Exploratory Study on Safety of PEEK Knee Prosthesis

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Informed consent form

Project Name: Prospective, single-arm, single-center exploratory study on safety of PEEK knee prosthesis

Protocol version: V3.1 date:2021/06/23

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Dear patient:

We invite you to participate in a prospective, single-arm, single-center exploratory study on the safety of PEEK knee prostheses approved by Renji Hospital, Shanghai Jiaotong University School of Medicine. This research will be carried out in Renji Hospital affiliated to Shanghai Jiaotong University School of Medicine, and 10 subjects are expected to participate voluntarily. This study has been reviewed and approved by the ethics committee of Renji Hospital affiliated to Shanghai Jiaotong University School of Medicine.

This informed consent form will provide you some information to help you decide whether to participate in this clinical study. Please rest assured that whether or not you participate in this study is completely voluntary, and your decision will not affect your normal diagnosis and treatment rights in this hospital. If you choose to participate in this research, our research team will try our best to ensure your safety and rights during the research process!

Please read this informed consent form carefully. If you have any questions, please ask the investigator responsible for explaining the informed consent form for you.

Research Background

In 2016, the chief scientist Professor Wang You applied for the "13th Five-Year" National Key Research and Development Program (2016YFC1101802)-R&D and industrialization of wear-resistant, antibacterial, and biologically active fixed PEEK artificial joints (PEEK is short for polyetheretherketone).

After several years of hard work, the project has achieved substantial results. The results of the study show that the inflammatory response of the same number of PEEK particles is equivalent to that of HXLPE (highly cross-linked poly-ultra-high molecular weight ethylene) and better than metal joints (cobalt-chromium-molybdenum). On the basis of biological research, we also performed a goat total knee replacement experiment, 48-week imaging observation results showed that there was no prosthesis fracture, fracture around the prosthesis, insert prolapse, prosthesis loosening or sinking, etc., proving that the prosthesis is safe in the animal .

The Shanghai Biomaterials Research and Testing Center (with qualifications recognized by the National Food and Drug Administration) was entrusted to conduct a biocompatibility test on the final product of PEEK knee prosthesis in accordance with the requirements of national standards, and the test results met the requirements.

We entrusted a German company with international standards accredited qualifications to carry out 5 million and 10 million wear tests in accordance with international standards. The wear amount of the test is lower than that of similar metal knee joint prostheses. It is expected to prolong product life.

We entrusted Tianjin Medical Device Quality Supervision and Inspection Center (a subordinate unit of the State Food and Drug Administration) to inspect all product performance

and obtain a product qualification report.

We commissioned a German laboratory with international standards accredited qualifications to carry out a magnetic resonance compatibility test on the PEEK knee joint prosthesis in accordance with the standard requirements. The test results show that it is safe under the prescribed inspection mode.

Therefore, PEEK knee prosthesis is safe and can be used in this clinical study.

Research purposes

Evaluate the safety of PEEK knee prosthesis for total knee replacement.

Research object

Patients with osteoarthritis who have severe knee joint pain, instability, and deformity, severely hindered activities of daily living, and who have undergone conservative treatment ineffective or ineffective.

Subject

Inclusion Criteria:

- Male and female subjects aged 55 years of age or older and less than 74 years of age, younger subjects should have urgent need for surgery.
- Subjects skeletal maturity.
- Subjects appropriate for total knee replacement, such as noninflammatory degenerative joint diseases (such as osteoarthritis, traumatic arthritis, or ischemic necrosis); Inflammatory degenerative joint diseases (including rheumatoid arthritis); Correction of functional deformity.
- The diseased side knee appropriate for primary total knee arthroplasty .
- Subjects or guardian is willing and able to sign the informed consent form .

Exclusion Criteria:

- Subjects with knee instability or abnormal gait caused by neuromuscular insufficiency.
- Subjects with bilateral knee joint disease who are expected to require replacement of both knees during the course of the study (i.e., within the next 12 months) .
- Alcoholics, drug addicts and drug abusers.
- Subjects with severe diabetes (fasting blood glucose > 10mmol/L)
- Body Mass Index, BMI>35.
- Female subjects who are pregnant or lactating.
- Subjects have disease limited their participation in the investigation or have an existing condition that would compromise their participation and follow-up in this clinical investigation.
- In the month before inclusion, subjects who participated in clinical studies of other drugs, biological agents or medical devices and failed to meet the main research endpoints.
- Other conditions, in the opinion of the Investigator, are inappropriate for participation in this clinical investigation.

Elimination criteria:

Including but not limited to the following situations:

- Subjects draw by themselves for any reason. Subjects are unwilling or unable to continue the clinical research, and propose to the investigator to withdraw from the clinical research, requesting the termination of participation in the clinical research;
- Subjects did not clearly propose to withdraw from the study, but no longer received treatment and examination and was lost to follow-up;
- Subjects have an allergic reaction or/severe adverse event, etc., and the investigator judges that the subject should terminate the clinical research;
- Subjects suffer from other complications that are not suitable for continuing clinical research ;
- Subjects have poor compliances .

Exit criteria:

- Subjects withdrew informed consent.
- Serious violation of clinical research protocols.
- Women who became pregnant during the clinical research.
- Subjects death.
- Subjects who Lost to follow-up
- Principal InvestigatorRequest termination of clinical research.

Research process

This research will verify the safety of the research equipment through clinical research of new medical technology, and plan to complete the clinical study of 10 subjects. And the research lasts for 12 months after surgery, and you need to cooperate with the following research content:

(1) Follow up 1--7 days ~ before surgery(screening period):

The following preoperative data must be collected within 7 days prior to surgery (unless otherwise stated): ①Demographic data of subjects (gender, date of birth, ethnicity, height, weight, etc.); ②Vital signs (temperature, respiration, heart rate, blood pressure); ③Physical check;④Medical history: osteoporosis, malnutrition (calcium, phosphorus, protein, iron), anemia, hormone deficiency (growth hormone, parathyroid hormone, etc.), radiotherapy, surgery, history of diabetes, hypertension, coronary heart disease, lung function, immunological diseases, etc;⑤Enrollment screening;⑥Laboratory tests: blood routine, liver and kidney function, urine routine, erythrocyte sedimentation rate, C-reactive protein, coagulation function, D-dimer, hepatitis B five tests; ⑦ electrocardiogram⑧ X-ray examination; ⑨Magnetic resonance examination;⑩Knee function score;

（2） Follow up 2, (surgery day）:

① vital signs detection (temperature, respiration, heart rate, blood pressure); ② Checking enrollment screening; ③surgery; ④Selection of knee prosthesis size; ⑤Combination of drug use; ⑥Device defects; ⑦Record complications;⑧Adverse events/serious adverse events were recorded.

（3） Follow up 3(after surgery/before discharge):

Subjects may be discharged when clinically stable, in the opinion of the Investigator. The following assessments must be completed after surgery: ① vital signs detection

(temperature, respiration, heart rate, blood pressure); ② Checking enrollment screening; ③surgery; ④Selection of knee prosthesis size; ⑤Combination of drug use; ⑥Device defects; ⑦Record complications;⑧Adverse events/serious adverse events were recorded.

（4） Follow up 4(3 months after surgery):

Subjects can participate within the specified time window of ±14 days. In addition to completing the following assessment, staff should also answer all relevant questions raised by subjects.

① Laboratory tests: including blood routine, liver and kidney function, erythrocyte sedimentation rate, C-reactive protein; ② X-ray examination; Magnetic resonance examination; ④ Knee function score; (5) Combination of drug use; ⑥ Device defects; ⑦ Record complications; (8) Adverse events/serious adverse events were recorded.

（5） Follow up 5(6 months after surgery):

① Knee function score; ② Combination of drug use;

（6） Follow up 6(12 months after surgery):

① Laboratory tests: including blood routine, liver and kidney function, erythrocyte sedimentation rate, C-reactive protein; ② X-ray examination; Magnetic resonance examination; ④ thin slice CT; ⑤ Knee function score; ⑥ Combination of drug use; ⑦ Device defects; ⑧to record the complications; ⑨ Record adverse events/serious adverse events

Since this study is an exploratory study, all subjects will be retrospectively studied one year after the end of the study.

Replacement therapy

If you do not participate in this study, you may choose other commercially available knee prostheses for surgical treatment, or choose any other reasonable treatment method recommended by the investigator.

If you participate in this clinical study, if you withdraw from the study for any reason, the investigator may perform revision surgery using the prosthetic joint that is currently routinely used.

Possible risks and discomfort

（1） the pain; (2) Periprosthesis infection, acute postoperative wound infection, secondary deep wound infection and/or mild synovitis; (3) Wound hematoma, thromboembolic diseases, including lower extremity deep vein thrombosis, pulmonary thrombosis or myocardial infarction; (4) Skin necrosis or wound healing disorder; (5) vascular and nerve damage, temporary or permanent nerve damage may lead to pain or numbness of the limb; The postoperative instability of the artificial knee joint, dislocation, subluxation, excessive rotation, flexion contracture, reduced mobility, component loosening, abnormal stress concentration and allograft bone; There is heterotopic ossification, inflammation of ossification, and calcification or ossification around the joint that may interfere with joint movement. Calcification around the joint may lead to reduced range of motion; (8) the prosthesis loosened, worn or fractured; （9） Phase wear; （10） Bone resorption and osteolysis; （ 11 ） Fracture around the prosthesis; Patellar fracture,

patellar prosthesis loosening, fracture of knee extension device, other patellar impingement sign, etc. (12) Anatomical structure alignment defect, including knee alignment defect height reduction, unequal length of limbs, etc.; （13）Implantation of allogeneic materials in tissues may lead to histological responses of macrophages and fibroblasts; （14）Be-cement implantation syndrome; (15) Other complications include pressure ulcers, pulmonary infection, urinary tract infection, gastrointestinal bleeding, fat embolism syndrome, etc.

In view of the above risks, researchers will do a good job of prevention and emergency treatment. If the above or any discomfort occurs, you need to inform the researcher in the first time, and the investigator will give you relevant treatment according to your situation.

The expected benefit

If you are known to be allergic to metals, have severe osteoarthritis of the knee, and have strong indications and desire for surgery, it is very risky to undergo surgery under previous technical conditions. Once a metal allergy occurs, the consequences are unbearable. The choice of PEEK knee prosthesis completely avoids the risk of metal allergy, and can be as comfortable as ordinary people to accept surgery.

If you have a primary knee replacement and develop a metal allergy, suffer from chronic rashes, itching, knee pain and swelling, and limited function, consider a knee replacement a disaster. The PEEK knee prosthesis was selected for revision to completely remove the allergen, providing the possibility of a complete cure and relief of metal ion allergy.

If you need to have repeated MRI examination for a long time due to some diseases, the choice of PEEK knee prosthetic can be used for MRI examination under any magnetic field intensity without any concern.

Free treatment

The expenses incurred in this study are funded by the National Key Research and Development Program, so you do not need to pay the expenses related to the research.

The compensation

If you participate in this study and come to our hospital for follow-up 3 months and 12 months after the surgery, you will be given a transportation subsidy of RMB 500 for each follow-up, which will be paid in cash in a lump sum after the study.

Compensation

If any adverse event occurs during this clinical study, your attending physician will actively implement treatment.

This clinical study provides clinical research liability insurance for all subjects participating in the study. In the event of infection, loosening, fracture of the prosthesis, fractures and other reasons related to the device factors after the operation, the insurance company and the participating units of the scientific research project will jointly bear the cost of a revision and hospitalization. If the subject is injured in a traffic accident due to participating in this clinical research study, the insurance company will be responsible for it.

Attentions before, during and after the study

The function of the knee prosthesis is inherently inferior to that of the natural joint. Compared with the function before the operation, people will get improvement in the joint function with the artificial joint. Total knee replacement is a operation that will take you several months to recover. In order to discover possible problems related to the operation through related inspection items in time after the operation, please attend each visit on time. The service life of the knee prosthesis is determined by your weight and the force exerted on the joint, so please avoid excessive load activities and exercises after the operation, and avoid twisting the knee joint, including running, jumping, race walking and other behaviors, avoiding falling, bumps and other conditions in the daily, these factors may cause wear and tear of the prosthesis and infection, and cause joint loosening and other complications. If the prosthesis becomes loose after the operation, you may need corrective surgery. If corrective surgery is performed, the mobility and flexibility of the joint may not be restored in some cases, and the second repair surgery usually restores the knee joint function, and the effect is not as good as the first operation. Therefore, you should avoid excessive exercise post-operation, and you should have regular medical follow-up examinations. If you have the following symptoms post-operation, for example increased knee pain; pain or swelling in the calf or thigh; abnormal redness, heat or pus at the incision site; difficulty breathing or chest pain; fever over 38 ℃ etc, please go to the hospital for examination.

Confidentiality

Your personal information for participating in the research is confidential. Your name and identity will will be kept confidential and not appear in future reports or research-related publications. If it is necessary, inspectors, monitors, sponsors, management departments of company/agency supporting the project, and ethics committees can directly access your personal data in accordance with the prescribed procedures. You or your legal representative authorizes such access when signing the written informed consent.

Regaining the informed consent

①Changes in research plan, scope, and content;②Other changes during the research

Voluntary

You can decide not to participate in this study, or notify the investigator to withdraw from the study at any time. Your data will not be included in the study results, and any of your medical treatment and rights will not be affected.

If you need other treatments, do not follow the study plan, or have a study-related injury or for any other reason, the study physician can terminate you participation in this study.

You can learn about the information and research progress related to this research at any time. If new safety information related to this research occurs, we will notify you in time.

Subject's obligations

As a research subject, you have the following responsibilities: provide the true information about your medical history and current physical condition; tell the research physician about any discomforts you have experienced during the research; you are not allowed to take restricted drugs, food etc. (details list of the restricted drugs and foods); tell the research physician whether you have participated or are participating in other studies recently.

Contact

If you have questions related to this study, any discomfort or injury during the study, or questions about the rights of participants in this study, you can contact your physician _____ through _____.

If you have any questions or complaints to the researchers during the research process, you can contact the Ethics Committee of Renji Hospital Affiliated to Shanghai Jiaotong University School of Medicine at 021-68383364.

Subject Signature Page

Subject Consent Statement:

☐ I have read the above introduction about this study, and the research doctor has explained the research content to me in detail. Before signing the informed consent, I have no more questions about the study to consult. On this basis, I voluntarily participate in the clinical study described in this paper, and my decision is based on a full understanding of the risks and benefits that may arise from participating in this study. In addition, the researchers did not use deceit, inducement or coercion to force me to agree to participate in the study, and I know that I can unconditionally withdraw from the study at any stage.

☐ Due to the subject's incapacity or limited capacity, this informed consent shall be signed by his guardian or legal representative.

Subject's Signature:_____ Agent 's Signature : _____
Signature Date:_____ Signature Date: _____
Contact Information:_____ Contact Information: _____

---------Subjects who are unable to read the text (e.g., illiterate, visually impaired) will need to sign as a fair witness----------
Signature of Fair Witness: _____

Signature Date: _____

Contact Information: _____

The researchers stated:

I confirm that I have explained to the patient the details of this study, in particular the risks and benefits that may arise from participating in this study.

Investigator signature: _____
signature date :_____
Contact Information :_____

Note: This page is the subject's signature page, and the study physician will explain the study content and relevant information to the subject in detail. Informed consent shall be signed by the subject/guardian/legal representative and the study physician who will explain the study for the subject. If the subject has any questions about the study content, the investigator should immediately explain them in detail to the subject. After signing, the investigator and the subject shall each keep an original copy.