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Interview on brain imaging
Cyprus / Dr. Chrysa Tziakouri Shakalli

The ESR spoke with Dr. Chrysa Tziakouri Shakalli, vice director of the radiology department of Nicosia General Hospital and president of the Cyprus Radiological Society, about the range of modalities available in Cyprus and the role of imaging in neurology.

European Society of Radiology: Imaging is known for its ability to detect and diagnose diseases. What kind of brain diseases can imaging help to detect and diagnose?
Chrysa Tziakouri Shakalli: Imaging is a very important and useful diagnostic and therapeutic tool for many different brain conditions. In the past, before the early 1970s, diagnosis depended almost completely on clinical examination, as brain imaging was very primitive. In the last decades, impressive technological developments have been achieved, and imaging has become a major tool for the detection and diagnosis of brain diseases. Until the mid-70s, imaging depended on plain x-rays such as skull x-rays (diagnosing skull fractures, or predicting a mass by the shifting of the pineal gland and other indirect signs). Other methods based on plain x-rays, such as pneumoencephalograms, helped reach a diagnosis by depicting the distribution of air injected into the ventricles, and the old arteriograms based on the film changer systems could help identify space-occupying lesions by depicting the displacement of the cerebral vessels or depicting large aneurysms and AVMs.
Nowadays, the new advanced imaging modalities, including computed tomography (CT), angiography and especially magnetic resonance imaging (MRI), which remains the most important tool of neuroradiologists, help to detect and provide diagnosis for conditions such as brain tumours, cysts, metastases, multiple sclerosis (MS), brain atrophy or neurodegenerative diseases, stroke-related disorders, infarcts, vascular or venous pathologies, hydrocephalus, leukoencephalopathies, benign intracranial hypertension or hypotension, micro bleeds, post-traumatic changes, Creutzfeldt-Jakob disease (CJD), Parkinson's disease (PD), developmental anomalies, nerve diseases. Imaging techniques also provide information on cerebrospinal fluid (CSF) flow, functional information, etc.

ESR: How useful is imaging in brain disease management? Does it improve the understanding of disease or improve patient prognosis?
CTS: Imaging has an important role in the diagnosis of brain disorders, and in understanding the causes of brain diseases and how they can be treated. In addition, there is some evidence that MRI can be useful in terms of predicting the outcome of a patient's condition. In stroke patients, even an image of the brain can save a person's life. A prompt and precise diagnosis of cerebrovascular accident (CVA) can save a patient's life or can prevent a potential disability after. The expression 'time is brain' for stroke imaging is an example of how crucial brain imaging is for the diagnosis and prognosis; presenting the options for further therapeutic management by thrombolysis, endovascular thrombectomy, etc. Another example is the management of aneurysms before rupture or a case with subarachnoid haemorrhage. Accurate and optimal imaging gives us the opportunity for the best therapeutic options, such as embolisation, surgery, etc. Therefore, new imaging techniques improve dramatically the understanding of a disease and patient prognosis.

ESR: What kind of technology and techniques do radiologists use to image the brain? Are there any specific techniques for particular diseases?

CTS: Brain imaging techniques allow doctors and researchers to view activity and disorders within the human brain without invasive neurosurgery. There are a number of accepted, safe imaging techniques in use today in research facilities and hospitals throughout the world.
The main techniques for brain imaging are:

- ***Magnetic resonance imaging (MRI)*** Superior to other imaging modalities, MRI can show lesions that are not visible with computed tomography, including early cytotoxic oedema after ischaemic stroke, diffuse axonal injury after traumatic brain injury, and cortical laminar necrosis after cardiac arrest. Thus, MRI increases the accuracy of neurological diagnosis in critically ill patients. It also diagnoses certain brain infections or vasculitis, and can reveal brain abscesses. MRI is very important in the diagnosis of multiple sclerosis and can detect the condition in up to 95% of the patients, because of its ability to detect subtle changes in brain tissue. MRI can be quite useful in helping diagnose hormonal disorders that affect the brain, such as pituitary problems or Cushing's syndrome. While MRI scans alone cannot be used to diagnose conditions such as Alzheimer or Parkinson's disease, they are useful in visualising the brain changes in these disorders and assisting in their diagnosis.

- Following are the different applications and techniques of MRI:

  Functional magnetic resonance imaging (fMRI) is a technique used to measure brain activity by reflecting the hemodynamic responses related to neuronal activity. When a brain area is more active, it consumes more oxygen, and to meet this increased demand, blood flow increases to the active area. Therefore, it detects brain regions and networks associated with basic functions, such as motion, vision, and speech, but also memory, attention and comprehension, when certain cognitive tasks are performed. fMRI can be used to produce activation maps showing which parts of the brain are involved in a particular mental process. With image-guided surgery in the operating room, this technique is highly sensitive in predicting whether surgery in or near an eloquent brain region would lead to a deficit for that patient. The technique allows for the length of surgery to be reduced and can also be used for the optimised treatment planning of radiotherapy. Neuroplasticity changes can also be evaluated with fMRI.

  Diffusion-Weighted Imaging (DWI) quantitatively assesses tumour cellularity. Tumours with high cellularity, including primary central nervous system (CNS) lymphoma, glioblastomas (GBM), meduloblastoma and meningioma may often exhibit greater restricted diffusion compared with normal brain parenchyma. Follow-up of tumours with DWI after radio-chemotherapy helps us to evaluate the response to treatment, shown as a diminution of the cellularity of the lesion that is not related to the size of the lesion. Single or multiple ring-enhancing infectious lesions with oedema may resemble metastases with central necrotic cavity, but the central restricted diffusion shown in abscess (due to the relatively high viscosity of pus) distinguishes the two entities. Other pathologies with restricted diffusion are acute stroke, infection, diffuse axonal injury, etc. Progress in management of critically ill neurological patients has led to improved survival rates.

  Diffusion Tensor Imaging (DTI) allows the visualisation of direction and continuity of the nerve fibres of the CNS. It is used in neuro-navigation surgery of brain tumours, which may involve the pyramidal tracts to plan the optimal trajectory and ensure total resection of the lesions during an operation, as well as to decrease potential disability after an operation and to shorten the length of hospitalisation. DTI is an effective means of quantifying parameters of demyelination and axonal loss. The application of DTI in multiple sclerosis has yielded noteworthy results. Several other diseases have changes in DTI, including autism, dyslexia, etc. Diffusional kurtosis imaging (DKI) extends DTI and provides diffusional kurtosis metrics that are strongly linked to brain cellular microstructure. The extra information provided by DKI can also resolve intra-voxel fibre crossings and, thus, be used to improve fibre tractography of white matter. Susceptibility weighted imaging (SWI) detects haemorrhage and neoangiogenesis in tumours and helps us to understand the angiographic behaviour of lesions. This technique also facilitates the visualisation of displaced subarachnoid vessels.

High-resolution 3T SWI scanning is an accurate test for Parkinson's disease. The 'swallow tail' imaging feature, which is very similar to the tail of a swallow, is absent in Parkinson's disease. This sign is seen in healthy nigrosome but not in Parkinson's disease (the characteristic pathology of Parkinson's with structural change in substantia nigra). This is a breakthrough finding, as currently Parkinson's disease is mostly diagnosed by identifying symptoms like stiffness and tremor. Imaging tests to confirm the diagnosis are limited to expensive nuclear medical techniques, which are not widely available and associated with potentially harmful ionising radiation.

***MRI perfusion imaging (PI*)** assesses regional cerebral blood volume (rCBV) and flow (rCBF) during contrast administration. This depends on the vascularity of tumour and not on the breakdown of the blood-brain barrier that is shown as post-contrast enhancement. Therefore, tumour angiogenesis assessed by PI correlates better with tumour grade than contrast enhancement. PI may be used for the semi-quantitative evaluation of various parameters, which become altered as normal cerebral tissue progresses from ischaemia to infarction.

MR Spectroscopy (MRS) provides information regarding the chemical composition of tumours and other lesions through the relative or quantitative evaluation of the concentration of various metabolites. Chemical-shift imaging (CSI) allows the 2D/3D spatial mapping of the detectable metabolites. High-grade gliomas and primary CNS lymphomas manifest with elevation of the choline-creatine and choline-NAA ratios. However, there is significant overlap between the different glioma grades, and even acute demyelinating plaques may simulate tumours. In metastases, a high intratumoural choline peak is not associated with choline elevation in the peritumoural oedema, allowing the differentiation between metastases and infiltrating tumours. MRS is also useful for metabolic and other diseases.

- ***PET with 2-deoxy-2-[18F] fluoro-D-glucose (FDG)*** is the 'work horse' of brain tumour imaging with radiopharmaceuticals. The method is regarded as the best imaging tool for metastases, although it cannot detect small lesions. Currently, tested novel brain tumour radiotracers (e.g. radioactively labelled nucleoside and aminoacide analogues) are expected to improve sensitivity, specificity and diagnostic accuracy. PET amyloid-beta imaging is very important for the diagnosis of preclinical Alzheimer's disease and early treatment.

- ***Computed tomography (CT) – Multisided CT scanners.*** Although the application for brain imaging is MRI, CT scans remain the first-line examinations in many cases, and the first priority exams in some cases such as craniocerebral injuries and the diagnosis of subarachnoid haemorrhage. CT angiography is the first-choice technique to depict aneurysms, because they are more accurate and faster.

- ***Angiography Suits/Systems DSA Angiographies*.** The main application for brain imaging with angiography systems is the interpretation of vascular abnormities of the brain with the ability to proceed in endovascular therapy (interventional neuroradiology).

ESR: What is the difference between a radiologist and a radiographer? Who else involved in performing brain imaging exams?

CTS: A radiologist is a medical professional who is responsible for the imaging examination and consults the radiographer on the protocol to be followed. Upon completion of the imaging exam he/she reads the results and reports the diagnosis.

A radiographer is a health professional. He/she is the technologist performing the imaging exams, using x-rays or other imaging modalities, under the instruction of the radiologist.
Medical physicists are also involved; their role is to optimise the protocols for performing images, ensure quality of imaging and consult on radiation protection.
There is a common misunderstanding among patients as to who is the person that he/she meets in an imaging room. No one explains what the difference between a radiographer and a radiologist is. The name of their professions confuse patients, because in some countries like Cyprus and Greece, radiographers obtain by law the official title of technologists-radiologists instead of radiological technologists or radiographers, as it should actually be.

ESR: How many patients undergo brain imaging exams in your country each year?
CTS: According to government statistics, out of a population of 800,000, about 35,000 patients undergo MRI or CT brain scans every year. This figure represents patients visiting both public and private hospitals. There are no separate figures for the about 2,000,000 tourists who visit Cyprus every year.

ESR: Access to modern imaging equipment is important for brain imaging. Are hospitals in Cyprus equipped to provide the necessary exams?
CTS: Both government and private hospitals in Cyprus, are fully equipped with state-of-the-art equipment, such as MR scanners (1.5T and 3T), CT scanners (16, 64 and 256 slides). Also in the government's General Hospital in Nicosia there are angiography systems; one is biplane and used for embolisation of brain vascular lesions. The number of MRI (15) and CT scanners (20) seems to be more than enough compared to the population of the country.

ESR: In many countries there are waiting lists for MRI exams. How long can patients typically expect to wait for an exam in your country?
CTS: In Cyprus there are only waiting lists for MRI exams in government hospitals and these lists, especially for brain imaging, are only for follow-up and chronic cases; the maximum length is three to six months. For emergency cases, all patients in need can be examined on the same day, and inpatients undergo the examination within a week. In private hospitals there are no waiting lists.

ESR: As the global population gets older, the risk of developing neurocognitive and neurodegenerative disorders increases. How can imaging help tackle this issue?
CTS: With CT, PET and in particular MRI, any changes in the brain tissue can be visualised well ahead of clinical diseases symptoms. Therefore imaging, and especially MRI, provides opportunities to characterise the risk of developing neurocognitive and neurodegenerative disorders, and to distinguish pathological effects from those seen in normal ageing. There is also growing interest in the use of PET imaging, which can reveal β-amyloid build-up but does not yet have the spatial sensitivity of MRI. Ultimately, the range of imaging methods provides a more detailed characterisation of patients, and may allow correlations to be drawn between patient traits and response to therapies.
Extensive research in the field of neurodegenerative disorders and related diseases is run in many centres and hospitals all over the world. In Cyprus, several interesting studies are ongoing. For example a big research project is now run by the University of Cyprus, in association with a private diagnostic centre. This research focuses on several techniques, including perfusion with different methods, in patients with different stages of these diseases.
In another project, which is run by the Cyprus Institute of Neurology and Genetics (CING) in cooperation with the radiology department of Nicosia General Hospital, researchers study patients with multiple sclerosis, with an emphasis on prognosis of clinical symptoms related to neurodegenerative disorders, and the prevalence, nature and associated risk factors in dysphagia.

ESR: Some imaging techniques, like x-ray and CT, use ionising radiation. What risk does this radiation pose to the patient and what kind of safety measures are in place to protect the patient?
CTS: The predominant risk from typical medical radiation exposure is the risk of cancer and other effects after radiotherapy. The most powerful tool for minimising this risk is appropriate performance of the test and optimisation of radiological protection of the patient. These are the responsibility of the radiologists and medical physicists. The basic principle of patient protection in radiological investigations is that necessary diagnostic information of clinically satisfactory quality should be obtained with as low a dose as reasonably achievable.
In our country, we are trying to improve the law on radiation protection and have more control by government officers of the machine's performance and the radiation dose to both patients and staff. We are also trying to implement the European guidance on estimating population doses from medical x-ray procedures (Radiation Protection No 154—European Commission 2008).
The radiological report should include the dose of radiation for each examination. We try to optimise the dose and let our radiologists know about that, in order to save the patient from high doses of radiation, especially children and pregnant women. To achieve this, we calculate the patient's radiation doses in cooperation with medical physicists. We also participated in the ESR Eurosafe Imaging campaign, which was launched during ECR 2014, with our national society poster 'A review of computerised tomography utilisation in Cyprus'.
Continued training of all staff using x- rays, referral clinical doctors and the public is another way to reduce radiation doses. We also emphasise referrals for MRI rather than CT in order to reduce radiation dose.

ESR: What kind of role can imaging play in preventing and predicting brain diseases?
CTS: Imaging techniques have a great potential to act as pre-symptomatic predictors of disease as well as to chart the course of a disease. Neuroimaging has greatly advanced the understanding of brain function, physiology and the prediction of brain diseases. Relatives with a family member with cerebral aneurysms can be checked with a high resolution MR angiography to diagnose cerebral aneurysm before rupture. Carotids ultrasound may diagnose atheromatous plaques and the following treatment may prevent stroke. A domestic research study was done in Cyprus between 2004–2006 by the Cyprus Institute of Neurology and Genetics University (CING)on the investigation of carotid plaque and other factors for the prevention of cerebrovascular accidents, which proved the usefulness of the investigation of carotid plaque by screening ultrasound.
Using PET amyloid-beta imaging in preclinical Alzheimer's disease enables us to start early treatment.
Thanks to diffusion, perfusion and angiography, we make quick decisions for the recanalisation of the occluded vessel in order to prevent hemiplegia or other disability. With diffusion and contrast injection we are very sure about the diagnosis for an early treatment of abscess.

ESR: In general, patients don't see the radiologist. A patient will discuss the image with the neurologist, neurosurgeon or oncologist. When they ask a question, they're often told: "I'm not a radiologist". Why don't radiologists discuss the image with the patient first?
CTS: Decades ago, a physician thought the patient did not need to know, or might be harmed in some way by being informed. Recently, with the rise of patient rights and the principle of autonomy, it has become less common for physicians to withhold information from patients. Ultimate responsibility for decision-making is now understood to belong to patients, and it is impossible for them to make informed choices without having all the available information. This is one of the reasons why informed consent forms have become ubiquitous in healthcare. Yet, saying that the patient should be informed does not necessarily say who should do it. In developing a policy on informing patients of the results of imaging studies, radiologists should bear several points in mind. First, such policies should probably be uniform throughout a healthcare organisation, so that there are not wide divergences in practice across a

department. Second, it is generally good for radiologists to inform patients of normal results, to alleviate unwarranted anxiety. In some practices, radiologists may choose to delegate this responsibility to technologists, which is poor practice.
In general, it is good for radiologists and referring physicians to know one another well enough in order to handle such situations in advance. It is both a responsibility and a privilege for radiologists to play a role in communicating imaging results to patients. If radiology is to thrive in the future, the field needs to ensure that more radiologists also regard it as an important professional opportunity.

ESR: How expensive are radiological examinations to the health service and is there a risk that some of these examinations could be blocked by health technology assessment agencies deeming them to be not cost-effective? If so, how can patients help to ensure that these examinations are made available?
CTS: Up to this day, we don't have a national health system. We are now in the process of establishing one similar to the most successful systems in Europe. This system will be based on a national budget in which the screening programmes will not be included. All the screening programmes which have proved cost effective will, fortunately, remain under the control of the Ministry of Health with a separate budget. In addition, the Cyprus National Health System, which should be implemented in 2015, will give patients the chance to be forwarded directly to specialists. However, there is still a trend of blocking expensive radiological examinations, which will affect the quality of the health service.

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She is involved in teleradiology and tele-echography experiments with the University of Orléans in France, the University of Cyprus and the Cyprus University of Technology. She is also involved in many professional bodies in her country and in the establishment of a National Health System. She sits on a committee of the recently establish Eurasian Radiology Initiative.