CHIEF SCIENTIST OFFICE

CODE: TCS/21/03

RESEARCH PROJECT BRIEFING

Early Detection Of Alzheimer's Disease With GlucoCEST MRI: A Feasibility Study.

AIMS

Alzheimer's disease causes gradual problems with memory, thinking, and daily life. Treatments can help manage symptoms, but they cannot cure the disease. In Alzheimer's disease, brain cells become less able to use glucose (sugar) for energy. This can be measured using a scan called FDG PET scan (fluorodeoxyglucose Positron Emission Tomography), which involves injecting a small amount of radioactive sugar. However, PET scans are expensive and prioritised for cancer patients in the NHS. People with Alzheimer's disease are usually assessed using memory and blood tests, which can sometimes be unclear and may delay diagnosis. Brain magnetic resonance imaging (MRI) scans can show brain shrinkage which is linked to Alzheimer's disease, but this is not always accurate either.

The aim of this study was to investigate a new MRI technique that measures brain glucose in a similar way to an FDG-PET scan but using a standard hospital MRI scanner instead. We compared this new MRI method to a PET scan in people with Alzheimer's disease to see how closely the two approaches agree. We also compared people with Alzheimer's disease to healthy individuals of the same age and sex, to see whether there were differences between the two groups.

KEY FINDINGS

- Recruitment of participants, including 18 patients with Alzheimer's disease and 18 people without memory problems, was achievable enabling successful data collection. All participants tolerated the glucose drink without adverse effects.
- PET images in patients with Alzheimer's disease showed the expected reduction in glucose signal levels in brain areas associated with Alzheimer's disease.
- The MRI-based method (glucoCEST) showed relatively uniform signal across the brain and did not replicate the typical areas of reduced glucose seen on PET.
- We did not observe differences in MRI images between patients with Alzheimer's disease and healthy individuals.
- We did not observe differences in MRI images before and after drinking glucose in patients with Alzheimer's disease.
- The MRI-based method (glucoCEST) was not sensitive enough to detect the same brain changes seen with PET scans. This means the MRI technique needs further improvement before it can detect Alzheimer's disease in the same way as PET scans do.

WHAT DID THE STUDY INVOLVE?

Twenty-one patients with Alzheimer's disease aged 60 and above, along with 25 age- and sex-matched healthy individuals, were recruited for the study, which took place over a period of 2 years. Several participants had to be excluded due to having higher than normal fasting blood glucose levels, a marker of pre-diabetes. Eighteen patients and 18 healthy individuals were finally included.

All participants completed two types of memory test to assess memory decline and had a brain MRI scan after overnight fasting. During the scan, they consumed a sugary drink (75 g glucose diluted in 113 ml water) to measure how the brain uses sugar (Figure 1). The sugar is absorbed in the stomach, enters the blood, and is then carried to the brain. Blood sugar levels were measured before and after drink to ensure the body responded as expected. Following the MRI scan, patients were also invited to undergo an FDG PET scan within one week and this was used for comparison with the MRI scan. Only one individual without Alzheimer's disease had both MRI and PET scans.

The MRI scan was found to be highly sensitive to head movement, which affected image quality. Participants with Alzheimer's disease tended to move more than healthy individuals during the scan. Motion correction was applied to the images; however, some datasets had to be excluded due to excessive head movement.

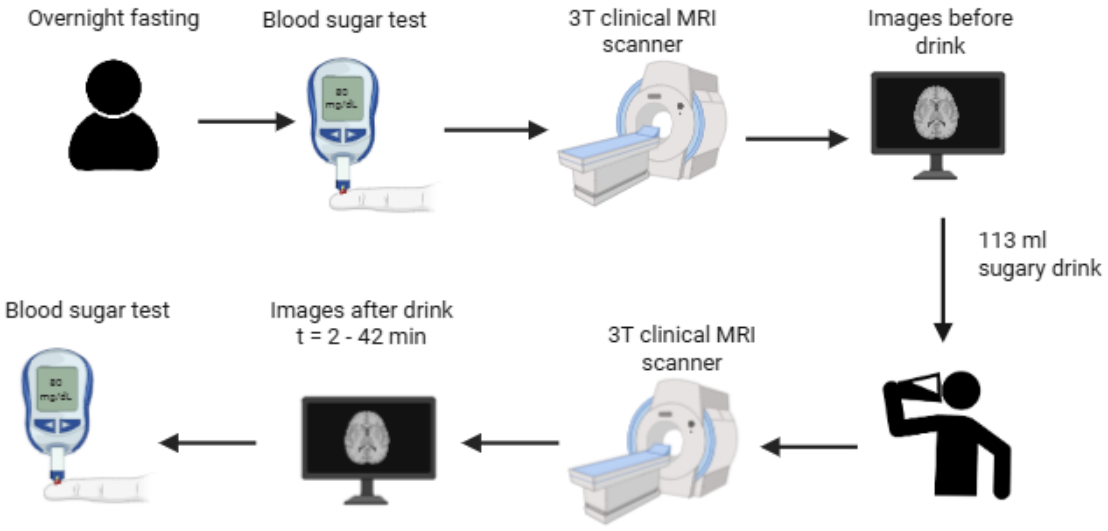

Figure 1: A diagram showing how the study was carried out for the collection of the MRI images.

WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

- We found it was feasible to recruit patients with Alzheimer's disease into the study with help from their carers when necessary. Most patients were able to follow the instructions and complete the full scan, allowing successful data collection in the majority of cases. All participants tolerated the glucose drink well without any adverse effects. Overall, the protocol was deliverable in a clinical research setting, with lessons learned to improve future study design.
- The PET scan showed clear differences in parts of the brain called the parietal and temporal regions—areas known to be affected in Alzheimer's disease—between people with Alzheimer's and one individual without the condition. In these regions, the signal was lower, meaning the brain was using less sugar than normal (Figure 2).
- The PET signal in these brain areas was linked to memory test scores, meaning lower brain activity was associated with worse memory, as expected.
- In contrast, the glucoCEST MRI scans did not show clear differences between patients and people without Alzheimer's disease. There was no sign of reduced sugar use in the parietal and temporal regions on glucoCEST MRI images (Figure 2).
- The glucoCEST MRI scans did not show any differences before and after drinking glucose in patients (Figure 3).
- There was no link between the MRI signal and the memory test scores, meaning that MRI images did not reflect memory function.
- The glucoCEST MRI scans did show the enlargement of the ventricles associated with Alzheimer's disease (Figure 2).
- Overall, the PET and MRI scans did not show the same results. Areas where the PET scan showed reduced glucose metabolism associated with Alzheimer's disease were not seen on the MRI scan. This means that glucoCEST did not match what was shown by the FDG PET scan (Figure 2).

WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

- Our findings show that while a glucoCEST MRI scan is feasible in patients with Alzheimer's disease it is not yet sensitive enough to detect the same brain changes seen on PET scans. These results highlight current limitations and suggest that future improvements, such as increasing brain glucose delivery, may help develop a more accessible MRI-based alternative for diagnosing Alzheimer's disease.

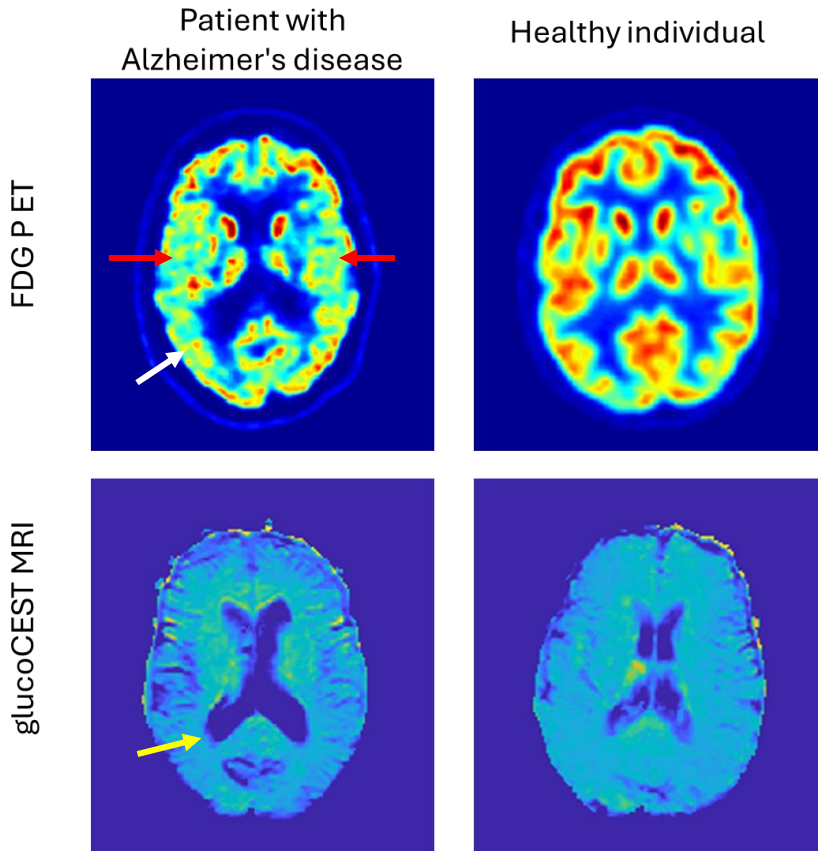

Figure 2: **Images from PET and glucoCEST MRI scans.** The top row shows PET scans, where reduced glucose metabolism can be seen in the Alzheimer's patient indicated by the blue colouring (left), compared to the healthy individual (right) in the temporal lobes (red arrows) and parietal lobes (white arrows). The bottom row shows corresponding glucoCEST MRI images, which did not show the same pattern of reduced metabolism in the patient and appear similar to the healthy individual. Enlargement of the ventricles (yellow arrow) is shown in patients as expected.

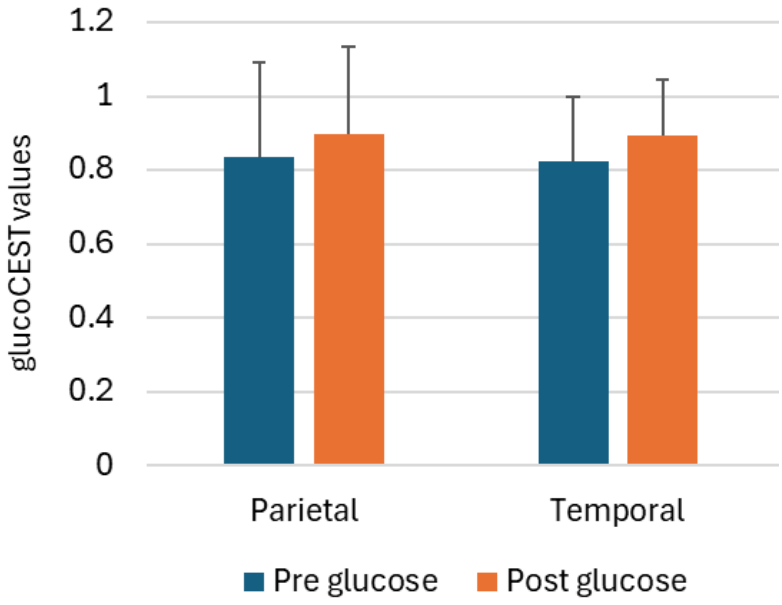

Figure 3: **Bar chart showing glucoCEST signal levels in patients before and after drinking glucose**. The measurements were taken from the parietal and temporal lobes—brain areas linked to Alzheimer's disease. There is no noticeable difference in the signal before (blue) and after (orange) the glucose drink.

WHAT IMPACT COULD THE FINDINGS HAVE?

In Scotland, the NHS prioritise PET scans for cancer imaging rather than dementia diagnosis. PET scans involves radiation exposure, are expensive, and are not widely available. Our aim was to test an alternative that could be implemented on standard clinical MRI scanners available in most large hospitals.

If this technique works reliably, it could offer a cheaper and more widely available way to diagnose dementia. This method would also be more suitable for repeated scans and could help support earlier diagnosis of Alzheimer's disease, allowing patients to start treatments sooner and potentially slow symptom progression. Although the results were negative, they are still important. They will help researchers understand the current limitations of the method and provide valuable information for improving its sensitivity in future studies. This will support further development of the technique towards possible use in diagnosing Alzheimer's disease in the future using MRI.

HOW WILL THE OUTCOMES BE DISSEMINATED?

This work has been presented at the Alzheimer's Research UK (ARUK) National Conference in 2023 and 2024 and at Scotland's Health Research and Innovation Conference in 2023. A manuscript reporting these findings is currently in preparation, with the intention of submitting it to a peer-reviewed journal (Scientific Reports).

Public and Patient Involvement (PPI) was integrated throughout the study. PPI members reviewed the study design prior to funding approval, and a dedicated PPI event was held in March 2024 to obtain feedback on the study concept and ensure its relevance and acceptability from a patient perspective. A link to this report will be sent to all of the participants with the opportunity for them to comment.

Once the manuscript is submitted, further funding will be sought from CSO to support a follow-on study incorporating improvements based on the findings of this work and feedback received from both scientific and patient engagement activities.

CONCLUSION

This was a feasibility study designed to test, for the first time, whether a new MRI-based method - glucoCEST- can measure how the brain uses glucose in people with Alzheimer's disease instead of the PET scan which is the current standard and most accurate method. A non-invasive approach was used in this study, where participants were given a sugary drink instead of receiving glucose through an intravenous injection as in PET. The study also examined whether it is practical to carry out this type of brain imaging in people with Alzheimer's disease, who may experience memory difficulties and find it challenging to remain still during scans. Overall, the study showed that it is feasible to scan this patient group using glucoCEST MRI. The results showed that after drinking glucose, the changes in brain signal were too small to be reliably measured using this method. However, the scan was still able to clearly show enlarged ventricles which are commonly seen in Alzheimer's disease. This suggests that while the method can show physical brain changes, it is not yet sensitive enough to measure glucose use after a drink. This suggests that an alternative method of delivering glucose, such as intravenous administration (as used in cancer brain imaging studies), may be needed in future work. These findings are important because they help guide how future studies should be designed and how the method can be improved to make it more sensitive. This study represents a fundamental early step towards developing an alternative to PET scan for diagnosing Alzheimer's disease. A successful alternative would be cheaper, would avoid exposure to radiation, and could be more widely available within the NHS in Scotland. At present, Alzheimer's disease is mainly diagnosed using memory and blood tests, which can sometimes be inconclusive and lead to delayed diagnosis. Earlier and more accurate diagnosis would allow treatment to start sooner, which may help slow disease progression and improve quality of life.

RESEARCH TEAM & CONTACT

Chief Investigator: Dr Gordon Waiter
Research fellow: Dr Vasiliki Mallikourti
Aberdeen Biomedical Imaging Centre,
University of Aberdeen

g.waiter@abdn.ac.uk

Additional Information
The project ended on 31st December 2025. It received £260,978 of funding from the Chief Scientist Office