

CRC BID provides a Clearer Picture of Epilepsy

¹⁸F labelled flumazenil shows promise in imaging of epilepsy

Epilepsy patients may enjoy better health outcomes if trials of a novel PET radiotracer developed by the Cooperative Research Centre for Biomedical Imaging Development Ltd (CRCBID) support the promising early results.

Flumazenil is a drug which targets GABA receptors in the brain. It is believed that there is a deficit of these receptors in the epileptic foci of epilepsy patients. Results from pilot studies of ¹⁸F-Flumazenil (¹⁸FMZ) suggest that Positron Emission Tomography (PET) imaging using this radiotracer accurately pinpoint this deficit and therefore localise the foci.

The clearer picture provided by ¹⁸FMZ PET imaging will be of particular help to patients whose seizure focus cannot be identified with Magnetic Resonance Imaging (MRI). Furthermore, in these patients ¹⁸FMZ PET can provide far more detailed information compared with traditional PET scans using ¹⁸Fluoro deoxy glucose, or FDG. This information could result in improved surgical planning and, potentially, less invasive procedures.

Chief investigator, Professor Terry O'Brien from the Royal Melbourne Hospital, says the early results are encouraging as they show real potential to improve the lives of people with epilepsy, who often suffer significant medical, psychological and economic difficulties as a result of their disorder.

"In about a third of people with epilepsy, the condition either cannot be controlled with medication or the side effects of the medication are simply unacceptable for the patient," Professor O'Brien explains.

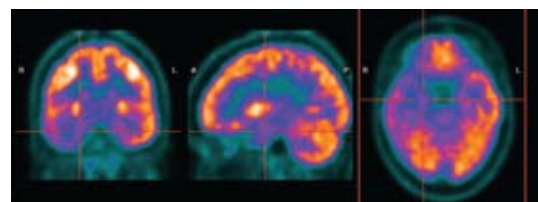
"For these people, neurological surgery can be a very effective treatment, yet it is currently only an option for a small number of people due to difficulties in localising the source of the seizure.

"This research is extremely important for these medication-resistant patients as ¹⁸FMZ may solve the issue for a significant number of them by allowing us to see exactly where the seizure onset is," Professor O'Brien says.

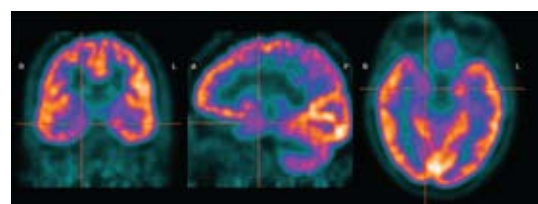
"With that clearer picture, doctors will be able to more confidently predict success with surgery and ultimately improve the lives of their patients."

Key Benefits of ¹⁸FMZ in Imaging for Epilepsy Patients

- **Clearly identifies location of seizure focus**
- **More precisely identifies and describes area of abnormality**
- **Easier, more accurate image analysis**
- **Improved surgical planning**
- **More targeted, less invasive surgery**
- **Feasible for widespread use in clinical practice**



Epilepsy patient FDG Scan



Epilepsy patient FMZ Scan

Pilot Study Delivers Positive Early Results

The human pilot study of ^{18}F FMZ is being conducted by the Royal Melbourne Hospital, Peter MacCallum Cancer Centre and CRC BID. This work builds upon pre-clinical research, recently published by CRCBID, which demonstrated that ^{18}F FMZ has high level of receptor specific uptake in an animal (rat) epilepsy model.

In the pilot study, human volunteers without disease are being imaged with ^{18}F FMZ PET at the Peter MacCallum Cancer Centre, along with epilepsy patients planned for surgery because of well defined abnormalities detected on routine MRI and ^{18}F Fluoro deoxy glucose (FDG) PET scans.

After this pilot study, CRCBID may sponsor clinical trials that will further evaluate the efficacy of ^{18}F FMZ in comparison to other methods. Such a trial would evaluate the performance of ^{18}F FMZ –PET against both MRI, which is not able to identify the seizure focus in a significant number of patients, and ^{18}F FDG PET which can predict a successful surgical result in many of these MRI negative patients, but often shows a relatively wide area of abnormality – much wider than that which needs to be removed for effective seizure control.

The early results indicate that ^{18}F FMZ produces a clearer and more detailed picture than these other options, potentially enabling more targeted, less invasive surgery, and therefore delivering better outcomes for the patient.

FMZ Gives a Clearer Picture

Previous work has indicated that FMZ may be a useful diagnostic radiotracer, but this work used a radiotracer with a short half-life.

“To date, investigators have used flumazenil labelled with the PET isotope carbon (^{11}C) which has a 20 minute half life – a very short time, making transport and multi-centre trials virtually impossible,” explain ANSTO project leader for CRCBID, Dr Andrew Katsifis.

“This practical limitation confined ^{11}C -FMZ PET scanning for epilepsy patients to the few research centres that have sophisticated radiotracer synthetic capabilities together with an onsite cyclotron for supply of ^{11}C .

“The challenge was to label this molecule with an atom of radioactive ^{18}F Fluorine rather than ^{11}C . Once achieved, we then optimised and automated the synthesis of ^{18}F FMZ for clinical use,” he said.

“The resulting ^{18}F FMZ has a significantly longer radioactive half-life of 109 minutes, enabling, for the first time, the possibility of more widespread clinical application of this agent in the care of epilepsy patients,” Dr Katsifis explains.

This outcome will not only be a welcome development for people with epilepsy, and those who manage their treatment and care, but may also be positive news for a number of other common brain conditions.

“ ^{18}F FMZ also has the potential to apply to the investigation of addiction, depression, dementia, neurotrauma and stroke” says Professor Rod Hicks, CRCBID’s Radiopharmaceutical Stream Leader, “and the CRCBID research team is exploring options to investigate some of these other conditions.”

CRC BID aims to develop and commercialise new radiotracers for clinical use to pinpoint disease to ultimately improve treatment and patient care. The CRC is founded on a collaborative arrangement between research and industry participants established and supported under the Australian Governments Cooperative Research Centres Programme. The participants include the Australian Nuclear Science and Technology Organisation, The Peter MacCallum Cancer Centre, The Garvan Institute of Medical Research, Monash University, Cyclotek, GE Healthcare and Berthold.



Cooperative Research Centres



A Clearer Picture of Health

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