THE CHEMISTRY OF RE-188 RADIOPHARMACEUTICALS: COULD RE-188 PLAY THE SAME ROLE IN THERAPY AS TC-99M IN DIAGNOSTICS?

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Radiopharmaceuticals incorporating the β- emitting radionuclide Re-188 are still attracting much interest for their potential application in nuclear medicine as therapeutic agents. There are many advantages of employing this class of radioactive compounds as briefly summarized in the following.

(1) Re-188 emits a high-energy β- particle (2.1 MeV) that can be efficiently used to deliver high-dose radiation to the target.

(2) Re-188 concomitantly emits a 155-keV γ photon that can be conveniently employed to obtain good-quality SPECT images of the biodistribution of Re-188 radiopharmaceuticals and, ultimately, following in vivo the course of the therapy.

(3) Re-188 has a relatively short half-life (17 hours) that may allow multiple treatments of the same patient's disease.

(4) Re-188 is a radiometal belonging to the same group of Tc-99m in the transition metal series of the Periodic Table, and shares with its cogener similar (though not identical) chemical properties that could be useful for designing a broad class of Re-188 radiopharmaceuticals having the same bioditribution properties of the corresponding Tc-99m analogues.

(5) Similarly to Tc-99m, the radionuclide Re-188 is produced in high-specific activity through the $^{188}W/^{188}Re$ transportable generator system.

A first challenge encountered in the attempt to develop efficient labeling procedures for Re-188 was related to the low radiochemical yield usually observed in tracer-level preparations of Re-188 radiopharmaceuticals starting from generator-produced $[^{188}ReO_4]$-. This drawback is commonly associated with the low value of the standard reduction potential of the tetraoxo anion as compared to the corresponding Tc-99m pertechnetate anion. In recent years, we reported a simple and efficient procedure for overcoming this problem based on a general chemical principle called 'expansion of the coordination sphere' and involving the addition to the reaction vial of an ancillary ligand (usually, chelating hard-donor Lewis'bases) favoring the conversion of the tetrahedral arrangement of $[^{188}ReO4]$- to a higher coordination geometry. Using this novel approach, we were able to obtain the high-yield preparation of a large number of Re-188 complexes having exactly the same molecular structure of the corresponding Tc-99m analogues, and clearly demonstrate that these matched-pairs of Tc-99m and Re-188 complexes fully exhibit the same biodistribution properties.

These findings opened the door to the application of a number of Re-188 radiopharmaceuticals to the treatment of different neoplastic diseases. In particular, we developed Re-188 radiopharmaceuticals for the therapy of the following tumours: (a) Re-188 labeled lipiodol for the treatment of hepatocellular carcinoma, (b) Re-188 labeled peptides for

the therapy of different types of peptide-receptor expressing tumors, and (c) Re-188 labeled biotin and bivalent haptens for the adjuvant treatment of breast cancer.

Recently, we devised a remotely controlled, multi-reaction, synthesis module for the preparation of different classes of Re-188 radiopharmaceuticals under conditions that dramatically decrease the radiation exposure of personnel involved in Re-188 production.