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Myelography and the 20th Century Localization of Spinal Cord Lesions

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Abstract
In this article, we commemorate the centenary of myelography, a neuroradiological procedure that, despite certain disadvantages, significantly contributed to the diagnosis and localization of spinal cord lesions during the 20th century. From the start, the use of myelography was characterized by different views regarding the potential dangers associated with the prolonged exposure of a "foreign body" to the central nervous system. Such differences in attitude resulted in divergent myelography practices; its precise indications, technical performance, and adopted contrast material remaining subject to variability until the procedure were eventually replaced by MRI at the close of the 20th century.

Introduction

In current clinical practice, MRI constitutes the predominant imaging modality for the diagnosis and localization of diseases affecting the spinal cord. In cases where MRI is contraindicated due to patient-related factors, the presence of an MRI-incompatible implanted devise, or expected significant artifacts, computed tomography (CT) myelography with intrathecal injection of contrast material continues to provide a useful alternative, particularly in the functional visualization of cerebrospinal fluid (CSF) leakage, spinal cord herniation, and spinal arachnoid cysts [1, 2].

The introduction of myelography dates back a century. Whereas patient history, neurological examination, and previous diagnostic tests had often been inconclusive in the diagnosis and localization of spinal cord lesions, myelography could starkly reveal the presence and location of these lesions on the radiogram, thereby significantly enhancing surgical planning and patient outcome. Initially, the application of myelography was largely limited to cases of suspected spinal cord tumors, but with the growing recognition of intervertebral disc herniation as a clinical entity amenable to surgery, its application expanded. Myelography was not, however, received without criticism. From the start, different attitudes regarding the dangers associated with the prolonged exposure of a "foreign body" to the central nervous system resulted in divergent myelography practices; its precise indications, technical performance, and contrast material remaining subject to variability until the procedure were eventually replaced by MRI at the close of the 20th century. In this

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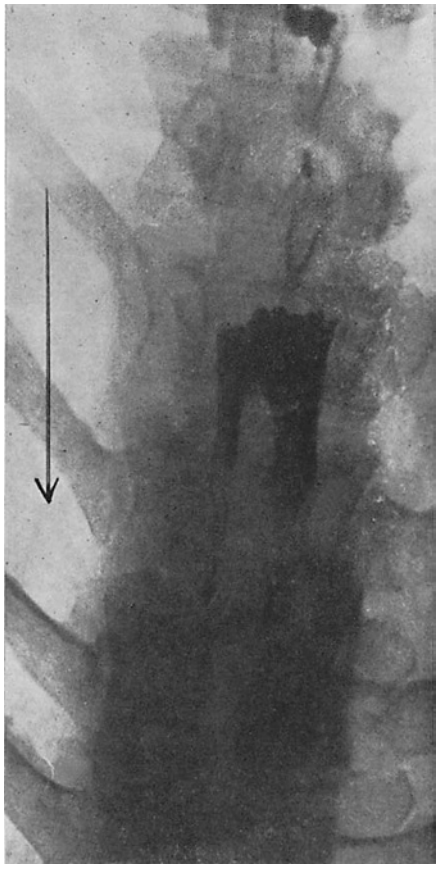

Fig. 1. Myelogram following intrathecal injection of Lipiodol, revealing a complete obstruction of the spinal canal caused by an intradural tumor [8].

article, we commemorate the centenary of myelography, a neuroradiological procedure that, despite certain disadvantages, significantly contributed to the diagnosis and localization of spinal cord lesions during the 20th century.

The Rise of Myelography

In 1919, American neurosurgeon Walter Dandy (1886–1946) first proposed the intrathecal injection of a substance opaque to X-rays as an aid to the localization of spinal cord lesions [3]. While introducing his technique of encephalography – which involved the lumbar injection of air to visualize tumor-induced alterations of the cerebral ventricles and subarachnoid space on the radiogram – Dandy suggested that the procedure could also be valuable in localizing spinal cord tumors. He postulated that if the spinal canal were to be obliterated by a tumor, the air would not be able to flow passed the point of obstruction and arrest at the level of the lesion, thereby sharply outlining its location. Due to paucity of suitable patients, however, Dandy was unable to test this hypothesis at the time. It would take until 1921 before the use of air myelography was first reported in the literature [4, 5].

In that same year, Paris physician Jean-Athanase Sicard (1872–1929) and his junior colleague Jacques Forestier (1890–1978) made a groundbreaking discovery [4–6]. For many years, Sicard had been performing intramuscular and subcutaneous injections of various iodized oils for the treatment of chronic pain and was struck by the high radiopacity and "absolute tolerance" of the body toward these substances. Postulating the potential value of iodized oils as a diagnostic tool, Sicard and Forestier started to experiment with injecting an iodized oil called Lipiodol into the lumbar epidural space. One day, Lipiodol was accidentally injected into the spinal canal. When the patient was found well, the French physicians at once realized the diagnostic potential of such intrathecal injections in the localization of spinal cord lesions [6].

Over subsequent years, Sicard and Forestier perfected their technique of contrast myelography: Lipiodol was injected into the spinal canal via suboccipital puncture with the patient in upright position. When the spinal canal was patent, the iodized oil would pass freely to the caudal cul-de-sac [7, 8]. In the presence of an obstruction, Lipiodol would come to a halt at the upper level of the lesion, starkly outlining its location on the radiogram (Fig. 1). The lower level of the lesion could subsequently be determined by the injection of Lipiodol via lumbar puncture with the patient in Trendelenburg position (Fig. 2) [7–9].

Negotiating a Foreign Substance

Contrast myelography was well received in the most of Europe, with the exception of Scandinavia. In the years following Sicard and Forestier's publications, many European physicians, particularly in France, Germany, and The Netherlands, reported on their positive experiences with the new diagnostic technique, which had enabled them to localize and successfully remove spinal cord tumors that would have otherwise remained undisclosed [10–12]. Their experiences with contrast myelography also seemed to support Sicard and Forestier's claim that intrathecal Lipiodol injections were well tolerated and devoid of serious discomfort or adverse events. As a result, contrast myelography rapidly became a routine proce-

dure in the diagnosis and localization of particularly spinal cord tumors in many European countries, leading Dutch neurologist Bernard Brouwer (1881–1949) and his surgical colleague Ignaz Oljenick (1888–1981), for instance, to argue that "it was not allowed at the present stage of medical science to send a patient to a surgeon with the diagnosis of a tumor of the spinal cord or of the cauda equina, without having first used Lipiodol" [12].

In North America, on the other hand, contrast myelography was met with opposition [13, 14]. While it was generally recognized that the technique could provide valuable diagnostic information, many American physicians objected to the notion of exposing the central nervous system to a "foreign body" that would remain present for an indefinite period [14, 15]. Such opposition was reinforced by occasional reports of adverse events associated with contrast myelography, most notably cyst formation, that started to appear halfway the 1920s [16]. Consequently, contrast myelography was only used as a last resort when neurological examination and other diagnostic tests – including chemical and manometric CSF analysis and air myelography – had failed to reveal the exact location of a spinal cord lesion.

The French originators of contrast myelography fiercely rejected the claim that Lipiodol acted as an irritating and harmful foreign body. In 1927, at a meeting of the Royal Society of Physicians in Edinburgh, Forestier held that Lipiodol did, in fact, not remain in the spinal canal for more than a few years [17]. In addition, he argued that histological specimens had shown "that there [was] no retention of the oil as a foreign body," and that the adverse events described in the literature had resulted from the use of expired Lipiodol. Based on his own experience, Forestier maintained that Lipiodol was absolutely harmless, stating that "when you use Lipiodol, you may do it sometimes with success, sometimes with failure, but never with any harm to the patient." Moreover, at the time of the Edinburgh meeting, Forestier was able to point at numerous other areas of medicine where Lipiodol was enthusiastically being embraced, including the fields of pulmonology, gynecology, and cyst surgery [17].

By the beginning of the 1930s, views and practices with regard to myelography diverged. Whereas, in Europe, intrathecal Lipiodol injections were performed on virtually all patients with suspected operable spinal cord lesions, North American physicians tended to use contrast myelography only as a last resort, preferring the use of air for its rapid absorbability, despite its lower radiopacity and tolerability. In Scandinavia, objections similar to those in North America led to the introduction of the water-soluble contrast agent Abrodil in 1931, which was not widely accepted due to its irritating effect on the meninges [18, 19]. The contrast agent Thorotrast was also introduced during this period but was abandoned for similar reasons.

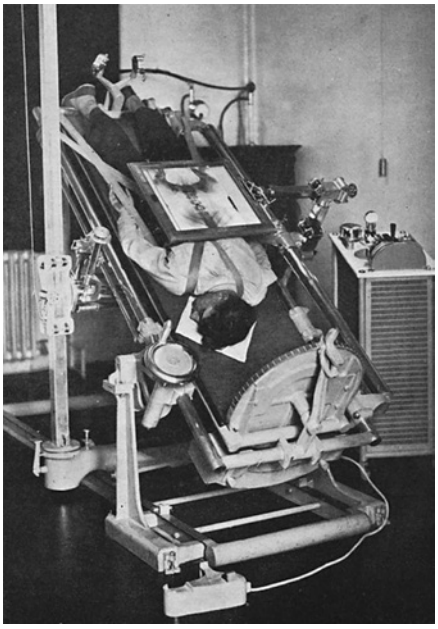

Fig. 2. Radiologic tilting table with patient in Trendelenburg position following the intrathecal injection of Lipiodol via lumbar puncture [8].

Expanding Indications

In 1934, American neurosurgeon William Mixter (1880–1958) and orthopedic surgeon Joseph Barr (1901–1964) firmly established herniation of the nucleus pulposus due to rupture of the intervertebral disc as a common and treatable cause of sciatic pain [20]. Over the subsequent decade, the treatment of herniated intervertebral discs became the hallmark of an effective, elegant, and minimally invasive neurosurgical intervention, offering relieve to many patients with previously untreatable low back pains and sciatica. Due to the high prevalence of herniated discs and frequent difficulty to localize them by clinical means, the use of contrast myelography rapidly expanded.

Nevertheless, persisting reluctance to the use of Lipiodol also prompted a revival of air, as besides being rapidly absorbed, air was relatively well-suited for outlining pathological changes of the caudal sac, the region where the vast majority of herniated discs occurred [21]. More-

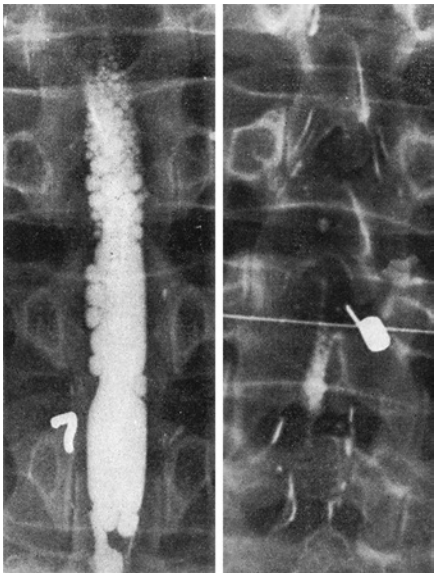

Fig. 3. Myelogram before (left) and after (right) the removal of Lipiodol from the spinal canal via lumbar puncture [22].

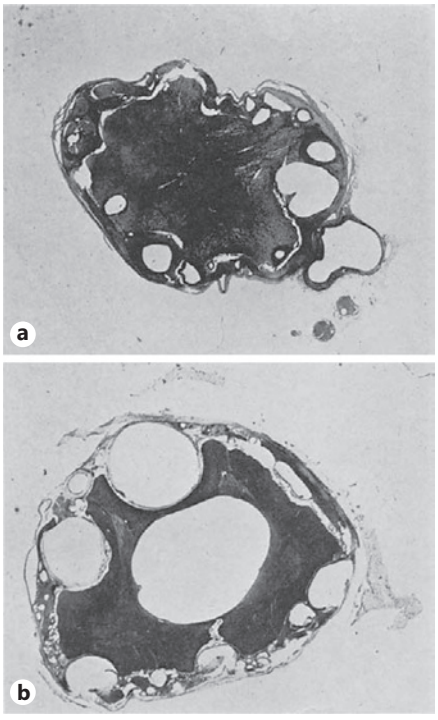

Fig. 4. Cyst formation in the spinal cords of dogs following intrathecal injection of Pantopaque (**a**) and Lipiodol (**b**) [24].

over, the recognition of intervertebral disc herniation as a clinical entity amenable to surgery made it essential to distinguish symptomatic herniated discs from other, inoperable causes of back pain and sciatica prior to intervention. The use of Lipiodol for this purpose was broadly considered undesirable, as there would be no chance to withdraw the substance from the spinal canal in case no operable lesion would be detected. In 1941, however, the odds were stacked back in favor of contrast myelography, when neuropathologist Charles Kubik (1891–1982) and radiologist Aubrey Hampton (1900–1955) introduced a simple procedure that allowed for the removal of iodized oil from the spinal canal via lumbar puncture, thereby effectively diminishing the main objection to the use of Lipiodol (Fig. 3) [22].

Despite effectively limiting the exposure of the central nervous system to Lipiodol, Kubik and Hampton's method had several shortcomings. For one, Lipiodol could often not be completely removed despite extensive manipulation of the puncture needle and the patient inevitably leaving part of the "foreign body" behind with all its potential consequences. Moreover, withdrawal of Lipiodol could be a rather painful endeavor – as nerve roots were often drawn against the point of the needle upon suction – complicated the myelography procedure and occasionally induced spinal hemorrhage. These drawbacks led some to refrain from using the method, either accepting the risk of having to leave behind Lipiodol in the spinal canal when no operation was pursued, or abandoning the use of iodized oils altogether in favor of air myelography. By the early 1940s, then, both air and Lipiodol were used as contrast agents in the diagnosis and localization of spinal cord lesions, but given the downsides that accompanied both substances, the search for a better contrast agent continued.

Search for Ideal Contrast

In 1944, a team of clinicians and scientists from the University of Rochester, NY, reported their experience with a new oil-based myelographic contrast agent ethyl iodophenylundecylate, marketed under the trade name Pantopaque [23]. Pantopaque was less viscous than Lipiodol, allowing the substance to be more easily removed from the spinal canal. Prior to its clinical application, the Rochester team had tested Pantopaque on dogs and found the substance to produce less discomfort and to be more rapidly absorbed than Lipiodol (even though, when left unremoved, Pantopaque also remained in the spinal canal for years) [24]. Moreover, postmortem analysis revealed that both contrast agents were encyst-

ed in the spinal canal, displaying a physiological response that was "essentially a foreign body reaction" [24]. Yet, the cysts in animals exposed to Pantopaque were smaller than in those subjected to Lipiodol (Fig. 4), reinforcing the notion of Pantopaque as a less noxious foreign body.

Pantopaque rapidly became the myelographic contrast agent of choice in many countries. Over subsequent decades, indications for contrast myelography loosened up and came to include various types of congenital nervous system anomalies, spine deformities, and vascular malformations [19]. Still, practices regarding the removal of Pantopaque continued to diverge, by and large reflecting earlier differences in attitude toward the risks associated with the prolonged exposure of a foreign body to the central nervous system. In the USA, the removal of Pantopaque following the procedure was beyond dispute. In the UK, on the other hand, Pantopaque was usually left in the spinal canal, despite occasional serious complications, including arachnoiditis, meningitis, embolism, hydrocephalus, and death [25].

Pantopaque remained the predominant contrast agent for myelography until the early 1970s, when the non-ionic water-soluble substance metrizamide was introduced in Scandinavia, and subsequently spread to the rest of Europe and North America [26]. Metrizamide's first appearance in Scandinavia was no mere coincidence, as Northern European physicians had traditionally favored the use of absorbable contrast media over oil-based substance. Whereas, similar to other water-soluble contrast agents – such as Abrodil and its successors iothalamate meglumine (Conray) and dimeglumine iocarmate (Dimer X) – metrizamide was rapidly absorbed by the body, the substance was found to be far less irritating than its predecessors, despite the frequent occurrence of headache, nausea, and, occasionally, seizures.

Noninvasive Alternatives

During the 1970s, the introduction and implementation of CT radically changed the diagnostic landscape of medicine, not least in the fields of neurology and neurosurgery. Being noninvasive, more cost-effective and able to detect far lateral spinal cord lesions that were frequently missed by myelography, CT came to replace myelography as the predominant aid in the diagnosis and localization of most lumbosacral lesions [27]. Myelography supplemented by CT was used when plain CT of the caudal spinal cord was inconclusive or when more cranial parts of the cord needed to be examined, where the lack of epidural fat limited the discriminative power of plain CT [28].

The clinical arrival of MRI, which allowed for the direct visualization of the spinal cord parenchyma and surrounding soft tissue without exposing the patient to ionizing radiation, greatly reduced the need for CT myelography at the close of the 20th century [29]. The development of MR myelography – heavily T2-weighted imaging that enhances the contrast between the CSF-containing spinal canal and its surrounding structures – further stimulated this decline [30]. Even though MRI has now replaced CT myelography as the preferred imaging modality in diseases affecting the spinal cord, the procedure continues to be used in cases where MRI is contraindicated, particularly in the functional visualization of CSF leakage, spinal cord herniation, and spinal arachnoid cysts [1, 2].

Conclusion

The history of myelography is characterized by divergent views with regard to the potential dangers associated with the prolonged exposure of a "foreign body" to the central nervous system. From the start, such different attitudes resulted in divergent clinical practices: in some places, contrast myelography was routinely used in the diagnosis and localization of spinal cord lesions, whereas in other places, the procedure was often dismissed or only invoked as a last resort. Even among those who, hesitantly or wholeheartedly, accepted myelography as a useful diagnostic tool, there was no consensus on when precisely the procedure was indicated, what contrast agent was to be used, and whether or not the substance was to be removed following the procedure. These divergent approaches to myelography persisted, despite accumulating experience and widespread availability of literature reporting on the merits and drawbacks associated with the procedure. Hence, the story of myelography aptly reveals the substantial variability that may exist across medical diagnostic practices, differences that are inevitably shaped by divergent local and national medical customs, ideas, and preconceptions.

Statement of Ethics

Not applicable.

Conflict of Interest Statement

The authors report no conflicts of interest.

Author Contributions

B.L. conceptualized the study and drafted the manuscript for intellectual content. P.K. conceptualized the study and revised the manuscript for intellectual content. R.G. conceptualized the study and revised the manuscript for intellectual content.

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