The basic science of nuclear medicine

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Abstract

In the era of increasing utilization of cross-sectional imaging in orthopaedic patients with computed tomography (CT) and magnetic resonance imaging (MRI), nuclear medicine (NM) techniques continue to occupy a valuable role in the investigation of these patients. It can provide crucial functional information in a variety of clinical settings that are encountered regularly in orthopaedic practice. It is important that the orthopaedic surgeon is aware of the modalities on offer and appreciates the relative strengths and limitations of these techniques. This article will describe the physical principles underlying NM imaging with single-photon and positron-emitting radiotracers. It will then go on to illustrate the clinical applications of these techniques as applied to pathological conditions of the bone, with particular emphasis on bone scintigraphy and state-of-the-art hybrid imaging techniques, which combine the strengths of functional and structural imaging: single-photon emission computed tomography/computed tomography (SPECT/CT) and positron emission tomography/computed tomography (PET/CT).

Keywords bone scintigraphy; nuclear medicine; PET; PET/CT; SPECT; SPECT/CT

Introduction

Nuclear medicine (NM) provides exquisitely sensitive functional imaging techniques that utilize trace amounts of radiopharmaceuticals to study physiological processes *in vivo*. Improved understanding of the biological processes that occur at a cellular level has recently led to a renaissance of interest in molecular imaging, which has its basis in NM with the introduction over half a century ago of iodine-131 (^{131}I) for imaging the thyroid gland.[1] Functional imaging achieved widespread clinical application with the ability to generate technetium-99m (^{99m}Tc) in the mid-1960s, a radiotracer that has optimal physical qualities for use in medical imaging and now forms the basis of over 75% of all nuclear medicine studies. More recently, further resurgence in clinical interest in NM has occurred with the advent of hybrid techniques, whereby fully diagnostic-quality anatomical imaging in the form of multi-detector (or 'multi-slice') computed tomography (CT) has been combined with the functional modalities of single-photon emission computed tomography (SPECT/CT) and positron emission tomography (PET/CT) in integrated hybrid scanners.[2–4] Overall, this has led to NM being at the vanguard of technological advancement in medical imaging at the present time. Many of these functional techniques have relevance to modern orthopaedic practice, and the orthopaedic surgeon should, therefore, possess some knowledge of the scope and limitations of modern NM modalities as applied to orthopaedic surgery. This article will describe the physical principles behind the basic techniques of NM imaging, and will then go on to demonstrate some of the main clinical applications of NM as applied to orthopaedic practice.

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The physics of nuclear medicine (NM) imaging

Common isotopes and radiopharmaceuticals

The ideal radiopharmaceutical should be specific to the pathway of interest, possess the requisite half-life, be sterile and pyrogen free, and should emit either gamma rays suitable for gamma-camera imaging or positrons suitable for PET scanning.[5] Radioactive nuclei that decay by other mechanisms, producing beta-particles or alpha-particles, only increase the radiation dose to the patient without providing signal to an external detector, and are therefore not useful as imaging tracers, although they have a role in targeted radiotherapy. Radiopharmaceuticals are regulated as medicines, and their manufacture must be carried out to good manufacturing practice (GMP) standards in order that they are safe to administer to patients.

Single-photon emitting tracers: the workhorse isotope for gamma-camera imaging is technetium-99m (^{99m}Tc), which has a six hours half-life and emits gamma rays of 140 keV energy. ^{99m}Tc is formed by the decay of its parent isotope molybdenum-99 (by beta emission), which leaves the ^{99m}Tc nucleus in a long-lived excited energy state (the "m" in 99mTc stands for "metastable"). ^{99m}Tc nuclei subsequently lose energy by the emission of the desired 140 keV gamma ray, with a half-life of six hours. The chemistry of technetium is not straightforward, but methods of attaching it to clinically interesting ligands have been developed, leading to a range of useful radiopharmaceuticals. The attraction of ^{99m}Tc is two-fold: (a) its near-ideal imaging properties and (b) the convenience of the generator system that makes it readily available to NM departments. The half-life of ^{99}Mo is 66 hours, which means that a generator need only be delivered once or twice per week, while fresh supplies of ^{99m}Tc can be eluted from it every day for the manufacture of radiopharmaceuticals for immediate use. Other radioisotopes are used for gamma-camera imaging, either when a longer half-life is required (e.g. to allow for imaging at 24 and 48 hours to detect the slow accumulation of the somatostatin analogue ^{111}Indium-octreotide), or where the ligand of interest is not amenable to labelling with ^{99m}Tc (Table 1).

Positron-emitting tracers: fluorine-18 (^{18}F) is the most commonly used PET tracer in clinical practice. In common with most PET tracers, ^{18}F is produced in a cyclotron, which is used to bombard a target of oxygen-18 enriched water with high-energy protons. With a half-life of 110 minutes, it is practicable to deliver supplies of ^{18}F-labelled radiopharmaceuticals to hospitals

Common single-photon radiopharmaceuticals	
Tc-99m diphosphonates	Skeletal metabolism
Tc-99m tetrofosmin	Myocardial perfusion
Tc-99m mercaptoacetyltriglycine (MAG3)	Dynamic renography
Tc-99m exametazime labelled leukocytes	Infection/inflammation imaging
In-111 pentetreotide	Somatostatin receptors
I-123 metaiodobenzylguanidine (mIBG)	Neuroectodermal tumours

Table 1

PET radiopharmaceuticals	
F-18-2-fluoro-2-deoxy-glucose (FDG)	Glucose metabolism
F-18 fluoride	Skeletal metabolism
F-18-choline	Prostate malignancy
F-18-MISO	Hypoxia imaging
Ga-68-DOTATATE	Somatostatin receptors

Table 2

from a cyclotron located 1 or 2 hours away, thus sharing the costs of running the cyclotron among several customers. The single most important ^{18}F-labelled radiopharmaceutical in clinical practice today is ^{18}F-2-fluoro-2-deoxy-D-glucose (^{18}F-FDG or FDG), which is a non-physiological analogue of glucose. Other ^{18}F-labelled radiopharmaceuticals are now being deployed clinically (Table 2), but FDG continues to account for the majority of PET scans undertaken currently.

Imaging principles and technology

There are two distinct modes of NM imaging: (a) single-photon emission imaging with a gamma camera and (b) positron emission tomography (PET) which is achieved with a PET scanner. The similarities of the two techniques are, in fact, greater than their technological differences. Both non-invasively produce images of the biodistribution of an administered radioactive tracer.

The life history of a gamma ray: from the point of emission, a gamma ray may travel straight out of the patient. However, it may be scattered (the Compton Effect), resulting in a lower-energy gamma ray travelling in a different direction from the original, or it may be totally absorbed (either by multiple Compton scatters, or by the photo-electric effect). Although NM detectors are energy selective, it is not practicable to reject all scattered photons, hence the resulting image will, to some extent, misrepresent the distribution of tracer in the patient, because of scattered photons seeming to have originated from somewhere other than their true point of emission. Scatter and attenuation are key confounding factors affecting the quantitative accuracy of NM images, and these effects can be corrected for more accurately in PET than in gamma-camera imaging.

Detecting gamma rays: most NM imaging systems are based on scintillation detectors (Figure 1). These use inorganic crystals that absorb gamma rays and then fluoresce, producing a shower of visible or ultraviolet photons. The fluorescent photon shower is converted into an electrical pulse by optically coupling the crystal to a photomultiplier tube (PMT). The magnitude of the electrical pulse produced is proportional to the gamma-ray energy absorbed by the crystal. There is growing interest in substituting the conventional PMT with silicon-based equivalents, so-called SiPMs.[6] These have the advantage of being unaffected by extraneous magnetic fields, which is highly desirable for the development of PET/MR systems.

Gamma-camera imaging: the essential features of the gamma camera have changed little since it was developed by Anger in the late 1950s, although camera performance has improved

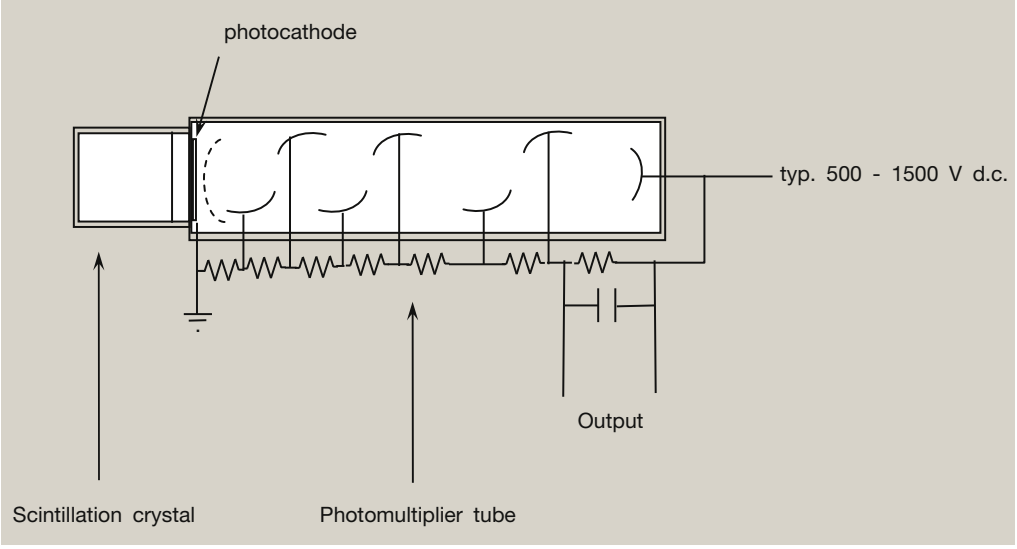

Figure 1 Schematic diagram of a basic scintillation detector. Fluorescent photons emitted by the scintillation crystal, following absorption of gamma-ray energy, stimulate emission of photoelectrons from the photomultiplier tube's photocathode, which are accelerated between the dynodes of the PMT generating a measurable charge pulse.