

PET/CT imaging of osteoblastic bone metastases with ^{68}Ga -bisphosphonates: first human study

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Bisphosphonates are well established ligands for $^{99\text{m}}\text{Tc}$ for planar and SPECT/CT imaging of osteoblastic metastases. A novel DOTA-based bisphosphonate, (4- $\{[\text{bis}(\text{-phosphonomethyl})\text{carbamoyl}]\text{methyl}\}$ -7,10-bis(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl)acetic acid (BPAMD) [1, 2], was labelled using the $^{68}\text{Ge}/^{68}\text{Ga}$ generator-derived positron emitter ^{68}Ga [3], resulting in the PET tracer ^{68}Ga]BPAMD.

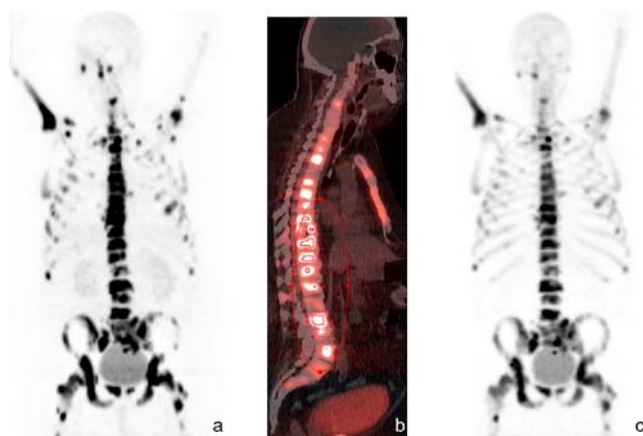
^{68}Ga]BPAMD was injected i.v. into a patient with known extensive bone metastases of prostate cancer. ^{68}Ga]BPAMD [maximum intensity projection (MIP) 50 min post-injection (p.i.), 462 MBq] revealed intense accumulation in multiple osteoblastic lesions in the central skeleton, ribs and proximal extremities: a = coronal PET, b = sagittal PET/CT. For comparison, c shows ^{18}F -fluoride PET (sagittal, MIP 90 min p.i., 270 MBq). Metastases were detected in the whole skeleton with a maximal standardized uptake value (SUV_{max}) of 77.1 and 62.1 in the 10th thoracic and L2 vertebra vs 39.1 and 39.2 for ^{18}F -fluoride, respectively.

The advantages of this new bone imaging PET tracer are the very high target to soft tissue ratios and fast clearance, its ease of use and the generator-based availability of ^{68}Ga which becomes especially important in these days of $^{99\text{m}}\text{Tc}$ 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/CT 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 palliation of bone pain.



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References

1. Kubíček V, Rudovský J, Kotek J, Hermann P, Vander Elst L, Muller RN, et al. A bisphosphonate monoamide analogue of DOTA: a potential agent for bone targeting. *J Am Chem Soc* 2005;127(47):16477–85.
2. Vitha T, Kubíček V, Hermann P, Elst LV, Muller RN, Kolar ZI, et al. Lanthanide(III) complexes of bis(phosphonate) monoamide analogues of DOTA: bone-seeking agents for imaging and therapy. *J Med Chem* 2008;51(3):677–83.
3. Zhernosekov KP, Filosofov DV, Baum RP, Aschoff P, Bihl H, Razbash AA, et al. Processing of generator-produced ^{68}Ga for medical application. *J Nucl Med* 2007;48(10):1741–8.

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