《招待講演 3》

Recent Advances in Radiopharmaceutical Development and Applications

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Recent advances in radiopharmaceutical development in three general areas will be discussed. The general areas are:

1. Development of new receptor based tumor imaging agents.

16α fluoro-17β estradiol (FES) was developed as an agent that can quantify estrogen receptor levels in tumors. Positron tomography has been used to compare the tumor uptake of FES with F-18 fluorodeoxyglucose (FDG) in women being evaluated for mass lesions of the breast. This comparative study shows that FES accurately predicts the estrogen receptor status of breast cancers while FDG appears more sensitive than FES for the detection of malignant lesions. Attempts have been made to prepare a more specific estrogen receptor ligand than FES. We have prepared some 21 other F-18 estradiol analogs. One of these 16β[F-18]fluoromoxesterol (FMOX) appear superior to FES in animal models. Preliminary human data suggests that FMOX may not be a superior imaging agent in humans. The reason for this is differing metabolic rates and pathways between animal models and humans. This has been confirmed by studies in isolated hepatocytes. Ligands for the androgen and progestin receptor system labeled with F-18 are also under development. In an attempt to extend the work with tumor receptor agents and PET to single photon emitting radionuclides, attempts have been made to radiolabel steroids with Tc-99m. An analog of the antiprogestin RU486 has been labeled with radionuclides of technetium and rhenium. Both of these labeled steroids show binding affinity higher than that of progesterone itself. Advances in the development of improved progestin technetium complexes as imaging agents for steroid receptor will be described.

2. Antibodies labeled with positron emitting radionuclides.

In the imaging of tumors using radiolabeled monoclonal antibodies, the use of PET gives increase sensitivity over conventional gamma camera imaging. An antibody (1A3) to colorectal carcinoma has been labeled with copper-64 using the bifunctional chelate Br-benzyl-TETA. The promising preclinical studies of this agent have led to the evaluation of copper-64 benzyl-TETA-Mab-1A3 in humans. Small colorectal tumor deposits were observed using PET and this labeled antibody. This application is of particular importance in quantifying human biodistribution of copper labeled antibodies prior to therapy using copper-67 labeled antibodies.

3. Advances in generator produced radionuclides.

Positron emitting generators such as the germanium-68/gallium-68 and zinc-62/copper-62 hold promise for the application of positron emission tomography in centers without cyclotrons. A zinc-62/copper-62 generator which produces >600 mCi of copper-62 at the time of preparation has been developed. A simple way to prepare copper (II) pyruvaldehyde bis-(N4-thiosemicarbazone) (PTSM) has been automated and used to prepare copper-62 PTSM for human use. This agent has been shown to be a useful agent to estimate perfusion in the brain, heart, kidney and tumors. Application of the germanium/gallium-68 generator is being utilized to investigate pulmonary transcapillary exchange rate in pulmonary disease. Labeling of proteins and peptides are also under development for various applications.