

## Hand-crafted and deep radiomics for the management of advanced cancer stages

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Impact statement

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Ouantitative image analysis through artificial intelligence (AI) has made great leaps in the past years, both through the development of machine learning (ML) methods using semantic and handcrafted (radiomics) features extracted from images, and through direct application of deep learning (DL) algorithms on images. While the development of these models requires a lot of time, coordination, and resources, the final product could be a tool that seamlessly integrates in the current clinical routine without adding workload. Ideally, when a patient enters the clinic and receives a scan, an automatic algorithm would (possibly after automatically delineating any regions of interest) analyze the image and combine this with other patient information in a prediction of any relevant clinical outcome. This is therefore not a tool that would replace a clinician, but rather augment them by condensing the available imaging, clinical, biological, and other information in a single understandable metric. In this thesis, we have contributed to this goal by attempting to solve relevant unmet clinical needs with routine imaging data. Several types of cancers were investigated for the predictive value of radiomics and DL in predicting future events and their complementary value to existing predictors, using large, multi-center datasets to create generalizable models.

All the studies included in this thesis are published in peer-reviewed open-access journals (Cancers, Frontiers in Oncology, Therapeutic advancements in oncology, British journal of radiology, PLOS ONE), and contribute to the field of science, specifically to precision medicine and cancer therapy because of a number of varying reasons. The study in chapter 2 provides an introduction to radiomics and the overview of the current radiomics as a scientific field. The studies in chapter 3 and 4 showed both a positive and negative result in predicting survival and tumor recurrence outcomes for patients with head and neck squamous cell carcinoma. This contrast in results highlights the downsides of radiomics, among others the need for high quality and high volume data to make effective models, and the existing problems in generalizability and reproducibility, and may serve as guidelines for future research. The study in chapter 5 shows that radiomics, while being able to predict development of brain metastases for patients with non-small cell lung cancer, could not outperform models based on clinical predictors. This emphasizes the relevance of existing data that radiomics does not seek to replace, but rather complement existing predictors built on clinical findings. The study in chapter 6 was a study on a large scale dataset of patients with brain metastasis to predict risk of radiation necrosis. In this study we thoroughly investigated pre-processing of MRI data, and the complementary value DL and radiomics have for prediction studies. Lastly, the study in chapter 7 was a study into slice spacing, which is one of the largest causes of guality discrepancy between images. A DL model to interpolate CT images can potentially address this by increasing the number of slices. In these studies, we have shown the potential of radiomics to be complementary to other clinical predictors, but also the need for future research mainly in the generalizability of the features from different scanners or different imaging protocols. We further think the next step for radiomics would be the inclusion in multi-center clinical trials, where control over the imaging parameters and inclusion of phantom scans could properly test the feasibility and generalizability of the developed models.

The results presented further have a number of (potential) societal impacts. We believe that radiomics, through the identification of tumor and patient subtypes, can play an important role in the realization of personalized medicine, instead of the current broader staging systems used based on clinical information. The risk stratification models presented would further allow for better informing of patients of their chance of survival or risk of side effects, and would allow for better selection of patients that are eligible for clinical trials. In addition, radiomics can be integrated clinically to perform, in an automated fashion, highly specific tasks done by a clinician now. This would lower clinicians' workloads, would save on time and money by using a machine that could do tasks in a fraction of the time a human could, and reduce the variability between doctors and clinics in performing these tasks. Lastly, radiomics would not replace clinicians by doing these tasks, but instead augment them, transforming the current clinician in an "Al-enhanced" clinician which would be better equipped to face the increasing workload in hospitals.