Symposium

Short-Lived Positron Emitters and Their Use in Nuclear Medicine: A Five-Year Experience

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The association of new methods of labeling with short-lived radioisotopes and of visualization in vivo of these labeled molecules by emission tomography allows regional studies of metabolism and physiologic parameters at different levels: fluid movements (cerebral blood flow, lung ventilation and perfusion, etc. . .), metabolism (oxygen, sugars, amino acids, etc. . .), barrier permeability (blood-brain barrier, etc. . .), and metabolism of drugs (receptor-ligand interactions). The success of such investigations depends on the simultaneous availability of three technological developments: Production of radioisotopes, labeling procedures and detection devices.

PRODUCTION OF SHORT-LIVED POSITRON EMITTER RADIOISOTOPES

Using a four particles cyclotron (Protons 21 MeV, deuterons 13 MeV, ^{4}He 24 MeV and ^{3}He 32 MeV), the following radioisotopes are currently produced:

^{15}O (T=2.05 min) as $^{15}O_2$, $C^{15}O_2$, and $H_2{}^{15}O$.

Labeled molecular oxygen and carbon dioxyde are produced on line and sent continously in a pure and sterile state into the examination room where they are inhaled by the patients for brain blood flow and oxygene consumption studies.

^{11}C (T=20.4 min) as ^{11}CO, $^{11}CO_2$, H^{11} CN, are also produced on line and sent to the chemistry lab. for labeling purposes.

^{13}N (T=10 min) as $^{13}N_2$ and $^{13}NH_3$,

^{18}F (T=112 min) as $^{18}F_2$ and $H^{18}F$.

Other isotopes as ^{19}Ne (T=17 sec) and ^{68}Ga (T=68 min) are also prepared for various applications.

LABELING PRODEDURES

Most of the labeling procedures are carried out with ^{11}C and rapid incorporation of this radioisotope have been studied using a 2 or 3 step-synthesis. Usually, high specific activity labeling is needed (0.5 to 1 Ci/μmole) and special care is taken to avoid isotopic dilution with stable carbon. It has been observed that in some specific cases interfering reactions may occur when working with high dilution of the labeled precursor.

The following molecules are routinely labeled:

^{11}C-methyl methionine, for pancreas visualization and brain protein synthesis,

^{11}C-chlorpromazine and ^{11}C-pimozide for brain dopamine receptor studies,

^{11}C-valium and ^{11}C-flunitrazepam for brain benzodiazepine receptors detection,

^{11}C-imipramine for lung uptake investigations,

^{11}C-etorphine for opiate receptors visualization.

All these molecules are produced in 50 to 100 mCi amounts and are sterile and pyrogen free. Semi automatic synthesis in lead shielded cells were developped in order, for the manipulators, to handle Curie quantities of carbon 11 safely.

MEDICAL APPLICATIONS UNDER STUDY USING POSITRON EMISSION TOMOGRAPHY

Regional cerebral blood flow (CBF) and oxygen extraction fraction (OEF) have been studied in patients suffering cerebrovascular diseases.

In recent brain infarction (less than 2 months) luxurious perfusion indicating a bad coupling between CBF and OEF is generally observed. Misery perfusion, which corresponds to an increase of OEF, was described for the first time in some patients suffering transient ischemic attacks. Normalization of this parameter has been observed in some of these patients after intra-extra cranial bypass surgery.

Using ^{11}C-methionine as precursor of brain protein synthesis, studies were performed in children suffering phenylketonuria and in old demented patients. Great modifications of labeled methionine uptake and incorporation in brain was observed.

Brain receptor visualization of receptors for neurotransmitters was tempted in baboons and humans. Specific brain distribution of drugs like chlorpromazine, flunitrazepam and pimozide were observed and displacement of some of them by cold drugs, indicating specific binding, was observed.

Other applications concerning lung ventilation, perfusion and metabolism as well as pancreas studies are currently pursued using positron emission tomography.

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