Review Article

The use of ^{18}F-FDG PET/CT for radiotherapy treatment planning in non-small cell lung cancer: a mini-review

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Abstract: In the past decades, the technical achievements in radiotherapy treatment planning and delivery, such as the use of intensity-modulated radiotherapy or the use of image-guided radiotherapy, alongside with the significant developments in molecular imaging and especially the use of positron-emission tomography (PET) have significantly improved radiotherapy treatment precision. In non-small cell lung cancer (NSCLC), the use of ^{18}F-fluoro-desoxy-glucose (^{18}F-FDG) positron-emission tomography/computed tomography (^{18}F-FDG-PET/CT) has a high accuracy for diagnostic workup, staging and response assessment but has been also implemented to optimize target volume concepts in NSCLC with high precision. These advances led, in the recent years, to an increased tumor control and improved outcomes. Especially in the context of emerging systemic treatments, such as immune checkpoint blockades (ICBs), the prevention of unnecessary irradiation of the lymphatic system might be very important. In the past years, several prospective randomized studies have been performed, aiming to optimize, standardize and develop new concepts in the target volume delineation especially in locally advanced NSCLC using different approaches. While the PET-Plan trial used a uniform target volume reduction based on the ^{18}F-FDG-PET/CT signal in the experimental arm, the PET boost trial and the RTOG 1106 used the ^{18}F-FDG-PET/CT information to define an additional boost volume for dose escalation. Within this mini-review, we provide an overview on the role of ^{18}F-FDG-PET/CT, the challenges and the benefits, in radiotherapy of NSCLC.

Keywords: Non-small cell lung cancer (NSCLC); radiotherapy; target volume delineation; ^{18}F-fluoro-desoxy-glucose positron-emission tomography/computed tomography (^{18}F-FDG-PET/CT)

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Introduction

Background

Radiotherapy plays a significant role in the treatment of non-small cell lung cancer (NSCLC) at every stage of the disease, from early stage to locally advanced and oligometastatic disease. ^{18}F-fluoro-desoxy-glucose (^{18}F-FDG) positron-emission tomography/computed tomography (^{18}F-FDG-PET/CT) is the standard extra-cranial staging modality for lung cancer patients in the primary setting but also for the detection of recurrences after initial treatment. ^{18}F-FDG-PET/CT shows a high sensitivity and specificity for the detection of nodal spread and distant metastases, leading to a better stratification and treatment allocation of the patients. Additionally, it serves as an excellent treatment planning modality for radiotherapy in locally advanced disease.

Rationale

In the past years, several prospective studies have evaluated the role of ^{18}F-FDG-PET/CT in the precise definition of the target volume but also for the definition of sub-volumes aiming at a further dose escalation. Furthermore, several radiomic features have been evaluated in order to predict local recurrences.

Objective

Herein we review the role of ^{18}F-FDG-PET/CT for radiotherapy treatment planning in NSCLC through the scope or recent advances and prospective trials performed over the past years.

Diagnosis and treatment volume delineation

Due to the higher accuracy in the identification of the nodal spread and differentiation between tumor and atelectasis, ^{18}F-DG-PET has been extensively used for the precise delineation of the radiotherapy panning target volume in of lung cancer patients, which has been previously highlighted in several publications (1). Additionally, the use of ^{18}F-FDG PET-based delineation of radiotherapy treatment volumes demonstrated an improvement on the inter-observer agreement (2).

Several studies compared the role of elective nodal irradiation (ENI) compared to involved filed radiotherapy (IFRT) in patients with locally advanced NSCLC treated with chemoradiation. In a meta-analysis by Li *et al.* (3), IFRT did not appear to increase the risk of elective nodal failures, while in a pooled analysis by Schild *et al.* (4) IFRT with 60 Gy was associated with more favorable overall survival and less toxicity than the use of ENI or higher radiotherapy dose. Nevertheless, most of these studies were not performed using a PET/CT for the definition of the target volume.

The prospective randomized PET-Plan trial aimed at investigating whether a ^{18}F-FDG-PET-based target volume definition compared to conventional planning, in patients with locally advanced NSCLC, was feasible and effective (5). In this multi-center, open-label, randomized, controlled trial, 205 patients with locally advanced inoperable stage II or III NSCLC, planed for chemoradiation were randomized concerning the definition of the planning target volume. In the conventional study arm A, target volumes based on ^{18}F-FDG-PET and CT plus ENI and tumor-associated atelectasis if present. In the experimental study arm B the definition of the target volume was based solely on ^{18}F-FDG-PET without the use of ENI. Both groups received an iso-toxic dose-escalated radiotherapy (60–70 Gy, 2 Gy per fraction) while the ENI was performed up to a total dose of 50 Gy in 2 Gy fraction. In the per-protocol set, the risk of loco-regional progression in the ^{18}F-FDG PET-based target volume (arm B) was lower than, that in the conventional arm A [14% (95% CI: 5–21%) *vs.* 29% (95% CI: 17–38%) at 1 year; HR 0.57 (95% CI: 0.30–1.06)]. Furthermore, the risk of loco-regional progression in arm B (^{18}F-FDG PET-based target volume) was also non-inferior that in the conventional arm A in the intention-to-treat analysis [17% (95% CI: 9–24%) *vs.* 30% (95% CI: 20–39%) at 1 year; HR 0.64 (95% CI: 0.37–1.10)] (5). Thus, the approach using an ^{18}F-FDG-PET based target volume definition should be followed, as smaller treatment volumes may lead to an improved local control or reduced toxicity and might also play a role in combination with immunotherapies.

Automatic contouring algorithms for the definition of the GTV

The use of automatic contouring algorithms for GTV delineation using an ^{18}F-FDG-PET is useful and time saving but should be used with caution. Contouring algorithms, should be previously calibrated and always be validated in clinical routine (6). A valid alternative is the consultation of an experienced imaging specialist. In the PET-Plan trial, a standardized individually calibrated contrast-oriented semi-automatic contouring algorithm, which had previously undergone multi-center calibration (7), was implemented in some cases. This algorithm was used as a starting point for GTV-contouring. Only an enlargement, but not reduction of the automatic generated volume by an experienced radiation oncologist was allowed. In any other case, visual contouring was performed together with radiation oncologists and diagnostic imaging colleagues (8,9). Several auto contouring algorithms using deep learning algorithms are now available but the reported failures, according to the AAPM Task Group 275, in detecting contouring errors in treatment targets is a big risk factor for treatment planning (10). In order to reduce the risk from contouring errors, automatic contouring error detection methods have been studied by several research groups and several quality assurance (QA) methods have been proposed (11,12).

Dose escalation strategies

Another significant clinical aspect, is the use of dose escalation strategies, made possible due to the better tumor visualization and precise target delineation in combination with the technical advances in radiotherapy planning, allowing a more precise delivery of higher doses. Several approaches have been suggested for dose escalation in radiotherapy of locally advanced NSCLC.

In the PET-Plan trial, an iso-toxic dose escalation (60–74 Gy, in 2 Gy per fraction) was applied in both study groups. The aim was to escalate the dose as high as possible while adhering to the pre-defined constraints for the organs at risk. In case that any constraint was exceeded, the highest safe dose level below (in 2 Gy steps) was used (5). The target volume reduction based on the ^{18}F-FDG PET-based target group (arm B) received significantly higher mean total doses (67.3 Gy) than in the conventional arm A (65.3 Gy). In total, higher doses (about 68 Gy or more) were more frequently applied in arm B than arm A [41 (47%) of 88 patients *vs.* 28 (33%) of 84 patients]. This resulted to a higher odds ratio in the patients receiving more than 65 Gy in the ^{18}F-FDG PET-based target group than in the conventional target group (P=0.0070). However, no effect of higher dose on overall or progression free survival could be shown.

In another prospective multicenter randomized controlled study, the PET Boost trial (13-15) patients received a hypo-fractionated radiotherapy with 24×2.75 Gy and were subsequently randomized between a simultaneously integrated boost (SIB) to the whole primary tumor (PTVwhole, arm A) or to the 50% maximum standardized uptake value (SUVmax) area of the primary tumor (arm B). The study accrued 107 patients (54 arm A and 53 arm B). The median escalated prescribed dose to the PTVwhole (arm A) was 3.25 Gy per fraction with a median total dose of 78 Gy. The median prescribed dose to the PTV50%SUVmax (arm B) was 3.5 Gy per fraction with a median total dose was 84 Gy. The 1-year freedom from local failure rate in all evaluable patients was 97% in arm A, and 91% in arm B, while the 1- and 3-year overall survival rates were 77% and 37% in arm A, and 62% and 33% in arm B, respectively. So, although no prognostic benefit was demonstrated, this study showed that in locally advanced NSCLC a homogeneous SIB, sparing central structures, was feasible, leading to local control rates but also showing a high rate of grade 3 early and late toxicities (14).

Another approach was used in the phase 2 clinical trial, involving 42 patients with stage II/III NSCLC from 2008 to 2012 in which conformal RT was individualized to a fixed risk of radiation induced lung toxicity (RILT , grade >2) and adaptively escalated during radiotherapy, to the residual tumor, using a mid-treatment FDG-PET. The dose was escalated up to a total dose of 86 Gy in 30 daily fractions. The in-field and local regional tumor control rates at 2 years were 82% (95% CI: 62–92%) and 62% (95% CI: 43–77%), respectively, showing overall a favorable local-regional tumor control. These results were evaluated in the RTOG 1106 trial (16).

In the subsequent multicenter randomized phase II study (RTOG 1106), patients with locally advanced stage III NSCLC were randomized by a 1:2 ratio to standard (60 Gy in 30 daily fractions) arm and adaptive therapy arm, in which the dose was individualized to 20 Gy mean lung dose (MLD) and adapted to the residual tumor on the mid-treatment FDG-PET/CT as in the previous study (17). All patients received a mid-treatment FDG-PET at 40 Gy. In the adaptive arm, the initial plan consisted of 2.2 Gy per fraction in 21 fractions followed by the adaptive boost using a variable prescription of 2.2–3.8 Gy per fraction for the final 9 fractions. Of 138 patients enrolled, 127 were eligible and analyzable. The median dose for the adaptive arm was 71 Gy *vs.* 60 Gy in the standard arm (P<0.01). The 2-year overall loco-regional progression free (LRPF) rates were 59.5% in the standard arm with a median LRPF of 27.5 months, while in the adaptive arm the 2-year LRPF rate was 54.6% with a median LRPF of 28.4 months. Overall, while there were no significant differences in overall survival, progression free survival or lung cancer specific survival between the two arms, this trial demonstrated the feasibility and safety of a biologically adaptive dose escalation. The in-field local regional tumor control results are not yet published (17).

Overall, no beneficial effect of radiotherapy dose escalation has been demonstrated so far. In the PET-Plan trial, there was no negative effect of dose escalation observed, but improved local control was not related to dose (5). Thus the improvement of local control in the PET-Plan cohort may be an effect of smaller treatment volumes rather than of dose escalation. Recently, more and more data show that normal tissue exposure, e.g., of heart, lung, blood pool and lymphatic tissues are related to outcome and possibly to the lack of an additional survival benefit.

Quality assurance

The PET-Plan trial included an extensive QA program which consisted from different components. The quality

assurance program included, a dummy run for the definition of the radiotherapy treatment volume, phantom calibrations of the PET-based target volume contouring, an expert panel review of the initial PET reading, and a blinded expert support for the response evaluation (5).

In the context of the PET-Plan trial, PET-reading in preparation of radiotherapy planning was investigated (18). A prospectively defined group of experts performed blinded reviews of the mediastinal nodal involvement in ^{18}F-FDG-PET/CT for all study patients, showing a high initial inter-observer disagreement (18). Subjective uncertainty was highly predictive for low agreement (18). The reading variability, is beyond anatomy, a major problem, potentially leading to deviations in the target volume definition between radiation oncologists, especially concerning the definition of the nodal target volume. This may be related to several factors such as education, experience and the individual complexity of each case. Overall, a joint discussion and agreement on detailed reading and reporting criteria reduces this effect (18). In general practice, sensitive reading of PET scans in the context of restricted target volumes is highly recommended, and in the presence of uncertainties, such as faintly positive nodes, they should be rather in- than excluded in the target volume. On the other hand, in cases where there is uncertainty concerning the inclusion of nodal areas with low pre-test probability in the target volume, they can be excluded, if their inclusion would lead to compromises in the treatment doses and/or concept (6). Additionally, a large part of the disagreements was related to different anatomical allocations of given findings.

Prediction of recurrence using serial scans with or without the use of radiomic features

In patients treated within multimodal protocols including induction chemotherapy, serial PET scans during induction treatment before radiotherapy or during chemoradiation, have been used, aiming to define individualized treatment adaptations, as previously reported or to acquire additional prognostic information (16,19). In some studies, several FDG-PET parameters such as the SUVmax or the metabolic tumor volume (MTV) or total lesion glycolysis (TLG) significantly correlated with the overall and progression free survival, and/or the local tumor control (19-22). Furthermore, the use of repeated ^{18}F-FDG PET in patients undergoing radiotherapy or chemoradiotherapy, either sequentially or concurrently, showed that a decrease in ^{18}F-FDG uptake in the primary tumor correlated with higher long-term overall survival rates (23). Additionally, in patients with NSCLC undergoing stereotactic body radiation therapy (SBRT), the use of ^{18}F-FDG PET-radiomics correlated with the local response and could be combined in a predictive model providing local relapse-related information (24). In another study, using 4D-PET/CT scans before treatment, and a 3D-scan during or after treatment, showed that the quantification of tumor FDG heterogeneity by area-under-the-curve of the cumulative standard-uptake-value histogram (δAUC_{CSH}) during chemoradiation correlated with the incidence of local recurrence and might be used for monitoring response or for further dose escalation in patients with NSCLC (25). Bowen *et al.* (26) developed a Voxel Forecast multiscale regression framework for predicting spatially variant tumor responses. Patients with a greater percentage of under-responding tumor voxels were classified as PETmid non-responders and had a worse overall survival compared to the rest of the patients. In general that the use of machine learning methods might add additional information and might be used for risk stratification.

Tumor volume reduction in combination with immunotherapy

The use of sequential immune checkpoint blockade (ICB) after definitive chemoradiation in locally advanced NSCLC led to a significantly better overall survival compared to definitive chemoradiation without sequential ICBs. On the other hand, radiotherapy leads to lymphodepletion which might have an impact on the efficacy of immunotherapies. In a prospective study including patients with advanced NSCLC receiving chemoradiation, the reduction of target volume margins and radiation dose (from 70 to 60 Gy) to the involved lymph nodes led to significantly lower acute toxicities and an improved overall survival (27). Moreover, the irradiation of the draining lymph nodes seems to restrain adaptive immune responses through several pathways. This is in line with the results of the PET-Plan trial, where in the absence of a dose effect, an improvement of loco-regional control by volume reduction was observed. As the irradiation of unaffected draining lymph nodes might decrease the immune response, it seems important to encourage future clinical studies using PET-based adjustment of the planning target volume for lung cancer and other tumors, especially in combination multimodal treatments including immunotherapy and chemoradiation (5).

Current recommendations for the use of ^{18}F-FDG-PET/CT in the definition of the radiotherapy target volume

One important aspect for the target volume definition is the variability that might emerge due to the lack of education, experience and complexity of the individual cases, especially concerning the lymph nodes. Thorough guidelines and recommendations might help reduce the inter-observer variability in the definition of the target volume, highlighting several aspects, which should be taken into account. First of all, the acquisition protocol should undergo institutional standardization (28), when PET data are co-registered with the planning CT for radiotherapy treatment planning. Additionally, the planning ^{18}F-FDG-PET/CT should be performed in treatment position using the same immobilization for imaging and treatment delivery in order to avoid geographic misses through a false co registration, and as previously described should be performed within 3 weeks before the treatment initiation (29). As patient movements may lead to incorrect hardware fusion, it is advised to evaluate the quality of the co-registration, before delineation. As outlined above, also contouring procedures should be institutionally standardized. Foremost, the ^{18}F-FDG-PET/CT scan should be performed within 3 weeks before start of radiotherapy, as there is a high probability of progression of 32% within 24 days while awaiting initiation of curative RT, which is associated with larger treatment volumes and worse survival (6) Thus, a diagnostic whole body ^{18}F-FDG-PET/CT, performed within 3 weeks before start of treatment, is mandatory (29).

Conclusions

The use of ^{18}F-FDG-PET/CT has led to a precise and standardized definition of the radiotherapy target volume and a reduction in the irradiated volumes, subsequently leading to an increased tumor control and improved outcomes in patients with locally advanced NSCLC treated with definitive chemoradiation.

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Footnote

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References

1. Gkika E, Oehlke O, Bunea H, et al. Biological imaging for individualized therapy in radiation oncology: part II medical and clinical aspects. Future Oncol 2018;14:751-69.
2. Steenbakkers RJ, Duppen JC, Fitton I, et al. Reduction of observer variation using matched CT-PET for lung cancer delineation: a three-dimensional analysis. Int J Radiat Oncol Biol Phys 2006;64:435-48.
3. Li R, Yu L, Lin S, et al. Involved field radiotherapy (IFRT) versus elective nodal irradiation (ENI) for locally advanced non-small cell lung cancer: a meta-analysis of incidence of elective nodal failure (ENF). Radiat Oncol 2016;11:124.
4. Schild SE, Fan W, Stinchcombe TE, et al. Toxicity Related to Radiotherapy Dose and Targeting Strategy: A Pooled Analysis of Cooperative Group Trials of Combined Modality Therapy for Locally Advanced Non-Small Cell

Lung Cancer. J Thorac Oncol 2019;14:298-303.
5. Nestle U, Schimek-Jasch T, Kremp S, et al. Imaging-based target volume reduction in chemoradiotherapy for locally advanced non-small-cell lung cancer (PET-Plan): a multicentre, open-label, randomised, controlled trial. Lancet Oncol 2020;21:581-92.
6. Nestle U, Le Pechoux C, De Ruysscher D. Evolving target volume concepts in locally advanced non-small cell lung cancer. Transl Lung Cancer Res 2021;10:1999-2010.
7. Schaefer A, Nestle U, Kremp S, et al. Multi-centre calibration of an adaptive thresholding method for PET-based delineation of tumour volumes in radiotherapy planning of lung cancer. Nuklearmedizin 2012;51:101-10.
8. Nestle U, Kremp S, Schaefer-Schuler A, et al. Comparison of different methods for delineation of 18F-FDG PET-positive tissue for target volume definition in radiotherapy of patients with non-Small cell lung cancer. J Nucl Med 2005;46:1342-8.
9. Schaefer A, Kremp S, Hellwig D, et al. A contrast-oriented algorithm for FDG-PET-based delineation of tumour volumes for the radiotherapy of lung cancer: derivation from phantom measurements and validation in patient data. Eur J Nucl Med Mol Imaging 2008;35:1989-99.
10. Ford E, Conroy L, Dong L, et al. Strategies for effective physics plan and chart review in radiation therapy: Report of AAPM Task Group 275. Med Phys 2020;47:e236-72.
11. Rhee DJ, Akinfenwa CPA, Rigaud B, et al. Automatic contouring QA method using a deep learning-based autocontouring system. J Appl Clin Med Phys 2022;23:e13647.
12. McIntosh C, Svistoun I, Purdie TG. Groupwise conditional random forests for automatic shape classification and contour quality assessment in radiotherapy planning. IEEE Trans Med Imaging 2013;32:1043-57.
13. Cooke S, De Ruysscher D, Reymen B, et al. OC-0609: The PET-boost trial: isotoxic homogeneous or FDG-directed dose escalation in stage II-III NSCLC. Radiotherapy and Oncology 2020;152:S345-S346.
14. van Diessen J, De Ruysscher D, Sonke JJ, et al. The acute and late toxicity results of a randomized phase II dose-escalation trial in non-small cell lung cancer (PET-boost trial). Radiother Oncol 2019;131:166-73.
15. van Elmpt W, De Ruysscher D, van der Salm A, et al. The PET-boost randomised phase II dose-escalation trial in non-small cell lung cancer. Radiother Oncol 2012;104:67-71.
16. Kong FM, Ten Haken RK, Schipper M, et al. Effect of Midtreatment PET/CT-Adapted Radiation Therapy With Concurrent Chemotherapy in Patients With Locally Advanced Non-Small-Cell Lung Cancer: A Phase 2 Clinical Trial. JAMA Oncol 2017;3:1358-65.
17. Kong F, Hu C, Machtay M, et al. OA02.04 Randomized Phase II Trial (RTOG1106) on Midtreatment PET/CT Guided Adaptive Radiotherapy in Locally Advanced Non-Small Cell Lung Cancer. J Thorac Oncol 2021;16:S104-S105.
18. Nestle U, Rischke HC, Eschmann SM, et al. Improved inter-observer agreement of an expert review panel in an oncology treatment trial--Insights from a structured interventional process. Eur J Cancer 2015;51:2525-33.
19. Lapa C, Nestle U, Albert NL, et al. Value of PET imaging for radiation therapy. Strahlenther Onkol 2021;197:1-23.
20. Roengvoraphoj O, Wijaya C, Eze C, et al. Analysis of primary tumor metabolic volume during chemoradiotherapy in locally advanced non-small cell lung cancer. Strahlenther Onkol 2018;194:107-15.
21. Bissonnette JP, Yap ML, Clarke K, et al. Serial 4DCT/4DPET imaging to predict and monitor response for locally-advanced non-small cell lung cancer chemo-radiotherapy. Radiother Oncol 2018;126:347-54.
22. Huang W, Zhou T, Ma L, et al. Standard uptake value and metabolic tumor volume of ^{18}F-FDG PET/CT predict short-term outcome early in the course of chemoradiotherapy in advanced non-small cell lung cancer. Eur J Nucl Med Mol Imaging 2011;38:1628-35.
23. van Elmpt W, Ollers M, Dingemans AM, et al. Response assessment using 18F-FDG PET early in the course of radiotherapy correlates with survival in advanced-stage non-small cell lung cancer. J Nucl Med 2012;53:1514-20.
24. Dissaux G, Visvikis D, Da-Ano R, et al. Pretreatment (18) F-FDG PET/CT Radiomics Predict Local Recurrence in Patients Treated with Stereotactic Body Radiotherapy for Early-Stage Non-Small Cell Lung Cancer: A Multicentric Study. J Nucl Med 2020;61:814-20.
25. Carles M, Fechter T, Radicioni G, et al. FDG-PET Radiomics for Response Monitoring in Non-Small-Cell Lung Cancer Treated with Radiation Therapy. Cancers (Basel) 2021;13:814.
26. Bowen SR, Hippe DS, Chaovalitwongse WA, et al. Voxel Forecast for Precision Oncology: Predicting Spatially Variant and Multiscale Cancer Therapy Response on Longitudinal Quantitative Molecular Imaging. Clin Cancer Res 2019;25:5027-37.
27. van Diessen JNA, Kwint M, Sonke JJ, et al. Safety and efficacy of reduced dose and margins to involved lymph

node metastases in locally advanced NSCLC patients. Radiother Oncol 2020;143:66-72.
28. van Herk M, Remeijer P, Rasch C, et al. The probability of correct target dosage: dose-population histograms for deriving treatment margins in radiotherapy. Int J Radiat Oncol Biol Phys 2000;47:1121-35.
29. Nestle U, De Ruysscher D, Ricardi U, et al. ESTRO ACROP guidelines for target volume definition in the treatment of locally advanced non-small cell lung cancer. Radiother Oncol 2018;127:1-5.

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