

Artificial intelligence in rectal cancer

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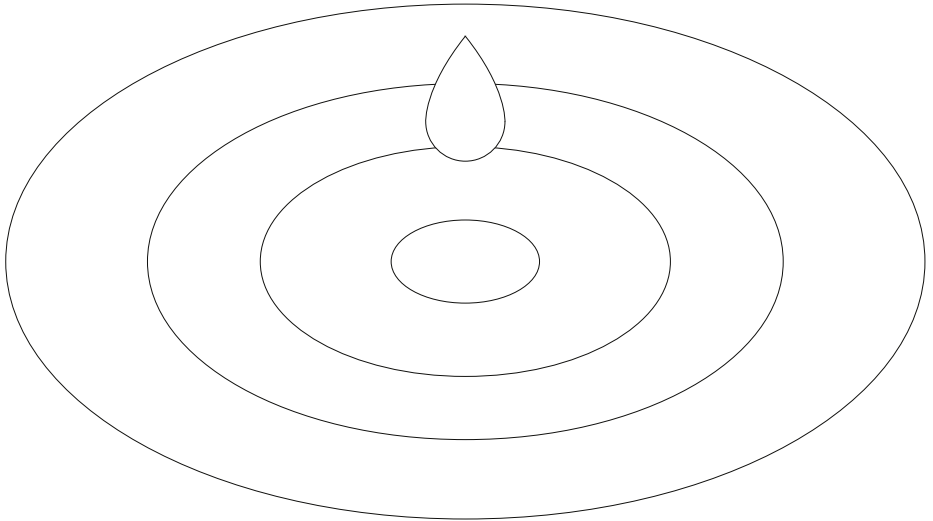
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Main aims and outcomes of this thesis

Medical imaging, such as Computed Tomography (CT), Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET), helps doctors to detect, stage and monitor tumors, which provides them with information that is crucial to help define the best possible treatment for each individual cancer patient. In current clinical practice, medical images are mainly assessed “qualitatively”, meaning that the images are assessed visually by trained radiologists, who report their findings in text reports. There are however also several ways to assess medical images quantitatively. Some simple quantitative tools are already being used in daily clinical practice, including for example size or signal intensity measurements. In recent years, the possibilities of quantitative medical imaging analysis have evolved tremendously. An important development in this field has been the introduction of radiomics. In radiomics, the phenotype of a target volume within a medical image (e.g., a cancer lesion on a CT or MRI scan) is captured through extraction of a large panel of “features”, calculated using advanced mathematical formulas. This allows for the extraction of much more information from the medical imaging than is visible by the “naked eye”¹. Using artificial intelligence (machine learning) computer methods, this information can be correlated to various clinical outcomes such as the response of a tumor to anti-cancer treatment. This way, the radiomics phenotype can be used to render imaging-biomarkers of disease that can be incorporated into clinical prediction models, which may ultimately act as decision-support tools to aid in further personalization of treatment for cancer patients.

In this thesis we addressed some of the key challenges in the radiomics workflow, using rectal cancer as a case example. Radiomics requires segmentation of the volume of interest within an image (e.g. a tumor lesion), which can be a very time consuming task requiring many hours of manual input from radiologists. The results in Chapters 2 and 3 show that fully-automatic segmentation of rectal tumors on MRI is feasible using artificial intelligence (AI) models, which can serve as a starting point and significantly reduce the amount of manual input required from radiologists. Another important prerequisite for successful radiomics analysis is the availability of good quality source images. Diffusion-weighted imaging (DWI) is nowadays an integral part of many oncologic MR imaging protocols and commonly used for quantitative MRI data analysis. In Chapter 4 we have shown that a simple intervention such as a preparatory micro-enema can help to greatly increase DWI scan quality. As shown in Chapter 3, this can contribute to improved performance of automatic segmentation protocols. A final challenge in the radiomics workflow is feature extraction, which is largely dependent on the mathematical formulas used and the implementation of these formulas in feature extraction software algorithms. In Chapter 5 we introduce *PyRadiomics*, an open-source toolkit for easy and reproducible feature extraction. It has been specifically developed for use in a community of radiomics researchers, aiming to increase the transparency and reproducibility of radiomics research by providing an easy go-to resource for feature extraction. In Chapter 6, we have put the radiomics workflow to the test in a clinical study and have shown that radiomics has potential to render valuable imaging biomarkers for pre-treatment prediction of response to neoadjuvant therapy in locally advanced rectal cancer.

Relevance

The results presented in this thesis may help future research in radiomics, paving the way on the road towards clinical implementation. The segmentation algorithms presented in Chapters 2 and 3 aim to automate the segmentation step of the radiomics workflow. Especially when combined with optimized acquisition protocols, these algorithms can act as support tools to greatly improve the efficiency and reduce the workload of image segmentation.

The *PyRadiomics* toolbox introduced in Chapter 5, with extensive documentation and publicly available source code, is aimed at widespread use by a global community of radiomics researchers. This removes the need for researchers to learn and implement radiomics features in custom-built code and contributes to increased reproducibility and comparability of published work. The success of *PyRadiomics* is reflected in its worldwide use – even serving as the radiomic feature extractor in several commercial products – and high number of citations for the paper² introducing this toolbox. Finally, results in Chapter 6 show the potential of radiomics for rendering valuable predictive biomarkers in rectal cancer. In future research, these may be incorporated into clinical prediction models, ultimately aiming to improve patient-tailored treatment planning and outcomes.

Target population

There are several groups who may benefit from the results presented in this thesis. The first are the researchers investigating the application of radiomics. Though this thesis is placed in the context of radiomics in rectal cancer, the workflow and challenges encountered – and the solutions offered in this thesis – can be generalized and applied to radiomics research in other oncological and non-oncological research fields.

Once properly validated in multicenter and prospective clinical studies, radiomics may aid healthcare professionals to build decision support models to better stratify patients, getting the right treatment to the right patient. However, before implementation into clinical workflows is feasible, the challenges described in the thesis need to be overcome.

Activities

The results presented in this thesis have been actively distributed, both through publication of results in peer-reviewed journals and presentation at multiple national and international conferences. The knowledge gained in this thesis is also currently being applied through new collaborations in follow-up research projects investigating radiomics and AI in rectal cancer as well as other tumor types. One such collaboration is an ongoing multicenter trial with participation of ten different centers in the Netherlands, including academic and oncology referral centers, but also several large teaching hospitals. This study aims to further build on the results acquired in chapter 6 by validating the predictive value of radiomics to predict rectal tumor response in a large multicenter dataset with large data heterogeneity, reflecting the regular clinical workflow.

The knowledge gained in this thesis is also incorporated into and distributed via the *PyRadiomics* platform. This is achieved through the public access and open-source nature of this toolbox, which is being used by a continuously growing community of researchers world-wide. *PyRadiomics* is now also part of the "Imaging Biomarker Standardization Initiative" (IBSI)³, which aims at standardization of radiomic feature extraction, regardless of software implementations.

Ultimately, biomarkers derived from medical imaging using radiomics and AI will most likely only be a part of the prediction. Like multidisciplinary tumor boards incorporating information from multiple aspects of healthcare, a combination of information derived from imaging as well as other clinical, histopathological and genetic sources will most likely result in higher performance than can be achieved with imaging data alone. To this end, collaboration between researchers of multiple disciplines is crucial to build the strongest possible clinical prediction models and decision-support tools that can really have an impact on patient management and ultimately treatment outcomes.

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