Role of Nuclear Cardiology in the Next Millennium

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About more than two decades ago, radionuclide methods were introduced for noninvasive clinical assessment of myocardial perfusion & ventricular function. The extensive research and development has established the clinical role of cardiovascular Nuclear medicine in modern cardiology. It is a dynamic field, each year new applications are introduced and established ones are refined. Tl-201 has been used as a potent myocardial perfusion imaging agent for more than 25 years for detection and evaluation of coronary artery disease (CAD) & the role of stress MUGA (multigated acquisition) with NG intervention has been established as an important investigation for ventricular function study of left ventricle with their ability to detect regional wall motion abnormality. Tc99m labelled agent such as sestamibi (cardiolite), tetrofosmin(Myoview), Teboroxime (cardiotec) are all reviewed and have been utilized as potent myocardial perfusion agents with the availability of additional informations such as left ventricular function, left ventricular cavity, systolic wall thickening, wall motion. Additionally pharmacologic stress myocardial perfusion imaging particularly I.V.adenosine / I.V dobutamine has provided an unique opportunity to evaluate myocardial perfusion during maximal coronary vasodilation is indicated in the early days of myocardial infarction to substitute submaximal predischarge exercise testing as a method for evaluating the extent of coronary disease & risk of future cardiac events in patients who are admitted with acute myocardial infarction & for patients who can not exercise for various reasons including physical limitations, lung disease, peripheral vascular disease, severe osteoarthritis, elderly aged persons etc. In the 1990's cardiovascular nuclear medicine has continued to face challenges posed by competing imaging modalities such as contrast echocardiography, magnetic resonance imaging, low dose I.V dobutamine

Echocardiography etc. To meet these challenges effectively, one should provide the highest quality newer nuclear cardiology procedures, educate the referring physicians & demonstrate the cost effectiveness of cardiovascular nuclear medicine procedures in the diagnosis & management of patients with coronary artery disease.
The following are some new innovations which will be soon available in the next millennium.

I. Early noninvasive detection of acute MI with Tc99 labelled Glucarate-

Tc99 glucarate has recently been reported to be an infarct avid agent. The feasibility of imaging with Tc99m glucarate has been evaluated for the early diagnosis of nonreperfused & reperfused myocardial infarction & has been well compared with the localization of administered in vivo In-III-antimyosin.

Usually the diagnosis of acute myocardial infarction is made on the basis of typical chest pain, the evolution of ECG changes & the pattern of serum cardiac enzyme release i.e CPK, CPK-MB fraction in the majority of patients. In several clinical instances these findings are less helpful such as in the differentiation of acute infarction from prolonged severe ischaemia , infarction in the presence of conduction abnormalities or infarct recurrence in the ECG territory of previous infarction , acute ischeamia syndrome, non'q' wave infarction . In such cases , the confirmation of diagnosis requires other noninvasive diagnostic aids. This diagnostic aid could be of greatest value if the occurrence of acute myocardial infarction could be established early to allow thrombolytic therapy. The time window amenable to thrombolysis is short. If a hot spot imaging agents are to fulfill this rule, it should target the infarct zone rapidly despite the persistently occluded status of the coronary artery. Already two infarct avid agents i.e Tc99 pyrrophosphate & In-III labelled antimyosin agents have not allowed the hyperacute localization and visualization of myocardial infarction, Tc99 glucarate a six carbon dicarboxylic acid has been shown to concentrate in the regions of myocardial necrosis. Tc99 glucarate 2^{nd} phase trial has shown adequate localization in experimental acute reperfused myocardial infarct in canine model on the day of the infarct. It has been demonstrated in the same model that glucarate uptake diminishes significantly by 48 to 72 hrs. after the acute event. The present study has been undertaken to evaluate the role of glucarate scintigraphy in the detection of acute nonreperfused myocardial infarction and to compare it with its

uptake in reperfused rabbit infarction as well as in severely ishaemic myocardial tissues.
Rapid blood clearance with a strong avidity of Tc99 glucarate for the necrotic myocardium enables generation of high target to background ratios early after experimental irreversible myocardial injury. Glucarate uptake occurs equally effective in reperfused & nonreperfused myocardial infarct models. In the canine model it has been found out that the percent injected dose per gram tracer localization is less with Tc99 glucarate than with Indium-III labelled antimyosin, target to background ratios as well as absolute radioisotope uptake is significantly greater with Tc-99 glucarate than with Indium-III antimyosin Fab. The patient study clearly reveals that high contrast images can be obtained within minutes after the onset of injury. If early glucarate uptake in myocardial infarction is confined in clinical studies, it may not only help direct the use of thrombolytic therapy in patients prsenting with equivocal diagnosis but also allow differentiation of acute from recent infarct.

II) Detection of active thrombus localization using Tc99 labelled/Indium-III fibrinogen inpatients of acute myocardial infarction.

Detection of active unstable thrombus/localization in major coronary arteries in one of the areas where radiolabelled fibrinogen will be helpful in differentiating unstable plaque from a stable plaque. This is crucial so far as the management of patients of acute M.I. is concerned. If radiolabelled Indium-III or Tc99m tagged fibrinogen reveals, a hot spot in the territory of the major coronary artery , then low molecular weight heparin will be able to dissolve the active unstable thrombus having no significant uptake by these fibrinogen labelled radioisotopes. The extensive research is going on all over the world to find out suitable radioisotope more specifically Technetium 99 labelled agent which is suitable for gamma camera energy & should be available readily. These unstable plaques/thrombus are quite dangerous as very often these plaques moves from one area to the other critical areas like occluding the major coronary artery resulting in a massive necrosis of the myocardial cells.

III) Combined use of I-123 BMIPP & perfusion tracer (Tl-201/Tc99m Sestamibi) in assessment of myocardial viability

Nuclear techniques have already established its role in diagnosis of ischaemic heart diseases & evaluation of ventricular function. One of the other important applications is the assessment of myocardial viability. Patients with ischaemic heart disease & LV

dysfunction may have significant amount of myocardium which is ischaemic but hibernating.

It is essential to identify viable myocardium since revascularisation can lead to resumption of normal function in these segments & hence improve the regional & global LV function, however several studies using stress & 3-4 hrs delayed Tl-201 images have demonstrated that nonreversible perfusion abnormalities frequently exhibit normal perfusion after coronary revascularization. So the recent publications indicate that conventional Tl-201 stress and rest (3-4hrs) imaging as mentioned above estimates the extent of infarction there by under estimating the viable and potentially jeopardized myocardium i.e stunned or hibernating myocardium. The current technique which is in clinical practice are reinjection of Tl-201 imaging , reinjection followed by 24 hrs. imaging , low dose I.V dobutamine echocardiography. In view of resting wall motion abnormalities on the one hand and the propensity of decreased perfusion either Tl-201/Tc-99m Sestamibi to overestimate myocardial scar on the other hand, metabolic imaging 18-F-FDG PET behaves as an additional techniques in myocardial segments with decreased perfusion (Tl-201/Tc-99m Sestamibi/NH3 Ammonia). Recently I-123 BMIPP (15-P-Iodophenyl-3-methly pentadecanoic acid) which in a fatty acid analogue represents an interesting alternative to 18-F-FDG (PET imaging tracers) . The combined use of I-123-15-P-IodoPhenyl-3-methyl pentadecanoic acid (BMIPP) and perfusion tracer (Tl-201/Tc99 Sestamibi) has been accurate regarding viability assessment in acute/subacute chronic phase of myocardial infarction . Usually a mismatch is seen between fatty acid and perfusion could identify chronically ischaemic but viable myocardium. It correlates well with the response of wall motion to I.V. low dose dobutamine, echocardiography and is more sensitive than sestamibi alone and for differentiating viable from scar segments. In the next millennium i.e 2000, cardiovascular nuclear medicine will also continue to face challenges by other imaging modalities. With these new innovations mentioned above and lot many still to come, Nuclear Cardiology speciality will continue to thrive as an important modality for the evaluation of patients with known or suspected cardiac disease.