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BRAINWATCH

DETECTING AND
DIAGNOSING BRAIN
DISEASES WITH
MEDICAL IMAGING

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WHAT IS A NEURORADIOLOGIST?

BY MAJDA M. THURNHER, TURGUT TALI, PAUL M. PARIZEL

The human brain is a unique, sophisticated and complicated structure. The brain consists of some 100 billion nerve cells (give or take a few billion). Each cell is connected to thousands of other nerve cells in an astonishingly complex network. In scientific terms, the brain is sometimes called 'the final frontier,' because its function is still not completely understood. Despite all research efforts, it will take many more years more to uncover its secrets. Together, the brain, spinal cord and peripheral nerves make up a complex information-processing and control system that is called the central nervous system (CNS). To look inside the brain and the way it works and to understand how it functions is the dream of many researchers and neuroscientists.

A neuroradiologist is a medical doctor who has special training in imaging procedures (diagnostic neuroradiology) and therapeutic procedures (interventional neuroradiology) in the brain and spine, as well as the associated blood vessels and skeletal elements. During their training, neuroradiologists acquire in-depth knowledge of the anatomy and physiology of the brain and spine. This is a prerequisite for proper interpretation of the diseases affecting the nervous system and for the treatment of some common disorders. This knowledge enables them to differentiate between normal variants, age-related changes and acute/chronic diseases. After recognising the abnormalities, the neuroradiologist will start investigating, incorporating imaging findings and clinical information, which ultimately leads to a specific diagnosis. In addition, interventional neuroradiologists can perform treatments of certain neurovascular dis-

orders (such as aneurysms or arteriovenous malformations) and interventions in the spine (for example in patients with chronic back pain). These interventional neuroradiological procedures are performed in a minimally invasive way, in close coordination with other specialists, such as neurosurgeons, neurologists or orthopaedic surgeons, to name but a few.

The list of diseases that can affect the brain is long and diverse. This includes infectious processes, benign and malignant tumours, traumatic lesions, metabolic disorders, demyelinating diseases and many more. Many neurological diseases cause lesions (a lesion is an area of abnormality in the brain or spinal cord), which can be analysed in detail. Important factors in the analysis of abnormalities are location, size, number of lesions, content characteristics (fat, water, and blood products), vessels, blood flow in the lesion, etc.

Different diseases affect different brain structures, making the location of abnormalities found on images an important factor in the analysis. One example is herpes simplex encephalitis (HSE), a life-threatening infection of the brain. However, it cannot be reliably distinguished from other neurologic disorders with similar symptoms when based on clinical symptoms alone. Abnormalities seen on imaging affecting specific parts of the brain (temporal lobes, limbic system) will facilitate the diagnosis, and treatment can be started immediately. Prompt initiation of therapy increases the probability of good outcomes; any delay in diagnosis and treatment increases the risk of severe neurological dysfunction.

The shape of the lesions is another important factor in the analysis of images. In multiple sclerosis (MS), multiple small oval-shaped lesions located close to the ventricular system can be detected. Ring-like lesions are indicative of abscesses or some brain tumours.

The neuroradiologist will choose the most appropriate technique that also provides the highest likelihood of a correct diagnosis, and can propose a minimally invasive treatment plan for certain conditions involving the intracranial or intraspinal blood vessels, and the spinal column. The most frequently used primary imaging technique to examine the brain is computed tomography (CT). Its wide availability and short examination time makes CT an excellent imaging tool for acute situations. With a CT scan, a neuroradiologist can diagnose or exclude diseases that require urgent therapeutic decisions. The most important diagnosis that requires a prompt CT scan of the brain is acute stroke or traumatic brain injury. CT provides information on the state of the brain parenchyma, the blood vessels, and brain tissue perfusion in patients with acute stroke; information necessary to make an adequate therapeutic decision. In the past, a major challenge was the availability of neuroradiologists to interpret these studies 24/7 (as quickly as possible and whenever needed). Today, this has been solved with the rapid delivery of high-quality image data to neuroradiologists wherever they may be, thanks to the use of high-speed internet access and excellent web-based PACS browsers.

Another technique, which is frequently used, is magnetic resonance imaging (MRI). This method provides

images, which are superior to CT in the detection and characterisation of brain and spine diseases. MRI is the preferred imaging modality in children as it does not use radiation. Imaging protocols can be tailored to clinical questions and suspected diseases. Modern MRI techniques, now widely available, are capable of answering the most relevant questions related to morphology and physiology of the diseases. The introduction of high-field MR scanners (3T) into clinical practice has opened up a new dimension in brain and spine imaging. With these machines, we can detect small vessels, small brain structures, brain fibres and lesions that measure only a few millimetres in size.

For many years, angiography was the only method for looking at the blood vessels of the brain and spinal cord. This invasive technique requires puncturing an artery and taking x-rays while injecting contrast medium into the blood vessels. Nowadays, newer non-invasive techniques, such as CT angiography (CTA) or MR angiography (MRA), only require intravenous injection of a contrast agent, with rapid imaging, while the contrast agent passes through the vessels. CT angiography has become a method of choice for evaluating patients with brain haemorrhage and aneurysms.

Brain tumour imaging is one of the most exciting fields in medicine. Excellence in diagnosing, delineating, and operating on brain tumours is necessary in order to prevent neurological deficits and improve the quality of the patient's life. There are new imaging techniques which have revolutionised pre-operative brain mapping functional MRI (fMRI). Diffusion tensor imaging

(DTI), perfusion imaging and MR spectroscopic imaging (MRS) are particularly important for surgical planning.

Interventional neuroradiology can be defined as image-guided treatment of neurological disorders by specially trained neuroradiologists. The last few years have been characterised by revolutionary advances in vascular neurointerventional radiology and spine procedures. Developments in technology and equipment have opened up a fascinating world of new possibilities. Minimally invasive endovascular treatments have been developed and optimised for numerous indications where, previously, open surgery was the only option. Thanks to the implementation of new angiographic equipment and new materials (such as stents, coils, catheters, etc.); we are now able to treat patients with less invasive techniques. In order to deal with complex neurovascular lesions, multidisciplinary teams have found their way into the neuro-angiography suite, which has become a viable alternative to the operating room. This has led to a significant increase in the number of neurovascular procedures and interventions. Similarly, new techniques have opened up opportunities for percutaneous neuroradiological treatment of spinal disorders, as an alternative to open surgical procedures.

In summary, both diagnostic neuroradiology (imaging) and interventional neuroradiology (therapeutic procedures) have been continuously improving over the last few decades. Research in the neurosciences continues to bring new insights into diseases of the brain and spine. Continuous efforts by neuro-researchers to understand the 'essence' of the diseases and find

their causes, efforts of neuroradiologists to learn how to interpret imaging findings, and efforts in improvement of neurointerventional procedures will ultimately lead to the improvement of patient outcomes and prognosis.

IMAGING BRAIN TUMOURS: THE NEURORADIOLOGIST AS THE CENTRAL CHAIR ON THE BRAIN TUMOUR BOARD

BY MAJDA M. THURNHER, PIA C. SUNDGREN

Clinical symptoms, combined with the results of a neurological examination, raise the initial suspicions that a person might have a brain tumour. The next step is to confirm or exclude the presence of a brain tumour by obtaining a scan of the patient's brain. This can be done with computed tomography (CT) or magnetic resonance imaging (MRI). CT scans can exclude or confirm the presence of a brain tumour. However, more detailed information about the tumour itself and its effects is only possible using MRI with a tailored imaging protocol. Brain tumour protocol includes a combination of MR techniques that lead to a precise diagnosis. Each MR technique provides complementary information, which is used to plan further steps and decide on therapy options. A one-stop multiparametric study, including conventional and advanced MR techniques on high-field MR scanners, is the state of the art in brain tumour imaging.

On conventional MR sequences, delineation of the tumour's borders and size, its location in the brain, blood products, calcifications, cysts, and the presence of oedema and mass effect are evaluated.

MR perfusion is a technique that allows insight into the tumour vasculature, distinguishing low (low cerebral blood volume CBV) from highly vascularised areas (high CBV). One of the important characteristics of the majority of malignant brain tumours is neoangiogenesis, the development of new vessels from pre-existing ones.

The general rule is the more aggressive the tumour, the more abnormal its vessels. With MR perfusion, it is possible to predict tumour biology and demonstrate changes in tumour behaviour (angiogenic switch from a benign tumour with normal vessels to a more aggressive tumour with abnormal vessels).

MR spectroscopy (MRS) can assess tumour biology and metabolic information about the tumour tissue.

Benign lesions have lower choline content than malignant tumours, and benign lesions have lower rCBV (regional cerebral blood volume) than malignant lesions. The combined measurement of choline and rCBV will have a higher sensitivity/specificity than either alone.

Another key feature of a brain tumour is its cellularity, which can be evaluated with diffusion-weighted MR imaging (DWI). Diffusion tensor imaging (DTI) has proven to be a useful tool for characterising tumours and defining white matter anatomy, as DTI can non-invasively trace neuronal tracts in the brain and spine. Not only does DTI enable visualisation of important white matter tracts in the brain, but it also allows neurosurgeons to better guide their surgical approach and resection of a tumour.

Susceptibility-weighted imaging (SWI) is a powerful tool for high-resolution imaging of the vasculature, detection of microbleeds and differentiation of malignant brain tumours from non-tumoural lesions.

Figure 1 shows typical MR characteristics of a low-grade glioma (LGG) in a 56-year-old male patient. FLAIR shows a high signal intensity lesion located in the right occipital lobe (1A), with no enhancement on post-contrast T1WI to be seen (1B). Isointensity on DWI and high ADC suggest low cellularity (1C, D), and low rCBV indicates low perfusion (1E), with no signs of neoangiogenesis on SWI (1F), and no white matter tracts disruption (1G). On MRS, a moderate choline increase can be observed (1H).

Figure 2 shows typical MR characteristics of a high-grade glioma (HGG) in a female patient. Axial FLAIR shows an inhomogeneous lesion in the right hemisphere with associated oedema, mass effect, and compression of the ventricle (2A), with irregular, peripheral enhancement can be detected on post-contrast T1WI (2B). On DWI/ADC, areas with low cellularity, as well as areas with high cellularity, can be detected (2C,D), high rCBV indicates high perfusion (2E), and black areas on SWI demonstrate neoangiogenesis (2F). DTI shows tract disruption and displacement (2G), and, on MRS, high choline, low NAA, and a high lactate peak confirm a high-grade malignancy (2H).

With the use of MR imaging it is possible to monitor changes in the brain tumour's appearance such as pathological events suggestive of increasing tumour grade, which are important for therapy decisions, as well as distinguishing tumour progression and tumour response from treatment associated changes. The changes in tumoural behaviour and response to treatment can be assessed with different MR imaging techniques. For example increased cellularity can be evaluated with the use of T2WI, DWI imaging, development of necrosis can be seen using T2WI and T1WI sequences, increased tumour vascularity can be demonstrated by sequences like PWI and SWI, and, finally, increased metabolic rates and tumour cell proliferation can be demonstrated by the use of MRS.

Therapy options for patients with brain tumours have greatly increased in recent years, with new potent drugs substantially increasing the survival rates for brain tumour patients. Imaging plays the central role in dis-

tinguishing tumour tissue (either residual tumour or recurrent tumour) from therapy-induced reactions and phenomena. The most common therapy-induced reaction is the so-called pseudo-progression in which the contrast enhancement of the residual tumour increases in volume and the surrounding oedema increases in size as a result of the ongoing treatment. In cases like this, the contrast enhancement and the oedema will subsequently decrease during continued unchanged treatment. The radiation treatment may result in damage to the brain, so-called radiation necrosis/radiation injury, and present with a similar picture as a progressive or recurrent tumour. In these cases, MRI might be helpful to distinguish between a progressive brain tumour and radiation injury. Less common is the pseudo-response, which occurs with specific treatment affecting the pathological vessels of the tumour. In pseudo-response the contrast enhancement decreases in the tumour despite the tumour still being present and this picture makes it appear as if the tumour is disappearing.

In the last decade, we have seen a progressive transition from anatomy-based neuroradiology to neuroimaging that includes functional, hemodynamic, metabolic, cellular, and cytoarchitectural information.

The neuroradiologist is an important member of the brain tumour board, comprising neurologists, neurosurgeons, neuropathologists, and oncologists.

Neuroimaging can answer crucial questions about the management of patients with brain tumours because it can characterise morphology and biology, as well as aid

in the grading of brain tumours. Furthermore, neuroimaging monitors and assesses treatment response, and subsequently influences patient therapy and prognosis.

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FIGURE 1A

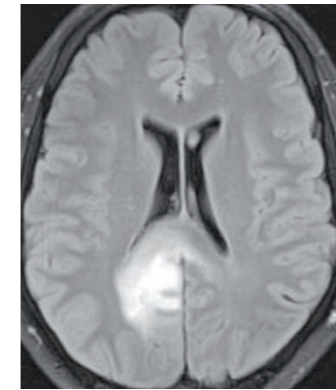


FIGURE 1B

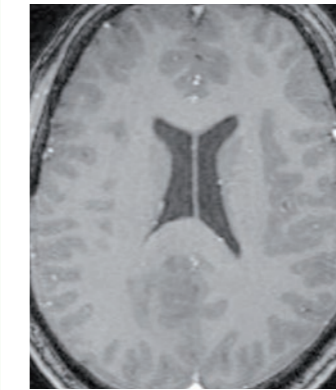


FIGURE 1C

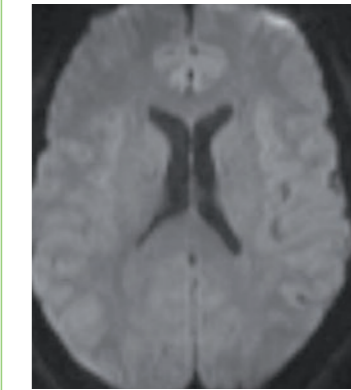


FIGURE 1D

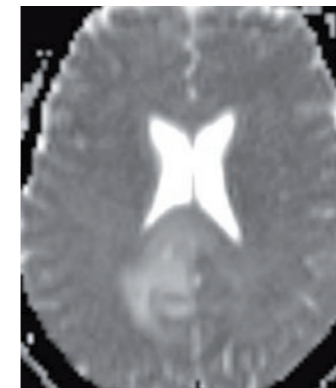


FIGURE 1E

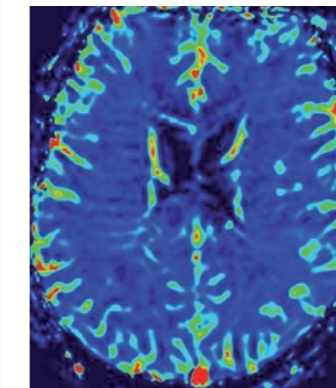


FIGURE 1F

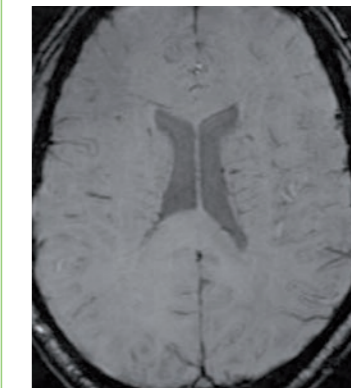


FIGURE 1G

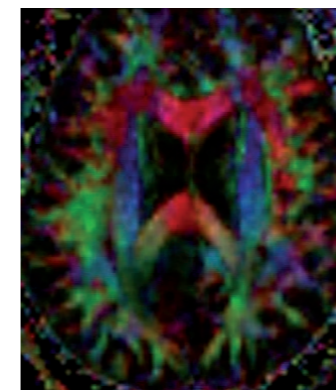


FIGURE 1H

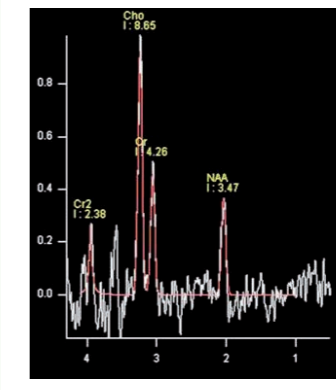


FIGURE 2A

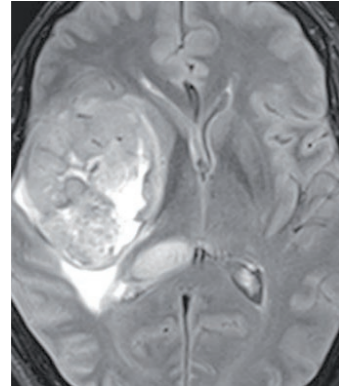


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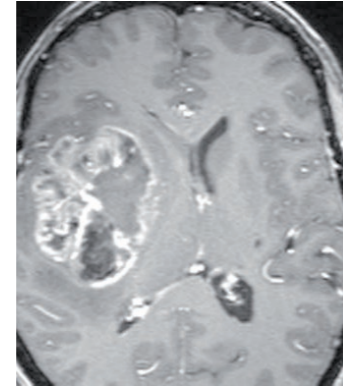


FIGURE 2C

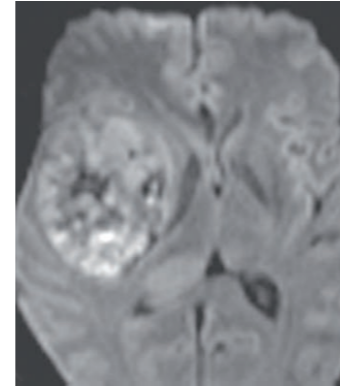


FIGURE 2D

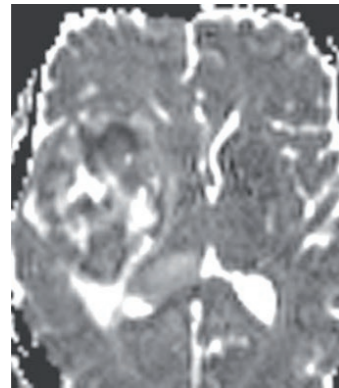


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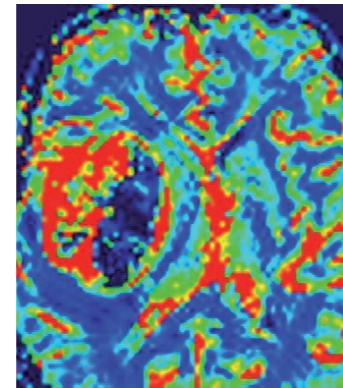


FIGURE 2F

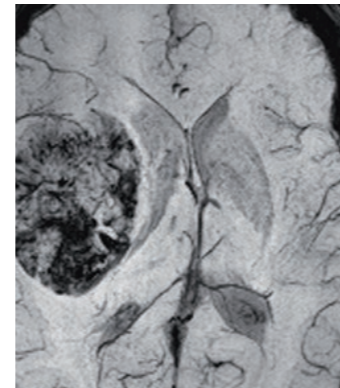


FIGURE 2G

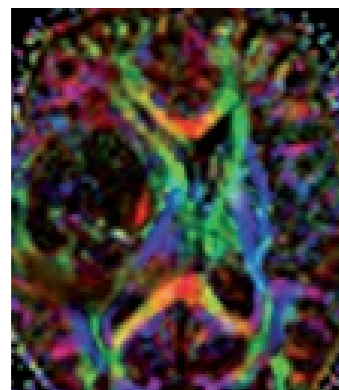


FIGURE 2H

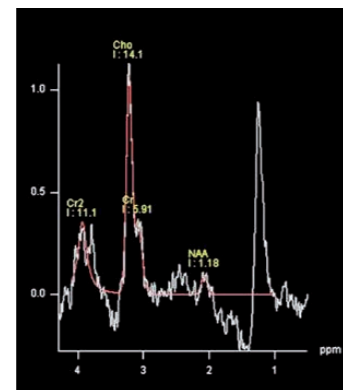


Figure 2 shows typical MR characteristics of a high-grade glioma (HGG) in a female patient. Axial FLAIR shows an inhomogeneous lesion in the right hemisphere with associated oedema, mass effect, and compression of the ventricle (2A), with irregular, peripheral enhancement can be detected on post-contrast T1WI (2B). On DWI/ADC, areas with low cellularity, as well as areas with high cellularity, can be detected (2C, D), high rCBV indicates high perfusion (2E), and black areas on SWI demonstrate neoangiogenesis (2F). DTI shows tract disruption and displacement (2G), and, on MRS, high choline, low NAA, and a high lactate peak confirm a high-grade malignancy (2H).

ADVANCED IMAGING TECHNIQUES IN THE DIAGNOSIS OF DEMENTIA: FROM STRUCTURE TO FUNCTION AND BACK AGAIN

BY PAUL M. PARIZEL, WIM VAN HECKE, SEBASTIAAN ENGELBORGHES

As the average life expectancy of the population increases, the prevalence of dementia is growing rapidly. Despite the vast and swiftly increasing numbers of patients with dementia, and notwithstanding the growing interest of press and politics, together with the emotional and financial burden of this debilitating condition, the disease remains largely underdiagnosed and undertreated. Within the medical and scientific community, there is a growing consensus that early and accurate diagnosis of dementia holds the key to better treatment response, timely counselling of patients and caregivers, and optimised disease management. This would delay institutionalisation, reduce the caregiver burden, and would be beneficial for patients,

medical and paramedical practitioners, as well as social and healthcare systems.

The most common type of dementia is Alzheimer's disease (AD), with an exponentially increasing prevalence with age. The clinical diagnosis of possible or probable AD is still based on excluding other systemic and brain disorders that could account for cognitive deterioration. The required diagnostic work-up, including clinical, technical and laboratory assessments, is time-consuming and expensive, and results, at best, in a diagnosis of probable AD confined to the dementia stage. A clinical diagnosis of probable AD has been shown to achieve average sensitivity and specificity values of 81% and 70% respectively.

Diagnostic tools that confirm the diagnosis of AD, rather than exclude all other possible causes, increase diagnostic certainty. A promising approach is the use of biochemical markers that are present in the cerebrospinal fluid (CSF). As the brain is in direct contact with the CSF, and as the flow of proteins to and from the CSF is restricted by the blood-CSF barrier, biochemical changes that reflect pathophysiological processes in the brain are likely to be reflected in the CSF. In 1998, a consensus report was published by the Working Group on Molecular and Biochemical Markers of Alzheimer's Disease that determined the requirements for an ideal biomarker for AD. In general, biomarkers should be able to detect a fundamental feature of AD pathology. The value of biomarkers should also be demonstrated in neuropathologically-confirmed dementia cases as neuropathology is still considered to be the gold standard of reference. In addition, diagnostic accuracy, sensitivity and specificity levels should be above 80%. The test itself should ideally be reliable and reproducible, non-invasive, simple to perform and inexpensive. CSF biomarkers that come closest to fulfilling these requirements are β -amyloid protein of 42 amino acids ($A\beta_{1-42}$), total tau protein (T-tau) and hyperphosphorylated tau (P-tau) in CSF. However, assessment of these biomarkers still means obtaining CSF through a lumbar puncture, which is an unpleasant, invasive, and time-consuming procedure.

Recently, the diagnostic criteria for AD were revised¹. Diagnostic criteria rely on the typical AD pattern of memory problems in combination with an AD biomarker. These criteria allow an early diagnosis to be made, even in the prodromal stage of the disease. The biomarkers

for early AD diagnosis that are currently in use reflect the deposition of amyloid (CSF $A\beta_{1-42}$ or positron emission tomography (PET) with amyloid ligands), formation of neurofibrillary tangles (CSF P-tau), neuronal degeneration (CSF T-tau), changes in brain metabolism (FDG-PET), as well as neuronal loss and volumetric changes in brain structures that cause the disease symptoms, such as the hippocampus through magnetic resonance imaging (MRI) of the brain.

High-resolution 3D anatomical MRI data sets allow the visualisation of structural changes in the brain in patients with dementia. These images can be acquired non-invasively in around five minutes. An overall brain volume reduction can be seen on and measured from these anatomical MRI data sets. As an example, the brain of a 32-year-old healthy woman and a 76-year-old woman with AD are shown in Figure 1. Using specialised software, the volume of the brain's grey matter (containing the neurons) and white matter (containing the axons, which connect different neurons) can be measured.

Although whole-brain volume loss can be observed in patients with AD, compared with age-matched healthy subjects, neuronal loss in AD patients is more significant in specific brain regions, such as the hippocampus [2]. Since the hippocampus is a brain structure which is responsible for memory and is affected in an early stage of the disease, volume loss in the hippocampus can be related to the early memory problems that occur in patients with AD. Reduction of the hippocampal volume, as measured on MRI, has been shown even in prodromal stages of AD² and can predict later conversion to AD

with about 80% accuracy³. In Figure 2, the hippocampi of a 70-year-old healthy subject (in green) and a 72-year-old patient with AD are shown (in red).

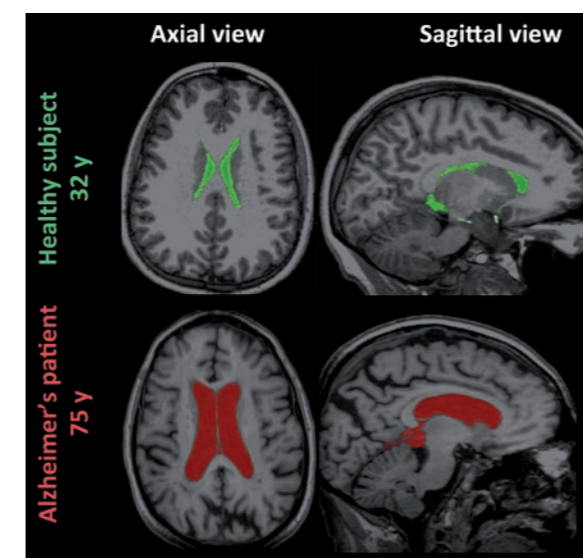
Another volumetric MRI method of interest for AD, and other types of dementia, is the cortical thickness measurement of the entire cortical mantle of the brain and, in particular, the neocortical association areas and the entorhinal cortex. Studies have demonstrated an accuracy of more than 90% in distinguishing AD patients from healthy controls by measuring the cortical thickness⁴.

In summary, advanced neuroimaging techniques offer new insights into the brain of dementia patients in a non-invasive, accurate and reproducible way. These methods not only generate insightful images of the anatomy and structure of the brain, but, more importantly, they provide quantitative measures which allow us to objectively assess the state of the brain of Alzheimer's patients, leading to a more accurate and early diagnosis. MRI holds great promise because it permits measurement of functional and structural parameters (such as cerebral blood flow, axonal myelination and changes in connectivity) without using ionising radiation. For the first time, advanced neuroimaging techniques can provide quantification of brain degeneration in dementia patients. We can expect these methods to significantly contribute towards an earlier and more accurate diagnosis of AD and other neurodegenerative brain disorders in the future.

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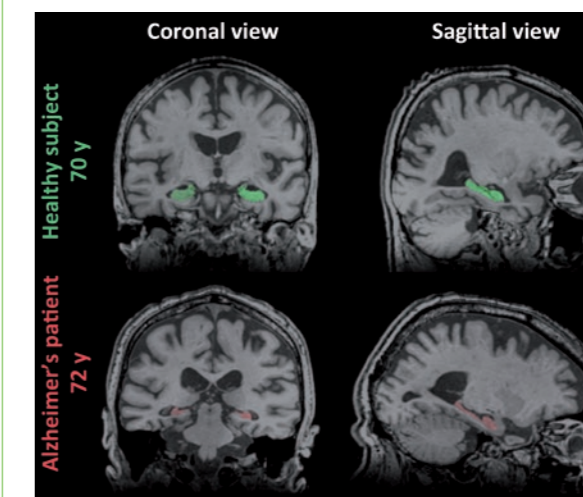
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FIGURE 1



Three-dimensional T1-weighted gradient echo images from the brain of a 32-year-old healthy woman (top row) and a 76-year-old woman with AD (bottom row), using axial (left column) and sagittal (right column) projections. In the patient with AD, the size of the brain ventricles (segmented and visualised in red) is much larger than in the healthy woman (ventricles shown in green). This increase in ventricular size represents atrophy (shrinking) of the brain parenchyma, which is a typical feature of AD.

FIGURE 2



Three-dimensional T1-weighted gradient echo images from the brain of a 70-year-old healthy individual (top row) and a 72-year-old patient with AD (bottom row), using coronal (left column) and sagittal (right column) projections. The grey matter of the hippocampus has been segmented and is visualised in green (healthy individual) and in red (AD patient). There is obvious volume loss in the AD patient, reflecting severe hippocampal atrophy.

MAGNETIC RESONANCE IMAGING IN THE DIAGNOSIS OF MULTIPLE SCLEROSIS

BY ÀLEX ROVIRA

INTRODUCTION

Multiple sclerosis (MS) is a chronic, persistent inflammatory demyelinating disease of the central nervous system (CNS), characterised pathologically by areas of inflammation, demyelination, axonal loss, and gliosis scattered throughout the CNS, mainly affecting the optic nerves, brainstem, spinal cord, and cerebellar and periventricular white matter. The causes of MS are still unknown, but it most likely results from an interplay between as yet unidentified environmental factors and susceptibility genes.

Relapses and progression are the two major clinical phenomena of prototypic MS. Relapses are considered the clinical expression of acute inflammatory demyelination spreading in the CNS. The remission of symptoms early in the disease is likely the result of remyelination, resolution of inflammation, and compensatory mechanisms such as redistribution of axolemmal sodium channels and cortical plasticity. In parallel with the demyelinating episodes, there may be damage to the exposed axons, leading to transection of the axons and retrograde neuronal degeneration. This process can be irreversible and is responsible for the accrual of disability that occurs as the disease progresses. Later in the disease, flare ups

of inflammatory activity occur less frequently, but the neurodegenerative process continues inexorably.

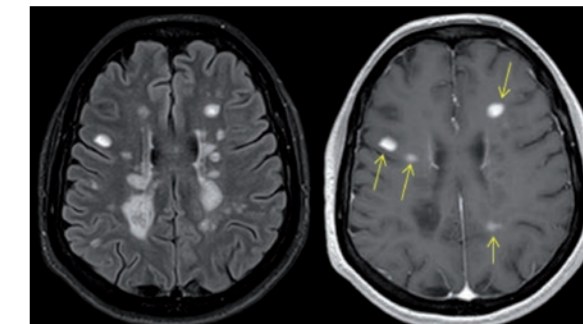
Immunomodulatory drugs such as beta-interferon, glatiramer acetate, natalizumab and fingolimod can alter the course of the disease, particularly in the relapsing phase of the disease, by reducing the number of relapses and accumulated lesions seen on magnetic resonance (MR) imaging, and by influencing the impact of the disease on disability.

IMPLEMENTATION OF MR IMAGING IN THE DIAGNOSIS OF MULTIPLE SCLEROSIS

The exact diagnosis of MS still remains challenging in some cases, as there is no single test (including biopsy) that can provide a definitive diagnosis of this disease. Over the last 20 years, the neurological community has adopted diagnostic criteria for MS, which have been modified several times following new evi-

dence and expert recommendations. With the availability of expensive disease-modifying treatments, which can be associated with serious side effects, and which are thought to be particularly effective in the early phases of the disease, an early and accurate diagnosis of MS is more important than ever. Diagnostic criteria for MS include clinical and paraclinical tests capable of demonstrating demyelinating lesions within the CNS disseminated across space and time, and capable of excluding alternative diagnosis that could mimic MS either clinically or radiologically. Although the diagnosis can be made on clinical presentation alone, MR imaging should be obtained to support the clinical diagnosis, and in a significant proportion of patients it can even replace some clinical criteria. This diagnostic value of MR imaging is based on its high sensitivity for detecting MS lesions within the brain and spinal cord, which make this technique not only the most important paraclinical tool for diagnosing MS, but also for understanding the natural history of the disease and monitoring the efficacy of disease-modifying treatments (Figure 1).

FIGURE 1



Conventional brain MR imaging in a patient with a diagnosis of MS. The T2-weighted image (left) shows the typical multifocal demyelinating lesions involving the white matter of both brain hemispheres. The contrast-enhanced T1-weighted image (right) demonstrates those lesions with abnormal blood-brain barrier permeability (arrows), a marker of inflammatory activity.

NON-CONVENTIONAL MR TECHNIQUES IN THE DIAGNOSIS OF MULTIPLE SCLEROSIS

There are pathologic and MR imaging data indicating that irreversible and diffuse tissue damage occurs at the earliest clinical stage of MS, and that the demonstration of this damage may be useful for identifying those patients with a higher risk of developing severe disability and cognitive impairment, and as a consequence those patients who may require early and aggressive treatment. Conventional MR techniques do not specifically detect the irreversible tissue damage within focal lesions and are insensitive to detecting diffuse damage in both white and grey matter. For that reason, a huge effort has been made in recent years to overcome these limitations.

Proton MR spectroscopy (¹H-MRS) has been used to assess the presence of tissue damage outside visible T₂ lesions in patients presenting a clinically isolated syndrome (CIS), the commonest form of presentation of MS. Several studies have shown a significant reduction in N-acetyl-aspartate (NAA) (a marker of neuroaxonal damage), and an increase in myo-inositol (a marker of glial cell activity) in the apparently normal white matter of CIS patients, which have been more prominent in those who subsequently converted to definite MS in the short-term follow-up.

Other MR techniques such as diffusion tensor imaging (DTI) and magnetisation transfer (MT) imaging have also shown, in group comparisons, significant differences in apparently normal brain tissue between CIS patients and healthy controls, and some value in predicting cognitive impairment and disability progression.

Although these non-conventional MR techniques provide valuable information about the degree and extent of tissue damage within the apparently normal brain tissue and for predicting the development of MS and disability in patients with CIS at a group level, they are yet to be adequately compared to conventional MR imaging for sensitivity and specificity in the diagnosis and differential diagnosis of MS in individual patients. Prospective studies are still required to systematically assess their real and added value to conventional MR techniques as diagnostic and prognostic measures, as well as their value to early treatment decision in individual patients.

FUTURE REQUIREMENTS AND CHALLENGES IN THE DIAGNOSTIC WORK-UP OF MULTIPLE SCLEROSIS

As a result of its high sensitivity, MR imaging has become the key diagnostic tool in the diagnosis of MS, as many imaging findings seen in MS patients are not specific to the disease. The McDonald

diagnostic criteria for MS have become less restrictive over time, possibly leading to the undesirable situation of MS overdiagnosis. Differential diagnosis is therefore a key issue in this context. The perivenular distribution pattern and increased iron deposition in MS lesions have been targeted in order to address this issue, particularly when MR systems operating at higher magnetic field strengths (≥ 3 T) are used. A relatively new sequence, susceptibility-weighted imaging (SWI), which has shown high sensitivity in detecting iron containing tissues and small veins due to their paramagnetic properties, has added value for these purposes particularly when co-registered and mixed with standard pulse sequences such as T₂-FLAIR. Recent experience with the implementation of SWI at 3.0T/7.0T in MS has shown that most focal chronic, and some acute, demyelinating lesions can be depicted as areas of low signal intensity likely representing iron deposition, and that a substantial proportion (higher than 40%) of MS lesions show a central vein (Figure 2). Future studies will have to demonstrate whether the incorporation of these imaging findings will further improve the specificity of MR imaging in the diagnosis of MS.

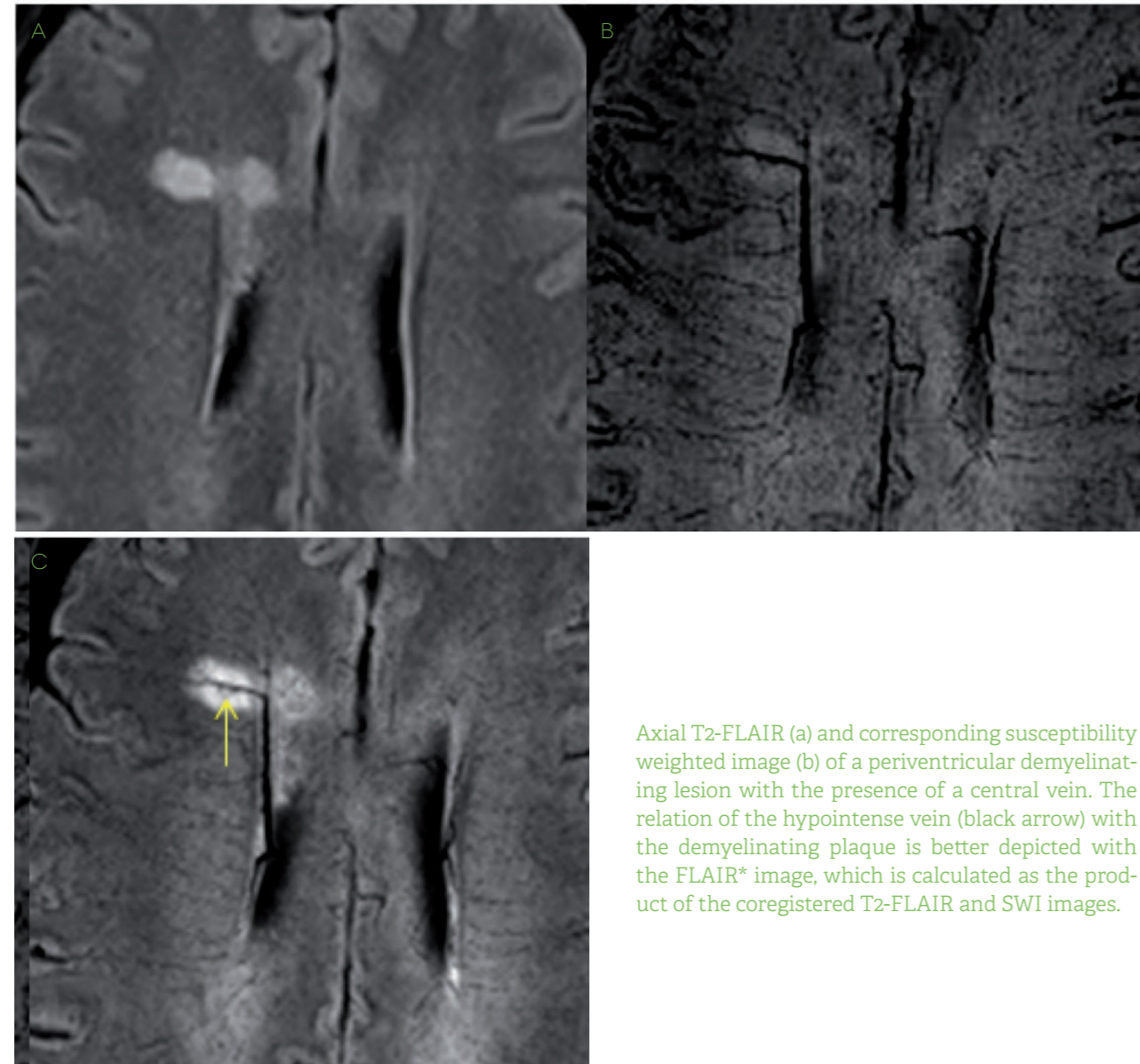
Another strategy is the incorporation of other important aspects of MS pathology such as the presence of cortical pathology. Cortical lesions are abundantly present in MS and may be better detected with dedicated pulse sequences such as the double inversion recovery (DIR) sequences. The advantage of these sequences becomes even more obvious when higher magnetic field strengths are used. This higher sensitivity may have some clinical relevance as identification of at least one intracor-

tical lesion may allow a more accurate identification of patients at risk of converting to clinically definite MS. However, imaging of cortical lesions at standard clinical field strength, even when using DIR sequences, is still suboptimal as a result of their limited sensitivity and reproducibility. Thus, while these sequences have made a major contribution to detecting focal cortical lesions in MS, providing important insights into the occurrence of cortical pathology in all subtypes of MS and their association with clinical disability and cognitive impairment, substantial research efforts are still needed before considering this technique within the standardised MR imaging protocol in the diagnostic work-up in clinical practice.

CONCLUSION

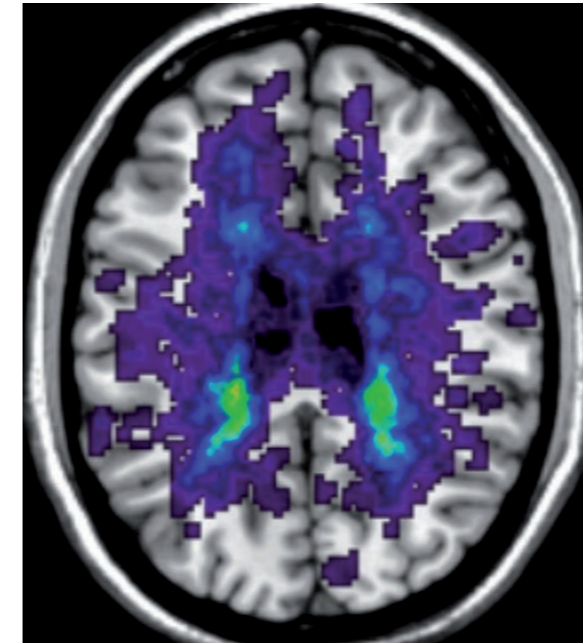
MR imaging has a major role in the overall diagnostic scheme of MS, as well as in selecting patients for immunomodulatory treatment, monitoring disease activity, and predicting treatment response. This important contribution of MR is based mainly on its unique sensitivity in detecting MS lesions and in assessing inflammatory activity in vivo, which is usually accomplished by using conventional MR techniques such as T₂-weighted and gadolinium-enhanced T₁-weighted images.

FIGURE 2



Axial T2-FLAIR (a) and corresponding susceptibility weighted image (b) of a periventricular demyelinating lesion with the presence of a central vein. The relation of the hypointense vein (black arrow) with the demyelinating plaque is better depicted with the FLAIR* image, which is calculated as the product of the coregistered T2-FLAIR and SWI images.

FIGURE 3



Lesion probability map obtained with brain MRI in a group of patients with multiple sclerosis. Colour intensity indicates those brain areas with a higher probability of containing multiple sclerosis lesions. (Provided by Cap de la Unitat de RM i de Neuroradiologia (IDI), Servei de Radiologia, Hospital Universitari Vall d'Hebron.)

MAGNETIC RESONANCE IMAGING IN THE DIAGNOSIS AND TREATMENT OF PARKINSON'S DISEASE

BY TAREK A. YOUSRY

INTRODUCTION

Parkinson's disease (PD) is the most common neurodegenerative disease after Alzheimer's disease (incidence 20 per 100,000 people and a prevalence of 150 per 100,000 people), followed by progressive supranuclear palsy (PSP) and multiple system atrophy (MSA).

Nigral cell loss underlies many of the movement disorders seen in the disease, but cell loss extends well beyond the dopaminergic system in the majority of patients. In PD as well as in MSA there is intracellular accumulation of an abnormally folded insoluble protein, alpha-synuclein, in the form of Lewy bodies in PD and largely as oligodendroglial, glial cytoplasmic inclusions (GCIs) in MSA. For this reason MSA and PD are classified as alpha-synucleinopathies. PSP and corticobasal degeneration (CBD) are characterised neuropathologically by neuronal loss, gliosis and the presence of tau-immunoreactive neuronal and glial cell inclusions affecting subcortical and some cortical regions. PSP and CBD are therefore classified as tauopathies. Recently, clinic-pathological studies

have indicated that these Parkinsonian diseases have overlapping areas of neuronal loss and that the spatial pattern of neurodegeneration correlates better with clinical features than the presence of one molecular pathology versus another (tauopathy versus synucleinopathy).

Patients with PD and with Parkinson-like symptoms are often a diagnostic challenge. The established diagnostic criteria are all clinical, but evidence from clinic-pathological studies reveals that 24% of those with a clinical diagnosis of PD have alternative diagnoses at post mortem, such as PSP, MSA, CBD, vascular disease and Alzheimer's disease (AD). The diagnosis can be particularly challenging in the early clinical phase (the first two years) as PD overlaps clinically with PSP, MSA, CBD and dementia with Lewy bodies (DLB). Accurate diagnosis in this phase, however, is important when specific disease-modifying therapies become available.

MRI IN THE DIAGNOSIS OF PARKINSON'S DISEASE

For a long time, the role of imaging in movement disorders was confined to the exclusion of secondary causes of Parkinsonism such as demyelination, tumours, normal pressure hydrocephalus and vascular disease.

However, conventional MRI has been instrumental in establishing criteria that assist in discriminating the different causes of Parkinsonism. A number of qualitative and quantitative methods have been developed to help differentiate atypical PD variants PSP and MSA from each other and from idiopathic PD.

The qualitative methods rely on changes of either the T2 signal or of the volume.

An example of changes in T2 signal is the pontine hyperintense 'hot cross bun sign' or 'cross sign' as well as the lateral hyperintense 'putaminal rim' sign in MSA. In PD, a decrease in T2 signal and a related decrease in the width of the pars compacta (PC) of the substantia nigra (SN) have been described but couldn't be replicated by many groups. Only recently was it possible, using high-field MR, to visualise more detailed aspects of the SN's complex anatomy. In the dorsolateral SN, a specific component of the PC-nigrosome-1 can be readily depicted on high-field 7T, as well as high-resolution 3T, using susceptibility weighted imaging (SWI) giving rise to a 'swallow tail' appearance, which is lost in PD. This sign seems to

have a high diagnostic accuracy for PD and has therefore the potential to become a new and easily applicable 3T MRI diagnostic tool for the diagnosis of PD (Figures 1-3).

Changes in volume affect specific regions, thereby altering their shape and form. In PSP, volume loss affects predominantly the mesencephalon, whereas in MSA it mainly affects the pons. The mesencephalic volume loss, present in at least 75-80% of clinically diagnosed PSP, led to the description of specific shapes the recognition of which would support the diagnosis of PSP. These shapes include the Hummingbird, the Morning Glory, and the King Penguin signs. These changes can be quantified by linear, area or volumetric measurements. For instance, a diameter of < 17mm has been shown to be highly specific of PSP when compared with MSA and PD.

In an effort to increase the sensitivity and specificity, more complex indices were suggested such as the mesencephalon-pons ratio and the MR Parkinsonism index (MRPI) (pons area/midbrain area multiplied by middle cerebellar peduncle width/superior cerebellar peduncle width) which was found to successfully differentiate MSA and controls on an individual basis.

Of great interest is the longitudinal volume measurement assessing whole-brain and regional atrophy rates. Regional rates of brainstem atrophy are greater than whole-brain rates of atrophy in PSP and MSA-P. Their different rates allow the differentiation of PSP and MSA-P from each other and from PD patients and healthy controls. This method has therefore the potential not only to

assist with the diagnosis, but also to monitor treatment and possibly serve as a secondary outcome measure.

Advanced MRI techniques also offer some promise: diffusion-weighted imaging can help distinguish between Parkinson's disease and other secondary causes of Parkinsonism though not between PSP and MSA. With magnetisation transfer imaging, changes are seen which are compatible with the pathology of the underlying disease, but these do not allow complete discrimination of the underlying pathological process.

MRI IN THE TREATMENT OF PARKINSON'S DISEASE

Functional stereotactic neurosurgery provides an effective treatment for Parkinson's disease patients whose motor symptoms are refractory to pharmacological treatment. The surgery aims at altering the function of target structures implicated in the generation of these symptoms, either by destroying them through ablation or by exposing them to a high frequency current emanating from an inserted electrode, a procedure known as deep brain stimulation (DBS). With DBS being a potentially reversible and safer procedure that 'mimics' the effect of a lesion and that can be performed bilaterally, ablative procedures declined and DBS became the method of choice. The target structures in PD patients are typically the subthalamic nucleus (STN) and the internal globus pallidum (GPi). Newer targets such as the

pedunclopontine nucleus (PPN) are under evaluation. However, the success of this approach depends heavily on the accuracy with which the target structures are reached. Pre-operative localisation of the target structures can be performed either directly from pre-operative MRI or through intraoperative recordings using micro-electrodes (MER), to identify characteristic activity of individual STN or pallidal neurons. There is an ongoing debate as to the advantages of each of these two methods. It is by now evident, however, that direct targeting is a relatively short, cost-effective and safe procedure, which starts and finishes with an MRI examination. The preoperative 'guidance-MRI' enables accurate and precise identification of the anatomy of the target structures. It is therefore ideally performed at a higher field strength (3T) with high spatial and contrast resolution sequences, specifically adapted to the structures to be targeted. At a field strength of 1.5T for example, the STN is very well visualised by a T2-weighted sequence, whereas the GPi is best visualised by a proton density-weighted sequence. SWI sequences are also proving to be very useful. The postoperative 'verification-MRI' needs to visualise the electrodes and their relationship to the target. The main emphasis is on safe imaging in the presence of intracerebral metal implants. The specific absorption rates of the sequences therefore have to be adjusted to ensure that energy deposition remains within safety margins.

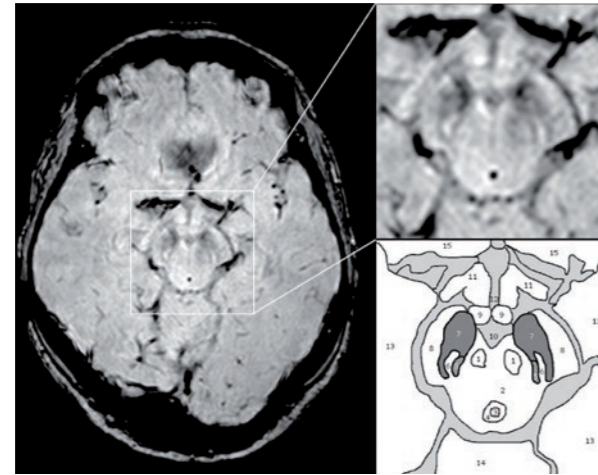
CONCLUSION

In summary, MRI is an integral part of the assessment and treatment of movement disorders. A number of diagnostic MR signs have been described that are very useful in the diagnosis of these diseases and that should be applied when reporting. Many, however, are best seen at late stages of the disease. There is therefore a clear need for the identification of early-stage disease markers. MR is, however, an essential part of the neurosurgical procedure which is typically MRI-planned and MRI-verified. Considerable care needs to be taken to optimise the appropriate sequences to ensure the overall success of the procedure.

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- Foltynie T1, Hariz MI. Surgical management of Parkinson's disease. *Expert Rev Neurother*. 2010;10(6):903-14.

FIGURE 1



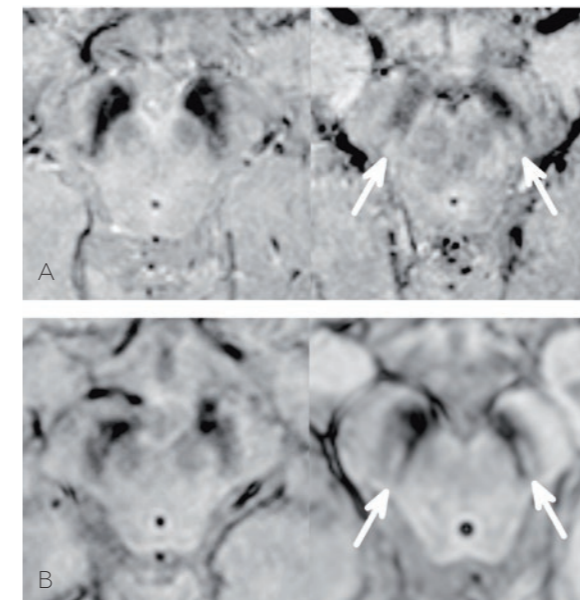
Substantia nigra anatomy on 3T-SWI – MRI. 3T-SWI axial slice just at the level of nigrosome-1 with magnification of the midbrain structures and a sketch outlining relevant anatomical structures: 1 red nucleus, 2 midbrain tegmentum, 3 aqueduct, 4 periaqueductal grey, 5 medial lemniscus, 6 nigrosome-1, 7 substantia nigra, 8 cerebral peduncle, 9 mammillary body, 10 inter-peduncular fossa, 11 optic radiation, 12 3rd ventricle, 13 temporal lobe, 14 cerebellum, 15 frontal lobe.

FIGURE 2



The red rumped swallow (*Cecropis daurica*). The tail of the swallow resembles the appearance of the healthy nigrosome-1 on HR-SWI MRI. Picture modified from Wikipedia: <http://en.wikipedia.org/wiki/Swallow>. Image rights transferred to public domain

FIGURE 3

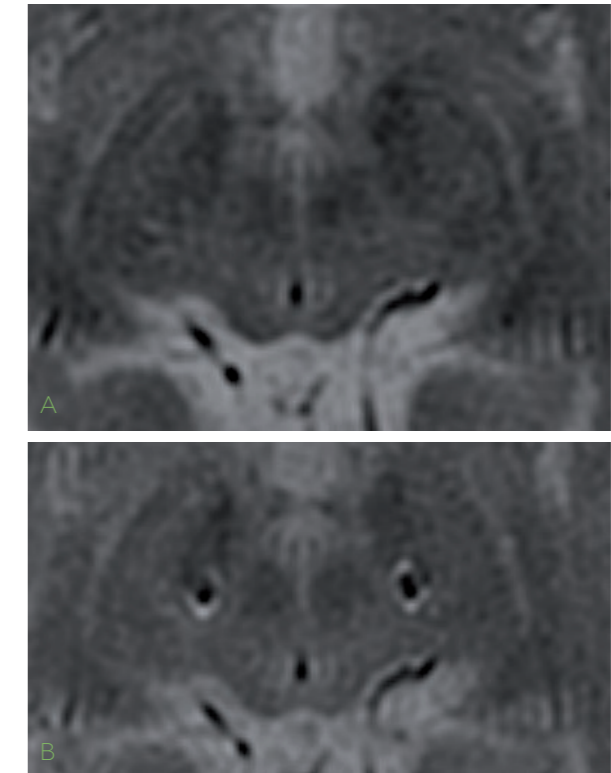


SWI MRI in PD and non-PD patients.

A. High resolution SWI MRI (3D gradient echo EPI, magnitude image) of a PD patient (left, 60 years, female, UPDRS: 53, HY score 3, nigrosome-1 absent bilaterally) and a control (right, 61 years, female, nigrosome-1 present bilaterally).

B. Clinical high resolution 3D-T2*/SWI MRI (Philips 'PRESTO' sequence), of a PD patient (left, 58 years old, male, nigrosome-1 absent bilaterally) and a non-PD patient (right, 70 years old, female, diagnosed with an aneurysmal subarachnoid haemorrhage, nigrosome-1 present bilaterally)

FIGURE 4



T2w images for guiding the DBS of the STN (a) and after the intervention, for verifying the position of the electrodes (b).

RADIOTHERAPY OF BRAIN MALIGNANCIES

BY MECHTHILD KRAUSE

INTRODUCTION

Radiotherapy, together with surgery and drug treatment, is one of the main pillars of cancer treatment. Today, about 60% of all cancer patients are treated with radiotherapy, and in 50% of all cancer cures radiotherapy is part of the treatment. In most cases, radiotherapy is applied as external-beam radiotherapy, which means a radiation beam is sent from a distance of several centimetres to the patient and the tumour. To ensure a high radiation dose within the tumour, while protecting the normal tissue around the treatment area, different beams from different directions are combined and crossed within the target area. Modern techniques that allow further improvement in precision are sometimes helpful, like stereotactic radiotherapy for very small tumours or intensity-modulated radiotherapy which can apply an inhomogeneous dose to irregular or concave target volumes. The standard type of radiotherapy is photon radiotherapy, i.e. high-energy x-rays. For some kinds of tumours, particle radiotherapy is more advantageous than photon radiotherapy, especially for tumours at the base of the skull or close to the spine, where a high radiation dose needs to be applied close to the organ at risk. For many other tumours, the value of particle radiotherapy is currently being tested. In general, radiotherapy applied alone or in combination with other anti-cancer treatments has the potential to permanently cure human tumours. The deactivation of tumour cells results from DNA damage to the tumour cells that can finally lead to cell death. With a few exceptions, radiotherapy dose is delivered in fractions that are applied daily. Between the fractions, the normal tissue

around the tumour has time to recover from radiation damage, thus reducing the risk of chronic side effects from radiotherapy.

WHAT KINDS OF BRAIN MALIGNANCIES ARE TREATED WITH RADIOTHERAPY?

Gliomas, i.e. tumours originating from the glial cells that support and protect neuronal cells in the brain, are distinguished by their histology in benign (WHO grade I/ II) and malignant tumours (WHO grade III/ IV). The most malignant tumour is the glioblastoma multiforme (WHO grade IV). If the overall status of the patient allows full treatment, then glioblastoma multiforme is usually treated after surgery or biopsy with radiotherapy combined with chemotherapy. WHO grade III tumours are also often treated with radiotherapy after surgery and depending on the specific features of the tumour chemotherapy is used in addition, or in some cases alternatively, to radiotherapy. Other very common reasons to perform radiotherapy treatment are brain metastases. If they are numerous, the whole brain will be irradiated with the aim of delaying further progression. If only one or very few brain metastases are present, they can be irradiated using high-precision radiotherapy techniques like stereotactic radiotherapy, which has the potential to completely remove the metastases with efficacy comparable to surgery.

In addition, there are many rare brain tumours where radiotherapy is part of the treatment, including paediatric tumours like medulloblastoma or ependymoma. In some benign tumours, like meningioma or acoustic neurinoma, stereotactic radiotherapy is an alternative to surgery, showing an equal level of long-term efficacy.

CLINICAL EXAMPLE: RADIOCHEMOTHERAPY OF GLIOBLASTOMA MULTIFORME

Glioblastoma multiforme is a very aggressive tumour entity that requires multi-modal treatment. If possible, the first step is tumour resection. After the wound has healed, patients receive radiotherapy combined with chemotherapy (Temozolomide) with the aim of deactivating residual tumour cells left after surgery. For the preparation of radiotherapy, a mask from thermoplastic material is made for the patient, which ensures consistent positioning of the head during treatment. A radiotherapy planning CT is performed and the post-operative MRI is overlaid to contour the radiotherapy target volume and the organs at risk. The target volume includes visible tumour areas, the surgical cavity and the brain tissue approximately 2cm around the cavity. The latter is targeted because glioblastoma cells usually spread relatively far around the visible tumour and can lead to rapid recurrences if not included in the

treatment region. A radiotherapy treatment plan is then completed by a physicist; the radiation dose distribution is optimised with the aim of homogeneously applying the prescribed radiation within the target volume and reducing doses to the normal tissue as much as possible.

Radiotherapy is then applied in 30 to 33 fractions, five days per week over six to six and a half weeks. One radiotherapy fraction lasts a few minutes. Chemotherapy with Temozolomide is prescribed for the whole treatment time and prolonged over 6 months afterwards. The whole treatment can in most cases be performed on an out-patient basis. During treatment, the patient is regularly seen by the physician, to check whether there are any side effects from the treatment. Blood cell counts and evaluation of liver enzymes, for example, are repeatedly performed to exclude side effects of the chemotherapy.

Besides this standard radiochemotherapy treatment, there are also treatment options for patients in poorer condition due to age, advanced tumour or other chronic diseases that may be present at the time. For such patients, the physician will decide whether radiotherapy with a reduced total dose or chemotherapy alone is a treatment option that may be applicable.

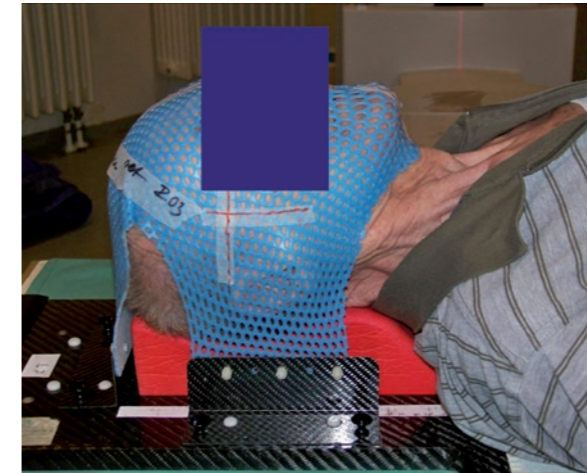
ARE THERE NEW TREATMENT OPTIONS FOR GLIOBLASTOMA MULTIFORME?

Radiochemotherapy, as described above, became the clinical standard nearly ten years ago and has, in comparison to radiotherapy without chemotherapy, improved the survival of patients with this aggressive disease. However, glioblastoma multiforme remains a disease that is seen as incurable. Thus, many efforts have been made to change this situation and improve treatment outcome. Such new treatments always need to be evaluated through clinical trials. In clinical trials, new treatment options are investigated under very well-controlled conditions, so that the risk to patients taking part in trials is very low, and the extremely standardised and controlled treatment and follow-up within a trial can often be seen as a considerable advantage for the patient. Glioblastoma trials aim to find markers that help to predict treatment outcome and select patients for specific treatments in order to establish new combined radiochemotherapy treatments and evaluate other radiotherapy beam modalities like protons. Patients who are willing to take part in clinical trials can help scientists to better understand the disease and improve the results of treatment.

SUMMARY

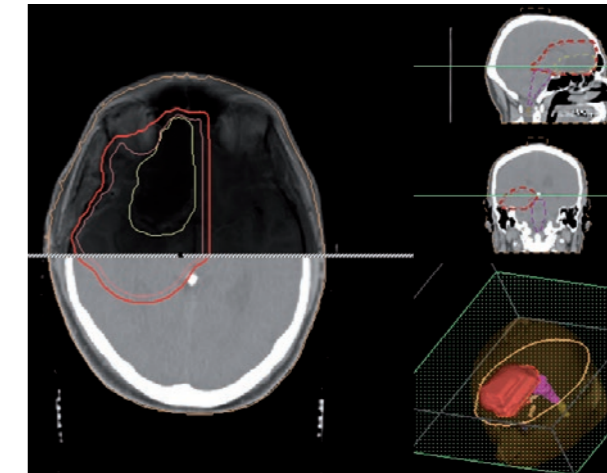
Overall, radiotherapy has made a number of considerable technical and biological advances within the last few decades. It is an effective and safe treatment option for different kinds of brain malignancies. Clinical trials are being performed to further improve radiotherapy, by evaluating new combined treatments or by investigating other beam qualities like protons for example.

FIGURE 1



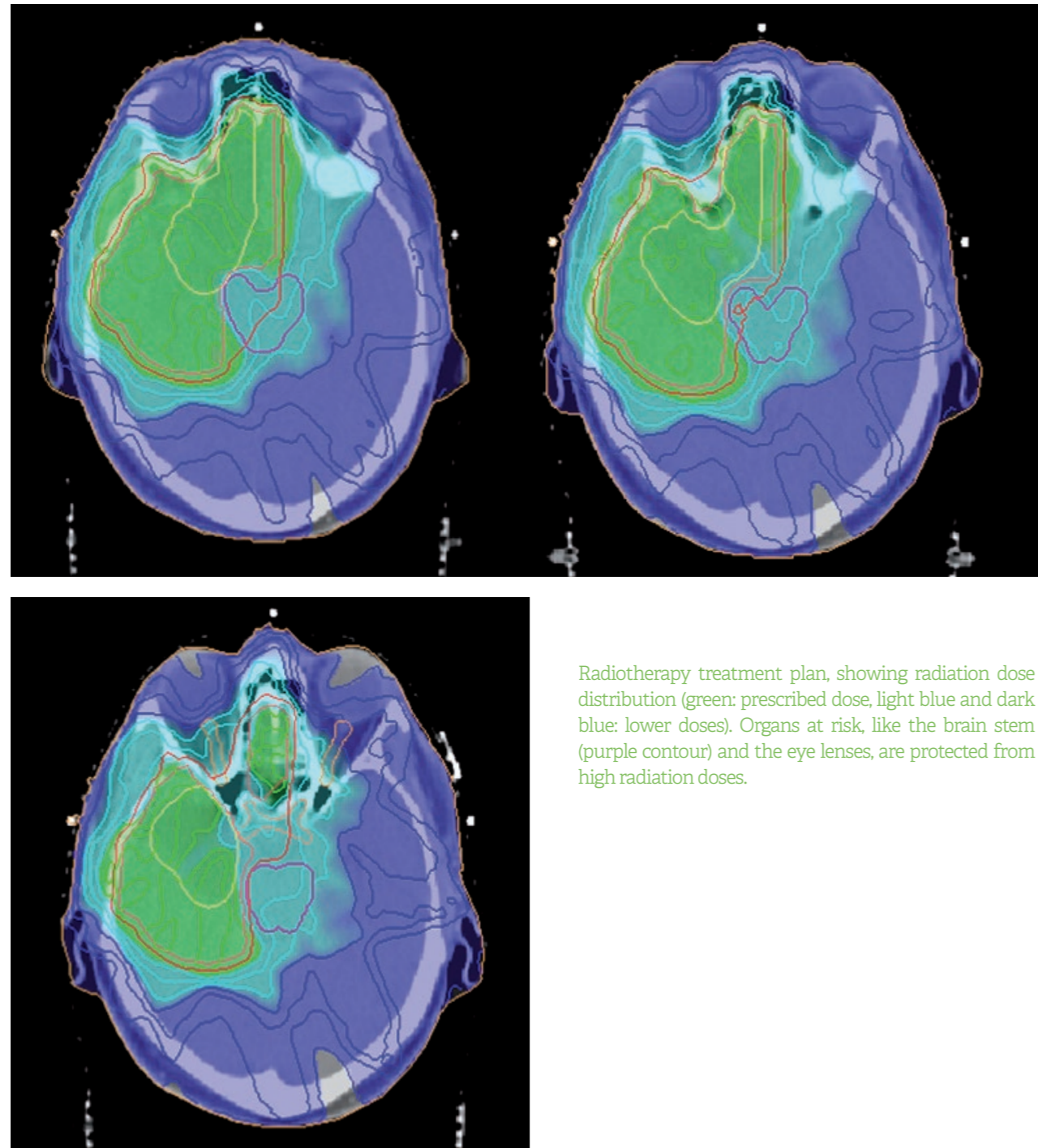
Patient positioned with mask.

FIGURE 2



Overlay of MRI and radiotherapy planning CT for contouring of the target region and normal tissue.

FIGURE 3



NEUROIMAGING RESEARCH

BY MAX WINTERMARK, RIVKA COLEN, CHRISTOPHER T. WHITLOW, GREG ZAHARCHUK (AMERICAN COLLEGE OF RADIOLOGY)

INTRODUCTION

Over the past decade, we have seen an explosion of innovation with respect to anatomical and functional neuroimaging techniques, providing exciting insights into new aspects of the human brain that transcend the simple visualization of anatomical structures. Newer and faster scanners, better image quality, higher magnetic field strength, as well as higher spatial and temporal resolution allow fully quantitative assessment of the brain's macroscopic structure, including its microstructural and functional organization, perfusion and metabolism. These developments include advancements in hardware, diverse methods of acquisition, methods for analysis, and novel application to clinical questions. The resultant exponential increase in highly granular neuroimaging data that can be collected over a relatively short acquisition period creates challenges, but also opportunities in terms of better characterization of neurological, neurosurgical and psychiatric disorders that arise from complex central nervous system dysfunction. Indeed, neuroimaging is now appropriately recognized as a "big data" technique, sharing a similar need with other data-rich methods for further innovation in analysis and meaningful information extraction, and also for integration with the other big data, such as genomics and proteomics. There is a continued need for this technology to be translated from basic science, 'bench top', into clinical practice, so that these remarkable advances in the ability to characterize the brain can benefit patients with neurological, neurosurgical and psychiatric disorders, so as to improve patient outcomes and alleviate human disease. Critical to this endeavor of

meaningful clinical translation is comparative effectiveness and outcome research in order to gain widespread acceptance in the modern, economically constrained healthcare system. This review article attempts to illustrate the different facets of these innovative anatomical and functional neuroimaging techniques, as well as the potential role of these methods as clinical tools for evaluating the range of diseases that affect the brain.

QUANTITATIVE NEUROIMAGING

Quantitative neuroimaging aims to extract physical parameters from CT, MR, PET, and SPECT images of the brain. Quantitative assessment of cerebral tissue and function provides the potential for unbiased and reproducible evaluation, as compared to the more traditional subjective visual interpretation, which is semi-quantitative at best. Quantitative neuroimaging approaches have begun to permeate into clinical practice due to the work of disease-specific consortia. For example, the Alzheimer's Disease Neuroimaging Initiative (ADNI) collected MRI, PET, genetics, cognitive test, CSF and blood biomarker data for investigation as potential predictors for the development of Alzheimer's disease.¹ Commercially available processing tools were developed from this endeavor that provide quantitative volumetric measurements of hippocampi and cerebral hemispheres, which can be compared with the normative ADNI database to provide output with respect to

age-dependent controls. Such tools provide utility in determining whether brain volume loss of one individual patient is part of expected senescent changes in the context of normal aging, or out of proportion for age, suggesting some type of dementia. These tools also facilitate the assessment of changes in brain volumes over time for characterizing the progression of mild cognitive impairment to Alzheimer's disease.

Quantitative neuroimaging is being heavily exploited as part of clinical trials using longitudinal and cross-sectional study designs with neuroimaging biomarkers for treatment selection or monitoring. Examples include imaging-based clinical trials of stroke, multiple sclerosis and brain tumor therapies. In stroke therapy trials, neuroimaging biomarkers such as the visualization of the ischemic penumbra, or tissue at risk of imminent cell death, can be used to select patients for stroke therapies and randomize them to treatment versus placebo groups for clinical trials.² The final infarct volume measured on follow-up imaging is another neuroimaging biomarker that can be used as a secondary endpoint. Similarly, serial neuroimaging is used as a secondary endpoint to monitor the effect of therapy for multiple sclerosis (for example, evolving number of white matter lesions) and brain tumors (for example, evolving size of enhancing and non-enhancing tumors). Though still not accepted by the Food and Drug Administration as primary outcome measures, these current research studies are laying the groundwork for future clinical practice.

Finally, the quantitative approach to neuroimaging is well-suited for statistical modeling and systematic image

analysis approaches based on canonical templates, or brain atlases for measurement of changes involving specific regions of interest that may be affected by central nervous system disease.³ Finally, new methods for quantitative evaluation of the brain as an integrated structural and functional network will be further discussed in the next section. These new approaches are considered by many to be critical for deciphering brain circuitry and the potential dysfunction of brain network connectivity that may be associated with a number of neurological and psychiatric disorders.

UNDERSTANDING BRAIN CIRCUITRY, BRAIN FUNCTION AND BRAIN DYSFUNCTION

Modern neuroimaging techniques allow the brain to be characterized as an integrated structural and functional network. The field of connectomics aims to understand the structural connectivity of brain networks, representing physical connections such as axons or fiber tracts. Structural connectivity can be observed either at the level of individual synapses (microconnectome) or at the level of fiber tracts between brain regions (macroconnectome). Structural magnetic resonance imaging (MRI), such as diffusion tensor imaging (DTI) and diffusion spectrum imaging (DSI) can provide information regarding struc-

tural connections of the macroconnectome.⁴ Functional MRI (fMRI) methods, such as blood oxygen level dependent (BOLD) imaging acquired during the resting-state can provide information regarding functional connectivity of the brain, identified as temporally correlated fluctuations in low-frequency BOLD signal between distributed regions.^{5,6} Functional connectivity can also be studied by measuring the electrical and magnetic activity associated with neuronal depolarization using electroencephalography (EEG) and magnetoencephalography (MEG), respectively.⁷⁻¹¹

The human connectome at the level of fiber tracts between brain regions has been shown to differ in patients with brain disorders compared to healthy control groups. Similar to genomics, the hope is to use connectomics as a clinical tool to identify biomarkers of disease that can be used to classify individual patients into diagnostic/prognostic groups and to predict outcomes related to therapeutic interventions. A variety of disorders affecting the brain have been associated with abnormalities of the connectome, including stroke, multiple sclerosis, brain tumors, epilepsy, neurodegenerative disorders, such as Alzheimer's dementia¹² and psychiatric diseases, such as depression and schizophrenia.

A number of hurdles must be overcome before diseases can be diagnosed and treated based upon the imaged connectome. Indeed, the pathophysiology of many diseases may result in relatively small or subtle abnormalities of the brain's functional or structural connectome compared to the structural organization of healthy controls. In addition, a given brain disorder may affect any

one of numerous individual networks or a combinations thereof. Methods to distinguish between group differences in the connectome, as are frequently reported in the literature, might not be sufficient to diagnose disease from which an individual patient suffers, and may be inadequate to indicate the best treatment option for that patient. As such, analysis tools to identify abnormalities of the connectome with high sensitivity and specificity for individual subject classification must be developed before meaningful clinical translation can be realized. In this regard, the field of connectomics is currently building large databases of structural and functional data, such as those of the Human Connectome Project¹³ and 1000 Functional Connectomes Project^{14,15} for conducting the necessary large-scale studies that may begin to better define the range of normal and abnormal with respect to the human connectome.

A better understanding of the brain function/dysfunction may also result from the new simultaneous PET-MRI scanner technology.¹⁶ Indeed, MRI represents the first-line diagnostic imaging modality for numerous indications, and a great number of specific PET tracers are available today to assess functional and molecular processes in the brain.¹⁷ For studying brain physiology, simultaneous acquisition may allow improved in vivo assessment of multiple neuropsychologic processes, such as changes in cerebral hemodynamics, including cerebral blood flow (CBF), volume (CBV), and oxygenation; and the relationship between metabolism and oxygen consumption (neurovascular coupling). Novel molecular probes enable the direct imaging of neuro-inflammation and microglial activation, hypoxia, necrosis,

and apoptosis. Before its integration with MRI, PET has largely been limited to studying physiology that was difficult to characterize with MRI, such as the decreased metabolism associated with interictal seizure imaging, or to distinguish recurrent brain tumors from radiation necrosis. Now that it is possible to combine PET and MRI in the same imaging session, the relative strengths of each individual technology can be brought to bear on the clinical questions, with the benefits of simultaneous acquisition and a minimum of patient inconvenience. For example, high-resolution CBV maps, created with MRI using ultrasmall superparamagnetic iron oxide (USPIO) nanoparticles, can be used to refine the calculation of oxygen extraction fraction measurements performed concurrently with oxygen-15 PET. Likewise, the high-resolution anatomical imaging that MRI excels in can be used to identify a region of focal cortical dysplasia in an epilepsy patient, which can then immediately be confirmed on accompanying fluorodeoxyglucose (FDG) PET images, which are inherently co-registered.

In addition, other disorders associated with changes in mental status, such as depression, dementia, schizophrenia, and obsessive-compulsive disorders, might be investigated in new ways, by combining anatomic, functional, and metabolic measurements during identical examination conditions. Simultaneous PET-MRI enables both spatial and temporal correlation of the signals, creating opportunities impossible to duplicate using sequentially acquired data. This is particularly important considering that a subject's mental state may change on time scales of minutes to even seconds while physiologic and metabolic changes can occur on the order of minutes in

some disease conditions, such as acute ischemic stroke or migraine. Likewise, similar rapid changes in baseline physiology can occur with therapeutic interventions. Because of this, PET-MRI will likely play a large role in the further understanding and treatment of psychiatric disorders.

BIG DATA

In recent years, an array of brain imaging techniques has been successfully employed to link individual differences in circuit function, structure or function in the living human brain with individual variations in the human genome. The central motivation behind imaging genomics is to use genetically informed brain imaging to pinpoint neurobiological mechanisms that contribute to behavioral intermediate phenotypes and disease states.

Clinically defined phenotypes are highly variable and there are inherent diagnostic uncertainties. In contrast to the relatively straightforward organization of the genome, the human phenome is a multidimensional search space with several neurobiological levels, spanning the proteome, cellular systems (e.g., signaling pathways), neural systems and cognitive and behavioral phenotypes. In a clinical context, the definition of symptoms and syndromes adds to the phenomic complexity. The genetic study of complex behavioral traits continues to mature along with that of complex neuropsychiatric disorders. A concept central to all these lines of research

entails the use of brain imaging to define intermediate phenotypes in humans. Compared to behavioral or syndromal phenotypes, intermediate imaging phenotypes may offer better mechanistic insights into how neural systems are affected by genetic variants and how this contributes to the emergence of brain disorders by virtue of their presumed closer proximity to genomic profiles.

The ongoing advances in neurogenetics will have a major impact on future study designs in the field of imaging genetics. New analytic methods and declining costs will prompt the use of more granular methods to map the human genome, including the detection of rare variants and copy number variations. This will require even larger sample sizes to detect robust genetic associations with complex multi-level phenotypes. Concurrently, this will pose unprecedented challenges for computational neuroscience. New neuroinformatics tools will have to be developed that can interrogate the highly multi-dimensional datasets acquired at multiple biological scales and can sufficiently capture the enormous genomic and phenomic complexity. Such tools may include supercomputers such as Watson. Winning the \$1 million 'Jeopardy!' challenge was just the tip of the iceberg for Watson, the IBM supercomputer that experts believe has the potential to revolutionize the neurosciences field. Powered by 90 servers and 360 computer chips, Watson was built in four years by IBM researchers seeking to develop a machine that could quickly answer complex questions. Using a probabilistic, evidence-based approach, Watson works to understand questions and develop answers – a capability critical to the technology's potential value to neurosciences and the understanding of the neurosci-

ences big data. Currently, Watson is being explored in the healthcare sector to help with big data analytics and adaptive learning.

STANDARDIZATION, DATA SHARING, AND RESEARCH NETWORKS

Significant resources around the world have been invested in anatomical and functional neuroimaging studies of central nervous system disease. Easier access to this large body of data would have profound impact on brain research. In particular, sharing data will accelerate progress in our fundamental understanding of the brain, lead to advances in the diagnosis and treatment of psychiatric and neurological disease, reduce the cost of research, increase the return on current research investments, and foster neuroimaging research and advances in clinical practice.

A trend toward increased sharing of neuroimaging data has emerged in recent years, illustrated by a number of initiatives. Groups such as Biomedical Informatics Research Network (BIRN), the Stroke Imaging Research Consortium (STIR), the Cancer Genome Atlas (TCGA), ADNI¹⁸ and Autism Brain Imaging Data Exchange (ABIDE)¹⁹ have produced the infrastructure to help groups share data. The development of common data elements (CDEs) has been encouraged and supported by

the NIH in order to facilitate the ability to merge multiple databases.^{20,21}

Nevertheless, a number of barriers continue to impede momentum. Many researchers and institutions remain uncertain about how to share data or lack the tools and expertise to participate in data sharing. Most of the data is not generally accessible, limited by issues of cost, privacy, and limited manpower. The use of electronic data capture methods for neuroimaging greatly simplifies the task of data collection and has the potential to help standardize many aspects of data sharing. The size and complexity of neuroimaging datasets and their associated challenges have increasingly attracted, in addition to radiologists, multidisciplinary communities of applied mathematicians, statisticians, image processors, data miners, and bioinformaticians who wish to apply their techniques to neuroimaging data. While their work may seem tangential to many neuroscientists, cross-disciplinary work may lead to major advances and even domain paradigm shifts. Neuroimaging will benefit tremendously from more multidisciplinary interactions, and a crucial first step in these collaborations will be for data to be available to those who work outside traditional neuroscience fields. This newly founded community has started work on several tools to ease and eventually automate the practice of data sharing. It is hoped that such tools will allow researchers to easily share raw, processed, and derived neuroimaging data, with appropriate metadata and provenance records, and will improve the reproducibility of neuroimaging studies.

The future of neuroimaging research will depend upon the integration of many types of data (e.g., multi-

modal imaging, imaging genomics, etc.). If robust anonymization can be assured and privacy concerns can be addressed, the aggregation of previously acquired datasets and results from many sites would already enable the creation of tremendously rich databases from which to test hypotheses. Neuroimaging may then enter an age where research could lean toward knowledge management rather than data management, and the construction of electronic systems that will accumulate results and information over which some reasoning can be done, eventually helping the construction of predictive models useful in brain diseases. As the overarching goal of scientific endeavor is to determine predictive models for the system under study, improvements to existing models are expected as new data are collected. Data availability is necessary for the construction of models based on large numbers of observations, as well as for the improvements or refutations of these models.

OUTCOME RESEARCH AND COMPARATIVE EFFECTIVENESS

A parallel direction that neuroimaging research needs to embrace is outcome research. In this day and age it is not sufficient to develop great neuroimaging tools and translate them to the clinics. Outcome research is required to inform the decisions of legislative bodies that make decisions related to healthcare, as well

as of financial bodies (governments, insurers, employers) who seek to minimize cost and waste while ensuring the provision of an acceptable level of care. Patients also have a significant stake in outcomes research because it facilitates their decision-making, both in deciding what intervention is best for them given their circumstances, and as members of the public who must ultimately pay for medical services. Outcomes research is applied clinical- and population-based research that studies and optimizes the end results of healthcare in terms of benefits to the patient and society. The intent of this research is to identify shortfalls in practice and to develop strategies to improve care. Like clinical trials, outcomes research seeks to provide evidence about which interventions work best for specific types of patients and under what circumstances. However, the evaluation methodology of outcomes research may include both experimental and non-experimental designs. Also, while traditional clinical trials focus primarily on therapeutic efficacy and safety, outcomes research may consider additional parameters such as cost, timeliness, convenience, geographical accessibility and patient preferences. Consequently, the field is more multi-disciplinary, involving not only neuroimagers and other healthcare providers but also medical economists, sociologists, and public health researchers, in addition to neuroimagers, healthcare professionals and the manufacturers of medical devices and/or pharmaceuticals.

TREATMENT

In addition to being a premier diagnostic modality, neuroimaging plays and will continue to play an important role in guiding therapy, including new therapeutics such as transcranial MR-guided focused ultrasound (MRgFUS). MRgFUS is an emerging technology that permits a highly concentrated focal point of ultrasound energy to be deposited to a target deep within the brain without an incision or craniotomy. MRgFUS is currently being investigated for a number of brain applications, including treatment of movement disorders, epilepsy, brain tumors, trigeminal neuralgia, and possibly intracranial hematomas. Other applications include treatment of bone metastases.

CONCLUSION

Three of the top five medical innovations of the last 25 years, as ranked by physicians, are related to imaging advances: magnetic resonance and computed tomography imaging, balloon angioplasty and mammography. These techniques are now firmly integrated into clinical practice, and radiology as a discipline deserves tremendous credit for the successful integration of physics and computer technology with clinical applications. These tremendous achievements are just the beginning, and neuroimaging is still in its infancy. The developments that lay ahead of us can barely be fathomed, but it is certain that they will shed a new light on our understanding of the brain, its miraculous struc-

ture and function, as well as the diseases that plague it. This will in turn hopefully open the way to new therapies and cures for the neurological, neurosurgical and psychiatric disorders that affect so many patients and levy their profound devastation on so many families.

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European Society of Radiology: What is the overall aim of your organisation and what exactly do you do to achieve this goal?

Donna Walsh: The European Federation of Neurological Associations (EFNA) is an umbrella group representing pan-European neurology patient groups. Our slogan, 'empowering patient neurology groups,' encapsulates our goals as an association. We strive to add capacity to our members, allowing them to be the most effective advocates possible in their own disease-specific areas. EFNA embraces the concept of partnership for progress: working at a high level with relevant stakeholders from the fields of policy, medical, scientific/research, industry, patient partners and other key opinion leaders.

ESR: How many patient organisations do you represent? How many members do you have? Who are they?

Donna Walsh: EFNA is an umbrella organisation comprising 19 predominantly pan-European disease-specific neurology patient organisations. These are Dystonia Europe, Euro-Ataxia, European Alliance for Restless Legs Syndrome (EARLS), European Alliance of Neuromuscular Disorders Associations (EAMDA), European Headache Alliance (EHA), European Huntington's Federation (EHF), European Multiple Sclerosis Platform (EMSP), European Myasthenia Gravis Association (EuMGA), European Network for Research in Alternating Hemiplegia in Childhood (ENRAH), European Polio Union, European Sex-

ual Health Alliance (ESHA), Guillain-Barre & Associated Inflammatory Neuropathies (GAIN), International Brain Tumour Alliance (IBTA), International Bureau for Epilepsy (IBE), Motor Neurone Disease Association (MND) – Europe, Pain Alliance Europe (PAE), Progressive Supranuclear Palsy Association – Europe (PSP-Europe), Stroke Alliance for Europe (SAFE), Trigeminal Neuralgia Association UK. As you can see, there are also some national organisations who are associate members and some international groups, in the absence of a pan-European association.

ESR: What are the most common brain diseases in Europe?

Donna Walsh: Brain disorders are very common and will affect one in three of us during our lifetime. They range from very prevalent disorders such as migraine (affecting up to 15% of the population) to very rare disorders. Most people will have heard of multiple sclerosis, dementia, Parkinson's disease, epilepsy, stroke, etc. But people often forget that sleep, mood, anxiety, addiction and eating disorders are also disorders of the brain. So brain disorders range from the genetic to the degenerative to the muscular and beyond!

ESR: Brain diseases affect an increasing number of people worldwide. Do you think current European health policies are well suited to tackling the issue?

"This year's IDoR focusing on brain imaging should highlight that radiology also plays a role in the management of brain disorders – and it is not just the domain of neurology. IDoR should also provide an example of best practice in highlighting collaboration between health professionals and patient organisations. EFNA would like to thank the ESR for including us in the planning for the day."

Donna Walsh is the executive director of the European Federation of Neurological Associations (EFNA). She has spent her career working with patient organisations in the neurology sector. Having studied for a BA in journalism at Dublin City University, she spent four years working as communications and information officer with the Migraine Association of Ireland. This led to her first position at the European level, as coordinator for the European Headache Alliance from 2010. In 2012, she was appointed EFNA executive director, and has since worked hard on establishing a new strategic direction for the organisation. She represents EFNA externally on numerous bodies, including the European Society of Radiology's Patient Advisory Group on Medical Imaging.

Donna Walsh: No. May 2013 was designated as European Month of the Brain (EMOB) by the European Commission to develop recommendations around health policy in Europe which would ensure brain disorders attracted a level of priority reflective of their burden and impact. Currently, revenues from central nervous system (CNS) drugs are predicted to decrease, prompting investors to withdraw their support. Many perceive the CNS disease research area as the most unpredictable and costly, with a high rate of failure. Hence, there exists a dilemma for investors in an area with high unmet need and potential for development, but with high risks. European health policy needs to be changed to ensure that investment in CNS is maintained and increased.

EMOB called for continued support for interdisciplinary research approaches, a more innovative and relevant approach to clinical development, new ways of implementing healthcare solutions, encouragement of data sharing, attracting and aligning public-private investment, rewarding innovative drug development, new technologies and healthcare delivery, and adapting the regulatory landscape. It also called for increased patient involvement and the eradication of stigma – issues of key concern to EFNA.

ESR: Brain cancer in particular affects more and more people. Is there enough emphasis on prevention and early detection in Europe in general?

Donna Walsh: Kathy Oliver, director of the International Brain Tumour Association (IBTA) says, “As far

as we currently know, brain tumours cannot be prevented. The only known causes of brain tumours to be determined to date are exposure to ionising radiation and some very rare, inherited syndromes. It seems that a change of lifestyle will not prevent people getting a brain tumour. So with regard to early detection, the sooner a brain tumour is diagnosed the better, but there is, as far as we know, no point in general population screening as brain tumours are an unpreventable rare disease.”

ESR: Some studies suggest mobile phones have an influence on the development of brain tumours. Has a clear link been established yet?

Donna Walsh: According to a summary by Cancer Research UK of historic and recent research, it seems unlikely that using a mobile phone can cause brain tumours, particularly as lab research hasn't shown a biological way this could happen. And rates of the brain tumours in question haven't seen an increase over time, despite mobile phone use booming. However, it also cautions that there isn't enough good evidence to say with absolute confidence that no risk exists. So, more research is needed.

ESR: Stroke can be lethal or disabling if not treated within the first six hours. Interventional radiologists can perform endovascular procedures to treat stroke

in that time. Do you think people know about this procedure?

Donna Walsh: According to Manuela Messmer-Wullen of the Stroke Alliance for Europe (and EFNA Board member), a radiologist seeing a patient in the early stages of a stroke can be very effective. However, most stroke patients are initially seen by a neurologist who will first attempt to treat the patient. This can mean that the patient will not see a radiologist in time for such an intervention. “Most people won't know that a radiologist is able to treat and solve such a big problem, so they won't ask to be treated this way,” says Manuela. “The problem with stroke is the lack of information and education in how to prevent, recognise and proceed.” Again more awareness is needed on the potential role of radiology in the diagnosis, management and treatment of the various neurological disorders.

ESR: Many European countries face significant health budget cuts, leading to shorter hospital stays and less access to modern equipment. How can patients benefit from state-of-the-art healthcare?

Donna Walsh: EFNA has a long track record of running workshops for patient advocates on issues such as health technology assessment (HTA) – as well as the wider issues of pricing, access and reimbursement of pharmaceuticals and medical devices. Therefore, we have an appreciation of the need to make innovative drugs and devices available within the constraints of today's limited resources. We believe that innovation should be rewarded (as I

mentioned earlier). But, more importantly, patients and health professionals need to work together to highlight how state-of-the-art healthcare applications can lead to prevention, better self-management, earlier diagnosis, less hospitalisation, etc. And this ultimately saves costs. Annually, brain disorders cost the European economy almost €800 billion. Many of these costs are indirect. Therefore, investment in treating and managing brain disorders is a smart investment!

ESR: The brain is a complex organ and physicians are only beginning to understand brain disease. What do patients need to hear from their physicians to better understand their pathology? What would patients need to hear from their radiologist, and how can both parties communicate better?

Donna Walsh: At the Joint Congress of European Neurology, EFNA ran a workshop entitled ‘Brain Disorders: The Communication Challenge’. These disorders really do pose a challenge for a number of reasons. Firstly, as you mention, the brain and its disorders are complex – so the physician needs to take time to ensure that the patient understands the diagnosis and its implications. Using pictures (or the image itself) can help overcome problems with medical/scientific technology. The patient should also be encouraged to ask questions and the physician should check regularly that they understand. We understand that, often, the patient will not

see the radiologist but will discuss the image with the neurologist, oncologist, neurosurgeon or another member of the healthcare team. This can cause difficulties if the patient has a question appropriate to the radiologist. A second problem is that many patients with neurological disorders are affected by a neurological deficit. These manifest in different ways, depending on the pathology, but can include memory difficulties, slurred/affected speech, problems with processing information, mood swings, etc. Again, this means more time is often needed, as well as the involvement of a case manager, family member or carer.

Finally, as a brain disorder diagnosis often means bad news, it is important for the physician to be honest with the patient and to set realistic expectations. It is also important that the patient is consulted in relation to their treatment/outcome preferences (which often differ from the physician's) and their acceptance of risk vs. benefit.

ESR: Do you think people have a good idea of what radiology has to offer today in brain disease management?

Donna Walsh: Traditionally, EFNA has worked closely with our neurologist colleagues at the European Federation of Neurological Societies (now merged with the ENS to form the European Academy of Neurology). However, EFNA has always been aware of the important role radiology plays in brain disorder management, as illustrated by our involvement in the Alliance for MRI. Also, we are increasingly aware of the need for a multidisciplinary approach in the management of brain disorders, which – of course – includes radiology.

However, having spoken to a number of the EFNA member organisations, it seems that while patients are aware of MRI, they are not as aware of its different techniques and applications. So we need to work together to create more awareness of MRI and to dispel many of the myths and misconceptions that may exist.

ESR: Do you think an initiative like IDoR, which focuses this year on brain imaging, can help in this regard?

Donna Walsh: This year's IDoR focusing on brain imaging should highlight that radiology also plays a role in the management of brain disorders – and it is not just the domain of neurology. IDoR also falls during the Year of the Brain 2014, which is being coordinated by the European Brain Council, so there are even more opportunities to position radiology in this field.

ESR: What other benefits do you think IDoR could bring?

Donna Walsh: IDoR should also provide an example of best practice in highlighting collaboration between health professionals and patient organisations. EFNA would like to thank the ESR for including us in the planning for the day.

European Society of Radiology: What is the overall aim of your organisation in Austria and what exactly do you do to achieve this goal?

Manuela Messmer-Wullen: Our mission is to inform the public about the burden of stroke, inform them on how to prevent stroke and support those who have been affected by stroke with information regarding their rehabilitation. We also provide support for carers, as well as information on where to find the right rehabilitation facilities, medical support, access to treatments, etc. We lobby, in general, for a better situation for stroke patients and their carers, to give them all a voice in the Austrian healthcare system. I do this work on a voluntary basis, without financial support from the state; projects are financed by individual funders. My personal investment of knowledge, time, energy and power is made in an effort to give stroke patients and their carers a better quality of life in Austria.

ESR: How many members do you have? Who are they?

Manuela Messmer-Wullen: In several Austrian states there are different groups run by individuals, therapeutic staff and medical professionals. SHÖ is the umbrella organisation for stroke patients and its membership is made up from many different patient groups who support their members across the country and within different fields.

ESR: Stroke affects an increasing number of people worldwide. Do you think current Austrian health policies are well suited to tackling the issue?

Manuela Messmer-Wullen: Not at all, there is no special information pointing out that stroke itself is a brain attack. Stroke is often obscured by the term 'cardiovascular disease'. This term is used by the media for simplicity and much of the public is unaware that it includes stroke. It would be more helpful to use the individual terms, stroke and heart attack more often. The public has to be informed about the danger of stroke and its possible consequences, like disability. Stroke affects the brain and can damage a lot of functions. Most people have no idea about these facts. Once they have this basic information about stroke, we can start educating them on how to prevent it. Stroke is the only brain disease that can, in certain circumstances, be prevented. People need to be informed of the necessary lifestyle changes.

ESR: Stroke can be lethal or disabling if not treated within the first six hours. In that time, interventional radiologists can perform endovascular procedures to treat stroke. Do you think people know about this procedure?

Manuela Messmer-Wullen: A radiologist seeing a patient in the early stages of a stroke can be very effective. However, most stroke patients are initially seen by a neuro-

"The problem with stroke is the lack of information and education on how to prevent, recognise and proceed. More awareness is needed on the potential role of radiology in the diagnosis, management and treatment of the various neurological disorders. IDoR can help if it speaks in the patient's language, and tries to inform them about the need to call the emergency services immediately and get the patient to a stroke unit as quickly as possible, where important treatments are routine work."

Manuela Messmer-Wullen is president of the Austrian Stroke Self-Help Association (Schlaganfallhilfe Österreich, SHÖ), as well as liaison officer and board member of the Stroke Alliance for Europe (SAFE). She is also an EFNA Board member. She has worked for different companies and agencies in Europe as a marketing & advertising manager, PR director and communications director. Her last active profession was Head of International Communications in Philips Speech Processing, 1992–2001. In 1997, she suffered a stroke during a business trip. The rehabilitation process and therapies took more than 7 years in total and at least 10 years to completely recover. In 2001, she left her paying job and in 2004 took over the presidency of SHÖ, which she founded together with a group of interested patients and professionals. That same year, a national umbrella Austrian Self-Help Association for health-related groups was founded and she helped create the statutes of this new organisation. Messmer-Wullen also played a key role in devising the statutes, constitution and mission statement of SAFE.

ogist who will first attempt to treat the patient. This can mean that the patient will not see a radiologist in time for such an intervention. Most people won't know that a radiologist is able to treat and solve such a serious problem, so they won't ask to be treated this way. The problem with stroke is the lack of information and education on how to prevent, recognise and proceed. Again more awareness is needed on the potential role of radiology in the diagnosis, management and treatment of the various neurological disorders.

ESR: What should you do when someone suffers a stroke?

Manuela Messmer-Wullen: You should immediately call the emergency services and inform them that the patient may be having a stroke. They will then bring the patient to the nearest stroke unit, or, if not available, to the nearest neurology department.

ESR: What should relatives bear in mind when a loved one has a stroke?

Manuela Messmer-Wullen: Stroke affects the personality of the patient as well. They often suffer from depression along with a lot of other different symptoms. When the patient leaves the hospital, the family never gets back the person they knew before. This situation is very difficult to understand and not treatable with medication, only through psychological treatment for both patient and carer, so that they can get to know each other again and understand each other's situation.

ESR: The brain is a complex organ and physicians are only beginning to understand brain disease. What do patients and their relatives need to hear from physicians to better understand their pathology? What would patients need to hear from their radiologist, and how can both parties communicate better?

Manuela Messmer-Wullen: This is a very comprehensive question. In terms of stroke, it would be helpful for people to appreciate that all functions of the body depend on the brain. If part of the brain is damaged by a stroke, the result is a corresponding defect which can affect bodily function. This can lead to some form of disability. In fact, most cases of adult-acquired disability are caused by stroke. To communicate with patients or their carers is very often a question of time and understanding people's reaction to tragic situations and problems; a question of human sensitivity and empathy. These attributes very often have no place in everyday clinical work. The problem is that stroke changes a life from one second to the other, and it takes time for patients and relatives to come to terms with the situation and commit to the major life changes that come with caring for a stroke patient; because the whole family will be affected by new problems.

If a patient's brain is damaged in the regions responsible for speech, a lot of different problems can arise. It could be that they have problems with comprehension or speech. It might mean a patient can no longer express themselves, can't understand what the doctor says, can't put words in the right sense, or can't speak at all. These

patients need very special treatment in communication, along with rehabilitation and therapy; most of them for the rest of their lives.

ESR: Do you think people have a good idea of what radiology has to offer stroke management today?

Manuela Messmer-Wullen: No, I don't think so. They don't because most of them have no idea about the disease itself. And radiology is a very technical discipline, which needs a lot of time to be explained in an understandable way.

ESR: Do you think an initiative like IDoR, which focuses this year on brain imaging, can help in this regard?

Manuela Messmer-Wullen: IDoR can help if it speaks in the patient's language, and tries to inform them about the need to call the emergency services immediately and get the patient to a stroke unit as quickly as possible, where important treatments are routine work.

ESR: What other benefits do you think IDoR could bring?

Manuela Messmer-Wullen: IDoR can help to build a relationship of confidence with the specialists who know how best to recognise and deal with stroke. It could also spread knowledge about the different ways of imaging

parts of people's body. This is a great opportunity to educate and inform patients; afterwards they will be more able to take responsibility and, hopefully, take better care of themselves.



Rivka R. Colen

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became a medical doctor in 1995, a neurologist in 2001 and received his PhD in medicine in 2004. He was appointed assistant professor at the University of Antwerp in 2004 and was promoted to associate professor in 2008. He was board certified in neurological revalidation in 2009. In 2011, he was appointed research professor of neurosciences & neurochemistry at the University of Antwerp and became full professor in 2014. Clinically, and with regard to research, Engelborghs specialises in neurodegenerative brain disorders that cause cognitive impairment and dementia. He is director of the Reference Center for Biological Markers of Dementia (BIODEM) at the Institute Born-Bunge of the University of Antwerp and coordinates the Memory Clinic of Antwerp (Hospital Network Antwerp), Belgium. He has authored and co-authored 186 PubMed-cited papers in international peer-reviewed journals and has an h-index of 38 (on September 2, 2014).



Mechthild Krause

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is director of the magnetic resonance unit and head of the department of neuroradiology at University Hospital Vall d'Hebron, Barcelona, Spain. He is also professor of radiology at the Autonomous University of Barcelona. He specialises in diagnostic neuroradiology; head & neck radiology, with a particular interest in demyelinating diseases; stroke; neuro-oncology; hepatic encephalopathy; and head & neck tumours. He is currently president of the Spanish Society of Neuroradiology, co-chairman of the European Multicenter Collaborative Research Network on MRI in Multiple Sclerosis (MAGNIMS), and a member of the Executive Committee of the European Society of Neuroradiology and the Spanish Society of Radiology. He has authored or co-authored more than 220 original papers, 25 review papers, 25 book chapters or monographs, and has delivered more than 400 conference presentations.



Pia C. Sundgren

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Wim Van Hecke

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Christopher Whitlow is associate professor at the department of radiology and the Translational Science Institute at Wake Forest School of Medicine in Winston-Salem, North Carolina, USA. He is a neuroradiologist and imaging neuroscientist, with expertise in combining advanced neuroimaging methods with network science and neuroinformatics approaches to study a variety of conditions affecting the brain, including psychiatric disorders, movement disorders, brain malignancy, diabetes, preterm birth and traumatic brain injury. He is director of the Wake Forest School of Medicine Combined MD/PhD Program. He also serves as co-chair of the American Society of Neuroradiology (ASNR) Study Group for the Clinical Translation of Functional and Diffusion MRI.



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