Minimally Invasive Procedures for the Treatment of Failed Back Surgery Syndrome

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Abstract
Failed back surgery syndrome has become unfortunately a common clinical entity. FBSS does not have one specific treatment because it does not have one specific cause. Some features are shared with chronic low back pain (CLBP) and some pathological processes are specific. Both pathologies are leading causes of disability in the industrialized world and costly medical and surgical treatments are continuously used despite their limited efficacy. Nonetheless, evidence based practice guidelines are systematically developed.

In this chapter we cautiously review the vast, complex and at times contradictory literature regarding the treatment of FBSS. Interventional Pain literature suggests that there is moderate evidence (small randomized or non randomized or single group or matched case controlled studies) for medial branch neurotomy and limited evidence (non experimental one or more center studies) for intra-discal treatments in mechanical low back pain. There is moderate evidence for the use of transforaminal steroid injections, lumbar percutaneous adhesiolysis and spinal endoscopy for painful lumbar radiculopathy and spinal cord stimulation and intrathecal pumps mostly after spinal surgery. In reality there is no gold standard for the treatment of FBSS but, these results seem promising.

Keywords: Failed back surgery; back pain; discography; nerve blocks; spinal cord stimulation; radio frequency lesions.

Introduction
Back pain is the most common cause of activity limitation in adults younger than 45 years, the second most frequent reason for visits to the physician, the fifth ranking cause of admission to hospital and the third most common cause of surgical procedures (Van Tulder et al., 2002). A letter to the British Medical Journal in October 2003, Dr Lina Talbot reported: “Every general practitioner has one – a patient who has had back surgery but hasn’t improved”. Around 20000 cases of failed back syndrome are produced each year in United Kingdom (Talbot, 2003).

Failed Back Surgery Syndrome (FBSS) does not implicate only surgery but also the medical pathway that leads to it (Fritsch et al., 1996). This syndrome constitutes a heterogeneous group of patients which have either their original cause of pain amenable to treatment or their original causes of pain non-amenable to surgery due to induced anatomical changes (Waguespack et al., 2002). Possible causes include correct operation but wrong diagnosis; correct diagnosis but wrong operation and wrong diagnosis and wrong operation; but also, correct diagnosis and correct surgery. The track to this clinical disaster is often paved with approximate diagnos-
tics, precipitation and lack of strategy. Yet with appropriate care, its incidence could be reduced. This clinical entity is endemic and deserves the highest priority (Porter et al., 1997). This chapter focuses on minimally invasive treatments but also on the prevention of the so-called Failed Back Surgery Syndrome.

Back pain is essentially a benign self-limiting condition. “Red flag conditions” are rare and may essentially be ruled out by taking a detailed history. Once this critical issue has been carefully considered, spinal surgery is never an emergency. This leaves us with the opportunity to review all the possible alternatives to improve the natural history of the disease before any non-reversible procedure is performed.

All the efforts must converge towards making a correct diagnosis. The past 15 years have brought essential diagnostic tools and important many studies show that the precision of diagnostic in chronic back pain can be performed (Schwarzer et al., 1994; Schwarzer et al., 1995a). These tests are not meant to replace surgery if indicated or conservative medical treatment when appropriate, their role is to assure a coherent working hypothesis.

In the early 80’s, 80% of “low back pain” patients were classified as “non-specific low back pain” (Kirwan, 1989). This was not a clear classification but probably the best at time. Today, thanks to a well defined taxonomy, precision diagnostic blocks and technological progresses, only 20% of patients remain in this “non-diagnostic category” (Merskey et al., 1994).

Another important step was to recognize that the classical “history – physical examination – radiological imaging” triad is necessary but not sufficient to determine the origin and the mechanism of pain (Strendler et al., 1997). History taking and physical examination did not improve during the last decades and all the possible progresses had to come either from advances in technology or from a different diagnostic approach. Although, anamnesis and clinical examination remain essential to the patient and the physician, they must be also oriented on the mechanism of pain and not only on its putative anatomical cause. This is particularly true in sub-acute and chronic situations for which, most of the time; a sole anatomical aetiology cannot be identified. Finally, minimally invasive procedures, such as spinal cord stimulation, may be superior to re-operation (North et al., 1994).

Prevalence and Cost

The prevalence of FBSS should be placed in the context of low back pain in general (Anderson et al., 1999; Bressler et al., 1999). The economic environment and local beliefs have an important influence on the type of treatment offered to low back pain patients. Comparing rates of back surgery in eleven countries, Cherkin and al demonstrated an almost linear increase in
spinal surgery with the per capita number of orthopaedic and neurosurgeons in the country (Cherkin et al., 1994). However, the adequate ratio neurosurgeon-orthopaedic surgeons/population needed per capita has not been defined and most probably cannot be determined.

The United States National Council on Compensation Insurance in Healthcare estimates the costs of work-related low back pain 8.8 billion US$, not taking into account lost work, lost tax revenue, and indemnity (Williams, 1998). Most costly are diagnostic procedures (25%), surgery (21%), and physical therapy (20%). The past 20 years have witnessed significant changes in the indications for, and use of, instrumentation in lumbar spine surgery. Between 1979 and 1990 there has been an increase of over 55% in the incidence of spine surgery for chronic low back pain (Gibson et al., 1999).

**Diagnostic Process in Chronic Low Back Pain**

In failed back patients, looking back often reveals important lacks in the diagnostic process. Anatomical and radiological observations do not focus on the mechanism of pain and often conclusions are drawn only from history taking and physical examination.

**Patient’s History**

Although no physician would deny patient’s history is essential, there is no evidence to support that this helps in establishing a correct diagnosis, moreover, the best method of history taking in chronic low back pain has neither been defined nor validated. History must assess the patient in a bio-psycho-social context, particularly in FBSS (Guzman et al., 2001). Psycho-social “red flags”, called yellow flags must be searched and a complete evaluation of the patient is mandatory if they are present (Deyo et al., 1992). Moreover, we recommend an interdisciplinary approach for these patients.

After unsuccessful surgery, with or without added pain, all history must be reviewed even before the operation because unfortunately often FBSS means failed diagnostic. From the biological point of view, the localisation and quality of the pain must be established.

**Localisation**: The origin of the main pain should be clearly defined, is the pain coming truly from the back? Couldn’t it be buttock pain or loin pain? If it is back pain, is lumbar spinal, sacral-spinal or lumbo-sacral spinal pain (Merskey et al., 1994). This precision is important since each condition suggests different diagnostics. If more than one pain is present, a link between them should not be presumed before a clear history has been drawn for each of them. If pain is clearly in the leg, could it be so-
matic referred pain? In order this question the quality of the pain will help in this regard.

Quality: somatic pain is characterized by deep, dull pressure-like pain and it must be differentiated from radicular neurogenic shooting or lancinating pain. Neurogenic pain will lead to a different diagnostic strategy and probably to another treatment (Fukui et al., 1997).

The other elements of history are all indicative without being essential. The mode of onset is not diagnostic. Spontaneous or explosive start is more alarming and serious conditions as infection, fracture and tumour must be ruled out, but in chronic low back pain these pathologies have usually already been eliminated, especially if the patient had spinal surgery.

The initial clinical presentation of the pain helps dividing patients with predominant low back versus leg pain and this may influence the diagnostic strategy which differs between the two groups.

Intensity of the pain is not a good indicator of the severity of the disease, but a comparison to baseline Visual Analog Scores (VAS) is useful to follow the patient along the treatment course.

Duration of pain is a more complex issue. For patients with chronic pain unlike acute pain, a multidisciplinary approach is essential.

An exhaustive list of therapeutic and diagnostic procedures that have been performed is mandatory. Not only must the individual procedures be listed but also the order in which they were performed.

Precipitating, aggravating and relieving factors have not been shown to have an important diagnostic value. Difficult social or psychological conditions must be evaluated and in the case of failed-back, interdisciplinary evaluation may raise crucial pitfalls. Most chronic pain patients have to some extent psycho-social distress. This may be only an aggravating factor or a more causal disorder. If not all pain patients need a psychosocial evaluation, failed back patients are probably good candidates for such an approach. In these patients, suffering and distress may be severe, and social context is most of the time disturbed as a consequence of the disease and the loss of self-esteem (Guzman et al., 2001).

**Physical Examination**

The reliability of a clinical sign is usually evaluated using a K score. K score measures the agreement between two individual observers and is always less than or equal to 1.0 (Cohen, 1960). In rare situations, K can be negative and this is the sign that two observers agree less than it would be expected just by chance. K scores inferior to 0.2 signs a poor agreement; between 0.2 and 0.4 slight agreement, 0.4 to 0.6 moderate agreements, 0.6 to 0.8 good agreement and 0.8 to 1.0 very good agreement. In low back pain evaluation, K scores range from 0.1 to 0.6. Compared to the neuro-
logical exam ranging between 0.6 and 0.9, it seems almost unreliable (Bogduk et al., 2002a).

These considerations demonstrate the limits of the clinical observation and shows how overconfident experienced clinicians may feel about their daily practice (Dreyfuss et al., 1996).

The patient however expects the physical exam, it means attention and care. Moreover, it is essential to orientate the physician towards more precise procedures but should never be considered independently.

Radiological Findings

Before surgery, it has been clearly demonstrated that plain x-ray of the lumbar spine, with or without the associated clinical examination, is not a valuable tool (Simmons et al., 2003). The lumbar spinal x-ray is not only of little value in the diagnostic of degenerative changes, it is also an insensitive method for diagnosing serious conditions in a general population of patients with low back pain (Van Den Bosch et al., 2004). Despite guidelines recommending its limited use, it is still often requested by general practitioners and even by specialists. This habit is not only expensive but may give a false impression of security to the patient and to his physician.

CT-scan imaging does not appear to affect treatment modalities in chronic back pain (Gilbert et al., 2004). Moreover, many asymptomatic patients have a pathological CT-scan (Wiesel, 1986). After surgery, the value of plain x-rays is not expected to be higher than before the operation. The value of MRI and CT-scan depends on numerous factors. For early post-operative complications, the validity of such exams is unquestionable, early complications like haematoma and infections are the perfect target for investigation. For recurrent chronic pain few months after spinal surgery, the evidence is not there. Two situations must be differentiated. First, is when surgery did not improve the pre-operative pain. In this case, no new radiological approach will do better than the preoperative one. Second, surgery has worsened the situation, then a new mechanical component must be looked for. In this situation, imaging the spine may offer new information. This new input should however be considered very cautiously for it might not be the cause of the worsening of pain.

MRI plays a key role in the investigation of chronic back pain and even more in FBSS. It reveals and excludes more lesions than either plain films or CT scan (Gilbert et al., 2004). Although most of the MRI will reveal mainly degenerative changes, some features may help to determine the "pain generator". High density zone (HIZ) is a feature that can occur in the posterior annulus of the lumbar intervertebral disc. It is seen in T2-weighted images. It constitutes the appearance in sagittal section of the circumferential portion of a grade IV annular fissures (Ricketson et al.,
Although HIZ will not detect all cases if internal disc disruption, when present, it is unlikely to be false-positive. This sign does not discriminate between patients with or without back pain, but applies to patients who do have back pain. This sign strongly suggests discogenic pain when present (Ito et al., 1998). Endplate changes also provide diagnostic indices for internal disc disruption (Braithwaite et al., 1998).

Normal MRI may also be useful as long as the discs are considered. Normal discs are unlikely to be the source of pain and the diagnostic investigations should first focus on other aetiologies. This may reduce the use of more invasive diagnostic procedures such as provocative discography.

**Minimally Invasive Approaches Diagnostic Procedures for Low Back Pain**

The precision diagnostic approach was developed to determine in conjunction with other diagnostic tools the cause or the causes of pain in low back pain. By stimulating or anesthetising specific structures, needle procedures can determine precisely the source of the patient’s pain (Steindler, 1938). These procedures can target the source of pain and unlike imaging studies determine whether the structure is generating pain or not. This approach is subject to control in order to ensure the validity of the test in each and every patient. The procedure requires fluoroscopy and special skills such as the ability to deliver a needle accurately and safely to the targeted structure.

Epidemiologically, three causes of back pain are predominant with or without surgery. Discogenic pain, Facet joint pain and SI joint pain (Manchikanti et al., 1999 a). For these three aetiologies, three test procedures are available in the investigation of chronic low back and FBBS pain: Discography, Medial Branch blocks and Sacro-iliac (SI) joint blocks.

Many FBSS patients present with a mixed clinical picture and multiple tests may be needed to determine the “pain generator”.

**Provocative Discography**

Discography involves the injection of radiographic contrast into the nucleus of an intervertebral disc. This invasive procedure is justified only if it provides new information that cannot be obtained by less invasive options. Discography does not compete with CT or MRI in the diagnosis of disc herniation. It is not only an anatomical diagnostic but mainly a functional test.

After a classical evaluation of the patient, including radiological exams, even when diseased structures have been identified with MRI for instance, most of the time, we still don’t know which structure causes pain. We still need a way to *reproduce* the pain as we try to do during the physical exam;
we still want a symptom related response. We then need to target the cause of the pain and its specific origin.

Provocation discography is achieved by distending the disc from the inside using medium contrast. Diseased discs are painful (Walsh et al., 1990). Although originally believed to be due to increased pressure on nerve roots in patients with herniations, pain occurs in patients with no evidence of herniation or disc-bulge and so must arise from the disc itself. Moreover, the reproduction of pain cannot be ascribed to a chemical effect of contrast medium or spillage of contrast medium into the epidural space, for it occurs without spillage, or if normal saline is used instead of contrast medium (Coppes, 1997).

Discography is performed under local anaesthesia; no or minimal sedation is required or desired. Heavily sedated patients may give partial to inadequate answers to the test. The patient, under sterile conditions lies prone. A posterolateral approach is used to enter the disc at the desired level. A well trained operator is necessary to perform a discography; a painful procedure due to inexperience will preclude a good and valid evaluation. A 22 G to 25 G needle 13 to 17 cm is used to enter the disc. Under the C-arm, lateral and a-p views are used to check the exact place of the tip of the needle. The contrast medium is injected into the disc and intensity and quality of pain are recorded as well as the pressure needed to induce pain (McNally et al., 1996). Discography findings are classified in two groups: symptomatic and radiological findings.

**Symptomatic findings:** An intact disc without any degenerative abnormalities will support pressures as high as 100 pounds per square inch; the injection is not very uncomfortable. In pathological conditions, the pressure needed to induce pain may vary a lot between subjects but should be below 50 PSI. Pain is recorded on a visual analog scale ranging from 0 being no pain to 10 rating unbearable pain. The patient should be blinded to the level of injection, not knowing if the control disc or the suspected disc is injected first. Evaluation must include quality of the pain, it should be similar to the usual patient’s complain.

**Radiological findings:** The procedure must be completed by a post-discography CT-scan. This exam determines the grade of fissure of a disc. A non injected image does not give this information. CT-scan evaluation of a discogram is looking at the repartition and shape of the injected dye. It must be planned immediately after the discography (Bernard et al., 1990). The disc can be either intact or ruptured or may present with internal disc disruption (IDD). IDD presents in four different stages. Grade I, II, III extend to the inner, middle and outer third of the annulus fibrosus, grade IV also extends circumferentially around the annulus assuming the shape of a ship’s anchor (Aprill et al., 1992). These fissures have no relation with degeneration, are not age related. A strong correlation as been dem-
onstrated between painful discography and IDD (Moneta et al., 1994). The reason why IDD is painful is not clearly established. Probably, in grade II, III and IV, the degradated matrix of the nucleus may chemically irritate the nerve endings of the outer third of the annulus (Heggeness et al., 1993). The second hypothesis is increased mechanical nociception due to mis-distribution of the charges on the diseased disc more sensitive to stress. These theories need further studies to be clearly demonstrated.

Provocative discography like any other diagnostic procedure in low back pain evaluation must not stand alone. It must be interpreted in the light of all the other information about the bio-psycho-social context of the patient. Viewed as an individual exam, this test has its limitations. The important issue is to be able to draw conclusions after a negative or a positive test.

In healthy young subjects with no pre-existing chronic painful illness, the false positive rate is extremely low. Walsh et al. in 1990 reported in a study on 10 volunteers. 16.7% of them had minimal pain on injection, 6.7% moderate pain and 3.3% “bad” pain (Walsh, 1990).

Further studies on older subjects suffering from chronic pain and on patients with significant psychometric features showed, as one would expect, higher false-positive rates. Carragee and al in 2000, conducted a prospective study including 30 patients. Little pain was elicited by low pressure injection of any anatomically normal disc. However, when discs although asymptomatic had fissuring of the annulus, the injection was painful. The main predictors of pain intensity were presence of chronic pain and abnormal psychometric scores (Carragee, 2000). As compared to the Walsh study, 40% of chronic pain group and 80% of the somatization group had at least one positive disc (Carragee, 2000).

In FBSS patients, discography is often used to evaluate recurrent or persistent back pain. Heggeness et al. reported in a retrospective study 83 patients who had undergone discography. 72% of them had a positive concordant pain response on injection of the previously operated disc. This may give a clue about the importance of the discogenic pain in FBSS patients (Heggeness, 1997).

Another study examined post-discectomy patients with or without persisting pain. 40% of the asymptomatic patients had positive injections on the previously operated level as compared to 63% in the symptomatic group. Moreover, considering the psychometric data, the rate of positive injections were the same in the two groups. Operated discs are painful in symptomatic as well in asymptomatic patients. Yet it remains true that concordant pain is reproduced in symptomatic patients. A damaged disc, symptomatic or not is usually painful when injected and according to the presence of associated aggravating factor, however the pain may be more intense (Carragee, 1999).
Future studies that focus on provocative discography should include a control discography on the adjacent level as proposed by the International Spinal Injection Society (ISIS). Since using a control discography with the provocative one, the false positive rate in normal discs is low even in the chronic pain population. Furthermore adding psychometric screening may help in reducing false-positive rate. As false-negative tests do not occur, we may conclude that all pathological discs are sensitive to provocative discography and with a good patient selection, reasonable diagnostic accuracy can be achieved. If the adjacent disc is used as a control, the specificity of this test will increase.

**Medial Branch Blocks**

Among the workers population, the prevalence of facet joint pain is 15% (Schwartzer, 1995 b). In an older group population, it increases up to 40% (Manchikanti, 1999 a). Not testing patients with back pain for zygapophyseal joint pain precludes the diagnostics in this proportion of patients and leads to further and perhaps futile investigations. After surgery, this remains valid and although the incidence is lower for other causes overpass this one, a significant proportion of patients will benefit from investigating the Z joint.

The zygapophyseal joint is innervated by the medial branch of the dorsal rami (Fig. 1).

Provocative saline Z-joint injection has been shown to induce pain in the back, the buttock and even down the leg in healthy volunteers. Anaesthetizing medial branches prevented the induction of pain in similar conditions (Kaplan, 1998).

Medial branch blocks are achieved under fluoroscopy guidance by specifically placing a needle onto the nerve and inject 0,5 ml of local anaesthetic (Bogduk, 1997). Each z-joint is innervated by two nerves blocked separately to anesthetize the joint. Single diagnostic blocks have a 47% false-positive rate. To achieve validity, controlled blocks must be performed with two local anaesthesia agents, a short and a long acting one (15% false positive blocks). If anaesthesia of the joint lasts longer with the second agent, the test is valid (Schwarzer, 1994).

**Sacro-Iliac Joint Blocks**

The sacro-iliac joint is responsible for 15% of low back pain (Schwartzer et al., 1995 c). S-I joint block is performed under fluoroscopy and a needle is introduced in the joint cavity. A contrast medium is used to insure correct placement of the needle tip (Slipman et al., 2002). A control block is mandatory to reach validity (Maigne, 1996).
To investigate leg pain or low back and leg pain associated with or without FBSS, trans-foraminal root sleeve injections, lumbar sympathetic blocks and spinal cord stimulation testing may be essential diagnostic tools and frequently determine the treatment.

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**Fig. 1. Schematic drawing of lumbar spine nerve supply.**

1. Medial branch dorsal ramus; 2. intervertebral disc; 3. communicating ramus; 4. sympathetic trunk; * = mamillo-accessory ligament

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**Minimally Invasive Approaches Diagnostic Procedures for Leg Pain**

To investigate leg pain or low back and leg pain associated with or without FBSS, trans-foraminal root sleeve injections, lumbar sympathetic blocks and spinal cord stimulation testing may be essential diagnostic tools and frequently determine the treatment.
Trans-Foraminal Diagnostic Injections

The clinical usefulness of nerve root blocks has been recognized as early as 1938 by Steindler and Luck (Steindler, 1938). Provocative response and anaesthesia of the nerve root have both been used as diagnostic procedures. In 1992, Nachemson indicated that selective nerve block provided important prognostic information about surgical outcome (Nachemson, 1992). It has also been shown that patients who failed to obtain sustained relief of radicular pain following the block (2% xylocaine 1 ml) were less likely to benefit from subsequent surgical intervention. The specificity of selective nerve root injection ranges from 94 to 100%. It is therefore a good prognostic factor, useful to determine the level in which surgery should be performed (Doodley, 1988).

The current literature provides moderate evidence of transforaminal epidural injections in the preoperative evaluation of patients with negative or non conclusive imaging studies, but with clinical findings of root irritation (Pang, 1998).

Algorithm for Diagnostic Assessment of Low Back Pain and FBSS

An algorithm to investigate low back pain must be based on the likelihood of the diagnosis. In 1995, Schwarzer et al. described the prevalence of the predominant aetiologies in low back pain. To investigate chronic back pain, minimally invasive tests have been developed during the last 15 years and there reproducibility and validity have been well documented (Bogduk, 2002 b). The quality of the test itself or the expertise of the physician performing the procedure is a necessary but not sufficient condition. The diagnostic must be established according to a clear strategy. Back versus leg pain must first be distinguished when possible and nociceptive differentiated from neuropathic pain. Physical examination will stress signs of radiculopathy versus pseudoradiculopathy. Although differentiating back from leg or radicular pain is particularly difficult to achieve in FBSS, the predominant features will determine the diagnosis process and later the treatment.

In each group, the next step consists in identifying the structure(s) responsible for the pain. The pain generator should be identified. In most non operated patients, a single cause of pain can be identified and treated. In operated patients, we face the possible overlap of multiple sources of pain. When surgery obviously has worsened the situation the question of a second and new pathological condition must be evaluated separately as a separate entity. Pain may be persist despite correct surgery for a correct diagnostic and further surgical treatment is impossible due to postoperative anatomical changes. The worst situation is when new symptoms follow sur-
Predominant back pain (Fig. 2): In chronic low back pain, the first exam is MRI. This exam will give the likelihood to orientate towards a discogenic pain or not. When the MRI shows abnormal discs, the level must be determined with multiple provocative discographies if needed. As discussed above, discography will help symptomatically and radiologically to determine the painful level. Operated discs, symptomatic or not do respond to provocative discography. In symptomatic operated patients the value of this test is not reduced. Therefore, when an operated patient is symptomatic it is of interest to know if injecting dye in the operated disc reproduces patient’s pain. It may still be the source of the pain. What we fail to have with this test is that asymptomatic disc may still generate pain as well.

In most cases, normal disc on MRI are not likely to cause pain. If they do, it is rare but when no other source of pain is found, it should not be forgotten that this hypothesis has not been tested.

When normal discs are demonstrated with MRI, the diagnostic strategy must be oriented towards other sources of pain, such as z-joints and SI
joints. The choice between these two is made according to their prevalence, older patients are more prone to suffer from diseased z-joint than young workers.

Unfortunately other sources of pain particularly after surgery, arachnoiditis, adhesions, fusion masses, damaged small nerves and neuromas do not have specific diagnostic tests. Moreover, no specific treatment follows these diagnoses.

**Predominant leg pain** (Fig. 3): When pain is in the leg, the quality of pain is helpful. History and clinical exam will help differentiate radiculopathy versus pseudoradiculopathy and by localising the level of radiculopathy. MRI findings will improve the accuracy of the diagnosis. Nociceptive and neuropathic pain should be differentiated. Transforaminal local anaesthetics injections will confirm and define the precise level of the radiculopathy. When an autonomic feature is associated to the painful leg, lumbar sympathetic blocks will also be diagnostic before an adequate therapy is chosen.

**Minimally Invasive Treatments for Low Back Pain**

A diagnostic strategy properly conducted leads to specific treatment. For the predominant causes of back pain, treatment is available. When no diagnosis can be established, the treatment will be symptomatic and when all medical and conservative treatments have failed, minimally invasive approach including spinal cord stimulation and intrathecal drug delivery systems will be used.
Intra-Discal-Electro-Therapy (IDET)

It is estimated that in a substantial percentage of patients with chronic back pain the lumbar disk is the pain generator. IDET was developed as an alternative for selected patients with chronic discogenic pain who have failed all conservative treatments and to whom the next step offered was arthrodesis. Intra-discal electrotherapy was developed because this last treatment was not the perfect response to discogenic pain and because no specific treatment was available for internal disc disruption.

The indication for IDET is demonstrated discogenic pain. As explained in the “provocative discography” section of this chapter, painful, low pressure, dye injection into the disc followed by CT-scan imaging constitute the selection criteria for intra-discal therapy.

Under local anaesthesia and under fluoroscopy guidance, a 17 gauge needle is placed into the centre of the disc to be treated. A navigable intradiscal catheter with a temperature-controlled thermal resistive coil is then deployed through the needle and navigated intradiscally under continuous two-plane fluoroscopic control. The catheter is navigated as far as possible adjacent to the inner posterior annulus. Once placement is optimal the catheter temperature is gradually raised according to a uniform protocol to 90°C over a period of 13 minutes and maintained at 90°C for 4 minutes. The 90°C catheter temperature creates annular temperatures of 60–65°C. Some authors advocate the use of prophylactic intradiscal antibiotics but no evidence shows it utility (Fig. 4).

Fig. 4. A-P view of a placement of an Intra-discal electrotherapy (IDET) catheter
The analgesic mechanism of IDET is thought to be related to the sealing of the radial fissures and to the destruction of the nerve endings in the annulus.

Observational studies have been conducted on IDET. Unfortunately, inclusion criteria did not include post discography CT-scan and control discography. However, significant improvement of pain scores and even improvement on disability questionnaire were observed. In 2002, Saal and al reported an outcome study on 58 patients with a two years follow-up. VAS, tolerance to the sitting position and SF-36 were reported at 6, 12, 24 months. At 24 months, 50% of patients reported a 4 point reduction on the VAS scale and similarly 78% of patients showed a 7 points improvement on the bodily pain scale of the SF-36 and 59% showed at least 14 points improvement. Moreover, these significant improvements were associated with no complication or adverse event (Saal et al., 2000; Saal et al., 2002).

A controlled study by Karazek and al on 36 patients with diagnosed internal disc disruption and a control group of 17 patients was conducted over 12 months. The control group was denied treatment by insurers and was treated with standard rehabilitation program. The control group did not improve except one patient. In the IDET group, after 12 months, 13 patients had no benefit and of the 23 that remained, 40% achieved 70% pain relief, 60% obtained at least 50% relief and 23% were completely relieved (Karazek et al., 2000). These results are encouraging for a still new and minimally invasive technique (Pauza et al., 2002).

**Medial Branch Radio-Frequency Lesionning**

A common technique to treat z-joint pain was the intra-articular steroids injection. This method did not pass the exam of controlled trial. Carette et al. demonstrated no more benefits with steroids than with intra-articular normal saline (Carette et al., 1991). Thus treatment of back pain by intra-articular steroids injection cannot be recommended.

The other method to prevent z-joint pain is denervation of the medial branches innervating the desired level. Two consecutive positive medial branch blocks with different local anaesthetics half-lives at the same levels predict an 80% pain reduction in 60% of patients 12 months after radio-frequency neurotomy (Dreyfuss et al., 1999). The treatment is achieved by lesionning the medial branches with a radio-frequency generator connected to a coated needle. The needle propagates a radio-frequency wave heating a small area around the non-coated to a preset temperature, generally 90°C for the defined time. This small area must surround the medial branch. To achieve perfect lesioning, the needle must be placed parallel to the nerve,
since the heated lesion is an ovoid shape that develops around but not extends the needle-tip.

**Minimally Invasive Treatments for Leg Pain**

Therapeutic approaches to leg pain are closely related to their underlying mechanism. Leg pain arising for low back pathology can be either inflammatory, or neuropathic.

**Therapeutic Epidural Injections**

Epidural steroid injection is probably the most frequent procedure performed to treat radicular pain. Technique is simple, and safe. Complications occur and may be related to the needle placement or to the drug administered. They include infections, dural tap and very rarely neurological damage (Nelson et al., 2001). Manchikanti et al. evaluated the effects of neuraxial steroids and found no significant effect of epidural steroids on weight and bone mass density (Manchikanti et al., 2000). Moreover, the commonly available steroid preparation can be safely used in the epidural space (Dunbar et al., 2002).

Three approaches to the epidural space are possible: Transforaminal, Inter-laminar or Caudal. The efficacy of epidural steroids injections has been questioned in many studies, most of them supporting the use of the technique (McQuay et al., 1998; Devulder, 1999). However, many studies either prospective or retrospective mixed the results of these three different techniques and did not consider the possible differences in the spread of the medication in the epidural space. Since, this problem has been addressed and in each of the three approaches differences have been shown (Price et al., 2000).

The most effective technique is probably the transforaminal approach (Karppinen et al., 2001). It is however associated with the highest complication rate and has been recently questioned. The most worrying complication is related to inadvertent injection of steroid solution into the Adamkiewicz artery (Houten et al., 2002). The entry of the artery into the foramen is subject to a high anatomical variability and enters between L2 to T9 in 85% of patients but may arise from the lower lumbar spine and even from as low as S1. To reduce the incidence of such complications, it is advisable not only aspirate on the syringe but also to inject dye before injecting a solution with potential aggregates prone to induce small vessels occlusions.

The combined evidence of caudal epidural steroid injections with randomised trials and prospective and retrospective trails is strong for short-term relief and moderate for long-term relief. It is a safe technique and should always be performed under fluoroscopy. Two studies have specifi-
cally addressed the problem of FBSS. Revel in a study including 60 patients showed significant improvement of symptoms in 49% of patients against 19% in the control group (Revel et al., 1996). However, another multicenter randomized study including 47 patients reported no short or long term benefit in this group of patients (Meadeb et al., 2001).

Trans-laminar epidural injections show moderate evidence for short term relief and no evidence for long-term relief. This may be due to the repartition of the solution in the epidural space, probably remaining in the posterior epidural compartment. It may also be related to the fact that most inter-laminar procedure are performed without fluoroscopic guidance.

**Percutaneous Epidural Neuroplasty (Racz Procedure) and Epiduroscopy**

If the effect of epidural steroid injections is local, i.e. a direct effect on the injured nerve root or on the “leaky disc”, it is essential that the steroid reach the site of injury. Historically, epidural steroid injections have been performed “blindly”, without any radiological guidance, however many factors may prohibit steroids from reaching the intended nerve root, such as scarring, adhesions, adipose tissue and septa, which may be present in the operated and non-operated backs. Thus theoretically drugs injected into a scarred epidural space will follow the path of least resistance, away from the painful site.

**Percutaneous epidural neuroplasty (Racz procedure):** It seems rational to assume that mobilization or dissolution of fibrosis may remove barriers that prevent application of drugs. Epidural neuroplasty (also known as Racz procedure) consists of accessing the epidural space in a caudal or transforaminal approach, injecting non-ionic contrast material (thus performing an epidurogram) in order to detect “filling defects” in the epidural space. This is followed by gentle manipulation of a metal reinforced catheter in order to liberate adhesions (“filling the defects”), and then injecting the targeted medication (Heavner et al., 1999). This procedure, which allows prolonged pain relief in refractory cases, has the advantage of targeted drug delivery, but has the disadvantage of an indirect, two dimensional vision of the presumed pathology.

The epidurographic diagnosis of spine pathology may be followed by neurolysis with the injection of corticosteroids, hypertonic saline and/or hyaluronidase. Two RCT and 3 retrospective evaluations showed pain relief up to a year, with cost effectiveness gains of up to 8,127 US$ per year per patient. When performed by appropriately skilled personnel this procedure has a low complication rate, however dural puncture, spinal cord compression, catheter shearing, hypertonic saline toxicity, infection and bleeding remain worrisome (Manchikanti et al., 1999 b).
Spinal Endoscopy: Even when injection is done under fluoroscopy, the image obtained is two-dimensional and can be misleading. Thus, epidural endoscopy provides us a three-dimensional, real-time, color view of anatomy-pathology in the epidural space.

Access of the epidural space with a flexible fibre-optic catheter via the sacral hiatus appears to be safe and efficient (Geurts et al., 2002). The procedure is done under local anaesthesia while continuously monitoring intra-epidural pressures, and patient’s response. Normal nerve roots when touched cause paraesthesia, diseased ones pain, so patient report is essential while gently performing adhesiolysis. The technique allows examination of the epidural space and its contents, targeted injection of medication, lysis of scar tissue (adhesiolysis) and (potentially) retrieval of foreign bodies (Kitahata, 2002). As technology grows new possibilities such as minimally invasive surgery, intraoperative nerve stimulation and immunobiological interference evolve, promising an important role of spinal endoscopy in the treatment of spinal pain.

In a prospective case series all patients undergoing epiduroscopy suffered from adhesions between nerve roots, dura and ligamentum flavum, 41% very dense, associated with previous surgery. If fibrosis is a result of chronic radiculitis, neurogenic inflammation and impaired fibrinolysis, repeat surgery will probably aggravate the situation and is thus ill advised. The authors hypothesize that adhesions obstruct radicular veins and interfere with the nervi vasorum, creating intra-neural edema and abnormal pain transmission. Dilution or “washing out” phospholipase A2 and synovial cytokines may also contribute to symptom improvement (Richardson et al., 2001).

In another recent study Igarashi et al. showed that epiduroscopy reduces back and leg pain among 58 elderly patients suffering spinal stenosis. Pain relief lasted more than a year after the procedure without any neurological complications, especially in patients suffering from abundant adhesions (Igarashi et al., 2004). This is of importance since persistent pain among patients suffering from FBSS is thought to be due to epidural scar. Furthermore, reservations about using this technique in patients suffering from a “restrictive” epidural space and thus fear from elevated intra-epidural pressures during the procedure, have been founded to be clinically debatable.

Spinal Cord Stimulation

Electrical stimulation has been used in the treatment of a variety of disease since the ancient Greeks. From the torpedo fish or “narke” inducing narcosis to the Faradization in the 18th century, electricity has been regarded as a therapeutic tool. In the end of the 19th and the early 20th century electricity has been disregarded in favor to emergent new pharmaceutical
agents and it is not until the early 60’s that electrotherapy reappeared. The publication by Wall and Merzack in 1965 of the “Gate control theory” of pain gave birth to the contemporary spinal cord stimulation (Melzack and Wall, 1965). The argument that electrical stimulation of large fibers would close the gate to input from the smaller diameter and unmyelinated A-delta and C fibers mediating pain was determinant to the success of SCS. Since, this hypothesis has been subject to criticism and we know now that it is not the only mechanism involve in pain control (Linderoth et al., 1999).

Spinal cord stimulation is achieved using a voltage-controlled pulse generator. It creates a potential difference between two outputs. The injected current is distributed in a 3-dimentional space made up of electrically conducting anatomical structures. The resulting 3-dimentional electric field can be represented by its potential distribution and by its current density distribution. These distributions can be visualized by isopotential line and isocurrent lines, respectively, as shown in the transverse section of spinal cord stimulation model. The stimulation induces mainly a depolarization of the nerve large myelinated fibers, both orthodromically and antidromically (Oakley et al., 2002).

The principle is to stimulate the dorsal column and interfere with the sensory information coming from the painful area. The analgesic mechanisms of SCS are however not clear. It is universally accepted that paresthesia coverage of the painful area, indicating the activation of the dorsal column, is necessary to obtain pain relief, it may however not be the mechanism of SCS. A possible stimulation target may be the dorsolateral funiculus which is known to contain descending pain controlling pathways. There is no convincing evidence for the involvement of opioid mechanism in the effect of SCS. Endorphins levels are not influenced by SCS and naloxone does not reverse pain relief induced by SCS (Meyerson et al., 1977). A possible role of GABA and adenosine in the analgesic action of SCS is suggested by animal and human studies indicating that GABA antagonists reverse partially the effect of SCS (Cui et al., 1996) and that a synergic effect of adenosine with SCS was observed (Cui et al., 1997).

The first spinal cord stimulator was placed in 1967 by Shealy by a D2-D3 laminectomy (Shealy et al., 1967). The first indication was cancer pain. Rapidly, it became clear that not all “pains” were sensible to SCS. Mainly, neuropathic pain was, nociceptive pain was not. Thanks to numerous publications on SCS, we now know that intermediate clinical states and other sympathetically maintained pain may be responsive to SCS which has progressively gained acceptance in a number of clinical pain syndromes including FBSS (Krames, 1999).

Implantable devices have a place in treatment of FBSS patients when all other conservative and minimally invasive tests and therapies have failed
to diagnose or treat a particular condition. This includes an important number of patients (North et al., 2002).

A proper patient selection is essential to achieve adequate pain relief with SCS. History is essential for the appropriate selection of the candidates to SCS. Pain characteristics and neuropathic features, must be searched, psychological screening may be useful. The evaluation of these crucial elements may lead to a shorter trial period, resulting in less infection rate and therapeutic failures.

In FBSS patients, leg pain responds better than axial back pain to SCS and neuropathic better than nociceptive, mechanical pain, the later almost non responsive to SCS.

With SCS, the active electrode, the cathode or negative electrode must be located near the level of the spinal cord dorsal columns that anatomically represents the level to be stimulated. The electrode is therefore placed in the epidural space under fluoroscopy guidance and with a patient awake and anesthetized locally at the needle entry point. The Tuohy needle is inserted into the epidural space using the loss of resistance technique and advanced rostrally up to the desired level. At this point, the external stimulator is connected and the patient is asked whether the stimulation, the paresthesia felt is covering the painful area or not. When the pain is unilateral, the electrode is placed on the side of the patient’s pain lateral to the midline on the homolateral dorsal column. If the pain is bilateral or axial, single or multiple electrodes must be placed on the midline or close to it.

SCS includes 3 components: The epidural electrode the connection between the epidural electrode and the battery and the Implantable-pulse-generator (IPG). A wide range of electrodes may be used. Two main categories are percutaneous leads and surgical leads, the later requiring laminotomy.

In failed-back patients, the implantation of the SCS is divided in three steps. The test electrode implantation performed under local anesthesia, the trial period ranging from one to four weeks and the IPG implantation commonly achieved under general anesthesia.

We think that placing a test lead without patient’s collaboration leads to a higher failure rate. The only indications for a direct implant of a surgical electrode are recurrent displacement of percutaneous leads or if a predicted target is in the area of prior surgery.

Trial period duration is debatable. Most authors recognize a one week test is minimal to obtain reasonable information to proceed to a definitive implantation. According to local practice the period extends from one to four weeks test. Criteria for a positive test are listed (Table 1).

The definitive implant requires connecting the implanted epidural lead to the connection, tunneled under the skin to the hypochondria where the IPG is placed.
Once the patient is implanted, treatment really begins. The surgical and trial periods are the easy part of the work. The follow-up of these patients is a dynamic process and may require long hours and programming is not always easy. Numerous consults may be needed and the willingness and patience of the physician and his team are essential.

Complications may be divided in 3 groups: surgical complications, device related and stimulation related complications.

Potential surgical complications include infection, spinal fluid leakage, hemorrhage and neurological injury. In 1995, Turner reviewed 31 studies referring between 0 to 12% infection rates, mean 5% (Turner et al., 1995).

In over 20 years, North’s group reported no major morbidity defined as neurological injury, meningitis or life-threatening infection (North et al., 1993). Electrode migration is the most common complication occurring 24% of the time (Turner et al., 1995). For this reason multichannel devices have been shown to be more reliable in this regard. It has also been advocated that paddle electrodes are more stable (North et al., 1997). Although no randomized studies have been published, it seems that paddle electrodes are associated with improved long term effectiveness, particularly for low back pain. This region needs high voltage stimulation and the design of the paddle leads with the stimulating electrode directed towards the dura unlike the percutaneous electrodes which directs all the usable current towards the medulla. This problem is of utmost importance for the development of new technology: What we really needed is a percutaneous paddle-like electrode.

Other problems like discomfort due to inadequate IPG position in the abdomen needing repositioning are uncommon.

Stimulation related discomfort is rare as it usually precludes definitive implant. If stimulation is painful or bothers the patient during the trial period, it is usually not a successful test and the electrode is removed. Patients usual complaint is related to posture induced changes in the intensity of stimulation. Important reprogramming sessions are mostly related to electrode displacement.

Most studies on SCS for FBSS are retrospective. Turner et al. reviewed 41 articles reporting approximately 50–60% of patients with FBSS describing a >50% pain reduction from the use of SCS (Turner et al., 1995). Hieu
et al., showed a long term efficacy in 63% of patients and fair in 22% after 42 months follow-up (Hieu et al., 1994).

Although no controlled studies have been conducted on SCS, recent prospective series reinforced the role of SCS in FBSS. North conducted a randomized comparison of SCS with re-operation with a 6 months cross-over arm in the study. 51 patients with FBSS consented to randomization. This study demonstrated a significant difference between patients who opted for cross over from SCS to re-operation but not visa versa and concluded that SCS is a viable alternative to re-operation (North et al., 1995).

Cost effectiveness can be evaluated comparing the estimated cost of therapy per year in groups treated by SCS versus alternative treatment. Bell et al. compared SCS versus surgeries and other alternative treatment over 5 years. The reduced demand for medical care of successfully SCS treated patients leads to the observation that SCS pays for itself in an average of 2.1 years (Bell et al., 1997).

Considering that SCS is an end stage technique used in patients in whom everything has failed, SCS is an effective treatment, particularly considering the low complication rate. However, new technology developments are needed to allow percutaneous placement of more efficient electrodes in terms of energy sparing and precision of current distribution (Deer et al., 2001).

Intrathecal Medications

The nature of back pain and the conjunction of nociceptive and neuropathic symptoms frequently reduce therapeutic margin of single or even complex medication, therefore, many FBSS patients fail to respond to oral or transcutaneous drug administration.

Nerve blocks have also limited efficacy, for these precise diagnostic tools do not always have a corresponding treatment. More invasive therapies must be cautiously examined for, as previously discussed in this review, the failure rate increases with the number of spinal re-operations and unless a specific target has really been identified recurrent surgery is not an option.

Intrathecal drug infusion is now well accepted as a treatment option when all conservative and etiologic treatment failed. These therapies have failed either because pain relief is inadequate or due to intolerable side effects.

When it comes to neuromodulation therapies, the choice between intrathecal medication and spinal cord stimulation is an important issue. SCS and Intrathecal drug infusion share common indications, but while SCS applies mainly to neuropathic symptoms, Intrathecal drug infusion also covers important nociceptives aspects of pain.
Once all other treatments have failed, a careful screening process of the candidates to an implantable therapy is needed. This screening can be divided into three steps.

The characteristics and localization of the pain must first be established. Low back versus leg pain and nociceptive versus neuropathic pain help in choosing the most appropriate approach between SCS and Intrathecal drug infusion. Hassenbusch et al. in a retrospective study in 1995 estimated that intrathecal infusion may be best for bilateral leg and back pain as compared to spinal cord stimulation (Hassenbusch et al., 1995).

No evidence has yet determined the adequacy of a particular treatment modality to select between spinal infusion and SCS, however, clinical practice is helpful in this regard. Although Intrathecal drug infusion may be efficient in a wide range of pain patterns and share common indications with SCS, the latter is easier for the patient and the physician. With SCS, no refills are needed, the patient may manage some stimulation parameters and there are no side-effects. Intrathecal drug delivery pumps need refilling and side-effects may be important. For these reasons, in common indications, it is only when SCS has failed that Intrathecal drug delivery should be used. For other indications like mixed pain patterns, Intrathecal drug infusion comes first.

Once the indication to Intrathecal drug delivery is determined, in a second step, patients must follow a medication trial and the most appropriate drugs must be tested.

The main principle is to first choose the most appropriate agent to the characteristics and localization of the pain. If not sufficient, it should be associated with a second medication. This second drug should be from another class of drugs. It should enhance the effect or complete the effect of the first drug by acting on other pain mechanisms like, for example, a local anesthetic if the first drug is an opioid.

Association of drugs may be required to achieve adequate analgesia but it will also complicate adaptations and changes of the medication as each drug concentration depends on the other. For example, to increase the delivery of one of three drugs mixed in the reservoir, the concentration of the others will need to be modified to keep their delivery flow constant. These sometimes complex therapies are needed and may be extremely efficient.

In most patients, morphine comes first. In a review of current practices Hassenbusch et al. determined that 98% of pain physicians who answered the questionnaire recalled using intrathecal morphine (Hassenbusch et al., 2000). The national outcomes registry for low back pain collected prospective data on 136 patients with chronic low back pain treated using intraspinal infusion via implanted devices, 81% of whom received morphine. Oswestry Low Back pain disability scale ratings after 12 months
improved by 47% in patients with back pain and in 31% in patients with leg pain (Deer T et al., 2004).

In Intrathecal drug delivery, besides side-effects of the infused drugs one may face other associated complications. Recent studies have confirmed the clinical observation that intrathecal morphine infusion was responsible for catheter-tip inflammatory masses. Coffey has recommended positioning the catheter tip in the lumbar thecal sac to minimize opioid dosage and concentration to the extent possible. It was also proposed to provide an attentive follow-up of patients to encourage early diagnosis and to reduce the risk of neurological injury in these patients (Coffey R J et al., 2002).

_Bupivacaine_ used mostly in association with opioids is a local anesthetic agent. Its use and safety in neuropathic pain syndromes has been widely recognized.

Up to maximum doses of 30–35 mg/day side effects are rare. Beyond 30 mg/day, and according to the place of the catheter tip, hypotension and motor weakness may be severe.

Less frequently used than morphine are mixtures: morphine+bupivacaïne (68% of pain physicians), hydromorphone (58% of pain physicians), morphine-clonidine, morphine-bupivacaïne-clonidine. Fentanyl and sufentanilly are also used alone or in mixed solutions. Combining drugs maximizes the effects and reduces the side-effects.

Although the above medications are used in a majority of patients new agents are in the pipeline and will soon be applied in clinical practice.

No definitive strategy has been established and the choice of the drug or the choice of the combination of drugs is specific to each and every patient. However, general principles are shared by pain specialists and guidelines have been proposed after reviewing current literature and practices by an expert panel in a polyanalgesic consensus conference in 2000, updated in 2003 (Bennett et al., 2000 a and Hassenbusch et al., 2004).

Although the acute cost of these implantable devices is high, the long term therapy is not more expensive than the conventional approaches (De Lissevoy et al., 1997).

New intra-thecal agents currently studied include midazolam, ketamine, neostigmine, gabapentine, ziconotide among others (Hassenbusch et al., 2004). These agents may be particularly helpful in the treatment of difficult neuropathic pain syndromes.

**Conclusions and Future**

The low back pain population includes a wide variety of patients (Walker, 2000). Not all patients should go through such diagnostic processes and treatments. 90% of acute back pain patients will resolve spontaneously in
the first three months and among the reminders not all will suffer enough to necessitate such approaches. For the small portion of the patients needing invasive therapies, non reversible procedures should take place only when a valid diagnostic strategy has been undertaken. In chronic back pain patients, surgery is never an emergency.

The principal problems leading to FBSS can be classified in 4 categories.

**Knowledge update:** All physicians taking care of low back pain patients should be aware of the leading epidemiological causes of acute and chronic back pain, of the headlines of the diagnostic algorithm in chronic back pain and detect the biological and psychological red flags.

**Common sense evidence:** Relying on history, physical examination and non MRI radiological findings may lead to wrong diagnostic, false security and sometimes to the wrong operation. Common sense is needed to treat low back pain but some historical evidences should be reconsidered.

**Diagnosis process:** Shortcuts from radiological findings to spinal surgery are not acceptable for chronic low back pain patients. Unless the source of pain can be determined precisely and that source possesses at least a mechanical component, surgery has no role.

**Surgery is not the ultimate solution:** The surgical approach must be confronted to a recent RCT comparing lumbar instrumented fusion with cognitive intervention and exercise in patients with chronic low back pain due to disk degeneration. This study was unable to detect any difference after one year in pain, analgesic consumption, satisfaction and return to work rate (Brox *et al.*, 2003). Moreover, when evaluating surgical results, it is important to consider radiographic fusion and functional outcome separately, thus improvement rate following surgery remains non conclusive. A comprehensive review suggests that 68% of patients have a satisfactory outcome following lumbar fusion; however, long term follow-up of decompressive laminectomy for lumbar spinal stenosis has shown no difference in outcome between surgical and non-surgical treatments (Turner *et al.*, 1992) (Iguchi *et al.*, 2000).

An 18 year follow-up in patients with spondylolisthesis showed that surgical interventions are indicated only for radiculopathies (Matsunaga *et al.*, 2000).

**Collaboration related:** Interdisciplinary approach is essential to investigate patients before surgery and to insure an adequate follow-up after. On the biological point of view, if surgery is performed only after a proper algorithm is followed, the target related procedure has the place it deserves; the adequate treatment.

We do not think the strategy described above will reduce the number of surgical procedures, but hopefully it may lead to more precise diagnosis and this will allow a better patient selection.
The trend is now for less invasive techniques and the industry have redirected their efforts towards the development of minimally invasive approaches. This economical and technological input will give birth to new high tech instruments. New ideas arise from our daily practice and a critical and constructive spirit will contribute to reduce the morbidity linked to our still incomplete understanding of pain and disability.

References