

DEVELOPMENT AND PERSPECTIVE OF PET RADIOPHARMACEUTICALS

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Perspective and strategy of the new business in PET area including radiopharmaceuticals will be discussed. In addition, the future direction of research as well as market size for PET radiopharmaceuticals, especially neurodegenerative disease imaging agents, prostate cancer imaging, will also be discussed.

I. NEW FLUORINATION METHOD IN A NONPOLAR PROTIC ALCOHOL SOLVENTS

The typical method for introducing fluorine, which is the best PET radioisotope, at a specific aliphatic molecular site is the nucleophilic displacement of the corresponding sulfonate or halide by fluoride ion. Ten years ago, we have developed a remarkable effect of using tertiary alcohols as a reaction medium for nucleophilic fluorination with alkali metal fluorides.^{1,2} The great efficacy of this method is a particular advantage in labeling radiopharmaceuticals with [¹⁸F]fluorine in high yield and purity, and in shorter times compared to conventional syntheses. In this new mechanism, the bulky, polarizable cation separates F⁻ from the protic solvent, which in turn acts as a base to reduce the unfavorable influence of the cation on the nucleophilicity of F⁻. We will use the term “flexible” fluoride to denote the unusual behavior of fluoride ion under these conditions.

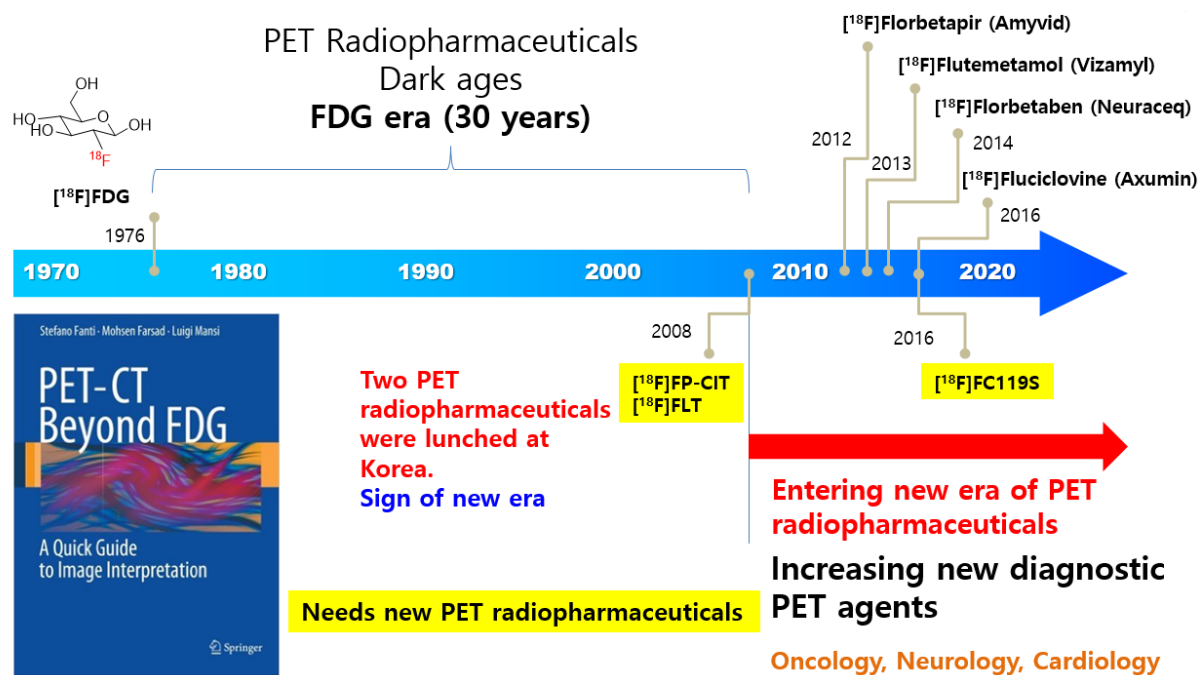
Using this new fluorination method, the development of several new radiopharmaceuticals such as [¹⁸F]FLT, [¹⁸F]FP-CIT, [¹⁸F]FES, and [¹⁸F]FMISO could be prepared in high yields.

II. NEW PET RADIOPHARMACEUTICALS IN MARKET

After FDG has been used since 1980s commercially, new F-18 labeled commercial PET radiopharmaceuticals have not been launched until 2008. Using this new fluorination method, two new radiopharmaceuticals [¹⁸F]FLT (cell proliferation imaging) and [¹⁸F]FP-CIT³ (Parkinson disease) were registered at Korea FDA in 2008. For your information, [¹⁸F]FLT and [¹⁸F]FP-CIT are commercially used for patients at Korea after getting the official permission from Korean FDA in 2008 spring. In 2002, ¹¹C-labeled [¹¹C]PIB (Pittsburgh compound B) was developed for imaging A β plaque in the brain of living subjects by modifying Thioflavin T, which has been used as a fluorescent dye for staining A β plaque in postmortem brains. [¹¹C]PIB exhibited good A β plaque binding in a living brain with an appropriate brain accumulation and washout ratio. Three F-18 labeled PET tracers have been approved by the U.S. Food and Drug Administration (FDA) in 2012 (AmyvidTM, Eli Lilly), 2013 (VizamylTM, GE Healthcare), and 2014 (NeuraceqTM, Piramal) as A β imaging agents and a secondary tool for the diagnosis of AD. We have also developed fourth F-18 labeled A β imaging PET tracer in NDA by Korean FDA in 2017 (Alzavue[®], FutureChem).

II. CONCLUSIONS

Based on this information, perspective, strategy, the future direction of research of the new business in PET radiopharmaceuticals - neurodegenerative disease imaging agents, prostate cancer imaging including some therapeutics will be discussed.



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