The Aarhus Neuromodulation Database

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Objectives: Spinal cord stimulation (SCS) is increasingly gaining widespread use as a treatment for chronic pain. A widely used electronic registry could play a pivotal role in improving this complex and cost-intensive treatment. We aimed to construct a comprehensive, universally available data base for SCS.

Materials and Methods: The design considerations behind a new online data base for SCS are presented; basic structure, technical issues, research applications, and future perspectives are described.

Results: The Aarhus Neuromodulation Database covers core SCS treatment parameters, including procedure-related details and complications, and features recording of key success parameters such as pain intensity, work status, and quality of life. It combines easy access to patient information with exhaustive data extraction options, and it can readily be adapted and expanded to suit different needs, including other neuromodulation treatment modalities.

Conclusions: We believe that the data base described in this article offers a powerful and versatile data collection tool suited for both clinicians and researchers in the field. The basic data base structure is immediately available on a no-cost basis, and we invite our colleagues to make use of the data base as part of the efforts to further the field of neuromodulation.

Keywords: Data base, electrical stimulation therapy, neuromodulation, registry, spinal cord stimulation

Conflict of Interest: Dr. Meier and Prof. Sørensen have received lecture fees from St. Jude Medical. Morten Flink is the proprietor of ITmedico. Ronnie Simonsen is an employee of ITmedico.

INTRODUCTION

Spinal cord stimulation (SCS) has been used to treat neuropathic pain for more than 40 years (1), and an increasing number of patients with different pain conditions are offered this type of treatment. In 2007, it was estimated that about 30,000 patients had received an SCS device that year in the United States alone (2). Despite its widespread use, there is surprisingly sparse information on the clinical parameters and mechanisms of SCS (3–5). One reason for this may be the lack of systematic access to data. A data base on SCS is an evident way to collect systematic information and to follow outcome. A few papers have referred to the existence of local or regional data bases, most prominently in Italy (6–8); yet to our knowledge, there is currently no universally accepted data base available for SCS.

A significant number of parameters require registration. Candidates for SCS treatment suffer from complex and chronic pain conditions and are usually thoroughly characterized, often through a combination of clinical observational data and questionnaires. The description of surgical procedures includes specifications of the implanted equipment, possible procedure-related complications, programming data, etc. Finally, extensive and multiple follow-up data are routinely generated both for research purposes and to satisfy requirements from reimbursement regulations.

Based on our experiences with collection and analysis of SCS data, we decided to construct a generic data base for SCS. In this technical note, we present the result of our efforts and a framework for further international collaboration.

METHODS (DATA BASE DESCRIPTION)

This section includes a detailed description of the data base design, including brief explanations of the choices made during the design process (Table 1).

For more information on author guidelines, an explanation of our peer review process, and conflict of interest informed consent policies, please go to http://www.wiley.com/bw/submit.asp?ref=1094-7159&site=1

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Table 1. We Identified Six Essential Criteria for a Generic SCS Data Base.

1. Inclusion of all relevant clinical data about patient demographics, pain conditions, former and current treatments, and indications for SCS.
2. Presentation of data in a fast and easy way.
3. Output in a format that allows for in-depth statistical analysis using commonly available statistical software packages.
4. Universal usability, independent of country, computer platform, preferred SCS equipment provider, and physician specialty.
5. A module-based design, allowing for future expansion and for easy adaptation to changing needs in neuromodulation treatments.

SCS, spinal cord stimulation.

Development Process
A preliminary framework of the data base was created using Microsoft Excel 2007 (Microsoft Corporation, Redmond, WA, USA). A spreadsheet was chosen, as its way of handling and presenting data is analogous to the format used in most statistical software. As part of the process, variables were named and defined; a number of analyses on the resulting data were carried out in Stata/IC 11 (StataCorp, College Station, TX, USA) to test the validity of the structure. The entire data base was then reconstructed using Microsoft Access 2007 to allow testing of the underlying structure in a more user-friendly and flexible data base environment. Input forms were designed to gain experience with data collection, and advice from colleagues inside and outside Denmark was incorporated.

In the final phase, a software company specialized in making clinical data bases (ITmedico, Aarhus, Denmark) was employed to completely reprogram the data base using customized software (ITmedico) written in Microsoft C# based on Microsoft.Net Framework v4. The data base is structured using Microsoft SQL Server 2008.

The data base author (KM) defined the structure on separate spreadsheets for each form detailing all variables and their internal relationship. Variable definitions include name, text label, format, value range, help notes, and descriptions. The variable definitions were supplemented with a total of 47 tables used to construct drop-down menu choices for a range of variables. Forty-three of the drop-down tables are generic for all countries; four tables (projects, implanters, centers, and referrals) can be tailored to the specific needs of other participating centers.

Output
As the data base was constructed with statistical analysis in mind, the output was designed as a row of variables in a universally available format, a comma-separated file (.csv). In the generated output, repeated variables (corresponding variables from different dates, e.g., scores from questionnaires) are supplied with the suffix [x], where x denotes the order in the chronology. Naming of variables adheres to common standards for statistical software (only lower case, no spaces or special characters except the underscore [ ]) to allow maximum compatibility. The complete data output is supplemented with three more manageable outputs listing patient data, procedure data, and project participants.

To allow for fast data entry as well as to ensure the reliability in the subsequent data analysis, we decided to eliminate unintended variation in responses by defining input options for a number of variables. Equipment names, outcome, indications, and complications are examples of variables entered via drop-down lists. Options in drop-down lists are recoded to numerical values in the output to facilitate data analysis (9). Missing data will be assigned a null value, marking them as missing, not 0.

A codebook detailing the various variables will be supplied to users along with the data base structure.

Internal Data Relations
In addition to assigning each patient in the data base a unique identification (ID), we opted to assign separate IDs to all procedures, allowing us to identify all implanted leads and implantable pulse generators (IPGs). This enables exact tracking of all implants, determining both the patient’s current and previous implant configuration. In addition, it allows users to examine the associations between complications, procedure parameters (including implantation, anesthesia, technique, indication, etc.), and equipment.

For choices relating to internal data base relations (e.g., linking a complication to a procedure or linking a complication to a clinical indication), a specially developed dynamic drop-down menu is used to reliably identify the options.

Technical Issues
The data base is constructed to run on all common browser clients based on Windows, Mac OS, or Android. There is no software client to download. Additionally, we chose to keep the interface simple with old monitors and mobile devices such as the Apple iPad, and less chance of losing perspective of things on the screen.

Data Security
The data base is accessed with a personal username and password. The communication between the user and the server is encrypted using minimum 128-bit secure sockets layer encryption. All logins, logouts, and login attempts are permanently logged, as are all access to, change in, or deletion of user data.

The Danish national server is housed in a state-of-the-art data center located in Denmark; all data are encrypted using 128-bit encryption.

Ethical and Legal Issues
The Danish Data Protection Agency approved the purpose and design of the data base. Before registration in the data base, all patients signed a consent form approved by the legal board of Central Denmark Region.

Structure
Centers providing SCS treatment and SCS follow-up employ widely varying assignments of tasks among staff members. Clinical
follow-up, medicine regulation and registration, programming of the IPG, etc., may all be performed by the same health-care provider, or the duties may be divided among several people. We therefore decided to provide separate forms (or work sheets) for various tasks (10); currently, 27 are implemented (Fig. 1).

Two forms (demographic and clinical data) are mandatory and not dated, as they are intended to be open for amendments as new information surfaces or the clinical condition progresses. The clinical data include details of the indications for SCS treatment (including diagnosis, triggering event, and symptom duration for up to four separate indications) and other information such as comorbidities we currently deem likely to be relevant for neurostimulation outcome or its complications. Additionally, one form (project participation) is not dated, as the data contained therein are assumed to be evolving through the course of a project. Unlike the two forms

1 Detailed information on substance abuse, psychiatric disorders, cardiovascular disease, neurologic disorders, and other diseases.
described above, multiple copies of the form may exist; one for each project the patient is registered for.

The remaining 24 forms are potentially recurring events and are thus identified by date. Six types of forms are currently included.

Visit/Examination (Two Forms)
This category includes forms for clinical visits and quantitative sensory testing. The clinical visit form is dynamic and contains questions relevant for preoperative evaluation and follow-up visits, respectively. A work status registration is included.

Registration of Analgesic Medication (One Form)
A text field is supplied for entering use of analgesics. For statistical purposes, an option is included to register regular use of analgesics (yes/no dropdown) in six major classes: opioids, tricyclic antidepressants, other antidepressants, anticonvulsives, nonsteroidal anti-inflammatory drugs, and other analgesics (e.g., dronabinol and ketamine) (11).

Questionnaires (Five Forms)
Questionnaires relating to quality of life, pain qualities and intensity, and psychosocial functioning play a key role in both clinical follow-up and research (12). Currently included items in the data base are Short Form 36 Health Survey v1.1 (13), the Pain Catastrophizing Scale (14), the Major Depression Inventory (15), a Generalized Anxiety Disorder ten-component score (16), EuroQoL-5D (17), and a form designed by the Danish Pain Research Center containing data on pain scores, work status, and patient-perceived treatment effect.

More items will be added regularly; currently, planned inclusions are the EuroQoL-5D, the Brief Pain Inventory, and the McGill Pain Questionnaire. The actual forms are the property of the respective developers and therefore are not included; the data base provides only a registration tool.

Procedure Registration (Eight Forms)
To avoid overly complex registration forms for surgical procedures, we decided to divide the procedures into three categories: Implantation, Revision (i.e., revising an existing implant without replacing it), and Explantation. Each procedure type is then divided into Percutaneous Lead, Surgical Lead, and IPG. Thus, a replacement of a percutaneous test lead with a surgical lead and concurrent implantation of an IPG would result in three forms: Explantation; Percutaneous Lead, Implantation; Surgical Lead, and Implantation; IPG. This system, while apparently cumbersome, breaks down a complicated procedure that may have several separate steps (each with their own possible complications) and an infinite combination of variables into three forms that take about 30–60 sec each to complete, yet gives a full account of each part.

Information registered in the forms includes, but is not limited to, anesthetic technique, and the precise localization of the implant. Leads, IPGs, and anchors from advanced neuromodulation systems (ANS)/St. Jude Medical, Boston Scientific, Medtronic, and Nevro are included; more will be added as new products are marketed.

Programming Registration (One Form)
Programming details vary immensely between patients. Different manufacturers employ different programming systems, the numbers of contacts on various leads may vary from 4 to 20, many patients have two or more leads implanted, and commonly patients are provided with several programs, each with optional stimsets. Due to the overwhelming complexity of programming issues (18–20), we chose to limit the programming registration to a simple text field. Thus, it does not allow for immediate statistical analysis without manual conversion but is instead designed as a tool primarily for managing patient treatment.

Complication Registration (Six Forms)
Registration and management of complications are crucial in both SCS therapy and research (21), and this area forms a core feature of the data base. Complications are identified as related to either the lead or the IPG and then selected from a list of commonly occurring problems. The complication can then be associated with a particular procedure selected from a drop-down list of previous procedures. Thus, all relevant data from the procedure in question will be linked with the complication, enabling detailed analysis of all occurring adverse events and their plausible causes. A sample flow chart is shown in Figure 2.

Features
Two dynamic fields were included to aid in the clinical follow-up of patients.

An upper-left field shows basic data about the patient, including the diagnosis and current treatment status. Data are automatically updated from the relevant forms. The basic data are supplied with a timeline, showing all events registered about the patient. To further increase clarity, various events are marked by different icons. The timeline can be sorted chronologically or by topic (Fig. 3).

Additionally, a separate screen was included, showing current implants (leads and IPGs) as well as latest programming data and medicine registration. Data for the screen are automatically updated from the data entered in the data base (Fig. 4).
Figure 3. Data base screenshot. The upper-left window offers basic information about the patient and his/her current treatment status. The left column is a graphic overview, also serving as a navigation frame for access to previous forms (click on an item to bring up the contents for viewing or editing). The timeline also can be sorted by category by removing the tick in the Sort Chronologically option. The main screen frame to the right is the primary input window. Dropdowns are used extensively to improve the speed and reliability of input.
DISCUSSION

Purpose of the Data Base
The purpose of the data base was to create a generic tool for researchers and healthcare providers working with SCS to collect systematic information about SCS. The authors of this paper represent three medical specialties commonly involved in SCS treatment (neurosurgery, anesthesiology, and neurology), as well as expertise in epidemiologic research and database construction. It is our view that the design of the data base reflects our multidisciplinary approach to registration of SCS treatment data. The data base designer (KM) is involved in SCS implanting, follow-up, and research, and the data base is constructed in such a way that it can be used for both clinical and research purposes.

Clinical Aspects
The quick-info box, the graphic representation of events (timeline), and the auto-updated overview of the current implant configuration, programming data, and used medicine together constitute the at-a-glance information we find most important to have available in our own clinical work. Additionally, the quickly accessed, chronologically sorted forms describing interventional procedures, complications, and detailed clinical data provide a concise distillate of relevant information.

The challenge was to strike the balance between registering all important information, yet not overburden users. If the users find the forms too detailed in a busy clinical setting, it is perfectly possible to skip sections or questions. Those data will be marked as missing in the output. Also, the module-based design allows users to employ the data base as a purely clinical tool, completely omitting more research-oriented options like questionnaires.

Research Aspects
Our ambition was to create a data collection tool powerful enough to aid in clarifying many of the general issues raised in relation to SCS treatment. Some of the questions we asked ourselves were the following:

- Is a trial stimulation a better tool in predicting long-term result than a thorough clinical screening?
- What is the cost-benefit ratio of SCS when work status and medicine expenses are included in a mixed patient population in different countries?
- Are certain anchors better at preventing lead migration than others?
- Should perioperative antibiotic coverage be mandatory?
- Is the patient’s level of preoperative expectations predictive of the long-term result?
- Is lumbar epidural access safe for implanting a cervical lead?
- Does symptom duration predict outcome in different indications?

We believe that the registry presented in this paper can give important information, allowing our community to suggest answers to not only these questions but numerous others as well. The crucial factor in achieving this aim will, obviously, still be our ability to provide enough data of a sufficiently high quality.

Figure 4. Hardware configuration overview, a separate screen designed to give at-a-glance view of core treatment data. All fields are automatically updated from the latest existing patient data in the data base.
International Collaboration
To fully unleash the potential in a systematic data analyzing tool, data should ideally be gathered from multiple centers. This is both advantageous not only due to the accumulated bulk of data but also because different approaches to treatment and follow-up regimens may reveal information not so readily obtained by a strictly national analysis. From the initial construction phase, the data base was intended for international collaboration, which gave rise to certain design considerations.

Flexibility
We knew that there would be considerable differences between centers not only in the surgical setup but also in the assignment of tasks to staff members, documentation traditions, follow-up setting and demands, etc. Thus, we chose to prioritize flexibility first and foremost. The disadvantage is clearly that the inconsistency in follow-up methods between centers will be directly reflected in the data base content. Conversely, we reckon that the opportunity to keep established work routines might encourage potential users of the data base to participate; thus, the added number of patients in the base would compensate for the diversity.

Legal and Technical Issues
We identified three potential obstacles for the formation of an international collaboration: confidence, economy, and legislative issues.
Confidence is both about trusting that data are kept safe and at the same time being confident that no one has unauthorized access to sensitive patient information or valuable research data.
Economy is the question if startup or running expenses will prohibit participation.
Finally, local or national data protection agencies or other regulations may constitute legal issues that are complex and often inscrutable for outsiders.
It is our view that the most obvious solution was to make the data base freely available, enabling collaborating countries, regions, or societies to host their own server, include their own users, and issue their own passwords. This shifts core responsibilities, like obtaining various official permissions, from developer to user; however, at the same time, it serves to overcome the obstacles outlined above. The fundamental data base structure will be locked to ensure consistency of variables. Updates and additions to the data base will be implemented globally to ensure continued data integrity. Depending on agreement, data can readily be merged, allowing collaborators to establish research networks across borders.

Data Reliability
The quality of data analysis depends on the quality of data registration. There is no way to prevent users from entering misleading data on purpose or by mistake (e.g., fail to register complications or tamper with follow-up feedback), but that issue is common to all public registries and not specific for neuromodulation. Users of the data base are free to form research collaborations with whomever they prefer, thus circumventing issues with data suspected of low quality.
We did attempt to avoid unintended interuser variation and errors in data entering. Wherever possible, variable outcomes are defined by drop-down menus (either a conventional dropdown or the specially tailored dynamic dropdown described in the Structure section), making them unequivocal. If a variable cannot meaningfully be defined by a drop-down menu, input is defined as narrowly as possible by validation rules and input masks (e.g., a certain variable may only be an integer between one and four).

More than 100 patients have been entered in the Danish data base with a combination of prospective and retrospective data without giving rise to more than minor adjustments of the structure. Furthermore, as all activity in the data base is logged on individual user level, administrators can trace all additions and modifications to existing patient data, making it possible to resolve possible disputes on validity.

FUTURE PLAN AND PERSPECTIVES
The following issues are planned for inclusion in 2012.

Generic Neuromodulation Data Base
The current version of the data base includes only SCS therapy for chronic pain. However, the structure is designed for seamless inclusion of other neuromodulation modalities and other indications. These upgrades to the data base will be merged with the current structure, ensuring consistency of use, continuity in patient treatment and registration, and conservation of existing user data.

Tailored Data Base Output
Data base output consists of a string of all variables, allowing for very detailed in-depth statistical analysis. This does, however, require statistical knowledge and software. In addition to the three existing supplementary outputs (patients, procedures, and projects), more user-friendly output formats are in the pipeline, enabling the user to create a graphic representation of treatment results, a customized graph depicting selected questionnaire scores and including important events.
Also planned is direct support of more output formats (Stata, SPSS, Statistica, SAS, and Excel) for added functionality.

The following issues are planned for inclusion in 2012.
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Graphic design: Axel Gruhn, Nuidag, Denmark.
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Intellectual contribution: Søren Paaske Johnsen, MD, PhD, Department of Clinical Epidemiology, Aarhus University Hospital, Denmark; Kari Mikael Sulikko, MD, Department of Neurosurgery, Seinäjoki Central Hospital, Finland; Philippe Mavrocordatos, MD, Clinique Cecil Lausanne, Switzerland; Thomas Peter Enggaard, MD, PhD, Department of Anesthesiology, Odense University Hospital, Denmark.

Authorship Statements

KM designed the data base and prepared the first draft of the manuscript. JCS, LN, and TSJ provided continual advice during the data base construction and revised the manuscript. MF and RS programmed the data base and contributed to the structural design. IM designed the data base output format.

All authors contributed to and approved the final manuscript.

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REFERENCES