

Microscopy & Imaging

Tackling Dementia with Cutting-Edge Brain Imaging Technology

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It's one of the sad truths about dementia that by the time symptoms start to appear, it's usually too late to reverse them. And as dementia grows into one of our most pressing public health issues, researchers urgently need the tools to help them detect the disorder in its earliest stages and develop effective treatments.

One of those tools – and one of the most valuable in the fight against dementia – is brain imaging technology. From detecting the build-up of toxic proteins in the brain, to learning more about how dementia takes hold at a cellular level, the deployment of magnetic resonance imaging (MRI) and positron emission tomography (PET) technologies can give scientists important insights into the development, progression and potential treatment of dementia.



PET MR Scanner - credit University of Manchester

Critical to this research will be new network of state-of-the-art PET-MR scanners established by Dementias Platform UK (DPUK), a public-private partnership funded by the UK's Medical Research Council that aims to speed up scientific advances in what has been a particularly stubborn area of research. The network of seven scanners, manufactured by Siemens and GE Healthcare and based at universities and hospitals across the UK, will build on existing brain imaging activities carried out under the auspices of DPUK.

Dr Julian Matthews, of the University of Manchester, is joint lead of the PET-MR project's harmonisation phase and chief investigator of a clinical study that will ensure these high-specification scanners are properly calibrated and providing consistent imaging results between sites. Dr Matthews said: "PET-MR is a new scanning technology which enables simultaneous acquisition of PET and MR data within a common scanning field of view, with minimal interference between the two imaging modalities. In the UK there are seven such scanners, which are all part of the DPUK network, with an eighth scanner due to complete installation in Sheffield in the near future.

"We envisage that this unique national network will provide accurate imaging biomarkers and thus enable highly effective clinical studies in the UK of new therapeutics in neurodegenerative disease, including - but not limited to - dementia. Additionally, although not yet established, this equipment has many potential benefits, such as reducing the scanning burden to patients who require both PET and MRI scans as part of their care, as well as being used in research where the clinical state of patients can change between scanning sessions."

Given PET-MR scanners are relatively new technology, their use in dementia research is not yet well understood. The harmonisation project run by Dr Matthews and colleagues will reduce the potential for variation between imaging sites and measure - in the words of the study protocol - the "repeatability and reproducibility" of testing across the UK as part of multi-centre DPUK cohort studies. Dr Matthews said: "Specifically, we need to understand the factors that result in variability in the measurements that we are making. Consequently, before using them in multi-centre clinical trials we need to harmonise how we use these scanners and once harmonised, measure the variability of the measurements.

"We have already conducted measurements on the scanners within the network using standard filled objects called 'phantoms'. These results were presented at the recent IEEE medical imaging conference in Manchester. This exercise enables us to qualify all seven scanners in the network and have measurements on the similarities and differences in the performance of the scanners.

"However, such phantom measurements are insufficient, as variations in human anatomy can affect the accuracy and precision of the measurements. To address this we plan to conduct a test-retest study where healthy elderly participants will have scans on two occasions. Some of the participants will be scanned twice at the same scanning site, but others will travel to a site with similar scanning equipment or, alternatively, with different scanning equipment. This will enable us to measure variability in these measurements and understand how much of the variability is due to the equipment being used, or the use of similar equipment at different sites," Dr Matthews added.

Once the harmonisation study has been completed and the scanners deemed ready for deployment in clinical research, it is envisaged that the network will provide huge opportunities for delivering critical advances in dementia research. The homogenised network will enable unprecedented longitudinal population-based studies - much larger than previously possible - which, in combination with genetics, proteomics and clinical phenotyping, are expected to identify the pathophysiological mechanisms that determine disease initiation and progression.

It will also provide a platform for large-scale clinical trials to modify disease progression and – researchers hope – ultimately even prevent the progression of mild cognitive deficits to dementia. Thus, the network of PET-MR scanners has enormous potential impact for the improvement of public health and reduction of the huge socio-economic costs associated with dementia.

The PET-MR scanners are part of DPUK's broader imaging network, led by Professor Franklin Aigbirhio of the University of Cambridge. The network arose, he commented, from the recognition that advanced imaging has a central role to play in dementia research – and the feeling that a networked approach to imaging technology would greatly enhance the impact of the major research programmes already being run by a number of individual universities.



Dr Julian Matthews



PET MR Team - credit University of Manchester

Professor Aigbirhio said: "In particular, we believed the network approach would bring together a larger critical mass of the range of skills needed for this type of interdisciplinary research, enhancing the sharing of ideas, technologies and best practice and establishing standard procedures across centres.

"Our overarching aim is to create a world-leading environment for applying advanced imaging to support experimental medicine and clinical trials in dementia research. Our objectives include sharing expertise and resources to enable more rapid uptake and application of technical advances - for example, novel radiopharmaceuticals or improved image analysis algorithms - as well as the establishment of common operating procedures and analyses for measuring outcomes, which will create an environment for rapid implementation of the highest-quality experimental medicine.

"We also aim to be a single point of access for a national imaging platform that will foster joint academic and industry dementia research towards the development of novel drugs."

Imaging brings unique insights to the field of dementia research that cannot be achieved through other means. Those insights include the ability to visualise and quantify directly in patients the biochemical and structural changes in the brain that are associated with dementia - for example, detecting the presence of toxic proteins in the brain before any symptoms occur.

And while combined PET-MR scanning for dementia research is still in its infancy as a technique, imaging technology more broadly is already achieving good results in the field. Professor Aigbirhio added: "We are gaining major insights into assessing the biodistribution and impact of the key toxic proteins associated with dementia: beta-amyloid and tau. Understanding how these proteins develop and vary in different parts of the brain will help us towards improved and earlier diagnosis of the different forms of dementia, as well as understanding their disease mechanisms.

"Brain imaging technology will also give us greater insights into other components of the dementia disorders, including the increase in inflammation and the effect on synapses. All of these are potential targets for developing vital new drugs for the treatment of dementia."

For more information on Dementias Platform UK, including the imaging network and PET-MR scanners, visit www.dementiasplatform.uk



Professor Franklin Aigbirhio - credit Alex Tyler



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