Medical imaging based biomarker to predict overall survival of lung cancer patients

Diem Vuong[1], et. al.

[1]*Department of Radiation Oncology, University Hospital Zurich, University of Zurich, Switzerland*

Background

Radiomics refers to the process of extracting a large number of quantitative imaging features that describes the intra-tumoral heterogeneity non-invasively using medical images. These features can be used to perform prognostic outcome modelling (Fig. 1).

Radiomics models are often based on single institution data. **Multi-centric** datasets reflect better the clinical reality, however they are highly heterogeneous in scanner and acquisition settings. Unstable features cannot be used for prognostic modelling.

Robustness studies are crucial to find features independent from e.g. scanner settings.

Aim: Comparison of model performance of CT radiomic overall survival (OS) model trained on multi-centric data with prior robust feature selection to a model on standardized data.

Materials and Methods

Imaging Data: Pre-treatment CT data from 121 stage IIIA/N2 NSCLC patients from a prospective Swiss multi-centric randomized trial (SAKK 16/00, neoadj. chemo- or radiochemotherapy prior to surgery).

Radiomic Features from primary tumor:

- shape (n=18)
- intensity (n=17)
- texture (n=137)
- wavelet features (n=1232)

Robustness Studies:

- Four robustness studies: contrast, convolution kernel, motion, interobserver variability (Fig. 2)
- Stability measure: intra-class correlation coefficient (> 0.9 considered stable)

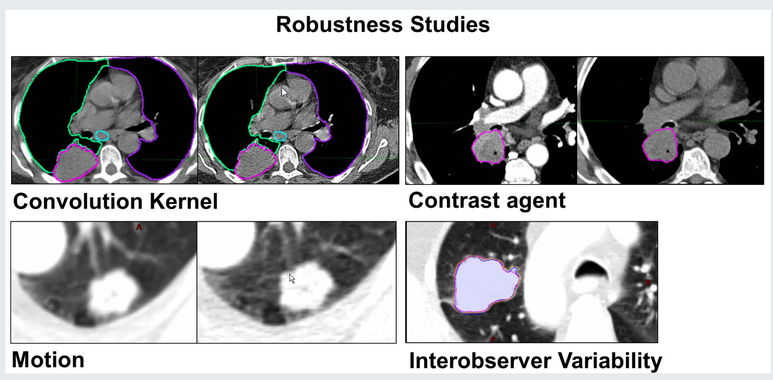

Fig. 2: Examplary CT scans shown for each robustness studies. Convoluton Kernel: Standard and Lung kernel. Motion: exhale of a 4D CT acquisition (most respiratory stable phase) with averaged CT scan. Contrast: contrast and non-contrast enhanced CT. Interobserver variability: Delineation variability between different delineators.

Models: Two OS radiomic models are developed as illustrated in Figure 3.

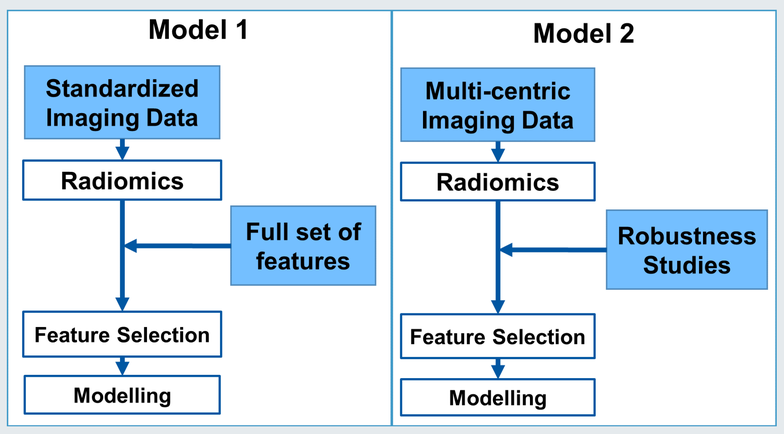

Fig. 3: Scheme of the two OS models.
Model 1: a patient sub-cohort characterized by a standardized imaging protocol (native CT, standard kernel, n = 84) is used. All radiomic features are used for the modelling.
Model 2: The entire heterogeneous patient cohort (n=121) is included but only pre-selection of robust radiomic features determined from the robustness studies are used for the modelling.

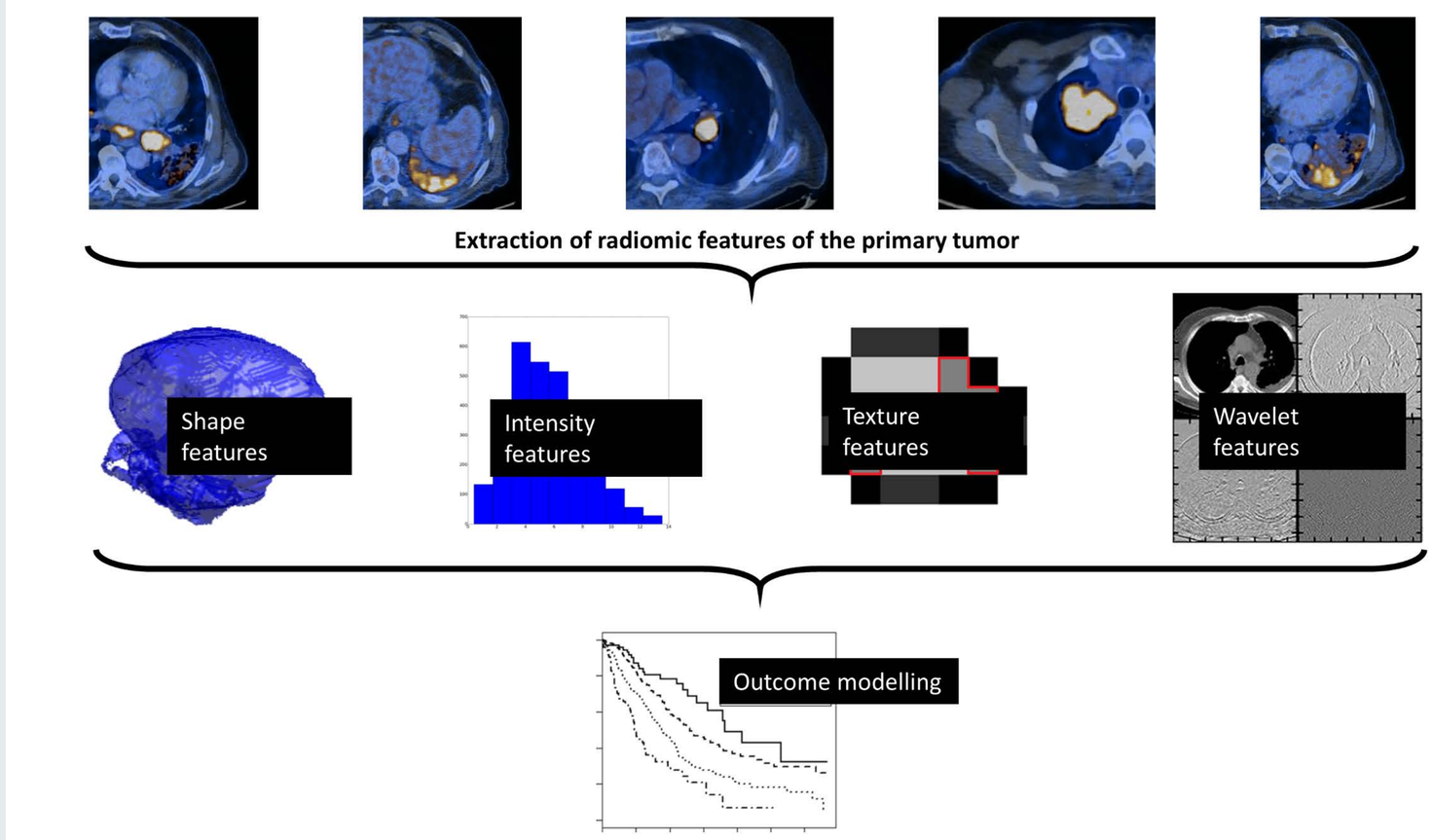

Fig. 1: Workflow of Radiomic based modelling used in this study. Primary tumors are manually delineated on the pre-treatment CT. In total, 1404 radiomic features are extracted from the delineated ROI. These features can be categorized in shape, intensity, texture and wavelet features. These features are then used to build the outcome model.

Model Development:

- Feature Selection: Principal Components Analysis
- Multivariate Cox Regression with backward selection.
- Validation: 10-fold cross-validation
- Performance measure: Concordance Index (CI)
- Performance comparison: bootstrap with resampling

First Results

Robustness of radiomic features

- 113 stable features among the four feature types, i.e. shape (n=8), intensity (n=0), texture (n=7) and wavelet (n=98).
- Convolution kernel was the largest influence on the robustness of the radiomic features (Fig. 4).

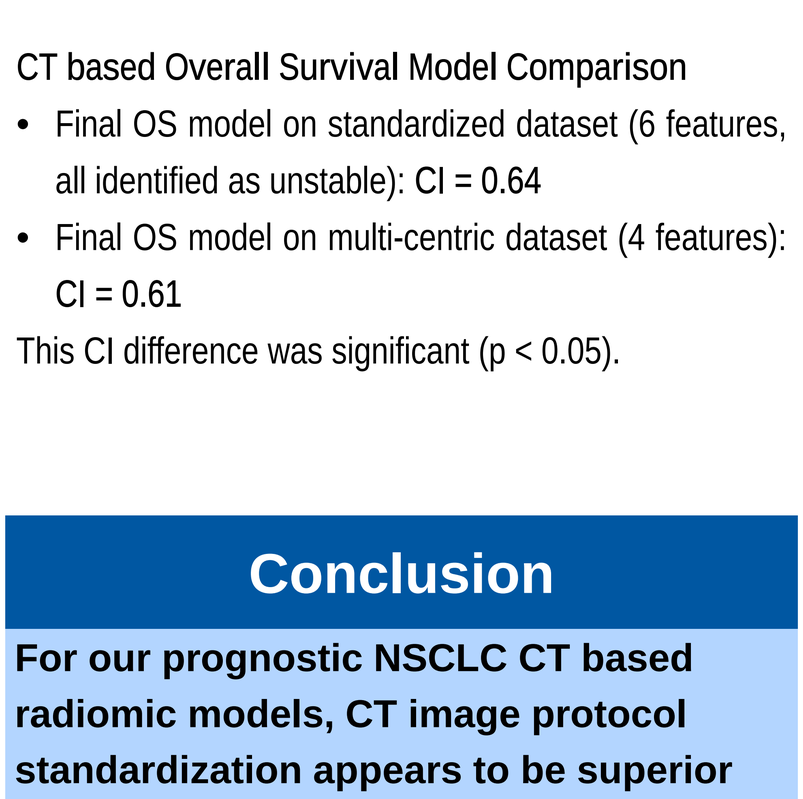

Fig. 4: Percentage of stable features among the four feature types shape, intensity, texture and wavelet for the four distinct robustness studies, i.e. interobserver delineation variability (IOV), contrast agent, reconstruction convolution kernel and respiratory motion. Highest stability was observed for IOV, lowest for convolution kernel.

CT based Overall Survival Model Comparison

- Final OS model on standardized dataset (6 features, all identified as unstable): CI = 0.64
- Final OS model on multi-centric dataset (4 features): CI = 0.61

This CI difference was significant ($p < 0.05$).

Conclusion

For our prognostic NSCLC CT based radiomic models, CT image protocol standardization appears to be superior to using larger but heterogeneous imaging data combined with prior robust feature selection.

Contact: Diem Vuong | diem.vuong@usz.ch
Rämistrasse 100, 8091 Zürich

Supervisors: Dr. Stephanie Tanadini-Lang | stephanie.tanadini-lang@usz.ch
Prof. Jan Unkelbach | jan.unkelbach@usz.ch