

^{68}Ga radiopharmaceuticals: past, present and future perspectives

Stefano Boschi, S.Orsola Hospital, Bologna, Italy

$^{68}\text{Ge}/^{68}\text{Ga}$ radionuclide generators have been investigated since 60's but it takes decades to approach a reliable level of $^{68}\text{Ge}/^{68}\text{Ga}$ generator design with chemical features adequate to radiometal labeling chemistry. More favourable chemistries were also developed; open chain complexing agents have almost completely been displaced by macrocyclic DOTA and NOTA-derived conjugates.

The most important driver for the development of ^{68}Ga radiopharmacy was the development of small tumour-affine peptides targeting somatostatin receptors. ^{68}Ga -DOTA-octreotide derivatives were the breakthrough vector molecules and fundamental to the development of present day ^{68}Ga radiopharmacy and the $^{68}\text{Ge}/^{68}\text{Ga}$ generators.

The striking diffusion and the exciting perspective of the ^{68}Ga radiopharmacy was the trigger for systematic chemical, radiochemical, technological and radiopharmaceutical efforts to guarantee reliable and medically approved $^{68}\text{Ge}/^{68}\text{Ga}$ generator systems along with automated and validated production processes, comprehensively and correctly implemented quality assurance system, to ensure that quality and safety of ^{68}Ga radiopharmaceuticals is adequate for the intended use.

Beside DOTA-Octreotide derivatives, a large number of ^{68}Ga labelled molecules has been developed and many others are used in pre-clinical studies. Myocardial perfusion, pulmonal blood flow, bone imaging, or membrane receptor status can be expected to be observable with sophisticated ^{68}Ga -PET analogues. Still there is room for improvement, which is reflected by the continuous increase in research papers from all areas of ^{68}Ga -based radiopharmaceutical chemistry.

Optimization of the chelating moieties in terms of thermodynamic stability and kinetic inertness, in terms of labelling efficacies and bi-functionality opens brilliant research and clinical perspectives.

Development of NOTA-derived bifunctional chelators has opened a brilliant future for almost unlimited application of ^{68}Ga in all fields of non-invasive molecular imaging with radioactive probes.