ERASMUS UNIVERSITEIT ROTTERDAM

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	*Division of Medical Physics, Erasmus MC Cancer Institute, The Netherlands*
Project Title:	*Daily online (re-)optimisation of radiation therapy*
Abstract:	*Development of an ultra-fast optimisation approach to solve large and complex problems within 1 minute. This is required to greatly improve cancer treatment by radiation therapy (radiotherapy).* Cancer is diagnosed yearly in around 12 million people worldwide. Radiotherapy is one of the three main treatment modalities. Prior to treatment, a patient-specific treatment plan is generated, based on medical images (Computer Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET)). The treatment plan defines treatment parameters like directions from which to irradiate the patient, intensity profiles, etc. Generation of a treatment plan is highly complex and involves mathematical optimisation. Generally, the treatment is delivered in several (up to 40) consecutive treatment days. An important limitation in current practice is that the patient's anatomy will generally differ from day to day, and from the pre-treatment imaging that served as the basis for generation of the treatment plan. As a result, the plan that was optimised for the pre-treatment anatomy will in general not be optimal for the daily treatments, which could result in a failure in curing the patient. In current clinical practice, tumours are treated with large margins to avoid these failures, but this will generally result in higher incidences of severe treatment-related morbidity (side effects) as large volumes of healthy tissues are irradiated to a high dose as well. Modern treatment units are equipped with in-room imaging, i.e. a CT-scan can be made daily with the patient on the treatment couch, awaiting for the daily treatmen fraction. The purpose of this project is to use the CT-scans for daily, very fast (re-)optimisation of the treatment plan, a procedure that is called adaptive radiotherapy (ART). The Erasmus MC is a front-runner in development of new approaches for radiotherapy treatment planning. We developed and clinically implemented a mathematical algorithm to fully automate treatment planning, i.e. without requiring manual interaction [1,2]. This is an important prerequisite for daily fast optimisations, as manual interaction is very time-consuming. Recently, we reduced the optimisation time by a factor of 12 by mathematically remodelling the multi-criteria optimisation problem [3]. Another technique in use is the

	plan-of-the-day approach, where the patient is treated with a plan from a database. This patient-specific database contains plans for different anatomical variations (determined by non-rigid image registration) [4,5]. Recently, our department purchased a robotic CyberKnife unit with an in-room diagnostic CT-scanner. It is believed that with this novel scanner with high quality images and the state-of-the-art treatment option of the CyberKnife, ART can be brought to a whole new level. In an on-going project, in-room diagnostic CT-scanners will also be installed in our future center for proton therapy. Your work will include the research, development, evaluation, and implementation of a suitable ultra-fast optimisation routine, capable of solving large multi-criteria problems. To reduce the complexity of the problem, practical warmstarting strategies may be required and need to be investigated. As the computed plan will be used directly for treatment, strict quality assurance is an essential element for succesful implementation. The work is embedded in a multi-disciplinary research group with radiation oncologists, mathematicians, (medical) physicists, computer scientists and imaging scientists. [1] Breedveld S, Storchi P, Voet P, Heijmen B *(2012)* **iCycle: Integrated, multicriterial beam angle, and profile optimization for generation of coplanar and noncoplanar IMRT plans** *Med Phys* **39** 951-963 (DOI: 10.1118/1.3676689) [2] Voet P, Dirkx M, Breedveld S, Fransen D, Levendag P, Heijmen B *(2013)* **Toward Fully Automated Multicriterial Plan Generation: A Prospective Clinical Study** *Int J Radiat Oncol Biol Phys* **85** 866-72 (DOI: 10.1016/j.ijrobp.2012.04.015) [3] Heijmen B, van Haveren R, Voet P, Breedveld S *(2014)* **A fast lexicographic optimizer for fully automated multi-objective plan generation** *Radiother. Oncol.* **111** S165-S166 [4] Vásquez Osorio E, Hoogeman M, Bondar L, Levendag P, Heijmen B *(2009)* **A novel flexible framework with automatic feature correspondence optimization for nonrigid registration in radiotherapy** *Med Phys* **36** 2848-59 (DOI: 10.1118/1.3134242) [5] Heijkoop S, Langerak T, Quint S, Bondar L, Mens J, Heijmen B, Hoogeman M *(2014)* **Clinical Implementation of an Online Adaptive Plan-of-the-Day Protocol for Nonrigid Motion Management in Locally Advanced Cervical Cancer IMRT** *Int J Radiat Oncol Biol Phys* (DOI: 10.1016/j.ijrobp.2014.06.046)

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Requirements of candidate:	Background: *Mathematics, Operations Research, Optimisation, Multi-Criteria Optimisation, Numerical Mathematics, Computer Science.* *The area of expertise is clearly oriented around mathematical optimisation. Considering the complexity of the problem, you should also be able to invent practical approaches for the problem.* Master degree: Yes IELTS Grade: 7.0 *(minimal 6.0 per component)* *or* TOEFL: *100 (minimal 20 per component)*
Supervisor information:	*Prof. dr. B.J.M. Heijmen* *b.heijmen@erasmusmc.nl* *Co-supervision by:* *Dr. S. Breedveld* *s.breedveld@erasmusmc.nl* *Websites:* *http://www.erasmusmc.nl/radiotherapie/research/radiationoncologymedicalphysicsandimaging/* *http://sebastiaanbreedveld.nl/*

Top-list of peer-review publications by Prof. dr. B.J.M. Heijmen (153 in total)

1. **Bondar L, Velema L, Mens JW, Zwijnenburg E, Heijmen B, Hoogeman M**
   Repeat CT-scan assessment of lymph node motion in locally advanced cervical cancer patients. Strahlenther Onkol. 2014 Aug 27. [Epub ahead of print]
2. **Heijkoop S, Langerak T, Quint S, Bondar L, Mens J, Heijmen B, Hoogeman M**
   Clinical Implementation of an Online Adaptive Plan-of-the-Day Protocol for Nonrigid Motion Management in Locally Advanced Cervical Cancer IMRT. Int J Radiat Oncol Biol Phys. 2014 Aug 20. pii: S0360-3016(14)03421-X. doi: 10.1016/j.ijrobp.2014.06.046. [Epub ahead of print]
3. **Van de Water S, Valli L, Aluwini S, Lanconelli N, Heijmen B, Hoogeman M**
   Intrafraction prostate translations and rotations during hypofractionated robotic radiation surgery: dosimetric impact of correction strategies and margins. Int J Radiat Oncol Biol Phys. 2014; 88(5): 1154-60.
4. **Voet P, Dirkx M, Breedveld S, Al-Mamgani A, Incrocci L, Heijmen B**
   Fully Automated Volumetric Modulated Arc Therapy Plan Generation for Prostate Cancer Patients. Int J Radiat Oncol Biol Phys. 2014; 88(5):1175-9
5. **Budiarto E, Keijzer M, Storchi P, Heemink A, Breedveld S, Heijmen B**
   Computation of mean and variance of the radiotherapy dose for PCA-modeled random shape and position variations of the target. Phys Med Biol. 2013; 59(2): 289-310.
6. **Thörnqvist S, Hysing L, Zolnay A, Söhn M, Hoogeman M, Muren L, Bentzen L, Heijmen B**
   Treatment simulations with a statistical deformable motion model to evaluate margins for multiple targets in radiotherapy for high-risk prostate cancer. Radiother Oncol. 2013 Oct 31. doi:pii: S0167-8140(13)00474-X. 10.1016/j.radonc.2013.09.012. [Epub ahead of print]
7. **Kraan A, van de Water S, Teguh D, Al-Mamgani A, Madden T, Kooy H, Heijmen B, Hoogeman M**

Dose Uncertainties in IMPT for Oropharyngeal Cancer in the Presence of Anatomical, Range, and Setup Errors. Int J Radiat Oncol Biol Phys. 2013; 87(5): 888-96.

8. **Leinders S, Breedveld S, Romero A, Schaart D, Seppenwoolde Y, Heijmen B**
Adaptive Liver Stereotactic Body Radiation Therapy: Automated Daily Plan Reoptimization Prevents Dose Delivery Degradation Caused by Anatomy Deformations. Int J Radiat Oncol Biol Phys. 2013; 87(5): 1016-21.
9. **Van de Water S, Kraan A, Breedveld S, Schillemans W, Teguh D, Kooy H, Madden T, Heijmen B, Hoogeman M**
Improved efficiency of multi-criteria IMPT treatment planning using iterative resampling of randomly placed pencil beams. Phys Med Biol. 2013; 58(19): 6969-6983.
10. **Ali A, Dirkx M, Cools R, Heijmen B**
Accurate IMRT fluence verification for prostate cancer patients using 'in-vivo' measured EPID images and in-room acquired kilovoltage cone-beam CT scans. Radiat Oncol. 2013; 8(1): 211.
11. **Gangsaas A, Astreinidou E, Quint S, Levendag P, Heijmen B**
Cone-beam computed tomography-guided positioning of laryngeal cancer patients with large interfraction time trends in setup and nonrigid anatomy variations. Int J Radiat Oncol Biol Phys. 2013; 87(2): 401-6.
12. **Thörnqvist S, Hysing L, Zolnay A, Söhn M, Hoogeman M, Muren L, Heijmen B**
Adaptive radiotherapy in locally advanced prostate cancer using a statistical deformable motion model. Acta Oncol. 2013; 52(7):1423-9.
13. **Ahmad R, Bondar L, Voet P, Mens J, Quint S, Dhawtal G, Heijmen B, Hoogeman M**
A margin-of-the-day online adaptive intensity-modulated radiotherapy strategy for cervical cancer provides superior treatment accuracy compared to clinically recommended margins: A dosimetric evaluation. Acta Oncol. 2013; 52(7): 1430-6.
14. **Osman S, Astreinidou E, Levendag P, Heijmen B**
Impact of geometric variations on delivered dose in highly focused single vocal cord IMRT. Acta Oncol. 2014; 53(2): 278-85.
15. **Bondar M, Hoogeman M, Schillemans W, Heijmen B**
Intra-patient semi-automated segmentation of the cervix-uterus in CT-images for adaptive radiotherapy of cervical cancer. Phys Med Biol. 2013; 58(15): 5317-5332.
16. **Wang Y, Zolnay A, Incrocci L, Joosten H, McNutt T, Heijmen B, Petit S**
A quality control model that uses PTV-rectal distances to predict the lowest achievable rectum dose, improves IMRT planning for patients with prostate cancer. Radiother Oncol. 2013; 107(3): 352-7.
17. **Voet P, Dirkx M, Breedveld S, Heijmen B**
Automated generation of IMRT treatment plans for prostate cancer patients with metal hip prostheses: Comparison of different planning strategies. Med Phys. 2013 Jul;40(7):071704. doi: 10.1118/1.4808117.
18. **Voet P, Dirkx M, Breedveld S, Fransen D, Levendag P, Heijmen B**
Toward Fully Automated Multicriterial Plan Generation: A Prospective Clinical Study. Int J Radiat Oncol Biol Phys. 2013; 85(3): 866-72.
19. **Bondar M, Hoogeman M, Mens J, Quint S, Ahmad R, Dhawtal G, Heijmen B**
Individualized nonadaptive and online-adaptive intensity-modulated radiotherapy treatment strategies for cervical cancer patients based on pretreatment acquired variable bladder filling computed tomography scans. Int J Radiat Oncol Biol Phys. 2012; 83(5):1617-23.
20. **Voet P, Breedveld S, Dirkx M, Levendag P, Heijmen B**
Integrated multicriterial optimization of beam angles and intensity profiles for coplanar and noncoplanar head and neck IMRT and implications for VMAT. Med Phys. 2012; 39(8): 4858-65.
21. **Rossi L, Breedveld S, Heijmen B, Voet P, Lanconelli N, Aluwini S**
On the beam direction search space in computerized non-coplanar beam angle optimization for IMRT-prostate SBRT. Phys Med Biol. 2012; 57(17): 5441-5458.
22. **Ahmad R, Hoogeman M, Quint S, Mens J, Vásquez Osorio E, Heijmen B**
Residual setup errors caused by rotation and non-rigid motion in prone-treated cervical cancer patients after online CBCT image-guidance. Radiother Oncol. 2012; 103(3): 322-6
23. **Vásquez Osorio E, Hoogeman M, Méndez Romero A, Wielopolski P, Zolnay A, Heijmen BJ**
Accurate CT/MR vessel-guided nonrigid registration of largely deformed livers. Med Phys. 2012; 39(5):2463-2477.
24. **Eriksen J, Beavis A, Coffey M, Leer J, Magrini S, Benstead K, Boelling T, Hjälm-Eriksson M, Kantor G, Maciejewski B, Mezeckis M, Oliveira A, Thirion P, Vitek P, Olsen D, Eudaldo T, Enghardt W, François P, Garibaldi C, Heijmen B, Josipovic M, Major T, Nikoletopoulos S, Rijnders A, Waligorski M, Wasilewska-Radwanska M, Mullaney L, Boejen A, Vaandering A, Vandevelde G, Verfaillie C, Pötter R**
The updated ESTRO core curricula 2011 for clinicians, medical physicists and RTTs in radiotherapy/radiation oncology. Radiother Oncol. 2012; 103(1): 103-108.
25. **Mutanga T, de Boer H, Rajan V, Dirkx M, van Os M, Incrocci L, Heijmen B**
Software-controlled, highly automated intrafraction prostate motion correction with intrafraction stereographic targeting: System description and clinical results. Med Phys. 2012; 39(3): 1314-21.
26. **Breedveld S, Storchi P, Voet P, Heijmen B**
iCycle: Integrated, multicriterial beam angle, and profile optimization for generation of coplanar and noncoplanar IMRT plans. Med Phys. 2012; 39(2): 951-963.

27. **Mutanga T, de Boer H, Rajan V, Dirkx M, Incrocci L, Heijmen B**
Day-to-Day Reproducibility of Prostate Intrafraction Motion Assessed by Multiple kV and MV Imaging of Implanted Markers During Treatment. Int J Radiat Oncol Biol Phys. 2012; 83(1): 400-7.
28. **Bondar L, Hoogeman M, Mens J, Dhawtal G, de Pree I, Ahmad R, Quint S, Heijmen B**
Toward an individualized target motion management for IMRT of cervical cancer based on model-predicted cervix-uterus shape and position. Radiother Oncol. 2011 May; 99(2): 240-5.
29. **Seppenwoolde Y, Wunderink W, Veen S, Storchi P, Méndez Romero A, Heijmen B**
Treatment precision of image-guided liver SBRT using implanted fiducial markers depends on marker-tumour distance. Phys Med Biol. 2011; 56(17): 5445-5468.
30. **Levendag P, Teguh D, Keskin-Cambay F, Al-Mamgani A, Rooij P, Astreinidou E, Kwa S, Heijmen B, Monserez D, Osman S**
Single vocal cord irradiation: A competitive treatment strategy in early glottic cancer. Radiother Oncol. 2011

(and 123 more publications ...)

Other publications

1. **Development of Procedures for In Vivo Dosimetry in Radiotherapy - IAEA Human Health Report No. 8.** (Contributor to drafting and reviewing)
2. **Heijmen B, de Lange M**
Implantable tumor markers for guidance of radiation therapy and multi-modality image registration. Chapter 12 in Contouring in Head&Neck Cancer, 2009, eds. Peter Levendag, Abrahim Al-Mamgani, David Teguh; Elsevier Professional Education, Munich.
3. **Levendag P, Teguh D, Heijmen B**
Oropharynx, Chapter 42 in Principles and Practice of Radiation Oncology, fifth edition, 2007; eds. Halperin EC, Perez CA and Brady LW; Wolters Kluwer|Lippincott Williams & Wilkins.
4. **Reynaert N, Van der Marck S, Schaart D, van der Zee W, Tomsej M, Van Vliet C, Jansen J, Coghe M, De Wagter C, Heijmen B**
Monte Carlo Treatment Planning: An Introduction, (Report 16 of the Netherlands Commission on radiation dosimetry) ISBN 90-78522-01-1, 2006
5. **Heijmen B, de Boer J, Levendag P**
"Current developments in electronic portal imaging"; chapter in: Mould RF (Ed) Progress in CT-3D Simulation 2003:133-141. Medical Innovative Technology GmbH, Bochum, Germany, ISBN: 3-00-011938-8