Voorstel MDO-opdracht
Opleiding Technische Geneeskunde
Universiteit Twente

A. Algemeen

1. Titel MDO-opdracht: **Comparison of pharmacokinetic parameters obtained by dynamic FDG-PET using two different, state-of-the-art commercial software packages.**

2. Gegevens instelling/indiener:

Naam indiener:	dr. E.P. Visser dr. L.F. de Geus-Oei, MD
Instelling/afdeling:	Nuclear Medicine, UMC St. Radboud, Nijmegen
Contactgegevens:	dr. E.P. Visser E-mail: e.visser@nucmed.umcn.nl Phone: 024 361 4081
Medisch begeleider:	dr. L.F. de Geus-Oei, MD drs. D. Vriens, MD
Technologisch begeleider (UT):	nog nader te bepalen

B. Faciliteiten

1. Welke faciliteiten zijn nodig voor een adequate uitvoering van de vraagstelling?
   - Dynamic FDG PET scans:
     - Database of approximately 80 patients and 220 scans available (stand-alone PET)
     - Data of patient scans already acquired on modern PET/CT scanner in ongoing research project is available. Patients are still being included in this study, total number of patients will be 53
   - Fast Dell workstations with 8-core CPUs
   - Inveon Research Workplace (Siemens)
   - PMod (PMod Technologies, Biomedical Image Quantification)

2. Wat zijn daarbij mogelijke risico's voor de voortgang van de opdracht?
   None

C. Overige opmerkingen

- The PET/CT scanner, software and data are available at the Radboud University Nijmegen Medical Centre, meaning that the students have to travel to Nijmegen. However, once the methods of analysis have become clear to the students, part of the work can also be performed at UTwente (or at the student's homes) using portable licenses ("dongle").

- The students can assist at the patient preparation (e.g. administration of radiopharmaceutical) and at the PET/CT scans of patients newly included in the advanced PET/CT study.
- Students are also invited to join some clinical meetings at the department of Medical Oncology to get more familiar with the broader context of this project and clinical patient care.
- The students can assist at the tumor resection by the thorax surgeon in the operation room (all patients undergoing PET/CT scan are scheduled for operation, see section below)

D. Inhoudelijke informatie MDO-opdracht

Omschrijving van de technisch geneeskundige vraagstelling:

PET/CT scans using FDG (radioactive analogue of glucose) are widely used for diagnosis of different types of tumours. Normally, static images are generated that are used by the nuclear medicine physician for therapy response monitoring, to identify metastases, or for general staging purposes.

To obtain more detailed information about e.g. the energy metabolism in the tumour, the tumour blood fraction, or tumour heterogeneity, dynamic FDG PET scans are made. The resulting time-dependent tumor signals are analyzed using pharmacokinetic models that describe the transport from blood vessels to the extravascular space, across the cell membrane, and finally, the FDG metabolism inside the tumor cells. The output of these models consists of several rate constants that describe the transport of FDG between these compartments, and the blood fraction in the tumour. It is generally believed that these kind of analyses yield better information about therapy response, survival, and staging than do static images [1-8].

Pharmacokinetic parameters are calculated from the time-dependent FDG concentration in blood plasma and the PET signal from the tumour. Until recently, the department of nuclear medicine at RUNMC used a “home-made” software package to analyze the dynamic FDG PET scans. However, several commercial software programmes have become available, the most advanced ones presently being Inveon Research Workplace (IRW) from Siemens Medical Solutions, and PMod from PMod Technologies, Biomedical Image Quantification.

Both software programmes are based on non-linear least squares curve fitting methods. Since the resulting tumour parameters can critically depend on choices with regard to starting parameters, subdivision in time frames, treatment of blood plasma input curves, etc. it is important to analyze the performance of these programmes upon variation of these parameters.

At present, several publications are available dealing with the outcome of dynamic FDG PET scans. However, none of these has adequately tackled the question as to how the choice of software package and model assumptions influence the resulting tumour parameters.

The proposed MDO project aims at the analyses of existing data of about 80 patients and 220 dynamic FDG PET scans using IRW and PMod. Moreover, the students will participate in ongoing research on non-small cell lung carcinoma using a more advanced PET/CT scanner for patients that have been selected for tumour resection at the department of surgery of RUNMC. Since the resected tumours are being analyzed with regard to pathology, additional information on tumour size and heterogeneity will be available serving as the “gold standard”.

In summary, the technical medicine questions of the MDO project are the following:

- To what extent are the resulting tumour parameters influenced by the choice of software package used for pharmacokinetic modelling?
- What are the critical choices with regard to e.g. starting values, choice of time framing, delay of tumour signal with respect to plasma curve, etc. influencing the resulting tumour parameters?

Remarks

- Although pharmacokinetic modeling is based on differential equations describing the transport and metabolism in an FDG compartment model, it is not required that the students fully understand the details of the mathematics involved.
- Since the proposed analyses are new and not yet available in the nuclear medicine literature, the students are encouraged to write or prepare a scientific paper dealing with the outcome of their project.
- Further information about dynamic FDG-PET research at nuclear medicine RUNMC can be found in references [1-5].

References

1. de Geus-Oei LF, van der Heijden HF, Visser EP, Hermsen R, van Hoorn BA, Timmer-Bonte JN, et al. Chemotherapy response evaluation with 18F-FDG PET in patients with non-small cell lung cancer. J Nucl Med. 2007;48:1592-8.
2. de Geus-Oei LF, van Laarhoven HW, Visser EP, Hermsen R, van Hoorn BA, Kamm YJ, et al. Chemotherapy response evaluation with FDG-PET in patients with colorectal cancer. Ann Oncol. 2008;19:348-52.
3. de Geus-Oei LF, Visser EP, Krabbe PF, van Hoorn BA, Koenders EB, Willemsen AT, et al. Comparison of image-derived and arterial input functions for estimating the rate of glucose metabolism in therapy-monitoring 18F-FDG PET studies. J Nucl Med. 2006;47:945-9.
4. Visser EP, Kienhorst LBE, de Geus-Oei L-F, Oyen WJG. Shortened dynamic FDG-PET protocol to determine the glucose metabolic rate in non-small cell lung carcinoma. Nuclear Science Symposium Conference Record, 2008 NSS '08 IEEE; 2008. p. 4455-8.
5. Visser EP, Philippens ME, Kienhorst L, Kaanders JH, Corstens FH, de Geus-Oei LF, et al. Comparison of tumor volumes derived from glucose metabolic rate maps and SUV maps in dynamic 18F-FDG PET. J Nucl Med. 2008;49:892-8.
6. Dimitrakopoulou-Strauss A, Hoffmann M, Bergner R, Uppenkamp M, Eisenhut M, Pan L, et al. Prediction of short-term survival in patients with advanced nonsmall cell lung cancer following chemotherapy based on 2-deoxy-2-[F-18]fluoro-D-glucose-positron emission tomography: a feasibility study. Mol Imaging Biol. 2007;9:308-17.
7. Dimitrakopoulou-Strauss A, Hoffmann M, Bergner R, Uppenkamp M, Haberkorn U, Strauss LG. Prediction of progression-free survival in patients with multiple myeloma following anthracycline-based chemotherapy based on dynamic FDG-PET. Clin Nucl Med. 2009;34:576-84.
8. Strauss LG, Klippel S, Pan L, Schonleben K, Haberkorn U, Dimitrakopoulou-Strauss A. Assessment of quantitative FDG PET data in primary colorectal tumours: which parameters are important with respect to tumour detection? Eur J Nucl Med Mol Imaging. 2007;34:868-77.