MEDIUM HALF-LIFE INORGANIC RADIONUCLIDES FOR PET IMAGING

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Introduction

In vivo radiotracer imaging continues to grow in importance and consideration is constantly given to the relative merits of the different techniques of radionuclide imaging and how they complement each other. The aim of this review is to highlight the role of inorganic medium-lived radionuclides within the field of Positron Emission Tomography (PET). PET has evolved around the use of short-lived radioactive tracers of natural organic elements such as $^{11}$C (20 min.), $^{13}$N (10 min.) and $^{15}$O (2 min.). Although fluorine is not a commonly natural constituent of organic molecules, $^{18}$F (110 min.), as a hydrogen analogue, is the radionuclide most commonly used and $^{18}$F-FDG is currently the most widely used PET radiotracer. This is due at least in part to the longer half-life of $^{18}$F which offers both practical and technical advantages to study prolonged biochemical interactions that are not possible even with the longest half-life organic radionuclide ($^{11}$C, 20 min.). This review therefore focuses on exploiting the use of medium half-life radionuclides in PET imaging. This expansion could aid in realising the true potential of PET by combining the sensitivity and quantitative accuracy of the technique with a large number of specific tracers developed for single photon imaging using for example, $^{99m}$Tc, $^{123}$I, $^{111}$In, $^{67}$Ga and $^{67}$Cu radionuclides. Here, the positron-emitters $^{94m}$Tc, $^{120}$I, $^{124}$I, $^{110}$In, $^{66}$Ga and $^{61}$Cu could be used as the PET imaging analogues. The abundance of inorganic positron-emitting radionuclides span a wide range of half-lives (~1-100 hours) and spectrum of chemical properties ranging from the alkali metals to transition elements to lanthanides and the halogens (although not strictly 'inorganic' elements, the halogens are included for completion). This diversity of physical, chemical and biochemical properties justifies further exploration into this area of inorganic PET in order to take advantage of the opportunities offered by such radionuclides in PET research. In addition to the practical benefits of medium half-life radiotracers, certain applications particularly in oncology, require tracer kinetics to be followed for periods exceeding the limits of conventional short-lived PET radionuclides. This is often necessary for pharmacokinetic studies of radiolabelled anti-cancer drugs and other molecules such as monoclonal antibodies (MAbs), where
tissue uptake kinetics far exceeding the 20 min. half-life of $^{11}\text{C}$ are not uncommon. This is further supported by our experience using the tamoxifen analogue, idoxifen [1], where peak levels of uptake into experimental tumours were not found until 24 hours post i.v. administration. This implies that $^{124}\text{I}$ with its 100 h half-life is a suitable PET radiolabel to study the pharmacokinetics of this anti-estrogen drug in breast cancer patients.

From a logistic point of view such a review is currently appropriate as PET facilities continue to expand, and concern has been raised with respect to the cost effectiveness of the technique. To this end, the use of inorganic tracers based on medium half-life and generator-produced radionuclides enables PET to be carried out at centres remote from a cyclotron. The longer half-life of such radionuclides allows regional distribution of a number of radiotracers to be a viable option and the goal of significantly reducing the cost of PET can finally be achieved.

The choice of inorganic radionuclides described here is based on realistic forecast in terms of their production, radiolabelling and imaging feasibility. These and other aspects pertinent to the radionuclides will be discussed in this chapter.

**Decay Properties of Inorganic PET Radionuclides**

Unlike the conventional short-lived PET radionuclides, the vast majority of inorganic positron-emitting radionuclides combine both electron capture (EC) and positron ($\beta^+$) decays as means to achieve stability. The emission of non-annihilation gamma-rays following EC decay results in an increase in the signal due to single events with a reduction in the 511 keV photon flux leading therefore to reduced sensitivity. This however does not negate their use as positron-emitting tracers thanks in part to the high detection efficiency of the coincident event compared to single photon imaging. The EC decay, however has implications on both image performance and radiation dosimetry. Table 1 lists the decay properties of the radionuclides that are related to PET imaging. The radionuclides included are those with half-lives $> 1$ hour and a positron emission rate of $\geq 19$. Decay data are from Lederer & Shirley [2] and Sowby [3]

**Radionuclide Production**

**RADIOPHYSICAL ASPECTS**

Compared to conventional PET radionuclides ($Z = 6-9$), the higher atomic number ($Z \sim 21-70$) of medium-lived radionuclides implies that higher energy particles are needed for their production. This is essential in order to overcome the higher coulomb barrier, a repulsive force between the incident particle and the target nucleus. Radionuclide yields however, are also modulated by the available phase space, spin changes and