

New Probe Sharpens Focus of Brain Cancer Therapy

The CRC for Biomedical Imaging Development Ltd's collaborative approach to imaging research is expediting the Australian development of fluoro ethyl tyrosine (FET) as a positron emission tomography (PET) tracer for brain tumour treatment planning.

Clinical Context – PET Imaging of Brain Tumours

Primary brain tumours are relatively common cancers, and both the tumours and the current treatments damage normal brain tissues, often resulting in major disability. Many brain tumours are highly aggressive and patients with high-grade tumours usually survive less than two years despite the very best treatment.

New ways to improve existing treatments like surgery, radiotherapy and chemotherapy (as well as new therapies that more specifically target the genetic and metabolic abnormalities causing these tumours) are constantly being devised. However, treatment can still be impaired because of limitations in defining the exact extent of the tumour, and in showing early on if therapy is having the desired effect.

Unlike computed tomography (CT) and magnetic resonance imaging (MRI) which display the structure of the body, positron emission tomography (PET) scanning makes the body's metabolic activity visible when short-lived radioactive substances known as radiotracers are introduced. Since the mid 1990's, PET has revolutionised cancer management by demonstrating differences in glucose metabolism between cancers and normal body tissues using a radiotracer known as fluoro deoxy glucose (FDG). PET using FDG has resulted in improved treatment for cancer patients by frequently providing diagnostic information that cannot be obtained as easily, or at all, using other techniques.

Contrast enhanced MRI is currently the major method for planning and monitoring brain tumour therapy. However,

in many cases it is difficult to decide if MRI abnormalities are due to scar tissue, tumour recurrence or the effect of radiation therapy, and in these patients metabolic imaging with FDG PET may be used to better guide treatment. Both imaging techniques are currently funded in Australia through Medicare.

The evaluation of brain tumours with FDG was one of the first applications of this radiotracer in cancer patients. However, researchers and clinicians are well aware of limitations in the use of FDG, such as the wide variability in the rate of FDG accumulation which is related closely to aggressiveness of the cancer. Also, the brain itself uses glucose as its preferred fuel so there is high uptake of FDG in normally-functioning brain tissues. These factors can complicate evaluation of low-grade brain tumours that require less aggressive treatment, and can delay detection of high-grade tumour recurrence after treatment.

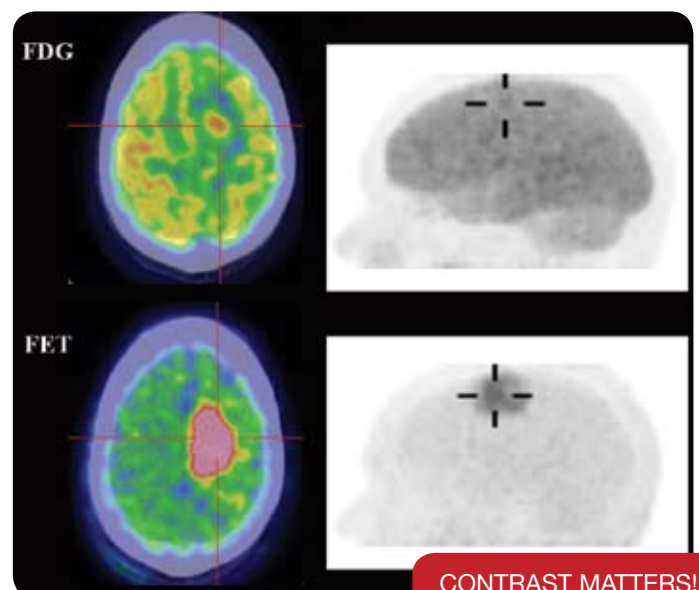
New Results - Amino Acid Radiotracers

The CRC for Biomedical Imaging Development Ltd (CRCBID) is researching the use of another type of metabolic probe for brain tumours, seeking to remove some of the limitations encountered when planning treatment using current imaging techniques. It has been known for many years that radio-labelled amino acids can determine the location of active brain tumour cells with a high degree of accuracy. This accuracy results because most tumours require much larger amounts of amino acids (the building blocks of protein) to support their disordered growth when compared to normal brain.

New PET Tracer Amino Acid transport- FET

Preliminary Peter MacCallum Cancer Centre data on 21 brain tumour patients with FDG & FET PET

- FET sensitivity 93%, specificity 100%, accuracy 96%.
- FDG sensitivity 27%, specificity 90%, accuracy 52%.



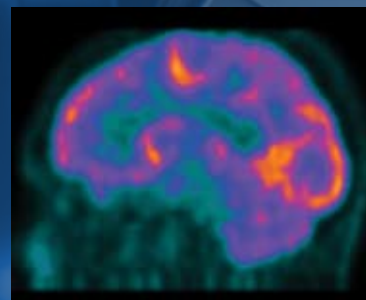
CONTRAST MATTERS!

To date, most of the radio-labelled amino acids have had limitations that prevented their widespread clinical application. The major limitation is that they were radio-labelled with Carbon-11 isotope, which has a half-life of only 20 minutes, and does not lend itself to transport. Where labelling has been performed with longer half-life isotopes such as Fluorine-18, the production yields have not been high enough to enable distribution.

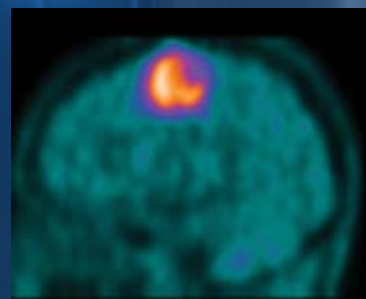
CRCBID has provided resources and infrastructure to study one such Fluorine-18 radio-labelled amino acid called, fluoro ethyl tyrosine or FET. In a pilot trial, conducted in patients with suspected and proven brain tumours at the Peter MacCallum Cancer Centre, standard PET scanning using FDG provided the correct treatment information on 13 of 25 occasions. In these patients, who participated in the trial because of difficulties in deciding the best treatment approach from their MRI scans, FET PET provided the correct information for treatment planning on 24 of 25 occasions.

Next Steps – Multi-Centre Study

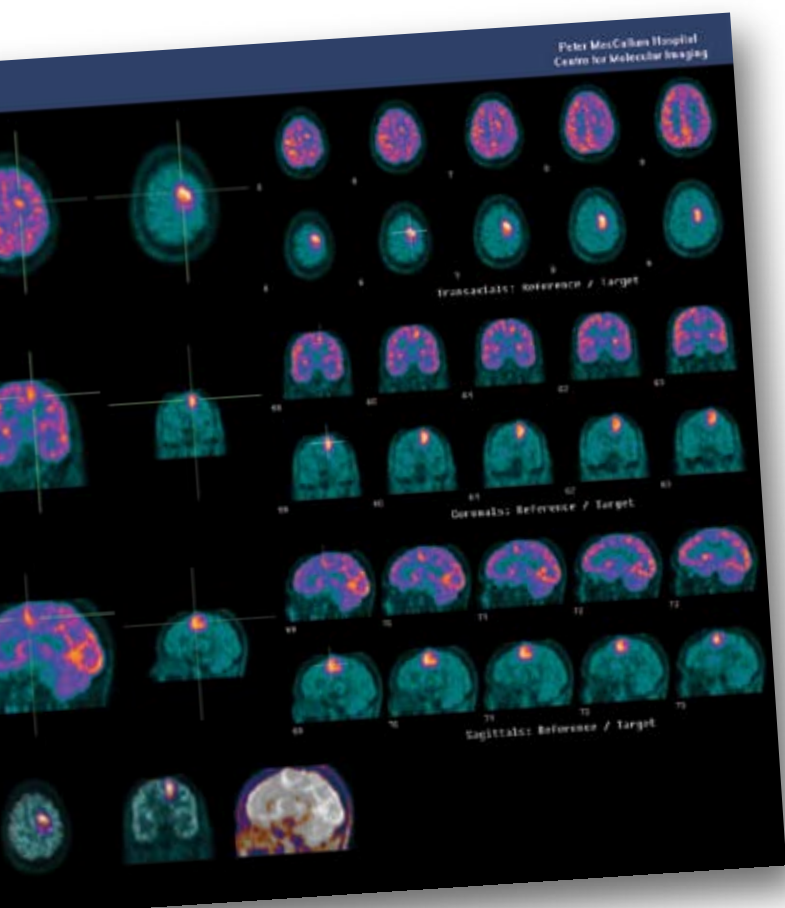
The promising results of this pilot study of FET PET scanning agree closely with results from international research institutions, and so CRCBID is moving to the next phase in its research pathway for FET.



The exact location and extent of the tumour was difficult to appreciate on an MRI scan (not shown), and the FDG PET scan done several days earlier



A low grade brain tumour that has recurred after radiotherapy is shown with great contrast on the PET scan using FET



CRCBID researchers at ANSTO and Peter MacCallum Cancer Centre have been refining the FET synthesis protocols to allow more efficient production, and thus more cost effective supply of the radiotracer. This innovation improves the efficiency of FET synthesis, making it feasible to supply PET facilities around Australia. FET will be produced in the Melbourne manufacturing laboratory of the CRCBID participant, Cyclotek. Work is well advanced on good manufacturing practice (GMP) production and certification of FET.

This manufacturing initiative will enable the many PET facilities that do not have onsite radiotracer production capability to participate in further research. To this end, new research protocols are being finalised that will allow the clinical utility of FET PET scanning to be validated in larger groups of patients. This concerted approach will facilitate rapid evaluation of FET scanning for planning brain tumour treatment. CRCBID is seeking to engage with PET centres around Australia, to allow additional data to be gathered regarding the efficacy of FET through a multi-centre study.

This work has been undertaken by the Cooperative Research Centre for Biomedical Imaging Development Ltd (CRCBID), established and supported under the Australian Government's Cooperative Research Centres Programme. CRCBID partners working on this project include Peter MacCallum Cancer Centre, ANSTO and local radiopharmaceutical manufacturer Cyclotek (Aust) Pty Ltd.

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