

Interim 18F-FDG Positron Emission Tomography/Computed Tomography during chemoradiotherapy in the management of cancer patients: A response

As outlined by Garibaldi *et al* in their recent letter (1), there is increasing interest in the use of Positron Emission Tomography – Computed Tomography (PET-CT) to demarcate the Biological Gross Tumour Volume (bGTV) for radical radiotherapy treatment. In head and neck cancers, 18F-Fluorodeoxyglucose (18F-FDG)-PET-CT defined volumes have been shown to correlate with pathological specimens better than other imaging modalities (2). Additionally, PET-CT carried out at baseline (3) and/or during treatment (4), may offer prognostic and/or predictive information (5, 6).

Adaptive radiotherapy (ART) - the alteration of a treatment plan based upon anatomical changes during radiotherapy - is a rapidly growing area. ART could improve normal tissue sparing (7) or, conversely, escalate radiotherapy doses to poorly responding tumours (8).

Garibaldi's critical review of the utility of interim PET-CT (iPET) in head and neck cancer treatment (9) concluded there was a need for further research into its predictive and/or prognostic role. They called for more homogenous cohorts of patients and treatment regimens, and a standardised method of analysing PET data.

The PEARL study (NCT number pending) is a multicentre phase II feasibility study designed to explore the potential of 18-FDG-PET-CT-based ART to reduce toxicity in radically treated patients with low risk (10) Human Papilloma Virus positive oropharyngeal squamous cell carcinoma. Patients will undergo iPET after 2 weeks of conventionally fractionated IMRT.

ATLAAS (Automatic decision-Tree Learning Algorithm for Advanced Segmentation of PET images), a machine learning tool, will define the bGTV on the baseline and interim PET-CT (11). We have shown that ATLAAS can be trained to outperform any other individual PET-based automated segmentation algorithm (12) and is a useful tool in the standardisation of PET-based segmentation within clinical radiotherapy trials.

PEARL will address many of the shortcomings identified by Garibaldi *et al*. Furthermore, PEARL will offer important insight into the feasibility of PET-based ART to improve outcomes.

REFERENCES

1. Garibaldi, C., Ferrari, M., Grana, C.M., Jereczek-Fossa, B.A., Cremonesi, M. Interim 18F-FDG positron emission tomography/computed tomography during chemoradiotherapy in the management of cancer patients. *Letters/Clin Oncol* 31 2019: p. 265 – 268
2. Daisne, J., Duprez, T., Weynand, B., Lonneux, M., Hamoir, M., Reyckler, H., *et al.*, Tumour volume in pharyngolaryngeal squamous cell carcinoma: Comparison of CT, MRI and FDG PET and validation with surgical specimens. *Radiology*, 2004, 233 (1): p.93 – 100
3. Chen, S., Hsieh, T., Yen, K., Yang, S., Wang, Y., Chien, C., *et al.*, Interim FDG PET/CT for predicting the outcome in patients with head and neck cancer. *Laryngoscope* 2014; 124: p. 2732 – 2738

4. Brun, E., Kjellen, E., Tennvall, J., Ohlsson, T., Sandell, A., Perfekt, R., et al., FDG PET studies during treatment: Prediction of therapeutic outcome in head and neck squamous cell carcinoma. *Head Neck Oncol* 2002: p. 127 – 135
5. Hentschel, M., Appold, S., Schreiber, A., Abolmaali, N., Abramyyuk, A., Dorr, W., et al., Early FDG PET at 10 or 20Gy during chemoradiotherapy is prognostic for locoregional control and overall survival. *Eur J Nucl Med Mol I*, 2011 38: p. 1203 – 1211
6. Min, M., Lin, P., Lee, M., Shon, I., Lin, M., Forstner, D., et al., Prognostic value of 2 – [18] Fluoro-2-deoxy-D-glucose positron emission therapy-computerised tomography scans carried out during and after radiation therapy for head and neck cancer using visual therapy response interpretation criteria. *Clin Oncol* 2016 28: p. 393 – 401
7. Hunter, K.U., Schipper, M., Feng, F., Lyden, T., Haxer, M., Murdoch-Kinch, C., et al., Toxicities affecting quality of life after chemo-IMRT of oropharyngeal cancer: Prospective study of patient-reported, observer-rated, and objective outcomes. *Int J Radiat Oncol* 2013 85(4): p. 935 – 940
8. Guerro-Urbano, T., 18F-FDG-PET Guided Dose-Painting with Intensity Modulated Radiotherapy in Oropharyngeal Tumours (FiGaRO). <https://clinicaltrials.gov/ct2/show/NCT02953197>
9. Garibaldi, C., Ronchi, S., Cremonesi, M., Gilardi, L., Travaini, L., Ferrari, M., et al., Interim FDG PET/CT during chemoradiation therapy in the management of head and neck cancer patients: A systematic review. *Int J Radiat Oncol* 2017, 98; 3: p. 555 – 573
10. Ang, K., Harris, J., Wheeler, R., Weber, R., Rosenthal, D., Nguyen-Tan, P., et al., Human Papillomavirus and survival of patients with oropharyngeal cancer. *N Engl J Med*, 2010, 363:p. 24 - 35
11. Berthon, B., Evans, M., Marshall, C., Palaniappan, N., Cole, N., Jayaprakasam, V., et al., Head and neck target delineation using a novel PET automated segmentation algorithm. *Radiother Oncol* 2017, 122: p. 242 – 247
12. Berthon, B., Spezi, E., Galavis, P., Shepherd, T., Apte, A., Hatt, M., et al. 2017. Toward a standard for the evaluation of PET-Auto-Segmentation methods following the recommendations of AAPM task group No. 211: Requirements and implementation. *Medical Physics* 44(8): p. 4098 - 4111