^{68}Ga-bisphosponates for imaging bone diseases

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Introduction: As ^{99m}Tc-bisphosphonates are well established tracers for the diagnosis of osteoblastic bone metastases using SPECT. Analogue attempts for PET using ^{68}Ga tracers would be potentially useful. Molecules combining a bisphosphonate bone-targeting structure and a macrocyclic complexing moiety for trivalent gallium could be considered as interesting vectors. A novel ^{68}Ga-DOTA-based bisphosphonate (BPAMD) was successfully synthesised and evaluated *in vivo* in humans.

Experimentalteil: Using the cation exchanger method for purification and concentration of the ^{68}Ge/^{68}Ga generator eluate the ligand BPAMD was ^{68}Ga -labelled in 85% yield within 10 min. The product was purified using a Strata-X-C cartridge for removing small amounts of free ^{68}Ga. After purification the acidic pH was adjusted and the product was passed trough a sterile filter. Quality control was performed by different radio-TLC systems and HPLC.

Results: In a first human *in vivo* study, the ^{68}Ga-BPAMD (MIP 50 min. p.i., 462 MBq) was injected i.v. into a patient with known extensive bone metastases of prostate cancer, as detected by [^{18}F]fluoride-PET. ^{68}Ga-BPAMD revealed intense accumulation in multiple osteoblastic lesions in the central skeleton, ribs, and proximal extremities. Metastases were detected in the whole skeleton with higher SUVmax (77.1 and 62.1 in the 10th thoracic and L2 vertebra) values compared to [^{18}F]fluoride (39.1 and 39.2).

Conclusions: Advantages of this new bone imaging PET-tracer are the very high target-to-soft-tissue ratios and ultrafast clearance, its ease of use and the generator-based availability of ^{68}Ga which becomes especially important in these days of ^{99m}Tc shortage. While [^{18}F]fluoride is adsorbed on bone surface and is related to blood flow, the bisphosphonate ^{68}Ga-BPAMD is taken up also by osteoclasts reflecting the farnesyl diphosphate synthase enzyme dynamics in the HMG-CoA reductase pathway. Since this pathway is mainly responsible for the osteoclastic bone destruction, ^{68}Ga-BPAMD may be superior in osteoclastic lesions.
Finally, ^{68}Ga-BPAMD seems to be an ideal PET -tracer to plan and monitor bisphosphonate therapy in several bone disorders like osteoporosis, osteitis deformans, bone metastases, multiple myeloma, osteogenesis imperfecta, etc. and also to monitor radionuclide therapy for bone palliation.

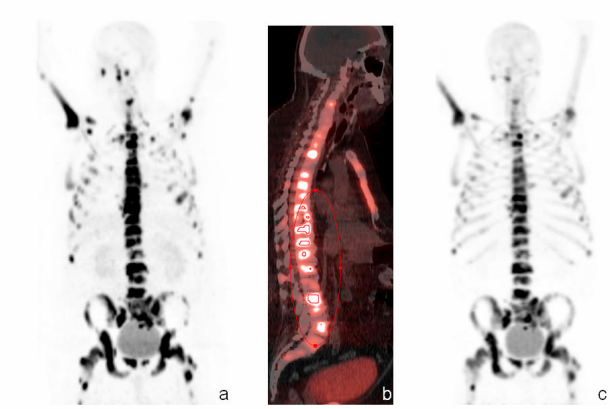

Figure 1: ^{68}Ga-BPAMD PET (MIP 50 min. p.i. of 468 MBq): intense accumulation of tracer in multiple osteoblastic lesions in the central skeleton, ribs, and proximal extremities (a). ^{68}Ga-BPAMD PET/CT (sagittal image): SUVmax 77.1 ([^{18}F]fluoride: 39.1) in 10th thoracic vertebra (b). [^{18}F]fluoride ion PET (MIP 90 min. p.i. of 270 MBq): SUVmax 39.2 (^{68}Ga-BPAMD 62.1) in L2 vertebra.

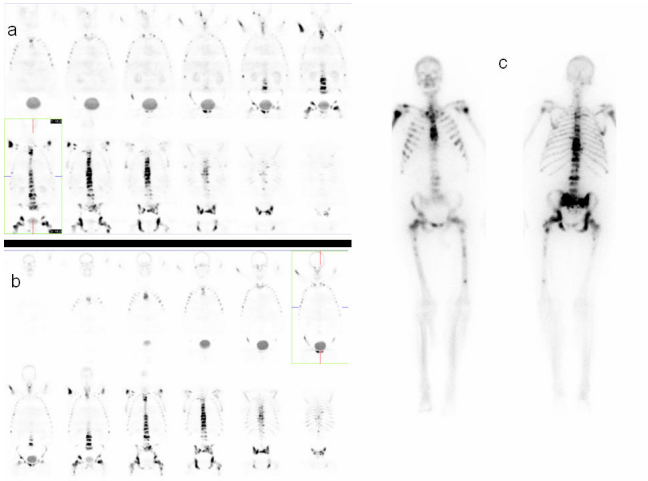

Figure 2: Comparison of ^{68}Ga-BPAMD (a) and [^{18}F]fluoride ion (b) coronal PET images: Similar high image quality, but slightly higher uptake in normal bone (e.g. ribs and left proximal humerus) in the sodium fluoride study; faint renal uptake of the ^{68}Ga-labelled tracer. Anterior and posterior images of the post therapy scans obtained 24 hrs after palliative radionuclide therapy with Sm-153 EDTMP are shown (c) on the right.

References

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