Medical Ethics Committee of West China Hospital of stomatology

Informed consent for scientific research involving human samples

Name and model specification of medical instrument used in the study: personalized titanium alloy bone plate

Project name: Application of 3D printed personalized titanium plates in orthognathic surgery A multicenter, prospective, randomized controlled trial.

Project Number: LCYJ2020-YF-1

Solution Version: LCYJ2020-YF-1-V02

Informed consent Version number: V03

Clinical trial institution：

- West China Hospital of Stomatology, Sichuan University
- Guiyang Hospital of Stomatology
- Southern Medical University Hospital of Stomatology (Guangdong Stomatology Hospital)
- Hospital of Stomatology, Jilin University

Informed Consent

Personal reading materials

Dear Participant:

You are invited to participate in a multicenter, prospective, randomized controlled trial of the Development of 3D Printed Personalized Titanium Plates and their Application in Orthognathic surgery. Please read this material carefully. You and your family, relatives, friends are welcome to ask questions and discuss issues regarding this project. The experiment scheme follows internationally accepted principles of the declaration of Helsinki and the state food and drug administration issued the Quality management code for clinical trials of medical devices. To ensure the scientific nature and reliability of the research, and to fully protect your personal rights and interests, this project has passed the hospital medical ethics committee review and has been approved by implementation.

The following describes the clinical trial background, purpose, method, benefits and possible risks or inconveniences you may face during the study, as well as your rights and interests of the medical devices used in the clinical trial. Please be sure to read them carefully before participating in the clinical trial. The information provided to you in this informed consent will help you to decide whether or not to participate in this clinical trial. If you have any questions, please ask the investigator responsible to ensure that you fully understand the relevant contents. Your participation in this trial is voluntary. If you agree to participate in this clinical trial, please sign the informed consent statement.

Background and study aim:

Internal rigid fixation is a common technique in the treatment of maxillofacial trauma, tumor and dentofacial deformity. Titanium alloy has many characteristics such as light weight, high strength, corrosion resistance and good biocompatibility. therefore, titanium plates are widely used to provide strong internal fixation of bone segments following different maxillofacial surgeries.

Currently, wide clinical use of commercially available titanium plates is produced and casted according to the fixed shape of the mold. However, the irregular shape of the maxillofacial bone surface makes the cast titanium plates unable to completely fit the contour of the bone surface of different shapes. for example, in orthognathic surgery, to correct dentofacial deformity the bone segment of patient’s jaws is moved resulting in a formation of steps between the segment. Therefore, titanium plates need to be bent to fit the bone surface. bending the titanium plate not only causes the surface

coating to shed off also wastes the operation time and increases the operation risk. It also makes the titanium plate more prone to metal fatigue and stress concentration, resulting in titanium plate fracture, screw loosening and other complications. Bending the titanium plates affect the accuracy of post operative results since fixing the bone segments according to the presurgical planning is difficult to achieve through using commercially used titanium plates.

The rapid development of digital technology, especially the development of 3D printing in oral and maxillofacial surgery makes the internal fixation easier and more accurate. 3D printing technology has gradually developed from the printing of resin guide plate to the 3D metal printing especially titanium alloy, which provides production of personalized titanium plate.

The aim of our study is to design 3-dimensional personalized printed titanium plate according to the patient's preoperative virtual planning simulation and utilize it in the actual operation. the advantages of using 3-D printed personalized titanium plates includes:

1. minimizing the operation time

2. more accurate postoperative results with better function and aesthetic outcomes through completely avoiding the titanium plate bending and its resultant problems.

At present, reports on the application of 3D printed titanium plates in orthognathic surgery inside the country and abroad are extremely limited, and only a few cases are reported. There are no corresponding experimental basic studies nor prospective, large-sample clinical studies. We plan to develop 3D printed personalized titanium plates and systematically study and evaluate the technical feasibility and clinical effect of 3D printed personalized titanium plates and compare it with commercial titanium plates through multi-center, large-sample randomized controlled trial.

1. Research purpose

a) To conduct A multi-center, large-sample randomized controlled trial to systematically study the technical feasibility of clinical application of 3D printed personalized titanium plates in orthognathic surgery.

b) To Compare and evaluate the effect of 3D printing personalized titanium plate objectively and accurately with commercial titanium plate.

2. Research process

How many people will take part in the trial?

About 100 people will take part in the study at four different medical facilities.

3. Methodology and content:

If you agree to participate in this study, please sign this informed consent form. This study is a multicenter, randomized controlled clinical trial. Subjects in the experimental group will use 3D printed personalized titanium plates, and subjects in the control group will use commercial titanium plates. Before entering the clinical study and after signing the informed consent the investigator will conduct a detailed screening of the relevant conditions of the subject according to the inclusion and exclusion criteria to determine whether you are or are not suitable to participate in the clinical study. After passing the relevant screening the subjects entered the clinical trial.

4. Research steps

- **Research process：**

  Screening → inclusion → implantation → observation and follow-up → extra ction → result analysis

a) Screening: Before you are enrolled in the study, your doctor will ask you for a medical history and perform physical, laboratory, imaging examination, and other necessary preoperative tests to determine whether you can participate in the study. The screening period is completed within 3 days.

b) Joining the research group: If you choose not to participate in the research out of the study, we pay you to join the team anyway. If you volunteer to participate in the study, you will follow the following steps.

c) Patients enrolled in the study were randomly assigned to either commercial or 3D-printed titanium plates by an independent statistician.

5. Commercial titanium plate group

(a) Completing preoperative orthodontic treatment and collecting preoperative data:

Spiral CT will be used to scan patients' heads and faces and collect radiological data. Laser scanning equipment will be also used to collect dental module data. The dental module data obtained by scanning were integrated with CT data. Data is then imported into related software for ratio analysis.

(b) Surgical simulation:

The deformity evaluation and surgical plan will be completed by the experienced surgeon based upon the patient's clinical and radiological examination. Followed by software simulation of the relevant orthognathic surgical procedures, the ideal face shape and occlusion will be obtained by adjusting the movement direction and distance of the bone block.

(c) Design and manufacture of osteotomy guide template and terminal occlus al splint:

According to the end bite the final splint will be designed, both terminal splint and resin osteotomy guide template will be generated by 3D printing.

(d) Mandibular surgery:

According to the preoperative surgical simulation plan and osteotomy guiding template the surgical operations will be performed. the mandible will be positioned according a terminal splint, finally the commercial titanium plate will be used for internal fixation of bone segments.

(e) Postoperative follow-up visit:

CT X-rays will be taken immediately after surgery, 1 month and 6 months post-operatively. The spiral CT to be taken 6 months after surgery is to observe the fixation and healing of the bone segments and the stability of titanium plates and screws.

(f) Titanium plate removal:

The titanium plates will be removed 6 to 8 months after the orthognathic surgery.

- **3D printing personalized titanium plate group**

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Spiral CT will be used to scan patients' heads and faces and collect data. The dental mold will be collected by laser scanning equipment. The dental modulus data obtained by scanning will be integrated with CT data. Data will be then imported into related software for ratio analysis.

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The deformity evaluation and surgical plan will be completed by the experienced surgeon using patient's specialized examination and imaging data. the relevant orthognathic surgical procedures will be simulated in the software, obtaining ideal face shape and occlusion by adjusting the movement direction and distance of the bone segment.

(c) Design and manufacture of osteotomy guide template and terminal occlus al splint:

According to the end bite the final splint will be designed, both terminal splint and resin osteotomy guide template will be generated by 3D printing.

(d) Design and production of 3D printing personalized titanium plate:

Model files of jaw position before and after surgery were sent to the machining c enter, and 3D titanium alloy printing technology was used to prepare 3D printed personalized titanium plates.

(e) Mandibular surgery:

According to the preoperative surgical simulation plan and osteotomy guiding template the surgical operations will be performed. the mandible will be positioned according a terminal splint, finally the commercial titanium plate will be used for internal fixation of bone segments.

(f) Postoperative follow-up visit:

CT X-rays will be taken immediately after surgery, 1 month and 6 months post-operatively. The spiral CT to be taken 6 months after surgery is to observe the fixation and healing of the bone segments and the stability of titanium plates and screws.

(g) Titanium plate removal:

The titanium plates will be removed 6 to 8 months after the orthognathic surgery.

Results analysis: data will be collected to determine whether the treatment you're receiving is safe and effective. Your physician will give you feedback about the clinical trial you underwent.

6. Other matters requiring your cooperation

During the clinical observation period you should follow the physician advice to receive surgical treatment and postoperative rehabilitation treatment. The specific operation and procedure will be carried out strictly in accordance with the Clinical Trial Protocol and clinical operation procedure. During the observation period regular follow-up will implicated according to the requirements of the doctor. During the follow-up, please report the changes of your condition to your doctor so that the doctor can judge whether the treatment you receive is effective and safe.

7. During your contribution in the study, you need to:

- You shall honestly report your related medical history including any allergies.
- You shall tell your doctor about any health problems you have during the study.
- You should not undergo any medical treatment or other treatment outside this study protocol.
- You should not perform other maxillofacial treatments on your own.

- You should follow instructions of researchers and study in charges.
- You can ask about anything that's unclear.
- Actively participates in a follow-up visit.

8. Funding sources of the experiment

Funding related to this study was provided by the scientific department of West China Hospital of Stomatology (Project No.: LCYJ2020-YF-1).

9. Possible benefits:

The participant will receive a routine orthognathic surgery. Although there is evidence that 3D printing of personalized titanium plates can improve the accuracy of orthognathic surgery, there is no guarantee that it does the same for every participant. Participant condition may or may not improve moreover or there may be the following risks and discomfort.

10. Possible risks or adverse events

An adverse event may occur during the clinical trial that may or may not be related to an experimental titanium plate. Although the titanium alloy material in this study has been systematically tested on animals to ensure the safety of the product before their use in human clinical trial, but uncertainty still exists regarding its clinical curative effect of individual. The adverse event may be due to either surgical risk or the application of medical apparatus and instruments that are likely to produce adverse events, Therefore, the risk of adverse events during your participation in the study cannot be ruled out. Patients undergoing jaw surgery occasionally experience complication such as redness, general rejection, local infection such as fever, inflammation, wound dehiscence, etc., most of these complications are related to the intervention itself and depends on the individual physiological characteristics but does not mean that any material defect or failure. If you experience any discomfort during the trial, you should contact your following physician who can judge and manage it in as soon as possible.

11. Medical treatment and economic compensation for injuries related to the study.

During the study, we will closely monitor adverse events perform a meticulous postoperative care and take active and preventive measures for any participant with injury related to this study. Orthognathic and Joint Surgery department of West China Hospital of Stomatology - Sichuan University will bear the treatment cost and corresponding economic compensation in accordance with Chinese laws and regulations.

12. Test groups to which they may be assigned

After signing the informed consent and passing the relevant screening, you will have a 50% chance of being in the trial group or the control group. During the experiment process you may also be transferred from the experimental group to the control group. For example, if 3D printed titanium plates are not suitable for patients in the experimental group during orthognathic surgery, commercial titanium plates will be used to complete the surgery, and patients in the control group will continue to complete follow-up.

13. Confidentiality of medical records

We will take all possible measures to ensure your privacy in accordance with the Declaration of Helsinki and the Code of Practice for the Management of Clinical Trials on Medical Devices. All information about your participation in the study including your medical history and medical records will be kept strictly confidential, and will not be disclosed to the public under any circumstances. Your personal identity will not be revealed in the report of the study results after its completion. To the extent permitted by laws and regulations, relevant medical personnel, members of ethics committees, and representatives of government administrative departments may review your medical records without violating the principle of confidentiality in order to verify the authenticity, accuracy, and reliability of the study data.

14. Free diagnosis and treatment programs and other relevant subsidies that may be obtained during the trial period

According to the clinical application, the titanium alloy bone plate and the standard treatment plan you have accepted are used. You will be examine and treated by clinically experienced doctors whom also will be ready to answer your questions and provide you with timely and thoughtful medical services. In addition, you will be compensated for the following expenses: free use of titanium plates and matching titanium screws; other surgical expenses, high-value consumables (including titanium plates and screws for bone grafting, traction screws for intermaxillary traction, etc.) and hospitalization expenses shall be paid by the subjects themselves. At the end of the study, the subject subsidy of RMB 500 will be paid. If you do not participate in the corresponding visit, the corresponding fee will not be paid.

15. Voluntary participation and withdrawal from the test

You may withdraw out of the study at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to withdraw out during the study you are encouraged to talk to your doctor first. Keeping your safety in consideration you may after withdrawal be subjected to some relevant examinations, and you can choose whether to willingly accept or refuse. The examinations include: vital signs,

specialized examination, laboratory examination, observational index of examination, the test related inspection fee shall be borne by the participant withdrawing out of the project. Meanwhile You are advised to perform the above examinations.

The investigator may terminate your participation in the study if you require additional diagnosis/treatment, you do not comply with the study plan, or for any other reasonable reason.

16. Rights and Responsibilities of subjects

- **Your rights**

The entire process of your participation in the study is voluntary. If you decide not to participate in this study, that will not affect other treatments you should receive. However, if you decide to participate you will be asked to sign this written informed consent. You have the right to withdraw from the trial at any stage without discrimination or unfair treatment, and your medical treatment and rights will not be affected.

- **Your responsibilities**

As a participant, you are required to provide true information about your medical history and current medical condition. You shall Inform the study in charge physician of any discomfort observed during the study. Do not accept any prescribed medical treatment or take any prescribed medicines or foods without prior consultion. You shall inform the study in charge physician if you have recently participated in or are currently participating in other studies. If you are a woman of childbearing age, you are required to strictly comply with the exclusion criteria of this study, and you are not allowed to plan pregnancy throughout the clinical study.

- **If you have problems or difficulties, whom to contact?**

If you have any questions related to this study, please contact your physician at:

If you have any questions relating to your rights/interests, or if you would like to report any difficulties, grievances or concerns you have encountered during your participation in this study, or if you would like to provide comments and suggestions in connection with this study, please contact the Hospital Ethics Committee at 028-85501479, email hxkqlunli@sina.com.

Finally, thank you again for reading this material. If you decide to participate in the study, please let your doctor know.

Informed Consent · Signature page of consent

Participant statement

I have been informed about the purpose, background, process, risks and benefits of this study. I also had plenty of time and opportunity to ask questions and I was satisfied with the answers.

I have been informed whom to contact if I have any questions or need further information, and whom to report difficulties, concerns, suggestions for research.

I have read this informed consent and agree to participate in this study. I understand that I may choose not to participate in the study or withdraw from the study at any time during the study without any reason.

I have learned that if my condition is worse or if I have a serious adverse reaction, I have the right to withdraw from the study; or if my research physician feels that it is not in my best interest to continue participating in the study, he/she will decide that I withdraw from the study without my consent; and the funder or regulator may terminate my participation during the study. If this happens the doctor will notify me promptly and the research doctor will discuss with me other options.

Finally, I received a copy of this informed consent form containing my signatures and the researcher and received a signed copy of the "informed consent form".

Participant 's signature: Date: Year/month/day

Contact Information of Participant:

Participant ID number

If the subject cannot sign the informed consent due to incapacity or other reasons, or the subject is a minor, his/her guardian shall sign the informed consent.

Signature of guardian: Date: Year month date

Relationship with Participant:

Reasons why subjects cannot sign the informed consent:

Investigator's Statement

I have accurately informed the subject about the contents of the informed consent form and answered the subject's questions, the subject is voluntarily participated in this study.

Investigator's signature: Date: Year month date

Contact Information: