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Application of Positron Emission Tomography in Head and Neck Cancer - An Overview

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Abstract: **High resolution cross sectional imaging dramatically improves the diagnosis and therapy of oncological patients primarily concerning the exact initial staging, differential diagnosis of recurrent tumours and therapy management. Positron emission tomography (PET) is a quantitative, functional diagnostic imaging modality using compounds labelled with positron-emitting radioisotopes to measure cell metabolism for both initial tumor staging and detection of tumour recurrence with a high diagnostic accuracy. Combined PET/CT is a unique imaging modality that permits anatomic and functional imaging on a single scan in comparison with PET alone. Nearly a decade after introduction of PET/CT, clinical combined PET/magnetic resonance imaging (PET/MRI) systems have become available commercially. PET/MRI system combines the unique features of MRI including excellent soft tissue contrast. Thus this paper portrays the usefulness of PET along with its recent advances in head and neck cancers.**

Keywords: **PET scan, FDG, Metastasis.**

I. INTRODUCTION

Oncological imaging plays an important role in head and neck cancers in the rapidly changing environment, diagnostic imaging should constantly head in the direction of more accurate diagnosis. The objective of diagnostic imaging is to provide information for the professional to be able to diagnose a condition, to provide accurate pre-treatment staging and to monitor the response to therapy. Positron Emission Tomography (PET) is a three-dimensional diagnostic imaging technology in nuclear medicine measuring physiological information necessary for the diagnosis of tumours based on increased regional metabolism .[1,10] PET provides new horizons in imaging and gives excellent information on tissue function of both normal and other pathological processes.

One of the most commonly used tracer for oncological examination is Fluorodeoxyglucose F18 (FDG) a glucose analog . FDG is transported and phosphorylated like glucose, but then trapped in the cells. [10]

History

- 1950- David E. Kuhl, Luke Chapman and Roy Edwards Introduced the concept of Emission and Transmission Tomography.[2,3]
- 1961, James Robertson and his associates built the first single-plane PET scan, nicknamed the ‘ head-shrinker.’[4]
- 1970-First Application of PC-I in tomographic mode.
- 1970s- Tatsuo Ido at the Brookhaven National Laboratory- first to describe the synthesis of 18F-FDG.
- 1972- James Robertson and Zang –Hee Cho were the first to propose a ring system, the current shape of PET.

In oncology, PET can be used in various modalities like tumour detection and differential diagnosis of benign and malignant tumours, tumour staging and prognostic stratification, evaluation of treatment response, restaging, detection of recurrent cancer, radiation treatment planning [5] and for the diagnosis of viable tumour tissue following chemotherapy.[10]

Furthermore, PET can have different places in the diagnostic pathway at the beginning of the pathway as a triage, at the end of the pathway as an add-on, or as a replacement for an existing diagnostic procedure in the pathway. [1] The sensitivity of PET FDG is dependent on the type and the size of the tumor.

II. RADIONUCLIDES AND RADIOTRACERS

Radionuclides used in PET scanning are typically isotopes with short half-lives such as carbon-11 (~20 min), nitrogen-13 (~10 min), oxygen-15 (~2 min), fluorine-18 (~110 min), or rubidum-82(~1.27 min).[10]

These radionuclides are incorporated either into compounds normally used by the body such as glucose (or glucose analogues), water or ammonia or into molecules that bind to receptors or other sites of drug action. Such labelled compounds are known as radiotracers.18F-FDG is an analog of glucose and as such ,a versatile radiopharmaceutical with major application in oncology.[9] FDG is now established as an important milestone in the evaluation of patients with variety of disorders. Due to the short half-lives of most positron-emitting radioisotopes, radiotracers have traditionally been produced using a cyclotron in close proximity to the PET imaging facility. [10]

Radiopharmaceuticals for Pet Studies

Tissue Perfusion

15 O-Water, 13N-ammonia, 62-Cu-pyruvaldehyde –bis –(N-4-methylthiosemicarbazone)

Transport and metabolism

11C-methionine,11C-thymidine,11C-tyrosine.18F-tyrosine, 13N-glutamate,

18F-deoxyuridine,18F-uridine,8-F-deoxyglucose

Cytostatic agents

13N-cisplatin, 18F-flurouracil .[10]

Indications

- In Oncology, PET imaging of tumours is performed to gain qualitative and quantitative data.
- To know Quantification of tissue perfusion.
- Evaluation of tumor metabolism.
- Transport of Amino acids.
- Tracing of radiolabeled cytostatic agents.
- Tumour detection and in differential diagnosis of benign and malignant tumours.
- Tumour staging.
- Prognostic stratification.
- Evaluation of treatment response.
- Restaging.
- Detection of recurrent cancer.
- Radiation treatment planning.[6]

III. PRINCIPLE OF PET SCAN

To conduct the scan, a short lived radioactive tracer isotope is injected. The tracer is chemically incorporated in to a biologically active molecule, after the waiting period of one hour. The active molecule becomes concentrated in tissues of interest then the subject is placed in the imaging scanner. As the radioisotope undergoes positron emission decay also known as positive beta decay, it emits a positron an antiparticle of the electron with opposite charge.

The emitted positron travels in tissue for a short distance typically less than 1 mm, but dependent on the isotope, during which time it loses kinetic energy, until it decelerates to a point where it can interact with an electron. The encounter annihilates both electron and positron, producing a pair of annihilation (gamma) photons moving in approximately opposite directions. These high energy photons 511 Kev have a much greater penetrating abilty. These are detected when they reach a scintillator in the scanning device, creating a burst of light which is detected by photomultiplier tubes or silicon avalanche photodiodes (Si APD).[6]

Advantages: It has the potential to yield physiological and functional Information necessary for the diagnosis of tumors, whole body screening with a single session, reduces ineffective treatments and costs, for the precise delineation of the tumor volume and provides prognostic information.[6,10]

Disadvantages: Limitation with respect to lesion localization [5], time consuming procedure, allergy to radiotracer, radioactive substance decays quickly and is effective only for a short period of time; resolution may not be as high as with other imaging technique, images are relatively noisy, false positive results. Diabetic patients or patients who have eaten within few hours can be adversely affected because of altered blood sugar, artifacts may be induced by Metallic implants and Imaging cost is expensive.6, 9.

However the advent of PET/CT now overcomes these limitations and permits the evaluation of both metabolic and anatomic characteristics of disease.

"Fusion imaging", always a promising "new" methodology has been kick-started by the combined PET/CT concept .[6] The most recent innovation in PET scanners is the dual-modality PET/CT.[7] By combining radiological (CT) and nuclear medicine (PET) imaging modalities, it is possible to add anatomical to functional information.[11,12.]

IV. COMBINATION OF PET WITH CT

PET/CT is now established as a imaging modality of choice in many clinical conditions, particularly in oncology. This combined technique improves diagnostic accuracy in comparision with PET alone. The PET acquisition typically occurs immediately after the CT acquisition to minimize the effects of patient motion. After reconstruction, the high resolution, anatomical images are overlaid with the functional images. Such image fusion has been shown to improve the diagnostic reliability.[11]

Indications

1. It permits the evaluation of both metabolic and anatomic characteristics of disease.

2. In detecting unknown primary tumour.

3. In detecting residual tumour.

4. In radiation treatment planning (IMRT)[6]

Limitations of PET/CT

1. T staging-Small T1 tumors, Superficial spread, perineural spread,

2. N staging- Nodal micrometastases, inflammatory lymph nodes, Necrotic lymph nodes.

3. Higher radiation dose with CT.[6]

Given the success that PET/CT imaging has experienced, however it is not surprising that considerable effort has been invested to develop hybrid PET/MRI devices. PET/MRI combines the unique features of MRI including excellent soft tissue contrast, diffusion-weighted imaging, dynamic contrast-enhanced imaging and other specialized sequences as well as MR spectroscopy with the quantitative physiologic information that is provided by PET.[8]

PET/MRI

The PET/MRI systems is best suited for clinical situations that are disease specific, organ specific related to diseases of the children or in those patients undergoing repeated imaging for whom cumulative radiation dose must be kept as low as reasonably achievable. PET/MRI also offers interesting opportunities for use of dual modality probes, clinic workflow,

optimized scan protocols, artifact handling, regulatory requirements, risks and safety considerations, training and credentialing needs for image interpretation, comparative effectiveness, cost-utility .[8]

Nevertheless PET/MRI provides unparalleled structural, metabolic, and functional information which can significantly impact diagnostic evaluation and affect clinical decision-making, patient management and potentially patient outcome. It may also enhance patient convenience by providing a "one-stop shop" diagnostic imaging work-up, reducing patient anxiety, total scan time, and recalls for repeat scanning. [8]

Indications:

- Assesment of response to gene therapy.
- Evaluation to stem cell delivery.
- Anatomical information in a relatively small compartment.
- For targeted biopsy.
- Hepatic metastasis.[10]

Advantages:

- Excellent soft tissue contrast and high accuracy.
- Reduced scan time by 50%.
- Patient comfort and convenience.[10]

V. COMPETITIVE ADVANTAGES OF PET/MRI OVER PET/CT

1. The unique features of MRI provide more robust imaging evaluation in certain clinical settings.
2. In clinical situations that are disease-specific, organ-specific, related to diseases of the children or in those patients undergoing repeated imaging for which cumulative radiation dose must be kept as low as reasonably achievable.
3. PET/MRI also offers interesting opportunities for use of dual modality probes.
4. It shows detailed views of moving organs or structures with higher anatomical variation.[8]

Future

PET/CT and PET/MRI are superior techniques that have grown over the years as understanding of this imaging modality has improved, including its advantages and limitations in defining and characterizing malignant disease and initial use in staging cancer. However, the changing demand to evaluate tumor angiogenesis, tumor hypoxia, tumor cell proliferation and tumor receptors, has led to the development of other specific tracers, which will get greater clinical acceptance with time.

VI. CONCLUSION

PET scanning is increasingly used because of its sensitivity for assessing early metabolic changes. Hybrid PET /CT has promoted the field of molecular imaging in head and neck cancer.PET/CT is accurate, quick and has become an indispensable modality in clinical imaging particularly in the management of onchologic patients . The long-term implications of simultaneous PET–MRI in oncology is more speculative as it relies on "emerging" or "future" applications requiring rigorous spatial and temporal co-registration of PET and MRI physiological, cellular and molecular data but it still offers interesting opportunities for use of dual modality probes in both research and clinical arenas. Multimodality imaging has made great strides in the imaging evaluation of patients with a variety of diseases.

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