Studies with N-13 Ammonia

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1. Schelbert	AJC 1982	To evaluate the detection of coronary artery disease in humans	-13 Normals -32 Patients	Rest/Stress (Dipyridamole)	Visual	97% Sensitivity (15/16 SVD, 6/6 2VD & 10/10 3VD) 90% of the coronary stenoses were correctly identified	N-13 Ammonia administered during pharmacologic coronary vasodilation is highly sensitive for non-invasive detection of CAD in humans and for estimating extent of disease
2. Konishi	Japanese Circulation Journal 1988	To evaluate the effect of surgery on myocardial perfusion and to predict graft status	-20 Patients	Rest/Stress	Visual	90% of pre-op ischemic segments normalized with surgery. Most persistent defects showed no post-operative change	Vessels to ischemic areas are suitable for bypass; vessels to persistent defects are not. Graft patency could be demonstrated by normal post op perfusion or improved perfusion from baseline to post-op. Graft occlusion could not be predicted. N-13 ammonia was useful for assessing effects of CABG, but not significantly superior to Tl-201 for only qualitative analysis
3. Hutchins	JACC 1990	To measure regional myocardial blood flow by quantitative analysis	-7 Healthy Volunteers	Rest-dipyridamole stress w/ hand grip exercise	Quantitative	Coronary Blood Flow and Coronary Flow Reserve were successfully measured	Quantification of myocardial blood flow is feasible with dynamic N-13 ammonia PET which may provide accurate noninvasive definition of function significance of CAD
4. Krivokapich	JACC 1991	To evaluate exercise myocardial blood flow after cardiac transplant	-10 Normal volunteers -12 Patients	Rest – Bicycle Exercise	Quantitative	Myocardial Blood Flow during exercise was not significantly different between groups (1.7 vs. 1.56 ml/min/gr)	Myocardial blood flow response to exercise stress is appropriate in transplant recipients and comparable to normal subjects
5. Himi	Am. Jour of Physiologic Imaging 1991	To assess the response of myocardial blood flow to Dipyridamole in different clinical set of subjects	-5 Normal volunteers -5 Hypertropic Cardiomyopathy -7 CAD	Rest – Dipyridamole Stress	Quantitative	Mean Regional MBF increased: 126% in normal volunteers 55% in HCM 19% in CAD Ischemic regions 76% in CAD Non-Ischemic regions	N-13 Ammonia PET can measure blood flow changes in response to Dipyridamole

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6. Dayanikli	Circulation 1994	To assess coronary artery flow reserve in asymptomatic middle age men w/ positive family history of CAD & high risk lipid profile	-16 High Risk -11 Low Risk	Rest – Adenosine Stress	Quantitative	Mean rest global myocardial blood flow was not significantly different. Mean stress global MBF was higher in low risk group. Coronary flow reserve was greater in low risk group	N-13 Ammonia PET can detect abnormal vasodilatory response to IV adenosine in asymptomatic male patients with a family history and high risk lipid profile. Assessment may allow early detection of preclinical CAD
7. DiCarli	Circulation 1995	To determine the relationship between myocardial blood flow and flow reserve to percent stenosis on quantitative arteriography	-18 Patients -10 Healthy Volunteers	Rest – Dipyridamole Stress	Quantitative	Myocardial blood flow and blood flow reserve were not significantly different in normal regions in patients with CAD and normal volunteers. PET estimate of myocardial blood flow reserve can differentiate coronary lesions of intermediate severity (50-70% & 70-90%)	Myocardial blood flow and coronary flow reserve by PET are inversely and non-linearly related to severity of coronary artery stenosis as defined by quantitative angiography.
8. Beanlands	JACC 1995	To determine the relationship between coronary artery flow reserve and coronary artery stenosis and determine if Flow Reserve is affected in areas supplied by vessels without significant coronary artery disease.	-27 Subjects -5 Young volunteers -7 Middle Age volunteers -15 patients with CAD	Rest – Adenosine Stress	Quantitative	CAD Flow Reserve None: 2.95 Mild: 2.09 Mod: 2.02 Severe: 1.30	Functional severity of CAD correlated well to angiographic severity. In patients, regions without significant angiographic stenoses had reduced coronary flow reserve indicating vascular reactivity was more diffusely impaired in patients with CAD than was suggested by angiography.
9. Duvernoy	J Nucl Cardiol 1995	To predict functional outcome after revascularization	-25 Patients w/ impaired regional wall motion	Rest Only	Semi-Quantitative	>85% of N-13 ammonia uptake in a segment is highly accurate in predicting normal post op regional wall motion, while <40% uptake of N-13 ammonia had normalization in only 13% of segments	N-13 ammonia uptake >80% or <40% of maximal uptake had excellent predictive value for functional outcome. N-13 ammonia uptake between 40% and 80% needed additional information for prediction.

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10. Campisi	Am Jour. Cardiology 1997	To evaluate blood flow in by pass grafts late after CABG	-15 Patients -10 Healthy Volunteers	Rest – Dipyridamole Stress	Quantitative	Rest myocardial blood flow did not differ between patients and controls, and was similar in normal myocardium supplied by SVG or LIMA. Hyperemic response and coronary flow reserve in normal myocardium supplied by grafts were less than that in controls.	Non-obstructive proliferative fibro-intimal changes of bypass conduits or atherosclerosis of the native resistance vessels may account for impaired hyperemic response
11. Muzik	JACC 1998	To correlate myocardial blood flow with the extent of coronary artery disease	-31 patients w/ CAD -20 normal Controls	Rest – Adenosine Stress	Quantitative	Myocardial blood flow and flow reserve were significantly different between normal subjects and patients with CAD of > 50% stenosis. There was also a significant difference between normal subjects and angiographically normal territories of patients with CAD.	N-13 ammonia PET provides high performance level for the detection and localization of CAD
12. Lancellotti	International Journal of Cardiac Imaging 1998	To assess the role of N-13 ammonia PET performed early after acute MI for predicting functional recovery	-17 patients with acute MI	Rest Only	Semi-Quantitative % Maximal Uptake	Segments with N-13 ammonia uptake ≥ 50% of maximum had significant improvement in wall thickening at F/U. < 50% uptake had no improvement. Predictive value for defining recovery with uptake > 63% was 86%. For absence of recovery (uptake < 50%) was 54%.	N-13 Ammonia PET early after myocardial infarction provides information regarding functional outcome
13. Duvernoy	JACC 1999	To compare myocardial blood flow in hyperlipidemic post-menopausal women and hyperlipidemic men	-15 Women -15 Men Non Diabetic, age and cholesterol level matched	Rest – Adenosine Stress	Quantitative	Women had higher rest and stress myocardial blood flow	A favorable lipid profile in women may be associated with preserved maximal blood flow in the myocardium

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14. Giorgetti	J Nucl Cardiol 1999	To correlate myocardial blood flow and flow reserve in patients with stress induced normalization of T-waves	14 Patients -7 with negative T-waves (NTW) that normalized during stress -7 with negative T-waves (NTW) that did not normalize during stress	Rest – Dipyridamole Stress	Quantitative	Resting blood flow was similar in both groups of normalized NTW inversion vs. persistent NTW inversion, but lower than in normal subjects. After dipyridamole, MBF was higher in patients with normalized NTW	Patients with NTW that normalize at stress have higher CFR, likely due to preserved coronary microcirculatory function, indicating myocardial viability
15. Shikama	Am J Cardiol 1999	To identify any association between an abnormality in myocardial perfusion and prognosis in patients with Idiopathic Dilated Cardiomyopathy (IDC)	26 Patients -17 Survivors -9 Non-Survivors 8 Normal Controls	Rest	Quantitative	Mean regional myocardial blood flow in survivors was lower than controls, but did not differ between non-survivors and controls. The co-efficient of variance (COV) of regional myocardial blood flow (measure of heterogeneity of myocardial perfusion) was higher in non-survivors than in either survivors or normal controls. Probability of 3 year survival was 33% if the COV was > median, 90% if the COV was < median.	Prognosis of patients with IDC is associated with the spatial heterogeneity of myocardial perfusion, not with initial absolute regional myocardial blood flow.
16. Kosa	JACC 1999	To evaluate myocardial flow reserve in patients early after coronary stent implantation	-14 Patients	Rest – Adenosine Stress	Quantitative	Rest and stress myocardial blood flow, and coronary flow reserve in areas supplied by stented coronary arteries did not differ significantly from that in remote areas	Coronary artery stents restore macroscopic integrity of epicardial arteries and results in early recovery of coronary flow reserve

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17. Yates	Pediatric Cardiology 2000	To evaluate myocardial perfusion in children after a surgical arterial switch procedure for correction of transposition of the great arteries	-11 Patients	Rest – Dipyridamole Stress	Quantitative	Rest myocardial blood flow was similar to reported adult rest values with a small, but significant increase in response to dipyridamole with a mean coronary flow reserve of 1.19	PET with N-13 ammonia is a reliable non-invasive method for evaluation of myocardial perfusion in small children, but data need to be interpreted with caution because normal data in children not available
18. Singh	JACC 2001	To assess myocardial blood flow and flow reserve in the systemic right ventricle in long term survivors of the Mustard operation	-11 Patients -13 Controls	Rest – Adenosine Stress	Quantitative	No difference was found in basal myocardial blood flow in the systemic RV of Mustard operation survivors and the systemic LV in normal controls. Hyperemic blood flows and, thus, myocardial flow reserve, were significantly lower in systemic RVs than in LVs.	Myocardial flow reserve is impaired in systemic right ventricles in survivors of the Mustard Operation, which may contribute to systemic ventricular dysfunction in these patients
19. Duvernoy	Journal of Gender-Specific Medicine 2001	To measure the effects of hormone replacement therapy on myocardial blood flow in post-menopausal women at high risk for coronary artery disease (Group I) and in women with documented coronary artery disease (Group II)	Group I -10 Patients Group II -8 Patients	Rest – Adenosine Stress	Quantitative	There was no difference in rest myocardial blood flow between Group I & II prior to therapy or at follow up. Stress myocardial blood flow and flow reserve were higher in Group I at baseline and at follow up.	Short term hormone replacement therapy in post-menopausal women did not result in improvements in myocardial blood flow or flow reserve.

Combined Studies with N-13 Ammonia and F-18 FDG

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1. Marshall	Circulation 1983	To determine the feasibility of PET to demonstrate the metabolic abnormalities of myocardial ischemia and infarction	-15 Patients with recent MI	Rest N-13 Ammonia Rest F-18 FDG	Visual	14/19 documented infarcts had concordantly decreased F-18 FDG & N-13 Ammonia uptake; 11 regions of ischemia identified with disproportionally increased F-18 FDG relative to N-13 Ammonia	N-13 Ammonia, in conjunction with F-18 FDG, has potential to identify and differentiate resting myocardial ischemia from infarction, and to assess tissue viability after an ischemic event.
2. Schwaiger	JACC 1986	To determine the prognostic value of metabolic indexes for functional tissue recovery	-13 Patients with recent MI	Rest N-13 Ammonia Rest F-18 FDG	Semiquantitative Circumferential Profile	16 segments with decreased N-13 Ammonia and decreased F-18 FDG had no functional recovery. 16 segments with decreased N-13 Ammonia but maintained F-18 FDG had variable functional recovery	In the subacute phase of MI, PET reveals high incidence of tissue viability in segment with decreased blood flow and impaired function. Absence of tissue metabolism is associated with irreversible injury, while preserved metabolic activity identifies variable outcome. PET may identify viable but jeopardized tissue.
3. Schwaiger	European Heart Journal 1987	To define regional blood flow and glucose metabolism in patients with acute MI and to correlate findings with coronary anatomy	-15 Patients	Rest N-13 Ammonia Rest F-18 FDG	Visual	20/37 segments had reduced blood flow and FDG uptake, consistent with necrosis. 17/37 segments had reduced blood flow, but maintained FDG uptake, suggesting residual viability. Wall motion analysis did not distinguish segments with PET criteria for viability vs. necrosis.	PET with N-13 Ammonia and F-18 FDG offers possibility to assess tissue viability early after ischemic injury where evaluation of wall motion fails to identify salvageable myocardium.

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4. Fudo	Amer Journal of Cardiology 1988	To evaluate blood flow and FDG uptake in patients with anterior MI	-22 Patients with prior MI	Rest and Exercise N-13 Ammonia Rest F-18 FDG	Visual	19/22 patients had decreased N-13 ammonia that corresponded to region of infarct. Hypoperfused areas expanded after exercise in 16/22 patients. F-18 FDG was observed in areas of hypoperfusion, especially in patients with hypokinesis and in exercise – induced hypoperfused areas	Metabolically active myocardium in infarcted areas, or areas of peri-infarct ischemia, can be visualized with F-18 FDG and stress N-13 Ammonia
5. Mody	JACC 1991	To determine if PET with N-13 Ammonia and F-18 FDG can distinguish cardiomyopathy of coronary artery disease from non-ischemic dilated cardiomyopathy	21 patients with severe LV dysfunction being evaluated for cardiac transplant -11 ischemic -10 non-ischemic by cardiac catheterization	Rest N-13 Ammonia Rest F-18 FDG	Visual and circumferential count profiles	N-13 Ammonia and F-18 FDG demonstrated fewer, and less severe, defects in dilated cardiomyopathy than in ischemic cardiomyopathy on visual assessment; Accuracy for distinguishing subgroups was 85%. With circumferential profile, patients with dilated cardiomyopathy had fewer ischemic and infarcted segments; sensitivity for distinguishing subgroups was 100%, and specificity was 80%	N-13 Ammonia and F-18 FDG PET is helpful in distinguishing patients with severe LV dysfunction secondary to coronary artery disease from patients with non-ischemic dilated cardiomyopathy. Circumferential profile analysis is superior to visual assessment
6. Krivokapich	American Heart Journal 1991	To detect exercise induced ischemia with N-13 Ammonia and F-18 FDG	-11 Normal Volunteers -16 Patients	Rest and Bicycle Exercise N-13 Ammonia Post-Exercise F-18 FDG	Semi-quantitative	Absolute net extractions of N-13 Ammonia at rest and exercise was not sensitive in detecting functionally significant CAD. Differences and ratios of F-18 FDG and N-13 Ammonia that had been normalized to the highest N-13 Ammonia uptake were able to objectively define flow – metabolism mismatches and identify functionally significant CAD	Exercise flow and metabolic imaging are superior to rest and exercise flow imaging for the detection of functionally significant CAD.

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7. Tamaki	Journal of Cardiology Suppl. 1991	To assess the predictive value of PET for identifying improvement in regional function after CABG	-25 Patients Before and After CABG	Rest N-13 Ammonia and F-18 FDG	Visual	68% accuracy (17/25) for predicting reversibility and 75% accuracy (25/33) for predicting non-reversibility of abnormal baseline perfusion. 78% accuracy (21/27) for predicting reversibility and 81% accuracy (21/26) for predicting non-reversibility of abnormal wall motion	Pre-operative metabolic imaging with PET appears useful for predicting response to CABG
8. Kambara	Japanese Circulation Journal 1992	To evaluate myocardial viability in comparison with Tl-201 SPECT and LV wall motion	-40 Patients with Anterior Wall MI	Stress and Redistribution Tl-201; Rest N-13 Ammonia and F-18 FDG	Visual	Of 197 fixed segments by Tl-201, 12% were normal and 36% were ischemic by PET criteria. 19/28 with infarct, and all 12 with non q-wave infarct had viable myocardium. LV wall motion was better in patients with normal PET findings compared to ischemia or scar.	Tl-201 SPECT significantly underestimates myocardial viability; PET is a promising tool for assessing presence of salvable myocardium
9. Nienaber	Circulation 1993	To evaluate regional blood flow and metabolism in symptomatic patients with hypertrophic cardiomyopathy	-13 Symptomatic Patients	Rest N-13 Ammonia and F-18 FDG in 13 patients, 4 of whom also had bicycle exercise N-13 Ammonia and F-18 FDG	Quantitative	At rest – blood flow lower but glucose utilization similar in hypertrophied compared to normal myocardium. With exercise – blood flow and glucose utilization failed to increase in hypertrophied and normal segments, but became more heterogeneously distributed in LV myocardium. Mismatched flow and metabolism indicating ischemia, noted in 3 patients at rest and 4 patients during exercise due to reduced blood flow with maintained glucose utilization.	Normal or elevated rates of glucose utilization and diminished blood flow in hypertrophied relative to normal myocardium suggests myocardial ischemia in symptomatic hypertrophic cardiomyopathy

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10. Sawada	JACC 1994	To determine the relative value of SPECT imaging at rest with Tc-99m sestamibi with PET for the detection of myocardial viability	-20 Patients with Prior MI	Rest Tc-99m sestamibi, N-13 Ammonia and F-18 FDG	Semi-Quantitative Circumferential Profiles	53% of segments with moderate perfusion defects (50-59% of peak activity), and 47% of segments with severe perfusion defects (<50% of peak activity) on T-c99m sestamibi were considered viable on PET.	Moderate and severe rest Tc-99m sestamibi defects frequently have metabolic evidence of viability. Tc-99m sestamibi SPECT yields larger perfusion defects than does N-13 Ammonia PET when the same threshold values are used.
11. Gewirtz	JACC 1994	To assess whether non-viable myocardium can be identified by quantitative measurements of regional myocardial blood flow	-26 Patients with Chronic MI	Rest N-13 Ammonia and F-18 FDG	Quantitative	Blood flow in normal zones was > border zones was > infarct zones. Mismatch between blood flow and F-18 FDG uptake (with one exception) was not observed in any segment with blood flow < 0.25 ml/min/g. All dyskinetic segments had blood flow < 0.25 ml/min/g. 43/45 segments with normal contraction, or only mild hypokinesis, had blood flow ≥ 0.39 ml/min/g	In patients with chronic MI, myocardial viability is unlikely when basal regional myocardial blood flow is < 0.25 ml/min/g

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12. DiCarli	JACC 1994	To determine whether angiographically visualized collateral vessels in patients with chronic CAD imply the presence of viable myocardium in asynergic regions subtended by completely occluded coronary arteries	42 Patients with Collateral Vessels Categorized is Absent, Minimal or Well Developed	Rest N-13 and F-18 FDG	Visual	No correlation was found between severity of perfusion defect by PET and grade of collateral vessels. Extent of mismatch was unrelated to the presence or magnitude of collateral vessels. Myocardial viability was usually present in severely hypokinetic regions (82%) but lower in akinetic-dyskinetic regions (49%). 58% of regions with, and 50% of regions without, collateral blood flow had mismatched PET consistent with viable myocardium. Collateral vessels were sensitive, but not specific for viability.	In patients with chornic CAD, angiographically visualized collateral vessels to asynergic myocardial regions subtended by occluded coronary arteries do not always imply the presence of viable myocardium.
13. DiCarli	American Journal of Cardiology 1994	To evaluate the prognostic value of PET, and its interrelation with choice of medical therapy or revascularization for predicting survival and improvement of heart failure in patients with CAD and LV dysfunction	-93 patients with CAD and LVEF <25% -50 patients had medical therapy -43 patients had surgical therapy	Rest N-13 Ammonia and F-18 FDG	Visual	Annual probability of survival of patients with mismatched PET receiving medical therapy was lower than those without mismatch (50% vs. 92%). Patients with mismatch who had CABG had higher survival than medical therapy (88% vs 50%). Mismatch predicted improvement in heart failure symptoms after CABG	PET mismatch in patients with CAD and severe LV dysfunction is associated with poor annual survival with medical therapy. Revascularization in patients with PET mismatch appears to be associated with improved survival and heart failure symptoms
14. Soufer	American Journal of Cardiology 1995	To compare detection of viable myocardium with Tc-99m sestamibi to PET	-37 Patients with CAD	Tc-99m sestamibi Rest N-13 Ammonia and F-18 FDG	Visual	71% concordance between Tc-99m sestamibi and N-13 Ammonia/F-18 FDG PET. Most discordance was in the inferior wall.	Tc-99m Sestamibi underestimates myocardial viability, as assessed by PET, predominately in the inferior wall.

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15. Beanlands	JACC 1997	To assess whether N-13 Ammonia alone can detect viable or non-viable myocardium, as defined by FDG PET	-16 patients 3 months after MI -6 Ischemic viable -10 non-viable scar	Rest dynamic N-13 Ammonia and F-18 FDG	Visual and Quantitative	FDG was reduced in patients with scar compared to normal patients with ischemic viable zones. Using N-13 kinetic modeling, flow and volume of distribution were reduced in hypoperfused regions of patients with scar (.36 vs. .65). For detection of viable myocardium, sensitivity was 100% and specificity was 80% for N-13 Ammonia flow > .45. Positive predictive value 86%; negative predictive value 100%	Patients with regions of blood flow ≤ 0.45 ml/min/g had scar. Viable myocardium had blood flow > 0.45 ml/min/g. N-13 Ammonia kinetic modeling can help differentiate between scar and ischemic, viable myocardium
16. Nakano	JACC 1999	To evaluate the clinical significance of reciprocal ST-segment depression associated with exercise induced ST segment elevation for detecting residual viability in an area of myocardial infarction.	-30 patients with prior Q-wave myocardial infarctions (15 anterior, 15 inferior)	Rest N-13 Ammonia and F-18 FDG	Visual	Reciprocal ST-segment depression was found in 16 patients. The presence and site of the infarct were determined with N-13 ammonia. FDG demonstrated residual tissue viability in the infarct area in all 16 patients with and in 3/14 without reciprocal ST-segment depression.	The occurrence of reciprocal ST segment depression associated with exercise induced ST-segment elevation in patients with prior Q-wave myocardial infarction who had single vessel disease indicates residual tissue viability in the infarct related area.
17. Schoder	JACC 1999	To evaluate the predictive accuracy of PET imaging in patients with coronary artery disease and diabetes mellitus	-40 patients (19 diabetic, 21 non-diabetic). Diabetics received insulin; non-diabetics received oral glucose administration	Rest N-13 Ammonia and F-18 FDG	Visual	FDG image quality and predictive accuracy were similar for both groups. Mismatched N-13 Ammonia to F-18 FDG for predicting improvement in LV function after revascularization had a sensitivity of 92% and specificity of 85% for diabetics and sensitivity of 94% and specificity of 79% for non-diabetics	The predictive accuracy of N-13 Ammonia blood flow/F-18 FDG is maintained in patients with diabetes mellitus when a clinically acceptable protocol is used.

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18. Vanoverschelde	American Journal of Cardiology 2000	To assess the time course of functional improvement after successful revascularization	-32 patients with coronary artery disease and chronic LV ischemic dysfunction who had CABG	Rest N-13 Ammonia and F-18 FDG in 29 patients	Quantitative	At follow up, 19 patients had improved LV function; 13 had persistent dysfunction. Pre-op reversibly dysfunctional segments had higher blood flow, higher glucose uptake and less increase in intracellular matrix on biopsy than did segments with persistent dysfunction.	The recovery of regional and global LV function after successful revascularization is progressive and follows a time course influenced by the extent of structural changes affecting cardiomyocytes