HHS Public Access

Author manuscript

Radiother Oncol. Author manuscript; available in PMC 2022 September 01.

Published in final edited form as:

Radiother Oncol. 2022 March ; 168: 37–39. doi:10.1016/j.radonc.2021.12.048.

Perspective paper about the joint EANM/SNMMI/ESTRO practice recommendations for the use of 2-[^{18}F]FDG-PET/CT external beam radiation treatment planning in lung cancer

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Ken Herrmann reports personal fees from Bayer, personal fees and other from Sofie Biosciences, personal fees from SIRTEX, non-financial support from ABX, personal fees from Adacap, personal fees from Curium, personal fees from Endocyte, grants and personal fees from BTG, personal fees from IPSEN, personal fees from Siemens Healthineers, personal fees from GE Healthcare, personal fees from Amgen, personal fees from Novartis, personal fees from ymabs, personal fees from Aktis Oncology, personal fees from Theragnostics, personal fees from Pharma15, outside the submitted work. - Rodney J. Hicks is on the Scientific Advisory Board of Telix Pharmaceuticals with any honoraria donated to his institution, he is a stock holder in this company, he is also an honorary Trustee of the International Cancer Imaging Society and honorary Board Member of Neuroendocrine Cancer Australia. - All the remaining authors declare no conflict of interest.

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Abstract

In “Joint EANM/SNMMI/ESTRO Practice Recommendations for the Use of 2-[18F]FDG-PET/CT External Beam Radiation Treatment Planning in Lung Cancer V1.0” clinical indications for PET-CT in (non-)small cell lung cancer are highlighted and selective nodal irradiation is discussed. Additionally, concepts about target definition, target delineation and treatment evaluation are reviewed.

Keywords

FDG-PET/CT; Non-small cell lung cancer; Small cell lung cancer; Radiation treatment planning; Treatment response assessment

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Recently, the “Joint EANM/SNMMI/ESTRO Practice Recommendations for the Use of 2-[^{18}F]FDG-PET/CT External Beam Radiation Treatment Planning in Lung Cancer V1.0” have been published. The aim of these recommendations is to provide specific evidence and expert opinion-based considerations on 2-[18F]fluoro-2-deoxy-D-glucose Positron Emission Tomography/Computed Tomography (2-[^{18}F]FDG-PET/CT) for radiation treatment (RT) planning in both non-small cell and small cell lung cancer (N)SCLC, in order to guide clinical management. Although 2-[^{18}F]FDG-PET/CT is routinely performed for lung cancer staging in standard clinical practice, this is the first joint EANM/SNMMI/ESTRO recommendation on PET/CT and RT planning in lung cancer [1-6].

2-[^{18}F]FDG-PET/CT is the recommended imaging modality for lung cancer staging. According to the NCCN, ESMO, ESTRO ACROP and EORTC recommendations, 2-[^{18}F]FDG-PET/CT plays a crucial role in RT planning in lung cancer, both of the primary tumour and lymph node metastases. 2-[^{18}F]FDG-PET/CT has been shown to lead to a change in target definition in 43% NSCLC and 26% SCLC patients [7]. Pre-therapeutic 2-[^{18}F]FDG-PET/CT has the advantage of reducing gross tumour volume (GTV) by improving tumour demarcation, e.g., in case of atelectasis or mediastinal infiltration, and increasing inter- and intra-observer reproducibility [8]. Moreover, it empowers selective nodal irradiation in both non-small cell and small cell lung cancer [9,10]. Of note, in patients treated with induction chemotherapy, the nodal volume for RT ought to include the lymph node stations, which were 2-[^{18}F]FDG-PET/CT positive at baseline evaluation. 2-[^{18}F]FDG-PET/CT staging after RT or radiochemotherapy (RCHT) enables response prediction, detection of residual or recurrent disease, and predicts overall survival after R(CH)T [11-13]. The cost of the 2-[^{18}F]FDG-PET/CT for staging is leveraged by optimizing delivery of RCHT for suitable stage 1–3 disease, while avoiding futile treatment in stage 4. Importantly, the lapse between 2-[^{18}F]FDG-PET/CT and RT should be <3 weeks.

In this guideline, clinical indications are highlighted and selective nodal irradiation is discussed. Additionally, concepts about target definition, target delineation and treatment evaluation are reviewed.

Recommendations about personnel, request, protocol, quality control, segmentation and report

RT planning in lung cancer is at the intersection of radiation oncology, nuclear medicine, and diagnostic radiology expertise. Treatment planning includes professionals trained in multimodality imaging according to interdisciplinary training programs [14]. The request for a 2-[^{18}F]FDG PET/CT in RT position should be written and contain all standard information for an oncological 2-[^{18}F] FDG PET/CT. Informed consent might need to be obtained for 2-[^{18}F]FDG PET/CT, according to national/institutional requirements. The acquisition and interpretation of imaging studies is guided by the clinical questions.

It is recommended that EANM/SNM procedural guidelines for tumour imaging and the EANM Research Ltd (EARL©) accreditation program are followed [15,16]. The administration of intravenous contrast improves primary tumour delineation, regional lymph nodes identification and organs at risk definition on CT. In such cases, kidney function and history of contrast allergy should be verified before injection. The PET/CT scanner should be equipped with a flat table-top and patient positioning devices for RT planning [17]. The CT component has to be calibrated and regularly checked for RT dose calculation accuracy. Patient setup should be performed with levelling lasers and reference ink to ensure accurate and reproducible alignment during RT [14]. Respiratory motion correction improves tumour localization, delineation, standardized uptake value (SUV) quantification and, consequently, dose delivery in RT [18].

Mutual training and close collaboration between radiation oncologists, nuclear medicine physicians, radiologists, expert physicians, technologists and clinical physicists are required.

Joint tumour delineation by a radiation oncologist and nuclear medicine physician increases quality and consistency. Several PET-based tumour volume delineation methods have been described and algorithms for semiautomatic 2-[^{18}F]FDG-PET segmentation, using artificial intelligence, have evolved in the last decade. Possible segmentation methods include manual, threshold-based, image processing and consensus methods [19]. Considering that different approaches are proposed for GTV delineation, it is recommended to develop departmental instructions, which should include testing the reproducibility of metabolic GTV delineation within the nuclear medicine department. Moreover, it is advisable to document the delineation method, including whenever appropriate the threshold used or other methodology. All delineation steps should be performed or supervised by radiation oncologists according to local practice and reviewed by another radiation oncologist.

2-[^{18}F]FDG PET/CT scans should preferably be reported by an appropriately trained and certified nuclear medicine physician, or a radiologist trained in 2-[^{18}F]FDG PET/CT image interpretation and with experience in lung malignancies. The report should contain the main clinical information, the clinical question, and technical details, including the fact that the PET/CT was performed in RT setting. It should also mention any imaging studies used for comparison, a conclusion answering to the clinical question and, whenever necessary, recommendations for follow-up. The use of a standardized report template is encouraged.

Future directions

Although the utility of 2-[^{18}F]FDG-PET/CT in RT planning in lung cancer has been based on a vast amount of evidence, several novel applications to improve delineation and dose administration are underway. The guideline briefly discuss new developments such as (1) the role of mid-treatment imaging in the earlier assessment of treatment response, enabling an alternative therapy and preventing unnecessary toxicity [20]; (2) PET/MRI that may be useful in cases with chest wall infiltration, superior sulcus tumours or para-spinal tumours [21]; (3) Radiomics improving lesions characterization by extracting additional quantitative data from medical image [22]; and (4) PET tracers other than 2-[^{18}F]FDG that have a potential role in imaging biological tumour processes and tumour heterogeneity (for example, to measure different levels of hypoxia, cell density, proliferation and vascularization), and which may provide complementary information to be used in RT dose definition.

Conclusion

2-[^{18}F]FDG-PET/CT has a large impact on the management and RT planning of lung cancer. The recently published joint recommendation by EANM, SNM and ESTRO provides summarized and updated information useful in clinical practice based on current evidence. Additionally, it addresses the recent developments considered for future application and stimulates a multidisciplinary approach to improve personalized treatment.

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