CHERE

PROJECT REPORT 18

Review of Positron Emission Tomography at Royal Prince Alfred Hospital

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Policy support is provided at all levels of the health care system by undertaking commissioned projects, through the provision of formal and informal advice as well as participation in working parties and committees.

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NOTE

This report was written and submitted to NSW Health Department in January 2000. Since this time circumstances relating to PET may have changed considerably. In particular, the costs cited in this report may have altered. The cost estimates prepared for the report have been re-estimated using 1998/99 and1999/00 costs, but this does not capture change in resource use.

1. INTRODUCTION

This report is a review of the clinical uses, impacts on clinical management, clinical outcome and resource use of Positron Emission Tomography (PET) at Royal Prince Alfred Hospital (RPAH). PET is a relatively new and resource intensive diagnostic technology which has a range of clinical applications, particularly in surgical oncology, neurology and cardiology (although the latter has become less important over time). At present there is only limited information on the clinical effectiveness and cost-effectiveness of the technology compared with other diagnostic technologies.

Specifically, PET is a functional imaging modality which is able to quantify physiological and biochemical processes in-vivo in humans, using short-lived radioisotopes called positron emitters. PET radioisotopes are produced by particle accelerators. PET uses the tracer method and image reconstruction techniques to provide a three dimensional depiction of metabolic events.

PET was initially introduced in the 1970s, but was primarily seen as a research tool with only limited clinical application. In the late 1980s and early 1990s there was increasing attention to the potential role of PET in a range of clinical applications. More recently, PET has been approved for Medicare reimbursement in the USA (in November 1997), specifically for imaging of lung nodules and staging of lung cancer.

PET was introduced in 1992 in Sydney at RPAH and in Melbourne at the Austin and Repatriation Medical Centre (ARMC). Since this time another two PET scanners have commenced operation at the Peter MacCullum Cancer Institute (1996) and the Wesley Hospital (1998). The PET unit at RPAH has now scanned over 6000 patients, with annual throughput increasing consistently since the unit commenced operation. Initially the emphasis was on cardiology and neurology scans. However, the majority of scans are now in oncology.

Since 1997 there has been limited Medicare reimbursement for PET scans undertaken at RPAH and ARMC. However, as yet, there has been only limited evaluation of the uses of PET and its impact on clinical management in Australia. CHERE has been commissioned by the NSW Department of Health to work with the PET unit at RPAH to undertake an evaluation of the role of the unit. The initial step in the process of this evaluation was to identify the scope and key

components of a comprehensive evaluation. In particular, two approaches to evaluation were identified as being necessary:

- Retrospective analysis, addressing the range of clinical applications of PET, the throughput of the Unit, the costs of undertaking a PET scan for different patient groups, and the impact of PET on patient outcomes; and
- Prospective analysis, addressing the impact of PET in specific identified applications, to provide an unbiased assessment of the impact of PET on clinical management, outcomes for patients and resource use.

Both components are seen as necessary to a comprehensive evaluation. The retrospective analysis is important in assessing how the role of PET has changed and in providing an overview of the role of PET. However, retrospective analyses are limited in that they are subject to a range of confounding factors, most importantly, there may be bias in the way patients were selected for PET scanning. Thus, the overall evaluation strategy has incorporated both components. The project commissioned by the NSW Department of Health was to undertake the retrospective analysis of throughput, costs and the outcomes of PET scans. In addition, CHERE, together with clinicians from Royal Prince Alfred Hospital developed an NHMRC project application to undertake a prospective evaluation of the role of PET in management of non-small cell lung cancer (NSCLC), which is one of the major current clinical applications of PET at RPAH. The prospective evaluation took the form of a randomised controlled trial incorporating economic evaluation. The project application was successful and recruitment for the trial commenced in April 1999, and was completed in December 2000. Follow-up of patients is continuing until December 2001.

This report presents the findings of the retrospective analysis of the role of the PET unit, particularly:

- Review of Australian and international literature on effectiveness and cost-effectiveness of PET compared with other diagnostic technologies, particularly for oncology;
- Summary of patient throughput, characteristics and reasons for scans for the period 1992-1998;
- Detailed analysis of reasons for scans for the period 1997-98;
- Estimated total and average costs for the PET unit, based on costing information for the period 1997-98.

2 Literature Review

In this section we briefly review the Australian and international literature evaluating the role of PET in clinical and research applications. In particular, we have focussed on the evaluation of PET as a diagnostic test, either as an adjunct or an alternative to existing diagnostic tests. As noted, clinical and research applications for PET have emerged in three broad disease groups: oncology, cardiology and neurology, with the most recent emphasis in both clinical applications and in the evaluation literature being on oncology. There is now a growing body of literature on evaluation of the role of PET in oncology, and, Robert and Milne (1999) report that more than 70% of referrals at the majority of international clinical PET centres now come from oncology departments.

Three recent reviews of the role of PET have been undertaken. In 1996, a report commissioned by the US Veterans Health Administration was finalised which included detailed systematic reviews of PET in a range of oncology applications and Alzheimer's disease (Flynn, Adams et al. 1996). This report found that the majority of the literature focussed on the feasibility of the use of PET and on diagnostic accuracy, with relatively few studies assessing efficacy or impact of PET on patient management. The report concluded that, at that stage, the evaluation literature was relatively under-developed, and it was difficult to draw conclusions about the utility of PET. For example, for diagnosis of Alzheimer's disease, while there was good evidence to support the accuracy of PET, there was not yet evidence available to support more widespread use of PET in management of Alzheimer's disease. For the use of PET in diagnosis and management of cancer, the report concluded that the literature was even less developed. Most studies were retrospectively analysed case series, with small patient numbers, lack of control groups, poor use of blinding and no randomisation.

In 1999, the National Health Service Research and Development Technology Assessment Program published a review of the state of knowledge regarding clinical applications of PET, partly as a basis for determining research priorities in relation to PET in the UK (Robert and Milne 1999). The conclusion of this report was similar to the previous US report. In particular, the authors note that "there is no good evidence to suggest how PET will affect the cost-effectiveness of the diagnosis, prognosis and management of patients", and they comment on the lack of large prospective studies. Thus, although there were increasing numbers of studies supporting the diagnostic accuracy of PET in a range of conditions, there was still very little information to assess the utility of PET in routine clinical practice, in terms of effectiveness or cost-effectiveness.

In 2000, the Department of Health and Aged Care produced a Commonwealth review of PET in Australia (Commonwealth Department of Health and Aged Care 2000). A key component of the review process was an evaluation of PET conducted by a Supporting Committee of the Medicare Services Advisory Committee (MSAC). MSAC explored the use of PET in six clinical indications including lung and colorectal cancer, coronary revascularisation, epilepsy, melanoma and glioma. The findings were largely consistent with the conclusions of existing reviews. It was concluded that there was insufficient evidence on PET's clinical or cost effectiveness with respect to the clinical indications reviewed and that conclusive evidence such as a randomised controlled trial is needed to explore the impact of PET on clinical management.

In our review of the literature we have focussed principally on the use of PET in oncology. Given the relatively recent publication of the MSAC review we have not replicated their work, but have focussed on identifying more recent papers. The main uses of PET in oncology identified were:

- Diagnosis — Differentiating between benign and malignant conditions and establishing the source of metastatic disease
- Staging — Defining the extent of disease
- Monitoring — Surveillance of treatment response
- Recurrence — Identifying recurrence

The most well-established uses of PET are in staging of lung cancer and in diagnosis of solitary pulmonary nodules. However, because of differences in clinical practice between the USA and Australia, the latter is less relevant in the Australian context. Potential uses of PET identified in the literature include the prediction of prognosis, tissue diagnosis and determining the best site for biopsy (Sarinas, Chitkara et al. 1999).

The findings of our review of the literature confirmed the findings of the three previous studies. The key issue that needs to be emphasised in relation to the evaluation of PET is that there are specific challenges in evaluating a diagnostic technology. The decision to perform a diagnostic test should be based on the usefulness of the information provided by the test. In other words, it should provide an accurate diagnosis, support the application of a specific efficacious treatment, and ultimately lead to a better or more cost-effective clinical outcome for the patient. In their review Robert and Milne (1999) note that Fineberg has classified three stages in the diagnostic process: production of a diagnostic output; the inclusion of that output into a diagnostic strategy

and choice of treatment; and the health outcome conditional upon treatment. In terms of evidence for the value of a diagnostic test, studies which focus on technical performance and diagnostic accuracy are only addressing the first of these stages. Ultimately, either prospective evaluations of management impact, or, at minimum, formal decision analyses based on rigorous assessment of sensitivity and specificity are necessary to address the second and third stages.

To date, published studies have focused on defining the accuracy of PET as a diagnostic test. A number of prospective studies have been published, but few of these incorporate assessment of how PET affects clinical decision making. There has been limited assessment of the impact of PET on clinical management, and virtually no assessment of the impact on patient outcomes and resource use. Some studies have extrapolated from the diagnostic properties of PET to the impact on patient management (Wahl, Quint et al. 1994; Lowe, Fletcher et al. 1998; Weder, Schmid et al. 1998). However, even among these studies, some authors note that they believe it would be unlikely that clinical management would be changed by the availability of the PET scan (Lowe, Fletcher et al. 1998). One recent paper, not included in either of the previous systematic reviews, does incorporate prospective assessment of the impact of PET on patient management, as well as follow-up of clinical outcomes (confirmation of diagnosis at surgery or through histology, as well as morbidity and mortality outcomes) (Saunders, Dussek et al. 1999). In this study 97 patients with confirmed or suspected resectable lung cancer were staged based on CT and conventional staging; CT alone; PET alone; and conventional, CT and PET. Management decisions were based on all diagnostic information and patients were followed up for up to 41 months. The study found that PET changed management in 37% of patients, although this figure included 15 patients for whom the operation was "enabled" by PET, suggesting that the inclusion criteria were not clearly defined. Of the 97 patients, 15 had a planned operation cancelled as a result of the PET scan.

There has been limited clinical evaluation of PET in the Australian context. A recent paper reports on the experience with PET at one Australian centre (Hicks, Binns et al. 1999). However, while the paper reports experience across a range of cancers suggesting that PET may have a role in changing management, the conclusions are based on case series, without clear description of the patient selection**.**

Economic evaluation

A Medline search (1990-2001; 'positron emission tomography' and 'cost-benefit analysis' exploded to all subheadings) was undertaken to locate papers addressing the cost-effectiveness of

PET. This was supplemented by other search strategies to locate the maximum number of papers. In all, 17 published economic evaluations were located, and are summarised in Table 1.

While the majority of papers conclude that PET is likely to be cost saving or to fall within an acceptable cost-effectiveness range relative to conventional management of oncology patients, this conclusion must be treated with considerable caution. All of the economic evaluations are subject to methodological flaws. In particular, none incorporate adequate follow-up of patient outcomes. Thus, even though decision tree modelling studies find that the use of PET in management of non-small cell lung cancer results in no change or an increase in life expectancy, this is the result of an assumption that avoidance of surgery in this group of patients reduces mortality. This assumption is not supported by any studies following up patient outcomes following incorporation of PET in the management strategy. In other studies there is no assessment of patient outcomes, and the analysis is restricted to comparison of costs based on the assumption that management will change and/or that patient outcomes will not be affected. Further, most studies incorporate only limited assessment of the costs of alternative strategies. More fundamentally, relative cost-effectiveness results are sensitive to the relative costs of procedures and it cannot be assumed that these costs are comparable across different settings.

TABLE 1: ECONOMIC EVALUATIONS OF THE ROLE OF PET 1990-2001

Author Year	**Study question Clinical application and alternative**	**Form Data sources**	**Outcome measure**	**Costing methods**	**Comments**
(Yao, Hoh et al. 1994)	Staging of malignant melanoma PET vs Conventional Staging	CMA Primary data (n=59)	Cost per patient	Hospital and medical charges (billed)	Cost per patient $4409 for conventional staging; $1950 for PET
(Patterson, Eisner et al. 1995)	Diagnosis of coronary artery disease Exercise ECTC vs SPECT vs PET vs coronary angiograph	CEA Mathematical model (clinical algorithms) based on Bayes' theorem and using primary data	Number of patients diagnosed with coronary artery disease. Cost per QALYs gained after therapy.	Published diagnostic and therapeutic costs	PET was the most cost-effective among patients with a pre test likelihood of coronary artery disease < 0.70.
(Gambhir, Hoh et al. 1996)	Staging NSCLC PET and CT vs CT alone	CEA Decision tree modelling using secondary data	Cost per LYS	Hospital and medical charges (billed)	CT plus PET resulted in a saving of $1154/patient without loss of life expectancy (however, impact on patient outcomes based on modelling assumptions)
(Valk, Pounds et al. 1996)	Management of NSCLC; SPN; Recurrent colorectal cancer; Metastatic melanoma; Recurrent head and neck cancer; Hodgkin's Disease PET and Conventional management vs Conventional Management; PET vs Conventional management	CMA Modelling based on retrospective analysis of primary data	Net costs (taking into account procedures avoided)	Medicare and DRG reimbursement	Not a comprehensive economic evaluation (methods not adequately described; not all costs taken into account; patient outcomes not followed up fully; patient selection criteria not clear) PET found to be cost saving for NSCLC & SPN (as an adjunct or as an alternative) PET found to be cost saving for colorectal cancer (adjunct or alternative) PET found to be cost saving for melanoma (adjunct or alternative) PET found to be cost saving for head and neck cancer (adjunct or alternative) PET not found to be cost saving for Hodgkin's disease

Author Year	**Study question Clinical application and alternative**	**Form Data sources**	**Outcome measure**	**Costing methods**	**Comments**
(Hoh, Glaspy et al. 1997)	Diagnosis of Hodgkin's Disease and Lymphoma PET vs Conventional (to diagnosis)	CMA Primary data	Cost comparison	Average prices for procedures from 5 local hospitals	PET found to be cost saving to the point of diagnosis: however, this was not a comprehensive economic evaluation and final management decisions were based on PET and conventional imaging results
(Adler, Faulhaber et al. 1997)	Breast cancer; Staging and management	CMA Modelling based on prospective primary data	Cost per patient	Hospital and medical charges	PET would potentially save $2300 per patient and avoid surgery
(Holmberg, Mohiuddin et al. 1997)	Coronary artery disease Comparison of two PET modalities (adenosine PET and dipyridamole PET)	CMA Primary data Retrospective, case-control	Cost per patient	Hospital costs	Adenosine found to be lower cost
(Scott, Shepherd et al. 1998)	NSCLC PET + CT versus CT alone (4 different PET plus CT strategies compared)	CEA Decision tree modelling using secondary data	Cost per LYS	Medicare reimbursed costs	Extends Gambhir, Hoh et al (1996) Strategy of PET following a negative CT scan resulted in a cost of $25000 per LYS compared with CT alone; Other strategies (PET + CT resulted in a cost of $70000-$137000 per LYS compared with CT alone) Note that the estimated reduction in mortality is based on the assumptions incorporated in the model and not based on any follow-up of patient outcomes
(Gambhir, Shepherd et al. 1998)	SPN 4 strategies compared watchful waiting; surgery; CT; CT + PET	Decision tree modelling using secondary data	LYS	Medicare reimbursed costs	CT plus PET found to be more cost-effective and potentially cost saving compared with CT alone for a pre-test probability of malignancy of 0.12-0.69
(von Schulthess, Steinert et al. 1998)	NSCLC PET vs CT Melanoma; PET vs Conventional Staging	CMA Modelling using primary data	Cost comparison	Medical and hospital charges	Not a comprehensive economic evaluation (impact on patient management only assessed hypothetically). PET found to be cost saving, but this is based on assumptions about the impact of PET on patient management

Author Year	Study question Clinical application and alternative	Form Data sources	Outcome measure	Costing methods	Comments
(Garber and Solomon 1999)	Coronary Artery Disease Diagnosis 5 diagnostic strategies compared: Angiography and initial testing + treadmill; planar thallium imaging; SPECT; stress echocardiography or PET	CEA Modelling using secondary data	QALYs	Medical and hospital charges	Incremental C-E ratio of PET vs SPECT greater than $640,000/QALY Echocardiography the most cost-effective strategy
(Derdeyn, Gage et al. 2000)	Symptomatic carotid occlusion PET vs no PET	CEA Markov model using prospective primary and secondary data	QALYs	Medicare reimbursement	Estimates were sensitive to a number of parameters.
(Klose, Leidl et al. 2000)	Staging of lymphomas PET vs CT, CT vs no diagnostics	CEA using prospective data	Percentage of correctly staged patients according a gold standard	Micro costing	Incremental cost-effectiveness ratio for CT vs no diagnostic and CT vs PET was 478 and 3133 euros in 1999. Cost per patient correctly staged by PET was 6.6 times higher than CT.
(Kosuda, Ichihara et al. 2000)	NSCLC CT vs CT and PET	CEA using a simulation based on past presenting patients	LYS	Hospital and outpatient (billed)	Cost is 2.18×10^5 yen per life year gained CT and PET is unlikely to be cost-effective; PET $100,000 yen
(Dietlein, Weber et al. 2000)	SPN Wait and watch or exploratory surgery vs transthoracic needle biopsy or PET Two alternative baseline strategies	CEA Decision tree analysis using secondary data on a target patient group	LYS	Reimbursement rates for medical, hospital and palliative therapy	Depending on the baseline strategy chosen, PET may lead to cost savings and additional life expectancy.
(Dietlein, Weber et al.	NSCLC Conventional staging vs	CEA Decision tree analysis	LYS	Reimbursement rates for medical, hospital	PET found to be more cost effective than CS when used in the patient group with normal-

Author Year	**Study question Clinical application and alternative**	**Form Data sources**	**Outcome measure**	**Costing methods**	**Comments**
2000)	PET A range of strategies were compared differing in terms of patient group (size of mediastinal lymph nodes and management strategies)	using secondary data on a target patient group		and palliative therapy	sized mediastinal lymph nodes. The findings are not clear for the patient group with enlarged mediastinal lymph nodes. In particular, exclusion from surgery on the basis of PET alone was cost saving, but resulted in reduced life expectancy.
(Miles 2001)	Staging NSCLC, breast cancer, recurrent colorectal cancer and myocardial viability PET and CT vs PET	CEA Decision tree modelling using re-worked secondary data	Cost per LYS	Medicare and DRG reimbursement	Underestimated cost of a PET scan at $950 in 1996-97 dollar terms CT plus PET resulted in a saving of $34.65/patient without loss of life expectancy (however, impact on patient outcomes based on modelling assumptions) PET as an adjunct to CT estimated to produce a saving of $360.03 per patient for preoperative staging lung cancer PET is not cost saving for axillary staging of breast cancer PET found to be cost saving for preoperative evaluation of recurrent colorectal cancer PET found to be cost saving for the assessment of myocardial viability

CMA: Cost minimisation analysis; CEA: Cost effectiveness analysis; LYS: Life years saved; QALYs: Quality adjusted life years

3 Overview of the Operation of the PET Unit

3.1 Background

The PET Unit at RPAH was established in 1992. The PET scanner was purchased at a cost of approximately $5 million dollars, funded by a collaborative effort involving Royal Prince Alfred Hospital (RPAH), the NSW Department of Health and private donations. The National Medical Cyclotron (NMC) was funded by the Commonwealth government, and is owned and operated by the Australian Nuclear Science and Technology Organisation (ANSTO). It was established on the campus of RPAH, at a cost of approximately $20 million.

The PET Unit began scanning in June 1992, and the annual throughput of patients in each year has increased consistently since then. Over 7000 patients have now been scanned. In 1999 (until November 30), 1356 studies were undertaken, comprising 400 neurological scans, 21 cardiac scans and 935 whole body (oncology) scans.

3.2 Operation of the PET Unit

The establishment of the PET Unit and the NMC in 1992 required extensive refurbishment of the PET suite within the hospital, involving the floor level being raised and complex air-conditioning being fitted. It also involved the installation of a rapid transport system under Missenden Road, to transport the PET radiotracers to the PET Suite. The total area of the PET Suite is 311 square metres. Since 1992 there has been extensive upgrading of the computer systems of the PET unit, to improve storage and retrieval of data.

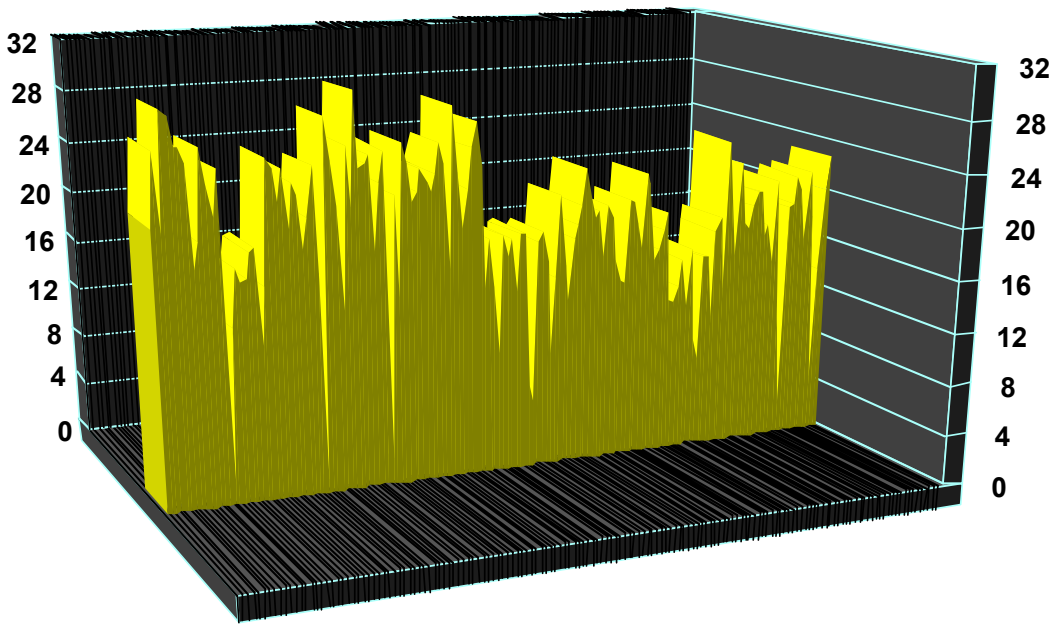
From the outset of the PET program, RPAH has had staff members from the PET unit located in the NMC who are responsible for production of PET tracers for RPAH. A typical production run for RPAH involves:

- set-up for production beginning at 0700 hrs,
- cyclotron irradiates PET target for 90 mins from 0730 - 0900 hrs,
- ^{18}F[1] is transferred to an automated radiochemistry box and synthesis takes place over 60 mins,
- a sample of the product is taken for quality control (QC) and
- product released 30 minutes later for human use at 1030 hrs.

[1] ^{18}F is a radioactive isotope with a half life of 110 minutes.

Average cyclotron beam time each week for RPA is 6 hrs. The amount of isotope produced each day is variable (Figure 1), although the amount paid by RPAH is per vial, regardless of the amount of isotope in the vial. Multiple patient doses are possible from a single batch of {18F}Flurodeoxyglucose (FDG)[2], because of its 110 minute half-life. The PET unit schedules its daily patient scanning as if an average yield will be available. The PET unit is advised at 1000 hrs of the amount of isotope that has been produced, and patients are then rescheduled accordingly. When the yield is low patient numbers are maintained by limiting the extent of some studies to shorten the time for data acquisition. In general, approximately 8 patients are scanned per day.

Figure 1: Daily FDG yields (in Giga Becquerels - GBqs) are shown on the vertical axes. The marked fluctuations in the yield of isotope show the unreliability of production and the vulnerability of RPA patient scanning to poor yields. When the yield is low patient numbers are maintained by limiting the extent of some studies to shorten the time for data acquisition.



Daily FDG yield in 1998

As soon as the isotope vial arrives in the PET unit (approximately 1030 hrs) the first patient is injected. Patients are managed throughout the day to a strict time schedule such that as soon as one patient leaves the scanning bed another is ready to be scanned. The larger the area to be scanned the longer the time needed on the bed and the greater the quantity of active isotope required. Most oncology studies are whole body studies requiring a scan from the neck to knee. The availability of isotope only after 1030 hrs

[2] FDG is the PET radiotracer

has cost implications, because most hospital activity is scheduled to occur during the normal working day. PET unit staff are often required to work overtime, and patients are often required to be scanned in the evening.

The process for each patient involves arrival at the unit followed by a consultation with either the PET unit director or the registrar to ensure they understand the process and to facilitate signing of a consent form. Patients are injected with the isotope approximately 45 minutes prior to scanning. Once injected, the patient is asked to remain still – this period is referred to as the uptake period. Patients for whom the area scanned includes the pelvis are fitted with a catheter. The duration of the scanning period is dependent mainly on the amount of the body to be scanned. After the scanning has finished it takes approximately 2 hours for the image reconstruction techniques to provide a 3-D depiction of dynamic metabolic events. The scan is assessed by the Director of the PET unit, and a report is sent to the referring physician. The findings may be passed to the referring physician by phone in cases where surgery is booked immediately following the scan.

The availability of the cyclotron is a limiting factor for the PET unit throughput. The NMC cyclotron is closed at weekends. It is also closed for maintenance every Monday and for 3 weeks over the Christmas / New Year period and for 2 weeks midyear, however in 1998 the midyear shutdown was not carried out.

3.3 Throughput

Table 2 summarises the annual throughput. The current annual throughput is approximately 1300 patients, and this has been relatively stable over the past three years. Given the current arrangements for provision of the service, which involves supply by the NMC of a single vial of isotope per day to the Unit on 4 days of the week, this throughput is likely to remain stable.

The Unit provides a state-wide PET imaging service for patients, and is the only PET unit in NSW. Less than 20 per cent of patients scanned reside within Central Sydney Area Health Service. Table 3 provides a summary of the place of residence of patients scanned during 1997-98.

TABLE 2: PATIENTS SCANNED IN THE 3 MAIN CLINICAL APPLICATIONS 1992-1999

Year	Cardiology	Neurology	Oncology	Total
1992 (June-Dec)	9	7	7	23
1993	64	151	220	443
1994	52	195	528	801
1995	43	200	853	1112
1996	24	177	652	864
1997	17	246	1024	1287
1998	18	196	1114	1328
1999 (Jan-Nov)	21	400	935	1356
Total	**248**	**1572**	**5333**	**7214**

TABLE 3: PLACE OF RESIDENCE OF PATIENTS SCANNED 1997-98

Place of residence	Number of patients
Central Sydney	206
South Eastern Sydney	145
Northern Sydney	198
Western Sydney	103
South West Sydney	154
Central Coast	94
Wentworth	24
Hunter	28
Illawarra	74
Macquarie	23
Mid Western	38
New England	15
Northern Rivers	11
Greater Murray	18
Southern	15
Mid North Coast	46
Far West	4
Unknown	14
Total NSW	**1210**
Interstate	**57**
Overseas	**20**
TOTAL	**1287**

3.4 Applications of PET at RPAH

Over the period of operation of the PET Unit there has been a shift in clinical emphasis towards oncology, which also reflects the trend internationally in the use of PET imaging. Over 80% of the throughput of the Unit is now in oncology, or more correctly 'surgical oncology' particularly staging of disease. Data from the RPA PET unit indicate that referrals for PET scans for patients with cancer mainly come from surgeons (approx 65%) and referrals from medical oncologists comprise only 14% of the total. A more detailed breakdown of the uses of the PET scanner, and the cancer

sites is provided later in this report. However, it should be noted that the current use of the scanner reflects existing knowledge of the effectiveness of PET as a diagnostic tool. Thus, there is an emphasis in the RPAH PET unit on lung cancer and melanoma, for which there is more evaluation evidence, both here and internationally. As new research evidence becomes available, there may be a further shift in clinical emphasis. Table 4 presents a breakdown by study type of all scans undertaken in 1997-98.

TABLE 4: PURPOSES OF SCAN BY STUDY TYPE 1997-98

Study Type	Sub Area	Number of Patients
Head	**Neurology**	
	Brain Tumours	198
	Degenerative	128
	Epilepsy	81
	Other	9
	Normal Volunteer/Research	49
Whole Body	**Oncology**	
	Lung	379
	Melanoma	132
	Gynaecological	34
	Soft Tissue	30
	Breast	21
	Head and Neck	9
	Urogenital	9
	Haemotological	6
	Unknown Primary	7
	Other cancers	8
	Gastro-intestinal	170
	Neurology	4
Cardiology	Cardiac Viability	13
Total		**1286**

Analysis of the PET Unit database and consultation with the Director of the PET Unit has identified the following main applications of PET at RPAH. These are identified in terms of the extent to which PET has the potential to provide additional information, and whether the additional information provided changes management.

Neurology and Neurosurgery

- NeuroDegenerative Disorders

The role of PET in dementia and other neurodegenerative disorders is to provide accurate diagnosis. Anatomical imaging studies (Computerised Tomography & Magnetic Resonance imaging) are usually normal in these conditions, PET can provide differentiate between dementia conditions, and can provide a diagnosis premortem

when anatomical imaging is unhelpful. The principal benefit of the PET scan in this case is the value of the information to the individual, the referring doctor and carers/family members. As treatments for dementia become available (already there are a number of agents that have been shown to delay the rate of disease progression in patients with suspected dementia in clinical trials) it is imperative that patients are correctly identified. In this context a PET scan will assist in determining more appropriate treatment, or in limiting unnecessary investigations. In 1997-98, 128 patients were scanned for neurological degenerative conditions.

- Brain Tumours

PET is used to provide information about the grade of a tumour, and to provide more accurate information to localise the most active tumour area for biopsy or excision by a neurosurgeon. In both cases, the benefit of PET is in determining the most appropriate treatment, particularly surgical treatment. Information about the grade of the tumour is used to determine whether patients are appropriate surgical candidates. In 1997-98, 198 patients were evaluated for brain tumours. Thus, almost half of the neurological referrals were for evaluation of tumours. PET can also be used for the surveillance of low-grade brain tumours avoiding alternative methods of monitoring. This use of PET may allow the earlier diagnosis of malignant transformation and earlier treatment may provide improved outcomes.

- Epilepsy

PET is used in epileptic patients who have refractory focal epilepsy to localise seizure foci. Thus, the PET scan may be used to provide additional diagnostic information to assist in management of epilepsy, in particular to select patients for whom surgery is likely to provide a benefit (that is, to determine whether surgery is likely to affect seizure control) but also to exclude patients with generalised epilepsy where surgery is of no benefit] and therefore to increase the probability of successful surgery. In 1997-98, 81 patients were scanned for epilepsy.

Cardiology

PET has been used to establish cardiac viability, to determine which patients are most likely to be successful candidates for revascularisation surgery. In 1992, this represented approximately 30% of the workload of the PET unit, but, in line with research evidence, this role has changed considerably. In 1997-98, only 13 patients

were scanned for this purpose. The benefit of a PET scan in this case is that it potentially provides better selection of surgical candidates, which may improve surgical outcomes.

Oncology

The main role of the PET Unit at RPAH over the past six years has been in a range of oncology applications in the pre-surgical setting. During 1997-98, patients were scanned for a range of cancers, including breast cancer, colorectal cancer, lung cancer, melanoma, gynaecological cancers, brain tumours and head and neck cancers. In general these patients have a whole body scan, and there are a number of possible purposes of the scan, as outlined below.

- Lung Cancer

PET is used to provide additional diagnostic information for patients with lung cancer. In 1997-98, 349 patients were referred for a whole body PET scan related to a primary diagnosis of lung cancer. The majority of patients referred for a PET scan have non-small cell lung cancer and the other large group is patients who are thought to have solitary pulmonary metastases from a range of malignancies including colorectal carcinoma, melanoma, breast cancer and soft tissue sarcomas.

The main use of the PET scan is to determine whether a patient is a suitable candidate for surgery prior to the final decision about treatment being made. PET is used to determine whether patients who have been diagnosed with StageI-II non-small cell lung cancer on other diagnostic tests have mediastinal node involvement (Stage III) or distant metastatic disease (Stage IV). Patients who have Stage III or IV cancer are generally not considered to be suitable candidates for surgery, although some patients with Stage IIIa non-small cell lung cancer may still have surgery following chemotherapy and PET in this instance is used to exclude Stage IV disease both before and at the completion of therapy. Thus, the main benefit of PET in this case is that it may avoid unnecessary and potentially fatal painful surgery.

PET is also used in some cases post-surgically to provide information about recurrence or to assess response to chemotherapy or radiotherapy. In this case, the benefit of PET is that it may provide information to determine the most appropriate treatment.

- Colorectal cancer

The PET scanner can be used for the accurate staging of disease, especially in those who are thought to have a solitary liver metastasis that would be amenable to surgery if there is not more widespread disease. This allows appropriate selection of candidates and enhances surgical outcomes.

- Melanoma

The PET scanner can be used for the staging of melanoma after initial diagnosis but it is mainly used in patients with metastatic melanoma prior to them undergoing surgical intervention that may include thoracic surgery, node dissection, hepatic resection or craniotomy. This may allow more appropriate treatment to be given.

- Head and Neck Cancer

Head and Neck surgery for ontological reasons distorts the anatomy of the region. Because of this the more functional PET scan may be more sensitive to early local recurrence than more structural diagnostic tools such as CT scanners. Early detection may offer more definitive and successful treatment.

- Gynaecological Cancer

The PET scanner is being used in ovarian cancer for two purposes; one to help aid the diagnosis of recurrence and the second is to assess the response to chemotherapeutic treatment. Earlier diagnosis of recurrence may allow improved therapeutic option selection. Assessing the response to treatment of ovarian cancer to chemotherapy may allow the early cessation of chemotherapy in those for whom it is not affecting the tumour, with quality of life and resource saving implications.

Summary

Thus, in summary, a number of potential benefits can be identified from the applications of PET at RPAH:

- Information for patients and clinicians

Even where the information from a PET scan does not affect clinical management, there may be benefits, particularly to patients from additional diagnostic information. This is particularly relevant in diagnosis of dementia conditions and in patients with other chronic conditions where treatment does not eradicate the disease and the natural history of these disorders is that there is disease progression over time.

- More appropriate clinical management

The PET scan may provide information that changes clinical management of the patient's condition. In many cases this may not provide a survival benefit (for example, in changed management of lung cancer), but there may be short term improvements in quality of life for patients, from avoidance of unnecessary surgery. However, as has been noted earlier, caution must be applied in assessing the extent to which PET changes clinical management. To evaluate this impact it is necessary to have an unbiased assessment of the management plan before and after the PET scan.

- Improved outcomes from treatment

The additional diagnostic information from the PET scan may lead to more localised and less invasive surgery or other treatment (for example, in surgical management of brain tumours, colorectal cancer, melanoma). This may improve the survival and quality of life outcomes from surgery.

- Resource use

Where PET changes clinical management it may avoid unnecessary resource use, for example, in the case of avoiding surgery. Whether this results in a net saving depends on the relative costs of the PET scan and the interventions avoided, and the proportion of patients for whom there is a change in management. As in the case of changes to clinical management, it is difficult to assess the amount of resource savings retrospectively.

- Allocative efficiency

Because PET may provide information which leads to better selection of patients for particular interventions, it may improve the allocative efficiency of service provision. In particular, there are allocative efficiency gains where there are resource constraints and where PET provides information which leads to more accurate decisions about which patients are likely to benefit from treatment. However, it should be noted that there are a number of questions that must be addressed in assessing the value of a PET scan in particular clinical applications:

- Will the PET scan provide additional diagnostic information? Is the information from the PET scan likely to change the diagnosis? Is the information more sensitive and/or more specific?
- Will the additional diagnostic information change the choice of treatment for the patient?
- Will any change in management result in changes in survival or quality of life outcomes for patients?
- Are there any other benefits/disbenefits to patients from the additional information?
- Is the change in management likely to lead to a net reduction in resource use, given the resource use associated with undertaking the scan?
- Is it feasible that PET would replace another diagnostic test, or is it likely to be used as an adjunct to other diagnostic tests?

4 Estimation of the Costs of PET

This section of the report outlines the methods and results of the costing undertaken for the PET Unit. Costs were estimated for the 1997-98 period, because a full year of financial data was available. The aims of the costing component of the project were:

- To estimate the total costs of the PET unit;
- To estimate the average cost of a PET scan;
- To determine whether average costs differ for different groups of patients;
- To estimate the short run marginal cost of a PET scan;
- To investigate how the costs of the PET unit would vary under different scenarios.

4.1 Estimation of the Total Costs of the PET Unit for 1997-98

The assumptions used to estimate the different components of total cost are outline below.

Recurrent Costs

- Staff salary costs were provided from the PET unit's accounts, with costs attributed to the PET unit based on information from the Director on the proportion of individuals' time allocated to the PET unit (some staff are shared between Nuclear Medicine and the PET unit). On costs were calculated as actual costs, again from the PET unit's accounts. On costs represent approximately 11 per cent of the total salary costs. Table 5 provides a summary of the staff profile of the PET unit.

TABLE 5: SUMMARY OF THE STAFF PROFILE OF THE PET UNIT

Staff Classification	**Number of Full Time Equivalents**
Scientific Officers	2.9
Medical Radiation Technologists	2.2
Nurse (Clinical Nurse Consultant)	1.0
Clerical	1.5
Cleaners	0.5
Medical (Registrar)	1.0
Medical (Senior Staff Specialist)	0.85

- Goods and services costs were provided from the PET unit's cost centre accounts. These costs included costs of medical supplies (other than isotope), stationery, computer software support, radiation monitoring and other operational goods and services.

- Isotope costs were based on actual charges made by ANSTO to Royal Prince Alfred Hospital. During 1997-98 177 vials of FDG-18, 10 vials of NH3 and 10 vials of 015 were provided to the PET Unit. Charging is on the basis of a set price per vial.

- Estimates of overhead costs were provided by the Finance Department of Royal Prince Alfred Hospital. These were based on the overhead cost allocation methods recommended in the NSW 1997/98 Costing Standards Manual. Overhead costs were estimated and attributed for Royal Prince Alfred Hospital and for Central Sydney Area Health Service.

- Repairs and Maintenance costs for the PET Unit were taken from two sources. Some maintenance costs for the Unit are separately reported in the Royal Prince Alfred financial accounts. However, this does not include the total cost of maintenance contracts because of the financial arrangements within the hospital, whereby global maintenance contracts are held, and not disaggregated to separate clinical units. Therefore estimates of the maintenance costs were also based on information provided by the Director of the PET unit and in a separate report on the activity of the PET Unit.

Capital Costs

- Building costs were estimated on the basis of an equivalent rental cost for the floor space occupied by the PET Unit. This was based on commercial rents for the area, of $225 per square metre (this was the mid point of estimates provided by local commercial real estate agents). The total floorspace of the PET unit was 311 square metres.

- Information on the costs of capital equipment for the operation of the PET unit was provided by the Director of the PET Unit and from NSW Department of Health files. This included the original purchase of the PET scanner and the refurbishment

of the PET unit (this cost was covered by ANSTO), but does not include the cost of construction of the cyclotron. The information provided was the best estimate of the original purchase price and the date of purchase for each item of capital equipment. The GDP implicit price deflator was used to convert the purchase price to 1997-98 dollars. It was assumed that the useful life of computer hardware was 5 years, and the useful life of other capital equipment was 10 years, and that there would be no residual value. Using these assumptions and a discount rate of 5%, an equivalent annual cost of capital equipment was calculated.

Table 6 summarises the total costs of the PET Unit for 1997-98. The total costs for the 1997-98 financial year were $2.5 million.

TABLE 6: TOTAL COSTS FOR THE PET UNIT 1997-98

Resource Item	**Total Costs 1997-98**	
Recurrent		
Staff	$630,270	
Isotope	$647,700	
Goods and Services (other)	$57,143	
Repairs and Maintenance	$226,633	
Overheads	$183,401	
Total Recurrent		$1,745,147
Capital		
Building	$69,975	
Equipment	$686,649	
Total Capital		$756,624
Total		$2,501,771

4.2 Estimation of the Average Costs per Patient for the PET Unit

During 1997-98, 1287 patients were scanned. Thus, the overall average cost per patient scanned was $1944. However, this is the average cost estimated across all scans and not taking account of differences in the resource use between different types of scans. It is possible to provide a more detailed assessment of the average costs of scanning particular groups of patients, based on patient-level information from the PET Unit data base, which includes information such as the total time for a scan, the amount of isotope. Costs were attributed to patients as outlined below.

Staff costs

Costs for those staff involved in the overall administration of the unit were averaged across all patients scanned during the year. This included costs for medical staff, the clinical nurse consultant, and administrative and cleaning staff. This allocation of costs

was made on the basis that where these staff were involved in direct patient care, the resource use was not likely to substantial vary with the nature of the scan and the length of time for the scan.
Costs for other staff, directly involved in scanning the patients were attributed to each patient on the basis of the total time for the scan.

Other recurrent costs
Isotope costs were calculated on a per patient basis, although this involves averaging across patients as follows. While the pet unit is charged a fixed amount for a vial of isotope, the amount of isotope in a vial is variable. Thus, in practice the per patient cost of isotope will vary on a daily basis, depending on the amount of isotope produced. However, as this variability in cost cannot be predicted, in calculating a cost per patient, an effective price per unit of isotope (measured in megabecs) was estimated over the whole year, and this was used to attribute costs to patients based on the amount of isotope the patient received.

Other goods and services were averaged across all patients scanned during the year, on the basis that the amount of consumables did not vary with the length of time for a scan or the nature of the scan.

Overhead costs were averaged across all patients, on the basis that these costs cover items of resource use which do not vary with the nature of the scan or the length of time for the scan.

Repairs and maintenance costs were attributed to patient on the basis of the total time for the scan. This reflects the fact that the majority of these costs relate to upkeep of the pet scanner, and so they should be allocated on the same basis as the capital equipment (see below).

Capital costs
Capital costs were attributed to patients based on the total time for the scan. This reflects the fact that the opportunity cost of additional time spent scanning a patient is the time forgone scanning additional patients.

Table 7 provides a summary of the average costs for different groups of patients. As would be expected, the most costly scans are whole body scans, because they require more time and more isotope to provide a full image of the body. A whole body scan generally requires 8 'beds' to complete the study (one 'bed' represents approximately 10 cm).

TABLE 7 AVERAGE COST OF A PET SCAN BY TYPE OF SCAN

Type of scan		**1997/1998**	**1998/1999**[1]	**1999/2000**[1]
All Scans		**$1,944**	**$1,994**	**$2,040**
Whole Body		**$1,963**	**$2,013**	**$2,060**
	Lung	$1,975	$2,026	$2,072
	Melanoma	$2,106	$2,160	$2,210
	Gynaecological	$1,929	$1,978	$2,024
	Soft Tissue	$1,869	$1,917	$1,961
	Breast	$1,981	$2,032	$2,079
	Head and Neck	$2,086	$2,139	$2,189
	Urogenital	$1,949	$1,999	$2,045
	Haemotological	$2,036	$2,088	$2,136
	Unknown Primary	$1,889	$1,937	$1,982
	Other cancers	$2,076	$2,129	$2,178
	Gastro-intestinal	$1,841	$1,888	$1,932
	Neurological	$1,755	$1,800	$1,841
Head		**$1,856**	**$1,904**	**$1,947**
	Brain Tumours	$1,681	$1,724	$1,764
	Degenerative	$1,842	$1,889	$1,933
	Epilepsy	$1,815	$1,862	$1,904
	Other	$1,852	$1,899	$1,943
	Normal Volunteer/ Research	$2,664	$2,732	$2,795
Cardiology	Cardiac Viability	**$3,900**	**$4,000**	**$4,092**

1. Average costs have been re-estimated for the 1998-1999 and1999-2000 period using the total health price index.

5. Conclusion

This report evaluated the clinical uses, impacts on clinical management, clinical outcome and resource use of Positron Emission Tomography (PET) at Royal Prince Alfred Hospital in Sydney.

A current literature review emphasised the increasing role PET scanning in oncology diagnosis and management. However, the clinical studies and economic evaluations of this role are limited and not generaliseable to the Australian context. To date, studies have focused on determining the accuracy of PET as a diagnostic tool. Few studies have incorporated assessment of how PET affects clinical decision making or impact on patient outcomes and resource use.

Since the introduction of the PET unit at RPA in 1992, throughput has increased three fold from 443 patients in 1993 to1328 patients in 1998. Consistent with international trends, the use of the PET scanner at RPA has shifted towards oncology applications, namely lung cancer, colorectal cancer and melanoma.

The total cost of the PET unit for the 1997-98 financial year was reported at $2,501,771. The average cost per patient scan was approximately $1,950. At a more detailed level, average costs were found to vary by type of scan with cardiology scans ($3,900) found to be more expensive than whole body ($1,963) and neurology scans ($1,856). The high relative neurology scan cost was partially attributed to the relatively expensive normal volunteer/research neurology scans. The increasing trend towards oncological scans may result in a decrease in the number of patients scanned as the demand for whole body scans increases.

Further evaluation of the activity of the PET unit at RPAH is necessary. In part this requirement will be fulfilled by the results of the randomised controlled trial currently being conducted on the role of PET in management of patients with Non-Small Cell Lung Cancer. However, it can also be supplemented by further analysis of existing throughput. Such analysis can only be undertaken when the appropriate data become available.

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