The Dynamic Dual-Mode Alignment Optimization and Intelligent Precision Knee Preservation System for Knee Osteoarthritis

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Scheme Abstract

Item Content

Project Name:

The Dynamic Dual-Mode Alignment Optimization and IntelligentPrecision Knee Preservation System for Knee Osteoarthritis

Research Objectives：

1. Clinical comparative study of neutral alignment vs. traditional alignment for knee preservation (completed); 2. Clinical comparative treatment of kinematic alignment vs. traditional alignment for knee preservation; 3. Clinical comparative study of 3D-printed guide plate-guided HTO vs. traditional surgery; 4. Optimization of preoperative surgical planning strategy based on CT imaging and verification of the accuracy of corresponding 3D-printed guide plates; 5. Accuracy verification of AR real-time feedback in intraoperative alignment adjustment for HTO

Study Subjects： Patients with knee osteoarthritis (KOA) requiring high tibial osteotomy (HTO) (K-L grade II-III)

Sample Size: Total: 120 cases (3 groups, 40 cases per group)

Inclusion Criteria:

1. Aged 40-70 years; 2. Unilateral medial compartment knee osteoarthritis (mild to moderate pain); 3. Mild to moderate varus deformity (5°-15°); 4. Coronal MRI shows medial meniscus extrusion (MME) > 3 mm, flexion contracture < 10°; 5. Intact lateral meniscus and cartilage; 6. Voluntarily sign informed consent

Exclusion Criteria:

1. Complicated with inflammatory arthritis (e.g., rheumatoid arthritis) or systemic inflammatory diseases; 2. Severe varus deformity (>10°) or flexion contracture >10°; 3. Lateral meniscus lesions (tear, discoid meniscus) or knee instability; 4. History of major knee trauma/infection/previous surgery; 5. Severe patellofemoral arthritis; 6. Advanced medial compartment osteoarthritis (bone-on-bone contact or knee subluxation); 7. Refusal of secondary arthroscopic review or study participation; 8. Failure to complete at least 12 months of follow-up; 9. Severe osteoporosis; 10. Cognitive impairment

Study Design:

This study adopts a prospective, multicenter, multi-module mixed design, combining

randomized controlled trial (RCT), prospective cohort study, and self-controlled study to systematically evaluate the effectiveness, accuracy, and clinical value of dynamic dual-mode alignment optimization (neutral position + kinematic alignment) and intelligent precision knee-preserving system (3D-printed guide plate, AR navigation).

1. Kinematic Alignment (KA) vs. Traditional Mechanical Alignment (MA) for Knee Preservation: Multicenter, assessor-blinded, three-arm parallel-group RCT. Group 1 (MA group): HTO guided by traditional mechanical axis alignment; Group 2 (KA group): HTO guided by personalized kinematic alignment based on dynamic knee kinematic assessment; Group 3 (DA group - Dynamic Dual-mode Alignment group): HTO guided by dynamic dual-mode alignment combining neutral alignment and KA.
2. 3D-Printed Guide Plate-Guided HTO vs. Traditional HTO: Multicenter, assessor-blinded RCT. Group A (Traditional group): Traditional manual HTO based on intraoperative fluoroscopy and empirical judgment; Group B (3D Guide Plate group): HTO based on optimized preoperative CT planning and 3D-printed osteotomy guide plate.
3. Optimization of CT-Based Preoperative Planning and Accuracy Verification of 3D-Printed Guide Plates: Prospective cohort study. Method: Preoperative virtual planning vs. postoperative actual results - 3D registration of postoperative CT data with preoperative planning data to quantitatively measure differences in key parameters (coronal MPTA angle, sagittal PTA angle, osteotomy depth, angle, osteotomy surface position, and deviation between planned and actual guide plate placement).
4. Accuracy Verification of AR Real-Time Feedback in Intraoperative HTO Alignment Adjustment: Prospective cohort study (self-controlled). Verification process: Step 1 (Routine Adjustment): Surgeon performs initial alignment adjustment and temporary fixation based on experience, fluoroscopy, and/or 3D guide plate (if used); Step 2 (AR-Guided Adjustment): Turn on AR navigation system, surgeon performs fine adjustment under AR real-time visualization feedback (showing deviation between current and target alignment); Step 3 (Final Confirmation): Confirm final alignment using standard fluoroscopy (full-length film).

Outcome Measures:

1. Alignment Comparison: Primary endpoint - 1-year postoperative WOMAC total score; Key secondary endpoints - 2-year postoperative KOOS score, VAS pain score, gait parameters,

reoperation rate.

2. Guide Plate vs. Traditional: Primary endpoint - Postoperative HKA planned-actual difference; Secondary endpoints - Operation time, fluoroscopy times, 6-week postoperative ROM, complication rate.
3. Guide Plate Accuracy: Primary endpoint - 3D registration error (MPTA/PPTA angle difference); Secondary endpoints - Osteotomy depth deviation (mm), guide plate clinical usability score.
4. AR Verification: Primary endpoint - Change in alignment deviation (HKA angle) before and after AR adjustment; Secondary endpoints - AR adjustment time, surgeon satisfaction score, system registration error.

Statistical Analysis:

A stratified statistical analysis framework will be adopted: For intergroup comparisons, continuous primary endpoints (WOMAC total score, MPTA angle difference) will use analysis of covariance to adjust baseline values; Kruskal-Wallis H test will be used for heterogeneous variance. Categorical variables (complication rate) will use chi-square test or Fisher's exact test, with Bonferroni correction for multiple comparisons among three groups. Repeated measurement data (multi-timepoint VAS/KOOS/ROM) will use linear mixed-effects model (LMM) to analyze time effect, intergroup effect, and interaction, with random intercept to control individual differences. For accuracy verification, paired t-test or Wilcoxon signed-rank test will compare systematic deviation between preoperative planning and postoperative measurement values; Bland-Altman consistency analysis will calculate 95% limits of agreement (LoA) and intraclass correlation coefficient (ICC) to evaluate measurement reliability. Correlation analysis will use Pearson/Spearman correlation coefficients to explore the association between alignment accuracy and clinical outcomes. All analyses will be based on the intention-to-treat (ITT) principle; missing data will use multiple imputation for sensitivity analysis. Two-tailed $\alpha=0.05$ will be set as the significance threshold, using SPSS 26.0 and R 4.3.1 software.

Study Duration: September 2026 - August 2028 (24 months)

1. Research Background

1.1 Clinical Problems to Be Solved and Necessity

Knee Osteoarthritis (KOA) is one of the major diseases with a rising global disability burden, especially medial unicompartmental OA combined with mechanical varus alignment, which has a significant incidence in middle-aged and elderly populations as well as young and middle-aged people with high sports demands. Its pathogenesis is closely related to lower limb alignment abnormalities: medial deviation of the mechanical axis leads to long-term excessive load on the medial compartment, accelerating cartilage degeneration and meniscal injury. High Tibial Osteotomy (HTO), as an important strategy for current knee-preserving treatment, aims to accurately adjust the overall alignment of the lower limb, transferring weight-bearing from the diseased medial compartment to the relatively healthy lateral compartment, thereby reducing mechanical stress in the lesioned area, delaying the degenerative process, and improving pain and function. This remodeling of the mechanical environment is clinically referred to as "joint restart," creating a biomechanical premise for cartilage repair and joint function recovery.

However, current mainstream preoperative planning for HTO mostly adopts a "one-size-fits-all" strategy based on static mechanical axis targets (e.g., Fujisawa point, approximately 62% of tibial plateau width), with multiple limitations:

- Neglect of individual differences: Significant differences exist in anatomical structure, soft tissue tension, meniscus and cartilage status, and gait kinematic patterns among different patients, making fixed targets unsuitable for all populations;
- Risk of overcorrection or undercorrection: Minor errors in the mechanical axis position can lead to significant changes in medial-lateral force, affecting clinical efficacy and long-term survival rate;
- Inconsistency between static and dynamic loading: Static imaging targets cannot accurately reflect dynamic load states such as walking and uphill/downhill walking, which may result in 达标 on imaging but unimproved or even worsened function and symptoms;
- Limited execution accuracy: Traditional operation methods relying on manual positioning and intraoperative fluoroscopy are highly dependent on surgeon experience, leading to easy deviation of key parameters such as HKA, MPTA, and PTS, while increasing radiation exposure and

operation time.

At present, there is a lack of an individualized precision knee-preserving system that can balance static accuracy and dynamic functional matching and can be widely promoted clinically. Especially in the context of no consensus on the "optimal target alignment," how to integrate static alignment (neutral or mild valgus) with dynamic functional indicators (e.g., knee adduction moment KAM, varus thrust), and realize a closed-loop of planning-execution-verification through digital means such as CT 3D planning, 3D-printed patient-specific instrumentation (PSI), and intraoperative augmented reality (AR) real-time feedback, has become an urgent clinical problem to be solved.

This study intends to construct and systematically verify a dual-mode alignment strategy of "static neutral target + dynamic functional target," combined with AI-assisted CT planning, 3D-printed PSI execution, and intraoperative AR fine adjustment, to achieve truly individualized precision orthopedics. Through rigorous verification from multiple dimensions such as kinematics, imaging, patient-reported outcomes (PROs), safety, and economics, it will provide high-quality evidence-based basis for clinical practice and promote KOA knee-preserving treatment to enter a new stage of functionalization and precision.

1.2 Epidemiology/Clinical/Instrument/Background

Knee Osteoarthritis (KOA) is one of the most common disabling musculoskeletal diseases worldwide. According to the Global Burden of Disease Study, the age-standardized prevalence of KOA worldwide was approximately 5.5%-7.1% in 2020, with a total of over 650 million patients; its prevalence has increased by more than 9% since 1990, and disability-adjusted life years (DALY) has increased by approximately 9.5%. Epidemiological surveys in China show that the total prevalence of KOA in people aged ≥40 years is 8.1%, with higher prevalence in women than men, and it increases significantly with age; in people aged ≥60 years, the prevalence can exceed 20%. With aging and obesity epidemics, the number of KOA patients is expected to continue to rise in the next 20 years, bringing a huge burden to the social labor force and medical system.

Total Knee Arthroplasty (TKA) can effectively relieve advanced symptoms, but the 10-year revision rate in young patients is significantly higher than that in the elderly, and revision surgery is complex and costly. Therefore, "delaying replacement and preserving joints" has important public health significance in this patient population. As the core surgical method for knee-preserving treatment,

High Tibial Osteotomy (HTO) has multiple advantages: it optimizes the lower limb alignment to reduce the load on the lesioned compartment and delay joint degeneration; unlike joint replacement, HTO retains the patient's own joint structure and proprioception, maintains the natural movement trajectory of the knee joint, and helps to better complete advanced functional activities such as squatting, running, and jumping; some patients can recover exercise ability after surgery and re-participate in daily exercise or even competitive sports; at the same time, HTO creates more ideal alignment and soft tissue conditions for patients who may need TKA in the future, thereby extending the service life of the joint and improving surgical effects.

In knee-preserving surgery, the core of HTO lies in optimizing the joint force environment by changing the lower limb alignment to delay disease progression. However, the difference between preoperative planning and intraoperative execution directly determines the accuracy of orthopedics and long-term efficacy. Although existing planning is mostly based on static mechanical axis targets, in practical application, alignment strategies need to be more refined and individualized according to the patient's soft tissue balance, meniscus and cartilage status, and gait kinematic characteristics.

In recent years, the application of digital auxiliary means in HTO has gradually emerged:

(1) Patient-Specific Instrumentation (PSI) can perform individualized osteotomy planning and guide plate production based on 3D images, showing high accuracy in coronal alignment (HKA, MPTA) and sagittal (PTS) control, while reducing intraoperative fluoroscopy times and operation time. However, its limitations include long production cycle, dependence on high-quality images, insufficient cross-center consistency, and lack of consistent evidence for its advantages in long-term functional outcomes and joint survival rate.

(2) Augmented reality (AR) or mixed reality navigation can provide real-time superimposed display of alignment and osteotomy information during surgery, realizing dynamic visualization and precise fine adjustment, which has potential in improving surgical controllability and reducing repeated fluoroscopy. However, it is currently mostly in the bench or small-sample clinical stage, with problems such as hardware dependence, affected registration accuracy, and visual field interference, and its translational value for patients' final functional benefits needs to be verified by large-scale clinical studies.

In summary, how to integrate individualized functional goals into planning while maintaining execution accuracy, and establish a digital precision knee-preserving system that can be stably

promoted under multicenter conditions, is the core problem to be solved urgently. The "dual-mode alignment + digital execution closed-loop" proposed in this study is a systematic solution to the above shortcomings.

1.3 Existing Evidence and Controversies

1.3.1 Clinical Evidence and Controversies of Target Alignment Strategies

At present, there is no unified consensus on the preoperative target alignment for HTO internationally. The mild valgus strategy represented by the Fujisawa point (WBL about 62–62.5%) is widely used, but in recent years, multiple studies have questioned the universality of this "fixed target" in all populations. Katagiri et al. (2023) reported that there was no significant difference in short-term clinical outcomes between neutral alignment and centralization strategy in patients with medial meniscus posterior root tear combined with varus. The prospective randomized controlled study of our team showed that there was no significant difference in postoperative functional recovery and pain improvement between neutral position and Fujisawa point target in patients with MMPRT combined with varus, while neutral position could avoid the risk of overcorrection in some patients. Other scholars have pointed out that excessive lateral shift of the Fujisawa point may increase lateral compartment stress and accelerate lateral cartilage degeneration. These results suggest that the optimal target alignment should consider individual anatomy, soft tissue, and dynamic load characteristics, rather than a "one-size-fits-all" model.

1.3.2 Accuracy and Limitations of Digital Execution Tools

Patient-specific guide plates (PSI) and computer-assisted surgery (CAS) are considered to improve the execution accuracy of HTO. Multiple systematic reviews and meta-analyses have confirmed that PSI is superior to traditional techniques in coronal alignment (HKA, MPTA) and sagittal (PTS) control, and can reduce intraoperative fluoroscopy time. However, there is no consistent conclusion on the advantages in long-term functional outcomes and joint survival rate; in addition, the production cycle, cost of PSI, and dependence on high-quality images limit its wide promotion in multicenter settings. Augmented reality (AR) navigation can provide real-time visualized superimposition of alignment and osteotomy information during surgery, helping to fine-tune alignment and reduce radiation exposure. Chui ECS et al.'s bench and cadaver tests verified the feasibility of markerless AR navigation, but its accuracy stability and translational value for patient function in large

clinical samples still need further verification.

1.3.3 Correlation between Kinematic Indicators and Clinical Outcomes

Gait studies have shown that peak knee adduction moment (KAM) and its impulse are important predictors of KOA pain and structural progression (Miyazaki T et al., 2002; Sharma L et al., 2017). At the same time, the presence of varus thrust is significantly associated with the occurrence and aggravation of KOA. However, existing HTO studies mostly use static image alignment as the main efficacy evaluation index, lacking systematic studies that link dynamic load indicators with static accuracy, functional outcomes, and safety. This leads to incomplete optimization of dynamic load distribution and symptoms in some patients even if static indicators are met.

1.3.4 Evidence Gaps to Be Addressed by This Study

Based on the above literature review, there is currently a lack of prospective multicenter clinical studies that combine individualized target alignment strategies with digital precision execution tools (PSI, AR) and simultaneously evaluate from the full chain of dynamic load-static alignment-patient-reported outcomes-safety. The design of this study is to fill this evidence gap, verify the real benefits of the "dual-mode alignment + digital closed-loop knee-preserving system" on multi-dimensional indicators, and provide high-quality evidence-based basis for KOA knee-preserving treatment.

2. Research Objectives

2.1 Primary Objective

To verify that the "dynamic dual-mode alignment optimization + intelligent precision knee-preserving system" (integrating multi-module technologies such as static/kinematic target alignment, CT-based preoperative 3D planning, 3D-printed guide plate guidance, and intraoperative AR real-time feedback) can achieve a more significant relative reduction in peak knee adduction moment (KAM) at 12 months postoperatively compared with traditional knee-preserving strategies, while maintaining or improving knee clinical function without increasing the incidence of perioperative and medium-to-long-term complications.

2.2 Secondary Objectives

(1) Improve static alignment accuracy and sagittal control ability;

(2) Improve dynamic load parameters such as varus thrust and KAM impulse;

(3) Improve patient-reported outcomes (PROs) scores and MCID compliance rate;

(4) Optimize perioperative process, reduce intraoperative radiation exposure and shorten operation time;

(5) Verify the safety and cost-effectiveness advantages of the scheme.

2.3 Sub-study Objectives

(1) Clinical Comparative Study of Neutral Alignment vs. Traditional Alignment for Knee Preservation (Completed): To compare the differences between the two static target alignments in KAM improvement and function enhancement, providing a benchmark for subsequent kinematic optimization.

(2) Clinical Comparative Treatment of Kinematic Alignment vs. Traditional Alignment for Knee Preservation: To verify the advantages of kinematic target alignment in reducing dynamic loads (KAM, varus thrust).

(3) Clinical Comparative Study of 3D-Printed Guide Plate-Guided HTO vs. Traditional Surgery: To evaluate the effect of PSI guide plate in improving alignment accuracy, reducing radiation and operation time.

(4) Optimization of Preoperative Surgical Planning Strategy Based on CT Imaging and Accuracy Verification of Corresponding 3D-Printed Guide Plates: To optimize preoperative 3D planning parameters and verify the accuracy of guide plate production and application.

(5) Accuracy Verification of AR Real-Time Feedback in Intraoperative HTO Alignment Adjustment: To compare the differences in intraoperative alignment adjustment accuracy and efficiency between AR navigation and traditional fluoroscopy.

3. Study Type

This is a prospective, randomized, controlled, partially blinded multicenter clinical study.

3.1 Overall Design Type

(1) Prospective: All cases preset inclusion criteria and research procedures before surgery, and follow up according to the established time window after surgery.

(2) Random Grouping: All sub-studies (except the completed "neutral alignment vs. traditional

alignment for knee preservation" comparative study) adopt computer random number table to assign subjects to experimental group or control group.

(3) Control Methods:

- Kinematic alignment vs. traditional static alignment;
- 3D-printed guide plate-guided HTO vs. traditional intraoperative fluoroscopy HTO;
- CT planning-optimized guide plate vs. conventional guide plate design;
- AR intraoperative real-time feedback vs. traditional fluoroscopy adjustment.

(4) Blinding: Due to obvious differences in intervention methods, surgeons and patients cannot be blinded; assessor blinding is adopted (postoperative imaging parameters, gait/kinematic data, and PROs scores are analyzed by independent assessors unaware of grouping information).

3.2 Sub-study Blinding and Randomization Details

(1) Kinematic vs. Traditional Alignment: 1:1 randomization; assessor blinding.

(2) 3D-Printed Guide Plate vs. Traditional HTO: 1:1 randomization; imaging and function assessor blinding.

(3) CT Planning Optimization vs. Conventional Planning: 1:1 randomization; postoperative imaging accuracy analysis by blinded measurement.

(4) AR Feedback vs. Traditional Fluoroscopy: 1:1 randomization; postoperative imaging and function assessor blinding.

(5) The completed study (neutral vs. traditional alignment) is a prospective randomized controlled design, and the results are used as methodological and effect size references, not included in the current random sequence.

3.3 Summary of Study Characteristics

(1) Study Type: Clinical interventional trial

(2) Design Attributes: Prospective, randomized, parallel-controlled, partially blinded, multicenter

(3) Main Evaluation Time Points: Preoperative baseline, 6 weeks, 3 months, 6 months, 12 months postoperatively

(4) Data Analysis Principle: Primary endpoints by intention-to-treat (ITT), safety endpoints by exposed population

4. Study Subjects and Case Selection

4.1 Inclusion Criteria

(1) Aged 40-70 years;

(2) Unilateral medial compartment knee osteoarthritis (mild to moderate pain);

(3) Mild to moderate varus deformity (5°-15°);

(4) Coronal MRI shows medial meniscus extrusion (MME) > 3 mm, flexion contracture < 10°;

(5) Intact lateral meniscus and cartilage;

(6) Voluntarily sign informed consent.

4.2 Exclusion Criteria

(1) Complicated with inflammatory arthritis (e.g., rheumatoid arthritis) or systemic inflammatory diseases;

(2) Severe varus deformity (>10°) or flexion contracture >10°;

(3) Lateral meniscus lesions (tear, discoid meniscus) or knee instability;

(4) History of major knee trauma/infection/previous surgery;

(5) Severe patellofemoral arthritis;

(6) Advanced medial compartment osteoarthritis (bone-on-bone contact or knee subluxation);

(7) Refusal of secondary arthroscopic review or study participation;

(8) Failure to complete at least 12 months of follow-up;

(9) Severe osteoporosis;

(10) Cognitive impairment.

5. Study Design

5.1 Intervention Measures

5.1.1 Intervention Group

The intervention group adopts the "dynamic dual-mode alignment optimization + intelligent precision knee-preserving system," integrating the following elements:

(1) Preoperative Planning:

- Static target alignment: Measure HKA, MPTA, JLCA, etc., based on full-length standing X-ray, and set orthopedic target (individualized ± neutral position).

- Kinematic target alignment: Calculate dual-mode comprehensive target using 3D gait analysis and ground reaction force data, combined with varus thrust, peak KAM, and KAM impulse.
- CT 3D reconstruction and surgical simulation: Acquire full-length femoral and tibial images using high-resolution CT (slice thickness ≤1mm), reconstruct 3D model, and set osteotomy plane, wedge opening amount, and hinge position.
- 3D-printed personalized guide plate (PSI): Design and print according to optimized planning data, including positioning guide plate and osteotomy guide groove.

(2) Intraoperative Operation:

- AR real-time feedback navigation: Register full-length lower limb images with 3D planning model during surgery to realize AR real-time superimposed display of alignment changes and dynamically adjust to planning target.
- Osteotomy technique: Single-plane opening wedge HTO (OWHTO) with locking plate fixation.
- Alignment confirmation: Recheck alignment and PTS under simulated weight-bearing, adjust opening amount or hinge position if necessary.

(3) Postoperative Management:

- Lower limb muscle strength training and range of motion (ROM) training from the first day after surgery;
- Partial weight-bearing on the ground 2–3 days after surgery (adjusted according to bone quality and fixation stability);
- Gradual full weight-bearing 3–4 weeks after surgery;
- Follow ERAS bundle care process, strengthen pain management and anti-thrombosis measures.

5.1.2 Control Group

The control group adopts traditional knee-preserving strategy, without kinematic alignment, personalized CT planning, 3D-printed guide plate, and AR real-time feedback. Specific measures are as follows:

(1) Preoperative Planning:

Only set traditional static orthopedic target (e.g., postoperative HKA≈183°) based on full-length standing X-ray, without kinematic evaluation and CT 3D planning.

(2) Intraoperative Operation:

Adopt traditional open high tibial osteotomy (OWHTO), with osteotomy and opening amount

confirmed by surgeon's experience and intraoperative conventional fluoroscopy; alignment adjustment based on estimation of mechanical axis under intraoperative fluoroscopy; no 3D-printed guide plate or AR navigation.

(3) Postoperative Management:

Implement routine rehabilitation and nursing programs with reference to the intervention group; consistent pain management and anti-thrombosis programs.

5.1.3 Concomitant Medication and Prohibited Medication Regulations

(1) Allowed: Routine analgesics (NSAIDs), anticoagulants (low molecular weight heparin or oral anticoagulants), bone health management drugs (e.g., calcium, vitamin D).

(2) Prohibited: Long-term systemic glucocorticoids; intra-articular injections outside the study scope (hyaluronic acid, hormones, etc.); other lower limb surgical interventions that may affect gait analysis.

All concomitant medications should be recorded and adjusted as covariates in data analysis.

5.2 Study Cycle and Visit Plan

5.2.1 Study Cycle

The total cycle of this study is 24 months, divided into four stages:

(1) Preparation Stage (Months 0–3): Team formation and training; formulation of SOP, improvement of case report form (CRF) and electronic data capture system (EDC); completion of ethical approval and pilot enrollment.

(2) Enrollment and Intervention Stage (Months 4–18): Allocate intervention group and control group according to randomization scheme; continuous case enrollment and intervention implementation; completion of preoperative baseline assessment and early postoperative follow-up.

(3) Follow-up and Data Collection Stage (Months 18–22): Complete clinical follow-up and testing according to preset visit points; ensure that the completion rate of 12-month primary endpoint assessment is ≥90%.

(4) Data Analysis and Conclusion Stage (Months 22–24): Data cleaning and statistical analysis; writing research report and paper submission.

5.2.2 Visit Points and Contents

Visit Point	Time Point	Main Contents
V0	Preoperative (on enrollment day or within 1 week before surgery)	- General information: Age, gender, BMI, course of disease, comorbidities - Laboratory tests: Blood routine, biochemical profile, coagulation function, blood glucose, liver and kidney function - Imaging: Lower extremity full-length standing X-ray, knee CT (required for intervention group), MRI (if meniscus/cartilage lesions exist) - Kinematic assessment: 3D gait analysis (peak KAM, KAM impulse, varus thrust) - Functional scales: KOOS, WOMAC, OKS, Lysholm, HSS - Safety assessment: Vital signs, electrocardiogram - Concomitant medication record
V1	Before discharge after surgery	- Intraoperative records: Osteotomy amount, hinge position, fixation method, fluoroscopy times/cumulative radiation dose, operation duration, blood loss - Postoperative imaging: Knee X-ray (including HKA, MPTA, PTS measurement) - Complication monitoring: Bleeding, infection, neurovascular injury, fracture, etc.
V2	6±1 weeks postoperatively	- Imaging: Knee X-ray (bone healing, alignment maintenance) - Functional assessment: ROM, weight-bearing ability - Complication monitoring: Incision healing, deep vein thrombosis, infection - Medication and rehabilitation compliance record
V3	3 months postoperatively (±2 weeks)	- Imaging: Lower extremity full-length standing X-ray (HKA, MPTA, JLCA, PTS) - Functional assessment: KOOS, WOMAC, OKS, Lysholm, HSS

		- Complication monitoring and rehabilitation progress - Record reintervention
V4	6 months postoperatively (±2 weeks)	- Kinematic assessment: Gait analysis (peak KAM, KAM impulse, varus thrust) - Functional assessment: Same as V3 - Imaging: Lower extremity full-length standing X-ray - Complication/reintervention record
V5	12±1 months postoperatively (primary endpoint assessment)	- Kinematic assessment: Gait analysis (peak KAM%Δ, KAM impulse, varus thrust) - Imaging: Lower extremity full-length standing X-ray (HKA hit rate, PTS error) - Functional scales: KOOS, WOMAC, OKS, Lysholm, HSS (calculate MCID compliance rate) - Perioperative and long-term complication record

5.3 Data and Quality Control

(1) Data at each visit point are entered into the EDC system and double-checked;

(2) Imaging and kinematic analysis are completed by independent assessors unaware of grouping information;

(3) A research progress and quality control meeting is held quarterly to ensure follow-up rate and data integrity.

5.4 Randomization and Blinding

(1) Kinematic vs. Traditional Alignment: 1:1 randomization; assessor blinding.

(2) 3D-Printed Guide Plate vs. Traditional HTO: 1:1 randomization; imaging and function assessor blinding.

(3) CT Planning Optimization vs. Conventional Planning: 1:1 randomization; postoperative imaging accuracy analysis by blinded measurement.

(4) AR Feedback vs. Traditional Fluoroscopy: 1:1 randomization; postoperative imaging and function

assessor blinding.

(5) The completed study (neutral vs. traditional alignment) is a prospective randomized controlled design, and the results are used as methodological and effect size references, not included in the current random sequence.

5.5 Other

5.5.1 Drug and Device Information

(1) Trial Devices:

- Personalized 3D-printed osteotomy guide plate (PSI): Designed based on preoperative high-resolution CT data 3D reconstruction and optimized planning, printed with medical-grade polyamide, in line with national Class III medical device registration requirements, and used once after sterilization.
- AR intraoperative real-time feedback navigation system: Adopts registered and verified augmented reality visualization platform, with functions of image superimposed display and real-time measurement of alignment deviation.
- Locking plate and screw: Medical titanium alloy material, certified by CE or NMPA.

(2) Routine Medications:

- Perioperative antibiotics (e.g., cephalosporins): Intravenous administration 30–60 minutes before surgery, discontinued within 48 hours after surgery; other sensitive antibiotics are selected if there is a drug allergy history.
- Anticoagulants: Subcutaneous injection of low molecular weight heparin sodium after surgery, once a day, then changed to oral anticoagulants (e.g., rivaroxaban) until 4 weeks after surgery; specific plan adjusted according to patient risk stratification.
- Analgesics: Select NSAIDs (e.g., celecoxib) or short-term weak opioids if necessary according to VAS pain score.

5.5.2 Drug Reduction, Delay and Discontinuation Procedures

(1) Antibiotics: If allergic reactions (rash, dyspnea, hypotension, etc.) occur after surgery, discontinue immediately and replace with sensitive alternative drugs; if there is no evidence of infection after surgery, discontinue strictly according to 48 hours.

(2) Anticoagulants: If active bleeding, platelets $<50\times10^9$/L, or severe coagulation dysfunction occurs,

discontinue immediately and give symptomatic treatment; if high-risk factors (e.g., severe venous thrombosis) occur in the early postoperative period, anticoagulation time can be extended.

(3) Analgesics: If severe gastrointestinal reactions, renal impairment, or drug allergy occur, adjust or discontinue NSAIDs, and give gastric mucosal protectants or change analgesic plans.

5.5.3 Measures to Ensure Subject Compliance

(1) Preoperative education: The research team explains the study process, intervention measures, and follow-up requirements to subjects and their families in detail, and provides written instructions and education manuals.

(2) Digital follow-up: Rely on the hospital follow-up management system or designated personnel to regularly send visit reminders, rehabilitation guidance, and medication prompts.

(3) Specialized follow-up: Each subject is assigned a fixed research coordinator responsible for regular telephone/video follow-up, answering patient questions, and supervising medication and rehabilitation compliance.

(4) Compliance monitoring: Record the patient's actual medication, rehabilitation implementation, and follow-up completion rate at each visit point; individualized intervention and supervision for subjects with insufficient compliance.

6. Outcome Measures and Evaluation Methods

Including primary study endpoints (usually 1), secondary study endpoints (not limited to 1), safety endpoints, exploratory endpoints, and their corresponding evaluation methods.

6.1 Primary Study Endpoint

Relative reduction rate of KAM (%ΔKAM): The percentage of relative reduction in peak KAM measured by gait analysis at 12±1 months postoperatively compared with preoperative baseline, reflecting the functional improvement of lower limb load redistribution in clinical practice.

- Evaluation method: A 3D gait analysis system (Vicon or equivalent with ≥100 Hz acquisition frequency) is used to collect walking data of subjects at self-selected speed, and the peak adduction moment during the gait cycle is calculated. The average value of three valid gait steps on both sides is taken, and %ΔKAM is calculated by comparing with baseline.

6.2 Secondary Study Endpoints

(1) Static alignment accuracy: MPTA planned-actual difference (measured by knee X-ray at 6 weeks postoperatively); HKA accuracy rate (proportion of HKA falling within ±2° target range in full-length standing X-ray at 12 months postoperatively).

(2) Sagittal control ability: PTS error value (difference between 12 months postoperatively and preoperative planning value, unit: °).

(3) Dynamic load indicators: KAM impulse (gait analysis integral value, reflecting cumulative joint load); Varus thrust amplitude (instantaneous coronal knee angle change in gait analysis).

(4) Patient-reported outcomes (PROs): Changes in KOOS, WOMAC, OKS, Lysholm, HSS scores and MCID compliance rate.

(5) Perioperative efficiency and radiation exposure: Operation time (minutes), intraoperative fluoroscopy times.

(6) Reoperation rate: Proportion of reoperation due to alignment failure, fracture, implant problems, etc., within 12 months of follow-up.

6.3 Safety Endpoints

(1) Incidence of complications during perioperative period (≤30 days) and follow-up period (≤12 months): Including incision infection, deep vein thrombosis, fracture, neurovascular injury, nonunion, loss of correction, internal fixation failure, etc.

(2) Incidence of serious adverse events (SAE): Death, life-threatening events, permanent functional loss, need for hospitalization or prolonged hospitalization, congenital abnormalities, etc.

(3) Changes in laboratory safety indicators: Proportion of significant abnormalities in blood routine, liver and kidney function, and coagulation function before and after surgery.

6.4 Exploratory Endpoints

(4) Correlation between alignment accuracy and clinical outcomes: Correlation between MPTA/HKA error and %ΔKAM, PROs score improvement.

(5) Economic indicators: Direct medical costs, reoperation costs, rehabilitation cycle, etc., between intervention group and control group.

(6) Relationship between AR navigation registration error and adjustment time: Explore the correlation between intraoperative AR system accuracy and operation efficiency.

6.5 Summary of Evaluation Methods

(1) Imaging indicators: Full-length standing X-ray and CT before surgery, 6 weeks, 3 months, 6 months, and 12 months after surgery are completed by two independent assessors unaware of grouping information using standardized measurement methods, and the average value is taken as the final result.

(2) Kinematic indicators: 3D gait analysis is completed by the same center and the same measurer using calibrated motion capture and force measurement system.

(3) Functional scores: Recorded by trained assessors through face-to-face or video visits to ensure the integrity of questionnaires.

(4) Safety monitoring: All adverse events are recorded in the case report form (CRF) and electronic data capture system (EDC), and regularly reviewed by the Data Safety Monitoring Board (DSMB).

7. Statistical Analysis

7.1 Sample Size Estimation

The primary endpoint of this study is the relative reduction rate of peak knee adduction moment (KAM) at 12 months postoperatively (%ΔKAM), designed as a multicenter, three-group parallel randomized controlled trial (kinematic alignment group, traditional alignment group, dynamic dual-mode alignment group), mainly analyzing the difference in %ΔKAM between groups.

Sample size calculation is completed using G*Power software, based on intergroup effect size f = 0.25 (medium effect size). According to previous pilot studies and previous literature reports (Katagiri 2023; our team's 2024 clinical data), the expected difference in %ΔKAM between the intervention group (dynamic dual-mode alignment optimization) and the traditional alignment group at 12 months postoperatively is $\Delta = 15\%$, and the standard deviation (σ) is about 20%. Setting significance level $\alpha=0.05$ (two-tailed) and test power $1-\beta=0.80$, calculated according to one-way analysis of variance (ANOVA) model, the required sample size per group is 34 cases. Considering that multiple group comparisons need Bonferroni correction ($\alpha'=0.05/3 \approx 0.0167$), the required sample size per group is increased to $n\approx40$ cases after recalculation.

To ensure study power and consider about 20% loss to follow-up or dropout rate, the final determination is: 50 cases per group; total sample size: 150 cases (3 groups).

7.2 Statistical Analysis of Study Data

Corresponding datasets (e.g., full analysis set, per-protocol set, and safety analysis set) can be selected for study endpoint analysis; corresponding data description forms and statistical analysis methods are selected according to endpoint evaluation indicators. The following data description forms and statistical analysis methods are for reference:

7.2.1 Analysis Datasets

(1) Full Analysis Set: Follows the intention-to-treat (ITT) principle, including all subjects randomly assigned and receiving at least one intervention; missing data is handled by multiple imputation.

(2) Per-Protocol Set (PPS): Includes subjects who strictly completed the intervention and main follow-up according to the study protocol, used to verify the robustness of study results.

(3) Safety Set (SS): Includes all subjects who received at least one study intervention and have safety assessment data, used for safety endpoint analysis.

7.2.2 Data Description

(1) Continuous variables: Describe the number of cases (n), mean ($\bar{x}$), standard deviation (SD), median (M), 25th and 75th percentiles (P25, P75), minimum (Min), and maximum (Max).

(2) Categorical variables: Describe the number of cases (n) and percentage (%) of each category.

7.2.3 Statistical Methods

(1) Distribution test: Shapiro-Wilk test is used to evaluate the normality of continuous variables, and Levene test is used to evaluate variance homogeneity.

(2) Intragroup pre-post comparison: Paired t-test is used if normally distributed; Wilcoxon signed-rank test is used if not normally distributed.

(3) Intergroup comparison: One-way analysis of variance (ANOVA) is used if normally distributed and homogeneous variance, with Bonferroni multiple comparison correction if necessary; Kruskal-Wallis H test is used if not normally distributed or heterogeneous variance, and Dunn method is used for pairwise comparison after test.

(4) Categorical variable comparison: Chi-square test is used; Fisher's exact probability method is used when expected frequency <5.

(5) Repeated measurement data (e.g., VAS, KOOS, WOMAC multi-timepoint data): Linear mixed-effects model (LMM) is used to analyze time effect, group effect, and their interaction,

with random effect term to control individual differences.

(6) Correlation analysis: Pearson or Spearman correlation coefficients are used to analyze the correlation between alignment accuracy and clinical outcomes.

(7) Consistency analysis (for comparison between planning and actual values): Bland-Altman method is used to calculate 95% limits of agreement, and intraclass correlation coefficient (ICC) is calculated to evaluate measurement reliability.

7.2.4 Statistical Significance

Unless otherwise specified, all statistical tests use two-tailed tests, with significance level set at $\alpha = 0.05$, and $P < 0.05$ is considered statistically significant. All analyses are completed using SPSS 26.0 (IBM Corp., Armonk, NY, USA) and R 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria) software.

8. Study Risks and Disposal Plans

This study is a multicenter clinical interventional study involving HTO, personalized 3D-printed guide plates, AR intraoperative navigation, and gait analysis. The following risks and corresponding disposal measures may exist:

8.1 Surgery-Related Risks

(1) Risks: Intraoperative bleeding, infection, neurovascular injury, fracture, nonunion or delayed union of osteotomy, implant failure, accelerated degeneration of lateral compartment cartilage, etc.

(2) Disposal Plans:

- Strictly screen subjects and exclude high-risk patients (e.g., severe osteoporosis, systemic infection, severe comorbidities).
- Surgeons must be chief doctors with rich HTO experience and familiar with PSI guide plate and AR navigation operation procedures.
- Follow aseptic principles during surgery, and prepare blood products if necessary; in case of neurovascular injury, perform microsurgical repair or vascular reconstruction immediately.
- For patients with delayed union or pseudarthrosis, give secondary intervention to promote bone healing (bone grafting, bone stimulation therapy, etc.).

8.2 Device Application-Related Risks

(1) Risks: Positioning deviation of PSI guide plate or AR navigation may reduce osteotomy accuracy and affect postoperative alignment; guide plate material allergy or foreign body reaction.

(2) Disposal Plans:

- All devices have passed medical device registration certification and are strictly disinfected and sterilized before use.
- Perform guide plate fitting and simulation exercise before surgery to ensure complete fit with the patient's bone surface.
- If large positioning deviation is found during surgery, immediately switch to traditional intraoperative fluoroscopy and mechanical axis measurement for correction.
- For patients with material allergy, replace with non-sensitizing material guide plate before surgery.

8.3 Drug Use-Related Risks

(1) Risks: Perioperative antibiotics may cause allergic reactions or drug resistance; anticoagulants may increase bleeding risk; NSAIDs may cause gastrointestinal adverse reactions.

(2) Disposal Plans:

- Inquire about drug allergy history before surgery and perform necessary skin tests.
- Anticoagulation plan is formulated according to patient's thrombosis risk stratification, and platelets and coagulation function are regularly monitored.
- For patients with peptic ulcer or high risk, combine with gastric mucosal protectants or select selective COX-2 inhibitors.

8.4 Imaging and Gait Analysis-Related Risks

(1) Risks: Fall risk during gait analysis; radiation exposure from imaging examinations.

(2) Disposal Plans:

- Arrange special personnel for protection during gait analysis and lay anti-slip mats on the ground.
- Imaging examinations follow the principle of "minimum necessary radiation," and low-dose mode is used as much as possible to reduce repeated shooting.

8.5 Data and Privacy Risks

(1) Risks: Personal privacy and medical data of subjects may be leaked.

(2) Disposal Plans:

- All data are replaced with unique codes instead of subject identity information and stored in an encrypted electronic data capture system.
- Data access is limited to authorized members of the research team, who sign confidentiality agreements.

8.6 Emergency Handling Mechanism

Each center sets up an emergency disposal team composed of multidisciplinary personnel from orthopedics, anesthesiology, critical care medicine, radiology, etc. In case of serious adverse events, report to the ethics committee and data safety monitoring committee within 24 hours, and start the emergency treatment process until the incident is resolved. Regularly conduct risk prevention and emergency disposal training for the research team to ensure that all types of emergencies can be handled in a timely and standardized manner.

9. Study Termination Criteria

To ensure the safety of subjects and maintain the scientificity and data integrity of the study, the entire study or individual subjects' participation in the study should be terminated when one of the following situations occurs:

9.1 Subject Safety-Related Reasons

(1) Any clinical adverse event (AE), severe abnormal laboratory test, or new comorbidity that the researcher believes will cause unacceptable risks to the subject or is not in their best interest if they continue to participate in the study.

(2) Severe adverse events (SAE) occur after surgery, which are highly correlated with study intervention after comprehensive evaluation, and continued study may lead to serious consequences.

9.2 Study Implementation and Methodology-Related Reasons

(1) Blind bottom leakage occurs (applicable to sub-studies implementing blinding), making it impossible to ensure the scientificity and fairness of results.

(2) Researchers or research centers seriously fail to comply with the study protocol (e.g., intervention operation, evaluation method, drug use, etc.) and cannot be corrected in time, affecting the

validity and comparability of study data.

(3) The Data Safety Monitoring Board (DSMB) finds that the primary endpoint cannot achieve the expected effect or there is a significant adverse trend opposite to the expected during regular evaluation.

9.3 Ethics and Management-Related Reasons

(1) The ethics committee requires the termination of the study based on safety, scientificity, or ethical principles.

(2) Higher management departments or funders issue termination orders due to major safety hazards, data quality problems, or policy adjustments in the study.

9.4 Subject's Personal Will

The subject or their legal representative proposes to voluntarily withdraw from the study and confirms after informed notification.

9.5 Termination Handling Process

Once a study termination situation occurs, researchers should immediately take measures to protect the safety of subjects and provide corresponding medical treatment if necessary. The reasons for termination and related materials must be detailed in the case report form (CRF) and electronic data capture system (EDC), and reported to the ethics committee and relevant regulatory authorities within 24 hours. Conduct a final follow-up on enrolled subjects and record their clinical status and outcomes.

10. Adverse Events and Disposal

Serious Adverse Event (SAE): refers to an adverse medical event that results in death, is life-threatening, causes permanent or severe disability or functional loss, requires hospitalization or prolongation of hospitalization, or is a congenital anomaly or birth defect in a subject after receiving the test drug.

Once an SAE occurs, the researcher shall report it within 24 hours after discovery and submit the SAE report form to the clinical research ethics committee for review of the adverse event, and record it. For death cases, report to the medical department in a timely manner in accordance with hospital regulations.

Treatment measures: Researchers need to take immediate measures to ensure that subjects receive timely clinical treatment, and follow up the outcome of their SAE until recovery or return to the baseline level.

11. Quality Control

Researchers will adopt standard operating procedures to ensure the implementation of the quality control and quality assurance system for clinical research. All observations and findings in clinical research will be verified to ensure data reliability and ensure that all conclusions in clinical research are derived from original data. Quality control is adopted at each stage of data processing to ensure that all data are reliable and processed correctly.

12. Ethical Requirements

(1) Before the start of the clinical study, the study protocol must be reviewed by the ethics committee, and the study can be implemented only after the review result is approved and a approval letter is signed.

(2) During the study, the WMA Declaration of Helsinki (2013), CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects (2016), and National Health Commission Measures for the Ethical Review of Life Science and Medical Research Involving Humans (2023) shall be followed.

(3) During the study, any modification of the clinical study protocol, informed consent form, recruitment materials, etc., must be approved by the ethics committee before implementation.

(4) Before each subject is enrolled in this study, the researcher must introduce the existing treatment methods, the purpose of this study, the study process and duration, examination operations, expected benefits and risks of the subject, possible money and time spent, and the subject's assignment to different groups in detail. In addition, researchers need to inform subjects that participation in this study is completely voluntary, and they have the right to withdraw from the study at any stage without discrimination or retaliation, and their medical treatment and rights will not be affected.

(5) After fully and detailed explanation of the study, the subject or their legal representative (for subjects with incapacity) signs the informed consent form and indicates the date. The researcher who executes the informed consent process also signs the name and date on the informed consent form. The informed consent form is in duplicate, one for the subject and one for the researcher.

13. Expected Progress and Completion Date

This study plans to start 1 month after approval by the ethics committee, with a total study period of 24 months. The specific progress arrangement is as follows:

(1) Preparation Stage (Months 0–3): Research team formation and training; formulation and improvement of standard operating procedures (SOP), case report form (CRF), and electronic data capture system (EDC); completion of ethical approval and pilot enrollment.

(2) Enrollment and Intervention Stage (Months 4–18): Continuous case enrollment and intervention implementation according to randomization scheme; completion of preoperative baseline assessment, surgery, and early postoperative follow-up.

(3) Follow-up and Data Collection Stage (Months 18–22): Completion of primary endpoint assessment (12 months postoperatively) and other follow-ups; ensure that the completion rate of primary endpoints is ≥90%.

(4) Data Analysis and Conclusion Stage (Months 22–24): Data cleaning and statistical analysis; writing research report and preparing SCI paper submission.

Expected Timeline:

- Start Time: September 2025
- Completion Time: August 2027

14. Participating Institutions and Responsibilities of All Parties

14.1 List of Research Centers

- Leading Institution: The First Affiliated Hospital of Wenzhou Medical University
- Collaborating Institutions: Beijing Jishuitan Hospital, Ningbo Sixth People's Hospital

14.2 Cooperative Units

- Imaging Data Processing Laboratory: Hubei Jiayi Hi-Tech Co., Ltd.
- 3D-Printed Guide Plate Manufacturer: Hubei Jiayi Hi-Tech Co., Ltd.
- CRO/SMO Company: Zhejiang Yaohui Pharmaceutical Technology Co., Ltd.

14.3 Responsibilities of Participating Institutions

Institution Name	Responsibilities
The First Affiliated Hospital of Wenzhou Medical University (Leading Institution)	Responsible for overall study design and protocol formulation; undertaking ethical approval and project registration; coordinating the implementation of each research center; responsible for data management and statistical analysis; formulating unified standards for primary endpoint assessment and training; leading paper writing and result release.
Beijing Jishuitan Hospital	Complete subject screening, enrollment, surgery, and follow-up according to the protocol; provide preoperative imaging and kinematic assessment data; participate in case quality control and difficult case discussion.
Ningbo Sixth People's Hospital	Complete case recruitment and intervention operations according to the protocol; cooperate in completing imaging and gait data collection; participate in research data sharing and safety monitoring. Hubei Jiayi Hi-Tech Co., Ltd. (Imaging Data Processing Laboratory) Provide a unified image measurement platform; independently analyze image registration and guide plate accuracy; issue standardized analysis reports.
Hubei Jiayi Hi-Tech Co., Ltd. (3D-Printed Guide Plate Manufacturer)	Produce personalized guide plates according to preoperative planning documents to ensure dimensional accuracy and qualified sterilization; provide production quality records and technical support.
Zhejiang Yaohui Pharmaceutical Technology Co., Ltd. (CRO/SMO Company)	Assist in multicenter case management, visit arrangement, data verification, and monitoring; ensure consistency, compliance, and high follow-up rate of data collection in each center.