Research protocol for "R&D of 3D printed personalized titanium plates and their application in orthognathic surgery"
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Abstract:

In order to compare the effects of the application of 3D printed personalized titanium plates and commercially available titanium plates on the operation time and bone movement accuracy in orthognathic surgery, this project intends to carry out multi-center, prospective and randomized controlled trials on the basis of the preliminary clinical trial using 3D printed personalized titanium plates for double jaw surgery. To achieve this objective and to accurately evaluate its effect this project is intended to include patients with dentofacial deformities who need orthognathic surgery, and randomly divide them into 3D printed personalized titanium plate group and commercially available titanium plate group. Both groups of patients will receive the same standard of treatment and have a solid internal fixation. patients will undergo CT radiographic examination at 7 days and 6 months postoperatively, the images will under three-dimensional reconstruction and uploaded to 3D slicer software program to observe the difference between the actual postoperative jaw position and the simulated jaw position in terms of displacement and direction. The secondary observation indicators are to evaluate the surgical operation time and titanium plate cost.

Keywords: 3D printing, personalized titanium plate, orthognathic surgery, prospective controlled trials

Research background

Rigid internal fixation is the common technique required in the treatment of maxillofacial trauma, tumors, and dentofacial deformities. Titanium alloys are widely used in surgery to provide rigid internal fixation to fix bone segment due to their light weight, high strength, corrosion resistance and good biocompatibility.

Currently the commercially available titanium plates used in clinical practice are produced and formed according to a mold with a fixed shape. While the morphology of the maxillofacial bone surfaces is irregular and the cast titanium plate cannot fully fit the bone surface contour of different forms. For example, step formation occurs between the bony

segments during fixation in patients with dentofacial deformities undergoing orthognathic surgery using commercially available titanium plate. Therefore, the titanium plate needs to be bent to fit the bone surface during surgery. The bending of the titanium plate will cause the surface coating of the titanium plate to shed off. also leads to the wastage of surgical time, increases the risk of surgery and affect the accuracy of bone position in a predetermined position. Bent titanium plate is prone to metal fatigue and stress concentration, resulting in complications such as titanium plate breaking and screw loosening.

The rapid development of digital technology, especially the development of 3D printing technology, provides imagination space for the further expansion of rigid internal fixation technology in oral and maxillofacial surgery. At present, 3D printing technology has gradually developed from the printing of resin guide plates to the 3D printing technology of metals, especially titanium alloys, which provides technical conditions for the subsequent personalized production of titanium plates. Our research aims to design a titanium plate that accurately fits the contour of the bone based on the patient's CT radiographic data. Personalized 3D printed titanium plate serves as a bridge between the preoperative virtual surgical simulation and the actual surgical operation. Use of personalized 3D printed titanium plate helps the surgeon to quickly and accurately move the bone segment to preoperatively planned position. moreover, avoids the various drawbacks caused by the bending of the titanium plate and obtaining better functions and aesthetic effects. Current reports on the application of 3D printed titanium plates in orthognathic surgery are extremely limited. Although few studies published in this regard but none of them were a prospective clinical large sample studies nor associated corresponding experimental basic research. Our study aims to develop 3D printed personalized titanium plates and systematically study the technical feasibility and clinical use effect of 3D printing personalized titanium plates through multi-center, large-sample randomized controlled trials, and compare them with commercially available titanium plates.

Objective of the study:

1. Study the technical feasibility of clinical application of 3D printing personalized titanium plates through multi-center large-sample randomized controlled trials.

2. Compare the post-operative accuracy between commercially available titanium plates and 3D printed personalized titanium plates.

Methodology

1. Inclusion criteria

Age ≥18

Patients with dentofacial deformities requiring orthognathic surgery.

Patients willing to participate in the clinical study and sign informed consent.

2. Exclusion criteria

Dental and maxillofacial deformities secondary to cleft lip and palate, tumor, trauma and iatrogenic factors

Syndromes such as partial face atrophy, first and second arch syndrome

Patients who had undergone previous jaw surgery.

3. Conditions for withdrawal or termination of the study:

Withdrawal of patients

- The patient asked to withdraw from the clinical study.
- Patients cannot complete relevant examinations as required which affects the data collection.
- The patients received other maxillofacial treatment without permission during the trial.
- Patients affected with diseases or serious complications during the study period for which need treatment or intervention which may affect the study program.

- **Termination of the study:**

If significant errors in clinical protocols were found in the study, which made it difficult to evaluate therapeutic efficacy.

- **Criteria for case shedding**

(1) Definition of shedding: study subjects who filled in informed consent and were screened qualified to enter the study are considered to be shedding cases as long as they did not complete the prescribed treatment cycle regardless of when and why they quit.

(2) The causes of shedding:

- Subjects could not complete relevant examinations as required or accept other treatment plans without permission during treatment;
- Patients failed to attend the required follow-up including those who were successfully operated but could not complete the whole course of treatment, so that incomplete clinical data collection affected the efficacy evaluation.
- patient discontinued the study due to serious adverse reactions or adverse events and complications that is not suitable for clinical trial treatment.

(3) Management of shedding cases

(1) in case the patient is shed off the investigator should make a close contact by telephone and shall give a door visit. Attempts to make appointment and bring back the patient to complete further follow-up as long as the patient condition permits.

(2) Cases of withdrawal due to adverse reactions or complications should be subjected to corresponding treatment measures according to the actual situation.

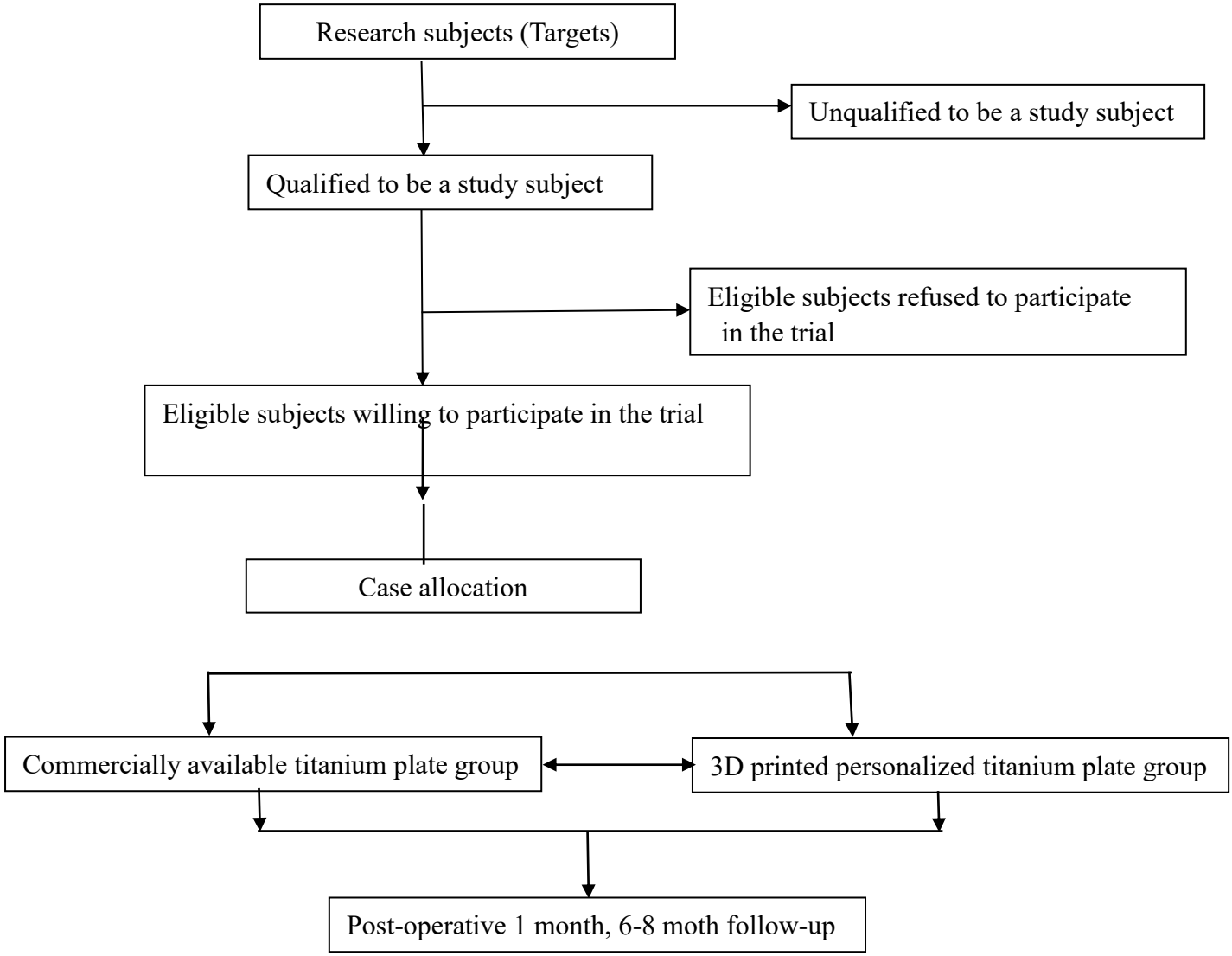
(3) Shedding cases relevant information should be kept properly for further comprehensive analysis.

(2) Sample size calculation

According to the accuracy and standard deviation of 3D printed titanium plate and commercially available titanium plate in orthognathic surgery guidance in pre-clinical trials and current literature reports, bilateral $\alpha=0.05$, $\beta=0.2$, then 40 patients should be included in each group. Considering the possibility of loss to follow-up, the sample size was set as 50 patients in each group.

(3) Randomization method

1. Research design



2. Case allocation

Patients who meet the inclusion criteria and agreed to participate in this clinical trial they will be then asked to sign the informed consent letter, and assigned to the 3D printed titanium plate group or commercial titanium plate group.

Blinding

This study cannot be blinded to surgeons. However, both subjects and evaluators were blinded.

4. Treatment plan

1. Commercial titanium plate group

(1) Complete preoperative orthodontic treatment and collecting preoperative data:

Spiral CT used to scan patients and collect data. Laser scanning equipment was used to collect tooth modulus data. The dental modulus data obtained by scanning were integrated with CT data. Data is imported into related software for analysis.

(2) Surgical simulation:

Following the deformity evaluation, the surgical plan will be completed by the experienced surgeon combined with the patient's clinical examination and imaging data. orthognathic surgical procedures will be simulated in the software and the ideal face shape and occlusion will be obtained by adjusting the movement direction and distance of the bone segments.

(3) Design and manufacture of final occlusal splint:

According to the final occlusal the splint will be designed and generated by 3D printing.

(4) Orthognathic surgery

According to the preoperative surgical simulation plan, surgical operations will be performed according to the osteotomy guide plate. The mandible will be positioned with a terminal plate finally a commercial titanium plate will be used for firm internal fixation.

(5) Postoperative follow-up visit:

The first CT scan x-rays will be taken immediately after surgery followed by another x-ray 1 month post-operatively to observe the accuracy of bone segment movement according to presurgical simulation. Another CT scan x-ray will be taken 6 months post-operatively to observe the fixation and healing of the bone segments and the stability of both titanium plates and screws.

(6) Titanium plate removal:

Re-admission 6-8 months postoperatively to remove titanium plate and screws.

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

1. **Design and production of 3D printing personalized titanium plate**: The model files of the preoperative and postoperative jaw positions are transferred to the machining center, and the 3D printed personalized titanium plates are prepared using 3D titanium printing technology.
2. **Orthognathic surgery:**

   According to the pre-operative surgical planning the osteotomy guide plate is used intra-operatively to carry out the surgery. The pre-drilled holes in the osteotomy guide will be used for the final fixation of 3D printed personalized plate. Finally, both jaws are placed in the presurgical planned position using the final resin splint.
3. **Postoperative follow-up:**

   First CT scan X-ray is to be taken immediate post-operative to observe the accuracy of bone segments positioning. the second X-rays will be taken 6 months post-operatively to observe the fixation and healing of the bone segments and the stability of titanium plates and titanium screws.
4. **Titanium plate removal:**

   Re-admission 6-8 months postoperatively to remove titanium plate and screws.

- **Observation indicators:**

  Main outcome measures: Accuracy of bone segment positioning between actual and simulated jaw surgery.

  Secondary outcome measures: 1. Operation time 2. The cost of titanium plate.

- **Risks and Benefits:**

All subjects included in the study are associated with dentofacial deformities and requiring orthognathic surgery so the surgery is considered to be a routine procedure. the possible risks are the conventional intraoperative and postoperative risks expected to happen with orthognathic surgery. If the 3D printing of titanium plates causes allergic reactions or rejection resulting in wound infection and prolongation of wound

healing the study in charge will consider surgical removal of 3D printed titanium plates and replace them with commercialized titanium plates at any time if necessary.

Benefits: Due to the application of 3D printed personalized titanium plates the subjects included in this clinical trial will able to have a short the surgical time and obtain higher surgical accuracy. Regardless of whether subjects are randomly assigned to 3D printed personalized titanium plate sets or commercially available titanium plate groups after enrollment, this clinical trial will provide subject willing to participate free titanium plates for orthognathic surgery. Each participant in and completed this clinical study will receive a grant of 500 yuan.

5. **Study quality control and assurance**

All participant will undergo required orthognathic surgery in all participating centers by highly qualified professors with vast surgical experience. Preoperative and postoperative imaging data and reconstructed models will be measured simultaneously by two software-skilled physicians who will be unaware of the intervention the patient is going to receive (evaluator blindness). The monitoring committee will also conduct a final review of the clinical data before conducting statistical analysis of the data.

6. **Ethical requirements**

The study will be conducted in full accordance with the ethical principles of the Declaration of Helsinki and the International Ethical Guidelines for The Identification of Biomedical Research issued by the Council of International Organizations of Medical Sciences. Respect of the human dignity, fairness and maximum effort will be made for the benefit of the participant and harm will be avoided as much as possible. all participants and their families will be informed about the clinical trial in detail prior to the conduction of it. they will also retain a copy of the informed consent.