# Study Protocol

## Observational Study of Sacral Nerve Function After Sacral Tumor Resection

### Background

Sacral tumors represent a rare subset of spinal neoplasms, accounting for only 1–7% of all spinal tumors. Among them, primary sacral tumors—such as chordoma and chondrosarcoma—are particularly uncommon. Due to their poor responsiveness to radiotherapy and chemotherapy, **en bloc surgical resection** remains the mainstay of treatment. However, early diagnosis is often difficult owing to their insidious onset, nonspecific symptoms, and limited detectability via routine musculoskeletal examinations.

For patients with primary malignant tumors of the sacrum, complete surgical excision is essential for achieving long-term tumor control and potential cure. Nevertheless, sacral resection is technically demanding. The anatomical complexity of the sacral region, proximity to critical neurovascular and visceral structures, and the frequent involvement of the presacral space or sacral canal contribute to a high risk of intraoperative complications, including massive hemorrhage and soft tissue defects. Multidisciplinary collaboration, especially with reconstructive surgeons, is frequently required to ensure adequate wound closure and functional restoration. Achieving negative surgical margins is critical for minimizing local recurrence.

To achieve complete tumor removal, surgeons may need to sacrifice sacral nerve roots, which can significantly compromise postoperative neurological function. Prior studies have demonstrated that **preservation of bilateral S2 roots** maintains normal gait in 56.2% of patients, while **bilateral S3 root preservation** increases this to 94.1%. With low-level sacral resections that spare nerve roots, all patients have been reported to retain normal ambulation. In contrast, bilateral S2 root sacrifice almost universally results in bowel and bladder dysfunction. Even unilateral S2 root preservation yields only 25% normal bladder function, which increases to 39.9% with bilateral preservation. Similarly, preservation of one or both S3 roots leads to 72.7% and 83.3% normal bladder function, respectively. For bowel function, bilateral S3 preservation is associated with 94% normal function, while single S3 root

preservation results in dysfunction in over 70% of cases. Notably, preservation of a single S4 root has been sufficient to maintain normal bowel and bladder function in 100% of patients. Motor outcomes are largely determined by S1 root involvement.

Thus, **sacral nerve root sacrifice** may result in profound motor, urinary, and bowel deficits, substantially affecting quality of life. However, failure to achieve complete resection may lead to local recurrence and eventual deterioration of the same functions. Therefore, optimizing the balance between radical resection and functional preservation remains a central challenge in sacral tumor surgery.

Despite the recognized importance of nerve root preservation, current literature on functional outcomes is limited by **retrospective design**, **small sample sizes**, and **non-standardized outcome metrics**, often using binary descriptors such as “normal” or “abnormal.” While some anatomical classifications—such as the use of the **S2/3 disc as a surgical landmark**—have been proposed, they primarily serve biomechanical or reconstructive purposes and lack correlation with functional outcomes. No prospective study has yet established a reliable, predictive model for post-surgical bladder and bowel function based on resection level or nerve root status.

This study therefore aims to address these limitations by conducting a **prospective observational cohort study** to evaluate postoperative neurological function—particularly motor, bladder, and bowel outcomes—following sacral tumor resection. The findings are expected to provide high-quality evidence to support surgical decision-making and improve individualized treatment planning for patients with sacral tumors.

**Objectives**

The primary objective of this study is to prospectively evaluate the functional outcomes following sacral tumor resection, with a specific focus on postoperative motor function, bowel function, and bladder function. By conducting systematic follow-up assessments, this study aims to investigate the key factors influencing neurological recovery and functional prognosis in patients undergoing sacral surgery.

A particular emphasis is placed on analyzing the relationship between postoperative

functional status and intraoperative variables, including the level of sacral osteotomy and the extent of sacral nerve root sacrifice. Additionally, the study seeks to document changes in neurological function and health-related quality of life over time using validated clinical instruments.

Ultimately, this single-center prospective study is designed to generate high-quality clinical evidence regarding the determinants of postoperative neurological outcomes. The findings are expected to inform surgical decision-making, facilitate the development of more precise operative strategies, and support the implementation of individualized treatment planning for patients with sacral tumors.

**Study Design and Overview**

**1.Overall Study Design and Plan**

This is a **single-center prospective observational study** conducted in patients diagnosed with sacral tumors. The study includes the following phases:

**Patient screening and eligibility confirmation**, based on clinical diagnosis of sacral tumors. Sample size was determined according to retrospective data and statistical power calculations.

**Enrollment** of eligible patients based on predefined inclusion and exclusion criteria, followed by **informed consent**.

**Comprehensive data collection** at multiple time points, including preoperative, intraoperative, and postoperative variables.

**Follow-up assessments** to monitor functional outcomes and complications.

**Data quality control and statistical analysis** of the results.

**2. Study Population**

The study population includes patients with a **confirmed diagnosis of sacral tumor** who are scheduled to undergo or have recently undergone surgical resection.

### 2.1 Inclusion Criteria

- Age between **12 and 80 years**.
- **Pathologically confirmed diagnosis** of a **primary sacral tumor** or **metastatic tumor from other solid malignancies**.
- Ability to understand the study and provision of **written informed consent**.

### 2.2 Exclusion Criteria

- Poor general condition deemed **unfit for surgery**.
- **Pre-existing diseases or surgical history** affecting bowel or bladder function.
- **Missing data** on intraoperative resection level or sacral nerve root management.
- **Pregnancy or lactation**.
- Incomplete follow-up or **loss to follow-up**.

### 2.3 Withdrawal Criteria

Patients may voluntarily withdraw from the study at any time, in accordance with ethical standards.

### 3 Sample Size and Grouping

Based on previous research and the primary endpoint (bowel function score at 12 months), the outcome is treated as a **continuous variable**. Sample size (N) was calculated using the following parameters:

- Significance level (α) = 0.05 → Z<sub>α/2</sub> = 1.96
- Power (1−β) = 0.80 → Z<sub>β</sub> = 0.84
- Standard deviation (σ): derived from prior data
- Expected effect size (d): minimal clinically significant difference

No interventional grouping will be used; analysis will be based on stratification by resection level and nerve preservation.

**4 Study Procedures and Data Collection**

**(1) Preoperative Assessment**

Patients undergo full clinical evaluation, including history-taking, physical examination, and imaging studies. After eligibility is confirmed and informed consent is signed, the following baseline data are collected:

**Demographics and clinical characteristics**: sex, age, BMI, prior treatments, surgical history

**Motor function**: Frankel grading system

**Bowel function**: Cleveland Constipation Score, Wexner Incontinence Score, anorectal manometry, rectal filling test

**Urinary function**: ICIQ-SF, Saito classification, uroflowmetry (Qmax, total volume, voiding time), urodynamics (bladder capacity, pressure, flow), post-void residual, compliance, bladder wall thickness

**Pain**: Visual Analog Scale (VAS)

**Quality of life**: QLQ-C30 questionnaire

**Other**: use of preoperative embolization or balloon occlusion

**(2) Intraoperative Data Collection:** Operative duration and blood loss, Transfusion requirement, Surgical approach and instrumentation, Level of sacral osteotomy, Sacral nerve root ligation or sacrifice, Tumor resection technique, Intraoperative bowel and neurovascular involvement or adhesions, Pelvic floor reconstruction, Intraoperative complications

**(3) Postoperative Follow-Up and Evaluation**:Follow-up assessments will be conducted at **2 weeks**, **3 months**, **6 months**, and **12 months** postoperatively. The following evaluations will be performed:

**Motor function**: Frankel score

**Bowel function**: Cleveland and Wexner scores, rectal pressure and filling tests

**Urinary function**: ICIQ-SF, Saito grading, uroflowmetry, urodynamics, bladder assessments

**Pain**: VAS (recorded as worst pain of the day), NSAID usage standardized; opioid use and corresponding VAS recorded

**Quality of life**: QLQ-C30

**Complications**: including thrombosis, surgical site infection, delayed wound healing, CSF leak, hemorrhage, pulmonary/urinary infections

**Psychosocial and economic impact**

**Disease control**: PFS and OS assessed via imaging (MRI) and symptom evaluation

**Adjuvant therapy**: regimen, dosage, duration, and adverse effects

**(4) Statistical Analysis**

All data will be analyzed using **SPSS software**. Continuous variables will be expressed as mean ± standard deviation and compared using t-tests. Statistical significance is defined as $p < 0.05$.

**Sample Size Calculation and Statistical Analysis**

**Sample Size Estimation**

The primary outcome of this study is the **bladder function score at 12 months postoperatively**, treated as a continuous variable. Sample size was calculated based on the following assumptions:

**Significance level (α)**: 0.05

**Power (1−β)**: 80%

**Estimated standard deviation (σ)**: 0.94, based on previously published data on bladder function scores following sacral tumor resection

**Minimum detectable effect size (d)**: 0.3, representing a clinically meaningful difference in functional outcome

Using the standard formula for comparing two means:77

$$N = \left( \frac{Z_{\alpha/2} + Z_{\beta}}{d/\sigma} \right)^2$$

Considering a 10% attrition rate, the **adjusted sample size** is:86

Given that the study will include **8–10 independent variables** for multivariate modeling, the sample size was also estimated using the rule-of-thumb for linear regression analysis, requiring **10–15 subjects per predictor variable**, resulting in a **minimum sample size of 80–150**.

In addition, using the power analysis formula for linear regression based on the expected coefficient of determination (**$R^2$**), the effect size **$f^2$** is defined as:

$$f^2 = \frac{R^2}{1 - R^2}$$

Assuming a small-to-moderate effect size and 10 predictors, a minimum of **45 subjects per predictor** is needed. To ensure statistical power and account for potential dropouts, the **final target sample size is set at 400 participants**.

**Statistical Analysis Plan**

All data will be analyzed using **SPSS version**. The analysis plan is as follows:

**Descriptive statistics** will be presented as means ±standard deviations for continuous variables and counts with percentages for categorical variables.

**Univariate analysis** will compare functional outcomes (e.g., bladder and bowel scores, motor function) between subgroups using **independent t-tests**, **chi-square tests**, or **Mann–Whitney U tests**, depending on data distribution.

**Multivariate linear regression** will be used to assess the association between surgical factors (e.g., resection level, nerve root sacrifice) and functional outcomes, controlling for covariates.**Repeated measures ANOVA** or **linear mixed models** may be used to assess longitudinal changes in functional scores over time.**Survival outcomes** such as progression-free survival (PFS) and overall survival (OS) will be estimated using **Kaplan–Meier methods** and compared using the **log-rank test**.A **two-sided p-value < 0.05** will be considered statistically significant.

References:

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# Informed Consent Form – Participant Information Sheet

**Dear Mr./Ms. _____,**

We sincerely invite you to participate in the clinical study titled **"Observational Study on Sacral Nerve Function Following Sacral Tumor Resection"**, conducted by the Department of _____.

Before you decide whether to participate, please carefully read this consent form. It contains information about the study's background, purpose, procedures, potential benefits and risks, and the protection of your rights. This document is designed to help you make an informed decision about your participation. If you have any questions, please do not hesitate to consult with the investigators. If you agree to participate, please sign this consent form and retain a copy for your records. This study protocol has been reviewed and approved by the Ethics Committee of Shanghai Changzheng Hospital.

## 1. Why is this study being conducted?

With advancements in surgical techniques and increasing expectations for quality of life, treatment of sacral tumors now emphasizes not only complete tumor resection but also postoperative recovery of neurological function and quality of life. The sacrifice of sacral nerve roots during surgery can severely impact bladder and bowel function, especially over longer survival periods. However, most existing studies only retrospectively describe the impact of nerve root ligation, with limited clinical applicability and predictive value.

This prospective observational study aims to analyze postoperative motor function and neurogenic bladder/bowel outcomes in patients undergoing sacral tumor resection. The goal is to identify key factors influencing functional outcomes and to establish correlations between these outcomes and variables such as the level of sacral osteotomy and nerve root sacrifice. By doing so, we hope to provide higher-level

clinical evidence and offer surgeons a more scientific basis for individualized surgical planning.

**2. Who is eligible to participate?**

**Inclusion criteria:**

1. Patients aged 12–80 years.
2. Diagnosed with primary sacral tumors or metastatic lesions from solid malignancies.
3. Voluntarily consent to participate and sign the informed consent form.

**Exclusion criteria:**

1. Medically unfit for surgery.
2. History of diseases or surgeries that impair bowel or bladder function.
3. Incomplete surgical records regarding sacral osteotomy or nerve root involvement.
4. Pregnancy or lactation.
5. Missing critical follow-up data or lost to follow-up.

**3. How many participants will be enrolled?**

Approximately 400 eligible participants will be enrolled in this study.

**4. How will the study be conducted?**

- **Preoperative Screening:** Medical history, physical examination, and imaging will confirm the diagnosis.
- **Informed Consent:** Eligible and willing participants will sign this form. Declining participation will not affect your treatment.

- **Data Collection:** This is a non-interventional study. We will only collect clinical data at designated timepoints.

**Assessments include:**

**Preoperative:**

- Basic information (age, gender, BMI, surgical history)
- Frankel motor function grading
- Cleveland Constipation Score & Wexner Incontinence Score
- Anorectal manometry & rectal compliance tests
- ICIQ-SF score & Saito urinary dysfunction grade
- Uroflowmetry (Qmax, volume, time), urodynamics (bladder capacity, detrusor pressure), bladder ultrasound (post-void residual, compliance, wall thickness)
- Pain (VAS)
- Quality of life (QLQ-C30)
- History of preoperative embolization or balloon occlusion

**Intraoperative:**

- Surgery duration, blood loss, osteotomy level, surgical approach
- Blood transfusion, instrumentation, nerve root ligation, resection technique
- Pelvic floor reconstruction, intestinal involvement, nerve adhesion

**Postoperative (2W, 3M, 6M, 12M):**

- Frankel motor function
- Bladder and bowel function (as above)
- Pain (VAS; standardized NSAID use; rescue opioid dose and timing)

- QLQ-C30
- Complications: thrombosis, wound infection, dehiscence, hematoma, CSF leak, pneumonia, UTI
- Psychological and economic burden
- Tumor control: PFS, OS (MRI, symptoms), adjuvant therapy (regimen, dose, duration, adverse effects)

**5. Risks and discomforts**

As this is an observational study, there are no additional clinical risks beyond standard care. However, scheduled follow-up assessments may cause minor inconvenience.

**6. Potential benefits**

You may not receive direct benefit. However, participation will help improve future care for sacral tumor patients. Regular follow-up may also support your ongoing recovery and treatment.

**7. Alternatives**

Refusal to participate will not affect your standard care. Your doctor will recommend alternative treatments as appropriate.

**8. Costs**

All follow-up consultations by attending physicians or higher will be provided free of charge for study participants.

**9. Management of injury**

In the unlikely event that study-related harm occurs, medical care will be provided and legal responsibilities fulfilled, unless the harm results from noncompliance with the protocol.

**10. Voluntary participation and withdrawal**

You may decline or withdraw at any time without penalty or loss of benefits. Investigators may also terminate your participation if deemed necessary for your safety or study integrity.

**11. Confidentiality**

Your privacy will be strictly protected. Identifiable information will only be accessible to study investigators, regulatory authorities, and ethics committees as needed. Results may be published without disclosing personal information.

**12. Other**

If any circumstances arise (e.g., protocol deviation, study termination, health risks), the investigator may withdraw you from the study for your safety.

**13. Contact information**

**Principal Investigator: Dr. X. Phone:**

For rights-related concerns, please contact the **Ethics Committee of Hospital**