Quantitative imaging analysis

Summary

Medical imaging has the capacity to non invasively analyse the phenotypic differences of tumors in three dimensions, and lately it has seen significant improvements due to advancements in the field of artificial intelligence. For example, radiomics, or quantitative image analysis – the high-throughput extraction of quantitative features from medical images and their correlation with diagnostic and prognostic outcomes – has been studied in particular to decode tumor phenotypes from a variety of modalities, including CT, magnetic resonance imaging, and positron emission tomography (PET). Thousands of quantitative radiomic characteristics may be retrieved from each area of interest (ROI) and examined further using machine learning algorithms to look for connections with biological and clinical end objectives.

In this thesis, our objectives are; 1) to evaluate the reproducibility of radiomic features extracted from the same scanner, or from different scanners with different CT acquisition parameters ; 2) to explore how the power of AI can be harnessed for the classification between different ILDs, potentially overcoming some of the current difficulties in the decision-making surrounding lung diseases. The thesis is divided into four parts:

Part 1: General introduction and outline of the thesis.
Part 2: Challenges in handcrafted radiomics.
Part 3: Application of handcrafted radiomics and deep learning on lung disease.
Part 4: General discussion and future perspective of the thesis.

In part 1, **chapter 2** provides a literature review to assess the present state of play in handcrafted radiomics and deep learning. We presented a thorough overview and update on the rapidly increasing field of quantitative imaging research in this review, with an emphasis on the two arms “handcrafted radiomics and deep learning.” The chapter discusses some of its shortcomings as well as instances of developing clinical implementations that serve as stepping stones toward precision medicine.

In part 2, several studies have been conducted to investigate the potential of handcrafted radiomics (HRFs). Nonetheless, a number of barriers to clinical integration of radiomics signatures have been discovered. Numerous research studies have been published on the sensitivity of HRFs to inter-reader variability, test-retest, and variations in imagining parameters. In this thesis (**chapters 3-6**), we showed that HRFs are sensitive to imagine variations using phantom and patient reproducibility studies. In addition, we examined the use of different harmonization methods on reducing the effect of different variations in imagining parameters.

In chapters 3-6, we assess the reproducibility of HRFs to the variations in CT parameters and the role of harmonization methods to address those variations. **Chapter 3** investigated the robustness of HRFs on a dataset consisting of 13 phantom CT scans. The scans were obtained from different vendors, with different CT parameters. The study's findings indicated that only a small percentage of handcrafted (HRFs) radiomics were robust to differences in the imaging settings examined. We also found that the performance of ComBat harmonization depends on the variations in imaging parameters.

Chapter 4 assess the reproducibility of hepatocellular carcinoma (HCC) HRFs, generated from various phases of contrast-enhanced CT images (CECT). For this study, HCC patients' arterial and venous CT scans were made accessible. The finding of the presented study showed that, when no image settings were changed, a subset of HRFs were shown to be reproducible in both phases. Moreover, the application of ComBat harmonization increased the number of reproducible features by 1% across phases.

In chapter 5, we investigated the use of Reconstruction Kernel Normalization (RKN) and ComBat harmonization to improve the reproducibility of HRFs across scans acquired with different reconstruction kernels. A total of 28 phantom scans collected on five distinct scanners types were assessed. The HRFs were extracted from the original scans and scans that were harmonized using the RKN method. Moreover, ComBat harmonization method was applied on both set of HRFs. The finding of this study showed that the majority of HRFs were found to be sensitive to the variations in the reconstruction kernels. Furthermore, the use of both RKN and ComBat harmonization methods significantly increased the number of reproducible HRFs compared to HRFs extracted from original scans.

In chapter 6, we also investigated the impact of changes in the in-plane spatial resolution (IPR) on the reproducibility of HRFs extracted from phantom scans (n=14) while all other imaging parameters were the same. We also examine the impact of ComBat harmonization on HRFs. The finding of this study revealed that the reproducibly of HRFs depends on the degree of the variations in pixel spacing.

Part 3 in this thesis is related to the application of radiomics and deep learning in different lung disorders. **In chapter 7,** we presented a summary of the existing researches on the use of handcrafted radiomics in lung cancer diagnosis, treatment response, and prognosis. In addition, applying HRFs in chronic obstructive pulmonary disease (COPD) has not been extensively investigated yet. We show examples of the potential use of HRFs in the diagnosis, treatment, and follow-up of COPD and future direction.

In chapter 8, the approach of HRFs was studied in order to predict different interstitial lung diseases (ILDs). The data for this study came from one center and two databases. The study

comprised four groups: 1) IPF with UIP pattern on HRCT, 2) IPF with UIP pattern confirmed by surgical lung biopsy, 3) non-IPF ILDs with surgical lung biopsy confirming the absence of a UIP pattern, and 4) healthy lung patients. To summarize, we were able to show that radiomic characteristics generated from HRCT images may be utilized to differentiate between a normal state and ILDs, as well as between IPF with a UIP pattern and ILDs with no UIP pattern as confirmed by surgical biopsy. Furthermore, our study found a significant difference in tracheal volume between individuals with normal, IPF/UIP, and non-IPF ILDs. The trachea volume was shown to be larger in IPF participants compared to normal and non-IPF ILDs.

In chapter 9, the use of both HRFs and DL was explored in this thesis to differentiate between different lung disorders – namely, IPF, and non-IPF ILDs subjects. In addition, in order to interpret the performance of HRFs and DL, interpretability methods were used. We also made use of ensemble learning methods to improve the performance of both HRFs and DL. In silico clinical trials were also used to compare the performance of medical experts with AI. Our results showcased the utility of HRFs and DL algorithms as a tool to support clinical decisions.

Finally, in part 4 (chapter 10) we extensively discussed the results of this thesis and the future perspective of both HRFs and deep learning.

Overall, this thesis verified a number of hypotheses concerning the uses of handcrafted radiomics and deep learning in medical image analysis. For handcrafted radiomics, we assessed the robustness of handcrafted radiomics analyses, which will aid in the development of generalizable radiomics signatures, and provided unique quantitative methods to measure the reproducibility of HRFs among scans obtained differently. For deep learning, we evaluated and demonstrated the potential of automated algorithms to improve clinical decision making. More specifically, a deep learning algorithm was developed that performed very well and has the potential to be used in clinical settings.

List of publications

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