

IMAGING IN DEMENTIA Venue: British Dental Association, London

CPD: 5 CREDITS



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BIR ANNUAL CONGRESS 2015 4–5 NOVEMBER LONDON

• Room 1 Day 1 Primers for the non-specialists

Session organised by Dr David Wilson, Consultant Interventional MSK Radiologist, Oxford University Hospitals NHS Trust

• Room 2 Radiation protection – current issues in molecular imaging and radiotherapy Session organised by Mr Andy Rogers, Head of Radiation Physics, Nottingham University Hospitals NHS Trust

View the full programme and register: www.bir.org.uk • Room 1 Day 2 *Clinical hybrid imaging in oncology* Session organised by Dr Gopinath Gnanasegaran, Consultant Physician in Nuclear Medicine, St Thomas' Hospital

• Room 2 *Emergency radiology – advances in trauma imaging and Essentials for the radiology trainee* Session organised by Dr Hardi Madani, Radiology Registrar, Royal Free London Hospital and Dr Ausami Abbas, Cardiothoracic Radiology Post CCT Welcome and thank you for coming to "Imaging in dementia" organised by The British Institute of Radiology.

We wish you a very enjoyable and educational experience.

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Programme

- 09:30 Registration and refreshments
- **09:55** Welcome and introduction Dr Adam Waldman, Consultant Neuroradiologist, Imperial College London
- **10:00** Clinical MRI in dementia Dr Adam Waldman, Consultant Neuroradiologist, Imperial College London
- 10:40 Refreshments
- **11:10** Volumetric/quantitative MRI Professor Frederik Barkhof, Professor of Neuroradiology and Scientific Director of the Image Analysis Center, Vrije University Medical Center
- **11:50** Imaging of metabolism and blood flow in dementia (MRI/PET) Dr Marion Smits, Associate Professor of Neuroradiology, Erasmus University, Rotterdam
- 12:30 Lunch
- **13:30** Clinical amyloid imaging Dr Zarni Win, Consultant Nuclear Medicine Radiologist, Imperial College Healthcare NHS Trust
- **14:10** Imaging tau and other pathological pathways Professor Alison Murray, Professor of Radiology, University of Aberdeen
- 14:50 Refreshments
- 15:20 Imaging in clinical trials

Professor Frederik Barkhof, Professor of Neuroradiology and Scientific Director of the Image Analysis Center, Vrije University Medical Center

- **16:00** Clinical impact of imaging in dementia—a clinician's perspective Dr Richard Perry, Consultant Neurologist, Imperial College Healthcare NHS Trust
- 16:30 Questions and discussion
- 17:15 Close of event

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Speaker profiles

Professor Frederik Barkhof Professor of Neuroradiology and Scientific Director of the Image Analysis Center, Vrije University Medical Center

Frederik Barkhof received his MD from VU University, Amsterdam, the Netherlands in 1988 and defended his PhD thesis in 1992, for which he received the Philips Prize for Radiology in 1992 and the Lucien Appel Prize for Neuroradiology in 1994. Since 2001 he serves as a full Professor in Neuroradiology at the department of Radiology and Nuclear Medicine at the VU University Medical Center (VUmc). He is a senior staff member of the MS Center Amsterdam, and Senior Consultant of the Alzheimer Center, VUmc. He is the Scientific Director of the Image Analysis Centre (IAC), involved in analysis of multicentre drug trials. Professor Barkhof was the chairman of the Dutch Society of Neuroradiology and the MAGNIMS study group for many years. He serves on the Editorial boards of Radiology, Brain, Multiple Sclerosis Journal, Neuroradiology and Neurology.

Professor Barkhof's research interests focus on childhood white matter disease, on multiple sclerosis (spinal cord MRI, grey matter, atrophy, histopathology correlations), on ageing (white matter lesions and microbleeds) and dementia (hippocampal atrophy in Alzheimer's and functional MR). He (co)authored more than 750 papers referenced in PubMed, has an H-factor of 86 and is author of the books "Neuroimaging in Dementia" and "Clinical applications of functional brain MRI".

Cumulatively, he has received more than 10 million euro grant money from various national and international funding agencies and performed contract research for all major pharmaceutical companies with cumulative contract value of more than 15 million euros. More than 30 PhD students graduated under his supervision and 2 of them have subsequently attained a full professorship.

Professor Alison Murray Professor of Radiology, University of Aberdeen

Alison Murray is the Roland Sutton Professor of Radiology at the University of Aberdeen. She is Director of the Aberdeen Biomedical Imaging Centre (www.abdn. ac.uk/ims/research/abic). ABIC comprises a diverse range of imaging scientists and clinicians and has a strong history of novel imaging development. Facilities include pre-clinical and clinical MRI, novel radiochemistry, cyclotron and pre-clinical and clinical PET CT, field cycling MRI and retinal imaging. She leads clinical brain imaging research in structural, functional and molecular imaging correlates of cognitive ageing and dementia, which includes MRI in the Aberdeen Birth Cohorts, and MRI and molecular imaging in clinical trials of novel tau aggregation inhibitor therapies in Alzheimer's disease. Particular interests are the relative contributions of vascular risk factors and subclinical Alzheimer's pathology to cognitive ageing and early life and life-course predictors of cognitive reserve and dementia risk. She is a founding and executive member of the Scottish Imaging Network: A Platform for Scientific Excellence (SINAPSE) (www.sinapse.ac.uk) a successful brain imaging pooling initiative, an executive member of the Scottish Dementia Research Consortium and President of the Scottish Radiological Society.

Dr Richard Perry Consultant Neurologist, Imperial College Healthcare NHS Trust

Richard Perry is a Consultant Neurologist and Honorary Senior Lecturer at Imperial College NHS Trust. Dr Perry gained his specialist clinical and research experience in cognition and memory disorders at the University of Cambridge Neurology Unit and the University of California San Francisco.

Since returning to London he has run memory clinics at Charing Cross Hospital and his area of special interest is in the early diagnosis and treatment of Alzheimer's disease. He runs a clinical trials team at Charing Cross that specialise in new disease modifying agents for Alzheimer's disease and other dementias. Over the last year he has been one of the early adopters of amyloid PET imaging in dementia assessment and works with neuroradiological and nuclear medicine colleagues in their dementia neuroimaging MDT. His clinical neurological work also includes assessment and care of patients with traumatic brain injury. He has both a specialist and general clinical neurology practice.

Dr Marion Smits Associate Professor of Neuroradiology, Erasmus University, Rotterdam

Marion Smits is Associate Professor of Neuroradiology and combines her clinical work as a Neuroradiologist with scientific research into advanced MR neuroimaging, such as functional MRI, diffusion tensor imaging (DTI) and perfusion imaging. She uses these techniques to visualise the brain's function and microstructure, and to study pathophysiological and regenerative processes in a variety of neurological diseases, such as stroke, dementia and brain tumours.

Marion combines her clinical expertise with scientific research and active participation in key European organisations, including the European Society of Radiology (ESR), the European Society of Neuroradiology (ESNR), the European Society for Magnetic Resonance in Medicine and Biology (ESMRMB), and the European Organisation for Research and Treatment of Cancer (EORTC).

Through her current research and position in the European COST-AID action BM1103 Arterial Spin Labeling (ASL) in dementia, she works towards translating this perfusion technique from the research arena to clinical practice. Her work has contributed to a recent white paper on recommendations for clinical implementation of ASL.

As a permanent faculty member of several European and national course organisations she lectures frequently on advanced MR neuroimaging. She is Course Director of the European School of MRI fMRI & DTI course, and Scientific Programme

Committee Chair of the ESMRMB scientific annual meeting 2015 in Edinburgh (UK). She has recently been elected as Congress President for the 2018 annual meeting of the ESNR.

Full list of publications: www.marionsmits.net/publications LinkedIn: nl.linkedin.com/in/marionsmits

Dr Adam Waldman Consultant Neuroradiologist, Imperial College London

Adam Waldman gained a PhD and undertook post-doctoral research in biophysics before training in medicine at Cambridge. He trained in radiology at University College Hospitals and subsequently in neuroradiology at the National Hospital for Neurology and Neurosurgery, Queen Square, London.

Dr Waldman has been Consultant Neuroradiologist at Imperial College Healthcare NHS Trust (formerly HHNT) since 2001. Since 2006 he has been departmental academic lead as Research Director for Radiology, and has also founded an academic training programme in clinical radiology.

He was awarded the 2009 Royal College of Radiologists Roentgen Professorship and medal, and holds honorary senior academic appointments at Imperial College London. His main research interests are in quantitative and physiological neuroimaging, particularly as applied to neuro-oncology and neurodegenerative dementias and neuroinflammatory disease.

Dr Zarni Win Consultant Nuclear Medicine Radiologist, Imperial College Healthcare NHS Trust

Zarni Win is a Dual Specialist Consultant Radiologist and Consultant Nuclear Medicine Physician, and is the Chief of Nuclear Medicine Service at Imperial College Healthcare NHS Trust (Hammersmith, Charing Cross and St Mary's Hospital). He trained in both specialities at the Hammersmith Hospital. He gained an MSc in nuclear medicine at King's College London, specialising in PET imaging and a BSc in psychology as an undergraduate. He is an expert in clinical amyloid plaque PET imaging with Amyvid, scanning the first clinical patient in the UK in December 2013 and having the largest series of clinical amyloid PET scans to date. He is an Amyvid PET trainer, for Eli Lily, training other radiologists and clinicians to read Amyvid PET scans, and also participates in their advisory panel. He is an expert in other novel PET tracers, such as gallium-68 DOTATATE, used in the investigation of neuroendocrine tumours and also runs nuclear medicine therapy clinics at Charing Cross and St Mary's hospitals.

Abstracts

Clinical MRI in dementia Dr Adam Waldman

The role of clinical MRI in dementia investigation will be discussed, with reference to differential diagnosis, cerebrovascular disease, common and rare neurodegenerative dementias, and other causes of cognitive impairment. The importance of clinical information, appropriate imaging protocols and reporting will be explored. The role and translation of emerging and quantitative methods will be introduced.

Volumetric/quantitative MRI Professor Frederik Barkhof

Compared to CT, the superior tissue contrast provided by MRI allows accurate segmentation of grey matter structures relevant in the setting of dementia. Robust segmentation techniques exist that allow volumetric assessment of crucial structures like the hippocampus. Especially atlas-based segmentations have markedly improved the accuracy of segmentation, although computation times can be prohibitive and off-line reconstructions hamper their implementation into a clinical setting. Vascular white matter lesions can also be quantified, which is informative especially in patients with strong vascular loading, where visual rating scales show ceiling effects. Beyond visible lesion and atrophy patterns, the quality of the (normal-appearing) brain tissue can be probed with quantitative MR techniques like diffusion tensor imaging (DTI), which may reveal widespread damage, often with a disease specific pattern (e.g. temporal lobe abnormalities in AD and frontal lobe involvement in FTD). Finally, quantitative perfusion information can be obtained using arterial spinal labelling (ASL) with similar diagnostic potential as FDG-PET.

Suggested reading:

• Barkhof F, Fox NC, Bastos-Leite AJ, Scheltens P. Neuroimaging in Dementia. Springer-Verlag Berlin Heidelberg (2011)

Imaging of metabolism and blood flow in dementia (MRI/PET) Dr Marion Smits

There is no single diagnostic test or biomarker to definitively diagnose dementia and its underlying neurodegenerative disorder. The differential diagnosis between dementia and more treatable conditions may be problematic. Differentiation between the several neurodegenerative disorders is often difficult, especially in a young dementia population in which atypical presentations prevail.

More accurate diagnosis can be obtained by metabolic brain imaging, such as fluorodeoxyglucose (FDG) positron emission tomography (PET). Arterial spin labeling (ASL) is a non-invasive MR imaging technique that measures brain perfusion. ASL has clear advantages over PET: patient burden and costs are much lower and

availability of MRI is much wider. Crucially, ASL can easily be added to the routinely performed structural MRI examination. Feasibility studies show that ASL provides reliable perfusion maps in dementia. In patients with established Alzheimer's disease and frontotemporal dementia, hypoperfusion patterns are seen that are similar to hypometabolism patterns seen with FDG-PET.

Learning objectives:

- To know the added value of metabolic/perfusion imaging for the diagnostic workup of patients with suspected dementia
- To know the imaging abnormalities related to common neurodegenerative disorders underlying dementia with metabolic/perfusion imaging
- To know the theoretical background and recommended implementation of ASL for clinical applications

Clinical amyloid imaging Dr Zarni Win

The first clinical amyloid PET scan was performed in the UK at Charing Cross Hospital, Imperial College Healthcare NHS Trust, the following day after the G8 Dementia Summit in London in December 2013, hosted by David Cameron. Since then, we have scanned over 50 patients, who have been carefully selected from our dementia MDT. The clinical impact of amyloid PET has been significant from day one, especially those with indeterminate clinical histories, and MRI scans. It is proving to be a reliable biomarker of amyloid plaque leading to change in management in a significant number of patients scanned. It is also proving to provide a better patient experience compared to other more invasive tests such as lumbar puncture for CSF analysis, which it is superceding.

The talk aims to discuss the pathophysiology of amyloid plaque deposition; seminal trials involving the licenced amyloid PET products; the different binary reading method of the current licenced tracers; examples of positive, negative, and "difficult" PET scans; the prognosis after a positive or a negative scan; comparison of amyloid brain PET or FDG brain PET in AD and FTD; and new uses of amyloid PET. The talk will also highlight the importance of careful patient selection through a dedicated dementia MDT, thereby effectively utilising what is a very powerful biomarker of Alzheimer's disease.

Imaging tau and other pathological pathways Professor Alison Murray

This presentation will discuss the role of neuropathologies other than amyloid and cerebrovascular disease in dementia, focussing on abnormal tau. It will illustrate how neuroimaging can contribute to routine diagnosis, to research and to clinical trials of novel therapies.

The following three areas will be covered:

• Alzheimer's disease (AD): evidence for abnormal tau, rather than amyloid as

the main driver of cognitive decline and dementia in AD; results from a phase 2 clinical trial of a novel tau aggregation inhibitor; current methods of diagnosing tau pathology using structural and molecular imaging

- Frontotemporal dementias (FTD): common clinical features; the different neuropathologies that can result in frontotemporal lobar degeneration; characteristic imaging findings on structural and molecular imaging and the main features that distinguish FTD from AD
- Lewy body disease (LBD): including Parkinson's disease dementia and dementia with Lewy bodies; the limited role of structural brain imaging in these diseases and the indications for and typical findings on molecular imaging

Learning points:

- Hyperphosphorylated tau neuropathology distribution in AD is the same as the pattern of atrophy on structural imaging and molecular imaging deficits on FDG PET and blood flow SPECT
- Frontotemporal lobar degeneration has different subtypes with around half having behavioural variant and half having primary progressive aphasia. Family history is present in around half and genetic causes are increasingly being found
- The distinction between Parkinson's disease dementia and dementia with Lewy bodies, both due to a synucleiopathy, is made due to the time between onset of dementia with respect to motor symptoms

Imaging in clinical trials Professor Frederik Barkhof

Both MRI and PET can be used beyond diagnostic purposes. Images harbour prognostic information and longitudinal imaging may reveal changes well before clinical deterioration occurs, providing a surrogate outcome for disease progression that is more sensitive and objective.

The role of imaging in trials encompasses four domains:

- Enrichment strategy—e.g. include only subjects with some degree of hippocampal atrophy
- In/exclusion—e.g. exclude subjects that are amyloid negative or have vascular loading
- Outcome measure—e.g. slowing atrophy rate or removing amyloid (target engagement)
- Safety monitoring—e.g. development of ARIA (amyloid-related imaging abnormalities)

Clinical impact of imaging in dementia—a clinician's perspective Dr Richard Perry

Imaging techniques are one set of tools that a clinician will use in assessing patients with memory or other cognitive symptoms. Which imaging technique depends on the question being asked.

At a very basic level the clinician may have to answer the question of whether the patient has 'dementia'. Dementia is a clinical syndrome characterised by progressive loss of memory and other cognitive functions with impairment of everyday activities, and as such, imaging contributes mostly in terms of excluding non-neurodegenerative causes of cognitive impairment such as hydrocephalus or space occupying lesions. Structural imaging with CT or MRI is sufficient for this. Although the NHS seems to be currently focused on improving rates of dementia diagnosis, many patients and clinicians are interested in addressing two other questions that arise when a patients is seen for assessment. Firstly, a clinician may have to determine whether a patient's symptoms are due to an underlying brain disease, or whether they could be a result of a psychologically based problem such as anxiety or depression. To answer this question a clinician needs tools that are markers of neuronal loss. If it looks as though the symptoms may be secondary to a form of brain disease, the next question is what is the nature, or underlying pathology of the brain disease. In answering these two guestions a clinician can attempt to reach an accurate sub-type diagnosis of dementia. In this situation, the investigative tools need to be pathology sensitive.

In this talk we will see how imaging techniques that are markers of neuronal loss such as MRI and FDG-PET can be used in clinical situations and how they relate to non-imaging techniques such as clinical assessments and neuropsychological assessments. We will discuss how patterns of regional atrophy, and white matter disease can be helpful in diagnostic terms. More recently, clinicians have access to investigative techniques that are pathology sensitive such as CSF analysis or amyloid PET imaging. By the combined use of markers of neuronal loss and markers of specific pathology, we will look at how clinicians can differentiate the earliest stages of the different dementias from normal ageing, and how to differentiate between the different dementia subtypes, particularly Alzheimer's disease and frontotemporal dementia.

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> BIR WESSEX SUMMER EVENT 19 JUNE 2015 CHICHESTER

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