Definitions

2-[18F]fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (FDG-PET/CT). Functional neuroimaging that uses a radio-active ligand to assess glucose metabolism in brain tissue. As it is a measure of brain function it is more sensitive to early changes than computed tomography (CT) or magnetic resonance imaging (MRI) which are measures of brain structure. The FDG-PET/CT combines an FDG-PET and CT scan, allowing both functional and structural neuroimaging simultaneously. It is widely used for oncology and increasingly available for dementia diagnosis.

Dopaminergic iodine-123-radiolabelled 2β-carbomethoxy-3β-(4-iodophenyl)-N-(3-fluoropropyl)nortropane single-photon emission computed tomography (FP-CIT SPECT or DaTscan). Functional neuroimaging that measures dopamine transport in the basal ganglia of the brain, supporting earlier diagnosis of Parkinson’s disease and dementia with Lewy bodies.

Perfusion hexamethylpropyleneamine oxime single-photon emission computed tomography (HMPAO-SPECT). Functional neuroimaging that assesses blood flow in the brain and is used for the same purposes as FDG-PET/CT.

Definitive diagnosis for the diseases causing dementia remains characteristic histopathology on post-mortem. Clinical diagnostic criteria rely on the cognitive profile supported by neuroimaging, which is becoming the primary investigation for suspected dementia, for detecting potentially reversible intra-cranial conditions and to aid in dementia sub-typing. Accurate diagnosis of the dementia subtype is extremely important for patients and their carers because the subtypes have differing clinical manifestations, genetics, pathophysiology, treatment options and prognoses. For example, fronto-temporal dementia (FTD) is different from Alzheimer’s disease (AD) in terms of earlier age of onset, higher genetic burden, prominent behavioural symptoms and poor response to acetylcholine-esterase inhibitors (ACIs).

NICE clinical guidelines recommend that structural neuroimaging with CT or MRI should be performed at least once in every patient with suspected dementia and that functional neuroimaging with HMPAO-SPECT or FDG-PET should be considered to help differentiate between AD, vascular dementia (VaD) and FTD if the diagnosis is in doubt. European guidelines attribute around 85% sensitivity and specificity to DaTscans for differentiating AD from DLB. NICE also recommends that functional neuroimaging with DaTscan should be used to help establish diagnosis in those with suspected dementia with Lewy bodies (DLB) if the diagnosis is in doubt. European guidelines attribute around 95% specificity in young onset dementia. NICE also recommends that functional neuroimaging with DaTscan should be used to help establish diagnosis in those with suspected dementia with Lewy bodies (DLB) if the diagnosis is in doubt. European guidelines attribute around 85% sensitivity and specificity to DaTscans for differentiating AD from DLB.

This article describes how we developed a business case for a pilot investment proposal leading to recurrent funding for 40 FDG-PET/CT and five DaTscans per year; the protocol for the service evaluation; and data from the first two years of operation.

Method

Developing a business case for a pilot investment proposal

The needs analysis. This project was established in partnership between the Memory Assessment Service (MAS) of 2gether NHS Foundation Trust, the radiology department of Gloucestershire Hospitals NHS Foundation Trust and Cobalt Health, Cheltenham. Before 2011, similar to many parts of the country, we did not have access to functional neuroimaging...
for dementia diagnosis in our county. Other counties in the region had access to HMPAO-SPECT scans for dementia diagnosis as part of historical block-contract commissioning arrangements. Our neurology and geriatric medicine colleagues had access to a limited number of DaTscans for differentiating benign tremor from Parkinson’s disease (PD) based on a business case that approximately 25% of the scans would be negative for PD, obviating the need for expensive, long-term anti-Parkinsonian medication which would recoup the initial cost of the scans.

A needs assessment survey of our MAS consultants revealed a surprisingly high estimated unmet need for 13 FDG-PET/CT or HMPAO-SPECT scans per month for differentiating FTD from AD and 11 DaTscans per month for confirming the diagnosis in suspected DLB. In 2010, an estimated 47% of the predicted dementia prevalence in our county was being diagnosed. A key aspiration set by our erstwhile Strategic Health Authority was to increase diagnosis rates to 60% by 2012, recognising the significant health and economic outcomes from timely diagnosis. MAS consultants also identified a particular unmet need for diagnosis in younger people, because there was no dedicated young-onset dementia service, and these patients often presented with atypical symptoms. It was felt that a functional neuroimaging for dementia service could potentially increase diagnosis rates in this population group and in those difficult to diagnose older patients.

Availability and costs – identifying local providers. FDG-PET/CT was available in our county at Cobalt Health, an independent charitable provider of imaging, predominantly for oncology. The FDG-PET ligand is off-patent, therefore the costs of these scans have significantly reduced. Providers of FDG-PET/CT scans for oncology in other parts of the country may be looking to expand into dementia diagnosis, creating an opportunity for locally commissioned services. Due to overall service demands on the gamma cameras, we had limited availability of HMPAO-SPECT slots and HMPAO-SPECT was more expensive in our county than brain FDG-PET/CT. Although the specific radiopharmaceuticals and instrumentation used in FDG-PET differ from those used in HMPAO-SPECT, the principles of interpretation, as well as the neurobiological processes underlying the use of the...
two modalities, are similar. Studies comparing neuropathological examination with FDG-PET have established reliable and consistent accuracy for diagnostic evaluations using FDG-PET with accuracies substantially exceeding those of comparable studies of the diagnostic value of HMPAO-SPECT. Therefore, for both financial and diagnostic accuracy reasons, FDG-PET was the functional neuroimaging modality preferred. Cobalt Health via subsidised charitable funds were able to provide the FDG-PET/CT scans at £350 per scan and DaTscans were available through Gloucestershire Hospital NHS Foundation Trust priced at £906 per scan in keeping with the NHS schedule of reference costs – as per which the comparative cost of a CT head without contrast is around £100 per scan and an MRI head without contrast is around £150 per scan.

Clinical and cost benefits. Access to functional neuroimaging could facilitate early and accurate diagnosis of dementia which, when followed by appropriate psychosocial support, can improve quality of life and delay care-home admission thereby reducing care-home costs – as detailed in the cost-effectiveness analysis used by the National Dementia Strategy to justify early diagnosis and intervention.

Although difficult to quantify, the scans may end years of diagnostic uncertainty, improving quality of life for patients and their families. Early diagnosis also prevents the burden and additional costs of further consultations and investigations. In our county, before the functional neuroimaging service, difficult to diagnose patients were often referred to tertiary centres, incurring further out-of-county expenses for the commissioners.

### Table 1. Sample characteristics from the results of the first two years of the service evaluation

<table>
<thead>
<tr>
<th>Sample characteristics</th>
<th>FDG-PET/CT</th>
<th>DaTscan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scans requested</td>
<td>79</td>
<td>11</td>
</tr>
<tr>
<td>Scans completed</td>
<td>76</td>
<td>10</td>
</tr>
<tr>
<td>Age</td>
<td>Mean: 67 years Range: 44–88 years</td>
<td>Mean: 78 years Range: 69–82 years</td>
</tr>
<tr>
<td>Gender (M:F)</td>
<td>42:34</td>
<td>9:1</td>
</tr>
<tr>
<td>Previous imaging done</td>
<td>CT: 51/76 (67%) MRI: 48/76 (63%)</td>
<td>CT: 9/10 (90%) MRI: 3/10 (30%)</td>
</tr>
<tr>
<td>Duration of cognitive symptoms</td>
<td>Mean: 33 months Range: 3 months to 15 years</td>
<td>Mean: 20 months Range: 3 months to 4 years</td>
</tr>
<tr>
<td>Memory Assessment Service (MAS) assessments done before scan:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuropsychology</td>
<td>44/64 (69%)</td>
<td>3/8 (38%)</td>
</tr>
<tr>
<td>Others (occupational therapy, speech and language therapy, physiotherapy)</td>
<td>32/69 (46%)</td>
<td>3/7 (43%)</td>
</tr>
<tr>
<td>Non-MAS assessments done before scan:</td>
<td>Total 22/66 (33%)</td>
<td>Total 5/8 (63%)</td>
</tr>
<tr>
<td>Physician referral only*</td>
<td>13/22 (59%)</td>
<td>3/5 (60%)</td>
</tr>
<tr>
<td>Other investigations only**</td>
<td>4/22 (18%)</td>
<td>1/5 (20%)</td>
</tr>
<tr>
<td>Physician referral and other investigations</td>
<td>5/22 (23%)</td>
<td>1/5 (20%)</td>
</tr>
</tbody>
</table>

*Physician referral – neurology, geriatric medicine, falls clinic, general medicine, tertiary centre. **Other investigations – CSF studies, EEG, genetics.

By allowing earlier and more reliable dementia subtype diagnosis, the service would enable earlier disease-specific treatments and would avoid certain treatments. For instance, if the scans confirmed diagnosis of AD, then treatment with ACIs or memantine may be beneficial as evidenced in the NICE appraisal. On the other hand, in FTD, ACIs are ineffective and may cause agitation, but serotonergic agents like trazadone and selective serotonin reuptake inhibitor (SSRI) anti-depressants may be effective for mood and behavioural disturbance.

Our business case postulated that if 25% of the FDG-PET/CT scans were positive for FTD, then the cost savings of avoiding long-term treatment with ACIs would recoup the initial costs of the scans. This was based on the cost of donepezil (Aricept) in 2011, but was rendered superfluous by the ACIs coming off-patent in 2012. If a DaTscan confirmed DLB, then treatment with antipsychotics would be avoided due to the risk of serious adverse reactions including increased mortality.
Other benefits of commissioning functional neuroimaging were ensuring our services became compliant with NICE and National Dementia Strategy recommendations, and ensuring equity of access for patients in our county.

The pilot study. An initial investment for 15 FDG-PET/CT and 15 DaTscans for a one-year pilot study was negotiated with our commissioners. This was realigned to 40 FDG-PET/CT and five DaTscans, based on demand, for the same funding. The results of the pilot were presented to the commissioners and as a poster at the International Psychogeriatric Association’s annual conference in 2012. Recurrent annual funding was agreed with the condition that regular case conferences be held between MAS clinicians and radiologists and service evaluation data be reported back to the commissioners annually.

Protocol for evaluating the service
Patients are referred from the old age psychiatry run memory clinics, using a standard referral form that collects sample characteristics, to the lead old age psychiatrist and lead radiologist for triaging. Those patients for whom the MAS pathway, including structural neuroimaging and neuropsychological testing, is not helpful in clarifying differential diagnosis of AD or FTD are considered for FDG-PET/CT. The diagnostic criteria used are the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA) criteria for AD\(^\text{10}\) and the consensus criteria for FTD.\(^\text{11}\) Similarly, those patients for whom the MAS pathway does not clarify differential diagnosis of AD or DLB are considered for a DaTscan.

<table>
<thead>
<tr>
<th>Sample evaluation reports:</th>
<th>FDG-PET/CT</th>
<th>DaTscan</th>
</tr>
</thead>
<tbody>
<tr>
<td>From scan reports:</td>
<td>n=76</td>
<td>n=10</td>
</tr>
<tr>
<td>Scan diagnosis:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal FDG-PET/CT scan</td>
<td>23/76 (30%)</td>
<td>–</td>
</tr>
<tr>
<td>Alzheimer’s disease (normal DaTscan)</td>
<td>32/76 (42%)</td>
<td>8/10 (80%)</td>
</tr>
<tr>
<td>Fronto-temporal dementia</td>
<td>11/76 (14%)</td>
<td>–</td>
</tr>
<tr>
<td>Vascular dementia</td>
<td>1/76 (1%)</td>
<td>–</td>
</tr>
<tr>
<td>Dementia with Lewy bodies</td>
<td>8/76 (11%)</td>
<td>2/10 (20%)</td>
</tr>
<tr>
<td>Inconclusive/non-specific</td>
<td>1/76 (1%)</td>
<td>–</td>
</tr>
</tbody>
</table>

From referrer feedback forms returned: 76/76 (100%) 10/10 (100%)

(i) Did the scan help clarify the diagnosis?
Yes: 61/76 (80%) 9/10 (90%)
No: 12/76 (16%) 1/10 (10%)
Not completed: 3/76 (4%) –

(ii) Final clinical diagnosis:
Alzheimer’s disease (AD): 30/76 (40%) 5/10 (50%)
Fronto-temporal dementia: 11/76 (14%) –
Vascular dementia (VaD)/cerebrovascular disease: 4/76 (5%) 2/10 (20%)
Dementia with Lewy bodies: 1/76 (1%) 2/10 (20%)
Mixed (AD + VaD) dementia: 1/76 (1%) –
Mild cognitive impairment: 4/76 (5%) –
Functional psychiatric (mood/psychosis/anxiety) disorder: 12/76 (16%) –
Unspecified dementia: 3/76 (4%) –
No dementia: 3/76 (4%) –
Other diagnosis (brain injury, drug-induced): 2/76 (3%) –
Diagnosis not clear, uncertain, unknown: 5/76 (7%) –
Diagnosis not recorded: 1/76 (1%) 1/10 (10%)

(iii) Investigations/consultations/treatments avoided as a result of the scan being available:
Repeat neuropsychological assessment: 25 3
MRI scans: 12 2
CT scans: 3 –
SPECT scans: 2 –
Neurology referrals: 8 3
Further clinical reviews/outpatients: 19 1
Tertiary centre referrals: 4 –
EEG: 5 2
Speech & language therapy assessment: 3 1
ECT: 2 –
Therapeutic trial with acetylcholine-esterase inhibitor: 6 –
CSF assay: – 1
Vasculitis screen: – 1
Prolonged hospital stay: 1 –
Other (‘probably hundreds’): 1 –
None recorded: 14 4

(iv) Referrer feedback on helpfulness of scan in diagnosis:
Very helpful: 36/76 (47%) 5/10 (50%)
Helpful: 26/76 (34%) 4/10 (40%)
Don’t know (not sure): 9/76 (12%) –
Unhelpful: 2/76 (3%) 1/10 (10%)
Very unhelpful: – –
Not completed: 3/76 (4%) –

From patient feedback forms returned: 51/76 (67%) 5/10 (50%)

Patient feedback on experience of scan:
Very pleasant: 21/51 (41%) 2/5 (40%)
Pleasant: 23/51 (45%) 2/5 (40%)
Don’t know (not sure): 5/51 (10%) 1/5 (20%)
Unpleasant: 2/51 (4%) –
Very unpleasant: – –

Table 2. Sample evaluation from the results of the first two years of the service evaluation.
The diagnostic criteria used are the DLB consortium consensus criteria.\textsuperscript{12}

All scans are double reported by radiologists experienced in the interpretation of functional neuroimaging. In line with standard clinical practice, during image interpretation there is full access to the clinical history and the findings of other structural imaging scans. Discordant findings are resolved by a third read and consensus arbitration.

Regular multidisciplinary meetings are held between consultant radiologists and the MAS clinicians to discuss the suitability of patients referred for functional neuroimaging, ensuing scan result and the clinical correlates.

Copies of scan reports are sent to the referring MAS clinician along with a referrer feedback form that collects data on: the final clinical diagnosis; helpfulness of the scan in making the diagnosis; the investigations, consultations and treatments avoided as a result of the scan; the estimated duration of diagnostic uncertainty avoided; and referrer satisfaction.

Feedback is also sought from patients immediately after the scans, and this includes patient satisfaction with the experience, comments, and suggestions for improvement.

Results
The results of the first two years of the service evaluation, from 1 June 2011 to 31 May 2013, are presented in Tables 1 and 2. In total there were 90 scans requested: 79 FDG-PET/CT scans and 11 DaTscans. Of these, 76 FDG-PET/CT scans and 10 DaTscans were completed. One FDG-PET/CT scan request was triaged out with MRI suggested instead, one FDG-PET/CT scan request was triaged out with DaTscan suggested instead, one FDG-PET/CT scan was not done as the patient was too ill to attend, and one DaTscan was not done because the patient was aggressive and did not accept intravenous cannulation.

We received 100% of the feedback forms from the memory clinic referrers. As shown in Table 2, the FDG-PET/CT scan report diagnosis of 42% AD and 14% FTD matches up with the final clinical diagnosis of 40% AD and 14% FTD. The overall mean estimated duration of diagnostic uncertainty avoided because of FDG-PET scan availability was 15 months and DaTscan was 13 months.

The referrers estimated a variety of different consultations, investigations or treatments that were avoided because of the availability of the scan. These included further MRI scans, repeat outpatient appointments, psychometric testing and tertiary centre referrals. Costing these up, as per the NHS schedule of reference costs, would match the initial costs of the scans and potentially make savings for our commissioners.\textsuperscript{5}

We received feedback forms from 67% of the patients who had the FDG-PET/CT scan and 50% of those who had the DaTscan. The majority of the feedback from the patients about their experience of the scan was positive, suggesting good acceptability. Of the 90 scans requested, ony one was not completed as the patient was too agitated and aggressive to comply, suggesting that the scans were well tolerated. Two patients who had the FDG-PET scan commented on unpleasant experiences – like the room being cold and claustrophobic – but none of the patients who had the DaTscan noted any unpleasant experiences. Feedback has been used by the providers to improve the scanning experience.

Discussion
The demographics of the sample are as one might expect. Patients referred for FDG-PET had a younger mean age than patients referred for DaTscan, consistent with the younger age at onset of FTD.\textsuperscript{1} The gender spread was biased towards male patients, particularly in the group referred for DaTscan. This may reflect the small sample size, but also suggests a preponderance of suspected DLB in male patients, as has been described previously.\textsuperscript{13} The mean MMSE score for both scan samples was 23/30 as expected for an early diagnosis service. Patients also had high rates of other investigations and consultations, compared to the typical patients attending MAS, perhaps reflecting their diagnostic complexity.

Memory clinic consultants were positive about the functional imaging service, evidenced not only by their 100% return rate of questionnaires, but also the feedback given. The number of scans requested did not exceed the allocated funding for 40 FDG-PET/CT and five DaTscans per year with only three requests having to be triaged out. To put things into perspective, a recently published audit cycle of neuroimaging in MAS showed that, in the re-audit, there were 150 referrals to MAS for a calendar month. Of these, 140 notes were identified and audited of which 106 (76%) had at least one structural scan.\textsuperscript{14} This would suggest appropriate use of the functional imaging service as second-line imaging. The 100% response rate and high levels of referrer satisfaction augur well for the continuing evaluation of the service as contracted by our commissioners.

Imaging was felt to have clarified the diagnosis in over 80% of both types of scans, with the FDG-PET/CT scan report diagnosis of
FTD and AD correlating with the final clinical diagnosis. The majority of the 30% normal FDG-PET/CT scans may have been given a final clinical diagnosis of a chronic functional psychiatric disorder, which is again expected as these can often mimic FTD. Only 11% of the FDG-PET/CT scans were reported as inconclusive.

It is beyond the scope of this article to look at the accuracy of the scan reports and, indeed, the final clinical diagnosis. Further research is planned to look at whether computerised quantitative analysis of FDG-PET/CT images, using various statistical packages, would improve the accuracy of scan reporting. Further, the patients with inconclusive FDG-PET scans may benefit from the newly licensed amyloid PET scans, to distinguish FTD from AD, in accordance with the recent Royal College of Physicians and Royal College of Radiologists guidance.15

The DaTscan sample may be too small to draw any meaningful conclusions, but it appears to have generated good referrer and patient satisfaction. The low DaTscan referral rate is possibly due to the relatively commissioned Parkinson’s disease service run by neurologists and elderly care physicians with access to DaTscaans.

The tables in this article are not intended to compare the two different scanning modalities, as they have very different indications, but are merely a convenient way of presenting the results.

It must be emphasised that none of these scans provide a definitive diagnosis of the dementia subtype, but merely assist with the clinical diagnosis. A review article by Shaik and Varma describes in detail the clinical assessment required for subtype diagnosis and its importance.16

Referrers estimated that the availability of the scans had avoided approximately one year of diagnostic uncertainty for their patients. This may have helped improve quality of life for both patients and their carers. An obvious limitation of this study is that the duration of diagnostic uncertainty and the investigations or consultations avoided as a result of the scans are estimates made by the referrers, who may have given positive feedback to ensure continued availability of the service.

It is hoped that this article may be helpful to clinicians in the other parts of the country in locally commissioning a similar service.

Dr Kuruvilla is a Consultant Psychiatrist in Old Age Psychiatry, Dr Phillips is a Higher Specialist Trainee in Old Age Psychiatry, and Dr Justin and Dr Rose are Core Trainees in Psychiatry, at 2gether NHS Foundation Trust, Charlton Lane Centre, Cheltenham. Professor Lyburn is a Consultant Radiologist at Gloucestershire Hospitals NHS Foundation Trust; Medical Director, Cobalt Health, Cheltenham; and Visiting Professor of Radiology, Cranfield University, Health Division

Acknowledgements

We would like to thank AD and JD, our patient and carer expert, for their input in developing, implementing and evaluating the service. We also thank Sharon Keeveren, Clinical Audit Officer of 2gether NHS Foundation Trust for help with the data collection and analysis.

Declaration of interests

Tarun Kuruvilla has received educational grants from Pfizer, Novartis, Lundbeck, Lilly and GE Healthcare to attend conferences, and speaker fees from GE Healthcare. Iain Lyburn has received speaker fees from GE Healthcare.

References