Science of Nuclear Energy and Radiation

Introduction to Nuclear Medicine

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Introduction.

Nuclear Medicine is the application of radioactive isotopes to the diagnosis and treatment of disease. The subject depends entirely upon the fact that a radioisotope of an element and a stable isotope of the same element have identical chemical properties but different physical properties. For example suppose we have one atom of stable iodine, ${}_{53}I^{127}$, and one atom of ${}_{53}I^{131}$. The same atomic number (53) means that the number of protons in the nucleus and the number of electrons is the same for each atom and that they will behave in the same manner chemically. This means for example that if both atoms were present in the circulating blood of a person, both atoms could be trapped by the thyroid gland. The thyroid gland is a small butterfly shaped gland in the neck which weighs about 20 grams. Its purpose in life is to extract iodine from circulating blood and to synthesize that iodine into the thyroid hormones tri-iodothyronine and thyroxine which are involved in many metabolic processes in the body. At some time after the radioactive atom enters the gland it will decay. If the emitted radiation is detected then we can ask such questions as:

<u>what fraction of an oral dose of I^{131} given to a patient actually ends up in the thyroid gland at some time after the dose?</u>

Obviously one of the factors which determines this amount is the ability of the gland to extract iodine from the circulation. This is the basis of a “thyroid uptake test”. Normally about 25% of the I^{131} dose is present in the gland at 24 hours after administration. Numbers much greater than 35% would represent an overactive gland or hyperthyroidism or thyrotoxicosis. Numbers below about 10% would represent an underactive gland or hypothyroidism or myxoedema. This type of application requires the ability to measure the amount of I^{131} present in the thyroid gland. Another question to be asked is:

<u>what is the spatial distribution of the radioactive iodine in the thyroid gland?</u>

The purpose of such a measurement or “thyroid scan” would be to identify abnormalities in the size or location of functioning thyroid tissue and to detect regions within the gland which were either overactive or underactive and could correspond to various abnormalities. This type of application will require a detector such as a gamma camera which only allows the detection and localisation of gamma rays emitted in a certain direction.

Most diagnostic procedures in Nuclear Medicine measure the amount of radioactivity present in an organ or the spatial distribution of activity and Nuclear Medicine can be considered as a discipline which assesses the functional state of an organ rather than defines the anatomy of an organ. The anatomy of organs is much better examined using x-rays in a Department of Radiology. The difference between image quality in Radiology and Nuclear Medicine arises principally from the fact that x-rays are switched on and off at the beginning and end of the study and so all the x-rays which give a radiation dose to tissues are used to form the image. In Nuclear Medicine, radioactivity is injected before a procedure and remains in the body until cleared by natural biological processes. The radiation dose is accumulated throughout the time radioactivity is present but only a small fraction of the emitted gamma rays are used to form the image. In Nuclear Medicine the number of gamma rays available is much less than the number of x-rays available in Radiology. Hence x-ray pictures have more detail and resolution than gamma ray images.

The Administration of Activity to People

For any Nuclear Medicine procedure the amount of radioactivity administered is small and will not interfere with any normal metabolic process. Such quantities are termed tracers. The typical radiation dose received by a patient (the effective dose) during a Nuclear Medicine procedure is 1 - 4 mSv. This can be compared to the average effective dose which everyone receives from natural radiation and radioactivity which is 2 mSv per year.

The presence of a radioactive atom is identified when it decays and the emitted radiation is detected. If the requirement is to measure radioactivity in a sample of blood or urine, then radioactive isotopes which emit either beta particles or gamma rays can be used. Typically beta particles have ranges in tissue or water of tenths of a mm whereas gamma rays will penetrate a few cm. If we need to image the distribution of radioactivity within the body then we can only use radioisotopes which emit the more penetrating gamma rays since they have to be detected from outside the body. The most commonly used radioisotope is ^{99m}Tc which has a half life of 6 hours and emits a gamma ray of 140 kev.

If we wish to test the functional state of an organ within the body, we have to exploit various natural biological mechanisms in order to introduce radioactivity into the organ. For example in the case of the thyroid gland we exploited the process of **active transport** by which the thyroid cells lining blood vessels transport iodine across the cell membrane from blood into the cell and ultimately into the gland.

Another mechanism is **capillary blockage** which is the mechanism used to introduce radioactive particles into the lung. If you inject radioactive particles into an arm vein, the venous blood will carry the particles back to the heart which then pumps the blood to the lung for reoxygenation, the exchange of oxygen and carbon dioxide. If the particles are 20 microns or so in diameter they will jam in the small capillaries of the lung. This is strictly a mechanical process and the particles eventually break down and are cleared from the lung. Nevertheless whilst a fraction of the blood capillaries are blocked a spatially sensitive detector, or gamma camera, can measure the distribution of radioactivity which will represent the distribution of blood flow to the lungs. Such a distribution can be altered dramatically in the presence of pulmonary embolism or lung cancer.

A third exploitable mechanism is **phagocytosis**. One of the functions of the liver is to remove colloidal material from the blood stream. Consequently if we introduce a radioactive colloid (particle size ~50nm) into blood, the liver will extract the radioactivity enabling an image to be produced by a gamma camera.

The **localization** of materials to an anatomical **compartment** can be used for diagnostic purposes. For example radioactive material can be mixed with food and the rate at which the food empties from the stomach can be measured. In this way abnormalities associated with delayed gastric emptying can be detected. It is also possible to restict tracers to compartments in the body such as blood, plasma, extracellular fluid or total body water. Such tracers can be used to measure the volume of fluid within each compartment.

The chemical nature of certain elements means that they have specific locations in the body. For example, some ions generally exist outside of cells (eg: sodium) while others exist inside cells (eg: potassium). Some elements are principally located within the skeleton (eg: calcium). The mechanisms responsible for these distributions can be exploited to introduce radioactivity into an organ by **exchange diffusion**. For example, thallium is a chemical analogue of potassium. After injection some thallium will be present in heart muscle and areas of defective function due to an infarct for example can be detected especially if the study is performed whilst the subject is exercising.

Finally, a substance such as pyrophosphate which has a role in the regulation of calcification processes in the skeleton, can be used to obtain bone scans. The amount of radioactively labelled pyrophosphate delivered to a particular bone site will depend on **blood flow** and the rate of bone uptake of the radiopharmaceutical. Consequently it is possible to image the skeleton according to important metabolic processes. If the blood flow to bone and/or bone cell activity is increased then the greater will be the activity delivered to and detected in the affected region. Abnormalities such as bone injuries, bone cancer or Paget's disease will show up on the bone scan.

Detectors in Nuclear Medicine.

The work horse of most nuclear medicine departments is the Anger camera which consists of a collimator, a crystal and a light detection system.

The collimator: The collimator is a device for restricting the radiation that reaches the detector. It consists essentially of a number of parallel holes in a lead disc so that only gamma rays travelling perpendicularly to the collimator face can pass through the holes. The typical energy of a gamma ray used in Nuclear Medicine is 140keV. The half value layer in lead for such gamma rays is about 0.3mm. Consequently the holes of a collimator need to be separated by about 1 mm to provide adequate collimation.

The crystal: The crystal is a device for converting electromagnetic radiation in the form of gamma rays into electromagnetic radiation in the form of visible light. Most commonly, the crystal consists of inorganic sodium iodide which has a density of 3.7g cm^{-3}. The presence of iodine in the crystal and the relatively high density means that gamma rays readily interact and transfer their energy to the crystal. This energy is re-emitted in the form of blue light which can be detected by a photomultiplier tube.

The light detection system: The location of a light flash in the NaI crystal corresponds to the location of the radioactive atom within the organ of interest. The light detection system converts this information into (x,y) coordinates within the plane of the crystal. The accumulation of many such events represents the projection of the 3D distribution of activity onto the 2D plane of the NaI crystal.

A bone scan can be performed after injection of ^{99m}Tc-diphosphonate and waiting for a short time while activity clears from blood and tissues and accumulates in bone. A normal bone scan is shown with the image on the left being obtained from the back and the right hand image from the front of the patient. There is activity in the thyroid gland and the stomach showing that some of the ^{99m}Tc has been freed and is circulating as TcO_4which can be taken up by the salivary glands, the thyroid gland and by the stomach. Most of the radioactivity accumulates in the ends of the long bones, in the ribs and the spine with little activity in the shafts of the long bones. This reflects the distribution of blood flow to the skeleton and the expected locations of greater bone cell activity. Here is what happens to the bone scan when there are multiple secondaries in the skeleton. This is from a patient with prostate cancer who had normal x-rays. However you can see that metastases are present in the ribs, the spine and at the shoulder. The secondaries originating from the primary cancer in the prostate have invaded the skeleton and have disturbed bone cell metabolism so that there is an increased uptake of the radiopharmaceutical. This is an example of a bone scan in a patient with Paget's disease. You can see that there are specific bones in the skeleton where the uptake of the radiopharmaceutical is greatly increased. This is due to both an increase in cell activity and an increased blood flow. In fact in some Paget's patients the affected limb can actually feel hot to the touch because of the increased blood flow. The cause of the disease is unknown and suggested causes range from a virus carried by house pets to long term exposure to environmental or occupational lead. In contrast to the Paget's disease scan, there may be abnormalities observed on a scan because of a lack of uptake of radioactivity as well as excessive uptake.

The ability of radioisotopes to measure time dependent processes is illustrated well by kidney scans. A radioactive tracer has been injected which is cleared from the blood stream through the kidneys. At the top left is a picture taken 3 minutes after injection at which time some of the the activity is in the kidneys but much is still within the circulation. At 13 minutes after injection, much of the activity has been processed by the kidneys and can be seen accumulating in the bladder after passing through the ureters. At 17 minutes after injection, the activity in one kidney has started to decline while the other kidney still contains the radioisotope apparently because of this blockage in the ureter. Thirty seven minutes after injection the flow from this kidney is still impaired.

Positron Emission Tomography.

At McMaster any Nuclear Medicine presentation is considered to be incomplete unless positron emission tomography (PET) is at least mentioned. PET scanning exists because of the limitations of imaging with a standard gamma camera. The difficulty is that, just as in standard x-ray imaging, the picture is a projection image which compresses the true spatial distribution of radioactivity onto a single plane. This means that abnormal increases or decreases in activity may not be visible and are lost in the general background radioactivity. PET scanning is one approach to obtaining true 3D images. Radioisotopes which decay by emitting a positron (^{18}F, ^{11}C, ^{13}N, ^{15}O) can be used to synthesize many radiopharmaceuticals. When a positron is emitted, the particle travels a very short distance and is annihilated by interacting with an electron. Two gamma rays are created which travel in opposite directions. If a pair of opposed detectors each identify an annihilation gamma ray at the same instant, then a positron decay probably occured on the line joining the two detectors. A ring of detectors is capable of detecting many annihilation events. If sufficient lines of interaction are identified then an image of the distribution of radioactivity can be reconstructed. For example, PET scans can view the distribution of a ^{18}F labelled neurotransmitter in a slice taken through the head. The distribution of activity is colour coded with the red being “hotter” than the blue. These two areas of increased activity are the caudate nuclei which are actively processing the neurotransmitter. It is also apparent that activity is accumulating in the scalp outside the brain. This activity represents metabolised radiopharmaceutical. The extent to which different regions of the brain are functioning and the respose of brain tissue to external stimuli can be tested in both normal and disease states using PET. For example an epiletic fit suffered by a child during a PET scan shows up as a dramatic increase in labelled glucose activity in a defined region of the brain.

It is incorrect to give the impression that all Nuclear Medicine procedures depend on imaging techniques and I want to give two non-imaging examples. First it is possible to diagnose the presence of bile acid deconjugation by bacteria in the bowel. Normally bile acids are secreted by the liver into the small bowel where they aid in the digestion of food. These bile acids are very efficiently returned to the liver further down the small bowel. Normally only 3% of bile acids pass into the large bowel where the presence of bacteria break down the acids into products which are absorbed. One of the final products of metabolism is carbon dioxide which is excreted through the lungs. If a normal person is given ^{14}C labelled bile acid then a small amount of $^{14}CO_2$ will be expired and can be detected. If for a variety of reasons, bacteria have invaded the small bowel, then bile acids will be broken down and absorbed and the amount of expired $^{14}CO_2$ will be greater than expected. The increased loss of bile acids will affect the ability of the small bowel to digest food. Another common syndrome is rapid transit of material through the bowel which decreases the return of bile acids to the liver and again will lead to increased exhalation of $^{14}CO_2$. In this example, a patient demonstrates increased activity in the breath following the administration of ^{14}C labelled bile acid. After treatment with the antibiotic tetracycline, the pattern returns to a more normal level. However some weeks later there is evidence that the condition is re-establishing itself. This suggests surgical correction is necessary after which the pattern was normal.

Another procedure common to Nuclear Medicine Departments is bone densitometry which does not even involve the administration of radioactivity. The technique depends on measuring the relative attenuation of a beam of photons which consists of gamma rays or x-rays of two distinct energies. If the two energies are chosen correctly the ratio of the attenuations of each energy group is sensitive to the amount of bone in the beam. A typical study involves the distal femur, a very important bone with respect to the disease osteoporosis.

Conclusion:

The diagnostic sub-specialty of Nuclear Medicine is based on the manipulation of radioactive substances and their emissions so that the functional state of organs and tissues can be quantitated. The discipline has evolved through the collaborations of physicians, chemists, pharmacists and physicists. Nuclear Medicine represents one of the major benefits to society arising from the development of nuclear energy during the 20th century.