Visualization and quantification of tumour biology for personalized radiotherapy

Valorization addendum

Social relevance and target groups

Cancer is one of the leading causes of mortality and morbidity worldwide. For many cancer types, the survival remains poor despite substantial advances in treatment options. In this thesis, we examined the tumour biology with different functional imaging modalities. A better understanding of the tumour biology and the tumour characteristics related to treatment resistance could improve current treatment options and help the development of new therapies.

To achieve the best treatment results, it is crucial to select the treatment with the highest expected benefit as quick as possible. Therapy could be adapted based on the patient prognosis. For example, treatment could be intensified in patients with poor prognosis, while in patients with a good prognosis, de-escalation of therapy dose could be considered. We used biomarkers derived from several functional imaging modalities to stratify patients based on their expected prognosis and to evaluate the expected treatment benefit. We showed that functional imaging could be used to redistribute the dose in the tumour and sculpt the dose for a specific case to better target the most resistant areas.

The ultimate aim of treatment personalization is to include the preference of the patient in the treatment decision; to balance increasing local tumour control and limiting toxicities to the surrounding healthy tissues based on the patient preference. Personalization will first of all affect the patient, their family, and the physician. In addition, it will befit the general population since cancer is a worldwide health problem. Improving treatment options will economically benefit the whole society.

Activities and products

A subset of the images acquired for the research presented in this thesis is publicly available (www.cancerdata.org). ^{89}Zr-cetuximab PET/CT images of head and neck cancer patients, and HX4 PET/CT and FDG PET/CT images of non-small cell lung cancer patients are provided. The treatment plans generated for the planning study of Chapter 5 are also available on the same website. Researchers and other interested parties are free to reuse the images for their own research questions.

The methodologies used in Chapter 6 en Chapter 7 are largely based on open-source software. The performed image registration, the generation of the supervoxels, and the clustering of the supervoxels were all performed using freely available software. The methodology described in these chapters to combine multiparamteric images can easily be implemented and reused in other projects.

Functional imaging could have an important role in the further development of prediction models. Prediction models are being developed to support physicians in clinical decision-making. With the vast amount of information available for every

patient, it becomes increasingly difficult for a physician to consider and incorporate all this information. Prediction models can combine data of multiple sources to predict patient prognosis. Some examples from the Maastro clinic research group are already available on www.predictcancer.org. Functional imaging, e.g. HX4 PET/CT imaging, has the potential to further improve these models and better support the physicians. Eventually, these prediction models could be integrated in decision support systems to help the patient in selecting a personalized treatment.

Innovation

Although the research presented in this thesis is based on a limited number of patients, the data sets are unique and difficult to acquire. To our knowledge, there is only one other clinical trial using ^{89}Zr-cetuximab PET images. In that trial, ten patients with advanced colorectal cancer were included. Our studies are the first to visualize and quantify ^{89}Zr-cetuximab PET uptake in head and neck cancer patients.

The combination of multiple functional images, as presented in Chapter 6 and Chapter 7, provides a unique insight in multiple tumour characteristics at the same time. With the increasing amount of data available, analysis methods are required that can manage multiple scans and can combine the knowledge. In Chapter 7 we provided an example of such a workflow.

In Chapter 4, we showed the prognostic value of hypoxia HX4 PET/CT imaging in non-small cell lung cancer. Although hypoxia PET imaging has shown to be prognostic before in several tumour types, this is the first study that shows the prognostic value of the novel hypoxia PET tracer HX4.

Schedule and implementation

The benefit of boosting specific radioresistant parts of the tumour is still under clinical evaluation. Maastro clinic is participating in a prospective phase II trial in non-small cell lung cancer (NCT01024829). Several other studies are ongoing, as discussed in the general discussion of this thesis. The results of these clinical trials will give more insight into the potential of such a strategy.

The prognostic value of the hypoxia PET marker HX4, needs to be further validated in a larger patient cohort. After validation, it can be implemented in prediction models. The prediction of hypoxia based on other imaging modalities (CT, FDG PET and DCE-CT) as presented in Chapter 6, could serve as a an alternative to hypoxia PET that is easier to implement in a clinical workflow.

Combining multiple imaging data sets will become proportionally important with the increasing amount of data available. The workflows presented in this thesis are based on several open-source packages and could be directly applied to other data.