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EDITORIAL COMMENTARY

Evaluation of response: is ^{18}F-FDG PET the answer?

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A recent paper from the University of Cologne [1] cast some doubts on the usefulness of ^{18}F-FDG PET in evaluating the response to chemotherapy of patients affected by oesophageal carcinoma. The authors reported on 55 patients recruited from a prospective trial on neoadjuvant radio-chemotherapy. Patients were studied before and at least 3 weeks after the completion of the treatment. Maximum and mean standardized uptake value (SUV) were measured using two different methods and compared with the histopathology assessment of tumour regression. Briefly, the authors reported that: (1) baseline SUV values were higher in responders; (2) after therapy, SUV was lower in responders; and (3) there were no significant differences between the SUV values of responders and those of non-responders. The conclusion of this paper is that ^{18}F-FDG PET is not a suitable tool for measuring response to radio-chemotherapy in oesophageal carcinoma.

Besides several differences in patient populations and technical aspects between studies, these conclusions cast some doubts on the reports by the Munich group, which assessed ^{18}F-FDG PET as a useful tool in evaluating response in patients with carcinoma of the oesophagogastric junction [2–4]. Levine reported results going in the same direction on patients affected by locally advanced oesophageal cancer [5]. Also, some reviews on the use of ^{18}F-FDG PET in oesophageal carcinoma [6, 7] concluded enthusiastically on the future use of ^{18}F-FDG PET not only for staging, but also for prognostic stratification and response evaluation.

It must be underlined that other authors [8–10] were already critical of the use of ^{18}F-FDG PET in making important clinical decisions on patient treatments.

Oesophageal carcinoma is only one of the solid tumours and lymphomas that are studied with ^{18}F-FDG PET in order to assess tumour response to radiation and chemotherapy treatments, which has been recently summarized [11] in a literature review.

Above and beyond the general enthusiasm which every new application of nuclear medicine procedures evokes in the nuclear medicine community, we have to be aware that controversial results may emerge in the medium and long term when limited series of patients are studied. Moreover, the large variety of pathologic types of tumours which may be studied must be carefully taken into consideration, as they have different biological behaviour, which ends up in a different capacity to take up a particular biological probe such as ^{18}F-FDG.

The first issued to be faced and solved is the standardization of the technical parameters. We, as nuclear medicine physicians, should do our best to establish some standard parameters to be employed when assessing solid tumours. These parameters are not required to have a general value for all tumour types, but must be determined for as many tumours as possible. This is not an easy task, but the consensus conference on Hodgkin's lymphoma [12] demonstrated that it is possible, and some efforts have already been made on the technical issues concerning multicentre trials [13]. General issues like ROI drawing and timing of acquisition must be the subject of harmonization pro-

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grammes in order to yield more reproducible results. In this setting, EANM and other European societies may play a leading role trying to get different scientists together.

Timing of response evaluation is also critical: standardization of protocols for both chemo-resistance and chemo-sensitivity assessment in different tumours should be strongly put forward, along with all the considerations related to the different chemotherapeutic agents used and the combined radiation along with chemotherapy regimens. Yet again, this is a tough task, particularly because protocols vary within different tumour types.

The hypothesis of metabolic stunning, proposed by Schmidt and co-workers [1] as a possible explanation of the poor results of ^{18}F-FDG PET in their study, reminds us that we have to be sure to be aware of what molecular imaging is showing us: ^{18}F-FDG uptake is not the imaging of the general metabolic activity of a tumour mass, but of particular processes related to glucose utilization by cancer cells. I understand this is common knowledge among nuclear medicine specialists, but this may not always be true for oncologists and surgeons.

These last considerations open the way to discussion on the use of radiopharmaceuticals other than ^{18}F-FDG. New probes are going to allow us to obtain better response assessments, showing images of specific processes inside the tumour mass, but we still have to establish which radiopharmaceutical should be used in a particular tumour at a particular stage. Therefore, standardization is going to be a future issue for non-^{18}F-FDG PET.

My personal view is that we should concentrate on the standardization of our procedures, to have them widely accepted by the medical community and to maximize their benefits to patient care.

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