

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Departments of Nuclear Medicine and Radiology, Erasmus MC Rotterdam
Project Title:	High resolution and high sensitivity preclinical multimodal imaging of cancer.
Abstract:	<p>In the search for a more individualized approach to cancer therapy, a good understanding of oncogenic processes and the interaction of (novel) drugs with both tumor tissue and normal tissue is crucial. Through preclinical studies in animal models of cancer we are able to increase our knowledge and understanding of these processes. Major benefit in such preclinical studies is obtained from the use of sophisticated imaging systems specifically designed for non-invasive in vivo imaging of small laboratory animals. Additional benefit is obtained from the use of multi-modality imaging approaches such as SPECT-CT and SPECT-MRI through which molecular as well as anatomical and functional information of biological processes in vivo can be obtained.</p> <p>When imaging small laboratory animals, both high resolution and high sensitivity capabilities are required. In recent years different vendors have developed multi-pinhole SPECT imaging devices. By utilizing pinhole magnification the required high image resolution for small animal scanners is obtained at the cost of reduced sensitivity. New collimators and systems have been introduced to mitigate the loss of sensitivity. In our departments we have two newly developed microSPECT systems that are integrated with either a CT scanner or an MRI scanner. The SPECT cameras in these systems are equipped with state of the art high sensitivity collimators. A higher sensitivity makes imaging with a higher temporal resolution possible and enables the visualization of fast dynamic physiological processes. Performance characteristics, including quantitative capabilities and temporal resolution, for these systems should be determined for a range of isotopes in combination with anatomical and or functional information. Quantitative imaging with high temporal resolution (5-10s time frames) in combination with pharmacokinetic models could open up a whole new range of applications for preclinical imaging in view of the development of new treatment strategies for cancer patients.</p> <p>Aim of the project: Evaluation and optimization of the high resolution and high sensitivity capabilities of two highly advanced multimodal preclinical imaging systems in a cancer research setting.</p>

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	<p>Plan of investigation:</p> <ol style="list-style-type: none"> 1. Systematic evaluation of the performance capabilities of two new preclinical imaging systems using relevant phantoms. 2. Optimization of imaging protocols for molecular and functional cancer imaging using relevant radiotracers in combination with anatomical and or functional imaging strategies. 3. Evaluation of new imaging techniques in selected animal tumor models.
<p>Requirements of candidate:</p>	<p>The candidate is required to:</p> <ul style="list-style-type: none"> - Have a background in (medical) physics or (biomedical) engineering - Have affinity with biomedical research - Have affinity with sophisticated imaging techniques - Have good people interaction skills for working in a team with people from different academic backgrounds. <p>Master degree: Yes IELTS Grade: 7.0 (<i>minimal 6.0 per component</i>) or TOEFL: 100 (<i>minimal 20 per component</i>)</p>
<p>Supervisor information:</p>	<p>Overall supervisor:</p> <p>Prof. dr. M. de Jong, PhD Head of the preclinical imaging group Departments of Nuclear Medicine and Radiology m.dejong@erasmusmc.nl</p> <p>Primary supervisors:</p> <p>Dr. Monique R. Bernsen, PhD Assistant professor of molecular imaging Departments of Nuclear Medicine and Radiology m.bernsen@erasmusmc.nl</p> <p>Marcel Segbers, MSc Clinical Physicist Department of Nuclear Medicine m.segbers@erasmusmc.nl</p> <p>http://www.erasmusmc.nl/amie/</p>

Selected publications of the past three years:

- 1: de Jong M, Essers J, van Weerden WM. Imaging preclinical tumour models: improving translational power. *Nat Rev Cancer*. 2014 Jul;14(7):481-93. doi: 10.1038/nrc3751. Epub 2014 Jun 19. Review. PubMed PMID: 24943811.
- 2: Pool SE, Kam BL, Koning GA, Konijnenberg M, Ten Hagen TL, Breeman WA, Krenning EP, de Jong M, van Eijck CH. [(111)In-DTPA]octreotide tumor uptake in GEPNET liver metastases after intra-arterial administration: an overview of preclinical and clinical observations and implications for tumor radiation dose after peptide radionuclide therapy. *Cancer Biother Radiopharm*. 2014 May;29(4):179-87. doi: 10.1089/cbr.2013.1552. PubMed PMID: 24820805.
- 3: Bernsen MR, Vaissier PE, Van Holen R, Booij J, Beekman FJ, de Jong M. The role of preclinical SPECT in oncological and neurological research in combination with either CT or MRI. *Eur J Nucl Med Mol Imaging*. 2014 May;41 Suppl 1:S36-49. PubMed PMID: 24895751.
- 4: Tatsi A, Maina T, Cescato R, Waser B, Krenning EP, de Jong M, Cordopatis P, Reubi JC, Nock BA. [DOTA]Somatostatin-14 analogs and their (111)In-radioligands: effects of decreasing ring-size on sst1-5 profile, stability and tumor targeting. *Eur J Med Chem*. 2014 Feb 12;73:30-7. doi: 10.1016/j.ejmech.2013.12.003. Epub 2013 Dec 16. PubMed PMID: 24378707.
- 5: Bison SM, Konijnenberg MW, Melis M, Pool SE, Bernsen MR, Teunissen JJ, Kwekkeboom DJ, de Jong M. Peptide receptor radionuclide therapy using radiolabeled somatostatin analogs: focus on future developments. *Clin Transl Imaging*. 2014;2:55-66. Epub 2014 Mar 5. Review. PubMed PMID: 24765618;
- 6: Bison SM, Pool SE, Koelewijn SJ, van der Graaf LM, Groen HC, Melis M, de Jong M. Peptide receptor radionuclide therapy (PRRT) with [(177)Lu-DOTA(0),Tyr(3)]octreotate in combination with RAD001 treatment: further investigations on tumor metastasis and response in the rat pancreatic CA20948 tumor model. *EJNMMI Res*. 2014 May 30;4:21. doi: 10.1186/s13550-014-0021-y. eCollection 2014. PubMed PMID: 24995150;
- 7: De Blois E, Schroeder RP J, De Ridder CM A, Van Weerden WM, Breeman WA P, De Jong M. Improving radiopeptide pharmacokinetics by adjusting experimental conditions for bombesin receptor-mediated imaging of prostate cancer. *Q J Nucl Med Mol Imaging*. 2013 Jun 19. [Epub ahead of print] PubMed PMID: 23778459.
- 8: Piscaer TM, Sandker M, van der Jagt OP, Verhaar JA, de Jong M, Weinans H. Real-time assessment of bone metabolism in small animal models for osteoarthritis using multi pinhole-SPECT/CT. *Osteoarthritis Cartilage*. 2013 Jun;21(6):882-8. doi: 10.1016/j.joca.2013.03.004. Epub 2013 Mar 14. PubMed PMID: 23499675.
- 9: Guenoun J, Ruggiero A, Doeswijk G, Janssens RC, Koning GA, Kotek G, Krestin GP, Bernsen MR. In vivo quantitative assessment of cell viability of gadolinium or iron-labeled cells using MRI and bioluminescence imaging. *Contrast Media Mol Imaging*. 2013 Mar-Apr;8(2):165-74. doi: 10.1002/cmmi.1513. PubMed PMID: 23281289.
- 10: Pool SE, Bison S, Koelewijn SJ, van der Graaf LM, Melis M, Krenning EP, de Jong M. mTOR inhibitor RAD001 promotes metastasis in a rat model of pancreatic neuroendocrine cancer. *Cancer Res*. 2013 Jan 1;73(1):12-8. doi: 10.1158/0008-5472.CAN-11-2089. Epub 2012 Nov 13. PubMed PMID: 23149918.
- 11: Bol K, Haack JC, Groen HC, Niessen WJ, Bernsen MR, de Jong M, Veenland JF. Can DCE-MRI explain the heterogeneity in radiopeptide uptake imaged by SPECT in a pancreatic neuroendocrine tumor model? *PLoS One*. 2013 Oct 8;8(10):e77076. doi: 10.1371/journal.pone.0077076. eCollection 2013. PubMed PMID: 24116203; PubMed Central PMCID: PMC3792933.
- 12: Bernsen MR, Ruggiero A, van Straten M, Kotek G, Haack JC, Wielopolski PA,

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	<p>Krestin GP. Computed tomography and magnetic resonance imaging. <i>Recent Results Cancer Res.</i> 2013;187:3-63. doi: 10.1007/978-3-642-10853-2_1. Review. PubMed PMID: 23179877.</p> <p>13: Plenge E, Poot DH, Bernsen M, Kotek G, Houston G, Wielopolski P, van der Weerd L, Niessen WJ, Meijering E. Super-resolution methods in MRI: can they improve the trade-off between resolution, signal-to-noise ratio, and acquisition time? <i>Magn Reson Med.</i> 2012 Dec;68(6):1983-93. doi: 10.1002/mrm.24187. Epub 2012 Feb 1. PubMed PMID: 22298247.</p> <p>14: Melis M, Valkema R, Krenning EP, de Jong M. Reduction of renal uptake of radiolabeled octreotate by amifostine coadministration. <i>J Nucl Med.</i> 2012 May;53(5):749-53. doi: 10.2967/jnumed.111.098665. Epub 2012 Apr 10. PubMed PMID: 22496587.</p> <p>15: Kotek G, van Tiel ST, Wielopolski PA, Houston GC, Krestin GP, Bernsen MR. Cell quantification: evolution of compartmentalization and distribution of iron-oxide particles and labeled cells. <i>Contrast Media Mol Imaging.</i> 2012 Mar-Apr;7(2):195-203. doi: 10.1002/cmmi.481. PubMed PMID: 22434632.</p> <p>16: Pool SE, ten Hagen TL, Koelewijn S, de Jong M, Koning GA. Multimodality imaging of somatostatin receptor-positive tumors with nuclear and bioluminescence imaging. <i>Mol Imaging.</i> 2012 Feb;11(1):27-32. PubMed PMID: 22418025.</p> <p>17: Guenoun J, Koning GA, Doeswijk G, Bosman L, Wielopolski PA, Krestin GP, Bernsen MR. Cationic Gd-DTPA liposomes for highly efficient labeling of mesenchymal stem cells and cell tracking with MRI. <i>Cell Transplant.</i> 2012;21(1):191-205. doi: 10.3727/096368911X593118. Epub 2011 Sep 16. PubMed PMID: 21929868.</p> <p>18: Konijnenberg MW, de Jong M. Preclinical animal research on therapy dosimetry with dual isotopes. <i>Eur J Nucl Med Mol Imaging.</i> 2011 May;38 Suppl 1:S19-27. doi: 10.1007/s00259-011-1774-4. Epub 2011 Apr 1. Review. PubMed PMID: 21484379;</p> <p>19: van Buul GM, Kotek G, Wielopolski PA, Farrell E, Bos PK, Weinans H, Grohnert AU, Jahr H, Verhaar JA, Krestin GP, van Osch GJ, Bernsen MR. Clinically translatable cell tracking and quantification by MRI in cartilage repair using superparamagnetic iron oxides. <i>PLoS One.</i> 2011 Feb 23;6(2):e17001. doi: 10.1371/journal.pone.0017001. PubMed PMID: 21373640</p> <p>20: Alic L, Haeck JC, Bol K, Klein S, van Tiel ST, Wielopolski PA, de Jong M, Niessen WJ, Bernsen M, Veenland JF. Facilitating tumor functional assessment by spatially relating 3D tumor histology and in vivo MRI: image registration approach. <i>PLoS One.</i> 2011;6(8):e22835. doi: 10.1371/journal.pone.0022835. PubMed PMID: 21897840</p>
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