Chapter 1

Introduction & Outline of the Thesis

Sciatica, more accurately called lumbosacral radicular syndrome or sciatica neuralgia, is one of the most common lumbar-spine disorders. Sciatica is generally defined as pain radiating to the leg below the knee following a dermatomal pattern.[1] It is probable that human's upright posture and relative longevity have exposed our species to a special, unwelcome affinity for lumbar disc syndrome and associated sciatica.[2] The prevalence of sciatic symptoms reported in the literature varies considerably ranging from 1.6% in the general population to 43% in a selected working population.[3] The natural history of acute sciatica is in general favorable, although a substantial proportion (up to 30%) continues to have pain for one year or longer.[1, 4, 5] Sciatica is associated with significant short- and sometimes long-term morbidity. This affliction, certainly in the industrialized countries, ranks as one of the most costly and ubiquitous medical problems.[6]

THE LONG WAY TOWARD OVERCOMING THE SCIENTIFIC CONFUSION

In classical literature sciatica has been of great interest to Greco-Roman and Eastern scientists and physicians.[7] The Greek physician Hippocrates (460-370 BC) is generally believed to be the first to describe the treatment for sciatica. Since ancient times many etiological explanations for sciatica have been proposed. Domenico Cotugnio (1736-1822), a skilled Italian physician and anatomist, was the first to really add something new to the description of sciatica in his 1764 seminal paper "De ischiade nervosa commentarius".[7, 8] He explained the sciatic complaints as a consequence of neuritis or edema of the sciatic nerve. As treatment he recommended cautery, saying that he had never seen a failure after this procedure (a triumph that might be explained by the reluctance of patients to return to his care after having suffered unbearable pain during treatment, and so unabling him to really measure the effectiveness of this procedure).[7] For years this inflammation of the sciatic nerve, described as sciatic neuritis, was the origin of pain. In 1857 Rudolf Virchow (1821-1902) described the traumatic rupture of an intervertebral disc, which afterwards became known as "Virchow Tumor".[9] In 1858 the famous German pathologist Hubert von Luschka (1820-1875) discovered at autopsy several instances of asymptomatic herniated lumbar discs, which he erroneously described as cartilaginous tumors of the disc.[10] He speculated that in more advanced cases this finding might produce neurological complaints.

With the introduction of effective anesthesia in the second half of the 19th century it became possible to operate upon the vertebral column and observe anatomic relationships.[7] In 1909, the German neurosurgeon Fedor Krause (1857-1937) and his neurologist colleague Hermann Oppenheim (1858-1919) reported on the removal of an "enchondroma", which in retrospect must have been a ruptured disc.[11] In 1911 Joel Goldthwait (1866-1961) reported on a patient with recurrent sciatica and low back pain, in whom Harvey Cushing (1869-1939) had performed a negative surgical exploration.[12] Despite that no lesion was found Goldwait believed that a "disclocated" disc, not evident at surgery, could have produced sciatica. In 1915 Charles Elsberg (1871-1948) reported "a surgical cure for sciatica" effected by the removal of a piece of ruptured ligamentum of "subflavum" which was compromising a nerve root.[7, 13] In 1929 the famous neurosurgeon Walter Dandy (1886-1946) at John Hopkins found cartilagi-

nous fragments lying loose in the spinal canal which he believed might well produce sciatica by compressing the adjacent nerve roots.[14] He even argued that by their removal, the patient's pain and suffering could be cured. Unfortunately, the importance of this paper went largely unrecognized as he continued to call these disc protrusions tumors.

In 1932 the prominent neurosurgeon William Jason Mixter (1880-1958) (Figure 1) and his orthopaedic colleague Joseph Seaton Barr (1901-1964) questioned whether "enchondromas" were truly the cause of sciatica and set out to review all of the previously diagnosed "enchondromas" at Massachusets General Hospital.[15] They observed that most of these cases were pathologically identical to normal disc material. Mixter later would recall that "this made us certain that we were dealing with a considerable group of lesions previously described as neoplasm, but undoubtedly of traumatic origin."[16] They concluded that enchondromas, Schmorl's nodules, and ruptured intervertebral discs were one and the same, and that the lesion was a common cause of the classic signs and symptoms of sciatica. Their ideas were met with considerable resistance at first. Mixter reports that he had asked for permission from the surgical executive committee at Massachusets General Hospital to present his findings at a meeting of the Massachusetts Medical Society, and "permission was refused on the ground that the subject was far too controversial to be given in such a meeting."[15, 16] In the spring of 1933 Barr did get a chance to present their work to a group at the Brigham Hospital Reunion, but the article essentially failed to spark any interest.[15] Finally, Mixter and Barr's report was read before the New England Surgical Society on September 30, 1933. In their famous publication in the August 2 issue of the New England Journal of Medicine in 1934 they stated[17]:

Figure 1. *Dr. William Jason Mixter, neurosurgeon*

"We conclude from this study: that a herniation of the nucleus pulposus into the spinal canal, or as we prefer to call it, rupture of the intervertebral disc, is a not uncommon cause of symptoms. That the lesion frequently has been mistaken for cartilaginous neoplasm arising from the intervertebral disc… That the treatment of this disease is surgical and that the results obtained are very satisfactory if compression has not been too prolonged".

This landmark report of Mixter and Barr greatly revolutionized medical think at the time, ushering in a greater interest in the lumbar disc as a source of sciatica and in the surgical treatment of such a disorder. In fact the report caused a shift in clinical management from largely conservative to that of surgery, which has come to be known as the "Dynasty of the Disc".[15, 18] Surgery for back and leg pain in association with nerve root compression has become one of the most commonly performed operative procedures worldwide.

REVIVAL OF SCIENTIFIC CONFUSION

Walter Dandy (1886-1946) introduced air myelography in 1918 at the Johns Hopkins Hospital for the diagnosis of space- occupying brain lesions. The difficulties in properly performing this procedure limited its widespread use in the spine. In 1920 the French neurologist and radiologist Jean Sicard (1872-1929) introduced iodinated contrast myelography, allowing the relatively accurate diagnosis of intraspinal pathology.[19] In subsequent decades the accuracy and safety of this diagnostic procedure were greatly improved.

In 1977 the first Magnetic Resonance Imaging (MRI) body scan of a human being was performed.[20, 21] Within a few years spinal MR imaging became available and was rapidly becoming the imaging modality of choice for most spinal disorders. However, the high-resolution images which allowed many investigators to detect an enormous variety of previously unappreciated anatomical variations in patients undergoing diagnostic workups for sciatica, also caused scientific confusion of our understanding of sciatia.[22] For example, in the early nineties of the 20th century several MRI studies showed a high prevalence of disc herniations ranging from 20 to 76% in persons without any symptoms.[23-25] Even in patients who were re-imaged after earlier disc surgery, MRI studies have found herniations in up to 53% of persons who at the time of the re-imaging had no symptoms.[26-28] Despite this scientific confusion, however, MRI is considered the imaging procedure of choice for patients suspected of lumbar disc herniations[23, 29] and is frequently performed in patients with persistent or recurrent symptoms of sciatica.[30] Moreover, abnormal MRI findings frequently result in surgical treatment or other invasive procedures such as epidural injections.[31, 32]

The controversy discussed above challenges our understanding of sciatica and the value of MRI in patients with sciatica. Many anatomical abnormalities detected with high-resolution imaging may not be of clinical consequence but are now exposing patients to interventions with potential risks. Establishing correlations between MRI findings and clinical outcome in patients with sciatica may not only help improve our understanding of the etiology of sciatica,

but it may also provide anchor points for new therapeutic approaches or fine-tuning of existing therapeutic strategies. To uncover the relevance of imaging findings it does not only require knowledge regarding their prevalence, but also their behavior of change with time, spectrum of changes and their relation with clinical outcome.[33] As the source for determining the clinical relevance of MR imaging findings data from the Sciatica Trial will be used in this thesis.

The Sciatica Trial is a multicentre prospective randomized controlled trial among patients with 6-12 weeks sciatica and disc herniation on MRI. An early surgery strategy was compared to prolonged conservative care for an additional 6 months followed by surgery for patients who did not improve or who did request it earlier because of aggravating symptoms.[34, 35] The trial showed faster recovery after early surgery as compared to a strategy of prolonged conservative care with surgery if needed, but there were no significant differences in clinical outcomes after one year. The randomized patients were part of a larger group of patients with sciatica who underwent a baseline MRI to assess the eligibility for the sciatica trial. All patients who underwent MRI (regardless of participation in the randomized controlled trial) were followed up for one year. Furthermore, all randomized patients underwent MRI at baseline and after one year. The 12 months evaluation period was selected since postoperative fibrosis usually stabilizes by 6 months, with no further changes at 12 months.[36]

OBJECTIVE AND OUTLINE OF THIS THESIS

The main objective of this thesis is to uncover the relationship between MRI findings and clinical outcome in patients with sciatica. As with any diagnostic study requiring expert reading, interpretation of MRI findings may be inconsistent between examiners. In **chapter 2** results are reported regarding the intra- and inter-observer variation in MRI evaluation among two neuroradiologists and one neurosurgeon who routinely assess spinal MRIs. It has been suggested that inconsistency in interpretation may lead to alternative treatment options between clinicians and therefore may impact the outcome of patient treatment. In **chapter 3** clinical outcome results are reported of patients in whom spine specialists independently agreed about the presence of a disc herniation or nerve root compression, those with inconsistent MRI interpretation, and those in whom spine specialists independently agreed about the absence of those findings.

The natural history of acute sciatica is in general favorable, although a substantial proportion (up to 30%) receives surgery. **Chapter 4** presents the results of both qualitative and quantitative MRI evaluations in predicting surgery for sciatica in a group of prolonged conservative care patients.

Patients with sciatica frequently complain about associated back pain. **Chapter 5** reports on the MRI differences between patients who suffer from sciatica with disabling back pain as compared to patients who suffered from predominantly sciatica, and on the significance of these MRI differences for prognosis.

Despite being scientifically debated, MRI is frequently repeated in patients with persistent or recurrent symptoms of sciatica. **Chapter 6** reports on the 1-year MRI findings of sciatica patients who were treated with either surgery or conservative treatment, changes of MRI findings over time, and their correlation with clinical outcome.

In the search for causes of associated back pain in patients with sciatica, vertebral endplate signal changes (VESC, also called Modic changes) visualized by MRI have been proposed as a possible cause. VESC are a frequent surgical indication to perform a fixation of two or more vertebrae in the lower spine or replacing the disc by a prothesis. **Chapter 7** reports on VESC findings, changes of VESC findings over time and the correlation between VESC findings and back pain in sciatica.

Gadolinium-enhanced MRI is frequently performed in patients with persistent or recurrent symptoms of sciatica after surgical treatment, as it has been proposed to differentiate between postoperative epidural scar tissue and recurrent disc herniation: scar tissue has a homogenous enhancement pattern while disc herniation usually lacks central enhancement. **Chapter 8** reports on the reliability of enhancement findings, their prevalence and their correlation with clinical outcome.

A synthesis and discussion about the results are given in **chapter 9**. The dissertation is concluded with a summary in **chapter 10.**

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