Major contributions to science

My research is focused on radiotherapy treatment planning and addresses 3 main problems:

1. Development of the mathematical optimization algorithms for radiotherapy planning, i.e. further development of radiotherapy treatment planning systems.
2. Determining how radiation should be delivered over time. This includes the fractionation scheme, but also scheduling and combining radiation with other therapies.
3. Identifying the region to be irradiated based on biomedical imaging and models of microscopic progression of tumors, i.e. target volume delineation and dose prescription.

1. Treatment plan optimization for IMRT and IMPT

Throughout my career, I have been working on the improvement of radiotherapy treatment planning systems, in particular the development of Intensity-modulated radiation therapy with high energy X-rays (IMRT) and Protons (IMPT). The focus has been on the development of new mathematical optimization algorithms. This area of research has a strong translational aspect: Through collaboration with industry partners (Philips Healthcare), research results are integrated into commercial treatment planning systems and are made available for clinical use. In addition, the work is integrated into the in-house proton planning system that is used and developed at Massachusetts General Hospital. Over the years, I have been working on a variety of topics on treatment plan optimization including direct aperture optimization (DAO), volumetric-modulated arc therapy (VMAT), and multi-criteria optimization (MCO). I am frequently invited to give presentations or write book chapters on this topic, e.g. for the widely used text book edited by Faiz Khan.

J. Unkelbach. Intensity-modulated radiation therapy: Photons. in F. Khan et al (editors), Treatment Planning in Radiation Oncology, 4th edition (Chapter 10), Wolters Kluwer, 2016

The main contribution to the field during the initial years of my career relates to the handling of uncertainties in treatment planning. During therapy, numerous errors may occur: Such errors include incorrect positioning of the patient during irradiation, organ movements, and an incorrect patient model due to imaging artifacts. Such errors may severely degrade the quality of radiotherapy treatment plans, especially in proton radiotherapy. My research aims at improving error handling in radiotherapy by directly incorporating uncertainty into the optimization of IMRT and IMPT treatment plans. This can be achieved via robust und stochastic programming techniques. In collaboration with industry partners, this research is now implemented into the first commercial treatment planning systems. The following publication on this topic has received 180 citations by June 2018.

J. Unkelbach, B. Martin, M. Soukup, and T. Bortfeld. Reducing the sensitivity of IMPT treatment plans to setup errors and range uncertainties via probabilistic treatment planning. Med.Phys. 2009;36:149-163

2. Fractionation and optimizing radiotherapy over time

My second area of research is the optimization of radiotherapy treatments over time. This includes the problem of fractionation and the development of treatment schedules that optimally exploit fractionation effects in tumors and normal tissues. An innovative contribution to this field is the concept of spatiotemporal fractionation. This work demonstrated that there can be an advantage of dilivering distinct dose distributions in different fractions. This chalenges the century-old paradigm that each fraction delivers the same dose. The main publications are:

J. Unkelbach, D. Papp, Gaddy MR, Andratschke N, Hong T, Guckenberger M. Spatiotemporal fractionation schemes for liver stereotactic body radiotherapy. Radiother Oncol. 2017 Nov;125(2):357-364

J. Unkelbach, M. Bussière, P. Chapman, J. Loeffler, H. Shih. Spatiotemporal Fractionation Schemes for Irradiating Large Cerebral Arteriovenous Malformations. Int. J. Rad. Onc. Biol. Phys., 2016;95(3):1067-1074

J. Unkelbach, D. Papp. The emergence of nonuniform spatiotemporal fractionation schemes within the standard BED model. Med. Phys., 2015;42:2234-2241

This work also received a conference award at the AAPM annual meeting in 2013.

J. Unkelbach, C. Zeng, M. Engelsman. The Emergence of Nonuniform Spatiotemporal Fractionation Schemes within the Standard BED Model. Med Phys 2013;40(6):551-551.

3. Target delineation and dose prescription

Research in medical physics has refined the technical precision of treatment planning and delivery to a high level of sophistication. However, quantitative methods to determine the biological target volume and optimal dose distribution often lag behind. Improvements to tumor delineation require an interdisciplinary approach that involves imaging, statistical analysis of clinical data, and mathematical modeling. In particular, the integration of advanced imaging modalities in radiotherapy treatment planning bears potential. This includes positron emission tomography (PET) to measure the metabolic activity of tumors, as well as advanced magnetic resonance imaging (MRI) to measure physiological properties of tumors, such as blood perfusion. Such an interdisciplinary approach has been pursued for a project on tumor growth modeling for gliomas, the most common primary brain tumor. Gliomas are known to infiltrate the brain parenchyma far beyond the tumor mass visible on current imaging modalities, which represents a challenge for radiotherapy planning. Phenomenological tumor growth models can be used to assess the microscopic infiltrative spread of tumor cells while accounting for the observed anisotropic growth patterns of these tumors. Medical image processing methods are used to personalize the tumor growth model to the brain anatomy of the patient at hand. Two important publications from this domain are:

J. Unkelbach, B. H. Menze, E. Konukoglu, F. Dittmann, M. Le, N. Ayache, and H. Shih. Radiotherapy planning for glioblastoma based on a tumor growth model: improving target volume delineation. Phys. Med. Biol. 2014; 59(3):747-770

J. Unkelbach, B. H. Menze, E. Konukoglu, F. Dittmann, N. Ayache, and H. Shih. Radiotherapy planning for glioblastoma based on a tumor growth model: implications for spatial dose redistribution. Phys. Med. Biol. 2014; 59(3):771-790