Magnetic Resonance-Neurography- a proposal to establish public access facility in London

Since Marie Curie's discovery, X-ray imaging has been an essential part of clinical investigations to facilitate diagnostic and treatment of patients. Up until the 1970s plain radiographs were the stalwart of imaging diagnostics, 3D application of this technique led to Computer tomographic (CT) scans. Complications of this imaging modality includes irradiation of the patient and though it provides excellent imaging of hard tissues, specifically bone and teeth, the resolution of soft tissues is poor.

Magnetic resonance imaging (MRI), a non-irradiating modality of imaging, uses strong magnetic fields and radio waves to produce detailed images of body tissues containing water. The magnetic field energises the Proton molecules in bodily tissues, which then release energy during the relaxation phase and the amount of proton energy released by each tissue reflects the water content and pattern of that tissue, allowing differentiating between various soft tissues for example grey and white brain tissues, muscles, ligaments, heart, liver, spleen etc Resolution can be increased by using higher Tesla scanners(measure of magnetic strength), with no side effects for the patient except for those with metal implants or certain pacemakers who cannot be scanned.

With stronger scanners (standard 1.5 -3T and now research is using 8T) the resolution can be improved, however if the volume of the tissue is small or the water content like surrounding structures, differentiating for nerves, for example, is very difficult. In the last 5 years with the development of Magnetic Resonance Neurography (MRN) we can see nerve structures clearly for the first time. This includes not just large structure like spinal column or sciatic nerve but much smaller nerves.

What is MRN? Magnetic resonance neurography (also called MRN or MR neurography) refers to MR imaging dedicated to the peripheral nerves, brain and spinal cord MRN uses the dedicated MRI sequences, often with the addition of a contrast medium (Gadolinium is injected into the space around the spinal cord and helps to highlight nerve tissue) and additional magnetic coils made specifically for different regions of the body are used. Specific imaging paradigms have been developed for different regions of the body thus enhancing the visibility of nerve tissue of interest.

Why is MRN such an important development? For the first time we can identify healthy and abnormal nerves using this technique.

What is the application of MRN?

MR neurography can image nerves anywhere in the body, although it is most used in the diagnosis of abnormalities of the brachial plexus, lumbosacral plexus, thoracic outlet, and sciatic nerves. MRN can be performed at any time after nerve injury, as opposed to electrodiagnostic studies, which usually require a two- to three-week waiting period after abnormalities can be detected. Including Nerve damage or trauma, tumour, inflammation, radiation damage, compression related to disc disease or entrapment (i.e. thoracic outlet, "piriformis"/extraspinal sciatica) are some of the more common nerve diseases that are evaluated with MRN.

Why should there be improved access for MRN? It is a novel development, with evidenced based benefit for many patients with a plethora of different conditions. MRN is a novel technique and its applications are being investigated. There is total lack of access to MRN in the UK and only available in Belgium in Europe. There are already many centres in the US offering public access for MRN (see list and costs appendix 1).

MRN is increasingly being recognised as the imaging modality of choice for neurological conditions. Peripheral neuropathies account for the most frequent disorders seen by neurologists, and causes are manifold. The traditional diagnostic gold-standard consists of clinical neurologic examinations supplemented by nerve conduction studies. Due to well-known limitations of standard diagnostics and atypical clinical presentations, establishing the correct diagnosis can be challenging but is critical for appropriate therapies. In focal neuropathies, whether traumatic or due to nerve entrapment, MRN has improved the diagnostic accuracy by directly visualizing underlying nerve lesions and providing information on the exact lesion localization, extension, and spatial distribution, thereby assisting surgical planning. Notably, the differentiation between distally located, complete cross-sectional nerve

lesions, and more proximally located lesions involving only certain fascicles within a nerve can hold difficulties that MRN can overcome, when basic technical requirements to achieve sufficient spatial resolution are implemented.

Chhabra, A., Madhuranthakam, A.J. & Andreisek, G. Magnetic resonance neurography: current perspectives and literature review. *Eur Radiol* 28, 698–707 (2018). https://doi.org/10.1007/s00330-017-4976-8

MRN protocols have helped in imaging nerve tissue with greater clarity thereby helping in the identification, localisation and classification of nerve lesions with greater confidence than was possible till now. Upadhyaya V, Upadhyaya DN, Kumar A, Pandey AK, Gujral R, Singh AK. Magnetic resonance neurography of the brachial plexus. Indian J Plast Surg. 2015 May-Aug;48(2):129-37. doi: 10.4103/0970-0358.163045. PMID: 26424974; PMCID: PMC4564494.

Specific recognised developments in diagnostic using MRN

- Due to the depth of the brachial plexus and its complex anatomy, brachial plexus lesions are often difficult to characterize and treat.[7] Furthermore, conditions such as cervical spondylosis-related radiculopathy or cervical disc herniation present similar to brachial plexopathies.[7] [8] [9] Thus, a precise technique is required for evaluation. MRN has become a valuable diagnostic tool for brachial plexopathies caused by trauma, acute or chronic inflammation, brachial plexus tumors, and thoracic outlet syndrome[10] [11] as it can locate the site of neurologic compromise with a high degree of precision.

- Upper extremity (UE) nerve entrapments often present with mild symptoms, such as numbness or tingling that can progress to pain and/or functional deficits.[15] In some cases, symptoms may deviate from the classic presentation for compressive neuropathy. Unfortunately, diagnosis may be delayed or missed altogether due to the difficulty of discerning the underlying cause of clinical symptoms. Ulnar and median nerve entrapment can progress to atrophy and loss of function in the intrinsic hand muscles in advanced stages, and early diagnosis is needed to maximize functional recovery. Currently, there are limited data assessing MRN as a means of evaluating UE nerve entrapments. Current literature suggests that MRN is a more precise tool than NCS and EMG in determining the exact site of UE nerve entrapment and assessing nerve recovery following surgical intervention
- Patients with lower extremity entrapment neuropathy, an under-recognized cause of pain and functional impairment, often present with nonspecific symptoms, which makes it difficult to distinguish from more common, nonneurologic causes of pain.[28] MRN has been used to evaluate causes of tibial nerve dysfunction, such as tarsal tunnel syndrome, Morton's neuroma, median plantar nerve entrapment, and lateral plantar nerve compression.[29] It has also been used to visualize femoral nerve abnormalities caused by conditions including lumbar plexopathy, nerve sheath tumors, trauma, and chronic inflammatory demyelinating polyradiculoneuropathy. One prospective study included 239 patients presenting with leg pain in the sciatic nerve distribution and either inconclusive diagnosis or unsuccessful prior lumbar spine surgery.[38] MRN was performed on all patients and was able to distinguish patients with piriformis syndrome (from patients with similar symptoms) with 93% specificity and 64% sensitivity.[38]
- Diabetic peripheral neuropathy (DPN) is common in diabetics and can cause irreversible nerve damage. DPN also increases risk of diabetic foot ulcers which, if left untreated, may lead to amputation.[41] [42] Historically, changes in the nerve microstructure in the lower extremity peripheral nervous system have been evaluated by NCS and nerve biopsy, both of which measure structural changes indirectly.[43] To prevent progression of DPN, noninvasive diagnostics with high sensitivity are needed for early detection. MRN is a promising imaging tool that may be employed as a diagnostic marker in the early detection of DPN in diabetic patients. Early detection may assist in preventing the progression of DPN to debilitating conditions that negatively impact quality of life.

- Pelvic pain- MRN use in chronic lumbosacral and pelvic pain led to a meaningful change in diagnosis and treatment. After MRN, conservative treatment and injections provided pain relief; however, patients benefited more from surgery than from any other treatment.

  Riham Dessouky, Yin Xi, Kelly M. Scott, Mohammed Khaleel, Kevin Gill, Stephanie Jones, Dalia N. Khalifa, Hazim I. Tantawy, Magdy A. Aidaros, Avneesh Chhabra. Magnetic Resonance Neurography in Chronic Lumbosacral and Pelvic Pain: Diagnostic and Management Impact–Institutional Audit. World Neurosurgery, Volume 114,2018, Pages e77-e113, ISSN 1878-8750,https://doi.org/10.1016/j.wneu.2018.02.072.

- Peripheral nerve injury PNI, including brachial and lumbar plexus injuries, occurs in ~5% of all traumas.[48] These injuries are most often a result of motor vehicle accidents, falls, or penetrating trauma.[49] The radial, ulnar, and median nerves are the most commonly injured UE nerves, and the sciatic, peroneal, femoral, and tibial nerves are most often affected in lower extremities.[50] Delayed diagnosis of PNI may be attributed to a variety of comorbid factors. An ischemic or badly injured limb can complicate physical examination.[48] In bedridden patients, lower extremity nerve defects may not clearly manifest until the patient is mobilized.[48] These PNIs can have a delayed presentation, secondary to musculoskeletal injuries, such as compression from hematoma, compartment syndrome, or complications from management of concurrently injured tissues.[48] Failure to address injured nerves in a timely manner can lead to long-term functional deficits. When physical examinations are inconclusive or highlight a high index of suspicion, early detection using MRN can prevent permanent damage that could lead to decreased strength, limited range of motion, or loss of sensation and/or proprioception.[51] [52] MRN has been utilized in a variety of nerve injury patterns to provide insights beyond traditional assessment modalities. The current literature indicates that MRN has the potential to improve clinical outcomes, particularly in nerve defects that are either difficult to detect or require early intervention. After closed injuries, it may be difficult to distinguish between nerve injuries that have the potential to recover on their own (neurapraxic and axonometric) from those that do not (neurotmetic) and require surgery.[53] Advantages of MRN include early characterization of the location and grade of nerve injury and improved accuracy when compared with NCS and EMG. Published data suggest that MRN could be a valuable addition to the diagnostic algorithm for traumatic nerve injuries, especially when traditional assessment tools are not able to accurately diagnose nerve conditions. Delayed diagnosis of PNI leads to delayed treatment, thus narrowing the scope of available treatment options. Ultimately, this can result in long-lasting functional deficits and impaired quality of life.[51] [56] Historically, PNIs have been diagnosed by clinical symptoms and indirect and/or invasive methods of evaluating nerve function, such as NCS and EMG.[51] [56] While these tools remain essential to diagnostic and postoperative workups, they do not adequately address the full spectrum of nerve injuries seen in a clinical setting. Given the gaps in the current nerve assessment algorithm, MRN has recently been used to supplement traditional techniques for both pre- and postoperative characterization of nerve structures. MRN can provide high-quality images of structures in difficult anatomical areas without a skilled operator, locate the precise location of nerve injury, and visualize signs of secondary muscle denervation, thus addressing many shortcomings of the current diagnostic/monitoring algorithm.[20] [28] [51] Injured nerves will exhibit hyperintense signal on T2W images within 24 hours of injury, reflecting a nonspecific response of the nerve to injury.[17] [28] In the case of nerve entrapment, nerve hyperintensity is most prominent at the site of entrapment, allowing localization of the nerve lesion.[17]

  Ku V Cox C Mikeska Mikesky A, McKay B. J Magnetic Resonance Neurography for Evaluation of Peripheral Nerves. Brachial Plex Peripher Nerve Inj 2021; 16(01): e17-e23 DOI: 10.1055/s-0041-1729176

  Kollmer, J., Bendszus, M. Magnetic Resonance Neurography: Improved Diagnosis of Peripheral Neuropathies. *Neurotherapeutics* 18, 2368–2383 (2021). https://doi.org/10.1007/s13311-021-01166-8

- Muscle denervation related to acute nerve injury MRN also provides excellent soft tissue contrast, allowing for visualization of downstream muscle injury and high contrast resolution between surrounding fat and vascular structures.[20] Signs of muscle denervation can be visualized distal to the site of nerve injury with diffuse muscle signal alterations and without hemorrhage or fascial edema.[17] In an acute setting, often within 48 hours of injury, denervated muscle displays hyperintense signals on T2W images due to increased extracellular fluid and edema.[20] [57] In chronic muscle denervation, due to volume loss and fatty infiltration, denervated muscle displays hyperintense signals on T1W images, indicating irreversible end-stage disease and muscle atrophy.[20] [28] Thus, being able to understand the extent and duration of a nerve deficit through the differentiation of acute versus chronic muscle denervation on MRN allows physicians to make better informed decisions about the time frame of surgical intervention.

- Preoperative location of important neural structures prior to cancer surgery and routine dental implants and wisdom teeth extractions
  Van der Cruyssen F, Croonenborghs TM, Renton T, Hermans R, Politis C, Jacobs R, Casselman J. Magnetic resonance neurography of the head and neck: state of the art, anatomy, pathology and future perspectives. Br J Radiol. 2021 Mar 1;94(1119):20200798. doi: 10.1259/bjr.20200798. Epub 2021 Jan 29. PMID: 33513024; PMCID: PMC8011265.
  Kwon D, Lee C, Chae Y, Kwon IJ, Kim SM, Lee JH. Clinical validation of the 3-dimensional double-echo steady-state with water excitation sequence of MR neurography for preoperative facial and lingual nerve identification. Imaging Sci Dent. 2022 Sep;52(3):259-266. doi: 10.5624/isd.20220035. Epub 2022 May 13. PMID: 36238701; PMCID: PMC9530289.
  Al-Haj Husain A, Valdec S, Stadlinger B, Rücker M, Piccirelli M, Winklhofer S. Preoperative visualization of the lingual nerve by 3D double-echo steady-state MRI in surgical third molar extraction treatment. Clin Oral Investig. 2022 Feb;26(2):2043-2053. doi: 10.1007/s00784-021-04185-z. Epub 2021 Sep 29. PMID: 34586501; PMCID: PMC8816737.

- Orofacial pain conditions
  3D CRANI is reliable for the visualization of the extraforaminal cranial and occipital nerves. Intravenous gadolinium significantly improves MR neurography when applying this sequence. Benchmarking data are published to allow future assessment of the 3D CRANI sequence in patients with pathology of the extraforaminal cranial and occipital nerves.
  Casselman J, Van der Cruyssen F, Vanhove F, Peeters R, Hermans R, Politis C, Jacobs R. 3D CRANI, a novel MR neurography sequence, can reliable visualise the extraforaminal cranial and occipital nerves. Eur Radiol. 2023 Apr;33(4):2861-2870. doi: 10.1007/s00330-022-09269-2. Epub 2022 Nov 26. PMID: 36435876; PMCID: PMC10017653.

Who will benefit from access to MRN? What conditions and what proportion of the population?

There are a significant number of applications including a large proportion of the population who would benefit from MRN access, for earlier and more accurate diagnosis and provide earlier intervention where needed to improve outcomes. Conventional MRI The diagnostic value of non-nerve-selective MRI sequences for post traumatic neuropathic pain is low and has little impact on clinical management.

Peeters F, Van der Cruyssen F, Casselman JW, Hermans R, Renton T, Jacobs R, Politis C. The Diagnostic Value of Magnetic Resonance Imaging in Posttraumatic Trigeminal Neuropathic Pain. J Oral Facial Pain Headache. 2021 Winter;35(1):35-40. doi: 10.11607/ofph.2732. PMID: 33730125.

Headaches There are approximately 45 million Americans complaining of headaches each year. That works out to about one in every six people or 16.54% of the population.

Back pain 7.5% of the world's population has low back pain. 8 out of 10 people in the U.S. will experience LBP in their lifetime. Women, individuals aged older than 30 and people who are classed as obese are at a greater risk of developing LBP.

Neck Pain Childs et al reported that at any given time, 10% to 20% of the population reports neck problems, with 54% of individuals having experienced neck pain within the last 6 months.

Diabetic neuropathy It is estimated that 415 million people are living with diabetes in the world, which is estimated to be 1 in 11 of the world's adult population. 46% of people with diabetes are undiagnosed. Diabetic peripheral neuropathy eventually affects nearly 50% of adults with diabetes during their lifetime, and is associated with substantial morbidity including pain, foot ulcers, and lower limb amputation.

Peripheral nerve entrapment The most common nerve entrapment injury is carpal tunnel syndrome, which has an estimated prevalence of 3 percent in the general population and 5 to 15 percent in the industrial setting. 34% of patients with traumatic brain injury during the postacute care suffer from PNI and 1,3% of all trauma victims suffer from PNI. The estimated community prevalence of neuropathic pain from the clinical examination (gold standard) was 9.8%.

Orofacial pain The prevalence of orofacial pain is around 17% to 26%, out of which 7% to 11% is chronic. Most patients, therefore, suffer acute pain that is in the most part secondary to dental or intraoral soft tissue pathology.

Dentistry routine dental implant surgery and wisdom tooth extraction isa high volume surgical field and both can imjure peripheral nerve if risk assessment in not undertaken correctly. Currently CT scans are the standard assessment but there is increasing evidence that MRN would be a preferred no irradiation risk assessment method for patients undergoing this surgery

Other applications Cranial nerve pathology which may include; ophthalmic conditions, vestibular (hearing), Cochlear (dizinness and balance), frozen shoulder, dystonias, swallowing problems, brain tumours affecting neural tissue and other conditions.

Urgent peripheral nerve repair

Any peripheral nerve and spinal cord injury would benefit from MRN to establish degree and cause of injury and grade the injury appropriately, allowing timely surgery to take place, Surgery is frequently delays as clinical evaluation and other electrophysiological tests do not differentiate nerve injuries from bruising or grade the injuries thus delay essential surgery which would improve outcomes when undertaken earlier. Van der Cruyssen F, Palla B, Jacobs R, Politis C, Zuniga J, Renton T. Consensus guidelines on training, diagnosis, treatment and follow-up care of trigeminal nerve injuries. Int J Oral Maxillofac Surg. 2024 Jan;53(1):68-77. doi: 10.1016/j.ijom.2023.06.003. Epub 2023 Jun 24. PMID: 37365073.

Market review

Currently no one is offering private MR Neurography in Europe

South florida https://uniqueimaging.com/mr-neuro/

UCSF https://radiology.ucsf.edu/patient-care/services/mr-neurography#:~:text=MR%20neurography%2C%20or%20magnetic%20resonance,nerves%20beyond%20the%20spinal%20canal.

Cost of private routine MRI

Brain and head £199

https://mriplus.co.uk/body-parts/brain-and-head?campaignid=18859802559&adgroupid=142885430586&creative=634098871805&network=g&device=c&matchtype=b&keyword=mri%20scan%20brain&adpos=&utm_term=mri%20scan%20brain&utm_campaign=&utm_source=adwords&utm_medium=ppc&hsa_acc=8312871601&hsa_cam=18859802559&hsa_grp=142885430586&hsa_ad=634098871805&hsa_src=g&hsa_tgt=kwd-150622605&hsa_kw=mri%20scan%20brain&hsa_mt=b&hsa_net=adwords&hsa_ver=3&utm_term=mri%20scan%20brain&utm_campaign=Brain+MRI+Scan&utm_source=adwords&utm_medium=ppc&hsa_acc=8312871601&hsa_cam=18859802559&hsa_grp=142885430586&hsa_ad=634098871805&hsa_src=g&hsa_tgt=kwd-150622605&hsa_kw=mri%20scan%20brain&hsa_mt=b&hsa_net=adwords&hsa_ver=3&gad_source=1&gclid=Cj0KCQiAz8GuBhCxARIsAOpzk8zC5TKSP61XIBpdhLH7lxlqOQKV6YQpDcIM2U2ZELoryvDgfp336ewaAq_NEALw_wcB

Head and neck MRI

https://visithealth.london/product/brain-mri/

Head +/_ angiogram £750

Head £720

Whole spine £1200

https://www.google.com/search?q=full+body+mr+scan&oq=full+body+mr+scan&gs_lcrp=EgZjaHJvbWUyBggAEEUYOTIJCAEQABgNGIAEMgkIAhAAGA0YgAQyCQgDEAAYDRiABDISCAQQLhgNGK8BGMcBGIAEGI4FMgkIBRAAGA0YgAQyCQgGEAAYDRiABDIJCAcQABgNGIAEMgkICBAAGA0YgAQyCQgJEAAYDRiABNIBCDgyMzdqMGo3qAIAsAIA&sourceid=chrome&ie=UTF-8

whole body £1250

https://mriplus.co.uk/body-parts/full-body-scan

whole body scan report 2 days £2999 or 7 days £999

- Brain (including MRA of blood vessels)
- Neck blood vessels (MRA of Carotid arteries)
- Chest (not including heart or lungs)
- Abdomen (including overview of liver, kidneys, spleen, pancreas, gallbladder)
- Pelvis (Female: includes uterus, ovaries and urinary bladder, Male: includes prostate and urinary bladder)

Costs for setting up the service

Potential to use an existing Seimans MRI scanner at ST Georges Hospital

Use Frederics paradigm and head coil

May need other coils?

Setting up costs ???

Running costs

- St Georges Fee for use of radiological suite and specific MR scanner (Out of hours?)
- Radiographers
- Radiologist
- technician
- Admin set up for reporting and appointment arrangements
- Website
- Social media and marketing