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Applications of Molecular Imaging

Single-photon emission tomography (SPET) and positron emission tomography (PET) can be used to visualise molecular alterations in the living subject, allowing alterations in metabolic pathways to be seen, and facilitating early diagnosis and treatment of disease. FDG-PET has already been accepted as an essential tool in the staging and re-staging of many tumours. In this article, we summarise the role of molecular imaging in evaluating therapy in oncology.

PET-CT Increases Accuracy

FDG PET-CT is characterised by a high accuracy of neoplastic lesion detection. Along with diagnosis, staging, detection of relapse, restaging and follow-up, one of the main applications of PET-CT is the assessment of therapy response and treatment planning. In routine practice, structural and tumour volume changes are used to guide therapeutic strategies and to measure the disease-free and overall survival. However, tissue metabolism changes more rapidly than morphology, and changes in tumour FDG uptake may therefore predate alterations in volume. A typical example is malignant lymphomas, in which anatomical imaging after the completion of therapy often reveals residual masses that could represent either persistent disease or fibrotic tissue. Early identification of patients with residual disease resistant to radio- o chemotherapy can provide a basis for alternative treatment strategies and decrease the costs and side-effects of unsuccessful therapy. the metabolic imaging provided by FDG-PET offers functional tissue characterisation that is useful for assessing response to therapy. Accordingly, a number of studies have addressed the utility of FDG-PET for early response assessment during treatment of lymphomas.

Early Response Assessment

Patients with malignancies other than lymphoma can also benefit from early response assessment: appraisal of changes in tumour size by conventional imaging after several cycles of chemotherapy or radiotherapy can require a lot of time. Furthermore, response evaluation with morphological imaging methods does not correlate well with pathologic response, with changes at the cellular level or with tumour viability. In contrast, FDG-PET is able to detect cell behaviour and thus to identify potential residual tumour disease.

The use of FDG-PET as a surrogate tool for monitoring therapy response offers better patient care by individualising treatment and avoiding ineffective chemotherapy. various examples can be cited, including breast, lung and rectal cancer:

1. FDG-PET can predict response after a few cycles of standardised chemotherapy for metastatic breast cancer, and is also a valid method for prognostic stratification in patients with metastatic breast cancer treated with high-dose chemotherapy.
2. Patients with stage III or Iv non-small cell lung cancer are usually treated with chemotherapy or chemotherapy plus radiation therapy, but conventional imaging sometimes cannot reliably distinguish necrotic tumour or fibrotic scar from residual tumour tissue. By contrast, FDG-PET allows evaluation of the pathologic response soon after radical radiotherapy or chemoradiotherapy. In addition, in comparison with CT scan findings, FDG-PET results show a significantly closer association with overall survival.
3. Management of locally advanced rectal cancer includes treatment with chemotherapy plus radiation therapy before surgery. Several works in the literature have underlined the importance of FDG-PET in assessing neo-adjuvant therapy response owing to its intrinsic capability to recognise early changes in the metabolic behaviour of tumours.

Assessment of Response to Targeted Therapies

Another interesting application of PET is assessment of response to targeted therapies. Although many agents have failed, some drugs such as bevacizumab, trastuzumab, cetuximab, gefitinib and erlotinib have already become part of the standard of care for common tumours including breast, colorectal, ovarian, lung and head and neck cancers. Furthermore, imatinib has shown unsurpassed efficacy in the less widespread, but aggressive, chronic myeloid leukaemia and gastrointestinal stromal tumours. Until now, no predictor of response to targeted therapy has been validated, but the selection of patients likely to benefit from tyrosine kinase inhibitors is mandatory, for clinical and economic reasons.

These new drugs, which are mostly antibodies, are very expensive and their effectiveness is limited to a percentage of patients. Molecular imaging is a novel and potentially valuable tool to identify patients who can benefit from these treatments and to evaluate the response to therapy in those patients selected for treatment. As already mentioned, PET is able to provide information about tumour metabolism, such as glucose consumption or proliferative activity, which can be used as an early predictor of therapy response. Moreover, some centres are trying to assess the in vivo distribution of these target molecules and the response or resistance to targeted agents using radiolabelled tyrosine kinase inhibitors or monoclonal antibodies.

PET Informs Decision-Making

Like other imaging exams, PET can be used to inform decision- making, e.g. whether a surgical approach is advisable, which intervention will be most appropriate and whether advanced therapies are feasible. In addition, molecular imaging could be employed to personalise therapy by guiding radiation therapy planning (the most significant example is intensity-modulated radiation therapy) and improving definition of tumour target volumes. Although CT remains the gold standard for depicting anatomy for the purpose of target volume definition and dose calculation, PET-CT could help with respect to the dose constraints for organs at risk, if the hypermetabolic component is smaller than the morphological appearance of the tumour, reducing the gross tumour volume. Further, PET could permit the inclusion of FDG-avid, but non-enlarged, lymph nodes within the field of treatment or could modify TNM staging, resulting in a shift in treatment modality from curative to palliative.

Conclusions

In conclusion, PET is an exceptional non-invasive tool, which can provide qualitative and quantitative in vivo assessment of biological processes. PET-CT is currently a very accurate method for diagnosis, staging, post-treatment evaluation, restaging and follow-up of many tumours. The impact of PET imaging on cancer therapy management is significant and many studies have considered its role in relation to radiotherapy, chemotherapy and appraisal of new drugs. Steady developments in cancer biology, radiochemistry and physics will provide rich soil for the further growth of molecular imaging.

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