PhD in Bioengineering Final Defense

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PhD Marco Bologna

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PhD student:	**MARCO BOLOGNA – XXXII Cycle**
Thesis title:	MRI - Based radiomic analysis for rare tumors: optimization of a workflow for retrospective multicentric studies
Advisor:	**Prof. LUCA MAINARDI**

Abstract:

The main purpose of this thesis was the optimization of a workflow for the radiomic analysis of Magnetic Resonance Images (MRI) acquired with uncontrolled image acquisition protocols. The secondary aim was the application of the optimized workflow to build prognostic models for Overall Survival (OS) for Head and Neck Cancer (HNC) and Soft Tissue Sarcoma (STS), in order to show the feasibility of using radiomics in multi-centric and/or multi-protocol datasets. The first part of the work focused on a series of stability analyses per-formed using a virtual phantom (Brain Web). The aim of these studies was two-fold:
1) to evaluate the effect of image pre processing on the stability to imaging-related variability;
2) to select the features that are stable to such variations, in order to use them for the following analysis.
Intensity standardization, image denoising, voxel size resampling and bias field correction were considered as potentially useful pre processing steps. Intra-class Correlation Coefficient (ICC) was used to quantify features stability and features with ICC>0.75 were considered stable. All the pre processing steps (Gaussian filtering, N4ITK Bias field correction, B-spline spatial re-sampling and intensity standardization) had positive effects in increasing the stability of radiomic features. When including all the previous pre-processing step, 550 features, based on both T1-weighted (T1w) and T2-weighted (T2w) MRI were identified as stable, out of a total of 1072 (536per image type).Stability to uncertainties of the region of interest (ROI) was also investigated. Two sources of variability were considered: multiple segmentation and geometrical transformations of the ROI. Both tests were performed on real images of STS and HNC, considering T1w, T2w and apparent diffusion coefficient maps (ADC). In each test, features with ICC>0.75 were considered stable. In total, 701 and 1057 features out of 1608 were stable for HNC and STS respectively. After properly combining these stable features sets with the results previously obtained on the Brain Web dataset, the number of stable features was reduced to 410 and 617. These two sets of features were used for successive studies. The post processing of the features was also optimized. In particular, features normalization and feature selection/dimensionality reduction were optimized in order to maximize the performance of a Cox proportional hazard regression model. Four different features normalization algorithms and2 different features selection pipelines were tested. Harrell's C-index was used to quantify the models performance. It was found that the combination of Z-score normalization and a series of different features selection (pairwise correlation and cross-validated Multivariate-Cox) lead to the best performance in a retrospective multi-centric HNC dataset (C-index 0.67).After the optimization based on the results of the previous analyses, the radiomic workflow was used to identify signatures that were prognostic of OS in HNC and STS. In HNC, a five-feature radiomic signature had a good prognostic value in both cross-validation (C-index 0.67) and independent validation (C-index 0.63) and in both cases, the radiomic features improved the prognosis when added to the clinical ones (from 0.67 to 0.69 and from 0.69 to 0.72 for the cross-validation and independent validation respectively). Similar results were found after cross-validation of a radiomic model in STS (C-index 0.74, 0.74 and 0.78 for the radiomic, clinical and combined model).The results show that with the right processing, radiomic analysis from non-standardized images is possible and provides consistent improvements in the prognostic performance of survival model for OS

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