

PET-CT: Imaging for Future Radiotherapy

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The cancer cell differs in subtle ways from the normal cell. These differences are exploited by the biological techniques of Nuclear Medicine to image cancer and distinguish cancer from non malignant tumours and from normal tissues. The different components on the cancer cell surface are in part due to up-regulation of receptors and the exposure of new antigens through the architectural disruption of the tissue by the malignant process. The increasing use of radiolabelled peptides and monoclonal antibodies in diagnosis and therapy demonstrate this. One of the most powerful techniques is Positron Emission Tomography, PET, which makes use of the cancer cells extra need for more food than the normal cell in particular more sugar glucose. The cancer cell has developed a more efficient ways of taking up a greater amount of sugar from the blood than most normal cells. Fluoro-DeoxyGlucose, FDG, is similar to glucose in that it is taken up rapidly by the cancer cell, but unlike glucose it is not digested by the cancer cell. FDG, containing F-18, produced in a Cyclotron, has to be made on site or delivered as FDG to the PET centre because of its short half-life of 110 minutes. This means that appointments for patients have to be scheduled very tightly and one is not able to make allowances for any delays in a patient's arrival for the study.

The PET system is about 100 times more sensitive than the gamma camera. As well as detecting cancer at its primary site in the lung, colon, head and neck or breast, it is also able to detect if the cancer has spread to bone or liver and or to lymph nodes close by, a problem for Xray-CT and MRI, if the nodes are of normal size. It is able to detect the cancer cells that are active in a tumour, whose size may be less than that apparent on CT. Alternatively cancer may be larger than its apparent radiological size due to the spread its fingers of cells into tissues. These can be seen by radiolabelled peptides and monoclonal antibodies due to their high amplification factor (up to 10,000 binding sites per cell) and may be seen by PET (up-regulation of the Glucose transporter by up to a factor of five and of the Hexokinase enzyme by a similar factor), but cannot be seen by CT or MRI. The physical techniques of radiology require a mass to detect disease.

The biological approach based on FDG has some disadvantages such as increased uptake in fractures and some infections since inflammatory cells also eat glucose avidly. CT can detect fractures and sites of inflammation and help to avoid making mistakes in the interpretation of PET studies. The location of the sites of focal uptake of PET FDG in soft tissues may be difficult to appreciate. When co-

located by co-registration and fusion to CT all becomes clear. Conversely focal uptake of PET FDG may aid the interpretation of a difficult CT scan by highlighting the abnormality on fusion. Thus the combination of the Biological and the Physical approach to cancer improves the sensitivity of CT (such as detecting cancer in normal sized lymph nodes) and improves the localisation and specificity of PET imaging (avoiding misinterpreting inflammatory disease). The evaluation of the effects of chemotherapy through serial imaging of the patient is also improved as the biological response usually precedes the physical change. This combination of PET and CT may be by using a dual imaging system or by multimodality software fusion imaging. The advantage of a dual imaging system is that the throughput of patients can be almost doubled as compared to PET alone since the time consuming attenuation correction procedure is avoided. It is substituted by a one minute CT based attenuation correction. Although the lower energy of the CT does not match that of a 511 Kev positron emitter, a bi-linear transform above and below zero Hounsfield numbers compensates for this. PET-CT and multimodality fusion between any set of PET, CT, SPECT and MRI image volume data, these are the state of the art imaging of cancer.

The combined biological and physical representation of the site and extent of cancer can be transferred and co-registered by software fusion with the radiotherapy plan. This makes the plan more accurate so the radiation therapy can be directed with greater intensity to the most active or the most radio-resistant areas and be better at avoiding normal tissues. This is through Intensity Modulated Radiation Therapy, IMRT. For example the introduction of new PET agent F-18-Miso for hypoxia enables IMRT on the basis of this imaging, to deliver a higher dose to the radio-resistant hypoxic volume within the tumour. The most advanced commercial IMRT system, which is called Tomotherapy, contains opposite to the therapy source a CT scanner, to which PET-CT images may be fused. It has, unlike the conventional Linear Accelerator, a helical therapy track, similar to the change from CT to spiral CT. These advanced systems are beginning to replace the old Linear Accelerators. The combination of a new PET-CT system, image volume data fusion and Tomotherapy will give the most advanced and accurate therapy planning and treatment for cancer.

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