Information for the Participant and Informed Consent Form for Participation in the Research Experiment

This Participant Information and Informed Consent Form for Participation in the Study is addressed to men and women with metastatic spinal disease.

Title of the Research Experiment: "Application of a carbon pedicle stabilization system in the surgical treatment of metastatic spinal tumors and stereotactic radiotherapy planning – a prospective, randomized study"

Name and Surname of the Principal Investigator: Kamil Krystkiewicz, MD, PhD

Center Details:

Sponsor Name: Copernicus Memorial Hospital in Łódź, Comprehensive Cancer and Traumatology Center, Pabianicka Str. 62, 93-513 Łódź

Name and Surname of the Research Experiment Participant: .....

This informed consent form consists of two parts:

- **Information for the Participant (containing information about the research experiment),**
- **Statement of consent to participate in the study (to be signed if you agree to participate in the study) along with the attachments.**

You will receive a complete copy of the informed consent form.

PART I: INFORMATION FOR THE RESEARCH EXPERIMENT PARTICIPANT

Introduction

Dear Madam / Sir, Wherever the term "Study" written with a capital letter is used in this document, it refers to the research experiment.

Please read the detailed information below regarding the objectives and rules of the research in which we would like to propose your participation. Your participation in this Study is entirely voluntary. Regardless of your decision, the hospital will continue to provide you with services—nothing in this regard will change.

You have the right to withdraw from the experiment at any stage without any consequences. Withdrawal from participation in the experiment does not affect the level and scope of health services provided to you.

This form consists of two parts:

- Participant Information (containing information about the research experiment);

- Statement of Consent to Participate in the Study (to be signed if you agree to participate in the Study) along with an appendix in the form of consent to process the research experiment participant's personal data.

If the document contains terms you do not understand, the doctor will explain all incomprehensible terms to you. If any questions arise later, you will be able to ask the Investigator or a member of the research team.

Confidentiality of personal data will be maintained. Named personal data will be excluded from any Study report or scientific publication.

Every Study Participant is covered by insurance against harm arising from participation in the Study. The policy number covering the experiment's insurance will be provided by the Investigator upon request at any time.

Biobanking

Every Study Participant will have the opportunity to join a scientific program conducted by the Medical Research Agency (ABM) involving the collection and biobanking of biological material. For this purpose, you will receive an additional informed consent form with all necessary information prepared by the ABM. The entity responsible for biobanking the biological material is the ABM.

Purpose of the Research Experiment

Metastases of neoplastic disease to the spine pose a serious clinical problem in oncology. Bones are the third most common organ where metastases are localized, and the spine is the skeletal element where they are most frequently located. The natural history of metastatic spinal disease is the remodeling of the normal bone structure. These changes increase the susceptibility of the affected bony elements of the spine to fractures, even under slight load. Surgical treatment is undertaken in cases of spinal cord compression, instability, spinal deformity, or pain resistant to radiotherapy.

The standard of treatment in most cases is spinal instrumentation using screws inserted into the vertebral bodies, connected by a rod secured with nuts. The basic material from which the implants are made is titanium alloy. Unfortunately, this material causes image distortion in computed tomography (CT) or magnetic resonance imaging (MRI). This hinders further radiotherapy planning and determination of the optimal dose that would spare healthy tissues, as well as postoperative check-ups aimed at assessing local recurrence.

As a solution to this problem, we see the application of X-ray translucent implants based on carbon fibers, which do not cause the image distortion typical of titanium implants. According to current knowledge, both stabilization methods are biomechanically equivalent. However, the use of carbon systems offers additional benefits for the patient in the form of easier and more effective planning of subsequent treatment (radiotherapy) and more efficient diagnostics of recurrence or disease progression.

In the Study, you will be randomly assigned to one of the Study arms (groups):
- Arm I: Pedicle stabilization with a titanium system, followed by stereotactic spinal radiotherapy at a dose of 5×5 Gy (25 Gy total dose).
- Arm II: Pedicle stabilization with a translucent composite system made of carbon fibers and PEEK, followed by stereotactic spinal radiotherapy at a dose of 5×5 Gy (25 Gy total dose).
- Arm III: Pedicle stabilization with a titanium system, followed by stereotactic spinal radiotherapy at a dose of 5×5 Gy (25 Gy total dose) as the first stage of treatment, and pedicle stabilization with a titanium system in the second stage of treatment.

Obligations Related to Participation in the Research Experiment

The Participant is obliged to:attend visits according to the planned visit schedule, undergo all procedures specified in the Study protocol. All medical procedures in the conducted Study will be performed with the Participant's consent. Refusal by the Participant to undergo a medical procedure specified in the Study protocol will be tantamount to exclusion from further participation in the Study. The Participant is obliged to inform the research team about their well-being and observed symptoms. The Participant may not participate in any other research experiment during the Study.

It is important that when making the decision to participate in the Study, you accept its course and purpose and are willing to participate in it until its completion or until you withdraw your consent to participate in the Study. Until you complete and sign the informed consent form below, none of the Study procedures can be performed on you.

Selection and Number of Participants and Conditions for Participation in the Research Experiment

A total of 226 Participants will take part in the Study. If, during the research experiment, it turns out that a potential Study Participant experiences events/factors preventing further participation in the Study or the risk to the Participant associated with participation in the Study increases, the Principal Investigator may exclude the Participant from the Study, despite earlier qualification.

Voluntary Participation in the Research Experiment

Your participation in this Study is entirely voluntary. The decision to participate is yours. You have the right to withdraw from participation in the experiment at any stage without any consequences. Withdrawal from participation in the experiment does not affect the level and scope of healthcare services provided to you.

Types of Research Interventions

The Study will involve randomly assigning you to one of the three Study arms (groups of Study Participants), performing radiotherapy, and implementing the treatment strategy.

Before starting the Study, a series of medical procedures listed below, which are necessary for conducting the research experiment, will be performed on you. Various management strategies are used in metastatic spinal disease. One of them is a surgical intervention involving the removal of the tumor infiltration causing compression of the neural structures and the restoration of spinal stability using implant systems embedded in the bone. Another element of treatment involves various radiotherapy techniques. Within the scope of the study, the effectiveness of various composite materials used in stabilization systems in the planning and effectiveness of radiotherapy for metastatic spinal tumors will be assessed. Additionally, during the study, the patient's blood and tumor tissue material will be collected to assess the expression of genes involved in the process of bone formation and bone tissue atrophy.

Procedures and Protocol of the Research Experiment

Description of the Process and Duration of the Research Experiment

Your treatment process will proceed in accordance with the current recommendations developed by the Polish Society of Spinal Surgery.

After your admission to the Neurosurgery Department at the Center, further management and care will proceed according to the following plan:

- A nursing interview will be conducted with you, and you will be familiarized with the structure and topography of the Department.
- Blood will be drawn from you for routine laboratory tests (complete blood count, coagulogram, ionogram, urea, creatinine, ESR, inflammatory parameters, total protein, albumins, HBs antigen, antibodies against HCV, blood type, hormonal tests depending on underlying diseases). The amount of blood drawn depends on the number of tests and is usually a few milliliters.

- After the blood type is determined, blood will be drawn again from you to secure and cross-match blood products for the procedure.
- Depending on the needs, an imaging study will be performed on you—spinal CT, spinal MRI, functional X-ray, or scoliosis X-ray (postural X-ray of the entire spine). The purpose and interpretation of each test, if ordered, will be discussed with you by the neurosurgeon.

The doctor will discuss the procedure, method of treatment, possible complications, their treatment, and prevention with you.

- If necessary, embolization of the tumor will be performed on you by interventional radiologists on the order of the neurosurgeon. This procedure is used when the tumor is highly vascularized to reduce the risk of intraoperative bleeding. This procedure is performed in the vascular laboratory under anxiolysis and sedation, i.e., partial sleep.
- In the following days, surgical treatment is planned—surgery under general anesthesia. During the surgical treatment, a 5 ml blood sample will be taken from you to assess molecular markers of bone turnover, and fragments of tumor tissue will be routinely collected for histopathological examination. After the procedure, you will be placed under observation, which is conducted by the anesthesiology team in the Postoperative Room. After observation and in the absence of alarming symptoms, you will be transported back to the Neurosurgery Department at the Center, where you will continue to be monitored by the Department staff.
- Within the first postoperative day, a CT scan will be performed on you to assess the implant placement. In the case of correct implant positioning, internal rehabilitation will be planned for you, aimed at improving and initiating functioning within one day after the procedure. If implant repositioning is necessary, you will be informed about another surgical procedure under general anesthesia aimed at inserting the implants in a new location.
- In the following postoperative days, your blood count will be routinely assessed to determine the need for blood product transfusion. The schedule for other postoperative tests depends on the clinical course of your case.
- Dressing changes and assessment of the wound and pain will be performed daily.

On the day of discharge, the attending physician will talk to you about recommendations and further postoperative management.

After meeting the criteria for inclusion in the research experiment, you will be randomly assigned to one of the three groups described in the previous part of the information brochure. The term ‘randomly assigned’ means that the treatment scheme will be assigned to you by chance, based on a coin toss or drawing lots from a hat. You have the same chance of drawing any of the three possible Study arms (groups of Study Participants).

After assignment to one of the groups, the doctor will talk to you about treatment options and its continuation.

This Study will be conducted for a total of 5 years. After the completion of hospital treatment, a follow-up visit will take place at the Neurosurgery Clinic at the Center within one month. During this visit, your health condition, the state of the postoperative wound, and pain assessment will be evaluated. In addition, a neurological examination will assess your neurological status. A control spinal MRI with contrast will be planned.

Subsequently, visits and tests will take place regularly every 3 months. At each visit, the Investigator will inform you about the results of previous tests and further planned treatment. In case information is obtained that could influence your decision to continue participation in the study, you will have the opportunity to consent to the continuation of participation in the Study or to withdraw from the study.

Unknown Procedures

Due to the uncertainty of whether carbon implants offer an advantage over classic titanium implants in the group of patients with oncological spinal disease, they must be compared. The recognized scientific methods that allow for a reliable comparison of treatment results in both groups of patients involve dividing the subjects into different groups. This is done randomly, and the process is called randomization. As a result, the patient is assigned to the appropriate group in the study, without the possibility of influencing this decision by either the Investigator or the Participant.

At this stage, it should be stated that each group receives the best possible therapy recognized in the treatment process of oncological spinal disease, and the patient may withdraw from participation in the study at any stage. The purpose of randomization is to exclude a phenomenon that would assign patients to study groups in a non-random, preferential manner. Such a phenomenon is unfavorable and can falsify the results of the scientific study. The remaining procedures used as part of the study are standard for the treatment process.

After the completion of the hospital treatment process, your further treatment will be conducted on an outpatient basis during visits to the Center's Neurosurgery Clinic. The study plan assumes visits every 3 months, during which your condition will be assessed clinically and radiologically by a neurosurgery specialist.

In case of health problems after discharge from the hospital, you will be able to receive medical assistance at the Center's Emergency Room or telephone advice at the number _____ (the number of the doctor's room in the Neurosurgery Department at the Center). If contact with the Investigators is necessary, the staff will discuss your clinical problem by phone and arrange a follow-up visit in the outpatient clinic or the Department if a physical examination is necessary. If re-hospitalization is required, you will be treated in the Neurosurgery Department of the Center according to the best state of knowledge.

In the event of adverse drug reactions that are routinely used in treatment, medical and nursing actions consistent with the current state of medical knowledge will be applied. If further surgical treatment is necessary in the future, you have the right and will be treated in accordance with the study results.

During the study, with your consent, biological material (blood, tumor biopsies) will be biobanked. The biological material will be used exclusively for scientific purposes and will not be used for commercial purposes. As a Study Participant, you have the right to view the results of the scientific study while maintaining the anonymity and privacy of the Participants.

Risk

Oncological procedures within the spine are high-risk procedures. Their performance is associated with the possibility of complications related to the surgical activity—neurological deficits (muscle weakness, impaired touch sensation, temperature, gait disturbances), wound healing problems, or hospital care complications—pneumonia, thrombosis, pulmonary embolism.

All procedures used (surgical treatment, radiotherapy) are standard, typical for the treatment process of oncological spinal disease. Participation in the Study does not involve additional risk for you. The only difference between the evaluated groups is the type of implant used, or rather the material it is made of. Both products are commercially available and registered for the treatment of spinal pathologies. Each of them exhibits good biocompatibility, and no complications related to the material used have been demonstrated, except for hypersensitivities, i.e., an allergic reaction to the given material.

If anything raises your doubts, you should inform the doctor and ask questions at every stage of the study. A team of trained doctors and nurses will supervise the entire course of the study and your health and safety.

In the event of a sudden serious deterioration of your health or well-being related to participation in the Study, appropriate treatment will be implemented. The Center is equipped with the necessary equipment needed to provide emergency assistance, if necessary. It is important that any previously unexperienced, alarming symptoms, if they occur, are immediately reported to the doctor or nurse by you.

Note: Concealment or providing false information about your health status during the qualification procedures may cause serious health complications during the study. All adverse events (any unexpected medical event) will be recorded, and medical personnel will take necessary actions aimed at reducing their negative consequences.

Benefits

The primary benefit of participating in the Study for you is the regular outpatient visits arranged by the Staff. The program includes visits to the Neurosurgery Clinic every 3 months, including clinical and radiological assessment of your spine.

Remuneration / Reimbursement of Costs

You will not incur any additional costs due to participation in this Study. You are not expected to pay for the procedures or tests required as part of this Study. You will be responsible for bearing the costs of your standard medical care, including procedures and medications not covered by the Study that your Study physician or general practitioner requires as part of standard medical care. You will not receive any compensation for participating in this research experiment.

Data Confidentiality

Your personal data collected for the purpose of the conducted Study and processed by the Research Team will be secured and protected against unauthorized access. The information collected as part of the Study will be confidential, accessible only to the Investigators and the Research Team. Data enabling the identification of Participants will not be published anywhere.

Sharing the Results of the Experiment, Including the Provision of a Summary of the Research Experiment Results

After the completion of the Study, the results will be scientifically and statistically processed. The results of the experiment, containing conclusions and statistical summaries (without Participants' personal data), will be published in medical journals and at scientific conferences. Data allowing the identification of the Participant's identity will not be published. Participants will not be informed about the Study results.

Right to Refuse or Withdraw Participation in the Research Experiment

You do not have to participate in the Study if you do not want to. Refusal to participate will not affect your current treatment conducted at the Research Center in any way. You may stop participating in the Study at any time, and you will not lose the benefits to which you are entitled as a patient. Such a decision will not affect the treatment received at the Center in any way.

Source of Study Funding

The Study will be financed from funds from a grant from the Medical Research Agency.

Contact Opportunities

If you have any questions, you can ask them now or later, even after the Study has started and at any time during its duration. If you wish to ask something later, you can contact:

Investigating Physician at the Center	
Phone Number	

In the event of any additional information about the research experiment that may affect your willingness to continue participation in the Study, the Investigator (the doctor conducting the Study) is obliged to immediately provide it to the Participant.

The design of this research experiment has been verified by the Bioethics Committee at the Medical University of Łódź and has received a positive opinion. The Bioethics Committee is a group of people whose task is to protect research Participants from harm/detriment that may be associated with the Study.

If you would like to obtain further information about the Bioethics Committee, please contact the Bioethics Committee Secretariat by phone at: (42) 271 11 23 or by email at: komisja.bioetyczna@iczmp.edu.pl.

In the event of any adverse symptoms, depending on the clinical symptoms, please contact the Emergency Notification Center (CPR) by phone at 112 or report to the nearest Emergency Department (SOR).

PART II: Statement of Voluntary Consent to Participate in the Study

Statement of the Person Consenting to Participate in the Study

I have read or have had the above information read to me. I have had the opportunity to ask questions about this information and have received satisfactory answers to all my questions. I voluntarily give / do not give consent (strike out as appropriate) to participate in this study as a Participant. I am aware that by consenting to participate in the Study, I simultaneously consent to the disclosure of my medical records to the Investigator and the Research Team to the extent necessary for the conducted Study.

I give consent: **YES** **NO** *(strike out as appropriate)*

Participant's Name and Surname (in block letters) _____

Participant's Signature _____

Signature Date _____

Statement of the Investigator / Person Obtaining Consent

I declare that I have discussed the presented study with the potential Study Participant using understandable, possibly simple language, and provided explanations regarding the essence and significance of the Study. I confirm that the Participant had the opportunity to ask questions about the Study, and I answered the questions asked by the Participant truthfully and to the best of my ability. I confirm that the Participant was not coerced into giving consent, and the consent was given freely and voluntarily.

A copy of this informed consent form was handed to the Participant.

Name and Surname of the Investigator / Person Obtaining Consent (in block letters) _____

Investigator's / Person's Obtaining Concent Signature _____

Signature Date _____

INFORMATION CLAUSE CONCERNING THE PROCESSING OF PERSONAL DATA
of the Research Experiment Participant

The Information Clause concerning the processing of personal data of the Research Experiment Participant, hereinafter referred to as the Study.

To ensure transparency in the processing of personal data in connection with participation in the scientific Study, we would like to inform you that:

Data Administrator Details

- The Administrator of the personal data of the Study Participant is Copernicus Memorial Hospital, Comprehensive Cancer and Traumatology Center in Łódź, hereinafter referred to as the Hospital.
- Hospital contact details: 93-513 Łódź, Pabianicka Str. 62, tel.: +48 42 689 5000, e-mail: szpital@kopernik.lodz.pl.
- If you have questions about data processing, please address them by post to the Hospital address or by email to the Data Protection Officer, Mr. Tomasz Zdzienicki (iod@kopernik.lodz.pl).

Purpose of Data Processing

The Study Participant's data will be processed for the purpose of:
- Realization of the scientific Study entitled: "Application of a carbon pedicle stabilization system in the surgical treatment of metastatic spinal tumors and stereotactic radiotherapy planning – a prospective, randomized study".

Legal Basis for Data Processing

The personal data of the Study Participant are processed with the Participant's consent based on:

- Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation), hereinafter referred to as the GDPR,
- the Act of 5 December 1996 on the profession of doctor and dentist,
- the Act of 14 July 1983 on the national archival resource and archives.

Sources of Data Acquisition

The Hospital may obtain the personal data of the Study Participant:

- directly from the Participant,
- from other healthcare entities that obtain appropriate consent from the Participant to participate in the Study.

Data Recipients

Recipients of the Participant's data may include:

- entities authorized to obtain them on the basis of legal provisions (courts, police, authorities conducting proceedings and controls),
- entities providing services for the Hospital:
  - legal,
  - support for IT systems used by the Administrator.

Storage Period

The personal data of the Study Participant contained in the Study files will be processed for a period of 20 years from the end of the calendar year in which the final resolution on the issuance of an opinion on the Study by the Bioethics Committee was issued. The data contained in the scientific Study files cannot be deleted before the expiry of the above-mentioned period. The Study documentation will be archived in accordance with art. 5 of the Act of 14 July 1983 on the national archival resource and archives.

Rights of Individuals

In connection with the processing of personal data, the Participant can:

- obtain access to the content of their data,
- demand their rectification,
- demand the restriction of processing or deletion of certain data if the Study documentation storage period has expired,
- object to processing,
- demand all information concerning the processing of the Participant's data.

If you believe that the processing of personal data violates the provisions of the GDPR, you have the right to lodge a complaint with the supervisory authority, i.e.: to the President of the Personal Data Protection Office, 00-193 Warsaw, ul. Stawki 2.

Consequences of Not Providing Data

Participation in the scientific Study is voluntary. If the Participant agrees to participate in the Study, it is necessary to obtain their personal data contained, among others, in the medical records. Refusal to provide the personal data of the Study Participant will result in the exclusion of the Participant from participation in the Study. Refusal to participate in the scientific Study does not affect the process of providing medical assistance to the patient.

Automated Decision-Making

The Participant's data will not be processed in an automated manner, including in the form of profiling.

Transfer of Data to a Third Country

We do not plan to transfer the Participant's data to third countries that do not guarantee an adequate level of data protection.

Consent to the Disclosure of Medical Records for Scientific Purposes

If the Participant agrees to participate in the scientific Study, they thereby consent to the disclosure of their medical records to the Research Team to the extent necessary for the conduct of the Study.

Below we provide the exact legal basis for the processing of the Study Participant's data:

Action / Scope of Data	**Additional Information**
Scope of processed data:	Range of data: - identification data contained in medical records, - special categories of data: health information contained in the medical records used for the purposes of the Study. Range of medical records used in the scientific Study: - descriptions from diagnostic imaging (CT, MRI), - histopathological test results.
Acquisition and processing of personal data for the purpose of the Study	art. 6 sec. 1 lit. c) and art. 9 sec. 2 lit. j) of the GDPR in connection with: - art. 25 of the Act of 5 December 1996 on the professions of doctor and dentist
Defense against claims	art. 6 sec. 1 lit. f) and art. 9 sec. 2 lit. f) of the GDPR in connection
Archiving of Study files	art. 6 sec. 1 lit. c) and art. 9 sec. 2 lit. j) of the GDPR in connection with: - art. 29 point 21. of the Act of 5 December 1996 on the professions of doctor and dentist, - art. 5 of the Act of 14 July 1983 on the national archival resource and archives

Participant's Name and Surname (in block letters) _____

Participant's Signature _____

Date of Signature _____