Title

Predicting lung cancer response to radiotherapy with pre- and early post-treatment [^{18}F]FDG PET/CT imaging

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Keywords / Topics

++B14 Lung (including Mesothelioma)

Authors

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Aim

This study aims to investigate the **potential power of metabolic features** extracted from pre- and early post-treatment [^{18}F]FDG PET/CT images of primary and secondary lung cancer lesions **to predict local response to radiotherapy one year after treatment**.

Materials and Methods

156 lung lesions from 95 oncology patients (66±10 y.o., 55 female), treated with radiotherapy alone or chemoradiotherapy, were retrospectively included. All patients underwent **pre-treatment** (up to 3 months before radiotherapy) and **one-year post-treatment** [^{18}F]FDG PET/CT scans. From these, for a subgroup of 142 lesions, an **early post-treatment** [^{18}F]FDG PET/CT (3 to 6 months post-radiotherapy) was also available.

Demographic (age, sex), **clinical** (primary tumor, staging, treatment combination), and **dosimetry-related features** (clinical tumor volume, total dose, and percentage of dose cover) were collected. **[^{18}F]FDG uptake-related features** (8 first-order and 4 geometry-based) were extracted from treated lesions. Segmentation was performed semi-automatically with an adaptive Bayesian classifier [1].

Classification into responder/non-responder lesion was based on clinical reports from one-year post-treatment PET/CT.

Figure 1 represents an example of the features collected for each lesion and the one-year classification into responder and non-responder.

The association between features and response was assessed using **univariate and multivariate logistic regression**. Multivariate classification performance was assessed with the area under the receiver operating characteristic curve (AUC) and balanced accuracy (BAcc). Leave-one-out cross-validation (LOOCV) was further performed to assess evaluation metrics' reproducibility.

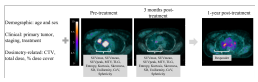

Fig. 1: Features collected from clinical records (demographic, clinical and dosimetric related features) and extracted from pre and 3 months post-treatment [18F]FDG PET/CT images (8 first-order and 4 geometry-based features). These features were used to predict local response to radiotherapy one year after treatment. At one year post-treatment, and based on [18F]FDG PET/CT clinical report, lesions were classified as responder or non-responder. CTV: clinical tumor volume; MTV: metabolic tumor volume; TLG: total lesion glycolysis; SD: standard deviation; CoV: coefficient of variation.

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Results

100 out of 156 lung lesions responded to treatment (92 out of 142 lesions in the subset with early post-treatment **PET/CT**).

Table 1 shows the *p*-value results for features studied in the univariate analysis. No demographic, clinical, or dosimetric features were significantly associated with the response. **Association with response was significant** ($p<0.05$) **for kurtosis, skewness, and coefficient of variation (CoV)** from the pre-treatment [^{18}F]FDG uptake; **and for SUV_{max}, SUV_{mean}, and SUV_{peak}** from early post-treatment [^{18}F]FDG uptake. In Figure 2 are boxplots representing the distribution of the features significantly associated with the response by group (responder and non-responder).

The multivariate models achieved the following significant AUC and BAcc: 0.70 and 0.55 for the model with demographic, clinical and dosimetry-related features; 0.72 and 0.65 for the model based on pre-treatment [^{18}F]FDG uptake; 0.79 and 0.73 for the model based on the early post-treatment [^{18}F]FDG uptake, and 0.86 and 0.75 for the model combining features from both pre-and early post-treatment [^{18}F]FDG uptake. In Figure 3 are the operating characteristic curves for each model.

When applying LOOCV, there was a decrease in BAcc to 0.54, 0.61, 0.66, and 0.66, respectively, for the above-mentioned models.

Variables	Logistic regression p-value
Demographic	
Age	0.15
Sex	0.57
Clinical	
Primary tumor	0.56
Staging	0.60
Treatment combination	0.21
Dosimetry related features	
CTV	0.20
Total dose	0.13
Dose cover	0.37
Pre-RT PET based features	
SUVmax	0.77
SUVpeak	0.99
SUVmean	0.74
Entropy	0.12
Kurtosis	**0.05**
Skewness	**0.02**
SD	0.66
MTV	0.25
TLG	0.20
Uniformity	0.06
CoV	**0.05**
Sphericity	0.29
Post-RT PET based features	
SUVmax	**0.01**
SUVpeak	**0.005**
SUVmean	**0.006**
Entropy	0.93
Kurtosis	0.21
Skewness	0.49
SD	0.94
MTV	0.10
TLG	0.06
Uniformity	0.22
CoV	0.97
Sphericity	0.07

Tab. 1: Univariate analysis with logistic regression for demographic, clinical, dosimetry-related features and [18F]FDG uptake-related features (early and post-treatment PET).

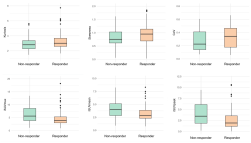

Fig. 2: Boxplots of the features associated with the response at one year (kurtosis, skewness and coefficient of variation (CoV) from the pre-treatment [18F]FDG uptake; and SUVmax, SUVmean, and SUVpeak from early post-treatment [18F]FDG uptake).

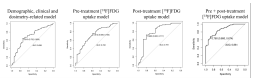

Fig. 3: Operating characteristic curves for the model with demographic, clinical and dosimetry-related features, the model based on pre-treatment [18F]FDG uptake, the model based on post-treatment [18F]FDG uptake and the model combining features from both pre- and early post-treatment [18F]FDG uptake.

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Conclusion

This preliminary study showed that **[^{18}F]FDG uptake-based features** from lung cancer lesions **may have value in predicting local response to radiotherapy/chemoradiotherapy**. Further studies, with larger data sampling and stratified tumors, are needed to evaluate the potential added value of these features.

References

[1] Constantino et al, doi:10.1007/s10278-023-00823-y

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