Department of Neurosurgery, University Hospital Münster

Department of Neurosurgery, University of Leiden

Multicenter trial on surgical outcome and quality of life in juxta-medullary tumors

Study Protocol

Coordinating Investigator:

PD Dr. med. Michael Schwake

Klinik für Neurochirurgie

Universitätsklinikum Münster

Albert-Schweitzer-Campus 1, Geb. A1

48189 Münster, Germany

Version 2.4

7.3.2025

Table of Contents

1. Synopsis

	Synopsis
Coordinating investigator	PD Dr. Michael Schwake, Klinik für Neurochirurgie, Universitätsklinikum Münster, Albert-Schweitzer-Campus 1, Geb. A1, 48149 Münster, Germany
Investigators	Michael Schwake, MD
Title	Multi-center-registry trial on surgical outcome and quality of life in juxta-medullary tumors
Indication	Adult patients operated on juxta-medullary tumors
Study objectives	**Primary objectives:** Primary objectives are to assess and define benchmarks of the surgical outcome in the form of extent of resection, functionality, and quality of life after resection of juxta medullary tumors **Secondary objectives:** Assessment of variables leading to better outcome through regression analysis: 1. Influence of surgical approach on functionality, pain, and quality of life 2. Comparison between patient with severe neurological (McCormick scale 3-5) to patients with mild deficits (McCormick 1-2) 3. Role of IOM in extent of resection and neurological deficits Assessment of treatment variations: 1. Assessment of risk factors for incomplete resection 2. Non inferiority of unilateral approach to achieve gross total resection of spinal meningioma, schwannoma and cauda ependymoma 3. Role of bed rest after surgery to prevent cerebro-spinal fluid leakage 4. Influence of laminectomy on cerebro-spinal fluid leakage Quality indicators: assessments of length of hospital stay, 30- and 90-days re-admissions, 30- and 90-days re-surgery, nosocomial infections
Inclusion/ Exclusion criteria	**Inclusion criteria** • Adult, age ≥18 years, patients treated on intraspinal, extra medullary tumor • Patients must have sufficient cognitive and language skills to give informed consent

	Exclusion criteria • Absence of informed consent • Lack of ability to consent • Primary bone tumors invading the intra-spinal space • Vertebral metastasis
Outcome(s)	**Primary Outcome** • Quality of life based on the questionnaire (EQ-D5) • Extent of tumor resection (see CRF): according to surgeon: 1. Meningioma: Simpson grade 1 and 2 2. Schwannoma: complete resection, including nerve root 3. Cauda ependymoma: complete resection, including filum terminale according to postoperative MRI, 3 months after surgery 4. Other: surgeon's decision • Neurological status (McCormick Score) (see CRF), 3 months after surgery **Secondary Outcome** Imaging: preoperative and postoperative MRI (3 months) according CRF • Volumetry • Spinal canal occupancy ratio in % Further patient reported outcomes: • Functionality: Neck disability index (NDI) for tumors in the cervical spine, Oswestry disability index (ODI) for tumors in the thoracic and lumbar spine (see CRF) • Local and radicular pain (VAS 1-10) (see CFR) • Neurological status: motor function of each limb, ataxia and gait (mJOA score) (see CRF) • HADS score- based score for anxiety • Questionnaire on bladder, bowl, sexual functionality

	Quality indicators (QI): Length of hospital stay 30- and 90-days readmission Nosocomial infections Blood loss Duration of surgery Progression of the disease or recurrence Other adverse events Mortality Assessment of adverse events according to Common Terminology Criteria for Adveres Events (CTCAE) 5.0 and severity according to the Ibañez scale (see CRF) CSF leakage is defined as one, when CSF leakage is identified on imaging of clinicaly and treatment is required: operative or conservative (Lumbar drain for example) Postoperative kyphosis of deformity is defined, when symptomatic (for example pain) or evident on imaging (for example kyphotic fracture on MRI)
Study design	Registry trial
Statistical analysis	**Primary Outcome** Improvement of neurological function, quality of life, and extent of resection **Secondary Outcome** Descriptive data analysis of clinical parameters is performed. Confidence intervals for relevant treatment effects are calculated using univariate and multi-variate statistical tests
Number of cases	100 patients
Time period	February 2025 until June 2027
Number of centers	N= X

Study Centers	In Germany (Planned): 1) Klinik für Neurochirurgie, Universitätsklinikum Münster. Direktor Prof. W. Stummer. Projektleiter PD Dr. Schwake 2) Klinik für Neurochirurgie, Universitätsmedizin Cottbus, Direktor Prof. E. Shiban. Ebenfalls Projektleiter https://mul-ct.de/medizinische-universitaet/einrichtungen-von-a-z/kliniken-departments-sektionen.php?object=contact&id_object=36&tab=ueber-uns 3) Klinik für Neurochirurgie, Universitätsklinikum Eppendorf. Komm. Direktoren Priv.-Doz. Dr. med. Lasse Dührsen und Priv.-Doz. Dr. med. Hanno Meyer. Projektleiter: PD Dr. Malte Mohme https://www.uke.de/kliniken-institute/kliniken/neurochirurgie 4) Klinik für Neurochirurgie, Universitätsklinikum Köln, Direktor Prof. Dr. Goldbrunner. Projektleiter Dr. Lenschow https://neurochirurgie.uk-koeln.de/klinik/direktor-team/ 5) Klinik für Neurochirurgie, Universitätsklinikum Freiburg. Direktor Prof. Dr. Beck. Projektleiter: Prof. Dr. Klingler https://www.uniklinik-freiburg.de/neurochirurgie.html 6) Other interested centers abroad: St. Gallen/ Zürich/ Geneva/ Bern/ Innsbruck

1.2 Flow chart

	Admission	Surgery	Discharge	3 months follow up	12 months follow up*
Assessment of inclusion and exclusion criteria	X				
Informed consent/assent	X				
neurological status: motor function, ataxia, reflexes, cauda symptoms	X		X	X	X
VAS Back pain, radiculopathy	X		X	X	X
McCormic score	X		X	X	X
Imaging (MRI)	X			X	X
EQ-5D	X			X	X
mJOA/NDI/ODI and further scores	X			X	X
Approach		X			
LOS			X		
30 and 90 days readmission				X	
Adjuvant treatment				X	X
Adverse events	X	X	X	X	X

* Further follow and documentation is possible and recommended

2. Introduction

2.1 Background information

Juxta-medullary tumors are mostly benign tumors in the spinal canal that may cause neurological deficits due to spinal cord or nerve root compression. The knowledge about the natural course of the disease, optimal treatment regarding timing of surgery and surgical approach are based on case series from different institutions around the world (Montano et al., 2016; M. Safaee et al., 2015, 2016; M. M. Safaee et al., 2017; Safavi-Abbasi et al., 2008; Schwake et al., 2018; Takahashi et al., 2022. Moreover, little is known about the long-term clinical and functional outcome after tumor resection, indicators of quality of treatment and quality of life after surgery.

Main treatment option of juxta-medullary tumors is a neurosurgical resection. The main goal of the surgery is to decompress the neuro structures in order to reveal neurological deficits. However, achieving gross total resection (GTR) is important in order to achieve long progression free survival (PFS) (Lenzi et al., 2017; Nanda et al., 2015; Ottenhausen et al., 2019; Ozawa et al., 2007). Therefore, the surgeon should choose the appropriate surgical approach to achieve these goals. Several publications show that GTR, whenever possible, is essential, as subtotal resection is the main reason of tumor regrowth or recurrence. Moreover, revision surgery due to tumor recurrence is one of the main risk factors of unfavorable outcome, probably to intradural adhesions, related to the first procedure. Due to the mostly benign nature of juxtamedullary tumors, it would be very difficult to evaluate overall survival (OS) and progression free survival (PFS) within this progressive registry in the short run. For this reason, data should be kept for late cohort analysis after longer intervals. Probably up to 20 years, as previous publications reported recurrence of spinal meningioma after GTR 10 years or more after surgery.

On the other hand, too large exposure may lead to impaired recovery after surgery, eventual higher blood loss during surgery and thus longer stay in hospital (LOS) and impaired quality of life. Moreover, extensive bone resection may lead to spinal instability requiring instrumentation, during index surgery or during further follow up in case of postoperative deformity (Abumi et al., 1990; Jiang et al., 2022; Lee & Teo, 2004; Mummaneni et al., 2020; Raysi Dehcordi et al., 2012).

In addition to the oncological outcome, the neurological outcome is also very important. Depending on the localization of the tumor, its form and compression of intra-spinal structures such as the spinal cord or nerve roots many patients develop neurological deficits. Besides GTR the other goal of resection is the neurological recovery of these patients. Previous reports show that the time point of surgery is important in order to achieve full recovery (Schwake et al., 2018). However, most of the data is derived from retrospective case series. One of the aims of this registry is to prove this hypothesis. These neurological deficits are, as mentioned above, related to the localization of the tumor within the spine, Tumors in the cervical spine would cause mainly gait ataxia, spasticity, and weakness in the upper extremities while tumors in the lumbar spine would lead to deficits in the lower extremities in combination to disturbances of bladder, bowl, and sexual functions. These functions should be evaluated and monitored, before and after treatment.

Other concerns are safety requirements in order to prevent peri-operative complications. For example, the role of intra-operative neurophysiological monitoring. Some authors recommend the utilization intra operative monitoring, however, the evidence level is very low (Jesse et al., 2022; Thakur et al., 2021). Other open questions are for example the utility of microscope, methods for dura closure and thrombosis prevention.

On the other hand, some tumors can be treated with irradiation, some studies showed efficacy of this method mainly in the case of Schwannomas and meningiomas. In case of residual tumor or tumor progression irradiation can be also performed to prevent further growth (Chang & Lee, 2013).

Lastly, in comparison to the methods mentioned above, a wait-and-see approach can be used for asymptomatic patients or those with mild symptoms. In this case, clinical and imaging examinations are performed at regular intervals to check the neurological status and the tumor. This can also be done for longer periods of time because of the benign nature of these tumors with the slow growth. in case of new neurological deficits of or progression surgical treatment should be advocated. Overall, it is not certain at what point therapy is indicated, especially in asymptomatic patients. Because many of these tumors are discovered by coincidence during imaging, which was performed due to other symptoms.

2.2 Rationale of the study

The rationale of the trial is to define benchmarks on quality of life, functionality and neurological outcome after resection of juxtamedullary tumors. Furthermore, to assess and define benchmarks of quality indicators of the treatment. These measurements would be essential for future studies.

Further rationales are to find out the optimal timing, method, and approach to treat juxta-medullary tumors. Because of the low incidence of juxta-medullary tumors, a multi-center trial seems to be essential. This would allow us to analyze a large number of patients, much more than any other published paper. Moreover, the different protocols and standards approaches in each center would allow conducting Comparative Effectiveness Research (CER).

2.3 Aims

The goal of this study is to establish a multicenter cohort of patients operated on juxtamedullary tumors. With especial emphasis on functional outcome, quality indicators (QI) and quality of life after surgery three months after surgery. Causes of unfavorable outcome should be determined (Schipmann et al., 2017, 2019).

The main hypothesis is that early and less-invasive surgery with maximal extents of resection would lead to a more favorable outcome. In the future the registry would help assessing further hypothesis can be answered on the base of comparative effectiveness research (CER), examples of these hypothesis are:

1. Functional and neurological outcome in comparison to preoperative status. Comparison between Panties with good preoperative McCormick score (1-2) and those with a high preoperative score (3-5).
2. Risk-factors for non-favorable outcome
3. Non-Inferiority to achieve gross total resection via unilateral approaches
4. Question whether laminectomy as approach may cause mor pain and impact quality of life
5. Risk factors for the development of CFS Leaks
6. Does bed rest prevent CSF leaks
7. Does laminectomy elevate the risk of CSF leaks
8. Does the utility of intraoperative neurophysiological monitoring (IOM) influence surgical outcome: rate of GTR and neurological outcome
9. Rate of postoperative kyphosis and deformity in laminectomy in comparison to non-laminectomy

10. Is facetectomy required for GTR of dumbbell tumors?
11. Risk factors for non-complete resection

Primary outcomes are determined by:

- Quality of life based on the questionnaire (EQ-D5)
- Extent of tumor resection (see CRF):

  according to surgeon:

  1. Meningioma: Simpson grade 1 and 2

  2. Schwannoma: complete resection, including nerve root

  3. Cauda ependymoma: complete resection, including filum terminale

  according to postoperative MRI, 3 months after surgery

  4. Other: surgeon's decision
- Neurological status (McCormick Score) (see CRF), 3 months after surgery

Secondary Outcome

Imaging: preoperative and postoperative MRI

- Volumetry
- Spinal canal occupancy ratio in %

Further patient reported outcomes:

- Functionality: Neck disability index (NDI) for tumors in the cervical spine, Oswestry disability index (ODI) for tumors in the thoracic and lumbar spine (see CRF)
- Local and radicular pain (VAS 1-10) (see CFR)
- Neurological status: motor function of each limb, ataxia and gait (mJOA score) (see CRF)
- HADS score- based score for anxiety
- Questionnaire on bladder, bowl, sexual functionality

Quality indicators (QI):

Length of hospital stay

30- and 90-days readmission

Nosocomial infections

Blood loss

Duration of surgery

Progression of the disease or recurrence

Other adverse events

Mortality

Assessment of adverse events according to Common Terminology Criteria for Adveres Events (CTCAE) 5.0 and severity according to the Ibañez scale (see CRF)

CSF leakage is defined as one, when CSF leakage is identified on imaging of clinicaly and treatment is required: operative or conservative (Lumbar drain for example)

Postoperative kyphosis of deformity is defined, when symptomatic (for example pain) or evident on imaging (for example kyphotic fracture on MRI)

2.3 Methodology

All patients treated in one of the study centers are recorded in a databank (Redcap, see below), which includes information about admission, symptoms, other diseases, treatment, quality indicators and questionnaires regarding quality of life and functionality. Data should be recorded in an anonymized in each center (see below).

For the analysis the CRF includes information about admission, surgery, discharge, and 3 months (90 days) after surgery. In addition, patients should fill out questionnaires on quality of life (EQ-D5) and functionality (ODI or NDI). Later, yearly visits can be completed to have long term results in the future regarding progression free survival (PFS) and overall survival (OS). The CRF is attached to this document.

Univariate and multivariate statistics would be applied to prove which variables might lead to a favorable or unfavorable outcome.

A minimum number of one hundred (N=100) inclusions seems to be adequate in order to perform reasonable analysis. In the event of nonsufficient recruitment, results and further recruitment would be discussed two years after initiation of the study, and annually thereafter.

2.4 Risk-Benefit Analysis

2.4.1 Risk expected for participants

No risk whatsoever awaits the participants in the study. All examinations and interventions will be performed according to clinical routine. Refusal to participate in the study will not result in any disadvantages for the patients. Participants will be treated exactly like non-study participants, based on the therapy standards of the respective study center

2.4.2 Benefit expected for participants

There is no specific benefit for the participants by taking part in the study

2.4.3 Benefit expected for medical science

The study should determine factors that influence the outcome (degree of resection, neurology, quality of life functionality, pain) of the patients. Furthermore, it would determine factors that influence the quality of treatment (length of stay, 30-day readmission, complications, infections etc.).

2.4.4 Benefit expected for the society:

A postoperatively impaired quality of life, severe neurological deficit, or functionality often leads to high costs in the health and social care systems. Therefore, knowledge of influencing factors is also of imminent societal importance.

In addition, quality indicators of therapy should be determined. These are also important for society. Improving the quality of therapy, for example, by reducing the length of stay, postoperative complications can also reduce treatment costs.

2.4.5. List of possible adverse events

Cerebrospinal Fluid (CSF) Leak:

- **Incidence:** Approximately (aprox. 1-4 %)

Details: A study involving 398 patients reported a CSF leak-related complication rate of 4.27%. The use of 6-0 Prolene sutures for dural closure was associated with a lower leak rate compared to 5-0 silk sutures.

Neurological Deficits:

- **Incidence:** Weakness (aprox. 5-20%), new sensory deficits (aprox. 4-16.7%)

Details: In a cohort of 135 patients undergoing spinal tumor resection, postoperative complications included weakness in 20% and new sensory deficits in 16.7% of patients.

Infections:

- **Incidence:** Superficial wound infection (aprox. 1.9%)

Details: Among 52 patients treated with a microscopic keyhole approach for spinal intradural extramedullary tumors, 1.9% experienced a superficial wound infection.

Bowel and Bladder Dysfunction:

- **Incidence:** aprox. 3.7%

Details: Urinary and renal complications were observed in 3.7% of patients after spinal cord tumor surgery.

Spinal Deformities:

Details: Extensive surgical procedures, especially those involving significant bone removal, may lead

to postoperative spinal deformities, necessitating further corrective measures.

General Surgical Complications:

Details: As with any major surgical procedure, there are inherent risks of complications such as bleeding, infection, and adverse reactions to anesthesia

Further adverse events are listed in the CRF.

3. Study Sites and Study Population

3.1 Study Site Selection

Due to the rare nature of juxta-medullary tumors and in order to have the opportunity to compare different treatment methods, the trial is planned as a multi-center trial.
So far, 5 centers have expressed interest in participating in the study.

3.2 Study Population

3.2.1 Inclusion Criteria

- Adult, age ≥18 years, patients treated on intraspinal, extra medullary tumor
- Patients must have sufficient cognitive and language skills to give informed consent

3.2.2 Exclusion Criteria

- Absence of informed consent
- Lack of ability to consent
- Primary bone tumors
- Vertebral metastasis

3.2.3 Distribution of Gender in the Study Population

All patients treated on juxta-medullary tumors can be invited to participate in the study; distribution of Gender varies depending on histology. For example, spinal meningiomas are up to 80% in female patients (Schwake et al., 2018).

4. Patient Registration

Patients who are cared for at one of the study sites and who are possibly eligible will be invited for study participation. Once written informed consent in participation has been given, the center can register the patient in the electronic data base (Redcap).

Should inclusion criteria fail, or exclusion criteria arise during the following screening process, the patient must be reported to the study coordinator immediately and the patient will be withdrawn from the study.

5. Assessment of Safety

Patients are treated according to the protocol of each center, the participation in the trial does not cause any disadvantage for these patients. Both patients' safety and possible adverse events are

subjects of this study.

6. Statistics

6.1 Primary outcome

Comparative analysis of pre-operative, post-operative, neurological status, and questionnaires

6.2 Secondary outcome

Descriptive data analysis of clinical parameters will be performed. Confidence intervals for relevant treatment effects are calculated using univariate and multi-variate statistical tests.

Patients' data will be compared to historical cohorts and equivalence, or superiority of care will be described.

Further analysis will be performed as comparative effectiveness research (CER) as described above. When applicable cohorts will be matched in a case-control mode.

7. Documentation, Data Management, Archiving

7.1 Patient Identification List

All patient data will be collected in a pseudonymized form. The pseudonym is given automatically during registration by Redcap.

7.2 Source Data / Source documents

Source data are, within the meaning of the ICH E6 Guideline, all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data will be documented in various source documents (e.g. hospital records, doctor's report, patient' diaries or evaluation checklists, imaging) and then entered into the electronic Case Report Form (eCRF).

7.3 Recording of Data / Case Report Form (CRF)

Data will be recorded electronically using Redcap, an EDC (Electronic Data Capture) system. For the documentation of study data, the investigator will be given access to an electronic CRF (eCRF) for each recruited patient. Only persons authorized to enter data into the eCRF will have access to the EDC system. All users will be trained to use the EDC system and will comply with the instructions in the study-specific user manual. They will have continuous access to the data and reports of study patients at their own study site. The investigator is responsible for ensuring that the study data will be documented correctly, completely and in a timely manner. A study team physician takes on responsibility for the collected data by signing electronically.

7.4 Data Management

For data management, the validated data management system redcap will be used. All entered data will be stored on servers of the University of Münster. The servers are located in a secure data center and behind a firewall in the network of the University of Münster. A backup of the data will be saved on a daily basis and all data changes will be recorded in an audit trail.

All data will be checked for plausibility during initial data entry. Missing or non-plausible data are highlighted by the system right at input at the clinical study site and may be corrected immediately. Thereafter, according to the data validation plan, further data checks will be performed with regard to completeness and plausibility by the study coordinator. In case of non-plausible or missing data, queries will be sent to the study site.

7.5 Archiving

After the end of the trial the originals of all trial specific documents (Trial Master File) including originals of the CRFs will be stored by the sponsor for at least 10 years in accordance with the applicable regulations (GCP-Verordnung §13(10)), EU directive 536/2914 and applicable EU directives on medical devices).

Furthermore, the investigator stores the ISF (Investigator Site File) including copies of the CRFs for the time period given above.

No trial data or documents must be destroyed without prior written agreement between the study coordinator and the investigators or their designee. queries must be resolved by authorized members of the investigator`s staff in the respective study site in a timely manner.

After completion of data entry and data processing, the database will be locked and the data will be exported for statistical analysis. The investigator will receive a CD-ROM of the eCRF data for archiving at the clinical study site.

8. Monitoring, Audits and Inspections

8.1 Monitoring

A quality assurance audit may be conducted by the study coordinator or one other assigned person. The quality assurance auditor must be provided access to all medical records, the investigator's study-related files and correspondence, and the informed consent documentation that is relevant to this study.

9. Ethical and Regulatory Requirements

9.1 Declaration of Helsinki and Legal Requirements

The study will be conducted in compliance with the declaration of Helsinki (current version, October 2024), the current legal provisions regarding data protection, and the principles of Good Clinical Practice (GCP).

The present study will not be started in a center before the competent ethics committee has given a favorable opinion and an approval by the relevant competent federal authority has been obtained.

Besides, for each participating study site a favorable opinion of the respective ethics committee is required.

In case of substantial amendments, a new application will be submitted to the ethics committees and/or the competent federal authorities. Changes will not be implemented in a country unless the competent ethics committee has given a favorable opinion and/or the competent authority has granted an approval.

Issues, which always require a favorable opinion of the ethics committee, are for example:

1. Inclusion of additional study sites,
2. Change of the investigator or his deputy,
3. Changes in any documents addressed to study participants or in any study information addressed to potential study participants.

9.2 Patient Information and Informed Consent

Prior to inclusion into the study, the investigator informs each patient and/or the legal guardians about nature, significance, implications, and risks of the study as well as about the patient's right to withdraw from study participation at any time without any resulting detriment.

With respect to data protection, the investigator furthermore informs that pseudonymized health data will be stored electronically and transmitted to various persons/institutions as explicitly described in the patient information and consent forms.

Patients/legal guardians will furthermore be informed that, if relevant for study evaluation, data once collected cannot be erased after withdrawal of informed consent.

Further, they provide the opportunity for clarification of any study issues.

The patient and/or the parents/legal guardians will be given adequate opportunity to decide whether to or not to participate in this study.

The consent form and the data protection statement are incorporated and archived with the investigator files. In the patient's file it will be stated that the patient is participating in this study and that these documents are archived in the investigator files.

If the Patients/legal guardians are unable to write, in exceptional cases, instead of the written consent required, oral consent in the presence of at least one witness, who was also present during the conversation about the study, may be given. The witness may not be anyone working at the study site nor a member of the investigating team. The orally given consent has to be documented in writing, dated and signed by the witness.

In case of any study issue which requires a change of the patient information sheet, patients and or their parents/legal guardians already included into the study must, if relevant to them, be informed about these issues orally and in writing and their written consent in further study participation must be obtained.

9.3 Financing

External funding is currently not planned. If funding is requested and approved during the course of the study, the Ethics Committee must be notified immediately.

9.4 Adherence to the Protocol

The Investigator must adhere to the protocol as detailed in this document. Dependent on competence, substantial changes to the protocol will require written favorable opinion by the ethics committee and/or written approval by the competent authority prior to implementation. This does not apply for appropriate urgent safety measures taken to protect the subjects against any immediate hazard.

Any deviations from the protocol must be fully documented in the source documentation and recorded and explained in the CRF.

10 Study Registration, Reporting and Publication

10.1 Study registration

The study is registered in a clinical trials database, which is accessible to the public (www.clinicaltrials.gov; ~~NCT04738162~~). ???

10.2 Publication Policy

After complete data collection and analysis, the study results will be published. Single publications such as lectures, posters or papers principally require the approval of the Principal Investigator. Inquiries by the press or the public regarding study results are only to be answered by the Principal Investigator.

A manuscript is to be prepared by the Principal Investigator or by a designated co-worker after completing statistical analysis***. All contributors*** would be considered as co-authors. The co-authors are required either to agree to the manuscript or to indicate any requests for changes within 4 weeks after receiving the draft of the manuscript to the lead author. Should they fail to meet this requirement agreement will be assumed.

11. Supplements:

11.1 EQ-5D-5L Questionnaire (© 2009 EuroQol Group EQ-5D™ is a trademark of the EuroQol Group)

MOBILITY

I have no problems in walking about

I have slight problems in walking about

I have moderate problems in walking about

I have severe problems in walking about

I am unable to walk about

SELF-CARE

I have no problems washing or dressing myself

I have slight problems washing or dressing myself

I have moderate problems washing or dressing myself

I have severe problems washing or dressing myself

I am unable to wash or dress myself

USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)

I have no pain or discomfort

I have slight pain or discomfort

I have moderate pain or discomfort

I have severe pain or discomfort

I have extreme pain or discomfort

PAIN / DISCOMFORT

I have no pain or discomfort

I have slight pain or discomfort

I have moderate pain or discomfort

I have severe pain or discomfort

I have extreme pain or discomfort

ANXIETY / DEPRESSION

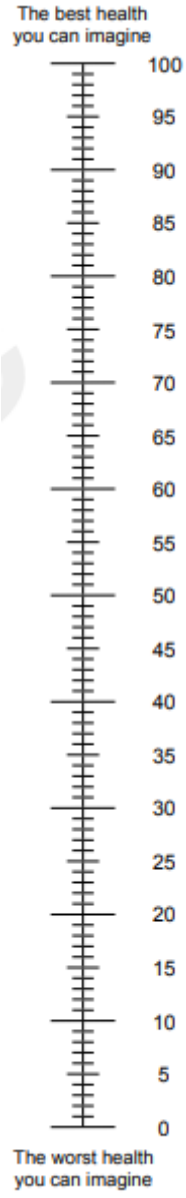
I am not anxious or depressed

I am slightly anxious or depressed

I am moderately anxious or depressed

I am severely anxious or depressed

I am extremely anxious or depressed



We would like to know how good or bad your health is TODAY.

- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine. 0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

11.2 Neck disability index (NDI) (Vernon, 2008)

Originally published in 1991 in the Journal of Manipulative and Physiological Therapeutics, the Neck Disability Index (NDI) is an instrument to measure patient-reported disability secondary to neck pain. It was developed utilizing the Oswestry Low Back Pain Index as a model and therefore, at the time of its creation, was distinguished from other simpler pain assessments by examining patient function with respect to activities of daily living.

The instrument has 10 items and patients rate their pain from 0 (no pain) to 5 (worst imaginable pain). Individual item responses are summed to a total score, where 0 points indicate no activity limitations, and 50 points indicate complete activity limitation. This instrument may be useful in patients with chronic or acute onset neck pain and in patients with musculoskeletal complaints or with cervical radiculopathy.

1. **Pain Intensity:**

I have no pain at the moment +0

The pain is very mild at the moment +1

The pain is moderate at the moment +2

The pain is fairly severe at the moment +3

The pain is very severe at the moment +4

The pain is the worst imaginable at the moment +5

2. Personal Care (Washing, Dressing, etc.)

I can look after myself normally without causing extra pain +0

I can look after myself normally but it causes extra pain +1

It is painful to look after myself and I am slow and careful +2

I need some help but can manage most of my personal care +3

I need help every day in most aspects of self care +4

I do not get dressed, I wash with difficulty and stay in bed +5

3. Lifting

I can lift heavy weights without extra pain +0

can lift heavy weights but it gives extra pain +1

Pain prevents me lifting heavy weights off the floor, but I can manage if they are conveniently placed, for example on a table +2

Pain prevents me from lifting heavy weights but I can manage light to medium weights if they are conveniently positioned +3

I can only lift very light weights +4

I cannot lift or carry anything +5

4. Reading

I can read as much as I want to with no pain in my neck +0

I can read as much as I want to with slight pain in my neck +1

I can read as much as I want with moderate pain in my neck +2

I can't read as much as I want because of moderate pain in my neck +3

I can't hardly read at all because of severe pain in my neck +4

I cannot read at all +5

5. Headaches

I have no headaches at all +0

I have slight headaches, which come infrequently +1

I have moderate headaches, which come infrequently +2

I have moderate headaches, which come frequently +3

I have severe headaches, which come frequently +4

I have headaches almost all the time +5

6. Concentration

I can concentrate fully when I want to with no difficulty +0

I can concentrate fully when I want to with slight difficulty +1

I have a fair degree of difficulty in concentrating when I want to +2

I have a lot of difficulty in concentrating when I want to +3

I have a great deal of difficulty in concentrating when I want to +4

I cannot concentrate at all +5

7. Work

I can do as much work as I want to +0

I can only do my usual work, but no more +1

I can do most of my usual work, but no more +2

I can't do my usual work +3

I can hardly do any work at all +4

I can't do any work at all +5

8. Driving

I can drive my car without any neck pain +0

I can drive my car as long as I want with slight pain in my neck +1

I can drive my car as long as I want with moderate pain in my neck +2

I can't drive my car as long as I want because of moderate pain in my neck +3

I can hardly drive at all because of severe pain in my neck +4

I can't drive my car at all +5

9. Sleeping

I have no trouble sleeping +0

My sleep is slightly disturbed (less than 1 hr sleepless) +1

My sleep is mildly disturbed (1-2 hrs sleepless) +2

My sleep is moderately disturbed (2-3 hrs sleepless) +3

My sleep is greatly disturbed (3-5 hrs sleepless) +4

My sleep is completely disturbed (5-7 hrs sleepless) +5

10. Recreation

I am able to engage in all recreational activities with no neck pain at all +0

I am able to engage in all my recreational activities, with some pain in my neck +1

I am able to engage in most, but not all of my usual recreational activities because of pain in my neck +2

I am able to engage in a few of my usual recreational activities because of pain in my neck +3

I can hardly do any recreational activities because of pain in my neck +4

I can't do any recreational activities at all +5

11.3 Oswestry disability Index (ODI) (Fairbank & Pynsent, 2000)

Originally published in 1980 in *Physiotherapy*, the Oswestry Disability Index (ODI) is an outcome measure that was designed to assess function in activities of daily living for those with acute or chronic back pain.

The ODI consists of 10 patient-completed questions in which the response options are presented as 6-point Likert scales. Scores range from 0% (no disability) to 100% (most severe disability

1. Pain Intensity

I have no pain at the moment +0

The pain is very mild at the moment +1

The pain is moderate at the moment +2

The pain is fairly severe at the moment +3

The pain is very severe at the moment +4

The pain is the worst imaginable at the moment +5

2. Personal Care (Washing, Dressing, etc.)

I can look after myself normally without causing extra pain +0

I can look after myself normally but it causes extra pain +1

It is painful to look after myself and I am slow and careful +2

I need some help but can manage most of my personal care +3

I need help every day in most aspects of self-care +4

I do not get dressed, I wash with difficulty and stay in bed +5

3. Lifting

I can lift heavy weights without extra pain +0

I can lift heavy weights, but it gives extra pain +1

Pain prevents me lifting heavy weights off the floor, but I can manage if they are conveniently placed, for example on a table +2

Pain prevents me from lifting heavy weights but I can manage light to medium weights if they are conveniently positioned +3

I can only lift very light weights +4

I cannot lift or carry anything at all +5

4. Walking

Pain does not prevent me walking any distance +0

Pain prevents me from walking more than 1 mile +1

Pain prevents me from walking more than ½ mile +2

Pain prevents me from walking more than 100 yards +3

I can only walk using a stick or crutches +4

I am in bed most of the time +5

5. Sitting

I can sit in any chair as long as I like +0

I can only sit in my favorite chair as long as I like +1

Pain prevents me sitting more than 1 hour +2

Pain prevents me from sitting more than 30 minutes +3

Pain prevents me from sitting more than 10 minutes +4

Pain prevents me from sitting at all +5

6. Standing

I can stand as long as I want without extra pain +0

I can stand as long as I want but it gives me extra pain +1

Pain prevents from standing for more than 1 hour +2

Pain prevents me from standing for more than 30 minutes +3

Pain prevents me from standing for more than 10 minutes +4

Pain prevents me from standing at all +5

7. Sleeping

My sleep is never disturbed by pain +0

My sleep is occasionally disturbed by pain +1

Because of pain I have less than 6 hours sleep +2

Because of pain I have less than 4 hours sleep +3

Because of pain I have less than 2 hours sleep +4

Pain prevents me from sleeping at all +5

8. Sex life (if applicable)

My sex life is normal and causes no extra pain +0

My sex life is normal but causes some extra pain +1

My sex life is nearly normal but is very painful +2

My sex life is severely restricted by pain +3

My sex life is nearly absent because of pain +4

Pain prevents any sex life at all +5

9. Social life

My social life is normal and gives me no extra pain +0

My social life is normal but increases the degree of pain +1

Pain has no significant effect on my social life apart from limiting my more energetic interests, for example sport +2

Pain has restricted my social life and I do not go out as often +3

Pain has restricted my social life to my home +4

I have no social life because of pain +5

10. Travelling

I can travel anywhere without pain +0

I can travel anywhere but it gives me extra pain +1

Pain is bad but I manage journeys over two hours +2

Pain restricts me to journeys of less than 1 hour +3

Pain restricts me to short necessary journeys under 30 minutes +4

Pain prevents me from travelling except to receive treatment +5

11.4 Modified Japanese Orthopedic Association (mJOA) score (Tetreault et al., 2017)

mJOA Scoring Criteria (18-point version)

Upper Extremity Motor Dysfunction (max score: 5)

0: I am unable to move my hands at all

1: I can move my hands a little, but I am unable to feed myself

2: I can feed myself but, I am unable to button my shirt

3: I can button up my shirt, but I find it very difficult and it takes a long time

4: I can button my shirt with only slight difficulty

5: My hands work normally

Lower Extremity Motor Dysfunction (max score: 7)

0: I am paralysed and unable to move or feel my legs

1: I can feel my legs but I am unable to move them at all

2: I can move my legs but I cannot walk

3: I can walk but I require a walking aid

4: Able I can walk up and down stairs, but I have to hold the handrail

5: I am a little unsteady on my feet, but I can walk up and down stairs without holding the handrail

6: I am a little unsteady, but I can walk unaided

7: My legs are unaffected

Sensory Dysfunction of Upper Extremity (max score: 3)

0: I am unable to feel my hands

1: I have pain or severe loss of feeling (including numbness, tingling) in my hands

2: I have mild loss of feeling (including numbness, tingling) in my hands

3: I have no loss of feeling in my hands

Sphincter function (max score: 3)

0: I cannot control when I pass urine

1: I have marked difficulty passing urine

2: I have mild difficulty passing urine

3: I have no difficulty passing urine

Score Interpretation

15-17: Mild myelopathy

12-14: Moderate myelopathy

0-11: Severe myelopathy

11.5 bladder, bowl, and sexual functionality

Sensation in the "saddle" area (buttocks, medial hips)

- Normal
- Paresthesia
- Reduced sensation
- Absent sensation

Bladder function:

- Normal function
- Mild dysfunction (occasional incontinence, but mostly continent)
- Moderate dysfunction (frequent incontinence, but some control)
- Severe dysfunction (total incontinence)

Bowel function - Low Anterior Resection Syndrome (LARS) Score (Bittorf et al., 2003)**:**

1. Incontinence for Flatus:
   - Never: 0 points
   - Less than once per week: 4 points
   - At least once per week: 7 points
   - Daily: 10 points

.

2. Incontinence for Liquid Stool:

- Never: 0 points
- Less than once per week: 3 points
- At least once per week: 7 points
- Daily: 13 points

3. Frequency of Bowel Movements:

- 1 time per day or less: 0 points
- 2-3 times per day: 4 points
- 4-6 times per day: 7 points
- 7 or more times per day: 11 points

4. Clustering (Having multiple bowel movements in a short period):

- Never: 0 points
- Less than once per week: 9 points
- At least once per week: 11 points
- Daily: 13 points

5. Urgency (Sudden need to defecate):

- Never: 0 points
- Less than once per week: 11 points
- At least once per week: 16 points
- Daily: 18 points

Interpretation of Total Score:

- No LARS (0-20 points): Indicates normal or near-normal bowel function.

- Minor LARS (21-29 points): Indicates minor bowel dysfunction that may occasionally impact daily activities.

- Major LARS (30-42 points): Indicates significant bowel dysfunction with frequent symptoms that substantially impact daily life and quality of life.

Sexual functions

Male

- Normal erectile and ejaculatory function
- Mild erectile or ejaculatory dysfunction (able to have intercourse with mild difficulty)
- Moderate erectile or ejaculatory dysfunction (intercourse possible with significant difficulty or partial erection)
- Severe erectile or ejaculatory dysfunction (intercourse rarely or not possible)
- Complete loss of erectile and ejaculatory function

Female

- Normal sexual function
- Mild dysfunction (decreased arousal or lubrication, but able to have intercourse)
- Moderate dysfunction (significant difficulty with arousal or lubrication, painful intercourse)
- Severe dysfunction (intercourse rarely or not possible due to dysfunction)
- Complete loss of sexual function

11.6 Hospital Anxiety and Depression Scale (HADS) score (Stern, 2014):

Tick the box beside the reply that is closest to how you have been feeling in the past week.

Don't take too long over you replies: your immediate is best.

Don't take too long over you replies: your immediate is best.

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			**I feel restless as I have to be on the move:**
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all

		Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful:			**I get sudden feelings of panic:**
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			**I can enjoy a good book or radio or TV program:**
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not Often	2		Not often
	3	Not at all	3		Very seldom

Please check you have answered all the questions

Scoring:

Total score: Depression (D) _____ Anxiety (A) _____

0-7 = Normal

8-10 = Borderline abnormal (borderline case)

11-21 = Abnormal (case)

11.8 McCormick scale

Filled by investigation according to neurological examination

1 Neurologically intact, ambulates normally, may have minimal dysesthesia

2 mild motor or sensory deficit; patient maintains functional independence

3 moderate deficit, limitation of function, independent with external aid

4 severe motor or sensory deficit, limit of function with a dependent patient

5 paraplegic or quadriplegic, even if there is flickering movement

11.9 classification of postoperative complications according Landriel Ibanez classification for neurosurgical complications: (Ibañez et al., 2011)

1. grade I represents any non-life-threatening complication treated without invasive procedures

2. grade II is complications requiring invasive management

3. grade III is life-threatening adverse events requiring treatment in an intensive care unit (ICU)

4. grade IV is death as a result of complications. We sought to compare our results with reports from the literature.

12. References:

Abumi, K., Panjabi, M. M., Kramer, K. M., Duranceau, J., Oxland, T., & Crisco, J. J. (1990). Biomechanical evaluation of lumbar spinal stability after graded facetectomies. *Spine*, *15*(11), 1142–1147. https://doi.org/10.1097/00007632-199011010-00011

Bittorf, B., Stadelmaier, U., Merkel, S., Hohenberger, W., & Matzel, K. E. (2003). Does anastomotic leakage affect functional outcome after rectal resection for cancer? *Langenbeck's Archives of Surgery*, *387*(11–12), 406–410. https://doi.org/10.1007/S00423-003-0349-7

Chang, U. K., & Lee, D. H. (2013). Stereotactic radiosurgery for spinal neoplasms: current status and future perspective. *Journal of Neurosurgical Sciences*, *57*(2), 87–101. https://pubmed.ncbi.nlm.nih.gov/23676858/

Fairbank, J. C. T., & Pynsent, P. B. (2000). The oswestry disability index. *Spine*, *25*(22), 2940–2953. https://doi.org/10.1097/00007632-200011150-00017

Ibanez, F. A. L., Hem, S., Ajler, P., Vecchi, E., Ciraolo, C., Baccanelli, M., Tramontano, R., Knezevich, F., & Carrizo, A. (2011). A new classification of complications in neurosurgery. *World Neurosurgery*, *75*(5–6), 709–715. https://doi.org/10.1016/J.WNEU.2010.11.010

Jesse, C. M., Alvarez Abut, P., Wermelinger, J., Raabe, A., Schär, R. T., & Seidel, K. (2022). Functional Outcome in Spinal Meningioma Surgery and Use of Intraoperative Neurophysiological Monitoring. *Cancers*, *14*(16), 3989. https://doi.org/10.3390/CANCERS14163989

Jiang, Y. W., Xu, X. J., Wang, R., & Chen, C. M. (2022). Tubular minimally invasive resection of McCormick type II paraspinal schwannoma: preliminary experience. *British Journal of Neurosurgery*. https://doi.org/10.1080/02688697.2022.2057433

Lee, K. K., & Teo, E. C. (2004). Effects of laminectomy and facetectomy on the stability of the lumbar motion segment. *Medical Engineering & Physics*, *26*(3), 183–192. https://doi.org/10.1016/J.MEDENGPHY.2003.11.006

Lenzi, J., Anichini, G., Landi, A., Piciocchi, A., Passacantilli, E., Pedace, F., Delfini, R., & Santoro, A. (2017). Spinal Nerves Schwannomas: Experience on 367 Cases-Historic Overview on How Clinical, Radiological, and Surgical Practices Have Changed over a Course of 60 Years. *Neurology Research International*, *2017*. https://doi.org/10.1155/2017/3568359

Montano, N., D'Alessandris, Q. G., D'Ercole, M., Lauretti, L., Pallini, R., di Bonaventura, R., la Rocca, G., Bianchi, F., & Fernandez, E. (2016). Tumors of the peripheral nervous system: analysis of prognostic factors in a series with long-term follow-up and review of the literature. *Journal of Neurosurgery*, *125*(2), 363–371. https://doi.org/10.3171/2015.6.JNS15596

Mummaneni, P. v., Park, P., Shaffrey, C. I., Wang, M. Y., Uribe, J. S., Fessler, R. G., Chou, D., Kanter, A. S., Okonkwo, D. O., Mundis, G. M., Eastlack, R. K., Nunley, P. D., Anand, N., Virk, M. S., Lenke, L. G., Than, K. D., Robinson, L. C., & Fu, K. M. (2020). The MISDEF2 algorithm: An updated algorithm for patient selection in minimally invasive deformity surgery. *Journal of Neurosurgery: Spine*, *32*(2), 221–228. https://doi.org/10.3171/2019.7.SPINE181104

Nanda, A., Kukreja, S., Ambekar, S., Bollam, P., & Sin, A. H. (2015). Surgical Strategies in the

Management of Spinal Nerve Sheath Tumors. *World Neurosurgery*, *83*(6), 886–899. https://doi.org/10.1016/J.WNEU.2015.01.020

Ottenhausen, M., Ntoulias, G., Bodhinayake, I., Ruppert, F. H., Schreiber, S., Förschler, A., Boockvar, J. A., & Jödicke, A. (2019). Intradural spinal tumors in adults—update on management and outcome. *Neurosurgical Review*, *42*(2), 371–388. https://doi.org/10.1007/s10143-018-0957-x

Ozawa, H., Kokubun, S., Aizawa, T., Hoshikawa, T., & Kawahara, C. (2007). Spinal dumbbell tumors: An analysis of a series of 118 cases. *Journal of Neurosurgery: Spine*, *7*(6), 587–593. https://doi.org/10.3171/SPI-07/12/587

Raysi Dehcordi, S., Marzi, S., Ricci, A., di Cola, F., & Galzio, R. J. (2012). Less invasive approaches for the treatment of cervical schwannomas: our experience. *European Spine Journal : Official Publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, *21*(5), 887–896. https://doi.org/10.1007/S00586-011-2118-6

Safaee, M. M., Lyon, R., Barbaro, N. M., Chou, D., Mummaneni, P. v., Weinstein, P. R., Chin, C. T., Tihan, T., & Ames, C. P. (2017). Neurological outcomes and surgical complications in 221 spinal nerve sheath tumors. *Journal of Neurosurgery. Spine*, *26*(1), 103–111. https://doi.org/10.3171/2016.5.SPINE15974

Safaee, M., Oh, T., Barbaro, N. M., Chou, D., Mummaneni, P. v., Weinstein, P. R., Tihan, T., & Ames, C. P. (2016). Results of Spinal Fusion After Spinal Nerve Sheath Tumor Resection. *World Neurosurgery*, *90*, 6–13. https://doi.org/10.1016/J.WNEU.2016.01.015

Safaee, M., Parsa, A. T., Barbaro, N. M., Chou, D., Mummaneni, P. v., Weinstein, P. R., Tihan, T., & Ames, C. P. (2015). Association of tumor location, extent of resection, and neurofibromatosis status with clinical outcomes for 221 spinal nerve sheath tumors. *Neurosurgical Focus*, *39*(2), E5. https://doi.org/10.3171/2015.5.FOCUS15183

Safavi-Abbasi, S., Senoglu, M., Theodore, N., Workman, R. K., Gharabaghi, A., Feiz-Erfan, I., Spetzler, R. F., & Sonntag, V. K. H. (2008). Microsurgical management of spinal schwannomas: evaluation of 128 cases. *Journal of Neurosurgery. Spine*, *9*(1), 40–47. https://doi.org/10.3171/SPI/2008/9/7/040

Schwake, M., Adeli, A., Sporns, P., Ewelt, C., Schmitz, T., Sicking, J., Hess, K., Cäcilia Spille, D., Paulus, W., Stummer, W., & Brokinkel, B. (2018). Spinal meningiomas - Risks and potential of an increasing age at the time of surgery. *Journal of Clinical Neuroscience*, *57*, 86–92. https://doi.org/10.1016/j.jocn.2018.08.030

Stern, A. F. (2014). The Hospital Anxiety and Depression Scale. *Occupational Medicine*, *64*(5), 393–394. https://doi.org/10.1093/OCCMED/KQU024

Takahashi, T., Hirai, T., Yoshii, T., Inose, H., Yuasa, M., Matsukura, Y., Morishita, S., Kobayashi, Y., Utagawa, K., Kawabata, A., Hashimoto, J., Tanaka, T., Motoyoshi, T., Hashimoto, M., Kawabata, S., & Okawa, A. (2022). Risk factors for recurrence and regrowth of spinal schwannoma. *Journal of Orthopaedic Science : Official Journal of the Japanese Orthopaedic Association*. https://doi.org/10.1016/J.JOS.2022.03.003

Tetreault, L., Kopjar, B., Nouri, A., Arnold, P., Barbagallo, G., Bartels, R., Qiang, Z., Singh, A., Zileli, M., Vaccaro, A., & Fehlings, M. G. (2017). The modified Japanese Orthopaedic Association scale: establishing criteria for mild, moderate and severe impairment in patients with degenerative cervical myelopathy. *European Spine Journal*, *26*(1), 78–84. https://doi.org/10.1007/S00586-016-4660-8,

Thakur, J., Ulrich, C. T., Schär, R. T., Seidel, K., Raabe, A., & Jesse, C. M. (2021). The surgical challenge of ossified ventrolateral spinal meningiomas: tricks and pearls for managing large ossified meningiomas of the thoracic spine. *Journal of Neurosurgery. Spine*, *35*(4), 516–526. https://doi.org/10.3171/2020.12.SPINE201526

Vernon, H. (2008). The Neck Disability Index: State-of-the-Art, 1991-2008. *Journal of Manipulative and Physiological Therapeutics*, *31*(7), 491–502. https://doi.org/10.1016/j.jmpt.2008.08.006