PET myocardial perfusion imaging using generator produced Rubidium-82 :
A review.

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Myocardial perfusion imaging can be performed using SPECT or positron emission tomography. Positron emitting radionuclides can be employed non-invasively to assess persons who have any of a variety of disease states and pathophysiologic alterations for regional perfusion, metabolism and the status of myocardial sympathetic innervations. PET afford quantitative non invasive imaging of regional concentration of positron emitting tracer (1) The capability for quantitation exists because photon attenuation can be measured and appropriately corrected for and because of in depth independent spatial resolution. Several positron emitting radionuclides like N-13 ammonia, 0-15 water or initial image of C-11 acetate have been demonstrated to be useful for assessing regional myocardial blood flow . Myocardial perfusion imaging with positron emitter can be done without onsite cyclotron which is relatively complicated with onsite source of generator produced myocardial perfusion tracer i.e Rubidium-82.

Rb-82 is a monovalent cation that is generator produced and has an ultra short half life of 75 seconds (2). Sr.82 is the parent isotope in the generator system producing Rb-82. This generator has almost no break through of strontium and is eluted with normal saline and has useful life of 4-6 weeks. Serial evaluations of regional myocardial perfusion can be made at intervals as short as 5 minutes. After intravenous injection it takes the tracer between 60 to 90 seconds to clear from the blood after which myocardial images are acquired. Because of short physical half life doses required are in the range of 40 to 60 mCi to achieve good counting statistics. The first pass extraction of Rb-82 at rest is approximately 50-60% and extraction decreases at hyperemic blood flow rates. (3). The first pass myocardial extraction is

lower than that of N-13 ammonia and Tl-201 , yet myocardial uptake is proportional to flow in physiologic range. Rb-82 perfusion imaging is usually performed before and after vasodilator stress rather than with exercise. Infarcted myocardium does not retain intravenously administered Rb-82 . After administration it washes out rapidly from damaged myocardial cells following the initial uptake phase (4). A mixture of reversible and irreversible myocardial tissue in the field of view results in an intermediate level of Rb-82 washout that is proportional to the percentage of viable or infarcted tissue.

Tomography data from Rb-82 images can be displayed using polar maps utilizing the bulls-eye approach with the apex located at the center and base at the rim. Both relative and absolute flow reserve can be depicted on quantitative polar maps of Rb-82 activity. In this manner the rest and stress images are functionally interrelated. Three dimentional (3-D) topographic displays of Rb-82 cardiac activity are more quantitative with respect to the polar maps. The 3-D topographic maps of cardiac positron emission tomography (PET) image are derived from the short-axis data.

PET is clinically for detection of CAD using intravenous dypiridmole or adenosine injection in conjunction with Rb-82 as tracer of blood flow (6-9). In this procedure, baseline myocardial perfusion is first assessed, followed by evaluation of regional perfusion after pharmacologic stress. A transmission image is initially acquired for 200,000K counts with Germanium-68 ring or rod source which takes about 20-30 min. Subsequently emission image were acquired at rest and stress for 5-7 minutes with optimal counts of > 40,000K counts. An automated quantitative analysis programmed may enhance accuracy and reproducibility of cardiac PET flow studies. The sensitivity and specificity of PET MPI are superior to other non invasive tests. Four studies involving a total of 342 patients have made direct comparisons of Tl-201 SPECT and PET MPI (10). In addition a survey of numerous studies of PET MPI in 1391 patients found excellent sensitivity (92% ; CI=90%-94%) and specificity (90% CI=88% to 92%) Churchwell et al has also shown greater accuracy in a blinded analysis of the accuracy of developed in their laboratory(76). Patterson et al also shown significantly better result with Rb-82 PET than their own SPECT Tl-201 results. These comparisons and Emory University's extensive clinical experiences (over 30,000 SPECT Tl-201 and over 2,000 PET Rb-82 studies) provides concluding evidence that PET Rb-82 is superior to SPECT Tl-201 or myocardial perfusion imaging (10). Though all patients with intermediate risk of coronary artery disease

can undergo PET MPI it is preferable to SPECT MPI in a subgroup of patients with attenuation problems i.e. large patients, women, breast implant or left mastectomy, chest wall deformity, left pleural or pericardial effusion. However it must be emphasized that the attenuation problems in SPECT cannot be predicted with confidence from examination of body habitus . There is incremental benefit caused by greater specificity and sensitivity which gives rise to incremental economic benefit caused by more accurate tests like Rb-82 PET MPI. (10)

PET Rb-82 imaging for myocardial viability

PET imaging of blood flow using Rb-82 may proved to be a useful approach to identifying viable myocardium. Myocardial viability is predicted on the fact that metabolically active myocardium must have some flow preservation. Estimation of myocardial membrane integrity based upon Rb-82 tissue kinetics compare favourably with myocardial uptake of FDG(11). The rationale for the use of Rb-82 imaging for 329 assessing myocardial viability is based on the concept that transiently ischemia but viable myocardium can retain extracted Rb-82 where as nonviable myocardium exhibits back diffusion of tracer(12). Upon delivery by coronary blood flow the myocardium , Rb-82 is extracted by normal cells, where it equilibrates with the intracellular potassium pool. If these cells are necrotic and can not retain the tracer, it washes out rapidly after initial distribution. The rate of Rb-82 washout can be measured by rapid sequential PET imaging.

PET Rb-82 imaging shows perfusion and can be performed at stress and rest. It has major advantages over SPECT due to attenuation correction, better spatial resolution and counting statistics. These stress-rest images which show reversibility as one indicator of viability and the severity of the defect at rest should be related to the severity of myocardial infarction. (13). A novel approach has been taken to this problem of detecting viability by imaging Rb-82 with PET in "list mode" to compare early versus late Rb-82 images after injection at rest. After waiting 1-0 to 1.5 minutes for blood pool clearance, defects present on the first 100 seconds of data acquired after rest injection are compared with the data acquired devoting the subsequent 320 seconds of the 7 minutes acquisition. Experimental studies in animals with external radiation detectors placed on the epicardium of the heart have confirmed initial uptake by even necrotic myocardium but subsequent release of the Rb-82 with a mark decrease (wash out) of actual Rb-82 activity on the late images e.g. wash out (13). Thus if a defect present on the "early" rest image gets substantially worse on the "late" rest image it is considered sign of

necrotic myocardial that had "early" uptake but insufficient viable myocardium to retain the Rb-82 . In contrast a defect that stays the same between "early" and "late" images would indicate viable myocardium and could retain the Rb-82 tracers. The validity of this technique seems to be supported by its ability to predict response to revascularisation and 3 years prognosis in a study of 30 patients (14).

Conclusion:

Rb-82 PET myocardial perfusion imaging is most accurate non invasive modality for evaluation of coronary artery disease. This procedure also has shown efficacy in community and private hospitals in the world. The cost effectiveness of Rb-82 generator as the method of choice will heavily depend on the number of patients although it is an attractive proposition to cyclotron produced positron emitters. Rb-82 PET cardiac imaging might become routine when " All PET" based Nuclear medicine becomes a reality during the next decades.

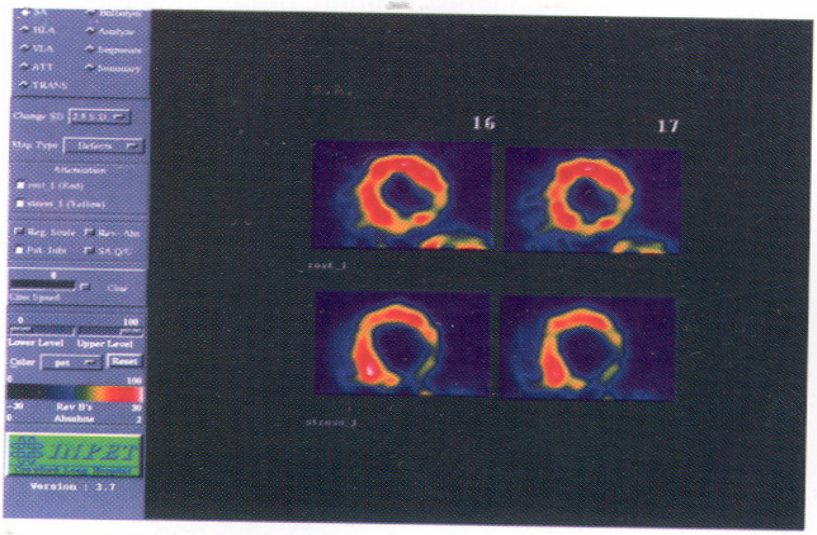

Fig-1 : Rb-82 PET stress and rest images in short axis showing anterior wall ischemia and lateral wall peri infarct ischemia.

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