The Introduction and Development of Clinical PET in the United Kingdom

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Twenty-five years ago (half the life of the BNMS) in 1990 clinical PET imaging began to be accepted as an important clinical diagnostic tool (Fig. 14.1).

There were then approximately 60 pet centres in the United States 20 in Japan and even six in Belgium however there was not a single clinical PET service in the United Kingdom in spite of the fact that the Medical Cyclotron and PET unit at the Hammersmith Hospital was at the cutting edge of research in this area.

In 1990, during a post prandial stroll back to our hotel during EANM conference, Desmond Croft (Gastroenterologist and head of Nuclear Medicine at St Thomas' hospital) and I discussed the possibility of establishing the first clinical PET Centre in the UK. Guys and St Thomas' Medical schools had been united in 1984 to form the joint United Medical and Dental Schools (UMDS) but the two hospitals remained separate entities (although later merging to form one hospital trust) We felt at the time that a single PET centre supported by both hospitals and based in the medical school would make it more likely that we could raise the necessary support and critically the funding.

Looking back to that time Twenty-five years ago it is interesting to note that the proposal was based mainly on neuropsychiatric indications (predominantly to identify pre-surgical sites of focal epilepsy and early diagnosis of Alzheimer's disease) and Cardiological applications (viability of ischaemic compromised myocardium) there was some early evidence from the United States and elsewhere that applications in cancer might assume a greater importance which at that time was restricted mainly to brain tumour recurrence and some early work in staging and recurrent Lung cancer.

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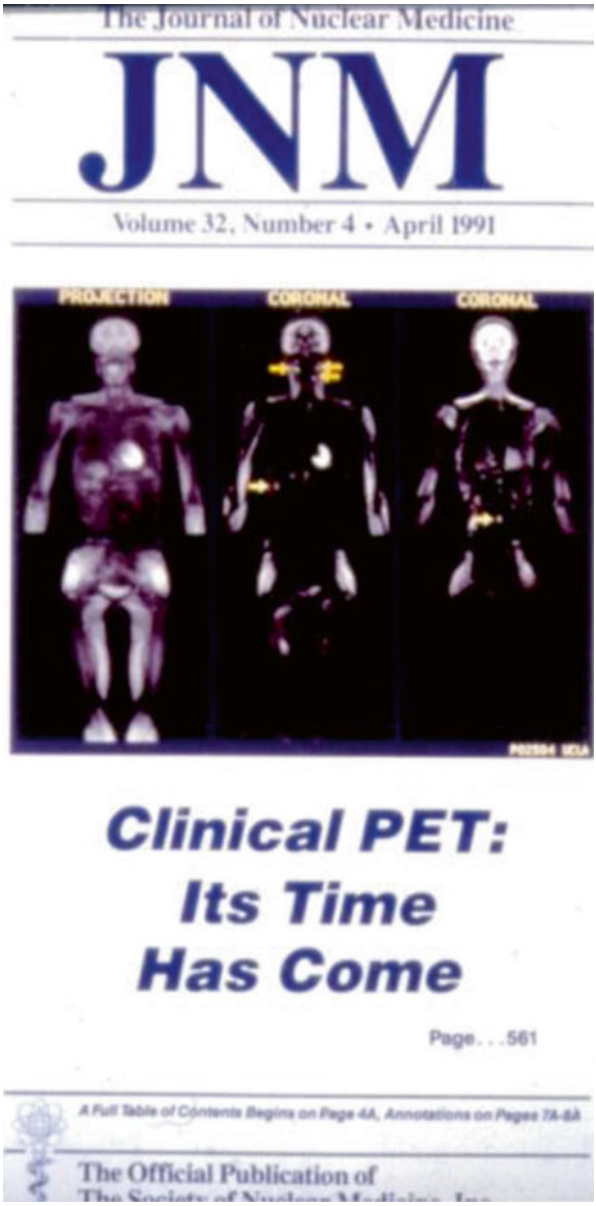

Fig. 14.1 Clinical PET its time has come recorded on the cover of the *Journal of Nuclear Medicine* in 1991

The concept we discussed that evening was to develop a clinical PET centre which was both a clinical service and a clinical research centre which would encompass a small medical cyclotron with a radiochemistry laboratory, with clinical PET scan imaging facilities at Guys hospital and St Thomas' Hospital with the whole centre functioning as a single entity. This plan seemed to make the likelihood of success higher as initial estimates suggested that around £5 million would need to be raised.

Fig. 14.2 Ex deputy prime minister under Margaret Thatcher-Lord William Whitelaw with Brit Ekland

The proposals were presented to UMDS and the boards of both Hospital Trusts and after considerable discussion the plan was supported by both the hospitals and Medical School with the new centre in the newly created division of Radiological Sciences. At that time Trusts were very separate from the academic school and were more risk adverse. The absolute 'proviso' was that we must raise the capital funding and the centre should be financially self supporting with all staff and running costs to be covered by charging for scan referrals, selling radiotracers from the radiochemistry unit as well as grants supporting clinical research projects.

After an initial period of planning and costing, with significant support from the Hammersmith PET group, even though there were some who did not believe that it was appropriate to use PET for clinical purposes! Early funding was raised from several sponsors before a formal fundraising program was established. We were fortunate in persuading the ex deputy prime minister under Margaret Thatcher-Lord William "every Prime Minister should have a Willie" Whitelaw to chair the appeal aptly named 'The Living Image appeal' Fig. 14.2.

The first formal meeting of which took place in December 1991 in the House of Lords! Lord Whitelaw proved to be an excellent chairman and within 6 months approximately 2.3 million had been raised and work to establish the centre was underway. The cyclotron itself was to be installed in the basement of St Thomas's Hospital with an imaging centre on the ground floor above and the second unit was incorporated in the physics Department below the nuclear medicine department at

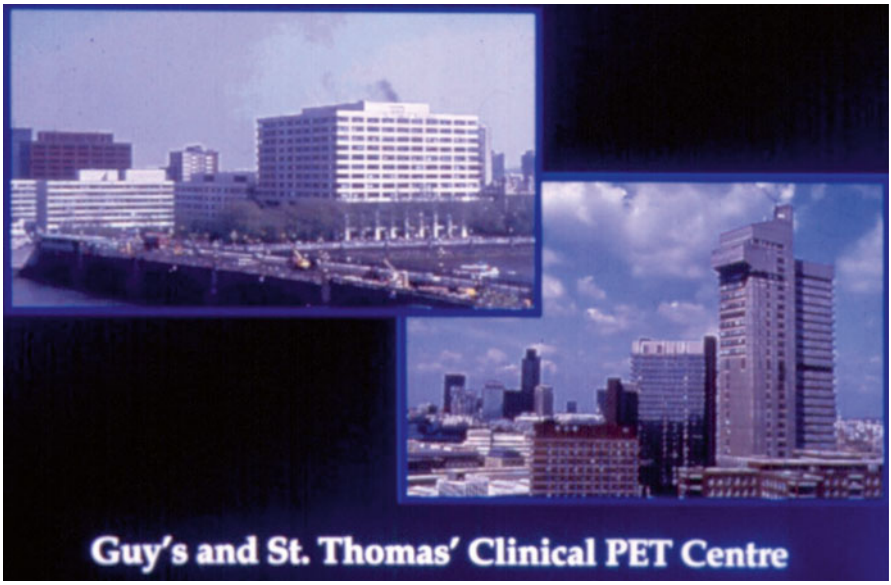

Fig. 14.3 The first clinical PET centre in the UK was finally opened in August 1992

Guys Hospital. Figure 14.3 shows St Thomas Hospital overlooking the river Thames on the left and Guy's Hospital tower on the right (Fig. 14.4).

During 1994 the 'Living image appeal' was discontinued as the total sum of £5 million had been reached and the centre was a going concern with significant external funded referrals and further income raised by selling cyclotron produced radiopharmaceuticals to increasing numbers of developing clinical PET facilities around the country. Added to this was the clinical research grants which had been gained.

It is interesting to note that by the end of the first year approximately 28 % of the clinical scans were referrals for cancer; diagnosis and treatment monitoring and by 1994 the figure had risen to 48 % currently the figure runs at over 90 %. Around half of the scans were for clinical purposes and approximately half for funded clinical research projects and all staff and running costs were being covered by the income from these sources. On the basis of our original projections (Neuropsychiatric and Cardiac) it has to be doubted whether the project would have been financially viable, but that is now history.

It is difficult to overestimate the importance of an effective team, with no formal training, to run a unit of this type, both then and now. Everybody: administrative, technical, radiographers scientists (Physics, Chemists and Computer scientists) as well as doctors, were essential and remain essential to the effective working of a unit of this type. Twenty-five years ago it was a very steep learning curve for everyone involved, particularly for the medical staff for whom formal training in clinical PET was not generally available. Also there was little available in the literature this meant learning and reporting the appearances of abnormal PET scans equally important was learning the range of normal variations of the physiological

Fig. 14.4 HRH Prince Charles at the formal opening of the Clinical PET centre. Prof Michael Maisey and Dr Tony Gee, Radio chemist demonstrates the equipment to Prince Charles on the *right*

distribution of tracer. A significant innovation in organisation was the blind double reading whereby each scan was read independently, disagreements discussed and agreed upon or referred to a third reader. I believe using this method we moved up the learning curve more rapidly and avoided many potentially serious errors: an arrangement which continues today.

Although we had expected to be mainly involved in neuropsychiatric and Cardiological applications it became clear that cancer would form a huge amount of the workload of clinical PET and this has continued. It was always expected that a range of biological traces would be involved however the fundamental tracer Fluorodeoxy Glucose (FDG) proved to be by far the most important and remains so today.

Gradually with the clinical success from referrals many other centres invested in PET imaging devices, as long as it was possible to obtain the appropriate tracers without the necessity of establishing at cyclotron and a radiochemistry unit the costs could be kept down there are now medical cyclotrons and diagnostic PET units in the UK many of which are commercial subcontracted to NHS of which about half are mobile systems including two suppliers of PET tracers (FDG, F-Choline and 18F Fluoride).

Anatomic localisation of the sites of tracer uptake in around 10 % of the cases remained a clinical problem for reporting scans. Early research work, in conjunction with our Radiological sciences computer imaging group, combining PET images with more conventional CT and MRI images Fig. 14.5 based on computer-generated image fusion was productive.

This image fusion, of course, was later taken on by the commercial manufacturers incorporating CT and later MR into the imaging device itself (PET/CT) which

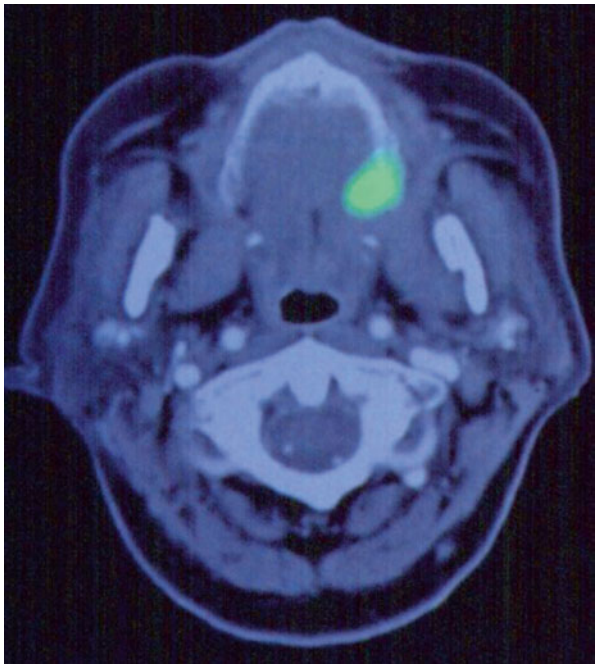

Fig. 14.5 PET and CT fused image of the skull

permitted accurate localisation as well as quicker attenuation correction, 8 patients/day was then maximum throughput, now about twice that rate is possible. The vast majority of PET devices are now PET CT devices and a few, including a new one at the Guys St Thomas's PET centre, incorporate MRI (PET/MR). This has also meant that non radiology trained Nuclear Medicine staff have had to undertake more formal training in cross sectional anatomical imaging.

The future remains exciting with further development of specific radio traces, in addition to FDG: F-Choline is routine for prostate cancer, 68Gallium for neuroendocrine tumours and 68Gallium PSMA has just become commercially available. An area that we thought at the time would be important; combined PET and MR spectroscopy has not as yet delivered any significant advances.

In 2015 25 years after the start of the first UK PET centre the whole unit has been refurbished with 2 new PET/CT scanners and a high field 3 T PET/MR scanner for clinical and basic research including spectroscopy. There is a PET / CT planned for the new cancer centre in 2016. In addition cyclotron and chemistry laboratories are being refurbished and is now probably the best equipped and most productive unit in the UK and I'm proud to have been associated with the onset and introduction of clinical PET into the United Kingdom. Research continues to be of great importance and a short selection of some key research publications below.

Michael Maisey After completing an MD based on an 131 biological assay for long acting thyroid-stimulating (LATS) I went to the United States in 1970 as a trainee Fellow at the Johns Hopkins Hospital in Baltimore in Nuclear Medicine. Johns Hopkins Nuclear Medicine under Henry Wagner was regarded at that time as the leading training centre for nuclear medicine worldwide. After spending 2 years there and gaining the American Boards in Nuclear Medicine I returned in 1972 to be appointed consultant in Nuclear Medicine at Guy's Hospital to establish the first nuclear medicine department in that hospital.

After 12 years in this post he was appointed Professor of Radiological Sciences with a remit to organise undergraduate and postgraduate teaching and research in diagnostic imaging into one organisation with strong science base. A significant early achievement was to obtain the first high field strength MRI machine and to give opportunities for the skills and roles of non-medical scientists within the discipline. In 1992 the U.K.'s first clinical PET centre for diagnosis and research was established within the division of radiological sciences.

Amongst other things I was president of BNMS and later the British Institute of Radiology retiring in 2003.