general purpose planar/SPECT systems, and they proved particularly useful for brain SPECT as detectors could be rotated quite close to the head. Fast dynamic acquisition could also be achieved, a feature lacking in more recent dual head systems. Although

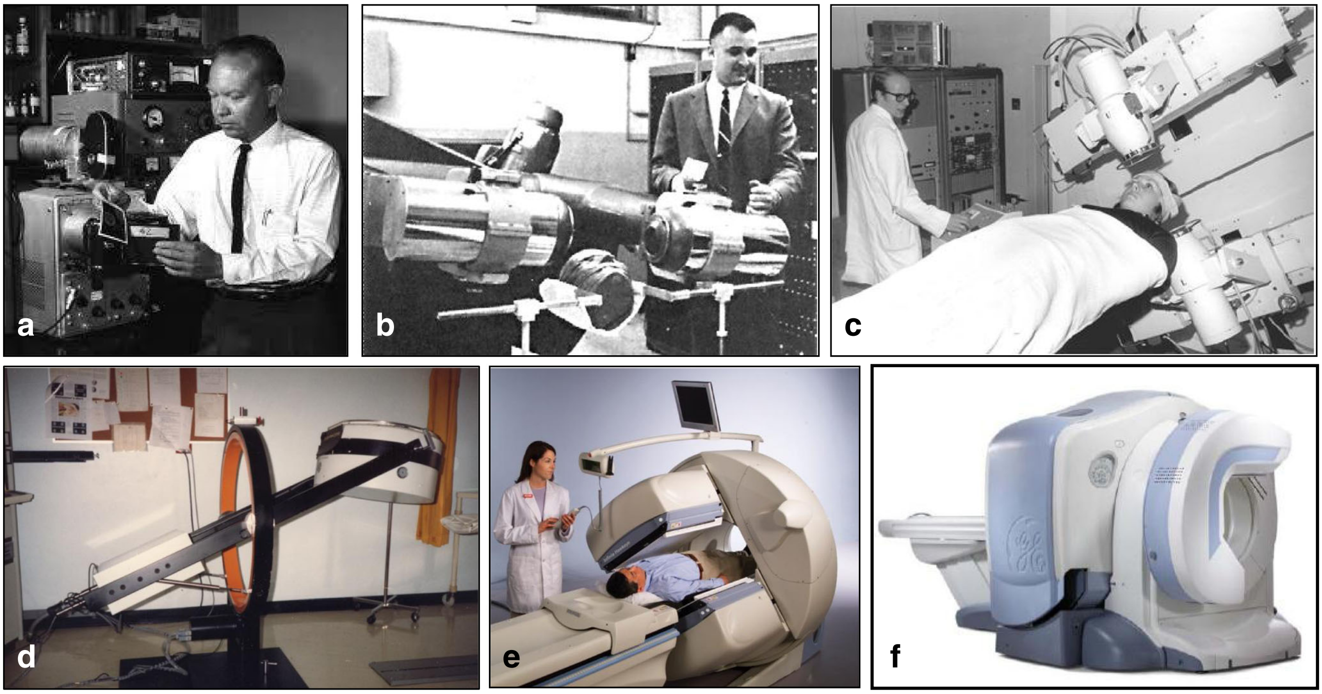

Fig. 1 The evolution of SPECT. **a** Hal Anger, inventor of the gamma camera (1958) and other tomographic systems (1967) [10, 19]; **b** David Kuhl with an early tomographic scanner (1968) [6, 8]; **c** Ian Keyes with the Aberdeen section scanner (1972) [9]. **d** The original cantilevered GE 400 T SPECT system (1983) [17]; **e** GE dual head Infinia Hawkeye (2006); **f** GE Discovery NM530c (Alcyone) with diagnostic CT option (2009). Dates are approximate

popular at the time, these were superseded by dual detector systems that offered more flexibility in detector position, less opportunity for truncation and more general application. These proved particularly popular when positioned at right angles for 180° cardiac tomographic acquisition.

The dramatic early development should not be underestimated as the early pioneers established much of the methodology that remains today. The development of fast computer algorithms (e.g. the fast Fourier transform) and the introduction of the first computers into medical imaging in the early 1970s certainly acted as a stimulus for image reconstruction, which previously had to be performed by optical techniques. The introduction of filtered back projection as a standard technique for CT reconstruction was readily adopted as the standard approach to reconstruction in SPECT and PET. This replaced earlier time-consuming algebraic iterative methods which at the time overstretched the capability of state-of-the-art computers and tended to be limited to university settings where large mainframe computers were installed. Ironically iterative reconstruction techniques such as maximum likelihood reconstruction using ordered subsets (OSEM) [18] are now in widespread use, not only for SPECT and PET but also for CT.

Focal plane tomography

One line of development followed the principles established in earlier work on X-ray longitudinal tomography (so-called focal plane tomography). This relies on imaging one plane in focus while other planes above and below the selected plane are out of focus. Clearly this is not true tomography since out of focus information is not removed. Nevertheless the technique does enhance contrast in the selected plane and is a technique still routinely used in diagnostic radiology. The rectilinear scanner fitted with a focused collimator was inherently tomographic and had to be carefully positioned so as to exploit this feature. Anger further developed the rectilinear scanning technique, replacing the detector with a small Anger-type camera with focused collimator [19]. By using selected degrees of magnification and compensation for projection position on the detector, the acquired data could be transformed after acquisition so as to enhance a set of planes rather than a single focal plane. The instrument formed the basis of the Searle Phocon commercial system which became popular for whole-body bone imaging. A similar device was also constructed in Aberdeen by Myers et al. [20].

Other focal plane systems were designed by McAfee et al. [21] based on the use of a slant-hole collimator in combination with camera translation, and by others including Walker [22], Freedman [23] and Muellehner [24, 25] using various designs that involved rotation of a slant-hole collimator, with or without combined movement of detector or bed. Many of these designs have similarity to early longitudinal tomographic X-ray designs but their use tended to be limited, lacking the flexibility and superior tomographic capability of a rotating gamma camera.

Two additional early approaches to focal plane tomography have been further developed more recently to enable true tomography (best described as limited angle tomography). The first of these was the use of multipinhole imaging using a stationary large-field gamma camera, popularized for cardiac imaging in the late 1970s [26]. The multiple views obtained by the multiple pinholes were simply recombined using various degrees of magnification and translation so as to digitally enhance selected planes in the heart. A similar stationary multipinhole system forms the basis of the recently introduced GE Discovery NM530c (Alcyone; see section Organ-specific systems), except that full tomographic reconstruction is now employed rather than focal plane transformation. Multipinhole designs have had particular appeal in preclinical imaging where magnification can be used to advantage to achieve outstanding resolution [27]. Coded aperture imaging was also originally used as a means of achieving focal plane tomography, a technique that continues to be of interest to the research community. The early use of Fresnel zone plates and associated optical decoding [28] had limited success but did stimulate other approaches to image encoding including time-varying coded apertures used in Michigan [29, 30].

Other early novel designs

There were many other innovative SPECT designs explored during the early years of development and, interestingly, some of the ideas used underpin more recent developments. Brill and Patton and the group at Vanderbilt initially developed single-slice multiprobe systems, but one innovation was the rotation of each probe around its axis [31, 32], similar to the acquisition geometry of the recent D-SPECT system based on cadmium zinc telluride (CZT) (see section Organ-specific systems). A further innovation detectors from the same group at Vanderbilt [33] was the design of a multiprobe system (with focused collimators) where the probe was moved in a rectilinear fashion, translating towards the patient rather than simply performing a linear motion at each projection angle. The so-called Orthoscanner formed the basis of the Cleon commercial system (Union Carbide) [34, 35], which was later further developed at Harvard [36] and marketed by Strichman. The Cleon system, designed specifically for brain imaging, produced impressive images, even by today's standards. Like so many innovative systems it initially lacked the computer power to support the complex reconstruction that is now possible.

Several other groups have a long history of development of SPECT systems. It is clear that systems designed for a specific application can yield optimal performance and early development focused particularly on brain SPECT. Of particular note was the development at Michigan of a range of scanners designed by Rogers and colleagues. The development extended their early work with coded apertures for focal plane imaging to incorporate these in full-ring tomographic systems. But subsequent work instead involved the introduction of slit-slat collimators (combination of parallel slats in the axial direction and a slit which acts as a pinhole in the transaxial direction) [37, 38]. Slit-slat collimators continue to be of interest in current SPECT designs for use in brain and breast imaging [39, 40]. The Michigan group continued to explore SPECT development using Compton cameras (see section Current SPECT design concepts).

Other early commercial brain SPECT systems included the Tomomatic marketed by Medimatic specifically for cerebral blood flow studies [41] with a design similar to Kuhl's Mark IV scanner. Further innovative designs originated from Genna and Smith [42] who used an annular detector with a rotating multisegment collimator; this was marketed as Ceraspect by Digital Scintigraphics. In Japan the Headtome was developed as a dual purpose SPECT and PET system, and formed the basis for a series of brain imaging systems developed in conjunction with Shimadzu [43]. Hitachi also developed a dedicated brain SPECT system based on four gamma cameras [44]. A further group that deserves specific mention is the laboratory of Barrett in Arizona, the source of many novel ideas for tomographic system designs. Early work included the use of coded apertures for the FastSPECT system [45], a stationary system designed for dynamic brain studies that was later adapted for preclinical imaging. The group has continued to develop a range of innovative systems for both human and preclinical imaging (see later sections).

Organ-specific systems

It is notable that many of these dedicated SPECT systems were designed specifically for use in brain studies, an area in which significantly improved performance can be gained. Unfortunately, in most centres the referral rate for brain studies has never reached sufficient numbers to warrant dedicated technology, except for specialist units that have focused on brain research using single photon emitters. In the research setting PET has evolved as the more attractive technology for this purpose, particularly with the range of ligands suitable for receptor studies. Consequently there has been insufficient demand for brain-only SPECT to sustain the market. Recently other organ-specific SPECT systems have attracted greater market interest, especially for use in cardiac perfusion imaging. Dedicated breast scanning SPECT systems are also showing promise (see for example Brzymialhiewicz et al. [46]) but have not yet reached widespread use.

Nuclear cardiology has become an important sector in the application of nuclear medicine with relatively large referral rates that justify dedicated equipment. In recent years there has been an explosion in systems specifically designed for cardiac use including small field-of-view cameras (e.g. GE Ventri), specialized collimators (e.g. Siemens IQ SPECT), desktop stationary systems that embody small rotating detectors (e.g. Cardiodesk) and specialized systems of novel design (several papers review the options [47–50]). These include DigiRad's system that uses a stationary detector with rotating chair [51], reminiscent of the early methods developed by Anger and others. The system is compact using CsI detectors and solid-state pin-diode readout. The same detectors are also used for transmission imaging (see section Transmission scanning). One system (CardiArc) has been designed based on a rotating slit-slat design similar to that used in the SPRINT systems from Michigan, although this development largely continues in a research environment [52].

Two systems have been commercially released based on CZT technology (Fig. 2) where the appeal is that compact design can be achieved with significantly improved energy resolution compared to sodium iodide, well suited to multi-radionuclide studies [53]. The GE Discovery NM 530c (Alcyone) uses 19 separate multi-element detectors (8 × 8 cm), each with a pinhole collimator centred on a common region that encompasses the heart [54, 55]. This approach follows a recent resurrection of human multi-pinhole imaging [56]. The system permits acquisition of high-quality cardiac perfusion studies in roughly one-third of the time required by a conventional dual detector SPECT system. The 3-D reconstruction models the exact system geometry accounting also for the system resolution.

The D-SPECT system (originally developed by Spectrum Dynamics) also uses similar CZT technology, in this case using nine 4 × 16cm multi-element detectors, each programmed to rotate on its axis [57, 58]. In this case the detectors can be programmed to preferentially acquire from a preselected subvolume containing the heart. Similar performance gains are achieved to that demonstrated by the Alcyone. Both the GE and Spectrum Dynamics systems facilitate dynamic acquisition taking advantage of the high count-rate capability of CZT. Using region-centric acquisition, the D-SPECT can acquire dynamics at 3–6 s per frame. In the NM 530c the detectors are stationary so that any temporal sampling rate can be selected. It is interesting that all four of the above novel systems have some resemblance to very early system designs (see Fig. 3).

Current SPECT design concepts

There are some aspects of SPECT design that are of continuing interest and that may influence future development. The concept of 'adaptive' SPECT has been introduced by Barrett et al. [59], the aim being to design systems that not only can be adapted to different applications but also may be adapted to an individual and even the measured count-rate and projected counts in real time. The system design can be quite complex and demands extremely fast processing in order to obtain immediate feedback (see for example Freed et al. [60] and Moore et al. [61]). The D-SPECT is to some extent such a system since the detectors can be programmed to acquire for specific times over a selected range of angles predetermined during a scout scan. There is scope for further exploitation of this approach.

In addition to the adoption of CZT, there are other new technologies that are impacting on instrument design, especially solid-state readout systems (see Pichler and Ziegler [62]). The recent motivation for much of this development has been the search for components that can operate in a magnetic field and so are well suited to the development of PET/MRI. The options for solid-state readout include pin diodes (PD), avalanche photodiodes (APD) including position-sensitive devices (PSAPD) [63], silicon photomultipliers (SiPM) [64, 65] and silicon drift detectors (SDD) [66, 67]. In the case of SPECT there has also been recent interest in the combination of SPECT and MRI, particularly in the preclinical community, and so there has been interest in alternative SPECT components that

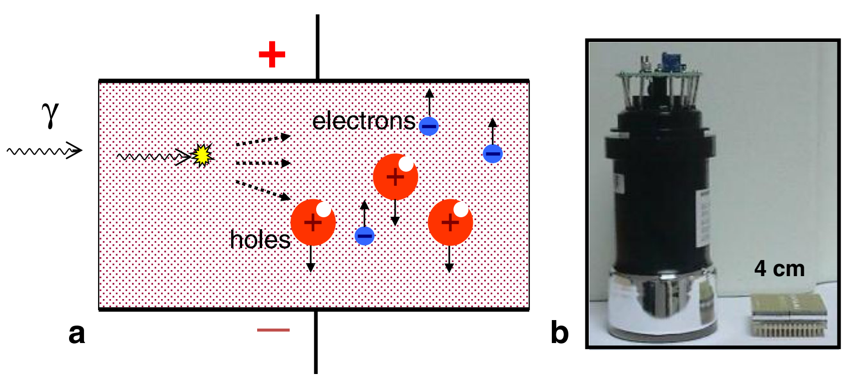

Fig. 2 Cadmium zinc telluride (CZT) operation. **a** Gamma radiation interacts to create electron–hole pairs that are attracted to the anode and cathode, resulting in direct electrical signal. **b** Compact system design is possible due to the small size of a CZT array compared to the photomultiplier tubes used in conventional gamma cameras [53]

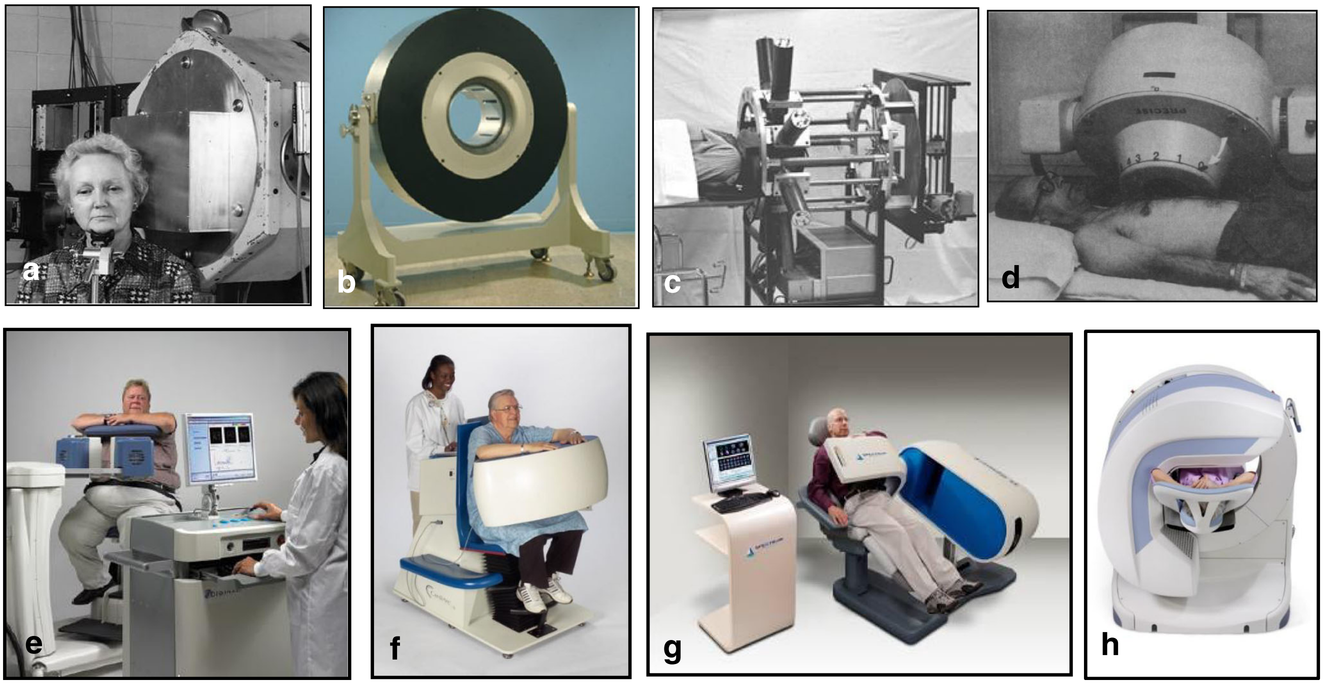

Fig. 3 Back to the future: original innovations (**a–d**) with recent related 'reinventions' (**e–h**). **a**, **e** Rotating patient (**a** Donner Laboratories, 1974 [12]; **e** Digirad system, 2010 [51]). **b**, **f** application of slit-slat collimation (**b** SPRINT, Michigan, 1982 [37, 38]; **f** CardiArc system, 2009). **c**, **g** use of rotating detectors (**c** Tomoscanner, Vanderbilt, 1969 [31]; **g** Spectrum Dynamics D-SPECT, 2009 [57, 58]). **d**, **h** Systems with multi-pinhole collimators (**d** Seven-pinhole, Denver, 1978 [26]; **h** GE Discovery NM530c, 2010 [54, 55]). Dates are approximate

could support this potential application. As in the case of PET, these developments can influence the overall strategy in SPECT design rather than being simply of benefit to the specialized application. Preclinical SPECT inserts have been designed using CZT [68, 69] necessitating correction for magnetic field effects on CZT performance. The choice of readout system best suited to SPECT is, however, a topic of continuing debate The SiPM (Fig. 4a) has rapidly gained in popularity in recent years, especially for potential use as a suitably fast readout for PET, with superior timing capability to conventional photomultiplier tube readout. For single photon emitters the main obstacle is increased readout noise due to the lower number of light photons produced by low-energy emission (e.g. 140 keV). SDDs (Fig. 4b) are relatively slow and so not well suited to the high count-rates and fast timing required for PET. However, they have low electronic noise and high quantum efficiency without the need for amplification and so have superior signal to noise characteristics for the lower energy emissions of relevance to SPECT. Multiple SDDs have recently been tiled for use on medium-sized detectors (10×10 cm) [70] and they are currently being investigated as candidates for future MRI-compatible SPECT systems [71] (FP7 INSERT project 305311) although optimal performance may require cooling. Further efforts to design detectors with superior intrinsic resolution have included experimentation with charge-coupled devices (CCD) similar to those used in modern compact optical cameras (e.g. electron multiplying CCD) [72–74]. To date, however, these efforts have largely been focused on potential preclinical and ex-vivo detectors for very low-energy emitters (e.g. ^{125}I).

The adoption of solid-state detectors and/or readout enables design of future detectors with improved intrinsic spatial resolution compared to that of the current gamma camera. The problem is that this improvement yields minimal impact if these detectors are combined with conventional parallel-hole collimators. Alternatives must be found. An approach, suggested again by the group in Arizona [75] and developed also at Utrecht [76], is to use detectors with high intrinsic resolution in combination with multiple pinhole collimators placed relatively close to the detectors. This involves minification (rather than the more commonly expected magnification) which results in improved sensitivity, while maintaining system resolution to a level that is similar to or marginally better than that of conventional SPECT systems. Much of this work has been motivated by the successful development of high-resolution multi-pinhole systems for preclinical SPECT [77, 78], a topic beyond the scope of this review. The compact design and robustness of solid-state systems makes these attractive as components for organ-specific applications and provides freedom in geometry well suited to adaptive systems. Clearly the compact design is essential for insertion inside a magnet, which now appears to be possible.

The ultimate goal would be to remove or replace the conventional SPECT collimator to improve sensitivity. The

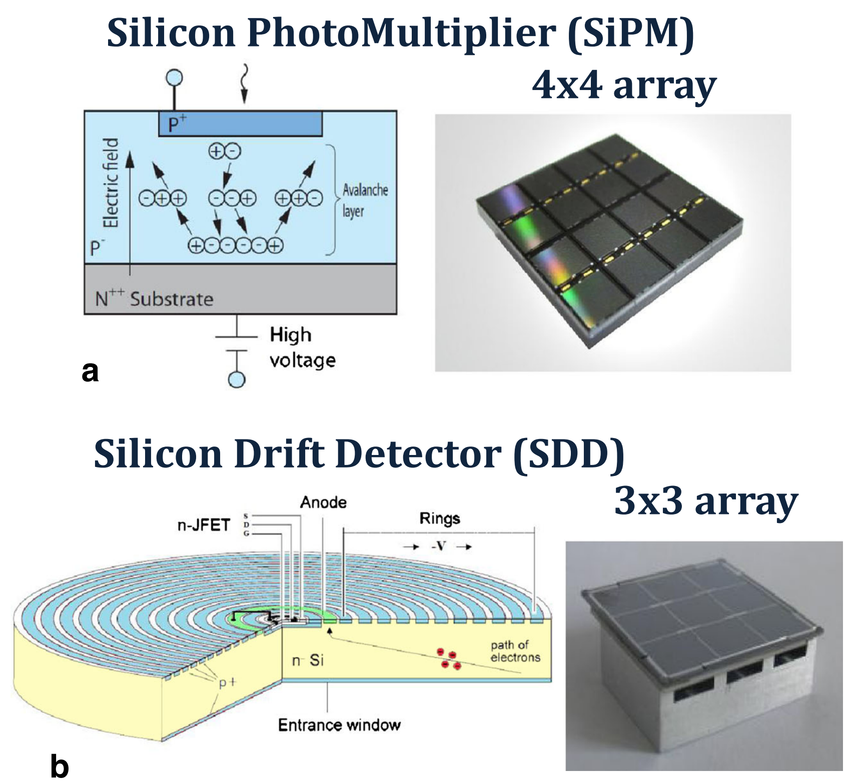

Fig. 4 Solid-state readout options for SPECT. **a** The silicon photomultiplier (SiPM) is effectively an APD operating in Geiger mode [64, 65]. **b** Silicon drift detector (SDD) collects charge at a central anode resulting from light photons detected within the sensitive silicon volume [66, 67]

Compton camera was suggested many years ago as a means to achieve this [79] and considerable early development of 'electronic collimation' was undertaken by Singh and colleagues [80, 81], who demonstrated potential gains in signal to noise ratio at moderately high energies. The principle (Fig. 5) is to use a second high-energy resolution solid-state detector such as silicon in place of the collimator, measuring the deposited energy that results from Compton interaction of a photon in the detector so that the angle of the incident photon can be estimated. Knowledge of this angle in combination with the position of the photon detected in the primary detector indicates the probable location of the emitted photon which can be accounted for during reconstruction. The group at Michigan have undertaken extensive research in developing a Compton-based ring camera (C-SPRINT) [82] and the interested reader will find the discussion of Rogers et al. [83] particularly useful to gain an insight into the potential of and issues concerning Compton systems.

There has always been considerable promise in Compton imaging as significant sensitivity gains have been demonstrated in simulation studies, but unfortunately, particularly at the lower photon energies of clinical interest, the uncertainty associated with measurement due to geometric effects, electronic noise and physical effects (e.g. Doppler broadening and polarization) places considerable demands on both the instrument design (need energy resolution <1 keV) and reconstruction algorithm. An approach that some groups have explored more recently is to use miniature cloud chambers to measure the direction of the recoil electron that is a byproduct of the Compton interaction so as to reduce uncertainty in the photon origin [84, 85]. An interesting possible development is the use of a PET detector ring in combination with Compton detection of single photons (see Rogers et al. [83]); this could be used to augment PET

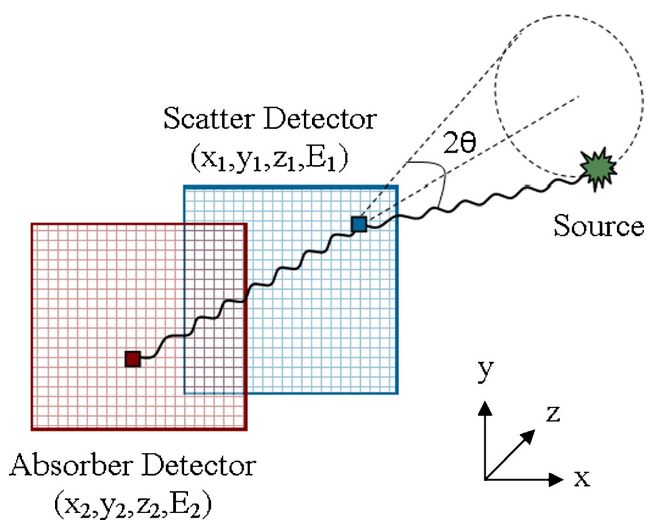

Fig. 5 The Compton camera. Photons are Compton scattered in a high-energy resolution solid-state detector, recording the location of interaction and energy deposited, which reflects the angle of scatter (θ). When the scattered photon is detected in the primary absorber detector the origin of the emitted photon can be estimated as lying somewhere on the surface of a cone of aperture 2θ. This information can be used during reconstruction

coincidence detection. The performance of Silicon detectors has improved in recent years [86], so perhaps this work will ultimately lead to future clinical systems that eliminate the conventional collimator. For an excellent review of detector technology applicable to SPECT instruments see Peterson and Furenlid [87]. This includes a discussion of alternative detector materials (scintillators and semiconductors) that are not discussed here (see also Moses and Shah [88]).

As image reconstruction algorithms have improved and computers get faster every year there has been considerable attention given to improving the system model that describes the emission and detection process, applicable to any desired SPECT geometry. This has led to considerable innovation in design of collimators and system geometry. Examples include the multifocus collimator used in the IQ SPECT system (Siemens) [89], the rotating slat collimator that acquires plane integrals instead of line integrals with appropriately altered reconstruction algorithms [90–92], and many variations on multipinhole and multiple slant-hole designs [93, 94] that provide multiple views from a single camera orientation. In general, iterative reconstruction can adapt to virtually any system geometry, within the constraint that sufficient sampling is used. Despite the high volume of published work many innovations fall short of clinical implementation; possible reasons are the marginal benefits demonstrated compared to conventional SPECT acquisition, lack of general availability of specialized reconstruction software and the substantial validation work required prior to commercial release.

Transmission scanning

It is not the purpose of this article to include a historical review of CT, so coverage is limited to developments leading to the ultimate use of SPECT/CT as an important dual modality device. We distinguish transmission scanning from X-ray CT, the former being based on the use of an external radionuclide as a transmission source rather than X-rays. See Bailey [95] for an excellent overview of transmission scanning in emission tomography which includes its historical development. Transmission scanning for the purpose of attenuation correction has for many years been an important component of PET, especially as direct correction for PET attenuation was recognized at an early stage of development as being straightforward, involving multiplicative correction of projections prior to reconstruction (although more recently corrected as part of the system model using iterative reconstruction). It was this capability that earned PET its reputation as a quantitative technique. Transmission scanning was used for estimating body contours in planar studies at an early date in rectilinear scanners and early gamma cameras. It proved useful in correction for attenuation in quantification of whole-body uptake using dual opposed planar acquisitions [96] and is still used for this purpose in serial whole-body studies used for estimation of internal dosimetry.

Transmission tomography was demonstrated by Kuhl et al. [7] prior to the introduction of X-ray CT using an ^{241}Am source. However, first reports of the use of a ^{99m}Tc flood source were not published until the mid 1980s [97–99]. In fact a little-read paper by Morozumi et al. (in Japanese) predates these papers [100]. The use of ^{99m}Tc precluded simultaneous emission/transmission acquisition, but the introduction of ^{153}Gd by Bailey et al. facilitated the first combined imaging, albeit requiring correction of downscatter from the emission source [101]. Incorporation of the measured attenuation in reconstruction is not straightforward, especially in the case of inhomogeneous attenuation and at the time iterative algorithms were too slow for clinical use. This motivated the development of efficient iterative reconstruction algorithms culminating with the development of OSEM [18]. This was followed by the development and subsequent commercial release of a range of transmission solutions that included multiple line sources (Siemens) [102], a high-energy source that penetrated the collimator (Picker's Beacon) [103, 104], a rod source and fanbeam collimator implemented on a triple head system [105, 106] and the scanning line source (adopted by ADAC, Elscint, GE Healthcare, Picker and SMV) [107]. The scanning line source (Fig. 6a, c) used both spatial and energy discrimination to separate emission and transmission data, significantly reducing the amount of downscatter. A further development of a scanning point source in combination with a fanbeam collimator, which adopted a similar strategy with further reduced downscatter, was not commercialized [108]. These systems were offered as options on the range of gamma cameras available at the time and led to recommendations by ASNC and SNM for attenuation correction to be adopted as a standard procedure for cardiac perfusion SPECT [109]. Despite these directives, transmission scanning failed to be universally accepted, partly due to deficiencies in the commercial devices and associated reconstruction software that were sold. The limitations were clearly exposed in a paper by O'Conner [110] in which results were reported for data acquired on several commercial transmission systems. Virtually all systems had identified artefacts in the SPECT reconstruction with the exception of the Hawkeye (SPECT/CT) which compared favourably with PET/CT.

The beginnings of SPECT/CT

Around the same time as the development of SPECT transmission, the group led by Hasegawa at UCSF described

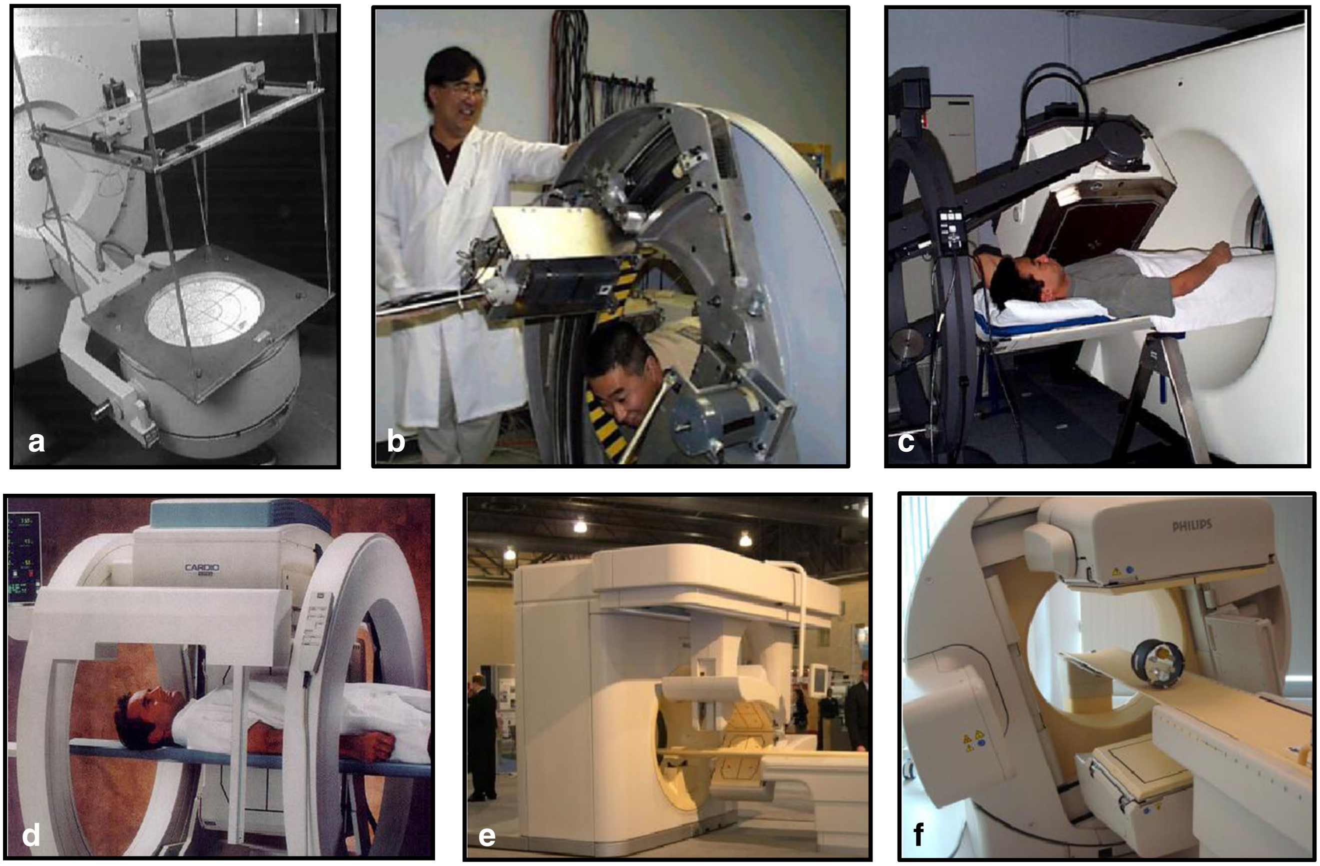

Fig. 6 Development of transmission scanning and SPECT/CT. **a** The original scanning line source in Sydney (1992) [104], **b** the late Bruce Hasegawa (UCSF) with the first prototype SPECT/CT (1992) [108, 109]; **c** the UCSF combined use of SPECT and CT (1996) [110]. **d** ADAC's implementation of the scanning line source (1996); **e** the ADAC/Philips SKYLight system attached to a diagnostic CT gantry (2005); **f** the Philips Brightview flat panel system (2009) [116]

designs for a proposed combined SPECT/CT scanner [111, 112] (Fig. 6b). This system was never used for patient studies, but the UCSF group later published work in which a third-generation CT scanner was used for cardiac attenuation estimation in conjunction with an adjacent gamma camera [113] (Fig. 6c), a technique at the time considered by some as total overkill for the solution of attenuation correction. Yet this was to herald the introduction of dual modality imaging as known today! The commercial interest in attenuation correction at that time was further motivated by the introduction of gamma camera based coincidence imaging which for a brief time offered a low-cost solution for everyday PET. These systems would require transmission measurement so as to permit attenuation correction but would not support rotating rod sources as used in PET systems at that time. The SPECT/CT prototype developed by Hasegawa and colleagues formed the basis for the development of the first commercial SPECT/CT system, introduced by GE as the Hawkeye in 1999, predating the commercial introduction of PET/CT the following year. The Hawkeye system used a low-cost dental X-ray tube to provide low-dose CT, with a slow rotation speed (25 s) and thick single slice acquisition (1 cm) [114]. As a result CT acquisition was relatively slow for the axial extent covering the heart, let alone more extensive whole-body surveys. Note that this is in contrast to the CT system introduced with PET, which was a standard fully diagnostic system. Despite these limitations good low-contrast object detectability (contrast to noise ratio) was demonstrated at low doses using this system, better than could be achieved with a conventional CT system operating at similar dose levels [115].

The original Hawkeye was later upgraded to a four-slice system and more recently fully diagnostic CT options have become available (with 16-slice or 64-slice options). In the more recent years further SPECT/CT systems have been released with a range of CT capabilities. For example, Siemens offered the Symbia system, initially offering a basic one-slice system with options of additional slices that now include a 16-slice option. Phillips initially offered a fully diagnostic CT system coupled with their SKYLight system which involved mounting dual gamma cameras on the main CT gantry (Fig. 6e). A similar SKYLight system was combined with a standard older generation CT system by installing a bed that could move on rails between the CT and SPECT systems, demonstrating that a low-cost installation could be implemented [116]. Given the relatively low utility of the CT systems compared to a clinical diagnostic radiology installation there is opportunity for more cost-effective solutions that include sharing a single CT system across several SPECT systems [117].

The uncertain role of CT in combination with SPECT has been very much reflected in the vendor attitude to product development. Understandably, a balance between cost and utility has had to be met. With technical developments in the last decade fully diagnostic multislice CT integrated with SPECT is now available from most vendors. Also innovative low-cost CT technology including flat-panel detectors have been introduced. As mentioned above, the DigiRad system acquires emission and X-ray transmission sequentially using the same detectors with only slight detector adjustment to account for the transmission source geometry [118]. The rotation of the patient for the transmission scan reproduces techniques originally introduced in X-ray tomography in the 1940s and 1950s (see Webb [5] for historical details). Detector technology has been more recently improved to provide very good energy resolution (7.5 %) and spatial resolution with very low radiation doses [119], providing a practical low-cost solution specifically for cardiac attenuation correction.

Philips has introduced a flat-panel X-ray detector for cone-beam CT acquisition [120], which conveniently attaches to the SPECT gantry (Fig. 6f) and produces good contrast images with isotropic voxels, well suited to the angular reorientation commonly used in nuclear medicine. The system offers sufficiently fast rotation to permit breath-holding (12 s). Alternatively a slower acquisition (60 s) can be selected for cardiac attenuation correction to permit averaging during shallow breathing, which can avoid the problematic respiratory mismatch between SPECT and CT that occurs with breath-hold CT. The system produces high-resolution subvolume CT reconstruction that is particularly well suited to the imaging of small bones, an area in which localization of focal tracer uptake is important.

There has been continuing controversy as to the level of CT that is required to complement SPECT, some arguing that the low resolution of SPECT should only warrant lower performance CT. Increasingly, however, this opinion is being over-turned. There is a case for designing low-cost systems specifically for attenuation correction, especially in the case of cardiac-specific SPECT systems where attenuation correction is strongly indicated [109]. The geometry of these systems is not always amenable to incorporation of a CT tube and detector, and alternative approaches to attenuation correction based only on emission data may be possible [121, 122]. It was really the introduction of PET/CT that demonstrated the need for high-quality fast-acquisition CT, not only for attenuation correction and localization but as a part of a truly diagnostic dual modality system, in which the combination of modalities has been clearly demonstrated to be clinically worth more than the sum of the parts [123, 124]. This led to a rapid acceptance of PET/CT as the system of choice, replacing PET-only devices. The transition for SPECT/CT has been much more gradual, reflecting the less-frequent use of SPECT and the broader use of SPECT systems for both planar and tomographic studies. This has been further reflected in the initial trend to introduce low-cost, low-performance CT systems rather than state-of-the-art systems, recognizing the difficulty in justifying cost given the limited clinical demand, but also conscious of the additional radiation burden. Unfortunately, this probably contributed to the initial slow acceptance of SPECT/CT with non-diagnostic CT being used solely for attenuation correction and/or general localization rather than for providing a truly complementary diagnostic modality. There is, however, growing acceptance of the merits of SPECT/CT and growing confidence in the quantitative accuracy that can be achieved in SPECT utilizing CT information (see following article).

So what is the future of SPECT/CT? It is clear that SPECT imaging provides better contrast than planar imaging and an opportunity to quantify in-vivo activity distribution. The inherent difficulties in interpreting SPECT are very much improved with CT localization, and there is a clear trend towards using SPECT/CT for a wider range of applications. SPECT studies continue to be more time-consuming than planar studies, and so reduction of acquisition time is a definite goal of suppliers, achieved either by improving system sensitivity or introducing more sophisticated reconstruction algorithms to control noise (potentially taking advantage of prior information provided by CT). It is conceivable that SPECT/CT acquisition could replace planar imaging, provided that patient throughput is maintained and diagnostic capability enhanced or at least maintained. As in past years, the area of focus for nuclear medicine studies changes; major developments in disease classification and treatment can shift the emphasis in practice, e.g. anticipated needs in dementia. The recent technological developments are well suited to organ-specific imaging with potential to provide enhanced performance, adapted to the imaging task. Of course, optimal SPECT designs are not always well suited to integration with CT and compact systems suitable for mobile application may have to be used in isolation. The collimator continues to be the main barrier to progress, but despite efforts to develop electronic collimation, a major breakthrough in this technology is unlikely. Multipinhole collimators in combination with high intrinsic resolution show greater potential. The possibility to acquire dual or multiple radionuclides continues to provide SPECT with a major advantage over PET, although this capability is not widely exploited. Dynamic SPECT may see some resurgence in interest for kinetic studies that formed the basis for much earlier planar studies. Indeed this may also stimulate interest in re-evaluating tracers that were deemed unsuitable for static imaging due to their unsuitable pharmacokinetics. Accurate attenuation correction (via CT) is important for quantification in such studies. There is little doubt that, in the foreseeable future, demand for SPECT/CT is likely to be maintained.

Summary

My hope is that this article stimulates admiration for the early pioneers who developed SPECT and SPECT/CT, and who had the vision for how this could impact on clinical practice. Since the earliest demonstrations by Kuhl and colleagues, there have been many innovative developments, and there continue to be advances that take advantage of new technology. In 30 years since the commercial availability of the first rotating camera SPECT systems there has been significant progress in the reliability and performance of available systems and increasing use in a wide range of applications. Continuing improvements in detector technology offer further scope for future novel system designs, particularly for organ-specific or adaptive applications, although ultimate performance continues to be largely limited by physical collimation. SPECT/CT was introduced commercially in 1999 and its initial clinical acceptance was relatively slow. However, there have been improvements in technology with a steady increase in the number of installed systems, accompanied by increasing evidence of clinical usefulness. The combination of SPECT and CT provides the capability for truly quantitative multiradionuclide investigation which traditionally has been difficult to achieve in the clinical setting. SPECT/CT imaging has reached maturity as a viable option for mainstream nuclear medicine.

Acknowledgments and omissions In an overview of this type it is difficult to ensure that facts are correct and that the many people who contributed to the development are appropriately recognized. I therefore offer apologies for any omissions or errors in this article. Thanks to Angela da Silva for details on the Philips Brightview system. Thanks also to Carlo Fiorini and Paulo Busca at POLIMI, Milan, for discussion and diagrams on solid-state readout systems. UCL and UCLH are supported by the National Institute for Health Research University College London Hospitals Biomedical Research Centre.

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