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Cardiac Nuclear Medicine

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ABSTRACT

Nuclear Medicine is a multidisciplinary technology used for diagnostic purpose. Cardiac nuclear medicine imaging is used to determine coronary artery disease and cardiomyopathy. It also may be used to determine whether heart has been damaged by chemotherapy or radiotherapy. Nuclear medicine uses trace amounts of radioactive materials called radio-tracers or radio-pharmaceuticals that are inhaled, swallowed or injected into the bloodstream. These radio-tracer travels through the area being examined and gives off energy in the form of gamma rays which are detected by gamma camera[1] and a computer to create images of the inside the body based on Artificial Neural Network[2]. ANN (an Artificial Intelligence technology) serves as a tool for detecting and localizing diseases while a radio-tracer travels across the body [2]. About heart ailments diagnosis is done using information contained in myocardial perfusion scintigrams[1]

Nuclear Medicine Imaging can be superimposed with CT or MRI to produce special views so called co-registration or fusion of images. Nowadays we have single unit of SPECT/CT and PET/CT that are able to perform both imaging examination at the same time. Artificial intelligence serves as a tool for detecting and localising coronary artery disease mostly by using information contained in myocardial perfusion scintigrams[12]. The myocardial perfusion images were preprocessed in order to decrease the number of variables and to extract relevant features from the images. This preprocessing was accomplished by a 2-D Fourier transformation that used both rest and stress images [3]. Nuclear medicine imaging provides unique information that often cannot be obtained using other imaging procedures.

Keywords: *radio-tracer, radio activity, scintigram, cardiac nuclear medicines, gamma camera, artificial intelligence, artificial neural network*

Introduction

Nuclear medicine is the branch of medicine that deals with the use of radio-active substances in research, diagnosis and treatment. It is a branch of medical imaging that uses trace amount of radioactive elements to diagnose and determine the severity and treatment for many types of disease as in cancers, heart disease, gastro-intestinal, endocrine, neurological disorders and other abnormalities inside the body[1].

Radioactive materials so used are termed as radio-tracers that are given to patient intravenously, swallowed or inhaled. These radio tracer travels through the area being examined and gives off energy in the form of gamma rays. These gamma rays detected by a special camera called gamma camera. [1].

Radionuclide when introduced into the body is often chemically bound to a complex that acts characteristically within the body are carrier molecules. This helps us to be able to pinpoint molecular activity within the body[4]. This offers potential to identify the disease in its earlier stages as well as a patient's immediate response to therapeutic interventions. Cardiac nuclear medicine imaging evaluates the heart for coronary artery disease and cardiomyopathy[1,12]. It also may be used to help determine whether the heart has been damaged by chemotherapy or radiotherapy. Nuclear medicine uses small amounts of radioactive materials called radio-tracers that are typically injected into the bloodstream, inhaled or swallowed. The radio-tracer travels through the area being examined and gives off energy in the form of gamma rays which are detected by a gamma camera and a computer to create images of the inside of your body. Nuclear medicine imaging provides unique information that often cannot be obtained using other imaging procedures [1].

Some common uses of procedures [1]

- Cardiac nuclear medicine imaging is also performed:
- To visualise blood flow patterns to the heart walls, called a myocardial perfusion scan.
- To evaluate the presence and extent of suspected or known coronary artery disease.
- To determine the extent of injury to the heart following a heart attack, or myocardial infarction.
- To evaluate the results of bypass surgery or other re-vascularisation procedures designed to restore blood supply to the heart.
- In conjunction with an electrocardiogram (ECG), to evaluate heart-wall movement and overall heart function with a technique called cardiac gating.

Diagnosis, Imaging and Instrumentation

Cardiac single photon emission computed tomography (SPECT) and positron emission tomography (PET) are increasingly being used in the evaluation of patients with suspected or known coronary artery disease by assessing myocardial viability and perfusion and providing invaluable diagnostic and prognostic information [12]. With their capacity to quantify left ventricular function as well as coronary flow reserve, these myocardial perfusion imaging techniques are superior to other methods for the detection of multi-vessel coronary artery disease and potentially, for risk stratification and prediction of cardiac events[8]. Hybrid SPECT/CT and PET/CT scanners allow identification of flow-limiting coronary lesions and therefore offering great potential for both diagnosis and management [19,25]. Advances in molecular biology of the cardiovascular system have helped to develop the molecular imaging which may be useful to evaluate targeted molecular and cellular abnormalities in the future. SPECT imaging has superseded planar perfusion imaging. Multiple planar images of the heart using photons (γ-rays) emitted by radio-pharmaceuticals are acquired by rotating detector heads around the patient, and myocardial perfusion images are reconstructed using principles close to CT imaging[10]. It is widely available and used to assess myocardial perfusion as well as ventricular function in suspected IHD[31]. Since its introduction in the late 1980s for routine clinical practice, the principle has remained the same; however, there have been several significant modifications for better and optimal imaging of the heart, for example 180°acquisitions have almost entirely replaced 360° acquisitions. This has resulted in faster acquisition times, in particular by using two-headed cameras at a 90° angle. Back-projection reconstruction of the images has now been mostly replaced by iterative reconstruction. This technique requires high computing power as it is calculation intensive. Although it has routinely been available in nuclear medicine since the 1990s, its use has been widespread only in the last decade. This technique is now being introduced to CT imaging owing to the even higher computing power required for higher resolution of CT images[19,20].The most common radio-tracers used in cardiac PET are ammonia (13NH3) and rubidium(82Rb) chloride for assessing myocardial perfusion and 2-(fluorine-18) fluoro-2-deoxy-d-glucose(FDG) for evaluating myocardial glucose metabolism. 13NH3 has a first-pass extraction of 80%and requires energy for myocardial uptake. As with SPECT myocardial perfusion agents, up take is linear over a wide range of myocardial blood flow rates except at very high flow rates. Imaging with 13NH3 requires either an on-site cyclotron or proximity to a regional positron radiopharmaceutical source center. [14] 82RbCl is a potassium analog that has a first-pass extraction of 65% and also requires energy formyocardial uptake. Repeat studies may be performed due to its very short half-life. An advantage of 82RbCl over 13NH3 is that it is produced by a strontium-82/82Rb generator without the need for a costly cyclotron. [14,19]

FDG is used in the evaluation of glucose utilization in Ischemic myocardium with suppressed mitochondrial β-oxidation of fatty acids. Ng et al showed that insulin infusion in the fasting state reduced myocardial extraction of free fatty acids by 85% and stimulated myocardial uptake of both FDG and glucose. FDG uptake is heterogeneous in normal myocardium in the fasting state in diabetic patients as well as in patients with normal glucose tolerance. Increased FDG up take is seen in ischemic tissue, whereas markedly reduced or absent uptake indicates scar. Oral glucose loading and continuous infusion of insulin, potassium, and glucose have been used to enhance myocardial FDG up take

[20,22,]. In a study by Knuuti et al, images obtained in non-diabetic patients after insulin infusion were of higher quality than those obtained after oral glucose loading. Oh take et al reported similar findings in patients with non–insulin-dependent diabetes. Some investigators have described insulin infusion as cumbersome for routine clinical use. Oral glucose loading and bolus injections of insulin have been suggested as possible alternatives[20,22].

Less commonly used PET radio-tracers are carbon-11 acetate for assessing regional myocardialoxygen consumption, C-11 palmitate for measuring fatty acid metabolism, and oxygen-15 water for quantifying myocardial blood flow [25].

Radio-pharmaceuticals

Myocardial perfusion: Thallium-201 chloride was the first pharmaceutical to be widely used clinically for imaging myocardial perfusion. It is an excellent agent for imaging perfusion and is still used to image the heart in many centres. Because of its relatively long half-life and low energy X-ray emission, it is not the ideal agent for imaging, giving a relatively large radiation dose with lower image quality than technetium agents. It behaves like the K^+ ion (via Na/KATPase), and is redistributed fairly rapidly, starting 20 min after injection [20, 22,].Ischemic heart disease: Nuclear Medicine plays an important role in detection of is chemic heart disease either reversible or irreversible (IHD), using a dedicated radio-pharmaceuticals in detection clinically, the most commonly used radio-pharmaceuticals are 99mTc-Sestamibi,99m Tc-Tetrofosmin and 201Tl. This study focused on using counts/second /pixel(c/s/p), reversibility% among arteries i.e. LAD, LCX and RCA in evaluation of 99mTc-MIBI and 201TL bio-distribution in both conditions of stress and rest, and the factors affecting reversibility such as age, gender and obesity[17].

Coronary heart disease

Radionuclide stress testing involves injecting a radioactive is otope(typically thallium or cardiolite) into the patient's vein after which an image of the patient's heart becomes visible with a special camera. The radioactive isotopes are absorbed by the normal heart muscle. Nuclear images are obtained in the resting condition, and again immediately following exercise. The two sets of images are then compared. During exercise, if a blockage in a coronary artery results in diminished blood flow to a part of the cardiac muscle, this region of the heart will appear as a relative "cold spot" on the nuclear scan. This cold spot is not visible on the images that are taken while the patient is at rest (when coronary flow is adequate). Radionuclide stress testing, while more time-consuming and expensive than a simple ECST, greatly enhances the accuracy in diagnosing coronary heart disease[10].

Artificial Neural Network

Artificial neural networks serve as a tool for detecting and localising coronary artery disease mostly by using information contained in myocardial perfusion scintigrams. Neural network diagnosed coronary artery disease in a population of patients ranging from 74 to 410. The diagnosed cases of coronary artery disease by artificial neural networks was comparable to agold standard, which consisted of a coronary-angiography, the interpretation of myocardial perfusion studies by two human experts or all clinical patient data including ECG analysis, results of a physical exercise test as well as the patient's history. All the applied models of artificial neural networks had a three layer structure and a feed forward flow of information. Each neural network consisted of three layers: an input layer, a hidden layer and an output layer. The number of neurons in an input layer varied between 11 and 256 depending on the used matrix of scintigrams and other data, whereas the number of neurons in a hidden layer ranged from 3 to140. An output layer consisted of one, two or eight units. Input signals of an artificial neural network which diagnosed coronary artery disease used all the clinical data[31]. The myocardial perfusion images were pre-processed in order to decrease the number of variables and to extract relevant features from the images. This pre-processing was accomplished by a two dimensional Fourier transformation that used both rest and stress images. After this transformation, 30 values were selected constituting the real and imaginary part of the Fourier coefficients were used to the input neurons. Other studies have used additional features: male or female, an exercise test, resting ECG, the heart rate and workload. The characteristics of the input signals of the artificial neural network (ANN) were designed so that each neuron would represent pixels of bull's eye images. [25,32] When the output layer contained one neuron that encoded whether coronary artery disease was present or not the results were binary values such as 0 or 1. Another study contained eight output neurons that encoded coronary artery disease and the severity of disease was based on a classification into seven abnormal categories and one normal case. In most of the studies, training of artificial neural networks was based on the back propagation algorithm. It used commercial computer software that simulated artificial neural networks from among JETNET3.0, MichiZane, VieNet2. The list contains the number of neurons, each layer of artificial neural networks (an input layer, hidden and output), the learning method (BP, Bayes) and the number of patients. It is based on the available studies in which artificial neural networks have been applied to predict coronary artery disease and have been shown to perform even better than experienced [32].

1st Case study[16]

A 58 year old male presents to the ER with chest pain.

Past medical history:

1. Coronary disease.
2. Cocaine abuse.
3. Questionable history of emphysema.
4. The patient has chronic joint pain problems.

Family history: Positive for hypertension. His brother died of a heart attack at age 45.

Social history:

The patient lives in the country. He has worked at odd jobs most of his life, working in farming. He has a smoking habit, currently of 4-5 cigarettes a day, more in the past. He smokes crack cocaine on a weekly basis; although he indicates that he is trying to cut back. He does not have any history of alcohol abuse or significant use. Hospital Course: On June 4, 2003 a 58-year-oldAfrican-American gentleman with history of emphysema was transferred from another hospital with dynamic EKG changes and chest pain that occurred four to five hours prior to presentation, did not really subside with rest, which usually subsides the patient's pain. The patient admitted cocaine use five days prior to presentation. The patient also admitted to increased chest pain episodes and shortness of breath on exertion for three to four weeks. The patient was admitted to the CCU. He was started on Integralin, aspirin, Simvastatin. Beta blocker was held due to cocaine use. The patient was taken to the cath lab on 6/5/03, which showed disease in the left circumflex, mid 60% in the large thrombus. The patient received PCIstenting to the mid left circumflex and OM III. LV-gram showed a 30% EF with severe lateralhypokinesis. Decadron was continued post procedure for 18 hours. He was also started on Plavix. The patient's tropon in peaked at 166 and then trended downward afterward. Echo was done to reevaluate bilateral function, showing an EF of 30%. On 6/6/03 Amlodipine was added in an effort to decrease coronary spasm. It was decided to hold beta blocker due to patient's cocaine use and due to patient's very low blood pressure no ACE inhibitor was started at this time with plans to start at some point in the future as an outpatient. The patient was transferred to Team One cardiology and remained stable. He was discharged on 6/9/03.The patient returned to the hospital on August 17th. He has been unable to afford refills of his medications and thus has not been on any medicines for months. The patient also has history of crack cocaine abuse and continues his habit even after multiple warnings as to the adverse effects on his coronary disease that this would invoke. The patient had smoked crack cocaine the day before presentation and had experienced substernal chest pain with typical angina symptoms the afternoon and evening before the morning of presentation. His symptoms did not improve and seemed to get worse. He had associated nausea and vomiting with shortness of breath. Ref: [16] The patient presented to the ER and was given nitroglycerine with some relief of pain. The patient was admitted to the CCU service. He was put on oxygen and serial cardiac enzymes were ordered. He was started on a heparin drip in addition to Plavix and aspirin. He was not started on a beta blocker due to his history of cocaine use and his heart rate and blood pressure were actually within good parameters. He had lipid studies and was started on a statin. He was given no additional nitroglycerin or morphine as the patient did not have recurrent chest pain during hospitalisation. Urine drug screen was positive for cocaine. The cardiology service recommended coronary angiogram the following day. The patient however did not want to have any invasive testing particularly anything such as an angiogram.

Lab values: cardiac injury level

Test Test result Range Unit

CK-Total 3201 50-260 IU/L

CK-MB 280 0.2-5 ng/ml

CK-Relat. Index 8.8 0-2.4

Troop in I 166 0-1.4 ng/ml

Due to the patient's history of problems with affording medications and general social problems including illicit drug use, a social worker was contacted for assistance in helping this patient get medical assistance and into some kind of drug rehabilitation program. The patient did seem interested in drug abuse treatment and was given extensive information on possible treatment programs that he could enroll himself in by our social worker. The patient continued to refuse invasive testing, but did consent to a nuclear medicine stress test. Nuclear Medicine IV Persantine Stress. The resting ECG showed sinus rhythm with T-wave abnormalities. Resting heart rate was 59 bpm and blood pressure was 82/62. Following Persantine injection, the heart rate was 75 bpm and blood pressure was 84/50. The patient complained of shortness of breath, but denied any chest pain. There were no significant ST changes over baseline. Impression: Normal heart rate response to IV-persantine without significant ST changes over baseline. The patient did complain of shortness of breath during the exam. Myocardial Perfusion Study with SPECT. 10.8 mCi of 99m TcSestamibi was infused at rest. SPECT images of the myocardium were obtained at approximately one hour delay. Subsequently, 39 mg of IV Persantine were infused over four minutes for pharmacy logical stressing. Seven minutes into the Persantine Stress Test, the patient was injected with 31.8 mCi of 99m TcSestamibi, and the imaging sequence was repeated. A large fixed perfusion defect is seen involving the entire lateral wall, the anterolateral wall, distal anterior wall, apex, and inferolateral wall. This is primarily fixed. There may be a very small amount of reversibility involving the anterior wall. The septal wall is the only normal appearing wall. A Thallium viability study is recommended to evaluate if any of this myocardium might, in fact, be hibernating. (not performed)

Impression: Large fixed perfusion defect involving the lateral, inferior, apex, in ferolateral walls. A thallium viability is recommended to evaluate for hibernating myocardium. The patient's physician was notified of this result. Quantitative gated SPECT: Quantitative gated SPECT study was performed during the stress acquisition. The end diastolic volume was calculated at 180cc. The end systolic volume was calculated at 148cc. The left ventricular ejection fraction was calculated at 18 percent. There is dyskinesis involving the apex on the CINE images.

Impression: Dilated left ventricular with severe global hypokinesis and dyskinesis of the apex, with an ejection fraction of 18 percent. The patient was discharged after three days displaying no recurrent pain or other angina-like symptoms. The patient was discharged in stable condition with cardiac diet and advised to limit activity to non-stressful activities for the next month. He was also strongly advised to stay away from drugs of abuse and to enroll himself in a drug treatment program. The patient was also started on lisinopril at 10 mg p.o.q.d. in addition to other medicines.

Medications on discharge:

1. Zocor 20 mg p.o.q.d.
2. Lisinopril 10 mg p.o.q.d.
3. Aspirin 325 mg p.o.q.d.
4. Plavix 75 mg p.o.q.d.
5. Spironolactone 25 mg p.o.q.d.
6. Nitroglycerin SL prn

Four days following the discharge of the patient he presented himself to the ER because of some difficulty breathing and swallowing and was found to have angioedema of the uvula and bottom lip. He presented with complaints of lip swelling x 1 day. He denies chest pain, diaphoresis. He had a small amount of cocaine on the day prior to admission. He was admitted to observation, and given IV Benadryl as well as H2 Cimetidine p.o. q.8h. He was started on hydrocortisone and had one administration of epinephrine. His shortness of breath and difficulty swallowing subsided. It was believed that he experienced an allergic reaction to the Lisinopril. The patient was discharged the following day after evaluation by internal medicine. Patient was without complaints, and instructed not to continue the ace inhibitor at this point, and once again instructed on the importance of cessation of cocaine. Only four days following his last admission, the patient was once again admitted. On the day of this admission the patient elapsed and was unresponsive. MEMS were called and shocked the patient by EED. The patient was shocked six times, and then started on Lidocaine 100mg IV and brought to the MICU at UAMS. He was sedated and intubated on arrival. Aspiration pneumon it is was suspected and the patient was started on Clindamycin and Cefepime. Chest x-ray later showed left lower lobe infiltrate. The patient continued to spike temperatures and his white continued to increase. The patient was started on aspirin, Plavix, heparin, and IV Amiodarone was loaded. The Infectious Disease team saw the patient and recommended starting gatifloxacin, vancomycin, and Imipenim and stopping the

Clindamycin and the Cefepimebecause they felt that, because of the patient's recent hospitalization, he would be treated fornoscomial organisms as well. The patient was started on vancomycin and imipenem IV, butgatifloxacin was held because it has an interaction with Amiodarone.An echocardiogram was repeated and showed that the EF had improved to 30-35%. The patient continued to improve on the IV antibiotics and became afebrile. The white count started to decrease. His hemoglobin and hematocrit was noted to be low but stable. Social work was consulted and discussed plans to go to a rehab unit with the patient. However, the patient became evasive and did not wish to be sent to a rehab unit. The patient also refused an IV line and IV antibiotics had to be stopped. Therefore, he was started on 400 mg q.d. of p.o.gatifloxacin for seven more days. The patient contacted his family and was discharged 14 days after his admission. The patient was given two follow up appointments and also instructed concerning his medications. The patient was also once again advised on refraining from alcohol or further cocaine use and the risk of sudden cardiac death.

2ND CASE STUDY [17]

A 48 year old black woman admitted who is suffering from hypertension and chest pain.

Height: 5'5"; Weight: 194 lbs.

ECG Results:

- Normal Sinus Rhythm
- Nonspecific T-wave abnormality
- Otherwise normal ECG
- Ventricular Rate 64 bpm

Nuclear Medicine: She was referred to the nuclear medicine department for evaluation of possible myocardial ischemia.

IV Persantine Stress. Under rest conditions the patient was injected with 0.56 mg per kg of IV Persantine (47 mg total) over 4 minutes. The resting heart rate was 59 beats per minute and blood pressure was 99/56. The EKG demonstrated normal sinus rhythm without acute change. Following Persantine infusion the heart rate measured 75 beats per minute and blood pressure was 110/74. The patient reported no systemic symptoms.

Imoression: Physiologic response to IV Persantine without Ischemic change identified.

Myocardial Perfusion Study with SPECT: At rest the patient received an IV injection of 11 mCi of Tc-99m Sestamibi. SPECT images of the myocardium were obtained after a 1hour delay. Seven minutes into the Persantine infusion the patient received an additional 32 mCi of Tc-99m Sestamibi and the imaging sequence repeated.

Post stress images demonstrate a defect in perfusion involving the anterior wall of the left ventricle.

Impression: Reversible defect involving the anterior wall of the left ventricle. The findings are consistent with a lad distribution lesion.

Quantitative Gated SPECT: Gated SPECT imaging was performed during stress acquisition. The left ventricular end diastolic volume was calculated at 79 cc, the end systolic volume at 32 cc, and the left ventricular ejection fraction at 62 percent.

Impression: Normal quantitative gated SPECT. The referring physician in the family medicine service was notified of the results.

The patient left the hospital after the procedure. Her physician called her at home and told her the results of her positive stress test that morning and told her to go to the ER. The patient said she was experiencing significant exertional chest pain, but no nausea, diaphoresis, dizziness, or dyspnea. The patient complained of chest pain with heart racing and said she was not feeling well. She said she would go to the ER tonight.

Conclusion

A complete assessment of many cardiac disorders, particularly CAD, requires both anatomical and functional information. This can be obtained in a variety of ways and the common imaging techniques overlap in their capabilities, particularly for the assessment of myocardial viability, function, and coronary anatomy. NICE guidance in the UK on the assessment of patients newly presenting with possible angina states that the accuracy and cost of the techniques are similar, and that choice between them can be based on local availability and expertise. While their accuracy might be similar in ideal hands, it is not known if the newer perfusion techniques perform as well in the real world and there have been no robust comparative studies of cost effectiveness. Each of the techniques is supported by appropriateness criteria that overlap in the common ground of patients with an intermediate likelihood of coronary artery disease (CAD).One important difference between echocardiography, nuclear cardiology, cardiovascular MRI, and CT is that they have been developed in the hands of different specialists, such as cardiology, nuclear medicine, or radiology. Professional and financial considerations mean that a technique is more likely to be used if it is in the hands of the referring physician. Thus, in some cases, the choice is made in the best interests of the doctor rather than the patient. There are considerable differences between countries in this regard. The interests of the imaging industry have also in some cases influenced the development of techniques. Such a situation should not prevail. The group agreed that a balanced use of cardiac imaging will best be achieved by education of users and providers of imaging services, and that this should be independent as far as possible of the background training of the specialist, be it cardiology, nuclear medicine, or radiology. The group was also optimistic that increasing collaboration between specialists and subspecialists would allow the best interests of the patient to prevail and the impressive developments in all areas of cardiac imaging in recent years to be translated into better outcomes for patients.[free articles, news].

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