Contribution ID: **245** Type: **Verbal**

In vivo ²¹²Pb/²¹²Bi generator using liposomes

Bi-212 is a potentially interesting alpha radionuclide for targeted alpha therapy. The principle is based on the stable binding of alpha emitting radionuclides to cancer selective carrier molecules, such as antibodies or peptides. The challenge is to deliver the radioactive atoms to the target with the objective to find the right balance between toxicity and anti-tumour effect.
Considering its short period (t1/2=60.6 min), Bi-212 is limited to situations where the labelled carrier molecule rapidly accumulates in the target tumor. To expand the range of applications, an interesting method is to use its parent, Pb-212 (t1/2=10.6 h), which will generate in vivo Bi-212. Data in the literature show that the classical chelation approach does not work. Although the chelating agent used (DOTA) is known to form strong complexes with both Bi and Pb, a significant part of Bi escapes from the carrier molecule as a result of the radioactive transformation Pb-212 / Bi-212 [1].
An interesting alternative is to use liposomes [2]. Once Pb-212 is encapsulated in its internal compartment, the phospholipidic membrane prevents Bi release provided that the liposome size is large enough (~ 100 nm). In this work, liposomes functionalised with DTPA at the surface are used. Once complexed with In, the In-DTPA species corresponds to the recognition site for the targeting. An active encapsulation was tested, i.e. the liposomes are preformed before the encapsulation, using a methodology implying the Chelex-100 resin. DTPA is present in the internal compartment (0.025 M) to keep Pb-212 in the core as an anionic complex after its uptake. The passage of the membrane was obtained using different weak complexing agents (1,10-phenanthroline-2,9-dicarboxylic acid (DCP), 2,3-dimercapto-1-propanol (BAL), sodium acetate), the one leading to the best results being acetate. Under the optimised conditions ([Pb]tot = 10-9 M (Pb-212 activity of 700 Bq), [liposome] = 2.5 mM, 65°C), 64% of Pb was shown to be encapsulated after 1 hour leading to 1 liposome labelled per 100.
The stability of the labelled liposomes was moitored in biological media using chromatographic techniques (HPLC, AF4: Asymmetrical Flow Field-Flow Fractionation) coupled with a gamma detection.

[1] Mirzadeh, S.; Kumar K. ; Gansow O., The Chemical Fate of 212Bi-DOTA Formed by b- decay of 212Pb(DOTA)2-. Radiochimica Acta, 1993, 60, 1-10.
[2] Henriksen G.; Schoultz B.; Hoff P.; Larsen, R., Potential in vivo generator for alpha-particle therapy with 212Bi: Presentation of a system to minimize escape of daughter nuclide after decay of 212Pb to 212Bi, Radiochimica acta, 2003, 91, 109-113.

Primary author: Ms LE DU, Alicia (Subatech)

Co-authors: Mr FAIVRE CHAUVET, Alain (Inserm U892); Mr MONTAVON, Gilles (Subatech); Mr BARBET, Jacques (Inserm U892); Mrs MOUGIN-DEGRAEF, Marie (Inserm U892); Mr BOTOSOA, Patrick Eliot (Inserm U892); Mrs HUCLIER, Sandrine (Subatech)

Presenter: Ms LE DU, Alicia (Subatech)

Track Classification: Nuclear Methods in Medicine, Radiopharmaceuticals and Radiodiagnostics, Labelled Compounds