Economic Analysis of Clinical Positron Emission Tomography of the Heart with Rubidium-82

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This report describes a cost analysis for clinical positron emission tomography (PET) of the heart using generator produced rubidium-82 (^{82}Rb). Considered sequentially are the clinical problem, current noninvasive radionuclide methods, positron emission tomograph, and the cost of PET per study. Also analyzed are the costs of PET versus thallium imaging in the management of chest pain, for screening asymptomatic men at high risk for coronary artery disease and for evaluating myocardial viability after myocardial infarction or thrombolytic therapy. Noninvasive assessment of coronary artery stenosis and myocardial ischemia/viability in symptomatic or asymptomatic subjects remains a major medical problem because the sensitivity and specificity of thallium imaging are only 70–85% and 50–70%, respectively, in recent studies. Cardiac positron imaging has an accuracy for noninvasive diagnosis of coronary artery disease in symptomatic or asymptomatic patients with a sensitivity and specificity of 95–98%. It can also be used for assessing physiologic stenosis severity, for imaging myocardial infarction and viability, for assessing effects of interventions such as thrombolysis, percutaneous transluminal coronary angioplasty (PTCA) or bypass surgery on myocardial perfusion, metabolism or coronary flow reserve, for assessing collateral function noninvasively in man, and for diagnosing cardiomyopathy not due to coronary artery disease. Although the cost for cardiac PET with ^{82}Rb may be modestly higher than for ^{201}Tl, the greater diagnostic yield of PET results in comparable or lower overall medical management costs than no diagnostic tests/interventions and lower overall costs compared to thallium imaging for evaluating patients with chest pain, asymptomatic high risk males, and patients after acute myocardial infarction/thrombolysis for myocardial viability.

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The introduction of new medical technology into widespread clinical use requires analysis of the benefits to patient care compared to the costs of its introduction and application versus existing technology. The analysis is inherently inexact for several reasons. It reduces subjective benefits of individual well being to statistical or monetary equivalents for comparison to other technologies or to alternative approaches. In addition, since the technology is new, by definition there is no exact or controlled past record on which to base cost and benefit projections. However, for positron emission tomography (PET) there are extensive publications on the specific clinical advantages for cardiac imaging in suitably large numbers of patients. The technology is also sufficiently advanced from the stage of university based development to manufacturing that cost and operating projections are reasonably accurate.

Translation of the subjective benefits for patients into cost equivalents for analytic purposes is always uncertain and at best only "reasonable". The benefit-cost equivalences for the current analysis are not intended to imply value judgements on other technologies, current medical practices, or the value of human well being or life. Rather, this analysis is made because the current evolutionary stage of PET provides an opportunity to analyze, understand, and optimize the introduction of a major new medical technology for economical patient care.

This cost analysis for clinical PET of the heart using generator produced rubidium-82 (^{82}Rb) is undertaken by approaching sequentially the clinical problem, cur-

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rent noninvasive radionuclide methods, PET, the cost of PET per study, and costs of PET versus thallium imaging, or no intervention, for evaluation of chest pain, of asymptomatic men at high risk for coronary artery disease, and of myocardial viability after myocardial infarction or thrombolysis therapy.

THE CLINICAL PROBLEM

Accurate noninvasive assessment of coronary artery stenosis and myocardial ischemia/viability in symptomatic or asymptomatic subjects remains a major medical problem for a number of reasons. Coronary heart disease continues to be the leading cause of death in most technologically advanced countries, responsible for one-third to one-half of all deaths between the ages of 35 and 64 yr old. Much of this heart disease is asymptomatic until some serious clinical event occurs. For example, 40% to 60% of patients with sudden death or myocardial infarction present with no prior symptoms (*1–4*). Up to 13% of middle aged men in the general population have coronary artery disease (*5,6*), most without symptoms. Silent ischemia is increasingly recognized in symptomatic and asymptomatic individuals (*7*) and has an unfavorable prognosis when observed in patients with recent unstable angina (*8*) or during exercise testing (*9*).

Finally, the community model of mass intervention for coronary atherosclerosis has been of questionable benefit compared with the medical model of intervention by risk factor control in specific individuals (*10*). However, even assuming its effectiveness, the medical model of risk factor control is limited by the low sensitivity and specificity with which risk factors identify individuals who have significant coronary artery disease (*11*). For example, two-thirds of healthy adult males, aged 40–55 yr, with the highest cholesterol and blood pressure risk factors remain well over the subsequent 25 yr (*12*).

Therefore, important questions are how to detect coronary artery disease and how to quantify it (*13–15*), particularly when atypical symptoms or absence of symptoms provide no clinical guide to severity or therapy that would prevent sudden death or myocardial infarction. Physiologic measures of stenosis severity, multidimensional anatomic quantitative analysis of stenoses and/or metabolic measurements of myocardial ischemia thus become necessary to select patients for appropriate coronary procedures and to avoid unnecessary ones. With the availability of effective drugs and radical lifestyle change to reduce cholesterol, selection of patients for medical therapy also requires noninvasive evaluation to assess severity and progression/regression of coronary artery disease.

As thrombolysis for acute myocardial infarction has become widespread, identification of ischemic, viable myocardium is essential for deciding upon definitive follow-up procedures such as PTCA or bypass surgery. For a completed myocardial infarction without remaining viable tissue, further interventions are not indicated. For patients with substantial ischemic viable myocardium continuing at risk, PTCA or bypass surgery may be indicated. Therefore, a reliable method for identifying ischemic, viable myocardium, and its extent would substantially reduce unnecessary procedures and select those patients for whom a follow-up procedure would be most beneficial.

CURRENT NONINVASIVE RADIONUCLIDE METHODS

Although they are important for evaluating patients with angina pectoris, current noninvasive diagnostic techniques have limited diagnostic yield, particularly for assessing patients at high risk for coronary disease or having abnormal exercise tests with atypical or no symptoms (*11,13–16*). The sensitivity, specificity, and/or predictive accuracy of exercise thallium imaging in earlier literature is 80–90% in symptomatic patients (*17–19*) but ranges down to 50% in more recent studies (*20–23*). One reason for low specificity in recent studies may be because patients with negative thallium stress tests no longer undergo cardiac catheterization. The catheterized population in a study would be biased by this exclusion of normals, thereby reducing calculated specificity. However, a large recent study with a sensitivity of 76% and specificity of 49% was not biased by this selection because all 832 subjects, asymptomatic Air Force personnel, had coronary arteriograms (*22*). Predictive accuracy falls low enough in asymptomatic populations (low prevalence) as to be of limited value for routine diagnostic testing (*20,22–26*) in patients with high risk factors. However, routine yearly treadmill testing is now commonly done in asymptomatic individuals despite limited demonstrated efficacy for clinical diagnosis in these circumstances. Consequently, an accurate method for assessing coronary artery disease and ischemic or viable myocardium in symptomatic or asymptomatic individuals would be useful.

Currently, bypass surgery or PTCA is commonly done after thrombolysis therapy with only limited evidence for remaining viable myocardium. The most commonly used approach for assessing viability is redistribution on late thallium images (*27,28*). However, myocardial uptake of fluorodeoxyglucose by positron imaging as a direct measure of metabolic viability is reportedly better than redistribution of thallium for identifying viable myocardium (*29*). Since it is common practice to carry out PTCA or bypass surgery after thrombolysis therapy, an accurate method for assessing viability would be an important addendum to our current diagnostic armamentarium, particularly if un-

necessary procedures or surgery could be substantially reduced in patients who have had thrombolysis therapy.

POSITRON EMISSION TOMOGRAPHY

The concept of coronary flow reserve as a functional measure of stenosis severity was initially proposed in 1974 by Gould et al. and was subsequently developed as a physiologic diagnostic method using i.v. dipyridamole (*30–40*). However, the application of this concept for clinical studies has been limited by the lack of quantitative imaging techniques until positron imaging became fully developed for clinical use. In the past, PET has been a complicated, expensive technology requiring a team of radiochemists, physicists, and physicians to carry out research studies providing important medical-scientific information, but limited in clinical application because of their complexity. The technology has now evolved into routinely applicable clinical equipment/procedures which provide information not previously obtainable and having significant impact on medical diagnosis and therapy.

Positron imaging of the heart with either generator produced ^{82}Rb or cyclotron produced nitrogen-13 (^{13}N) ammonia or fluorine-18 deoxyglucose is suitable for accurate noninvasive-invasive diagnosis of coronary artery disease in symptomatic or asymptomatic patients with a sensitivity and specificity of 95–98% (*38,40–42*), for assessing physiologic stenosis severity (*38,40,43–45*), for imaging myocardial infarction (*46–54*) and viability (*29,47–53*), for assessing effects of interventions such as thrombolysis or PTCA on myocardial perfusion or coronary flow reserve or bypass surgery on function and metabolism (*29,49,51,55*), for assessing three-dimensional regional left ventricular function (*40,56*), for assessing collateral function noninvasively in man (*14,57*), and for diagnosing cardiomyopathy not a result of coronary artery disease (*58,59*). These sophisticated clinical applications are feasible due to the unique capacity of positron imaging for quantitative analysis of myocardial perfusion and metabolism. Positron imaging therefore provides the basis for specific therapeutic approaches in the management of heart disease, particularly of coronary artery disease.

Although a cyclotron and radiochemist are necessary for the broad spectrum of metabolic studies, the ^{82}Rb generator provides a source of positron radionuclide without a cyclotron (*60*), allowing routine clinical studies of cardiac perfusion and function. Rubidium is an alkali metal analogue of potassium and similar in its chemical and biological properties. It is rapidly concentrated by the myocardium with a first-pass extraction of 60% at resting flow levels, but falls to 20–30% at high flows (*61–63*). By comparison, first pass myocardial extraction of [^{13}N]ammonia is somewhat higher, 70%, falling to approximately 25%–35% at high flows (*64,65*). For equal millicurie doses, rubidium images contain fewer counts than ammonia images due to the short half-life of Rb. However, with appropriately larger doses of ^{82}Rb used clinically (40 mCi to 50 mCi), images are comparable to those of [^{13}N]ammonia (*40*) for the same or lower radiation exposure. Rubidium-82, because of its short half-life (75 sec), is particularly well suited for repeated or sequential myocardial imaging, allowing rapid patient throughput. It is therefore useful in acute clinical situations in which the patient's condition is changing rapidly or for studies before and after an intervention such as dipyridamole stress or PTCA in a private lab where patient volume is essential.

Economic Analysis of Clinical Positron Emission Tomography

Cost per PET study using ^{82}Rb

In order to analyze the cost and therefore charges per PET study, a realistic pro forma is shown below using the following assumptions:

1. A study for assessing myocardial perfusion consists of rest and dipyridamole stress images.
2. The PET scanner price for complete turnkey operations is $2,400,000 with $461,000 down and a $1,939,000 loan at 12% interest.
3. Bad debt: 20.00%.
4. Tax rate: 34.00%.
5. Inflation: 6.00%.
6. Charge per study: $1,200.

The analysis is shown in Table 1 for a charge of $1,200 per study for the technical fee without a physicians professional fee, considered later. Bad debt refers to studies done for which incomplete or no payment is made. A steady state of eight patients per day is assumed. Expenses include salaries for technical staff to operate the PET facility and a maintenance contract for the scanner beginning in the second year, the first year being covered by warranty. Costs of the ^{82}Rb generator are estimated to be $20,000 per generator, purchased each month.

The internal rate of return on investment in the PET facility for an optimal case load of eight patients per day at a charge of $1,200 each is 17%. This return is reasonable for the investment made relative to the risks of maintaining case load and collecting 80% or more of payments due. A fall in daily case load of only two patients to six/day reduces the internal rate of return to 7%. A return of 7% is comparable to that from a bank savings account or Certified Deposit and is inadequate for the investment risk. For a charge of $1,200 per study, the breakeven point in the first year is five patients per day, shown in Figure 1. For this analysis, cost includes interest and taxes and bad debt have been deducted from revenues.

TABLE 1
Proforma for Clinical Cardiac PET with ^{82}Rb

Assumptions						
	Camera price:	$2,400,000	Amt down:	$461,000	Loan value:	$1,939,000
	Interest rate:	12.00%	Bad debt:	20.00%	Price:	$1,200
	Tax rate:	34.00%	Inflation:	6.00%		

PET studies	Year 1	Year 2	Year 3	Year 4	Year 5
Daily average	4	6	8	8	8
Volume/year	1040	1560	2080	2080	2080
Charge/study ($)	1200	1272	1348	1429	1515
Revenue ($)	1248000	1984320	2804506	2972776	3151142
Less Bad debt ($)	249600	396864	560901	594555	630228
Net Revenue ($)	998400	1587456	2243604	2378221	2520914
Expenses ($)					
Technician	30000	31800	33708	35730	37874
Nurse	30000	31800	33708	35730	37874
Depreciation	480000	480000	480000	480000	480000
Maintenance	0	254400	254400	254400	254400
Isotope (Rb-82)	240000	254400	269664	285844	302994
Rent/overhead	20000	21200	22472	23820	25250
Utilities	10000	10600	11236	11910	12625
Admin/secr	50000	53000	56180	59551	63124
Supplies	52000	82680	110240	110240	110240
Crash cart	26000	67416	71461	75749	80294
Total expenses ($)	938000	1287296	1343069	1372975	1404675
EBIT*	60400	300160	900536	1005246	1116239
Interest	216476	178288	135257	86768	32130
EBT†	−156076	121872	765279	918478	1084109
Less taxes	−53066	41436	260195	312282	368597
EAT‡	−103010	80436	505084	606195	715512
Add back dep	461000	461000	461000	461000	461000
After tax CF§	357990	541436	966084	1067195	1176512
IRR** on investment of $2,400,000 at end of 5 yr					17%/year

* Earnings before interest and taxes.
† Earnings before taxes.
‡ Earnings after taxes.
§ Cash flow.
¶ Depreciation.
** Internal rate of return.

A decrease in payment to $1,000 per study becomes borderline at eight patients per day with an internal rate of return of only 7%, again comparable to a bank savings account. At this charge per study, a decrease in case load to six/day results in an internal rate of return of minus 3%, a loss. As shown in Figure 2 the breakeven point at a charge of $1,000 per study is ~6.5 cases per day.

Based on this analysis, the technical charge for clinical PET with ^{82}Rb should be $1,200 per study with a case load of six to eight studies/day. Fewer studies or lower charges are not economical. With professional fee, the total cost would be $1,500 per study. The question then arises: What is the impact or societal cost/benefit relative to current thallium perfusion imaging that is less costly per study but also has a lower diagnostic yield and therefore incurs real additional costs resulting from less accurate diagnosis?

Economic Analysis of PET For Evaluating Patients with Chest Pain

The following assumptions and analysis are hypothetical for purposes of illustration based on available data and/or conservative, reasonable estimates. The purpose is to determine whether the greater diagnostic yield of PET compensates for its greater cost per study compared to thallium exercise testing such that the overall costs of medical management based on PET imaging is comparable (or not) to that for thallium imaging for assessing patients with chest pain.

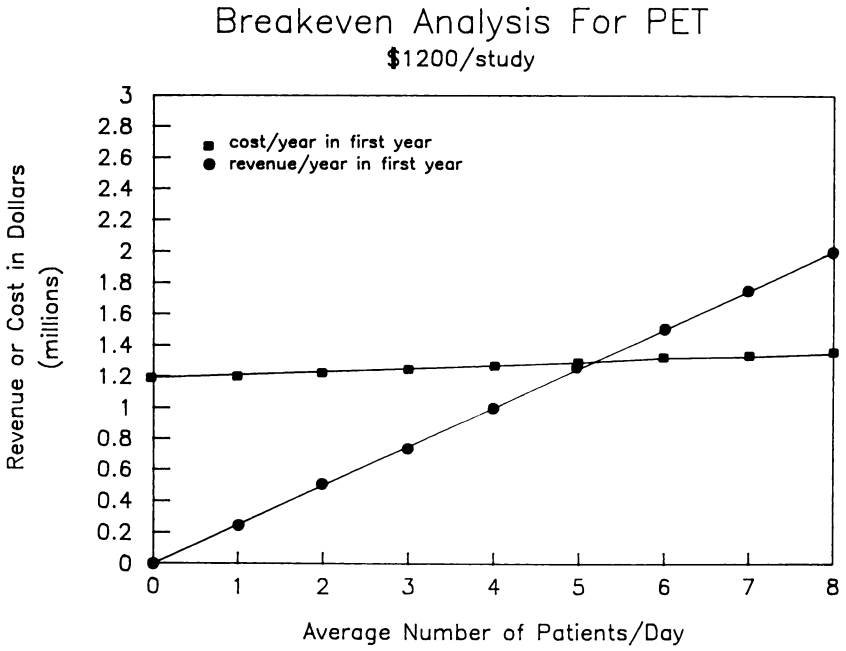

FIGURE 1
Breakeven analysis for PET operations at $1200 per cardiac study, including rest and stress images. Vertical axis shows revenue or cost in millions of dollars per year and horizontal axis shows average number of patients studied per day. Breakeven is approximately five patients per day.

Assumptions

1. Analysis is per 100 patients with chest pain.
2. Prevalence of significant coronary artery disease by coronary arteriography in this group is 25% (*24*).
3. Based on recent publications through 1988, sensitivity of stress thallium imaging ranges 76% to 93% here assumed to be 85%, and specificity ranges down to 49% here assumed to be 60% based on the largest, most recent reports, for false-positive results of 40% (*11,17–26*). However, no direct comparisons of PET with stress thallium have been carried out in a population with mild or equivocal chest pain where the prevalence of disease is ~25%.
4. Cost of exercise thallium testing is $950 per study including professional fee.
5. Sensitivity and specificity of PET is 95% or higher (*38,40,41,66*).
6. Cost of PET is $1,500 per study ($1,200 technical fee plus $300 physicians fee).
7. Coronary arteriography at a total cost of $6,000 per patient including professional fees is done in all patients with a positive noninvasive test.

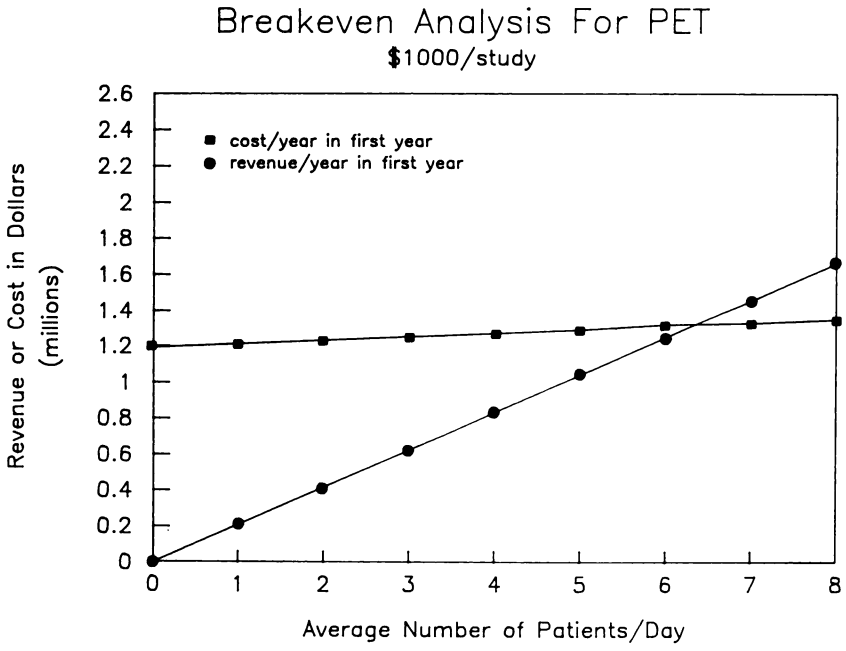

FIGURE 2
Breakeven analysis for PET operations at $1000 per cardiac study, including rest and stress images. Vertical axis shows revenue or cost in millions of dollars per year and horizontal axis shows average number of patients studied per day. Breakeven is approximately 6.5 patients per day.

8. Of those patients with significant CAD, 85% are treatable either by percutaneous transluminal coronary angioplasty (PTCA) or saphenous vein bypass grafting (SVBG).
9. Half of patients with treatable significant CAD by coronary arteriography have PTCA at a cost of $10,000 each and half have SVBG at a cost of $20,000 each.

Analysis of cost of medical management based on exercise thallium imaging

1. Of 100 patients with chest pain, 25 have significant CAD and 75 do not based on prevalence of 25%.
2. The total number of positive thallium tests are (25) (85%) + (40%) (75) = 21.3 + 30 = 51.3.
3. Therefore, 51.3 patients undergo coronary arteriography based on a positive thallium test.
4. Of these 51.3 patients, 21.3 have significant CAD and 30 do not as shown in Step 2 above.
5. Of the 21.3 with CAD, 18 are treatable with interventions (85%), of whom nine have SVBG and nine have PTCA.
6. Of the 25 patients with CAD, (25) (15%) = 3.75 patients have normal exercise thallium tests, are not further studied and therefore are "missed".
7. Total cost of medical management based on thallium imaging is

Thallium Test:	100 × $950	=	$95,000
Coronary Arteriog.	51.3 × $6,000	=	$307,800
PTCA	9 × 10,000	=	$90,000
SVBG	9 × 20,000	=	$180,000
	Total Cost		$672,800

Analysis of cost of medical management based on PET using ^{82}Rb

1. Total number of positive PET tests are (95%) (25) + (5%) (75) = 23.8 + 3.8 = 26.6.
2. Therefore, 26.6 patients have coronary arteriography based on PET.
3. Of these 26.6 patients, 23.8 have significant CAD and 3.8 do not as shown in Step 1 above.
4. Of the 23.8 with CAD, 20.2 are treatable (85%), ten by PTCA and ten by SVBG.
5. Of the 25 patients with CAD, (25) (5%) = 1.25 patients have normal PET tests, are not cathed and therefore are "missed".
6. Total cost of medical management based on PET is

PET	100 × $1,500	=	$150,000
Coronary arteriog.	26.6 × 6,000	=	$159,600
PTCA	10 × 10,000	=	$100,000
SVBG	10 × 20,000	=	$200,000
	Total cost		$609,600

These figures show that PET is comparable or less costly than thallium imaging for the diagnosis and management of patients with chest pain. The reason is that a large number of patients with positive stress thallium tests and normal coronary arteries undergo coronary arteriography whereas these patients are more likely to have normal PET scans and thereby avoid catheterization. In addition, for PET, 1.25 patients are "missed" versus 3.75 patients for thallium imaging.

For calculating the potential economic impact of the lower diagnostic yield with thallium imaging, the following additional assumptions and analysis for loss of wages/productivity were made.

1. Because it identifies mild (earlier) CAD, a normal PET study need not be repeated for 5 yr since this time period would likely be required for clinically severe coronary artery narrowing to develop from stenoses mild enough to produce no stress perfusion defect by PET.
2. Mortality of those individuals with severe CAD, missed and untreated, ranges from 6% to 25%, and is here assumed to be 7%/yr (*2,9,67–74*). For the 5-yr period following a PET scan, the cumulative mortality in the missed patients is therefore 35%. Although the prognosis is purportedly good in patients with normal exercise thallium tests in the presence of angiographically proven CAD, such studies are likely to be strongly biased by the exclusion from the study population of those patients who have already had PTCA, bypass surgery, sudden death or myocardial infarction. Accordingly, we have used the known mortality of patients with angiographically severe disease.
3. Yearly wages lost at $30,000/yr for 5 yr is $150,000; cost of mortality per deceased person is $5,000 for a total expense of $155,000 per deceased person.
4. For a mortality of 7%/yr, over a 5-yr period following diagnostic evaluation, the mortality is (35%) (3.75) = 1.31 deaths/5 yr in the "missed" cases after thallium testing versus (35%) (1.25) = 0.44 deaths/5 yr in the "missed" cases after PET. Medical management based on thallium imaging therefore theoretically incurs a mortality of 1.31/0.44 or 3.0 times that for PET with corresponding losses of wages/productivity and cost of mortality.
5. Loss of wages and productivity over a five year period due to mortality in the "missed" are

Thallium	1.3 × $155,000	=	$201,500
PET	0.44 × 155,000	=	$68,200

6. The total combined cost of medical management of those patients diagnosed as having CAD and wages lost due to mortality in the missed, untreated individuals over a 5-year period per 100 patients would be

	Medical Costs		Lost Productivity		
Thallium	$672,800	+	$201,500	=	$874,302
PET	$609,600	+	$68,200	=	$677,802

Conclusions for evaluating chest pain

Although the cost of cardiac PET with ^{82}Rb at $1,500 per study is higher than for thallium imaging at $950 per study, the greater diagnostic yield of PET theoretically results in lower overall costs of medical management compared to thallium imaging for evaluating patients with chest pain. These results are summarized in Table 2.

TABLE 2
Economic Analysis of PET for Dx/Rx Chest Pain

	Thallium	PET
Patients Dx/Rx	18	20
Cost of tests/100	$ 95,000	$150,000
Coronary arteriography	307,000	159,600
PTCA, SVBG	270,000	300,000
Total direct costs	$672,800	$609,600
Lost productivity/5 yr	$201,500	$ 68,200
Direct costs + lost productivity	$874,302	$677,802
Mortality persons/5 yr	1.31	0.44

PET for Evaluating Asymptomatic Individuals with Risk Factors

Screening of asymptomatic individuals for CAD has generally been considered inappropriate for several reasons. The limited diagnostic yield of standard noninvasive testing does not provide good identification of normals and abnormals. For this limited diagnostic yield, cost of current noninvasive testing leading to large numbers of normal patients undergoing coronary arteriography is excessive, thereby making "screening" tests inappropriate. In the past, interventional therapy, especially bypass surgery, was also not appropriate for this group because symptoms of angina pectoris have been the primary criterion for surgery. However, PET technology for accurate noninvasive diagnosis, mechanical intervention, and pharmacologic therapy have now evolved sufficiently to reconsider the potential impact of this approach. For high risk individuals defined as males 45 to 65 yr old with one or more risk factors of smoking, hypertension, hypercholesterolemia (or abnormal HDL/LDL ratios) and/or family history of CAD, prevalence of CAD is 15% to 35% (*5,6,26*) with disease that is anatomically severe ranging from 7% to 35% (*26*). Using an approach like that above for chest pain, the cost of screening for and treating severe coronary artery disease in asymptomatic individuals with risk factors for coronary atherosclerosis can also be analyzed. The total direct cost of screening by PET and cost of therapy per 100 individuals with risk factors is calculated to be less than the direct care costs plus lost productivity of an unscreened group with risk factor subject to the recognized prevalence of sudden death, myocardial infarction, or subsequent angina (*2,9,67–74*). However, the assumptions on productivity, such as salary, make this analysis more debatable since it involves the difficult question of economic equivalents of life and mortality.

The currently reported specificity is 50–75% for thallium imaging (*11,17–26*) particularly in asymptomatic patients. If all such patients with positive thallium studies were catheterized, approximately one-half to one-third would have normal coronary arteries. The cost of doing arteriography in this large number of patients without disease makes the total costs of medical management by thallium imaging more expensive than PET for this application.

PET for the Postinfarction Patient

Similar logic can be applied to the postmyocardial infarction patient. Fifty to seventy percent of patients or myocardial segments have significant remaining viable myocardium after myocardial infarction (*29,48,49*), 85% of which demonstrate improved contractile function after reperfusion (*48*). By thallium redistribution studies, only half of these patients have viable myocardium (*29*) with the balance being classified as completed infarctions without viable myocardium when they in fact have viable tissue by PET studies. Mortality after myocardial infarction ranges 7% to 30% (*2,67,69,70–74*) without revascularization or reperfusion. Consequently, the difference in accuracy between PET and thallium for identifying patients with viable myocardium can be analyzed in terms of differences in mortality, lost productivity, and direct care costs. Because of its greater accuracy in identifying patients with viable myocardium appropriate for PTCA or bypass surgery, unnecessary procedures can be avoided and mortality/morbidity can be minimized at cost savings that offset the modestly higher costs of PET compared to thallium. In this application, the overall costs of medical management based on PET can be shown to be comparable or less than for thallium imaging.

OVERALL ECONOMIC ANALYSIS OF CLINICAL CARDIAC PET WITH ^{82}Rb

Although the cost for a PET study with ^{82}Rb may be somewhat higher than for a ^{201}Tl study, the greater diagnostic yield of PET results in comparable or lower overall medical management costs than no diagnostic tests/interventions and comparable or lower overall costs than thallium imaging for evaluating patients with chest pain, asymptomatic high risk males and patients after acute myocardial infarction/thrombolysis for myocardial viability.

Radiation Burden

The radiation burden to patients by positron tracers of ^{82}Rb, [^{13}N]ammonia, and [^{18}F]FDG are generally comparable or lower than standard cardiac nuclear tracers such as ^{201}Tl because the half-life of the positron tracers are short. Optimal clinical benefit with most appropriate choice of test, its safe application, and proper interpretation within the clinical context of a specific patient for a given radiation dose make positron imaging an optimal clinical tool with relatively low radiation burden to patient and staff.

Personnel and Facility Requirements

Two types of facilities for cardiac PET are appropriate. The first is a positron camera utilizing generator produced ^{82}Rb in the absence of a cyclotron. The second includes a cyclotron-radiochemistry complex. For clinical studies, both facilities would require a room ~15 ft by 15 ft for the camera with an attached smaller space 10 ft × 10 ft as a computer room, control console, and reading center. Appropriate cardiac drugs and resuscitation equipment are required in the imaging room, including defibrillation, intubation facilities, and emergency cardiac drugs. Since the stress provided for the screening test utilizes intravenous dipyridamole, appropriate EKG monitoring should be available. Physician supervision is necessary for carrying out these studies due to the infusion of vasoactive drugs comparable to exercise stress. On occasion, patients with coronary artery disease undergoing dipyridamole-hand grip stress develop angina pectoris which requires reversal utilizing intravenous aminophylline. Aminophylline is effective in reversing the effects of dipyridamole quickly. Consequently, the test sequence may be well controlled. A cardiologist is essential for evaluating the patient during the test in order to determine whether this reversal step is necessary.

Available positron cameras have become sufficiently dedicated with operational software transparent to the user that a technician can carry out the procedure under the supervision of a physician. Physicians with expertise in physiologic cardiovascular imaging are the appropriate individuals for choosing the appropriate patients, the study to be done, and for carrying out the test protocol, for study interpretation, and for supervising the program. Such physicians may be cardiologists, nuclear medicine physicians, or radiologists with knowledge of cardiovascular imaging, cardiovascular physiology, coronary arteriography, and particularly clinical management of cardiac disease including cardiac emergencies, resuscitation, arrhythmias, and cardiac arrest.

Status with Regulatory Agencies

PET cameras are now commercially distributed as a Class II device registered with the FDA using Form 510K under FDA guidelines USDHHS Section 21CFR 807, Class II (Performance Standards), Premarket Notification for Medical Devices under a grandfather clause for preexisting technology. The cost analysis for a cyclotron source of positron radiotracers is beyond the scope of this study. Intravenous dipyridamole for stress perfusion imaging and the ^{82}Rb generator are both currently being reviewed by the Food and Drug Administration. This analysis shows the potential value of the ^{82}Rb generator for positron imaging when it becomes available for widespread use.

CONCLUSIONS

For medical centers with PET facilities, cardiac positron imaging serves as a routine diagnostic clinical tool for the following reasons:

1. Cardiac PET provides information not previously available for better diagnosis and management of cardiac disease. This new information includes the accurate, noninvasive diagnosis of coronary artery disease in asymptomatic or symptomatic patients, the noninvasive assessment of coronary stenosis severity, myocardial infarct imaging, assessment of myocardial viability, collateral function, and cardiomyopathy.
2. Cardiac positron imaging may utilize generator produced ^{82}Rb or a variety of cyclotron produced metabolic and flow radiotracers to obtain unique data on myocardial perfusion, function, infarction and viability, having major clinical and research significance. Either asymptomatic or symptomatic patients may be studied with high accuracy on an outpatient or inpatient basis.
3. Although the cost of PET with ^{82}Rb per study is higher than thallium imaging, the greater diagnostic yield of PET results in comparable or lower overall medical costs than no diagnostic tests/interventions and comparable or lower costs than thallium imaging for evaluating patients with chest pain, for screening asymptomatic high risk males and for assessing myocardial viability in patients after myocardial infarction or thrombolysis therapy.

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