Sacral Anterior Root Stimulation (SARS) and Visceral Function Outcomes in Spinal Cord Injury–A Systematic Review of the Literature Over Four Decades

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Forty years of sacral anterior roots stimulation

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Sacral Anterior Root Stimulation (SARS) and visceral function outcomes in spinal cord injury – a systematic review of literature over four decades

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Abstract

Study design: Systematic Review

Objectives: The sacral anterior root stimulator (SARS) was developed 40 years ago to restore urinary and bowel functions to individuals with spinal cord injury (SCI). Mostly used to restore lower urinary tract function, SARS implantation is coupled with sacral deafferentation to counteract the problems of chronic detrusor sphincter dyssynergia and detrusor overactivity. In this article, we systematically review 40 years of SARS implantation and assess the medical added-value of this approach in accordance with the PRISMA guidelines (Preferred Reporting Items for Systematic reviews and Meta-Analyses). We identified four axes of investigation: i) impact on visceral functions, ii) implantation safety and device reliability, iii) individuals quality of life, and iv) additional information about the procedure.

Methods: Three databases were consulted: *Pubmed*, *EBSCOhost* and *Pascal*. 219 abstracts were screened and 38 publications were retained for analysis (1,147 implantations).

Results: The SARS technique showed good clinical results (85.9% of individuals used their implant for micturition and 67.9% to ease bowel movements) and improved individual quality of life. Conversely, several sources of complications were reported after implantation (surgical complications, failures etc.).

Conclusions: Despite promising results, a decline in implantations was observed. This decline can be linked to the complication rate, as well as to the development of new therapeutics (botulinum toxin, etc.) and directions for research (spinal cord stimulation) that may have an impact on people. Nevertheless, the lack of alternatives in the short-term suggests that the SARS implant is still relevant for the restoration of visceral functions after SCI.

Introduction

Spinal cord injuries (SCI) have disastrous consequences for individuals, who, in addition to the motor impairments, must deal with sexual, bowel and urinary problems. Beyond their impact on health, these disorders have psychosocial implications that must not be neglected. Regarding lower urinary tract (LUT) function, SCI results in a communication breakdown between supraspinal and spinal levels that not only manifests by the loss of voluntary control of micturition but also by an exacerbation of reflex processes. Adult neurogenic lower urinary tract dysfunction (ANLUTD) refers to the urological symptoms associated with these disturbances and expresses clinically by two major problems: the disruption of the detrusor activity (detrusor overactivity – DO or detrusor underactivity – DU) and the detrusor sphincter dyssynergia (DSD).

In order to restore urinary function, a device based on a strategy of functional electrical stimulation (FES) – more specifically, sacral anterior root stimulation (SARS) – was developed 40 years ago (implantation of the first person in 1976 and entering into the market in 1982) (1): the Brindley-Finetech® implant (or SARS implant). Stimulation electrodes are surgically disposed on S2 to S5 sacral anterior roots – i.e., roots composed of pelvic motor axons – and the device exploits the anatomical and physiological characteristics of the urinary tract to induce micturition. The detrusor being made up of slow dynamic smooth muscle fibers and the external urethral sphincter of fast dynamic striated muscle fibers; post-stimulus voiding is enabled by applying intermittent electrical stimulation. Indeed, at each stimulation cycle (3 seconds stimulation at 25 Hz followed by 6 seconds rest), the detrusor and the striated sphincter simultaneously contract and then relax asynchronously (striated sphincter relaxes instantly while detrusor contraction persists for a short time); this asynchrony is the source of a pressure gradient favorable to micturition. Default stimulation parameters – ie bladder-specific settings – might subsequently be adapted to either facilitate defecation (lengthening of stimulation cycles – 10 secs on then 20 secs off) or sustained erection in male individuals (decrease of stimulation frequency at either 8 or 12 Hz).

However, the Brindley device does not handle DO by itself as bladder contractions at low filling are still likely induced by the disturbed sacral reflex arch. Sacral deafferentation (i.e., sectioning of the sacral posterior roots, procedure called rhizotomy) is often coupled with SARS implantation to prevent DO – and, consequently, promote bladder compliance – but results in the potentially irreversible loss of spared perineal sensation and function (erection and ejaculation in men, vaginal lubrication in women, defecation).

Recent technological improvements paved the way to optimized sacral stimulation paradigms likely to renew the interest for SARS-like approaches. In this context, reviewing the impact of Brindley implantation in patients with traumatic SCI seems an important step towards development of upgraded implants/strategies.

Methods

We reviewed 40 years of Brindley implant use – from 1976 to 2020 – by analyzing the data in terms of i) visceral function results, ii) occurrences of adverse effects, iii) quality of life impact/considerations, and iv) additional aspects, especially long-term concerns – e.g., impact of laminectomies on spinal stability or compatibility with MRI exams.

Literature search

This systematic review was performed according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) recommendations. Three databases were searched: *Pubmed (main database), EBSCOhost (medical database)* and *Pascal (European and French database)* based on keywords selected by an engineer (TG) and a physician specialized in physical and rehabilitation medicine (CF). No language or date restrictions were applied and the last search was performed in August 2020. The search was carried out using the terms “sacral anterior root stimulator”, “implantable neurostimulator”, “neural prostheses”, “electrical stimulation therapy”, “neurogenic bladder”, “urinary incontinence”, “urinary retention, “bowel function”, “acceptability”, “failures”, “quality of life” and “psychology” confined to additional filters like “human species” and “adult” in *Pubmed*. The abstracts of all identified studies were screened by TG according to inclusion criteria defined with the senior authors. Only articles related to SARS in adults with SCI of traumatic origin were kept for analysis whatever their level of evidence (from cohort study to single subject design) or the number of implanted individuals (from large groups of persons to case study). TG then reviewed the selected articles in full text according to a review protocol designed in collaboration with CF, CA-C and DG. Manual inspection of the reference lists of all included papers was carried out to identify studies that were not captured by the online search (Figure 1) and senior authors undertook a repeat review to ensure inclusion of all relevant articles.

Study selection

Evaluating the action of the SARS procedure implies assessing its impact in terms of improved visceral functions – LUT, defecation and erection – but also the risks inherent to implantation (surgery, technical failures, etc.). The impact of SARS on quality of life was also investigated in this literature review, as were several additional findings on long-term follow-up (compatibility with MRI exams, etc.).

Studies from the same research group were carefully inspected and only studies with significantly different numbers of individuals, sufficient temporal gaps and different population characteristics were kept for the first analysis. Two-part studies were treated separately when they reported results in two different axes of research.

Raw data extraction and presentation

First, the main characteristics of each paper were extracted. The nature of the article (retrospective, prospective study, case study etc.), the year of publication and the main features of the investigated population (number of individuals, age, type of lesions, etc.) were examined. The level of evidence and the risk of bias were assessed at the same time using the recommendations of the Oxford Centre for Evidence-Based Medicine and the Cochrane's Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool (2) respectively.

The article contents were analyzed through four reading grids, one for each axis, and the following information was extracted and combined in a table format:

- *Urological, intestinal, and sexual benefits*: use of the SARS implant for micturition, defecation and sexual purposes; bladder volume; volume of residual urine; incontinence episodes; urinary tract infections; autonomic dysreflexia before and after surgery.

- *Implantation procedure and reliability:* sacral deafferentation and implantation procedure; complications following surgery; implant failures; impact on peoples' everyday lives and long-term side effects; other considerations (benefits, etc.).
- *Individuals' quality of life*: population; survey modalities; results.
- *Studies providing additional information*.

Data analysis

Given the large amount of generated data and in order to avoid patient redundancy, articles authorships as well as medical centres location were extracted from each paper before grouping them by geographic areas – Austria, France, Germany, Netherlands, North America, South America, Spain, Switzerland and United Kingdom (Table 1, 2 and 3) – allowing for a better tracking of implanted individuals for advanced analysis. For the same medical centre, according to their level of evidence and bias, articles were primarily used for main analysis or only for data completion precluding multiple computation of data from a single individual. In the same way, only publication stating data from the same individuals before and after implantation were used for computation of urologic outcomes while data from multicentric studies – including the three articles authored by GS Brindley – were reported separately. Last, the mean values of the most salient variables in each of these table were calculated on the generated dataset in order to obtain a summary statement of the literature.

Statistical analysis

When available, standard deviations associated with pre- and post-implantation bladder and residual urine volumes were extracted for statistical analysis. After ensuring independence between study-level variances and sample sizes (plots of squared standard deviation versus sample size complemented with a monotony assessment using a spearman coefficient), inverse variance weighting was used to implement both a fixed effect and a random effect meta-analytic model (Hunter and Schmidt model [HSM] (3)). Indicators of heterogeneity H^2 and I^2 provided insights upon models' relevance and confirmed the validity of the HSM model. After obtaining the meta-analysis global estimates and standard errors, 95% confidence interval values were drawn from a t-distribution (t-score being more conservative than z-score). For qualitative indicators – presence/absence of UTI or incontinent episode, statistics were drawn from a t distribution after comparison of pre and post implantation ratios. 95% confidence intervals were then used to determine significance for α=5%. These statistical analyses were carried out using the Metalab toolbox developed in Matlab (4).

Results

Research process and study design

The flow diagram of the literature search is shown in Figure 1. At the end of the selection process, 38 articles were retained for analysis including 24 retrospective studies (5–28), 4 prospective studies (29–32), 4 cross-sectional studies (33–36), 4 case reports (37–40), 1 survey (41) and 1 basic research article (42).

Among these publications, 6 dealt with individuals quality of life (29,30,33–36), and 8 others – including two case reports – were placed in the category "Other considerations" (5,6,37–42). The axes "Benefits for visceral functions" and "Implantation procedure and reliability" regrouped the 24 remaining publications.

The raw data from these studies were compiled in a table format – five tables in total, one combining the population characteristics plus one for each axis of investigation (Supplementary Tab.1, Supplementary Tab.2, Supplementary Tab.3, Table 4 and Table 5). Among these 38 publications, data from 4 multicentric studies (Supplementary Table 4) were subsequently withdrawn from analysis (15–17,22) as they were grouping results from several medical centers and precluded individualized follow-up.

Two additional figures investigated the risk of bias (Supplementary Fig.1) and the level of evidence (Supplementary Fig.2) of these studies. Interestingly, a gradual shift was observed from visceral benefits and implant reliability to quality of life issues over the last decades while wider considerations such as the long-term outcome of implanted persons emerged rather recently (Supplementary Fig.2).

Data analysis

A total of 1,147 implanted persons were tracked in 34 articles including 712 men and 435 women (Table 1). Individuals' mean age at the time of implantation was 36 years (ranged between 26.3 and 40 years, n=1,091) while 467 (31.3%) persons had tetraplegia and 680 (68.7%) paraplegia. The mean time between spinal injury and implantation was 8.45 years (varied from 1.86 to 11.17 years, n=1,097) and the mean post-implantation follow-up was 12.3 years (between 4.4 and 14.6 years, n=957). Implantations were performed on people with complete SCI in 88.9% [77-100%] of cases (mean [range of the means by geographical areas], n=1124).

Benefits for visceral functions

The impact of the Brindley implant on urinary, intestinal and sexual functions was initially reported in 24 studies. Of these 24 studies, 50% were ranked as level II or III, while the remaining 50% were categorized as level IV or V (Table 2).

Among the 1,147 individuals identified with SARS implant, 880 individuals were asked for their current situation and 85.9% [73-100%] stated using their implant for micturition. Their averaged bladder capacity significantly increased from 198 mL [173-264 mL] before implantation to 480 mL [401-546 mL] (n=751) after implantation (HSM for 295 individuals (10,17,19,30,32): mean increase in bladder volume = 279 mL; 95% Confidence Interval [CI], +191 to +354 mL), whereas the mean volume of residual urine after micturition decreased significantly from 131 mL [90-157 mL] (n=57) to 46 mL [16-85.7 mL] (HSM for 72 people (11,12,17,30): mean decrease in residual urine = - 97 mL; 95% CI, -71 to -122 mL). Urinary incontinence affected 86% [61-100%] and 35.5% [7-65%] of the individuals before and after implantation respectively (n=691; t-distribution, $p<0.05$). Urinary tract infections decreased from 6.3 to 1.3 episodes per year in the German group (n=464) while the overall percentage of persons affected by urinary tract infections in other areas dropped from 93% [87.7-100%] to 39% [15-78%] (n=402, t-distribution, $p<0.05$).

In addition to the LUT data, 67.9% [29-100%] of the patients (n=654) used their implant to facilitate bowel movements, while 62.1% [30-100%] of the male individuals (n=143 of 230 males) were able to obtain stimulation-induced erections. Finally, the proportion of individuals with autonomic dysreflexia decreased from 43.3% [16-66%] to 3% [0-9%] after implantation (n=895).

<u>Implantation procedure and reliability</u>

SARS implant reliability and impact on individuals with SCI was assessed by five modalities: i) nature of the surgical procedure, ii) surgical complications, iii) implant failures, iv) long-term complications, and v) additional information (benefits of the implantation, problems using the implant, etc.). The corresponding data were drawn from 22 publications gathering 989 implanted individuals from 10 level II or III studies – 45.5% – and 12 level IV or V publications – 54.5% (Table 3).

In 83.3% of individuals, Brindley devices were implanted intradurally. Sacral deafferentation was attempted in 99.4% of cases with a success rate of 93.9%. A total of 34 immediate post-surgical complications occurred after the initial surgery (3.4% - infections, cerebrospinal fluid leakage, etc.). Adverse effects caused by the implant/stimulation were reported in 54 cases (5.5%: muscle spasms, stimulus pain, infections, etc.), whereas 209 implant faults (21.1% of implants) were reported leading to 136 revision surgeries (surgeries to replace implant failures: 13.7%). Last, the SARS procedure proved to be insufficient in 63 persons (6.3%) who faced persistent urinary disorders (incontinence, sphincterotomy, etc.).

Nevertheless, the cleanest database on the subject remains Brindley's 1995 publication overviewing the 500 first implanted individuals (8) (Supplementary Tab.4).

Patient quality of life

Six publications were classed in this axis (Table 4; 488 individuals: 138 from level II and 350 from level III studies). In a nutshell, two distinct groups emerged and the conclusions drawn by Wielink et al. (29), Vastenholt et al. (33) and Rasmussen et al. (35) differed slightly from those of Creasey et al. (30), Martens et al. (34) and Zaer et al. (36).

For Wielink et al. (29) and Vastenholt et al. (33), implantation had an overall beneficial impact on individuals but this improvement was either not statistically significant (Wielink et al. (29)) or concerned only half the persons (people expectations met in 49% of cases in Vastenholt et al. (33)). Rasmussen et al. (35), for their part, only assessed quality of life related to bowel function in implanted individuals with no real improvement.

Conversely, no reservation was expressed about the positive impact of implantation in Creasey et al. (30)(improvement in 86.8% of the cases), Martens et al. (34) (results from Qualiveen and SF-36 questionnaire) and Zaer et al. (36) (overall satisfaction of implanted individuals and improvements of bladder function), for which a clear improvement in individual's quality of life was demonstrated.

Additional information

Eight publications were retained to complement this review as they were dealing with aspects little or not documented in previous studies (Table 5; 204 individuals from level IV or V studies including 4 case studies). Among these papers, six dealt directly with the consequences of implantation (5,6,37–40), while the last two (41,42) were focused on the prospects of this design of implant.

Lopez de Heredia et al. (5) concluded on the safety of MRI examination in implanted persons when conducting examinations in a 1.5 Tesla system – a central concern for the follow-up of people with SCI. Krebs et al. (6) showed no significant alteration of bladder contraction during stimulation-induced micturition in 111 patients 11.7 years after implantation.

Conversely, Soni et al. (37) questioned the long-term impact of laminectomy on spinal balance by reporting fractures of L4 and L5 vertebral bodies in one patient that induced a deterioration in his condition eventually leading to the cessation of implant use. Vaidyanathan et al. (38) and Bramall et al. (40) reported implant infections with complete removal of the device while Pannek et al. (39) reported the case of a patient with life-threatening autonomic dysreflexia for whom sacral deafferentation was necessary but who refused SARS implantation – raising genuine questions about the psychological impact of neuroprosthetic implantation.

Dealing with the future of the SARS implant, Kirkham et al. (42) investigated simultaneous stimulation of both anterior and posterior roots to restore LUT function without sacral deafferentation but concluded to the failure of the investigated procedure while Sanders et al. (41) attempted to identify patients' preferences for future neuroprostheses and highlighted the major role of the benefit-risk ratio on implant acceptability.

Discussion

Level of evidence

This systematic review gathered 1,147 implanted individuals from 34 publications. These 34 articles presented unequal levels of evidence (studies with a control group/level II: 2; prospective studies/level III: 11; retrospective studies/level IV: 11; case studies and short communications/level V: 10) as well as unequal risk of bias (supplementary Fig.1).

The number of publications classed under each axis of research proved also highly variable (Supplementary Fig.2). Most of the collected data related either to clinical results on visceral functions (n=24) or implant reliability (n=22). Only a few dealt with quality of life (n=6), although these studies had the highest level of evidence (level II or III) while long-term considerations were often limited to low-evidence articles (8 articles: levels IV or V including 4 case studies).

Assessment of Brindley implantation

a) Benefit/risk balance

For all clinical examinations – bladder capacity, volume of residual urine, incontinence episodes, urinary infections, facilitation of bowel movements, autonomic dysreflexia – a gain of function was systematically observed as a results of a combined SARS and sacral deafferentation procedure in all the investigated studies (Table 2).

Apart from the imponderables of such a procedure – i.e., surgery, electronic device implantation and sacral deafferentation – discomfort resulted mostly from surgical complications or implant failures that were corrected spontaneously (leak of cerebrospinal fluid, neuropraxia etc.) or after a second surgery (cable replacement, second extradural implantation) (Table 3). Deafferentation was responsible for constipation or erectile dysfunction but had a rather unpredictable impact on fecal incontinence; promoting stress incontinence of feces – by reducing reflex contraction of the anal sphincter – in one hand or decreasing fecal incontinence by reducing bowel reflex contractions in the other hand.

The aging of the implanted population raised previously unknown issues, such as the impact of laminectomy on spine balance or the safety of MRI exams (implant successfully tested with 1.5 Tesla MR System (5) while manufacturer documentation reports safe procedures with > 0.5 Tesla machines). Brindley also reported two death in his follow-up of the first 500 implanted individuals (7,8) – one due to renal failure and the other from primary bladder carcinomatosis (Supplementary Tab.3) – but none was mentioned in the 34 retained studies.

As patients' expectations for the implant are often very high – and legitimately so – these unexpected drawbacks might have engendered frustration despite the overall success of the procedure. This might explain the results – globally positive but somewhat contrasted – of quality of life studies (Table 4).

b) Decline in the use of the implant

In addition to the SARS implant, other competing solutions – surgical and drug approaches – emerged in recent years offering patients and medical staff several therapeutic alternatives especially to treat refractory DO (43). Surgical solutions include augmentation enterocystoplasty and/or continent cystostomy and offer the advantage of achieving both sustainable results and an optimal action on DO but constitute unique invasive procedures. Medication approaches may also be prescribed such as semi-invasive botulinum toxin injections. However, repeated injections are needed to achieve a significant decrease in DO emphasizing the transient impact of this procedure and the discontinuous nature of the generated effect – discontinuity that generates discomfort in patients waiting for renewal of the injection. Finally, both botulinum toxin and surgical approaches do not enable patients to get away from intermittent (self-) catheterization to manage DSD issues.

From an economic perspective, additional reports concluded the cumulative cost of treatment with the neuroprosthesis – including the cost of the device, its implantation and maintenance – to be equaled of those of conventional care on a time horizon between 5- and 8-years post-implantation (comparison before and after implantation (29,44)). Subsequent studies further investigated the cost-effectiveness ratio of the SARS approach to deeply inform decision makers of the opportunity to reimburse this procedure (versus a control group (45,46)) and provided recommendations in favor of the Finetech-Brindley implant. Nevertheless, these conclusions were a bit contrasted by the mixed results reported in studies focused on the quality of life of the implanted population (29,30,33–36). Thus, in the vast majority of cases, the cost of the procedure is still largely borne by patients while some alternatives are cheaper on a shorter term and more easily reimbursed by the health care system. This lead to a potentially insurmountable financial burden on interested individuals that will dissuade them from opting for the neuroprosthesis and may further explain, at least in part, the decline in implantation. Likewise, the gradual decline in implantation leads to a reduction in trained surgical services and to an even greater reduction in the number of prescriptions making this approach slowly falling back into anonymity.

Beyond the aforementioned factors, the rise of the Internet facilitates public access to recent scientific advances and raises expectation for the development of a medium-term comprehensive solution (stem-cell therapy, neuroprosthesis etc.). Patients are therefore more likely to preserve their "neurological capital" – and so to reject any deafferentation – and to suspend all surgical procedures while waiting for this new solution.

Distrust of some patients with regard to the implantation of electronic devices for ideological considerations may also constitute a limiting factor.

c) Targeted population

SARS is therefore one of the solutions to overcome visceral deficiency but by both its nature and the incidence of adverse effects, the generalization of its recourse is unlikely; secondary ejaculatory dysfunction and loss of sensitivity already precluding deafferentation in persons with incomplete lesions. However, since the population of patients with a spinal cord injury is very disparate – particularly with respect to the lesion profiles or the age of the individuals – SARS implant may still be relevant for certain categories of patients:

- Aging patient with paraplegia or tetraplegia (woman or man) in trouble to continue self-catheterization.

- Women with paraplegia or tetraplegia, able to perform self-catheterization, to transfer and to undress but confronted with residual incontinence (DO – different form stress incontinence) that cannot be collected by a specific device equivalent to the penile sheath in men.

- Women or men with paraplegia or tetraplegia who can no longer or cannot apply intermittent self-catheterization due to overweight or obesity.

- Patient with paraplegia or tetraplegia (woman or man) who refuses self-catheterization for practical reasons or to avoid urinary tract infections.

Although ANULTD management is very much dependent on the patient's medical condition and willingness, several studies have helped to deeply revise the current therapeutic arsenal to provide easy-to-follow treatment guidelines applicable to large cohorts of patients. Based on the objective to be achieved: i) continence with intermittent catheterization, ii) continence without catheterization, or iii) reflex micturition, several therapeutic stratagems might be implemented to help patients with DO or DSD – see Denys et al (47), Wyndaele et al (48) or Anquetil et al (43) for more details. Nevertheless, it might be worth complementing these guidelines by mentioning that Brindley implantation is not precluding future urological surgeries when, conversely, prior urological intervention is likely to prevent SARS procedure.

Study limitations

The lack of randomized or multi-group studies reduced the level of certainty of this systematic review. This situation can be explained by the difficulty of setting up randomized protocols because of both the invasiveness of surgery and people high expectations about implantation. It might also be due to the relative paucity of complete spinal cord injury as examiners might have anticipated that such a randomization would had decrease their recruitment potential. Similarly, setting up cross-over studies seems very unlikely because of the sacral deafferentation. Most of the publications on SARS have come from neurosurgical departments and, unsurprisingly, many of these studies dealt exclusively with urological and surgical outcomes, while few focused on patient quality of life.

As the selected studies were performed at different location across the globe, differing surgeries, post-surgical treatment care and rehabilitation may have affected outcomes. Only few studies reporting fragmentary data were thus available for individuals implanted in Spain or United Kingdom. Absence of a systematic report of pre and post-surgery data – as well as their respective variances – further undermine the impact of our conclusions by drastically reducing the number of implanted people eligible for final analysis. Discrepancies in follow-up periods and reporting procedures, especially regarding postoperative complication/care and quality of life assessment, also make synthetizing these data extremely difficult – our study is, to the best of our knowledge, the first systematic review on the SARS implant. In the same way, as this literature review extending over four decades, both the surgical approach and the implant reliability were continuously refined for the succeeding studies. Originally implanted without deafferentation, outcomes of the first/pioneer studies were likely impacted by the preservation of a disturbed sacral reflex arch in some individuals while management of side effects has progressively improved over time. Ultimately, as patient long term follow-up is often ensured by clinical centers close to the patients' homes, long-term assessment of large cohorts of individuals remains a challenge. It is therefore not surprising that most of the publications related to long-term implantation consequences are case studies.

Future directions

The main limitation of the implantation procedure remains the systematic posterior root rhizotomy. New stimulation strategies are currently studied to bypass this procedure and are mainly based on direct spinal cord stimulation (49,50) or on a combination of spinal roots and pudendal nerve stimulation. These main approaches are the so called "LION approach" (51), the sphincter fatigue procedure (52), the blocking technique (53,54) and the high frequency technique (55).

Conclusions

Despite generally positive results on visceral functions – especially LUT function – the number of Brindley implantation procedures has declined in recent years. Although the risks inherent to this procedure was minimized, the emergence of mini-invasive therapeutic alternatives such as botulinum toxin therapy has limited its use. The deafferentation coupled with the implantation procedure dissuades many persons frightened by its very invasive nature. However, sacral deafferentation might still constitute a valid alternative in individuals with a botulinum toxin-resistant bladder and might still be considered in competition with more widespread urological surgeries such as enterocystoplasty.

The rehabilitation of visceral functions remains a major concern of individuals with SCI, and thus many research teams are dedicated to finding less invasive solutions or alternatives that are likely to offer these persons a dramatic gain in quality of life. Nonetheless, the lack of alternatives in the short term suggests that the SARS and SARS-like implants are still relevant within the therapeutic arsenal.

Data Archiving

All data generated or analysed during this study are included in this published article.

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Conflict of Interest Statement

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

TG was responsible for designing the review protocol, conducting the search, screening potentially eligible studies, extracting and analyzing data, interpreting results, creating tables, and writing the report.

CF was responsible for designing the review protocol, conducting the search and assessing potentially eligible studies. He contributed to writing the report and interpreting results.

CAC and DG contributed to the review protocol and provided feedback on the report.

CD, LB, JRV interpreting results and provided feedback on the report.

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Figure Legends

Figure 1. Flow diagram of the literature search

Table 1. Study and patient characteristics per geographic areas

Table 2. Benefits for visceral functions (geographic areas)

Table 3. Implantation procedure and reliability axis

Table 4. Patient quality of life

Table 5. Additional information

Supplementary Figure Legends

Supplementary Fig.1. Cochrane's Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) plot

Supplementary Fig.2 – Articles characteristics. a) Distribution of the selected publications classified according to their topics and their year of publication, b) Strength of evidence of the selected articles

Supplementary Tab.1. Study and patient characteristics (all studies)

Supplementary Tab.2. Benefits for visceral functions (all studies)

Supplementary Tab.3. Implantation procedure and reliability axis (all studies)

Supplementary Tab.4. Multicentric studies

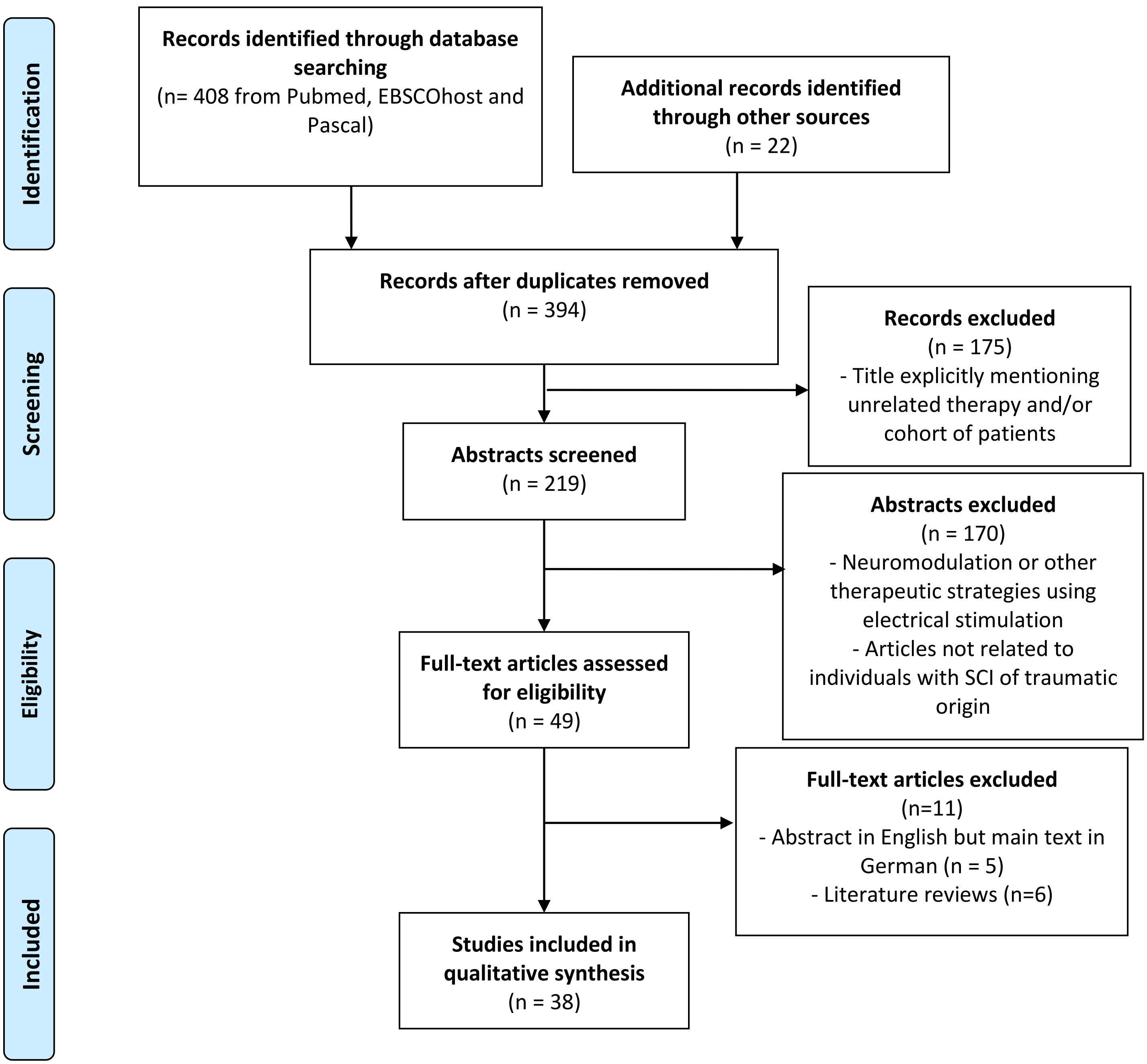
Identification
Screening
Eligibility
Included
Records identified through database searching
(n= 408 from Pubmed, EBSCOhost and Pascal)
Additional records identified through other sources
(n = 22)
Records after duplicates removed
(n = 394)
Records excluded
(n = 175)
- Title explicitly mentioning unrelated therapy and/or cohort of patients
Abstracts screened
(n = 219)
Abstracts excluded
(n = 170)
- Neuromodulation or other therapeutic strategies using electrical stimulation
- Articles not related to individuals with SCI of traumatic origin
Full-text articles assessed for eligibility
(n = 49)
Full-text articles excluded
(n=11)
- Abstract in English but main text in German (n = 5)
- Literature reviews (n=6)
Studies included in qualitative synthesis
(n = 38)

Table 1 – Study and patients characteristics per geographic areas

Location and period of publication [First to Last papers]	Identified groups	References* and level of evidence	% of male patient	Mean age at the time of implantation (in years)	Lesion profile T – Tetraplegia P – Paraplegia	% of complete SCI	Mean age of the lesion at the time of implantation (in years)	Mean patient follow up after implantation (in years)
Austria [1988-1993]	Innsbruck	[Made88] – IV [Made93] – V	27 -> n=30	26.3 -> n=7	Trauma: 30 T – 10 / P – 20 -> n=30	97 -> n=30	1.86 -> n=7	<8 -> n=30
United Kingdom [1988-2012]	Cardiff Sheffield Southport	[Robi88] – IV [MacD90] – III [Kirk02] – IV [Soni04] – V [Vaid09] – V [DeHe12] – IV	91.75 -> n=24	34.5 -> n=2	Trauma: 24 T – 9 / P – 15 -> n=24	91.75 -> n=24	4.96 -> n=24	10.5 -> n=2
France [1993-2004]	Bordeaux Le Mans Montpellier Nantes	[Bara93] – V [Egon93] – V [Egon98] – IV [Bauc01] – III [Hame04] – IV	65.1 -> n=120	33.6 -> n=116	Trauma: 116 Unspecified: 4 T – 48 / P – 72 -> n=120	85.8 -> n=120	6.6 -> n=116	5.34 -> n=116
Spain [1993]	Barcelona	[Sarr93] – V	14.3 -> n=7	-	Trauma: 7 T – 3 / P – 4 -> n=7	-	-	-
Netherlands [1996-2011]	Enschede Nijmegen Rotterdam	[VanK96] – IV [VanK97] – III [Wiel97] – III [VanD99] – III [Vast03] – II [Mart11] – II	68.6 -> n=89	37.1 -> n=89	Trauma: 89 T – 25 / P – 64 -> n=89	100 -> n=89	6.67 -> n=89	4.8 -> n=89
Switzerland [1998-2017]	Nottwil Zurich	[Schu98] – III [Pann10] – V [Kras14] – III [Kreb17] – IV	57.1 -> n=147	39.2 -> n=147	Trauma: 147 T – 58 / P – 89 -> n=147	95.9 -> n=147	11.17 -> n=147	14.05 -> n=147
North America [2001-2016]	Cleveland New York Philadelphia San Diego Stanford Toronto	[Crea01] – III [Sand11] – IV [Bram16] – V	70 -> n=23	40 -> n=23	Trauma: 23 T – 6 / P – 17 -> n=23	100 -> n=23	7 -> n=23	> 1 year but some results are missing -> n=23
Germany [2003-2018]	Bad Wildungen	[Saue03] – V [Kutz05] – IV [Kutz07] – IV [Rasm15] – III [Zaer18] – III	57 -> n=587	34.9 -> n=587	Trauma: 561 Other specified causes: 26 T – 266 / P – 321 -> n=587	84.5 -> n=587	8.9 -> n=587	14.6 -> n=587
South America [2016-2020]	Medellin Santiago de Chile	[Cast16] – III [Ramo] – V	89.2 -> n=120	38.7 -> n=120	Trauma: 103 Unspecified: 17 T – 42 / P – 78 -> n=120	92.3 -> n=104	7.25 -> n=104	4.4 -> n=16

*References presented as the four first letters of the first author surname followed by the two last digits of the year of publication; -> n = total number of implanted individuals with available information for each area

Table 2 – Benefits on visceral functions (geographic areas)

Location	Use of SARS for micturition (%)	Mean bladder capacity (volume in ml)		Mean residual urine (volume in ml)		Incontinent episodes (%)		Urinary tract infections		Autonomic dysreflexia (%)		Use for defecation (%)	Use for erection (% of male)
		Before	After	Before	After	Before	After	Before	After	Before	After		
Austria	90 -> n=30	209 -> n=7	435 -> n=7	116 -> n=7	27 -> n=7	100 -> n=30	7 -> n=30	-	0 -> n=7	-	-	29 -> n=7	100 -> n=1
United Kingdom	73 -> n=22	-	-	-	-	-	32 -> n=22	-	-	-	-	50 (SARS alone) -> n=12	30 -> n=20
France	89.7 -> n=116	203 -> n=112	546.4 -> n=112	90 -> n =19	25 -> n =19	98.8 -> n=112	11.58 -> n=112	100 -> n=93	29 -> n=93	21.7 -> n=112	0 -> n=112	52.6 -> n=116	65.2 -> n=75
Spain	100 -> n=7	-	>400 in all patients -> n=7	-	<50 in all patients -> n=7	-	0 -> n=7	-	-	-	-	100 -> n=7	100 -> n=1
Netherlands	87.1 -> n=84	285.4 -> n=52	571.2 -> n=37	104.7 -> n=52	64.9 at one year -> n=37	90 (daytime) 96 (night) -> n=52	27 (daytime) 14 (night) at one year -> n=37	98 -> n=37	59 -> n=37	15.9 -> n=47	4.25 -> n=47	46.7 -> n=84	62.3 -> n=61
Switzerland	79.6 -> n=147	264.4 -> n=147	476.7 -> n=147	157 -> n =10	16 -> n =10	60.9 -> n=137	38.3 -> n=137	87.7 -> 147	51.7 -> n=147	62.6 -> n=147	7.5 -> n=147	-	-
North America	78 -> n=21	256.9 -> n=21	>401 -> n=21	159.6 -> n=21	85.7 -> n=21	82.6 -> n=21	64.8 -> n=21	100 -> n=21	78.3 -> n=21	34.8 -> n=21	8.7 -> n=21	61 (systematic use) -> n=21	-
Germany	86.2 -> n=333	173 -> n=464	470 -> n=464	-	-	86 -> n=287	52 -> n=287	6.3 per year -> n=464	1.2 per year -> n=464	40.3 -> n=464	0.4 -> n=464	73 ->287	-
South America	90.5 -> n=120	-	362 -> n=104	-	<50 -> n=120	100 -> n=104	14.4 -> n=104	91 -> n=104	15 -> n=104	66.3 -> n=104	5.8 -> n=104	88.8 -> n=120	66.7 -> n=72

-> n = total number of implanted individuals with available information for each area

Table 3 - Implantation procedure and reliability axis (geographic areas)

Author	Deafferentation and Implantation procedure	Complications following surgery	Implant failures	Impact on patients everyday life and long term side effects	Additional information
Austria ->N=30	SARS implantation and deafferentation of roots for whom anterior component induced detrusor contractions – first patients – then extension to all sacral posterior roots. 26 intradural implant and 4 extradural implantation	- Second deafferentation (n=5) -> successful procedure for 4 of them	-	- Suspicion of Wallerian degeneration in one patient for whom electromicturition was impossible at the time of the study	- Severe autonomic dysreflexia disappeared in on patient - Statement claiming that SARS procedure improved all patients Quality of life as well as no patient has regretted the operation
United Kingdom ->N=24	Intradural implantation in all cases with or without S2-S4 rhizotomy – e.g. 9 implantation with and 3 without deafferentation in Sheffield group (n=12)	- Suspicion of anterior roots damage (n=2) - Cerebrospinal fluid leakage (n=2)	-	- Patient with pelvic pain awaiting for rhizotomy (n=1) - Somatic muscle spasms (n=1, preventing implant-driven micturition) - Muscle spasms when using SARS implant for erection (n=6 -> never used for sexual purposes) - Sphincterotomy proposed (n=4 -> two refused and did not use the implant) - Hydronephrosis pre-implantation (n=4): * Resolved in two cases * One patient relapsed * Grade IV reflux with urgent sphincterotomy in one patients - Spine fractures due to the laminectomy leaded to intractable spasms and cessation of implant use (n=1) - Infection leading to complete removal of the device 2 years after implantation (n=1)	- No constipation and reduced time for bowel evacuation reported by the Sheffield group
France ->N=116	- Intradural rhizotomy and implantation (n=103) – Intradural rhizotomy and extradural implantation (n=13)	- Cerebrospinal fluid leakage (n=6) - Nearly complete denervation (n=5, intradural implantation, stimulator could be use after recovery in 3 patients) - Neuropraxia (n=1) -> Recovery after few months (n=1) - Partial denervation (n=5, with good results few months post-implantation) - Second deafferentation (n=4) - Discomfort at the subcutaneous receptor (subsequently displaced, n=2)	- Extradural implantation due to intradural electrode failure (n=1) - Replacement of receiver block (n=6) - Cable failures (n=4) - Cable disconnection (n=4) - Charger failure (n=3)	- Transitory spasticity was mentioned but not quantitatively documented. - Infection leading to implant removal (n=2) - Deterioration of detrusor responses (n=5) - Bladder fibrosis (n=1) - Persistent sphincter dyssynergia (n=3, patient refused sphincterotomy or conus deafferentation) - Persistent Wallerian degeneration (n=1) - Second sphincterotomy (n=4, all continent) - Pyelonephritis (n=1) - Renal problems leaded to nephrotomy (n=1)	Benefit: - Preoperative vesicoureteral reflux disappeared (n=3)
Spain ->N=7	Extradural implantation and deafferentation at the conus medullaris in all patients	The receiver block was placed too low in patient abdominal wall and broke through the skin (n=1) -> It was replaced higher up	-	-	Benefit: - Upper urinary tract dilatation improved in one patient

Netherlands ->N=84	Intradural sacral posterior rhizotomy (S2-S5) and intradural SARS implantation in all patients	- Second deafferentation (n=3) - Neuropraxie (n=1) - Cerebrospinal fluid leakage (n=3) - Wound infection (n=1) - Nerve damage (n=2) * 1 permanent * 1 recovered - Detrusor weakness (n=4) -> Problems solved several years after surgery	- External equipment (n=23 in total) * Cable fracture (n=16) * Transmitter defects (n=7) - Internal equipment (n=4 in total). * 3 receiver replacements	- Strong lower limbs contractions during stimulation-induced erection (n=12) - Strong motor responses to stimulation (n=1) - Fibrosis around sacral roots (n=2) - Root failures (n=1, but deafferentation enable complete continence) - Detrusor weakness (n=2) - Sphincter weakness (n=1) - Implant infection (n=1) -> Replacement of the intradural implant by an extradural one - AHR induced by stimulation (n=2) - Intrathecal baclofen pump (n=2)	- Stimulation-induced erections not used for sexual intercourse - Upper urinary tract dilatation solved in 2 patients - Creatinine clearance returned to normal values after implantation (n=32) - Preoperative vesicoureteral reflux was reduced (n=1) or disappeared (n=1) - No interference between SARS and baclofen pump
Switzerland ->N=147	Intradural implantation and deafferentation S2 to S5 in all cases	- Incomplete rhizotomy (n=8) with second deafferentation (n=4) - Cerebrospinal fluid leakage (n=8) - Infection (n=3)	- Defect of cables (n=19) - Defect of stimulation plate (n=19) - Dislocation of the stimulator plate (n=16) - Undetermined cause of stimulator failure (n=15)	- Additional urological interventions in 43 patients * 22 Outlet obstruction * 10 Vesicoureteral reflux * 10 Incontinence * 9 Urethral strictures - Problems with condom fixation (n=3) - AHR persisted and occurred during implant-driven voiding despite complete sacral deafferentation (n=8)	- In 54 patients, a total of 83 surgical revisions were performed (17 patients underwent more than one revision)
North America ->N=21	Extradural implantation and intradural rhizotomy S2-S5 in all cases	- Temporary nerve damage (n=2, recovery within 3 months) - Incomplete rhizotomy with second deafferentation (n=1)	-	- Increased lower limb spasticity (n=2) - Infection leading to complete removal of the device 26 years after implantation (n=1) - Increase in incontinence episodes (n=4) - Fracture of the second lumbar vertebra 5 months after surgery which caused compression of the cauda equina (n=1)	Benefit: - Reduced time for bowel evacuation
Germany ->N=440	Intradural deafferentation and implantation. Rhizotomy performed in all surgery with a success rate of 95.2%	- Cerebrospinal fluid leak (n=6) - Infection of the implant (n=5) with further reimplantation in 4 cases - Dehiscent wound (n=2) - Hemorrhages (n=2, no further treatment) - Second rhizotomy (n=8 at conus terminlis to interrupt dysreflexia)	- 81 Implant defects -> 44 repair surgeries * 26 Receiver exchange and cable repair * 6 Cable repair alone * 12 Extradural implant with 1 withdrawal due to an infection	- Bladder overdistension and neurogenic failures are mentioned but not quantitatively documented.	- Bladder spasticity stopped in 97% of all cases. - Recovery of kidney function is mentioned
South America ->N=120	Extradural implantation and posterior rhizotomy of S2-S5 sacral roots (n=104) or S2-S4 roots (n=16)	- Neuropraxia with spontaneous resolution after 12 months (n=2)	- Failure of the receiver block (n=1) - Malfunction/damage of the external hardware mostly due to operator misuse (n=10)	- Infections few months after implantation (n=2) - Cable extrusion (n=2) - Extrusion of the receiver block (n=4)	- Stimulation-induced erections rarely used for sexual intercourse

-> N = total number of implanted individuals with available information for each area; n = number of corresponding adverse events for each area

Table 4 - Patient's quality of life

Author	Population	Survey modalities	Results
Wielink et al, 1997	52 implanted patients. Questionnaires completed at baseline, 3 months, 6 months and 1 year follow-up	Final survey designed by using 4 indicators - the Nottingham Health Profile - the Karnofsky Performance Index - the Affect Balance Scale - Self-developed items + Cost effectiveness study	<u>Quality of life:</u> - The Nottingham Health Profile covers several aspects such as "energy", "sleep", "emotional reaction" and "social isolation". It did not show significant improvement after implantation. - The Karnofsky Performance Index, initially designed in cancer research to quantify "objective" quality of life aspects, did not show significant improvement after implantation. - The Affect Balance Scale assessing experienced well-being improved significantly after SARS implantation. - Before implantation patients showed problems with bladder emptying and incontinence especially during everyday life tasks. <u>Cost-effectiveness:</u> - Costs of treatment with SARS are high in the first 2.5 years (implantation surgery and stay in hospital) - These SARS costs are earned back after 8 years compared to conventional treatment costs. - The saving of money increases with the long term effects
Creasey et al, 2001	18 implanted patients whose completed a 6-month follow-up	User satisfaction survey designed by the authors	<u>6 Items with 5 possible responses (Strongly agree / Agree / Neutral / Disagree / Strongly disagree):</u> - Patient satisfaction *SA: 67% *A: 28% *N: 0% *D: 5% *SD: 0% - Quality of life improvement *SA: 44% *A: 50% *N: 5% *D: 0% *SD: 0% - Correspondence with patients expectations *SA: 29% *A: 59% *N: 0% *D: 12% *SD: 0% - Improvement in patient independence *SA: 39% *A: 39% *N: 22% *D: 0% *SD: 0% - System ease of use *SA: 28% *A: 61% *N: 0% *D: 11% *SD: 0% - Reduction in urinary tract infections *SA: 44% *A: 33% *N: 6% *D: 11% *SD: 6%
Vastenholt et al, 2003	Comparison between two populations: - 37 implanted patients with a 7 years follow-up period - 400 SCI patients whose results are reported in the manual of the Qualiveen questionnaire	Use of the Qualiveen questionnaire which is a disease specific questionnaire composed of two parts: - Impact of urinary problems - Quality of life of SCI patients + Patient expectations	<u>Qualiveen results:</u> - Impact of urinary problems on patients quality of life is smaller in the implanted patients group compared to the control group. - The overall quality of life is higher in implanted patients versus control patients <u>Patient's experiences and expectations:</u> - Patients expectations with respect to micturition: *Expectations met: 62% *Partially met: 32% - Concerning defecation: *Expectations met: 38% *Partially met: 30% - Use of SARS for erection in male patients: *Expectations met: 47% Almost 90% patient would chose again for surgery and would recommend implantation
Martens et al, 2011	Comparison between 3 populations: - Brindley group (n=46)	Survey designed with 3 components: - the Qualiveen questionnaire	<u>Qualiveen questionnaire</u> - Impact of urinary problems: * Patients who used SARS mentioned less limitations, constraints, fears and bad feelings concerning their urinary problems. - Overall quality of life:

	- Rhizotomy group (Brindley procedure without use of the implant – n=27) - Control group (n=28)	- the SF-36 which mesures the general health - Questions regarding urinary tract infections and continence	* Better general quality of life for the Brindley group * Better general quality of life for the rhizotomy group compared to the control group but not statistically significant. - Brindley group > Rhizotomy group > Control group <u>SF-36 Questionnaire:</u> - Higher scores in Brindley group versus Rhizotomy group and control group indicating better general health and social functioning <u>Clinical results:</u> - Continence rate (% of patients totally continent): *Brindley group 52% *Rhizotomy group 33% *Control group 14% - Urinary tract infections (% of patients without infections): *Brindley group 50% *Rhizotomy group 15% *Control group 36%
Rasmussen et al, 2015 and Zaer et al, 2018	587 implanted patients. Questionnaires completed by 333 patients and only responses from those who are using the SARS for bowel function were analyzed in Rasmussen et al (n=277 – 145 males and 132 females) while only those using the SARS for bladder function were analyzed in Zaer et al (n=287– 154 males and 133 females).	Combination of data from both showed results from 7 indicators - 1 for overall satisfaction: Visual analog scale (VAS), - 1 for bladder function: VAS - 1 for sexual function: VAS (n=284 – 154 males and 130 females) - 4 assessing bowel function: VAS for overall severity of bowel symptoms; Neurogenic bowel dysfunction score; St Marks incontinence score and Cleveland constipation score	<u>Overall satisfaction:</u> - VAS ranged from 0 (worst) to 10 (best). For the subject that are still using their implant, the median VAS score was 10 (range: 0-10). <u>Bladder function (for individuals using their implant):</u> - VAS ranged from 0 (minor) to 10 (major nuisance). VAS score dropped from 9 (range: 7-10) at baseline to 3 (1-5) at follow up. <u>Sexual function (for individuals using their implant):</u> - VAS ranged from 0 (no satisfaction) to 10 (no problems). Males: No statistical difference between before and after (0.41 versus 0.47) even if males ability of performing intercourse decreased. Females: slightly decrease from 6 (range: 0-10) to 5 (0-10) without reaching statistical significance. In the same way, no statistical difference between before and after regarding capability of orgasm, usage of sexual aids or medicine and ability of having sexual intercourse. <u>Bowel symptoms (for individuals using their implant):</u> - VAS for overall severity of bowel symptoms, range 0 (worst) to 10 (best), was 6 (range: 4-8) before implantation and 4 (2-6) at follow up. - Neurogenic bowel dysfunction score (0-6 very minor, 7-9 minor, 10-13 moderate, 14+ severe dysfunction) was 17 (range: 11-21) before SARS procedure and 11 (9-15) at follow-up. - St Marks incontinence score (0=perfect continence, 24=totally incontinence) remains 4 before and after implantation (range: 0-7 and 0-5 respectively). - Cleveland constipation score (0=minimal, 30=worst constipation) slightly decrease from 7 (range: 6-10) at baseline to 6 (4-8) at follow-up.

Table 5 – Additional information

Author	Deafferentation	General description
Kirkham et al, 2002	- Extradural (80%) or intradural (20%) implantation of SARS - No rhizotomy	Implantation of SARS implant on both anterior and posterior roots for neuromodulation purposes. In all patient, stimulation increase bladder capacity and reflex erection was preserved. However, micturition was only elicited in one patient - Patient for whom micturition cannot be for sure imputed to implant use.
Soni et al, 2004	intradural implantation of SARS and S2, S3 and S4 posterior roots rhizotomy	A patient using SARS implant for micturition noticed progressively increasing spasms. These spasms required intrathecal baclofen therapy but subsequent lumbar spine fractures – L4 and L5 vertebral bodies – leaded to intractable spasms and to cessation of implant use.
Vaidyanathan et al, 2009	- Intradural rhizotomy and implantation	Person with SCI with a history of bladder calculus underwent sacral deafferentation and SARS implantation. Chronic infections by Pseudomonas aeruginosa led to implant removal, causing loss of bladder emptying. Deafferentation and failed implantation induced severe constipation and loss of – reflex – penile erection. The long-term consequences of unsuccessful bladder stimulator surgery had dramatic effects on patient quality of life.
Pannek et al, 2010	Intradural rhizotomy without implantation	S2 to S5 deafferentation as a salvage procedure in a patient with life-threatening autonomic dysreflexia. This bladder-triggered dysreflexia even leading to cardiac arrest, it was decided to perform sacral deafferentation to prevent further critical episodes. The patient nevertheless rejected any implant and 3 month after surgery declare himself content with suprapubic catheter while no episodes of autonomic dysreflexia occurred.
Sanders et al, 2011	NA[a]	Patient preferences for next generation of neural prostheses. A fractional factorial study was designed to identify patient preferences regarding new neuroprosthetic devices. This study aimed to identify the key features for implant attractiveness and compared three stimulation modalities: Brindley implant, pudendal nerve stimulation and Brindley system without dorsal rhizotomy. In a nutshell, “side effects” and invasiveness seemed to be the most important features while patient preferences established the following ranking: Brindley system without dorsal rhizotomy > pudendal nerve stimulation > Brindley implant.
De Heredia et al, 2012	NA[a]	Investigation of MRI exams impact on SARS implant in 18 patients. A total of 44 MRI examinations were performed, 34 at 0.2 Tesla and 21 at 1.5 Tesla. Side effects: Two MRI on the same patient were stopped due to interference with the SARS (toe movements at 0.2 Tesla, a subsequent MRI at 1.5 Tesla was performed without complications). No other adverse effects could be directly attributed to MRI exams.
Bramall et al, 2016	- Intradural implantation of SARS - No rhizotomy	Person with SCI remained incontinent after SARS implantation leading his physician to remove the receiver block while leaving the electrodes and associated wires. Repeated skin breakdown with wired extrusion happened in subsequent patient medical history ultimately leading to a chronic Staphylocccus aureus infection and sacral osteomyelitis 26 years after implantation. Definitive management involved complete removal of the device and the intradural phlegmon as well as ligation of the thecal sac and flap reconstruction.
Krebs et al, 2016	- Intradural rhizotomy and implantation	Long-term follow up of detrusor contractions in spinal cord injured individuals implanted with sacral anterior root stimulator (mean follow-up=11.7 years). Detrusor pressures induced by stimulation decreased over time without reaching statistical significance. This decrease neither resulted in an increase in the number of daily stimulation-induced voiding nor in an increase in residual urine after voiding. The origin of the deterioration of bladder contraction remains unknown even if neurogenic deterioration in the wake of SCI, long-term SAR or aging are likely to be incriminated.

[a]NA: Not applicable

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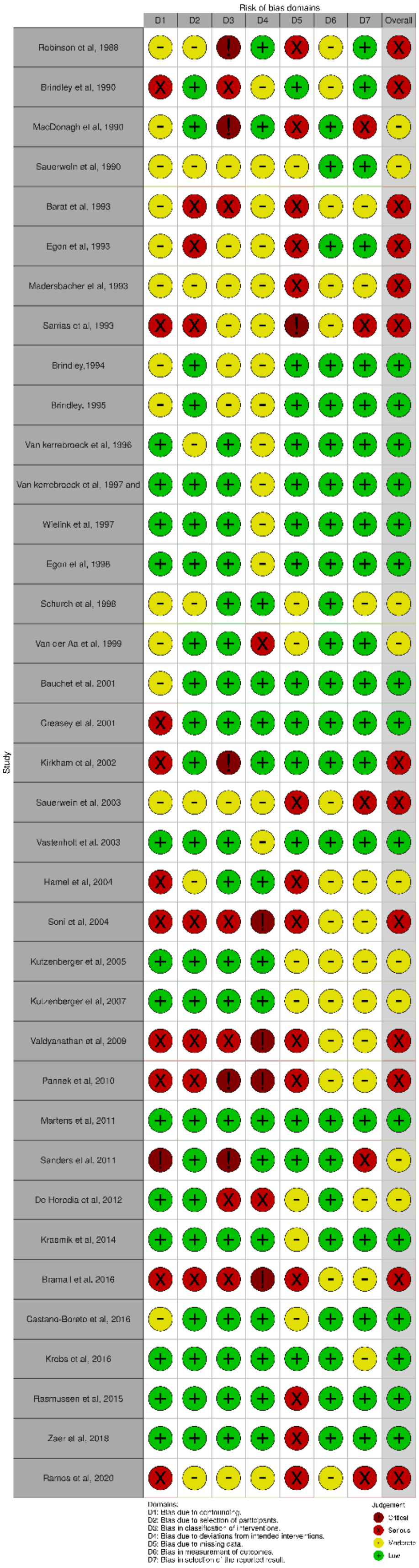
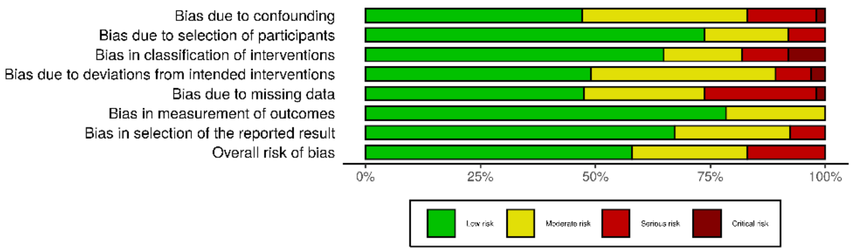
Supplementary Fig.1 – Cochrane's Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) plot





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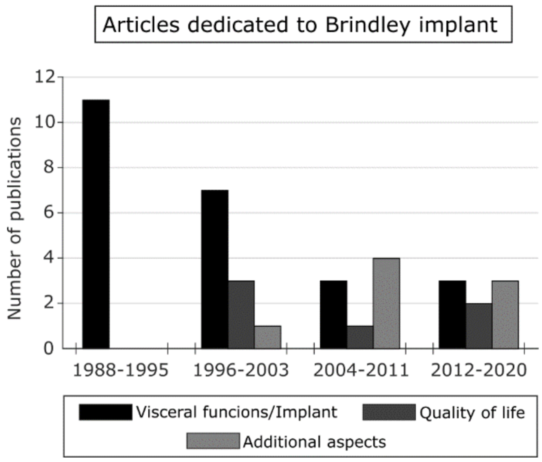
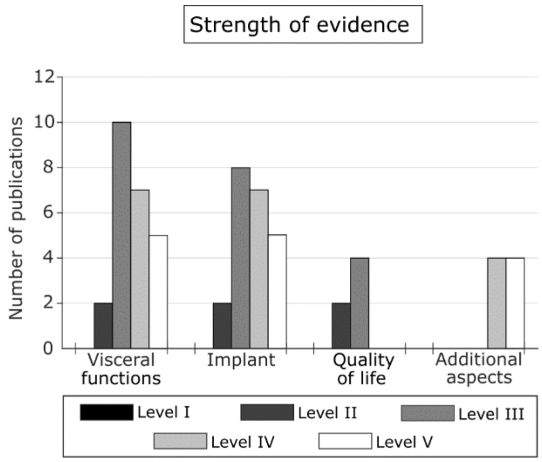
Supplementary Fig.2 – Articles characteristics. a) Distribution of the selected publications classified according to their topics and their year of publication, b) Strength of evidence of the selected articles





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Supplementary Tab.1 – Study and patient characteristics (all studies)

Authors	Number of patients / % of male patient	Mean age in years (*)	Lesion profile T – Tetraplegia P – Paraplegia	% of complete SCI	Mean age of the lesion at the time of implantation (in years)	Patients follow up after implantation (in years)	Study type	Level of evidence
Madersbacher et al, 1988	7/14	26.3 [17-45]	Trauma: 7 T – 3 / P – 4	86	1.86 [1-3]	- [0.5-2]	RS	IV
Robinson et al, 1988	22 / 91	-	Trauma: 22 T – 7 / P – 15	91	4.5 [1-22]	-	RS	IV
Brindley et al, 1990	50 / 76	32.08 [57-19][a]	Trauma: 48 T – 10 / P – 38 MS: 2	77.08	-	- [5-11]	RS	IV
MacDonagh et al, 1990	12 / 75	-	Trauma: 12 T – 2 / P – 10	100	> 2	2.2 [0.25-6]	PS	III
Sauerwein et al, 1990	12 / 50	36 [24-52][a]	Trauma: 12 T – 1 / P – 11	83.3	9 [1-27]	1.31 [2.5-0.08]	RS	IV
Barat et al, 1993	9 / -	-	-	-	-	-	RS – SC	V
Egon et al, 1993	30/ 70	-	-	-	-	-	RS – SC	V
Madersbacher et al, 1993	30 / 27	-	Trauma: 30 T – 10 / P – 20	97	-	< 8	RS	V
Sarrias et al, 1993	7 / 14.3	-	Trauma: 7 T – 3 / P – 4	-	-	-	RS – SC	V
Brindley, 1994 and Brindley, 1995	500 / 54.2	-	Trauma: 378 T – 122 / P – 256 Unspecified : 98	85.5	-	4.07 [0.25-16.1]	RS	III
Van kerrebroeck et al, 1996	52 / 55.8	32.9 [16-57][a]	Trauma: 52 T – 11 / P – 41	100	6.25 [0.75-22.5]	3.2 [0.25-6.33]	RS	IV
Van kerrebroeck et al, 1997 and Wielink et al, 1997	52 / 78.85	28.5 [16-54][ab]	Trauma: 52 T – 11 / P – 41	100	6.4 [0.75-24.8]	1.14	PS	III
Egon et al, 1998	96/ 73.1	38.9 [23-66][a]	Trauma: 96 T – 41 / P – 55	82.3	6.67 [1-21]	5.52 [0.5-14]	RS	IV
Schurch et al, 1998	10 / 30	28.7 [18-42][a]	Trauma: 10 T – 5 / P – 5	90	5.23 [1.2-16.7]	3.8 [1.92-6.03]	RS	III
Van der Aa et al, 1999	38 / 86.8	35.03 [18-59][a]	Trauma: 38 T – 9 / P – 29	100	6.95 [1-39]	- [0.25-12]	RS	III
Bauchet et al, 2001	20 / 30	34 [17-53][a]	Trauma: 20 T – 6 / P – 14	100	6,25 [1.25-23.83]	4.5 [1-8.5]	RS	III
Creasey et al, 2001	23 / 70	40 [14-67][a]	Trauma: 23 T – 6 / P – 17	100	7 [2-26]	> 1 year but some results are missing	PS	III
Kirkham et al, 2002	5 / 100	37.2 [32-46][a]	Trauma: 5 P – 5	100	8.4	-	RA	IV
Sauerwein et al, 2003	427 / 33	34[a]	Unspecified: 427	-	-	6.2	RS – SC	V
Vastenholt et al, 2003	37 / 86.52	43	Trauma: 47	100	7.25	7.1	CSS	II

		[23-63][b]	T – 14 / P – 23		[0.9-39.25]	[1.3-13.25]		
Hamel et al, 2004	4/100	-	Unspecified: 4 T – 1 / P – 3	100	-	- [0.5-1.75]	RS	IV
Soni et al, 2004	1 / 100	46[a°]	-	100	17	8	CR	V
Kutzenberger et al, 2005	464 / 31	-	Unspecified: 464 P – 464	-	-	6.6 [0.5-17]	RS – SC	IV
Kutzenberger, 2007	464/53	33 [14-67][a]	Trauma: 436 Other specified causes: 28 T – 190 / P – 274	75	[0.5-46]	8.6 [1.5-18]	RS	IV
Vaidyanathan et al, 2009	1/100	23	Trauma: 1 T – 1	100	3	13	CR	V
Pannek et al, 2010	1 / 100	53 [a°]	Trauma: 1 P – 1	100	34 - rhizotomy only	0.25	CR	V
Martens et al, 2011	Group #1 -Brindley 46 / 78	48 [33-67][b]	Unspecified: 46	-	8	13 [1-19]	CSS	II
	Group #2 -Rhizotomy 27 / 81	47 [26-66][b]	Unspecified: 27	-	5	14 [3-21]		
	Group #3 - Control 28 / 79	42 [20-75][b]	Unspecified: 28	100	NA	NA		
Sanders et al, 2011	66 / 89.4	50.6 (sd :1.9)[b]	Trauma: 66 T – 38 / P – 28	31.6	NA	NA	RA	IV
De Heredia et al, 2012	18 / 66.6	First MRI: 46 [24-69]	Unspecified: 18 T – 2 / P – 16	-	7 [1-18]	0.5 years after MRI exam	RS	IV
Krasmik et al, 2014	137 / 59.1	40 (sd: 12.4)[a]	Trauma: 137 T – 53 / P – 84	96.35	11.6 (sd: 10.2)	14.8 (sd: 5.3)	RS	III
Bramall et al, 2016	1/100	36	Trauma: 1 P – 1	100	14	26	CR	V
Castano-Boreto et al, 2016	104 / 91.3	38 (sd:10)[a]	Trauma: 103 Unspecified: 1 T – 34 / P – 70	92.3	6.5 (sd: 4.9)	-	RS	III
Krebs et al, 2016	111/53	-	Unspecified: T – 39 / P – 72	-	8.6	11.7 [5-24.9]	RS	IV
Rasmussen et al, 2015 and Zaer et al, 2018	587/57	34.9	Trauma: 561 Other specified causes: 26 T – 266 / P – 321	84.5	8.9 [0-49]	14.6 [1-25]	CSS	III
Ramos et al, 2020	16/81	43 [31-59][a]	Unspecified: 16 T – 8 / P – 8	-	-	4.4	RS-SC	V

[a] is the age at time of implantation, [b]corresponds to the age at interview completion and ° are absolute values instead of mean values. [] corresponds to data range. (sd) corresponds to data standard deviation. RS: Retrospective Study, PS: Prospective study, SC: Short Communication, CR: Case Report, CSS: Cross-sectional study, RA: Research Article. NA: Not Applicable.

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Supplementary Tab.2 – Benefits for visceral functions (all studies)

Author	Use of SARS for micturition (%)	Bladder capacity (ml)		Residual urine (ml)		Incontinent episodes (%)		Urinary tract infections		Autonomic dysreflexia (%)		Use for defecation (%)	Use for erection (%)
		Before	After	Before	After	Before	After	Before	After	Before	After		
Madersbacher et al, 1988 (n=7)	100	209 [80-350]	350< [350-500<]	130 [50-200]	27 [10-40]	-	-	-	0	-	-	29	100 (1/1 male)
Robinson et al, 1988 (n=22)	73	-	-	-	-	-	32	-	-	-	-	-	30 (6/20 males)
Brindley et al, 1990 (n=48)[a]	85.4	-	-	-	-	-	44 (SARS users)	-	29.2% (SARS users)	-	-	56.2	43.2 (16/37 males)
MacDonagh et al, 1990 (n=12)	100	-	-	-	-	-	-	-	-	-	-	50 (SARS alone)	-
Sauerwein et al, 1990 (n=12)	75	-	565	-	<50 in 75% of patients	75	25	-	-	-	-	-	-
Egon et al, 1993 (n=30)	90	-	-	-	<50 in 83% of patients	-	-	-	-	-	-	-	-
Madersbacher et al, 1993 (n=30)	90	-	-	-	<50	100	7	-	-	-	-	-	-
Sarrias et al, 1993 (n=7)	100	-	>400 in all patients	-	<50 in all patients	-	0	-	-	-	-	100	100 (1 male patient)
Brindley, 1994 and Brindley, 1995 (n=479)[a]	86.2	-	-	-	-	-	-	-	-	-	-	-	-
Van kerrebroeck et al, 1996 (n=47)[a]	87.2	-	590 (sd: 104) [374-792]	-	<50 in all patients	-	8.5	4.2 per year [2-12]	1.4 per year [0-2]	15.9	4.25	36.2	62 (18/29 males)
Van kerrebroeck et al, 1997 and Wielink et al, 1997 (n=52)	100	285.4 [20-780]	571.2 [260-806]	104.7 [0-600]	45.6 [0-600] at one year (n=31)	90 (daytime) 96 (night)	21 (daytime) 12 (night) at one year	92% 1.94 per year [0-15]	27% 0.31 at one year [0-3]	13.5	5.8	Clear benefit mentioned for 2/3 of the patients	78 (32/41 males)
Egon et al, 1998 (n=93)[a]	89.3	206	564	-	-	98.6	11.8	100	29	22.9	0	54.8	70.8 (46/65)
Schurch et al, 1998 (n=10)	100	160 (sd: 82)	>500 in all cases	157 (sd: 138)	16 (sd: 22)	100	-	80%	60%	80	80	-	-
Van der Aa et al, 1999 (n=37)[a]	91.9	>400 in 24% of patients (9/37)	>400 in 94.6% of patients (35/37)	>60 in 78.8%	<60 in 73%	-	16.2	-	-	-	-	73	87.9 (29/33 males)

Bauchet et al, 2001 (n=19)[a]	89.5	190 [40-600]	460 [350-800]	90 [0-500]	25 [0-90]	100	10.5	100	-	15.8	0	42.1	0 (0/6 males)
Creasey et al, 2001 (n=21)[a]	78	256,9	>401	159.6	85.7	82.6	64.8 (11/17)	100 %	78.3%	34.8	8.7	61 (systematic use)	-
Sauerwein et al, 2003 (n=427)	98	-	-	-	-	-	-	6.4 per year	1.2 per year	-	-	95	-
Vastenholt et al, 2003 (n=37)	87	-	-	-	-	-	43 (daytime) 30 % (night)	98%	59%	-	-	60 - clear benefit in stool evacuation	62.5 (20/32 males)
Hamel et al, 2004 (n=4)	100	-	>400 in all patients	-	<50 in all patients	-	25	-	-	-	-	50	75 but not used (3/4 males)
Kutzenberger et al, 2005 (n=464)	90.5	173	470	-	-	-	17	6.3 per year	1.2 per year	40.3	0.4	86.4	-
Kutzenberger, 2007 (n= 440)	95.4	173	476	-	-	-	17	6.3/year	1.2/year	-	0.4	91	-
Krasmik et al, 2014 (n=137)	78.1	272 (sd: 143)	475 (sd: 83)	-	96 (sd: 177)	60.9	38.3	88.3% 6.2 per year (sd: 4.5)	51.1% 2.5 per year (sd: 2.6)	61.3	2.2	-	-
Castano-Boreto et al, 2016 (n=104)	91	-	362 (sd : 108)	-	<50	100	14.4	91%	15%	66.3	5.8	88	64.2 (61/95 males)
Rasmussen et al, 2015 and Zaer et al, 2018 (n=333/287)	86.2	-	-	-	-	86	52	-	-	-	-	73	-
Ramos et al, 2020 (n=16)	87.5	-	-	-	<50 in all patients	-	-	-	37.5 (SARS users)	-	-	94	85 (11/13 males)

[a]Number of patients that completed the follow-up period (when different from the total number of patients involved in the initial study -> Figures related to bladder functions were then computed based on this number)

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Supplementary Tab.3 – Implantation procedure and reliability axis (all studies)

Author	Deafferentation and Implantation procedure	Complications following surgery	Implant failures	Impact on patients everyday life and long term side effects	Additional information
Robinson et al, 1988 (n=22)	-	Neuropraxia (n=1)	-	- Patient with pelvic pain awaiting for rhizotomy (n=1) - Somatic muscle spasms (n=1, preventing implant-driven micturition) - Muscle spasms when using SARS implant for erection (n=6 -> Implant never used for sexual purposes) - Sphincterotomy proposed (n=4 -> two refused and did not use the implant) - Hydronephrosis pre-implantation (n=4): * Resolved in two cases * One patient relapsed * Grade IV reflux with urgent sphincterotomy in one patients	-
Brindley et al, 1990 (n=48)	-	-	- 37.5% of patients reported implant failures --> 25 failures in total - Receiver block failure (n=7) - New implantation due to cable break (n=1) - Cable break (n=5) - Connector failures (n=12)	- 17% of users noted increased spasms - Backache (n=2) - Stimulus pain (n=1) - Pain leading patient to stop implant use (n=2) - Increased sweating (n=6) - Occasional headache (n=1) - Occasional autonomic dysreflexia (n=1) - Loss of reflex erections (n=8) - Increased constipation (n=4)	-
MacDonagh et al, 1990 (n=12)	Intradural implantation in all cases and S2-S4 rhizotomy in 75% of patients	- Suspicion of anterior roots damage (n=2) - Cerebrospinal fluid leakage (n=2)	-	-	- No reports of constipation in any patients Benefit: - Reduced time for bowel evacuation in any patient
Sauerwein et al, 1990 (n=12)	Initially: -Intradural implantation without rhizotomy (16.7% of patients) -> Implants replaced by extradural devices with extradural rhizotomy Finally: -Extradural implant and extradural rhizotomy in all patients	- Cerebrospinal fluid leakage (n=1) - Root damage in all patients (n=12) - Incomplete deafferentation (n=2 and one more is suspected).	-	-	-

Barat et al, 1993 (n=9)	Deafferentation in all patients but 3 incomplete procedure (without S2 or S4 cutting)	-	-	- Stress incontinence (n=3) - Reflex incontinence (n=3) - Mixed incontinence (n=2) - Second deafferentation needed in 3 patients (spread to S1 in two cases)	Benefit: - 3 patients recovered continence
Egon et al, 1993 (n=30)	-	- Major denervation -> Nearly complete bladder denervation (n=2, maximal recovery after 1 year) - Neuropraxia (n=1) -> Recovery after few months (n=1) - Partial denervation (n=5, with good results few months post-implantation)	-	- Secondary loss of bladder contractions (n=3)	-
Madersbacher et al, 1993 (n=30)	SARS implantation and deafferentation of roots for whom anterior component induced detrusor contractions – in first patients – then extension to all sacral posterior roots with better results. 27 intradural implant and 4 extradural implantation	Suspicion of Wallerian degeneration in one patient for whom electromicturition was impossible at the time of the study	-	- Second deafferentation (n=5) -> successful procedure for 4 of them	- Severe autonomic dysreflexia disappeared in on patient - Statement claiming that SARS procedure improved all patients Quality of life as well as no patient has regretted the operation
Sarrias et al, 1993 (n=7)	Extradural implantation and deafferentation at the conus medullaris in all patients	The receiver block was placed too low in patient abdominal wall and one of the device corners broke through one of the skin creases (n=1) -> It was replaced higher up and cause no further trouble	-	-	Benefit: - Patient satisfaction - one patient with upper urinary tract dilatation showed improvement after 6 months of implant-driven micturition.
Brindley, 1994 and Brindley, 1995 (n=479)	- Implantation: * 88.2 % intradural * 4.6% Extradural * 7.2% Unknown - Rhizotomy: * 73.6% Rhizotomy * 10.4% No rhizotomy * 16% Unknown	- Infection following surgery and device explantation (n=3)	- Implant failures in 72 of the 500 first patients * 56 repairs + 21 second failures ▪ 9 replaced ▪ 12 repaired + 3 third failures ▪ 1 replaced ▪ 2 repaired * 9 replaced by a new stimulator with extradural electrodes + 2 failures ▪ 2 repaired * 5 Implant needed no repair since implant-driven micturition remained good	- Infection and explantation during follow-up (n=1) - Exposition of the receiver block (n=5) - 95 surgery performed to remedy faults in implant: * 75 repair procedures (cables, receiver block) -> These operations were followed by infections in two cases. * 20 implantations of a new device -> followed by infection and explantation in one case. - Death due to renal failure (n=1) - Deterioration of the upper urinary tract (n=11) -> Including one patient deceased from carcinomatosis, primary in the bladder - Second deafferentation (n=39) - Spinal roots deterioration during follow up (n=8)	-

			* 2 waiting to be repaired - Total number of failures = 98 * 18 receiver failures * 18 connector failures * 3 cable fractures * 42 cables outside their receiver blocks * 17 Unknown	- Failures of implant driven micturition due to overstretching of bladder wall (n=5) -> recovery in all cases.	
Van kerrebroeck et al, 1996 (n=47)	Intradural implantation and posterior rhizotomy in all cases	- Cerebrospinal fluid leakage (n=2) - Wound infection (n=1) - Nerve damage (n=2) * 1 permanent * 1 recovered	-No implant failure (only mention of minor problems with the external control boxes)	- Spasticity return to preoperative levels - Second deafferentation (n=3) - Implant infection (n=1) -> Replacement of the intradural implant by an extradural one - AHR induced by stimulation (n=2) - Strong lower limbs contraction s during stimulation-induced erection (n=12) - Intrathecal baclofen pump (n=2)	Benefits: - Upper urinary tract dilatation solved in 2 patients - Creatinine clearance returned to normal values after implantation (n=32) - Preoperative vesicoureteral reflux was reduced (n=1) or disappeared (n=1) - No interference between SARS and baclofen pump
Van kerrebroeck et al, 1997 and Wielink et al, 1997 (n=52)	Intradural implantation and intradural sacral posterior root rhizotomy (S2, S3 and S4)	- Difficulties to split anterior and posterior roots (n=3) -> Persistent reflex post-operatively needed second deafferentation - Persistent neuropraxia (n=1, resolved at 18 months) - Cerebrospinal fluid leakage (n=2)	- Minor problems with the external control box are mentioned - Cable fracture (n=1, 18 months after surgery)	-	Benefits: - Upper urinary tract dilatation solved in 2 patients (6 weeks after rhizotomy) - Vesicoureteral reflux observed in 6 ureters in 4 patients improved in all cases
Egon et al, 1998 (n=93)	- 90.7% Intradural implantation	- Cerebrospinal fluid leakage (n=3) - Nearly complete denervation (n=5, intradural implantation, stimulator could be use after recovery in 3 patients)	- Receivers failure (n=5, all were replaced) - Cable failures (n=4)	- Transitory spasticity was mentioned but not quantitatively documented. In some cases, ablation of S1 and L5 posterior roots to abolish triceps surae spasticity - Infection leading to implant removal (n=2) - Second deafferentation in 4.3% of patients due to persistent detrusor reflex activity. - Deterioration of detrusor responses (n=5) - Persistent sphincter dyssynergia (n=3, patient refused sphincterotomy or conus deafferentation) - Persistent Wallerian degeneration (n=1) - Second sphincterotomy (n=4, all continent) - Renal problems leaded to nephrotomy (n=1)	Benefit: - Preoperative vesicoureteral reflux disappeared (n=3)
Schurch et al, 1998 (n=10)	Intradural implantation and sacral deafferentation in all cases	- Surgical incomplete deafferentation (n=4)	-	- AHR persisted and occurred during implant-driven voiding despite complete sacral deafferentation (n=8 and unknown condition in 1 patient)	- DSD resolved in all cases - No lower limb or trunk contraction during stimulation in all patients.
Van der Aa et al, 1999	Intradural sacral posterior rhizotomy (S2-S5) and		-Receiver block failure (n=3)		

(n=37)*	intradural SARS implantation in all patients				
Bauchet et al 2001 (n=19)	Intradural implantation and S2/S3 rhizotomy with S4/S5 roots crushing in all cases	- Cerebrospinal fluid leak (n=2) - Discomfort at the subcutaneous receptor (subsequently displaced, n=2)	- Extradural implantation due to intradural electrode failure (n=1) - Replacement of receiver block (n=1) - Cable disconnection (n=4) - Charger failure (n=3)	- Bladder fibrosis (n=1) - Pyelonephritis (n=1)	One woman cannot use her implant at work because of inappropriate toilets
Creasey et al, 2001 (n=23)	Extradural implantation and intradural rhizotomy S2-S5 in all cases	- Temporary nerve damage (n=2, recovery within 3 months)	-	- Increased lower limb spasticity (n=2) - Incomplete rhizotomy with second deafferentation (n=1) - Increase in incontinence episodes (n=4) - Fracture of the second lumbar vertebra 5 months after surgery which caused compression of the cauda equina (n=1)	Benefit: - Reduced time for bowel evacuation
Sauerwein et al, 2003 (n=427)	-	-	-	-	- Bladder spasticity stopped in 97% of all cases. - Recovery of kidney function is mentioned
Vastenholt et al, 2003 (n=37)	-	- Cerebrospinal fluid leakage (n=1) - Neuropraxie (n=1) - Detrusor weakness (n=4) Problems solved several years after surgery	-External equipment (One failure per 17 and per 38 user-years, n=23) * Cable fracture (n=16) * Transmitter defects (n=7) - Internal equipment (One per 66 user-years, n=4 in total). * 3 receiver replacements	- Strong motor responses to stimulation (n=1) - Fibrosis around sacral roots (n=2) - Root failures (n=1, but deafferentation enable complete continence) - Detrusor weakness (n=2) - Sphincter weakness (n=1)	-Erection never used for sexual intercourse
Hamel et al, 2004	Intradural rhizotomy and extradural implantation	- Cerebrospinal fluid leakage spontaneously resolved (n=1)	-	-	-
Kutzenberger et al, 2005 (n=464)	Deafferentation performed in all surgery with a success rate of 94.1%	- Cerebrospinal fluid leak (n=6) - Infection of the implant (n=5) - Dehiscent wound (n=2) - Hemorrhages (n=2, requiring no further treatment)	- 70 Implant defects -> 34 repair surgery were necessary * 16 Receiver exchange and cable repair * 5 Cable repair alone * 9 Extradural implant	- Second deafferentation (n=8 to interrupt dysreflexia) - Bladder overdistension and neurogenic failures are mentioned but not quantitatively documented.	-
Kutzenberger et al, 2007 (n=440)	Intradural deafferentation and implantation. Rhizotomy performed in all surgery with a success rate of 95.2%	- Cerebrospinal fluid leak (n=6) - Infection of the implant (n=5) with further reimplantation in 4 cases - Dehiscent wound (n=2) - Hemorrhages (n=2, requiring no further treatment)	- 81 Implant defects -> 44 repair surgery were necessary * 26 Receiver exchange and cable repair * 6 Cable repair alone * 12 Extradural implant with 1 further withdrawal due to an infection	- Second deafferentation (n=8 at conus terminlis to interrupt dysreflexia) - Bladder overdistension and neurogenic failures are mentioned but not quantitatively documented.	-

Krasmik et al, 2014 (n=137)	Intradural implantation and deafferentation S2 to S5 in all cases	- Cerebrospinal fluid leakage (n=8) - Infection (n=3)	- Defect of cables (n=19) - Defect of stimulation plate (n=19) - Dislocation of the stimulator plate (n=16) - Undetermined cause of stimulator failure (n=15)	-Incomplete rhizotomy with second deafferentation at the conus medullaris (n=4) - Additional urological interventions in 43 patients * 22 Outlet obstruction * 10 Vesicoureteral reflux * 10 Incontinence * 9 Urethral strictures - Problems with condom fixation (n=3)	In 54 patients, a total of 83 surgical revisions were performed (17 patients underwent more than one revision)
Castano-Boreto et al, 2016 (n=104)	Extradural implantation and posterior rhizotomy of S2-S5 sacral roots in all cases	-	- Failure of the receiver block (n=1)	- Infections few months after implantation (n=2) - Cable extrusion (n=2) - Extrusion of the receiver block (n=2)	-
Ramos et al, 2020 (n=16)	SARS implantation and deafferentation S2 to S4 in all cases	Neuropraxia with spontaneous resolution after 12 months (n=2)	- Malfunction/damage of the external hardware mostly due to operator misuse (n=10)	- Extrusion of the receiver block (n=2)	- 85% of patient obtained stimulation-induced erections but only 2 use SARS (6 patients sexually active before SARS procedure – 4 using a penile prosthesis)

- : Not Documented.

Guiho T, Azevedo-Coste C, Bauchet L, Delleci C, Vignes JR, Guiraud, D, Fattal C. Forty Sacral Anterior Root Stimulation and visceral function outcomes in spinal cord injury – A systematic review of the literature over four decades, World Neurosurgery, 2021.

Supplementary Tab.4 – Multicentric studies

Study and patients characteristics

Authors	Number of patients / % of male patient	Mean age in years (*)	Lesion profile T – Tetraplegia P – Paraplegia	% of complete SCI	Mean age of the lesion at the time of implantation (in years)	Patients follow up after implantation (in years)	Study type	Level of evidence
Sauerwein et al, 1990	12 / 50	36 [24-52][a]	Trauma: 12 T – 1 / P – 11	83.3	9 [1-27]	1.31 [2.5-0.08]	RS	IV
Brindley et al, 1990	50 / 76	32.08 [57-19][a]	Trauma: 48 T – 10 / P – 38 MS: 2	77.08	-	- [5-11]	RS	IV
Brindley, 1994 and Brindley, 1995	500 / 54.2	-	Trauma: 378 T – 122 / P – 256 Unspecified : 98	85.5	-	4.07 [0.25-16.1]	RS	III

Benefits on visceral functions

Author	Use of SARS for micturition (%)	Bladder volume (ml)		Residual urine (ml)		Incontinent episodes (%)		Urinary tract infections		Autonomic dysreflexia (%)		Use for defecation (%)	Use for erection (%)
		Before	After	Before	After	Before	After	Before	After	Before	After		
Sauerwein et al, 1990 (n=12)	75	-	565	-	<50 in 75% of patients	75	25	-	-	-	-	-	-
Brindley et al, 1990 (n=48)[a]	85.4	-	-	-	-	-	44 (SARS users)	-	29.2% (SARS users)	-	-	56.2	43.2 (16/37 males)
Brindley, 1994 and Brindley, 1995 (n=479)[a]	86.2	-	-	-	-	-	-	-	-	-	-	-	-

Implantation procedure and reliability axis

Author	Deafferentation and Implantation procedure	Complications following surgery	Implant failures	Impact on patients everyday life and long term side effects	Additional information
Sauerwein et al, 1990 (n=12)	Initially: -Intradural implantation without rhizotomy (16.7% of patients) ->	- Cerebrospinal fluid leakage (n=1)	-	-	-

	Implants replaced by extradural devices with extradural rhizotomy Finally: -Extradural implant and extradural rhizotomy in all patients	- Root damage in all patients (n=12) - Incomplete deafferentation (n=2 and one more is suspected).			
Brindley et al, 1990 (n=48)	-	-	- 37.5% of patients reported implant failures --> 25 failures in total - Receiver block failure (n=7) - New implantation due to cable break (n=1) - Cable break (n=5) - Connector failures (n=12)	- 17% of users noted increased spasms - Backache (n=2) - Stimulus pain (n=1) and pain leading to stop implant use (n=2) - Increased sweating (n=6) - Occasional headache (n=1) - Occasional autonomic dysreflexia (n=1) - Loss of reflex erections (n=8) and Increased constipation (n=4)	-
Brindley, 1994 and Brindley, 1995 (n=479)	- Implantation: * 88.2 % intradural * 4.6% Extradural * 7.2% Unknown - Rhizotomy: * 73.6% Rhizotomy * 10.4% No rhizotomy * 16% Unknown	- Infection following surgery and device explantation (n=3)	- Implant failures in 72 of the 500 first patients * 56 repairs -> 21 second failures ▪ 9 replaced and 12 repaired -> 3 third failures ▪ 1 replaced ▪ 2 repaired * 9 replaced by a new stimulator with extradural electrodes -> 2 failures ▪ 2 repaired * 5 Implant needed no repair since implant-driven micturition remained good * 2 waiting to be repaired - Total number of failures = 98 * 18 receiver failures * 18 connector failures * 3 cable fractures * 42 cables outside their receiver blocks * 17 Unknown	- Infection and explantation during follow-up (n=1) - Exposition of the receiver block (n=5) - 95 surgery performed to remedy faults in implant: * 75 repair procedures (cables, receiver block) -> 2 infections * 20 implantations of a new device -> 1 infection and explantation - Death due to renal failure (n=1) - Deterioration of the upper urinary tract (n=11) -> Including one death from carcinomatosis, primary in the bladder - Second deafferentation (n=39) - Spinal roots deterioration during follow up (n=8) - Failures of implant driven micturition due to overstretching of bladder wall (n=5) -> recovery in all cases.	-